11-Step Enantioselective Synthesis of (–)-Lomaiviticin Aglycon

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Supporting Information

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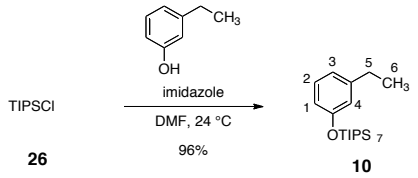
General Experimental Procedures. All reactions were performed in single-neck, flame-dried, round-bottomed flasks fitted with rubber septa under a positive pressure of argon, unless otherwise noted. Air- and moisture-sensitive liquids were transferred via syringe or stainless steel cannula, or were handled in a nitrogen-filled drybox (working oxygen level <1 ppm). Organic solutions were concentrated by rotary evaporation at 30–33 °C. Normal and reverse phase flash-column chromatography was performed as described by Still et al.[1] Normal phase purifications employ silica gel (60 Å, 40–63 μm particle size) purchased from Sorbent Technologies (Atlanta, GA). Reverse phase purifications employ C_{18}-labeled silica gel (125 Å, 55–105 μm particle size) purchased from Waters Corporation (Milford, MA). Analytical thin-layered chromatography (TLC) was performed using glass plates pre-coated with silica gel (0.25 mm, 60 Å pore size) impregnated with a fluorescent indicator (254 nm). Preparative TLC (PTLC) was performed using glass plates precoated with silica gel (1.0 mm, 60 Å pore size) impregnated with a fluorescent indicator (254 nm). TLC plates were visualized by exposure to ultraviolet light (UV) and/or submersion in aqueous ceric ammonium molybdate solution (CAM), acidic *p*-anisaldehyde solution (PAA), or aqueous potassium permanganate solution ($KMnO_4$), followed by brief heating on a hot plate (120 °C, 10–15 s).

Materials. Commercial solvents and reagents were used as received with the following exceptions. Benzene, dichloromethane, and toluene were purified according to the method of Pangborn et al.[2] Acetonitrile, *N,N*-di-*iso*-propylethylamine, and triethylamine were distilled from calcium hydride under an atmosphere of nitrogen immediately before use. Tetrahydrofuran was distilled from sodium/benzophenone under an atmosphere of nitrogen immediately before use. Methanol was distilled from magnesium methoxide under an atmosphere of nitrogen immediately before use. Chloromethyl methyl ether, hexamethylphosphoramide, and trimethylsilylchloride were distilled from calcium hydride and stored under nitrogen. 4-Å Molecular sieves were activated by heating overnight in vacuo (200 °C, 200 mTorr), stored in a gravity oven (120 °C), and were flame-dried in vacuo (100 mTorr) immediately before use. Tris(diethylamino)sulfonium difluorotrimethylsilicate [TASF(Et)] was prepared by a modification[3] of Middleton's procedure,[4] and was stored in a nitrogen-filled drybox at –20 °C. Polymer-bound triphenylphosphine (styrene-divinylbenzene copolymer, 20% cross-linked, 3.00 mmol triphenylphosphine/gram resin) was obtained from Strem Chemicals (Newburyport, MA) and was stored in a nitrogen-filled drybox. Manganese tris(hexafluoroacetylacetonate) was prepared according to the procedure of Mayer and co-workers[5] and was sublimed in vacuo (60–70 °C, 200 mTorr) immediately before use. Solutions of trifluoromethanesulfonyl azide in hexanes were prepared according to the procedure of Charette and co-workers.[6] The concentration of trifluoromethanesulfonyl azide was determined by ^{19}F NMR analysis using α,α,α-trifluoroacetophenone as an internal standard (TfN_3 δ = –76.34; $PhCOCF_3$ δ = –72.11), as described by Wong and co-workers.[7] 2,3-Dibromo-5,6-dihydroxynapthoquinone (**30**) was prepared according to the procedure of Huot and Brassard.[8] Mesitylaldehyde dimethyl acetal was prepared according to the procedure of Myers and co-workers.[9]

Instrumentation. Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded at 400 or 500 MHz at 24 °C, unless otherwise noted. Chemical shifts are expressed in parts per million (ppm, δ scale) downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($(CD_3)_2NCHO$, δ 8.03; $CHCl_3$, δ 7.26; C_6HD_5, δ 7.15; CHD_2OD, 3.31). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and/or multiple resonances, br = broad, app = apparent), integration, coupling constant in Hertz, and assignment. Proton-decoupled carbon nuclear magnetic resonance spectra (^{13}C NMR) were recorded at 100 or 125 MHz at 24 °C, unless otherwise noted. Chemical shifts are expressed in parts per million (ppm, δ scale) downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent [$(CD_3)_2N\mathbf{C}DO$, δ 163.2; C_6D_6, δ 128.0; $CDCl_3$, δ 77.0; CD_3OD, δ 49.0]. Distortionless enhancement by polarization transfer spectra [DEPT (135)] were recorded at 100 or 125 MHz at 24 °C, unless otherwise noted. ^{13}C NMR and DEPT (135) data are combined and represented as follows: chemical shift, carbon type [obtained from DEPT (135) experiments]. Attenuated total reflectance Fourier transform infrared spectra (ATR-FTIR)

were obtained using a Thermo Electron Corporation Nicolet 6700 FTIR spectrometer referenced to a polystyrene standard. Data are represented as follows: frequency of absorption (cm^{-1}), intensity of absorption (s = strong, m = medium, w = weak, br = broad). Analytical ultra high-performance liquid chromatography/mass spectrometry (UPLC/MS) was performed on a Waters UPLC/MS instrument equipped with a reverse-phase C_{18} column (1.7 μm particle size, 2.1 × 50 mm), dual atmospheric pressure chemical ionization (API)/electrospray (ESI) mass spectrometry detector, and photodiode array detector. Samples were eluted with a linear gradient of 20% acetonitrile–water containing 0.1% formic acid→100% acetonitrile containing 0.1% formic acid over 3 min, followed by 100% acetonitrile containing 0.1% formic acid for 1 min, at a flow rate of 800 μL/min. Analytical UPLC/MS data are represented as follows: retention time (t_R) in minutes. Analytical chiral stationary phase HPLC was performed on an Agilent 1100 series HPLC instrument equipped with a CHIRALPAK® AD column and photodiode array detector. Samples were eluted with 0.5% ethanol–hexanes at a flow rate of 800 μL/min. Analytical chiral stationary phase chromatographic data are represented as follows: retention time (t_R) in minutes. High-resolution mass spectrometry (HRMS) were obtained at the W. M. Keck Foundation Biotechnology Resource Laboratory at Yale University or using a Waters UPLC/HRMS instrument equipped with a dual API/ESI high-resolution mass spectrometry detector and photodiode array detector. Unless otherwise noted, samples were eluted over a reverse-phase C_{18} column (1.7 μm particle size, 2.1 × 50 mm) with a linear gradient of 5% acetonitrile–water containing 0.1% formic acid→95% acetonitrile–water containing 0.1% formic acid over 1.6 min, followed by 100% acetonitrile containing 0.1% formic acid for 1 min, at a flow rate of 600 μL/min. Optical rotations were measured on a Perkin Elmer polarimeter equipped with a sodium (589 nm, D) lamp. Optical rotation data are represented as follows: specific rotation ($[\alpha]_\lambda^T$), concentration (mg/mL), and solvent.

Synthetic Procedures.[10]

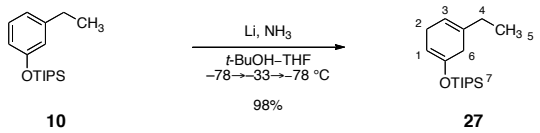


26 **10**

Synthesis of O-*(Tri-iso-propylsilyl)-3-ethylphenol (**10**):*

3-Ethylphenol (149 mL, 1.22 mol, 1.15 equiv) and tri-*iso*-propylchlorosilane (**26**, 226 mL, 1.06 mol, 1 equiv) were added in sequence to a stirred solution of imidazole (145 g, 2.13 mol, 2.00 equiv) in *N,N*-dimethylformamide (500 mL) at 24 °C. The homogenous mixture gradually became biphasic, and the biphasic mixture was vigorously stirred for 20 h at 24 °C. The product mixture was poured into a separatory funnel that had been charged with 50% ether–hexanes (2 L) and 1 N aqueous sulfuric acid solution (3 L). The layers that formed were separated and the organic layer was washed sequentially with 1 N aqueous sodium hydroxide solution (3 × 1 L) and saturated aqueous sodium chloride solution (500 mL). The washed organic layer was dried over sodium sulfate, and the dried solution was filtered. The filtrate was concentrated to afford the silylether **10** as a clear, colorless liquid (293 g, 96%). The silyl ether was utilized without further purification.

R_f = 0.62 (1% ether–hexanes; $KMnO_4$). ^{1}H NMR (400 MHz, $CDCl_3$), δ 7.12 (t, 1H, J = 8.0 Hz, H_2), 6.78 (d, 1H, J = 7.6 Hz, H_1), 6.74 (s, 1H, H_4), 6.70 (dd, 1H, J = 8.0, 2.0 Hz, H_3), 2.60 (q, 2H, J = 8.0 Hz, H_5), 1.31–1.20 (m, 6H, H_6/$H_{7\text{-methine}}$), 1.12 (d, 18H, J = 8.0 Hz, $H_{7\text{-methyl}}$). ^{13}C NMR (100 MHz, $CDCl_3$), δ 156.0 (C), 145.8 (C), 129.0 (CH), 120.5 (CH), 119.5 (CH), 117.0 (CH), 28.8 (CH_2), 17.9 (6 × CH_3), 15.5 (CH_3), 12.7 (3 × CH). IR (ATR-FTIR), cm^{-1}: 2944 (s), 2866 (s), 1603 (s), 1274 (s). HRMS-CI(m/z): $[M+H]^+$ calcd for $C_{17}H_{31}OSi$, 279.2139; found, 279.2138.

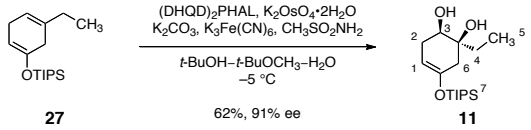


10 **27**

*Birch Reduction of the Enoxysilane **10**:*

A 5-L 3-neck round-bottomed flask fitted with two septa and a dry-ice condenser was charged with tetrahydrofuran (900 mL) and *tert*-butyl alcohol (198 mL). The resulting mixture was cooled to –78 °C. Dry ice and acetone were added to the reflux condenser, and then anhydrous ammonia (~1.6 L) was condensed into the cold reaction vessel. Finely divided lithium metal (13.6 g, 1.94 mol, 6.00 equiv) and the silylether **10** (90.0 g, 324 mmol, 1 equiv) were then added in sequence. Upon completion of the addition, the cooling bath was warmed to –30 °C and the mixture was allowed to reflux. The reaction mixture was stirred for 50 min at reflux, and then was treated with additional *tert*-butyl alcohol (99 mL). The diluted mixture was stirred for 25 min at reflux and then was cooled to –78 °C. The cooled mixture was treated with solid ammonium chloride (ca. 100 g) and was stirred at –78 °C (external cooling) until the blue color discharged (ca. 10 min). The product mixture was warmed over 3 h to 24 °C (***Warning: Large quantities of ammonia gas are released on warming. This operation should be performed in a well-ventilated fume hood)***. The warmed solution was diluted with water (600 mL), and the resulting biphasic mixture was transferred to a separatory funnel. The layers that formed were separated, and the aqueous layer was extracted with pentane (3 × 600 mL). The organic layers were combined and the combined organic layers were dried over sodium sulfate. The dried solution was filtered, and the filtrate was concentrated to afford the diene **27** as a clear, colorless oil (90.0 g, 98%).

R_f = 0.58 (1% ether–hexanes; $KMnO_4$). ^{1}H NMR (400 MHz, $CDCl_3$), δ 5.40 (bs, 1H, H_3), 4.89 (bs, 1H, H_1), 2.76 (bs, 2H, H_2/H_6), 2.66 (m, 2H, H_2/H_6), 2.03 (q, 2H, J = 7.2 Hz, H_4), 1.21 (m, 3H, $H_{7\text{-methine}}$), 1.17 (d, 18H, J = 6.8 Hz, $H_{7\text{-methyl}}$), 1.07 (t, 3H, J = 7.2 Hz, H_5). ^{13}C NMR (100 MHz, $CDCl_3$), δ 148.2 (C), 136.4 (C), 116.8 (CH), 100.1 (CH), 33.7 (CH_2), 29.6 (CH_2), 27.2 (CH_2), 18.0 (6 × CH_3), 12.7 (3 × CH), 12.0 (CH_3). IR (ATR-FTIR), cm^{-1}: 2944 (s), 2866 (s), 1697 (m), 1665 (m), 1216 (s). HRMS-CI(m/z): $[M+H]^+$ calcd for $C_{17}H_{33}OSi$, 281.2296; found, 281.2294.

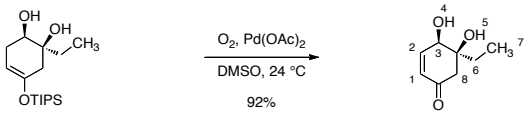


27 **11**

*Dihydroxylation of the Cyclohexadiene **27**:*

$(DHQD)_2PHAL$ (1.67 g, 2.14 mmol, 0.01 equiv), potassium osmate dihydrate (788 mg, 2.14 mmol, 0.01 equiv), methanesulfonamide (20.4 g, 214 mmol, 1.00 equiv), potassium carbonate (88.8 g, 643 mmol, 3.01 equiv) and potassium ferricyanide (212 g, 644 mmol, 3.01 equiv) were added in sequence to a mixture of *tert*-butylmethyl ether (300 mL), *tert*-butyl alcohol (550 mL), and water (850 mL) at 24 °C. The resulting mixture stirred for 15 min at 24 °C and then was cooled to –5 °C. The cyclohexadiene **27** (60.0 g, 214 mmol, 1 equiv) was then added. The reaction mixture was stirred for 40 h at –5 °C. The product mixture was transferred to a separatory funnel that had been charged with ethyl acetate (1 L) and distilled water (2 L). The layers that formed were separated, and the aqueous layer was extracted with ethyl acetate (3 × 1 L). The organic layers were combined and the combined organic layers were washed sequentially with 10% aqueous sodium thiosulfate solution (w/v, 500 mL), saturated aqueous sodium bicarbonate solution (500 mL), and saturated aqueous sodium chloride solution (500 mL). The washed organic layer was dried over sodium sulfate, and the dried solution was filtered. The filtrate was concentrated and the residue obtained was purified by flash-column chromatography (eluting with 15% ethyl acetate–hexanes initially, grading to 50% ethyl acetate–hexanes, one step) to afford the diol **11** as a clear, colorless oil (42.0 g, 62%). The enantiomeric excess of the diol **11** was determined to be 91% by chiral stationary phase HPLC analysis of the enone **28** (vide infra).

R_f = 0.35 (30% ethyl acetate–hexanes; $KMnO_4$). ^1H NMR (400 MHz, $CDCl_3$), δ 4.68 (t, 1H, J = 4.0 Hz, H_1), 3.63 (dd, 1H, J = 11.6, 6.0 Hz, H_3), 2.34 (m, 1H, H_2), 2.20 (m, 3H, $H_2/2 \times H_6$), 2.02 (s, 1H, OH), 1.89 (d, 1H, J = 6.8 Hz, OH), 1.57 (m, 2H, H_4), 1.13 (m, 3H, $H_{7\text{-methine}}$), 1.07 (d, 18H, J = 6.0 Hz, $H_{7\text{-methyl}}$), 0.95 (t, 3H, J = 7.6 Hz, H_5). ^{13}C NMR (125 MHz, $CDCl_3$), δ 148.6 (C), 98.5 (CH), 74.2 (C), 71.2 (CH), 39.5 (CH_2), 30.2 (CH_2), 29.8 (CH_2), 18.4 (6 × CH_3), 13.0 (3 × CH), 7.7 (CH_3). IR (ATR-FTIR), cm^{-1}: 3391 (s), 2942 (s), 2866 (s), 1673 (s), 1196 (s). HRMS-CI(m/z): $[M+H]^+$ calcd for $C_{17}H_{35}O_3Si$, 315.2350; found, 315.2350.

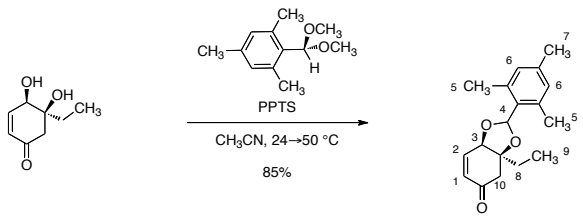


11 **12**

*Oxidation of the Diol **11**:*

A 500-mL round-bottomed flask was charged sequentially with a Teflon-coated stirbar, the diol **11** (9.60 g, 30.6 mmol, 1 equiv), and dimethyl sulfoxide (15.3 mL). Palladium(II) acetate (685 mg, 3.06 mmol, 0.10 equiv) was then added. The headspace in the flask was purged with dioxygen by three sequential evacuation–refill cycles (P < 700 mTorr for each evacuation; a balloon of dioxygen was used to fill the flask). The resulting mixture was stirred under a balloon of dixoygen for 10 h at 24 °C. The headspace in the flask was then purged again three times with dioxygen, and stirring was continued for an additional 7 h at 24 °C under a balloon of dioxygen. The product mixture was purified directly by flash-column chromatography (eluting with 45% acetone–hexanes) to afford the enone **12** as a viscous, colorless oil (4.41 g, 92%).

R_f = 0.20 (70% ethyl acetate–hexanes; UV, PAA). ^{1}H NMR (500 MHz, $CDCl_3$), δ 6.74 (dd, 1H, J = 10.0, 2.5 Hz, H_2), 6.04 (ddd, 1H, J = 11.0, 2.0, 1.0 Hz, H_1), 4.38 (dt, 1H, J = 9.0, 2.5 Hz, H_3), 2.76 (d, 1H, J = 8.5 Hz, H_4), 2.64 (dd, 1H, J = 16.5, 0.5 Hz, H_8), 2.48 (d, 1H, J = 16.5 Hz, H_8), 2.26 (s, 1H, H_5), 1.72 (app q, 2H, J = 7.5 Hz, H_6), 0.97 (t, 3H, J = 8.0 Hz, H_7). ^{13}C NMR (125 MHz, $CDCl_3$), δ 198.3 (C), 149.8 (CH), 128.9 (CH), 76.8 (C), 70.1 (CH), 46.1 (CH_2), 31.2 (CH_2), 7.9 (CH_3). IR (NaCl, thin film), cm^{-1}: 3407 (s), 1675 (m), 1463 (w), 1385 (w). HRMS-CI (*m/z*): $[M + H]^+$ calcd for $C_8H_{13}O_3$, 157.0859; found, 157.0855.



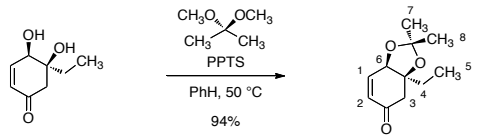
12 **13**

1:1 dr

*Mesityl Protection of Enone **12**:*

Mesitylaldehyde dimethylacetal (11.0 g, 56.5 mmol, 2.01 equiv) and pyridinium *para*-toluenesulfonate (710 mg, 2.83 mmol, 0.10 equiv) were added in sequence to a stirred solution of the enone **12** (4.39 g, 28.1 mmol, 1 equiv) in acetonitrile (140 mL) at 24 °C. The resulting mixture was stirred for 1 h at 24 °C, and then was placed in an oil bath that had been preheated to 50 °C. The reaction mixture was stirred and heated for 45 min at 50 °C. The product solution was cooled over 10 min to 24 °C. Triethylamine (8.00 mL, 57.8 mmol, 2.06 eq) was then added to the cooled solution. The resulting mixture was poured into a separatory funnel that had been charged with saturated aqueous sodium bicarbonate solution (400 mL). The layers that formed were separated, and the aqueous layer was extracted with ethyl acetate (3 × 250 mL). The organic layers were combined and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue obtained was purified by flash-column chromatography (eluting with 25% ether–hexanes) to afford the acetal **13** as a clear, colorless oil (6.82 g, 85%, 1:1 mixture of diastereomers).

R_f = 0.76 (60% ethyl acetate–hexanes; UV, PAA). ^{1}H NMR (500 MHz, $CDCl_3$; 1:1 mixture of diastereomers, * denotes second diastereomer), δ 6.90–6.86 (m, 2H, H_2/H_{2*}), 6.82 (s, 2H, H_6), 6.81 (s, 2H, H_{6*}), 6.30–6.27 (m, 3H, H_4/H_{4*}/H_1), 6.20 (d, 1H, J = 10.5 Hz, H_{1*}), 4.53 (d, 1H, J = 4.0 Hz, H_3), 4.46 (d, 1H, J = 4.0 Hz, H_{3*}), 3.01 (d, 1H, J = 17.0 Hz, H_{10*}), 2.93 (d, 1H, J = 16.5 Hz, H_{10}), 2.72 (d, 1H, J = 16.0 Hz, H_{10}), 2.70 (d, 2H, J = 16.5 Hz, H_{10*}), 2.42 (s, 6H, H_5), 2.37 (s, 6H, H_{5*}), 2.25 (s, 3H, H_7), 2.24 (s, 3H, H_{7*}), 2.04–1.91 (m, 2H, H_8/H_{8*}), 1.89–1.81 (m, 1H, H_8), 1.80–1.73 (m, 1H, H_{8*}), 1.04–0.97 (m, 6H, H_9/H_{9*}). ^{13}C NMR (125 MHz, $CDCl_3$; 1:1 mixture of diastereomers, * denotes second diastereomer), δ 197.4 (C), 196.7 (C*), 142.9 (CH), 142.6 (CH*), 139.1 (C), 139.0 (C*), 137.9 (1 × C, 1 × C*), 131.6 (CH), 130.5 (CH*), 130.3 (2 × CH), 130.2 (2 × CH*), 127.5 (C), 126.9 (C*), 100.2 (1 × CH, 1 × CH*), 82.3 (2 × C), 81.1 (2 × C*), 75.2 (CH), 74.9 (CH*), 45.0 (CH_2), 43.6 (CH_2*), 32.9 (CH_2), 31.1 (CH_2*), 20.9 (2 × CH_3), 20.5 (2 × CH_3*), 20.3 (1 × CH_3, 1 × CH_3*), 8.2 (CH_3), 7.3 (CH_3*). IR (ATR-FTIR), cm^{-1}: 2970 (w), 1687 (s), 1448 (m). HRMS-CI (*m/z*): $[M + Na]^+$ calcd for $C_{18}H_{22}O_3Na$, 309.1462; found, 309.1461.



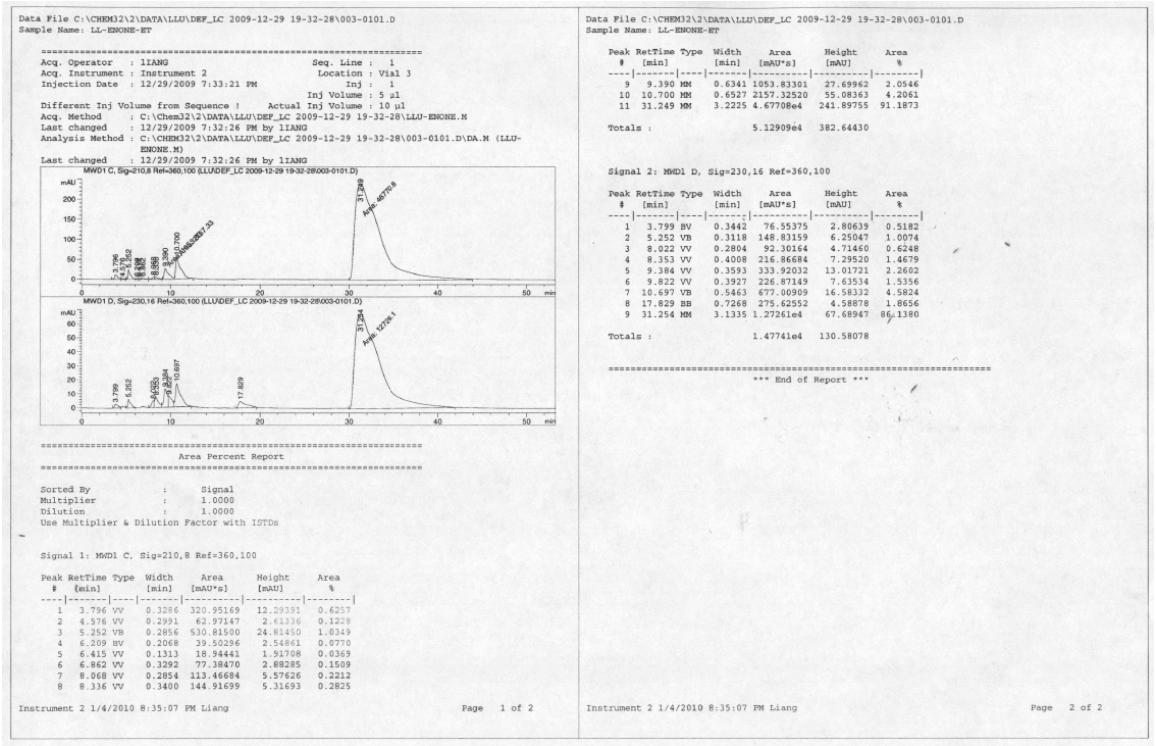
12 **28**

*Synthesis of the Acetonide **28**:*

2,2-Dimethoxypropane (1.22 mL, 10.0 mmol, 5.00 equiv) and pyridinium *para*-toluenesulfonate (50.0 mg, 200 µmol, 0.10 equiv) were added in sequence to a stirred solution of the enone **12** (312 mg, 2.00 mmol, 1 equiv) in benzene (20 mL) at 24 °C. The resulting mixture was stirred for 5 min at 24 °C and then was heated to 50 °C. The reaction mixture was stirred and heated for 1 h at 50 °C. The product mixture was cooled to 24 °C and the cooled solution was diluted with distilled water (20 mL). The diluted solution was transferred to a separatory funnel and the layers that formed were separated. The aqueous layer was extracted with ethyl acetate (6 × 30 mL). The organic layers were combined and the combined organic layers were dried over sodium sulfate. The dried solution was filtered, and the filtrate was concentrated. The residue obtained was purified by flash-column chromatography (eluting with 70% ethyl acetate–hexanes) to furnish the acetonide **28** as a white crystalline solid (374 mg, 94%).

R_f = 0.30 (20% ethyl acetate–hexanes; UV, PAA). ^{1}H NMR (500 MHz, $CDCl_3$), δ 6.78 (dd, 1H, J = 10.0, 3.5 Hz, H_1), 6.11 (d, 1H, J = 10.5 Hz, H_2), 4.46 (dd, 1H, J = 3.5, 0.5 Hz, H_6), 2.88 (d, 1H, J = 16.5 Hz, H_3), 2.51 (d, 1H, J = 16.5 Hz, H_3), 1.85−1.74 (m, 1H, H_4), 1.71−1.60 (m, 1H, H_4), 1.44 (s, 3H, H_7/H_8), 1.39 (s, 3H, H_7/H_8), 0.97 (t, 3H, J = 7.5 Hz, H_5). ^{13}C NMR (125 MHz, $CDCl_3$), δ 197.1 (C), 144.1 (CH), 130.6 (CH), 110.0 (C), 83.2 (CH), 74.7 (C), 44.7(CH_2), 31.4 (CH_2), 28.4 (CH_3), 28.3 (CH_3), 7.7 (CH_3). IR (NaCl, thin film), cm^{-1}: 2989 (s), 2880 (w), 1691 (s), 1389 (m), 1164 (w), 896 (w). HRMS-CI (*m/z*): [M + H]$^+$ calcd for $C_{11}H_{17}O_3$, 197.1172; found, 197.1168.

The enantiomeric excess of the acetonide **28** was determined to be 91% by chiral stationary phase HPLC analysis ($t_{R(major)}$ = 31.249 min; $t_{R(minor)}$ = 10.700 min].



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Area Percent Report

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Use Multiplier & Dilution Factor with ISTDs

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6	6.862	VV	0.3292	77.38470	2.88285	0.1509
7	8.068	VV	0.2854	113.46684	5.57626	0.2212
8	8.336	VV	0.3400	144.91699	5.31693	0.2825

Instrument 2 1/4/2010 8:35:07 PM Liang Page 1 of 2

Data File C:\CHEM32\2\DATA\LLU\DEF_LC 2009-12-29 19-32-28\003-0101.D
Sample Name: LL-ENONE-ET

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
9	9.390	MM	0.6341	1053.83301	27.69962	2.0546
10	10.700	MM	0.6527	2157.32520	55.08363	4.2061
11	31.249	MM	3.2225	4.67708e4	241.89755	91.1873
Totals :				5.12909e4	382.64430	

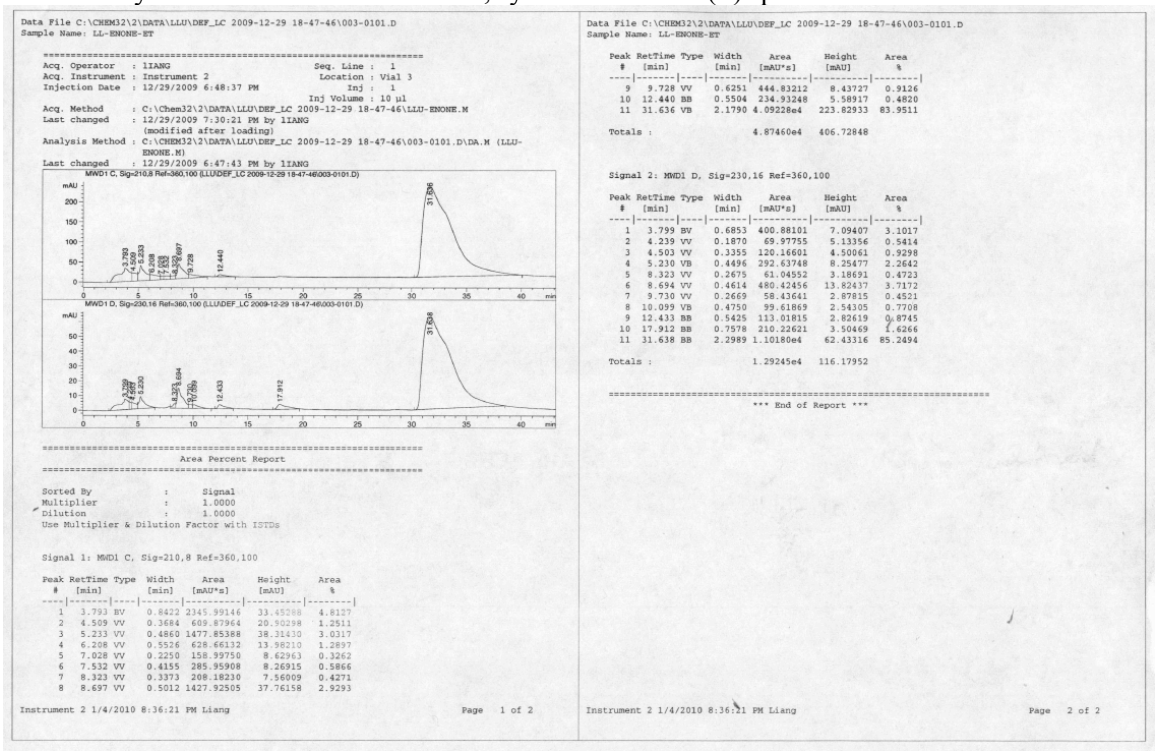
Signal 2: MWD1 D, Sig=230,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.799	BV	0.3442	76.55375	2.80639	0.5182
2	5.252	VB	0.3118	148.83159	6.25047	1.0074
3	8.022	VV	0.2804	92.30164	4.71460	0.6248
4	8.353	VV	0.4008	216.86684	7.29520	1.4679
5	9.384	VV	0.3593	333.92032	13.01721	2.2602
6	9.822	VV	0.3927	226.87149	7.63534	1.5356
7	10.697	VB	0.5463	677.00909	16.58332	4.5824
8	17.829	BB	0.7268	275.62552	4.58878	1.8656
9	31.254	MM	3.1335	1.27261e4	67.68947	86.1380
Totals :				1.47741e4	130.58078	

*** End of Report ***

Instrument 2 1/4/2010 8:35:07 PM Liang Page 2 of 2

HPLC analysis of authentic stereoisomer, synthesized from (+)-quinic acid.[11]



Data File C:\CHEM32\2\DATA\LLU\DEF_LC 2009-12-29 18-47-46\003-0101.D
Sample Name: LL-ENONE-ET

Acq. Operator : lIANG Seq. Line : 1
Acq. Instrument : Instrument 2 Location : Vial 3
Injection Date : 12/29/2009 6:48:37 PM Inj : 1
Inj Volume : 10 µl
Acq. Method : C:\Chem32\2\DATA\LLU\DEF_LC 2009-12-29 18-47-46\LLU-ENONE.M
Last changed : 12/29/2009 7:30:21 PM by lIANG (modified after loading)
Analysis Method : C:\CHEM32\2\DATA\LLU\DEF_LC 2009-12-29 18-47-46\003-0101.D\DA.M (LLU-ENONE.M)
Last changed : 12/29/2009 6:47:43 PM by lIANG

MWD1 C, Sig=210,8 Ref=360,100 (LLU\DEF_LC 2009-12-29 18-47-46\003-0101.D)

MWD1 D, Sig=230,16 Ref=360,100 (LLU\DEF_LC 2009-12-29 18-47-46\003-0101.D)

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.793	BV	0.8422	2345.99146	33.45288	4.8127
2	4.509	VV	0.3684	609.87964	20.90298	1.2511
3	5.233	VV	0.4860	1477.85388	38.31430	3.0317
4	6.208	VV	0.5526	628.66132	13.98210	1.2897
5	7.028	VV	0.2250	158.99750	8.62963	0.3262
6	7.532	VV	0.4155	285.95908	8.26915	0.5866
7	8.323	VV	0.3373	208.18230	7.56009	0.4271
8	8.697	VV	0.5012	1427.92505	37.76158	2.9293

Instrument 2 1/4/2010 8:36:21 PM Liang Page 1 of 2

Data File C:\CHEM32\2\DATA\LLU\DEF_LC 2009-12-29 18-47-46\003-0101.D
Sample Name: LL-ENONE-ET

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
9	9.728	VV	0.6251	444.83212	8.43727	0.9126
10	12.440	BB	0.5504	234.93248	5.58917	0.4820
11	31.636	VB	2.1790	4.09228e4	223.82933	83.9511
Totals :				4.87460e4	406.72848	

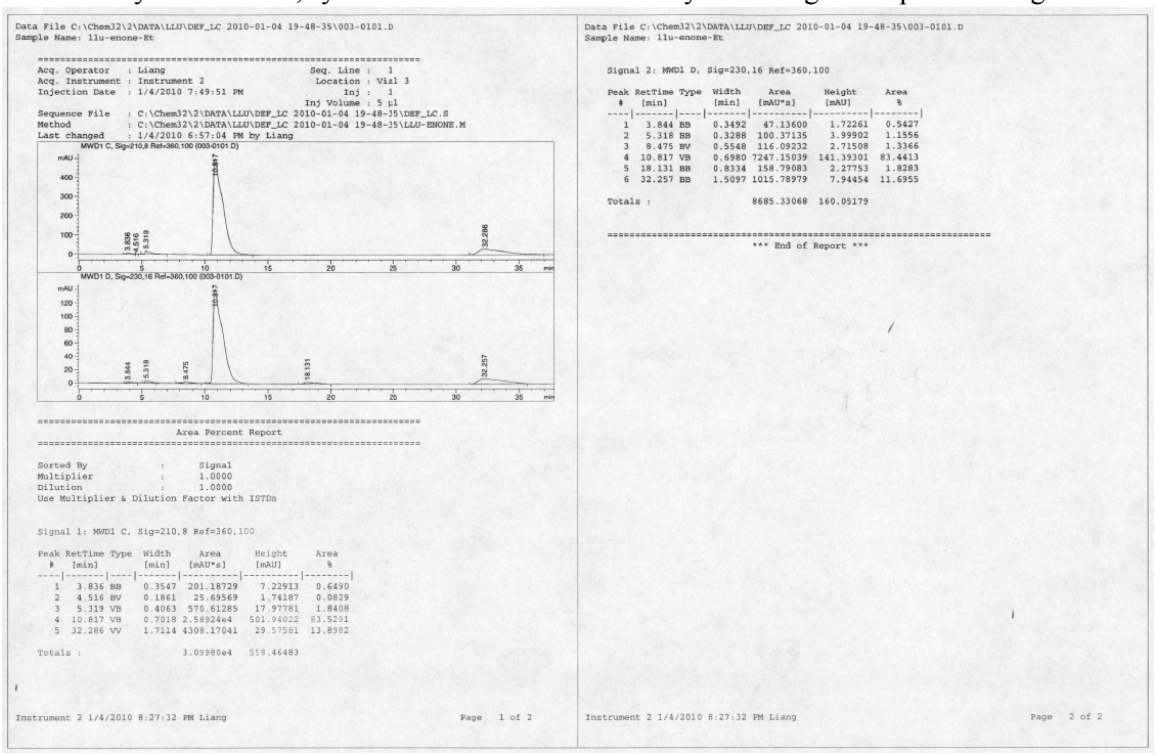
Signal 2: MWD1 D, Sig=230,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.799	BV	0.6853	400.88101	7.09407	3.1017
2	4.239	VV	0.1870	69.97755	5.13356	0.5414
3	4.503	VV	0.3355	120.16601	4.50061	0.9298
4	5.230	VB	0.4496	292.63748	8.25477	2.2642
5	8.323	VV	0.2675	61.04552	3.18691	0.4723
6	8.694	VV	0.4614	480.42456	13.82437	3.7172
7	9.730	VV	0.2669	58.43641	2.87815	0.4521
8	10.099	VB	0.4750	99.61869	2.54305	0.7708
9	12.433	BB	0.5425	113.01815	2.82619	0.8745
10	17.912	BB	0.7578	210.22621	3.50469	1.6266
11	31.638	BB	2.2989	1.10180e4	62.43316	85.2494
Totals :				1.29245e4	116.17952	

*** End of Report ***

Instrument 2 1/4/2010 8:36:21 PM Liang Page 2 of 2

HPLC analysis of ***ent*-28**, synthesized from the diene **27** by an analogous sequence using AD-mix-α.



Data File C:\Chem32\2\DATA\LLU\DEF_LC 2010-01-04 19-48-35\003-0101.D
Sample Name: llu-enone-Et

Acq. Operator : Liang
Acq. Instrument : Instrument 2
Injection Date : 1/4/2010 7:49:51 PM
Seq. Line : 1
Location : Vial 3
Inj : 1
Inj Volume : 5 µl
Sequence File : C:\Chem32\2\DATA\LLU\DEF_LC 2010-01-04 19-48-35\DEF_LC.S
Method : C:\Chem32\2\DATA\LLU\DEF_LC 2010-01-04 19-48-35\LLU-ENONE.M
Last changed : 1/4/2010 6:57:04 PM by Liang

MWD1 C, Sig=210,8 Ref=360,100 (003-0101.D)

MWD1 D, Sig=230,16 Ref=360,100 (003-0101.D)

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.836	BB	0.3547	201.18729	7.22913	0.6490
2	4.516	BV	0.1861	25.69569	1.74187	0.0829
3	5.319	VB	0.4063	570.61285	17.97781	1.8408
4	10.817	VB	0.7018	2.58924e4	501.94022	83.5291
5	32.286	VV	1.7114	4308.17041	29.57581	13.8992
Totals :				3.09980e4	558.46483	

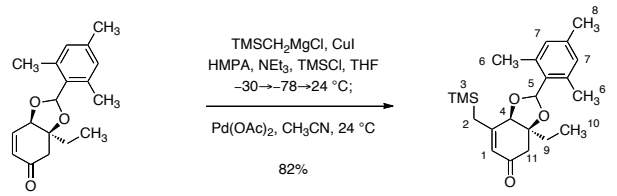
Instrument 2 1/4/2010 8:27:32 PM Liang Page 1 of 2

Signal 2: MWD1 D, Sig=230,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.844	BB	0.3492	47.13600	1.72261	0.5427
2	5.318	BB	0.3288	100.37135	3.99902	1.1556
3	8.475	BV	0.5548	116.09232	2.71508	1.3366
4	10.817	VB	0.6980	7247.15039	141.39301	83.4413
5	18.131	BB	0.8334	158.79083	2.27753	1.8283
6	32.257	BB	1.5097	1015.78979	7.94454	11.6955
Totals :				8685.33068	160.05179	

*** End of Report ***

Instrument 2 1/4/2010 8:27:32 PM Liang Page 2 of 2



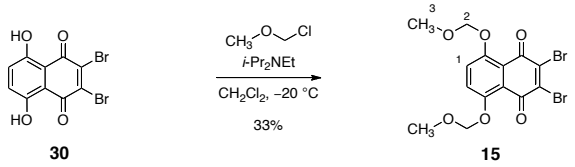
*Synthesis of the β-(Trimethylsilylmethyl)-α,β-unsaturated Ketone **14**:*

Cuprous iodide (101 mg, 534 μmol, 0.10 equiv) was added to a stirred solution of trimethylsilylmethylmagnesium chloride in ether (1.00 M, 5.88 mL, 5.88 mmol, 1.10 equiv) at 24 °C. The resulting solution was cooled to −30 °C, to afford a cloudy suspension. A solution of the cyclohexenone **13** [1.53 g, 5.34 mmol, 1 equiv; dried by azeotropic distillation with benzene (2 mL)] in tetrahydrofuran (1.0 mL) was then added dropwise via cannula. The flask containing the cyclohexenone **13** was rinsed with tetrahydrofuran (2 × 1.3 mL) and the rinses were added to the reaction vessel via cannula. The reaction mixture was cooled to −50 °C and then was stirred at this temperature for 30 min. The mixture was then was cooled to −60 °C and hexamethylphosphoramide (1.02 mL, 5.88 mmol, 1.10 equiv), triethylamine (1.48 mL, 10.7 mmol, 2.00 equiv), and trimethylsilyl chloride (982 μL, 10.7 mmol, 2.00 equiv) were added in sequence to the cooled solution. The resulting mixture was further cooled to −78 °C, and was stirred at this temperature for 1 h. The product mixture was warmed over 10 min to 24 °C, and the warmed solution was stirred for 10 min at 24 °C. The product mixture was diluted with ether (100 mL) and the diluted solution was poured into a separatory funnel that had been charged with saturated aqueous sodium bicarbonate solution (80 mL). The layers that formed were separated, and the aqueous layer was extracted with ether (100 mL). Each organic layer was washed separately with saturated aqueous sodium bicarbonate solution (2 × 50 mL) and saturated aqueous sodium chloride solution (50 mL). The organic layers were combined and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue obtained was dissolved in ether (20 mL) and the resulting solution was eluted over a pad of silica gel (2 × 5 cm). The pad of silica gel was washed with ether (3 × 10 mL), and the filtrates were combined. The combined filtrates were concentrated to afford the enoxysilane **29** as a clear, colorless oil (2.39 g).

Palladium(II) acetate (1.32 g, 5.87 mmol, 1.10 equiv) was added to a stirred solution of the enoxysilane **29** (2.39 g, 5.34 mmol, 1 equiv) in acetonitrile (53 mL) at 24 °C. The resulting black mixture was stirred for 12 h at 24 °C. The product mixture was diluted with ether (100 mL) and the diluted solution was filtered through a pad of celite (5 × 5 cm). The celite pad was washed with ether (3 × 25 mL) and the filtrates were combined. The combined filtrates were concentrated to dryness, and the residue obtained was purified by flash-column chromatography (eluting with 20% ether–hexanes) to afford the β-(trimethylsilylmethyl)-α,β-unsaturated ketone **14** as a clear, colorless oil (1.63 g, 82%, 1:1 mixture of diastereomers).

R_f = 0.33 (20% ether–hexanes; UV, PAA). ^{1}H NMR (400 MHz, $CDCl_3$; 1:1 mixture of diastereomers, * denotes second diastereomer), δ 6.83 (s, 2H, H_7), 6.81 (s, 2H, H_{7*}), 6.32 (s, 1H, H_5), 6.26 (s, 1H, H_{5*}), 5.95 (s, 1H, H_1), 5.91 (s, 1H, H_{1*}), 4.27 (s, 1H, H_4), 4.23 (s, 1H, H_{4*}), 2.94 (d, 1H, J = 16.8 Hz, H_{2*}), 2.85 (d, 1H, J = 16.0 Hz, H_2), 2.68–2.63 (m, 2H, H_2/H_{2*}), 2.43 (s, 6H, H_6), 2.38 (s, 6H, H_{6*}), 2.25 (s, 3H, H_8), 2.24 (s, 3H, H_{8*}), 2.15–2.10 (m, 2H, H_{11}/H_{11*}), 2.00–1.81 (m, 5H, H_{11}/2 × H_9/H_{11*}/H_{9*}), 1.79–1.70 (m, 1H, H_{9*}), 1.00 (app t, 6H, J = 7.6 Hz, H_{10}/H_{10*}), 0.11 (bs, 18H, H_3/H_{3*}). ^{13}C NMR (100 MHz, $CDCl_3$; 1:1 mixture of diastereomers, * denotes second diastereomer), δ 196.4 (C), 195.9 (C*), 159.0 (C), 158.6 (C*), 139.0 (C), 138.9 (C*), 137.9 (2 × C), 137.8 (2 × C*), 130.2 (2 × CH, 2 × CH*), 127.7 (C), 126.9 (C*),

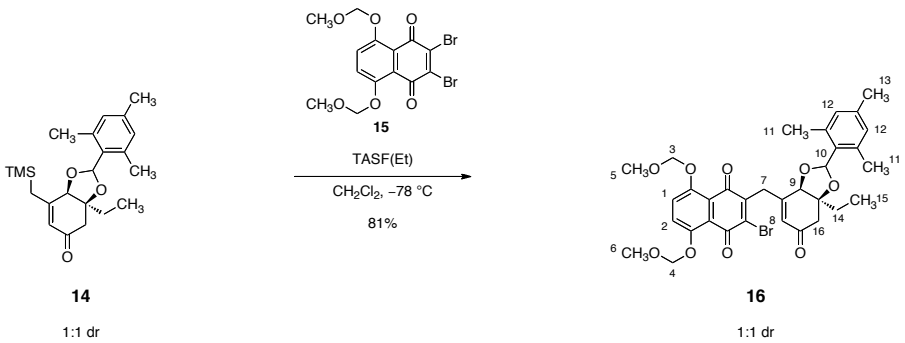
125.7 (CH), 125.3 (CH*), 99.8 (CH), 99.7 (CH*), 82.1 (C), 80.6 (C*), 79.3 (CH), 79.0 (CH*), 44.6 (CH_2), 42.1 (CH_2*), 32.5 (CH_2), 31.5 (CH_2*), 27.7 (CH_2), 27.2 (CH_2*), 20.8 (1 × CH_3, 1 × CH_3*), 20.2 (2 × CH_3, 2 × CH_3*), 8.1 (CH_3), 7.4 (CH_3*), −1.1 (3 × CH_3, 3 × CH_3*). IR (ATR-FTIR), cm^{-1}: 1663 (m), 1614 (w), 905 (s). HRMS-CI(m/z): $[M+H]^+$ calcd for $C_{22}H_{33}O_3Si$, 373.2194; found, 373.2197.



*Synthesis of 2,3-Dibromo-5,8-di(methoxymethyloxy)napthoquinone (**15**):*

Chloromethyl methyl ether (7.50 mL, 101 mmol, 4.83 equiv) was added to a solution of 2,3-dibromo-5,8-dihydroxynapthoquinone (**30**, 7.00 g, 20.2 mmol, 1 equiv) in dichloromethane (290 mL) at –20 °C. *N,N*-Di-*iso*-propylethylamine (25.4 mL, 144 mmol, 7.00 eq) was added dropwise via syringe pump over 4 h to the cold mixture. Upon completion of the addition, the reaction mixture was stirred for 8 h at –20 °C. The product mixture was diluted with saturated aqueous sodium bicarbonate solution (200 mL) and the diluted solution was warmed over 20 min to 24 °C. The warmed biphasic mixture was transferred to a separatory funnel and the layers that formed were separated. The aqueous layer was extracted with dichloromethane (2 × 50 mL) and the organic layers were combined. The combined organic layers were dried over sodium sulfate and the dried solution was filtered. The filtrate was concentrated and the residue obtained was purified by flash-column chromatography on deactivated silica gel (6% w/w distilled water; eluting with 30% ethyl acetate–hexanes initially, grading to 7% ethyl acetate–dichloromethane, one step) to afford the quinone **15** as a red solid (2.90 g, 33%).

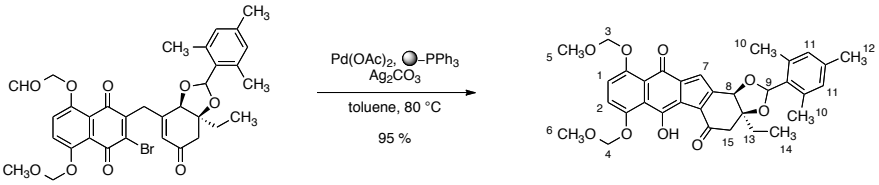
R_f = 0.74 (40% ethyl acetate–hexanes; UV, CAM). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52 (s, 2H, H_1), 5.29 (s, 4H, H_2), 3.54 (s, 6H, H_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ 174.7 (C), 153.0 (C), 141.8 (C), 125.1 (CH), 120.7 (C), 95.8 (CH_2), 56.7 (CH_3). IR (ATR-FTIR), cm^{-1}: 2936 (w), 1665 (m), 1144 (m), 896 (m). HRMS-CI (*m/z*): $[M + H]^+$ calcd for $C_{14}H_{13}{}^{79/79;79/81;81/81}Br_2O_6$, 434.9079/436.9058/438.9038; found, 434.9071/436.9042/438.9020.



*Coupling of 2,3-Dibromo-5,8-di(methoxymethyloxy)napthoquinone (**15**) And The β-(Trimethylsilylmethyl)-α,β-unsaturated Ketone **14**:*

A neat mixture of 2,3-dibromo-5,8-di(methoxymethyloxy)napthoquinone (**15**, 4.77 g, 10.9 mmol, 4.00 equiv) and the β-(trimethylsilylmethyl)-α,β-unsaturated ketone **14** (1.02 g, 2.74 mmol, 1 equiv) was prepared in a 1-L round-bottomed flask. The mixture was dried by azeotropic distillation with benzene (3 × 20 mL). The dried mixture was dissolved in dichloromethane (690 mL) and was stirred at 24 °C until homogenous (ca. 10 min). The resulting red, homogenous mixture was cooled to –78 °C. A solution of TASF(Et) (1.48 g, 4.11 mmol, 1.50 equiv) in dichloromethane (9.0 mL) was added dropwise via cannula to the cold, stirred solution. The resulting black mixture was stirred for 15 min at –78 °C. The cold product mixture was diluted with 0.1 M aqueous sodium phosphate buffer solution (pH 7, 400 mL). The diluted solution was warmed over 45 min to 24 °C. The resulting biphasic mixture was transferred to a separatory funnel and the layers that formed were separated. The aqueous layer was extracted with dichloromethane (3 × 100 mL). The organic layers were combined and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue obtained was diluted with dichloromethane (100 mL) and the diluted solution was filtered to partially remove unreacted quinone **15**. The filtrate was concentrated and the residue obtained was purified by flash-column chromatography (eluting with 5% ethyl acetate–dichloromethane initially, grading to 40% ethyl acetate–dichloromethane, one step) to afford the coupled product **16** as a red solid (1.45 g, 81%, 1:1 mixture of diastereomers).

R_f = 0.55 (20% ethyl acetate–hexanes; UV, PAA). ^{1}H NMR (400 MHz, $CDCl_3$; 1:1 mixture of diastereomers, * denotes second diastereomer), δ 7.40 (app s, 2H, H_1/H_2), 7.39 (d, 1H, J = 9.2 Hz, H_{1*}/H_{2*}), 7.37 (d, 1H, J = 9.2 Hz, H_{1*}/H_{2*}), 6.74 (s, 2H, H_{12}), 6.69 (s, 2H, H_{12*}), 6.20 (bs, 2H, H_{10}/H_{10*}), 5.93 (s, 1H, H_8), 5.87 (s, 1H, H_{8*}), 5.24–5.15 (m, 8H, $H_3/H_4/H_{3*}/H_{4*}$), 4.53 (s, 1H, H_9), 4.45 (s, 1H, H_{9*}), 4.04–3.96 (m, 2H, H_7/H_{7*}), 3.71–3.65 (m, 2H, H_7/H_{7*}), 3.50 (bs, 6H, $H_6/H_5/H_{6*}/H_{5*}$), 3.47 (s, 3H, H_{6*}/H_{5*}), 3.46 (s, 3H, H_6/H_5), 2.90 (d, 1H, J = 16.8 Hz, H_{16*}), 2.85 (d, 1H, J = 16.4 Hz, H_{16}), 2.63–2.59 (m, 2H, H_{16}/H_{16*}), 2.35 (s, 6H, H_{11}), 2.27 (s, 6H, H_{11*}), 2.19 (s, 3H, H_{13}), 2.17 (s, 3H, H_{13*}), 2.00–1.91 (m, 2H, H_{14}/H_{14*}), 1.87–1.79 (m, 1H, H_{14}), 1.78–1.69 (m, 1H, H_{14*}), 0.95 (t, 3H, J = 7.2 Hz, H_{15*}), 0.93 (t, 3H, J = 7.6 Hz, H_{15}). ^{13}C NMR (100 MHz, $CDCl_3$; 1:1 mixture of diastereomers, * denotes second diastereomer), δ 196.5 (C), 196.1 (C*), 180.1 (C), 180.0 (C*), 175.9 (1 × C, 1 × C*), 152.8 (C), 152.7 (C*), 152.3 (2 × C), 152.2 (C*), 152.1 (C*), 146.5 (C), 146.4 (C*), 139.9 (2 × C), 138.7 (2 × C*), 137.7 (2 × C), 137.6 (2 × C*), 129.9 (2 × CH, 2 × CH*), 127.8 (CH), 127.1 (CH*), 127.0 (C), 126.7 (C*), 124.6 (2 × CH), 124.5 (2 × CH*), 121.1 (C), 120.9 (C*), 120.8 (1 × C, 1 × C*), 100.0 (CH), 99.9 (CH*), 95.6 (CH_2), 95.5 (CH_2*), 95.4 (1 × CH_2, 1 × CH_2*), 82.1 (C), 81.1 (C*), 78.4 (CH), 78.3 (CH*), 56.4 (2 × CH_3), 56.3 (2 × CH_3*), 44.5 (CH_2), 43.0 (CH_2*), 36.3 (CH_2), 36.0 (CH_2*), 33.0 (CH_2), 30.9 (CH_2*), 20.7 (1 × CH_3, 1 × CH_3*), 20.2 (2 × CH_3), 20.1 (2 × CH_3*), 8.0 (CH_3), 7.2 (CH_3*). IR (ATR-FTIR), cm^{-1}: 1670 (s), 1467 (s), 1255 (s), 1151 (s). HRMS-CI(m/z): $[M + Na]^+$ calcd for $C_{33}H_{35}Br^{79/81}O_9Na$, 677.1357/679.1337; found, 677.1359/679.1356.



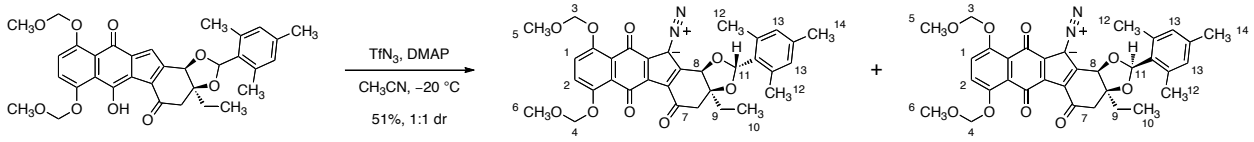
16
1:1 dr

17
1:1 dr

*Cyclization of the Coupled Product **16**:*

A mixture of palladium(II) acetate (485 mg, 2.17 mmol, 1.00 equiv), polymer-supported triphenylphosphine (1.08 g, 3.25 mmol triphenylphosphine, 1.50 equiv], and silver(I) carbonate (1.19 g, 4.33 mmol, 2.00 equiv) were added to a stirred solution of the coupled product **16** [1.42 g, 2.17 mmol, 1 equiv; dried by azeotropic distillation with benzene (5 mL)] in toluene (110 mL) at 24 °C. The resulting mixture was placed in an oil bath that had been preheated to 80 °C. The reaction mixture was stirred and heated for 2 h at 80 °C. The product solution was cooled over 10 min to 24 °C and the cooled solution was filtered over a celite pad (6 × 8 cm). The celite pad was washed with ethyl acetate (4 × 50 mL) and dichloromethane (2 × 50 mL). The filtrates were combined and the combined filtrates were concentrated to dryness. The residue obtained was purified by flash-column chromatography (eluting with 25% acetone–hexanes initially, grading to 3% methanol–dichloromethane, one step) to afford the cyclized product **17** as a dark purple solid (1.17 g, 95%, 1:1 mixture of diastereomers).

R_f = 0.70 (2% methanol-dichloromethane; UV, CAM). ^{1}H NMR (500 MHz, $CDCl_3$; 1:1 mixture of diastereomers, * denotes second diastereomer), δ 7.47–7.40 (m, 4H, $H_1/H_2/H_{1*}/H_{2*}$), 7.07 (s, 1H, H_{7*}), 7.05 (s, 1H, H_7), 6.82 (s, 2H, H_{11}), 6.77 (s, 2H, H_{11*}), 6.38 (s, 1H, H_9), 6.35 (s, 1H, H_{9*}), 5.32 (app d, 4H, J = 1.5 Hz, $H_3/H_4/H_{3*}/H_{4*}$), 5.27 (bs, 4H, $H_3/H_4/H_{3*}/H_{4*}$), 5.04 (s, 1H, H_8), 5.01 (s, 1H, H_{8*}), 3.59 (s, 6H, $H_5/H_6/H_{5*}/H_{6*}$), 3.56 (s, 6H, $H_5/H_6/H_{5*}/H_{6*}$), 3.34 (d, 1H, J = 19.0 Hz, H_{15*}), 3.25 (d, 1H, J = 18.5 Hz, H_{15}), 3.04–2.99 (m, 2H, H_{15}/H_{15*}), 2.44 (s, 6H, H_{10}), 2.31 (s, 6H, H_{10*}), 2.25 (s, 3H, H_{12}), 2.21 (s, 3H, H_{12*}), 2.09–2.01 (m, 2H, H_{13}/H_{13*}), 2.00–1.92 (m, 1H, H_{13}), 1.92–1.84 (m, 1H, H_{13*}), 1.02 (t, 3H, J = 7.5 Hz, H_{14*}), 0.98 (t, 3H, J = 7.5 Hz, H_{14}). ^{13}C NMR (125 MHz, $CDCl_3$; 1:1 mixture of diastereomers, * denotes second diastereomer), δ 190.6 (C), 190.1 (C*), 180.7 (1 × C, 1 × C*), 175.5 (C), 175.4 (C*), 154.5 (2 × C), 154.3 (2 × C*), 144.2 (C), 144.0 (C*), 139.0 (C), 138.9 (C*), 137.9 (2 × C), 137.8 (2 × C*), 130.2 (2 × CH, 2 × CH*), 128.1 (2 × C), 127.4 (2 × CH), 127.0 (2 × C*), 125.1 (2 × CH*), 124.4 (C), 124.3 (C*), 122.8 (C), 122.5 (1 × CH, 1 × CH*, 1 × C*), 122.3 (C), 122.2 (C*), 121.6 (C), 121.3 (C*), 101.1 (CH), 100.5 (CH*), 96.4 (2 × CH_2), 96.3 (CH_2*), 96.2 (CH_2*), 85.2 (C), 83.2 (C*), 75.5 (CH), 74.8 (CH*), 56.7 (2 × CH_3), 56.7 (CH_3*), 56.6 (CH_3*), 43.3 (CH_2), 40.2 (CH_2*), 32.3 (CH_2), 31.8 (CH_2*), 20.9 (1 × CH_3, 1 × CH_3*), 20.4 (2 × CH_3), 20.3 (2 × CH_3*), 8.6 (CH_3), 7.8 (CH_3*). IR (ATR-FTIR), cm^{-1}: 2966 (b), 1595 (s), 1562 (s), 1462 (m). HRMS-CI(m/z): $[M + H]^+$ calcd for $C_{33}H_{35}O_9$, 575.2281; found, 575.2295.



17

1:1 dr

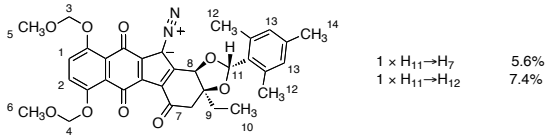
18

19

*Diazotransfer to the Cyclized Product **17**:*

4-Dimethylaminopyridine (1.53 g, 12.5 mmol, 5.00 equiv) was added to a stirred solution of the cyclized product **17** [550 mg, 917 μmol, 1 equiv; dried by azeotropic distillation with benzene (2 mL)] at 24 °C. The resulting mixture was stirred for 2 min at 24 °C, and then was cooled to –20 °C over 5 min. A solution of trifluoromethanesulfonyl azide in hexanes (273 mM, 8.39 mL, 2.29 mmol, 2.50 equiv) was added dropwise via syringe to the cooled solution at –20 °C. The resulting mixture was stirred for 2 h at –20 °C. The product mixture was diluted with saturated aqueous sodium bicarbonate solution (60 mL). The diluted solution was poured into a separatory funnel that had been charged with ethyl acetate (350 mL), and the layers that formed were separated. The organic layer was washed sequentially with 1 N aqueous sulfuric acid solution (2 × 150 mL), saturated aqueous sodium bicarbonate solution (3 × 150 mL), and saturated aqueous sodium chloride solution (1 × 150 mL). The washed organic layer was dried over sodium sulfate and the dried solution was filtered. The filtrate was concentrated and the residue obtained was examined by ^{1}H NMR (1:1 mixture of diastereomers). The residue was then purified by flash-column chromatography (eluting with 60% ethyl acetate-hexanes) to afford separately the *exo*-mesityl diazofluorene **18** (yellow solid, 128 mg, 22%) and the *endo*-mesityl diazofluorene **19** (yellow solid, 164 mg, 29%).

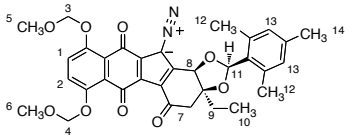
The stereochemistry of the mesityl acetal protecting group was determined by NOE analysis.



18

Exo-Mesityl Diazofluorene **18**:

R_f = 0.75 (90% ethyl acetate–hexanes; UV). t_R = 2.06. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49 (d, 1H, J = 9.5 Hz, H_1/H_2), 7.44 (d, 1H, J = 9.5 Hz, H_1/H_2), 6.84 (s, 2H, H_{13}), 6.32 (s, 1H, H_{11}), 5.31 (app s, 2H, H_3/H_4), 5.26 (app s, 2H, H_3/H_4), 5.09 (s, 1H, H_8), 3.56 (s, 3H, H_5/H_6), 3.55 (s, 3H, H_5/H_6), 3.14 (d, 1H, J = 15.0 Hz, H_7), 2.92 (d, 1H, J = 15.0 Hz, H_7), 2.41 (s, 6H, H_{12}), 2.25 (s, 3H, H_{14}), 2.06–1.93 (m, 2H, H_9), 1.04 (t, 3H, J = 7.5 Hz, H_{10}). ^{13}C NMR (125 MHz, $CDCl_3$): δ 188.7 (C), 179.3 (C), 178.0 (C), 153.1 (C), 153.0 (C), 143.9 (C), 139.3 (C), 138.0 (2 × C), 134.0 (C), 130.2 (2 × CH), 129.2 (C), 127.3 (CH), 127.1 (C), 126.1 (C), 125.7 (C), 123.4 (CH), 122.0 (C), 101.0 (CH), 96.7 (CH_2), 95.7 (CH_2), 84.9 (C), 76.2 (C), 72.9 (CH), 56.6 (CH_3), 56.5 (CH_3), 46.0 (CH_2), 32.8 (CH_2), 20.9 (CH_3), 20.3 (2 × CH_3), 8.3 (CH_3). IR (ATR-FTIR), cm^{-1}: 2927 (m), 2139 (s), 1684 (s), 1443 (s). HRMS-CI (*m/z*): $[M + H]^+$ calcd for $C_{33}H_{33}N_2O_9$, 601.2181; found, 601.2209.



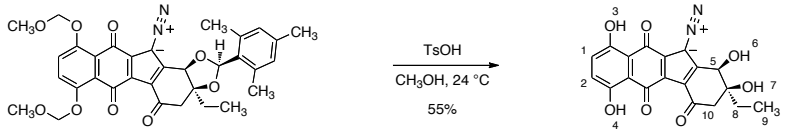
$1 \times H_{11} \rightarrow H_8$	2.5%
$1 \times H_{11} \rightarrow H_{12}$	7.4%
$1 \times H_{11} \rightarrow H_9$	3.4%
$1 \times H_{11} \rightarrow H_9$	1.4%
$1 \times H_{11} \rightarrow H_{10}$	0.9%

19

Endo-Mesityl Diazofluorene **19**:

R_f = 0.64 (90% ethyl acetate–hexanes; UV). t_R = 1.97. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49 (d, 1H, J = 9.5 Hz, H_1/H_2), 7.44 (d, 1H, J = 9.5 Hz, H_1/H_2), 6.77 (s, 2H, H_{13}), 6.37 (s, 1H, H_{11}), 5.32–5.26 (m, 4H, H_3/H_4), 5.09 (s, 1H, H_8), 3.57 (s, 3H, H_5/H_6), 3.55 (s, 3H, H_5/H_6), 3.22 (d, 1H, J = 16.0 Hz, H_7), 2.89 (d, 1H, J = 16.0 Hz, H_7), 2.24 (s, 6H, H_{12}), 2.21 (s, 3H, H_{14}), 2.15–2.11 (m, 1H, H_9), 1.88–1.84 (m, 1H, H_9), 1.07 (t, 3H, J = 7.5 Hz, H_{10}). ^{13}C NMR (125 MHz, $CDCl_3$): δ 188.0 (C), 179.2 (C), 178.0 (C), 153.1 (C), 153.0 (C), 144.8 (C), 139.3 (C), 138.0 (2 × C), 133.8 (C), 130.2 (2 × CH), 129.3 (C), 127.3 (CH), 126.5 (C), 125.8 (C), 124.9 (C), 123.4 (CH), 122.0 (C), 100.8 (CH), 96.8 (CH_2), 95.7 (CH_2), 84.3 (C), 76.1 (C), 72.8 (CH), 56.6 (CH_3), 56.6 (CH_3), 47.2 (CH_2), 30.6 (CH_2), 20.8 (CH_3), 20.2 (2 × CH_3), 7.5 (CH_3). IR (ATR-FTIR), cm^{-1}: 2926 (m), 2137 (s), 1686 (s), 1443 (s). HRMS-CI (*m/z*): $[M + H]^+$ calcd for $C_{33}H_{33}N_2O_9$, 601.2181; found, 601.2186.

Either diazofluorene **18** or **19** could be fully deprotected to afford the monomeric lomaiviticin aglycon **31**. A representative procedure follows.

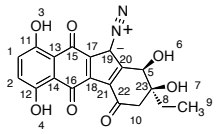


19 **31**

Deprotection of the Endo-*Mesityl Diazofluorene **19**:*

A solution of *para*-toluenesulfonic acid in methanol (10.0 mM, 833 μL, 8.33 μmol, 0.25 equiv) was added to a stirred solution of the *endo*-mesityl diazofluorene **19** (20.0 mg, 33.3 μmol, 1 equiv) in methanol (3.4 mL) at 24 °C. The resulting mixture was stirred for 3 h 20 min at 24 °C. The product mixture was diluted sequentially with distilled water (2.0 mL) and *N,N*-dimethylformamide (1.0 mL). The diluted reaction mixture was loaded directly onto a column of reverse phase silica gel. The mixture was eluted with acetonitrile–water (10% acetonitrile–water initially, grading to 30% acetonitrile–water, one step) to afford the lomaiviticin monomer aglycon **31** as a purple solid (7.0 mg, 55%). ^{1}H NMR data (THF-d_8) were in agreement with those previously reported.[12] The purified monomer aglycon **31** was found to be stable for at least 3 d at 24 °C in d_7-DMF.

R_f = 0.37 (5% methanol–dichloromethane; UV, CAM). t_R = 0.86. ^{1}H NMR (500 MHz, d_7-DMF): δ 13.41 (s, 1H, H_3/H_4), 12.54 (s, 1H, H_3/H_4), 7.37 (d, 1H, J = 9.5 Hz, H_1/H_2), 7.33 (d, 1H, J = 9.5 Hz, H_1/H_2), 6.27 (d, 1H, J = 8.5 Hz, H_6), 5.26 (d, 1H, J = 8.5 Hz, H_5), 4.78 (s, 1H, H_7), 2.82 (d, 1H, J = 17.0 Hz, H_{10}), 2.59 (d, 1H, J = 15.5 Hz, H_{10}), 1.83–1.79 (m, 2H, H_8), 1.00 (t, 3H, J = 7.5 Hz, H_9). ^{13}C NMR (125 MHz, DMF-d_7): δ 189.7 (C), 183.8 (C), 183.5 (C), 159.1 (C), 158.5 (C), 155.3 (C), 131.9 (C), 131.0 (C), 129.2 (CH), 128.9 (CH), 125.7 (C), 114.4 (C), 113.6 (C), 81.2 (C), 79.1 (C), 72.1 (CH), 50.2 (CH_2), 31.6 (CH_2), 8.8 (CH_3). IR (ATR-FTIR), cm^{-1}: 3647 (m), 2956 (s), 2173 (m), 1441 (s). $[\alpha]_D^{20}$ −20 (*c* 0.01, THF). HRMS-CI (*m/z*): $[M + H]^+$ calcd for $C_{19}H_{15}N_2O_7$, 383.0879; found, 383.0875.



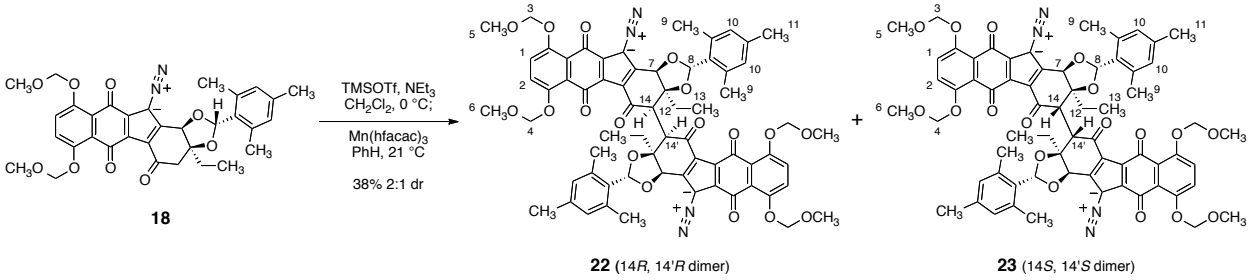
31

Table of NMR Data and C–H couplings (d_7-DMF):

Position	δH	Multiplicity, Integration, *J*-Value	δC	HMBC $_{(H-C)}$
1	7.37	d, 1H, J = 9.5 Hz	129.2	C_{11}, C_{13}
2	7.33	d, 1H, J = 9.5 Hz	128.9	C_{12}, C_{13}
3	13.41	s, 1H	–	C_1, C_{13}, C_{11}
4	12.54	s, 1H	–	C_2, C_{12}, C_{14}
5	5.26	d, 1H, J = 8.5 Hz	72.1	C_8, C_{19}, C_{20}, C_{21}
6	6.27	d, 1H, J = 8.5 Hz	–	–
7	4.78	s, 1H	–	–
8	1.83–1.79	m, 2H	31.6	C_5, C_9, C_{10}, C_{23}
9	1.00	t, 3H, J = 7.5 Hz	8.8	C_8, C_{23}
10	2.82	d, 1H, J = 17.0 Hz	50.2	C_5, C_8, C_{21}, C_{22}, C_{23}
	2.59	d, 2H, J = 15.5 Hz	50.2	C_5, C_8, C_{21}, C_{22}, C_{23}
11	–	–	158.5	
12	–	–	159.1	
13	–	–	114.4	
14	–	–	113.6	
15	–	–	183.8	
16	–	–	183.5	
17	–	–	131.9	
18	–	–	131.0	
19	–	–	81.2	
20	–	–	155.3	
21	–	–	125.7	
22	–	–	189.7	
23	–	–	79.1	

* C_1, C_3, C_{11}, C_{13}, C_{15}, and C_{17} are interchangeable with C_2, C_4, C_{12}, C_{14}, C_{16}, and C_{18}, respectively.

Oxidative Dimerization of the Exo-*Mesityl Diazofluorene **18**:*



*Dimerization of Diazofluorene **18**:*

Triethylamine (115 μL, 831 μmol, 5.00 equiv) and trimethylsilyl trifluoromethanesulfonate (75.3 μL, 417 μmol, 2.50 equiv) were added in sequence to a stirred solution of the *exo*-mesityl diazofluorene **18** [100 mg, 167 μmol, 1 equiv; dried by azeotropic distillation with benzene (2 × 5.0 mL)] in dichloromethane (8.4 mL) at 0 °C. The resulting mixture was stirred for 20 min at 0 °C. The red product mixture was diluted with methanol (600 μL) and the diluted solution was transferred to a separatory funnel that had been charged with 0.1 M aqueous sodium phosphate buffer solution (pH 7, 50 mL) and dichloromethane (100 mL). The layers that formed were separated and the aqueous layer was extracted with dichloromethane (2 × 15 mL). The organic layers were combined and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to afford the trimethylsilyl enoxysilane of **18** (**20**) as a red oil.

A solution of manganese tris(hexafluoroacetylacetonate) in benzene (80.0 mM, 2.50 mL, 200 μmol, 1.20 equiv) was added rapidly via syringe to a vigorously stirred solution of the enoxysilane **20** [167 μmol, 1 equiv; dried by azeotropic distillation with benzene (2 × 2 mL)] in benzene (3.0 mL) at 24 °C. The reaction mixture was stirred for 2.5 min at 24 °C and then was diluted with methanol (2.0 mL). The diluted solution was transferred to a separatory funnel that had been charged with 50% ethyl acetate–hexanes (200 mL) and 1 N aqueous sodium hydroxide solution (30 mL). The separatory funnel was sealed and the sealed funnel was vigorously shaken. The layers that formed were separated and the organic layer was washed sequentially with 1 N aqueous sodium hydroxide solution (3 × 30 mL), saturated aqueous sodium bicarbonate solution (50 mL), distilled water (50 mL) and saturated aqueous sodium chloride solution (50 mL). The organic layer was dried over sodium sulfate and the dried solution was filtered. The filtrate was concentrated and the residue obtained was purified by flash-column chromatography (eluting with 30% acetone–hexanes) to afford separately the (14*R*,14'*R*)-dimeric diazofluorene **22** (orange solid, 26.4 mg, 26%), the (14*S*,14'*S*)-dimeric diazofluorene **23** (orange solid, 12.0 mg, 12%) and recovered diazofluorene **18** (yellow solid, 30.1 mg, 30%).

(14*R*,14'*R*)-Dimeric Diazofluorene **22**:

Note: ^{1}H and ^{13}C NMR data are normalized to the monomeric structure.

R_f = 0.41 (40% acetone–hexanes; UV, ANIS). t_R = 2.77. ^{1}H NMR [500 MHz, 10% $CDCl_3$–CD_3OD (v/v)]: δ 7.37 (s, 1H, H_8), 7.26 (app s, 2H, H_1/H_2), 6.86 (s, 2H, H_{10}), 5.41 (s, 1H, H_7), 5.25 (d, 2H, J = 7.0 Hz, H_3/H_4), 5.18 (d, 1H, J = 7.0 Hz, H_3/H_4), 5.14 (d, 1H, J = 7.0 Hz, H_3/H_4), 5.00 (d, 1H, J = 7.0 Hz, H_3/H_4), 3.85 (s, 1H, H_{14}), 3.52 (s, 3H, H_5/H_6), 3.42 (s, 3H, H_5/H_6), 2.62 (s, 6H, H_9), 2.27 (s, 3H, H_{11}), 2.08–1.98 (m, 2H, H_{12}), 1.05 (t, 3H, J = 7.5 Hz, H_{13}). ^{13}C NMR [125 MHz, $CDCl_3$–CD_3OD (10% v/v)]: 192.2 (C), 180.4 (C), 179.0 (C), 154.2 (C), 153.8 (C), 147.3 (C), 140.3 (C), 140.0 (C), 135.9 (C), 131.2 (2 × CH), 129.7 (C), 129.6 (C), 126.8 (CH), 126.3 (C), 125.5 (C), 125.1 (CH), 123.0 (C), 105.0 (CH), 97.1 (CH_2), 97.0 (CH_2), 86.7 (C), 78.9 (C), 75.6 (CH), 57.2 (CH_3), 56.9 (CH_3), 55.1 (CH), 37.3 (CH_2), 21.2 (3

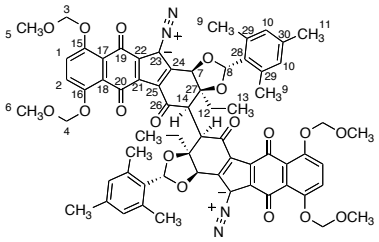
× CH_3), 9.2 (CH_3). IR (ATR-FTIR), cm^{-1}: 2957 (m), 2161 (s), 2029 (s), 1686 (s), 1443 (s). HRMS-CI (*m/z*): $[M + H]^+$ calcd for $C_{66}H_{63}N_4O_{18}$, 1199.4137; found, 1199.4136.

(14*S*,14'*S*)-Dimeric Diazofluorene **23**:

Note: ^1H and ^{13}C NMR data are normalized to the monomeric structure.

R_f = 0.58 (40% acetone–hexanes; UV, ANIS). t_R = 3.03. ^1H NMR (500 MHz, $CDCl_3$): δ 7.54 (d, 1H, J = 9.5 Hz, H_1/H_2), 7.34 (d, 1H, J = 9.5 Hz, H_1/H_2), 6.75 (s, 2H, H_{10}), 5.67 (s, 1H, H_8), 5.57 (s, 1H, H_7), 5.38 (d, 1H, J = 7.5 Hz, H_3/H_4), 5.27 (d, 1H, J = 7.0 Hz, H_3/H_4), 5.08 (d, 1H, J = 7.0 Hz, H_3/H_4), 5.04 (d, 1H, J = 6.5 Hz, H_3/H_4), 3.62 (s, 1H, H_{14}), 3.60 (s, 3H, H_5/H_6), 3.48 (s, 3H, H_5/H_6), 2.82–2.77 (m, 1H, H_{12}), 2.28 (s, 6H, H_9), 2.25–2.19 (m, 4H, H_{11}/H_{12}), 1.07 (t, 3H, J = 7.0 Hz, H_{13}). ^{13}C NMR (125 MHz, $CDCl_3$): 191.0 (C), 178.0 (C), 177.9 (C), 153.7 (C), 152.7 (C), 142.0 (C), 138.5 (C), 137.5 (2 × C), 133.8 (C), 130.1 (2 × CH), 129.0 (C), 127.6 (C), 126.5 (C), 126.3 (CH), 124.5 (CH), 124.4 (C), 121.7 (C), 101.2 (CH), 96.1 (2 × CH_2), 86.7 (C), 76.8 (C, determined indirectly by HMBC), 73.0 (CH), 56.5 (CH_3), 56.4 (CH_3), 55.7 (CH), 28.8 (CH_2), 20.8 (3 × CH_3), 7.2 (CH_3). IR (ATR-FTIR), cm^{-1}: 2966 (m), 2160 (s), 2030 (m), 1688 (s). HRMS-CI (*m/z*): $[M + H]^+$ calcd for $C_{66}H_{63}N_4O_{18}$, 1199.4137; found, 1199.4120.

(14*R*,14'*R*)-Dimeric Diazofluorene 22:



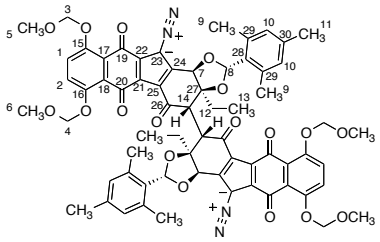
22 (14*R*, 14'*R* dimer)

Table of NMR Data and C–H couplings (10% CD_3OD–$CDCl_3$):

Position	δH	Multiplicity, Integration, *J*-Value	δC	HMBC (H-C)
1	7.26	app s, 1H	126.8	C_{15}, C_{17}, C_{19}
2	7.26	app s, 1H	125.1	C_{16}, C_{18}, C_{20}
3	5.25	d, 1H, J = 7.0 Hz	97.1	C_5, C_{15}
	5.18	d, 1H, J = 7.0 Hz	97.1	C_5, C_{15}
4	5.14	d, 1H, J = 7.0 Hz	97.0	C_6, C_{16}
	5.00	d, 1H, J = 7.0 Hz	97.0	C_6, C_{16}
5	3.52	s, 3H	57.2	C_3
6	3.42	s, 3H	56.9	C_4
7	5.41	s, 1H	75.6	C_8, C_{12}, C_{14}, C_{23}, C_{24}, C_{25}, C_{27}
8	7.37	s, 1H	105.0	C_{28}, C_{29}
9	2.62	s, 3H	21.2	C_{10}, C_{28}, C_{29}
10	6.86	s, 1H	131.2	C_9/C_{11}, C_{10}, C_{28}, C_{29}
11	2.27	s, 3H	21.2	C_{10}, C_{30}
12	2.08–1.98	m, 2H	37.3	C_7, C_{13}, C_{14}, C_{27}
13	1.05	t, 3H, J = 7.5 Hz	9.2	C_{12}, C_{27}
14	3.85	s, 1H	55.2	C_7, C_{12}, C_{14}, C_{25}, C_{26}, C_{27}
15	–	–	153.9	
16	–	–	154.2	
17	–	–	125.5	
18	–	–	123.0	
19	–	–	179.0	
20	–	–	180.4	
21	–	–	129.7	
22	–	–	135.9	
23	–	–	78.6	
24	–	–	147.3	
25	–	–	126.3	
26	–	–	192.2	
27	–	–	86.7	
28	–	–	129.6	
29	–	–	140.0	
30	–	–	140.3	

* C_1, C_3, C_5, C_{15}, C_{17}, C_{19}, and C_{22} are interchangeable with C_2, C_4, C_6, C_{16}, C_{18}, C_{20}, and C_{21}, respectively.

(14*S*,14'*S*)-Dimeric Diazofluorene 23:

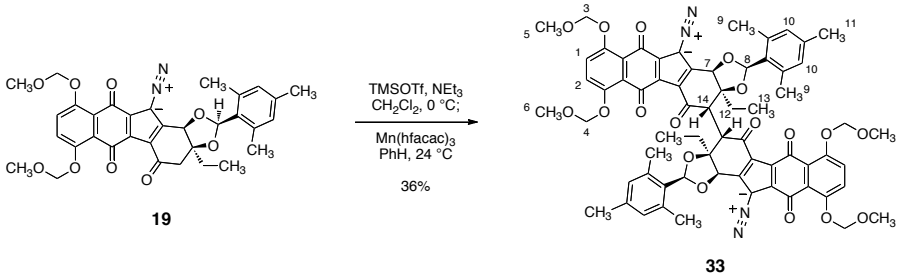


23 (14*S*, 14'*S* dimer)

Table of NMR Data and C–H couplings ($CDCl_3$):

Position	δH	Mult, J-Value	δC	HMBC (H-C)
1	7.54	d, 1H, J = 9.5 Hz	126.3	C_{15}, C_{17}, C_{19}
2	7.34	d, 1H, J = 9.5 Hz	124.4	C_{16}, C_{18}, C_{20}
3	5.38	d, 1H, J = 7.5 Hz	96.1	C_5, C_{15}
3*	5.27	d, 1H, J = 7.0 Hz	96.1	C_5, C_{15}
4	5.08	d, 1H, J = 7.0 Hz	96,1	C_6, C_{16}
4*	5.04	d, 1H, J = 6.5 Hz	96.1	C_6, C_{16}
5	3.60	s, 3H	56.5	C_3
6	3.48	s, 3H	56.4	C_4
7	5.57	s, 1H	73.0	C_8, C_{12}, C_{23}, C_{24}, C_{25}
8	5.67	s, 1H	101.2	C_{28}, C_{29}
9	2.28	s, 3H	20.8	C_{10}, C_{28}, C_{29}
10	6.75	s, 1H	130.1	C_8, C_9/C_{11}, C_{10}, C_{28}, C_{29}
11	2.20	s, 3H	20.8	C_{10}, C_{30}
12	2.82–2.77	m, 2H	28.8	C_7, C_{13}, C_{14}, C_{27}
13	1.07	t, 3H, J = 7.0 Hz	7.2	C_{12}, C_{27}
14	3.62	s, 1H	55.7	C_7, C_{14}, C_{25}, C_{26}, C_{27}
15	–	–	152.7	
16	–	–	153.7	
17	–	–	124.4	
18	–	–	121.7	
19	–	–	177.9	
20	–	–	178.0	
21	–	–	133.8	
22	–	–	126.5	
23	–	–	76.8	
24	–	–	142.0	
25	–	–	129.0	
26	–	–	191.0	
27	–	–	86.7	
28	–	–	127.6	
29	–	–	137.5	
30	–	–	138.5	

* C_1, C_3, C_5, C_{15}, C_{17}, C_{19}, C_{22} are interchangeable with C_2, C_4, C_6, C_{16}, C_{18}, C_{20}, C_{21} respectively.



19 **33**

Dimerization of The Endo-*Mesityl Diazofluorene **19**:*

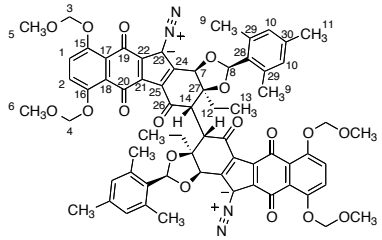
Triethylamine (69.0 μL, 500 μmol, 5.00 equiv) and trimethylsilyl trifluoromethanesulfonate (45.0 μL, 250 μmol, 2.50 equiv) were added in sequence to a stirred solution of the *endo*-mesityl diazofluorene **19** (60.0 mg, 100 μmol, 1 equiv) in dichloromethane (5.0 mL) at 0 °C. The resulting mixture was stirred for 5 min at 0 °C. The product mixture was diluted sequentially with methanol (390 μL) and 0.1 M aqueous sodium phosphate buffer solution (pH 7, 5 mL). The diluted solution was transferred to a separatory funnel and the layers that formed were separated. The aqueous layer was extracted with dichloromethane (2 × 5 mL). The organic layers were combined and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated to afford the trimethylsilyl enoxysilane of **19** (**32**) as a red oil.

A solution of manganese tris(hexafluoroacetylacetonate) in benzene (80.0 mM, 1.50 mL, 120 μmol, 1.20 equiv) was added rapidly via syringe to a vigorously stirred solution of the enoxysilane **32** [100 μmol, 1 equiv; dried by azeotropic distillation with benzene (2 × 500 μL)] in benzene (1.8 mL) at 24 °C. The reaction mixture was stirred for 1.0 min at 24 °C and then was diluted with methanol (780 μL). The diluted solution was transferred to a separatory funnel that had been charged with 25% ethyl acetate–hexanes (150 mL) and 1 N aqueous sodium hydroxide solution (100 mL). The separatory funnel was sealed and the sealed funnel was vigorously shaken. The layers that formed were separated and the organic layer was washed sequentially with 1 N aqueous sodium hydroxide solution (2 × 100 mL), saturated aqueous sodium bicarbonate solution (100 mL), distilled water (100 mL) and saturated aqueous sodium chloride solution (100 mL). The organic layer was dried over sodium sulfate and the dried solution was filtered. The filtrate was concentrated and the residue obtained was purified by flash-column chromatography (eluting with 30% acetone–hexanes) to afford the (14*S*,14'*S*)-dimeric diazofluorene **33** as an orange solid (21.6 mg, 36%).

Note: ^{1}H and ^{13}C NMR data are normalized to the monomeric structure.

R_f = 0.28 (70% ethyl acetate–hexanes; UV). t_R = 2.90. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42 (d, 1H, J = 9.0 Hz, H_1/H_2), 7.22 (d, 1H, J = 9.0 Hz, H_1/H_2), 6.60 (s, 2H, H_{10}), 6.30 (s, 1H, H_8), 5.27 (d, 1H, J = 7.0 Hz, H_3/H_4), 5.24 (s, 1H, H_7), 5.15 (d, 1H, J = 7.0 Hz, H_3/H_4), 4.97–4.93 (m, 2H, H_3/H_4), 3.71 (s, 1H, H_{14}), 3.51 (s, 3H, H_5/H_6), 3.39 (s, 3H, H_5/H_6), 2.97–2.92 (m, 1H, H_{12}), 2.39–2.35 (m, 1H, H_{12}), 2.08 (s, 3H, H_{11}), 1.99 (s, 6H, H_9), 1.13 (t, 3H, J = 7.5 Hz, H_{13}). ^{13}C NMR (125 MHz, $CDCl_3$): 190.4 (C), 178.4 (C), 177.9 (C), 154.1 (C), 153.0 (C), 146.4 (C), 139.3 (C), 138.3 (2 × C), 133.7 (C), 130.6 (2 × C), 127.5 (C), 127.1 (C), 126.8 (C), 125.7 (C), 125.0 (C), 124.8 (C), 122.2 (C), 100.4 (C), 96.7 (C), 96.6 (C), 88.8 (C), 78.2 (C), 71.5 (C), 56.9 (C), 56.8 (C), 54.5 (C), 23.3 (C), 21.2 (C), 20.7 (2 × C), 6.8 (C). IR (ATR-FTIR), cm^{-1}: 2967 (s), 2141 (m), 1686 (m), 1443 (m). HRMS-CI (*m/z*): $[M + H]^+$ calcd for $C_{66}H_{63}N_4O_{18}$, 1199.4137; found, 1199.4136.

(14*S*,14'*S*)-Dimeric Diazofluorene 33:

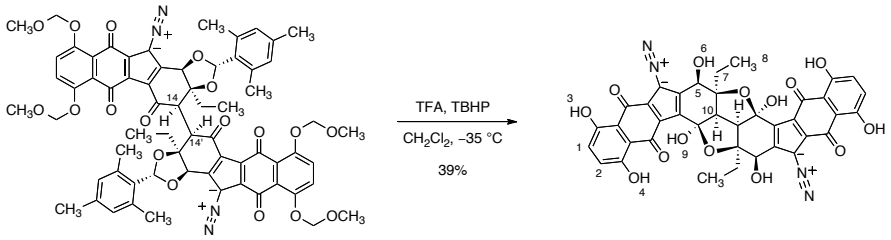


33 (14*S*, 14'*S* dimer)

Table of NMR Data and C–H couplings ($CDCl_3$):

Position	δH	Mult, J-Value	δC	HMBC (H-C)
1	7.42	d, 1H, J = 9.0 Hz	126.8	C_{15}, C_{17}
2	7.22	d, 1H, J = 9.0 Hz	124.8	C_{16}, C_{18}, C_{20}
3	4.97–4.93	m, 2H	96.6	C_5, C_{15}
4	5.27	d, 1H, J = 7.0 Hz	96.7	C_6, C_{16}
4*	5.15	d, 1H, J = 7.0 Hz	96.7	C_6, C_{16}
5	3.51	s, 3H	56.9	C_3
6	3.39	s, 3H	56.8	C_4
7	5.24	s, 1H	71.5	C_8, C_{12}, C_{23}, C_{24}, C_{25}
8	6.30	s, 1H	100.4	C_{28}, C_{29}
9	1.99	s, 3H	20.7	C_{10}/C_{12}, C_{30}, C_{31}/C_{33}
10	6.60	s, 1H	130.6	C_9/C_{13}, C_{31}/C_{33}
11	2.08	s, 3H	21.2	C_{10}/C_{12}, C_{32}
12	2.97–2.22, 2.39–2.35	m, 2H	23.3	C_7, C_{15}, C_{16}, C_{29}
13	1.13	t, 3H, J = 7.5 Hz	6.8	C_{14}, C_{29}
14	3.71	s, 1H	54.5	C_7, C_{16}, C_{27}, C_{28}, C_{29}
15	–	–	153.9	
16	–	–	153.0	
17	–	–	125.7	
18	–	–	122.2	
19	–	–	177.9	
20	–	–	178.4	
21	–	–	138.3	
22	–	–	133.7	
23	–	–	78.2	
24	–	–	146.4	
25	–	–	125.7	
26	–	–	190.4	
27	–	–	88.6	
28	–	–	127.1	
29	–	–	127.5	
30	–	–	139.2	

* C_1, C_3, C_5, C_{15}, C_{17}, C_{19}, and C_{22} are interchangeable with C_2, C_4, C_6, C_{16}, C_{18}, C_{20}, and C_{21}, respectively.



22 (14*R*, 14'*R* dimer) lomaiviticin aglycon (**3**)

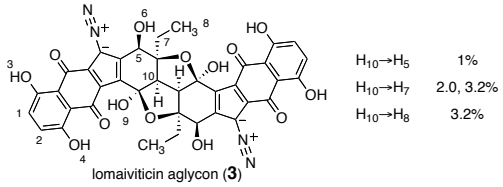
*Deprotection of The (14R,14'R)-Dimeric Diazofluorene **22**:*

A 100-mL round-bottomed flask was charged with a solution of the (14*R*, 14'*R*)-dimeric diazofluorene **22** (10.0 mg, 8.34 μmol, 1 equiv) in 20% dichloromethane–benzene (v/v, 2.0 mL). The solution was concentrated to dryness at 24 °C. The residue obtained was dissolved in dichloromethane (1.2 mL) and solution of anhydrous *tert*-butylhydroperoxide in decane (5.5 M, 400 μL, 2.20 mmol, 264 equiv) was added. The resulting orange, homogeneous mixture was cooled to –35 °C. Trifluoroacetic acid (400 μL, 5.23 mmol, 627 equiv) was then added dropwise over 1 min via syringe to the cold mixture. The reaction mixture was stirred for 13 h at –35 °C. The purple product mixture was cooled to –78 °C (mixture freezes on cooling). Dichloromethane (33 mL) and 0.1 M aqueous sodium phosphate buffer solution (pH 7, 50 mL) were then added in sequence via syringe pump at a rate of 1 mL/min. Upon completion of the addition, the cooling bath was removed and the biphasic mixture was allowed to warm to 21 °C over 1.5 h. The resulting biphasic solution was transferred to a separatory funnel and the layers that formed were separated. The aqueous layer was extracted with dichloromethane (10 mL). The organic layers were combined and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue obtained was purified by PTLC (pre-developed with 100% ethyl acetate, eluting with 100% ethyl acetate followed by 5% methanol–dichloromethane) to afford the lomaiviticin aglycon **3** as a purple solid (2.5 mg, 39%). ***Note:*** The ketone tautomer of lomaiviticin aglycon (**25**) was detected as the major species in solution (LC/MS analysis, t_R = 1.55), but was observed to cyclize upon purification by preparative TLC. A procedure to isolate mixtures containing **25** is described below.

R_f = 0.15 (100% ethyl acetate; UV, ANIS). t_R = 1.26. IR (ATR-FTIR), cm^{-1}: 2922 (s), 2146 (s), 1591 (s), 1445 (s). $[\alpha]_D^{20} = -177°$ (*c* 0.022, $CHCl_3$). HRMS-CI (*m/z*): $[M - OH]^+$ calcd for $C_{38}H_{26}N_4O_{13}$, 745.1418; found, 745.1418. The aglycon **3** is only sparingly soluble in methanol-d_4. NMR spectral data in chloroform-*d*, *N,N*-dimethylformamide-d_7, and 30% *N,N*-dimethylformamide-d_7–methanol-d_4 are provided below.

^{1}H NMR (400 MHz, $CDCl_3$): δ 12.77 (s, 1H, H_3/H_4), 12.62 (s, 1H, H_3/H_4), 7.19 (d, 1H, J = 9.2 Hz, H_1/H_2), 7.15 (d, 1H, J = 9.2 Hz, H_1/H_2), 5.59 (s, 1H, H_9), 4.98 (d, 1H, J = 10.4 Hz, H_5), 3.67 (s, 1H, H_{10}), 2.83 (d, 1H, J = 11.2 Hz, H_6), 2.42–2.36 (m, 1H, H_7), 2.25–2.17 (m, 1H, H_7), 1.20 (t, 3H, J = 7.6 Hz, H_8). ^{13}C NMR (125 MHz, $CDCl_3$): 184.5 (C), 181.5 (C), 158.5 (C), 158.3 (C), 136.7 (C), 132.3 (C), 129.6 (CH), 129.3 (CH), 127.6 (C), 126.9 (C), 112.9 (C), 112.5 (C), 99.4 (C), 88.6 (C), 68.5 (CH), 61.9 (CH), 32.1 (CH_2), 9.8 (CH_3). *The diazo carbon was not observed due to co-resonance with the residual chloroform peak; this carbon atom was observed at 78.9 in d_7-DMF (vide infra).

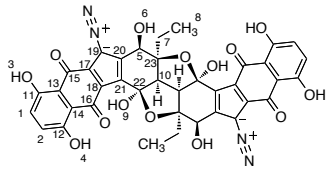
The following NOEs were observed on irradiation of H-10 ($CDCl_3$):



^{1}H NMR (400 MHz, d_7-DMF): δ 13.27 (s, 1H, H_3/H_4), 12.27 (s, 1H, H_3/H_4), 7.25 (d, 1H, J = 7.2 Hz, H_1/H_2), 7.18 (d, 1H, J = 7.6 Hz, H_1/H_2), 6.46 (s, 1H, H_9), 4.94 (d, 1H, J = 7.6 Hz, H_6), 4.69 (d, 1H, J = 7.6 Hz, H_5), 3.30 (s, 1H, H_{10}), 2.04–1.97 (m, 1H, H_7), 1.93–1.89 (m, 1H, H_7), 1.03 (t, 3H, J = 6.0 Hz, H_8). ^{13}C NMR (125 MHz, d_7-DMF): 184.3 (C), 181.9 (C), 159.1 (C), 158.6 (C), 142.0 (C), 131.4 (C), 130.9 (CH), 130.7 (CH), 129.6 (C), 127.9 (C), 114.2 (C), 113.4 (C), 102.7 (C), 90.1 (C), 78.9 (C), 70.3 (CH), 61.9 (CH), 31.4 (determined indirectly by HMBC, CH_2), 10.1 (CH_3).

^{1}H NMR [500 MHz, 30% d_7-DMF–CD_3OD (v/v)]: δ 7.30 (d, 1H, J = 9.5 Hz, H_1/H_2), 7.27 (d, 1H, J = 9.5 Hz, H_1/H_2), 4.81 (s, 1H, H_5), 3.41 (s, 1H, H_{10}), 2.16–2.05 (m, 2H, H_7), 1.20 (t, 3H, J = 7.5 Hz, H_8). ^{13}C NMR [125 MHz, 30% d_7-DMF–CD_3OD (v/v)]: 184.8 (C), 182.4 (C), 159.1 (C), 158.7 (C), 141.8 (C), 132.2 (C), 130.6 (CH), 130.4 (C), 129.6 (CH), 128.1 (C), 114.6 (C), 113.7 (C), 102.9 (C), 90.6 (C), 70.4 (CH), 62.1 (CH), 31.5 (determined indirectly by HMQC, CH_2), 10.0 (CH_3).

Lomaiviticin Aglycon (3):

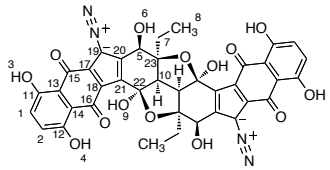


lomaiviticin aglycon (**3**)

Table of NMR Data and C–H couplings ($CDCl_3$):

Position	δH	Mult, J-Value	δC	HMBC $_{(H-C)}$
1	7.19	d, 1H, J = 9.2 Hz	129.6	C_{11}, C_{13}
2	7.15	d, 1H, J = 9.2 Hz	129.3	C_{12}, C_{14}
3	12.77	s, 1H	–	C_1, C_{11}, C_{13}
4	12.62	s, 1H	–	C_2, C_{12}, C_{14}
5	4.98	d, 1H, J = 11.2 Hz	68.5	–
6	2.83	d, 1H, J = 10.4 Hz	–	–
7	2.42–2.36	m, 1H	32.1	C_5, C_8, C_{10}, C_{23}
7*	2.25–2.17	m, 1H	32.1	C_5, C_8, C_{10}, C_{23}
8	1.20	t, 3H, J = 7.6 Hz	9.8	C_7, C_{23}
9	5.59	s, 1H	–	C_{10}, C_{22}
10	3.67	s, 1H	61.9	C_{10}, C_{22}
11	–	–	158.5	
12	–	–	158.3	
13	–	–	112.9	
14	–	–	112.5	
15	–	–	184.5	
16	–	–	181.5	
17	–	–	132.3	
18	–	–	127.6	
19	–	–	–	
20	–	–	136.7	
21	–	–	126.9	
22	–	–	99.4	
23	–	–	88.6	

Lomaiviticin Aglycon (3):

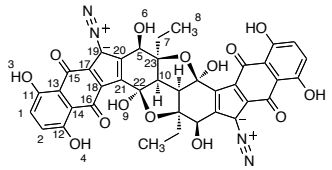


lomaiviticin aglycon (**3**)

Table of NMR Data and C–H couplings (d_7-DMF):

Position	δH	Mult, J-Value	δC	HMBC $_{(H-C)}$
1	7.25	d, 1H, J = 7.2 Hz	129.6	C_{11}, C_{13}
2	7.18	d, 1H, J = 7.6 Hz	127.9	C_{12}, C_{14}
3	13.27	s, 1H	–	C_1, C_{11}, C_{13}
4	12.27	s, 1H	–	C_2, C_{12}, C_{14}
5	4.69	d, 1H, J = 7.6 Hz	70.3	C_{20}, C_{21}
6	4.94	d, 1H, J = 7.6 Hz	–	C_5, C_{23}, C_{20}
7	2.04–1.97	m, 1H	31.4	C_8, C_{23}
7*	1.93–1.89	m, 1H	31.4	C_8, C_{23}
8	1.03	t, 3H, J = 6.0 Hz	10.1	C_7, C_{23}
9	6.46	s, 1H	–	C_{10}, C_{21}, C_{22}
10	3.30	s, 1H	61.9	C_7, C_{10}, C_{21}, C_{22}
11	–		159.1	
12	–		158.6	
13	–	–	114.2	
14	–	–	113.4	
15	–	–	184.3	
16	–	–	181.9	
17	–	–	130.9	
18	–	–	130.7	
19	–	–	78.9	
20	–	–	142.0	
21	–	–	131.4	
22	–	–	102.7	
23	–	–	90.1	

Lomaiviticin Aglycon (3):



lomaiviticin aglycon (**3**)

Table of NMR Data and C–H couplings (30% d_7-DMF–CD_3OD):

Position	δH	Mult, J-Value	δC	HMBC (H-C)
1	7.30	d, 1H, J = 9.5 Hz	130.6	C_{11}, C_{13}
2	7.27	d, 1H, J = 9.5 Hz	129.6	C_{12}, C_{14}
3	–	s, 1H	–	–
4	–	s, 1H	–	–
5	4.81	s, 1H	70.4	C_{20}, C_{21}
6	–	–	–	–
7	2.16–2.05	m, 2H	31.5	–
8	1.20	t, 3H, J = 7.5 Hz	10.0	C_7, C_{23}
9	–	–	–	–
10	3.41	s, 1H	62.1	C_7, C_{10}, C_{21}, C_{22}
11	–		159.1	
12	–		158.7	
13	–	–	114.6	
14	–	–	113.7	
15	–	–	184.8	
16	–	–	182.4	
17	–	–	130.4	
18	–	–	128.1	
19	–	–	–	
20	–	–	141.8	
21	–	–	132.2	
22	–	–	102.9	
23	–	–	90.6	

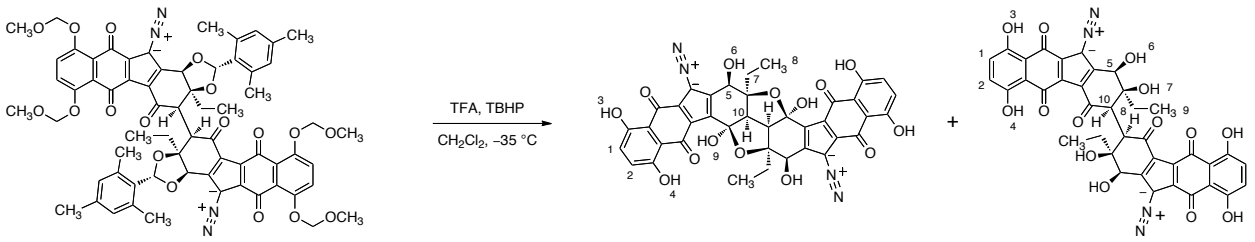
Comparison of lomaiviticin aglycon (**3**) and lomaiviticin B (**2**). Data for **2** taken from ref. 13. Note: The aglycon **3** is only sparingly soluble in methanol-d_4.

Comparison of ^{1}H NMR Data

Posn (this work)	Posn (ref. 13)	Lomaiv B (CD_3OD)	**3** (d_7-DMF)	**3** ($CDCl_3$)	**3** (30% d_7-DMF–CD_3OD)
10	2	2.64 (br s)	3.3 (s)	3.67 (s)	3.41 (s)
5	4	4.99 (br s)	4.69 (s)	4.98 (s)	4.81 (s)
1	8	7.23 (br s)	7.25 (d, 7.2)	7.19 (d, 9.2)	7.3 (d, 9.5)
2	9	7.22 (br s)	7.18 (d, 7.6)	7.15 (d, 9.2)	7.27 (d, 9.5)
7	12	1.82 (m)	2.04–1.97 (m)	2.42–2.36 (m)	2.16–2.05 (m)
7*	12	1.70 (m)	1.93–1.89 (m)	2.25–2.17 (m)	2.16–2.05 (m)
8	13	0.93 (t, 7)	1.03 (t, 6.0)	1.2 (t, 7.6)	1.2 (t, 7.5)

Comparison of ^{13}C NMR Data

Posn (this work)	Posn (ref. 13)	Lomaiv B (CD_3OD)	**3** (d_7-DMF)	**3** ($CDCl_3$)	**3** (30% d_7-DMF–CD_3OD)
22	1	96.5	102.7	99.4	102.9
10	2	44	61.9	61.9	62.1
23	3	78	90.1	88.6	90.6
5	4	78.1	70.3	68.5	70.4
20	4a	141.7	142	136.7	141.8
19	5	76.1	78.9	not obs.	not obs.
17	5a	133.4	130.9	132.3	130.4
15	6	186.2	184.3	184.5	184.8
13	6a	114.3	114.2	112.9	114.6
11	7	159.3	159.1	158.5	159.1
1	8	130.1	129.6	129.6	130.6
2	9	130.4	127.9	129.3	129.6
12	10	159.2	158.6	158.3	158.7
14	10a	114.5	113.4	112.5	113.7
16	11	183.6	181.9	181.5	182.4
18	11a	130.3	130.7	127.6	128.1
21	11b	125.1	131.4	126.9	132.2
7	12	25.5	31.4	32.1	31.5
8	13	7.5	10.1	9.8	10



*Procedure To Obtain Mixtures of Lomaiviticin Aglycon (**3**) And The Ketone Tautomer **25**:*

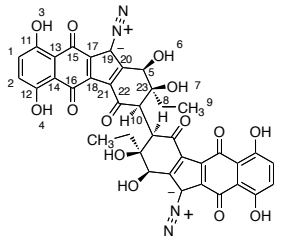
Mixtures of lomaiviticin aglycon (**3**) and the ketone tautomer **25** were isolated when the reaction mixture, obtained as described above, was purified in the following manner:

The unpurified reaction mixture was redissolved in dichloromethane (500 μL) and loaded onto a 4-g cartridge of silica gel (Silia*Sep*® HP flash cartridge, 15–40 μm, 60 Å, purchased from Silicycle, Inc, Quebec, CA). The sample was purified using a Biotage Isolera purification system, eluting with a linear gradient of 1% methanol–dichloromethane→10% methanol–dichloromethane over 14 column volumes at a flow rate of 12 mL/min. Samples purified in this manner contained a mixture of **25**:**3** in variable ratios (10:1–2:1). The ketone tautomer of lomaiviticin aglycon (**25**) was observed to convert to lomaiviticin aglycon (**3**) on standing in chloroform-*d* at 24 °C. Selected NMR data are shown below. Analytically pure samples of **25** could not be obtained owing to its facile conversion to **3**.

Ketone Tautomer of Lomaiviticin Aglycon (**25**):

t_R = 1.55. ^{1}H NMR (500 MHz, $CDCl_3$): δ 12.94 (s, 1H, H_3/H_4), 12.43 (s, 1H, H_3/H_4), 7.15–7.12 (m, 2H, H_1/H_2), 6.09 (s, 1H, H_7), 5.11 (d, 1H, J = 11.0 Hz, H_5), 3.35 (s, 1H, H_{10}), 2.26–2.21 (m, 1H, H_8), 2.09–2.02 (m, 1H, H_8), 1.13 (t, 3H, J = 7.5 Hz, H_9). HRMS-CI (*m/z*): [M + H]+ calcd for $C_{38}H_{27}N_4O_{14}$, 763.1524; found, 763.1526.

Ketone Tautomer of Lomaiviticin Aglycon (25):



25

Table of NMR Data and C–H couplings ($CDCl_3$):

Position	δH	Mult, J-Value	δC (determined indirectly via HMBC and HMQC experiments)	HMBC $_{(H\text{–}C)}$
1	7.15–7.12	m, 1H	130.4	C_{11}
2	7.15–7.12	m, 1H	130.4	C_{12}
3	12.94	s, 1H	–	C_1, C_{11}, C_{13}
4	12.43	s, 1H	–	C_2, C_{12}, C_{14}
5	5.11	d, 1H, J = 11.0 Hz	68.4	–
6	–	–	–	–
7	6.09	s, 1H	–	–
8	2.26–2.21	m, 1H	33.3	C_9, C_{10}, C_{23}
8*	2.09–2.02	m, 1H	33.3	C_9, C_{10}, C_{23}
9	1.13	t, 3H, J = 7.5 Hz	9.3	C_8, C_{23}
10	3.35	s, 1H	52.7	C_{10}, C_{22}, C_{23}
11	–	–	158.4	
12	–	–	158.4	
13	–	–	112.7	
14	–	–	112.7	
22	–	–	191.7	
23	–	–	77.1	

* C_1, C_3, C_{11}, C_{13} are interchangeable with C_2, C_4, C_{12}, C_{14} respectively.

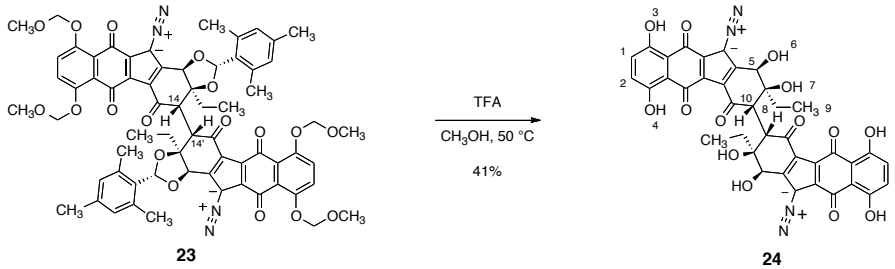
Comparison of the ketone tautomer of lomaiviticin aglycon (**25**) and lomaiviticin A (**1**). Data for **1** taken from ref. 13. Partial ^{13}C NMR data was obtained for the ketone tautomer of lomaiviticin aglycon (**25**) by HMBC and HMQC experiments.

Comparison of ^{1}H NMR Data

Posn (this work)	Posn (ref. 13)	Lomaiv A (**1**) (CD_3OD)	**25** ($CDCl_3$)
10	2	4.00 (br s)	3.35 (s)
5	4	5.33 (br s)	5.11 (s)
	8	7.24 (d, 9.4)	7.15–7.12
1			(m)
	9	7.16 (d, 9.4)	7.15–7.12
2			(m)
	12	2.21 (m)	2.26–2.21
8			(m)
	12	2.12 (m)	2.09–2.02
8*			(m)
9	13	1.24 (t, 7)	1.3 (t, 7.5)

Comparison of ^{13}C NMR Data

Posn (this work)	Posn (ref. 13)	Lomaiv A (**1**) (CD_3OD)	**25** ($CDCl_3$)
22	1	198.4	191.7
10	2	47.6	52.7
23	3	83.6	77.1
5	4	67.3	68.4
13	6a	113.4	112.7
11	7	160.4	158.4
1	8	131.1	130.4
2	9	131.3	130.4
12	10	159.4	158.4
14	10a	114.4	112.7
8	12	29.9	33.3
9	13	9.6	9.3



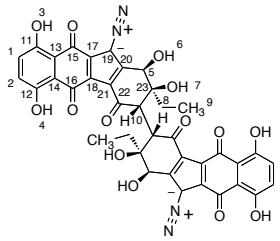
*Deprotection of The (14S,14'S)-Dimeric Diazofluorene **23**:*

Trifluoroacetic acid (300 μL, 20% v/v) was added to a stirred solution of the (14*S*,14'*S*)-dimeric diazofluorene **23** (15.0 mg, 12.5 μmol, 1 equiv) in methanol (1.6 mL) at 24 °C. The resulting mixture was placed in an oil bath that had been preheated to 50 °C. The reaction mixture was stirred and heated for 2 h at 50 °C. The product mixture was cooled to 24 °C, and the cooled solution was concentrated to dryness under a stream of nitrogen. The residue obtained was dissolved in methanol (2 mL) and *N,N*-dimethylformamide (1 mL). The diluted reaction mixture was loaded directly onto a column of reverse phase silica gel. The mixture was eluted using acetonitrile–water (10% acetonitrile–water initially, grading to 50% acetonitrile–water, one step) to afford the (10*S*, 10'*S*)-lomaiviticin aglycon diastereomer **24** as a purple solid (3.9 mg, 41%).

Note: ^{1}H and ^{13}C NMR data are normalized to the monomeric structure.

R_f = 0.43 (5% methanol–dichloromethane; UV). t_R = 0.98. ^{1}H NMR (500 MHz, d_7-DMF): δ 13.22 (s, 1H, H_3/H_4), 12.10 (s, 1H, H_3/H_4), 7.25 (d, 1H, J = 9.5 Hz, H_1/H_2), 7.13 (d, 1H, J = 9.5 Hz, H_1/H_2), 6.19 (d, 1H, J = 9.0 Hz, H_6), 5.26 (d, 1H, J = 9.0 Hz, H_5), 4.91 (s, 1H, H_7), 3.12 (s, 1H, H_{10}), 2.27–2.22 (m, 1H, H_{14}), 2.02–1.97 (m, 1H, H_{14}), 1.09 (t, 3H, J = 7.5 Hz, H_9). ^{13}C NMR (125 MHz, $CDCl_3$): 193.4 (C), 183.2 (C), 182.2 (C), 159.3 (C), 158.5 (C), 151.2 (C), 132.9 (C), 130.9 (CH), 129.8 (CH), 127.9 (C), 127.4 (C), 113.8 (C), 112.7 (C), 81.4 (C), 80.2 (C), 69.6 (CH), 60.1 (CH), 28.1 (CH_2), 7.8 (CH_3). IR (ATR-FTIR), cm^{-1}: 2922 (s), 2152 (m), 1661 (m), 1445 (m). HRMS-CI (*m/z*): [M + H]+ calcd for $C_{38}H_{27}N_4O_{14}$, 763.1524; found, 763.1522.

(10*S*, 10'*S*)-Lomaiviticin Aglycon Diastereomer 24:

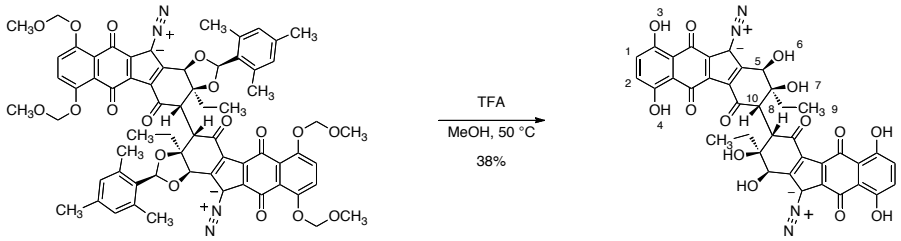


24

Table of NMR Data and C–H couplings (d_7-DMF):

Position	δH	Mult, J-Value	δC	HMBC $_{(H-C)}$
1	7.25	d, 1H, J = 9.5 Hz	130.9	C_{11}, C_{13}
2	7.13	d, 1H, J = 9.5 Hz	129.8	C_{12}, C_{14}
3	13.22	s, 1H	–	C_1, C_{11}, C_{13}
4	12.10	s, 1H	–	C_2, C_{12}, C_{14}
5	5.26	d, 1H, J = 9.0 Hz	69.6	C_{20}, C_{21}
6	6.19	d, 1H, J = 9.0 Hz	–	C_5, C_{20}
7	4.91	s, 1H	–	C_5, C_{10}, C_{23}
8	2.27–2.22	m, 1H	28.1	C_5, C_9, C_{10}, C_{23}
8*	2.02–1.97	m, 1H	28.1	C_5, C_9, C_{10}, C_{23}
9	1.09	t, 3H, J = 7.5 Hz	7.8	C_8, C_{19}
10	3.12	s, 1H	60.1	C_5, C_{10}, C_{19}, C_{21}, C_{22}
11	–	–	159.5	
12	–	–	158.5	
13	–	–	113.8	
14	–	–	112.7	
15	–	–	183.2	
16	–	–	182.2	
17	–	–	132.9	
18	–	–	127.9	
19	–	–	80.2	
20	–	–	151.2	
21	–	–	127.4	
22	–	–	193.4	
23	–	–	81.4	

* C_1, C_3, C_{11}, C_{13}, C_{15}, C_{17} are interchangeable with C_2, C_4, C_{12}, C_{14}, C_{16}, C_{18} respectively.



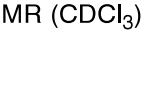
33 24

*Deprotection of The (14S,14'S)-Endo-mesityl-dimeric Diazofluorene **33**:*

Trifluoroacetic acid (360 μL, 20% v/v) was added to a stirred solution of the (14*S*,14'*S*)-*endo*-mesityl-dimeric diazofluorene **33** (21.6 mg, 18.0 μmol, 1 equiv) in methanol (1.8 mL) at 24 °C. The resulting mixture was placed in an oil bath that had been preheated to 50 °C. The reaction mixture was stirred and heated for 4 h at 50 °C. The product mixture was cooled to 24 °C and the cooled solution was concentrated to dryness under a stream of nitrogen. The residue obtained was dissolved in a mixture of methanol-, and was purified by elution over a column of reverse phase silica gel (eluting with 10% acetonitrile–water initially, grading to 50% acetonitrile–water, one step) to afford the (10*S*, 10'*S*)-lomaiviticin aglycon diastereomer **24** as a purple solid (5.2 mg, 38%). ^{1}H NMR and UPLC/MS data of **24** obtained in this manner were indistinguishable from the product obtained by deprotection of the (14*S*,14'*S*)-dimeric diazofluorene **23** (vide supra).

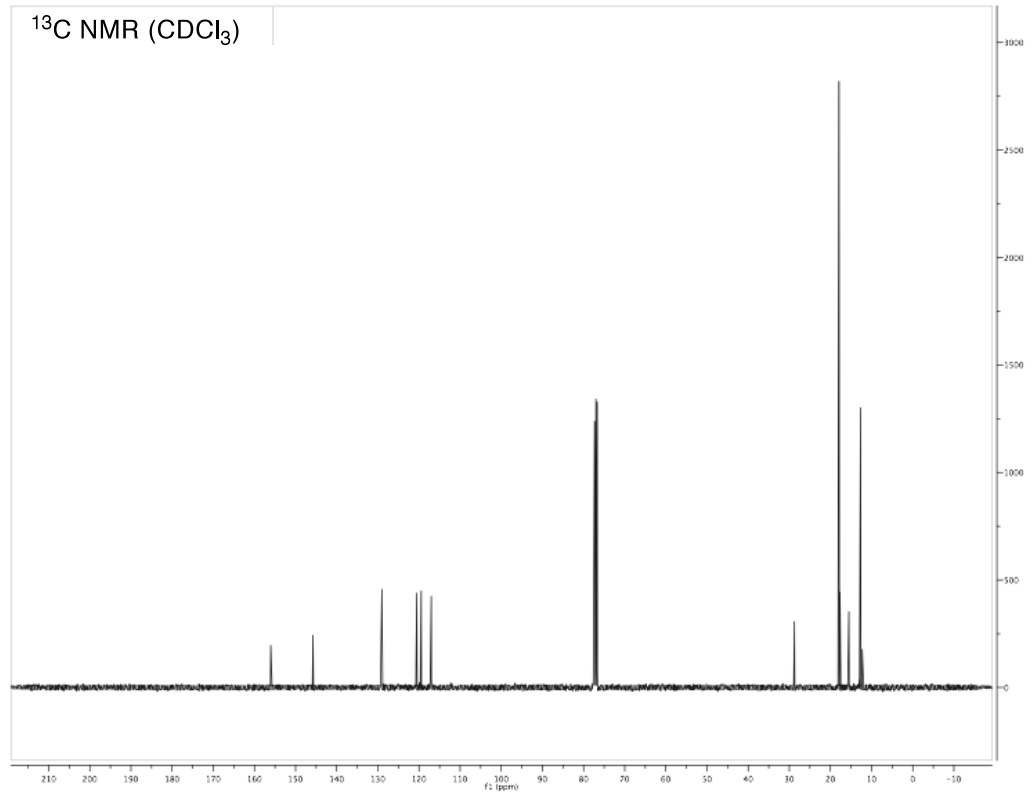
Catalog of Nuclear Magnetic Resonance and Infrared Spectra

^{1}H NMR ($CDCl_3$)

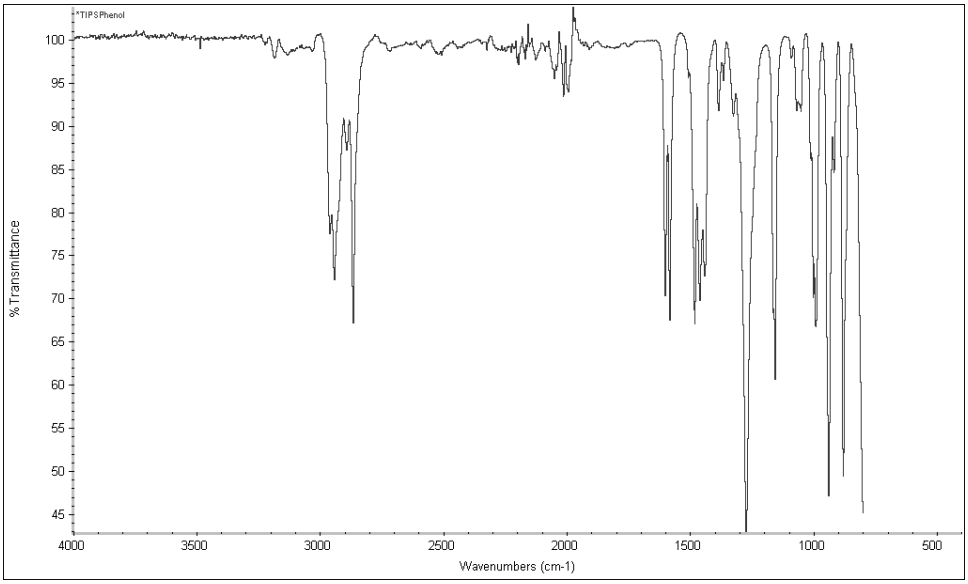


10

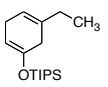
^{13}C NMR ($CDCl_3$)



IR

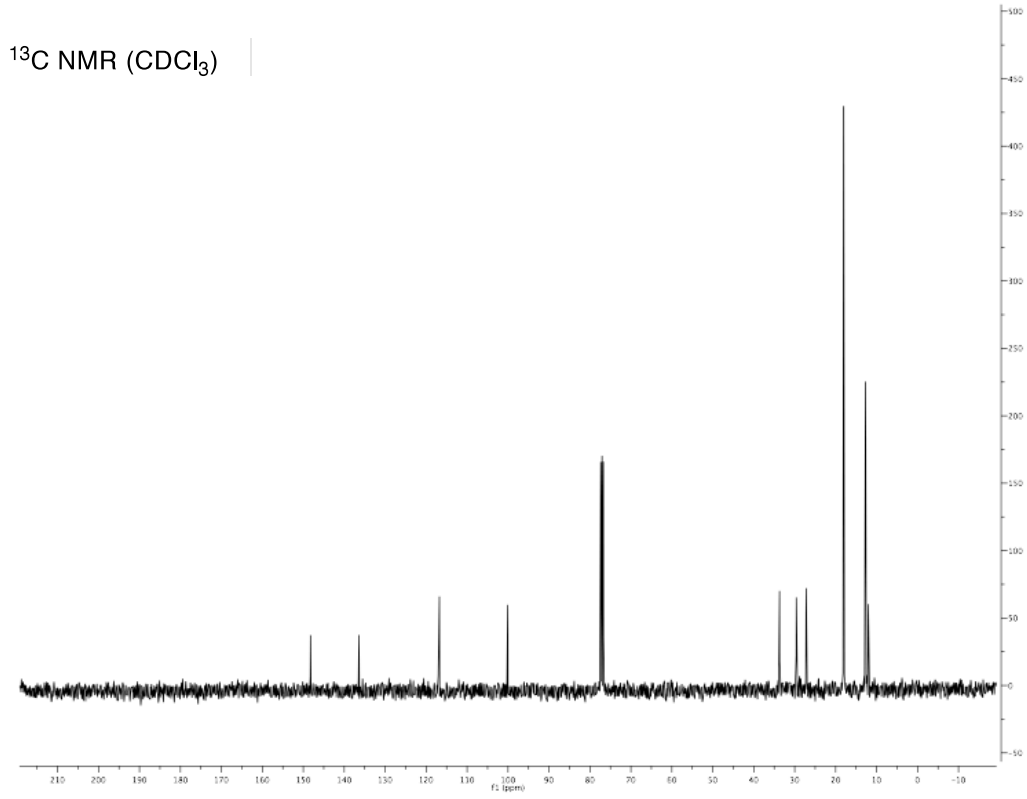

*TIPSPhenol
% Transmittance
100
95
90
85
80
75
70
65
60
55
50
45
4000
3500
3000
2500
2000
1500
1000
500
Wavenumbers (cm-1)

^{1}H NMR ($CDCl_3$)

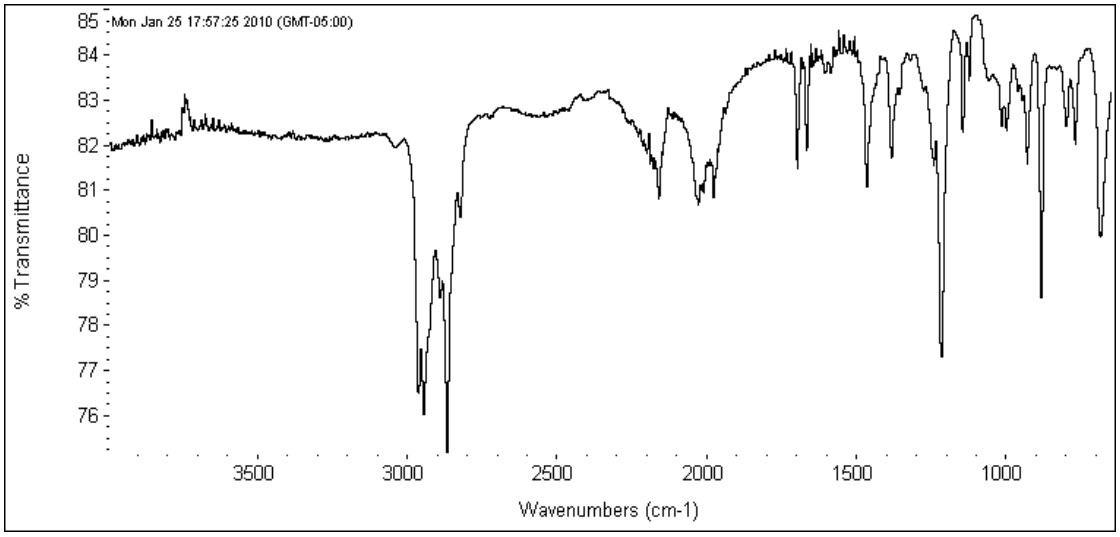


27

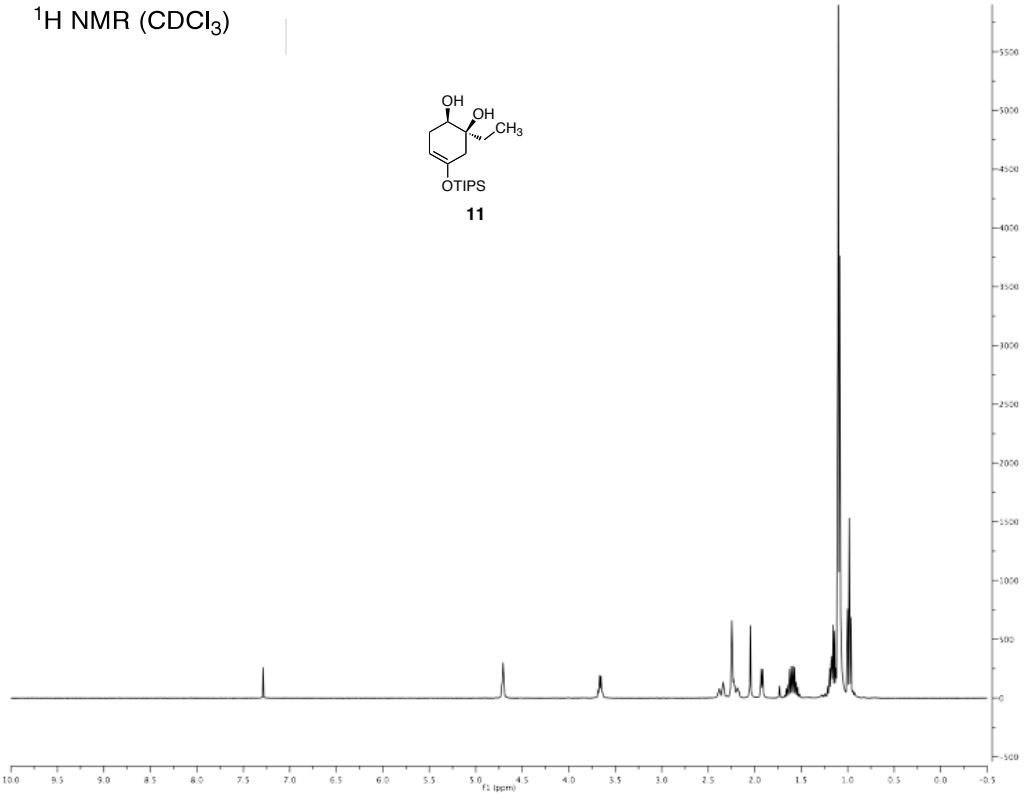
^{13}C NMR ($CDCl_3$)



IR

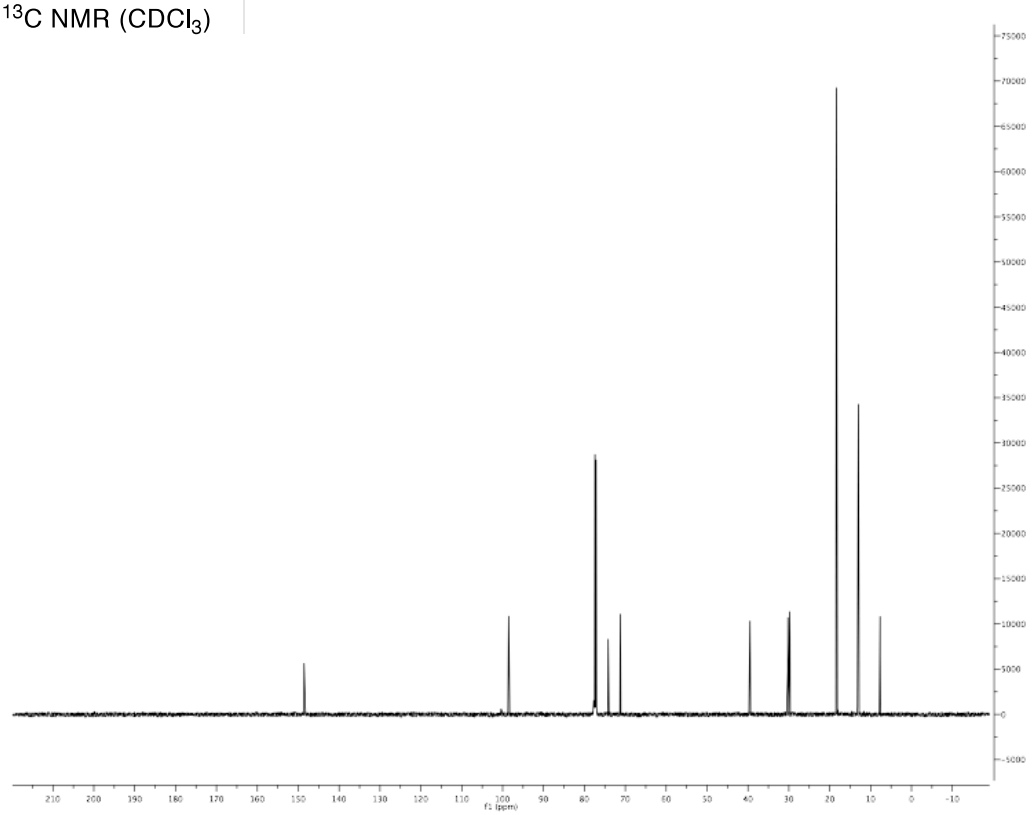

Mon Jan 25 17:57:25 2010 (GMT-05:00)
% Transmittance
85
84
83
82
81
80
79
78
77
76
3500
3000
2500
2000
1500
1000
Wavenumbers (cm-1)

^{1}H NMR ($CDCl_3$)

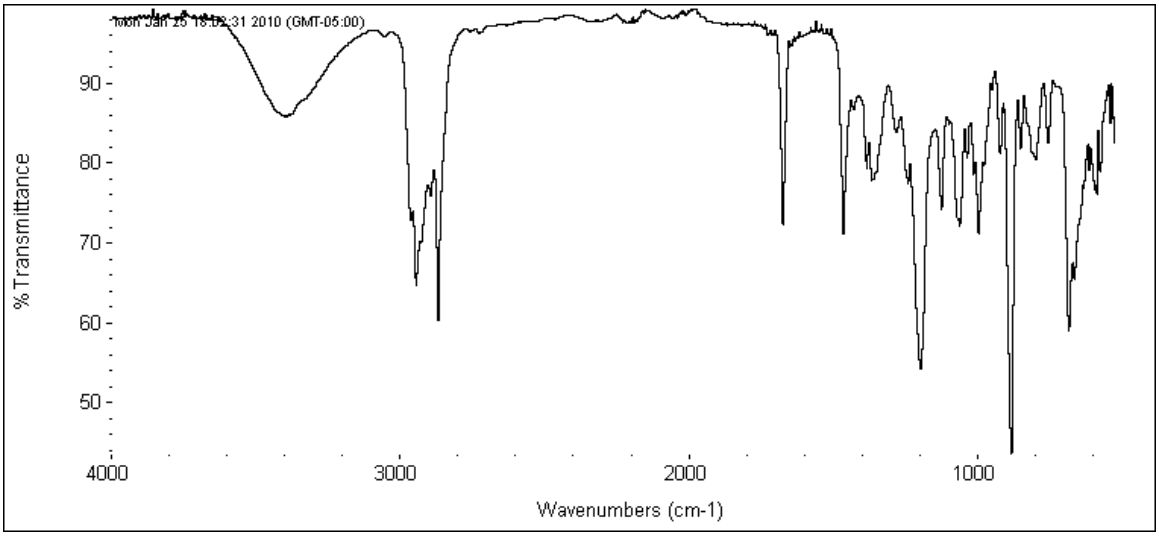


11

^{13}C NMR ($CDCl_3$)



IR


% Transmittance
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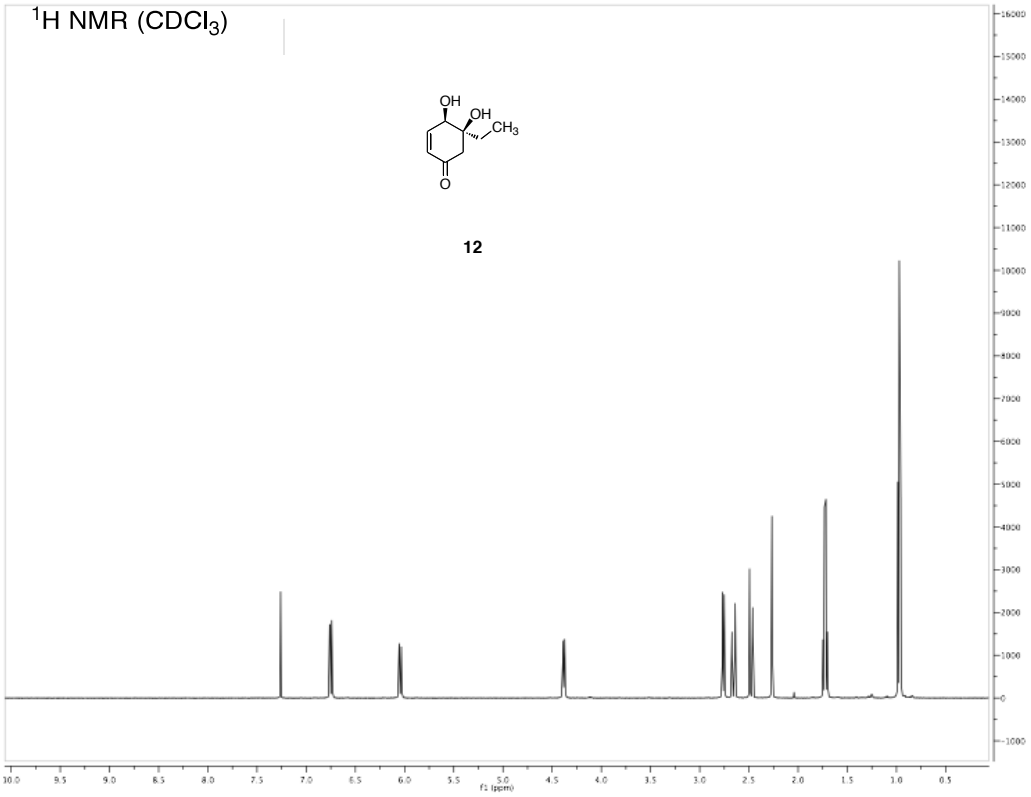
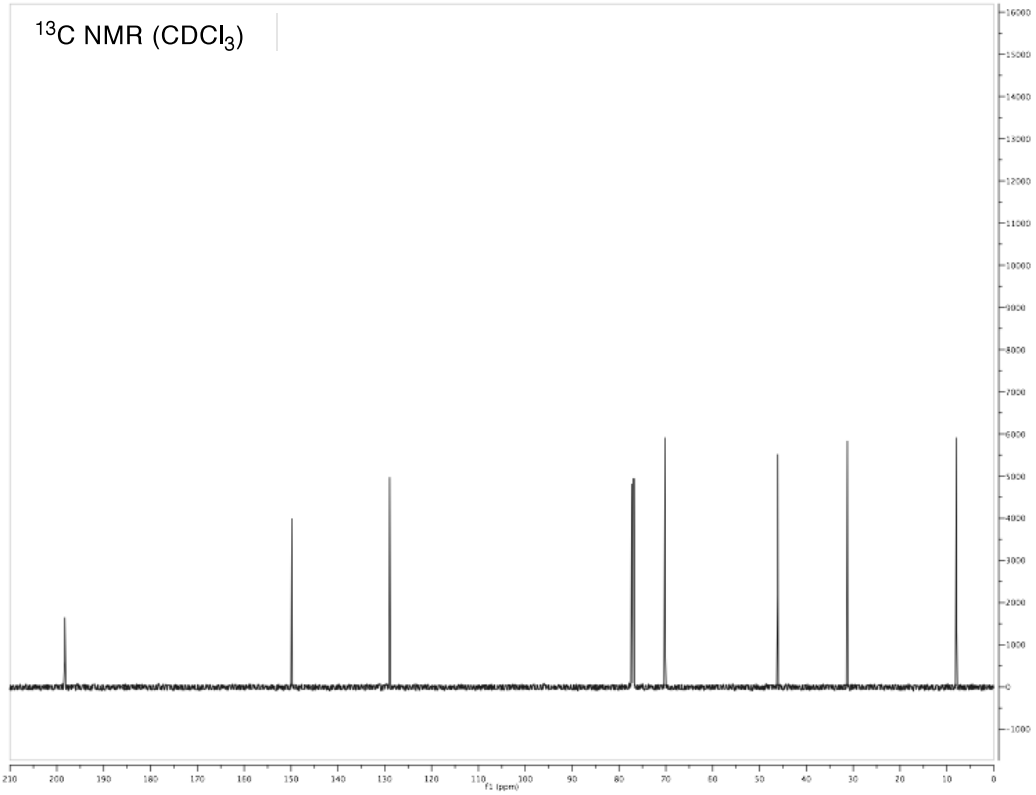
80
70
60
50
4000
3000
2000
1000
Wavenumbers (cm-1)

^{1}H NMR ($CDCl_3$)

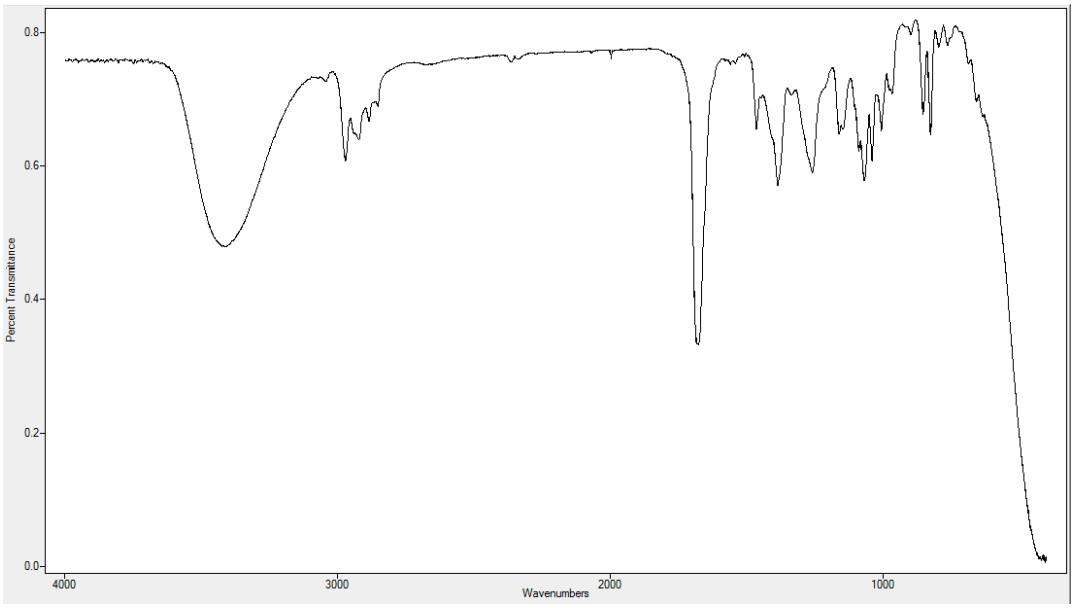


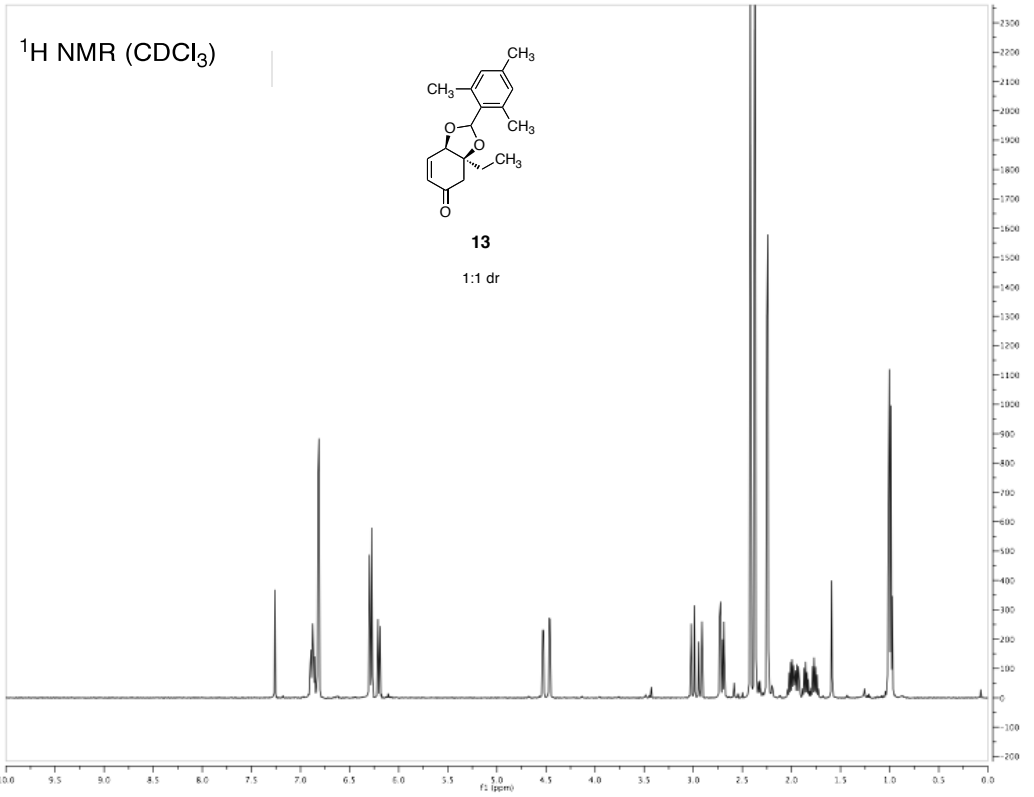
12

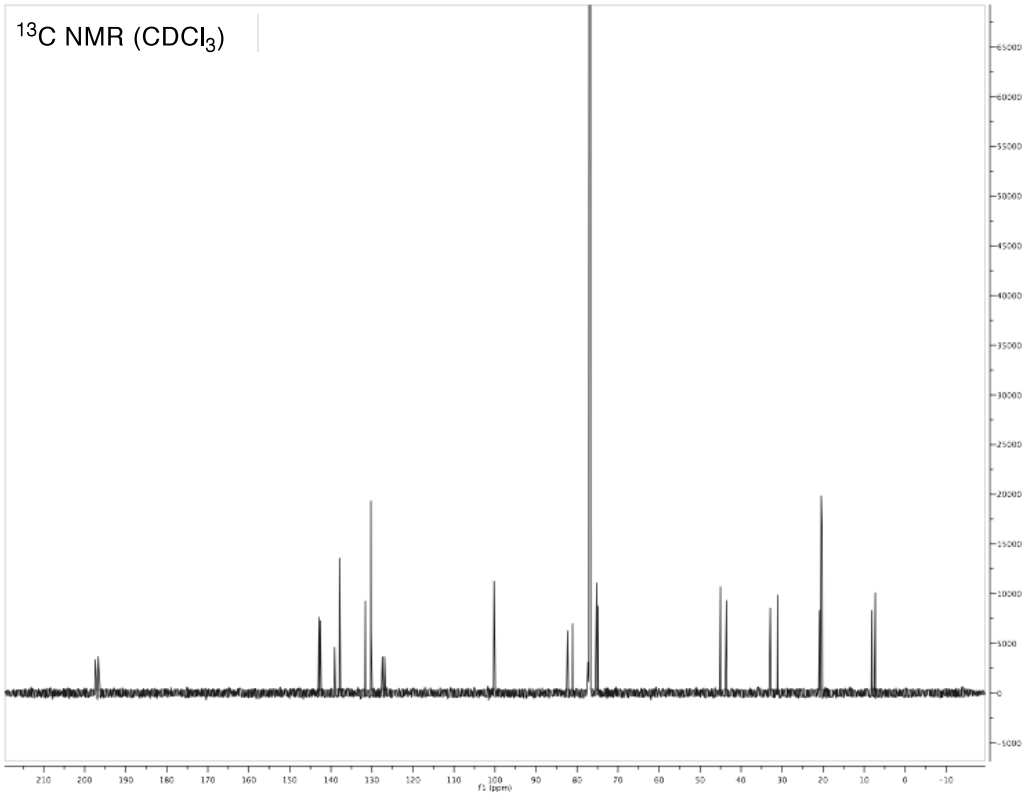


^{13}C NMR ($CDCl_3$)

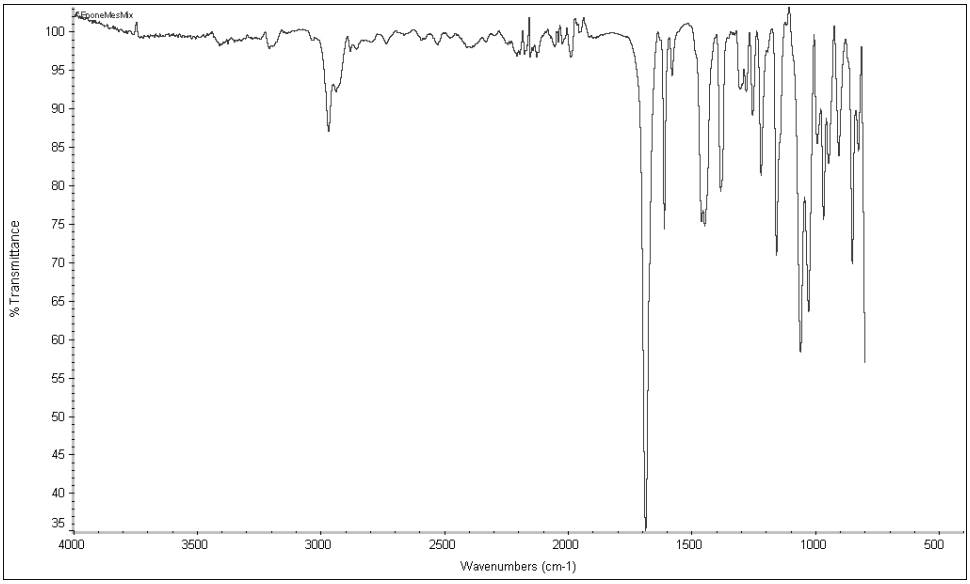
IR


0.8
0.6
0.4
0.2
0.0
Percent Transmittance
4000
3000
2000
1000
Wavenumbers

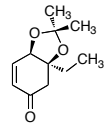

^{1}H NMR ($CDCl_3$)
CH3
CH3
CH3
O
O
CH3
O
13
1:1 dr


^{13}C NMR ($CDCl_3$)

IR

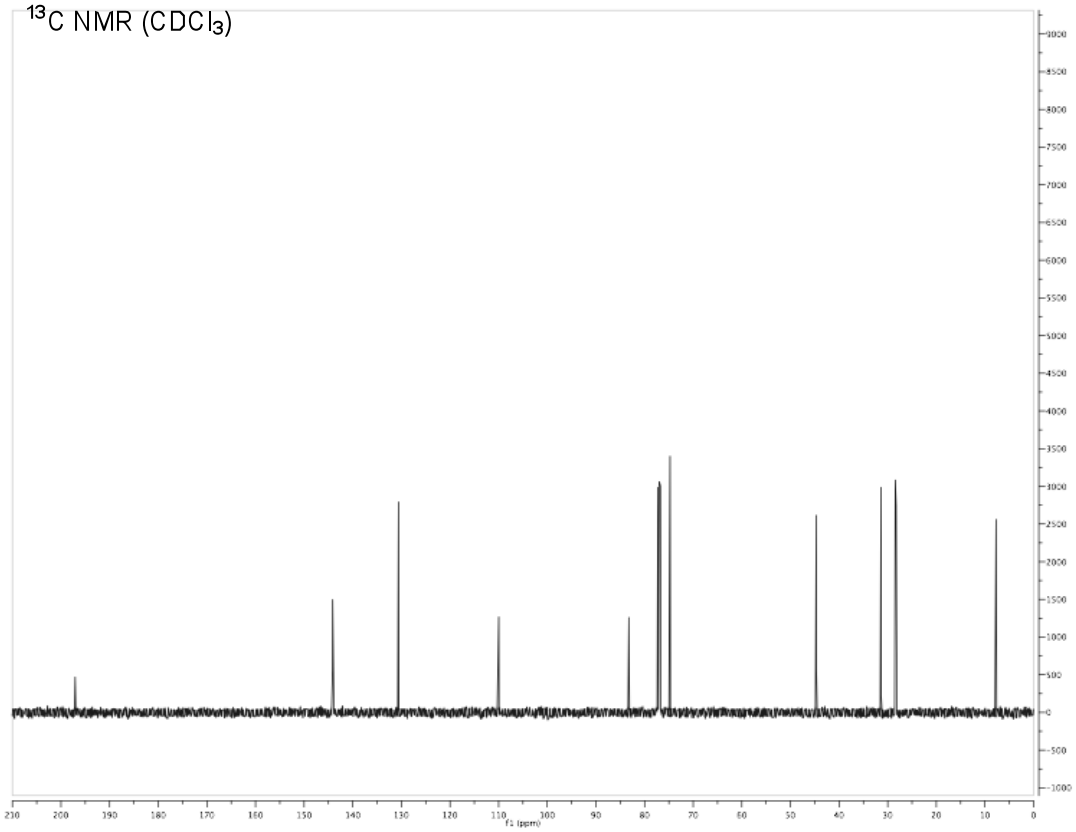

%Transmittance
Wavenumbers (cm-1)
4000
3500
3000
2500
2000
1500
1000
500

^{1}H NMR ($CDCl_3$)

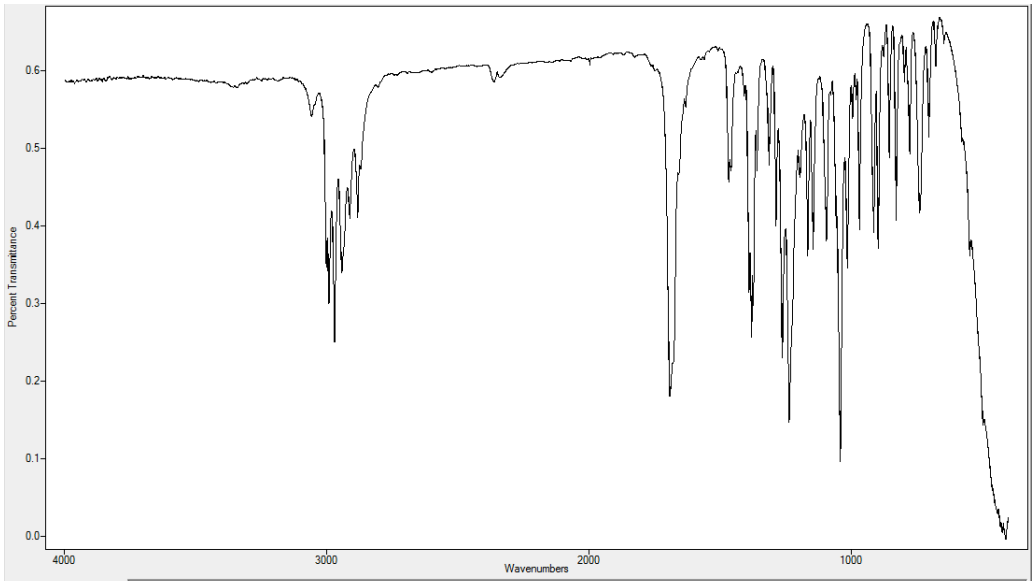


28

^{13}C NMR ($CDCl_3$)



IR


Percent Transmittance
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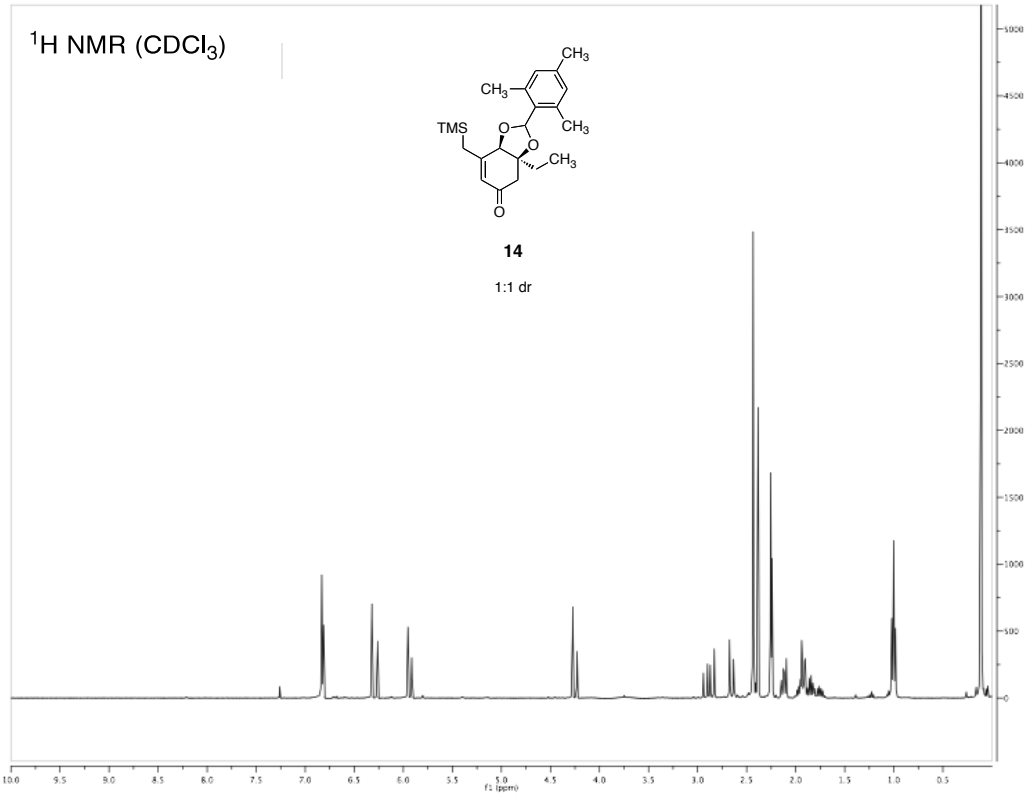
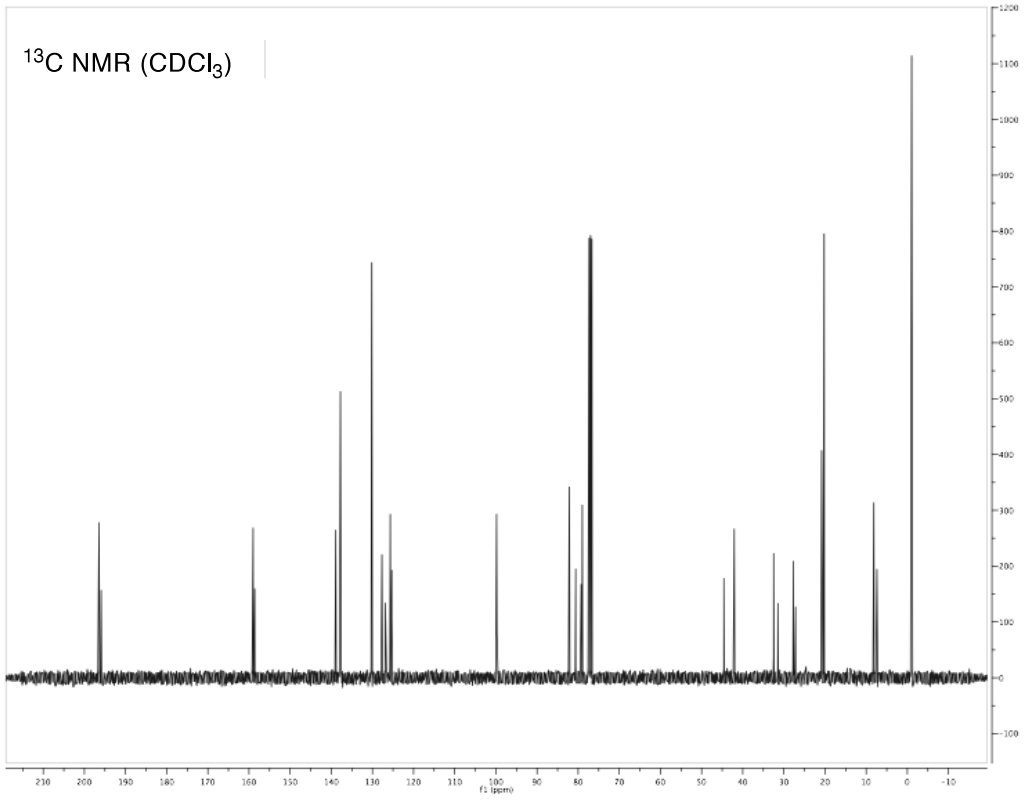
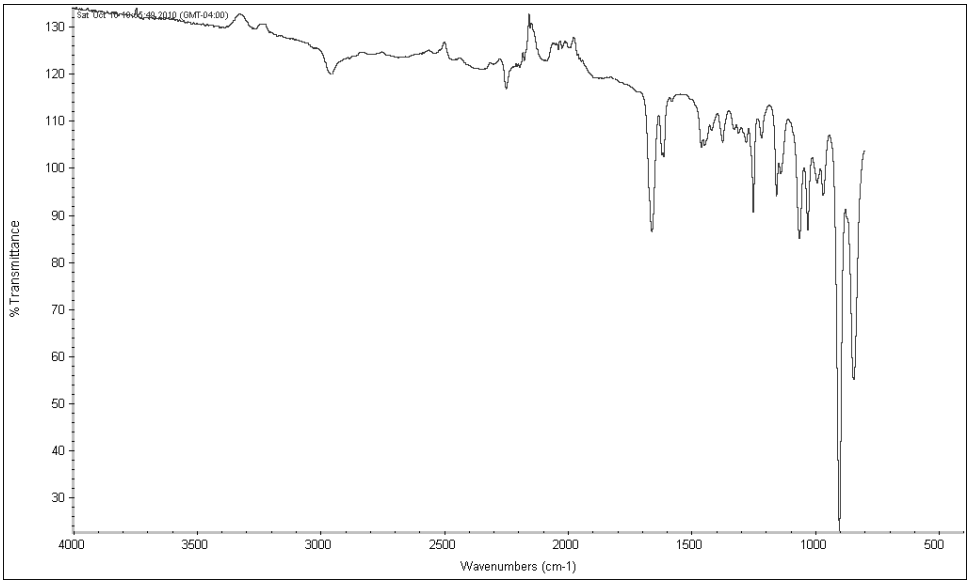
0.3
0.2
0.1
0.0
4000
3000
2000
1000
Wavenumbers


^{1}H NMR ($CDCl_3$)
TMS
O
O
O
CH_3
CH_3
CH_3
CH_3
14
1:1 dr


^{13}C NMR ($CDCl_3$)

IR


% Transmittance
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120
110
100
90
80
70
60
50
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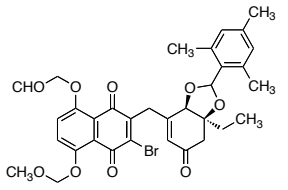
30
4000
3500
3000
2500
2000
1500
1000
500
Wavenumbers (cm-1)

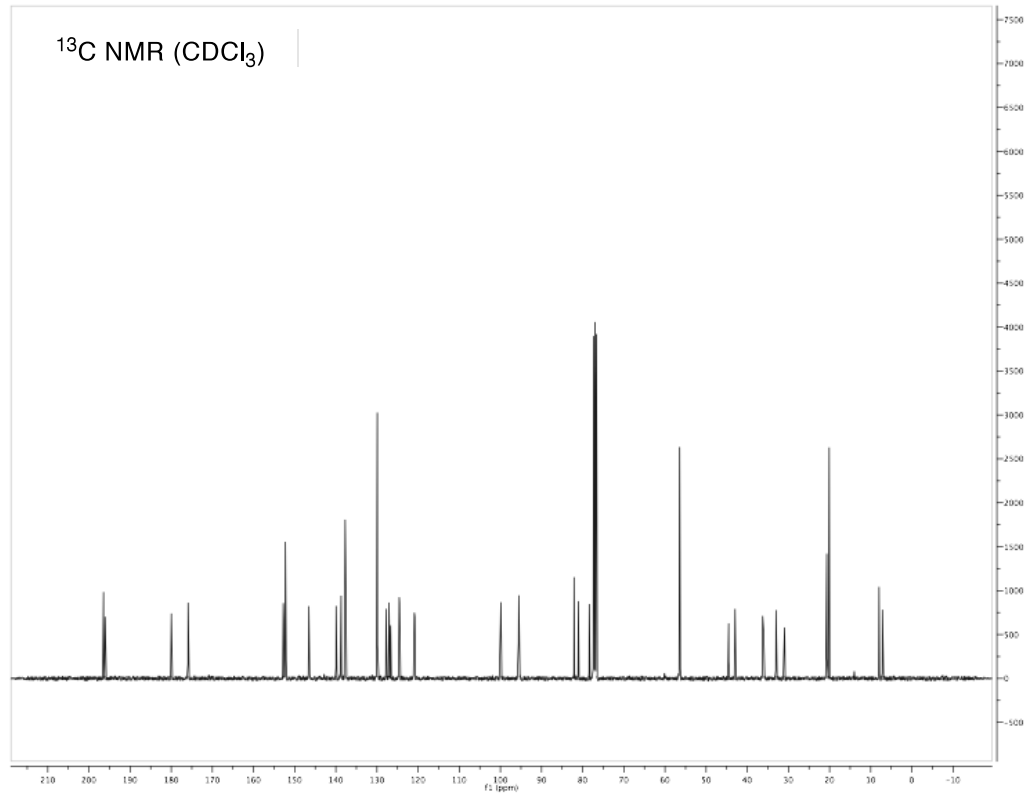
^{1}H NMR ($CDCl_3$)



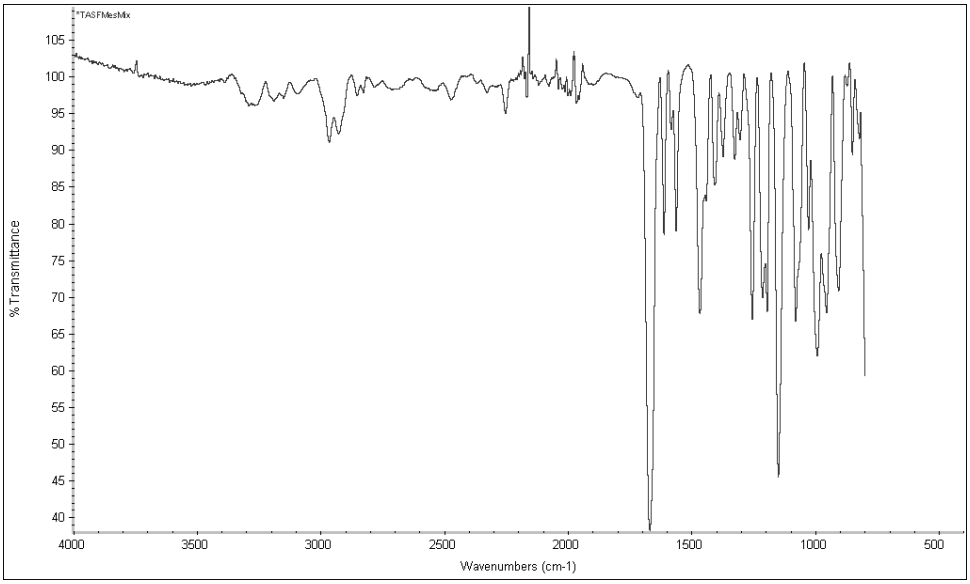
16

1:1 dr

^{13}C NMR ($CDCl_3$)



IR


*TASFMesMix
%Transmittance
105
100
95
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85
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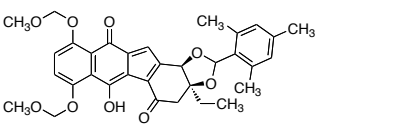
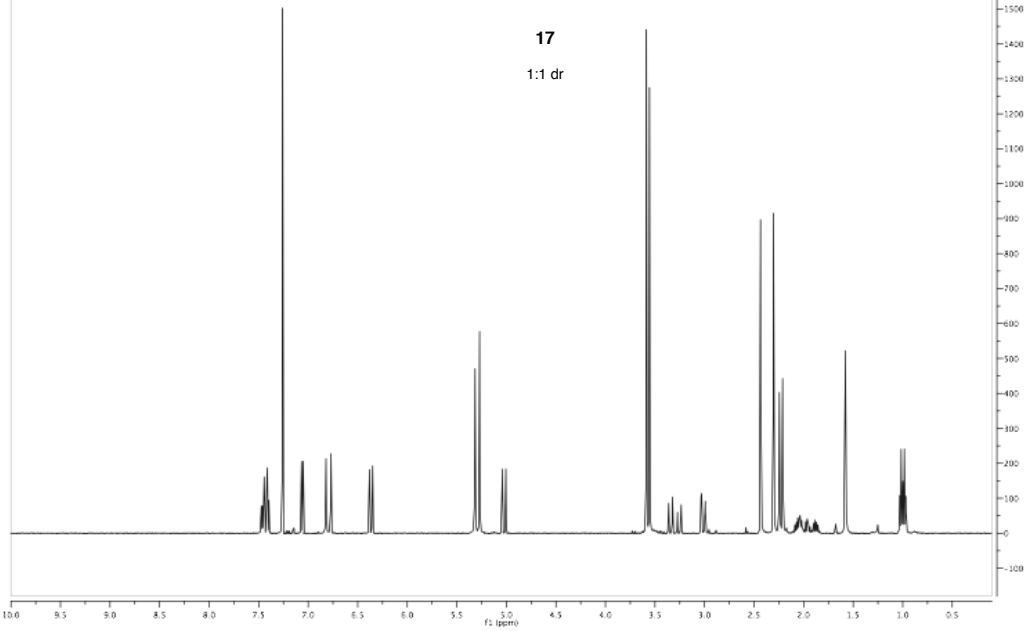
75
70
65
60
55
50
45
40
4000
3500
3000
2500
2000
1500
1000
500
Wavenumbers (cm-1)

^{1}H NMR ($CDCl_3$)

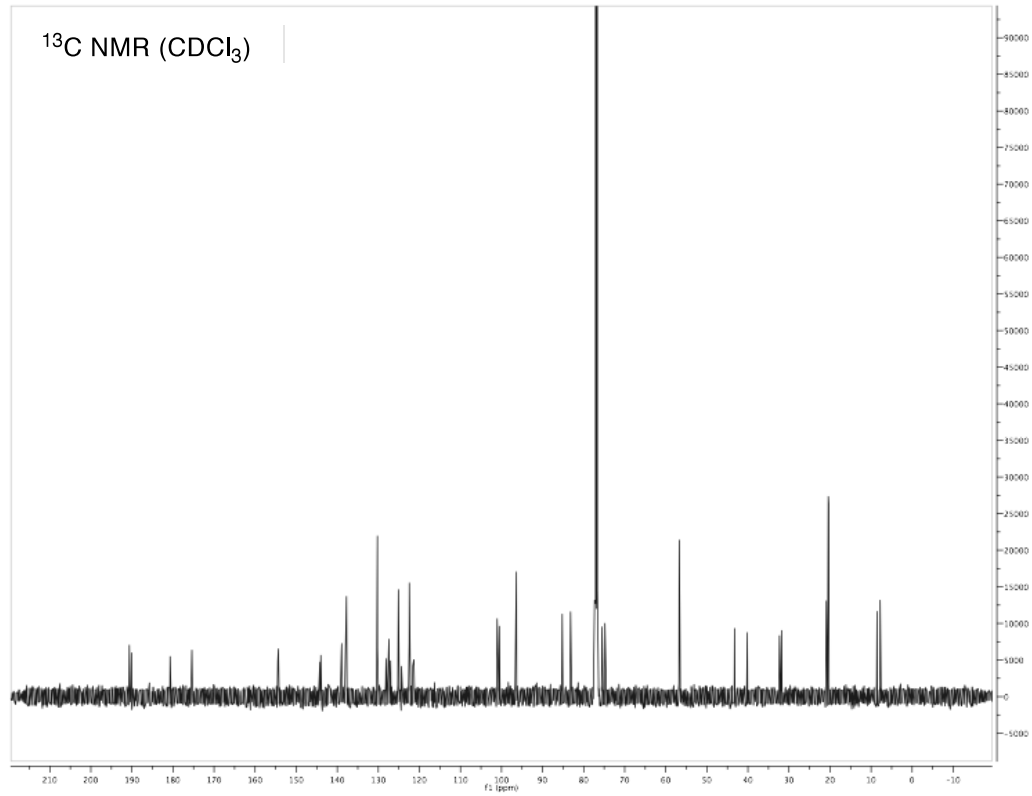


17

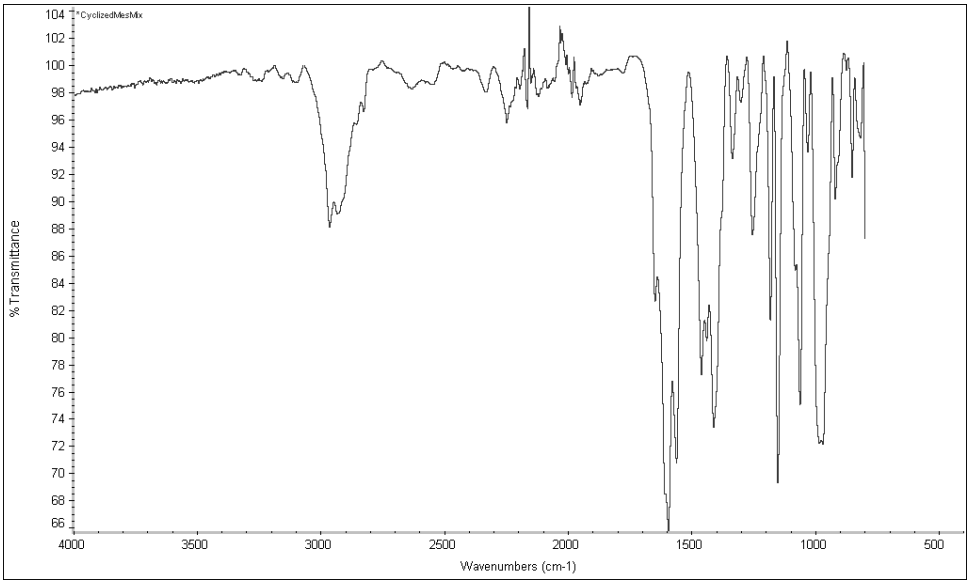
1:1 dr



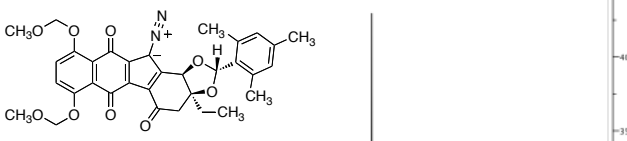
^{13}C NMR ($CDCl_3$)



IR

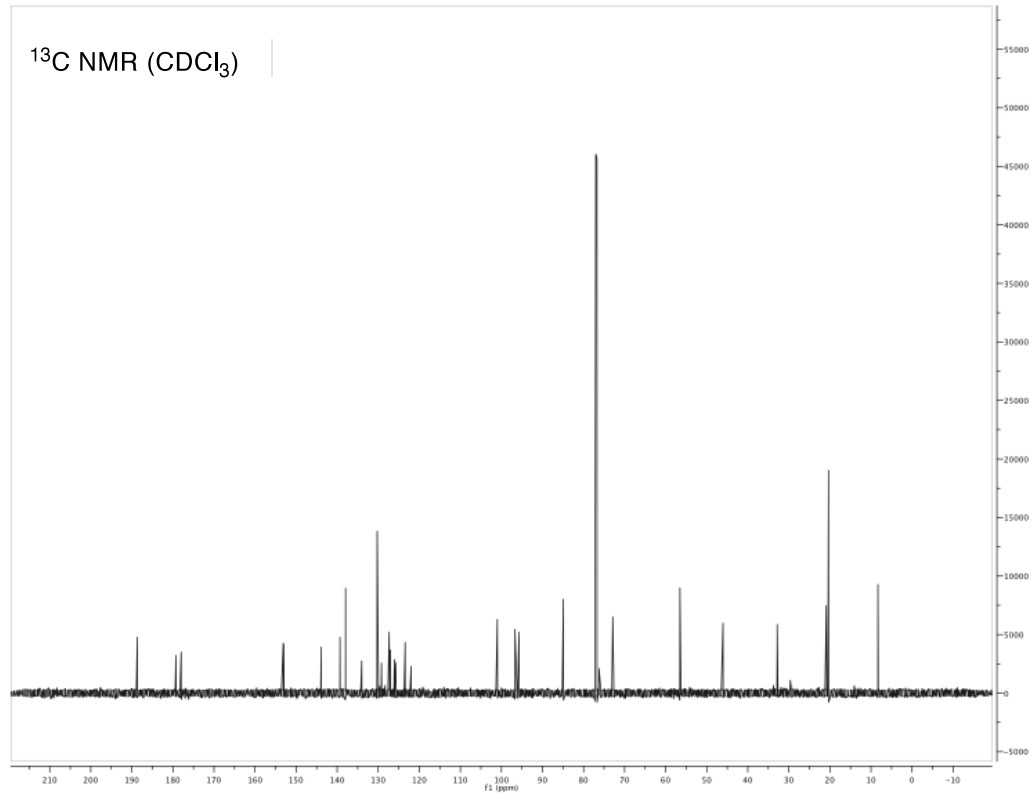

*CyclizedMesMix
%Transmittance
Wavenumbers (cm-1)
104
102
100
98
96
94
92
90
88
86
84
82
80
78
76
74
72
70
68
66
4000
3500
3000
2500
2000
1500
1000
500

^{1}H NMR ($CDCl_3$)

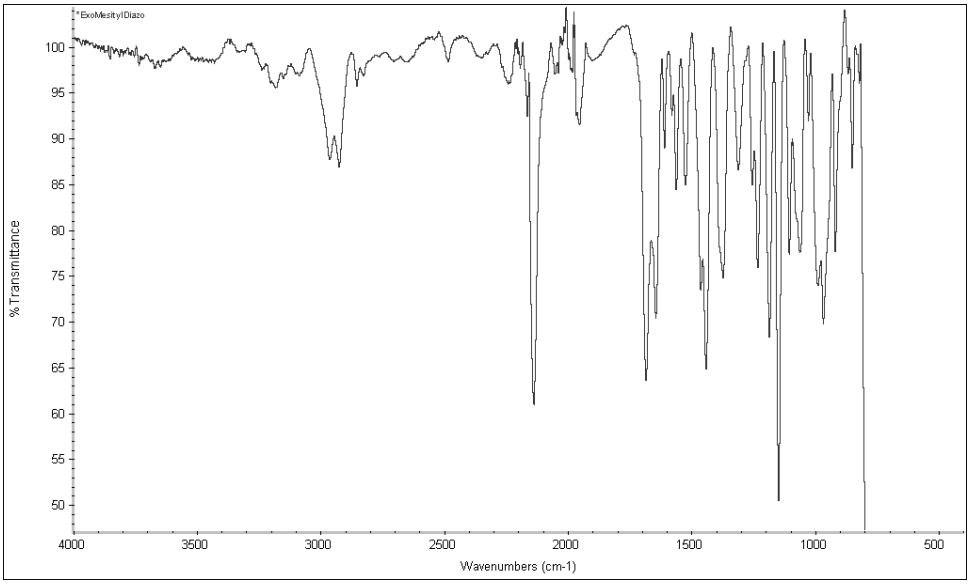


18

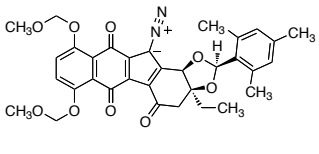
^{13}C NMR ($CDCl_3$)



IR

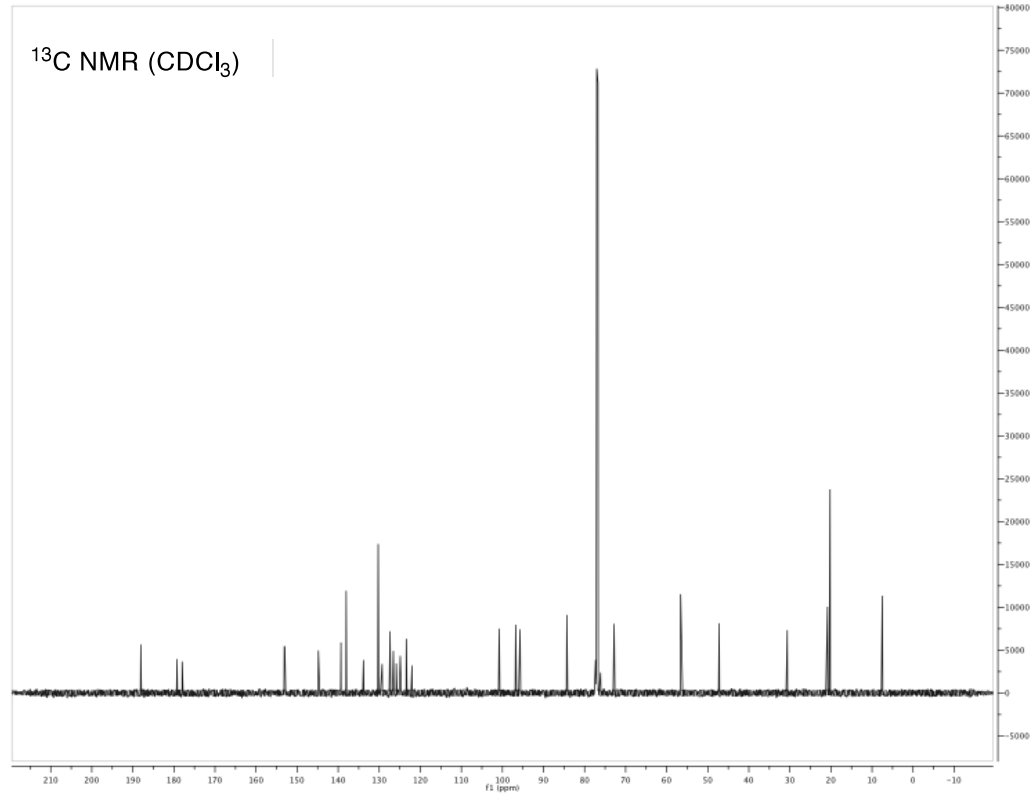

*ExoMesitylDiazo
%Transmittance
100
95
90
85
80
75
70
65
60
55
50
4000
3500
3000
2500
2000
1500
1000
500
Wavenumbers (cm-1)

^{1}H NMR ($CDCl_3$)

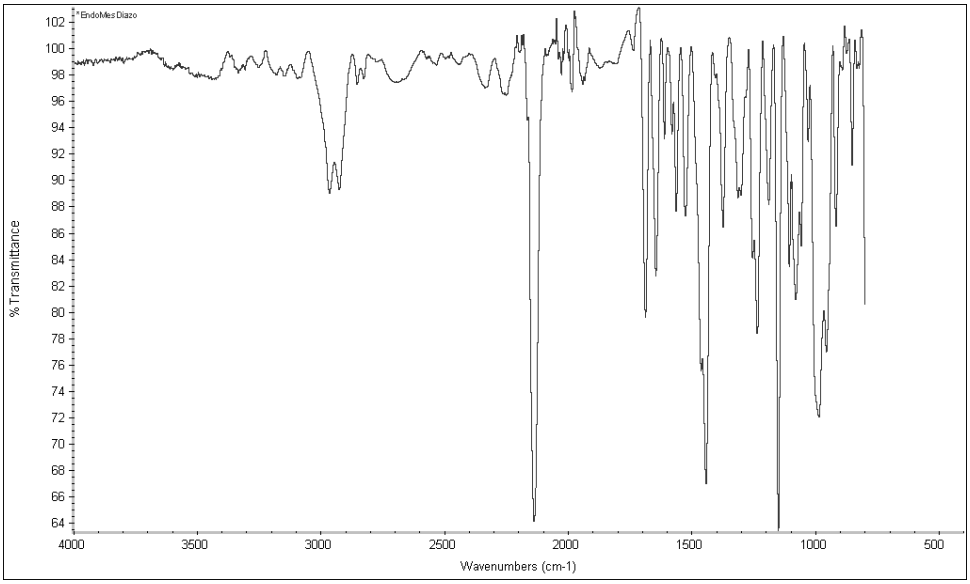


19

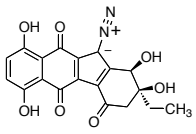
^{13}C NMR ($CDCl_3$)



IR

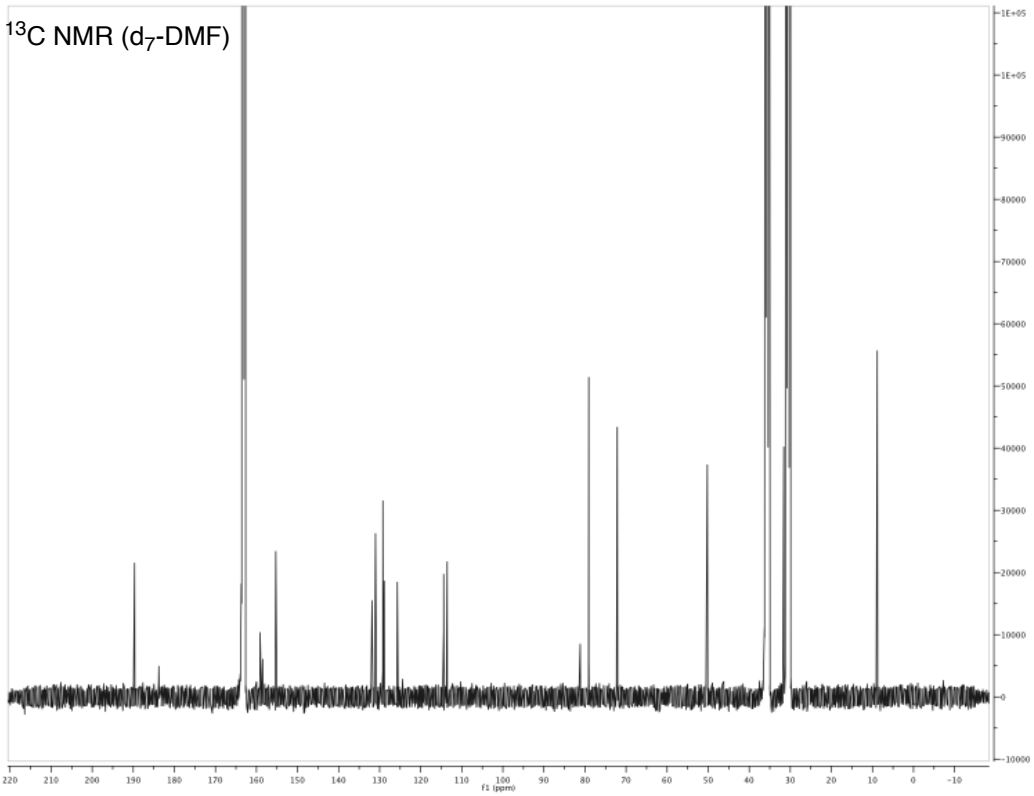

*EndoMes Diazo
% Transmittance
Wavenumbers (cm-1)
102
100
98
96
94
92
90
88
86
84
82
80
78
76
74
72
70
68
66
64
4000
3500
3000
2500
2000
1500
1000
500

^{1}H NMR (d_7-DMF)

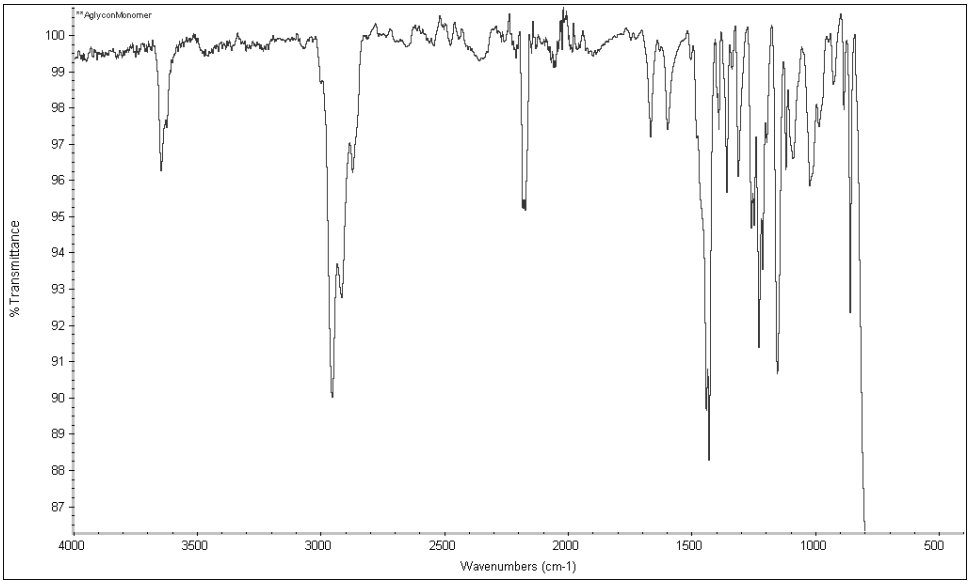


31

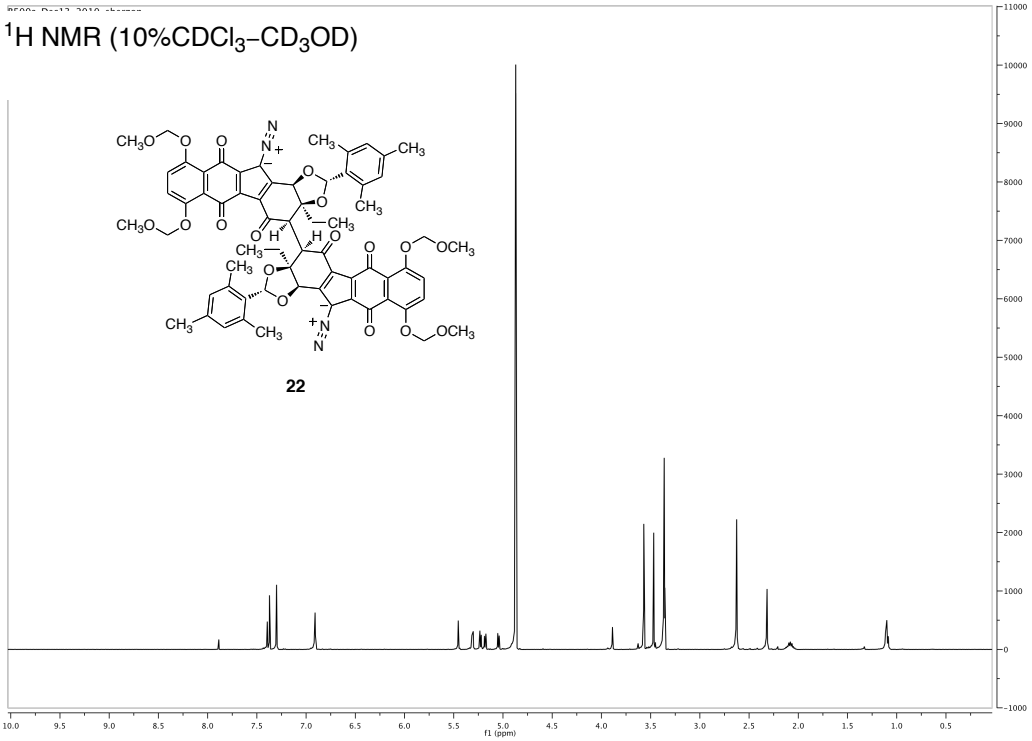
^{13}C NMR (d_7-DMF)



IR

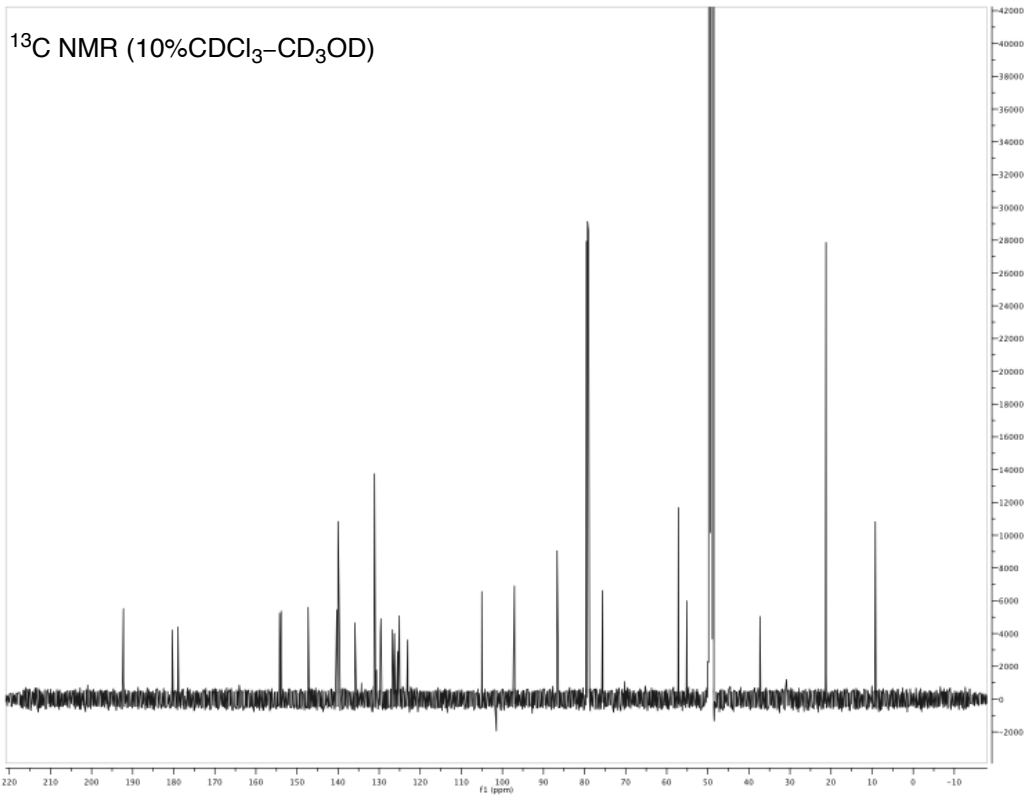

**AglyconMonomer
% Transmittance
100
99
98
97
96
95
94
93
92
91
90
89
88
87
4000
3500
3000
2500
2000
1500
1000
500
Wavenumbers (cm-1)

^{1}H NMR (10%$CDCl_3$–CD_3OD)

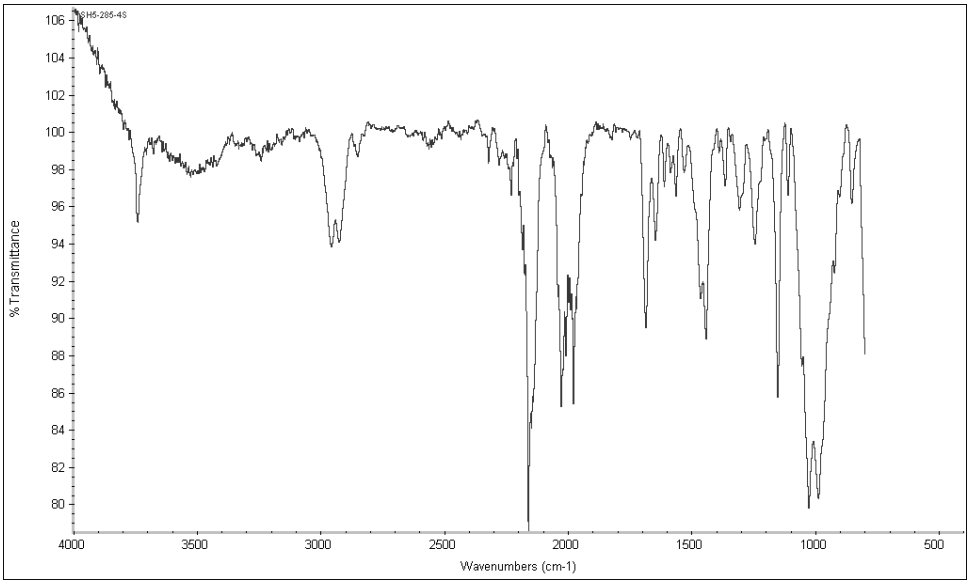


22

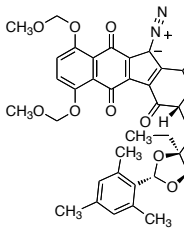
^{13}C NMR (10%$CDCl_3$–CD_3OD)



IR

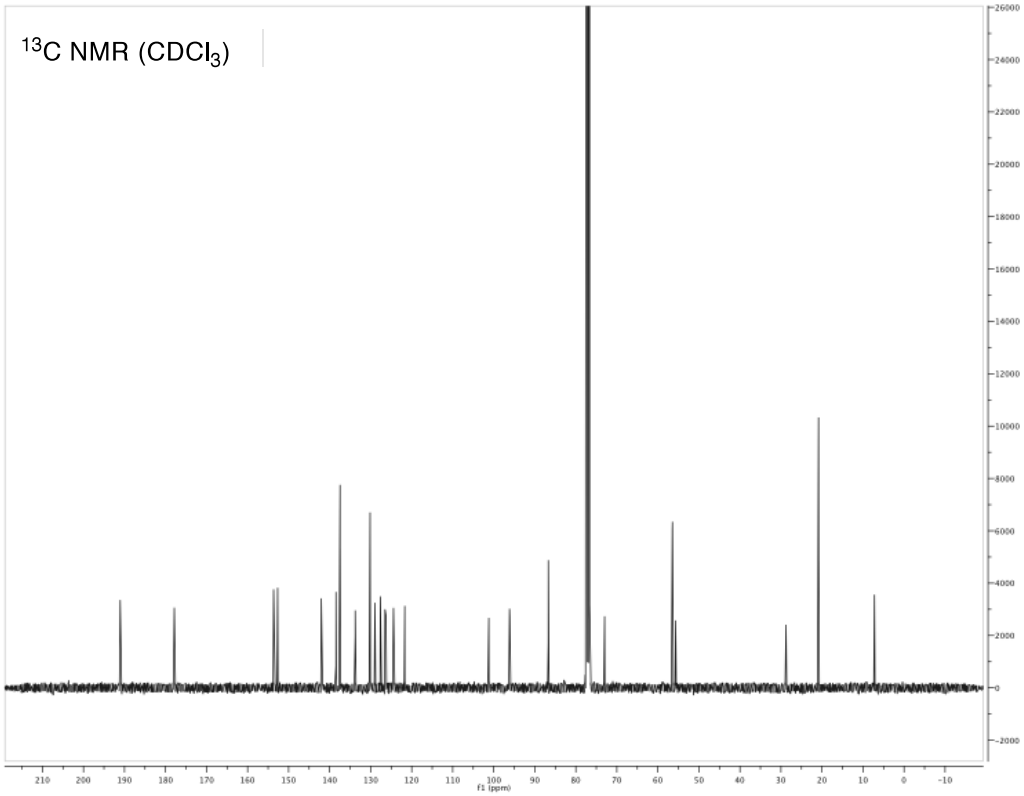

SH5-285-4S
% Transmittance
106
104
102
100
98
96
94
92
90
88
86
84
82
80
4000
3500
3000
2500
2000
1500
1000
500
Wavenumbers (cm-1)

^{1}H NMR ($CDCl_3$)

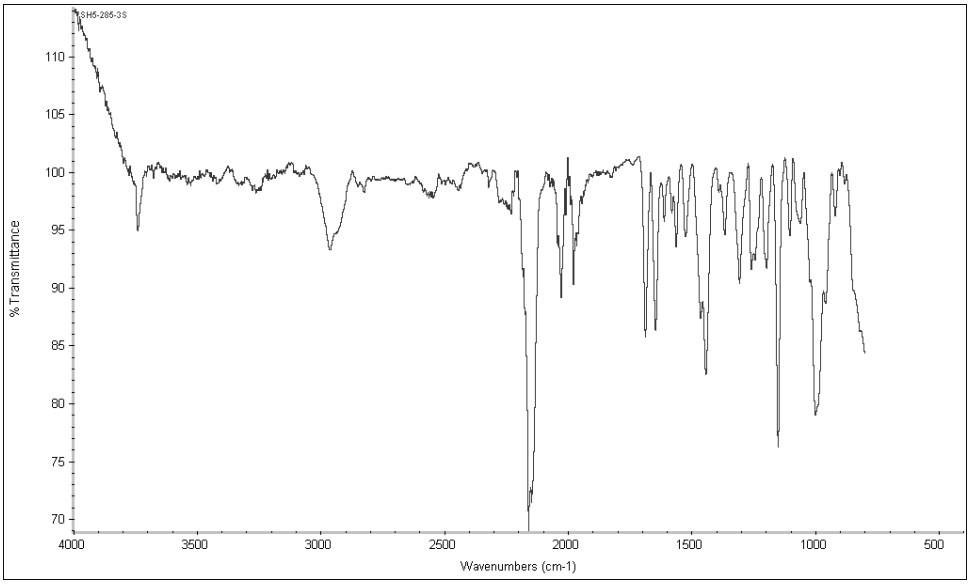


23

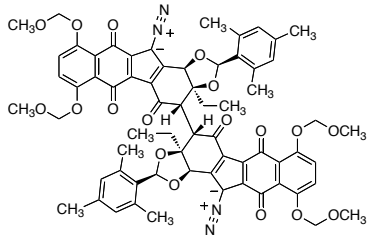
^{13}C NMR ($CDCl_3$)



IR

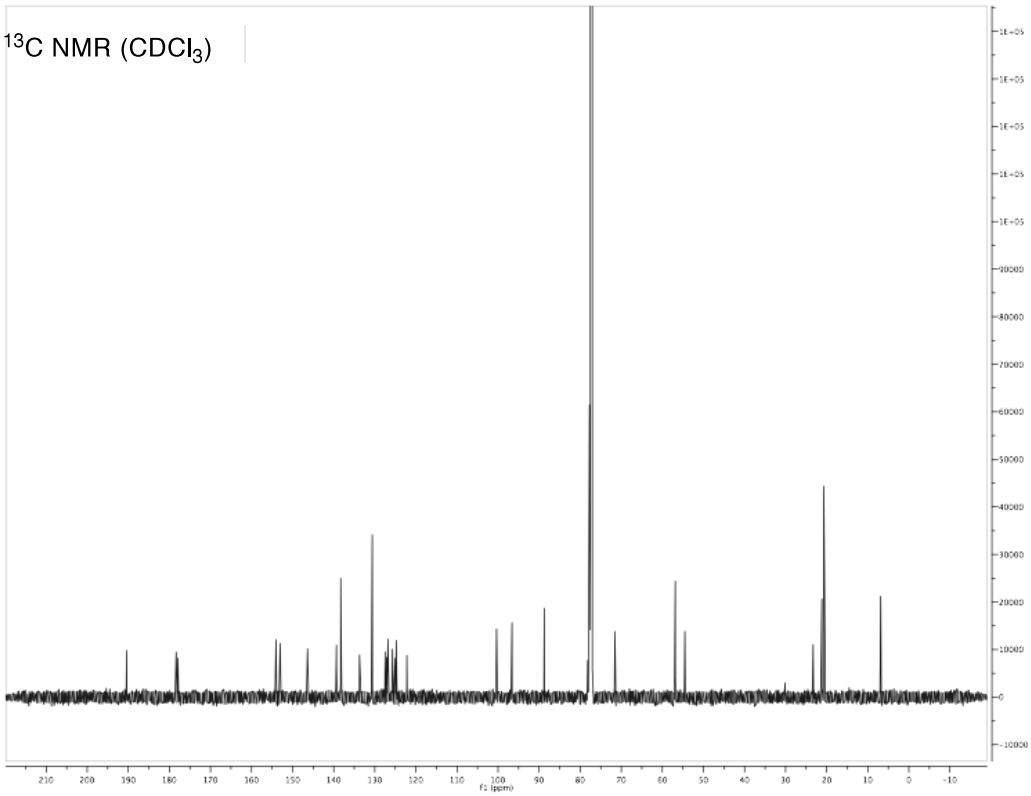

SH5-285-3S
% Transmittance
110
105
100
95
90
85
80
75
70
4000
3500
3000
2500
2000
1500
1000
500
Wavenumbers (cm-1)

^{1}H NMR ($CDCl_3$)

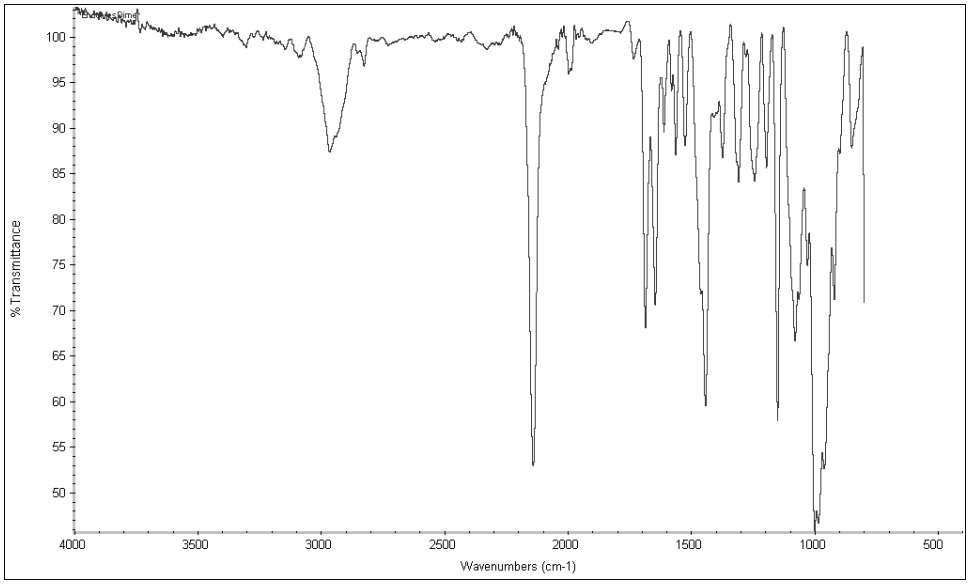


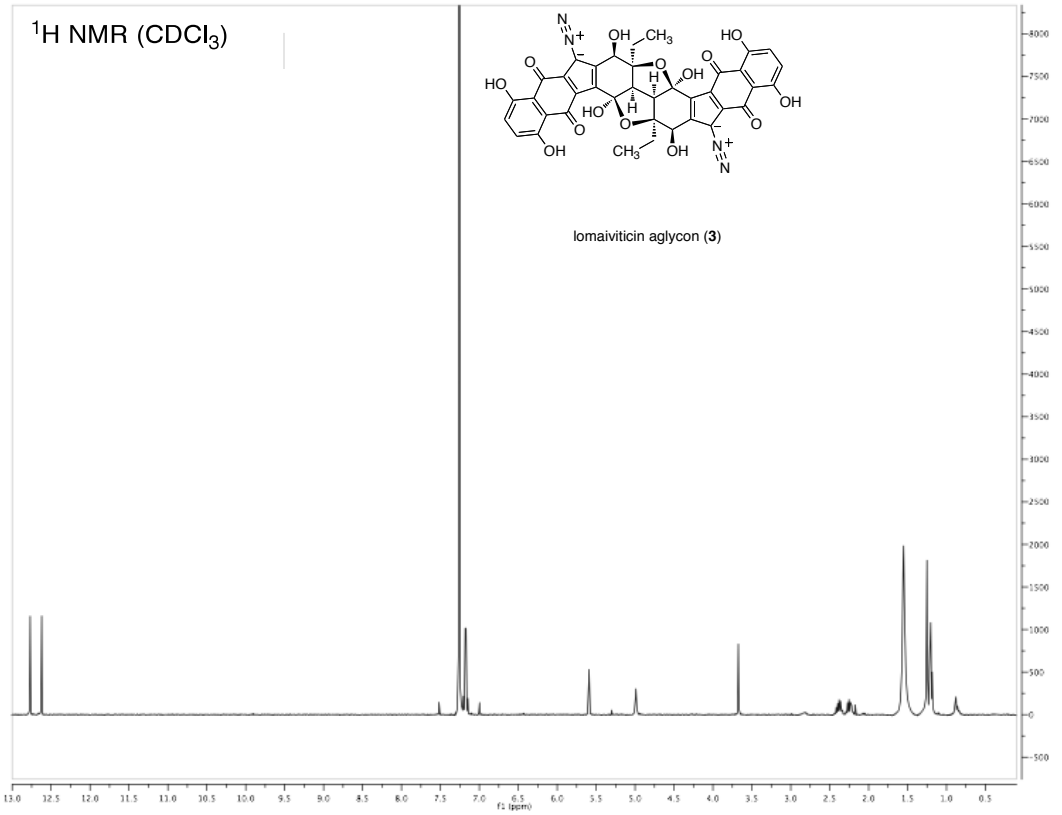
33

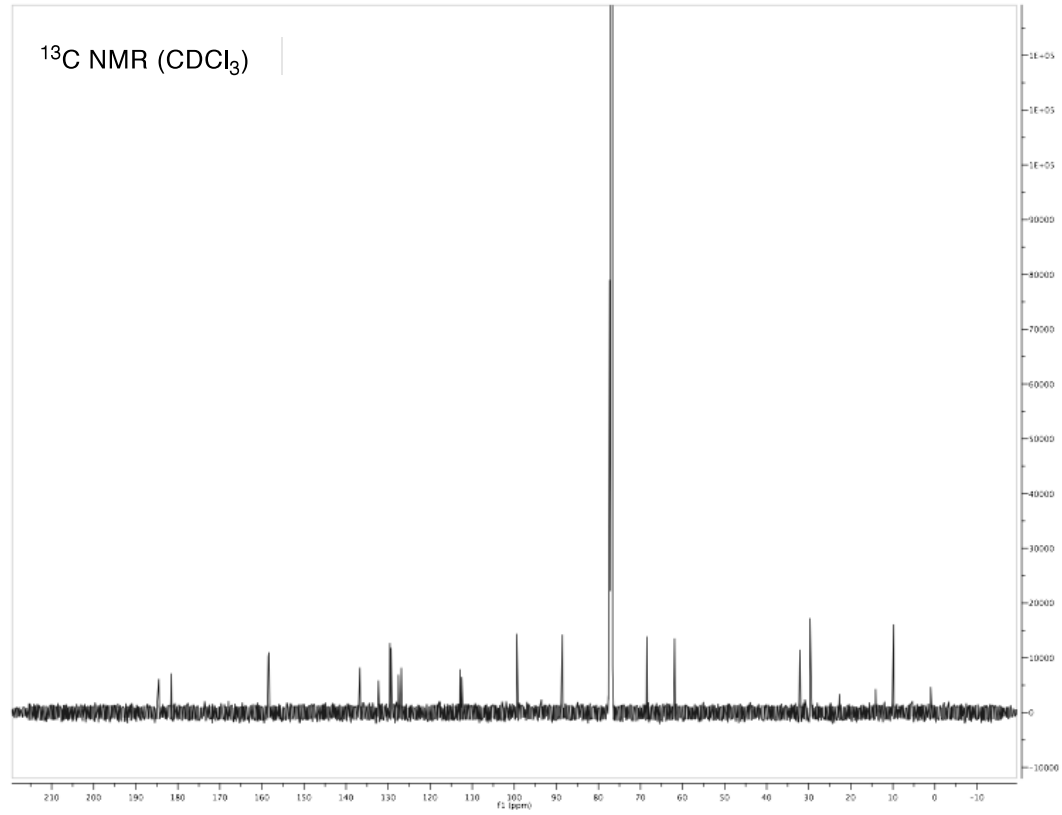
^{13}C NMR ($CDCl_3$)



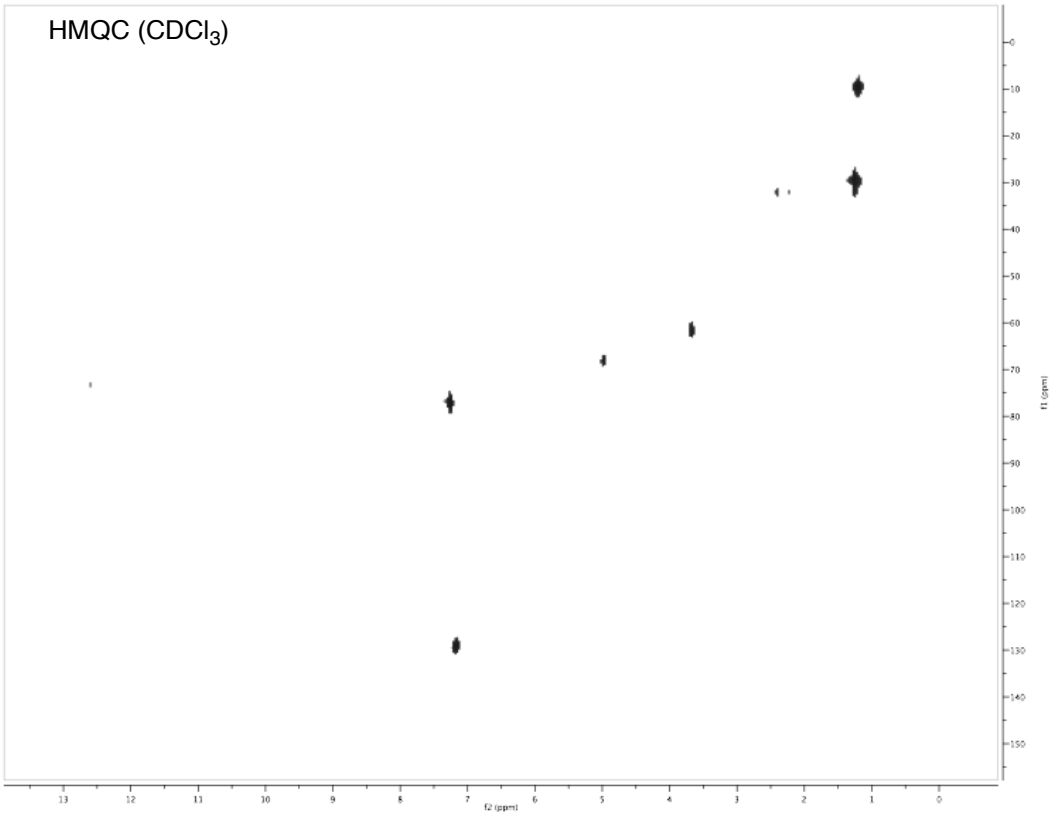
IR


% Transmittance
100
95
90
85
80
75
70
65
60
55
50
4000
3500
3000
2500
2000
1500
1000
500
Wavenumbers (cm-1)

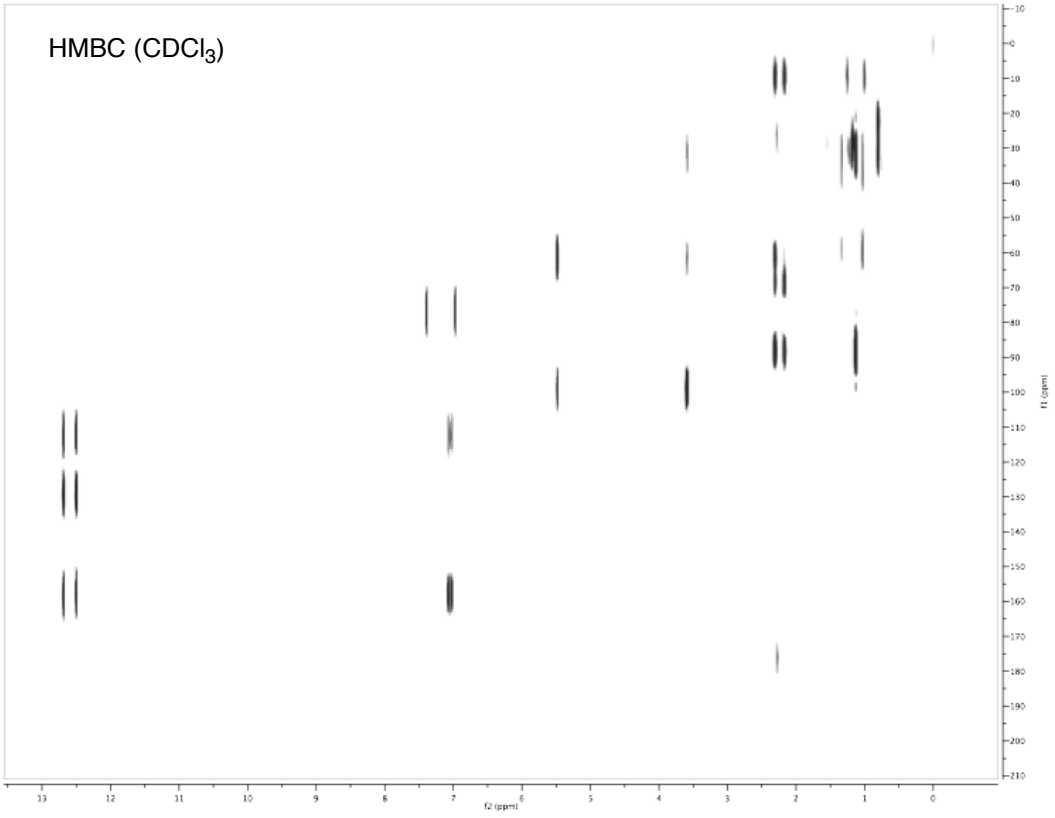

^{1}H NMR ($CDCl_3$)
lomaiviticin aglycon (**3**)

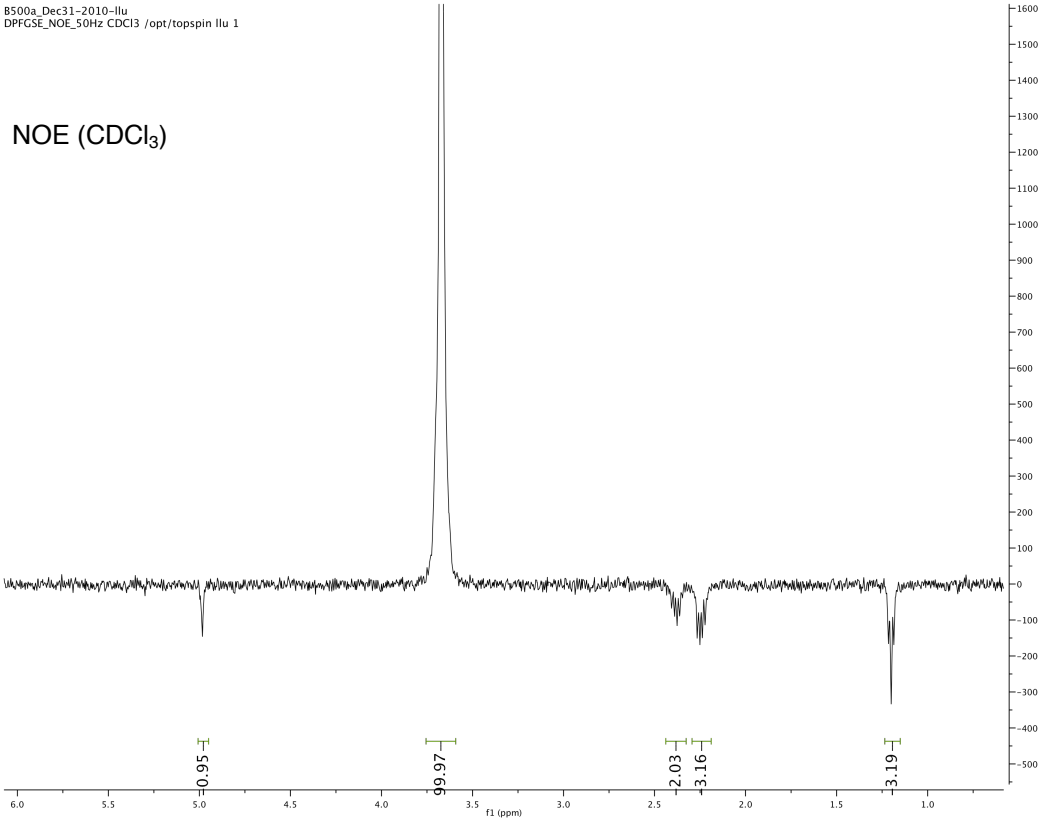

^{13}C NMR ($CDCl_3$)

HMQC ($CDCl_3$)

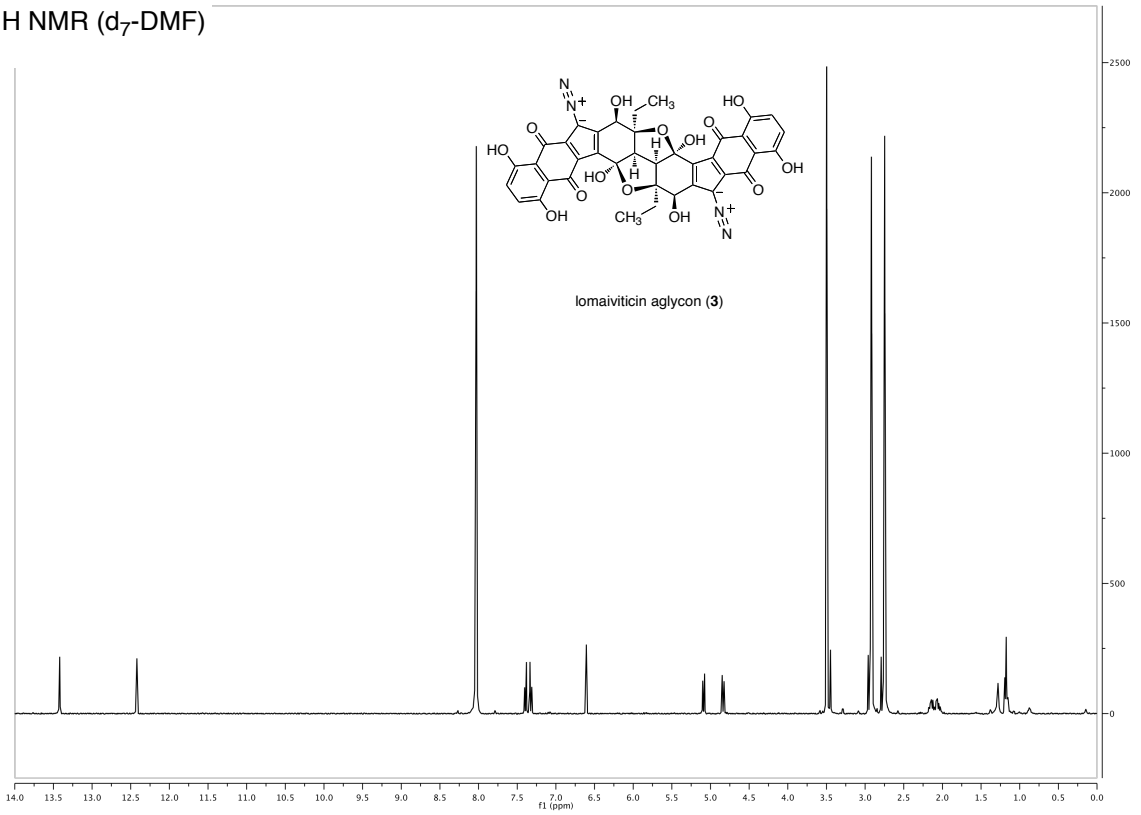


HMBC ($CDCl_3$)

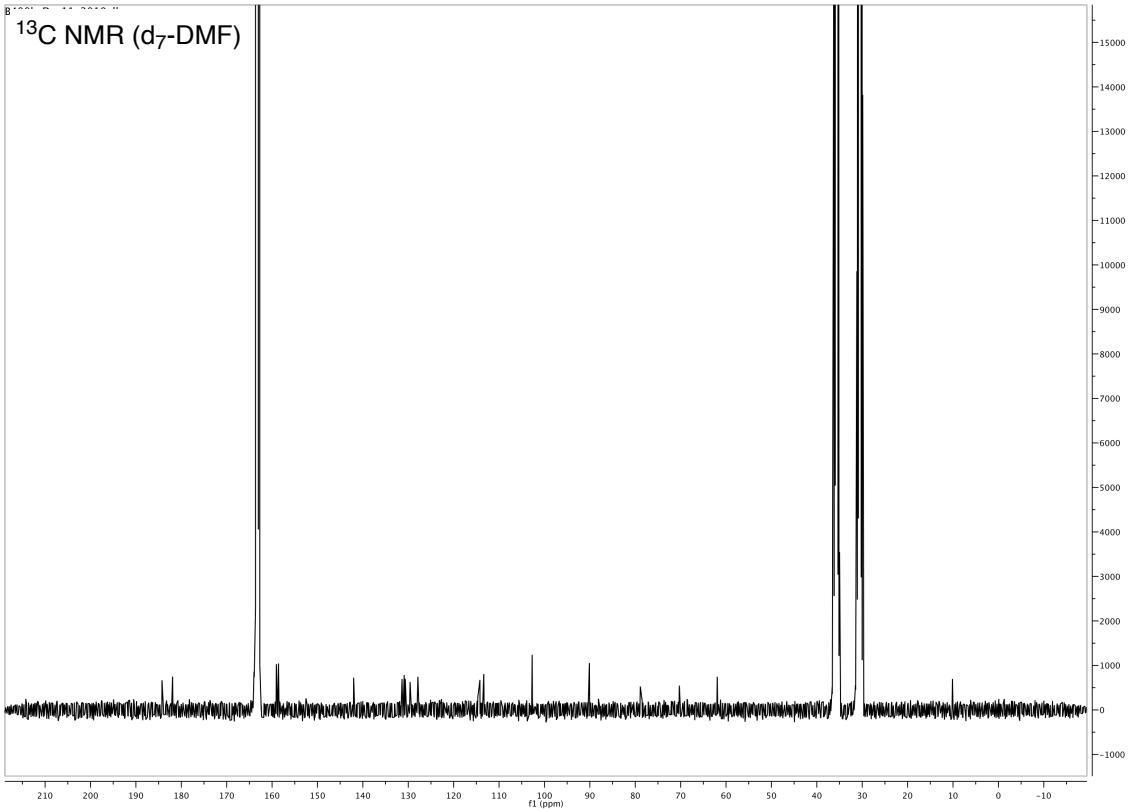


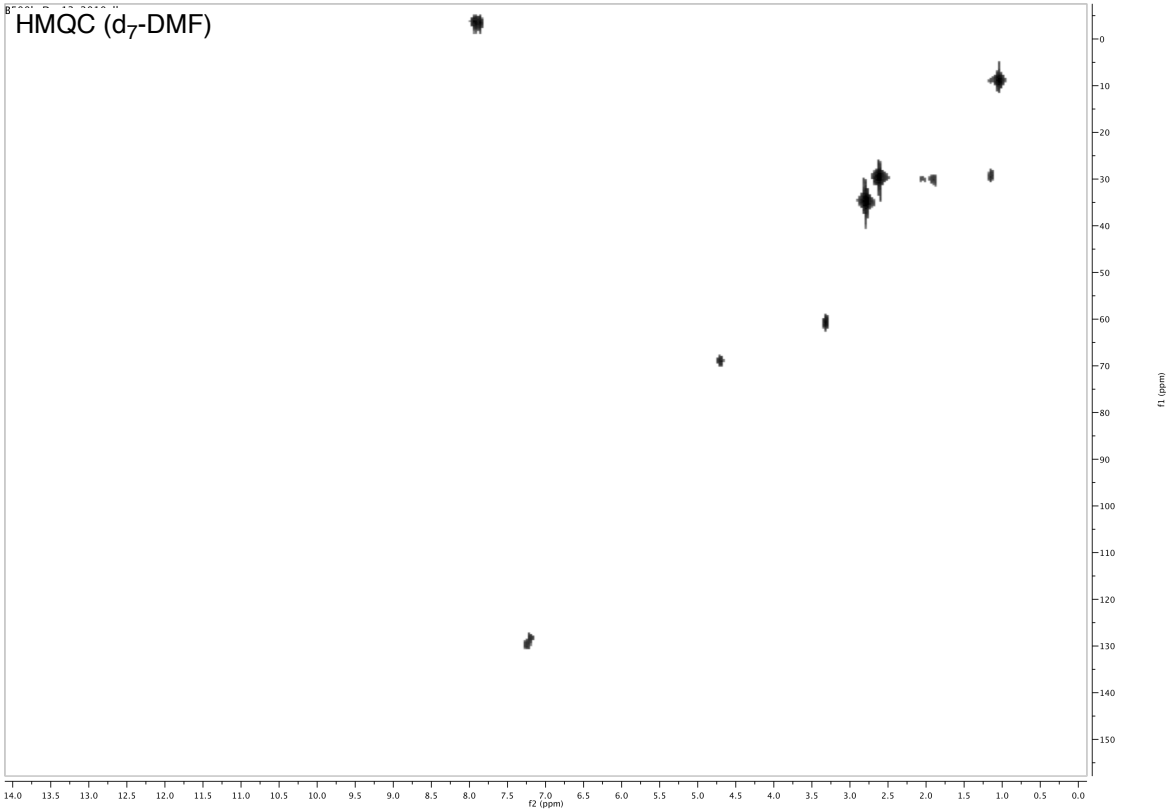

B500a_Dec31-2010-llu
DPFGSE_NOE_50Hz CDCl3 /opt/topspin llu 1
NOE ($CDCl_3$)
0.95
99.97
2.03
3.16
3.19
f1 (ppm)

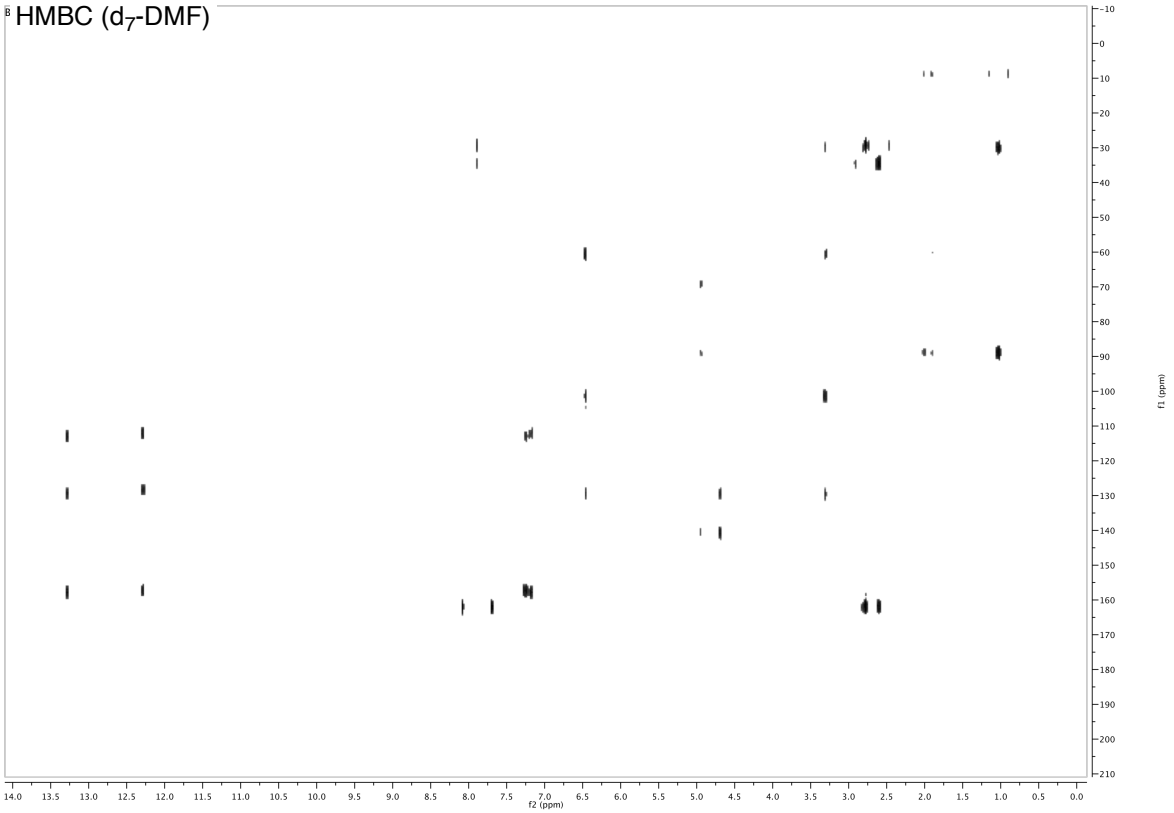
^{1}H NMR (d_7-DMF)



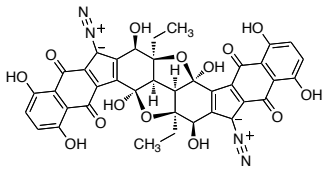
^{13}C NMR (d_7-DMF)




HMQC (d_7-DMF)
f2 (ppm)
f1 (ppm)

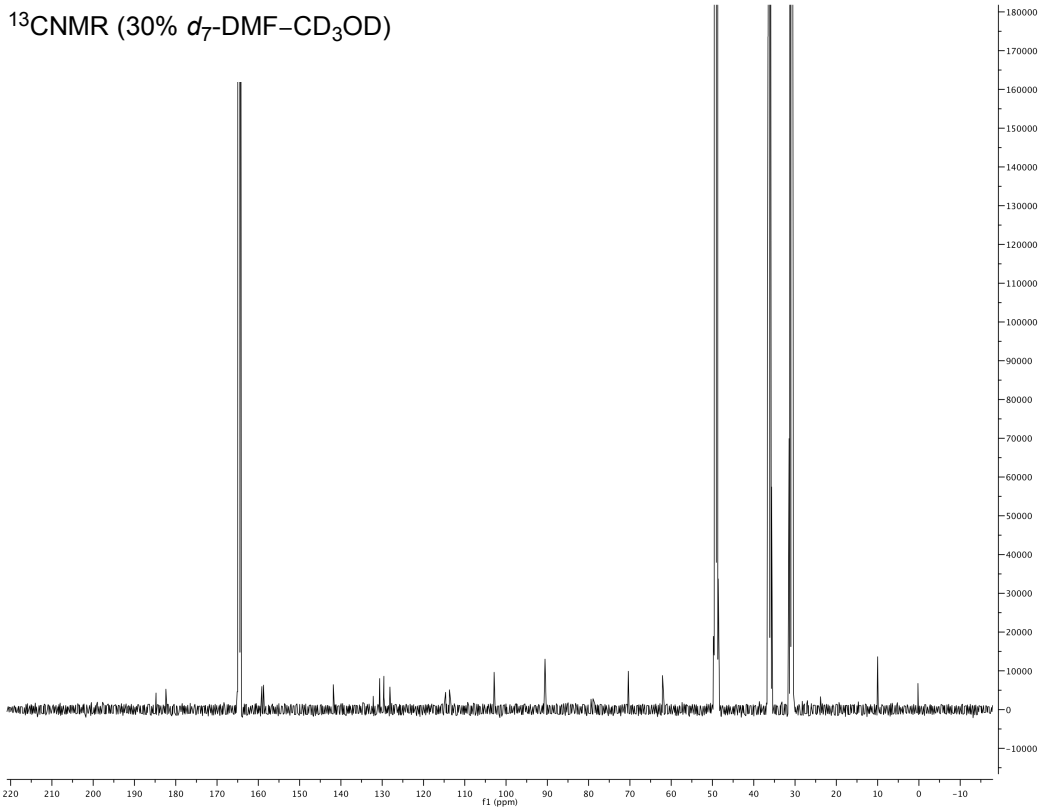

HMBC (d_7-DMF)
f2 (ppm)
f1 (ppm)

^{1}HNMR (30% d_7-DMF–CD_3OD)

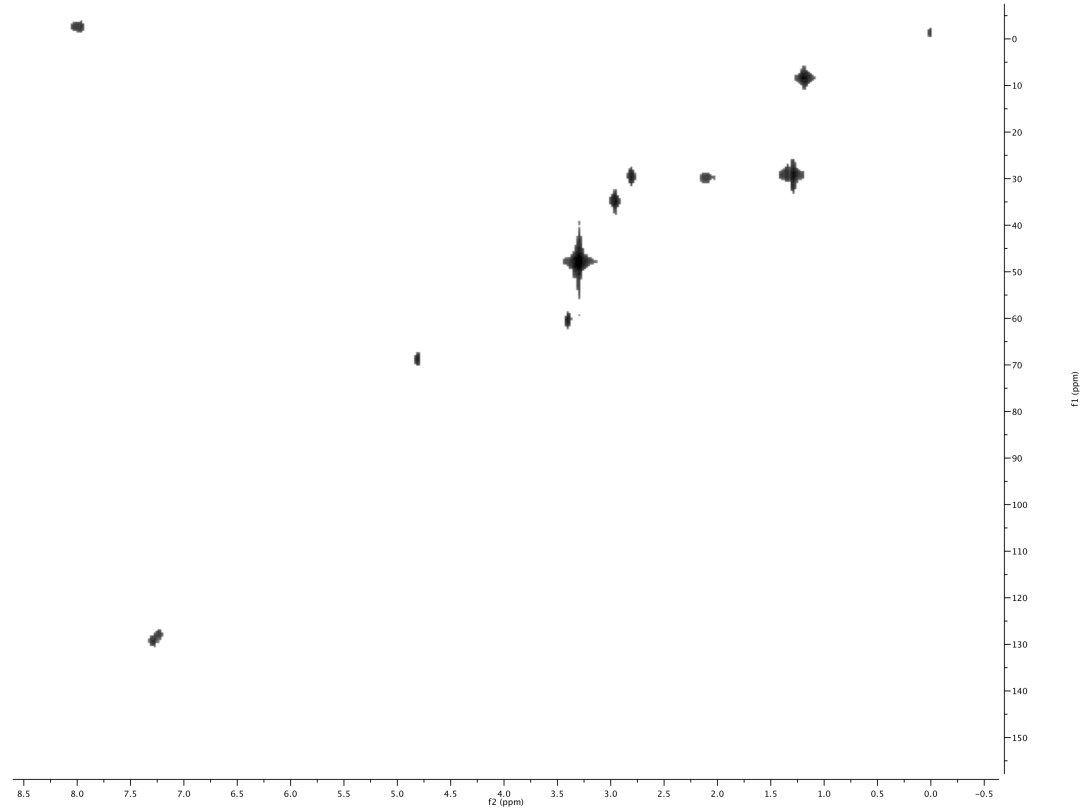


lomaiviticin aglycon (**3**)

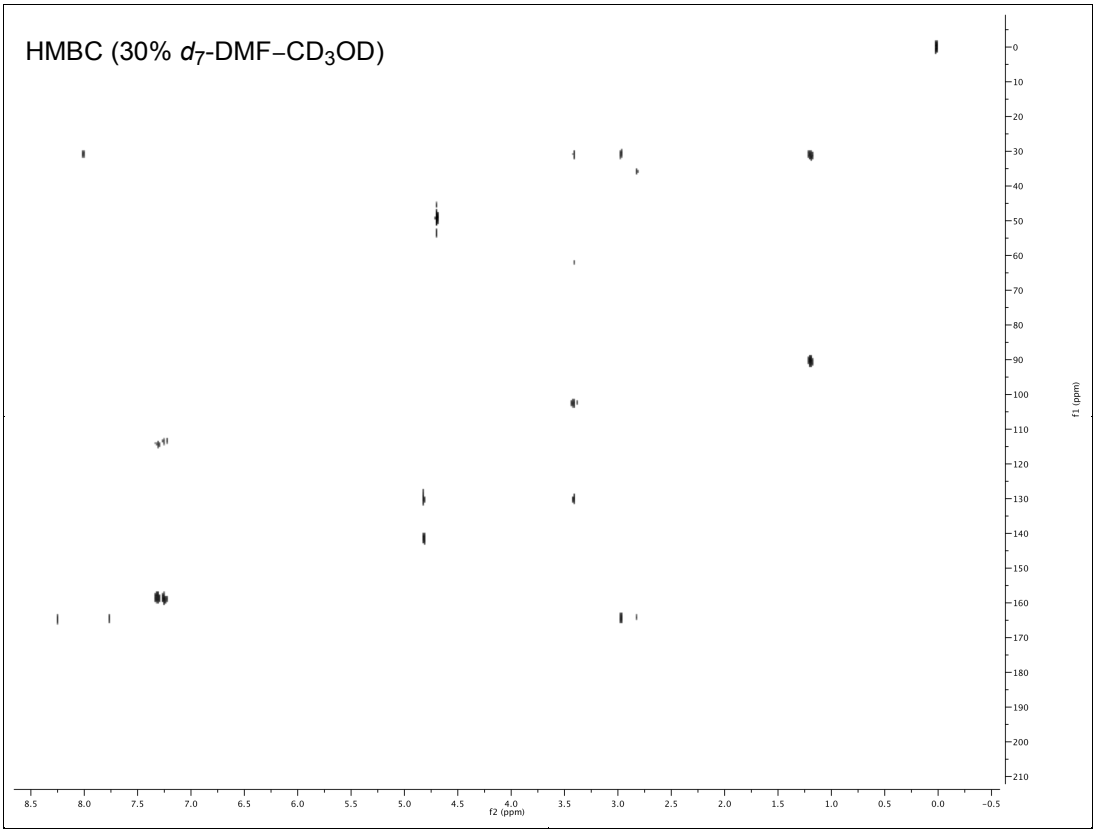
^{13}CNMR (30% d_7-DMF–CD_3OD)



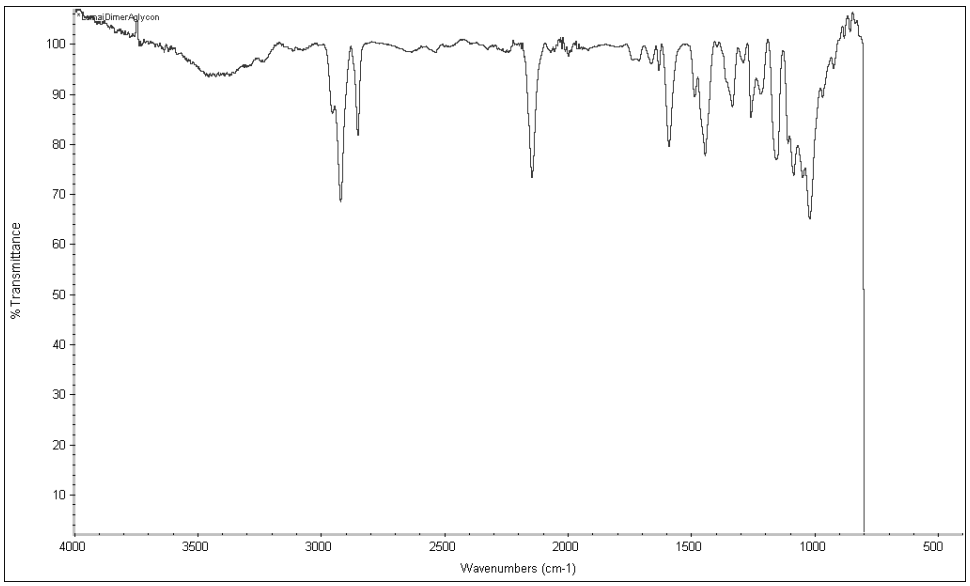
HMQC (30% d_7-DMF–CD_3OD)

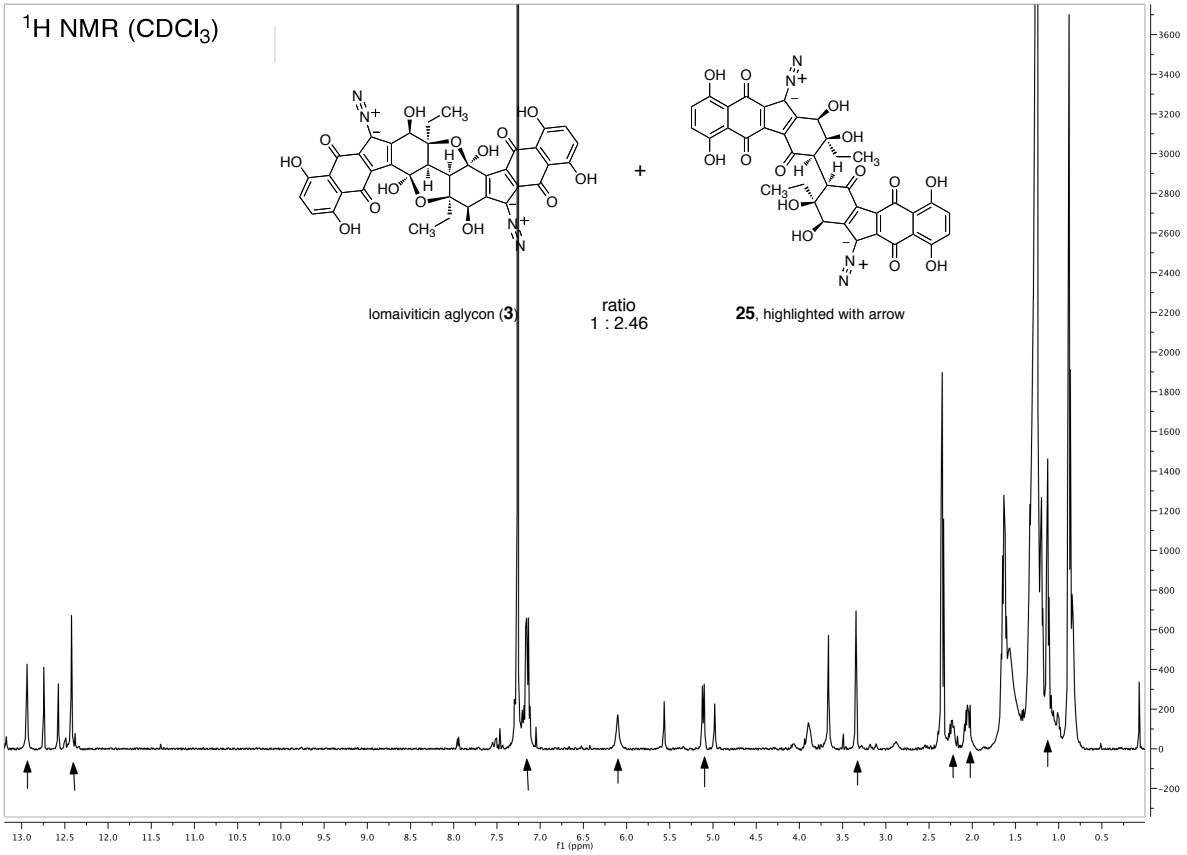


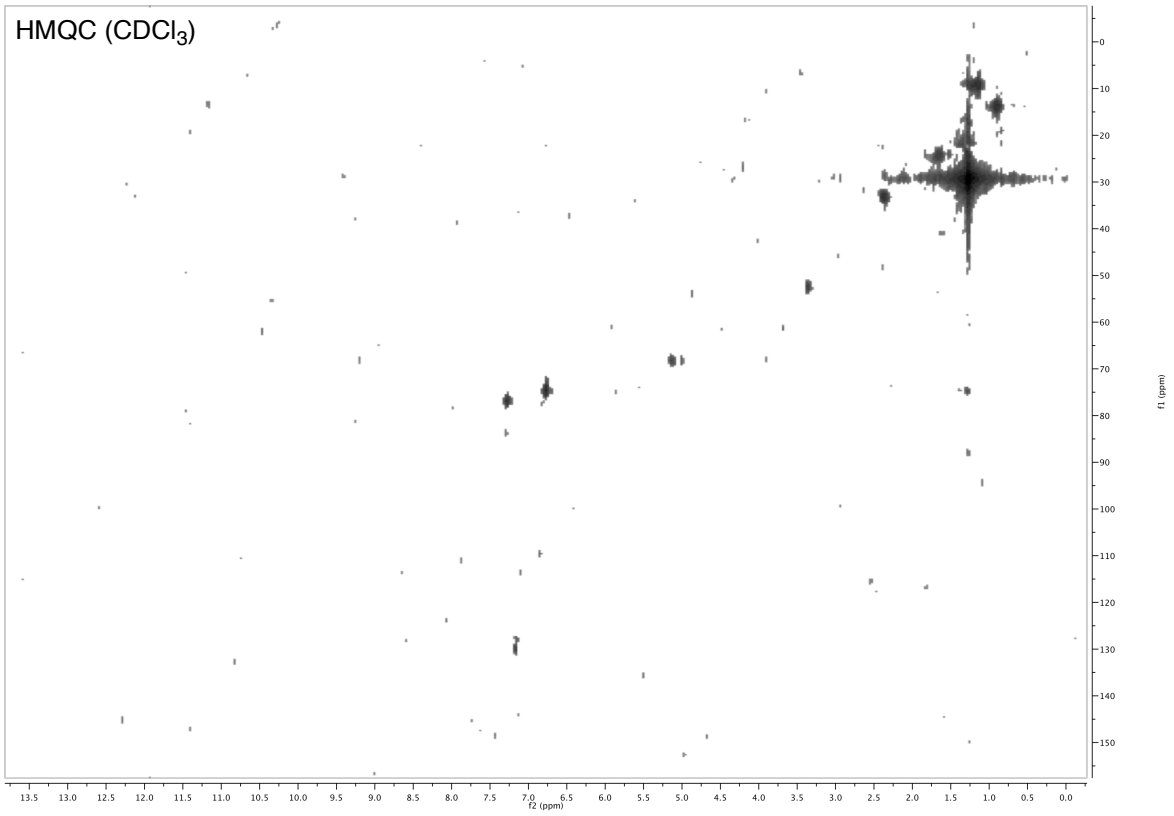
HMBC (30% d_7-DMF–CD_3OD)

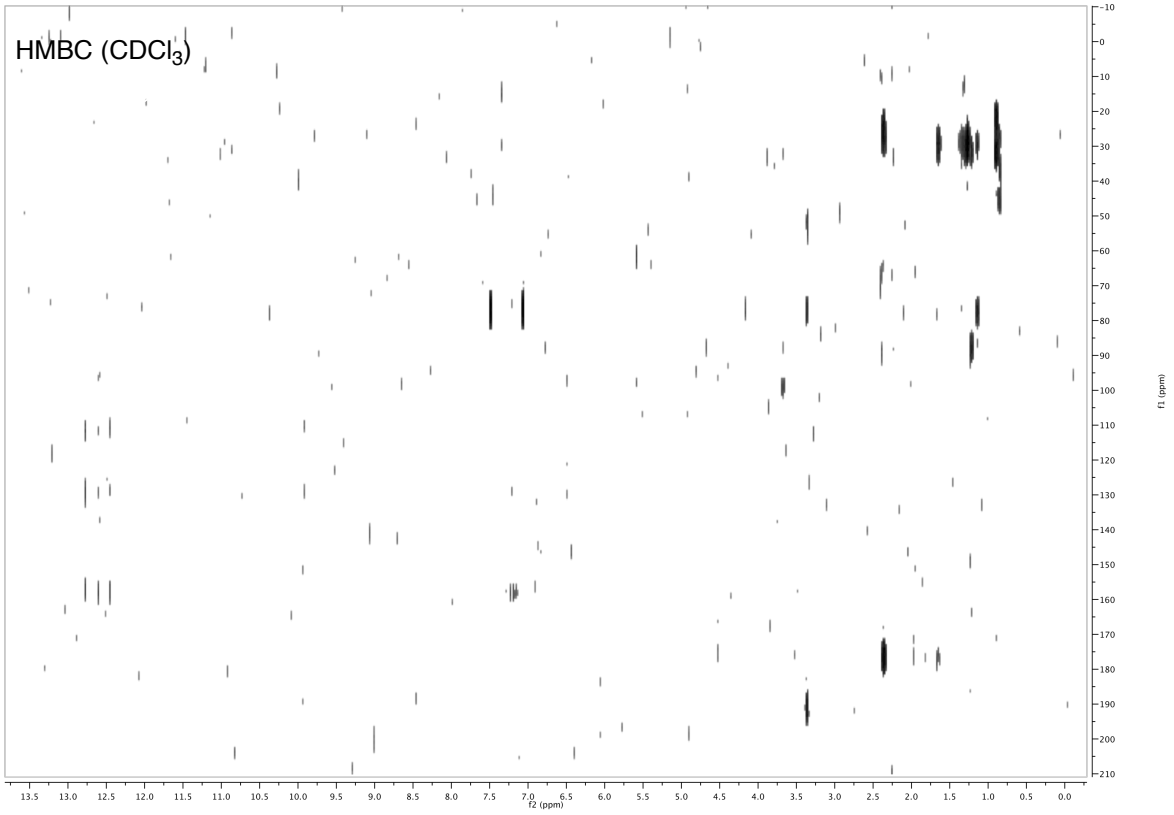


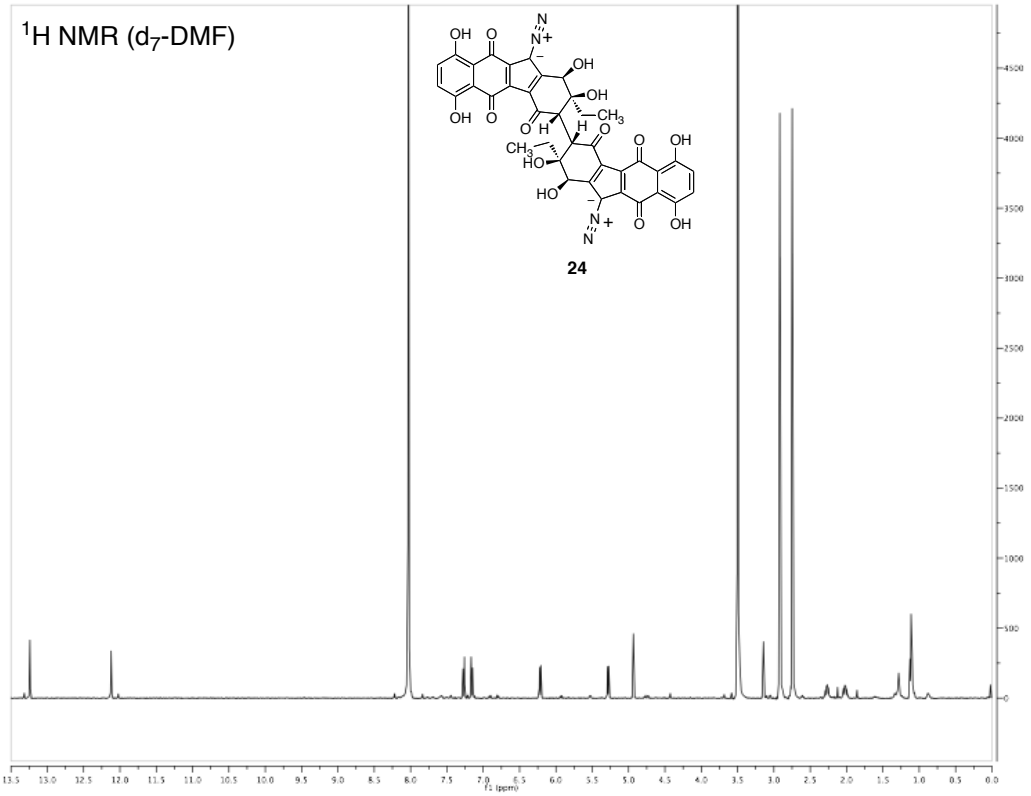
IR


BenzylDimerAglycon
% Transmittance
100
90
80
70
60
50
40
30
20
10
4000
3500
3000
2500
2000
1500
1000
500
Wavenumbers (cm-1)

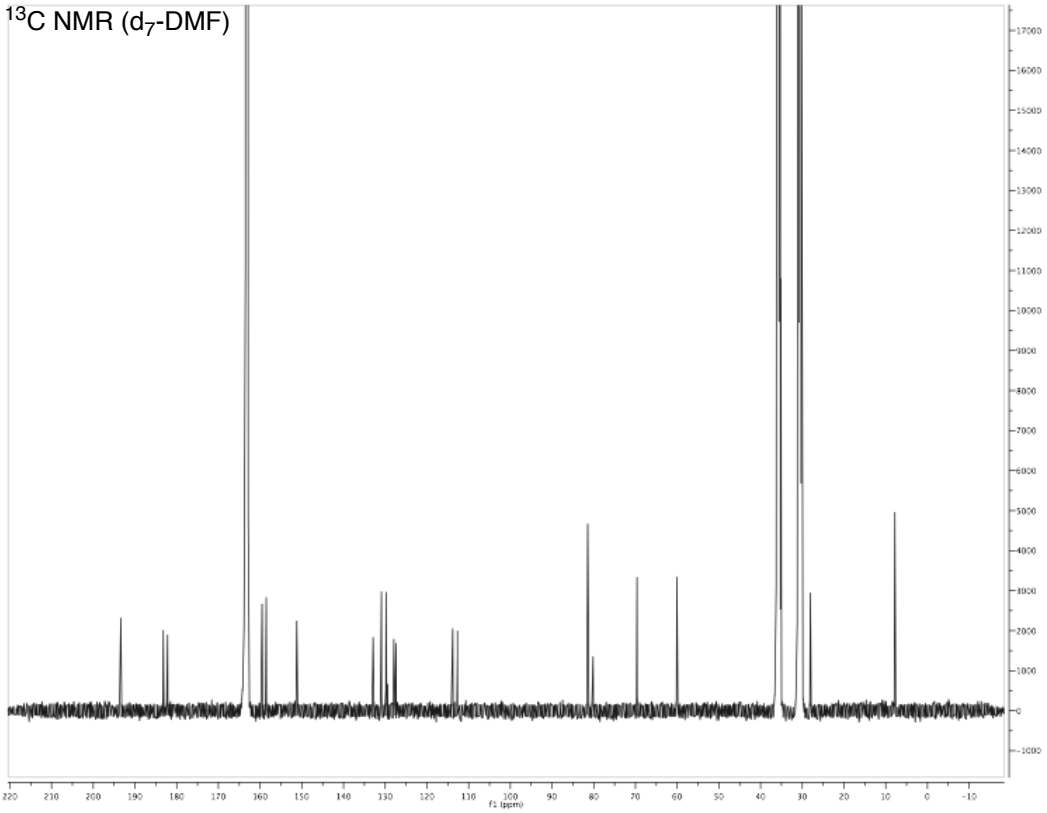

^{1}H NMR ($CDCl_3$)
lomaiviticin aglycon (**3**)
ratio
1 : 2.46
25, highlighted with arrow
f1 (ppm)


HMQC ($CDCl_3$)
f2 (ppm)
f1 (ppm)

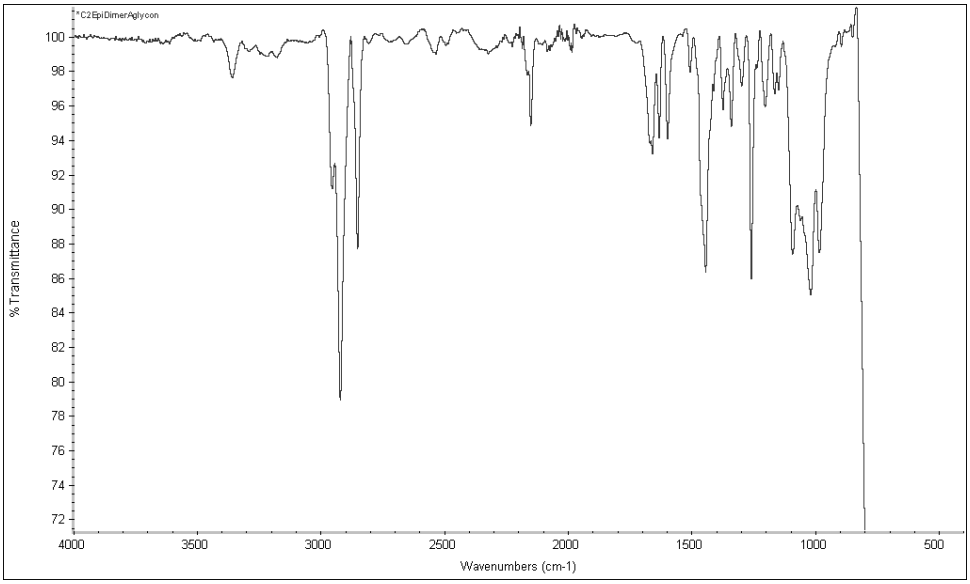

HMBC ($CDCl_3$)
f2 (ppm)
f1 (ppm)



24



IR


*C2EpiDimerAglycon
% Transmittance
100
98
96
94
92
90
88
86
84
82
80
78
76
74
72
4000
3500
3000
2500
2000
1500
1000
500
Wavenumbers (cm-1)

Bibliography.

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10. For clarity, synthetic intermediates not described in the manuscript are numbered in the Supporting Information beginning with 27.
11. Gholap, S. L.; Woo, C. M.; Ravikumar, P. C.; Herzon, S. B. *Org. Lett.* **2009**, *11*, 4322.
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