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

Supporting Information

Gold(I)- Catalyzed Addition of Aldehydes to Cyclopropylidene Bearing 6-Aryl-1,5-Enynes

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Supporting Information

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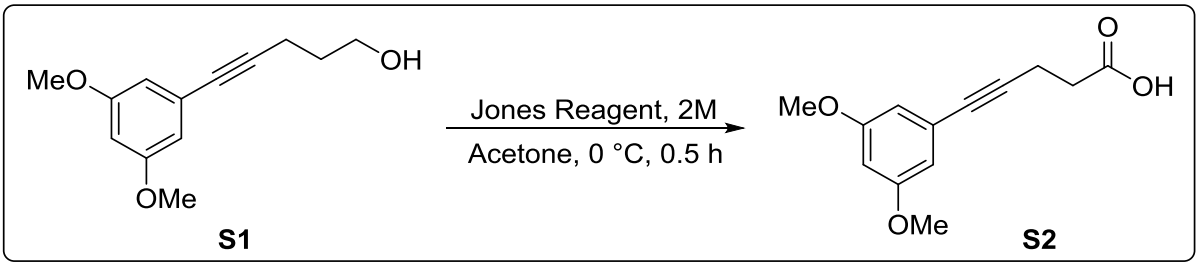
1. Experimental Details and Complex Characterization Data

1.1 General Methods

Unless otherwise stated, all commercially available reagents were used as received. Anhydrous tetrahydrofuran (THF, Stabilized, 99.9%, Acros Organics, purchased from Fisher Scientific) and anhydrous 1,4-dioxane (99.8%, purchased from Sigma Aldrich) were used as received. Anhydrous dichloromethane and diethyl ether were passed through a column of alumina.[1] The polymer-bound 2,6-di-tert-butylpyridine (200-400 mesh, ~1.8 mmol/g loading, 1 % cross-linked with divinylbenzene) was purchased from Sigma Aldrich. Column chromatography was performed using SilaFlash P60 40-63 µm (230-400 mesh). Thin layer chromatography (TLC) was performed on SiliCycle Silica Gel 60 F254 plates and was visualized with UV light and either $KMnO_4$ stain or 2,4–dinitrophenylhydrazine stain. NMR spectra were recorded on a Bruker Avance 400, 500 or 600 MHz spectrometer. All deuterated solvents were used as received from Cambridge Isotope Laboratories, Inc. The residual solvent protons (^1H) or the solvent carbons (^{13}C) were used as internal standards. ^1H NMR data are presented as follows: chemical shift in ppm (δ) downfield from tetramethylsilane (multiplicity, coupling constant, integration). The following abbreviations are used in reporting NMR data: s, singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublets; dt, doublet of triplets; ddd, doublet of doublet of doublets; m, multiplet. High resolution mass spectra for organic compounds were obtained on an Agilent Accurate LC-TOF Mass Spectrometer (Agilent Series 6220) operating in positive ion mode with an electrospray ionization source (fragmentor = 175 V) by Dr. Mee-Kyung Chung. The data were analyzed using an Agilent MassHunter Workstation Software, Qualitative Analysis (V.B.02.00). High resolution mass spectra for Au-containing intermediates were obtained with a hybrid LTQ FT (ICR 7T) (ThermoFisher, Bremen, Germany) mass spectrometer where samples were introduced via a micro-electrospray source and analyzed using Xcalibur (ThermoFisher, Breman, Germany) by the UNC Chapel Hill Chemistry Department Mass Spec Facility.

1.2 Preparation of 1b

1.2.1 Preparation of 5-(3,5-dimethoxyphenyl)pent-4-ynoic acid, S2



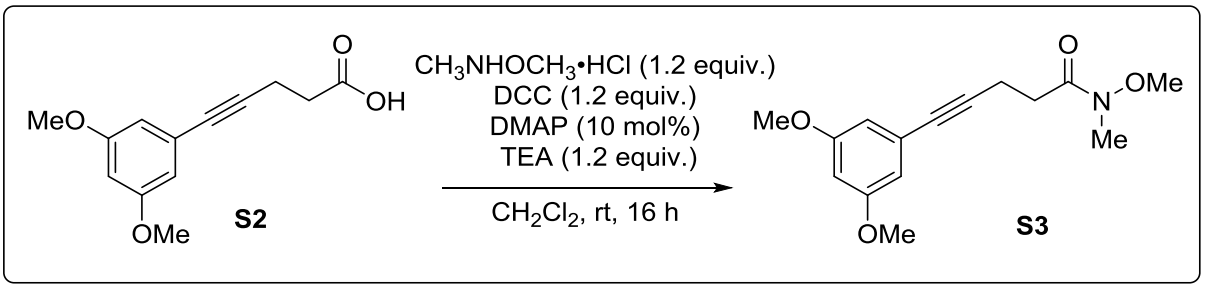
The alcohol **S1** was synthesized following a literature procedure.[2]

To a solution of alcohol **S1** (2.33 g, 10.58 mmol) in acetone (107 mL) at 0 °C was added Jones Reagent (2M, 17 mL) dropwise. The resulting solution was stirred for 30 minutes at 0 °C. Isopropanol (~10 mL) was added to quench the reaction, and the reaction mixture was extracted with H_2O/Et_2O. The organic layer was concentrated and extracted between Et_2O and 1 M NaOH.

The aqueous layer was washed with Et_2O and acidified by adding conc. HCl until reaching pH ~1. This was then extracted with Et_2O. The organic layer was washed with brine, dried over $MgSO_4$, filtered and concentrated to afford **S2** as a rusty orange solid, which was used without further purification (1.788 g, 72%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.55 (d, *J* = 2.3 Hz, 2H), 6.41 (t, *J* = 2.3 Hz, 1H), 3.77 (s, 6H), 2.75 – 2.68 (m, 4H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 176.6, 160.4, 124.7, 109.4, 101.4, 87.2, 81.3, 55.4, 33.1, 15.1. **HRMS** (ESI): calcd for $C_{13}H_{15}O_4$ $[M+H]^+$ 235.0965, found 235.0971.

1.2.2 Preparation of 5-(3,5-dimethoxyphenyl)-N-methoxy-N-methylpent-4-ynamide, S3

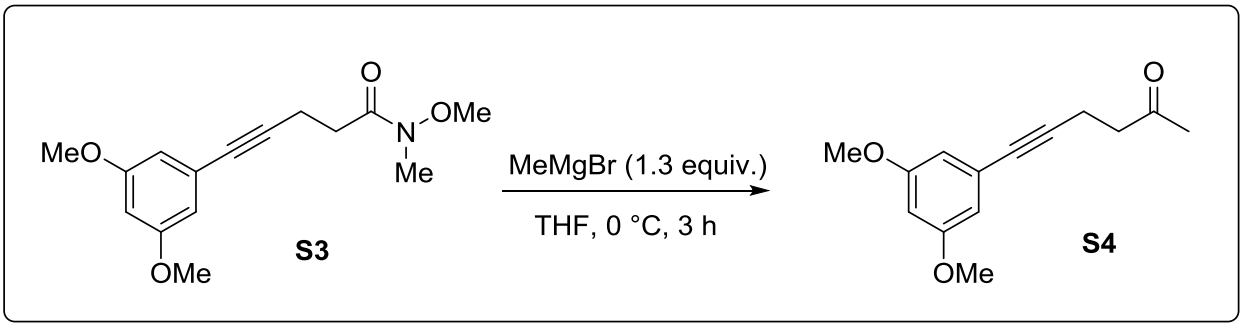


The following procedure was adapted from a literature procedure.[3]

To a solution of acid **S2** (0.871 g, 3.72 mmol) in CH_2Cl_2 (60 mL) at room temperature was added *N,O*-dimethylhydroxylamine hydrochloride (0.435 g, 4.46 mmol), *N,N'*-dicyclohexylcarbodiimide (0.920 g, 4.46 mmol), 4-(dimethylamino)pyridine (0.045 g, 0.372 mmol), and triethylamine (0.62 mL, 4.46 mmol). The reaction mixture was stirred at room temperature for 16 hours. H_2O (25 mL) was added to quench the reaction. The reaction mixture was extracted with CH_2Cl_2, and the organics were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The product was purified by silica gel column chromatography (Hexanes/EtOAc = 3:1) to afford the Weinreb amide as a viscous yellow oil (0.571 g, 55% yield).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.56 (d, *J* = 2.3 Hz, 2H), 6.40 (t, *J* = 2.3 Hz, 1H), 3.77 (s, 6H), 3.72 (s, 3H), 3.21 (s, 3H), 2.77 – 2.72 (m, 4H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 172.6, 160.4, 125.0, 109.4, 101.2, 88.7, 80.9, 61.4, 55.4, 32.2, 31.3, 14.9. **HRMS** (ESI): calcd for $C_{15}H_{20}NO_4$ $[M+H]^+$ 278.1387, found 278.1397.

1.2.3 Preparation of 6-(3,5-dimethoxyphenyl)hex-5-yn-2-one, S4

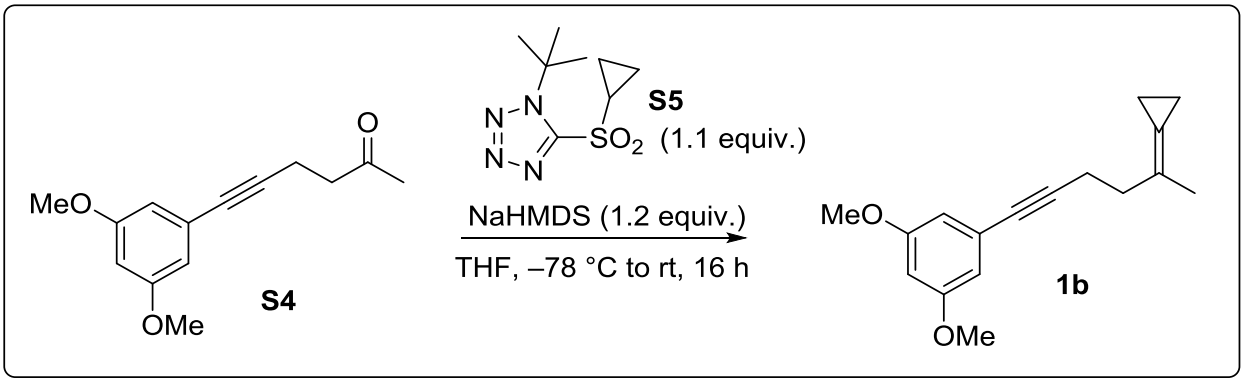


The following procedure was adapted from a literature procedure.[3]

To a solution of Weinreb amide **S3** (0.498 g, 1.80 mmol) in anhydrous THF (20 mL) at 0°C was slowly added a solution of MeMgBr (3 M in Et_2O, 0.78 mL, 2.34 mmol). The reaction mixture was stirred for 3 hours at 0°C. A saturated solution of NH_4Cl (25 mL) was added to quench the reaction, and the mixture was extracted with EtOAc. The organics were washed with brine, dried over $MgSO_4$, filtered and concentrated to afford the ketone as a pale yellow waxy solid (0.387 g, 92% yield). The product was taken to the next step without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.53 (d, *J* = 2.2, 2H), 6.40 (t, *J* = 2.2, 1H), 3.76 (s, 6H), 2.77 (t, *J* = 7.1, 2H), 2.65 (t, *J* = 7.1, 2H), 2.20 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 206.7, 160.6, 125.0, 109.5, 101.4, 88.3, 81.1, 55.5, 42.6, 30.1, 14.1. **HRMS** (ESI): calcd for $C_{14}H_{17}O_3$ $[M+H]^+$ 233.1172, found 233.1175.

1.2.4 Preparation of 1-(5-cyclopropylidenehex-1-yn-1-yl)-3,5-dimethoxybenzene, 1b



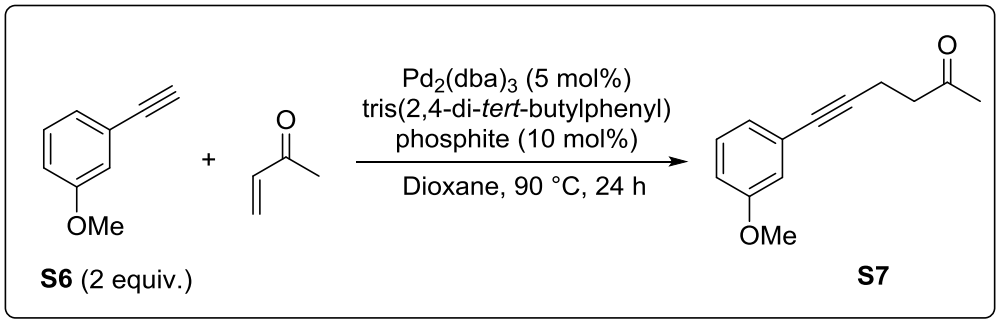
The Julia-Kocienski **S5** reagent was synthesized following a literature procedure.[4] The following procedure was adapted from a literature procedure.[3]

The ketone **S3** (0.387 g, 1.67 mmol) and Julia-Kocienski reagent **S5** (0.399 g, 1.73 mmol) were dissolved in anhydrous THF (20 mL) and cooled to –78 °C. Sodium bis(trimethylsilyl)amide (1 M in THF, 2 mL, 2 mmol) was added, and the reaction was allowed to warm to room temperature and stirred overnight. A saturated aqueous solution of NH_4Cl (10 mL) was added to quench, and the reaction mixture was extracted with Et_2O. The organics were washed with brine, dried over $MgSO_4$ and concentrated to afford a yellow oil. The crude product was purified by silica gel column chromatography (Hexanes:EtOAc 10:1) to give the title compound **1b** as a pale yellow oil (0.333 g, 78% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.53 (d, *J* = 2.1 Hz, 2H), 6.39 (t, *J* = 2.0 Hz, 1H), 3.77 (s, 6H), 2.60 (t, *J* = 7.6 Hz, 2H), 2.47 (t, *J* = 7.4 Hz, 2H), 1.86 (s, 3H), 1.11 (t, *J* = 5.9 Hz, 2H), 0.98 (t, *J* = 6.2 Hz, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 160.6, 125.5, 122.9, 116.7, 109.4, 101.1, 90.4, 80.6, 55.5, 36.0, 20.8, 18.2, 3.2, 1.6. **HRMS** (ESI): calcd for $C_{17}H_{21}O_2$ $[M+H]^+$ 257.1536, found 257.1535.

1.3 Preparation of Enyne 1c

1.3.1 Preparation of 6-(3-methoxyphenyl)hex-5-yn-2-one, S7

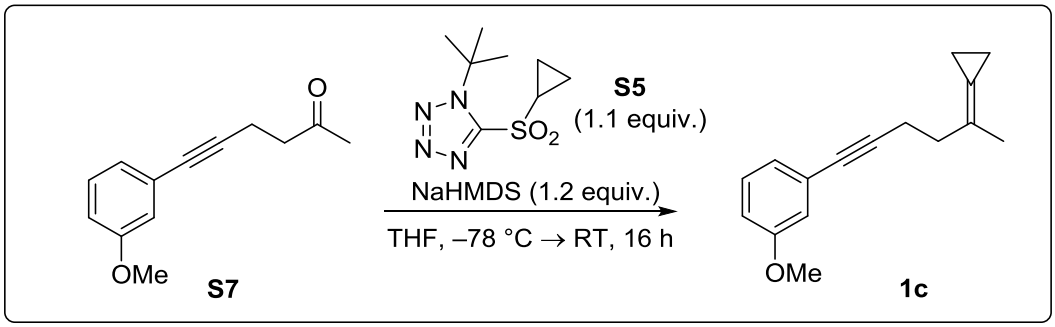


The alkyne **S6** was synthesized following a literature procedure.[5] The following procedure was adapted from a literature procedure.[6]

$Pd_2(dba)_3$ (0.250 g, 0.242 mmol) and tris(2,4-di-*tert*-butylphenyl) phosphite (0.313 g, 0.483 mmol) were added to a flame-dried Schlenk flask under N_2. Anhydrous dioxane (40 mL) was added and the resulting solution was sparged for 30 minutes. Methyl vinyl ketone (0.39 mL, 4.83 mmol) was added, and the reaction mixture was heated at 90 °C in a flask equipped with a reflux condenser under N_2. A solution of alkyne **S6** (1.278 g, 9.66 mmol) in dioxane (10 mL) was added dropwise to the reaction mixture over the course of 10 h, then continued to reflux for 14 h. The reaction was allowed to cool to room temperature, diluted with Et_2O, and filtered through a plug of Florisil®, eluting with Et_2O. The filtrate was concentrated and purified via silica gel column chromatography (Hexanes:EtOAc 30:1/ 20:1/ 10:1) to afford the title compound **S7** as a dark yellow oil (0.228 g, 23% yield).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.18 (t, *J* = 7.9 Hz, 1H), 6.97 (dt, *J* = 7.6, 1.2 Hz, 1H), 6.91 (dd, *J* = 2.7, 1.4 Hz, 1H), 6.83 (ddd, *J* = 8.2, 2.7, 0.9 Hz, 1H).3.79 (s, 3H), 2.77 (t, *J* = 7.3 Hz, 2H), 2.66 (t, *J* = 7.3 Hz, 2H), 2.21 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 206.7, 159.2, 129.3, 124.5, 124.1, 116.4, 114.4, 88.4, 80.9, 55.3, 42.5, 30.0, 14.0. **HRMS** (ESI): calcd for $C_{13}H_{15}O_2$ $[M+H]^+$ 203.1067, found 203.1067.

1.3.2 Preparation of 1-(5-cyclopropylidenehex-1-yn-1-yl)-3-methoxybenzene, 1c



The ketone **S7** (0.228 g, 1.13 mmol) and Julia-Kocienski reagent **S5** (0.286 g, 1.24 mmol) were dissolved in anhydrous THF (15 mL) and cooled to –78 °C. Sodium bis(trimethylsilyl)amide (1 M in THF, 1.4 mL, 1.4 mmol) was added, and the reaction was allowed to warm to room temperature and stirred overnight. A saturated aqueous solution of NH_4Cl (~10 mL) was added to quench, and the reaction mixture was extracted with Et_2O. The organics were washed with brine, dried over $MgSO_4$ and concentrated to afford the product as a pale yellow oil. The crude product was purified by silica gel column chromatography (Hexanes:EtOAc 30:1) to give the title compound **1c** as a pale yellow oil (0.091 g, 37% yield).

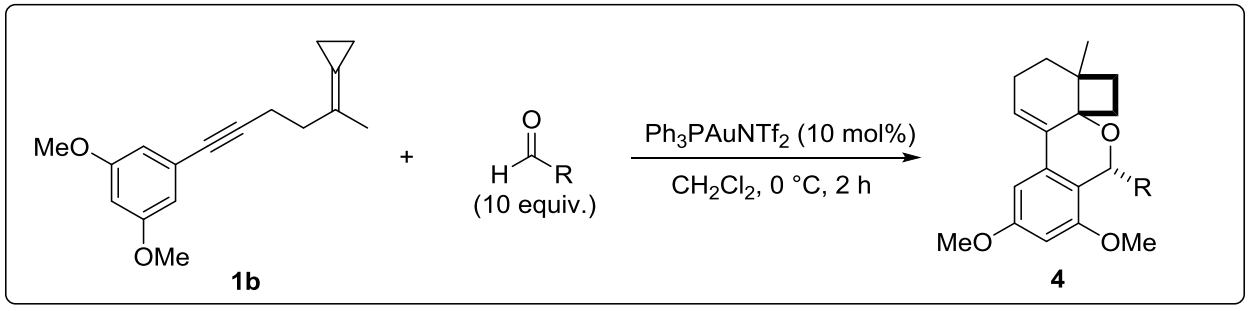
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.18 (t, *J* = 7.9 Hz, 1H), 6.96 (dt, *J* = 7.6, 1.2 Hz, 1H), 6.90 (dd, *J* = 2.6, 1.4 Hz, 1H), 6.82 (ddd, *J* = 8.4, 2.7, 0.9 Hz, 1H), 3.79 (s, 3H), 2.61 (t, *J* = 7.6 Hz, 2H), 2.47 (t, *J* = 7.5 Hz, 2H), 1.86 (s, 3H), 1.12 – 1.09 (t, *J* = 7.5 Hz, 2H), 0.99 – 0.97 (t, *J* = 7.4 Hz, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 159.2, 129.2, 125.1, 124.0, 122.7, 116.5, 116.3, 114.1, 90.4, 80.4, 55.2, 35.9, 20.7, 18.1, 3.1, 1.4. **HRMS** (ESI): calcd for $C_{16}H_{19}O$ $[M+H]^+$ 227.1430, found 227.1432.

1.4 Gold-Catalyzed Addition of Aldehydes to 1,5-Enynes

$Ph_3PAuNTf_2$ was synthesized following a literature procedure.[7]

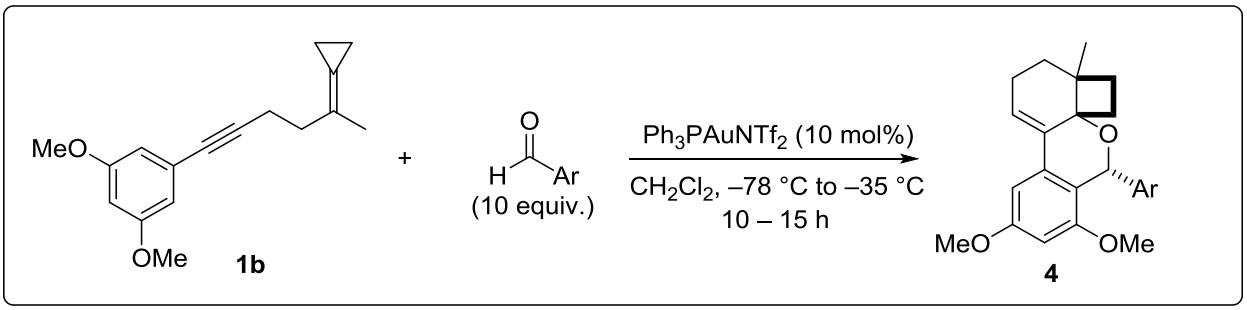
1.4.1 General procedure for Au-catalyzed addition of aldehydes to 1,5-enynes

Method A, procedure for aliphatic aldehydes, reaction run at 0 °C



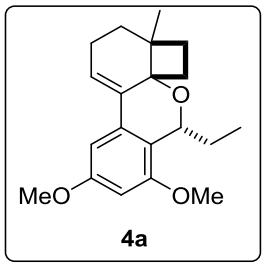
The 1,5-enyne **1b** (0.1 mmol) was dissolved in anhydrous CH_2Cl_2 (1 mL) in an oven-dried 1 dram vial. The aldehyde (1.0 mmol, 10 equiv.) was added to the vial, and the contents were stirred and cooled to 0°C in an ice bath. $Ph_3PAuNTf_2$ (0.01 mmol, 0.1 equiv.) was added to the vial, and the reaction mixture was stirred for 2 hours. Upon evaporation of the solvent under reduced pressure, the residue was purified by silica gel column chromatography to afford the polycyclic product in pure form.

Method B, procedure for aromatic aldehydes, reaction run at –35 °C



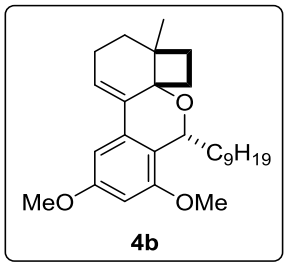
The 1,5-enyne **1b** (0.1 mmol) was dissolved in anhydrous CH_2Cl_2 (1 mL) in an oven-dried 1 dram vial. The aldehyde (1.0 mmol, 10 equiv.) was added to the vial, and the contents were stirred and cooled to –78°C in a dry ice/acetone bath. $Ph_3PAuNTf_2$ (0.01 mmol, 0.1 equiv.) was added to the vial, and the reaction mixture was transferred to a cryobath at –35 °C. The reaction was stirred for the appropriate reaction time (ca. 10-15 h), then warmed to room temperature. Upon evaporation of the solvent under reduced pressure, the residue was purified by silica gel column chromatography to afford the polycyclic product in pure form.

1.4.2 7-ethyl-8,10-dimethoxy-3a-methyl-2,3,3a,4,5,7-hexahydrobenzo[c]cyclobuta[i] chromene, 4a



Propionaldehyde was distilled prior to use. The product **4a** was prepared following Method A and purified using hexanes: ethyl acetate (10:1), (pale yellow oil, 91% yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 6.58 (d, *J* = 2.3 Hz, 1H), 6.33 (d, *J* = 2.3 Hz, 1H), 6.25 (dd, *J* = 5.0, 3.5 Hz, 1H), 4.82 (dd, *J* = 7.4, 3.3 Hz, 1H), 3.82 (s, 3H), 3.77 (s, 3H), 2.31 – 2.24 (m, 2H), 2.24 – 2.19 (m, 1H), 2.00 – 1.91 (m, 1H), 1.68 – 1.55 (m, 3H), 1.49 – 1.44 (m, 1H), 1.43 – 1.37 (m, 1H), 1.34 – 1.30 (m, 1H), 1.29 (s, 3H), 0.83 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$): δ = 159.0, 156.6, 135.6, 135.2, 120.1, 119.3, 99.8, 97.5, 71.7, 70.5, 55.3, 55.2, 42.3, 31.5, 29.2, 28.4, 22.6, 22.6, 22.0, 9.6. **HRMS** (ESI): calcd for $C_{20}H_{27}O_3$ $[M+H]^+$ 315.1955, found 315.1959.

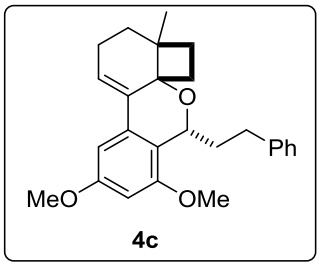
1.4.3 8,10-dimethoxy-3a-methyl-7-nonyl-2,3,3a,4,5,7-hexahydrobenzo[c]cyclobuta[i] chromene, 4b



4b

The product **4b** was prepared following Method A and purified using hexanes: ethyl acetate (10:1), (pale yellow oil, 85% yield). ^{1}H **NMR** (600 MHz, $CDCl_3$): δ = 6.57 (d, *J* = 2.3 Hz, 1H), 6.33 (d, *J* = 2.3 Hz, 1H), 6.24 (dd, *J* = 5.3, 3.2 Hz, 1H), 4.85 (dd, *J* = 8.0, 3.1 Hz, 1H), 3.82 (s, 3H), 3.76 (s, 3H), 2.30 – 2.25 (m, 2H), 2.24 – 2.19 (m, 1H), 1.96 – 1.89 (m, 1H), 1.62 – 1.55 (m, 3H), 1.48 – 1.43 (m, 1H), 1.43 – 1.38 (m, 1H), 1.31 – 1.28 (m, 1H), 1.28 (s, 3H), 1.27 – 1.21 (m, 14H), 0.87 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 159.0, 156.5, 135.6, 135.0, 120.1, 119.8, 99.8, 97.5, 71.7, 69.5, 55.3, 55.2, 42.4, 35.4, 32.0, 31.5, 29.7, 29.6, 29.5, 29.4, 29.2, 25.3, 22.7, 22.7, 22.6, 21.9, 14.2. **HRMS** (ESI): calcd for $C_{27}H_{41}O_3$ $[M+H]^+$ 413.3050, found 413.3049.

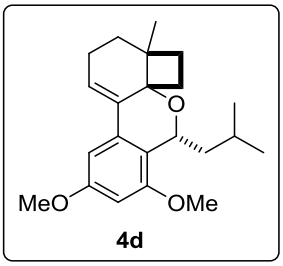
1.4.4 7-benzyl-8,10-dimethoxy-3a-methyl-2,3,3a,4,5,7-hexahydrobenzo[c]cyclobuta[i] chromene, 4c



4c

The product **4c** was synthesized following Method A and purified using hexanes: ethyl acetate (10:1), (yellow oil, 82% yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = δ 7.27 (d, *J* = 7.5 Hz, 2H), 7.22 (d, *J* = 7.5 Hz, 2H), 7.17 (t, *J* = 7.1 Hz, 1H), 6.62 (d, *J* = 2.3 Hz, 1H), 6.34 (d, *J* = 2.3 Hz, 1H), 6.33 – 6.29 (m, 1H), 4.89 (d, *J* = 7.7 Hz, 1H), 3.85 (s, 1H), 3.76 (s, 1H), 2.71 (t, *J* = 8.0 Hz, 2H), 2.40 – 2.22 (m, 4H), 1.99 – 1.91 (m, 1H), 1.65 – 1.57 (m, 2H), 1.54 – 1.44 (m, 2H), 1.39 – 1.34 (m, 4H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 159.1, 156.6, 143.2, 135.4, 135.0, 128.6, 128.1, 125.3, 120.1, 119.0, 105.4, 99.8, 97.5, 71.8, 68.8, 55.3, 55.1, 42.2, 36.7, 31.5, 31.1, 29.2, 22.7, 22.6, 22.0. **HRMS** (ESI): calcd for $C_{25}H_{28}NaO_3$ $[M+Na]^+$ 399.1931, found 399.1918.

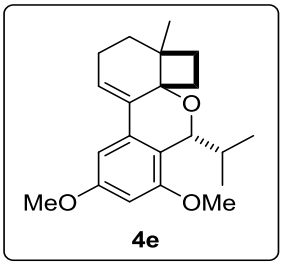
1.4.5 7-isobutyl-8,10-dimethoxy-3a-methyl-2,3,3a,4,5,7-hexahydrobenzo[c]cyclobuta[i] chromene, 4d



4d

The product **4d** was synthesized following Method A and purified using hexanes: ethyl acetate (10:1), (pale yellow oil, 78% yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 6.59 (d, *J* = 2.3 Hz, 1H), 6.33 (d, *J* = 2.3 Hz, 1H), 6.26 (dd, *J* = 5.3, 3.2 Hz, 2H), 4.91 (dd, *J* = 9.2, 2.7 Hz, 1H), 3.82 (s, 3H), 3.77 (s, 3H), 2.31 – 2.19 (m, 3H), 1.94 – 1.87 (m, 1H), 1.80 (ddd, *J* = 13.5, 9.4, 2.8 Hz, 1H), 1.62 – 1.52 (m, 2H), 1.49 – 1.36 (m, 3H), 1.28 (s, 3H), 0.96 (d, *J* = 6.5 Hz, 3H), 0.88 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 159.0, 156.5, 135.5, 134.8, 120.2, 120.0, 99.9, 97.6, 71.7, 68.0, 55.3, 55.1, 44.5, 42.3, 31.2, 29.1, 24.7, 23.9, 22.7, 22.6, 21.9, 21.7. **HRMS** (ESI): calcd for $C_{22}H_{31}O_3$ $[M+H]^+$ 343.2268, found 343.2271.

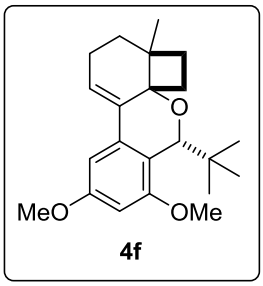
1.4.6 7-isopropyl-8,10-dimethoxy-3a-methyl-2,3,3a,4,5,7-hexahydrobenzo[c]cyclobuta[i] chromene, 4e



4e

The product **4e** was synthesized following Method B and purified using hexanes: ethyl acetate (10:1), (waxy yellow solid, 74% yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 6.55 (d, *J* = 2.3 Hz, 1H), 6.33 (d, *J* = 2.2 Hz, 1H), 6.20 (t, *J* = 4.3 Hz, 1H), 4.75 (d, *J* = 3.7 Hz, 1H), 3.82 (s, 3H), 3.76 (s, 3H), 2.27 (m, 3H), 2.23 – 2.15 (m, 1H), 1.69 – 1.54 (m, 2H), 1.46 (dt, *J* = 13.6, 4.7 Hz, 1H), 1.41 – 1.36 (m, 1H), 1.32 – 1.29 (m, 1H), 1.29 (s, 3H), 0.96 (d, *J* = 6.9 Hz, 3H), 0.59 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 159.0, 156.6, 135.9, 135.8, 120.1, 119.0, 99.9, 97.4, 73.4, 71.5, 55.3, 55.2, 42.7, 32.4, 32.2, 29.4, 22.7, 22.6, 22.1, 19.7, 16.0. **HRMS** (ESI): calcd for $C_{21}H_{29}O_3$ $[M+H]^+$ 329.2111, found 329.2114.

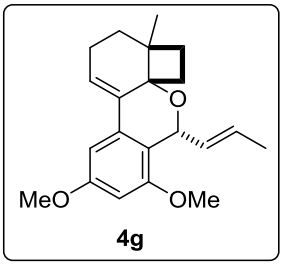
1.4.7 7-(tert-butyl)-8,10-dimethoxy-3a-methyl-2,3,3a,4,5,7-hexahydrobenzo[c]cyclobuta[i] chromene, 4f



4f

The product **4f** was synthesized following Method B and purified using hexanes: ethyl acetate (10:1), (pale yellow oil, 68% yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 6.49 (d, *J* = 2.3 Hz, 1H), 6.34 (d, *J* = 2.3 Hz, 1H), 6.14 (t, *J* = 4.2 Hz, 1H), 4.87 (s, 1H), 3.84 (s, 3H), 3.72 (s, 3H), 2.31 – 2.25 (m, 2H), 2.13 – 2.06 (m, 1H), 1.53 – 1.46 (m, 2H), 1.46 – 1.40 (m, 2H), 1.34 (s, 3H), 1.28 – 1.19 (m, 1H), 0.77 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 159.2, 157.4, 137.7, 137.4, 120.5, 116.9, 100.8, 97.0, 75.9, 72.1, 55.3, 54.8, 43.9, 39.7, 36.1, 29.1, 26.5, 23.1, 22.8, 21.8. **HRMS** (ESI): calcd for $C_{22}H_{31}O_3$ $[M+H]^+$ 343.2268, found 343.2269.

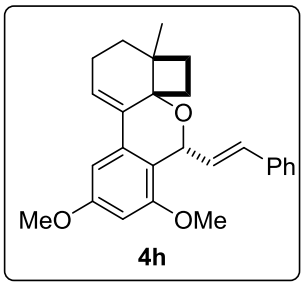
1.4.8 (E)-8,10-dimethoxy-3a-methyl-7-(prop-1-en-1-yl)-2,3,3a,4,5,7-hexahydrobenzo[c]-cyclobuta[i]chromene, 4g



4g

Crotonaldehyde (99% trans) was distilled prior to use. The product **4g** was synthesized following Method A and purified using hexanes: ethyl acetate (10:1), (white solid, 71% yield). **^{1}H NMR (**600 MHz, $CDCl_3$): δ = 6.58 (d, *J* = 2.4 Hz, 1H), 6.34 (d, *J* = 2.0 Hz, 1H), 6.26 (dd, *J* = 5.4, 3.2 Hz, 1H), 5.76 – 5.67 (m, 1H), 5.59 (ddd, *J* = 15.1, 6.1, 1.7 Hz, 1H), 5.29 (d, *J* = 6.1 Hz, 1H), 3.75 (s, 3H), 2.32 – 2.24 (m, 3H), 1.65 (d, *J* = 6.3 Hz, 3H), 1.64 – 1.55 (m, 3H), 1.47 – 1.40 (m, 2H), 1.31 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 159.3, 156.6, 135.2, 134.6, 131.7, 126.0, 120.8, 118.5, 100.0, 97.8, 72.3, 70.1, 55.3, 53.4, 42.5, 31.8, 29.1, 22.9, 22.6, 22.0, 17.9. **HRMS** (ESI): calcd for $C_{21}H_{27}O_3$ $[M+H]^+$ 327.1955, found 327.1960

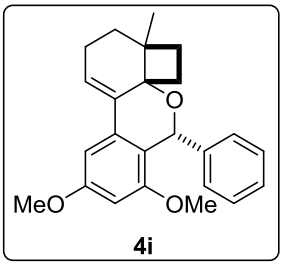
1.4.9 (E)-8,10-dimethoxy-3a-methyl-7-styryl-2,3,3a,4,5,7-hexahydrobenzo[c]cyclobuta[i] chromene, 4h



4h

The product **4h** was synthesized following Method A and purified using hexanes: ethyl acetate (10:1), (waxy yellow solid, 67% yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.34 (d, *J* = 6.8 Hz, 2H), 7.26 (t, *J* = 7.7 Hz, 2H), 7.17 (t, *J* = 7.3 Hz, 1H), 6.65 – 6.59 (m, 2H), 6.35 (d, *J* = 2.3 Hz, 1H), 6.36 – 6.30 (m, 1H), 6.30 (dd, *J* = 5.5, 3.0 Hz, 1H), 5.51 (d, *J* = 6.2 Hz, 2H), 3.83 (s, 3H), 3.76 (s, 3H), 2.37 – 2.27 (m, 3H), 1.69 (ddd, *J* = 11.0, 8.7, 2.6 Hz, 1H), 1.64 – 1.59 (m, 1H), 1.52 – 1.43 (m, 2H), 1.36 – 1.32 (m, 4H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 159.6, 156.7, 137.7, 135.1, 134.8, 130.6, 129.9, 128.3, 127.0, 126.5, 121.2, 117.8, 100.2, 97.8, 72.4, 70.2, 55.4, 55.3, 42.6, 32.0, 29.2, 22.9, 22.7, 22.0. **HRMS** (ESI): calcd for $C_{26}H_{29}O_3$ $[M+H]^+$ 389.2111, found 389.2120.

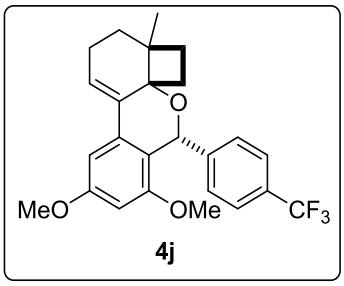
1.4.10 8,10-dimethoxy-3a-methyl-7-phenyl-2,3,3a,4,5,7-hexahydrobenzo[c]cyclobuta[i] chromene, 4i



4i

The product **4i** was synthesized following Method B and purified using dichloromethane: petroleum ether (1:1), (white solid, 88% yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.24 – 7.19 (m, 4H), 7.20 – 7.15 (m, 1H), 6.65 (d, *J* = 2.3 Hz, 1H), 6.34 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.26 (d, *J* = 2.2 Hz, 1H), 5.82 (s, 1H), 3.83 (s, 3H), 3.46 (s, 3H), 2.39 (q, *J* = 10.1 Hz, 1H), 2.32 – 2.26 (m, 2H), 1.71 (ddd, *J* = 11.0, 8.7, 2.5 Hz, 1H), 1.61 (q, *J* = 9.8 Hz, 1H), 1.42 (ddd, *J* = 13.6, 5.3, 3.4 Hz, 1H), 1.37 – 1.30 (m, 2H), 1.23 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 159.6, 156.8, 144.0, 135.1, 135.0, 128.1, 127.5, 126.8, 120.6, 118.7, 99.8, 98.0, 72.7, 72.7, 55.3, 55.1, 42.3, 31.3, 29.0, 22.8, 22.7, 21.9. **HRMS** (ESI): calcd for $C_{24}H_{27}O_3$ $[M+H]^+$ 363.1955, found 363.1973.

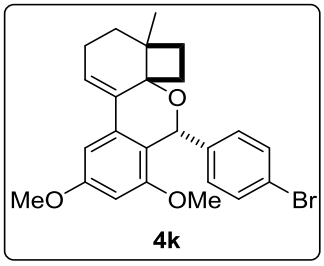
1.4.11 8,10-dimethoxy-3a-methyl-7-(4-(trifluoromethyl)phenyl)-2,3,3a,4,5,7-hexahydro-benzo[c]cyclobuta[i]chromene, 4j



4j

The product **4j** was synthesized following Method B and purified using dichloromethane: petroleum ether (1:1), (pale yellow crystalline solid, 86% yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.47 (d, *J* = 8.2 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 6.67 (d, *J* = 2.3 Hz, 1H), 6.38 (dd, *J* = 5.4, 3.2 Hz, 1H), 6.27 (d, *J* = 2.3 Hz, 1H), 5.86 (s, 1H), 3.83 (s, 3H), 3.48 (s, 3H), 2.40 (q, *J* = 10.1 Hz, 1H), 2.32 – 2.28 (m, 2H), 1.71 (ddd, *J* = 11.0, 8.7, 2.5 Hz, 1H), 1.63 (q, *J* = 9.5 Hz, 1H), 1.46 (ddd, *J* = 13.6, 5.2, 2.9 Hz, 1H), 1.39 – 1.33 (m, 2H), 1.23 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$): δ = 159.9, 156.6, 148.1, 135.0, 134.7, 128.9 (q, $^{2}J_{CF}$ = 32 Hz), 128.4, 124.5 (q, $^{3}J_{CF}$ = 3.8 Hz), 124.4 (q, $^{1}J_{CF}$ = 271.9 Hz), 121.1, 117.6, 99.9, 97.9, 72.8, 72.3, 55.3, 55.0, 42.2, 31.2, 29.0, 22.7, 22.6, 22.0. **^{19}F NMR** (376.3 MHz, $CDCl_3$): δ = -62.25. **HRMS** (ESI): calcd for $C_{25}H_{26}F_3O_3$ $[M+H]^+$ 431.1829, found 431.1833.

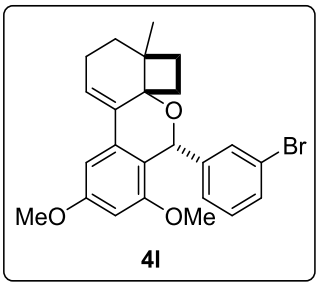
1.4.12 7-(4-bromophenyl)-8,10-dimethoxy-3a-methyl-2,3,3a,4,5,7-hexahydrobenzo[c] cyclobuta[i]chromene, 4k



4k

The product **4k** was synthesized following Method B and purified using dichloromethane: petroleum ether (1:1), (colorless crystalline solid, 85% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 7.33 (d, *J* = 8.4 Hz, 1H), 7.09 (d, *J* = 8.4 Hz, 1H), 6.65 (d, *J* = 2.3 Hz, 1H), 6.35 (dd, *J* = 5.0, 3.5 Hz, 1H), 6.26 (d, *J* = 2.3 Hz, 1H), 5.77 (s, 1H), 3.83 (s, 3H), 3.49 (s, 3H), 2.37 (q, *J* = 9.9 Hz, 1H), 2.31 – 2.27 (m, 2H), 1.70 (ddd, *J* = 10.9, 8.7, 2.5 Hz, 1H), 1.61 (q, *J* = 9.5 Hz, 1H), 1.44 (ddd, *J* = 13.6, 5.4, 3.1 Hz, 1H), 1.37 – 1.32 (m, 2H), 1.22 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 159.9, 156.8, 143.3, 135.1, 135.0, 130.8, 130.1, 121.0, 120.7, 118.1, 100.0, 98.0, 72.9, 72.3, 55.4, 55.2, 42.3, 31.3, 29.2, 22.8, 22.8, 22.1. **HRMS** (ESI): calcd for $C_{24}H_{27}BrO_3$ $[M+H]^+$ 441.1060, found 441.1044.

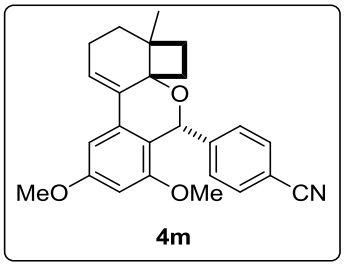
1.4.13 7-(3-bromophenyl)-8,10-dimethoxy-3a-methyl-2,3,3a,4,5,7-hexahydrobenzo[c] cyclobuta[i]chromene, 4l



4l

The product **4l** was synthesized following Method B and purified using dichloromethane: petroleum ether (1:1), (pale yellow crystalline solid, 73% yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.36 (t, *J* = 1.8 Hz, 1H), 7.30 (ddd, *J* = 7.8, 2.1, 1.2 Hz, 1H), 7.14 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.08 (t, *J* = 7.8 Hz, 1H), 6.65 (d, *J* = 2.3 Hz, 1H), 6.35 (dd, *J* = 5.4, 3.1 Hz, 1H), 6.27 (d, *J* = 2.2 Hz, 1H), 5.76 (s, 1H), 3.83 (s, 3H), 3.50 (s, 3H), 2.37 (q, *J* = 10.0 Hz, 1H), 2.31 – 2.27 (m, 2H), 1.69 (ddd, *J* = 11.0, 8.7, 2.5 Hz, 1H), 1.61 (q, *J* = 9.5 Hz, 1H), 1.44 (ddd, *J* = 13.6, 5.7, 2.8 Hz, 1H), 1.39 – 1.32 (m, 2H), 1.23 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 159.8, 156.7, 146.4, 135.0, 134.7, 131.2, 129.8, 129.2, 126.8, 121.5, 121.0, 117.8, 99.9, 98.0, 72.8, 72.2, 55.3, 55.1, 42.3, 31.2, 29.0, 22.7, 22.6, 22.0. **HRMS** (ESI): calcd for $C_{24}H_{25}BrNaO_3$ $[M+Na]^+$ 463.0879, found 463.0871.

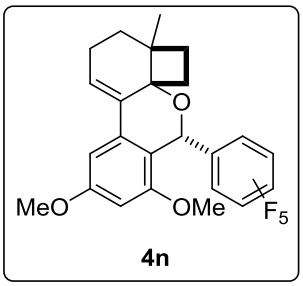
1.4.14 4-(8,10-dimethoxy-3a-methyl-2,3,3a,4,5,7-hexahydrobenzo[c]cyclobuta[i]chromen-7-yl)benzonitrile, 4m



4m

The product **4m** was synthesized following Method B and purified using dichloromethane: petroleum ether (1:1), (white crystalline solid, 64% yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.51 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.3 Hz, 2H), 6.65 (d, *J* = 2.3 Hz, 1H), 6.38 (dd, *J* = 5.5, 3.1 Hz, 1H), 6.25 (d, *J* = 2.3 Hz, 1H), 5.82 (s, 1H), 3.83 (s, 3H), 3.48 (s, 3H), 2.37 (q, *J* = 10.0 Hz, 1H), 2.33 – 2.28 (m, 2H), 1.70 (ddd, *J* = 10.9, 8.7, 2.5 Hz, 1H), 1.61 (d, *J* = 9.8 Hz, 1H), 1.46 (ddd, *J* = 13.6, 5.7, 2.9 Hz, 1H), 1.38 – 1.32 (m, 2H), 1.22 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 160.0, 156.5, 149.5, 134.9, 134.4, 131.6, 128.9, 121.3, 119.3, 117.0, 110.4, 99.9, 97.8, 72.9, 72.3, 55.3, 55.0, 42.2, 31.1, 29.0, 22.6, 22.6, 21.9. **HRMS** (ESI): calcd for $C_{25}H_{26}NO_3$ $[M+H]^+$ 388.1907, found 388.1910.

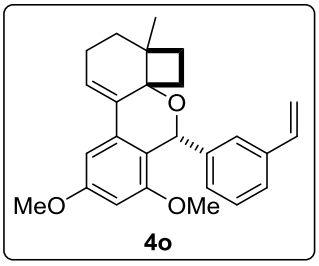
1.4.15 8,10-dimethoxy-3a-methyl-7-(perfluorophenyl)-2,3,3a,4,5,7-hexahydrobenzo[c] cyclobuta[i]chromene, 4n



4n

The product **4n** was synthesized following Method B and purified using dichloromethane: petroleum ether (1:1), (tan solid, 67% yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 6.66 (d, *J* = 2.3 Hz, 1H), 6.43 (dd, *J* = 5.9, 2.7 Hz, 1H), 6.25 (d, *J* = 2.3 Hz, 1H), 6.14 (s, 1H), 3.83 (s, 3H), 3.56 (s, 3H), 2.39 (q, *J* = 9.7, 8.7 Hz, 1H), 2.36 – 2.25 (m, 2H), 1.72 – 1.61 (m, 2H), 1.49 – 1.44 (m, 1H), 1.43 – 1.35 (m, 2H), 1.21 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 159.8, 156.1, 145.40 (d, $J_{C\text{-}F}$ = 254.8 Hz), 140.21 (d, $J_{C\text{-}F}$ = 251.8 Hz), 137.08 (d, $J_{C\text{-}F}$ = 248.8 Hz), 136.3, 134.9, 133.5, 121.1, 117.3, 114.6, 99.6, 97.5, 73.0, 63.4, 55.3, 55.2, 41.8, 30.0, 29.0, 22.6, 22.5, 22.0. **^{19}F NMR** (376 MHz, $CDCl_3$) δ = -143.20 (d, *J* = 16.3), -157.33 (t, *J* = 20.9), -164.19 (td, *J* = 21.3, 7.1). **HRMS** (ESI): calcd for $C_{24}H_{22}F_5O_3$ $[M+H]^+$ 453.1484, found .453.1493.

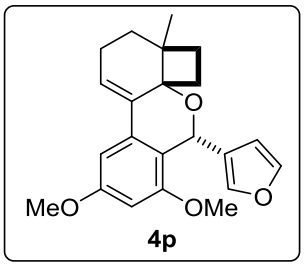
1.4.16 8,10-dimethoxy-3a-methyl-7-(3-vinylphenyl)-2,3,3a,4,5,7-hexahydrobenzo[c] cyclobuta[i]chromene, 4o



4o

The product **4o** was synthesized following Method B and purified using dichloromethane: petroleum ether (1:1), (white solid, 48% yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.28 (s, 1H), 7.24 (d, *J* = 7.8 Hz, 1H), 7.17 (t, *J* = 7.6 Hz, 1H), 7.08 (d, *J* = 7.5 Hz, 1H), 6.67 (dd, *J* = 17.6, 10.9 Hz, 1H), 6.65 (d, *J* = 2.3 Hz, 1H), 6.34 (t, *J* = 4.3 Hz, 1H), 6.27 (d, *J* = 2.2 Hz, 1H), 5.82 (s, 1H), 5.68 (d, *J* = 17.6 Hz, 1H), 5.17 (d, *J* = 10.9 Hz, 1H), 3.83 (s, 3H), 3.47 (s, 3H), 2.39 (q, *J* = 10.1 Hz, 1H), 2.32 – 2.26 (m, 2H), 1.71 (ddd, *J* = 11.0, 8.6, 2.5 Hz, 1H), 1.61 (q, *J* = 9.7 Hz, 1H), 1.44 – 1.40 (m, 1H), 1.36 – 1.31 (m, 2H), 1.23 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 159.6, 156.8, 144.3, 137.3, 136.7, 135.1, 135.1, 127.7, 127.7, 126.4, 124.6, 120.7, 118.6, 113.1, 99.9, 98.0, 72.8, 72.6, 55.3, 55.2, 42.3, 31.4, 29.0, 22.8, 22.7, 21.9. **HRMS** (ESI): calcd for $C_{26}H_{29}O_3$ $[M+H]^+$ 389.2111, found 389.2116.

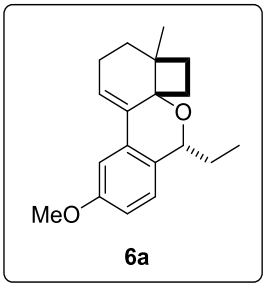
1.4.17 7-(furan-3-yl)-8,10-dimethoxy-3a-methyl-2,3,3a,4,5,7-hexahydrobenzo[c]cyclobuta [i]chromene, 4p



4p

The product **4p** was synthesized following Method B and purified using dichloromethane: petroleum ether (1:1), (yellow solid, 77% yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.23 (t, *J* = 1.7 Hz, 1H), 7.19 – 7.17 (m, 1H), 6.60 (d, *J* = 2.3 Hz, 1H), 6.33 (d, *J* = 2.3 Hz, 1H), 6.26 – 6.24 (m, 2H), 5.91 (s, 1H), 3.83 (s, 3H), 3.67 (s, 3H), 2.32 (q, *J* = 10.0 Hz, 1H), 2.28 – 2.24 (m, 2H), 1.69 (ddd, *J* = 11.1, 8.7, 2.6 Hz, 1H), 1.59 (q, *J* = 9.5 Hz, 1H), 1.45 – 1.40 (m, 1H), 1.34 – 1.28 (m, 2H), 1.27 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 159.7, 156.5, 141.9, 140.2, 135.3, 135.2, 128.2, 121.3, 118.3, 110.2, 100.2, 97.7, 72.7, 64.6, 55.3, 55.2, 42.8, 32.5, 29.0, 22.9, 22.7, 21.8. **HRMS** (ESI): calcd for $C_{22}H_{25}O_4$ $[M+H]^+$ 353.1747, found 353.1749.

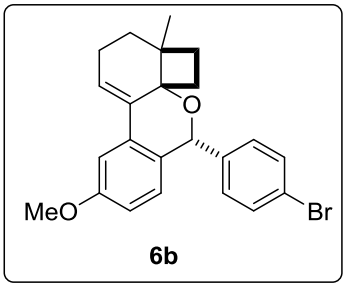
1.4.18 7-ethyl-10-methoxy-3a-methyl-2,3,3a,4,5,7-hexahydrobenzo[c]cyclobuta[i] chromene, 6a



6a

Propionaldehyde was distilled prior to use. The product **6a** was synthesized following Method A and purified using hexanes: ethyl acetate (9:1), (yellow oil, 79% yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.06 (d, *J* = 2.6 Hz, 1H), 6.99 (dd, *J* = 8.6, 0.9 Hz, 1H), 6.76 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.36 – 6.31 (m, 1H), 4.67 (dd, *J* = 8.7, 3.2 Hz, 1H), 3.81 (s, 3H), 2.36 – 2.26 (m, 3H), 2.06 – 1.99 (m, 1H), 1.72 – 1.63 (m, 3H), 1.48 – 1.41 (m, 2H), 1.35 (td, *J* = 10.8, 10.1, 2.1 Hz, 1H), 1.30 (s, 3H), 0.98 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 158.1, 134.7, 133.6, 130.0, 125.3, 119.9, 113.4, 108.1, 72.5, 71.7, 55.2, 41.9, 29.8, 29.3, 28.8, 22.6, 22.5, 21.6, 9.7. **HRMS** (ESI): calcd for $C_{19}H_{25}O_2$ $[M+H]^+$ 286.1883, found 286.1886.

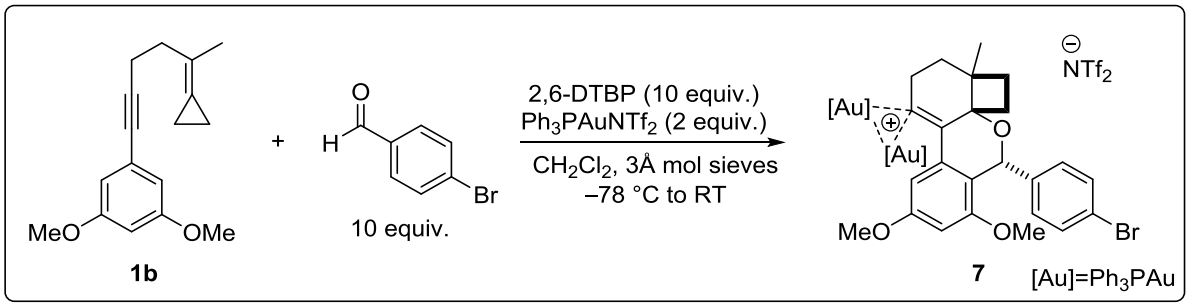
1.4.19 7-(4-bromophenyl)-10-methoxy-3a-methyl-2,3,3a,4,5,7-hexahydrobenzo[c] cyclobuta[i]chromene, 6b



6b

The product **6b** was synthesized following Method B and purified using dichloromethane: petroleum ether (1:1), (pale yellow crystalline solid, 74% yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.45 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.08 (d, *J* = 2.6 Hz, 1H), 6.64 (dd, *J* = 8.6, 2.6 Hz, 1H), 6.56 (dd, *J* = 8.6, 0.8 Hz, 1H), 6.42 (dd, *J* = 5.9, 2.9 Hz, 1H), 5.68 (s, 1H), 3.80 (s, 3H), 2.47 (q, *J* = 10.1 Hz, 1H), 2.37 – 2.29 (m, 2H), 1.83 (ddd, *J* = 11.1, 8.7, 2.6 Hz, 1H), 1.69 (q, *J* = 9.4 Hz, 1H), 1.51 – 1.46 (m, 1H), 1.45 – 1.38 (m, 2H), 1.23 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 158.4, 142.1, 134.1, 133.4, 131.4, 130.4, 128.9, 127.5, 121.7, 120.7, 113.4, 107.8, 74.5, 73.7, 55.2, 41.9, 29.9, 29.3, 22.7, 22.6, 21.7. **HRMS** (ESI): calcd for $C_{23}H_{23}BrNaO_2$ $[M+Na]^+$ 433.0774, found 433.0762.

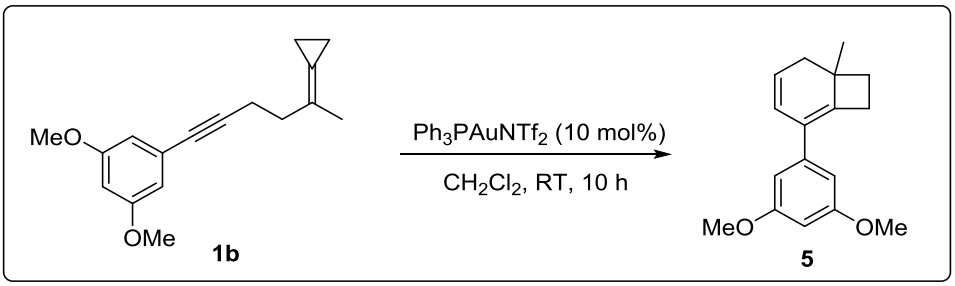
1.5 Isolation of Di-gold intermediate 7



In an oven dried vial, enyne **1b** (2 mg, 0.0078 mmol), 4-bromobenzaldehyde (14 mg, 0.078 mmol) and 2,6-di-*tert*-butylpyridine (polymer bound, 1.8 mmol/g loading; 43 mg, 0.078 mmol) were dissolved in 1 mL anhydrous CH_2Cl_2. Activated molecular sieves (~60 mg) were added. The solution was cooled to –78 °C. $Ph_3PAuNTf_2$ (11.5 mg, 0.0156 mmol) was added to the solution. The mixture was stirred and allowed to warm to room temperature. The solution was passed through a glass plug of cotton to remove the resin base, and the solvent was evaporated under reduced pressure. The resulting residue was washed with 2 mL anhydrous diethyl ether at –78 °C to remove excess aldehyde (**7** is slightly soluble in ether). The ether was discarded, and the residual solvent was removed under reduced pressure. The washing process was repeated 4 times, and resulted in an orange oil (4 mg, 0.0024 mmol, 31%). Protodemetallated product **4k** and $[(Ph_3P)_2Au]^+[NTf_2]^-$ were always observed as impurities. Continuous washing with ether

removed **4k**, but increased the $[(Ph_3P)_2Au]^+[NTf_2]^-$ impurity. **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 2.2, 1H), 7.59 – 7.35 (m, 30H), 6.80 (d, *J* = 8.4, 2H), 6.55 (d, *J* = 2.2, 1H), 6.49 (d, *J* = 8.3, 2H), 5.98 (s, 1H), 3.49 (s, 3H), 3.36 (s, 3H), 3.13 – 3.08 (m 1H), 2.68 – 2.58 (m, 2H), 1.84 – 1.71 (m, 3H), 1.53 – 1.48 (m, 1H), 1.45 – 1.40 (m, 1H), 1.28 (s, 3H).**^{13}C NMR** (151 MHz, $CDCl_3$): δ = 159.9, 156.9, 140.7, 134.1, 133.9, 133.8, 133.7, 133.6, 133.0, 132.5, 132.2, 130.6, 130.1, 129.7, 129.4, 129.4, 128.8, 128.4, 127.6, 127.2, 126.9, 121.0, 117.5, 103.0, 101.1, 74.2, 72.6, 55.4, 55.1, 34.9, 32.5, 29.7, 28.7, 22.9, 21.8. **^{31}P NMR** (243 MHz, $CDCl_3$): δ = 38.5 (1P), 33.6 (1P). **HRMS** (ESI): calcd for $C_{60}H_{54}O_3P_2Au_2Br_1$ $[M]^+$ 1357.2063, found 1357.2055. Note: ^{1}H, ^{13}C and ^{31}P NMR contain the $[(Ph_3P)_2Au]^+[NTf_2]^-$ impurity.

1.6 Isolation of Cycloisomer 5



In an oven dried vial, enyne **1b** (10 mg, 0.039 mmol) was dissolved in 1 mL anhydrous CH_2Cl_2. $Ph_3PAuNTf_2$ (2.9 mg, 0.00039 mmol) was added, and the mixture was stirred for 10 hours. Upon evaporation of the solvent under reduced pressure, the residue was purified by silica gel column chromatography (Hexanes: ethyl acetate 10:1) to afford the cycloisomer **5** in pure form (8.2 mg, 82% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 6.43 (d, *J* = 2.3, 2H), 6.34 (t, *J* = 2.3, 1H), 6.24 (dd, *J* = 9.7, 3.5, 1H), 5.82 (ddd, *J* = 8.9, 6.4, 1.8, 1H), 3.79 (s, 6H), 3.28 (dt, *J* = 17.6, 9.1, 1H), 2.92 – 2.81 (m, 1H), 2.31 (dt, *J* = 16.7, 3.0, 1H), 2.02 (dd, *J* = 16.6, 6.4, 1H), 1.96 (td, *J* = 9.9, 3.1, 1H), 1.86 (q, *J* = 8.8, 1H), 1.25 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ = 160.8, 143.9, 140.0, 126.0, 125.3, 124.1, 104.5, 98.7, 55.4, 40.7, 35.4, 34.5, 31.0, 20.8. **HRMS** (ESI): calcd for $C_{17}H_{20}O_2$ $[M+H]^+$ 257.1536, found 257.1536.

1.7 Experimental Procedure for Acid/Base Experiments

1.7.1 Reactions with acid.

$[Ph_2NH_2][BF_4]$ was synthesized according to a literature procedure.[8] In an oven dried vial, enyne **1b** (6 mg, 0.023 mmol), $[Ph_2NH_2][BF_4]$ (6 mg, 0.023 mmol), and propionaldehyde (8.5 µL, 0.117 mmol) were dissolved in 0.5 mL anhydrous CH_2Cl_2. $Ph_3PAuNTf_2$ (1.7 mg, 0.0023 mmol) was added, and the mixture was stirred for 1 hour. The solution was pushed through a short plug of silica gel, eluting with CH_2Cl_2, and analyzed by GCMS. This reaction was repeated with 5 equivalents of acid.

1.7.2 Reactions with base.

In an oven dried vial, enyne **1b** (6 mg, 0.023 mmol), N-methyldiphenylamine (4.1 µL, 0.023 mmol), and propionaldehyde (8.5 µL, 0.117 mmol) were dissolved in 0.5 mL anhydrous CH_2Cl_2. $Ph_3PAuNTf_2$ (1.7 mg, 0.0023 mmol) was added, and the mixture was stirred for 1 hour. The solution was pushed through a short plug of silica gel, eluting with CH_2Cl_2, and analyzed by GCMS. This reaction was repeated with 5 equivalents of base.

1.8 Experimental Procedure for Competition Experiments

In an NMR tube, enyne **1b** (8 mg, 0.031 mmol), p-CF_3-benzaldehyde (21 µL, 0.155 mmol), and benzaldehyde (16 µL, 0.155 mmol) were dissolved in 0.5 mL CD_2Cl_2. The reaction was cooled to –78 °C in a dry ice/acetone bath. $Ph_3PAuNTf_2$ (2.3 mg, 0.0031 mmol) was added, and the reaction was transferred to a cryobath set at –35 °C for 12 hours. The resulting mixture was analyzed by ^{1}H NMR. The reaction was repeated with p-anisaldehyde (19 µL, 0.155 mmol) in place of benzaldehyde.

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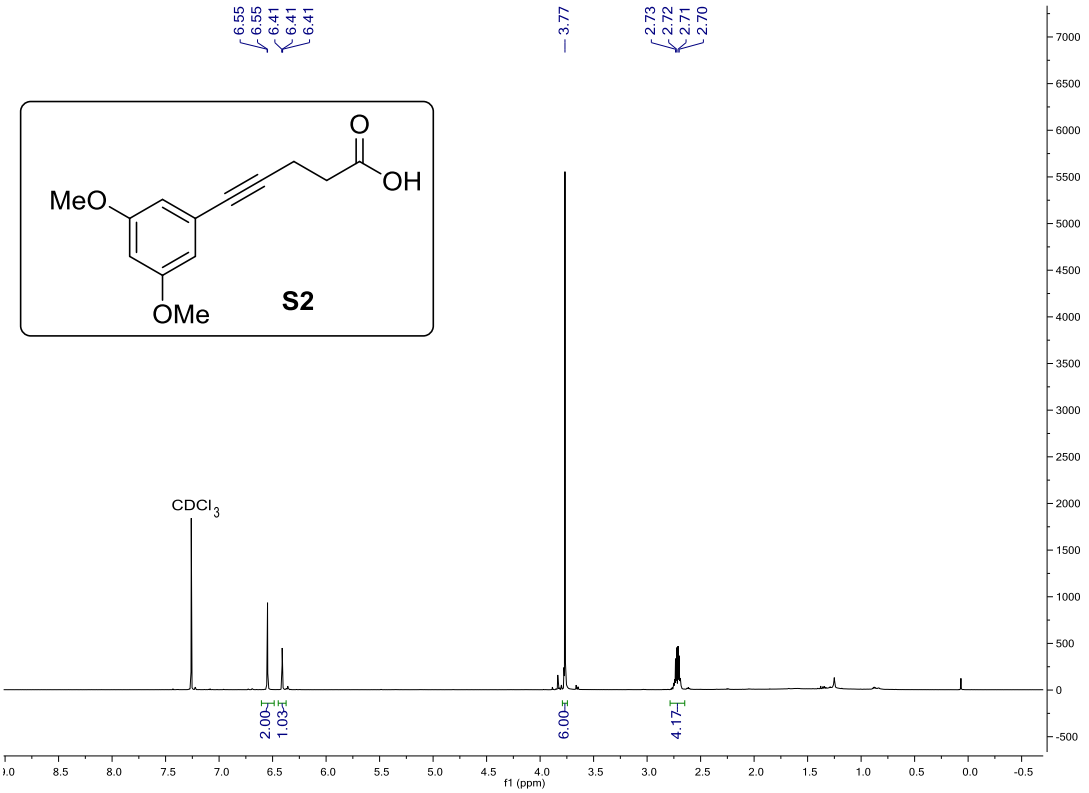
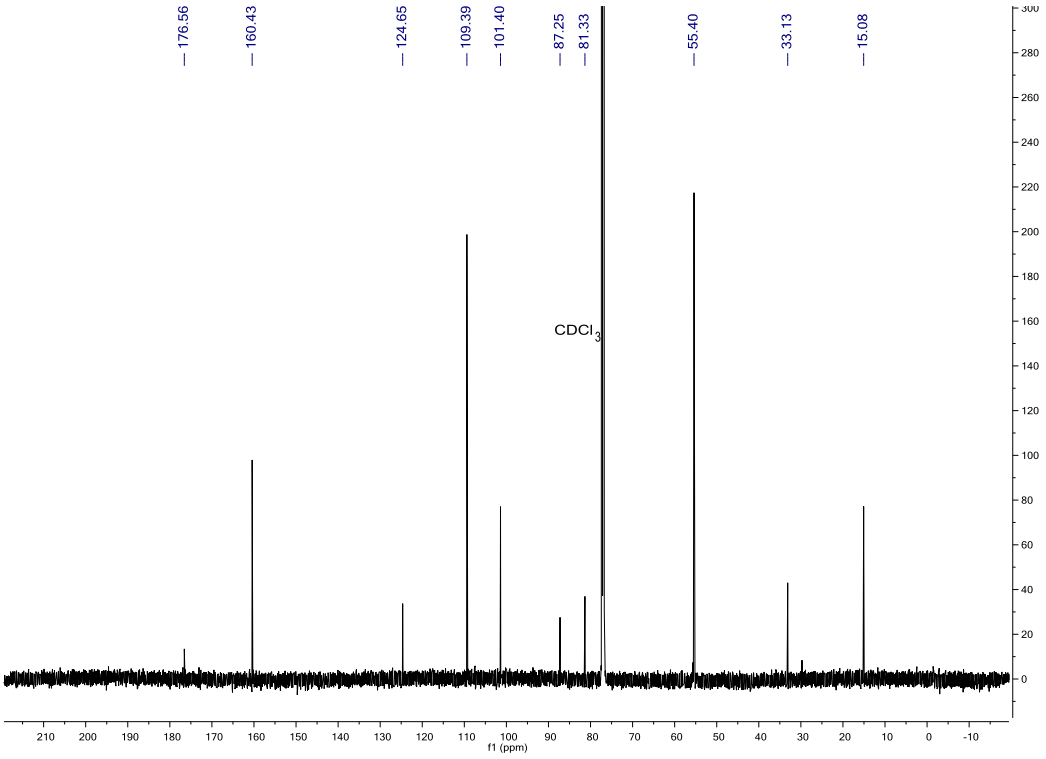
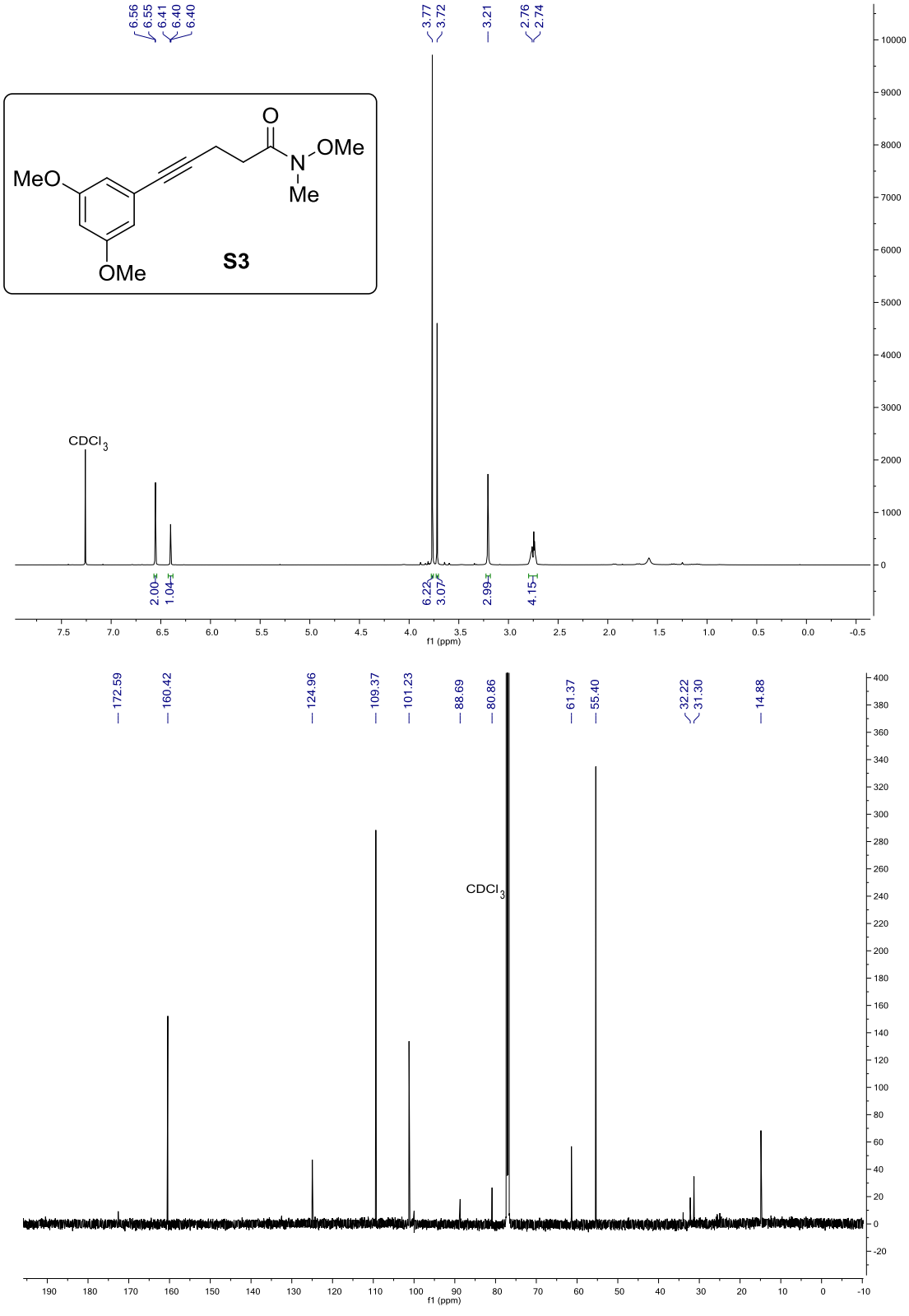
2. NMR Spectra for New Compounds

2.1 ^{1}H and ^{13}C NMR of S2 in $CDCl_3$ at 25 °C.

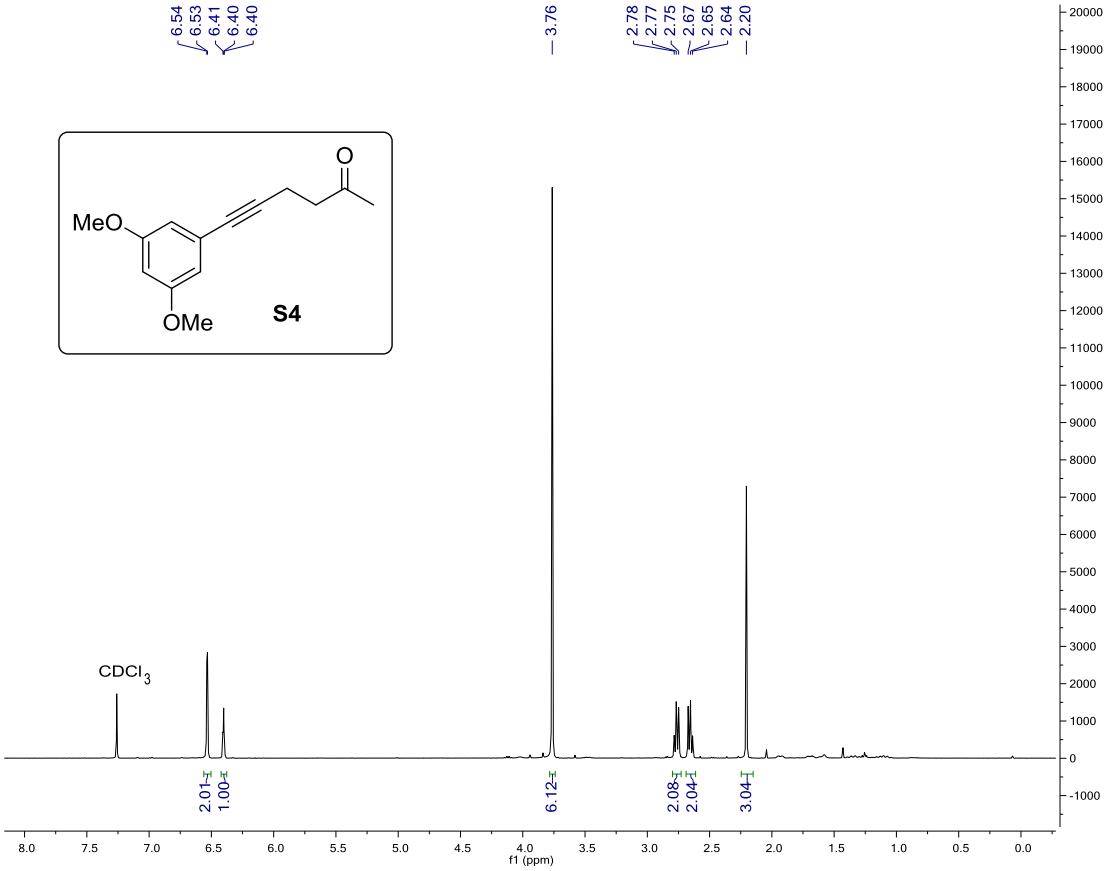


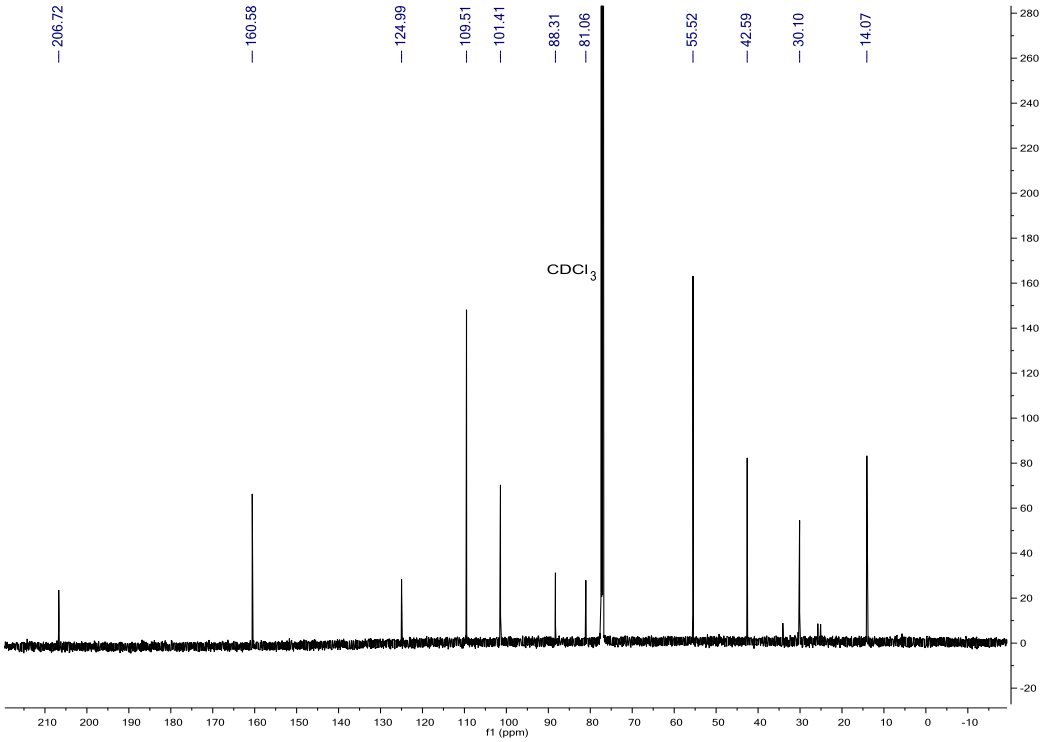


2.2 ^{1}H and ^{13}C NMR of S3 in $CDCl_3$ at 25 °C.

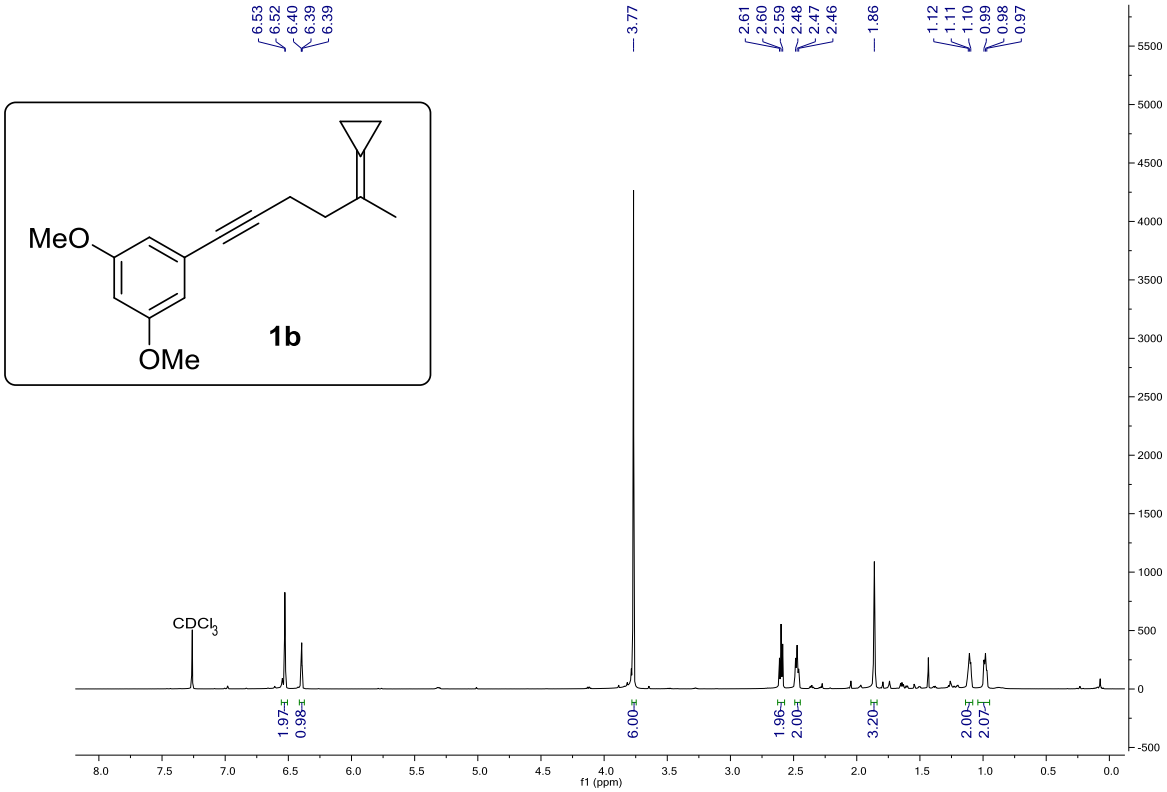


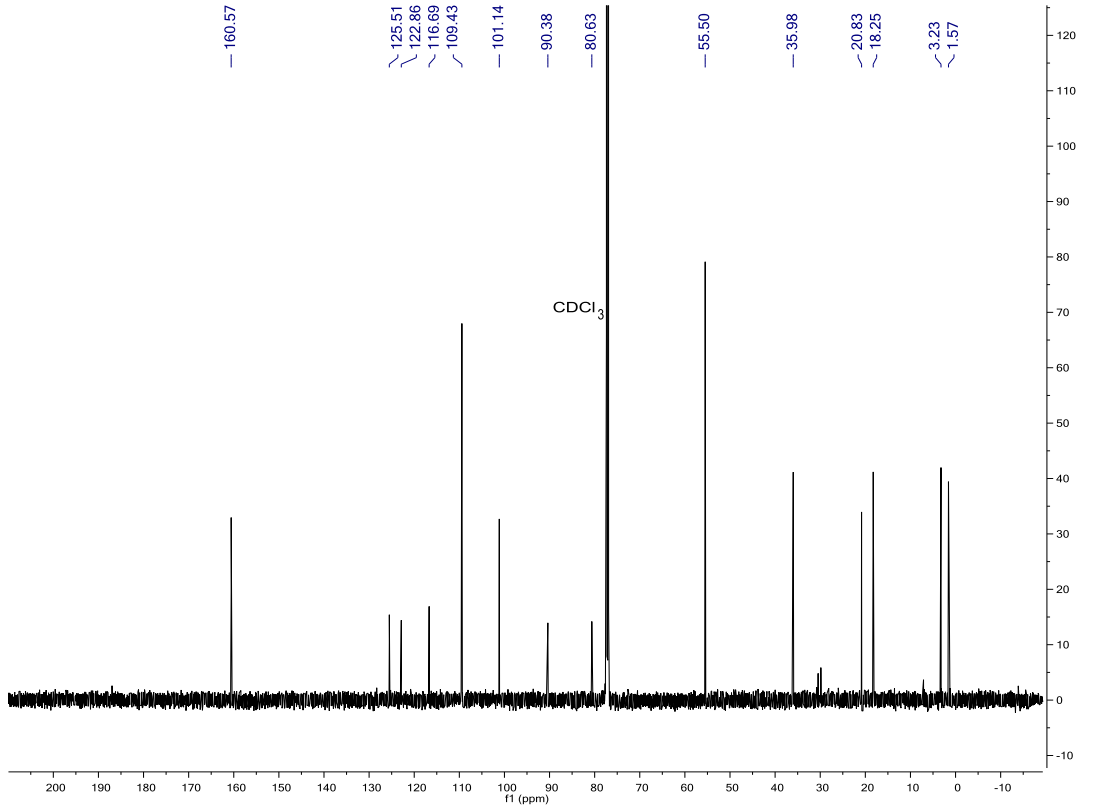
2.3 ^{1}H and ^{13}C NMR of S4 in $CDCl_3$ at 25 °C.



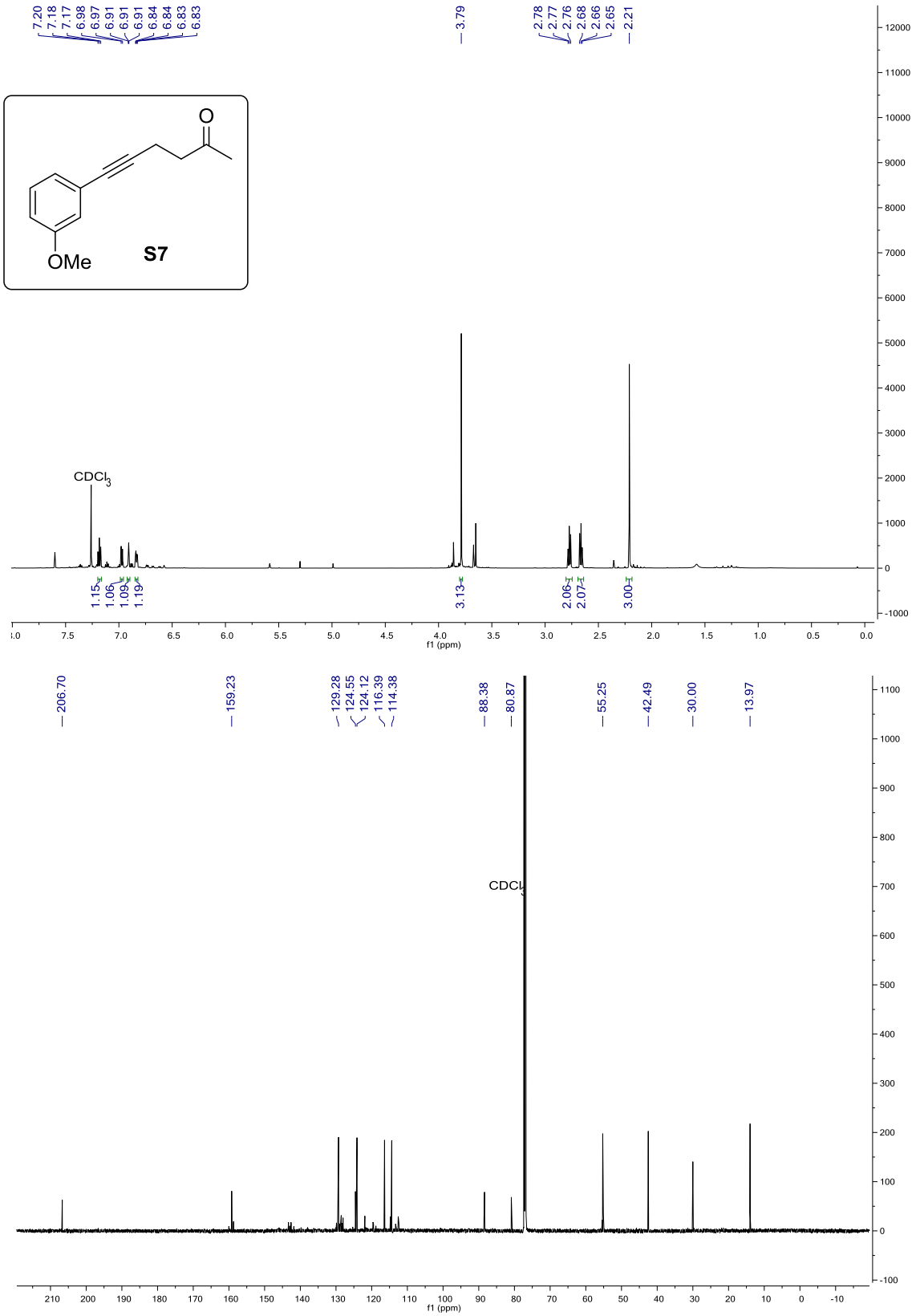


2.4 ^{1}H and ^{13}C NMR of 1b in $CDCl_3$ at 25 °C.

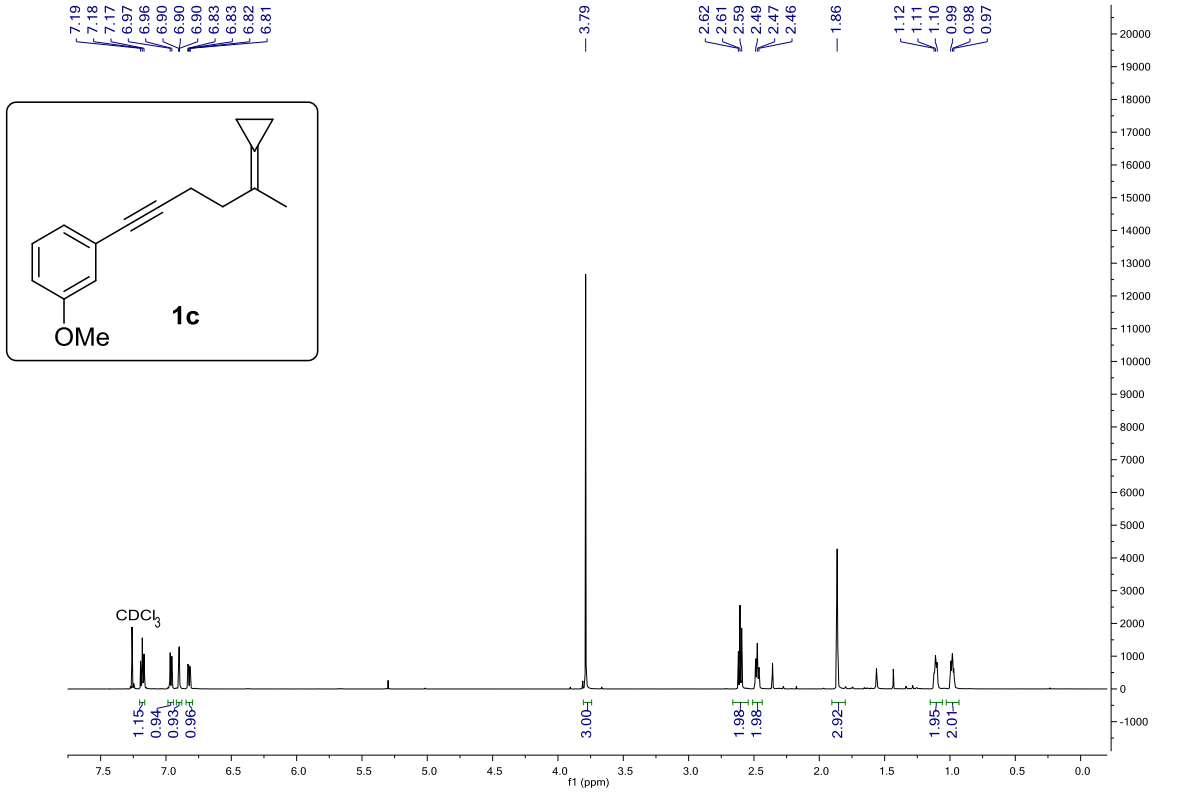


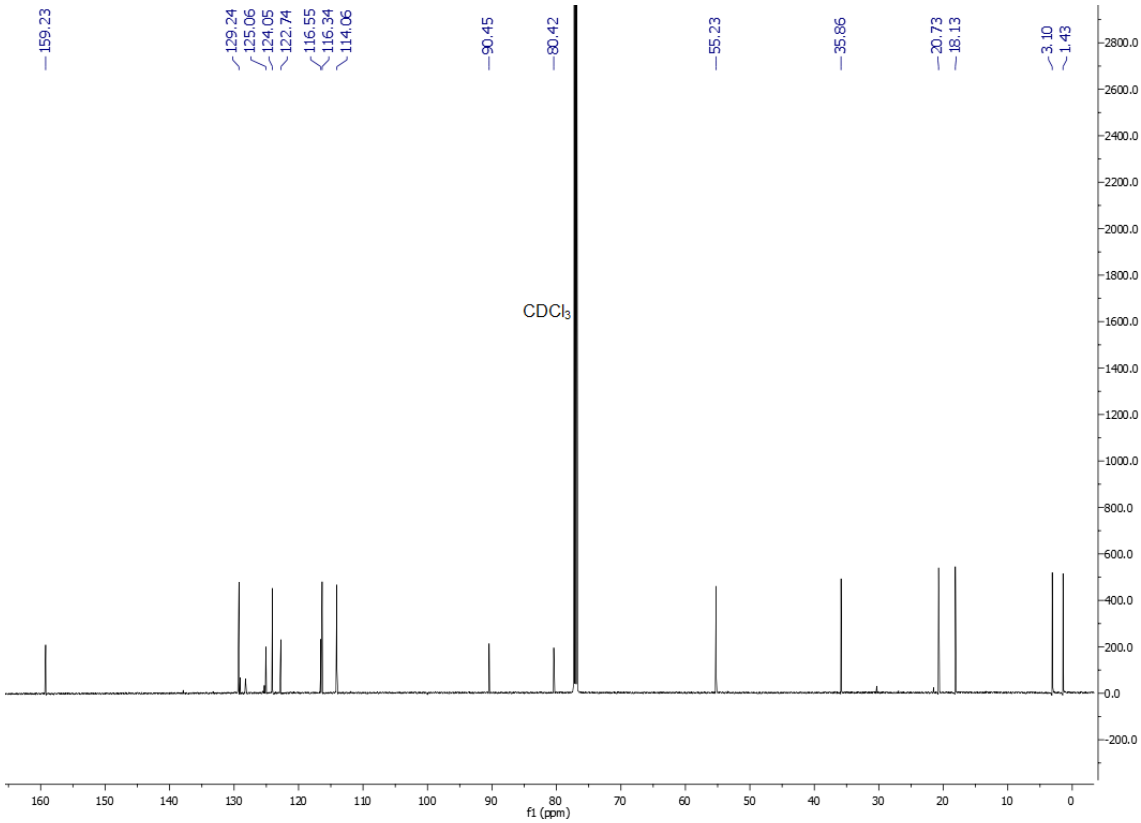


2.5 ^{1}H and ^{13}C NMR of S7 in $CDCl_3$ at 25 °C.

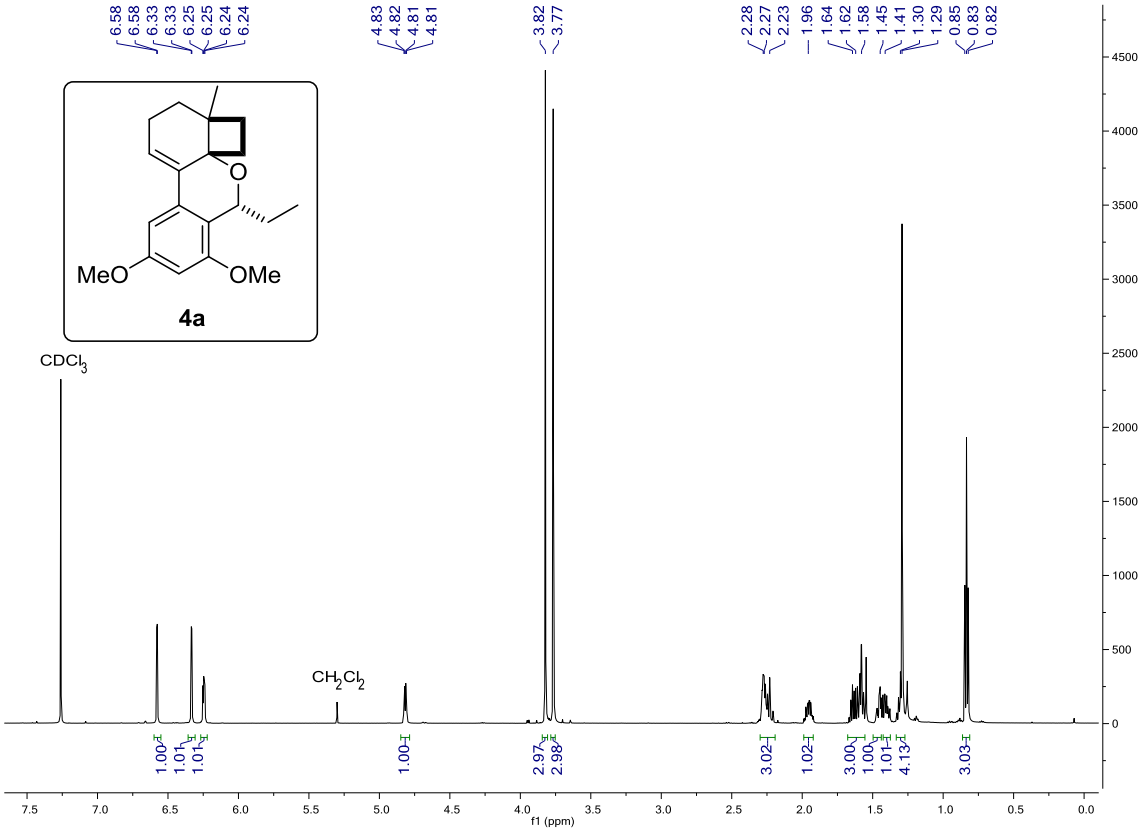


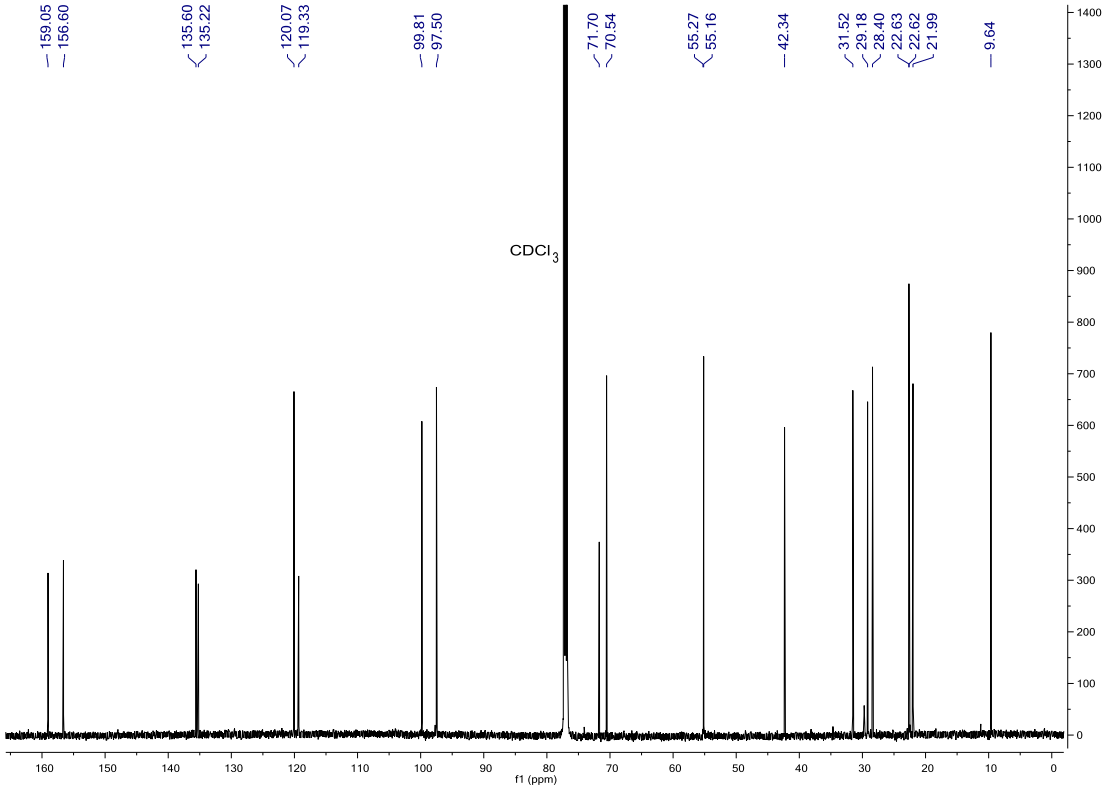
2.6 ^{1}H and ^{13}C NMR of 1c in $CDCl_3$ at 25 °C.



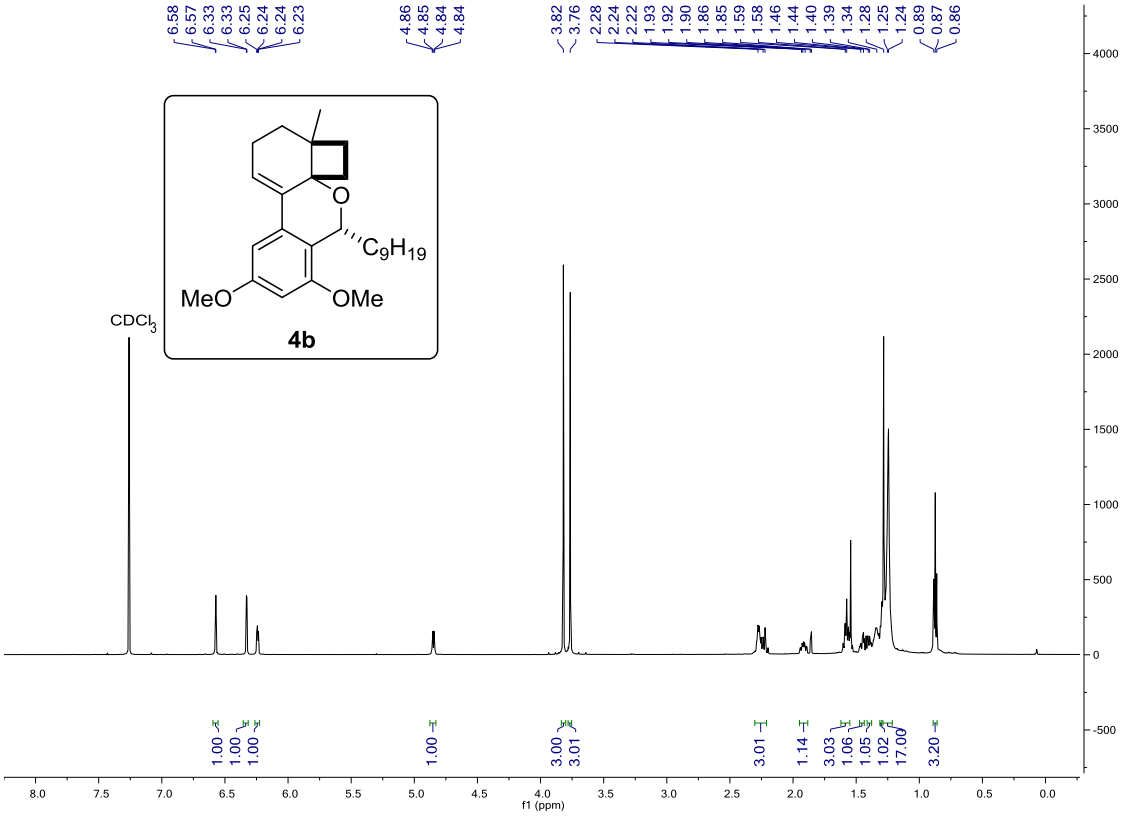


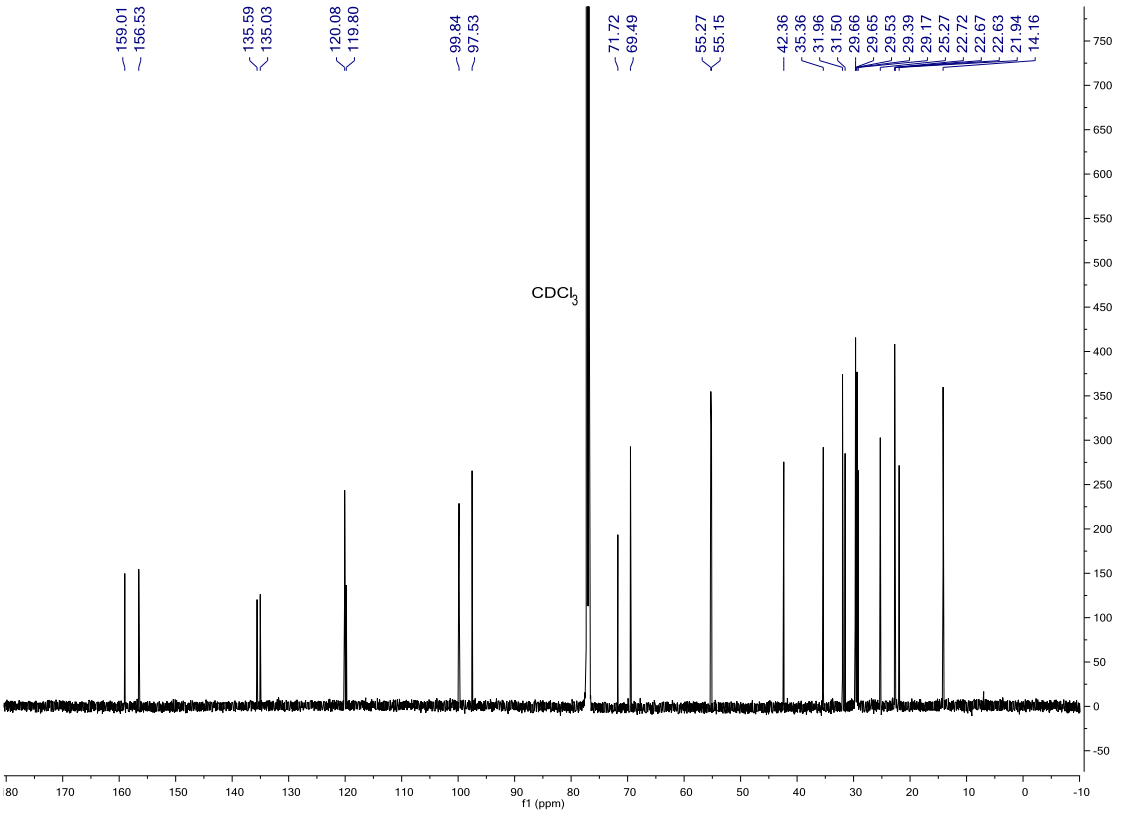
2.7 ^{1}H and ^{13}C NMR of 4a in $CDCl_3$ at 25 °C.



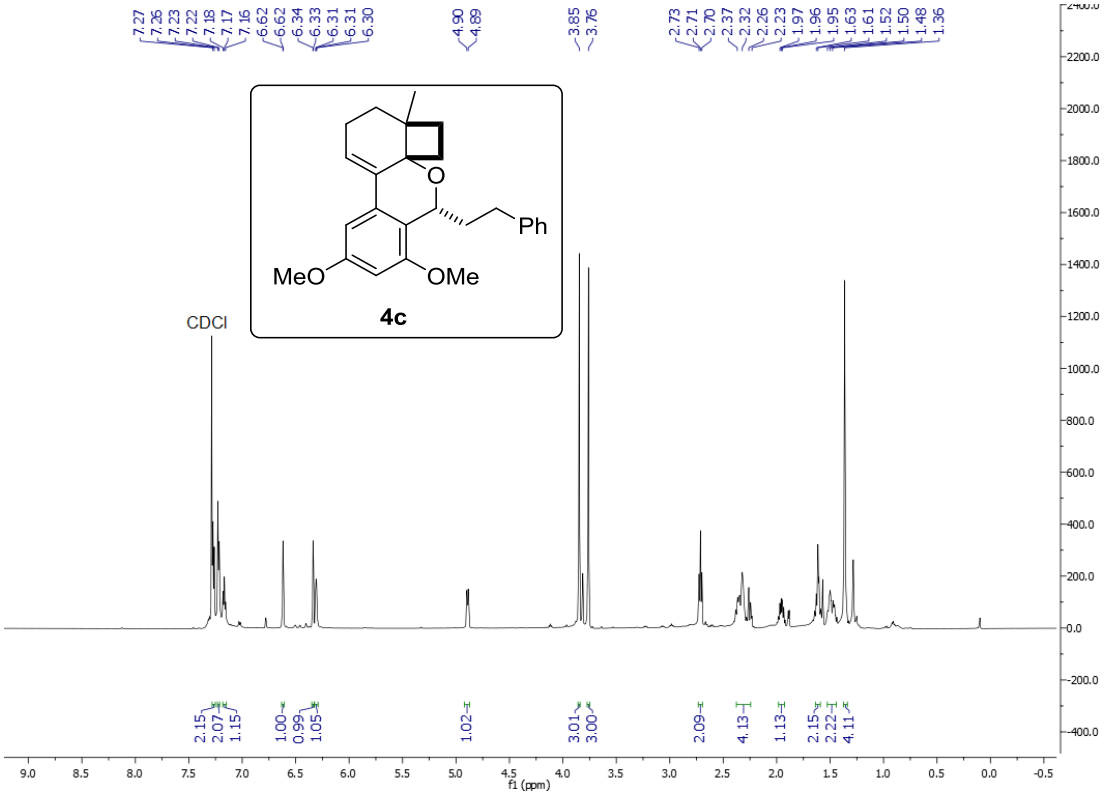


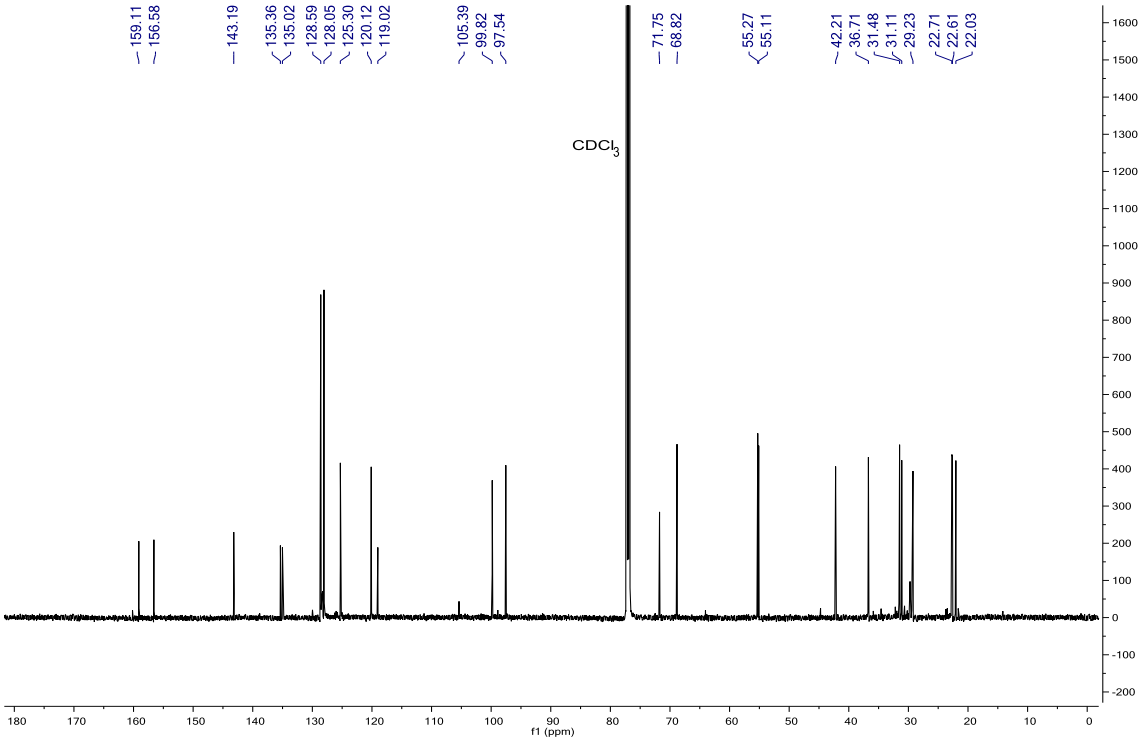
2.8 ^{1}H and ^{13}C NMR of 4b in $CDCl_3$ at 25 °C.



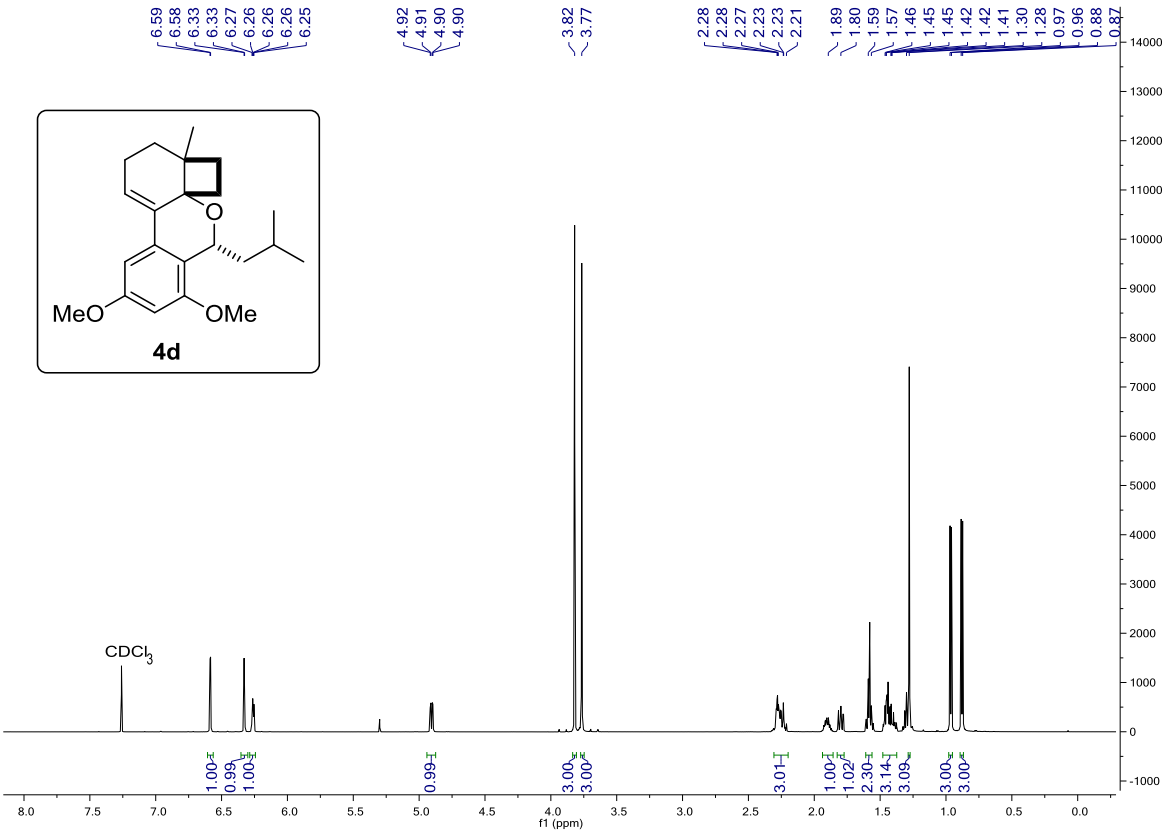


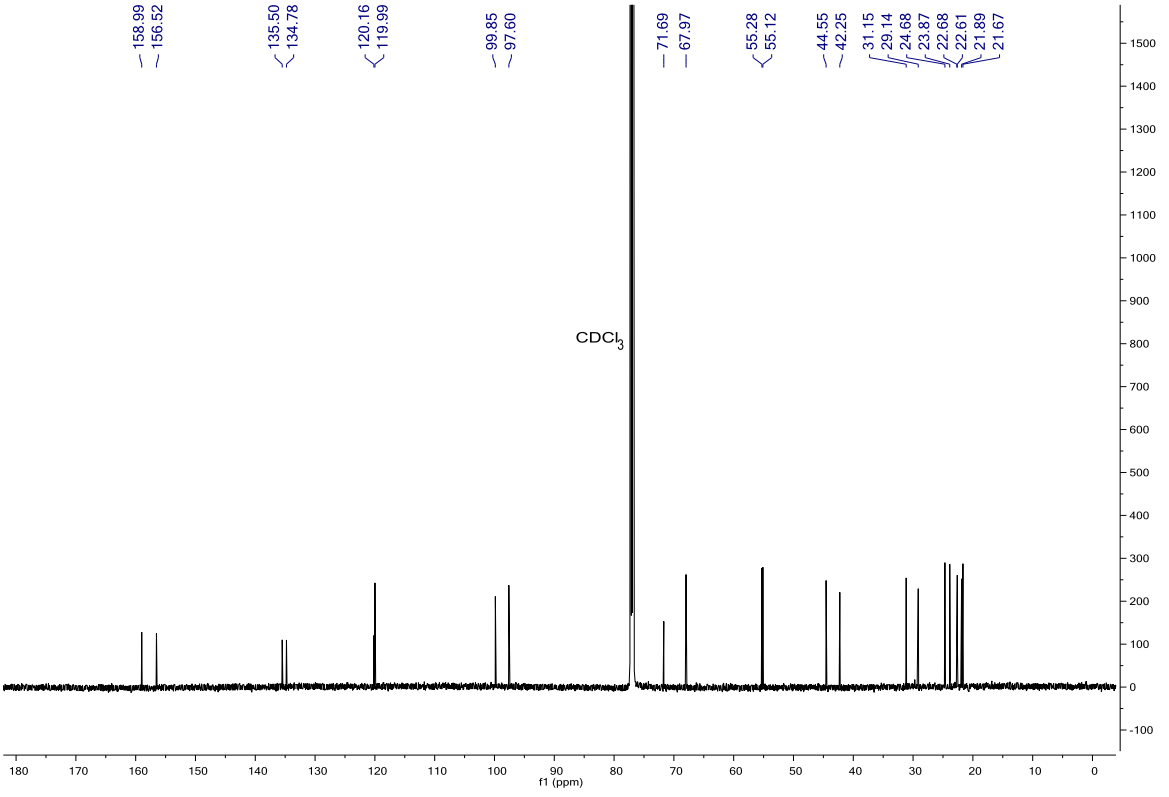
2.9 ^{1}H and ^{13}C NMR of 4c in $CDCl_3$ at 25 °C.



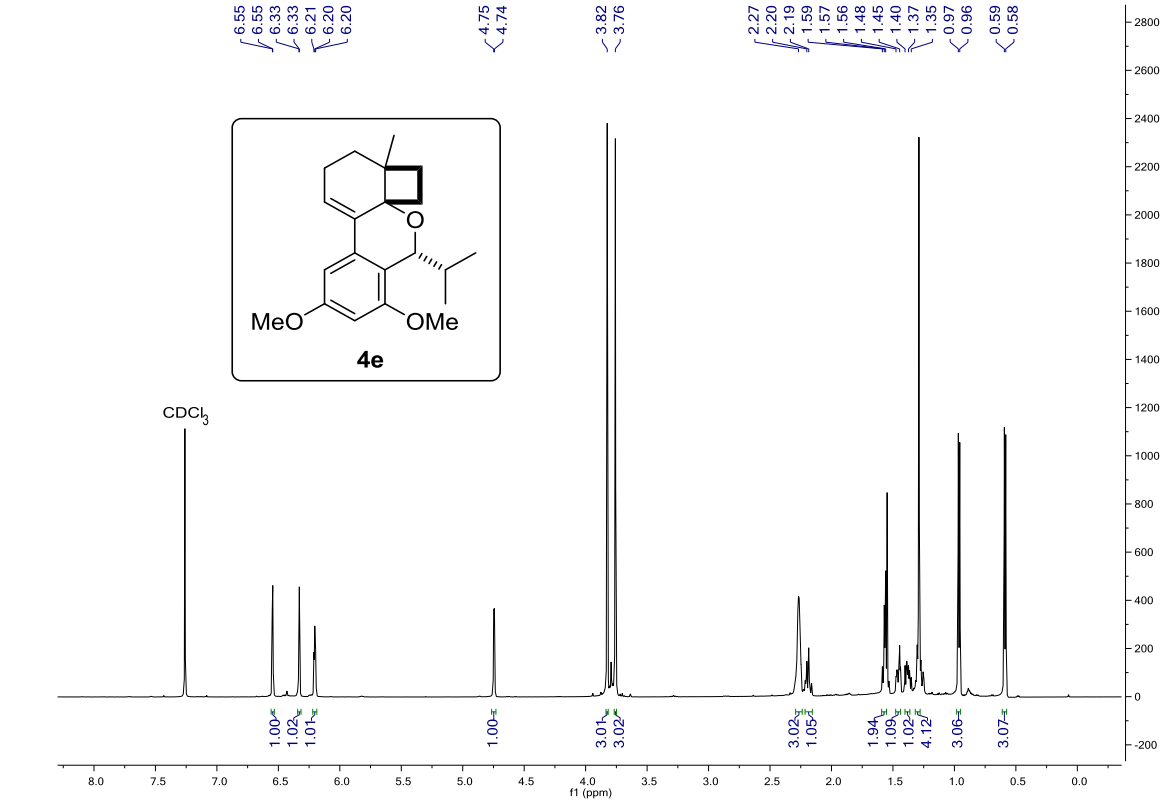


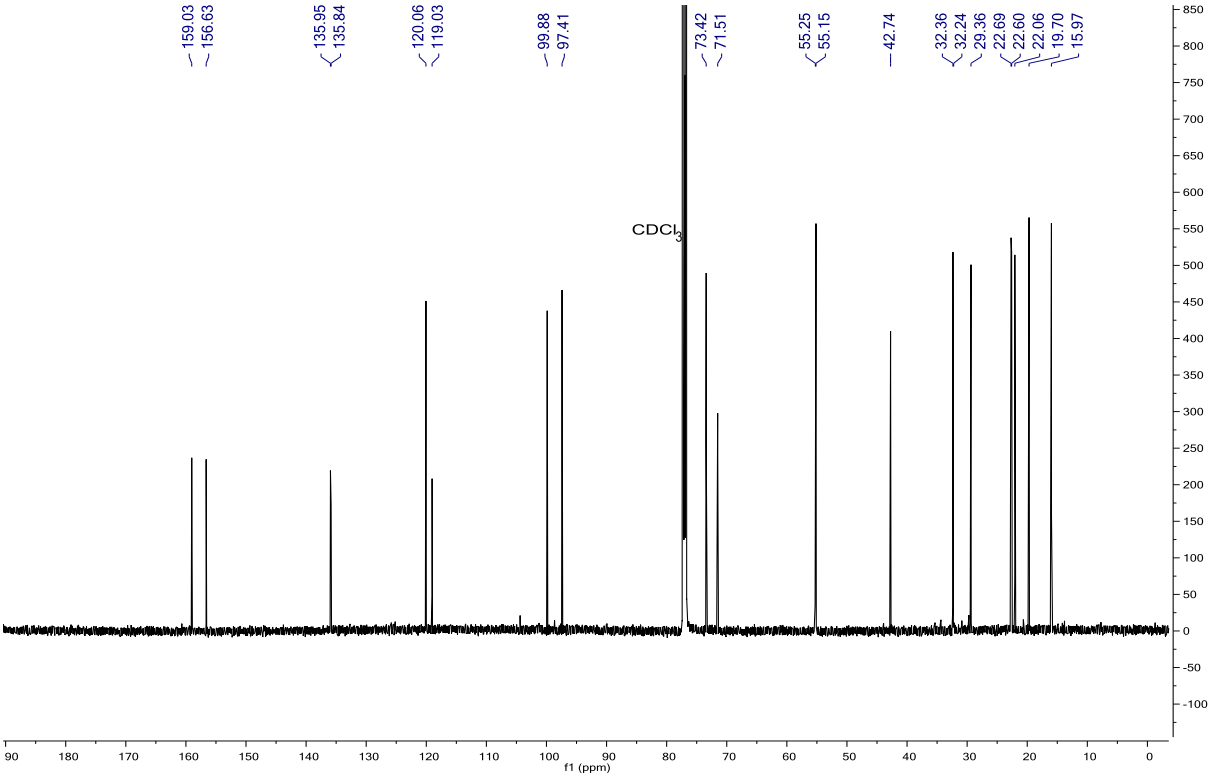
2.10 ^{1}H and ^{13}C NMR of 4d in $CDCl_3$ at 25 °C.



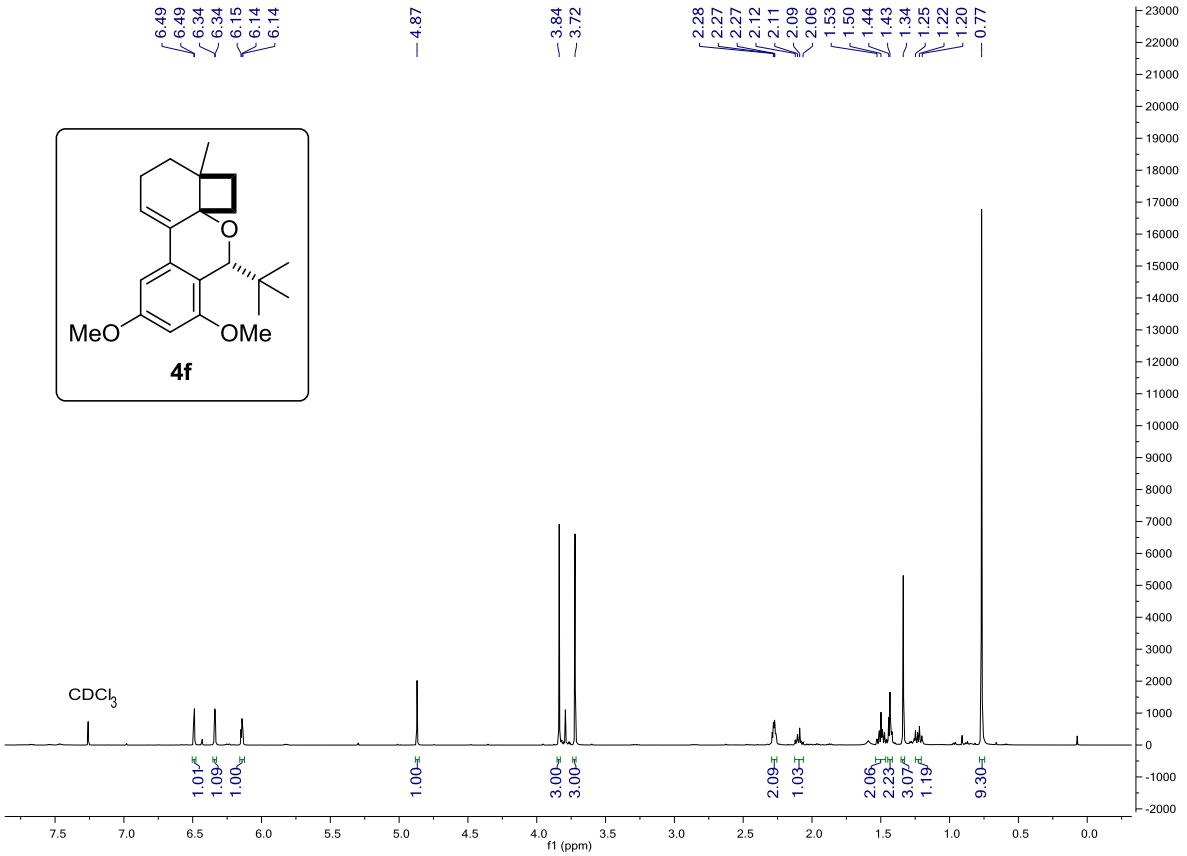


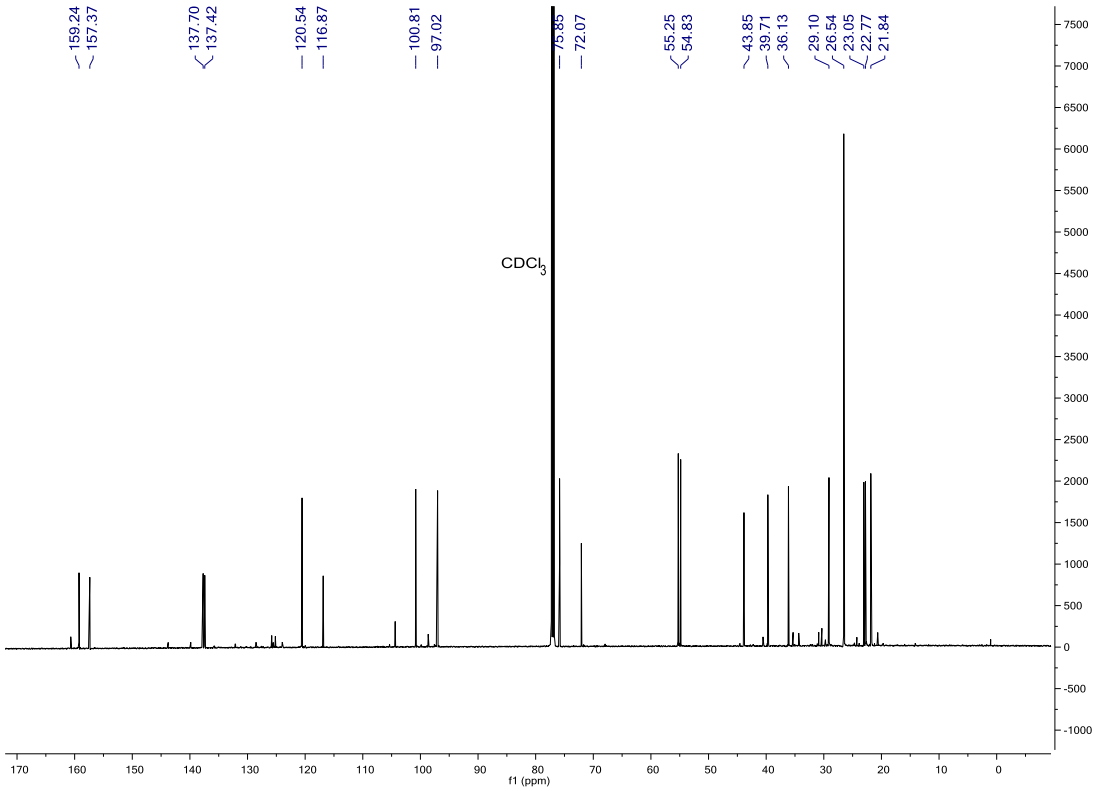
2.11 ^{1}H and ^{13}C NMR of 4e in $CDCl_3$ at 25 °C.



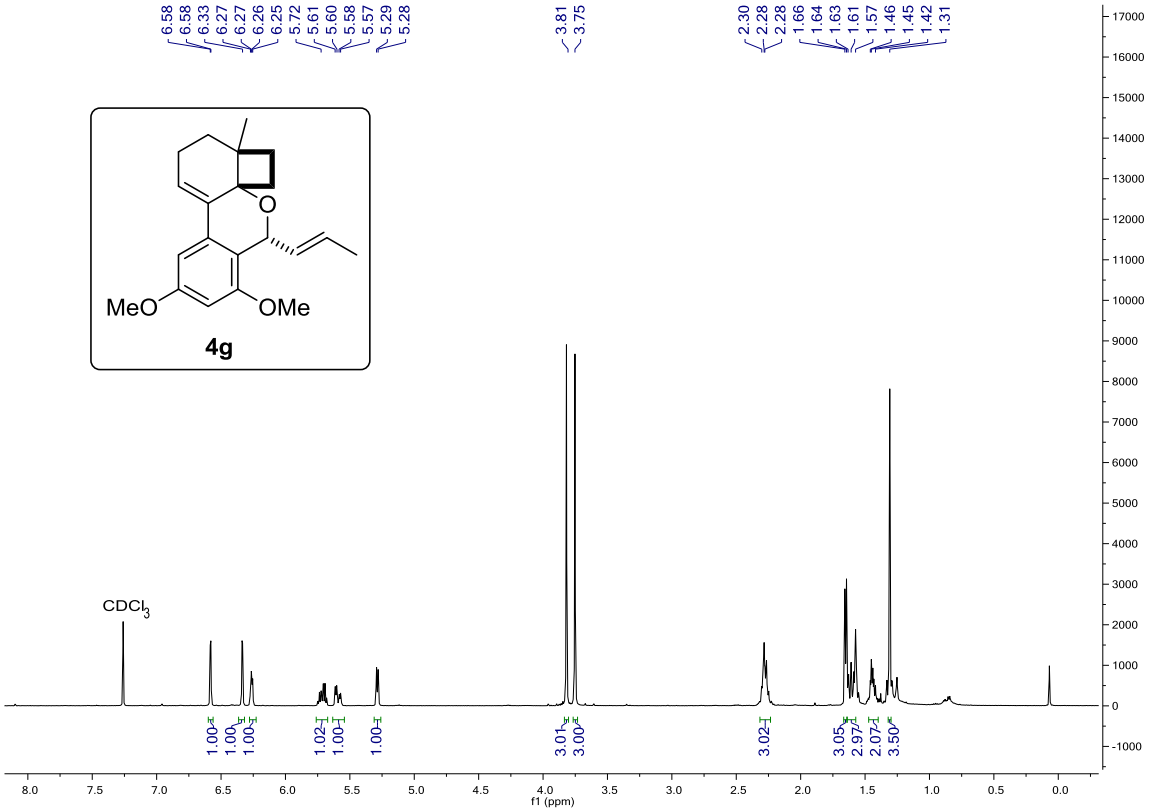


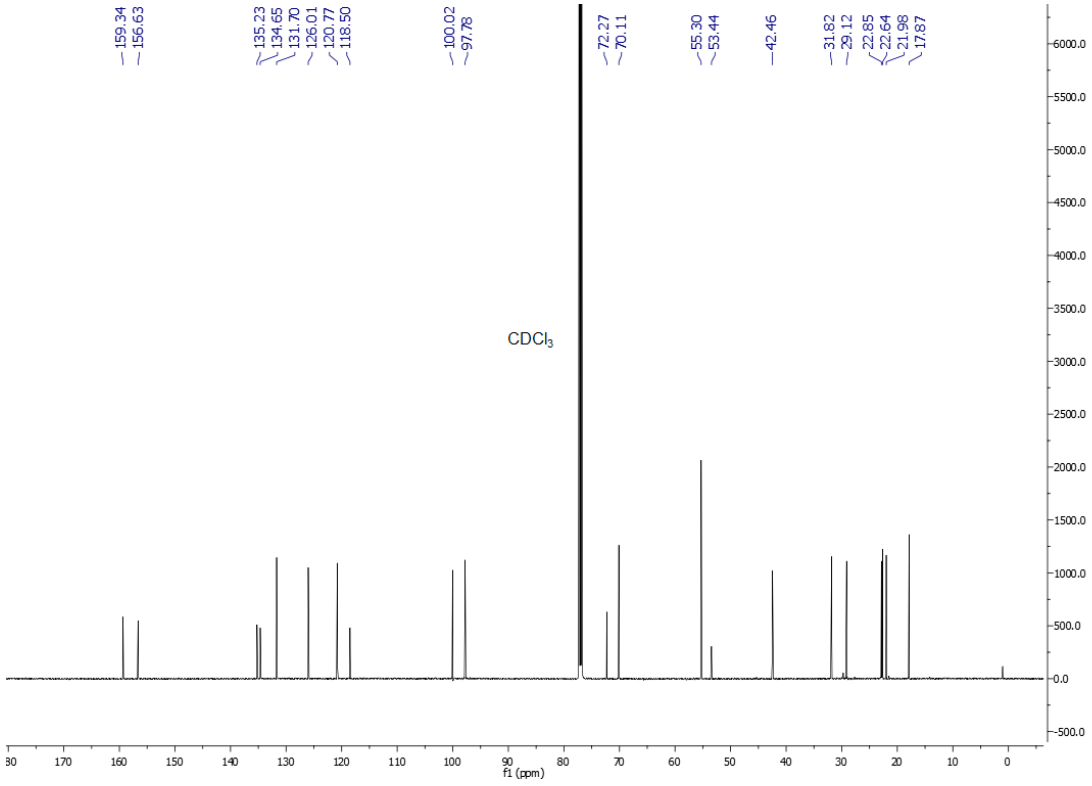
2.12 ^{1}H and ^{13}C NMR of 4f in $CDCl_3$ at 25 °C.



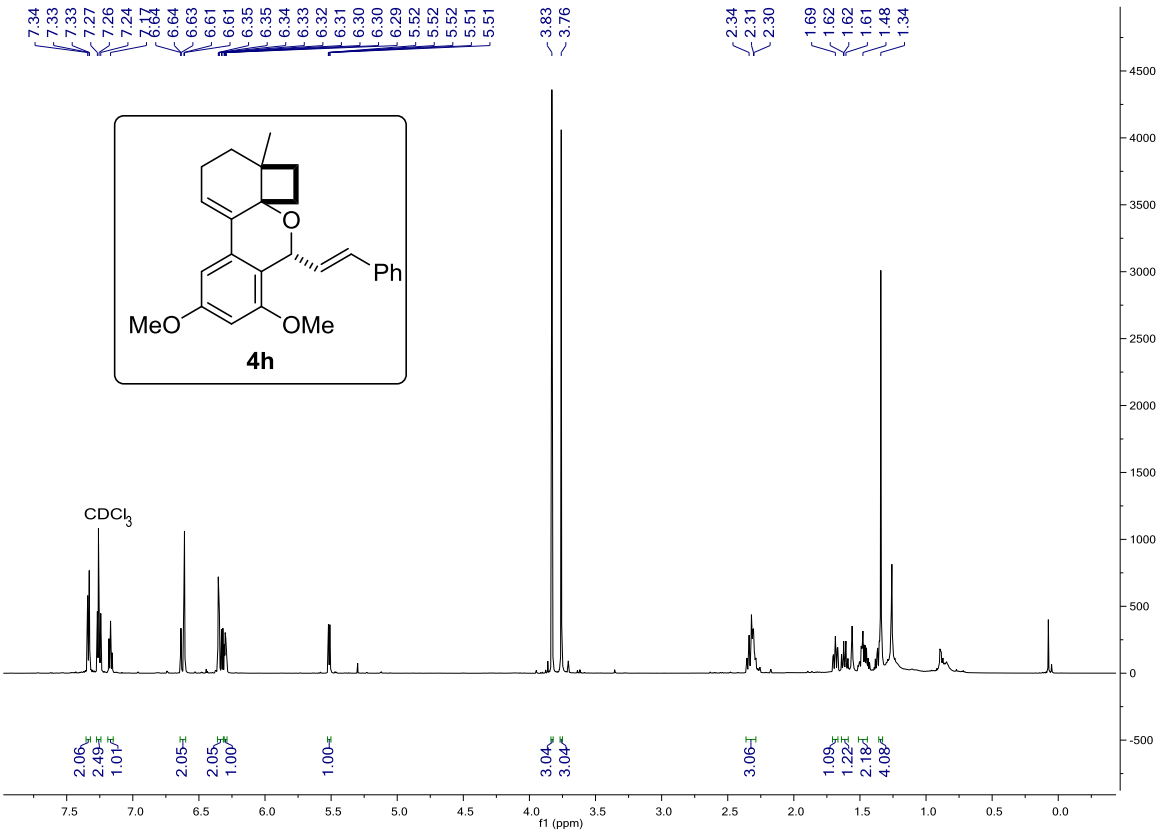


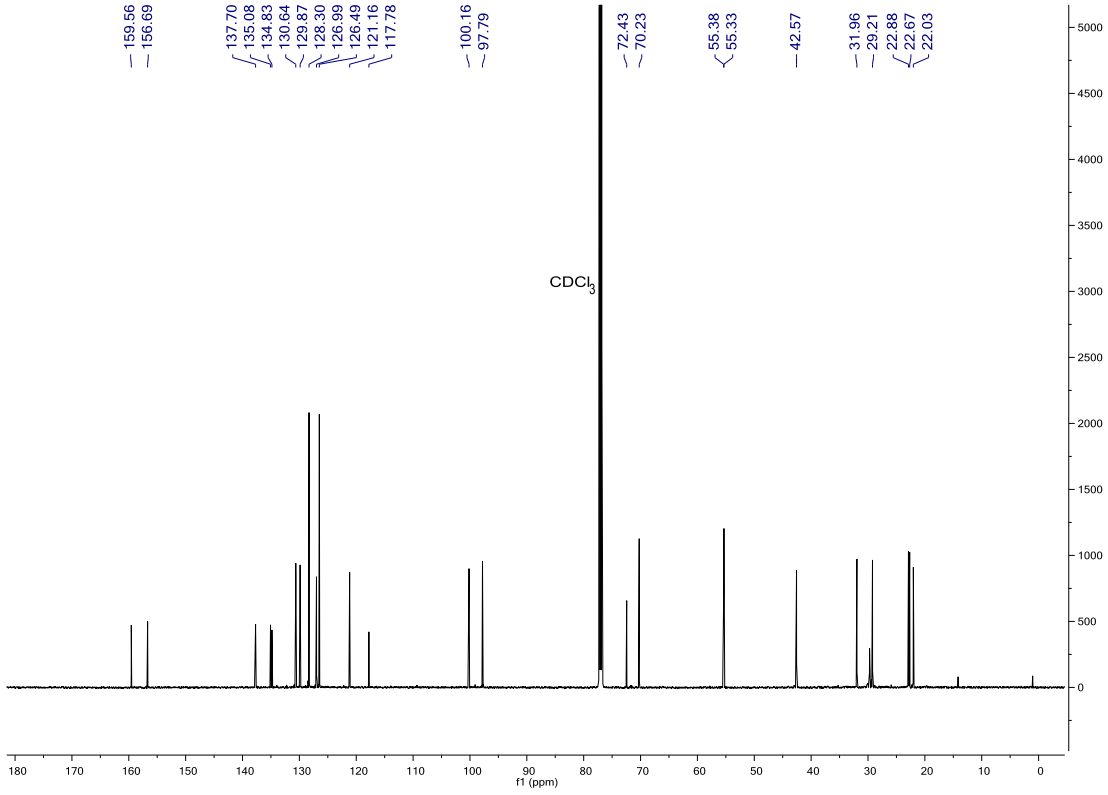
2.13 ^{1}H and ^{13}C NMR of 4g in $CDCl_3$ at 25 °C.



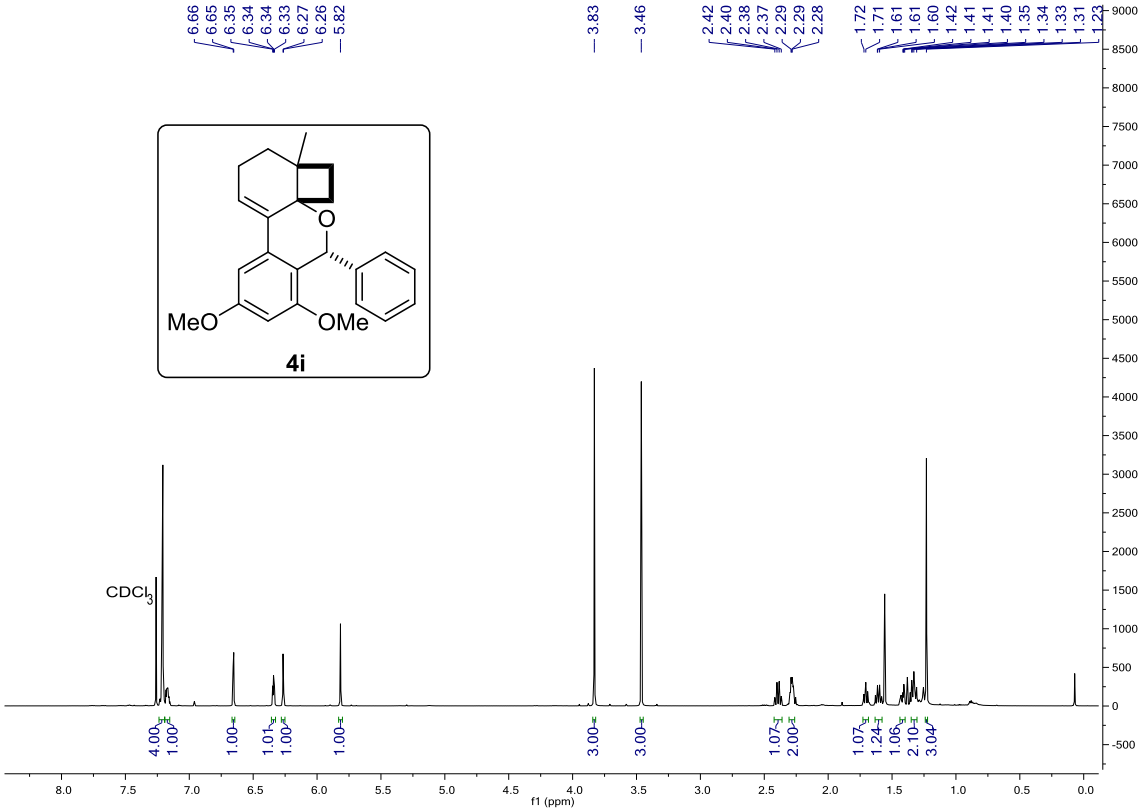


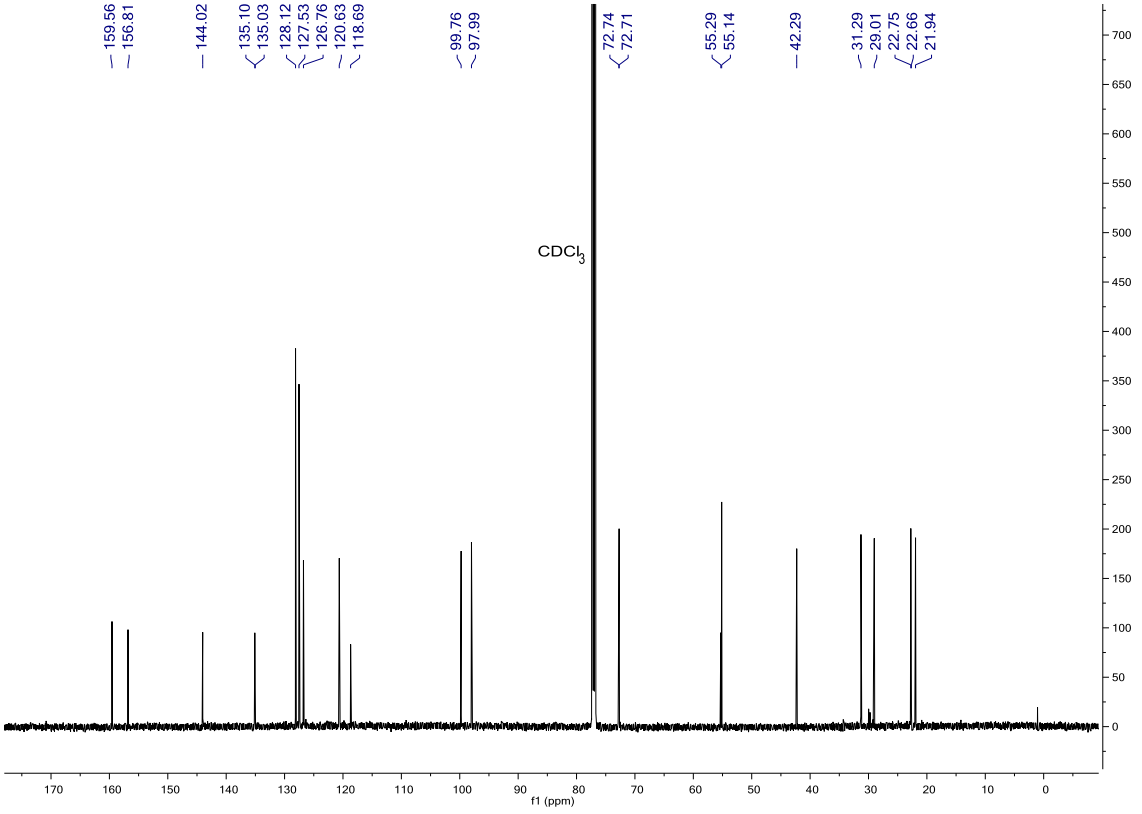
2.14 ^{1}H and ^{13}C NMR of 4h in $CDCl_3$ at 25 °C.



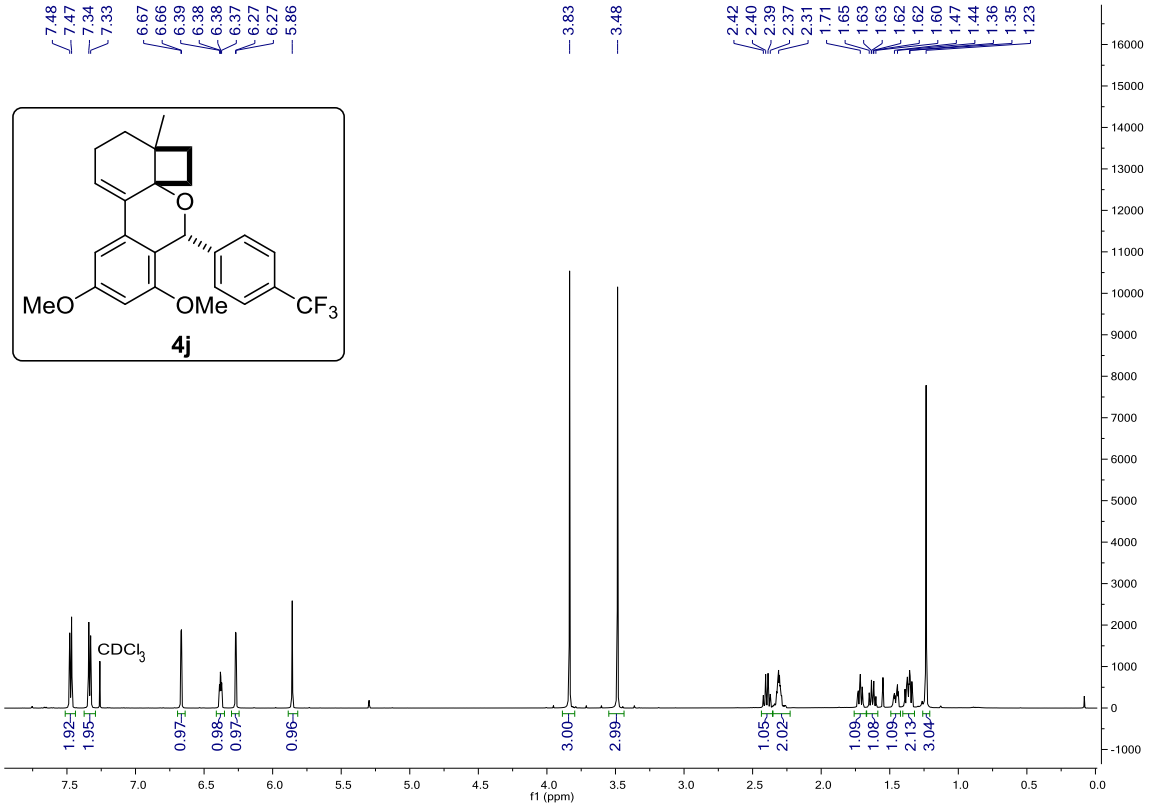


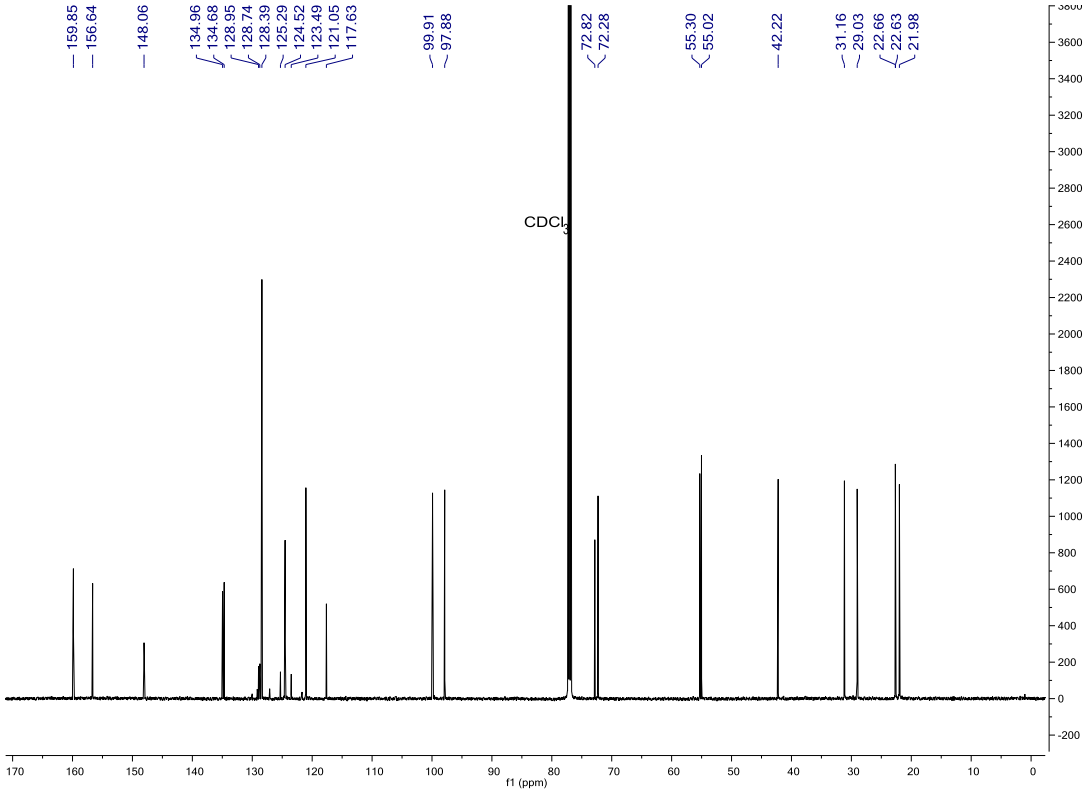
2.15 ^{1}H and ^{13}C NMR of 4i in $CDCl_3$ at 25 °C.

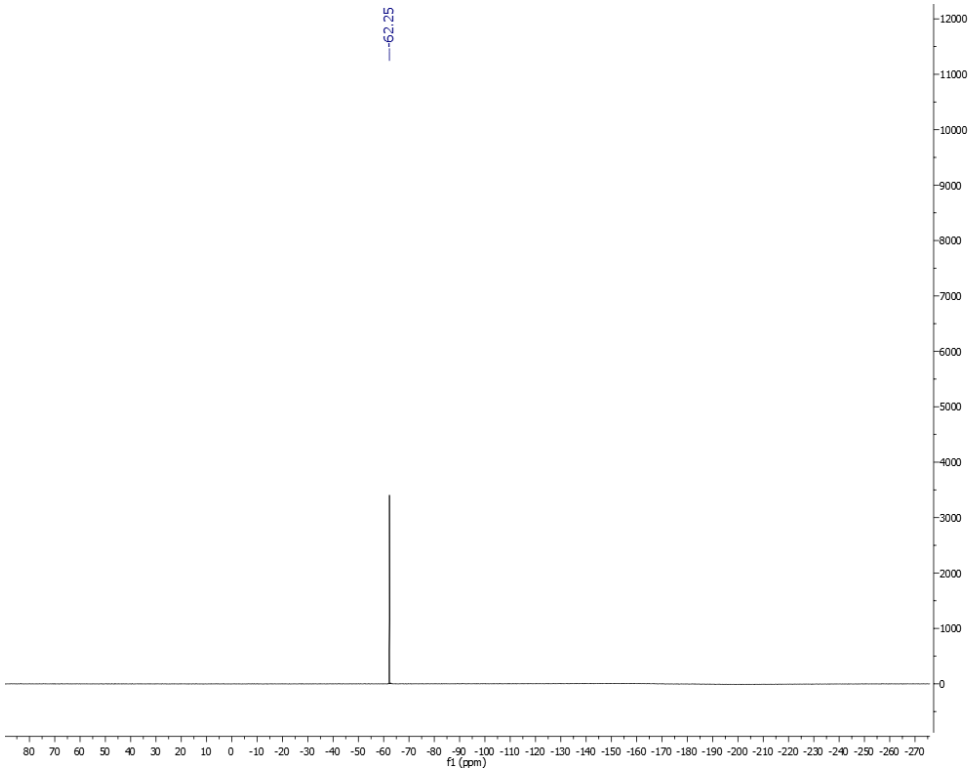




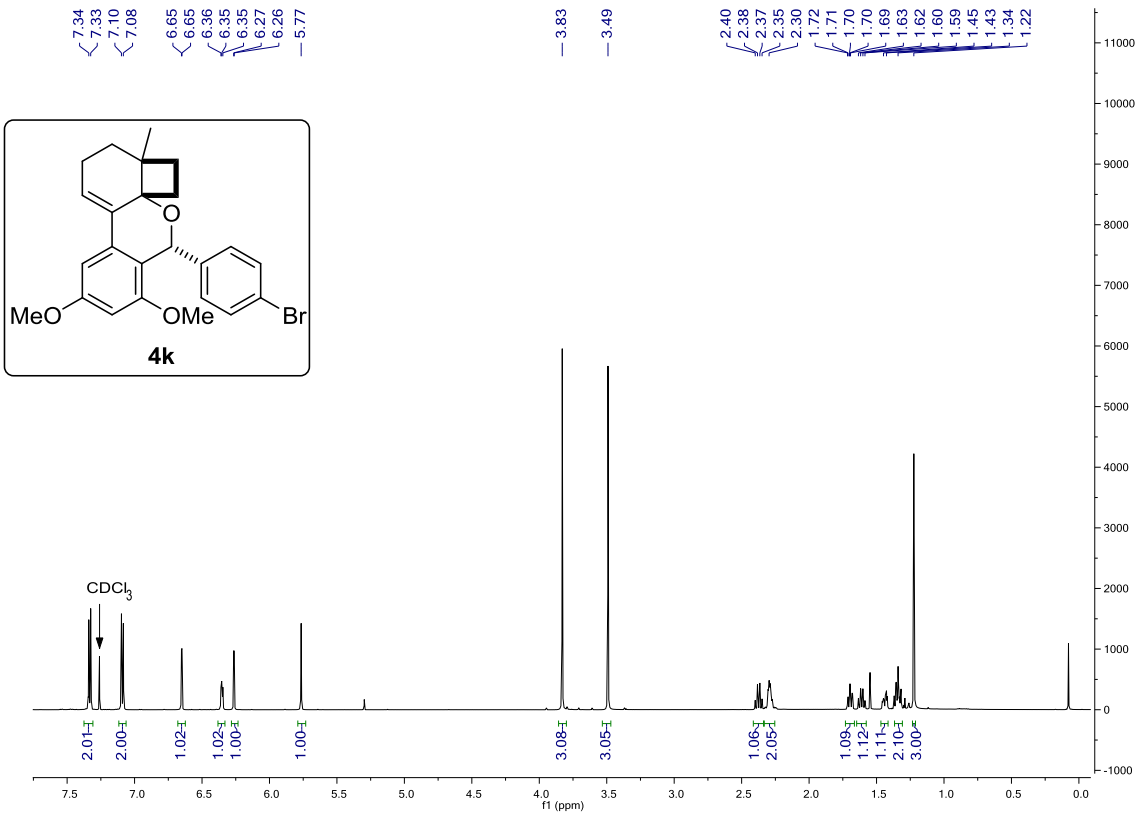
2.16 ^{1}H, ^{13}C, ^{19}F NMR of 4j in $CDCl_3$ at 25 °C.

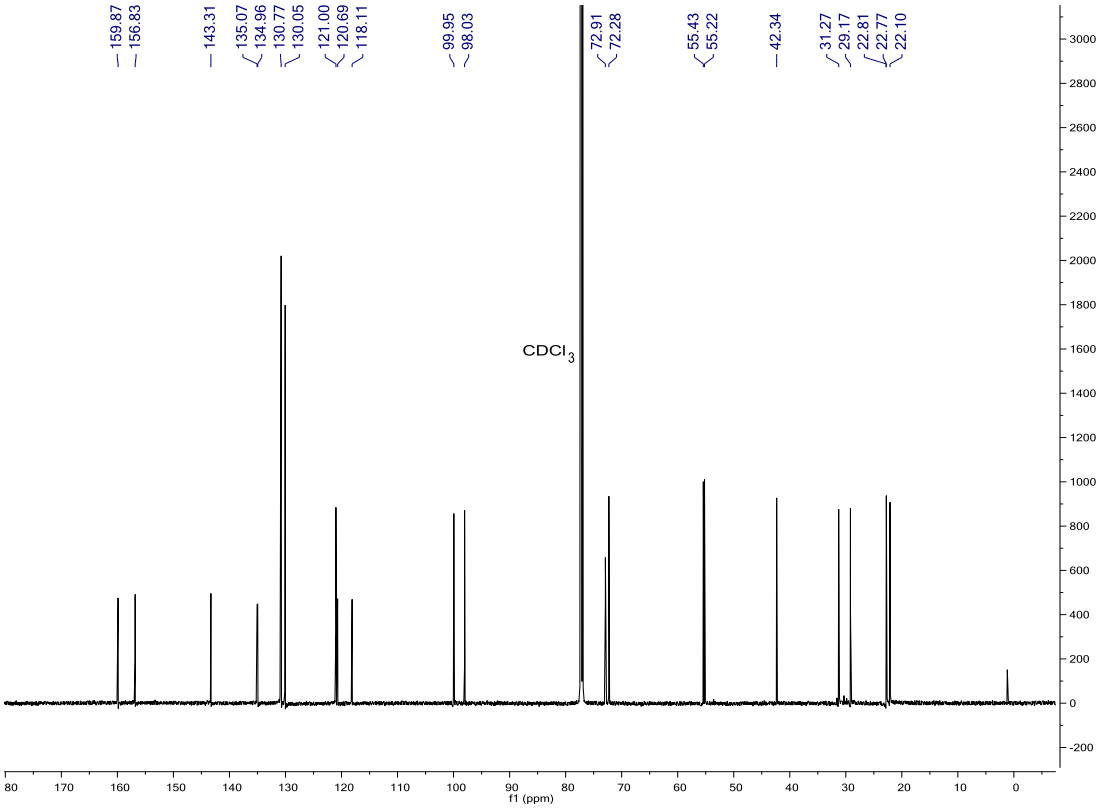




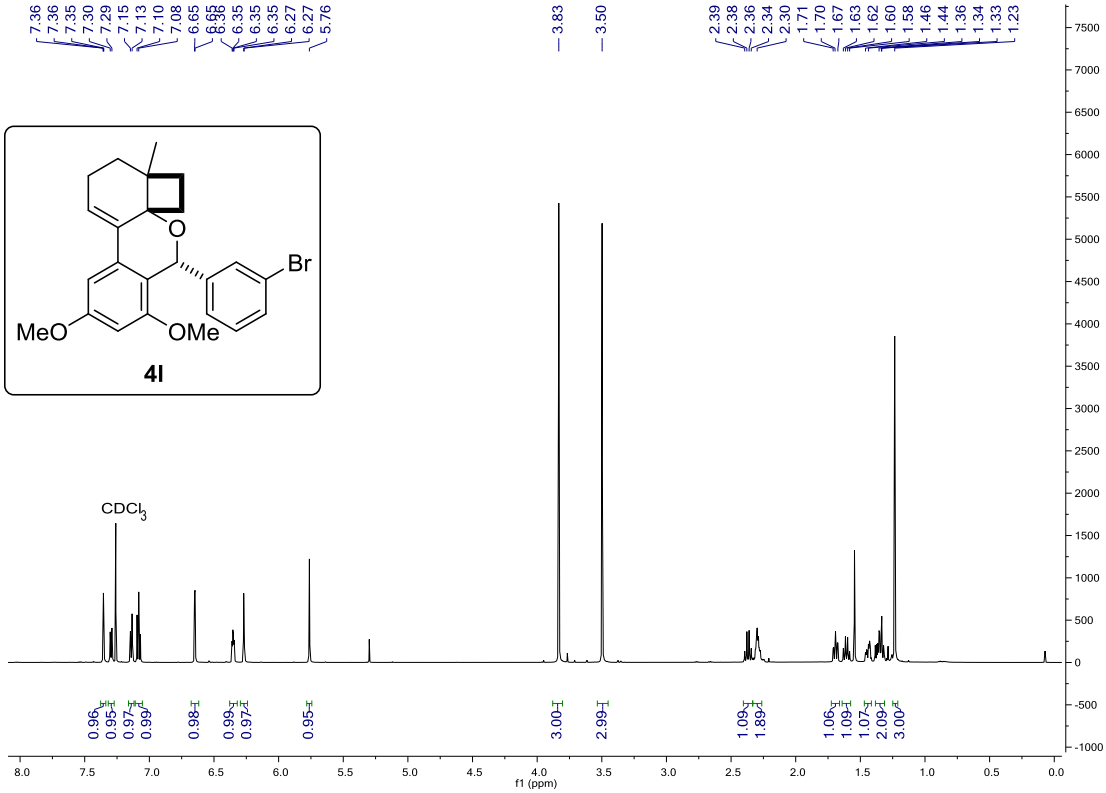


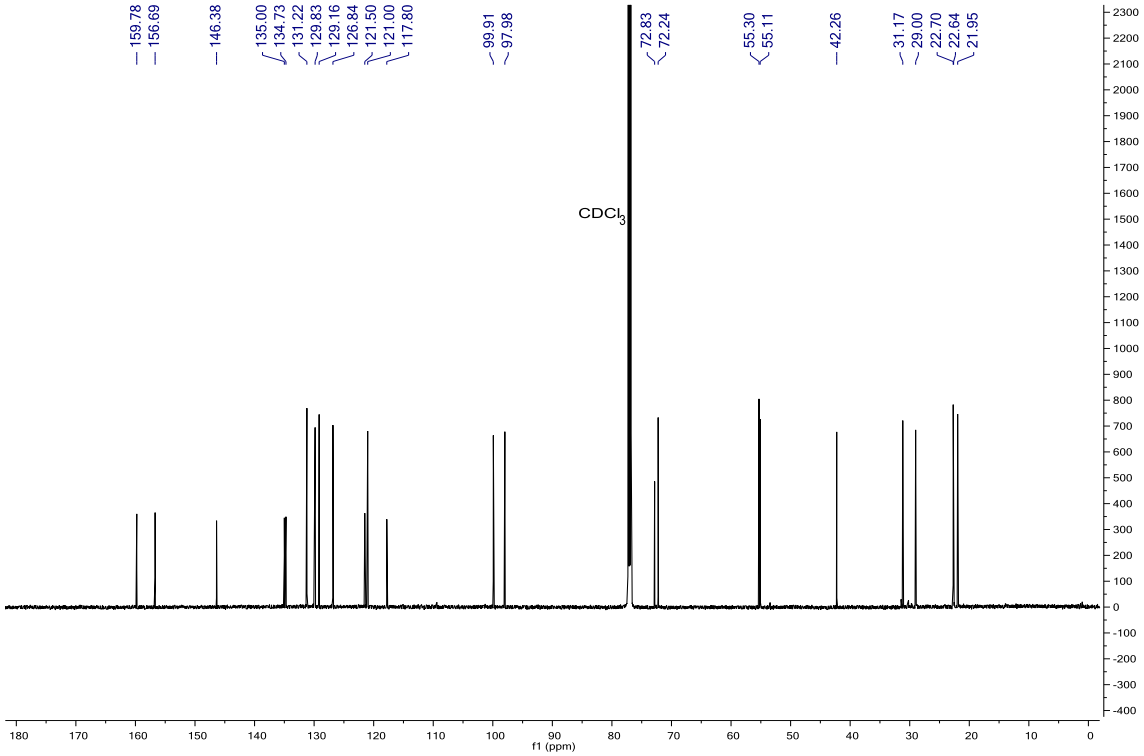
2.17 ^{1}H and ^{13}C NMR of 4k in $CDCl_3$ at 25 °C.



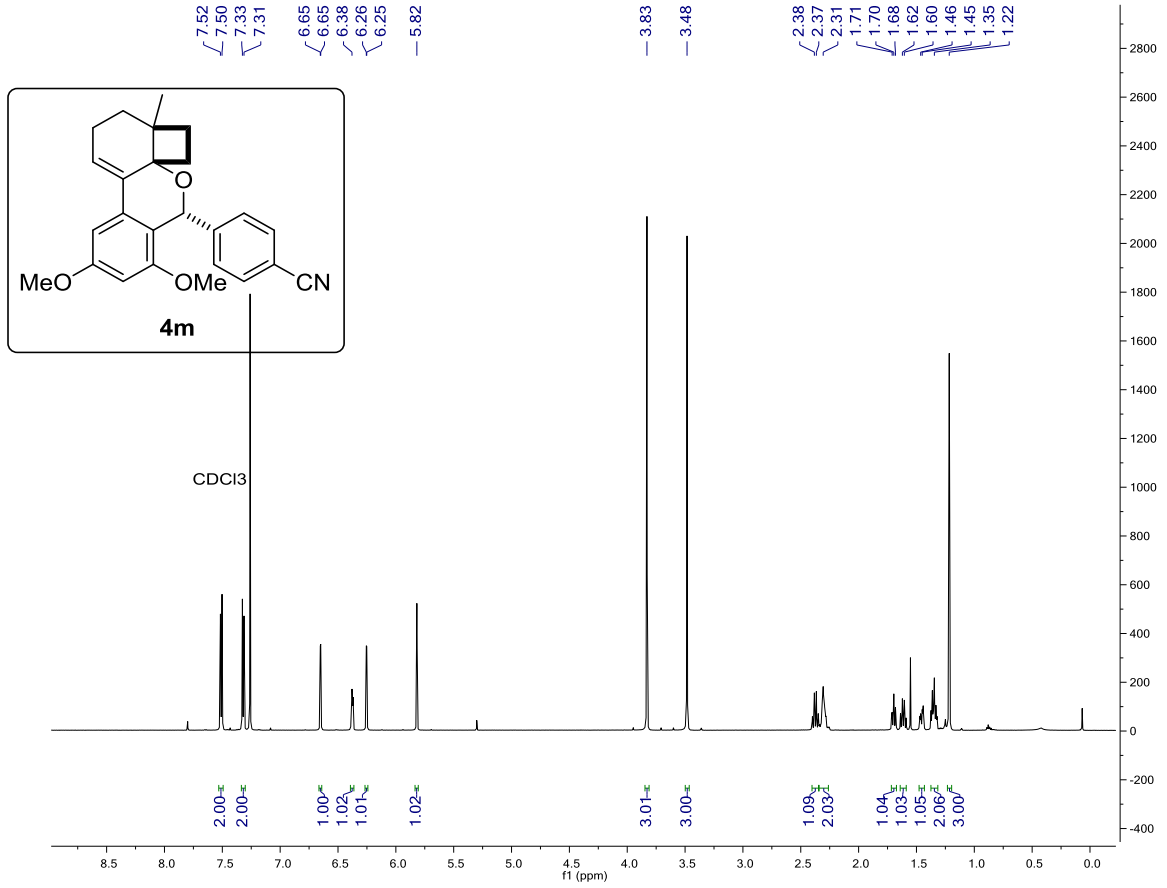


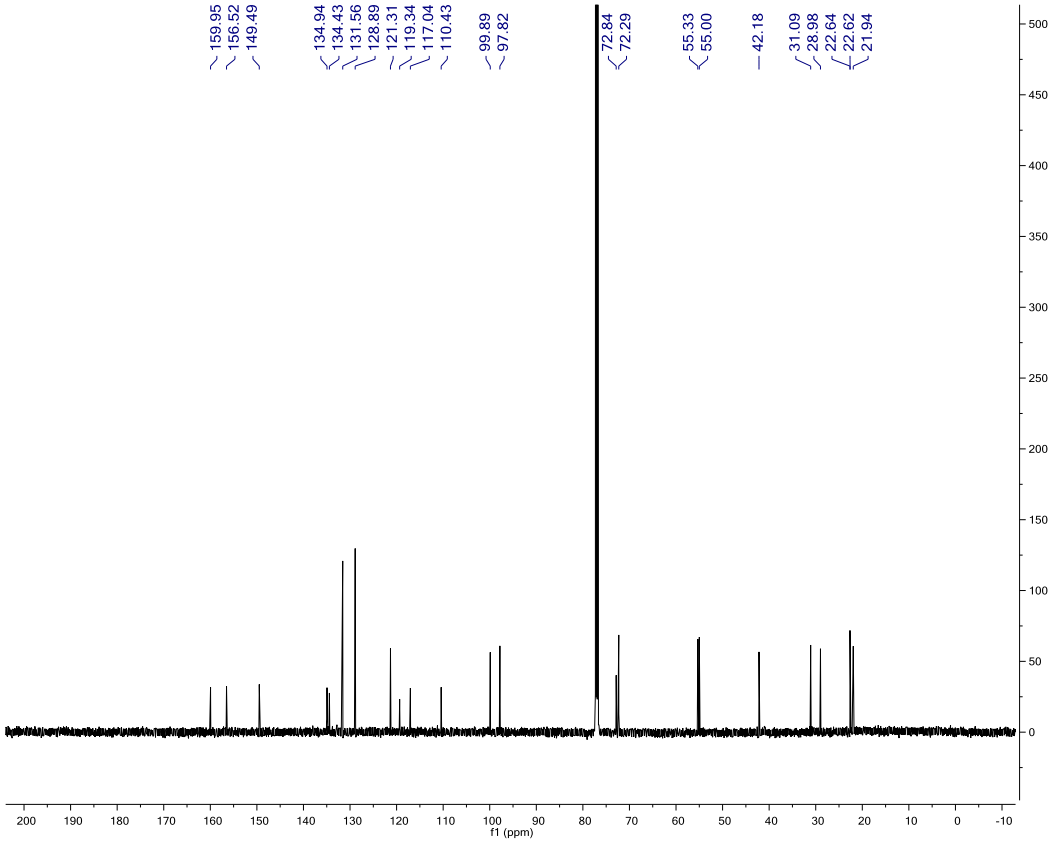
2.18 ^{1}H and ^{13}C NMR of 4l in $CDCl_3$ at 25 °C.



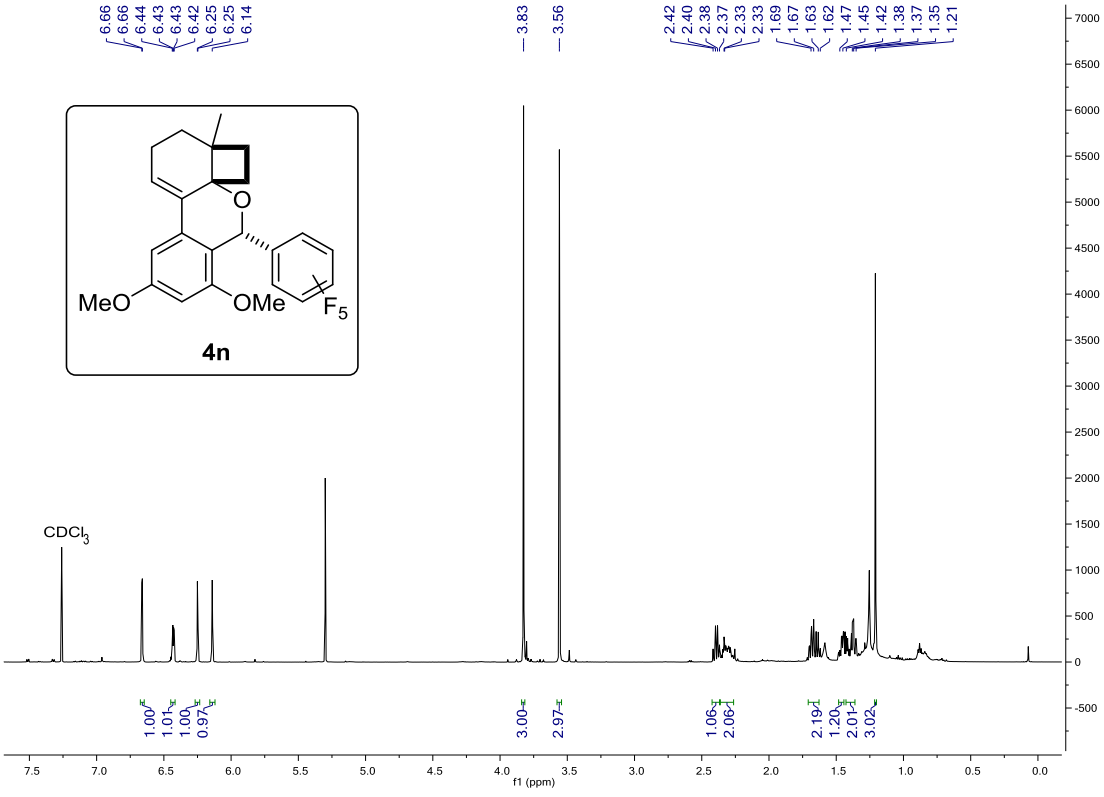


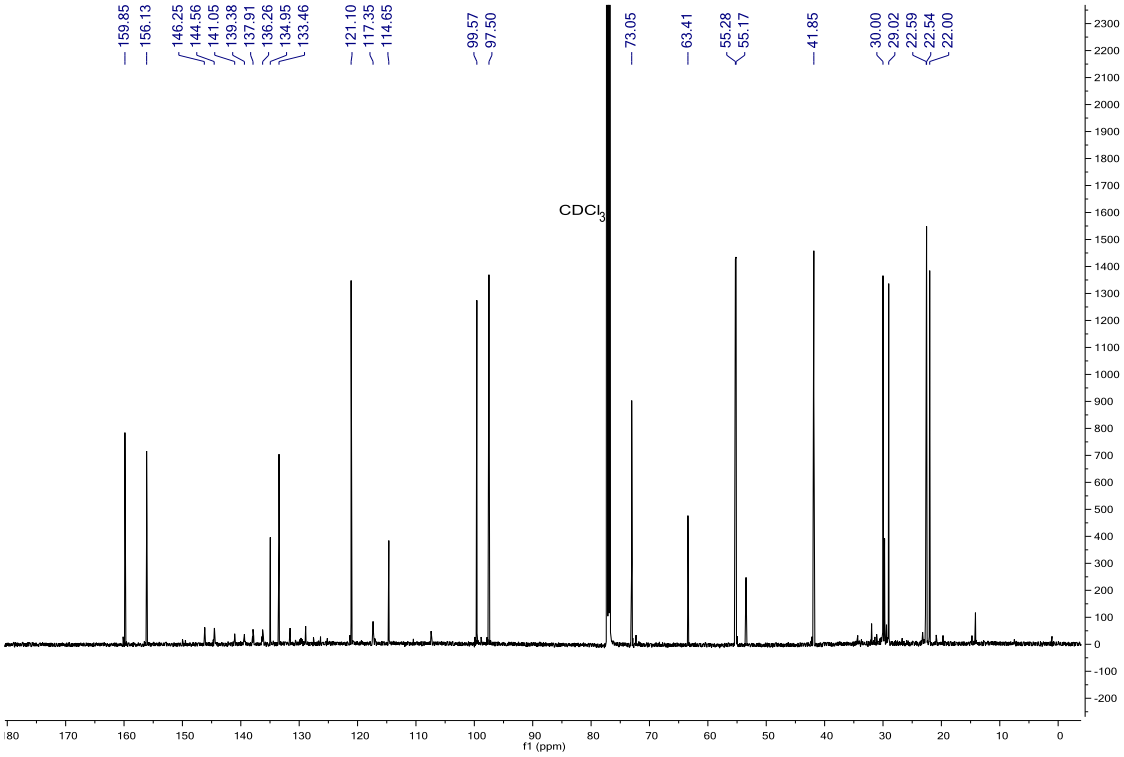
2.19 ^{1}H and ^{13}C NMR of 4m in $CDCl_3$ at 25 °C.

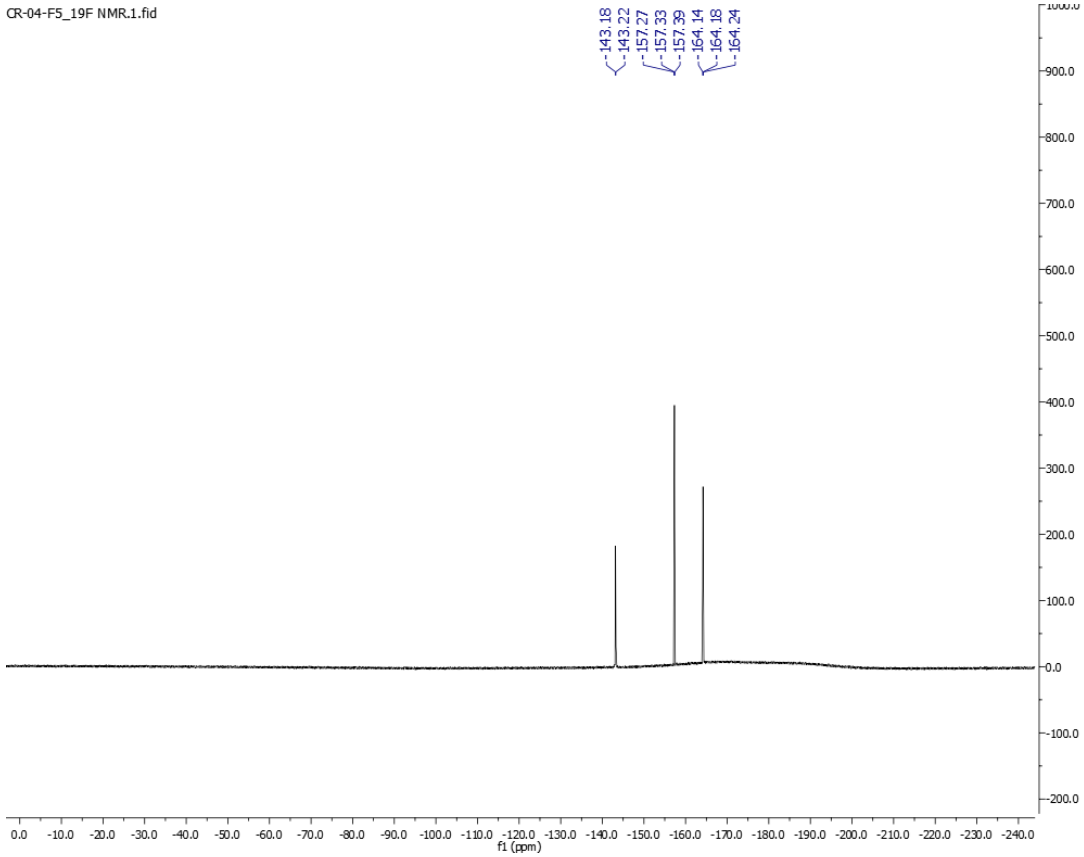




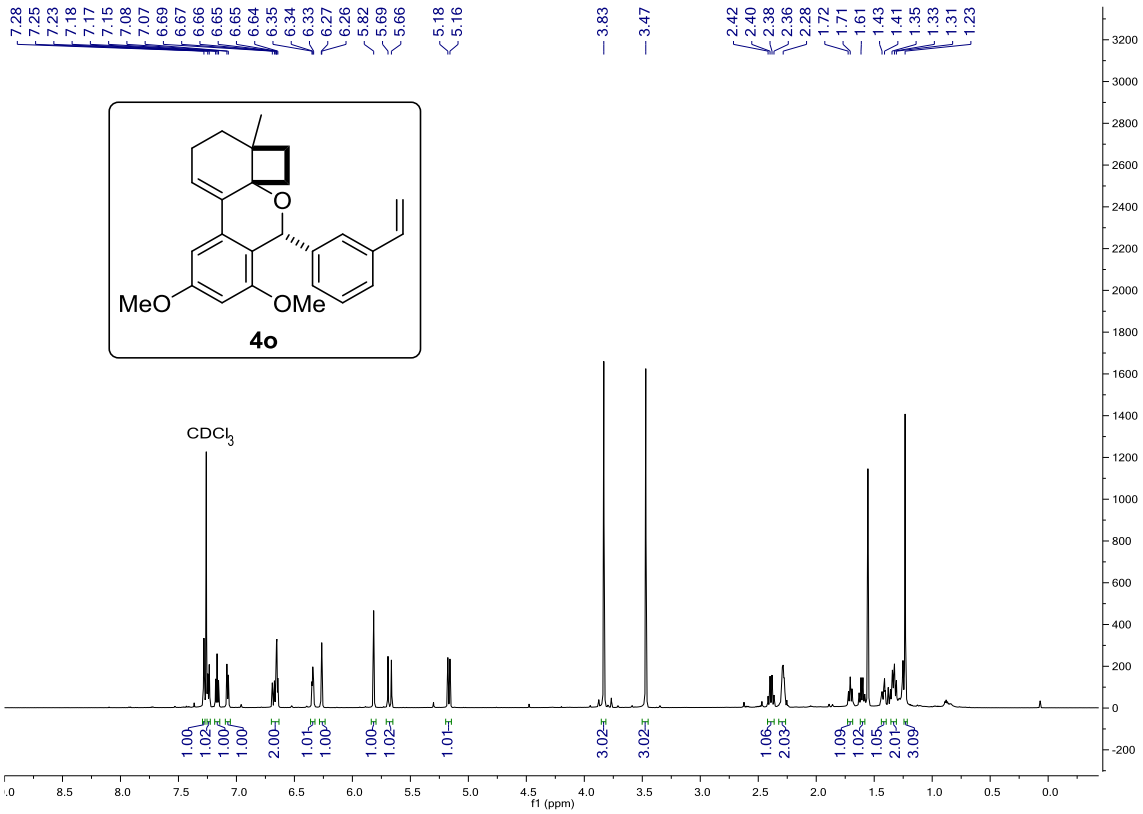
2.20 ^{1}H, ^{13}C and ^{19}F NMR of 4n in $CDCl_3$ at 25 °C.

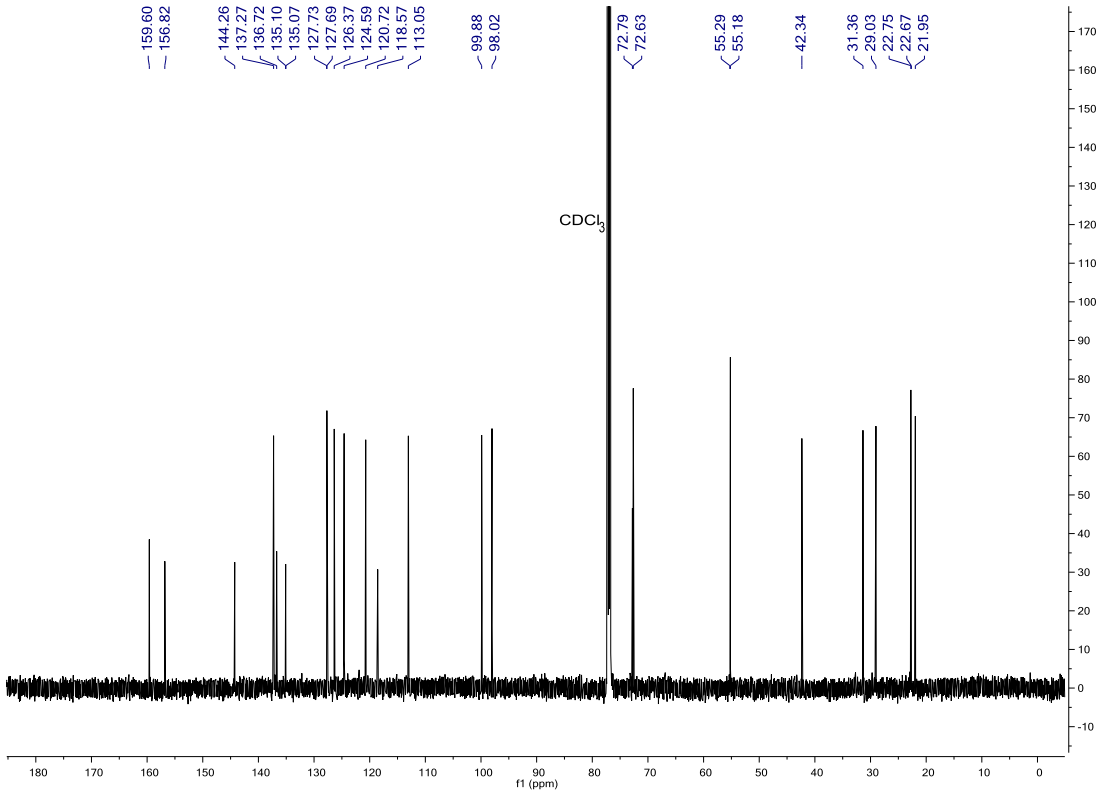



159.85
156.13
146.25
144.56
141.05
139.38
137.91
136.26
134.95
133.46
121.10
117.35
114.65
99.57
97.50
73.05
63.41
55.28
55.17
41.85
30.00
29.02
22.59
22.54
22.00
CDCl3
f1 (ppm)

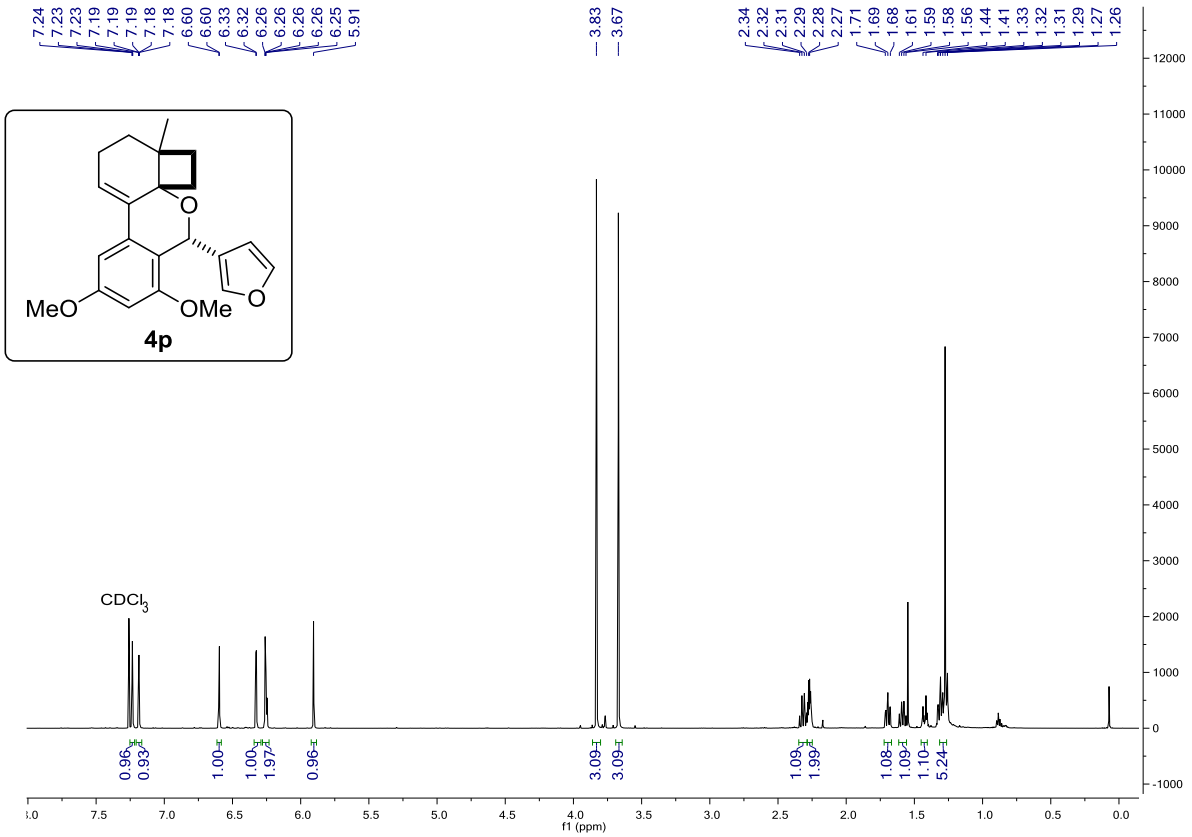

CR-04-F5_19F NMR.1.fid
-143.18
-143.22
-157.27
-157.33
-157.39
-164.14
-164.18
-164.24
f1 (ppm)

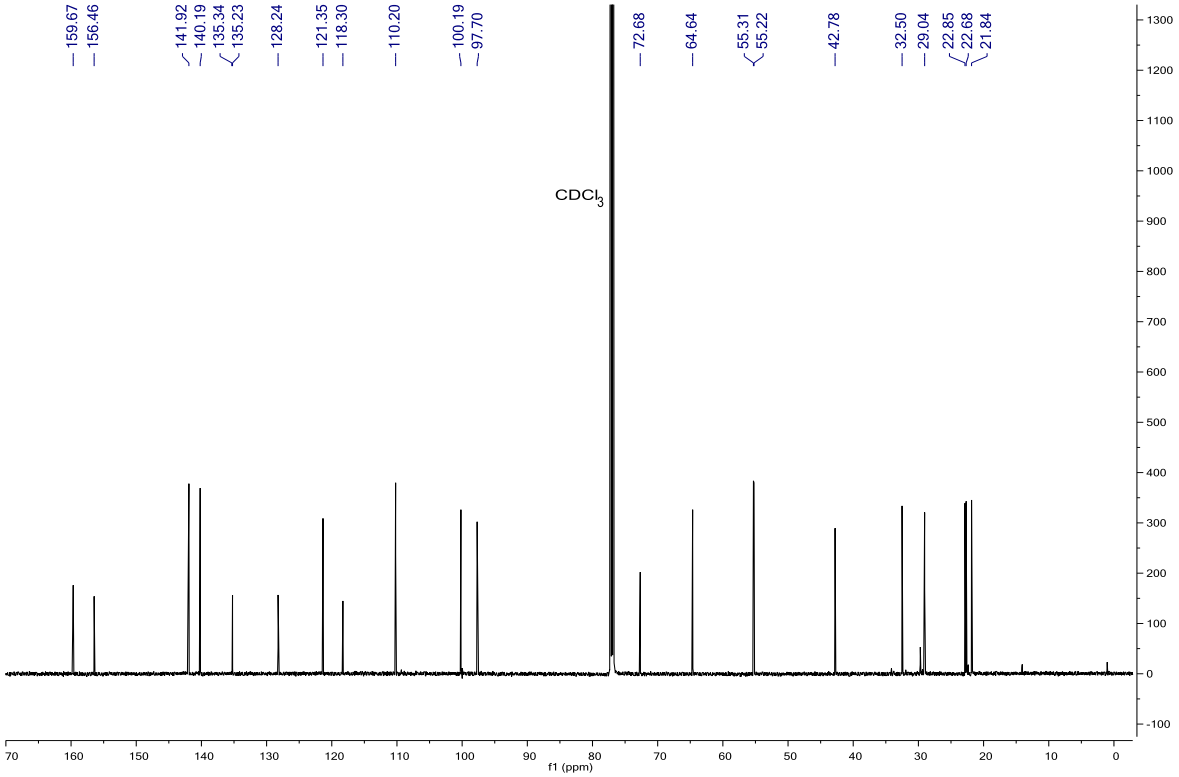
2.21 ^{1}H and ^{13}C NMR of 4o in $CDCl_3$ at 25 °C.



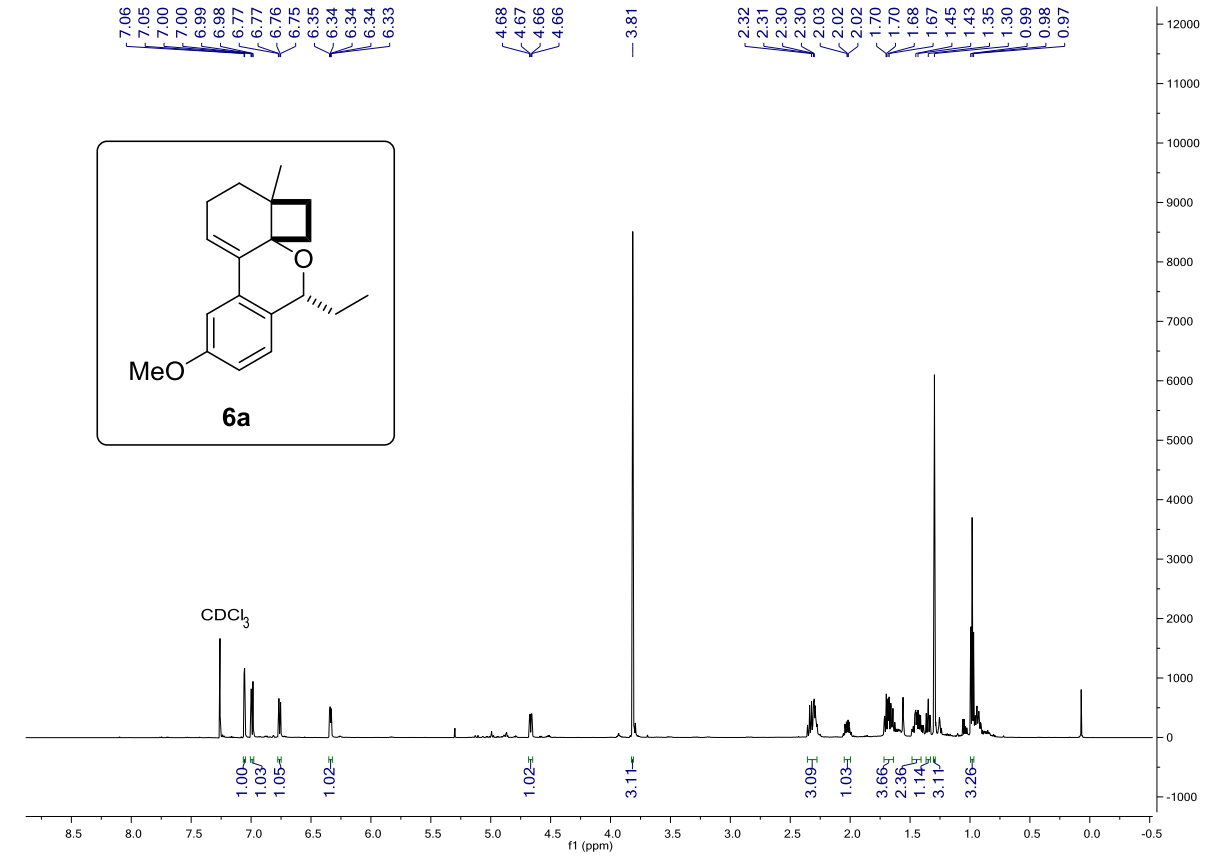


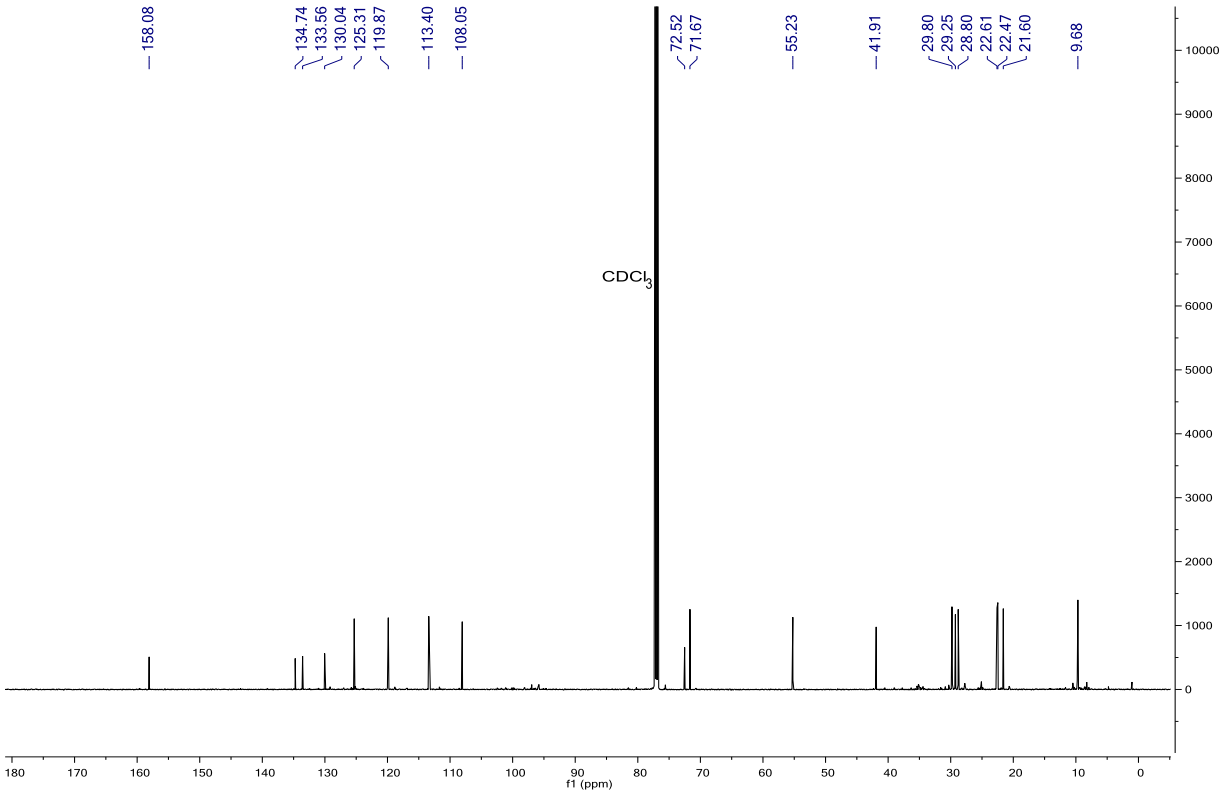
2.22 ^{1}H and ^{13}C NMR of 4p in $CDCl_3$ at 25 °C.



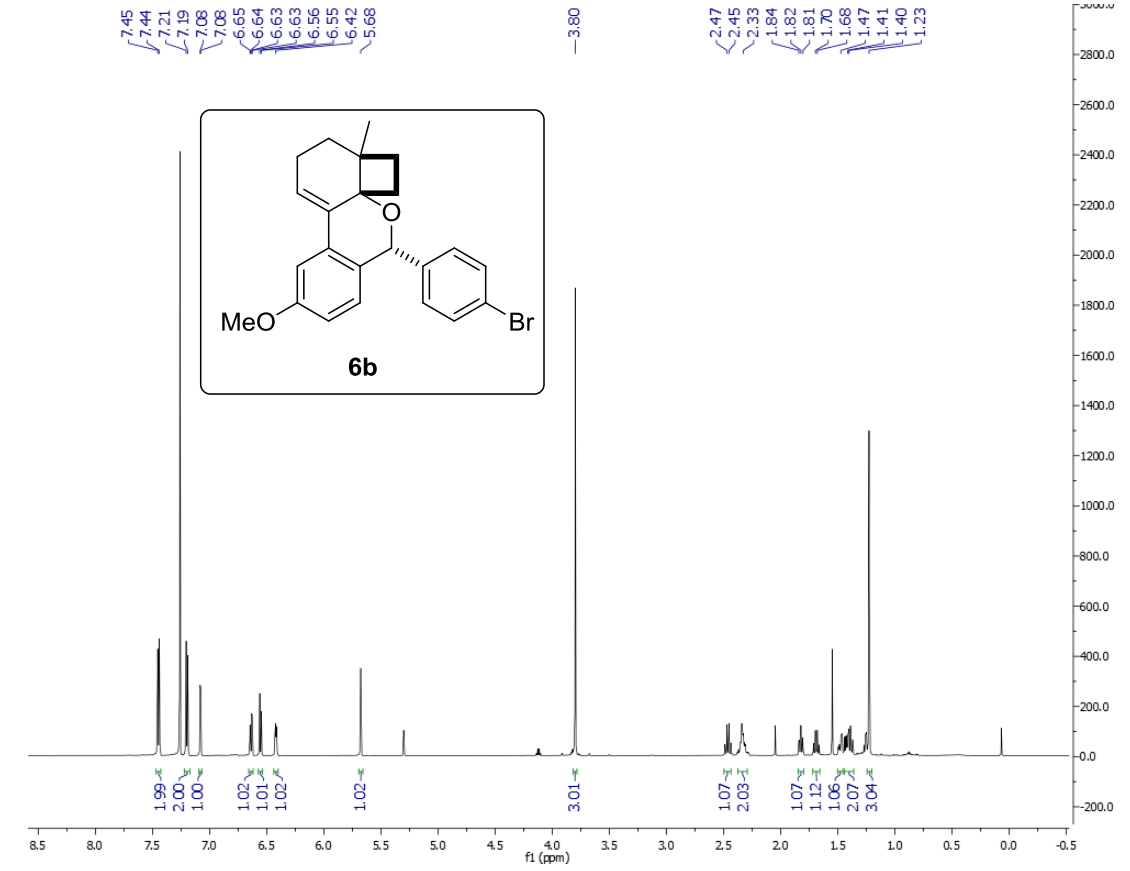


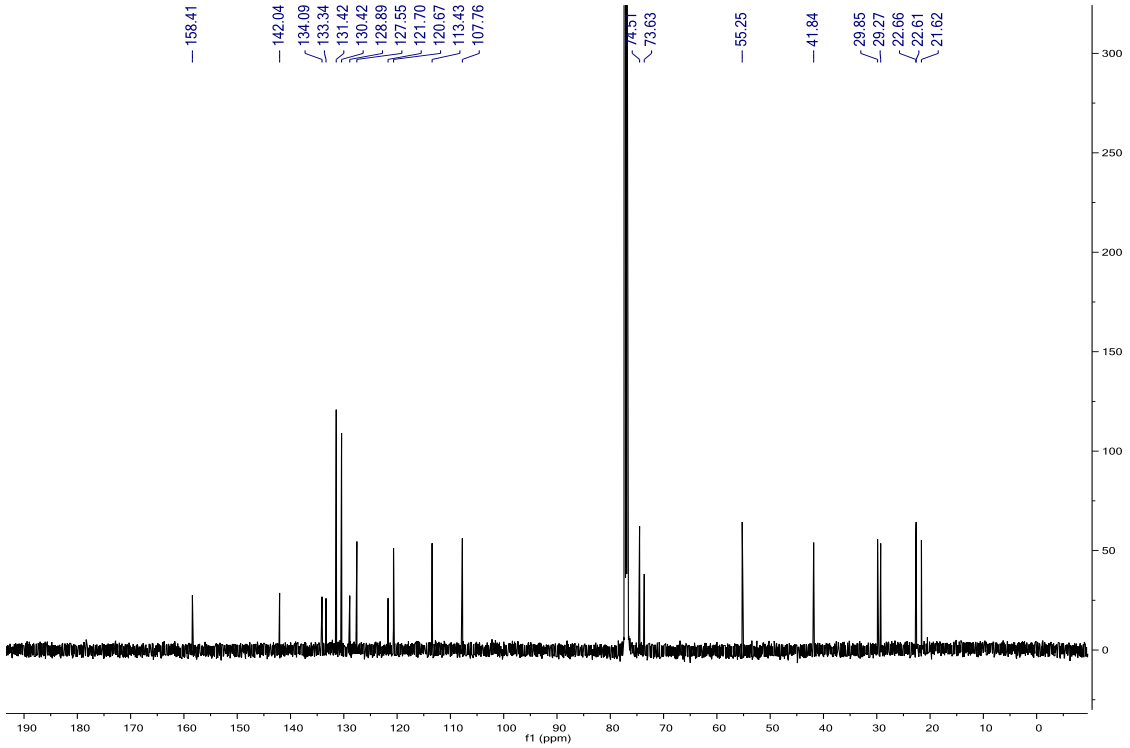
2.23 ^{1}H and ^{13}C NMR of 6a in $CDCl_3$ at 25 °C.



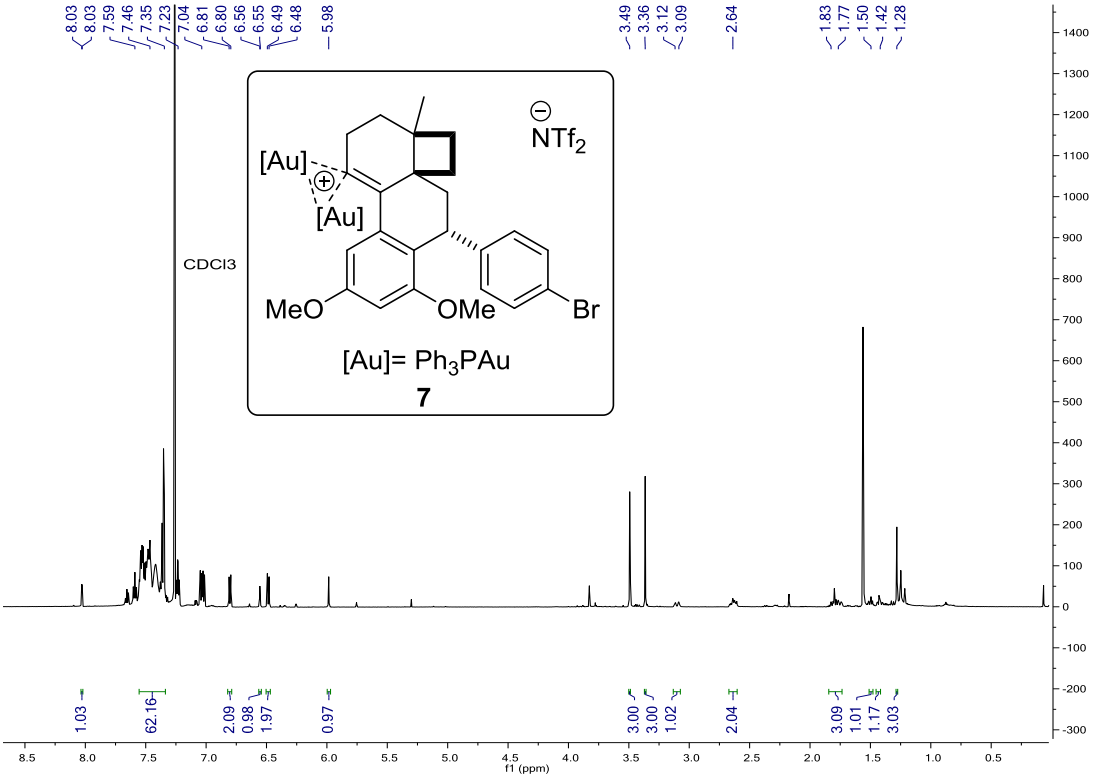


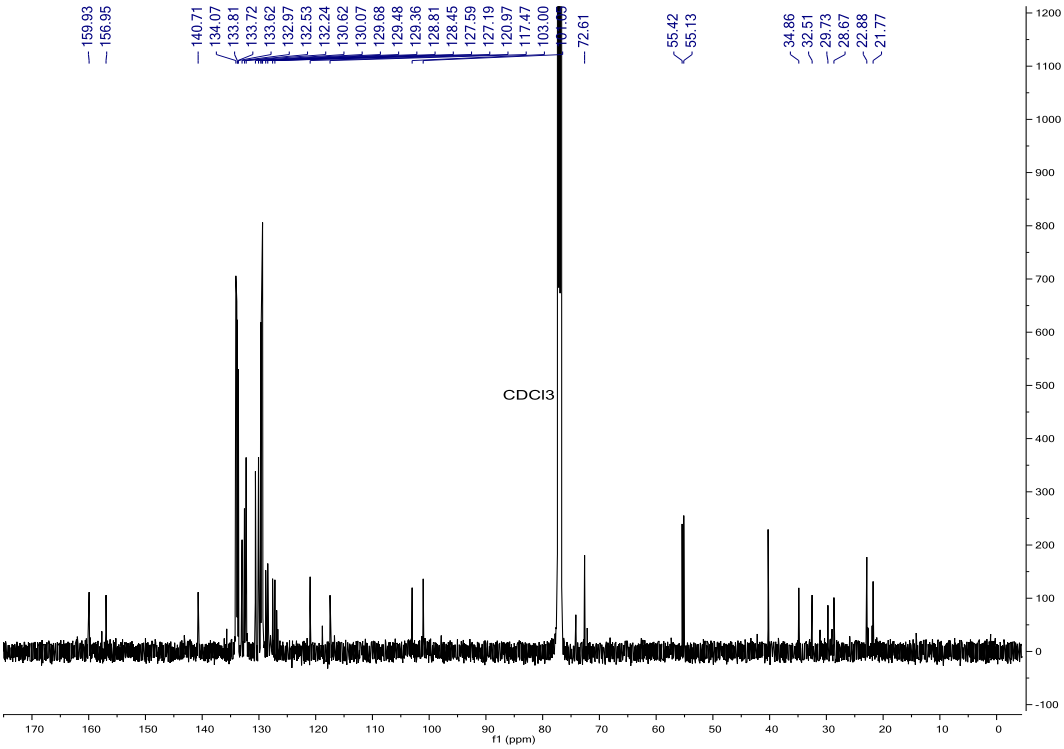
2.24 ^{1}H and ^{13}C NMR of 6b in $CDCl_3$ at 25 °C.

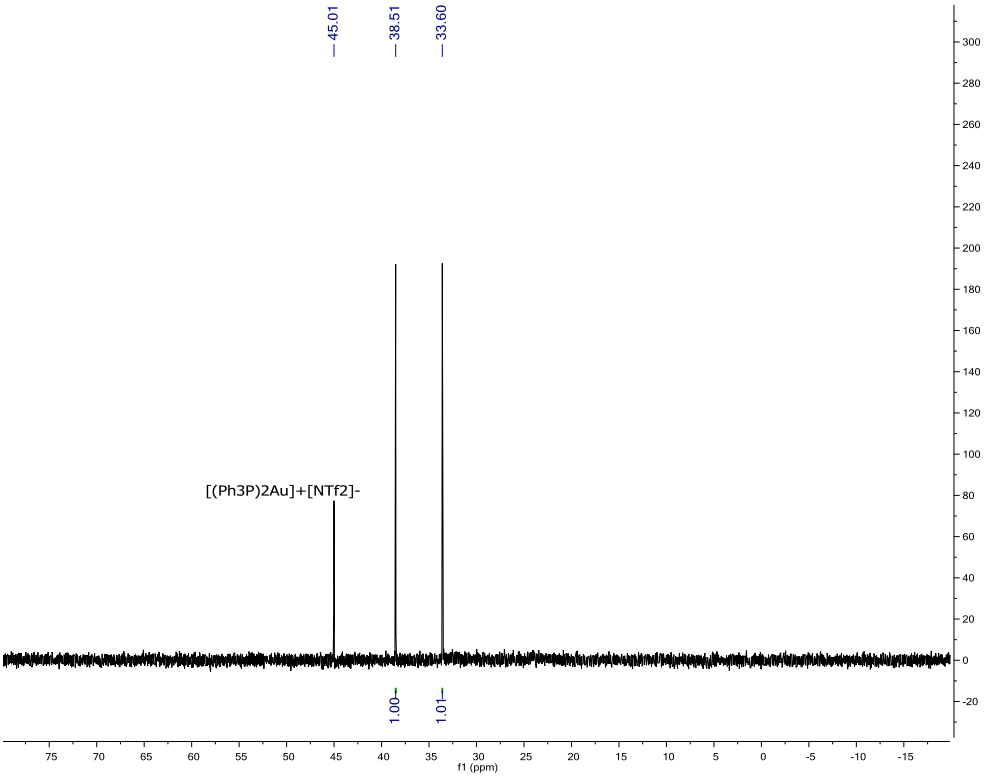




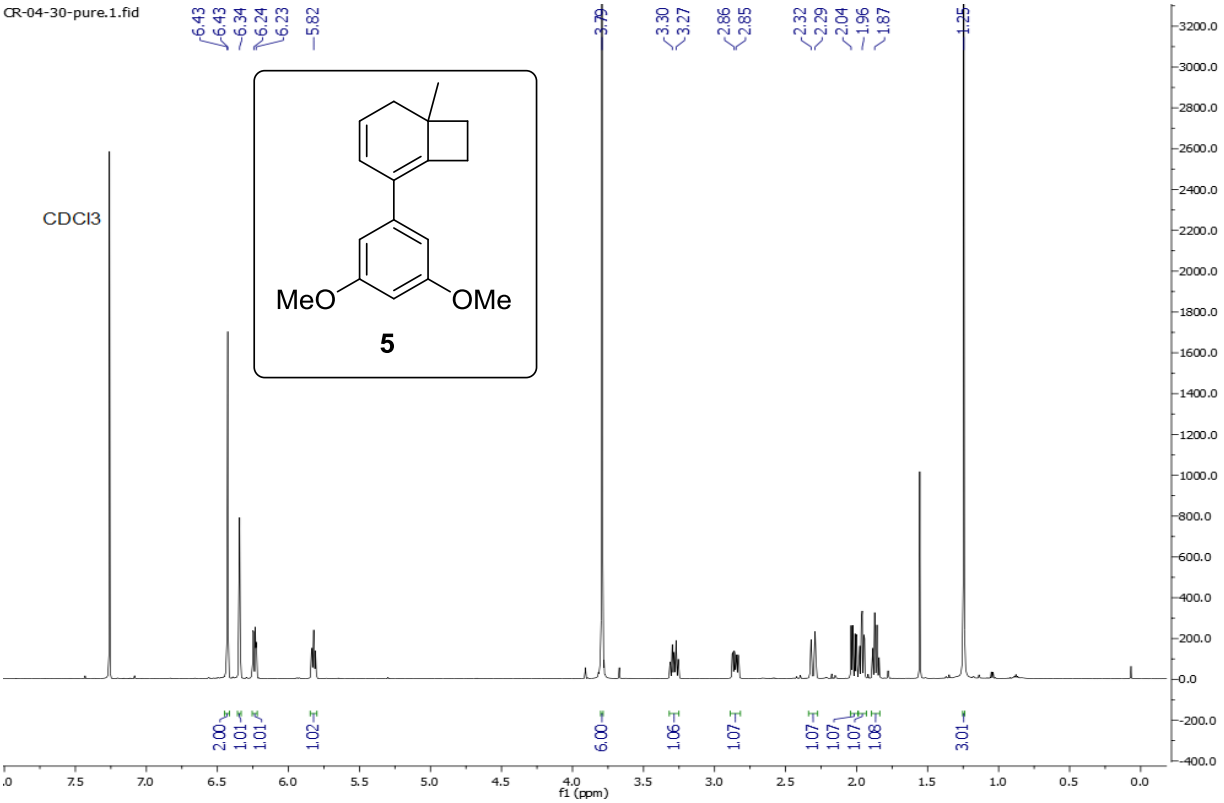
2.26 ^{1}H, ^{13}C, ^{31}P NMR of digold 7 in $CDCl_3$ at 25 °C

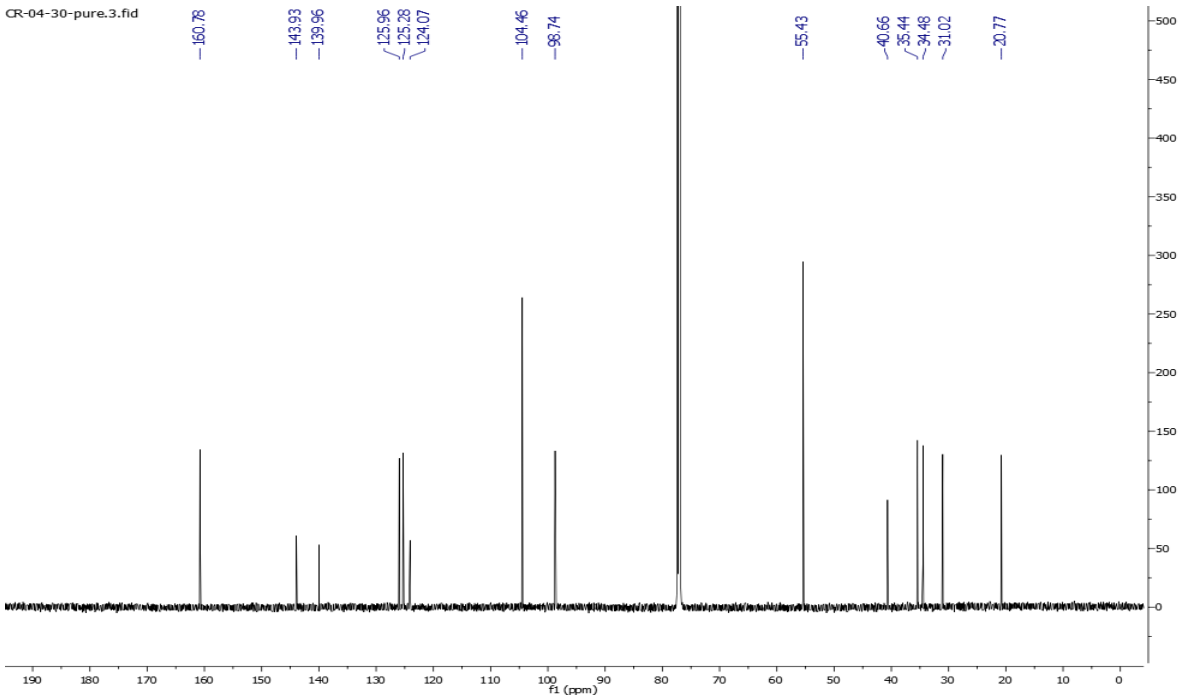






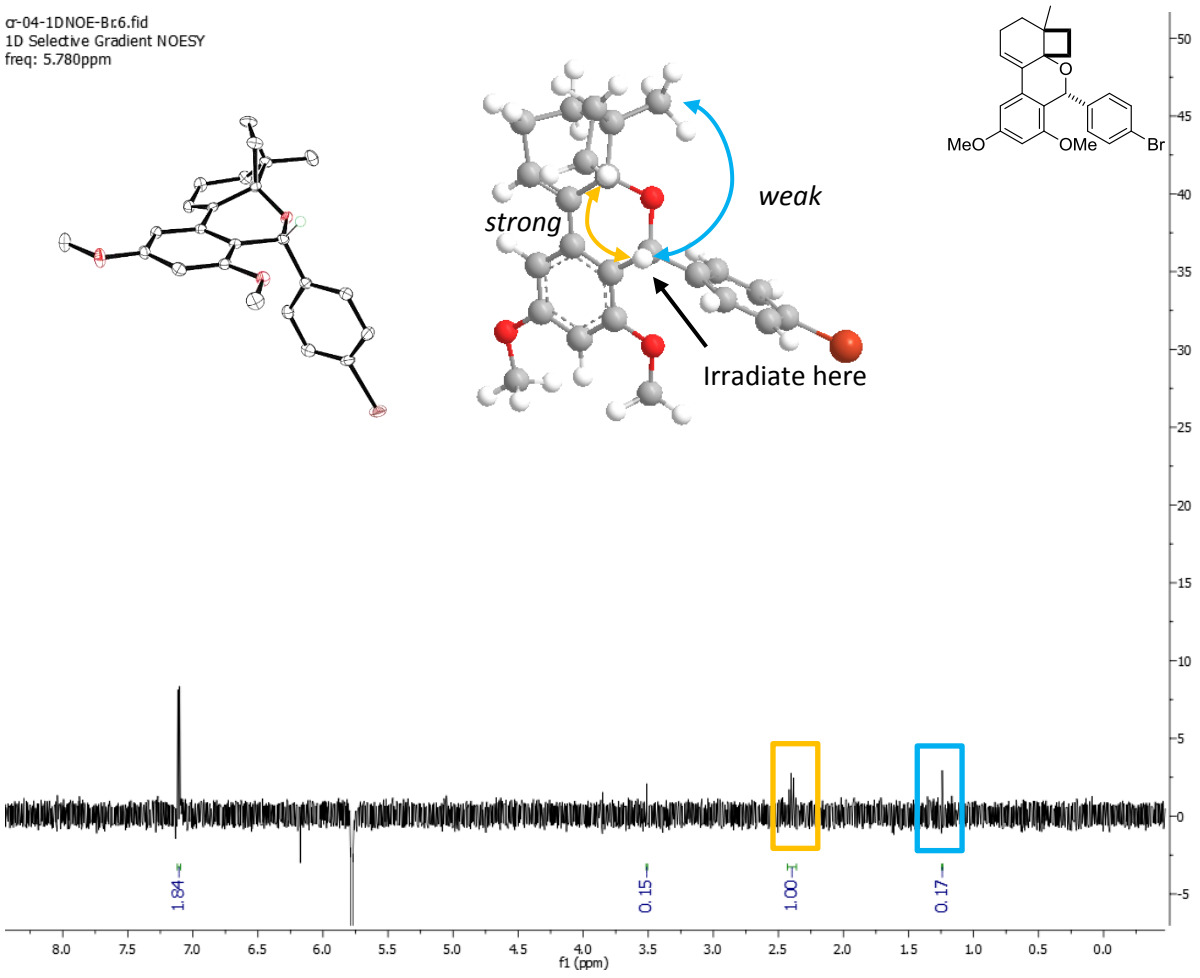
2.26 ^{1}H and ^{13}C NMR of cycloisomer 5 in $CDCl_3$ at 25 °C.



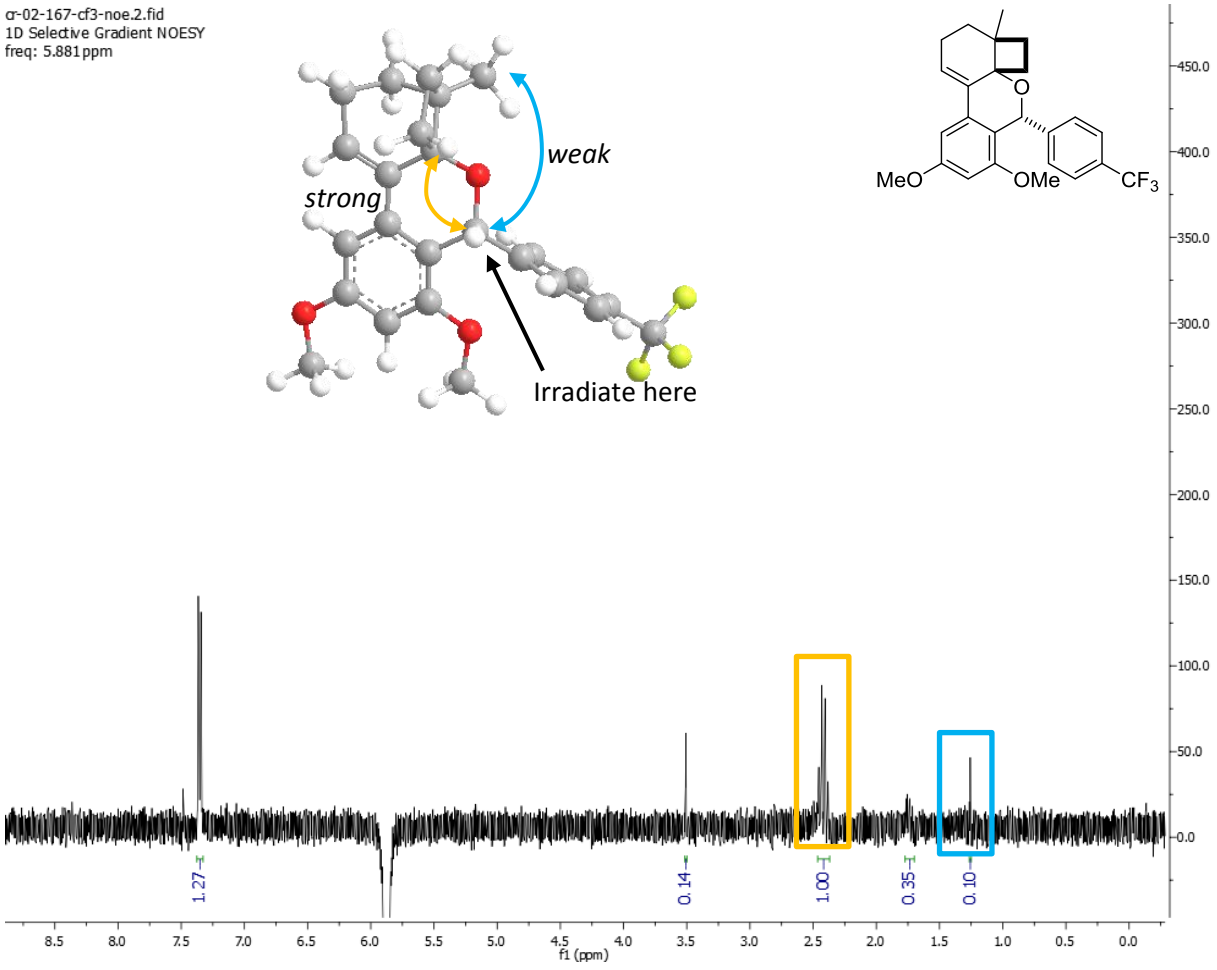

CR-04-30-pure.3.fid
160.78
143.93
139.96
125.96
125.28
124.07
104.46
98.74
55.43
40.66
35.44
34.48
31.02
20.77
f1 (ppm)

3. Gradient 1D NOESY Stereochemical Assignment

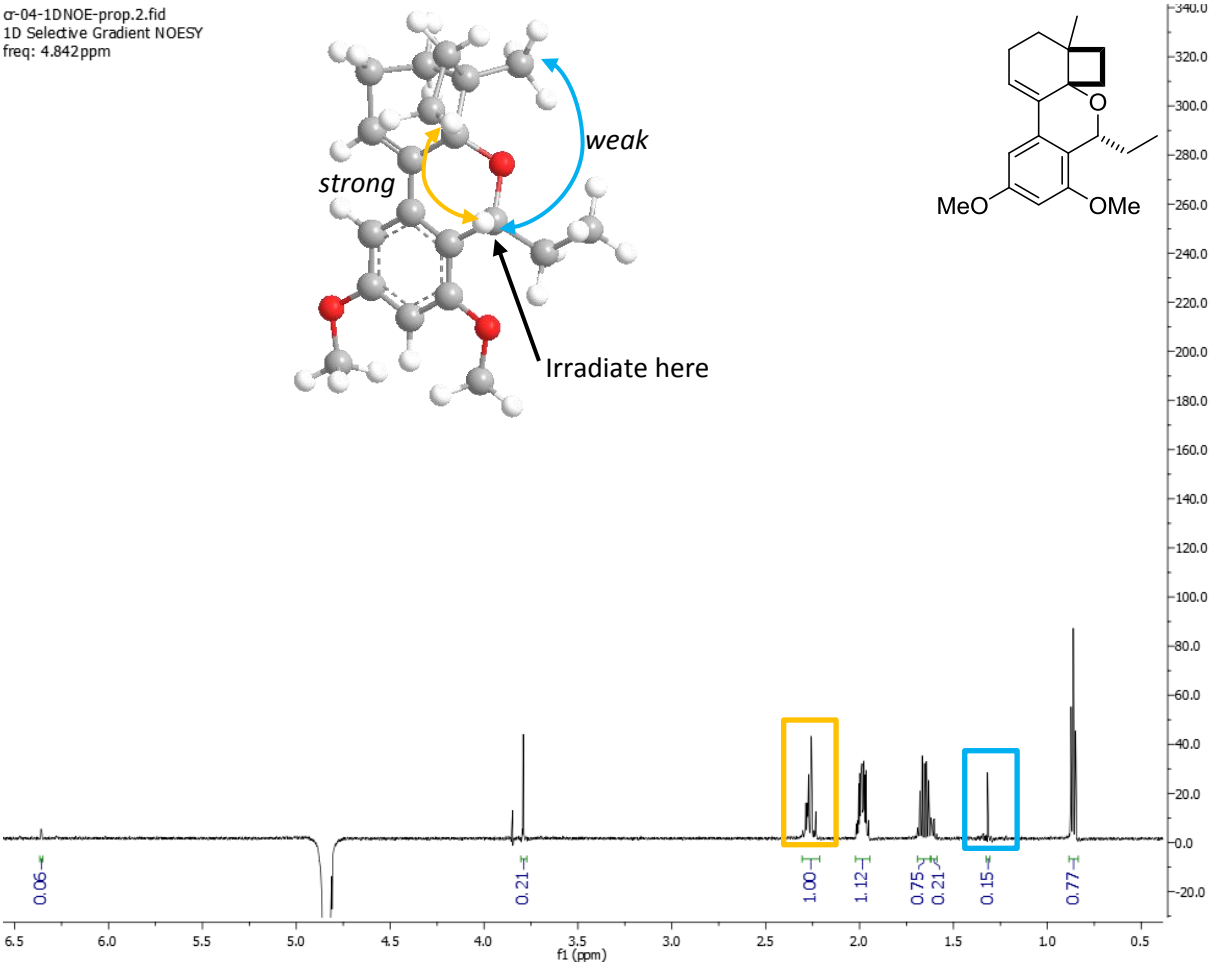
3.1 Stereochemistry of 4k confirmed via X-ray structure.



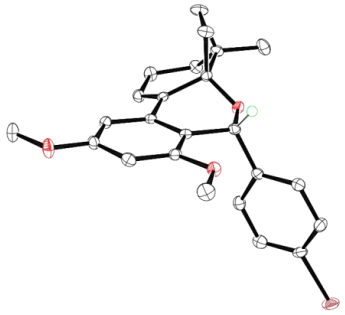
3.2 Stereochemical assignment of 4j



3.3 Stereochemical assignment of 4a



4. Single Crystal X-ray Diffraction Analysis



ORTEP representation of the solid state molecular structure of **4k**; ellipsoids drawn at 50% probability, only one enantiomer of the asymmetric unit, and the majority of hydrogen atoms are omitted for clarity.

Empirical formula	$2(C_{24}H_{25}BrO_{3})$	D_{calcd} (Mg m^{-3})	1.437
F_w	441.37	Radiation	Cu $K\alpha$
Colour, habit	Colourless, block	Absorption coeff. (μ) (mm^{-1})	2.92
Crystal dimensions (mm)	0.21 x 0.17 x 0.11	Absorption correction	Numerical SADABS 2014/5
Crystal system	Triclinic	*F*(000)	912
Space group	*P*-1	θ_{min} *to* θ_{max} (°)	3.1 to 70.1
Z	2	Measured reflections	20859
a (Å)	11.9878(6)	Independent reflections	7453 (R_{int}=0.021)
b (Å)	13.1429(7)	Data/restraints/parameters	7453/0/511
c (Å)	14.8309(8)	Maximum shift/error	0.004
α (°)	72.229(2)	Goodness-of-fit on F^2	1.05
β (°)	86.297(2)	Final *R* indices ($I > 2\sigma(I)$)	R_1 = 0.026 wR_2 = 0.066
γ (°)	66.705(2)	R indices (all data)	R_1 = 0.028 wR_2 = 0.067
Collection ranges	*h* = -9→14 *k* = -14→16 *l* = -18→18	absolute structure parameter	N/A
Temperature (K)	100	Extinction coefficient	N/A
Volume ($Å^3$)	2039.57 (19)	Largest diff. peak and hole (e $Å^{-3}$)	0.36 and -0.42