

A General Method for the Synthesis of Nonracemic *trans*-Epoxides: Concise Syntheses of *trans*-Epoxide Containing Insect Sex Pheromones

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Supporting Information

Experimental Procedures	pages 1-12
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General

All reactions described were performed under an atmosphere of dry argon using oven-dried glassware unless otherwise specified. THF, Et₂O, CH₂Cl₂ were used directly from an MBraun Solvent Purifier System (MB-SP Series). Commercial anhydrous EtOH (reagent grade) was used without further purification. Cold temperatures were maintained by the use of following reaction baths: 0 °C, ice-water; -30 °C, ethyl acetate-ethanol; -78 °C, acetone-dry ice. Flash chromatography was carried out with 230-400 mesh silica gel (E. Merck, Silica Gel 60) following the technique described by Still.¹ Concentration of solvents was accomplished with a Buchi rotary evaporator using acetone-dry-ice condenser and removal of trace solvents was accomplished with a Welch vacuum pump.

Gas chromatography (GC) analysis was performed on a Hewlett Packard model 6890 gas chromatograph, equipped with a flame ionization detector and a custom made fused silica column with a 1:1 mixture of heptakis-(2,6-di-*O*-methyl-3-*O*-pentyl)- β-cyclodextrin and OV-1701.^{2,3}

NMR spectra were recorded using deuteriochloroform (CDCl₃) as the solvent. Signal positions (δ) are given in parts per million from tetramethylsilane (δ 0) and were measured relative to the signal of the solvent (CDCl₃: δ 7.26, ¹H NMR; δ 77.0, ¹³C NMR). Coupling constants (*J* values) are given in Hertz (Hz) and are reported to the nearest 0.1 Hz. ¹H NMR spectral data are tabulated in the order: multiplicity (s, singlet; d, doublet; t, triplet; m, multiplet), number of protons, coupling constants. Proton nuclear magnetic resonance (¹H NMR) spectra were recorded on a Bruker Avance 600 equipped with a QNP cryoprobe (600 MHz) or Varian Inova 500 (500 MHz). Carbon nuclear magnetic resonance (¹³C NMR) spectra were recorded on a Bruker Avance 600 equipped with a QNP cryoprobe (150 MHz) or Varian Inova 500 (125 MHz).

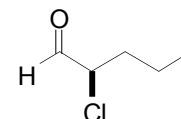
Infrared (IR) spectra were recorded on a MB-series Bomem/Hartman & Braun Fourier transform spectrophotometer with internal calibration as films between sodium chloride plates. Only selected, characteristic absorption data are provided for each compound.

Chemical ionization (CI) mass spectra were recorded on a Varian 4000 mass spectrometer at 70 eV. High-resolution electron impact (EI) and fast atom bombardment (FAB) mass spectra were recorded on a JEOL JMS-AX505HA mass spectrometer at 3 kV. Optical rotation was measured on a Perkin Elmer Polarimeter 341 at 589nm.

Preparation of (2*R*)-2-chloropentanal (10)

Procedure A:

To a cold (0 °C), stirred solution of pentanal (172 mg, 2.0 mmol) in CH₂Cl₂ (4 mL), was added L-prolinamide (23 mg, 0.2 mmol) and *N*-chlorosuccinimide (348 mg, 2.6 mmol). The reaction mixture was stirred for 1 hour and then allowed to slowly warm to room temperature over the course of 3 hours at which temperature it was stirred until complete consumption of pentanal (as determined by ¹H NMR spectroscopy). After this time, the mixture was diluted with pentanes (10 mL), cooled (-78 °C), filtered through a fritted funnel, and concentrated on a rotary evaporator in an ice water bath. The resulting oil was dissolved in pentanes (10 mL), cooled (-78 °C), filtered through a fritted funnel, and concentrated on a rotary evaporator in an ice-water bath to give (2*R*)-2-chloropentanal (**10**) (240 mg, >97% yield) as a clear oil.



Procedure B:

To a cold (-30 °C), stirred solution of (5*S*)-5-benzyl-2,2,3-trimethylimidazolidin-4-one (10.9 mg, 0.05 mmol) in acetone (2 mL), was added 2,3,4,5,6,6-hexachloro-2,4-cyclohexadien-1-one (361 mg, 1.2 mmol) and pentanal (86.1 mg, 1.0 mmol). The reaction mixture stirred at -30 °C until the aldehyde was consumed (as determined by ¹H NMR spectroscopy). After this time the mixture was filtered through Iatrobeads and eluted with Et₂O and concentrated on a rotary evaporator in an ice-water bath to provide (2*R*)-2-chloropentanal (**10**) (96.5 mg, 80% yield) as a clear oil.

¹H NMR (500 MHz, CDCl₃) δ: 9.44 (d, 1H, *J* = 2.5 Hz), 4.14 (ddd, 1H, *J* = 2.5, 5.0, 7.5 Hz), 1.90 (m, 1H), 1.77 (m, 1H), 1.47 (m, 2H), 0.91 (t, 3H, *J* = 7.0 Hz).

¹³C NMR (125 MHz, CDCl₃) δ: 195.2, 63.6, 33.8, 18.7, 13.2.

IR (neat): 2963, 2936, 2876, 2849, 1735, 1466, 1434, 1382, 1262, 1206, 1055 cm⁻¹

Exact mass calcd. for C₅H₁₀ClO: 121.5868; found: 121.5870.

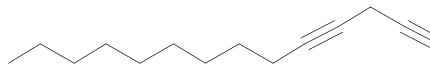
[α]_D²⁵: 11.2° (c = 0.8, CHCl₃)

The enantiomeric excess of **10** was determined by chiral GC analysis of the primary alcohol derived from the reduction of **10**. Thus, to a solution of (2*R*)-2-chloropentanal (**10**) (12 mg, 0.1 mmol) in MeOH (2 mL) was added NaBH₄ (10 mg, 0.25 mmol) and the resulting mixture was stirred at room temperature for 1 hour. The reaction mixture was then quenched with water (1 mL) and diluted with Et₂O (5 mL) and the phases were

separated. The organic phase was dried (MgSO_4) and concentrated to afford (2*R*)-2-chloropentanol. Separation of the enantiomers of 2-chloropentanol was accomplished by chiral GC. Temperature program: 70 °C held for 5 minutes then increased by 20 °C per minute until 150 °C and run for 30 minutes. t_R = 21.0 minutes ((*R*)-enantiomer); t_R = 21.8 minutes ((*S*)-enantiomer).

Preparation of tetradeca-1,4-diyne (23)

A stirred solution of 1-undecyne (40.8 mg, 0.4 mmol) and ethyl magnesium chloride (0.26 mL, 0.52 mmol, 2.0 M solution in Et_2O) in THF (4.0 mL) was heated at reflux for 2 hours. After this time, the solution was cooled to 0 °C, and copper (I) iodide (7.8 mg, 0.04 mmol) was added. After an additional 30 minutes at 0 °C, propargyl mesylate (69.6 mg, 0.52 mmol) was added in one portion and the resulting brown solution was stirred at room temperature for 2 hours. After this time the reaction mixture was treated with saturated aqueous NH_4Cl (5 mL) and the resulting mixture was diluted with Et_2O (20 mL) and the phases were separated. The organic phase was washed with brine (3 x 10 mL), dried (MgSO_4) and concentrated. Purification of the crude product by flash column chromatography (30 g of silica gel, 60:1 pentanes – diethyl ether) and removal of trace amounts of solvents (vacuum pump) afforded tetradeca-1,4-diyne (**23**) (70.0 mg, 92 %) as a light yellow oil.



^1H NMR (500 MHz, CDCl_3) δ : 3.15 (dt, 2H, J = 2.5, 2.4 Hz), 2.15 (tt, 2H, J = 2.5, 7.0 Hz), 2.06 (t, 1H, J = 2.4 Hz), 1.49 (m, 2H), 1.27-1.37 (m, 12H), 0.89 (t, 3H, J = 7.0 Hz).

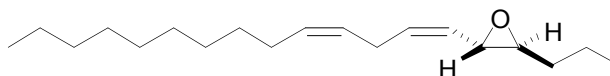
^{13}C NMR (125 MHz, CDCl_3) δ : 81.4, 79.0, 72.9, 68.3, 31.9, 29.5, 29.3, 29.1, 28.9, 28.7, 22.7, 18.7, 14.1, 9.6.

IR (neat): 3411, 3005, 2925, 2144, 1716, 1420, 1363, 1222, 1093, 902 cm^{-1}

MS (CI, m/z): 190.3 (M^+)

Preparation of (6*Z*,9*Z*,4*S*,5*S*)-4,5-epoxynonadeca-6,9-diene (1)

To a cold (-78 °C), stirred solution of tetradeca-1,4-diyne (**23**) (38 mg, 0.2 mmol) and dry THF (2 mL) was added *n*-butyllithium (0.1 mL, 0.2 mmol, 2.0 M in hexanes). After 30 seconds, a solution of (2*R*)-2-chloropentanal (**10**) (29 mg, 0.24 mmol) in THF (0.2 mL) was added and the resulting mixture was stirred for 5 minutes. After this time the light yellow solution was treated with saturated aqueous NH_4Cl (5 mL) and diluted with Et_2O (20 mL). The phases were separated and the organic phase was washed with brine (3 x 10 mL), dried (MgSO_4) and concentrated to provide the chlorohydrins **25** (>20:1 mixture of diastereomers as



determined by ^1H NMR spectroscopy) as a crude oil that was used without further purification.

To a cold ($0\text{ }^\circ\text{C}$), stirred solution of the crude chlorohydrins **25** (0.2 mmol) in EtOH (2.0 mL) was added Lindlar's catalyst (4.3 mg, 0.04 mmol) and quinoline (25.8 mg, 0.2 mmol) and the resulting suspension was stirred under an atmosphere of H_2 (balloon) for 2 hours at $0\text{ }^\circ\text{C}$. After this time KOH (16.8 mg, 0.3 mmol) was added and the suspension was stirred for an additional 30 minutes. The reaction mixture was then filtered through celite and the filtrate was diluted with pentanes (20 mL), and washed with brine (3 x 10 mL). The combined aqueous phases were extracted with pentanes (3 x 10 mL) and the combined organic phases were dried (MgSO_4) and concentrated. Purification of the crude product by flash column chromatography (45:1 hexanes: ethyl acetate) and removal of trace amounts of solvents (vacuum pump) afforded (6*Z*,9*Z*,4*S*,5*S*)-4,5-epoxynonadeca-6,9-diene (**1**) (45.7 mg, 82 %) as a clear oil.

The enantiomeric excess of (**1**) was determined to be 85% by chiral GC analysis. Temperature program: temperature set at $145\text{ }^\circ\text{C}$ for 80 minutes. $t_{\text{R}} = 57.1$ minutes ((*S,S*)-enantiomer); $t_{\text{R}} = 59.0$ minutes ((*R,R*)-enantiomer).

^1H NMR (500 MHz, CDCl_3) δ : 5.66 (dt, 1H, $J = 7.0, 10.5$ Hz), 5.33-5.46 (m, 2H), 5.07 (ddt, 1H, $J = 1.5, 9.0, 10.5$ Hz), 3.37 (dd, 1H, $J = 2.0, 9.0$ Hz), 2.96 (t, 2H, $J = 7.0$ Hz), 2.83 (dt, 1H, $J = 2.5, 5.5$ Hz), 2.06 (dt, 2H, $J = 7.5, 7.0$ Hz), 1.45-1.60 (m, 4H), 1.26-1.37 (m, 14H), 0.97 (t, 3H, $J = 7.0$ Hz), 0.88 (t, 3H, $J = 7.0$ Hz).

^{13}C NMR (125 MHz, CDCl_3) δ : 134.4, 131.1, 127.2, 126.7, 60.0, 54.3, 34.1, 31.9, 29.60, 29.59, 29.58, 29.33, 29.32, 27.3, 26.1, 22.7, 19.2, 14.1, 13.9.

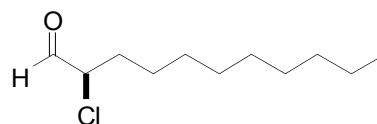
IR (neat): 3010, 2958, 2925, 2854, 1717, 1558 cm^{-1}

Exact mass calcd. for $\text{C}_{19}\text{H}_{33}\text{O}$: 277.4704; found: 277.4722.

$[\alpha]_{\text{D}}^{25}$: -11.6° ($c = 1.2$, CHCl_3); lit. -12.5 ($c = 4.1$, CHCl_3)⁴

Preparation of (2*R*)-2-chloroundecanal (12)

To a cold ($0\text{ }^\circ\text{C}$), stirred solution of undecanal (341 mg, 2.0 mmol) in dry CH_2Cl_2 (4 mL), was added L-prolinamide (23 mg, 0.2 mmol) and *N*-chlorosuccinimide (348 mg, 2.6 mmol). The reaction mixture was stirred for 1 hour and then allowed to slowly warm to room temperature over the course of 3 hours at which temperature it was stirred until complete consumption of undecanal (as determined by ^1H NMR spectroscopy). After this time, the mixture was diluted with pentanes (10 mL), cooled ($-78\text{ }^\circ\text{C}$), filtered through a fritted funnel, and concentrated on a rotary evaporator in an ice-water bath. The resulting oil was dissolved in pentanes (10 mL), cooled ($-78\text{ }^\circ\text{C}$), filtered through a fritted funnel, and concentrated on a rotary



evaporator in an ice-water bath to give (2*R*)-2-chloroundecanal (**12**) (400 mg, 97% yield) as a clear oil.

¹H NMR (500 MHz, CDCl₃) δ: 9.43 (d, 1H, *J* = 2.5 Hz), 4.11 (ddd, 1H, *J* = 2.5, 5.5, 7.5 Hz), 1.94 (m, 1H), 1.77 (m, 1H), 1.38- 1.47 (m, 2H), 1.20-1.30 (m, 12H), 0.91 (t, 3H, *J* = 7.0 Hz).

¹³C NMR (125 MHz, CDCl₃) δ: 195.1, 63.8, 31.9, 31.7, 29.3, 29.2, 29.1, 28.8, 25.4, 22.6, 14.0.

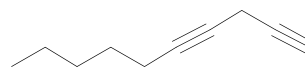
IR (neat): 3447, 2964, 2936, 2876, 2839, 1735, 1466, 1382, 1262, 1054 cm⁻¹

Exact mass calcd. for C₁₁H₂₀ClO: 203.7322; found: 203.7330.

[α]_D²⁵: 14.8° (c = 0.6, EtOH)

Preparation of deca-1,4-diyne (24)

A stirred solution of 1-heptyne (38.5 mg, 0.4 mmol) and ethyl magnesium chloride (0.26 mL, 0.52 mmol, 2.0 M solution in Et₂O) in dry THF (4 mL) was heated at reflux for 2 hours.



After this time, the solution was cooled to 0 °C, and copper (I) iodide (7.8 mg, 0.04 mmol) was added. After an additional 30 minutes at 0 °C, propargyl mesylate (69.6 mg, 0.52 mmol) was added in one portion and the brown solution was stirred at room temperature for 2 hours. After this time the reaction mixture was treated with saturated aqueous NH₄Cl (5 mL) and the resulting mixture was diluted with Et₂O (20 mL) and the phases were separated. The organic phase was washed with brine (3 x 10 mL), dried (MgSO₄) and concentrated. Purification of the crude product by flash column chromatography (30 g of silica gel, 60:1 pentanes – diethyl ether) and removal of trace amounts of solvents (vacuum pump) afforded deca-1,4-diyne (**24**) (49 mg, 91 %) as a light yellow oil.

¹H NMR (500 MHz, CDCl₃) δ: 3.14 (dt, 2H, *J* = 2.5, 2.4 Hz), 2.15 (tt, 2H, *J* = 2.5, 7.0 Hz), 2.05 (t, 1H, *J* = 2.4 Hz), 1.49 (tt, 2H, *J* = 7.0, 7.0 Hz), 1.20-1.35 (m, 4H), 0.89 (t, 3H, *J* = 7.0 Hz).

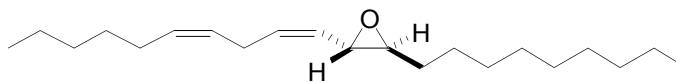
¹³C NMR (125 MHz, CDCl₃) δ: 81.3, 79.0, 72.9, 68.3, 31.0, 28.3, 22.2, 18.6, 14.0, 9.6.

IR (neat): 3015, 2921, 2854, 2214, 1713, 1467 cm⁻¹

MS (CI, *m/z*): 134.2 (M⁺)

Preparation of (6Z,9Z,11S,12S)-11,12-epoxyhenicosa-6,9-diene (2)

To a cold (-78 °C), stirred solution of deca-1,4-diyne (**24**) (26.8 mg, 0.2 mmol) in dry THF



(2 mL) was added *n*-butyllithium (0.1 mL, 0.2 mmol, 2.0 M in hexanes). After 30 seconds, a solution of (2*R*)-2-chloroundecanal (**12**) (49 mg, 0.24 mmol) in THF (0.2 mL) was added and the resulting mixture was stirred for 5 minutes. After this time the light yellow solution was treated with saturated aqueous NH₄Cl (5 mL) and diluted with Et₂O (20 mL). The phases were separated and the organic phase was washed with brine (3 x 10 mL), dried (MgSO₄) and concentrated to provide the chlorohydrins **26** (>20:1 mixture of diastereomers as determined by ¹H NMR spectroscopy) as a crude oil that was used without further purification.

To a cold (0 °C), stirred solution of the crude chlorohydrins **26** (0.2 mmol) in EtOH (2.0 mL) was added Lindlar's catalyst (4.3 mg, 0.04 mmol) and quinoline (25.8 mg, 0.2 mmol) and the resulting suspension was stirred under an atmosphere of H₂ (balloon) for 2 hours at 0 °C. After this time KOH (16.8 mg, 0.3 mmol) was added and the suspension was stirred for a further 30 minutes at 0 °C. The reaction mixture was then filtered through celite and the filtrate was diluted with pentanes (20 mL) and washed with brine (3 x 10 mL). The combined aqueous phases were extracted with pentanes (3 x 10 mL) and the combined organic phases were dried (MgSO₄) and concentrated. Purification of the crude product by flash column chromatography (45:1 hexanes: ethyl acetate) and removal of trace amounts of solvents (vacuum pump) afforded (6*Z*,9*Z*,11*S*,12*S*)-11,12-epoxyhenicosa-6,9-diene (**2**) (51.5 mg, 84 %) as a clear oil.

¹H NMR (500 MHz, CDCl₃) δ: 5.66 (dt, 1H, *J* = 7.0, 10.5 Hz), 5.33-5.47 (m, 2H), 5.06 (ddt, 1H, *J* = 1.5, 9.0, 10.5 Hz), 3.37 (dd, 1H, *J* = 2.0, 9.0 Hz), 2.96 (t, 2H, *J* = 7.0 Hz), 2.82 (dt, 1H, *J* = 2.0, 6.0 Hz), 2.06 (dt, 2H, *J* = 7.5, 7.0 Hz), 1.58 (m, 2H), 1.45 (m, 2H), 1.26-1.38 (m, 18H), 0.89 (t, 3H, *J* = 7.0 Hz), 0.88 (t, 3H, *J* = 7.0 Hz).

¹³C NMR (125 MHz, CDCl₃) δ: 134.3, 131.1, 127.3, 126.7, 60.2, 54.3, 32.1, 31.9, 31.5, 29.55, 29.52, 29.45, 29.30, 29.24, 27.2, 26.1, 25.9, 22.7, 22.6, 14.11, 14.07.

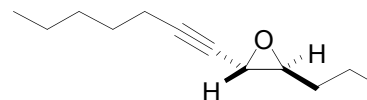
IR (neat): 3004, 2925, 2855, 1721, 1636 cm⁻¹

Exact mass calcd. for C₂₁H₃₉O: 307.5401; found: 307.5421.

[α]_D²⁵: -9.6° (c = 1.0, CHCl₃); lit. -10.8 (c = 1.08, CHCl₃)⁵

Preparation of (4*S*,5*S*)-4,5-epoxydodec-6-yne (19a)

To a cold (-78 °C), stirred solution of 1-heptyne (48.1 mg, 0.5 mmol) in dry THF (2.5 mL) was added *n*-butyllithium (0.25 mL, 0.5 mmol, 2.0 M in hexanes).



After the mixture had stirred for 10 minutes, a solution of (2*R*)-2-chloropentanal (**10**)

(66.3 mg, 0.55 mmol) in THF (0.25 mL) was added and the reaction mixture was stirred for an additional 10 minutes. After this time, the clear solution was treated with saturated aqueous NH_4Cl (5 mL) and diluted with Et_2O (20 mL). The phases were separated and the organic phase was washed with brine (3 x 10 mL), dried (MgSO_4) and concentrated to provide the chlorohydrins **18a** (>20:1 mixture of diastereomers as determined by ^1H NMR spectroscopy) as a crude oil that was used without further purification.

To a stirred solution of the crude chlorohydrins **18a** (0.5 mmol) in EtOH (2.5 mL) at room temperature was added KOH (84 mg, 1.5 mmol). After the mixture had been stirred for 30 minutes the resulting yellow solution was diluted with pentanes (20 mL) and washed with brine (3 x 10 mL). The aqueous phase was extracted with pentanes (3 x 10 mL) and the combined organic phases were dried (MgSO_4) and concentrated. Purification of the crude product by flash column chromatography (30:1 hexanes: ethyl acetate) and removal of trace amounts of solvents (vacuum pump) afforded (4*S*,5*S*)-4,5-epoxydodec-6-yne (**19a**) (75.2 mg, 86 %) as a light yellow oil.

The enantiomeric excess of **19a** was determined to be 85% by chiral GC analysis. Temperature program: temperature set at 100 °C for 30 minutes. t_R = 10.7 minutes ((*S,S*)-enantiomer); t_R = 11.4 minutes ((*R,R*)-enantiomer).

^1H NMR (500 MHz, CDCl_3) δ : 3.08 (dt, 1H, J = 2.0, 1.5 Hz), 3.02 (dt, 1H, J = 2.0, 5.0 Hz), 2.19 (dt, 2H, J = 1.5, 6.0 Hz), 1.44-1.54 (m, 6H), 1.26-1.38 (m, 4H), 0.96 (t, 3H, J = 7.0 Hz), 0.89 (t, 3H, J = 7 Hz).

^{13}C NMR (125 MHz, CDCl_3) δ : 84.9, 77.0, 60.6, 45.9, 34.0, 31.2, 38.3, 23.4, 19.2, 18.9, 14.1, 14.1.

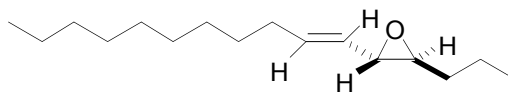
IR (neat): 2959, 2934, 2867, 2238, 1460, 1233, 1154, 898, 862 cm^{-1}

Exact mass calcd. for $\text{C}_{12}\text{H}_{21}\text{O}$: 181.2981; found: 181.2992.

$[\alpha]_D^{25}$: -3° (c = 0.8, CHCl_3)

Preparation of (6*E*,4*S*,5*S*)-4,5-epoxyhexadec-6-ene (19b)

To a cold (-78°C), stirred solution of (*E*)-1-iodoundec-1-ene (28.0 mg, 0.1 mmol)⁶ in dry THF (1.0 mL) was added *n*-butyllithium (0.05 mL, 0.1 mmol, 2.0 M in hexanes). After 10 minutes, a solution of (2*R*)-2-chloropentanal (**10**) (13.3 mg, 0.11 mmol) in THF (0.1 mL) was added and the reaction mixture was stirred for an additional 10 minutes. After this time, the clear solution was treated with saturated aqueous NH_4Cl (5 mL) and diluted with Et_2O (20 mL). The phases were separated and the organic phase was washed with brine (3 x 10 mL), dried (MgSO_4) and concentrated to provide the chlorohydrins **18b** (17:1 mixture of diastereomers as determined by ^1H NMR spectroscopy) as a crude oil which was used without further purification.



To a stirred solution of the crude chlorohydrins **18b** (0.1 mmol) in EtOH (1.0 mL) at room temperature was added KOH (17 mg, 0.3 mmol). After 30 minutes the resulting yellow solution was diluted with pentanes (20 mL) and washed with brine (3 x 10 mL). The combined aqueous phases were extracted with pentanes (3 x 10 mL) and the combined organic phases were dried (MgSO₄) and concentrated. Purification of the crude product by flash column chromatography (30:1 hexanes: ethyl acetate) and removal of trace amounts of solvents (vacuum pump) afforded (6*E*,4*S*,5*S*)-4,5-epoxyhexadec-6-ene (**19b**) (18 mg, 75 %) as a yellow oil.

¹H NMR (600 MHz, CDCl₃) δ: 5.90 (dt, 1H, *J* = 7.2, 15.6 Hz), 5.15 (dd, 1H, *J* = 8.4, 15.6 Hz), 3.07 (dd, 1H, *J* = 7.8, 8.4 Hz), 2.82 (m, 1H), 2.05 (dt, 2H, *J* = 7.2, 7.0 Hz), 1.53 (m, 6H), 1.37 (m, 2H), 1.26-1.30 (m, 10H), 0.95 (t, 3H, *J* = 7.2 Hz), 0.88 (t, 3H, *J* = 7.2 Hz).

¹³C NMR (150 MHz, CDCl₃) δ: 136.8, 127.4, 60.2, 58.8, 34.1, 32.4, 31.9, 29.5, 29.5, 29.3, 29.1, 28.9, 22.7, 19.2, 14.1, 14.0.

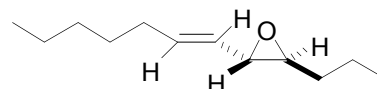
IR (neat): 2964, 2926, 2855, 1713, 1455, 1378, 965, 902 cm⁻¹

Exact mass calcd. for C₁₆H₃₀O: 238.4084; found: 238.4076.

[α]_D²⁵: -7.9° (c = 1.4, CHCl₃)

Preparation of (6*E*,4*S*,5*S*)-4,5-epoxydodec-6-ene (19c)

To a cold (-78 °C), stirred solution of (*E*)-1-iodohept-1-ene (112 mg, 0.5 mmol)⁷ in dry THF (5.0 mL) was added *n*-butyllithium (0.25 mL, 0.5 mmol, 2.0 M in hexanes). After 10 minutes, a solution of (2*R*)-2-chloropentanal (**10**) (66.3 mg, 0.55 mmol) in THF (0.5 mL) was added and the reaction mixture was stirred for an additional 10 minutes. After this time, the clear solution was treated with saturated aqueous NH₄Cl (5 mL) and diluted with Et₂O (20 mL). The phases were separated and the organic phase was washed with brine (3 x 10 mL), dried (MgSO₄) and concentrated to provide the chlorohydrins **18c** (13:1 mixture of diastereomers as determined by ¹H NMR spectroscopy) as a crude oil which was used without further purification.



To a stirred solution of the crude chlorohydrins **18c** (0.5 mmol) in EtOH (5.0 mL) at room temperature was added KOH (85 mg, 1.5 mmol). After 30 minutes the resulting yellow solution was diluted with pentanes (20 mL) and washed with brine (3 x 10 mL). The combined aqueous phases were extracted with pentanes (3 x 10 mL) and the combined organic phases were dried (MgSO₄) and concentrated. Purification of the crude product by flash column chromatography (30:1 hexanes: ethyl acetate) and removal of trace amounts of solvents (vacuum pump) afforded (6*E*,4*S*,5*S*)-4,5-epoxydodec-6-ene (**19c**) (79 mg, 87 %) as a yellow oil.

^1H NMR (500 MHz, CDCl_3) δ : 5.88 (dt, 1H, $J = 7.0, 15.5$ Hz), 5.15 (dd, 1H, $J = 9.0, 15.5$ Hz), 3.04 (m, 1H), 2.80 (m, 1H), 2.04 (dt, 2H, $J = 7.0, 7.0$ Hz), 1.24-1.55 (m, 10H), 0.95 (t, 3H, $J = 7.0$ Hz), 0.87 (t, 3H, $J = 7.5$ Hz).

^{13}C NMR (125 MHz, CDCl_3) δ : 136.6, 127.4, 60.2, 58.8, 34.0, 32.3, 31.3, 28.6, 22.5, 19.2, 14.0, 13.9.

IR (neat): 2950, 2922, 2860, 1710, 1440, 1322, 922 cm^{-1}

Exact mass calcd. for $\text{C}_{12}\text{H}_{23}\text{O}$: 183.3140; found: 183.3152.

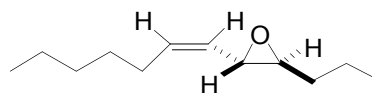
$[\alpha]_{\text{D}}^{25}$: -4.5° ($c = 0.6$, CHCl_3)

Determination of optical purity: to a stirred solution of (6*E*,4*S*,5*S*)-4,5-epoxydodec-6-ene (**19c**) (5 mg) in EtOH was added Pd/C (0.1 mol%) and the resulting suspension was stirred under an atmosphere of H_2 (balloon) for 3 hours. After this time, the reaction mixture was filtered through celite and concentrated and the crude oil was purified by flash chromatography (30:1 hexanes: ethyl acetate) to provide (4*S*,5*S*)-4,5-epoxydodecane. The observed specific rotation of this material ($[\alpha]_{\text{D}}^{25}$: -24.9) was consistent with that of a sample of (4*S*,5*S*)-4,5-epoxydodecane that was produced from (6*Z*,4*S*,5*S*)-4,5-epoxydodec-6-ene (**19d**) (85% ee as determined by chiral GC, see below) in the same manner ($[\alpha]_{\text{D}}^{25}$: -24.7).

Preparation of (6*Z*,4*S*,5*S*)-4,5-epoxydodec-6-ene (19d)

Procedure A:

To a cold (0 $^\circ\text{C}$), stirred solution of (4*S*,5*S*)-4,5-epoxydodec-6-yne (**19a**) (90.1 mg, 0.5 mmol) in EtOH (2.5 mL) was added Lindlar's catalyst (5.3 mg, 0.05 mmol) and quinoline (6.5 mg, 0.05 mmol) and the resulting suspension was stirred under an atmosphere of H_2 (balloon) for 30 minutes at 0 $^\circ\text{C}$. The reaction mixture was then filtered through celite and the filtrate was diluted with Et_2O (20 mL) and washed with brine (3 x 10 mL). The combined aqueous phases were extracted with Et_2O (3 x 10 mL) and the combined organic phases were dried (MgSO_4) and concentrated. Purification of the crude product by flash column chromatography (30:1 hexanes: ethyl acetate) and removal of trace amounts of solvents (vacuum pump) afforded (6*Z*,4*S*,5*S*)-4,5-epoxydodec-6-ene (**19d**) (85.7 mg, 94 %) as a light yellow oil.



Procedure B:

To a cold (-78°C), stirred solution of (*Z*)-1-iodohept-1-ene (112 mg, 0.5 mmol)⁸ in dry THF (5.0 mL) was added *n*-butyllithium (0.25 mL, 0.5 mmol, 2.0 M in hexanes). After 10 minutes, a solution of (2*R*)-2-chloropentanal (**10**) (66.3 mg, 0.55 mmol) in THF (0.5 mL) was added and the reaction mixture was stirred for an additional 10 minutes. After this time, the clear solution was treated with saturated aqueous NH_4Cl (5 mL) and diluted

with Et₂O (20 mL). The phases were separated and the organic phase was washed with brine (3 x 10 mL), dried (MgSO₄) and concentrated to provide the chlorohydrins **18d** (14:1 mixture of diastereomers as determined by ¹H NMR spectroscopy) as a crude oil which was used without further purification.

To a stirred solution of the crude chlorohydrins **18d** (0.5 mmol) in EtOH (5.0 mL) at room temperature was added KOH (85 mg, 1.5 mmol). After 30 minutes the resulting yellow solution was diluted with pentanes (20 mL) and washed with brine (3 x 10 mL). The combined aqueous phases were extracted with pentanes (3 x 10 mL) and the combined organic phases were dried (MgSO₄) and concentrated. Purification of the crude product by flash column chromatography (30:1 hexanes: ethyl acetate) and removal of trace amounts of solvents (vacuum pump) afforded (6*Z*,4*S*,5*S*)-4,5-epoxyhexadec-6-ene (**19d**) (70 mg, 77 %) as a yellow oil.

The enantiomeric excess of the epoxide **19d** derived from both procedures A and B was determined by chiral GC analysis to be 85%. Temperature program: temperature held at 70 °C for 50 minutes. *t*_R = 35.3 minutes ((*S,S*)-enantiomer); *t*_R = 36.4 minutes ((*R,R*)-enantiomer).

¹H NMR (500 MHz, CDCl₃) δ: 5.68 (dt, 1H, *J* = 7.5, 11.0 Hz), 5.03 (ddt, 1H, *J* = 1.5, 9.0, 11.0 Hz), 3.35 (dd, 1H, *J* = 2.5, 9.0 Hz), 2.81 (dt, 1H, *J* = 2.0, 5.0 Hz), 2.20 (m, 2H), 1.54-1.40 (m, 6H), 1.30 (m, 4H), 0.96 (t, 3H, *J* = 7.5 Hz), 0.89 (t, 3H, *J* = 7.5 Hz).

¹³C NMR (125 MHz, CDCl₃) δ: 136.5, 127.0, 60.0, 54.4, 34.1, 31.3, 29.2, 27.6, 22.5, 19.2, 14.0, 13.9.

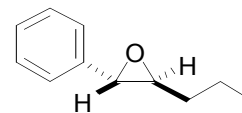
IR (neat): 3205, 2960, 2931, 2858, 1636, 1466, 1380, 901 cm⁻¹

Exact mass calcd. for C₁₂H₂₃O: 183.3140; found: 183.3152.

[α]_D²⁵: -9.7° (c = 1.4, CHCl₃)

Preparation of (4*S*,5*S*)-4,5-epoxy-5-phenylpentane (19e)

To a cold (-78 °C), stirred solution of bromobenzene (78.51 mg, 0.5 mmol) in dry THF (2.5 mL) under argon was added *n*-butyllithium (0.25 mL, 0.5 mmol, 2.0 M in hexanes). After 10 minutes a solution of (2*R*)-2-chloropentanal (**10**) (66.3 mg, 0.55 mmol) in THF (0.25 mL) was added and the reaction mixture was stirred for an additional 10 minutes. After this time, the clear solution was treated with saturated aqueous NH₄Cl (5 mL) and diluted with Et₂O (20 mL). The phases were separated and the organic phase was washed with brine (3 x 10 mL), dried (MgSO₄) and concentrated to provide the chlorohydrins **18e** (13:1 mixture of diastereomers as determined by ¹H NMR spectroscopy) as a crude oil which was used without further purification.



To a stirred solution of the crude chlorohydrins **18e** (0.5 mmol) in EtOH (2.5 mL) at room temperature was added KOH (84 mg, 1.5 mmol). After 30 minutes the resulting yellow solution was diluted with pentanes (20 mL) and washed with brine (3 x 10 mL). The combined aqueous phases were extracted with pentanes (3 x 10 mL) and the combined organic phases were dried (MgSO₄) and concentrated. Purification of the crude product by flash column chromatography (30:1 hexanes: ethyl acetate) and removal of trace amounts of solvents (vacuum pump) afforded (4*S*,5*S*)-4,5-epoxy-5-phenylpentane (**19e**) (68.4 mg, 84 %, d.r.= 14:1) as a light yellow oil.

¹H NMR (500 MHz, CDCl₃) δ: 7.36-7.27 (m, 5H), 3.61 (d, 1H, *J* = 2.0 Hz), 2.95 (dt, 1H, *J* = 2.0, 5.5 Hz), 1.64-1.70 (m, 2H), 1.52-1.58 (m, 2H), 1.00 (t, 3H, *J* = 7.5 Hz).

¹³C NMR (125 MHz, CDCl₃) δ: 138.1, 128.6, 128.2, 125.7, 63.3, 58.8, 34.6, 19.5, 14.2.

IR (neat): 3080, 3062, 3026, 2961, 2933, 2873, 1605, 1498, 1461, 1380, 1203, 870 cm⁻¹

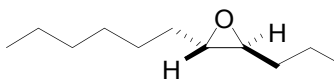
Exact mass calcd. for C₁₁H₁₄O: 162.2278; found: 162.2284.

[α]_D²⁵: -31.5° (c = 0.8, CHCl₃)

The enantiomeric excess of **19e** was determined by transformation to (2*S*)-1-phenylpentan-2-ol. Thus, a solution of (4*S*,5*S*)-4,5-epoxy-5-phenylpentane (**19e**) (16 mg, 0.1 mmol) and NaBH₄ (10 mg, 0.25 mmol) in MeOH (2 mL) was stirred at room temperature for 1 hour. The reaction mixture was then treated with water (1 mL), diluted with Et₂O (5 mL), and the phases were separated. The organic phase was dried (MgSO₄) and concentrated. Purification of the crude product by flash column chromatography (10:1 hexanes: ethyl acetate) and removal of trace amounts of solvents (vacuum pump) afforded (2*S*)-1-phenylpentan-2-ol. [α]_D²⁰ = 3.7° (obs.) (c = 1.1, EtOH); lit. 4.2° (c = 1.8, EtOH).⁹

Preparation of (4*S*,5*S*)-4,5-epoxyundecane (19f)

To a cold (-78 °C), stirred solution of *n*-hexyllithium (0.25 mL, 0.5 mmol, 2.0 M in hexanes) in dry THF (2.5 mL) was added a solution of (2*R*)-2-chloropentanal (**10**) (66.3 mg, 0.55 mmol) in THF (0.25 mL) and the reaction mixture was stirred for 10 minutes. After this time the clear solution was treated with saturated aqueous NH₄Cl (5 mL) and diluted with Et₂O (20 mL). The phases were separated and the organic phase was washed with brine (3 x 10 mL), dried (MgSO₄) and concentrated to provide the chlorohydrins **18f** (8:1 mixture of diastereomers as determined by ¹H NMR spectroscopy) as a crude oil which was used without further purification.



To a stirred solution of the crude chlorohydrins **18f** (0.5 mmol) in EtOH (2.5 mL) at room temperature was added KOH (84 mg, 1.5 mmol). After the mixture had been stirred for 30 minutes the resulting yellow solution was diluted with pentanes (20 mL) and washed with brine (3 x 10 mL). The combined aqueous phases were extracted with pentanes (3 x

10 mL) and the combined organic phases were dried (MgSO₄) and concentrated. Purification of the crude product by flash column chromatography (30:1 hexanes: ethyl acetate) and removal of trace amounts of solvents (vacuum pump) afforded (4*S*,5*S*)-4,5-epoxyundecane (**19f**) (67.3 mg, 79 %, d.r.= 8:1) as a light yellow oil.

¹H NMR (500 MHz, CDCl₃) δ: 2.66 (m, 2H), 1.50 (m, 8H), 1.29 (m, 6H), 0.95 (t, 3H, *J* = 7.0 Hz), 0.88 (t, 3H, *J* = 7.0 Hz).

¹³C NMR (125 MHz, CDCl₃) δ: 58.9, 58.8, 34.4, 32.3, 31.9, 29.3, 26.2, 22.7, 19.5, 14.2, 14.1.

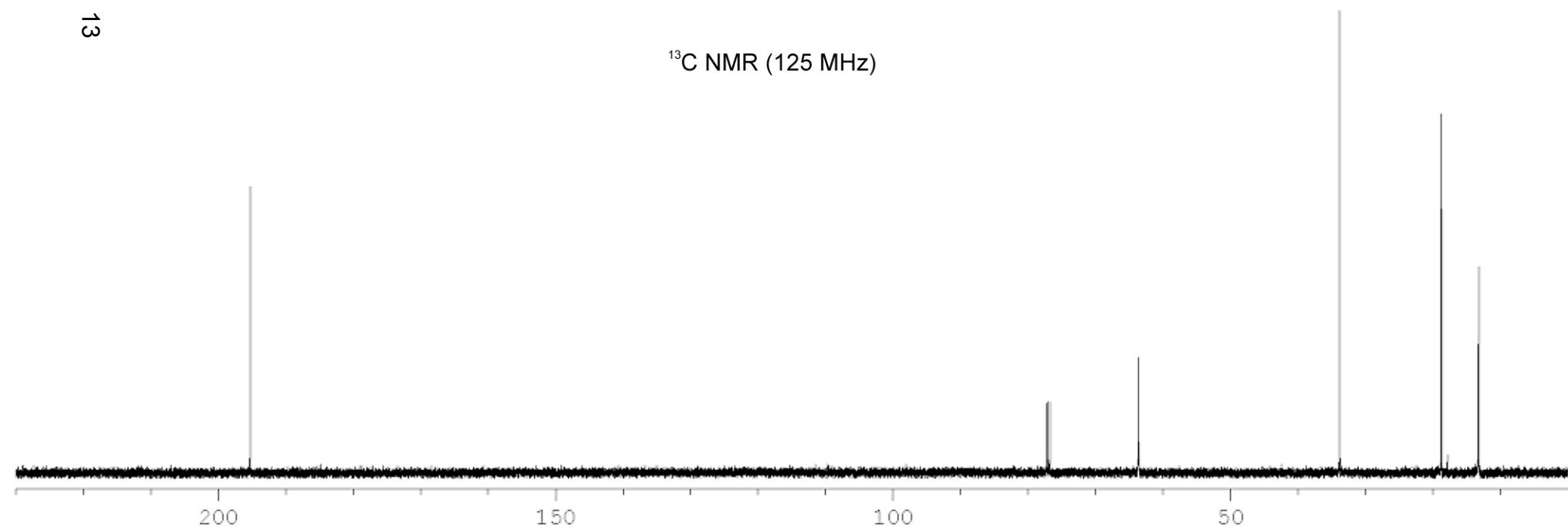
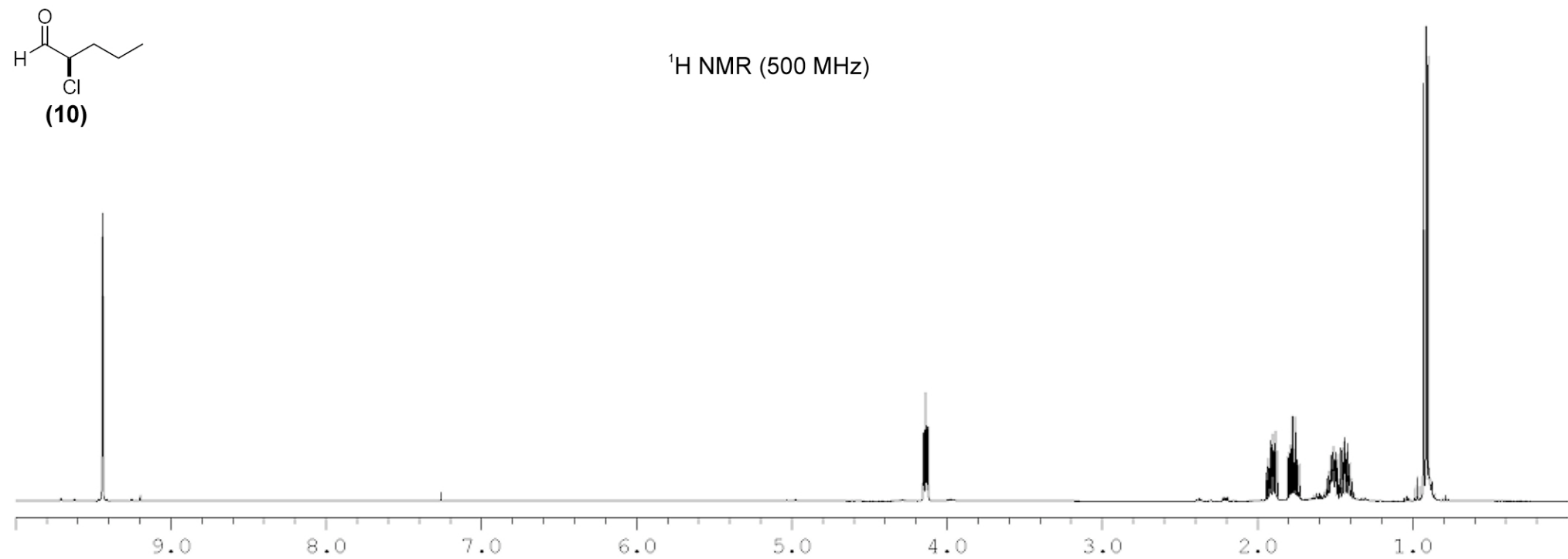
IR (neat): 2960, 2928, 2861, 1733, 1465, 1156, 1094, 904 cm⁻¹

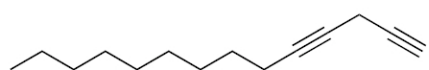
Exact mass calcd. for C₁₁H₂₂O: 170.2951; found: 170.2962.

[α]_D²⁵: -26.5° (c = 0.6, CHCl₃)

References

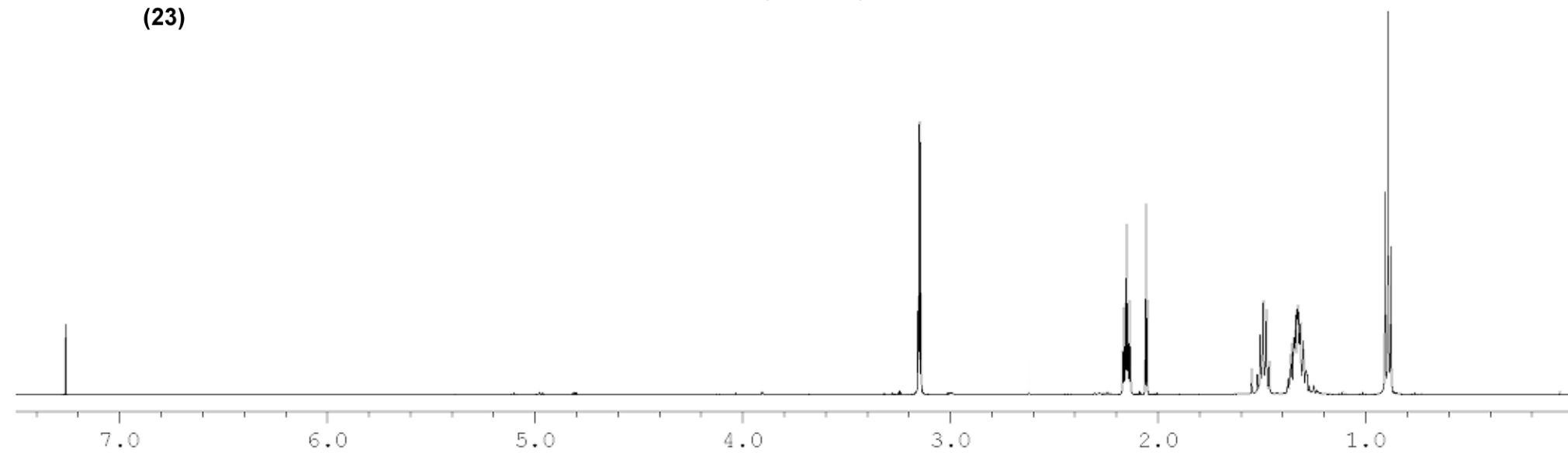
1. Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.*, **1978**, *43*, 2923.
2. König, W. A.; Gehrke, B.; Icheln, D.; Evers, P.; Donneck, J.; Wang, W. *J. High Resol. Chromatography*, **1992**, *15*, 367.
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4. Francke, W. *German Patent* 19814330.3, **1998**.
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6. (*E*)-1-iodoundec-1-ene was synthesized according to the procedure described in: Tius, M. A.; Busch-Petersen, J.; Yamashita, M. *Tetrahedron Lett.* **1998**, *52*, 930.
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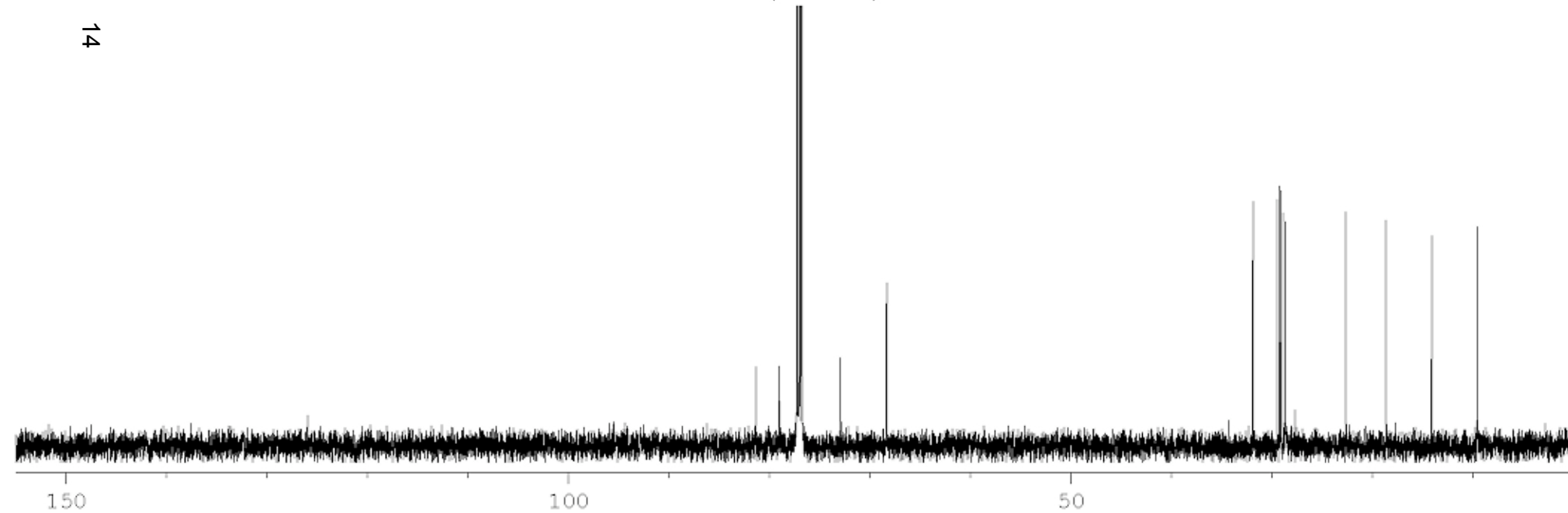


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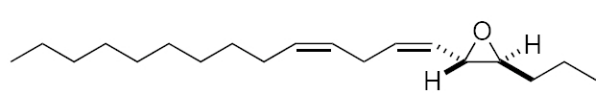
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^{13}C NMR (125 MHz)

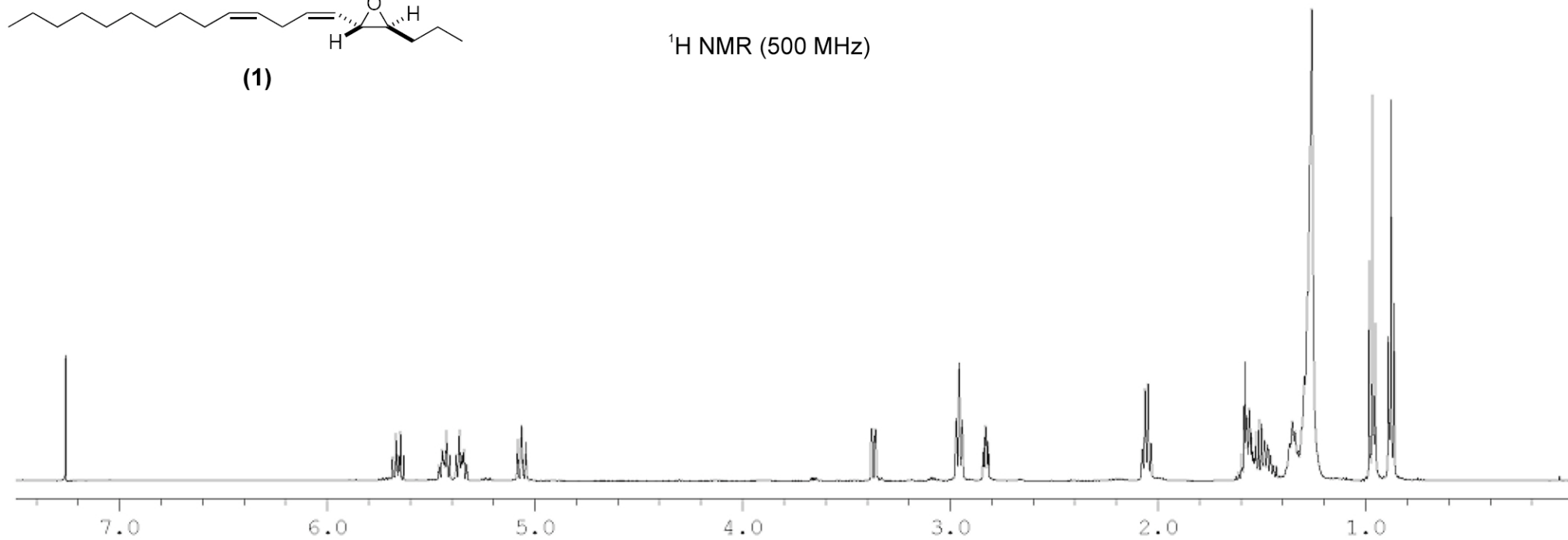


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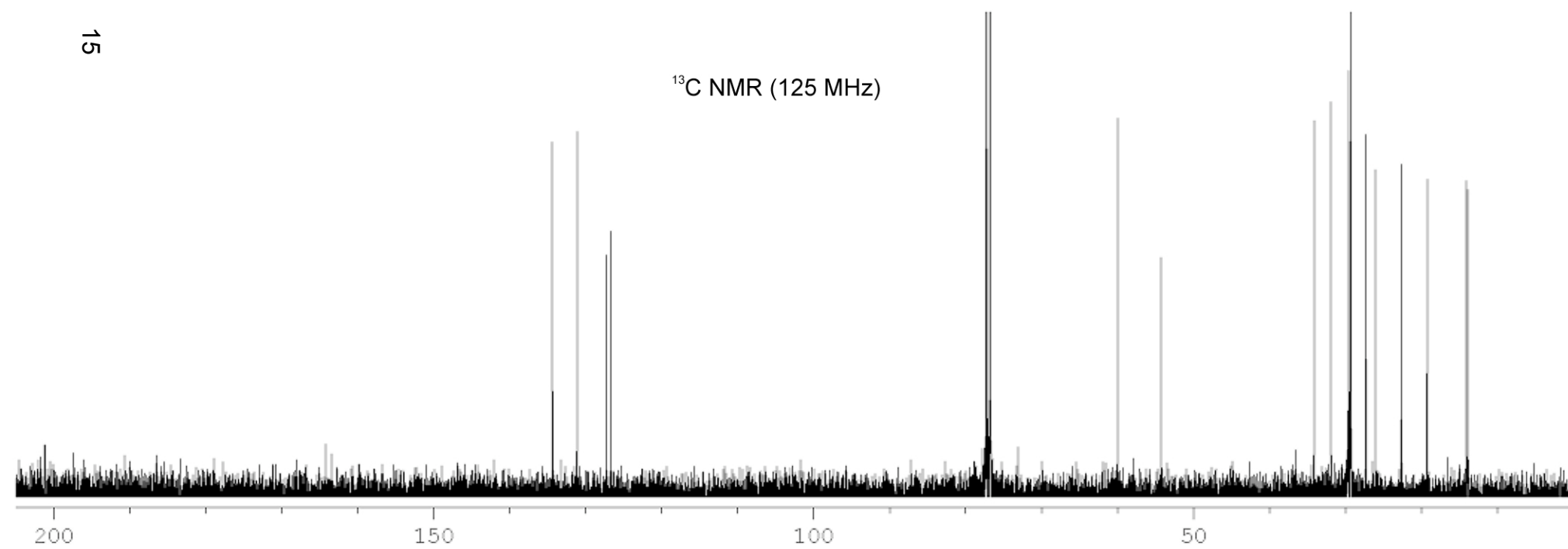


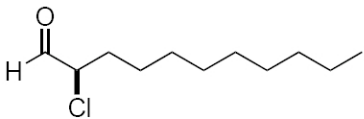
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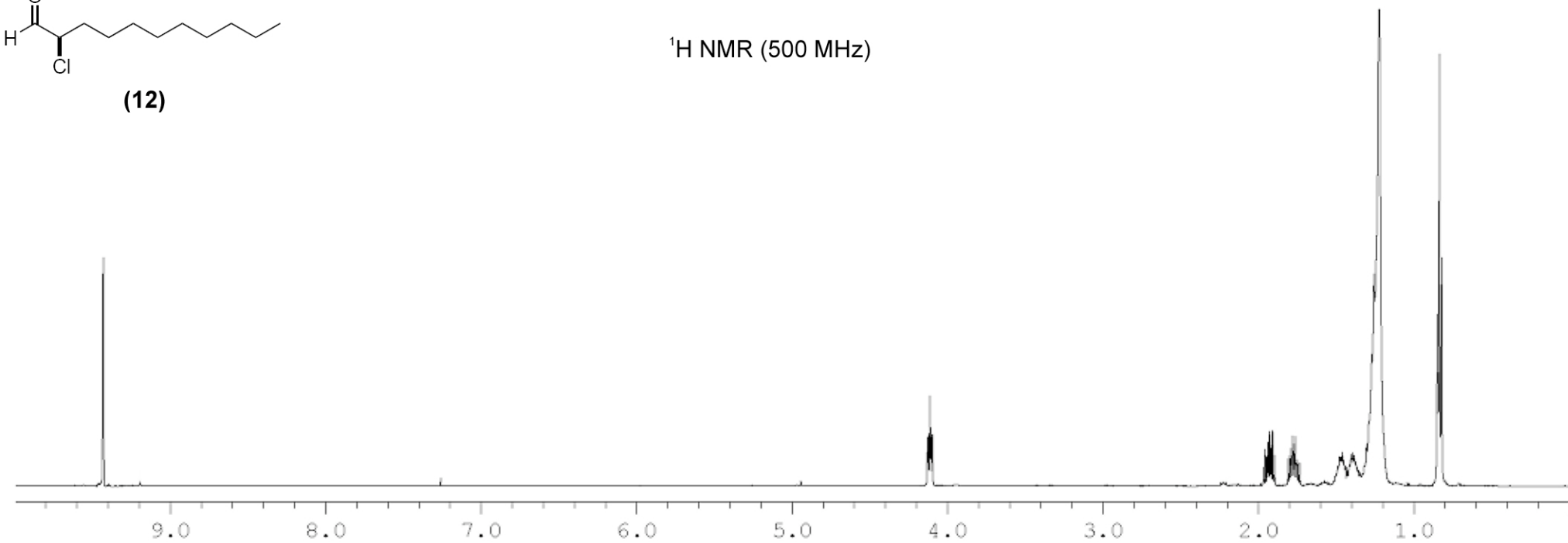
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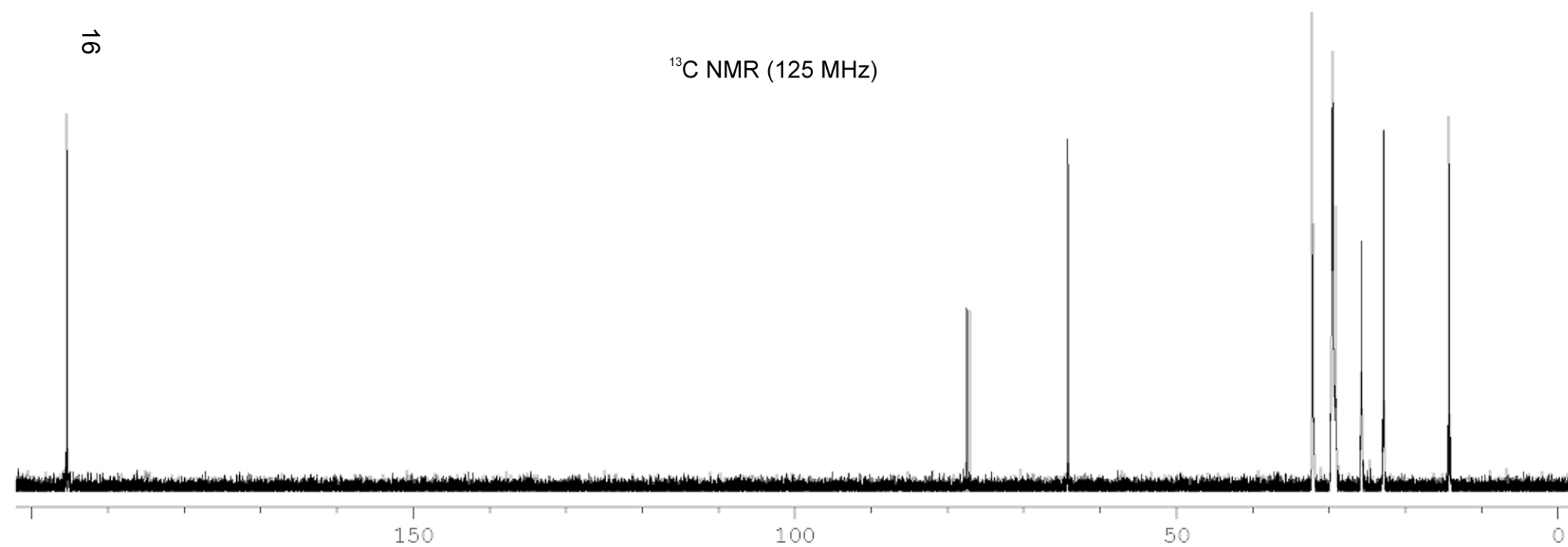
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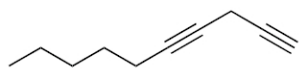
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16

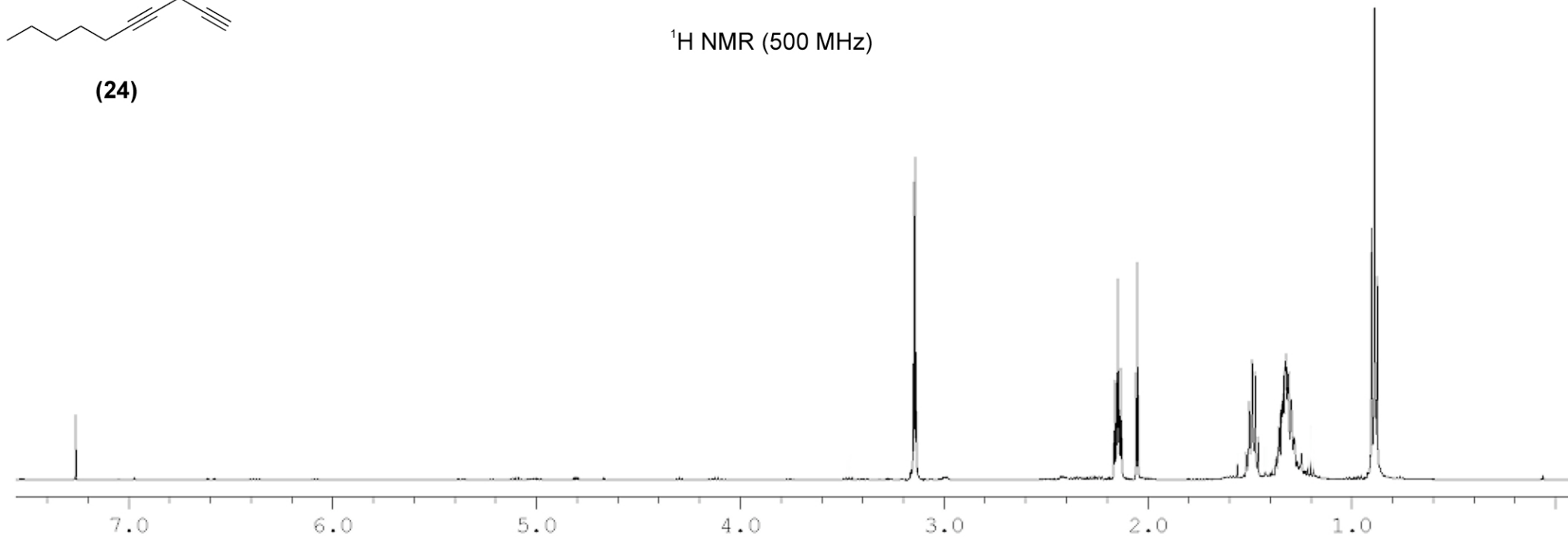
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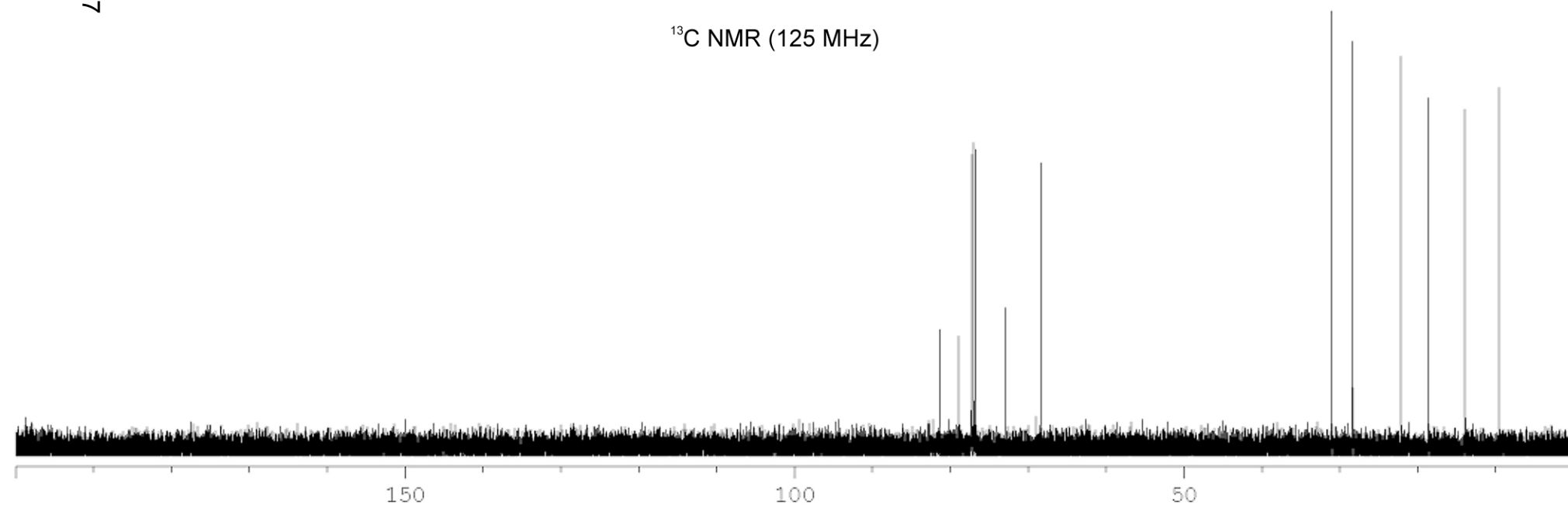
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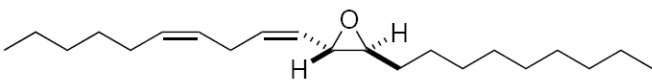
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17

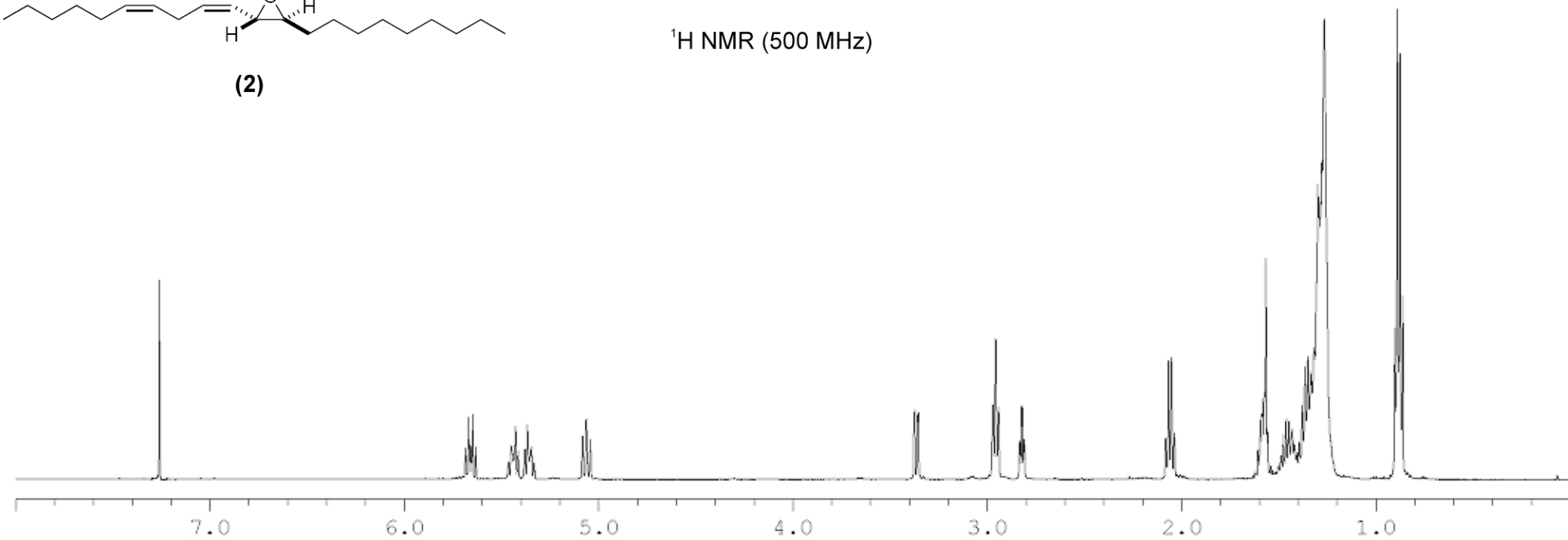
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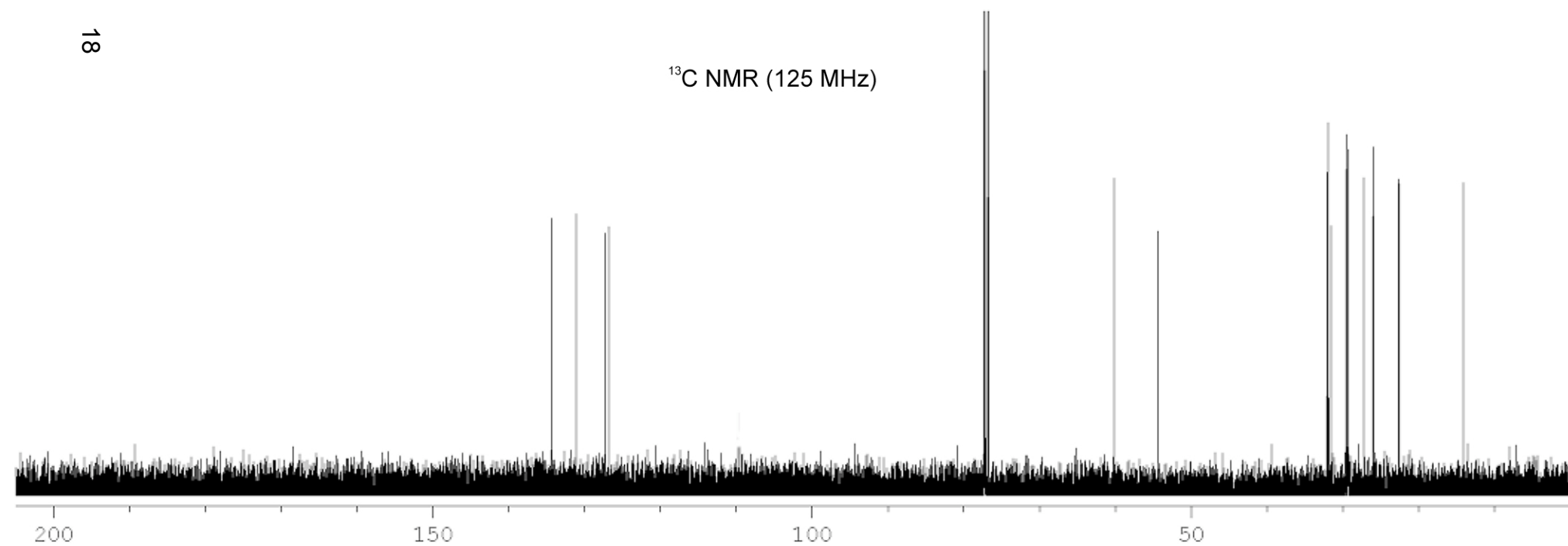
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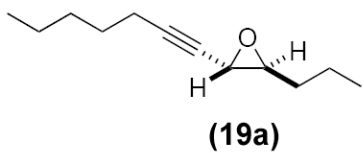
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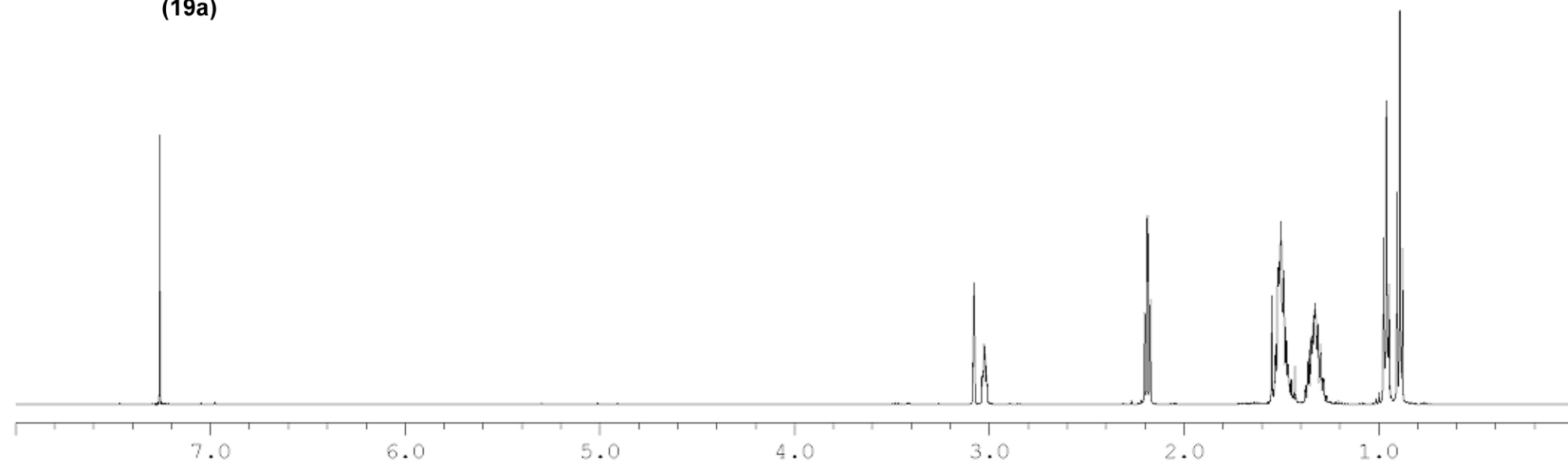
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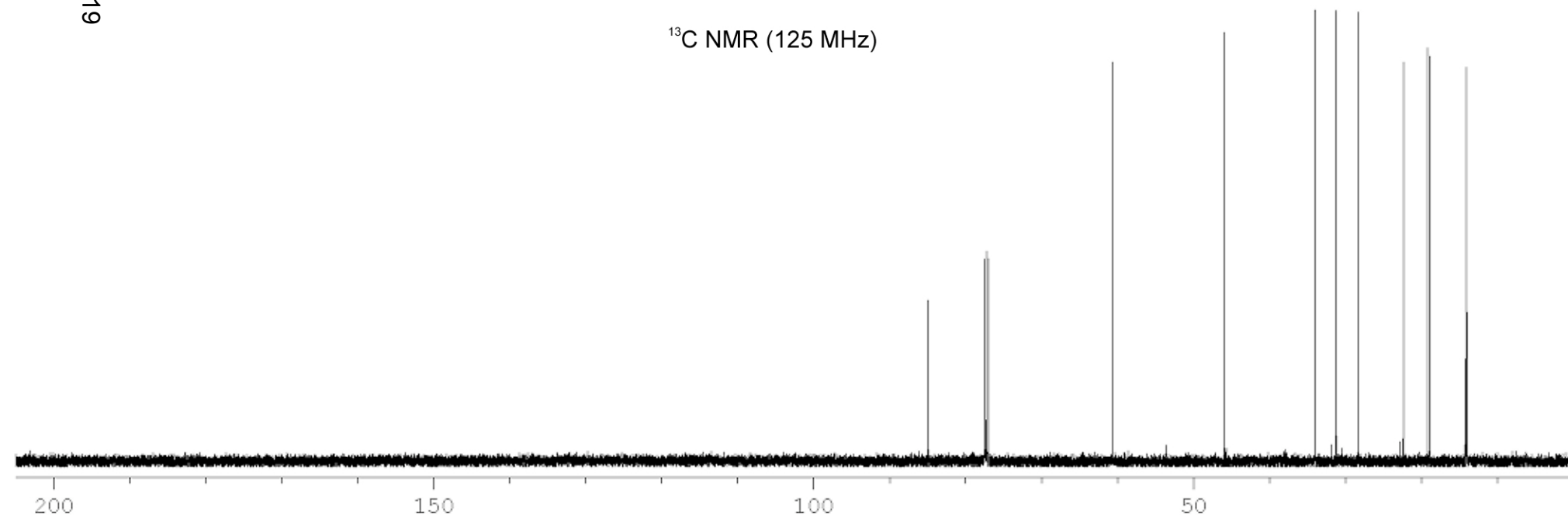


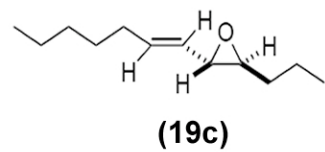
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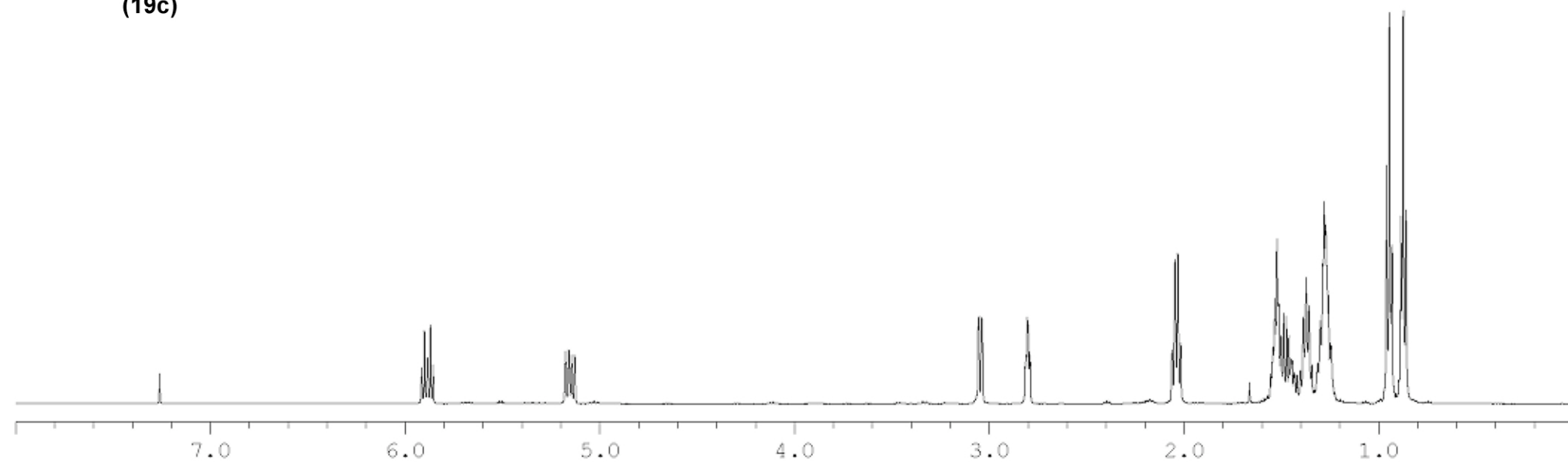
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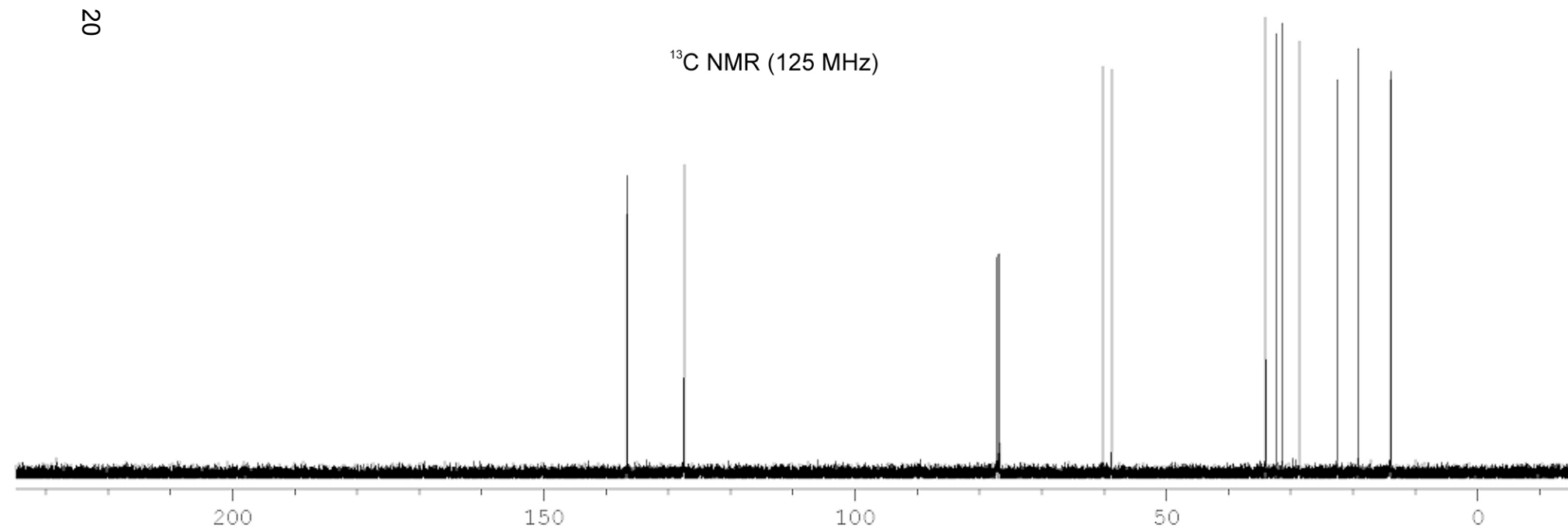


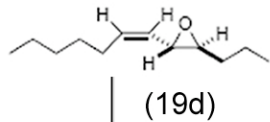


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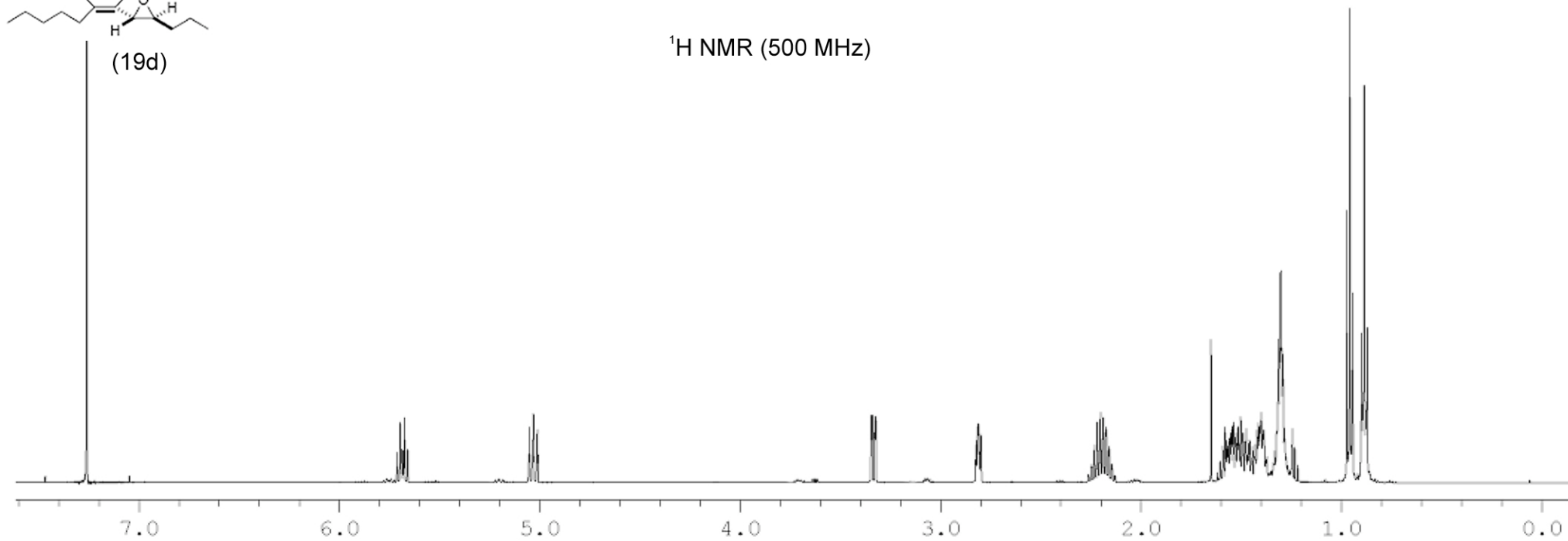


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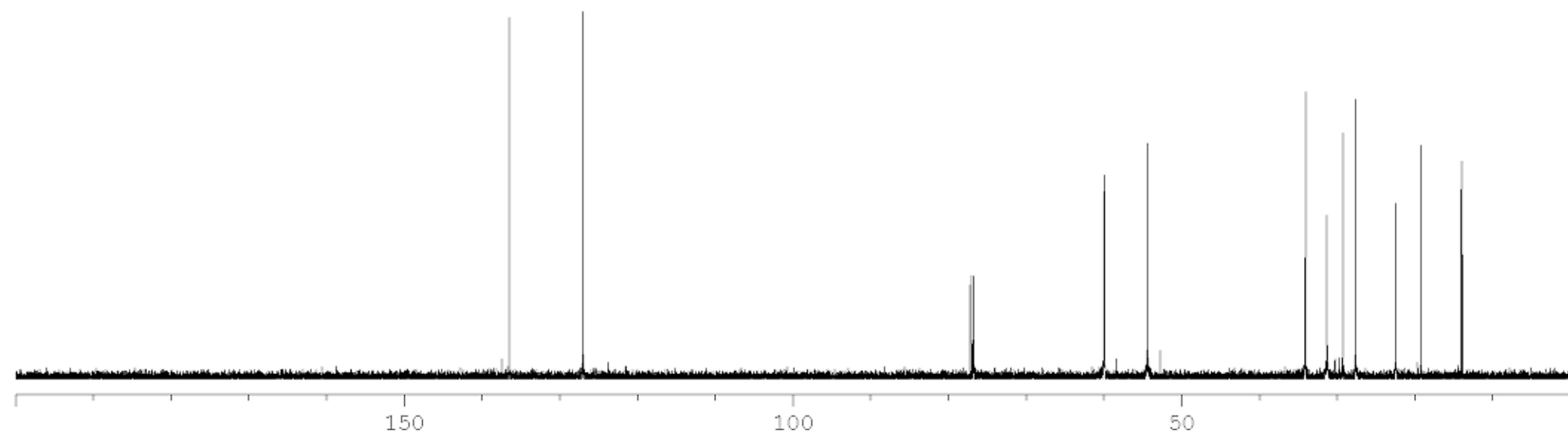


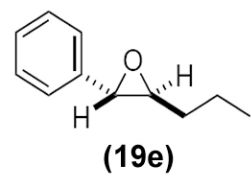


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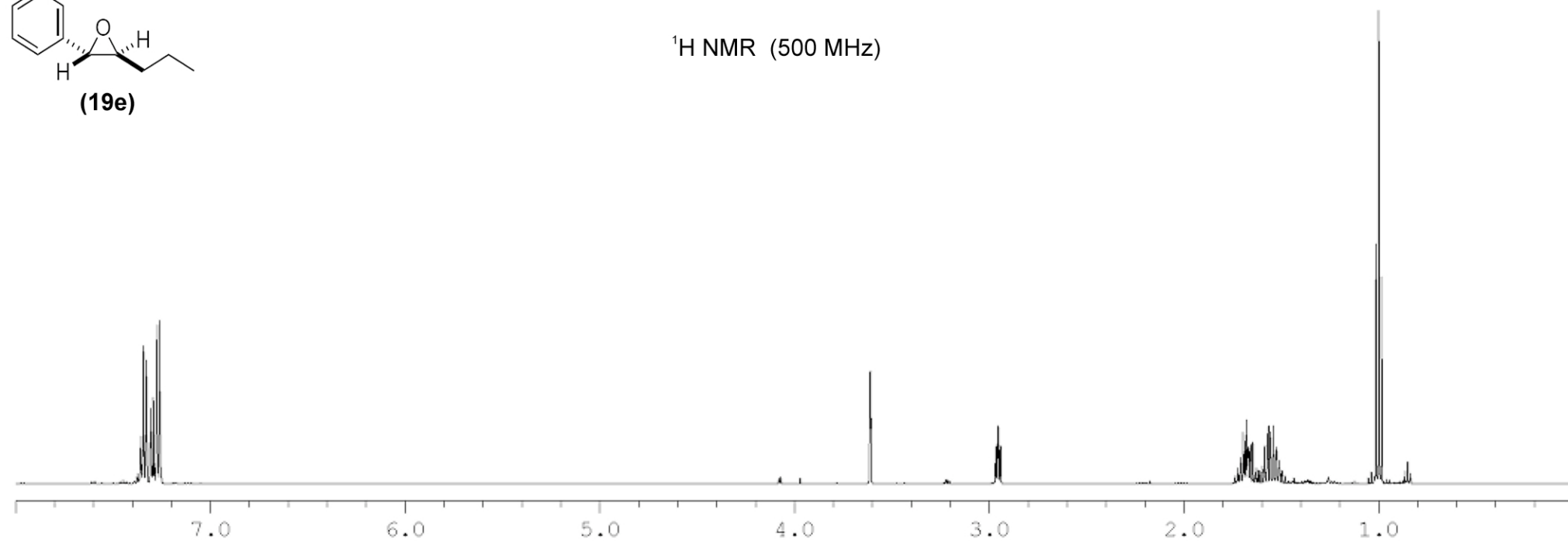


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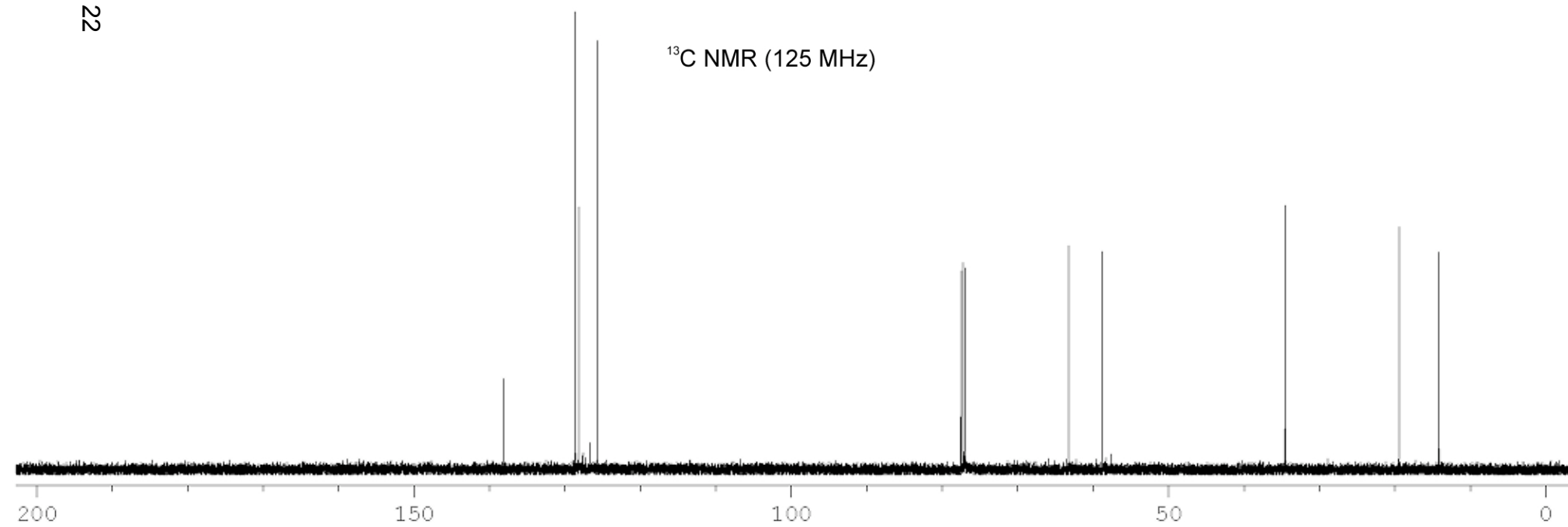


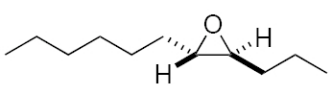
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22

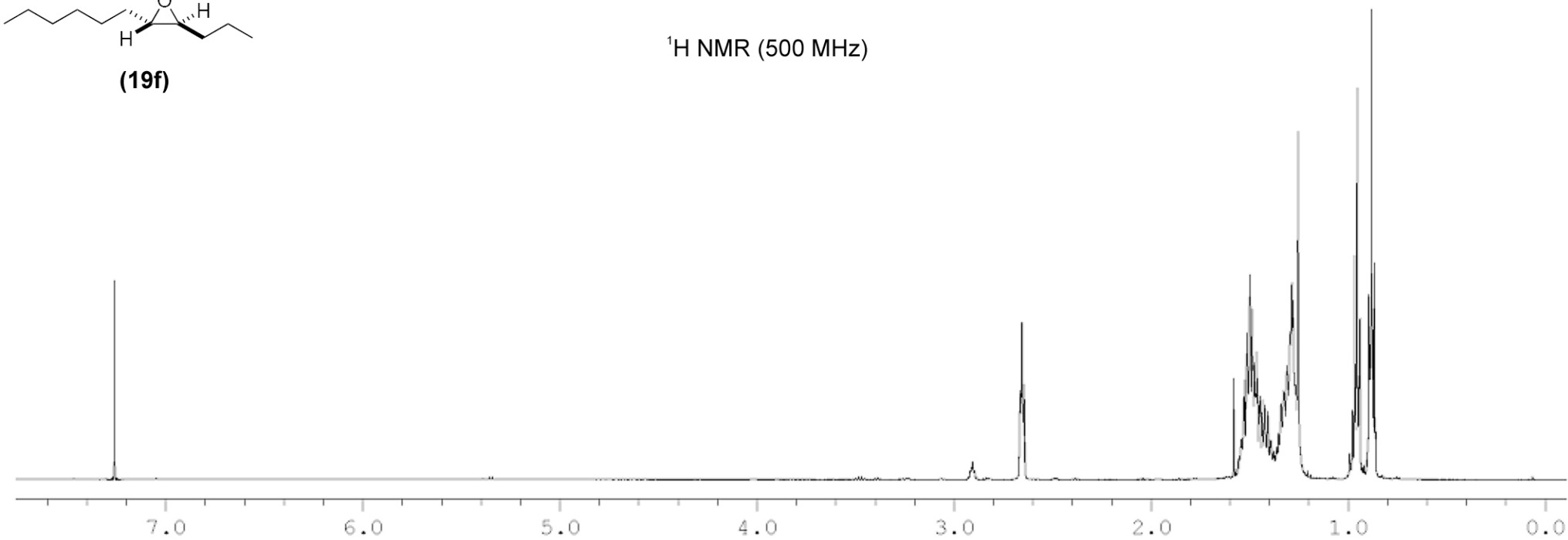
^{13}C NMR (125 MHz)





(19f)

^1H NMR (500 MHz)



23

^{13}C NMR (125 MHz)

