Supplementary Material for Organic & Biomolecular Chemistry

Synthesis of the guanacastepene A-B hydrazulene ring system through photochemical ring transposition

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Supporting Information

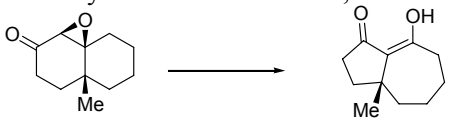
1. General Procedures

^{1}H NMR spectra were recorded at ambient probe temperatures on either a Brüker AC250 (250 MHz) or a Brüker DPX360 (360 MHz) instrument. The data is presented as follows: chemical shift (in ppm on the δ scale), integration, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet,), coupling constant (J, in hertz) and the assignment. ^{13}C NMR data were recorded at ambient probe temperatures on either a Brüker AC250 (62.9 MHz) or a Brüker DPX360 (90.5 MHz) instrument and are reported in ppm on the δ scale followed by the interpretation determined from the DEPT spectra.
Infra Red spectra were recorded on a JASCO FT/IR-460 plus instrument using 4mm sodium chloride plates. The wavelengths of the maximum absorbance (ν_{max}) are quoted in cm^{-1}. MS analysis was carried out at the EPSRC National Mass Spectrometry Service Centre, Swansea. Accurate mass measurements were obtained on a Finnigan MAT 900 XLT double focusing mass spectrometer. The data is recorded as the ionisation method followed by the calculated and measured masses. Melting points were determined on a Gallenkamp Electrothermal melting point apparatus and are uncorrected.
TLC was performed on Merck 60F_{254} silica plates and visualised by UV light and/or anisaldehyde[1] or potassium permanganate[2] stains. The compounds were purified by wet flash chromatography using Merck Kieselgel 60 (particle size 35-70) silica under a positive pressure. The eluent compositions are quoted as a percentage.
Anhydrous toluene, dichloromethane, tetrahydrofuran, diethyl ether, and methanol were obtained from an Innovative Technologies solvent purification system unless otherwise stated. Diisopropylamine and pyridine were distilled and stored over potassium hydroxide. *n*-Butyl lithium solutions were titrated against diphenylacetic acid in THF at 0 ºC immediately prior to use. All other chemicals were used as supplied except where otherwise stated in the text.

[1] Anisaldehyde stain was prepared as follows: Concentrated sulphuric acid (10 mL) was added carefully to a stirring solution of ethanol (200 mL) and *p*-methoxybenxaldehyde (10 mL).
[2] Potassium Permanganate stain was prepared as follows: 3g potassium permanganate, 20g potassium carbonate, 5mL 5% sodium hydroxide, 300mL water.

2. Synthesis of Individual Compounds

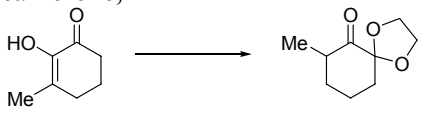
8-Hydroxy-3a-methyl-3,3a,4,5,6,7-hexahydro-2H-azulen-1-one, **9**



8 **9**

The epoxy ketone **8**[3] (48.6 mg, 0.27 mmol) was dissolved in ethanol (200 mL) and the solution deoxygenated by bubbling nitrogen through for 1 h. The solution was then immersed in an ice bath and exposed to UV radiation through a Pyrex filter for 6 h before being concentrated. The residue was purified by column chromatography (SiO_2, ethyl acetate/hexanes 9:1) to yield the title product **9** (24.5 mg, 50%) as a colourless oil, along with recovered starting material **8** (12.2 mg, 25%): **IR** (neat)/cm^{-1} ν_{max} 3398 (OH), 1645 (C=O), 1604 (C=O); **^{1}H NMR** (360 MHz, $CDCl_3$), δ 1.14 (3H, s), 1.41-1.47 (2H, m), 1.63-1.82 (6H, m), 2.32-2.39 (2H, m), 2.51-2.61 (2H, m), 14.24 (1H, s); **^{13}C NMR** (90.5 MHz, $CDCl_3$), δ 24.7 (CH_3), 26.4 (CH_2), 26.6 (CH_2), 36.0 (CH_2), 37.6 (CH_2), 39.0 (CH_2), 43.0 (C), 43.6 (CH_2), 119.8 (C), 183.0 (C), and 206.3 (C); **HRMS** (EI) m/z calcd. for $C_{11}H_{16}O_2$ 180.1145, found, 180.1145.

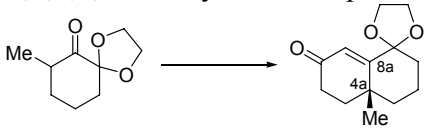
7-Methyl-1,4-dioxa-spiro[4.5]decan-6-one**, 22**



10 **22**

2-Hydroxy-3-methylcyclohex-2-enone[4] **10** (5.08 g, 0.040 mol) was dissolved in benzene (50 mL). To the stirring solution was added anhydrous ethylene glycol (2.70 mL, 3.01 g, 0.048 mol) and *p*-TsOH (cat). The resulting solution was then refluxed with a Dean and Stark trap for 6 h. TLC (EtOAc/Hexane 2:8) showed the reaction had not gone to completion so more ethylene glycol (0.22 ml, 0.198 g 3.19 mmol) was added and the solution stirred for a further 17 h after which time the reaction was shown to have gone to completion by TLC. The reaction was quenched with water (20 mL) and the layers separated. The organic layer was washed with sat aq $NaHCO_3$ (10 mL). The aqueous layers were extracted three times with diethyl ether (30 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated in *vacuo* to afford a yellow oil. Column chromatography (SiO_2, DCM) afforded the title compound **22** (2.91 g, 42%) as a yellow crystalline solid: **mp** = 83-85°C (DCM); **IR** (neat)/cm^{-1} ν_{max} 1729 (C=O), 1026 (C-O); **^{1}H NMR** (250 MHz, $CDCl_3$), δ 1.02 (3H, d, J = 6.5), 1.30 (1H, m), 1.73-2.09 (5H, m), 3.02 (1H, sept, J = 6.5), 3.74-4.06 (4H, m); **^{13}C NMR** (62.9 MHz, $CDCl_3$), δ 14.0 (CH_3), 22.0 (CH_2), 35.1 (CH_2), 37.2 (CH_2), 42.8 (CH), 64.4 (CH_2), 65.8 (CH_2), 107.1 (C) and 207.8 (C); **HRMS** (EI+) m/z calcd. for $C_9H_{14}O_3$ $[M]^+$ 170.0943, found 170.0942.

8-(1,3-dioxolane)-4a-methyl-4,4a,5,6,7,8-hexahydro-3*H*-naphthalen-2-one, **23**

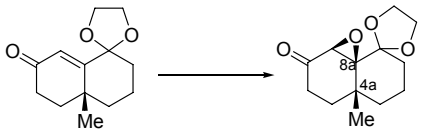


22 **23**

[3] R. C. Klix and R. D. Bach, *J. Org. Chem.*, 1987, **52**, 580-586.
[4] M. Utaka, Y. Fujii and A. Takeda, *Chem. Lett.*, 1986, 1103-1104.

Ketal protected 2-hydroxy-3-methylcyclohex-2-enone **22** (0.25 g, 1.49 mmol) was dissolved in methanol (10 mL) in a dry RB flask. The solution was transferred to a 2 neck RB flask, fitted with a reflux condenser, *via* a cannula. Sodium methoxide (0.018 g, 0.33 mmol) was dissolved in methanol (10 mL) and also transferred *via* cannula to the RB flask. To the stirring solution was added methyl vinyl ketone [MVK] (0.13 mL, 0.11 g, 1.53 mmol). The resulting solution was refluxed under N_2 for two hours. TLC (EtOAc/Hexane 2:8) showed the reaction had not gone to completion, prompting further reflux for an additional 16 h. TLC showed that the reaction had still not gone to completion so more MVK (0.13 mL, 0.11 g, 1.53 mmol) and sodium methoxide (cat amount) were added and the reaction was refluxed for a further 24 h after which time TLC showed complete reaction. Solid NH_4Cl was added and the methanol removed on a rotary evaporator. The resulting solid was partitioned between sat aq NH_4Cl (10 mL) and DCM (10 mL). The aqueous phase was extracted three times with DCM (20 mL) and the combined organic extracts dried ($MgSO_4$), filtered and concentrated to afford the title compound **23** (0.199 g, 60%) as a yellow crystalline solid: **mp** = 112-113ºC (ethyl acetate/hexanes); **IR** (neat)/cm^{-1} ν_{max} 1668 (C=O), 1028 (C-O); **^{1}H NMR** (250 MHz $CDCl_3$), δ 1.32 (3H, s), 1.63-1.99 (8H, m), 2.30-2.33 (2H, m), 3.72 (1H, m), 3.90-4.03 (3H, m), 6.06 (1H, s); **^{13}C NMR** (62.9 MHz, $CDCl_3$), δ 19.0 (CH_2), 22.5 (CH_3), 34.1 (CH_2), 37.0 (C), 37.0 (CH_2), 39.4 (CH_2), 40.8 (CH_2), 63.7 (CH_2), 65.5 (CH_2), 107.1 (C), 122.7 (CH), 164.6 (C) and 200.7 (C); **HRMS** (EI+) m/z calcd. for $C_{13}H_{18}O_3$ $[M]^+$ 222.1256, found, 222.1251.

8-(1,3-dioxolane)-4a-methyl-hexahydro-1-oxa-cyclopropa[*d*]naphthalen-2-one, **11**



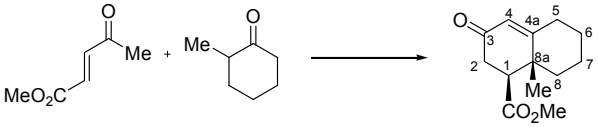
23 **11**

Enone **23** (1.01 g, 4.5 mmol) was dissolved in methanol (30 ml) and cooled to 0 ˚C. To the stirring solution was added $CeCl_3.7H_2O$ (2.52 g, 6.76 mmol). $NaBH_4$ (0.18 g, 4.83 mmol) was then added portion wise over approximately 10 min. The resulting solution was stirred for 30 min after which time TLC (EtOAc/Hexane 2:8) showed complete reaction. Acetone (20 mL) and solid NH_4Cl were added to the reaction mixture and the solvent was removed in *vacuo*. The product was then partitioned between sat aq NH_4Cl (10 mL) and diethyl ether (10 mL). The aqueous layer was extracted with diethyl ether (4 × 20mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated to yield the product allylic alcohol as a yellow oil (1.02 g, 100%) which was sufficiently pure to be used in the next step without further purification: **^{13}C NMR** (62.9 MHz, $CDCl_3$), δ 19.3 (CH_2), 24.6 (CH_3), 28.5 (CH_2), 35.9 (C), 37.6 (CH_2), 39.0 (CH_2), 41.4 (CH_2), 63.3 (CH_2), 64.9 (CH_2), 68.2 (CH), 107.7 (C), 125.3 (CH) and 142.7 (C); **HRMS** (EI+) m/z calcd. for $C_{13}H_{20}O_3$ $[M]^+$ 224.1412, found, 224.1414.

The allylic alcohol from the previous step (0.97 g, 4.31 mmol) was dissolved in DCM (30 mL) and cooled to 0 ˚C. To the stirring solution was added $NaHCO_3$ (0.72 g, 8.61 mmol). *m*-CPBA (1.37 g, 7.96 mmol) was then added portionwise over approx 15 min. The resulting solution was stirred for 5 h after which time TLC (EtOAc/Hexane 4:6) showed complete reaction. sat aq Solutions of $Na_2S_2O_3$ (10 mL) and $NaHCO_3$ (10 mL) were added and the layers separated. The aqueous layer was extracted with DCM (3 × 10 mL). The organic layers were combined, dried ($MgSO_4$), filtered and concentrated to yield a pale yellow oil. Column chromatography (SiO_2, EtOAc/hexane 3:7) yielded the product epoxy alcohol as a colourless oil (0.77 g, 75%): **IR** (neat)/cm^{-1} ν_{max} 3443 (O-H); **^{1}H NMR** (360 MHz, $CDCl_3$) δ 0.99 (1H, m), 1.20 (3H, s), 1.37-1.65 (8H, m), 1.65-1.89 (2H, m), 3.62 (1H, d, *J* = 4.4 Hz), 3.82-3.95 (2H, m), 4.04-4.13 (2H, m); **^{13}C NMR** (90.5 MHz, $CDCl_3$) δ 18.9 (CH_2), 23.8 (CH_3), 26.3 (CH_2), 32.0 (CH_2), 34.6 (C), 36.2 (CH_2), 36.3 (CH_2), 59.3 (CH), 64.3 (C), 65.5 (CH_2), 65.9 (CH_2) 68.8 (C) and 107.6 (C). **HRMS** (EI+) m/z calcd. for $C_{13}H_{20}O_4$ $[M]^+$ 240.1362, found, 240.1356.

The epoxy alcohol from the previous step (0.77 g, 3.22 mmol) was dissolved in DCM (50 mL) and cooled to 0 ºC. To the stirring solution was added PCC (1.75 g, 8.13 mmol) portion-wise over approximately 1 h. The resulting solution was stirred for 18 h after which time TLC (EtOAc/hexane 4:6) showed incomplete reaction. More PCC (0.71 g, 3.27 mmol) was carefully added at 0 ºC and the resulting solution was stirred for a further 6 h after which time the reaction had gone to completion. The solution was filtered (SiO_2, DCM) to remove the chromium salts, dried ($MgSO_4$), filtered and concentrated to yield the *α,β* epoxy ketone **11** (0.67g, 87%) as a white solid (dr >8:1). The solid was recrystallised from diethyl ether to yield the pure product as white needles: **mp** = 97-99 ºC (diethyl ether); **IR** (neat)/cm^{-1} ν_{max} 1712 (C=O); **^{1}H NMR** (360 MHz, $CDCl_3$) δ 1.33 (1H, m), 1.34 (3H, s), 1.46 (1H, m), 1.56-1.72 (3H, m), 1.82-1.99 (3H, m), 2.16-2.43 (2H, m), 3.40 (1H, s), 3.81-4.08 (4H, m); **^{13}C NMR** (90.5 MHz, $CDCl_3$) δ 18.9 (CH_2), 23.4 (CH_3), 32.6 (CH_2), 33.3 (CH_2), 34.7 (CH_2), 35.5 (C), 36.5 (CH_2), 58.2 (CH), 65.5 (CH_2), 65.7 (CH_2), 69.5 (C), 107.0 (C) and 206.1 (C); **HRMS** (EI+) m/z calcd. for $C_{13}H_{18}O_4$ $[M]^+$ 238.1200, found, 238.1200.

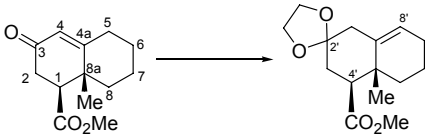
8a-Methyl-3-oxo-1,2,3,5,6,7,8,8a-octahydro-naphthalene-1-carboxylic acid methyl ester, **15**[5]



13 **14** **15**

Methyl 4-oxo-2-pentenoate (30.177g, 0.236 mol) and 2-methyl-cyclohexanone (28.7 mL, 0.236 mol) were dissolved in toluene (460 mL). A catalytic amount of TsOH (8.981g, 0.047 mol, 20 mol%) was added and the reaction mixture was refluxed under an atmosphere of nitrogen with a Dean-Stark trap for 48 h. The reaction was allowed to cool to room temperature and quenched with sat aq $NaHCO_3$ (100 mL). The aqueous phase was extracted with diethyl ether (4 × 50 mL). The organic layers were combined, washed with brine, dried ($MgSO_4$), filtered and concentrated. Purification by column chromatography (SiO_2, ethyl acetate/hexanes 2:8) yielded the title compound **15** (10.04 g, 20 %) as a white solid: **mp** 58-61 °C (hexanes); **IR** (neat)/cm^{-1} ν_{max} 2934 (C-H), 1731 (C=O), 1672 (C=O); **^{1}H NMR** (360 MHz, $CDCl_3$) δ 1.22 (3H, s, C(8a)C*H*$_3$), 1.32-1.48 (2H, m), 1.56-1.68 (2H, m), 1.86-2.00 (2H, m), 2.27-2.43 (3H, m), 2.71-2.92 (2H, m), 3.70 (3H, s, CO_2CH_3), 5.70 (1H, s, C(4)*H*); **^{13}C NMR** (90.5 MHz, $CDCl_3$) δ 197.3 (C), 172.3 (C), 168.9 (C), 124.2 (CH), 51.7 (CH_3), 51.2 (CH), 39.6 (CH_2), 38.7 (C), 36.4 (CH_2), 32.7 (CH_2), 26.6 (CH_2), 21.6 (CH_2) and 18.2 (CH_3); **HRMS** (ES+) m/z calcd. for $C_{13}H_{19}O_4$ $[M+H]^+$ 223.1329, found, 223.1329.

4'a-Methyl-3,4'.4'a,5',6',7'-hexahydro-1'*H*-spiro[[1,3]dioxolane-2,2'-naphthalene]-4'-carboxylic acid methyl ester, **24**



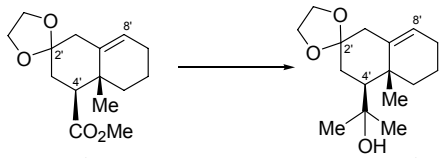
15 **24**

The enone **15** (3.28 g, 0.015 mol), ethylene glycol (1.25 mL, 0.022 mol) and a catalytic amount of TsOH were dissolved in benzene (100 mL). The resulting solution was refluxed under an atmosphere of nitrogen with a Dean-Stark trap for 18 h. The reaction mixture was allowed to cool to room temperature and quenched with sat aq $NaHCO_3$ (50 mL). The aqueous phase was extracted with diethyl ether (4 × 50 mL). The organic layers were combined, washed with brine (50 mL), dried ($MgSO_4$), filtered and concentrated. Purification by column chromatography (SiO_2, ethyl acetate/hexanes 2:8) yielded the title compound **24**

[5] J. E. McMurry and L. C. Blaszczak, *J. Org. Chem.*, 1974, **39**, 2217-2222.

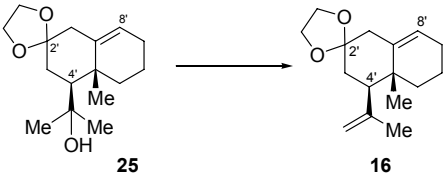
(3.641 g, 93 %) as a white solid: **mp** 44-46 °C; **IR** (neat)/cm^{-1} ν_{max} 2935 (C-H), 1731 (C=O); **^{1}H NMR** (360 MHz, $CDCl_3$) δ 1.13 (3H, s, C(4'a)CH_3), 1.58-1.69 (4H, m), 1.78 (1H, ddd, *J* = 3.4, 3.4, 13.8 Hz), 1.92-2.05 (2H, m), 2.09-2.17 (2H, m), 2.51-2.58 (2H, m), 3.67 (3H, s, CO_2CH_3), 3.92-3.99 (4H, m, O-CH_2-CH_2-O), 5.45 (1H, m, C(8')*H*); **^{13}C NMR** (90.5 MHz, $CDCl_3$) δ 173.8 (C), 138.8 (C), 124.1 (CH), 108.3 (C), 64.6 (CH_2), 64.4 (CH_2), 51.2 (CH_3), 51.1 (CH), 41.7 (CH_2), 37.1 (CH_2), 36.7 (C), 34.0 (CH_2), 25.4 (CH_2), 19.4 (CH_3) and 18.8 (CH_2); **HRMS** (EI+) m/z calcd. for $C_{15}H_{22}O_4$ $[M]^+$ 266.1513, found, 266.1505.

2-(4'a-Methyl-3,4'.4'a,5',6',7'-hexahydro-1'*H*-spiro[[1,3]dioxolane-2,2'-naphthalene]-4'-yl)-propan-2-ol, **25**



The protected ester **24** (3.641 g, 0.014 mol) was dissolved in tetrahydrofuran (50 mL) under an atmosphere of nitrogen. The solution was cooled to 0°C before adding methyl lithium (1.6 M, 21.9 mL, 0.035 mol) dropwise. The reaction was allowed to warm to room temperature and stirred over night. The solution was quenched with sat aq NH_4Cl (10 mL) after cooling to 0 °C. The aqueous layer was extracted with diethyl ether (4 × 15 mL). The organic layers were combined, washed with brine (30 mL), dried ($MgSO_4$), filtered and concentrated. Purification by column chromatography (SiO_2, ethyl acetate/hexanes 3:7) yielded the title compound **25** (2.867 g, 78 %) as a white solid: **mp** 39-41 °C (ethyl acetate/hexanes); **IR** (neat)/cm^{-1} ν_{max} 3398 (O-H), 2969 (C=O); **^{1}H NMR** (360 MHz, $CDCl_3$) δ 1.20 (3H, s, C(4'a)CH_3), 1.26 (3H, s, C(2)CH_3), 1.28 (3H, s, C(2)CH_3), 1.44-2.03 (9H, m) 2.05-2.22 (2H, m), 2.47 (1H, dd, *J* = 2.9, 13.5 Hz), 3.92-3.97 (4H, m, O-CH_2-CH_2-O), 5.36 (1H, m, C(8)*H*); **^{13}C NMR** (90.5 MHz, $CDCl_3$) δ 141.4 (C), 123.4 (CH), 108.9 (C), 75.1 (C), 64.2 (CH_2), 64.1 (CH_2), 54.4 (CH), 42.6 (CH_2), 39.5 (C), 39.2 (CH_2), 34.8 (CH_2), 32.0 (CH_3), 29.2 (CH_3), 25.3 (CH_2), 20.4 (CH_3) and 19.3 (CH_2); **HRMS** (ES+) m/z calcd. for $C_{16}H_{27}O_3$ $[M+H]^+$ 267.1955, found, 267.1956.

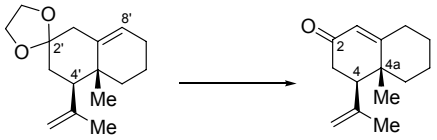
4'-Isopropenyl-4'a-methyl-3,4'.4'a,5',6',7'-hexahydro-1'*H*-spiro[[1,3]dioxolane-2,2'-naphthalene], **16**



The tertiary alcohol **25** (1.013 g, 3.8 mmol) was dissolved in pyridine (10 mL) under an atmosphere of nitrogen. Phosphoryl chloride (1.1 mL, 0.011 mol) was added dropwise and the resulting solution was stirred at room temperature for 18 h. The reaction was cooled to 0 °C before being quenched with water (10 mL). The aqueous phase was extracted with diethyl ether (3 × 20 mL). The combined organic layers were washed with aq HCl (20 mL, 1M), sat aq $NaHCO_3$ (20 mL) and brine (20 mL) before being dried ($MgSO_4$), filtered and concentrated in *vacuo*. Purification by column chromatography (SiO_2, ethyl acetate/hexanes 1:9) yielded the title compound **16** (0.705 g, 75 %) as a white solid: **mp** 38-41 °C (ethyl acetate/hexanes); **IR** (neat)/cm^{-1} ν_{max} 2939 (C-H); **^{1}H NMR** (360 MHz, $CDCl_3$) δ 1.06 (3H, s, C(4'a)CH_3), 1.44-1.62 (6H, m), 1.76 (3H, s, C(2)CH_2CH_3), 2.00 (2H, t, *J* = 13.5 Hz), 2.01-2.24 (2H, m), 2.52 (1H, dtd, *J* = 3.2, 5.5, 13.8 Hz), 3.93-3.97 (4H, m, O-CH_2-CH_2-O), 4.70 (1H, s, C(2)CH_2CH$_3$), 4.90 (1H, s, C(2)CH_2CH$_3$), 5.38 (1H, m, C(8')*H*); **^{13}C NMR** (90.5 MHz, $CDCl_3$) δ 145.7 (C), 140.7 (C), 122.8 (CH), 113.7 (CH_2), 109.0 (C), 64.4 (CH_2), 64.2 (CH_2), 51.6 (CH), 41.9 (CH_2), 37.6 (C), 37.4 (CH_2), 37.0 (CH_2),

25.7 (CH_2), 24.1 (CH_3), 19.3 (CH_3) and 18.9 (CH_2); **HRMS** (ES+) m/z calcd. for $C_{16}H_{25}O_2$ $[M+H]^+$ 249.1849, found, 249.1851.

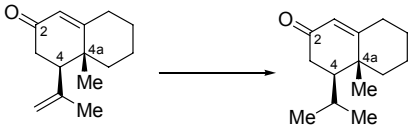
4-Isopropenyl-4a-methyl-4,4a,5,6,7,8-hexahydro-3*H*-naphthalen-2-one, **26**



16 **26**

The protected alkene **16** (0.045 g, 0.18 mmol) was dissolved in acetone (3 mL) and water (0.2 mL). TsOH (7.0 mg; 0.036 mmol, 20 mol%) was added and the solution was refluxed for 2.5 h. The reaction was allowed to cool to room temperature before being quenched with sat aq $NaHCO_3$ (10 mL). The aqueous phase was extracted with dichloromethane (4 × 15 mL). The combined organic layers were washed with brine (20 mL) before being dried ($MgSO_4$), filtered and concentrated in *vacuo*. Purification by column chromatography (SiO_2, ethyl acetate/hexanes 1:9) yielded the title compound **26** (0.030 g, 81 %) as a white solid: **mp** 28-31 °C (ethyl acetate/hexanes); **IR** (neat)/cm^{-1} ν_{max} 2931 (C-H), 1672 (C=O); **^{1}H NMR** (360 MHz, $CDCl_3$) δ 1.17 (3H, s, C(4a)CH_3), 1.25-1.43 (2H, m), 1.54-1.67 (2H, m), 1.79 (3H, s, CCH_2CH_3), 1.87-1.91 (2H, m, CH_2), 2.24-2.33 (2H, m), 2.38-2.48 (1H, m), 2.56-2.65 (2H, m), 4,76 (1H, s, CCH_2CH$_3$), 5.01 (1H, s, CCH_2CH$_3$), 5.75 (1H, s, C(1)*H*); **^{13}C NMR** (90.5 MHz, $CDCl_3$) δ 200.0 (C), 170.9 (C), 143.8 (C), 124.2 (CH), 115.4 (CH_2), 52.4 (CH), 40.0 (C), 39.7 (CH_2), 39.6 (CH_2), 32.9 (CH_2), 26.7 (CH_2), 23.7 (CH_3), 21.8 (CH_2) and 18.1 (CH_3); **HRMS** (ES+) m/z calcd. for $C_{14}H_{21}O$ $[M+H]^+$ 205.1587, found, 205.1585.

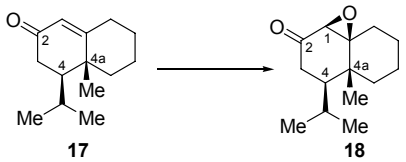
4-Isopropyl-4a-methyl-4,4a,5,6,7,8-hexahydro-3*H*-naphthalen-2-one, **17**



26 **17**

$(PPh_3)_3RhCl$ (0.034 g, 0.037 mmol, 10 mol%) was added to a solution of alkene **26** (0.075 g, 0.367 mmol) dissolved in methanol (10 mL). The resulting solution was placed in a high pressure reaction vessel and subjected to hydrogen at 15 bar for 12 h. The solution was concentrated and purified by column chromatography (SiO_2, 10% ethyl acetate in hexanes) to yield the title compound **17** (0.074 g, 99 %) as a white solid: **mp** 40-43 ºC (ethyl acetate/hexanes); **IR** (neat)/cm^{-1} ν_{max} 2936 (C-H), 1670 (C=O); **^{1}H NMR** (360 MHz, $CDCl_3$) δ 0.88 (3H, d, J = 6.9 Hz, CH(CH_3)$_A$(CH$_3$)$_B$), 0.94 (3H, d, J = 6.9 Hz, CH(CH$_3$)$_A$ (CH_3)$_B$), 1.16 (3H, s, C(4a)CH_3), 1.29-1.42 (2H, m), 1.58-1.77 (4H, m), 1.84-1.91 (1H, m), 1.98-2.12 (2H, m), 2.22-2.29 (2H, m), 2.40 (1H, m), 5.73 (1H, s, C(1)*H*); **^{13}C NMR** (90.5 MHz, $CDCl_3$) δ 200.8 (C), 171.3 (C), 124.4 (CH), 50.7 (CH), 40.6 (C), 38.9 (CH_2), 34.6 (CH_2), 32.8 (CH_2), 26.9 (CH_2), 24.9 (CH), 24.6 (CH_3), 21.8 (CH_2), 18.6 (CH_3) and 17.5 (CH_3); **HRMS** (ES+) m/z calcd. for $C_{14}H_{23}O$ $[M+H]^+$ 207.1743, found, 207.1741.

4-Isopropyl-4a-methyl-hexahydro-1-oxa-cyclopropa[*d*]naphthalen-2-one, **18**

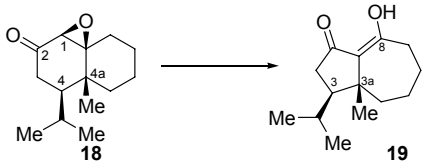


The ketone **17** (0.151g, 0.73 mmol) was dissolved in methanol (20 mL) and then cooled to 0 °C before $CeCl_3 \cdot 7H_2O$ (0.411 g, 1.67 mmol) and $NaBH_4$ (0.029 g, 0.75 mmol) were added. The resulting solution was stirred for 1 h at 0 °C. The reaction was quenched with acetone and solid NH_4Cl was added before being concentrated under reduced pressure. The resulting slurry was partitioned between water (15 mL) and diethyl ether (20 mL) and the layers separated. The aqueous phase was extracted with diethyl ether (5 × 20 mL). The combined organic layers were washed with brine (30 mL) before being dried ($MgSO_4$), filtered and concentrated to yield the allylic alcohol (0.149 g, 98 %) as a white solid which could be used without further purification.

The alcohol (0.149 g, 0.715 mmol) was dissolved in dichloromethane (7 mL) and the solution was cooled to 0 °C before $NaHCO_3$ (0.120 g, 0.143 mmol) and *m*CPBA (0.265 g, 1.07 mmol) were added. The resulting solution was stirred for 1.5 h at 0 °C and then quenched with aq sat $Na_2S_2O_5$ (10 mL) and the layers separated. The aqueous phase was extracted with dichloromethane (4 × 15 mL) and the combined organic layers were washed with brine (20 mL) before being dried ($MgSO_4$), filtered and concentrated. Column chromatography (SiO_2, ethyl acetate/hexanes 3:7) yielded the epoxide (0.150 g, 94 %) as a colourless oil: **^{1}H NMR** (360 MHz, $CDCl_3$) δ 0.78 (3H, d, J = 6.6 Hz, $CH(CH_3)_A(CH_3)_B$), 0.85 (3H, d, J = 6.6 Hz, $CH(CH_3)_A(CH_3)_B$), 1.01 (3H, s, C(4a)CH_3), 1.07-1.18 (2H, m), 1.24-1.41 (4H, m), 1.42-1.54 (2H, m), 1.73 (1H, m), 1.81 (1H, m), 1.92-2.01 (2H, m), 2.59 (1H, s, O*H*), 3.12 (1H, s, C(1)*H*), 3.87 (1H, dd, J = 6.4, 10.6 Hz); **^{13}C NMR** (90.5 MHz, $CDCl_3$) δ 70.4 (CH), 67.5 (C), 66.7 (CH), 51.3 (CH), 39.7 (CH_2), 36.3 (C), 32.3 (CH_2), 25.8 (CH_2), 25.4 (CH), 24.9 (CH_2), 24.4 (CH_3), 21.1 (CH_2), 18.5 (CH_3) and 16.3 (CH_3).

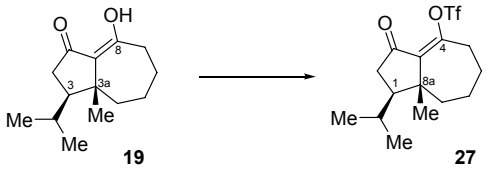
The epoxy-alcohol (0.150 g, 0.669 mmol) was dissolved in dichloromethane (10 mL) and cooled to 0 °C before PDC (0.394 g, 1.0 mmol) was added. The resulting solution was allowed to warm to room temperature and stirred for 18 h. More PDC (0.178 g, 0.472 mmol) was added and the solution was stirred for a further 17 h before being filtered through SiO_2, eluting with dichloromethane, and concentrated. Column chromatography (SiO_2, ethyl acetate/hexanes 1:9) yielded the title compound **18** (0.132 g, 89 %) as a colourless oil (dr>20:1): **IR** (neat)/cm^{-1} ν_{max} 2934 (C-H), 1718 (C=O); **^{1}H NMR** (360 MHz, $CDCl_3$) δ 0.82 (3H, d, J = 6.9 Hz, $CH(CH_3)_A(CH_3)_B$), 0.86 (3H, d, J = 6.9 Hz, $CH(CH_3)_A(CH_3)_B$), 1.18 (3H, s, C(4a)CH_3) 1.21-1.62 (5H, m), 1.68-2.07 (5H, m), 2.74 (1H, dd, J = 12.3, 12.3 Hz), 3.05 (1H, s), 5.29 (1H, s, C(1)*H*); **^{13}C NMR** (90.5 MHz, $CDCl_3$) δ 209.8 (C), 72.9 (C), 65.3 (CH), 55.8 (CH), 39.5 (CH_2), 37.8 (C), 33.6 (CH_2), 32.1 (CH_2), 26.3 (CH), 24.6 (CH_2), 24.0 (CH_3), 20.9 (CH_2), 18.3 (CH_3) and 16.5 (CH_3); **HRMS** (ES+) m/z calcd. for $C_{14}H_{26}O_2N$ $[M+NH_4]^+$ 240.1958, found, 240.1959.

8-Hydroxy-3-isopropyl-3a-methyl-3,3a,4,5,6,7-hexahydro-2*H*-azulene-1-one, **19**



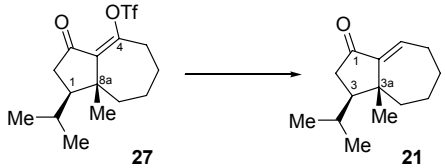
The epoxy ketone **18** (0.052 g, 0.23 mmol) was dissolved in ethanol (200 mL) and the solution deoxygenated by bubbling nitrogen through for 1 h. The solution was then immersed in an ice bath and exposed to UV radiation through a Pyrex filter for 9 h before being concentrated. Column chromatography (SiO_2, ethyl acetate/hexanes 1:9) afforded the desired product (29 mg, 56%) as a white solid, along with recovered starting material (0.012 g, 23%): **mp** 44-47 ºC (ethyl acetate/hexanes); **IR** (neat)/cm^{-1} ν_{max} 2959 (C-H), 2924 (C-H), 1613 (C=O); **^{1}H NMR** (360 MHz, $CDCl_3$) δ 0.92 (3H, d, J = 6.7 Hz, $CH(CH_3)_A$ $(CH_3)_B$), 1.02 (3H, d, J = 6.7 Hz, $CH(CH_3)_A(CH_3)_B$), 1.09 (3H, s, C(3a)CH_3), 1.20-1.80 (6H, m), 1.85 (1H, m), 2.10-2.40 (2H, m), 2.23-2.46 (2H, m), 2.59 (1H, m), 14.52 (1H, s, C(8)OH) ; **^{13}C NMR** (90.5 MHz, $CDCl_3$) δ 202.5 (C), 183.2 (C), 120.5 (C), 53.5 (CH), 44.8 (C), 41.3 (CH_2), 39.7 (CH_2), 36.8 (CH_2), 28.5 (CH), 25.3 (CH_2), 25.2 (CH_2), 24.0 (CH_3), 22.3 (CH_3) and 17.9 (CH_3); **HRMS** (EI+) m/z calcd. for $C_{14}H_{22}O_2$ $[M]^+$ 222.1614, found, 222.1614.

Trifluoromethanesulfonic acid 1-isopropyl-8a-methyl-3-oxo-1,2,3,5,6,7,8,8a octahydro-azulen-4-yl-ester, **27**



The enol **19** (0.050 g, 0.225 mmol) was dissolved in dichloromethane (5 mL) under nitrogen. The mixture was cooled to 0 °C before adding diisopropylethylamine (78 µl, 0.450 mmol) and trifluoromethansulfonic anhydride (56 µl, 0.338 mmol). After stirring for 1 h at 0 °C the reaction was quenched with water and the aqueous phase was extracted with dichloromethane (4 × 5 mL). The combined organic layers were washed with brine (10 mL) before being dried ($MgSO_4$), filtered and concentrated in *vacuo*. Purification by column chromatography (SiO_2, ethyl acetate/hexanes 1:9) yielded the title compound **27** (0.068 g, 86 %) as a yellow oil: **IR** (neat)/cm^{-1} ν_{max} 2934, 1427, 1208, 1242; **^{1}H NMR** (360 MHz, $CDCl_3$) δ 0.91 (3H, d, J = 6.4 Hz, $CHCH_3$), 1.00 (3H, d, J = 6.4 Hz, $CHCH_3$), 1.22 (3H, s, CH_3), 1.47-1.64 (2H, m), 1.71-2.02 (6H, m), 2.43-2.66 (4H, m); **^{13}C NMR** (90.5 MHz, $CDCl_3$) δ 17.9 (CH_3), 21.5 (CH_3), 23.2 (CH_3), 24.2 (CH_2), 24.6 (CH_2), 28.4 (CH), 34.7 (CH_2), 41.3 (CH_2), 44.0 (CH_2), 47.6 (C), 58.3 (CH), 113.0-123.6 ($-CF_3$), 138.0 (C), 150.7 (C), 199.2 (C).

3-isopropyl-3a-methyl-3-3a,4,5,6,7-hexahydro-2*H*-azulen-1-one, **21**[6]

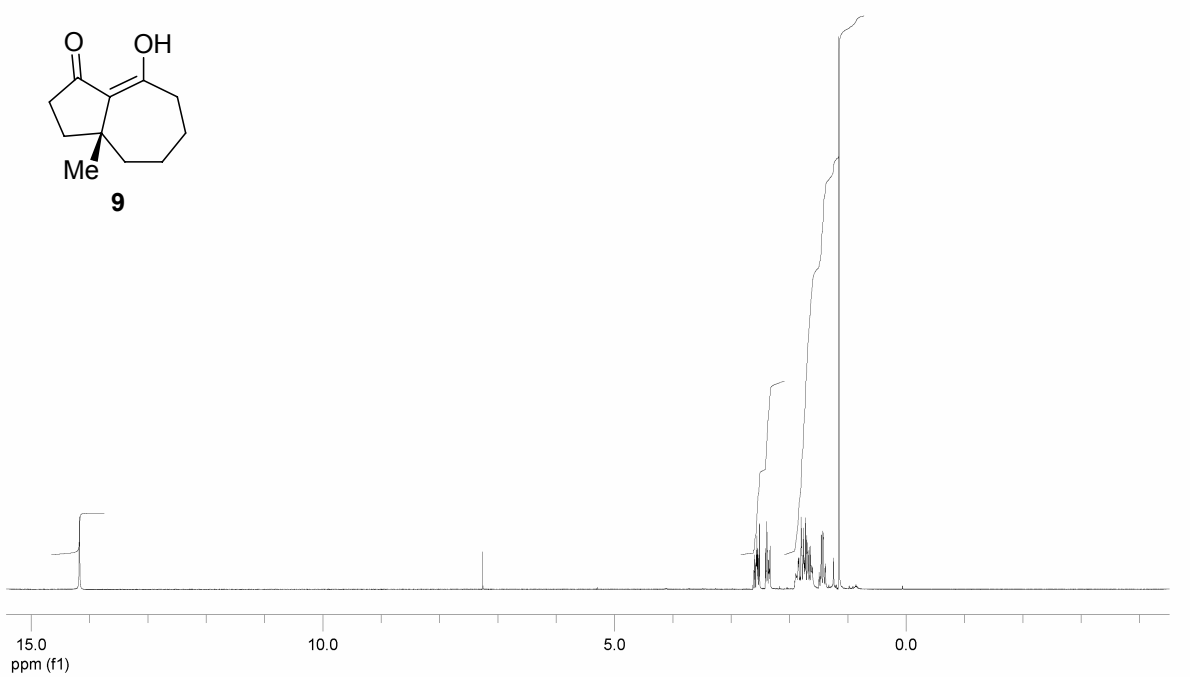


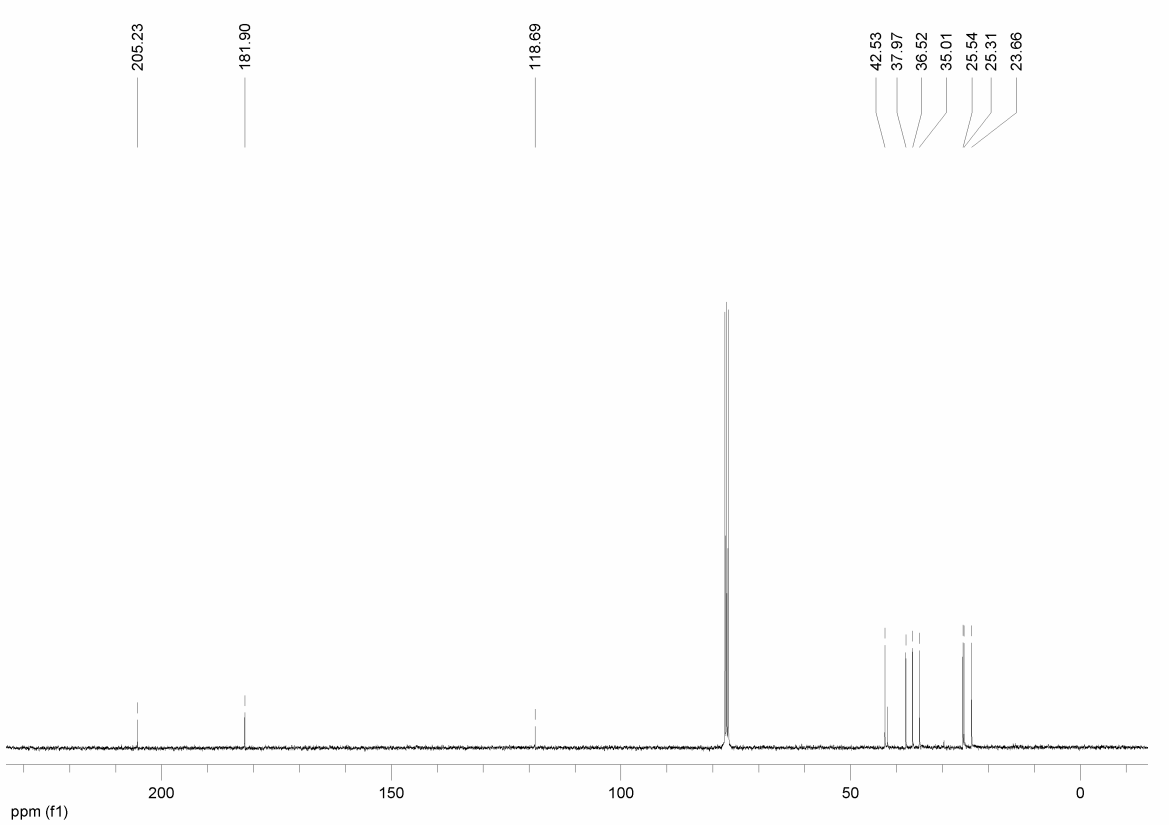
To a solution of **27** (0.065 g, 0.183 mmol) in DMF (3 mL) under nitrogen was added palladium acetate (catalytic amount), triphenylphosphine (catalytic amount), triethylamine (76 µl, 0.55 mmol) and formic acid (14 µl, 0.367 mmol); the solution was stirred for 16 h at 60 °C. The mixture was filtered through SiO_2 and purified by column chromatography (SiO_2, ethyl acetate/hexanes 1:9) to yield the title compound **21** (0.029 g, 76 %) as a colourless oil: **IR** (neat)/cm^{-1} ν_{max} 2926 (C-H), 1671 (C=O); **^{1}H NMR** (360 MHz, $CDCl_3$) δ 0.92 (3H, d, J = 6.6 Hz, $CH(CH_3)_A$ $(CH_3)_B$), 1.00 (3H, d, J = 6.6 Hz, $CH(CH_3)_A(CH_3)_B$), 1.14 (3H, s, C(3a)CH_3), 1.38-1.51 (2H, m), 1.61-1.72 (4H, m), 1.92 (1H, m), 2.04-2.13 (2H, m), 2.41-2.54 (2H,

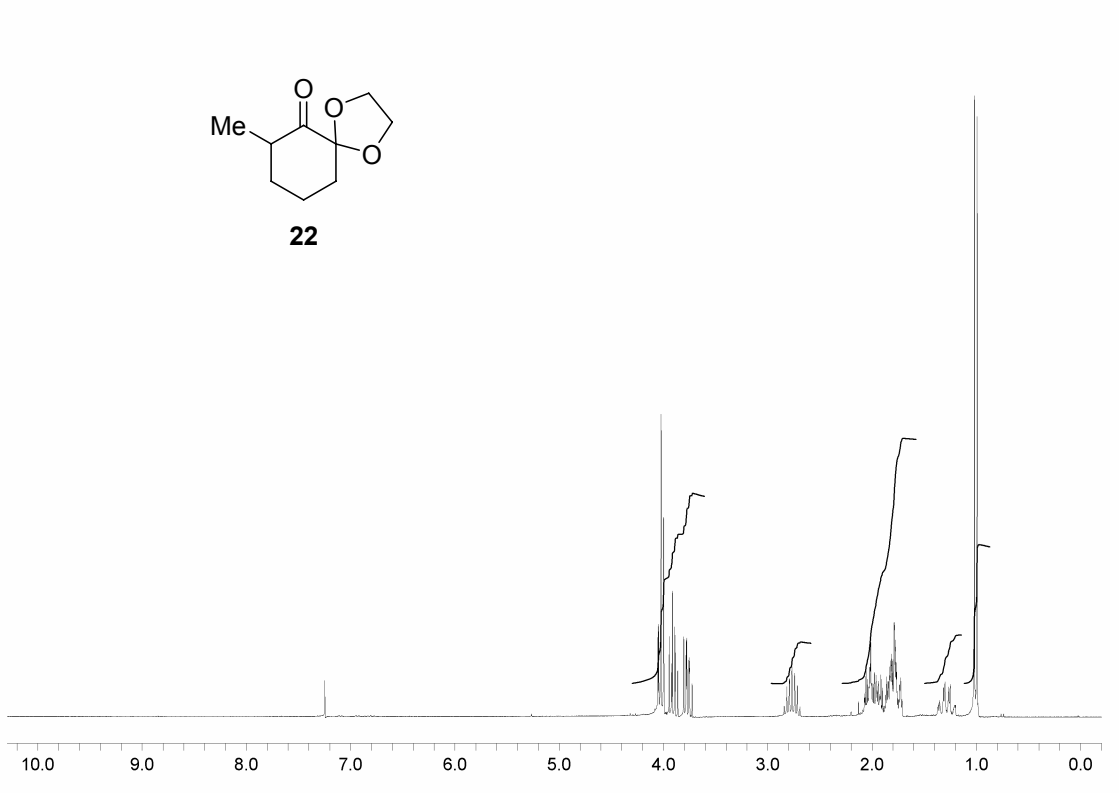
[6] P. Chiu and S. Li, *Org. Lett.*, 2004, **6**, 613-616.

m), 2.61 (1H, m), 6.78 (1H, dd, *J* = 2.4, 3.3 Hz, C(8)*H*); **^{13}C NMR** (90.5 MHz, $CDCl_3$) δ 200.7 (C), 152.6 (C), 141.0 (CH), 58.3 (CH), 47.9 (C), 43.9 (CH_2), 41.6 (CH_2), 34.8 (CH_2), 28.9 (CH), 25.4 (CH_2), 25.0 (CH_2), 23.4 (CH_3), 22.5 (CH_3) and 17.7 (CH_3).

3. NMR Spectra



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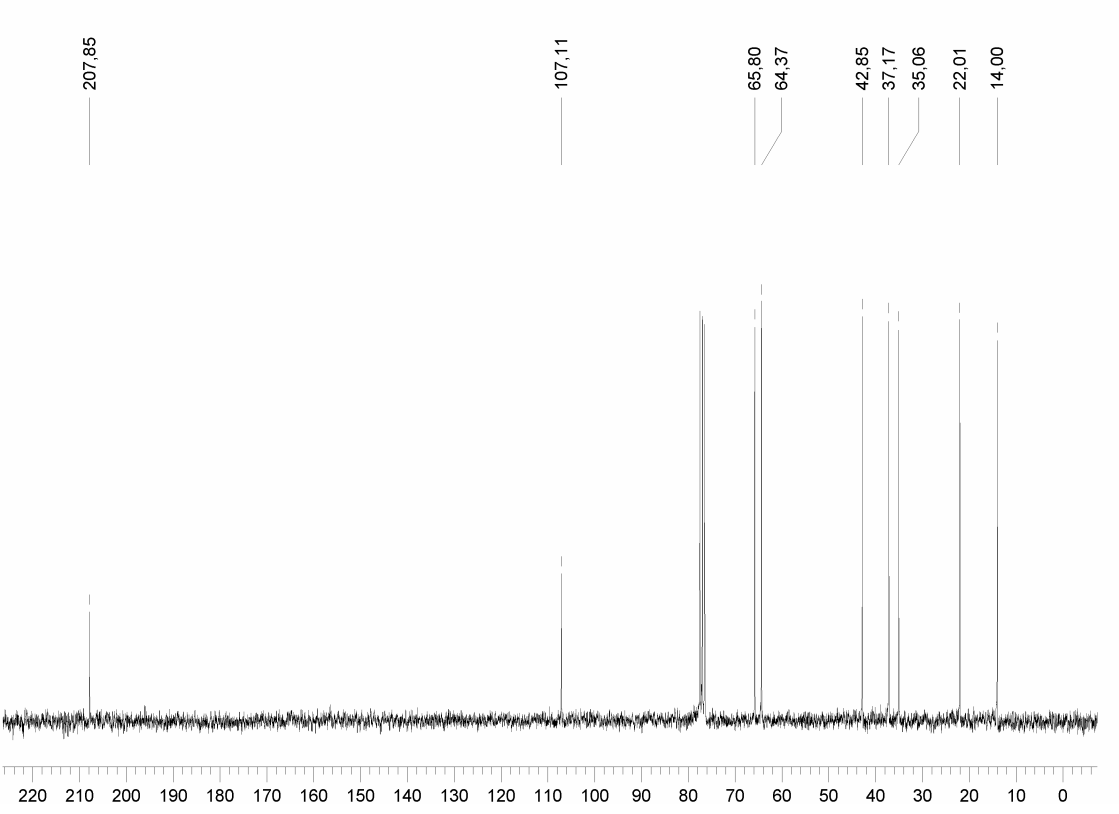
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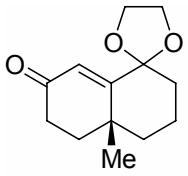
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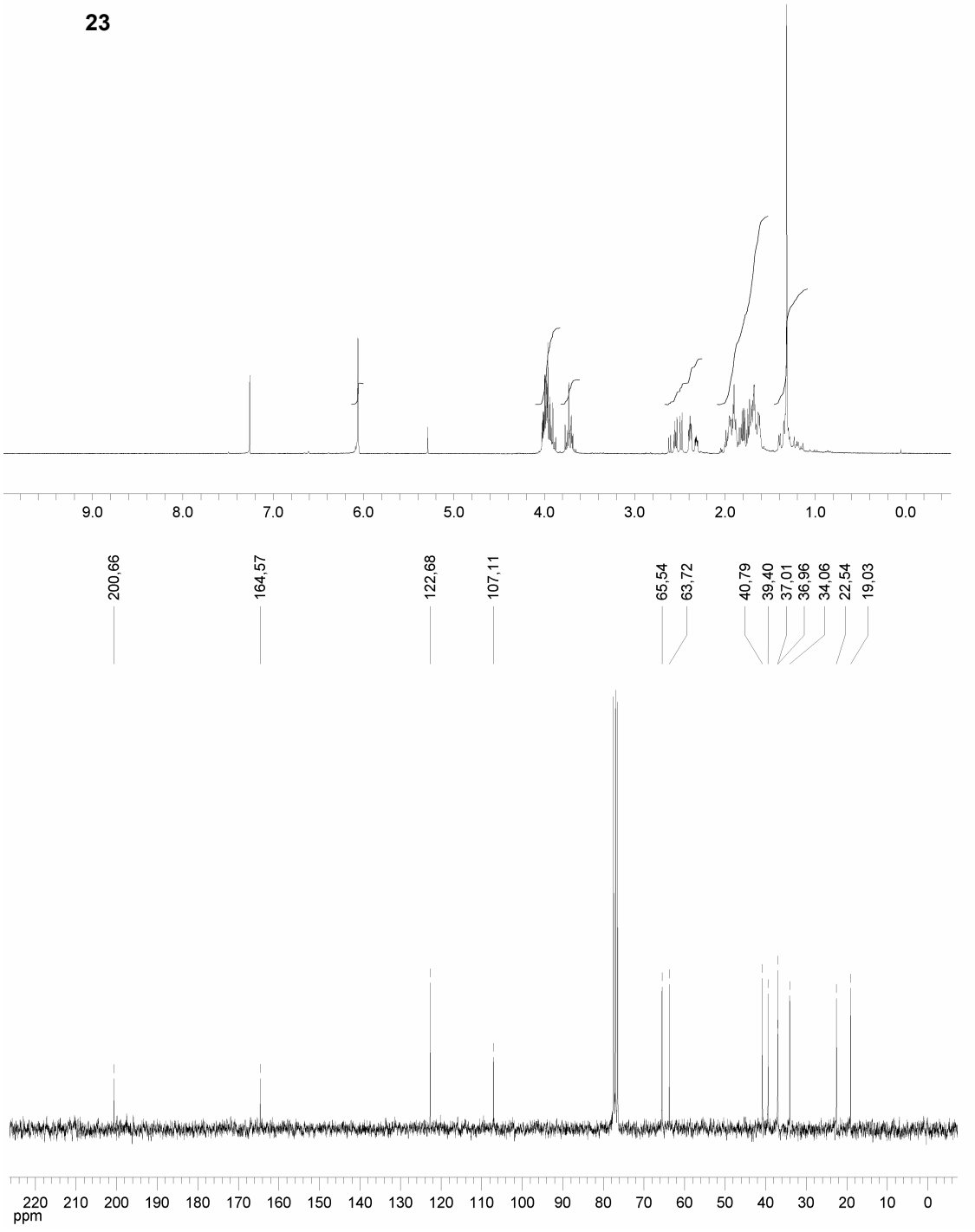
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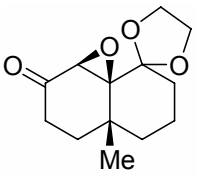
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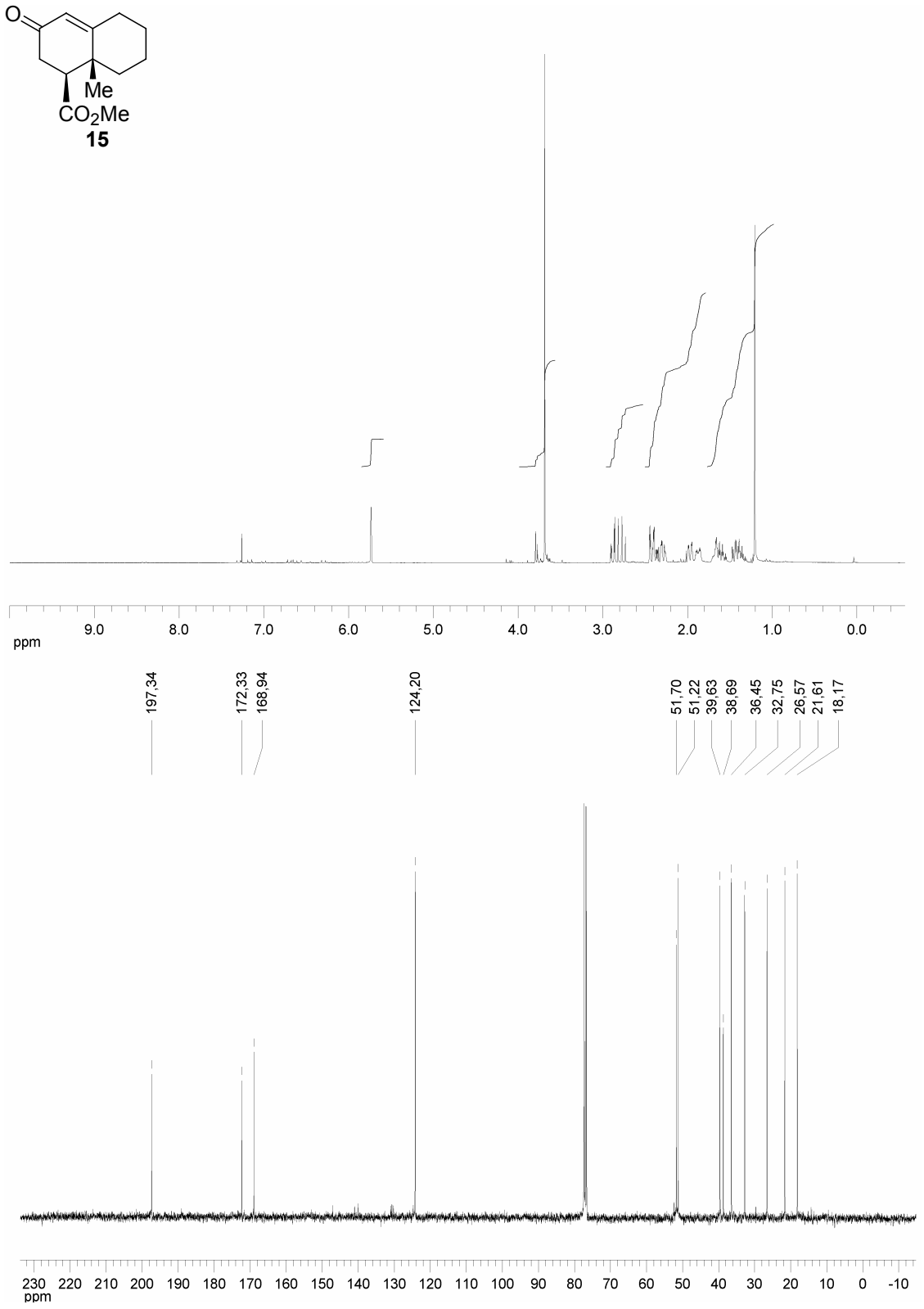
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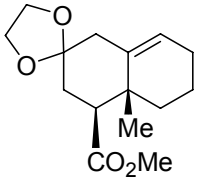
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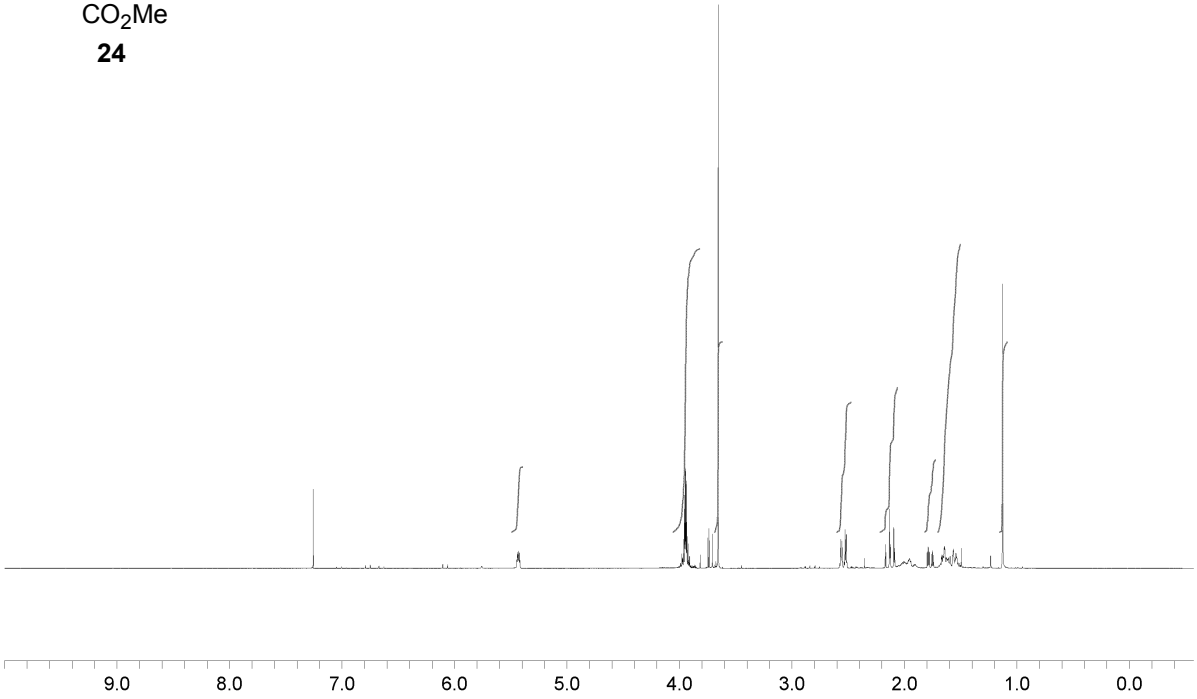
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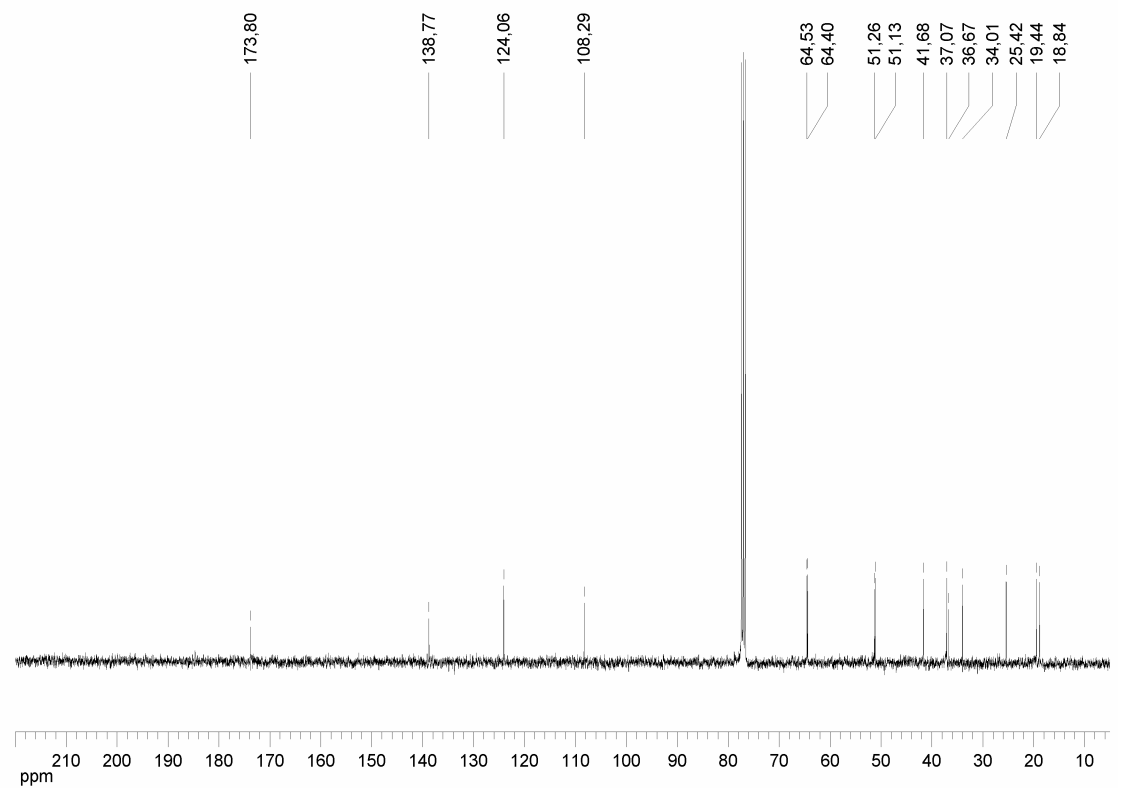
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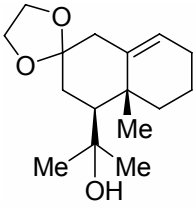
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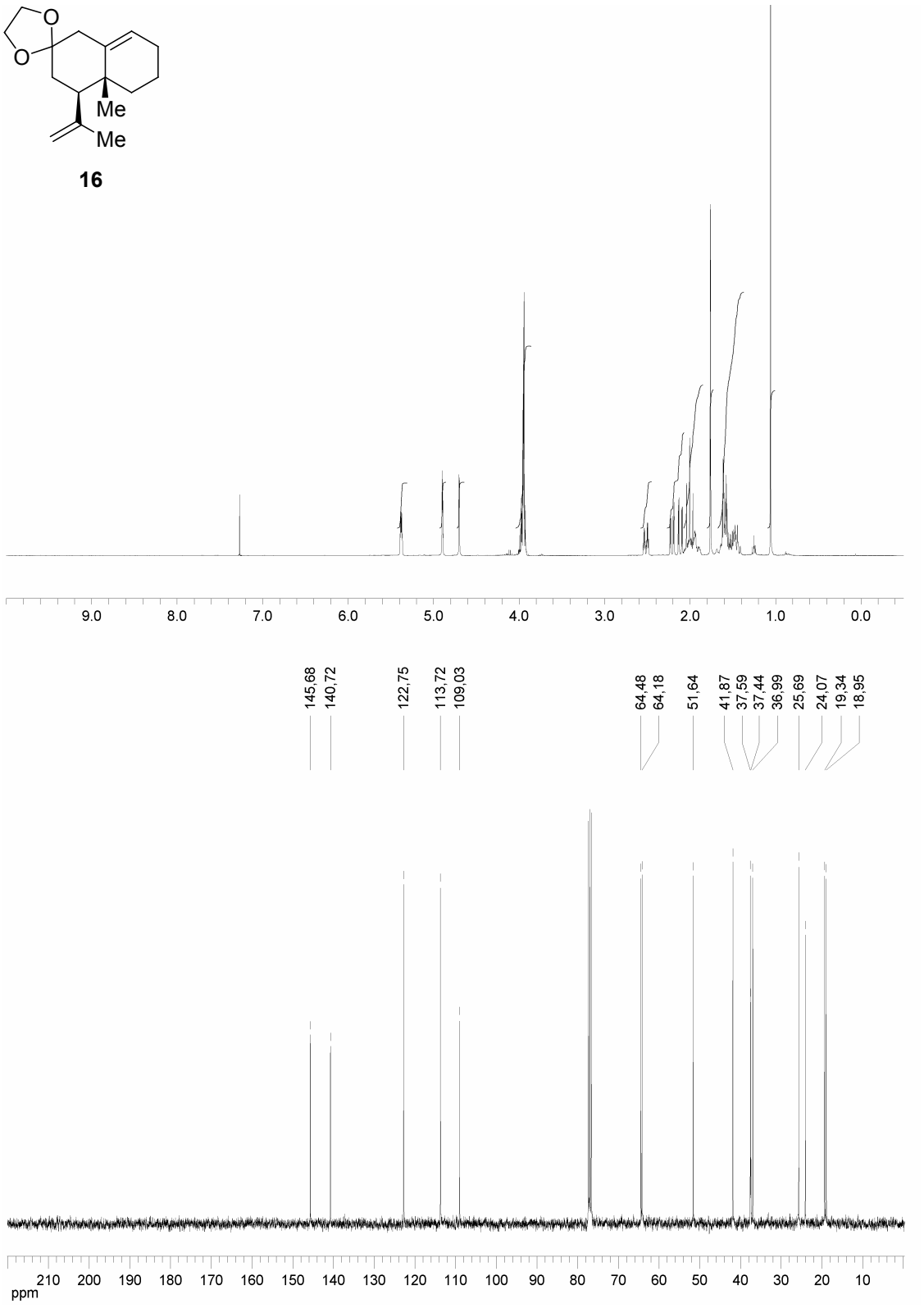
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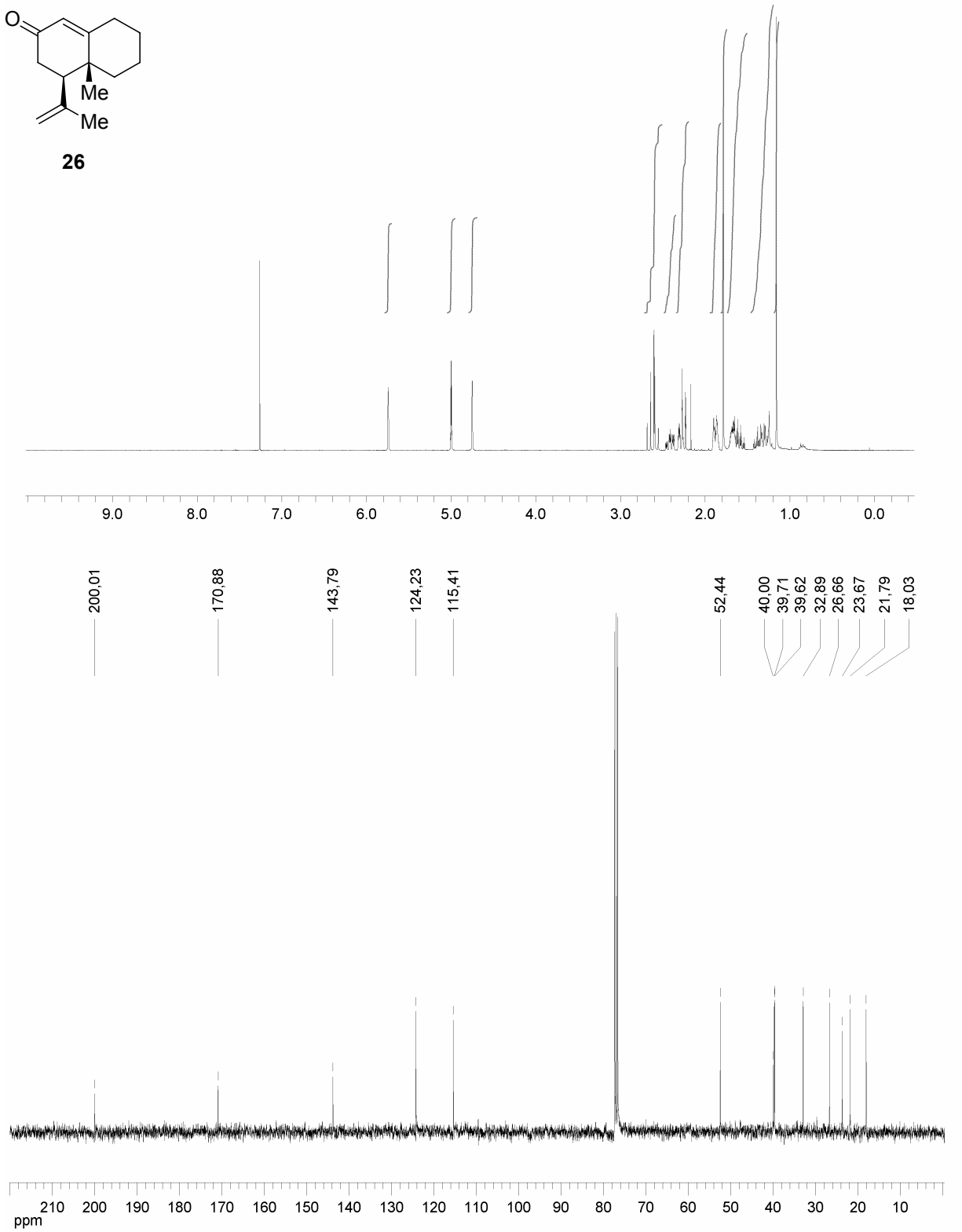
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143,79
124,23
115,41
52,44
40,00
39,71
39,62
32,89
26,66
23,67
21,79
18,03
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
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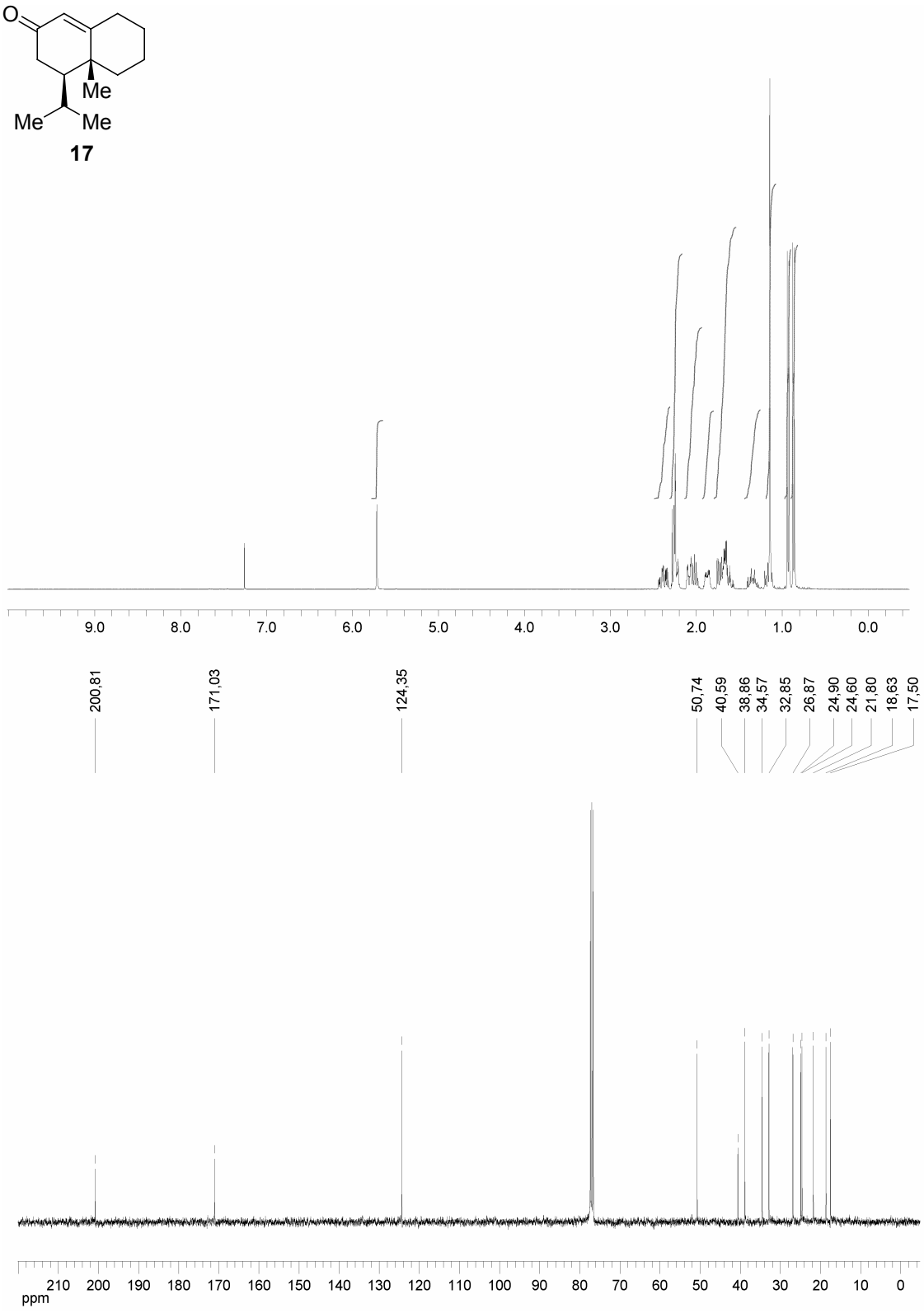
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Me
Me
Me
17
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8.0
7.0
6.0
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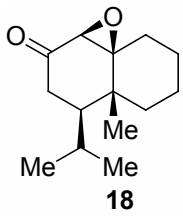
4.0
3.0
2.0
1.0
0.0
200,81
171,03
124,35
50,74
40,59
38,86
34,57
32,85
26,87
24,90
24,60
21,80
18,63
17,50
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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O
Me
Me
Me

18

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8.0
7.0
6.0
5.0
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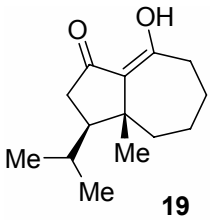
3.0
2.0
1.0
0.0
209,75
72,90
65,33
55,75
39,52
37,82
33,57
32,06
26,26
24,63
23,99
20,90
18,34
16,50
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
ppm


O
OH
Me
Me
Me

19

ppm
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12.0
11.0
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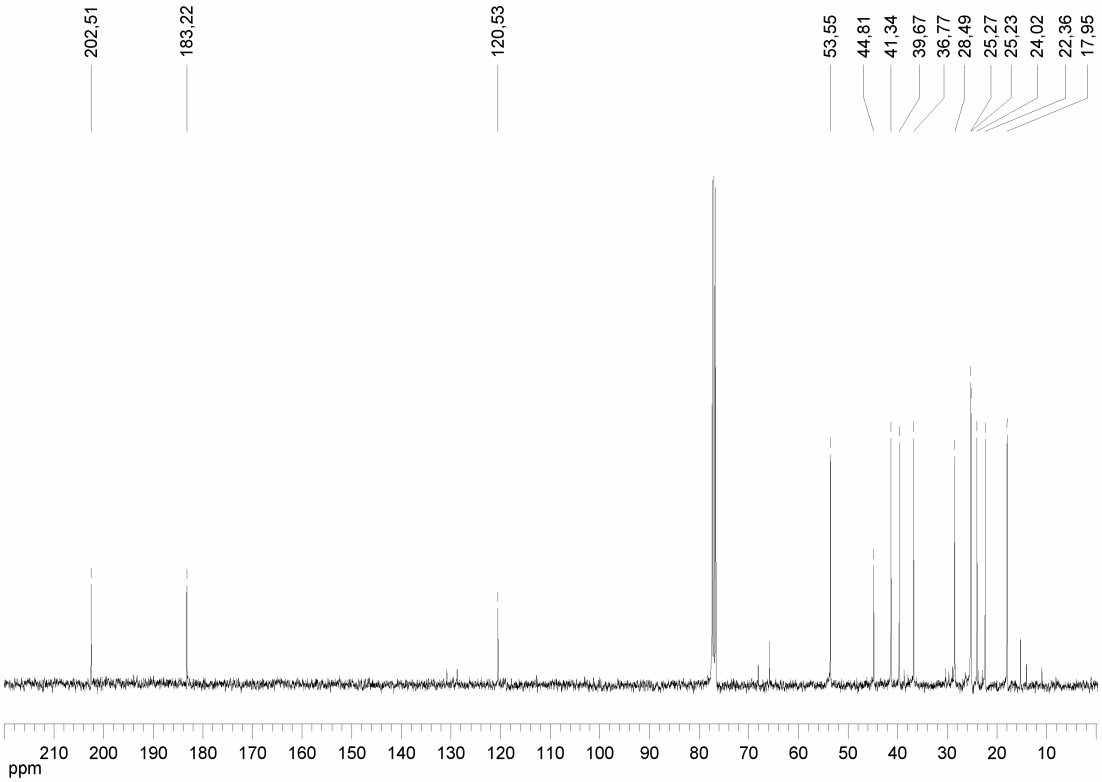
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0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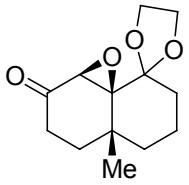
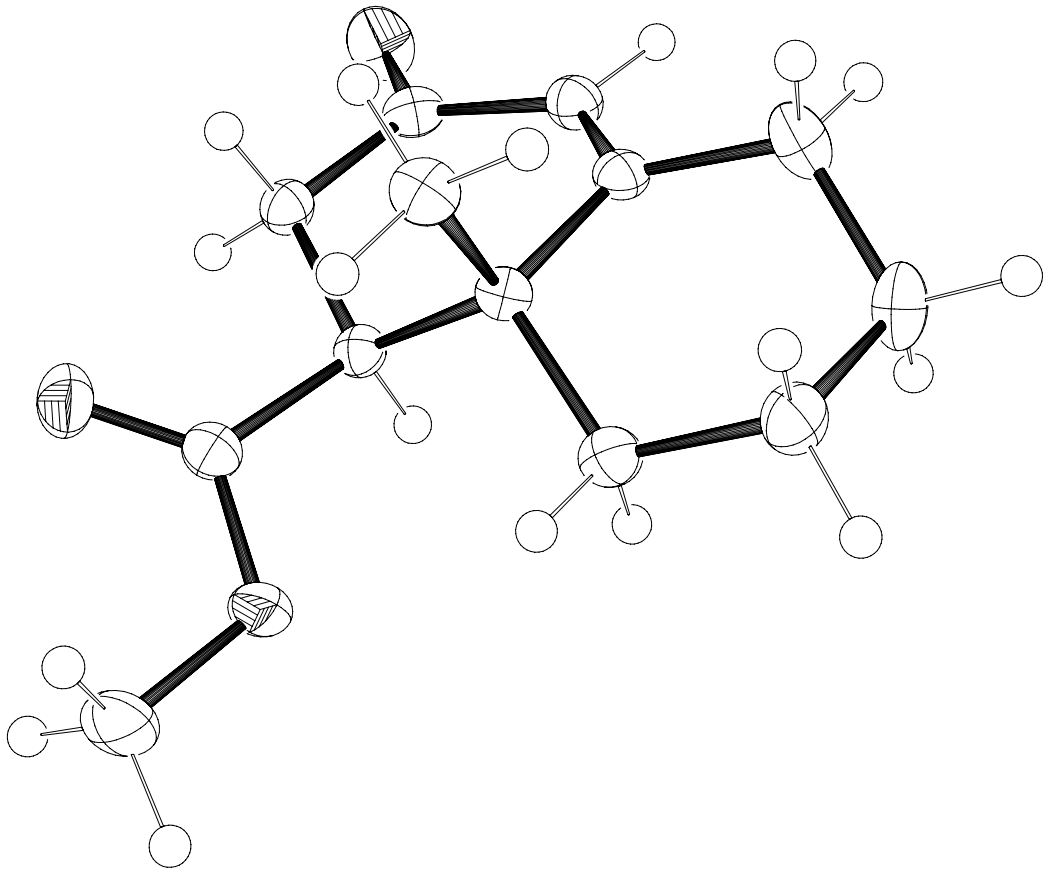
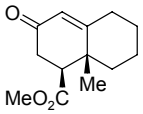
183,22
120,53
53,55
44,81
41,34
39,67
36,77
28,49
25,27
25,23
24,02
22,36
17,95
ppm
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

4. ORTEP Structures







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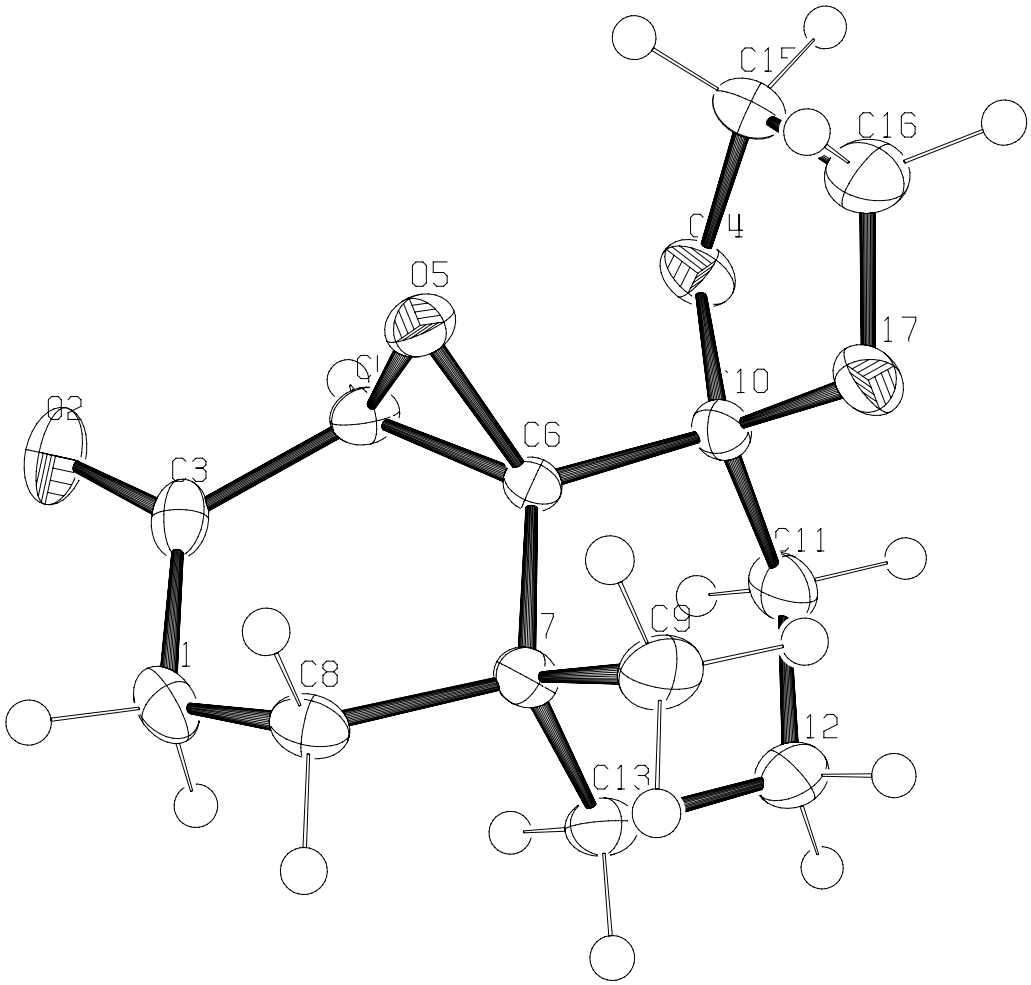

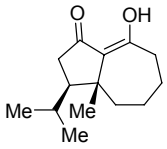

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