Total Synthesis of (+)-Allocyathin B_2

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Supplementary Informaiton

General Comments

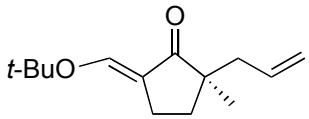
All reactions were performed under a nitrogen atmosphere unless otherwise indicated. Some solvents were freshly purified by column before use: acetonitrile, methylene chloride, toluene, benzene, triethylamine, dimethylformamide, tetrahydrofuran and pyridine and diethyl ether. Tetrahydrofuran for Negishi reaction was distilled from sodium benzophenone ketyl. Methanol was distilled from magnesium methoxide. All reagents were used as obtained unless otherwise noted.

Flash Chromatography was performed with EM Science silica gel (0.040-0.063 μm grade). Analytical thin-layer chromatography was performed with 0.2mm coated commercial silica gel plates (E. Merck, DC-Plasrikfolien, kieselgel 60 F_{254}). Melting points were obtained on a Thomas-Hoover apparatus in open capillary tubes and are uncorrected.

Proton nuclear magnetic resonance (^{1}H-NMR) data were acquired at 300 MHz on a Varian GEM-300, 400 MHz on a Varian GEM-400 and at 500 MHz on a Varian GEM-500 spectrometer. Chemical shifts are reported in delta (δ) units, in parts per million (ppm) downfield from tetramethylsilane, of in ppm relative to the singlet at 7.26ppm from chloroform-*d*. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; p, pentet; sept, septet; m, multiplet, br, broad. Carbon-13 nuclear magnetic resonance (^{13}C-NMR) data were acquired at 75 MHz on a Varian GEM-300, 100 MHz on a Varian GEM-400 and at 125 MHz on a Varian GEM-500 spectrometer. Chemical shifts are reported in ppm relative to the center line of a triplet at 77.0 ppm for choroform-*d.*

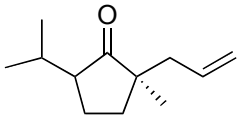
Infrared (IR) data were recorded as films on sodium chloride plates or a potassium bromide (KBr) pellets on a Perkin-Elmer Paragon 500 FT-IR spectrometers. Absorbance frequencies are reported in reciprocal centimeters (cm^{-1}). High resolution mass spectral data (HRMS) were obtained from Mass Spectrometry Resource, School of

Pharmacy, University of California-San Francisco, on a Kratos MS9 spectrometer at an ionizing current of 98 mA and an ionizing voltage of 70 eV. Elemental analyses (Anal.) were performed by M.-H.-W. Laboratories of Pheonix, AZ. Chiral HPLC analyses were performed on a Spectra Series P-100 chromatograph using the chiral column and heptane:*iso*-propanol mixtures indicated. Optical rotations were measured on a Jasco DIP-1000 digital polarimeter using 5cm cells and the sodium D line (589 nm) at ambient temperature in the solvent and concentration indicated.

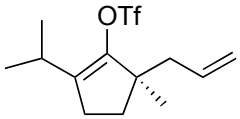


(*R*)-2-*tert*-Butoxymethylene-5-methyl-5-(2-propenyl)cyclopentanone (7). To a solution of LDA (67.0 mmol) in 170 mL of DME at –78 °C was added a solution of enol ether **6** (6.1 g, 33.5 mmol) in 10 mL of DME. After stirring at 0 °C for 15 min, the reaction was charged with *tert*-butanol (22.4 mL, 235 mmol) followed by a solution of trimethyltin chloride (6.67 g, 33.5 mmol) in 10 mL of DME. After stirring at 0 °C for 5 min, the reaction was cooled to –78 °C. Meanwhile, a solution of π-allyl palladium chloride dimmer (61.3 mg, 0.168 mmol) and (*S,S*)-ligand (230 mg, 0.335 mmol) in DME (10 mL) was stirred at room temperature for 10 min. The catalyst solution was charged with allyl acetate (4.0 mL, 36.8 mmol) and was then added to the enolate solution at –78 °C. The cooling bath was removed and the reaction was stirred at room temperature overnight. The reaction was diluted with 200 mL of ether and 200 mL of water. The layers were separated and the aqueous phase was extracted with ether (2 × 200 mL). The pooled organic extracts were washed with brine (1 × 200 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (10% ether/petroleum ether) to give enol ether **7** (6.20 g, 83%) as a colorless liquid. Determination of enantiomeric excess: chiral GC (cyclosil B, isotherm 120 °C) (+) enantiomer t_R = 74.825 min, (-) enantiomer t_R = 74.169 min. $[\alpha]_D$ = +25.2 (*c* 1.0, 23.7 °C, dichloromethane, 95% ee). IR (neat) 2977, 2869, 1708, 1630, 1458, 1371, 1265, 1156, 980, 945 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.50 (t, *J* = 2.5 Hz, 1 H), 5.68-5.76 (m, 1 H), 5.02 (d, *J* = 14.0 Hz, 2 H), 2.41-2.44 (m, 2 H), 2.13-2.15 (m, 2 H), 1.81-1.87 (m, 1 H), 1.55-1.60 (m, 1 H), 1.34 (s, 9 H), 1.00 (s, 3 H); ^{13}C NMR ($CDCl_3$, 125

MHz) δ 210.9, 149.0, 134.6, 117.6, 115.2, 79.8, 49.5, 41.3, 32.5, 28.3, 22.0, 21.3. Anal. Calc'd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.84; H, 10.18.

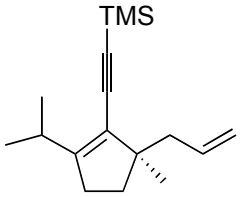


(*R*)-5-*Iso*propyl-2-methyl-2-(2-propenyl)cyclopentanone (8). Methyllithium (100 mL, 1.4 M solution in ether, 140 mmol) was added to a suspension of freshly purified copper(I) iodide (13.3 g, 70 mmol) in 180 mL of ether at –20 °C. The solution was stirred at –20 °C for 30 min at which point it was completely homogeneous. A solution of ketone **7** (6.22 g, 28.0 mmol) in 20 mL of ether was added dropwise. The reaction was allowed to warm to room temperature overnight and was then carefully poured into 200 mL of saturated NH_4Cl. The layers were separated and the aqueous solution was extracted with ether (2 × 200 mL). The ethereal extracts were pooled, washed with brine and $NaHCO_3$ (1 × 200 mL each), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (10% ether/petroleum ether) to give **8** (4.30 g, 86%) as a volatile colorless liquid (1:1 mixture of diastereomers). More practically, the volatile isopropyl ketone was concentrated to a minimal volume after purification and used in the next reaction with some residual solvent. IR (neat) 2960, 2872, 1732, 1640, 1457, 1370, 1065, 996, 916 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 5.59-5.68 (m, 1 H), 4.95-5.08 (m, 2 H), 1.43-2.10 (m, 8 H), 0.96 (d, J = 7.2 Hz, 3 H), 0.92 (s, 1.5 H), 0.89 (s, 1.5 H), 0.78 (d, J = 7.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 223.3, 223.2, 134.1, 133.6,118.1, 117.9, 55.8, 54.6, 48.7, 48.4, 42.0, 39.6, 33.2, 32.6, 27.4, 27.1, 22.5, 21.3, 21.1, 21.0, 20.6, 20.4, 18.5, 18.2; HRMS Calc'd for $C_{12}H_{20}O$ [M^+]: 180.1514; Found: 180.1508.



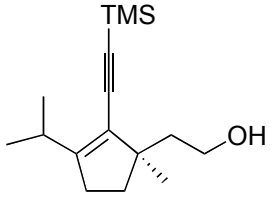
(*R*)-2-*Iso*propyl-5-methyl-5-(2-propenyl)cyclopentanone enol triflate (9). To a solution of LDA [prepared from diisopropylamine (3.63 mL, 25.9 mmol) and *n*-butyllithium (1.6 M in hexanes, 16.2 mL, 25.9 mmol) in 100 mL of THF at –78 °C was

added a solution of ketone **8** (3.9 g, 21.6 mmol) in 20 mL of THF. The reaction was stirred at 0 °C for 15 min and was then charged with a solution of *N*-phenyltrifluoromethanesulfonimide (10.8 g, 30.3 mmol) in 30 mL of THF. The reaction was stirred at room temperature for 2 h and was then diluted with 100 mL of ether and 100 mL of water. The layers were separated and the aqueous phase was extracted with ether (2 × 100 mL). The pooled extracts were washed with water and brine (1 × 150 mL each), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (petroleum ether to 5% ether/petroleum ether) to give **9** (6.41 g, 96%) as a colorless liquid. IR (neat) 3080, 2968, 2936, 2875, 1684, 1642, 1409, 1213, 1142, 1027, 843, 610 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.68-5.76 (m, 1 H), 5.02-5.07 (m, 2 H), 2.81 (p, *J* = 7 Hz, 1 H), 2.19-2.27 (m, 3 H), 2.08 (q, *J* = 8.0 Hz, 1 H), 1.90-1.95 (m, 1 H), 1.61-1.67 (m, 1 H), 1.12 (s, 3 H), 1.00 (d, *J* = 7.0 Hz, 3 H), 0.99 (d, *J* = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 144.9, 138.0, 134.2, 118.6, 117.9, 46.3, 43.0, 32.9, 25.7, 24.4, 23.8, 20.5, 20.2; HRMS Calc'd for $C_{10}H_{14}F_3O_3S$ [M-$C_3H_5^+$]: 271.0616. Found: 271.0618.



(*R*)-2-*Iso*propyl-5-methyl-5-(2-propenyl)-cyclopent-1-enylethynyl-trimethylsilane (5). To a prestirred solution (10 min) of $Pd_2dba_3.CHCl_3$ (471 mg, 0.455 mmol) and triphenylphosphine (953 mg, 3.64 mmol) in benzene (20 mL) was added triflate **9** (5.7 g, 18.2 mmol) at room temperature. The catalyst solution was transferred to a solution of copper(I) iodide (173.3 mg, 0.91 mmol), trimethylsilylacetylene (7.74 mL, 54.7 mmol), and *n*-butylamine (4.14 mL, 41.9 mmol) in benzene (30 mL). After being stirred at 50 °C for 18 h, the reaction was cooled to room temperature and diluted with 50 mL of water. The layers were separated and the organic layer was washed with 50 mL of brine, dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (5% ether/petroleum ether) to give alkyne **5** (4.18 g, 85%) as a colorless liquid. $[\alpha]_D$ = +8.72 (*c* 1.00, 25.3 °C, dichloromethane). IR (neat) 2960, 2870, 2138, 1250, 842 cm^{-1}; ^1H NMR ($CDCl_3$, 500

MHz) δ 5.71-5.80 (m, 1H), 4.96-5.02 (m, 2 H), 2.90 (sept, J = 7.0 Hz, 1 H), 2.14-2.29 (m, 3 H), 2.08 (dd, J = 13.5, 8 Hz, 1H), 1.75-1.81 (m, 1 H), 1.46-1.51 (m, 1 H), 1.05 (s, 3 H), 0.99 (d, J = 7.0 Hz, 6 H), 0.17 (s, 9 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 157.4, 136.0, 124.6, 116.6, 101.1, 99.1, 50.0, 44.5, 34.5, 19.1, 15.7, 21.0, 20.7, 0.2; HRMS Calc'd for $C_{17}H_{28}Si$ [M^+]: 260.1960. Found: 260.1958.

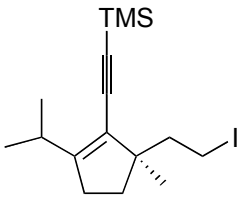


(*R*)-5-(2-Hydroxyethyl)-2-*iso*-propyl-5-methyl-cyclopent-1-enylethynyl-trimethylsilane (10). To a stirred solution of alkyne **5** (1.06g, 4.08 mmol) in CH_2Cl_2 (6 mL) was added NMO (1.685 g, 14.4 mmol) and OsO_4 (4% in water, 0.305 mL, 0.048 mmol) at room temperature. The mixture was stirred for 8 h and treated with ether (40 mL) and water (10 mL). After separation of the layers the organic phase was concentrated under reduced pressure to give the crude diol.

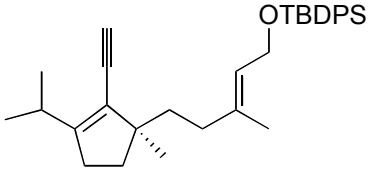
The crude diol was dissolved in acetone/water (4:1, 6 mL). To this mixture was added $NaIO_4$ (2.05 g, 9.6 mmol) at room temperature. The suspension was stirred for 1 h and treated with ether (60 mL) and water (15 mL). After separation of the layers the aqueous phase was extracted with ether (20 mL). The combined organic layers were washed with brine (10 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified with column chromatography (3% ether in petroleum ether) to furnish the corresponding aldehyde (930.6 mg, 87%) as a clear liquid.

To a solution of the aldehyde in MeOH (2 mL) was added $NaBH_4$ (134.3 mg, 3.55 mmol) at room temperature. The mixture was stirred for 10 min and concentrated under reduced pressure. The residue was treated with ether (60 mL) and water (10 mL). After separation of the layers the aqueous layer was extracted with ether (3 × 10 mL). The combined organic layers was washed with brine (10 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified with column chromatography (20% ether in petroleum ether) to furnish the compound **10** (888.1 mg, 94%) as a clear liquid, $[\alpha]_D$ = + 21.0 (*c* 1.10, 22.7 °C, chloroform). IR (neat) 3333, 2958, 2137, 1454, 1249, 842 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.65 (m, 2 H), 2.91 (sept, J =

7.2 Hz, 1 H), 2.29 (t, J = 7.5 Hz, 2 H), 1.80 (m, 2 H), 1.62 (m, 2 H), 1.08 (s, 3 H), 1.00 (s, 3 H), 0.98 (s, 3 H), 0.17 (s, 9 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.7, 124.3, 101.0, 99.6, 60.1, 48.9, 42.9, 36.0, 29.2, 29.0, 26.1, 20.8, 20.6, 0.1; HRMS Calc'd for $C_{16}H_{28}OSi$ [M^+]: 264.1909; Found: 264.1910.



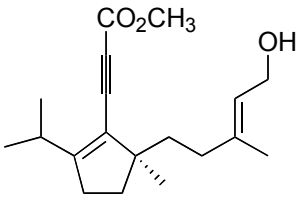
(*R*)-5-(2-Iodoethyl)-2-*iso*-propyl-5-methyl-cyclopent-1-enylethynyl-trimethylsilane (11). To a stirred solution of compound **10** (266 mg, 1.0 mmol) in CH_3CN and ether (3:5, 6.4 mL) was added PPh_3 (340.0 mg, 1.3 mmol), I_2 (355.3 mg, 1.4 mmol), and imidazole (102.1 mg, 1.5 mmol) at 0 °C. The mixture was stirred for 2 h at room temperature and treated with ether (40 mL) and saturated $NaHSO_3$ solution (20 mL). After separation of the layers the organic phase was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude material was purified with column chromatography (100% petroleum ether) to give compound **11** (363.3 mg, 97%) as a clear liquid, $[\alpha]_D$ = + 22.3 (*c* 1.30, 23.2 °C, dichloromethane). IR (neat) 2960, 2137, 1458, 1249 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.24 (m, 1 H), 3.16 (m, 1 H), 2.89 (sept, J = 7.2 Hz, 1 H), 2.28 (m, 2 H), 2.07 (m, 2 H), 1.76 (m, 1 H), 1.54 (m, 1 H), 1.05 (s, 3 H), 1.00 (d, J = 2.4 Hz, 3 H), 0.98 (d, J = 2.4 Hz, 3 H), 0.18 (s, 9 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.8, 123.3, 100.5, 99.9, 52.5, 45.5, 34.7, 29.2, 25.4, 20.9, 20.7, 1.5, 0.2; HRMS Calc'd for $C_{19}H_{27}ISi$ [M^+]: 374.0927; Found: 374.0928.



(*E*)-(*R*)-5-(2-Ethynyl-3-*iso*propyl-1-methyl-cyclopent-2-enyl)-3-methyl-pent-2-en-1-ol *tert*-butyldiphenyl ether (13). To a solution of the compound **11** (110 mg, 0.293 mmol) and anhydrous $ZnCl_2$ (39.8 mg, 0.293 mmol) in THF (3 mL) was added *t*-BuLi (1.4 M in pentane, 0.627 mL, 0.818 mmol) at –78 °C in 10 min. The mixture was stirred for 5 min at this temperature and warmed to room temperature for 1 h. The yellow

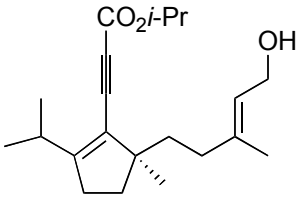
solution was transferred through cannular to a mixture of vinyl iodide **12** (100.4 mg, 0.322 mmol) and $Pd(PPh_3)_4$ (16.9 mg, 0.146 mmol) at room temperature. The reaction mixture was stirred overnight before the addition of ether (30 mL) and water (15 mL). After separation of the layers the aqueous layer was extracted with ether (2 ×10 mL). The combined organic layers was washed with brine (10 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified with column chromatography (3% ether in petroleum ether) to furnish the coupled product as a light yellow liquid which was contaminated with traces of unreacted vinyl iodide. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.62 (m, 4 H), 7.36 (m, 6 H), 5.27 (t, *J* = 4.2 Hz, 1 H), 4.15 (d, *J* = 6.0 Hz, 2 H), 2.92 (sept, *J* = 7.0 Hz, 1H), 2.27 (m, 2 H), 1.90 (m, 1 H), 1.77 (m, 1 H), 1.44 (m, 1 H), 1.38 (s, 3 H), 1.21-1.06 (m, 3 H), 1.00 (m, 3 H), 0.99 (s, 9 H), 0.98 (m, 6 H), 0.15 (s, 6 H).

To a solution of the above product in MeOH (2 mL) was added K_2CO_3 (80.7 mg, 0.585 mmol) at room temperature. The mixture was stirred for 1 h and treated with water (5 mL) and ether (15 mL). After separation of the layers the aqueous layer was extracted with ether (5 mL). The combined organic layers was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified with column chromatography (5% ether in petroleum ether) to provide compound **13** (53.2 mg, 74%) as a light yellow liquid, $[\alpha]_D$ = + 3.13 (*c* 1.46, 22.7°C, dichloromethane). IR (neat) 2959, 2137, 1462, 1112 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.70 (m, 4 H), 7.40 (m, 6 H), 5.38 (t, *J* = 4.2 Hz, 1 H), 4.21 (d, *J* = 6.0 Hz, 2 H), 3.10 (s, 1 H), 2.97 (sept, *J* = 7.0 Hz, 1H), 2.31 (m, 2 H), 1.95 (m, 2 H), 1.87 (m, 1 H), 1.78 (m, 1 H), 1.59 (m, 1 H), 1.48 (m, 2 H), 1.44 (s, 3 H), 1.09 (s, 3 H), 1.06 (d, *J* = 7.0 Hz, 3 H), 1.05 (s, 9 H), 1.02 (d, *J* = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 157.9, 137.9, 135.6, 134.1, 129.4, 127.6, 127.5, 123.6, 123.5, 81.7, 79.7, 61.2, 49.9, 38.3, 34.8, 34.7, 29.2, 26.8, 26.7, 26.0, 21.0, 20.8, 19.2, 16.4; HRMS Calc'd for $C_{33}H_{44}OSi$ [M^+]: 484.3161; Found: 484.3184.

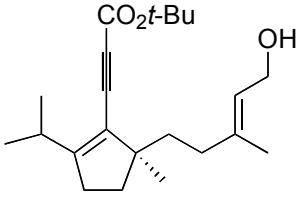


(*E*)-(*S*)-[5-(5-Hydroxy-3-methyl-pent-3-enyl)-2-*iso*propyl-5-methyl-cyclopent-1-enyl]-propynoic acid methyl ester (14a). To a solution of compound **13** (859.6 mg, 1.775 mmol) in THF (8 mL) was added *n*-BuLi (2.45 M in hexanes, 1.09 mL, 2.66 mmol) at –78 °C. The mixture was stirred at this temperature for 0.5 h before the addition of methyl chloroformate (335.5 mg, 3.33 mmol). The mixture was allowed to warm to room temperature and stirred overnight. The reaction was quenched by addition of water (10 mL) and ether (60 mL). The phases were separated and the aqueous layer was extracted with ether (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified with column chromatography (4% ether in petroleum ether) to furnish the ester (952.9 mg, 99%) as a clear liquid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.59 (m, 4 H), 7.30 (m, 6 H), 5.28 (m, 1 H), 4.11 (d, *J* = 6.3 Hz, 2 H), 3.69 (s, 3 H), 2.92 (sept, *J* = 6.3 Hz, 1H), 2.29 (t, *J* = 7.2 Hz, 2 H), 1.82 (m, 1 H), 1.76 (m, 2 H), 1.54 (m, 2 H), 1.52 (m, 1 H), 1.38 (m, 2 H), 1.34 (s, 3 H), 1.02 (s, 3 H), 0.95 (s, 9 H), 0.85 (d, *J* = 6.3 Hz, 3 H), 0.82 (d, *J* = 6.3 Hz, 3 H).

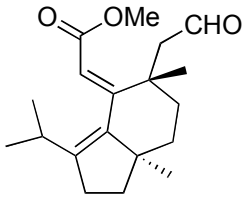
To a solution of above compound (952.9 mg, 1.775 mmol) in THF (8 mL) was added TBAF (1 M in THF, 2.13 mmol) at room temperature. The mixture was stirred for 1 h and quenched with addition of brine (10 mL) and ether (60 mL). The phases were separated and the aqueous layer was extracted with ether (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified with column chromatography (30% ether in petroleum ether) to furnish compound **14a** (280.7 mg, 52 %) as a clear liquid, $[\alpha]_D$ = + 18.9 (*c* 1.37, 22.5 °C, dichloromethane). IR (neat) 3398, 2959, 2201, 1712, 1434, 1272, 1243 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.39 (m, 1 H), 4.12 (d, *J* = 6.4 Hz, 2 H), 3.76 (s, 3 H), 2.97 (sept, *J* = 6.4 Hz, 1 H), 2.35 (m, 2 H), 1.88 (m, 1 H), 1.82 (m, 2 H), 1.66 (s, 3 H), 1.53 (m, 1 H), 1.51 (t, *J* = 8.8 Hz, 2 H), 1.09 (s, 3 H), 1.02 (d, *J* = 6.4 Hz, 3 H), 1.01 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.6, 154.9, 140.3, 123.1, 122.1, 85.9, 83.5, 59.4, 52.5, 50.3, 38.3, 34.9, 34.8, 30.0, 29.7, 26.0, 21.1; HRMS Calc'd for $C_{19}H_{28}O_3$ [M^+]: 304.2038; Found: 304.2040.



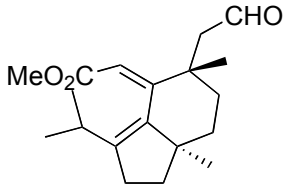
(*E*)-(*S*)-[5-(5-Hydroxy-3-methyl-pent-3-enyl)-2-*iso*propyl-5-methyl-cyclopent-1-enyl]-propynoic acid *iso*-propyl ester (14b). Following the similar procedure for the preparation of compound **14a**, compound **14b** was obtained as a light yellow oil, $[\alpha]_D$ = + 14.3 (*c* 1.75, 23.1 °C, dichloromethane). IR (neat) 3379, 2961, 2197, 1703, 1454, 1272, 1244, 1103 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.42 (t, *J* = 7.0 Hz, 1 H), 5.10 (sept, *J* = 6.5 Hz, 1 H), 4.14 (d, *J* = 7.0 Hz, 2 H), 3.00 (sept, *J* = 7.0 Hz, 1 H), 2.37 (m, 2 H), 1.99 (m, 1 H), 1.90 (m, 1 H), 1.82 (m, 1 H), 1.69 (s, 3 H), 1.63 (m, 1 H), 1.55 (m, 2 H), 1.31 (d, *J* = 6.5 Hz, 6 H), 1.11 (s, 3 H), 1.04 (d, *J* = 7.0 Hz, 3 H), 1.03 (d, *J* = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 164.8, 154.1, 140.3, 123.0, 122.2, 86.6, 82.5, 69.5, 59.4, 50.3, 38.2, 34.8, 34.8, 29.8, 29.6, 26.0, 21.7, 21.1, 20.8, 16.4; HRMS Calc'd for $C_{18}H_{25}O_3$ [M^+-C_3H_7]: 289.1804; Found: 289.1807.



(*E*)-(*S*)-[5-(5-Hydroxy-3-methyl-pent-3-enyl)-2-*iso*propyl-5-methyl-cyclopent-1-enyl]-propynoic acid *tert*-butyl ester (14c). Following the similar procedure for the preparation of compound **14a**, compound **14c** was obtained as a light yellow oil, $[\alpha]_D$ = + 32.9 (*c* 0.52, 24.0 °C, dichloromethane). IR (neat) 3383, 2962, 2194, 1703, 1456, 1370, 1284, 1151 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.43 (t, *J* = 7.2 Hz, 1 H), 4.14 (m, 2 H), 2.99 (sept, *J* = 6.8 Hz, 1 H), 2.37 (m, 2 H), 1.99 (m, 1 H), 1.90 (m, 1 H), 1.81 (m, 1 H), 1.69 (s, 3 H), 1.63 (m, 1 H), 1.57 (m, 2 H), 1.51 (s, 9 H), 1.10 (s, 3 H), 1.04 (d, *J* = 6.4 Hz, 3 H), 1.02 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 164.2, 153.6, 140.4, 123.0, 122.3, 87.6, 82.8, 80.6, 59.4, 50.3, 38.2, 34.8, 34.8, 29.8, 29.6, 28.0, 26.0, 21.1, 20.8, 16.4; HRMS Calc'd for $C_{18}H_{26}O_3$ [M^+-C_4H_8]: 290.1882; Found: 290.1878.



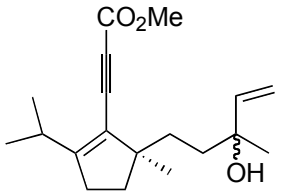
(*E*)-[(5*S*,7*aR*)-3-*Iso*propyl-5,7*a*-dimethyl-5-(2-oxo-ethyl)-1,2,5,6,7,7*a*-hexahydro-inden-4-ylidene]-acetic acid methyl ester (15a). To a solution of compound **14a** (296.8 mg, 0.976 mmol) in 2-butanone (9.7 mL) and DMF (71.3 mg, 0.976 mmol) was added $CpRu(CH_3CN)_3PF_6$ (84.7 mg, 0.195 mmol). The yellow solution was stirred at room temperature for 2 h and concentrated under reduced pressure. The crude material was purified by column chromatography (4% ether in petroleum ether) to give compounds **15a** (less polar)**, 16a** (more polar) and **17a** (most polar). Compound **15a** (100.4 mg, 34%, a clear liquid): $[\alpha]_D$ = + 373.2 (*c* 1.45, 24.2 °C, dichloromethane). IR (neat) 2956, 1718, 1607 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 9.82 (t, *J* = 3.5 Hz, 1 H), 5.59 (s, 1 H), 3.70 (s, 3 H), 3.03 (d, *J* = 3.5 Hz, 2 H), 2.62 (sept, *J* = 6.5 Hz, 1 H), 2.34 (m, 2 H), 1.73 (m, 2 H), 1.67 (m, 2 H), 1.43 (m, 2 H), 1.35 (s, 3 H), 1.00 (d, *J* = 6.5 Hz, 3 H), 0.99 (s, 3 H), 0.98 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 203.0, 166.8, 158.2, 146.6, 141.2, 116.3, 51.5, 50.5, 48.2, 40.5, 39.2. 36.1, 35.0, 28.6, 26.6, 25.2, 24.8, 21.6, 21.4; HRMS Calc'd for $C_{19}H_{28}O_3$ [M^+]: 304.2038; Found: 304.2027.



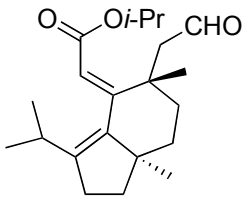
(*Z*)-[(5*S*,7a*R*)-3-*Iso*propyl-5,7*a*-dimethyl-5-(2-oxo-ethyl)-1,2,5,6,7,7*a*-hexahydro-inden-4-ylidene]-acetic acid methyl ester (16a). A clear liquid (83.6 mg, 28%): $[\alpha]_D$ = + 216.2 (*c* 2.30, 22.7 °C, dichloromethane). IR (neat) 2958, 1715, 1626, 1434, 1290, 1194 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 9.92 (t, *J* = 3.5 Hz, 1 H), 5.66 (s, 1 H), 3.64 (s, 3 H), 2.56 (dd, *J* = 15.0, 3.5 Hz, 1 H), 2.52 (dd, *J* = 15.0, 3.5 Hz, 1 H), 2.37 (m, 2 H), 2.42 (m, 2 H), 1.94 (m, 1 H), 1.79 (m, 1 H), 1.72 (m, 2 H), 1.18 (s, 3 H), 1.09 (s, 3 H), 0.90 (d, *J* = 9.0 Hz, 3 H), 0.98 (d, *J* = 9.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 198.3, 162.8, 155.3, 139.6, 131.3, 109.9, 49.2, 47.4, 47.0, 37.5, 34.4, 32.8, 32.4, 25.0,

23.2, 20.5, 19.7, 17.4, 15.3; HRMS Calc'd for $C_{19}H_{28}O_3$ [M^+]: 304.2038; Found: 304.2029.

131.3, 109.9, 49.2, 47.4, 47.0, 37.5, 34.4, 32.8, 32.4, 25.0, 23.2, 20.5, 19.7, 17.4, 15.3; HRMS Calc'd for $C_{19}H_{28}O_3$ [M^+]: 304.2038; Found: 304.2029.

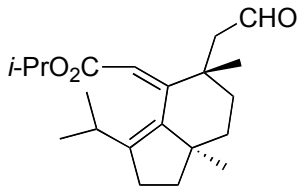


(5*R*)-[5-(3-Hydroxy-3-methyl-pent-4-enyl)-2-*iso*propyl-5-methyl-cyclopent-1-enyl]-propynoic acid methyl ester (17a). Light yellow oil (a mixture of two diastereomers, 31.4 mg, 30%). IR (neat) 3483, 2960, 2201, 1713, 1435, 1274, 1198 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 5.90 (dd, *J* = 13.6, 8.4 Hz, 1 H), 5.20 (d, *J* = 13.6 Hz, 1 H), 5.05 (d, *J* = 8.4 Hz, 1 H), 3.78 (s, 3 H), 2.97 (sept, *J* = 6.0 Hz, 1 H), 2.37 (m, 2 H), 1.79 (m, 2 H), 1.61 (m, 1 H), 1.54 (m, 1 H), 1.44 (m, 2 H), 1.28 (s, 3 H), 1.10 (s, 3 H), 1.04 (d, *J* = 4.0 Hz, 3 H), 1.03 (d, *J* = 4.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.6, 154.8, 145.0, 145.0, 122.0, 122.0, 111.8, 111.7, 85.9, 83.5, 73.1, 73.0, 52.0, 50.0, 37.2, 34.8, 34.7, 33.7, 33.6, 29.8, 29.7, 27.7, 27.5, 26.2, 26.0, 21.1, 20.8; HRMS Calc'd for $C_{19}H_{26}O_7$ [M^+-H_2O]: 286.1933; Found: 286.1940.

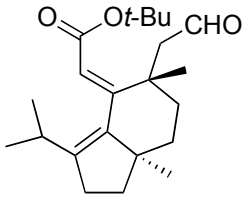


(*E*)-[(5*S*,7*aR*)-3-*Iso*propyl-5,7*a*-dimethyl-5-(2-oxo-ethyl)-1,2,5,6,7,7*a*-hexahydro-inden-4-ylidene]-acetic acid *iso*-propyl ester (15b). Following the similar procedure for the preparation of compound **15a** and **16a**, compound **15b** and **16b** were obtained as a light yellow oil (60% yield, a 1.5:1 mixture). **15b**: $[\alpha]_D$ = + 423.3 (*c* 0.91, 23.1 °C, dichloromethane). IR (neat) 1722, 1626, 1452, 1188, 1109 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 9.83 (t, *J* = 2.5 Hz, 1 H), 5.55 (s, 1 H), 4.99 (sept, *J* = 6.5 Hz, 1 H), 3.03 (dd, *J* = 16.5, 3.5 Hz, 1 H), 2.99 (dd, *J* = 16.5, 3.5 Hz, 1 H), 2.85 (sept, *J* = 6.5 Hz, 1H), 2.34 (m, 2 H), 1.74 (m, 1 H), 1.64 (m, 2 H), 1.57 (m, 1 H), 1.48 (dt, *J* = 9.0, 3.5 Hz,

1 H), 1.39 (m, 1 H), 1.35 (s, 3 H), 1.28 (d, J = 6.5 Hz, 3 H), 1.26 (d, J = 6.5 Hz, 3 H), 0.99 (m, 9 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 203.2, 166.2, 156.7, 146.3, 141.1, 117.4, 67.8, 50.8, 48.2, 40.4, 39.1. 36.2, 35.1, 28.5, 26.5, 25.3, 24.7, 21.8, 21.7, 21.4; HRMS Calc'd for $C_{21}H_{32}O_3$ [M^+]: 332.2351; Found: 332.2359.

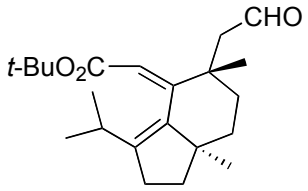


(*Z*)-[(5*S*,7*aR*)-3-*Iso*propyl-5,7*a*-dimethyl-5-(2-oxo-ethyl)-1,2,5,6,7,7*a*-hexahydro-inden-4-ylidene]-acetic acid *iso*-propyl ester (16b). $[\alpha]_D$ = + 196.9 (*c* 1.15, 23.8 °C, dichloromethane). IR (neat) 1722, 1626, 1452, 1188, 1109 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.93 (t, J = 3.0 Hz, 1 H), 5.62 (s, 1 H), 4.96 (sept, J = 6.5 Hz, 1 H), 2.55 (dd, J = 16.0, 3.0 Hz, 1 H), 2.52 (dd, J = 16.0, 3.0 Hz, 1 H), 2.43 (m, 2 H), 2.41 (m, 1 H), 1.95 (dt, J = 13.5, 4.0 Hz, 1 H), 1.80 (m, 1 H), 1.74 (m, 1 H), 1.57 (m, 2 H), 1.22 (dd, J = 6.5, 2.0 Hz, 6 H), 1.18 (s, 3 H), 1.10 (s, 3 H), 0.92 (dd, J = 6.5, 2.0 Hz, 6 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 202.6, 165.8, 158.6, 143.2, 135.5, 114.8, 67.1, 53.2, 51.4, 41.5, 38.4. 36.8, 36.5, 29.0, 27.2, 24.5, 23.8, 22.0, 21.4, 19.3; HRMS Calc'd for $C_{21}H_{32}O_3$ [M^+]: 332.2351; Found: 332.2359.

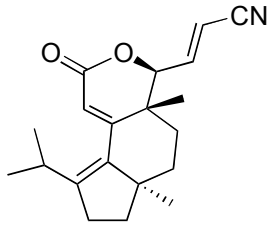


(*E*)-[(5*S*,7*aR*)-3-*Iso*-propyl-5,7*a*-dimethyl-5-(2-oxo-ethyl)-1,2,5,6,7,7*a*-hexahydro-inden-4-ylidene]-acetic acid *tert*-butyl ester (15c). Following the similar procedure for the preparation of compound **15a** and **16a**, compound **15c** and **16c** were obtained as a light yellow oil (55% yield, a 6.7:1 mixture). **15c**: $[\alpha]_D$ = + 266.0 (*c* 1.80, 23.7 °C, dichloromethane). IR (neat) 2959, 1750, 1708, 1456, 1368, 1143 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.83 (t, J = 3.6 Hz, 1 H), 5.51 (s, 1 H), 3.06 (dd, J = 18.0, 4.0 Hz, 1 H), 2.91 (dd, J = 18.0, 4.0 Hz, 1 H), 2.86 (sept, J = 6.8 Hz, 1H), 2.34 (m, 2 H), 1.71 (m, 2 H), 1.62 (m, 2 H), 1.51 (m, 1 H), 1.48 (s, 9 H), 1.42 (m, 1 H), 1.32 (s, 3 H), 1.01 (m, J = 6.4 Hz, 3 H), 0.99 (s, 3 H), 0.98 (d, J = 6.4 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ

203.3, 166.4, 154.2, 145.8, 140.9, 118.7, 80.6, 51.1, 48.2, 40.3, 38.9. 36.2, 35.3, 28.5, 28.1, 26.5, 25.5, 24.5, 21.6, 21.4; HRMS Calc'd for $C_{22}H_{34}O_3$ [M^+]: 346.2508; Found: 346.2508.

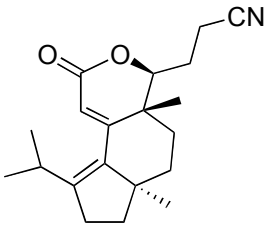


(*Z*)-[(5*S*,7*aR*)-3-*Iso*-propyl-5,7*a*-dimethyl-5-(2-oxo-ethyl)-1,2,5,6,7,7*a*-hexahydro-inden-4-ylidene]-acetic acid *tert*-butyl ester (16c). $[\alpha]_D$ = + 280.4 (*c* 1.80, 24.2 °C, dichloromethane). IR (neat) 2958, 1715, 1626, 1434, 1290, 1194 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.93 (t, *J* = 4.0 Hz, 1 H), 5.57 (s, 1 H), 2.54 (dd, *J* = 15.6, 4.0 Hz, 1 H), 2.50 (dd, *J* = 15.6, 4.0 Hz, 1 H), 2.43 (sept, *J* = 6.4 Hz, 1 H), 2.47 (m, 1 H), 1.93 (dt, *J* = 13.2, 4.0 Hz, 1 H), 1.80 (m, 1 H), 1.70 (m, 2 H), 1.58 (m, 2 H), 1.53 (m, 1 H), 1.44 (s, 9 H), 1.17 (s, 3 H), 1.09 (s, 3 H), 0.94 (d, *J* = 6.8 Hz, 3 H), 0.90 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 202.7, 165.0, 158.5, 142.8, 135.2, 115.8, 79.7, 53.3, 51.6, 41.5, 38.1, 36.9, 36.2, 29.0, 28.3, 28.0, 27.2, 24.6, 21.4, 19.4; HRMS Calc'd for $C_{22}H_{34}O_3$ [M^+]: 346.2508; Found: 346.2520.

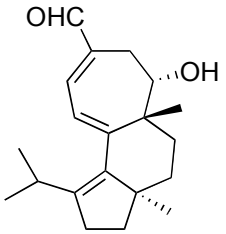


(*E*)-(3*S*,3*aR*,5*aR*)-3-(1-*Iso*propyl-3*a*,5*a*-dimethyl-8-oxo-2,3,3*a*,4,5,5*a*,6,8-octahydro-7-oxa-cyclopenta[*a*]naphthalen-6-yl)-acrylonitrile (20). To a solution of compound **15c** (20.7 mg, 0.060 mmol) and phenylsulphinyl acetonitrile (13.8 mg, 0.084 mmol) in benzene (0.6 mL) was added piperidine (7.1 mg, 0.084 mmol) at room temperature. The mixture was stirred for 36 h and directly purified by column chromatography (petroleum ether/ether, 2:1) to give compound **20** as a white solid (13.9 mg, 75%), mp. 130-131 °C, $[\alpha]_D$ = + 667.9 (*c* 0.57, 24.6 °C, dichloromethane). IR (neat) 2957, 2227, 1724, 1678, 1451, 1247 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 6.71 (dd, *J* = 16.0, 3.5 Hz, 1 H), 5.95 (dd, *J* = 16.0, 2.0 Hz, 1 H), 5.77 (s, 1 H), 4.75 (dd, *J* = 4.0, 2.0 Hz, 1 H), 2.89 (sept, *J* = 6.5 Hz, 1 H), 2.48 (m, 2 H), 1.84 (m, 2 H), 1.76 (m, 2 H), 1.65

(m, 2 H), 1.57 (s, 3 H), 1.05 (d, J = 7.0 Hz, 3 H), 0.99 (s, 3 H), 0.98 (s, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.8, 160.0, 153.1, 146.3, 133.8, 130.3, 116.7, 113.7, 103.1, 82.8, 48.4, 40.1, 39.0, 35.4, 32.3, 29.3, 27.1, 23.4, 21.6, 21.4, 17.8; HRMS Calc'd for $C_{20}H_{25}NO_2$ [M^+]: 311.1885; Found: 311.1865.



(3*S*,3*aR*,5*aR*)-3-(1-*Iso*-propyl-3*a*,5*a*-dimethyl-8-oxo-2,3,3*a*,4,5,5*a*,6,8-octahydro-7-oxa-cyclopenta[*a*]naphthalen-6-yl)-propionitrile (21). To a solution of compound **20** (13.9 mg, 0.045 mmol) in EtOAc (0.4 mL) was added 10% Pd/C (7.0 mg). The suspension was stirred under 1 atm H_2 for 6 h and filtered through a plug of celite. The filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (petroleum ether/ether, 1:1) to give compound **21** as white crystals (11.6 mg, 83%), mp. 155-156 °C, $[\alpha]_D$ = + 650.4 (*c* 0.22, 24.8 °C, dichloromethane). IR (neat) 2959, 2252, 1717, 1638, 1250 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.75 (s, 1 H), 4.16 (dd, J = 10.0 Hz, 3.2 Hz, 1 H), 2.90 (sept, J = 6.8 Hz, 1H), 2.68 (m, 2 H), 2.47 (m, 2 H), 1.96 (m, 2 H), 1.80 (dddd, J = 7.2, 7.2, 2.8, 2.8 Hz, 1 H), 1.80 (dd, J = 5.6, 2.4 Hz, 1 H), 1.72 (m, 2 H), 1.65 (m, 2 H), 1.04 (d, J = 6.8 Hz, 3 H), 1.01 (s, 3 H), 0.98 (s, 3 H), 0.97 (d, J = 6.8 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 164.9, 160.4, 152.3, 134.1, 119.1, 114.0, 83.0, 48.6, 39.1, 39.0, 35.7, 32.6, 29.3, 27.0, 25.3, 23.4, 21.6, 21.4, 17.0, 14.0; HRMS Calc'd for $C_{20}H_{27}NO_2$ [M^+]: 313.2042; Found: 313.2041.

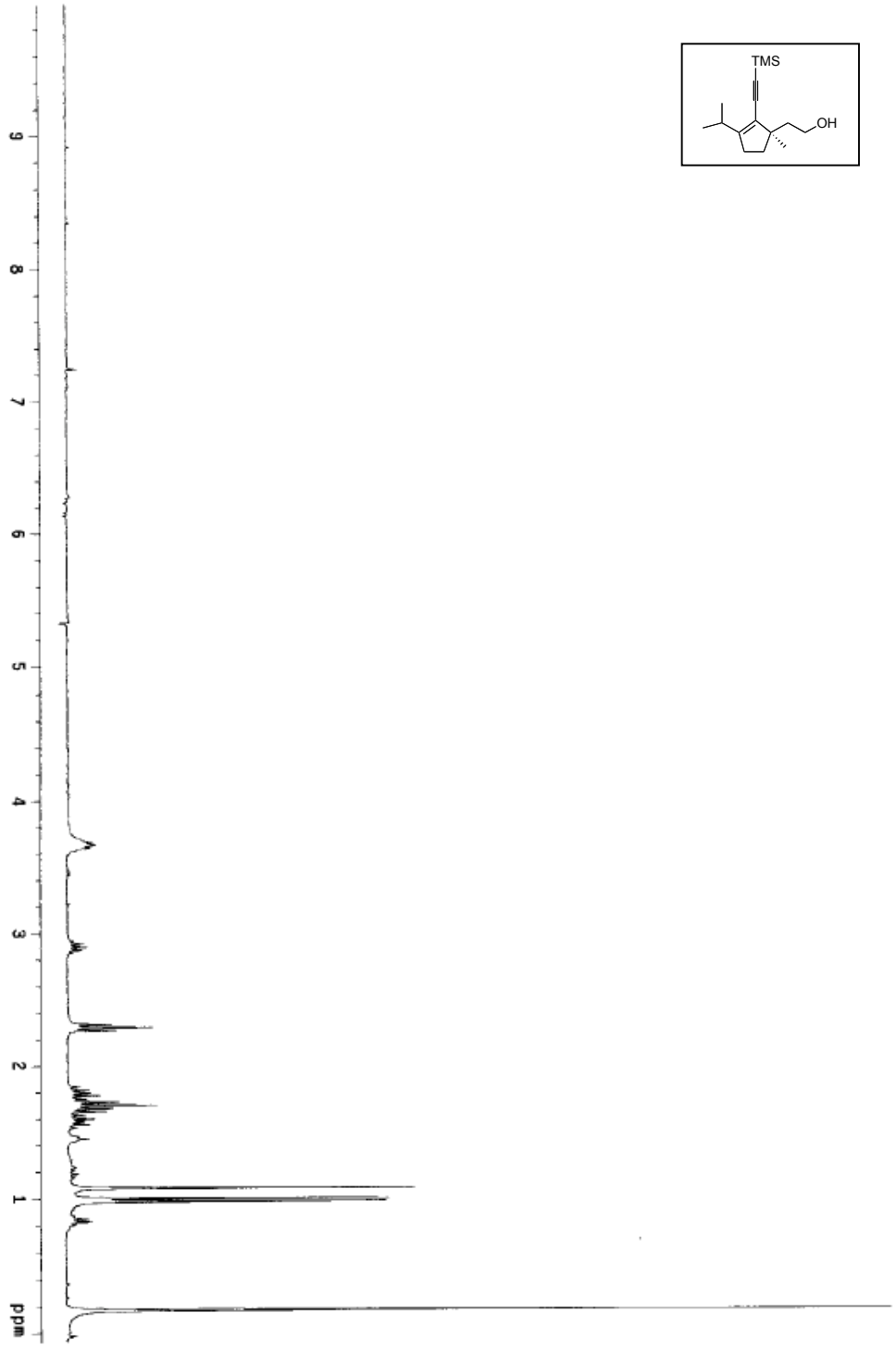


(+)-Allocyathin B_2 (1). To a solution of compound **21** (10 mg, 0.032 mmol) in CH_2Cl_2 (0.5 mL) was added DIBAL-H (1 M in hexanes, 0.128 mL, 0.128 mmol) at –78 °C. The mixture was stirred at this temperature for 2 h and quenched with addition of 1

M $NaHSO_4$ (0.4 mL). The suspension was warmed up to room temperature for 15 min and extracted with ether (2 × 5 mL). The organic layer was washed with brine (2 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude aldehyde **3** was used directly for the next step. Aldehyde **3**: ^{1}H NMR ($CDCl_3$, 500 MHz, mixture of two diastereomers) major: δ 9.88 (s, 1 H), 5.88 (m, 1 H), 5.22 (m, 1 H), 3.85 (d, *J* = 6.5 Hz, 1 H), 3.74 (m, 1 H), 3.66 (m, 1 H), 2.86 (m, 1 H), 2.57-2.39 (m, 4 H), 2.33 (m, 2 H), 1.98 (m, 1 H), 1.72 (m, 1 H), 1.67 (m, 2 H), 1.52 (m, 3 H), 1.35 (m, 2 H), 1.03 (m, 3 H), 0.99-0.96 (m, 6 H), 0.94 (s, 3 H); minor: δ 9.88 (s, 1 H), 5.37 (m, 1 H), 5.09 (m, 1 H), 3.87 (d, *J* = 6.5 Hz, 1 H), 3.75 (m, 1 H), 3.58 (m, 1 H), 2.86 (m, 1 H), 2.33 (m, 2 H), 1.98 (m, 1 H), 1.72 (m, 1 H), 1.67 (m, 2 H), 1.52 (m, 3 H), 1.35 (m, 2 H), 1.03 (m, 3 H), 0.99-0.96 (m, 6 H), 0.92 (s, 3 H).

To a solution of the crude aldehyde **3** in MeOH (1.0 mL) was added 5% KOH in MeOH (1.0 mL). The mixture was stirred at 60 °C for 1 h. The reaction was quenched with addition of 10% citric acid solution (3 mL) and was concentrated under reduced pressure. The aqueous residue was extracted with ether (2 × 5 mL). The combined organic layers were washed with brine (2 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (5:1 EtOAc/petroleum ether) to give (+)-allocyathin B_2 (**1**, 4.8 mg, 51 %) as a pale yellow oil, $[\alpha]_D$ = + 482.3 (*c* 0.18, 23.6 °C, methanol); lit. $[\alpha]_D$ = + 144 (*c* 0.18, methanol).[1] IR (neat) 3442, 1668, 1571, 2959 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.45 (s, 1 H), 6.82 (dd, *J* = 8.0, 6.5 Hz, 1 H), 5.94 (d, *J* = 8.0 Hz, 1 H), 3.73 (m, 1 H), 3.16 (dd, *J* = 18.5, 6.0 Hz, 1 H), 2.83 (sept, *J* = 6.5 Hz, 1 H), 2.55 (br, d, *J* = 18.5 Hz, 2 H), 2.53 (m, 1 H), 2.42 (dd, *J* = 9.5, 2.5 Hz, 1 H), 2.41 (d, *J* = 13.5 Hz, 1 H), 1.74 (ddd, *J* = 12.5, 7.5, 5.0 Hz, 1 H), 1.69-1.65 (m, 3 H), 1.61 (br, m, 1 H), 1.34 (dt, *J* = 14.0, 3.5 Hz), 1.05 (d, *J* = 7.0 Hz, 3 H), 1.00 (s, 3 H), 0.97 (d, *J* = 7.0 Hz, 3 H), 0.96 (s, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 194.2, 155.1, 146.5, 144.4, 151.8, 137.7, 119.3, 74.0, 49.1, 48.2, 38.2, 36.5, 33.9, 29.2, 29.0, 27.0, 26.5, 23.9, 21.5, 21.5; HRMS Calc'd for $C_{20}H_{28}O_2$ [M^+]: 300.2089; Found: 300.2077.

[1] Personal communication with Prof. Hirokazu Kawagishi.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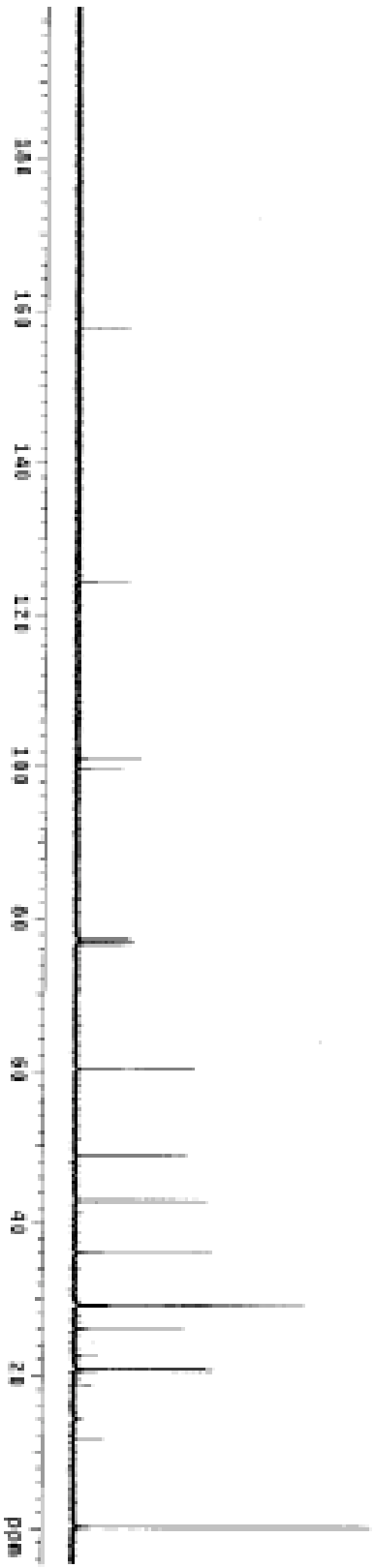
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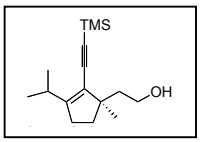
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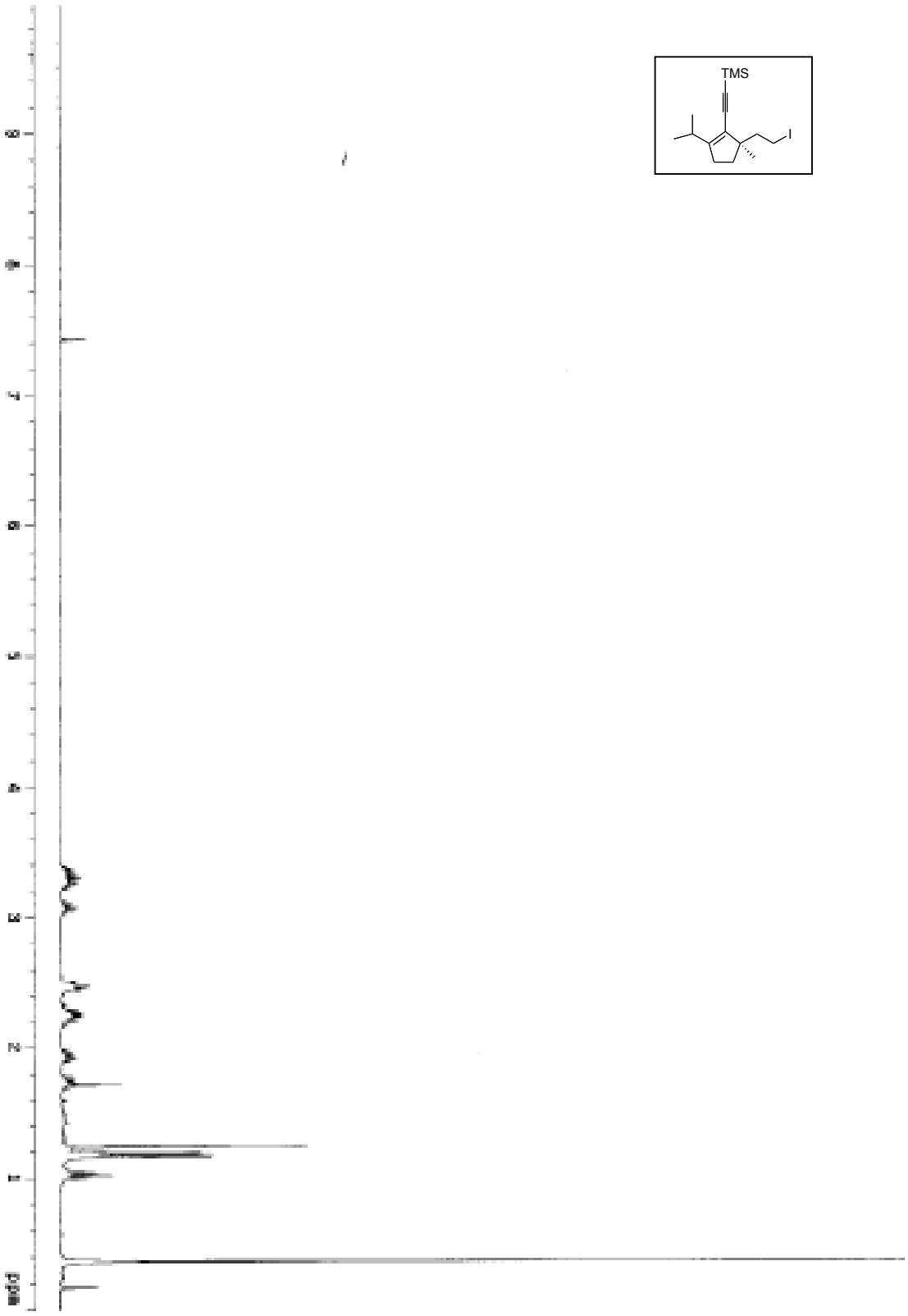
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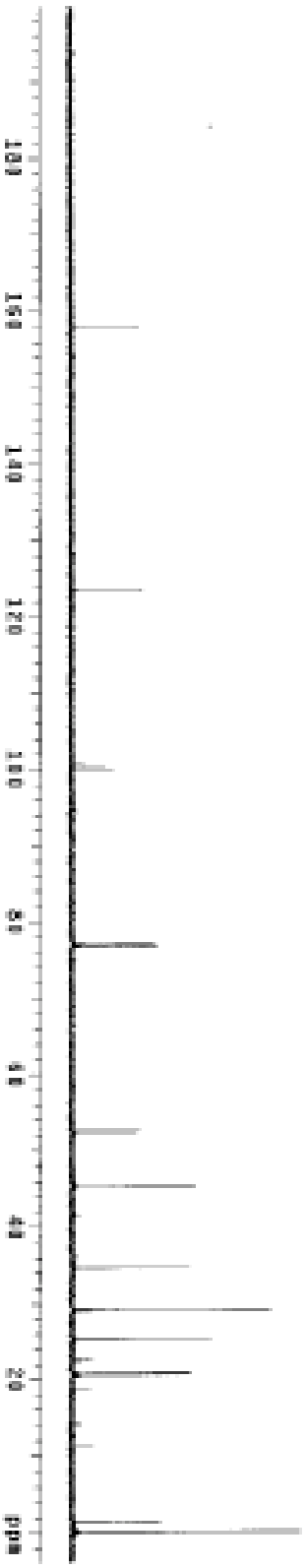
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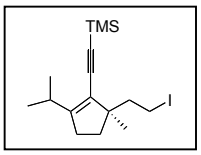
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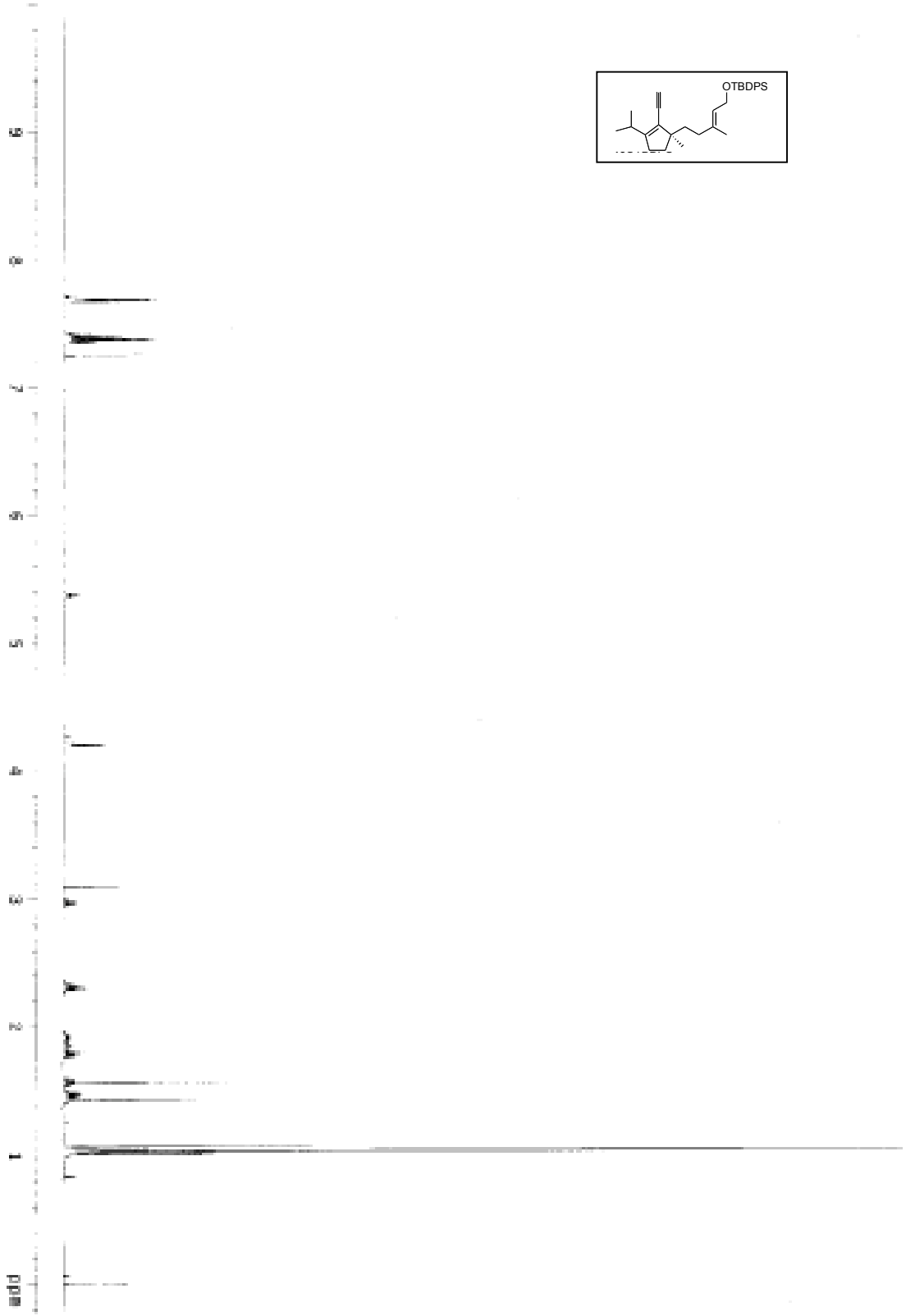
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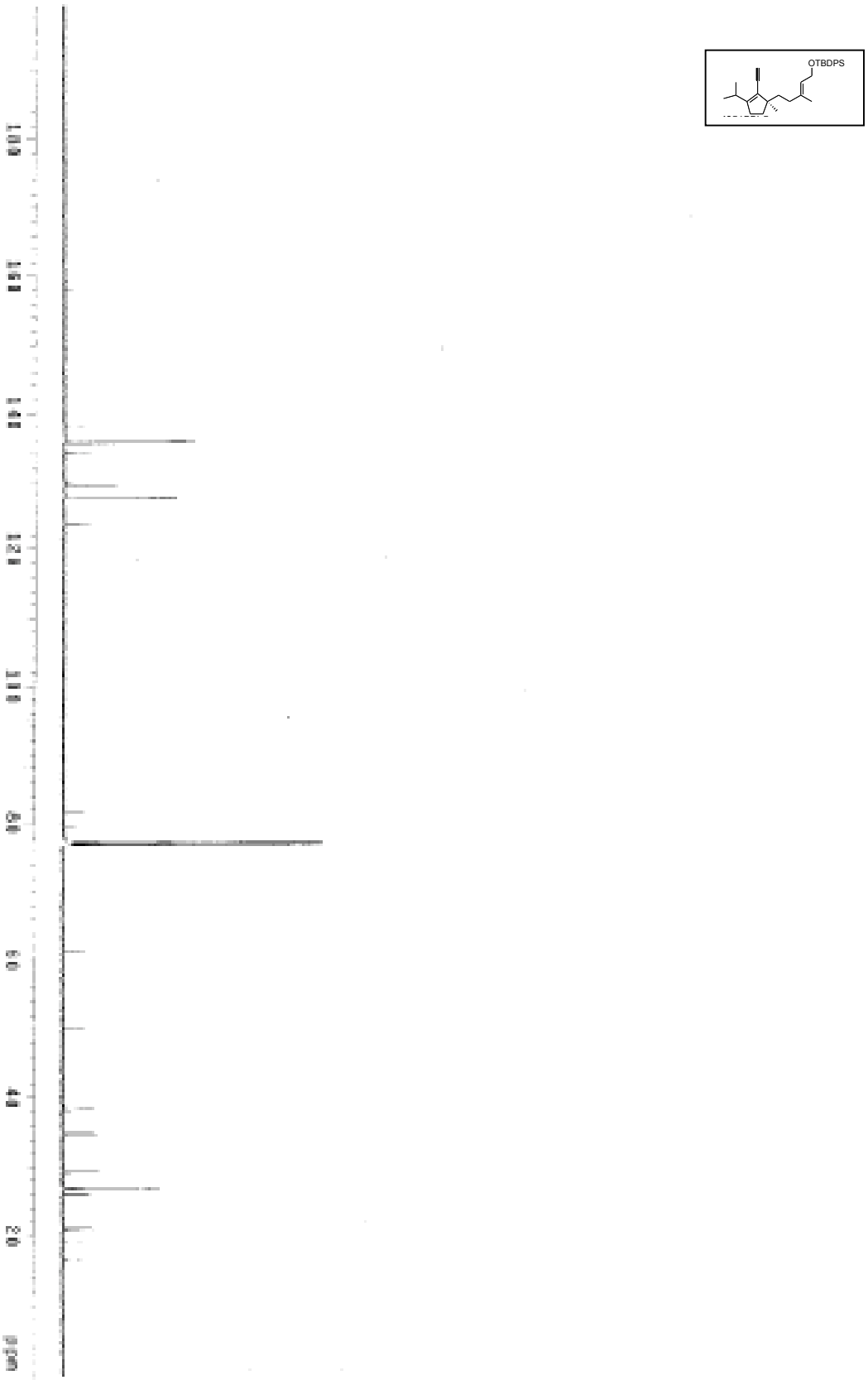
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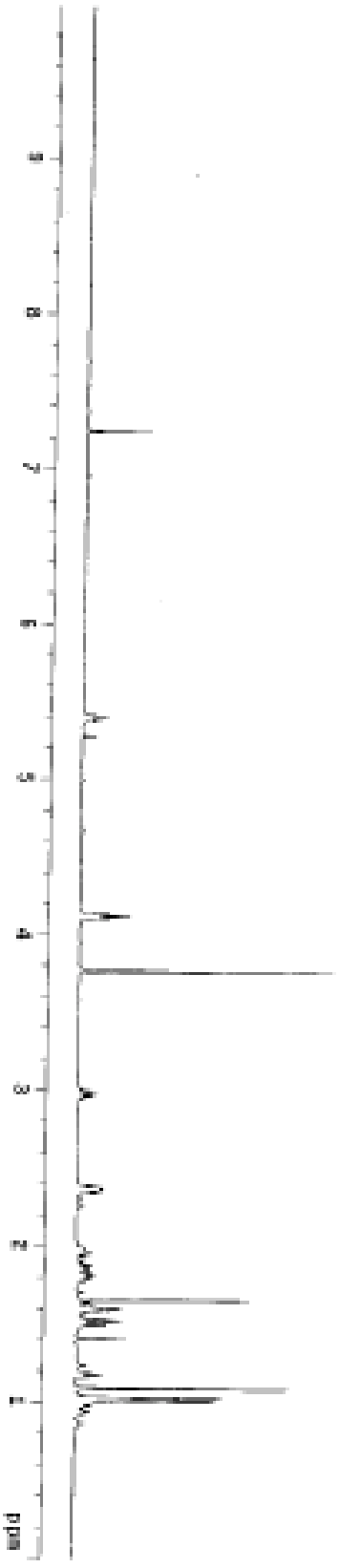
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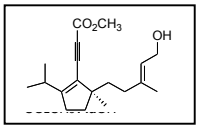
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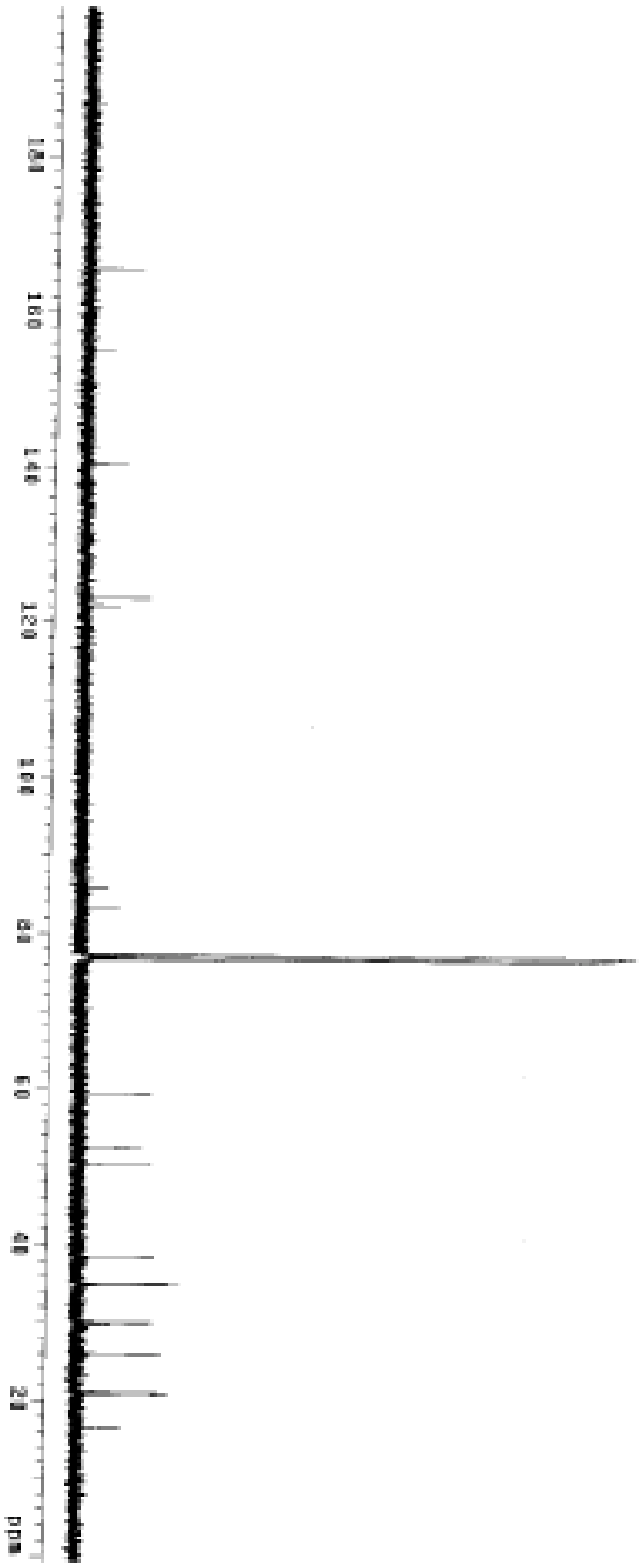
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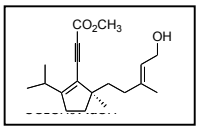
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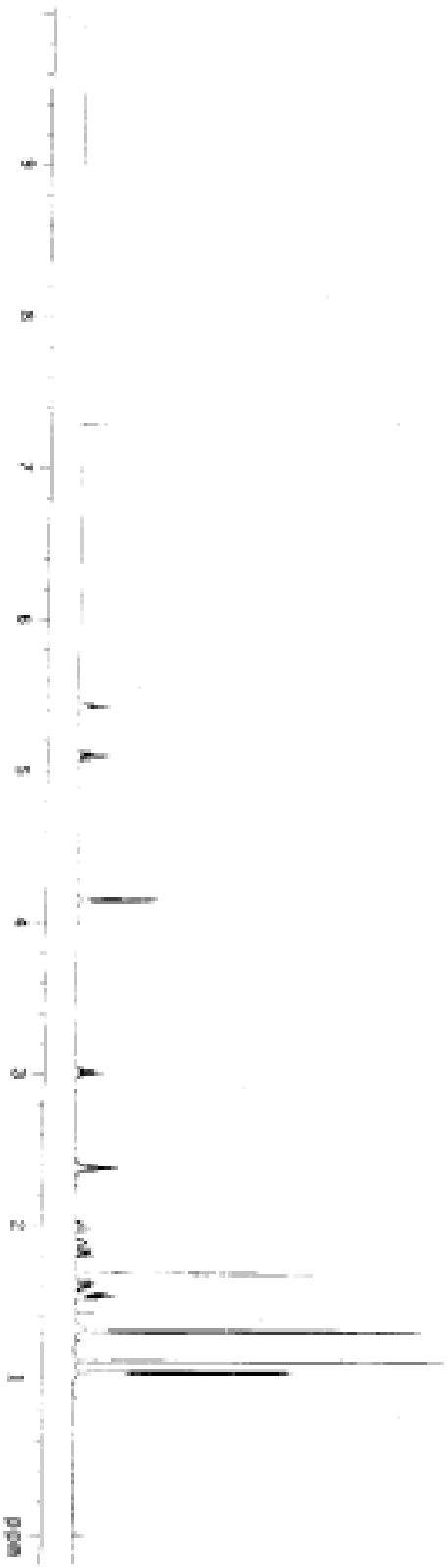

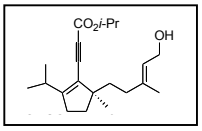
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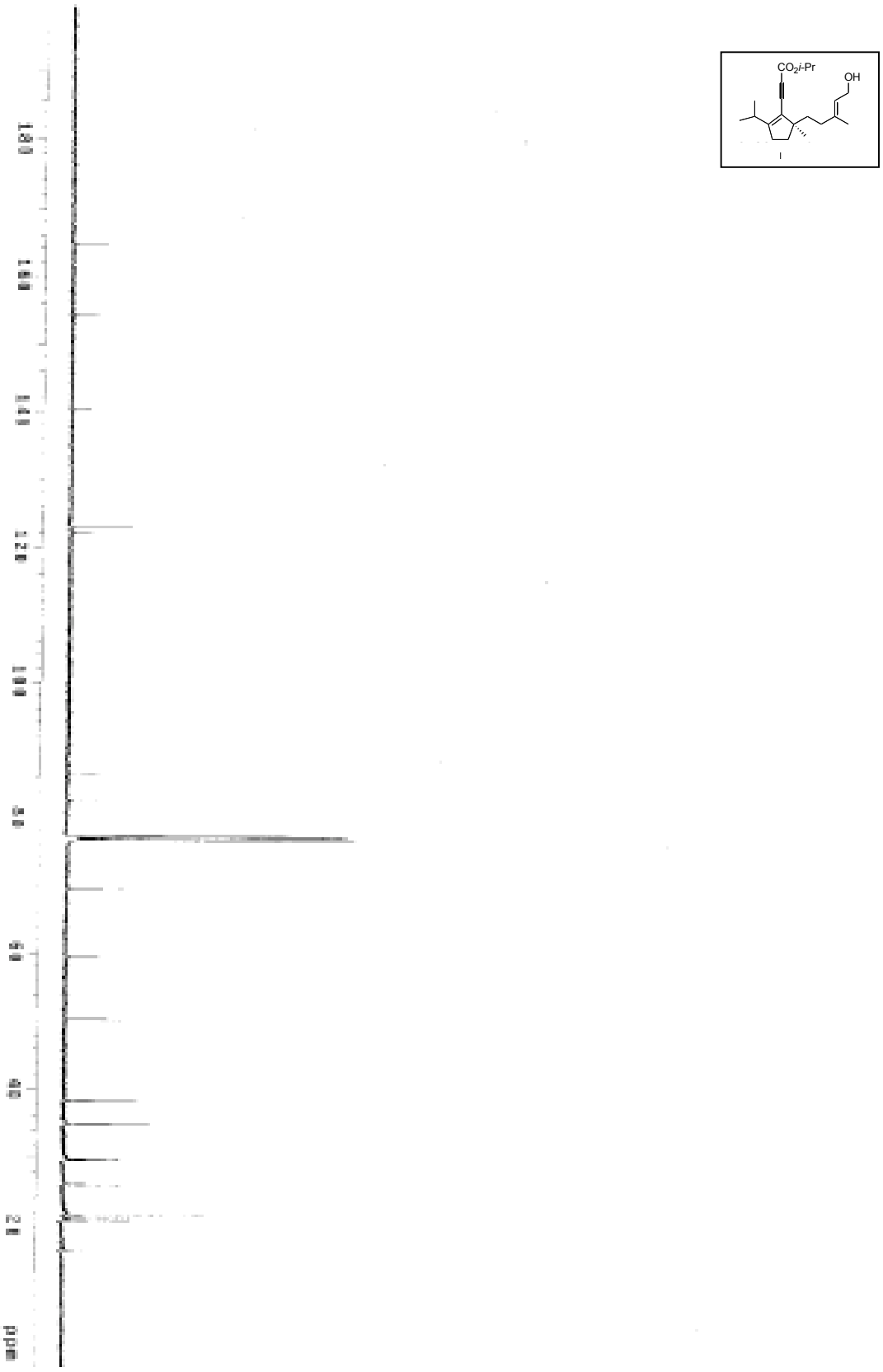
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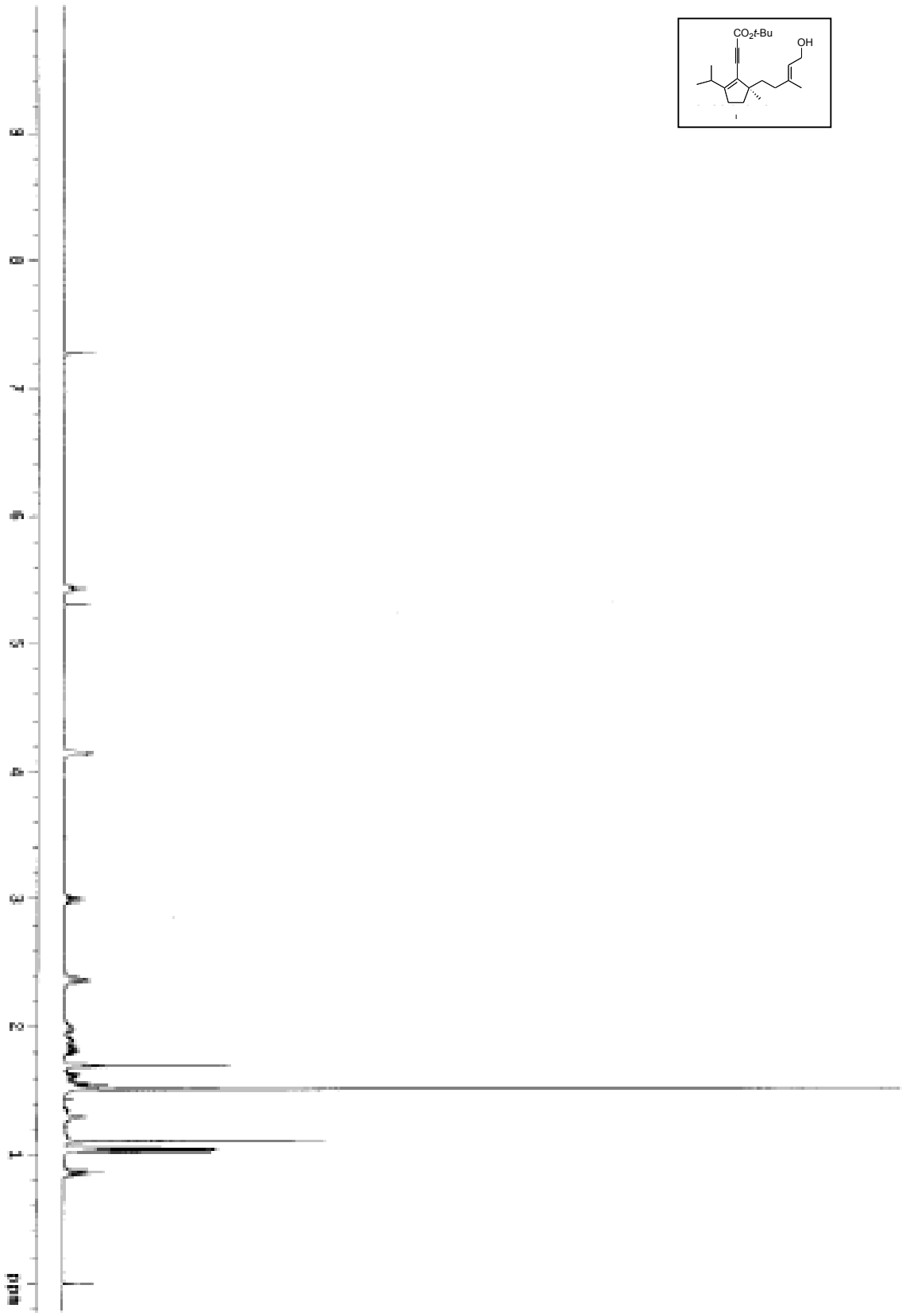
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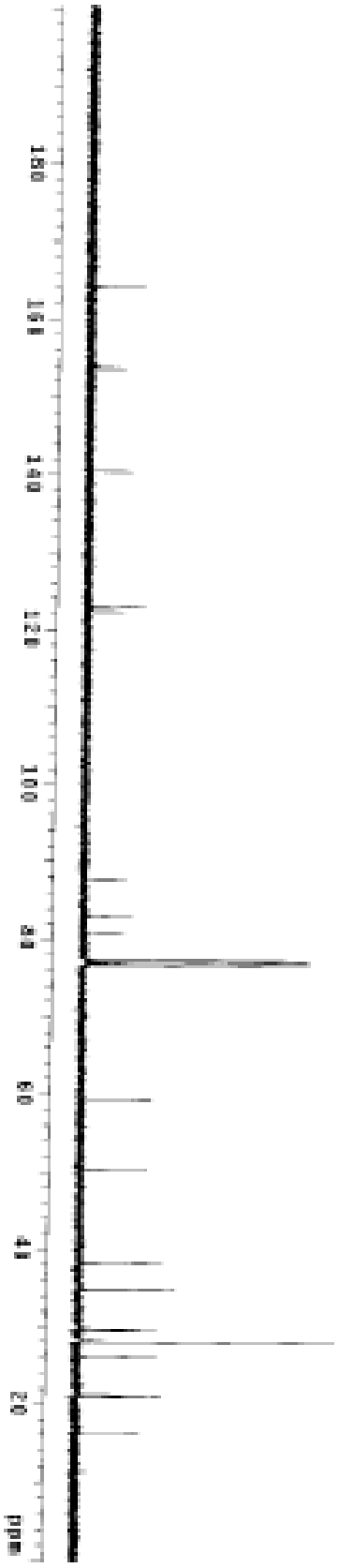
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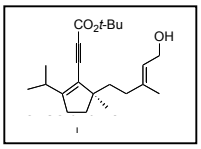
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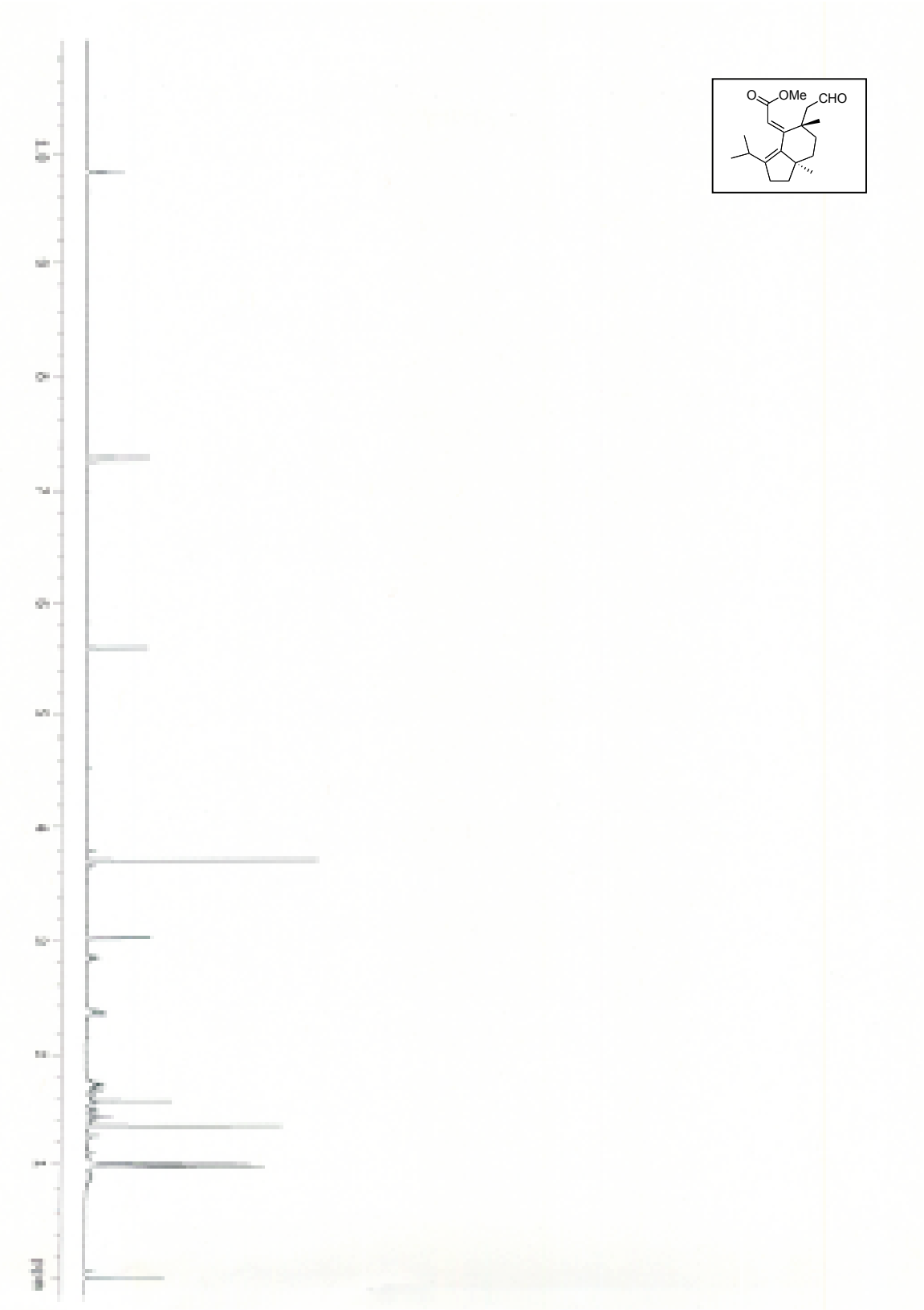
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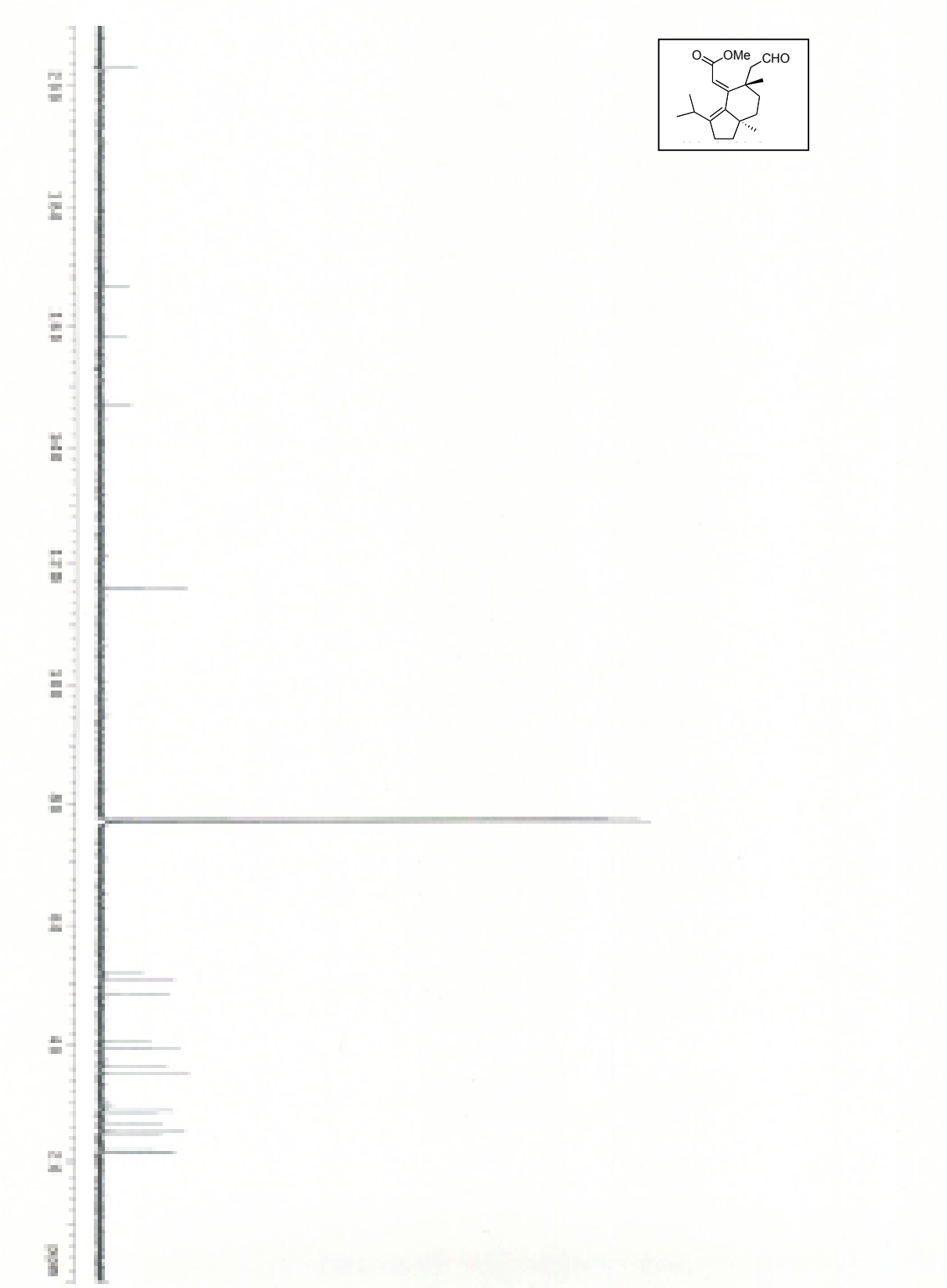
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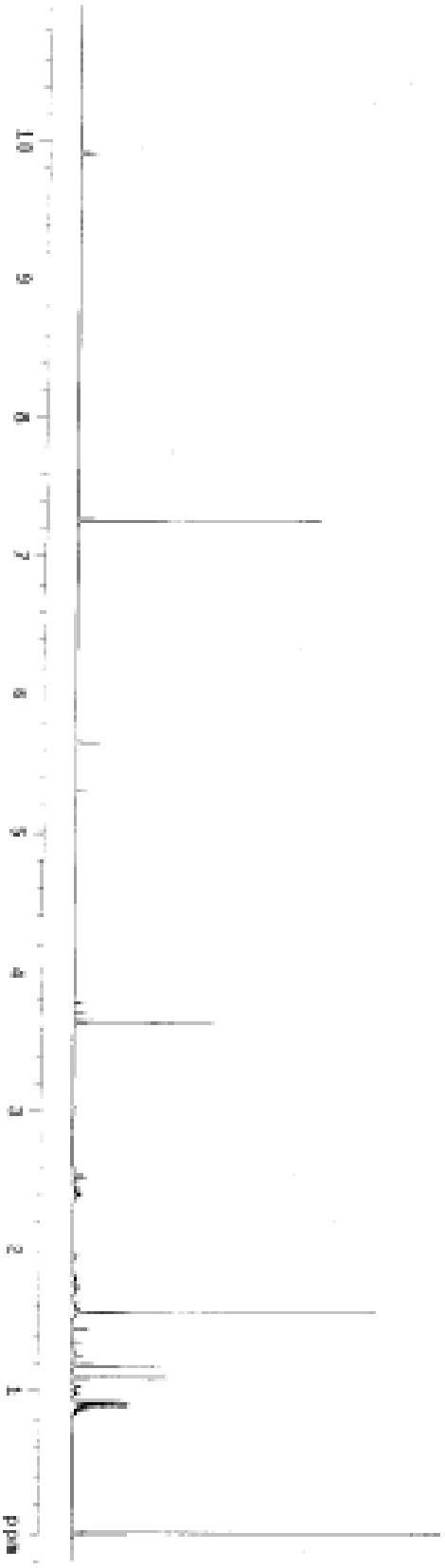
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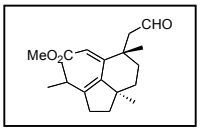
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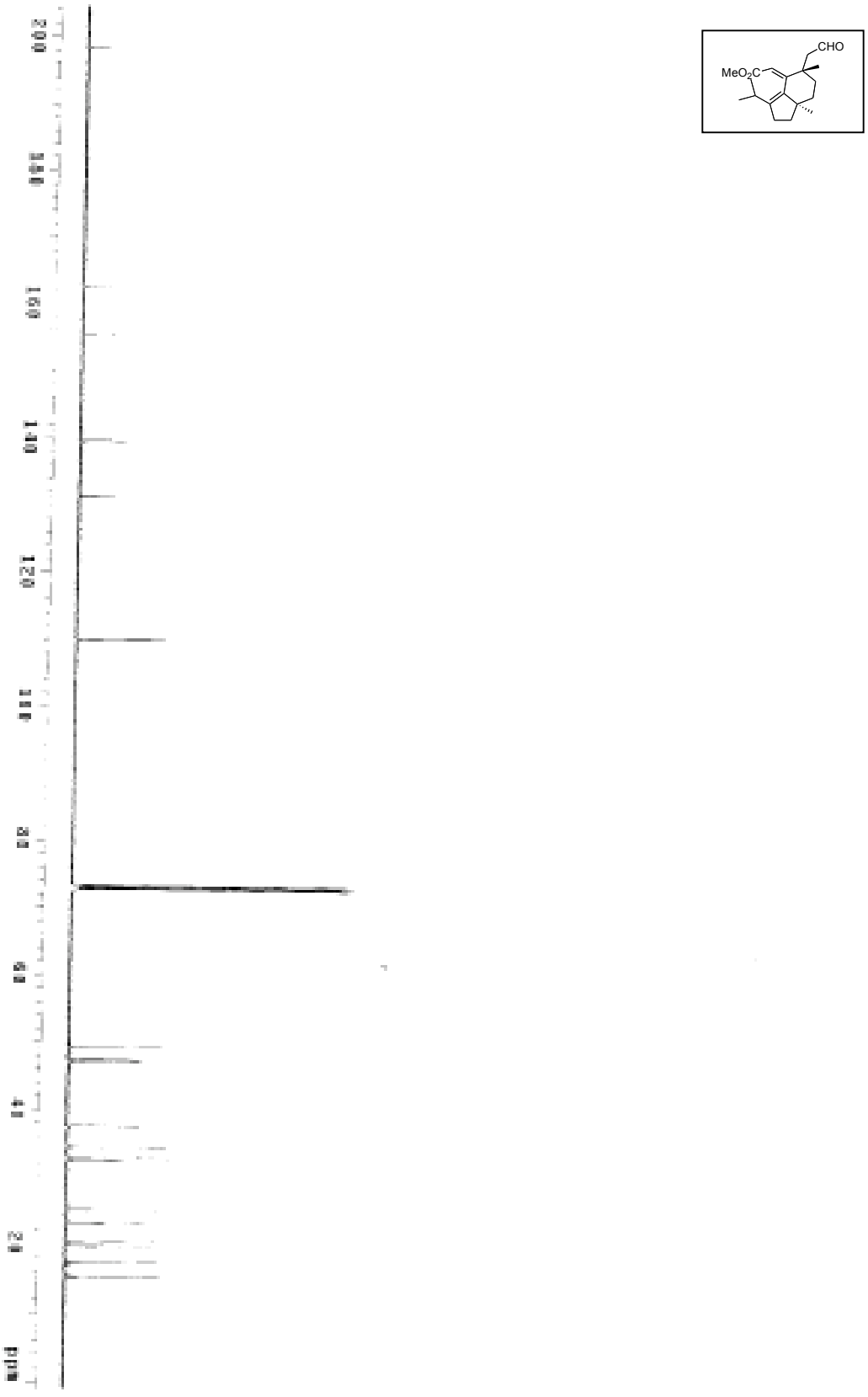
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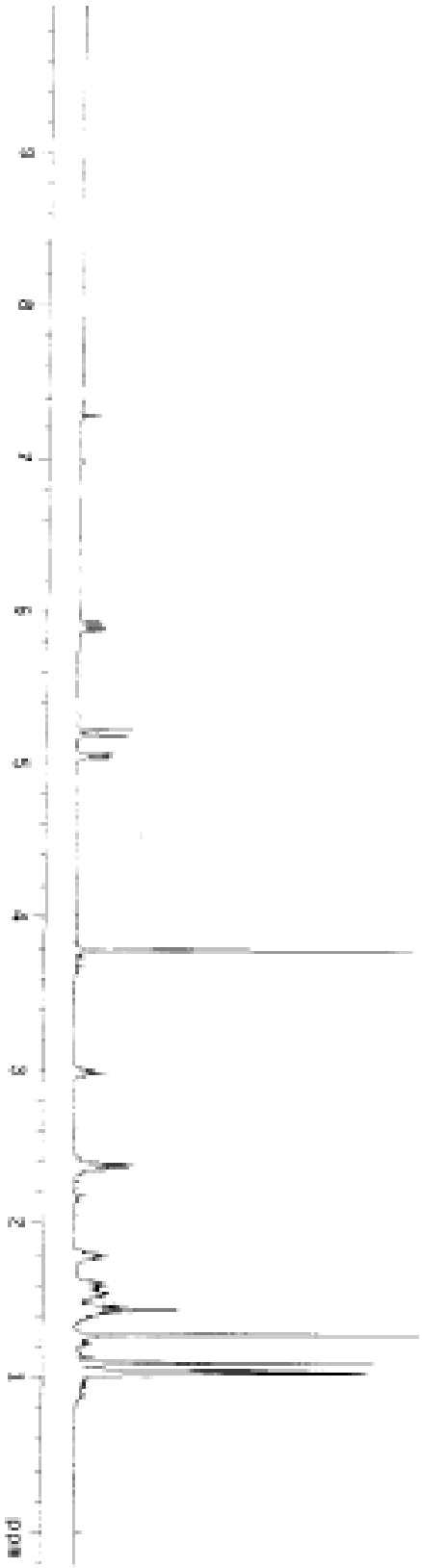

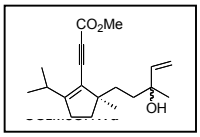
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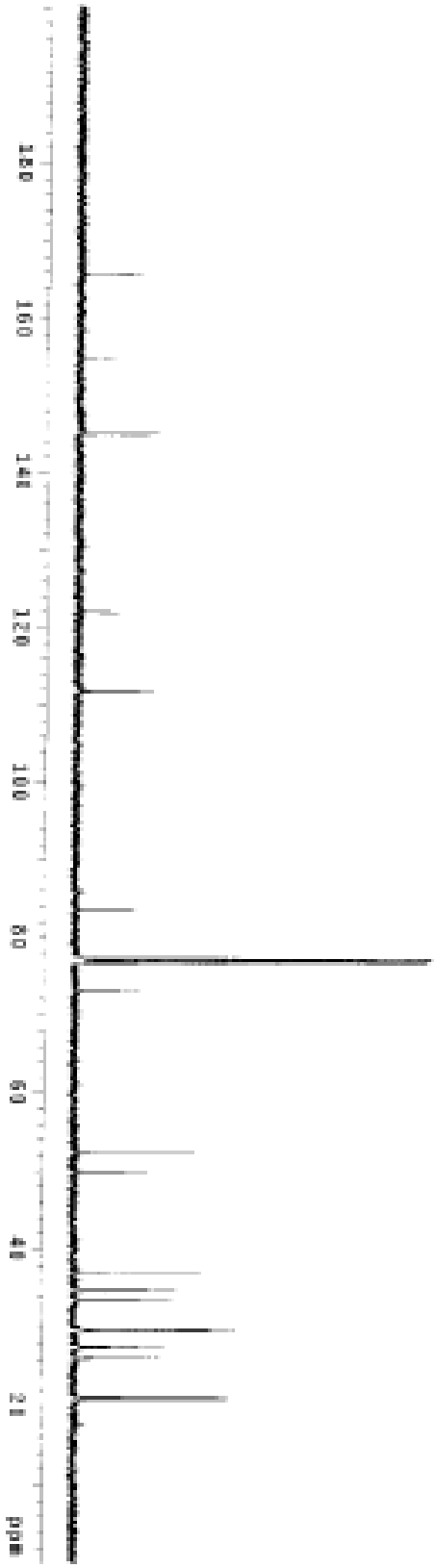
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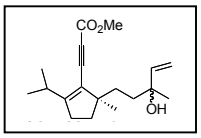
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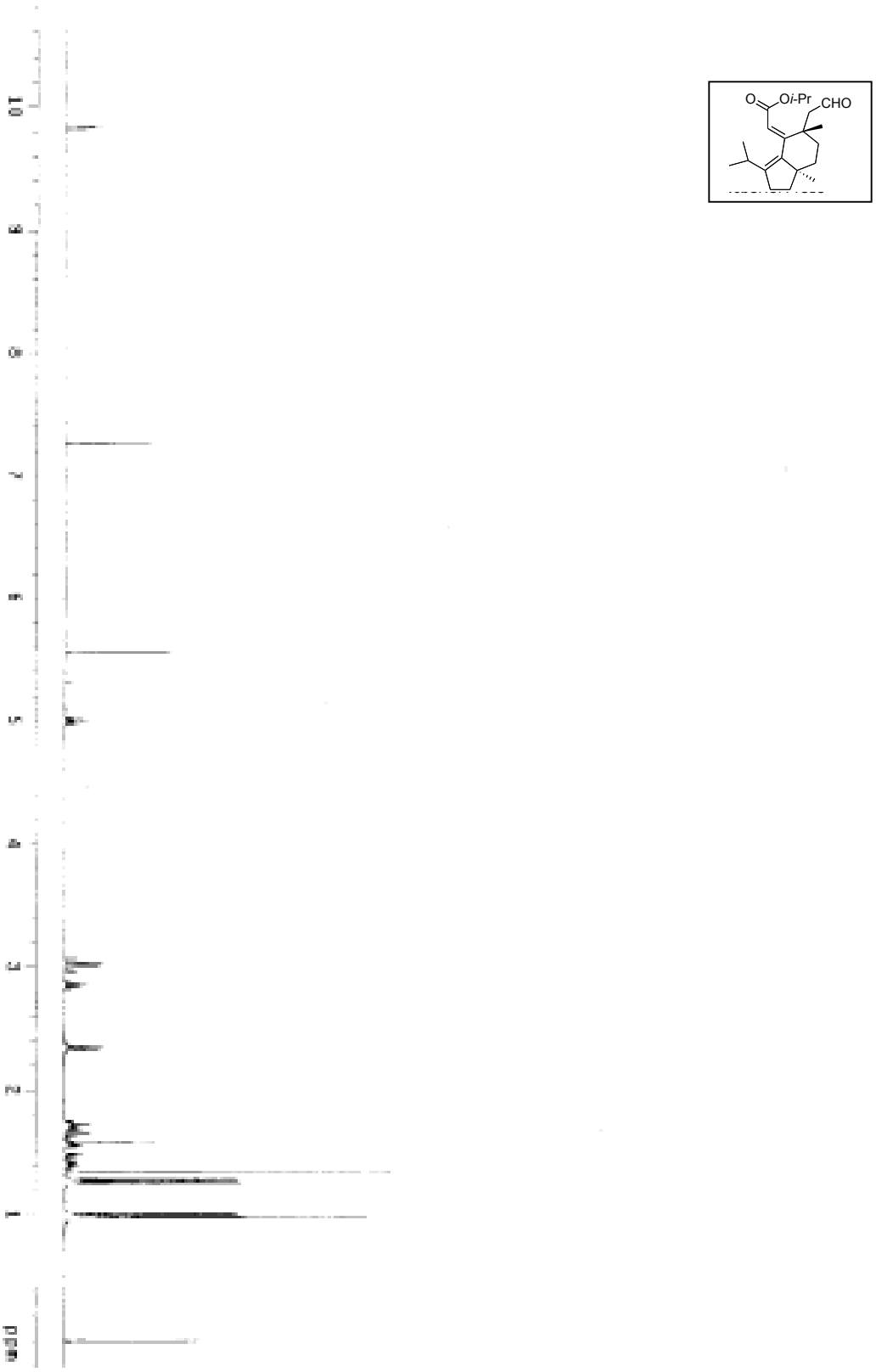
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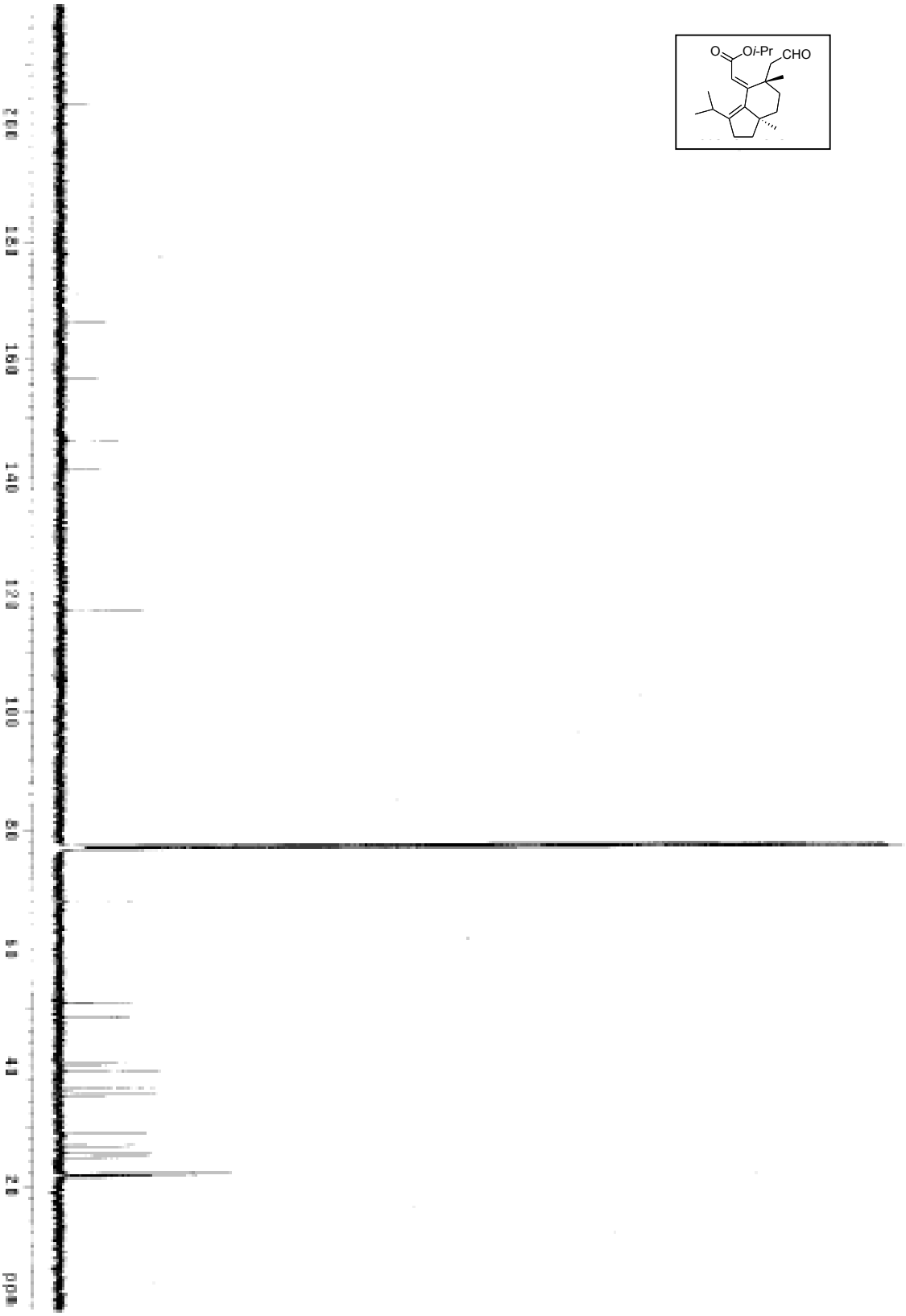
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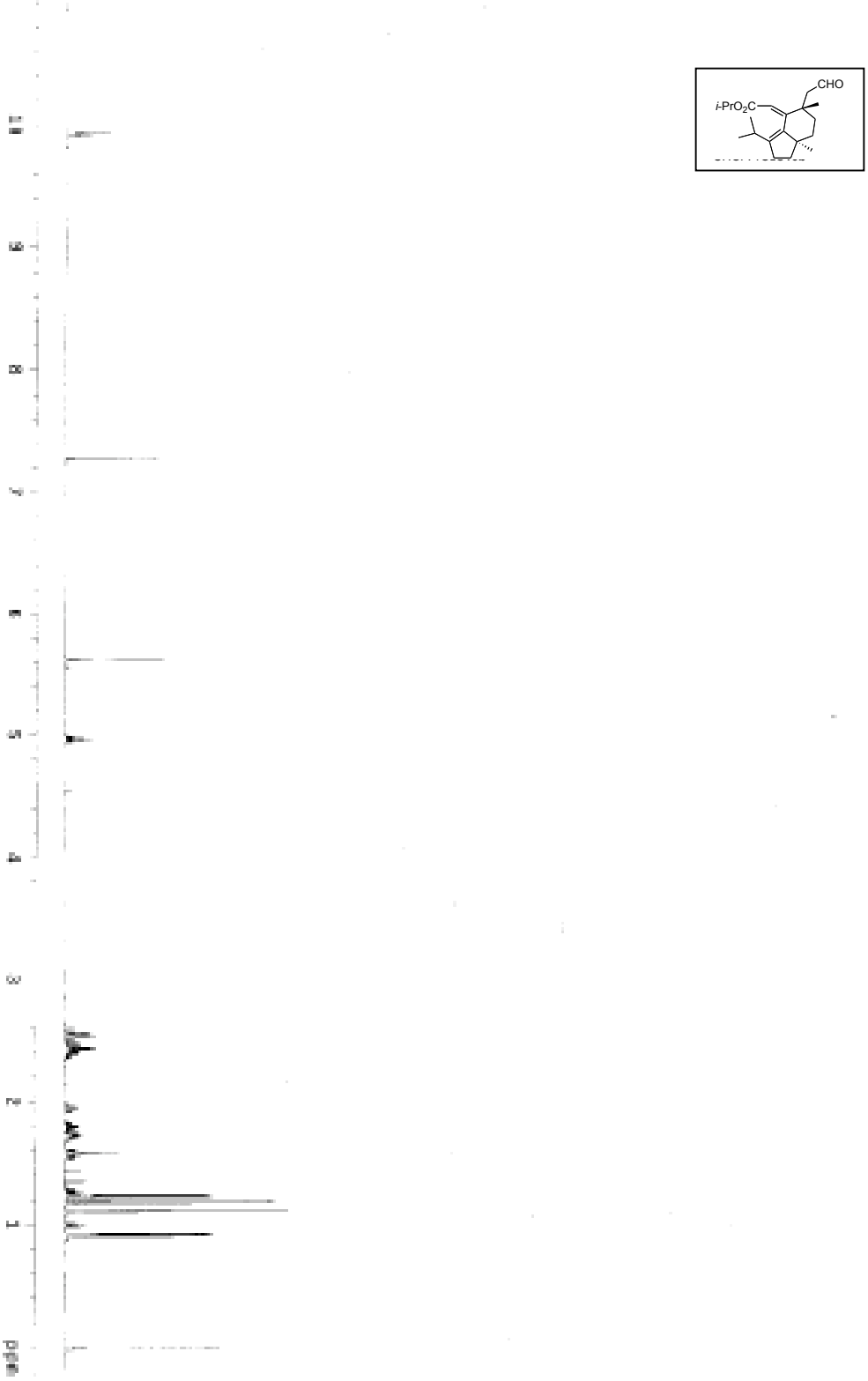
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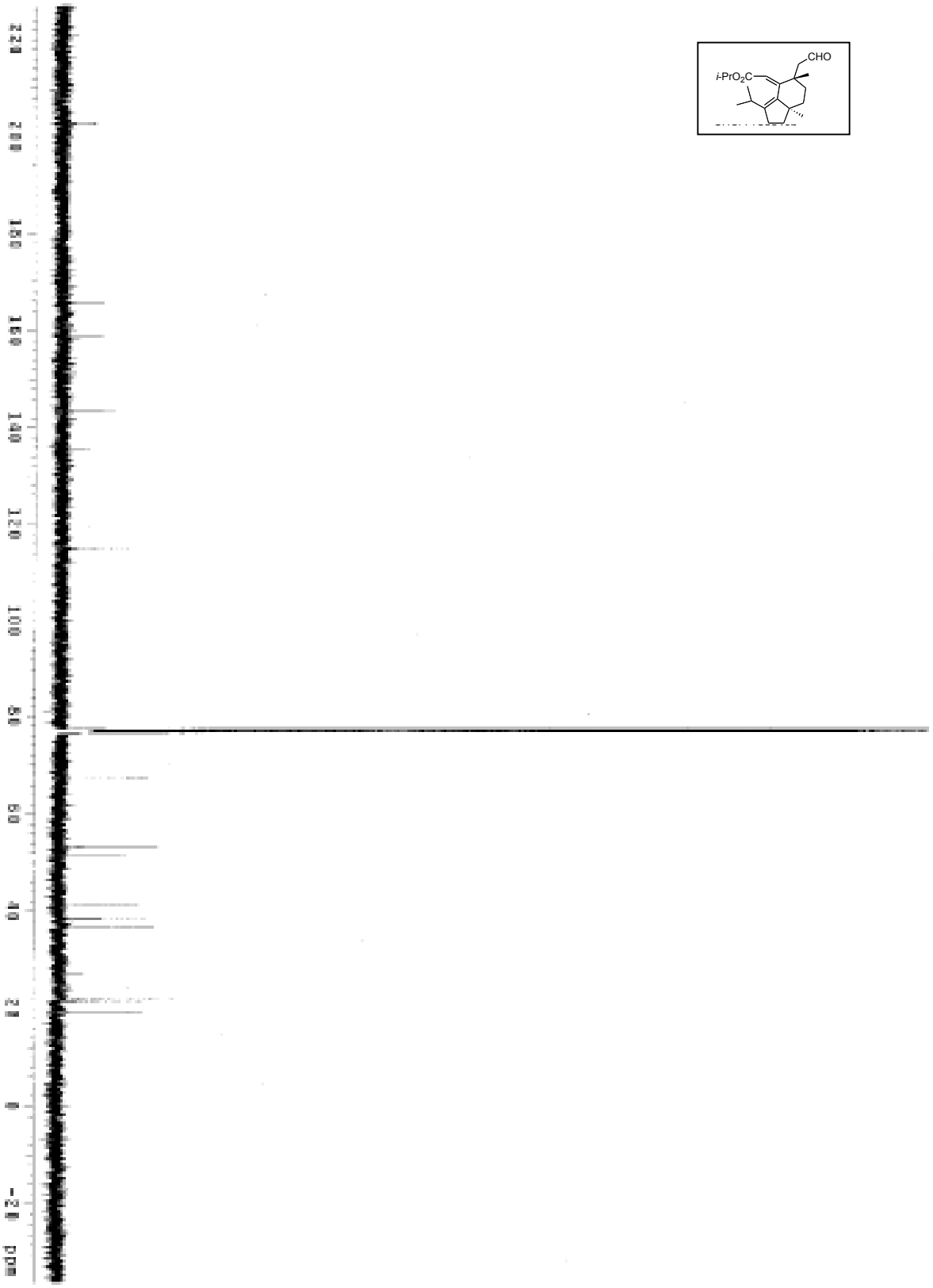
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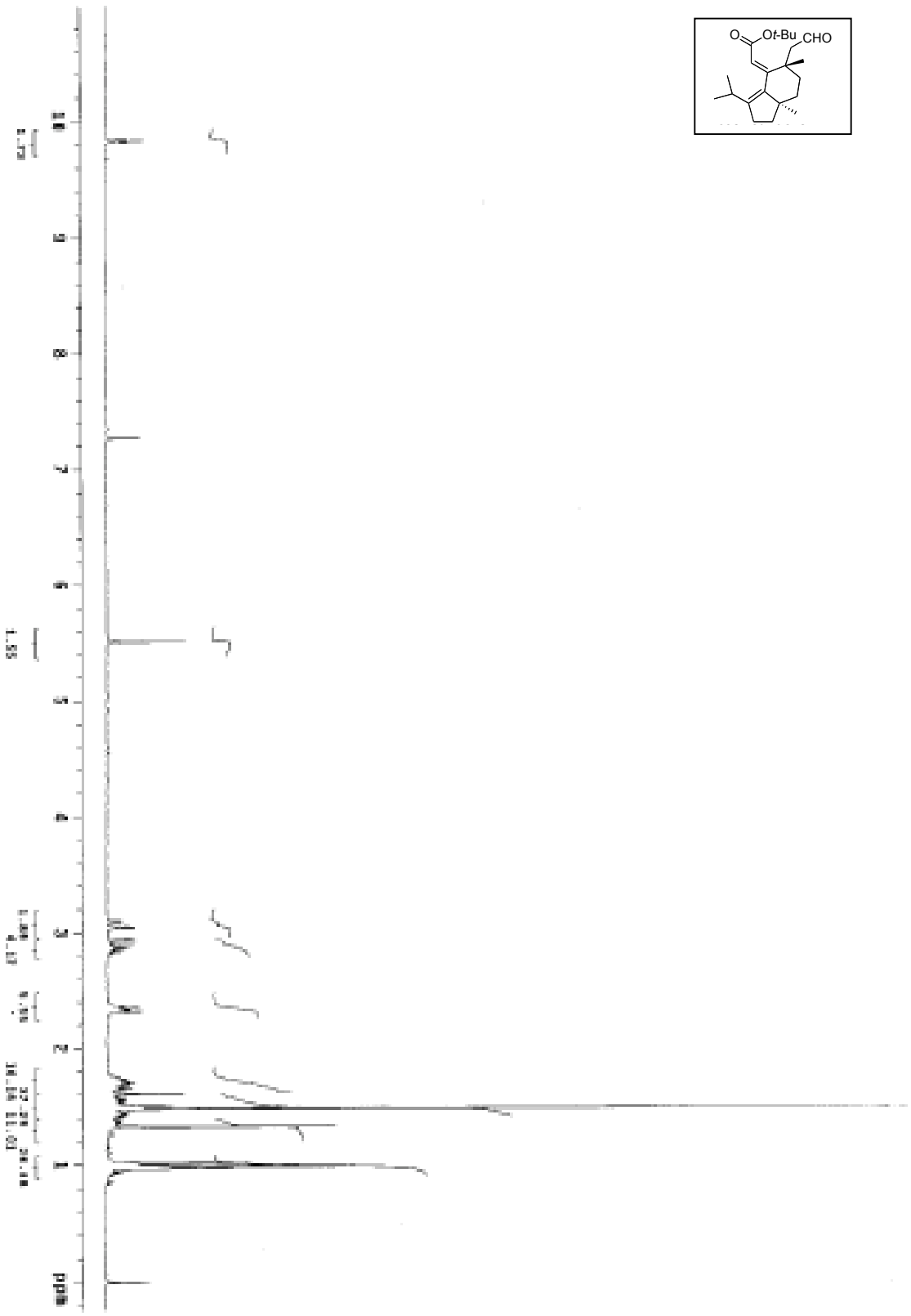
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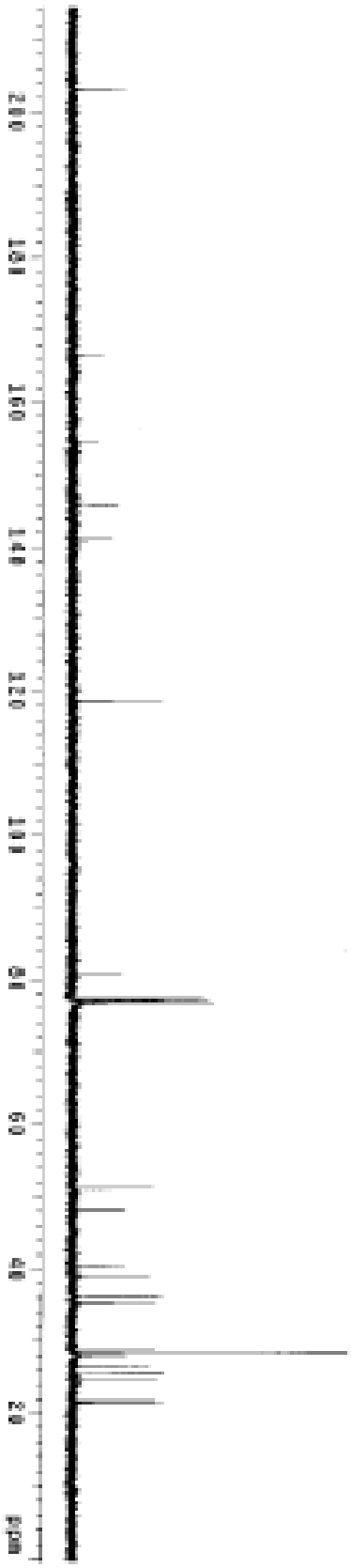
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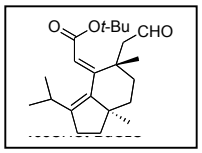
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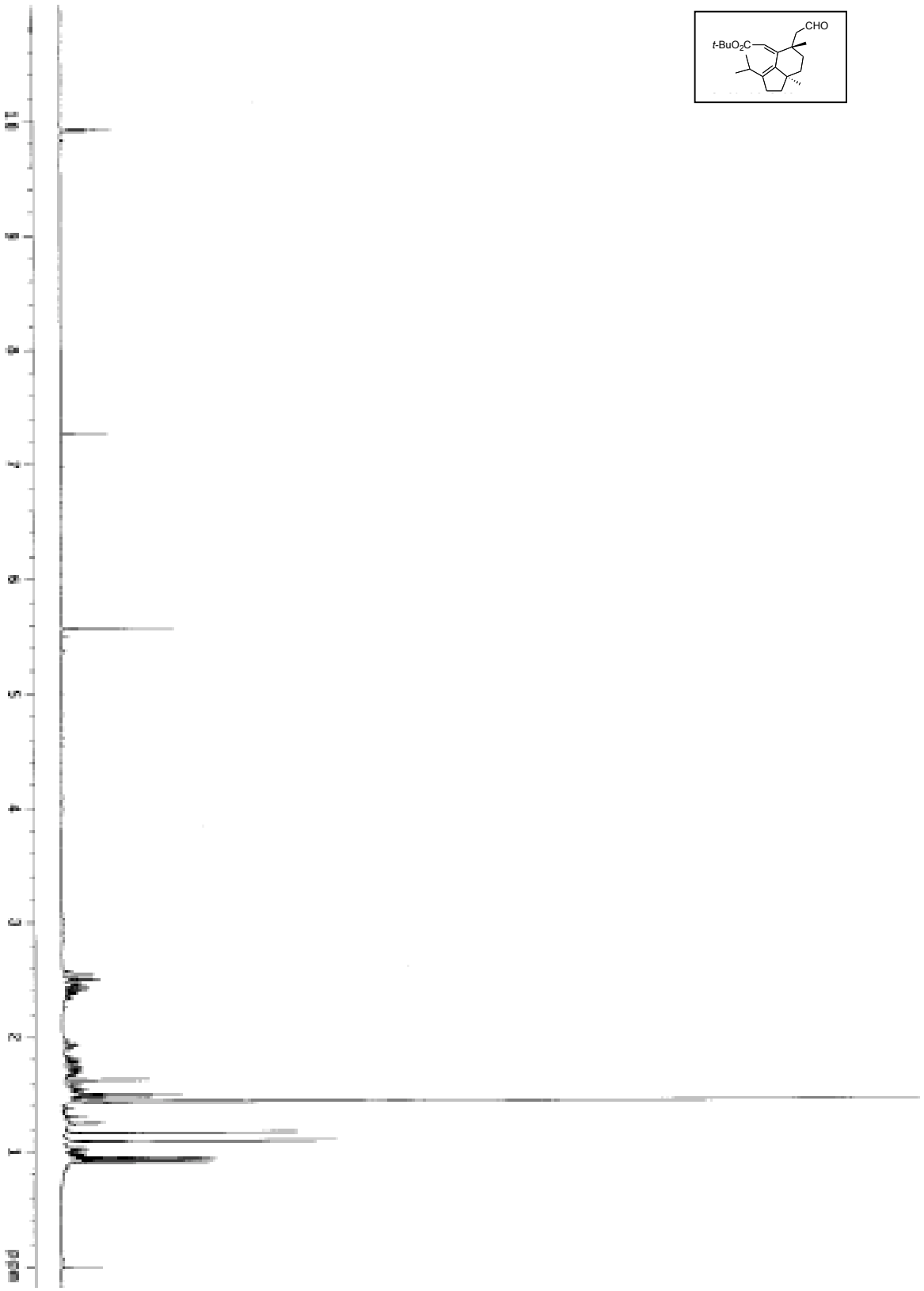
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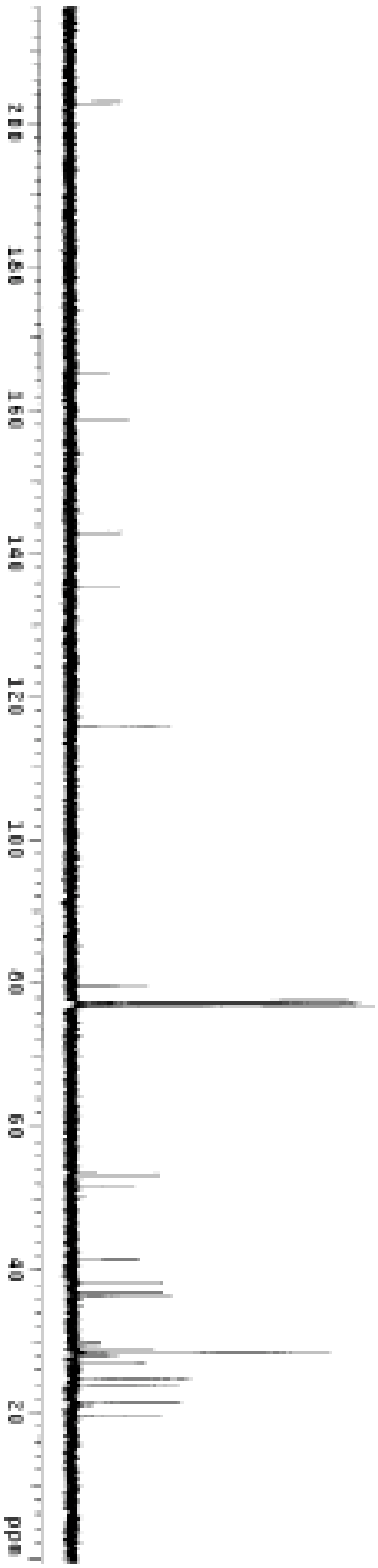
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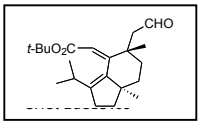
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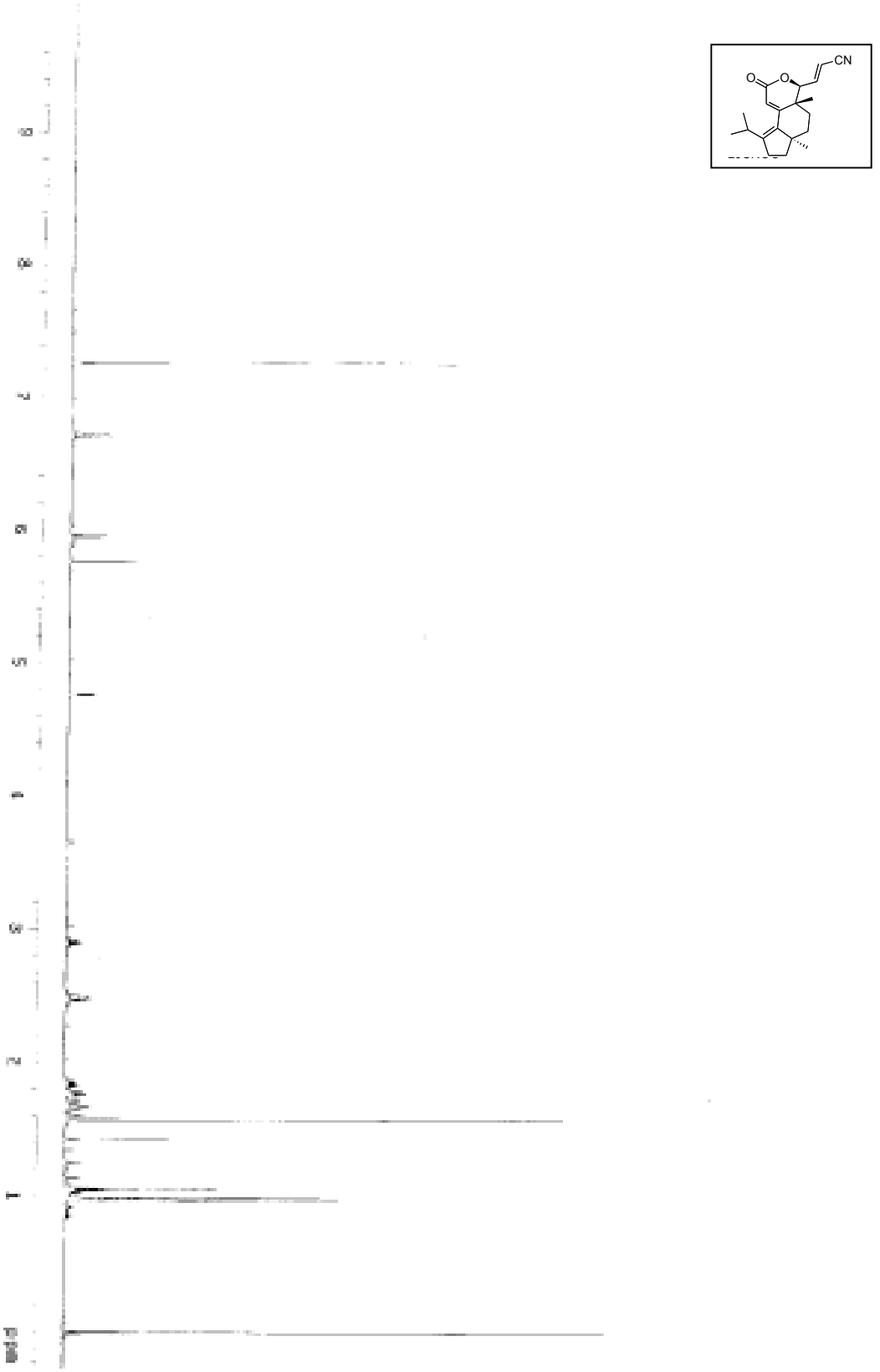
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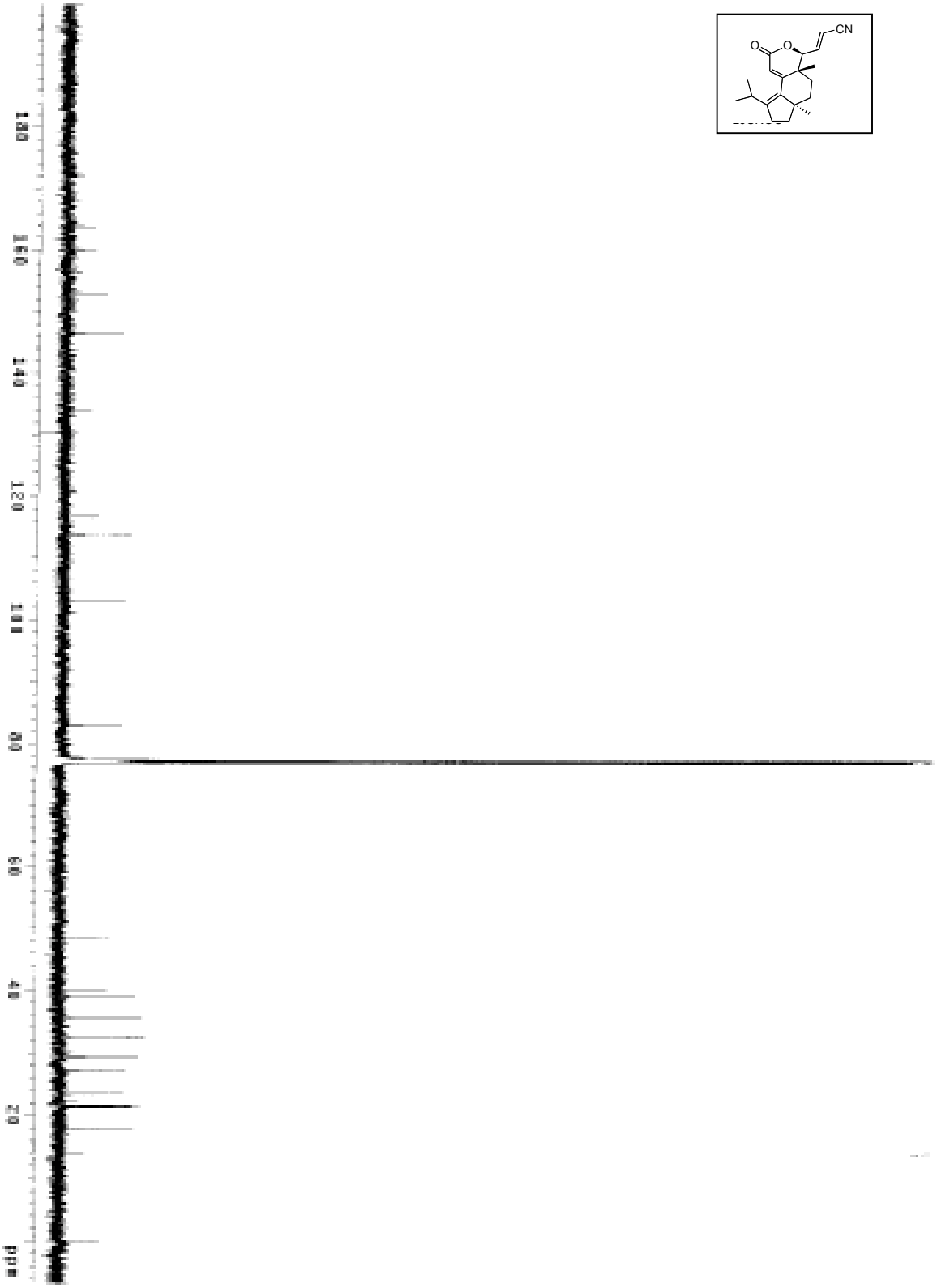
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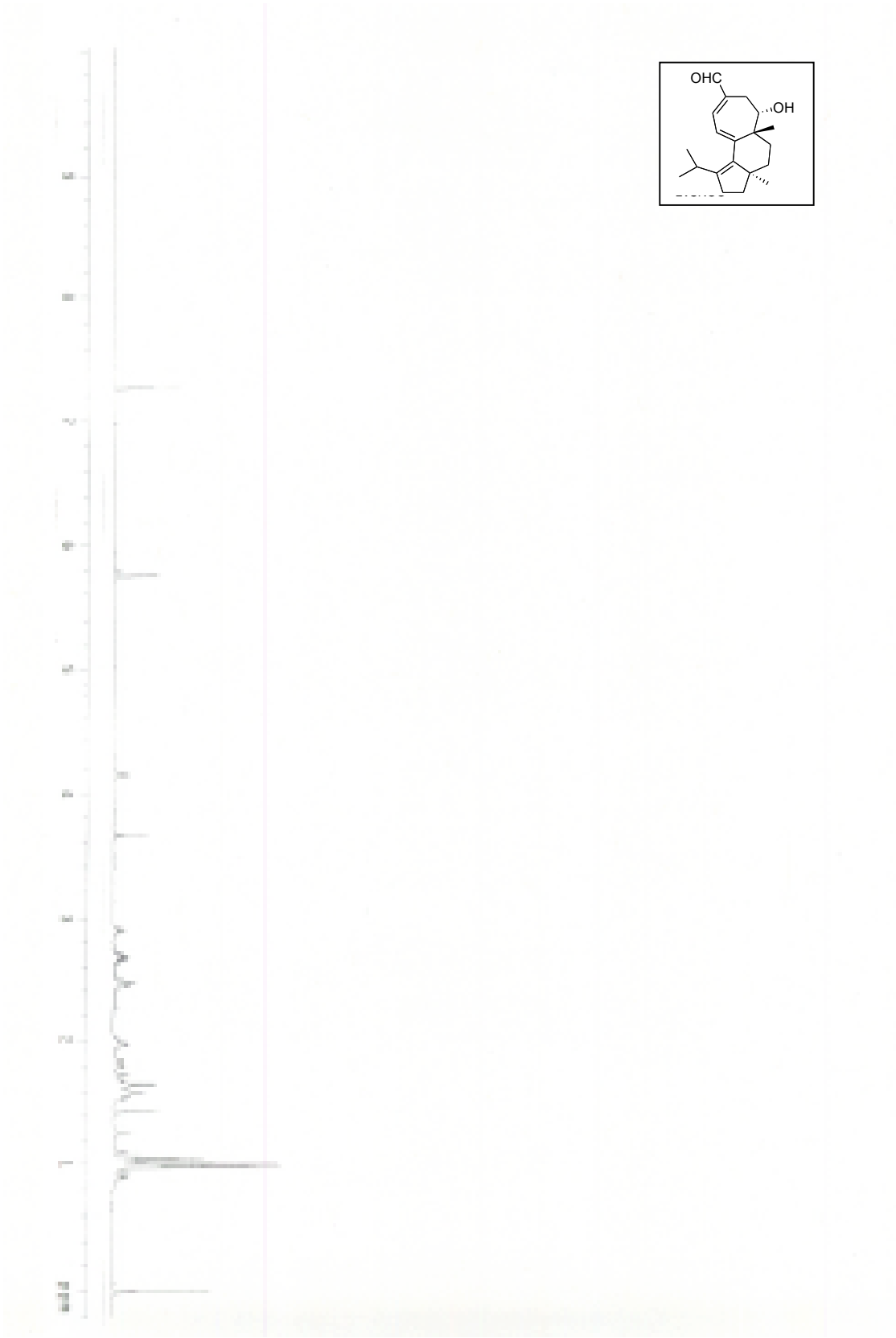
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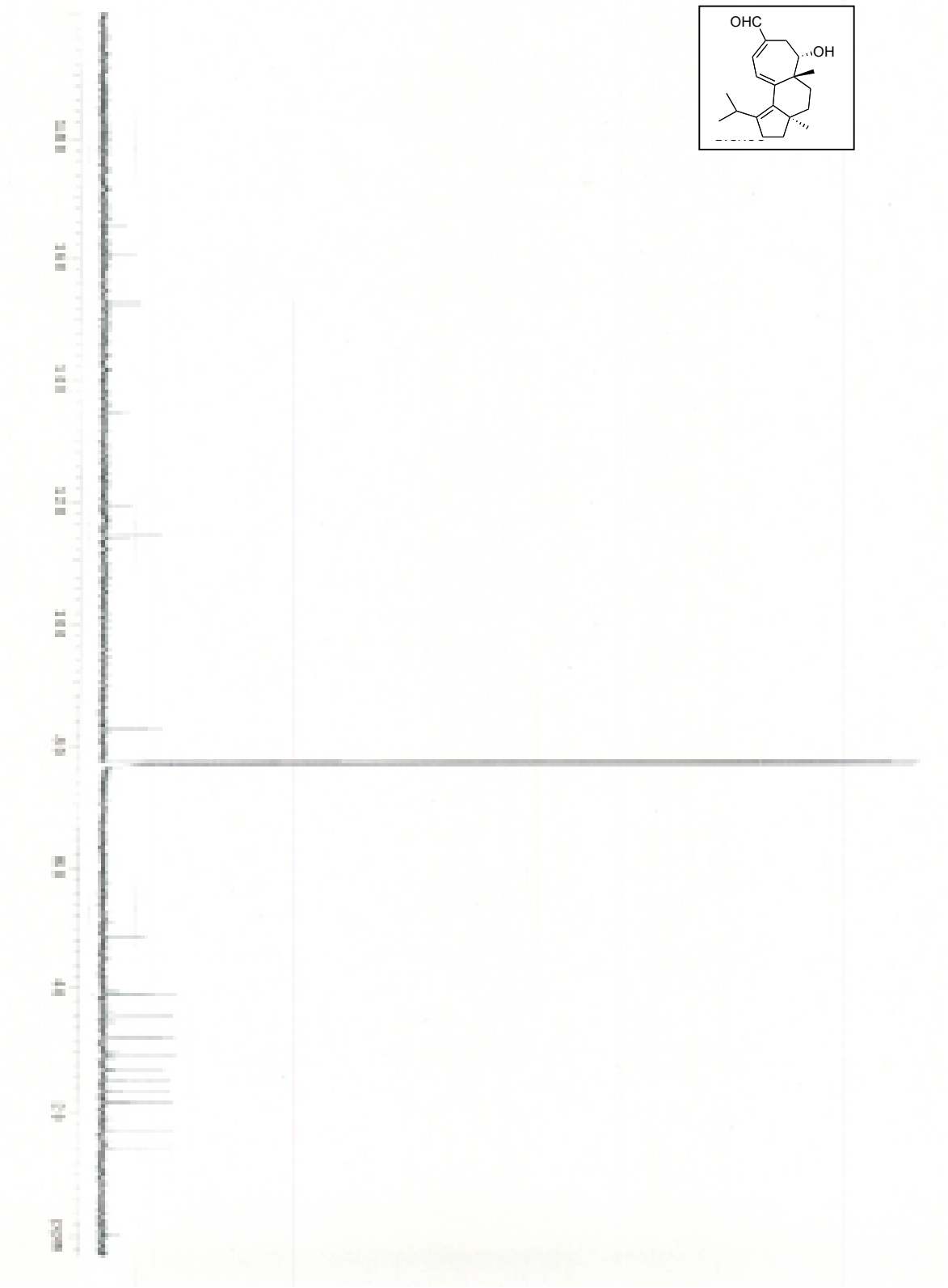
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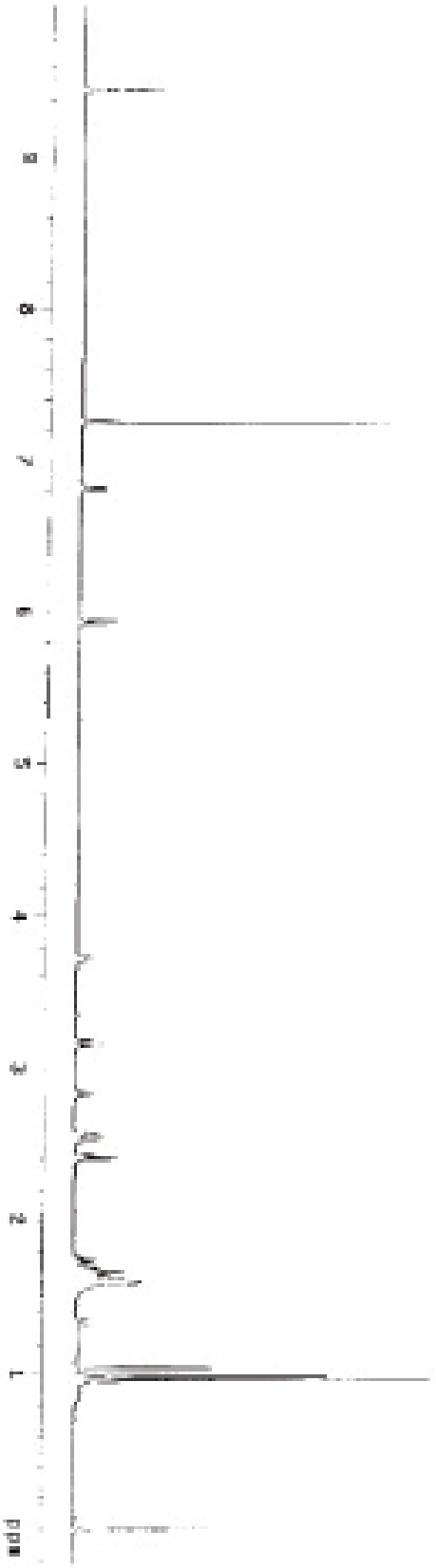

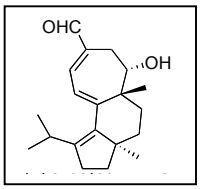
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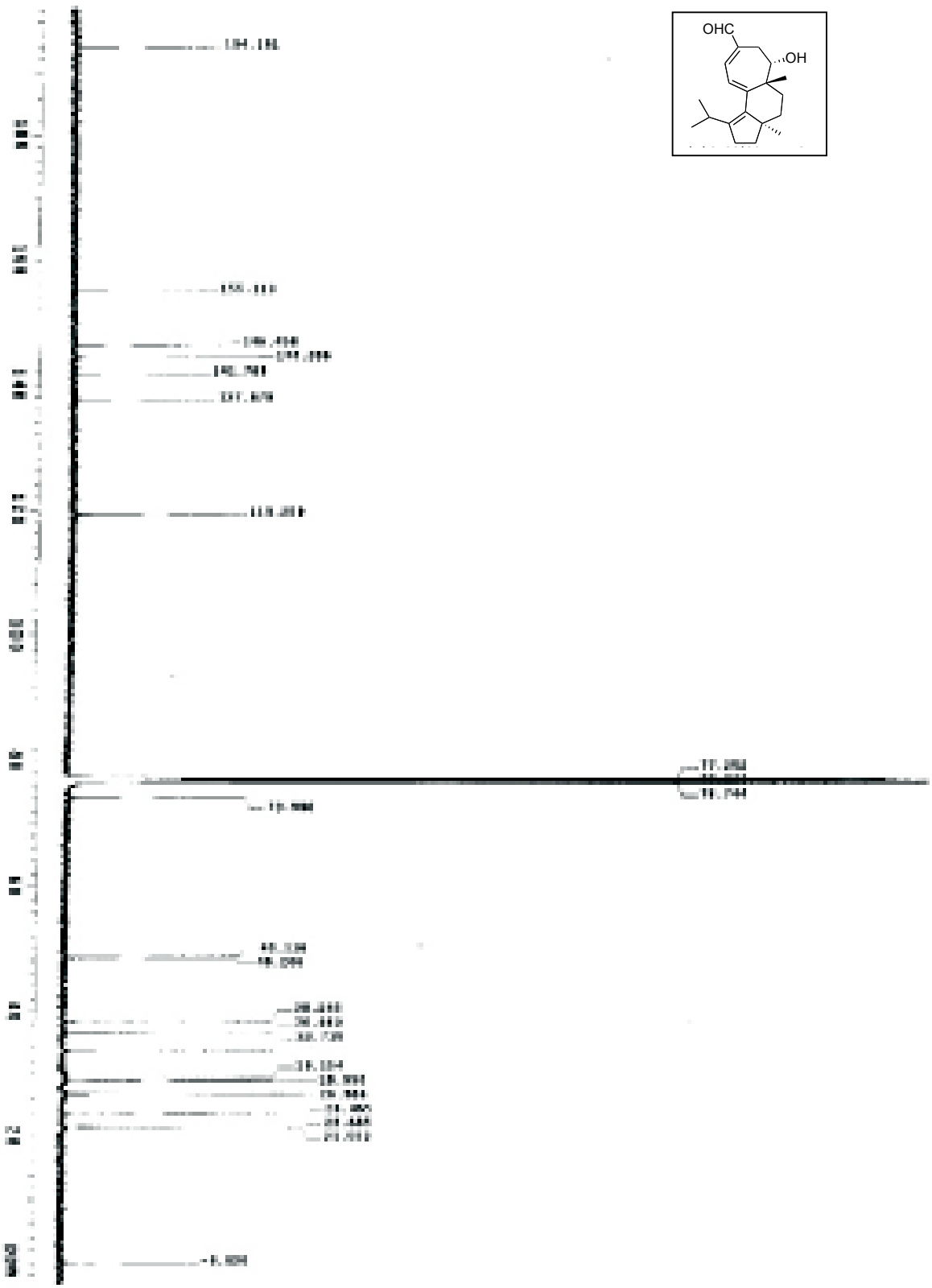
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