In situ Methylene Capping: A General Strategy for Efficient Stereo-Retentive Catalytic Olefin Metathesis. The Concept, Methodological Implications and Applications to Synthesis of Biologically Active Compounds

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SUPPORTING INFORMATION

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1. General

Unless otherwise noted, transformations were performed with distilled and degassed solvents under an atmosphere of dry N_2, in oven- (135 °C) or flame-dried glassware with standard dry box or vacuum line techniques. ^{1}H NMR spectra were recorded on a Varian Unity INOVA 400 (400 MHz), 500 (500 MHz) or a 600 (600 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance resulting from incomplete deuterium incorporation as the internal standard ($CDCl_3$: δ 7.26 ppm, DMSO-d_6: δ 2.50 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, br = broad, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on a Varian Unity INOVA 400 (100 MHz), 500 (125MHz), or 600 (151 MHz) spectrometers with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 77.16 ppm). High-resolution mass spectrometry was performed on a Micromass LCT ESI-MS and JEOL Accu TOF Dart (positive mode) at the Boston College Mass Spectrometry Facility. Melting points were determined using a Thomas Hoover Uni-melt capillary melting point apparatus. Infrared (IR) spectra were recorded on a Bruker FTIR Alpha (ATR Mode) spectrometer, ν_{max} in cm^{-1}. Bands are characterized as broad (br), strong (s), medium (m), or weak (w). Values for *E*:*Z* ratios of products were determined by analysis of ^{1}H NMR or quantitative ^{13}C NMR (13 second delay time) spectra. Specific rotations were measured using a Rudolph Research Analytical Autopol IV Polarimeter. In the olefin metathesis reaction, 100 torr vacuum is applied for 1-8 h, which often results in complete solvent evaporation.

Solvents

Tetrahydrofuran (THF) was distilled from Na/benzophenone. CH_2Cl_2 were purified under a positive pressure of dry argon gas by a modified Innovative Technologies purification system. $CDCl_3$ and DMSO-d_6 were purchased from Cambridge Isotope Laboratories and stored over activated 4Å molecular sieves prior to use. CH_3CN was used as received. Hexamethylphosphoramide (HMPA) was distilled from CaH_2 and stored over activated 4Å molecular sieves prior to use. Purification procedures of products were carried out with reagent grade solvents (Fisher) under bench-top conditions.

Reagents

(*Z*)-2-Butene (Aldrich) was dissolved in dried THF and stored in the freezer at –50 °C; Weight percent (wt %) was calculated based on the ^{1}H NMR analysis of the mixture. (*Z*)-3-hexene (Alfa Aesar), (*Z*)-5-decene (Alfa Aesar), hex-5-enoic acid (Aldrich), 3-buten-1-ol (Oakwood), 9-decen-1-ol (Aldrich), dec-9-enal (Aldrich), 2,6-dimethyloct-7-en-2-ol (dihydromyrcenol, Aldrich), 4-allylphenol (Aldrich), 1-decen-3-ol (TCI), (*Z*)-prop-1-en-1-ylbenzene (*cis*-β-methyl styrene, Aldrich), (*E*)-buta-1,3-dien-1-ylbenzene (Aldrich), dec-9-enoic acid (Aldrich), *N*-(3-dimethylaminopropyl)-*N*'-ethylcarbodiimide hydrochloride (EDC • HCl, Advanced ChemTech), 4-dimethylaminopyridine (DMAP, Advanced ChemTech), methyl 5-hexenoate (TCI), 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde (Combi-blocks), (*Z*)-1-bromoprop-1-ene (Aldrich), tetrakis(triphenylphosphine)palladium(0) ($Pd(PPh_4)_3$ (Strem)), *tetra*-*n*-butylammonium bromide (Aldrich), potassium hydroxide (Aldrich),

(*Z*)-4,4,5,5-tetramethyl-2-(prop-1-en-1-yl)-1,3,2-dioxaborolane (Aldrich), 1-bromopentane (Aldrich), Mg turnings (Aldrich), $BrCH_2CH_2Br$ (Aldrich), L-selectride (Aldrich), hydrogen fluoride pyridine (Aldrich) were used as received.

Benzyl pent-4-enoate (from 4-pentenoic acid (Aldrich)) and benzyl hex-5-enoate (from 5-hexenoic acid (Aldrich)) were prepared in analogy to reported procedures.[1]. 3-(But-3-en-1-yl)-1H-indole (from indole (Aldrich)),[2] (*E*)-1-(buta-1,3-dien-1-yl)-4-methoxybenzene (from *trans*-*p*-methoxycinnamaldehyde (Aldrich))[3], (*Z*)-1,2-dimethoxy-3-(prop-1-en-1-yl)benzene (from (*Z*)-1-bromoprop-1-ene (Aldrich))[4], *tert*-butyl (2-(but-3-en-1-ylamino)-2-oxoethyl)carbamate (from but-3-en-1-amine (Aldrich)), and (*S*)-*tert*-butyl (1-(but-3-en-1-ylamino)-3-methyl-1-oxobutan-2-yl)carbamate (from but-3-en-1-amine (Aldrich)) and (*S*)-*tert*-butyl (1-(but-3-en-1-ylamino)-4-(methylthio)-1-oxobutan-2-yl)carbamate (from but-3-en-1-amine (Aldrich))[5] were prepared according to a reported procedures. Undec-10-en-1-yl hex-5-enoate (from hex-5-enoic acid (Aldrich) and undec-10-en-1-ol (Aldrich)), hex-5-en-1-yl non-8-enoate (from non-8-enoic acid (Aldrich) and hex-5-en-1-ol (Aldrich)), non-8-en-1-yl hept-6-enoate (from hept-6-enoic acid (Aldrich) and non-8-en-1-ol (Aldrich)), dec-9-en-1-yl hept-6-enoate (from hept-6-enoic acid (Aldrich) and dec-9-en-1-ol (Aldrich)), undec-10-en-1-yl non-8-enoate (from non-8-enoic acid (Aldrich) and undec-10-en-1-ol (Aldrich)), undec-10-en-1-yl undec-10-enoate (from undec-10-enoic acid (Aldrich) and undec-10-en-1-ol (Aldrich), *N*-(undec-10-en-1-yl)hex-5-enamide, *N*-(undec-10-en-1-yl)undec-10-enamide,[6] nonadeca-1,18-dien-10-ol,[7] 2-(*N*-(undec-10-en-1-yl)undec-10-enamido)acetic acid,[8] 4-((*tert*-butyldimethylsilyl)oxy)cyclopent-2-en-1-one[9], (*S*,*E*)-*tert*-butyl((1-iodooct-1-en-3-yl)oxy)dimethylsilane,[10] and (6*S*,9*R*,15*S*,18*R*)-methyl 9,18-diallyl-15-benzyl-6-(4-hydroxybenzyl)-2,2-dimethyl-4,7,10,13,16-pentaoxo-3-oxa-5,8,11,14,17-pentaazanonadecan-19-oate[11] were prepared according to reported procedures.

Organometallic complexes

Complex **Ru-1a** (Aldrich) was used as received; **Ru-2a** was prepared according to a previously reported procedure.[12] **Ru-2b** was prepared according to previously reported procedure.[13]

2. Synthesis of compounds 1b-d by cross-metathesis

(*Z*)-Hept-5-enoic acid (1b). In a N_2-filled glovebox, an oven-dried vial equipped with a magnetic stir bar was charged with 5-hexenoic acid (**1a**, 14.5 mg, 0.127 mmol), *Z*-butene in THF (22 wt %, 647.0 mg, 2.54 mmol) and catechothiolate complex **Ru-2a** (1.0 mg, 0.00127 mmol, 100 μL THF). The mixture was allowed to stir for 1 h at 22 °C, after which the reaction was quenched by the addition of undistilled (wet) diethyl ether. The volatiles were then removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (10% ethyl acetate in hexanes) and filtered through a small plug of activated charcoal to afford **1b** (15.4 mg, 0.121 mmol, 95% yield) in >98:2 *Z:E* ratio as colorless oil. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 5.57–5.45 (m, 1H), 5.43–5.30 (m, 1H), 2.38 (t, *J* = 7.1 Hz, 2H), 2.11 (q, *J* = 7.3 Hz, 2H), 1.71 (p, *J* = 7.4 Hz, 2H), 1.60 (d, *J* = 6.8 Hz, 3H); **HRMS[M+H]$^+$** Calcd for $C_7H_{13}O_2$: 129.0916, found: 129.0913. The characterization data are consistent with these previously reported.[14]

(*Z*)-Oct-5-enoic acid (1c). In a N_2-filled glovebox, an oven-dried vial equipped with a magnetic stir bar was charged with 5-hexenoic acid (29.0 mg, 0.254 mmol), the *Z*-3-hexene (107.0 mg, 1.27 mmol) and **Ru-2a** (4.9 mg, 0.00635 mmol, 100 μL THF). The mixture was allowed to stir for 1 h at 22 °C, after which the reaction was quenched by wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (10% ethyl acetate in hexanes) and filtered through a small plug of activated charcoal to afford **1c** (29.8 mg, 0.211 mmol, 83% yield) in >98:2 *Z:E* ratio as colorless oil. **^{1}H NMR (600 MHz, $CDCl_3$):** δ 5.45–5.39 (m, 1H), 5.35–5.25 (m, 1H), 2.36 (t, *J*= 7.5 Hz, 2H), 2.10 (q, *J* = 7.4, 6.9 Hz, 2H), 2.03 (pd, *J* = 7.5, 1.5 Hz, 2H), 1.70 (p, *J* = 7.5 Hz, 2H), 0.95 (t, *J* = 7.5 Hz, 3H); **HRMS[M+H]$^+$** Calcd for $C_8H_{15}O_2$: 143.1072, found: 143.1068. The characterization data are consistent with these previously reported.[15]

(*Z*)-Dec-5-enoic acid (1d). In a N_2-filled glovebox, an oven-dried vial equipped with a magnetic stir bar was charged with 5-hexenoic acid (14.5 mg, 0.127 mmol), the (*Z*)-5-decene (90.0 mg, 1.27 mmol) and **Ru-2a** (2.4 mg, 0.00318 mmol, 100 μL THF). The mixture was allowed to stir for 1 h at 22 °C, after which the reaction was quenched by wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (10% ethyl acetate in hexanes) and filtered through a small plug of activated charcoal to afford **1d** (21.1 mg, 0.124 mmol, 98% yield) in >98:2 *Z:E* ratio as colorless oil. **^{1}H NMR (600 MHz, $CDCl_3$):** δ 5.46–5.38 (m, 1H), 5.36–5.29 (m, 1H), 2.36 (t, *J* = 7.5 Hz, 2H), 2.10 (q, *J* = 7.0 Hz, 2H), 2.02 (q, *J* = 6.8 Hz, 2H), 1.70 (p, *J* = 7.5 Hz, 2H), 1.35–1.28 (m, 4H), 0.92–0.87 (m, 3H); **HRMS[M+H]$^+$** Calcd for $C_{10}H_{19}O_2$: 171.1385, found: 171.1391. The characterization data are consistent with these previously reported.[16]

3. Procedure for synthesis of alkene 2 by homocoupling of alkenes 1a-d

(*Z*)-Dec-5-enedioic acid (2). In a N_2-filled glovebox, an oven-dried vial equipped with a magnetic stir bar was charged with **1b** (28.1 mg, 0.22 mmol) and a solution of **Ru-2a** (3.4 mg, 0.0044 mmol, 200 μL THF). The system was placed under 100 torr of vacuum and was allowed to stir for 8 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (10~20% ethyl acetate in hexanes) and filtered through a small plug of activated charcoal to afford **2** (16.3 mg, 0.16 mmol, 74% yield) in >98:2 *Z:E* as white solid. **M.p.**: 76−77 °C; **IR (neat):** 3021 (m), 2952 (m), 1703 (s), 1458 (m), 1410 (m), 1330 (m), 1244 (m), 1200 (m), 938 (m), 858 (m), 639 (s) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 11.19 (br, 2H), 5.42−5.36 (m, 2H), 2.36 (t, *J* = 7.3 Hz, 4H), 2.13−2.06 (m, 4H), 1.69 (p, *J* = 7.3 Hz, 4H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 180.3, 129.8, 33.5, 26.5, 24.6; **HRMS[M+H]$^+$** Calcd for $C_{10}H_{17}O_4$: 201.1127, Found: 201.1118.

4. Procedure for homocoupling with *Z*-butene as the methylene capping agent

In a N_2-filled glovebox, an oven-dried vial equipped with a magnetic stir bar was charged with the **1a** (14.5 mg, 0.127 mmol), unpurified *Z*-butene in THF (22 wt%, 650 mg, 1.27 mmol), and a solution of **Ru-2a** (1.0 mg, 0.00127 mmol, 200 μL THF), and then the vessel was sealed. The mixture was allowed to stir at 22 °C for 1 h, after which the volatiles were removed *in vacuo* (100 torr for 2 min). The flask containing the residue was charged with a solution of **Ru-2a** (2.0 mg, 0.00254 mmol in 200 μL THF) and the system was placed under 100 torr of vacuum

generated from a diaphragm pump. The resulting solution was allowed to stir for 8 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (10~20% ethyl acetate in hexanes) and filtered through a small plug of activated charcoal to afford **2** (17.8 mg, 0.089 mmol, 70% yield) in >98:2 *Z:E* as white solid.

5. Cross-metathesis with *Z*-butene as the methylene-capping agent

General procedure A: In a N_2-filled glove box, an oven-dried vial equipped with a magnetic stir bar was charged with the alkene substrates (1:3 ratio), unpurified *Z*-butene in THF and a solution of the appropriate amount of **Ru-2a** in THF. The vessel was then sealed. The mixture was allowed to stir at 22 °C for 1–16 h, after which the volatiles were removed *in vacuo* (100 torr, 2 min). The flask containing the residue was then charged with a solution of the appropriate amount of **Ru-2a** in THF and the system was placed under 100 torr of vacuum generated from a diaphragm pump. The resulting solution was allowed to stir for 1–8 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. Silica gel chromatography was used to obtain pure products.

General procedure B (for the reactions with α-branched terminal alkenes, *Z*-β-methyl styrenes and *Z*-1-propenylboronic acid ester): In a N_2-filled glove box, an oven-dried vial equipped with a magnetic stir bar was charged with the terminal alkene substrate, unpurified *Z*-2-butene (**3**) in THF and a solution of the appropriate amount of **-2** in THF. The vessel was then sealed. The mixture was allowed to stir at 22 °C for 1 h, after which the volatiles were removed *in vacuo* (100 torr, 2 min). The flask containing the residue was then charged with the other alkene (e.g. *cis*-β-methyl styrene) and a solution of the appropriate amount of **Ru-2a** in THF and the system was placed under 100 torr of vacuum generated from a diaphragm pump. The resulting solution was allowed to stir for 1–8 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. Purification was performed by silica gel chromatography.

(*Z*)-Benzyl-7-hydroxyhept-4-enoate (4). Following the general procedure A, in a N_2-filled glove box, an oven-dried vial equipped with a magnetic stir bar was charged with but-3-en-1-ol (7.2 mg, 0.10 mmol), benzyl pent-4-enoate (57.0 mg, 0.30 mmol) and *Z*-butene (**3**) in THF (36 wt %, 312.0 mg, 2.01 mmol) and a solution of **Ru-2a** (0.76 mg, 0.0010 mmol in 100 μL THF). The vessel was then sealed. The mixture was allowed to stir at 22 °C for 16 h, after which the volatiles were removed *in vacuo* (100 torr, 2 min). The flask containing the residue was then charged with a solution of **Ru-2a** (3.00 mg, 0.0040 mmol, 200 μL THF) and the system was placed under 100 torr of vacuum generated from a diaphragm pump. The resulting solution was allowed to stir for 8 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (15% ethyl acetate in hexanes) and filtered through a small plug of activated charcoal to afford olefin product **4** (13.2 mg, 0.056 mmol, 56% yield) in 95:5 *Z:E* ratio as colorless oil. **IR (neat):** 3386 (br), 3012 (m), 2946 (m), 1731 (s), 1498 (m), 1418 (m), 1258 (m), 1151 (s), 1047 (s), 735 (s), 696 (s), 503 (m)

cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.40–7.28 (m, 5H), 5.64–5.31 (m, 2H), 5.12 (s, 2H), 3.64 (t, *J* = 6.5 Hz, 2H), 2.47–2.40 (m, 4H), 2.34 (q, *J* = 6.3 Hz, 2H), 1.66 (br, 1H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 173.2, 136.1, 130.8, 128.7, 128.4, 128.4, 127.3, 66.4, 62.3, 34.2, 30.9, 22.9. **HRMS[M+H]$^+$** Calcd for $C_{14}H_{19}O_3$: 235.1334, Found: 235.1346.

(*Z*)-8-(Benzyloxy)-8-oxooct-4-enoic acid (5a). Following the general procedure A, in a N_2-filled glovebox, an oven-dried vial equipped with a magnetic stir bar was charged with benzyl pent-4-enoate (25.4 mg, 0.127 mmol) and hex-5-enoic acid (38.1 mg, 0.38 mmol), unpurified *Z*-2-butene in THF (22 wt %, 650 mg, 2.54 mmol) and a solution of **Ru-2a** (1.0 mg, 0.00127 mmol, 200 μL THF). The vessel was then sealed. The mixture was allowed to stir at 22 °C for 1 h, after which the volatiles were removed *in vacuo* (100 torr, 2 min). The flask containing the residue was then charged with a solution of **Ru-2a** (3.9 mg, 0.00508 mmol in 200 μL THF) and the system was placed under 100 torr of vacuum generated from a diaphragm pump. The resulting solution was allowed to stir for 8 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (10~20% ethyl acetate in hexanes) and filtered through a small plug of activated charcoal to afford **5a** (24.6 mg, 0.094 mmol, 74% yield) in >98:2 *Z*:*E* ratio as colorless oil. For the larger scale process, the above procedure was followed with benzyl pent-4-enoate (380.48 mg, 2.0 mmol) and hex-5-enoic acid (600.7 mg, 6.0 mmol), resulting in the formation of **5a** (293.8 mg, 1.117 mmol, 56% yield) in 98:2 *Z*:*E* ratio as colorless oil. **IR (neat):** 3011 (br), 2954 (w), 1734 (s), 1708 (s), 1454 (w), 1382 (w), 1258 (m), 1213 (m), 1152 (m), 738 (m), 689 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.38−7.30 (m, 5H), 5.41−5.39 (m, 2H), 5.12 (s, 2H), 2.43−2.37 (m, 8H); **^{13}C NMR (101 MHz, $CDCl_3$):** δ 178.3, 173.1, 136.1, 129.3, 128.9, 128.7, 128.4, 128.4, 66.4, 34.3, 33.9, 22.9, 22.6; **HRMS[M+H]$^+$** Calcd for $C_{15}H_{19}O_4$: 263.1283, found: 263.1292.

(*Z*)-8-(1H-Indol-3-yl)oct-5-enoic acid (5b). Following the general procedure A, in a N_2-filled glovebox, an oven-dried vial equipped with a magnetic stir bar was charged with the 3-(but-3-en-1-yl)-1*H*-indole (21.7 mg, 0.127 mmol) and hex-5-enoic acid (43.5 mg, 0.381 mmol), unpurified *Z*-2-butene in THF (36 wt %, 396 mg, 2.54 mmol) and a solution of **Ru-2a** (1.0 mg, 0.00127 mmol, 200 μL THF). The reaction vessel was then sealed. The mixture was allowed to stir at 22 °C for 1 h, after which the volatiles were removed *in vacuo* (100 torr, 2 min). The flask containing the residue was then charged with a solution of **Ru-2a** (3.9 mg, 0.00508 mmol, 200 μL THF) and the system was placed under 100 torr of vacuum generated from a diaphragm pump. The resulting solution was allowed to stir for 8 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (10~20% ethyl acetate in hexanes) and filtered through a small plug of activated charcoal to afford **5b** (19.0 mg, 0.074 mmol, 58% yield) in >98:2 *Z*:*E* ratio as colorless solid. **M.p.:** 65–67 °C; **IR (neat):** 3414 (m), 3055 (m), 3004 (m), 2927 (m), 2851 (m), 1701 (s), 1456 (m), 1419 (m), 1243 (m), 1090 (m), 1010 (m), 927 (w), 797 (m), 740 (s) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.90 (br, 1H), 7.63−7.59 (m, 1H), 7.34 (dt, *J* = 8.1, 0.9 Hz, 1H), 7.18 (ddd, *J* = 8.1, 7.0, 1.3 Hz, 1H), 7.11 (ddd, *J*= 8.1, 7.0, 1.1 Hz, 1H), 7.00 −6.97 (m, 1H), 5.60−5.48 (m, 1H), 5.42−5.31 (m, 1H), 2.82 (ddd, *J*= 7.6, 6.9, 0.9 Hz, 2H), 2.53−2.39 (m,

2H), 2.24 (t, *J* = 7.5 Hz, 2H), 2.12−1.98 (m, 2H), 1.68−1.55 (m, 2H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 179.9, 136.5, 130.9, 129.0, 127.7, 122.0, 121.4, 119.3, 119.0, 116.4, 111.2, 33.4, 28.0, 26.6, 25.4, 24.6; **HRMS[M+H]$^+$** Calcd for $C_{16}H_{20}O_2N$: 258.1494, found: 258.1502.

(*Z*)-14-Hydroxytetradec-5-enoic acid (5c). Following the general procedure A, in a N_2-filled glovebox, an oven-dried vial equipped with a magnetic stir bar was charged with the dec-9-en-1-ol (19.8 mg, 0.127 mmol) and hex-5-enoic acid (43.5 mg, 0.381 mmol), unpurified *Z*-butene in THF (22 wt %, 650 mg, 2.54 mmol) and a solution of **Ru-2a** (1.0 mg, 0.00127 mmol, 200 μL THF). The vessel was then sealed. The mixture was allowed to stir at 22 °C for 1 h, after which the volatiles were removed *in vacuo* (100 torr, 2 min). The flask containing the residue was then charged with a solution of **Ru-2a** (3.9 mg, 0.00508 mmol, 200 μL THF) and the system was placed under 100 torr of vacuum generated from a diaphragm pump. The resulting solution was allowed to stir for 8 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (10~20% ethyl acetate in hexanes) and filtered through a small plug of activated charcoal to afford **5c** (16.8 mg, 0.074 mmol, 58% yield) in >98:2 *Z*:*E* ratio ratio as colorless oil. **IR (neat):** 3336 (br), 3006 (m), 2925 (s), 2854 (m), 1707 (s), 1457 (m), 1409 (m), 1260 (m), 1023 (m), 862 (m), 801 (m), 722 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 6.08 (br, 1H), 5.45−5.37 (m, 1H), 5.35−5.29 (m, 1H), 3.65 (t, *J* = 6.6 Hz, 2H), 2.35 (t, *J* = 7.4 Hz, 2H), 2.10 (q, *J* = 7.4 Hz, 2H), 2.01 (q, *J* = 6.8 Hz, 2H), 1.69 (m, 2H), 1.62−1.48 (m, 2H), 1.41−1.22 (m, 10H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 178.4, 131.4, 128.5, 63.2, 33.4, 32.7, 29.6, 29.4, 29.3, 29.1, 27.3, 26.6, 25.7, 24.8; **HRMS[M+H]$^+$** Calcd for $C_{14}H_{27}O_3$: 243.1960, found: 243.1970.

(*Z*)-14-Oxotetradec-5-enoic acid (5d). Following the general procedure A, in a N_2-filled glovebox, an oven-dried vial equipped with a magnetic stir bar was charged with the undec-10-enal (19.6 mg, 0.127 mmol) and hex-5-enoic acid (43.5 mg, 0.381 mmol), unpurified *Z*-butene in THF (22 wt %, 650 mg, 2.54 mmol) and a solution (200 μL) of **Ru-2a** (1.0 mg, 0.00127 mmol, 200 μL THF). The vessel was sealed. The mixture was allowed to stir at 22 °C for 1 h, after which the volatiles were removed *in vacuo* (100 torr, 2 min). The flask containing the residue was then charged with a solution of **Ru-2a** (3.9 mg, 0.00508 mmol, 200 μL THF) and the system was placed under 100 torr of vacuum generated from a diaphragm pump. The resulting solution was allowed to stir for 8 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (10~20% ethyl acetate in hexanes) and filtered through a small plug of activated charcoal to afford **5d** (20.1 mg, 0.084 mmol, 66% yield) in >98:2 *Z*:*E* ratio as colorless oil. **IR (neat):** 3006 (m), 2925 (m), 2853 (m), 1705 (s), 1458 (m), 1411 (m), 1239 (m), 1161 (m), 938 (m), 724 (m) cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 9.76 (t, *J* = 1.9 Hz, 1H), 5.45−5.37 (m, 1H), 5.36−5.28 (m, 1H), 2.42 (td, *J* = 7.3, 1.9 Hz, 2H), 2.36 (t, *J* = 7.5 Hz, 3H), 2.09 (q, *J* = 7.1 Hz, 2H), 2.00 (q, *J* = 6.9 Hz, 2H), 1.73−1.67 (m, 2H), 1.65−1.60 (m, 2H), 1.33−1.28 (m, 10H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 203.2, 178.6, 131.4, 128.4, 44.1, 33.3, 29.8, 29.4, 29.4, 29.3, 29.3, 27.3, 26.6, 24.8, 22.2; **HRMS[M+H]$^+$** Calcd for $C_{15}H_{27}O_5$: 255.1960, found: 255.1967.

(*Z*)-8-((Benzyloxy)methoxy)-8-phenyloct-5-enoic acid (5e). Following the general procedure A, in a N_2-filled glovebox, an oven-dried vial equipped with a magnetic stir bar was charged

with the (1-((benzyloxy)methoxy)but-3-en-1-yl)benzene (34.0 mg, 0.127 mmol), hex-5-enoic acid (43.5 mg, 0.381 mmol), unpurified *Z*-2-butene in THF (22 wt %, 650 mg, 2.54 mmol) and a THF solution of **Ru-2a** (1.0 mg, 0.00127 mmol, 200 μL THF). The reaction vessel was then sealed. The mixture was allowed to stir at 22 °C for 1 h, after which the volatiles were removed *in vacuo* (100 torr, 2 min). The flask containing the residue was then charged with a solution of **Ru-2a** (3.9 mg, 0.00508 mmol, 200 μL THF) in and the system was placed under 100 torr of vacuum generated from a diaphragm pump. The resulting solution was allowed to stir for 8 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (10~20% ethyl acetate in hexanes) and filtered through a small plug of activated charcoal to afford **5e** (28.7 mg, 0.081 mmol, 64% yield) in >98:2 *Z*:*E* ratio as colorless oil. **IR (neat):** 3086 (m), 3062 (m), 3029 (m), 2932 (m), 1706 (s), 1454 (m), 1410 (m), 1239 (m), 1100 (m), 1036 (s), 1025 (s), 735 (m), 699 (s) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.38−7.26 (m, 10H), 5.51−5.39 (m, 2H), 4.73 (d, *J* = 7.0 Hz, 1H), 4.70 (d, *J* = 11.6 Hz, 1H), 4.68 (dd, *J* = 7.5, 6.1 Hz, 1H), 4.64 (d, *J* = 7.0 Hz, 1H), 4.50 (d, *J* = 11.7 Hz, 1H), 2.60 (dt, *J* = 14.7, 7.3 Hz, 1H), 2.45 (dt, *J* = 13.8, 6.4 Hz, 1H), 2.28 (t, *J* = 7.5 Hz, 2H), 2.06−1.99 (m, 2H), 1.64-1.58 (m, 2H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 179.6, 141.8, 138.0, 130.9, 128.5, 128.5, 128.1, 128.1, 127.8, 127.1, 126.6, 92.5, 78.3, 69.8, 35.9, 33.4, 26.7, 24.5; **HRMS[M+NH_4]$^+$** Calcd for $C_{22}H_{30}O_4N$: 372.2175, found: 372.2171.

(*Z*)-7-(3,4-Dimethoxyphenyl)hept-5-enoic acid (5f). Following the general procedure A, in a N_2-filled glovebox, an oven-dried vial equipped with a magnetic stir bar was charged with the 4-allyl-1,2-dimethoxybenzene (17.8 mg, 0.10 mmol), hex-5-enoic acid (34.2 mg, 0.30 mmol), unpurified *Z*-butene in THF (17 wt %, 660 mg, 2.00 mmol) and a solution of **Ru-2a** (0.76 mg, 0.0010 mmol in 200 μL THF). The vessel was sealed. The mixture was allowed to stir at 22 °C for 1 h, after which the volatiles were removed *in vacuo* (100 torr, 2 min). The flask containing the residue was then charged with a solution of **Ru-2a** (3.0 mg, 0.0040 mmol, 200 μL THF) and the system was placed under 100 torr of vacuum generated from a diaphragm pump. The resulting solution was allowed to stir for 8 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (10~20% ethyl acetate in hexanes) and filtered through a small plug of activated charcoal to afford **5f** (17.1 mg, 0.064 mmol, 64% yield) in 98:2 *Z*:*E* ratio as colorless oil. **IR (neat):** 3008 (m), 2937 (s), 2837 (m), 1737 (m), 1706 (s), 1513 (s), 1464 (m), 1260 (s), 1234 (s), 1139 (s), 1029 (s), 756 (m) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 6.80 (d, *J* = 7.9 Hz, 1H), 6.71 (d, *J* = 7.9 Hz, 1H), 6,70 (s, 1H), 5.65–5.56 (m, 1H), 5.53–5.42 (m, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.34 (d, *J* = 7.3 Hz, 2H), 2.40 (t, *J* = 7.5 Hz, 2H), 2.22 (q, *J* = 7.1 Hz, 2H), 1.76 (p, *J* = 7.5 Hz, 2H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 179.3, 149.1, 147.4, 133.6, 129.8, 129.30, 120.2, 111.8, 111.5, 56.1, 56.0, 33.5, 33.2, 26.6, 24.7; **HRMS[M+H]$^+$** Calcd for $C_{15}H_{21}O_4$: 265.1434, Found: 265.1450.

(*Z*)-Benzyl-7-(5-acetyl-2-hydroxyphenyl)hept-5-enoate (6a). Following the general procedure A, in a N_2-filled glovebox, an oven-dried vial equipped with a magnetic stir bar was charged with the 1-(3-allyl-4-hydroxyphenyl)ethanone (16.4 mg, 0.10 mmol) and benzyl hex-5-enoate (61.2 mg, 0.30 mmol), unpurified *Z*-butene in THF (24 wt %, 466 mg, 2.00 mmol)

and a solution of **Ru-2a** (0.76 mg, 0.0010 mmol, 200 μL THF). The vessel was sealed. The mixture was allowed to stir at 22 °C for 1 h, after which the volatiles were removed *in vacuo* (100 torr, 2 min). The flask containing the residue was then charged with a solution of **Ru-2a** (3.0 mg, 0.0040 mmol in 200 μL THF, 4.0 mol %) in and the system was placed under 100 torr of vacuum generated from a diaphragm pump. The resulting solution was allowed to stir for 8 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (10% ethyl acetate in hexanes) and filtered through a small plug of activated charcoal to afford **6a** (22.2 mg, 0.063 mmol, 63% yield) in 97:3 *Z*:*E* ratio as yellow oil. **IR (neat):** 3275 (br), 3011 (m), 2951 (m), 1733 (s), 1652 (m), 1588 (s), 1421 (m), 1357 (m), 1276 (s), 1150 (m), 966 (m), 824 (m), 699 (m) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.77–7.73 (m, 2H), 7.39–7.29 (m, 5H), 6.82 (d, *J* = 8.1 Hz, 1H), 5.90 (br, 1H), 5.67–5.48 (m, 2H), 5.13 (s, 2H), 3.39 (d, *J* = 4.9 Hz, 2H), 2.54 (s, 3H), 2.41 (t, *J* = 7.3 Hz, 2H), 2.26–2.20 (m, 2H), 1.79 (p, *J* = 7.3 Hz, 2H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 197.9, 174.0, 159.2, 136.0, 131.0, 130.9, 130.2, 129.0, 128.7, 128.4, 128.3, 127.9, 127.2, 115.5, 66.5, 33.8, 28.2, 26.7, 26.4, 24.8; **HRMS[M+H]$^+$** Calcd for $C_{22}H_{25}O_4$: 353.1747, Found: 353.1770.

Benzyl (*Z*)-11-hydroxy-7,11-dimethyldodec-5-enoate (6b). Following the general procedure B, in a N_2-filled glovebox, an oven-dried vial equipped with a magnetic stir bar was charged with the benzyl hex-5-enoate (77.7 mg, 0.381 mmol), unpurified *Z*-butene in THF (22 wt %, 650.0 mg, 2.54 mmol) and a solution of **Ru-2a** (1.0 mg, 0.00127 mmol, 200 μL THF). The vessel was sealed. The mixture was allowed to stir at 22 °C for 1 h, after which the volatiles were removed *in vacuo* (100 torr, 2 min). The flask containing the residue was then charged with dihydromyrcenol (19.8 mg, 0.13 mmol) and a solution of **Ru-2a** (4.0 mg, 0.0052 mmol, 200 μL THF) and the system was placed under 100 torr of vacuum generated from a diaphragm pump. The resulting solution was allowed to stir for 8 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (1~5% diethyl ether in hexanes) and filtered through a small plug of activated charcoal to afford **6b** (23.8 mg, 0.075 mmol, 58% yield) in >98:2*Z*:*E* ratio as colorless oil. **IR (neat):** 3527 (br), 3034 (m), 2933 (m), 2867 (w), 1735 (s), 1455 (m), 1376 (m), 1309 (w), 1159 (s), 976 (w), 747 (m), 697 (m) cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.38−7.31(m, 5H), 5.29−5.24 (m, 1H), 5.17−5.11 (m, 3H), 2.39−2.36 (m, 3H), 2.09−2.05 (m, 2H), 1.82−1.65 (m, 2H), 1.43−1.33 (m, 2H), 1.33−1.18 (m, 10H), 0.91 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR (126 MHz, $CDCl_3$):** δ 173.6, 137.5, 136.2, 128.7, 128.4, 128.3, 127.2, 71.1, 66.3, 44.2, 38.1, 33.9, 31.8, 29.4, 29.3, 27.0, 25.2, 22.4, 21.5; **HRMS[M+H-H_2O]$^+$** Calcd for $C_{21}H_{31}O_3$: 315.2324, found: 315.2309.

Benzyl (*Z*)-7-hydroxytetradec-5-enoate (6c). In a N_2-filled glovebox, an oven-dried vial equipped with a magnetic stir bar was charged with the benzyl pent-4-enoate (77.7 mg, 0.381 mmol) unpurified *Z*-butene in THF solution (2.54 mmol) and a THF solution (200 μL) of **Ru-2a** (1.0 mg, 0.00127 mmol). The vessel was sealed and the mixture was allowed to stir at 22 °C for 1 h. A separate oven-dried vial equipped with a magnetic stir bar was charged with dec-1-en-3-ol (19.8 mg, 0.127mmol) and unpurified *Z*-butene in THF (1.27 mmol) and a solution of **Ru-2a** (1.5 mg, 0.00191 mmol, 200 μL THF). The vessel was sealed and the solution was allowed to stir at 22 °C for 1 h. The mixtures were then combined and the

volatiles were removed *in vacuo* (100 torr for 2 mins). The flask containing the residue was charged with a solution of **Ru-2a** (4.9 mg, 0.00635 mmol in 200 μL THF) and the system was placed under 100 torr of vacuum generated from a diaphragm pump. The resulting solution was allowed to stir for 8 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (10% diethyl ether in hexanes) and filtered through a small plug of activated charcoal to afford **6c** (19.7 mg, 0.060 mmol, 47% yield) in 90:10 *Z*:*E* ratio as colorless oil. **IR (neat):** 3430 (br), 3034 (w), 3006 (m), 2926 (s), 2854 (m), 1737 (s), 1456 (m), 1380 (m), 1311 (m), 1234 (m), 1214 (m), 1153 (m), 1045 (m), 1003 (m), 750 (m), 697 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.38−7.31 (m, 5H), 5.43−5.38 (m, 2H), 5.12 (s, 2H), 4.34 (q, *J* = 6.7 Hz, 1H), 2.38 (t, *J* = 7.3 Hz, 2H), 2.23−2.04 (m, 2H), 1.82−1.67 (m, 2H), 1.60−1.53 (m, 2H), 1.45−1.23 (m, 10H), 0.88 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 173.6, 136.1, 134.1, 130.7, 128.7, 128.4, 128.4, 67.6, 66.4, 37.6, 33.7, 32.0, 29.7, 29.4, 27.0, 25.5, 24.9, 22.8, 14.3; **HRMS[M+H-H_2O]$^+$** Calcd for $C_{21}H_{31}O_2$: 315.2324, found: 315.2338.

(*Z*)-Benzyl 5-phenylpent-4-enoate (7a). Following the general procedure B, in a N_2-filled glovebox, an oven-dried vial equipped with a magnetic stir bar was charged with the benzyl pent-4-enoate (72.4 mg, 0.381 mmol), unpurified *Z*-2-butene in THF (22 wt %, 650 mg, 2.54 mmol) and a solution of **Ru-2a** (1.0 mg, 0.00127 mmol, 200 μL THF). The vessel was then sealed. The mixture was allowed to stir at 22 ^oC for 1 h, after which the volatiles were removed *in vacuo* (100 torr, 2 min). The flask containing the residue was then charged with (*Z*)-prop-1-en-1-ylbenzene (15.0 mg, 0.127 mmol, 200 μL THF) and a solution of **Ru-2a** (3.9 mg, 0.00508 mmol) and the system was placed under 100 torr of vacuum generated from a diaphragm pump. The resulting solution was allowed to stir for 8 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (1% ethyl acetate in hexanes) and filtered through a small plug of activated charcoal to afford **7a** (16.4 mg, 0.061 mmol, 48% yield) in 96:4 *Z*:*E* ratio as colorless oil. **IR (neat):** 3063 (w), 3012 (w), 2954 (w), 2922 (w), 1734 (s), 1494 (m), 1447 (m), 1381 (m), 1352 (m), 1512 (s), 751 (m), 697 (s) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.41−7.20 (m, 10H), 6.48 (d, *J* = 11.6 Hz, 1H), 5.65 (dt, *J*= 11.6 Hz, 7.2 Hz, 1H), 5.12 (s, 2H), 2.83−2.63 (m, 2H), 2.51 (t, *J* = 7.5 Hz, 2H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 172.9, 137.3, 136.1, 130.4, 130.4, 128.9, 128.7, 128.4, 128.3, 128.3, 126.9, 66.4, 34.6, 24.2; **HRMS[M+H]$^+$** Calcd For $C_{18}H_{19}O_2$: 267.1385, found: 267.1380.

(*Z*)-Benzyl 5-(3,4-dimethoxyphenyl)pent-4-enoate (7b). Following the general procedure B, in a N_2-filled glove box, an oven-dried vial equipped with a magnetic stir bar was charged with benzyl pent-4-enoate (28.5 mg, 0.050 mmol), *Z*-butene (**3**) in THF (24 wt %, 236 mg, 1.01 mmol) and a solution of catechothiolate complex **Ru-2a** (0.38 mg, 0.0005 mmol, 100 μL THF). The reaction vessel was then sealed. The mixture was allowed to stir at 22 °C for 1 h, after which the volatiles were removed *in vacuo* (100 torr, 2 min). The flask containing the residue was charged with (*Z*)-1,2-dimethoxy-4-(prop-1-en-1-yl)benzene (8.9 mg, 0.05 mmol), followed by a solution of **Ru-2a** (1.50 mg, 0.002 mmol, 200 μL THF) and the system was placed under 100 torr of vacuum generated from a diaphragm pump. The resulting solution was allowed to

stir for 4 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (5% ethyl acetate in hexanes) and filtered through a small plug of activated charcoal to afford **7b** (8.2 mg, 0.025 mmol, 50% yield) in 92:8 *Z:E* ratio as colorless oil. **IR (neat):** 3007 (m), 2934 (m), 2836 (m), 1733 (s), 1602 (m), 1514 (s), 1456 (m), 1257 (s), 1238 (s), 1141 (s), 1027 (s), 750 (m), 656 (m) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.37–7.28 (m, 5H), 6.87–6.79 (m, 3H), 6.40 (d, *J* = 11.6 Hz, 1H), 5.55 (dt, *J* = 11.6, 7.2 Hz, 1H), 5.12 (s, 2H), 3.88 (s, 3H), 3.85 (s, 3H), 2.70 (q, *J* = 7.5 Hz, 2H), 2.51 (t, *J* = 7.5 Hz, 2H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 172.9, 148.7, 148.1, 136.1, 130.3, 130.1, 129.1, 128.7, 128.4, 128.3, 121.4, 112.1, 111.1, 66.4, 56.1, 56.0, 34.6, 24.3; **HRMS[M+H]$^+$** Calcd for $C_{20}H_{23}O_4$: 327.1596, found: 327.1608.

(*Z*)-Methyl 6-(3-formylphenyl)hex-5-enoate (7c). Following the general procedure B, in a N_2-filled glove box, an oven-dried vial equipped with a magnetic stir bar was charged with methyl hex-5-enoate (19.2 mg, 0.15 mmol) and *Z*-butene (**3**) in THF (17 wt %, 334 mg, 1.01 mmol) and a solution of **Ru-2a** (0.38 mg, 0.00050 mmol, 100 μL THF). The vessel was sealed. The mixture was allowed to stir at 22 °C for 1 h, after which the volatiles were removed *in vacuo* (100 torr, 2 min). The flask containing the residue was then charged with (*Z*)-3-(prop-1-en-1-yl)-benzaldehyde (7.3 mg, 0.050 mmol), followed by a solution of **Ru-2a** (1.50 mg, 0.0020 mmol, 200 μL THF) and the system was placed under 100 torr of vacuum generated from a diaphragm pump. The resulting solution was allowed to stir for 4 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (1% diethyl ether in hexanes) and filtered through a small plug of activated charcoal to afford **7c** (7.4 mg, 0.032 mmol, 64% yield) in 96:4 *Z:E* ratio as colorless oil. **IR (neat):** 3013 (m), 2950 (m), 2927 (m), 2852 (m), 2728 (m), 1734 (s), 1700 (s), 1598 (m), 1436 (m), 1376 (m), 1222 (m), 1155 (m), (m), 808 (m), 685 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 10.03 (s, 1H), 7.77–7.73 (m, 2H), 7.56–7.48 (m, 2H), 6.50 (d, *J* = 11.6 Hz, 1H), 5.74 (dt, *J* = 11.6, 7.4 Hz, 1H), 3.63 (s, 3H), 2.42–2.30 (m, 4H), 1.85–1.75 (m, 2H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 192.5, 173.9, 138.5, 136.6, 134.8, 133.4, 130.0, 129.0, 128.6, 128.0, 51.7, 33.6, 28.0, 25.1. **HRMS[M+H]$^+$** Calcd for $C_{14}H_{17}O_3$: 233.1178, found: 233.1189.

(*Z*)-11-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)undec-10-enal (8). Following the general procedure B, in a N_2-filled glove box, an oven-dried vial equipped with a magnetic stir bar was charged with undec-10-enal (8.4 mg, 0.050 mmol), *Z*-butene (**3**) in THF (36 wt %, 78.0 mg, 0.50 mmol) and a solution of **Ru-2a** (0.38 mg, 0.00050 mmol, 100 μL THF). The vessel was then sealed, and the mixture was allowed to stir at 22 °C for 1 h, after which the volatiles were removed *in vacuo*. The flask containing the residue was then charged with (*Z*)-4,4,5,5-tetramethyl-2-(prop-1-en-1-yl)-1,3,2-dioxaborolane (25.2 mg, 0.15 mmol), followed by a solution of **Ru-2a** (1.50 mg, 0.0020 mmol, 200 μL THF) and the system was placed under 100 torr of vacuum generated from a diaphragm pump. The resulting solution was allowed to stir for 1 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (2% ethyl acetate in hexanes) and filtered through a small plug of activated charcoal to afford **8** (7.9 mg, 0.027

mmol, 54% yield) in 95:5 *Z:E* ratio as colorless oil. **IR (neat):** 2979 (m), 2926 (s), 2855 (m), 1727 (s), 1628 (s), 1436 (m), 1320 (m), 1259 (s), 1145 (s), 968 (m), 760 (m) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.76 (t, *J* = 1.9 Hz, 1H), 6.48–6.37 (m, 1H), 5.32 (d, *J* = 13.5 Hz, 1H), 2.48–2.34 (m, 4H), 1.66–1.58 (m, 2H), 1.44–1.20 (m, 22H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 203.1, 155.3, 82.9, 44.1, 32.3, 29.6, 29.5, 29.4, 29.3, 29.1, 25.0, 22.3; **HRMS[M+H]$^+$** Calcd for $C_{17}H_{32}BO_3$: 295.2445, found: 295.2446.

(5*Z*,7*E*)-12-Hydroxydodeca-5,7-dienoic acid (9a). Following the general procedure A, in a N_2-filled glovebox, an oven-dried vial equipped with a magnetic stir bar was charged with the (*E*)-octa-5,7-dien-1-ol (16.0 mg, 0.127 mmol) and 5-hexenoic acid (43.5 mg, 0.381 mmol), unpurified *Z*-butene in THF (24 wt %, 593 mg, 2.54 mmol) and a solution of **Ru-2a** (1.0 mg, 0.00127 mmol, 200 μL THF). The vessel was sealed, and the mixture was allowed to stir at 22 °C for 1 h, after which the volatiles were removed *in vacuo* (100 torr, 2 min). The flask containing the residue was then charged with a solution of **Ru-2a** (3.9 mg, 0.00508 mmol, 200 μL THF) and the system was placed under 100 torr of vacuum generated from a diaphragm pump. The resulting solution was allowed to stir for 8 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (10~50% ethyl acetate in hexanes) and filtered through a small plug of activated charcoal to afford **9a** (16.1mg, 0.076 mmol, 59% yield) in 95:5 *Z*:*E* ratio as colorless oil. **IR (neat):** 3017 (m), 2926 (m), 2856 (m), 1707 (s), 1456 (m), 1437 (m), 1409 (m), 1246 (m), 1056 (m), 986 (m), 949 (m), 740 (w) cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$)**: δ 6.30 (dd, *J* = 15.1, 11.0 Hz, 1H), 6.01 (t, *J* = 10.9 Hz, 1H), 5.67 (dt, *J* = 14.7, 6.9 Hz, 1H), 5.35–5.23 (m, 1H), 3.67 (t, *J* = 6.7 Hz, 2H), 2.37 (t, *J* = 7.2 Hz, 2H), 2.25 (q, *J* = 7.4 Hz, 2H), 2.14 (q, *J* = 7.2 Hz, 2H), 1.73 (p, *J* = 7.2 Hz, 2H), 1.60 (dt, *J* = 14.8, 6.7 Hz, 2H), 1.49 (p, *J* = 7.1 Hz, 2H); **^{13}C NMR (126 MHz, $CDCl_3$)**: δ 180.0, 134.6, 130.1, 128.5, 126.0, 63.0, 32.8, 32.3, 31.9, 26.8, 25.2, 24.5; **HRMS[M+H]$^+$** Calcd For $C_{12}H_{21}O_3$: 213.1491, found: 213.1495.

Benzyl (5*Z*,7*E*)-8-phenylocta-5,7-dienoate (9b). Following the general procedure A, in a N_2-filled glovebox, an oven-dried vial equipped with a magnetic stir bar was charged with the (*E*)-buta-1,3-dien-1-ylbenzene (16.5 mg, 0.127 mmol) and benzyl hex-5-enoate (77.7 mg, 0.381 mmol), unpurified *Z*-butene in THF (24 wt %, 593 mg, 2.54 mmol) and a solution of **Ru-2a** (1.0 mg, 0.00127 mmol, 200 μL THF). The vessel was then sealed, and the mixture was allowed to stir at 22 °C for 1 h, after which the volatiles were removed *in vacuo* (100 torr, 2 min). The flask containing the residue was then charged with a solution of **Ru-2a** (3.9 mg, 0.00508 mmol, 200 μL THF) and the system was placed under 100 torr of vacuum generated from a diaphragm pump. The resulting solution was allowed to stir for 8 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (1~2% diethyl ether in hexanes) and filtered through a small plug of activated charcoal to afford **9b** (31.0 mg, 0.10 mmol, 80% yield) in 97:3 *Z*:*E* ratio as colorless oil. **IR (neat):** 3061 (m), 3027 (w), 2937 (m), 1731 (s), 1493 (m), 1453 (m), 1413 (m), 1382 (m), 1310 (m), 1213 (s), 1912 (m), 1152 (m), 1073 (m), 985 (m), 946 (m), 732 (s), 694 (s) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.44–7.17 (m, 10H), 7.00 (ddd, *J* = 15.5, 11.1, 1.2 Hz, 1H), 6.52 (d, *J* = 15.5 Hz, 1H), 6.18 (t, *J* = 10.9 Hz, 1H), 5.46 (dt, *J* = 10.8, 7.7 Hz, 1H), 5.10 (s, 2H),

2.40 (t, *J* = 7.5 Hz, 2H), 2.33 (qd, *J* = 7.5, 1.4 Hz, 2H), 1.83–1.75 (m, 2H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 173.5, 137.6, 136.2, 134.2, 132.8, 131.6, 130.0, 128.7, 128.7, 128.3, 127.6, 126.5, 124.2, 66.3, 33.7, 27.4, 24.9; **HRMS[M+H]$^+$** Calcd for $C_{21}H_{23}O_2$: 307.1698, found: 307.1704.

Benzyl (5*Z*,7*E*)-8-(4-methoxyphenyl)octa-5,7-dienoate (9c). Following the general procedure A, in a N_2-filled glovebox, an oven-dried vial equipped with a magnetic stir bar was charged with the (*E*)-1-(buta-1,3-dien-1-yl)-4-methoxybenzene (20.3 mg, 0.127 mmol) and benzyl hex-5-enoate (77.7 mg, 0.381 mmol), unpurified *Z*-butene in THF (24 wt %, 593 mg, 2.54 mmol) and a solution of **Ru-2a** (1.0 mg, 0.00127 mmol, 200 μL THF). The vessel was then sealed, and the mixture was allowed to stir at 22 °C for 1 h, after which the volatiles were removed *in vacuo* (100 torr, 2 min). The flask containing the residue was then charged with a solution of **Ru-2a** (3.9 mg, 0.0051 mmol, 200 μL THF) and the system was placed under 100 torr of vacuum. The resulting solution was allowed to stir for 8 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (1~2% diethyl ether in hexanes) and filtered through a small plug of activated charcoal to afford **9c** (23.9 mg, 0.071 mmol, 56% yield) in 97:3 *Z*:*E* ratio as colorless oil. **IR (neat):** 3029 (w), 3004 (w), 2934 (w), 2836 (w), 1731 (s), 1602 (m), 1509 (s), 1455 (m), 1303 (m), 1245 (s), 1173 (s), 1153 (s), 1115 (w), 1030 (m), 982 (m), 947 (m), 862 (m), 745 (m), 697 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.37–7.30 (m, 7H), 6.91–6.85 (m, 3H), 6.49 (d, *J* = 15.5 Hz, 1H), 6.18 (t, *J* = 10.9 Hz, 1H), 5.45–5.41 (m, 1H), 5.12 (s, 2H), 3.82 (s, 3H), 2.42 (t, *J* = 7.5 Hz, 2H), 2.34 (q, *J* = 7.5 Hz, 2H), 1.81 (m, 2H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 173.5, 159.3, 136.2, 132.3, 130.5, 130.4, 130.1, 128.7, 128.3, 127.7, 122.3, 114.2, 66.3, 55.4, 33.7, 27.3, 25.0; **HRMS[M+H]$^+$** Calcd for $C_{22}H_{25}O_3$: 337.1804, found: 337.1816.

(*Z*)-Di-*tert*-butyl ((hex-3-ene-1,6-diylbis(azanediyl))bis(2-oxoethane-2,1-diyl))dicarbamate (10a). Following the general procedure A, in a N_2-filled glove box, an oven-dried vial equipped with a magnetic stir bar was charged with *tert*-butyl (2-(but-3-en-1-ylamino)-2-oxoethyl)carbamate (11.4 mg, 0.0050 mmol) and *Z*-butene (**3**) in THF (22 wt %, 256 mg, 1.00 mmol) and a solution of catechothiolate complex **Ru-2a** (0.38 mg, 0.00050 mmol in 100 μL THF). The vessel was then sealed. The mixture was allowed to stir at 22 °C for 4 h, after which the volatiles were removed *in vacuo*. The flask containing the residue was then charged with a solution of **Ru-2a** (1.50 mg, 0.0020 mmol in 200 μL THF) and the system was placed under 100 torr of vacuum generated from a diaphragm pump. The resulting solution was allowed to stir for 1 h at 22 °C under vacuum, and then for another 3 h without vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (2% CH_2Cl_2 in MeOH) and filtered through a small plug of activated charcoal to afford **10a** (9.4 mg, 0.022 mmol, 88% yield) in >98:2 *Z*:*E* ratio as white solid. **M.p.:** 52–53 °C; **IR (neat):** 3306 (s), 2976 (m), 2932 (s), 1698 (s), 1656 (s), 1524 (s), 1454 (m), 1365 (m), 1166 (s), 1050 (m), 864 (m), 731 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 6.62 (br, 2H), 5.45–5.40 (m, 4H), 3.77 (d, *J* = 5.5 Hz, 4H), 3.32 (q, *J* = 6.3 Hz, 4H), 2.25 (q, *J* = 6.2 Hz, 4H), 1.56–1.29 (m, 18H); **^{13}C NMR (101 MHz, $CDCl_3$):** δ 170.0, 156.4, 129.0, 80.3, 44.5, 39.0, 28.5, 27.7; **HRMS[M+H]$^+$** Calcd for $C_{20}H_{37}O_6N_4$: 429.2713, found: 429.2727.

(*S*,*Z*)-Benzyl 8-(2-((*tert*-butoxycarbonyl)amino)-3-methylbutanamido)oct-5-enoate (10b). Following the general procedure A, in a N_2-filled glove box, an oven-dried vial equipped with a magnetic stir bar was charged with (*S*)-*tert*-butyl (1-(but-3-en-1-ylamino)-3-methyl-1-oxobutan-2-yl)carbamate (27.0 mg, 0.10 mmol), benzyl hex-5-enoate (61.2 mg, 0.30 mmol, 3.00 equiv.), *Z*-2-butene (**3**) in THF (24 wt %, 468 mg, 2.00 mmol) and a solution of **Ru-2a** (0.76 mg, 0.001 mmol, 100 μL THF). The vessel was sealed, and the mixture was allowed to stir at 22 °C 16 h, after which the volatiles were removed *in vacuo* (100 torr, 2 min). The flask containing the residue was then charged with a solution of **Ru-2a** (3.00 mg, 0.004 mmol in 200 μL THF) and the system was placed under 100 torr of vacuum generated from a diaphragm pump. The resulting solution was allowed to stir for 8 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (20% ethyl acetate in hexanes) and filtered through a small plug of activated charcoal to afford **10b** (20.8 mg, 0.047 mmol, 47% yield) in 91:9 *Z:E* ratio (determined by quantitative ^{13}C NMR, relaxation time = 13 s) ratio as colorless oil. **$[\alpha]_D^{20}$** −15.4 (*c* 0.7, MeOH); **IR (neat):** 3312 (br), 3012 (w), 2963 (m), 2934 (s), 2873 (m), 1736 (s), 1652 (s), 1525 (m), 1455 (m), 1366 (m), 1245 (m), 1163 (m), 1016 (m), 873 (m), 806 (m), 698 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.42–7.28 (m, 5H), 6.06 (s, 1H), 5.43 (dt, *J* = 10.5, 7.6 Hz, 1H), 5.34 (dt, *J* = 10.5, 7.4 Hz, 1H), 5.11 (s, 2H), 5.08 (s, 1H), 3.86 (dd, *J* = 8.6, 6.4 Hz, 1H), 3.30–3.20 (m, 2H), 2.35 (t, *J* = 7.3 Hz, 2H), 2.18 (q, *J* = 6.9 Hz, 2H), 2.15–2.01 (m, 3H), 1.69 (p, *J* = 7.3 Hz, 2H), 1.43 (s, 9H), 0.93 (d, *J* = 6.7 Hz, 3H), 0.89 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 173.6, 171.7, 156.0, 136.1, 131.5, 128.7, 128.4, 128.4, 127.2, 79.9, 66.4, 60.2, 39.2, 33.7, 31.0, 28.5, 27.4, 26.7, 24.9, 19.5, 17.9; **HRMS[M+H]$^+$** Calcd for $C_{25}H_{39}O_5N_2$: 447.2859, found: 447.2878.

(*S*,*Z*)-Benzyl 8-(2-((*tert*-butoxycarbonyl)amino)-4-(methylthio)butanamido)oct-5-enoate (10c). Following the general procedure A, in a N_2-filled glove box, an oven-dried vial equipped with a magnetic stir bar was charged with (*S*)-*tert*-butyl (1-(but-3-en-1-ylamino)-4-(methylthio)-1-oxobutan-2-yl)carbamate (33.9 mg, 0.10 mmol), benzyl hex-5-enoate (61.2 mg, 0.30 mmol), *Z*-butene (**3**) in THF (24 wt %, 472 mg, 2.02 mmol) and a solution of **Ru-2a** (0.76 mg, 0.0010 mmol in 100 μL THF). The vessel was sealed, and the mixture was allowed to stir at 22 °C for 16 h, after which the volatiles were removed *in vacuo* (100 torr, 2 min). The flask containing the green oil residue was then charged with a solution of **Ru-2a** (3.00 mg, 0.0040 mmol, 200 μL THF) and the system was placed under 100 torr of vacuum generated from a diaphragm pump. The resulting solution was allowed to stir for 8 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (40% ethyl acetate in hexanes) and filtered through a small plug of activated charcoal to afford **10c** (24.4 mg, 0.051 mmol, 51% yield) in >98:2 *Z:E* ratio as colorless oil. **$[\alpha]_D^{20}$** −17.5 (*c* 0.8, MeOH); **IR (neat):** 3306 (br), 3013 (w), 2972 (m), 2929 (m), 1734 (m), 1656 (s), 1524 (s), 1455 (m), 1366 (m), 1246 (s), 1164 (s), 1025 (s), 752 (m), 698 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.41–7.28 (m, 5H), 6.30 (br, 1H), 5.44 (dt, *J* = 10.6, 7.4 Hz, 1H), 5.34 (dt, *J* = 10.6, 7.4 Hz, 1H), 5.28 (br, 1H), 5.11 (s, 2H), 4.22 (br, 1H), 3.32–3.18 (m, 2H), 2.58–2.46 (m, 2H), 2.36 (t, *J* = 7.3 Hz, 2H), 2.24–2.15 (m, 2H),

2.11–2.03 (m, 6H), 1.92–1.85 (m 1H), 1.74–1.66 (m, 2H), 1.43 (s, 9H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 173.6, 171.5, 155.7, 136.1, 131.6, 128.7, 128.4, 128.4, 127.0, 80.1, 66.4, 53.6, 39.2, 33.7, 32.0, 30.4, 28.5, 27.3, 26.7, 24.8, 15.4; **HRMS[M+H]$^+$** Calcd for $C_{25}H_{39}O_5N_2S$: 479.2580, found: 479.2566.

6. Preparation of compound 11b

(*Z*)-(*Z*)-Dodec-10-en-1-yl hept-5-enoate (11b). In a N_2-filled glove box, a solution of unpurified *Z*-2-butene (**3**) in THF (27 wt %, 416 mg, 2.00 mmol) was added to an oven-dried vial containing undec-10-en-1-yl hex-5-enoate (**11a**; 26.6 mg, 0.10 mmol), followed by a THF solution of **Ru-2a** (0.76 mg, 0.001 mmol, 250 μL THF). The vessel was sealed and the mixture was allowed to stir for 1 h at 22 °C. The reaction was then quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (1% diethyl ether in hexanes) and filtered through a small plug of activated charcoal to afford **11b** (26.2 mg, 0.089 mmol, 89% yield) in >98:2 *Z,Z:Z,E* ratio as colorless oil. **IR (neat):** 3014 (m), 2926 (s), 2855 (m), 1737 (s), 1454 (m), 1311 (m), 1238 (m), 1160 (s), 1035 (m), 699 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 5.54–5.26 (m, 4H), 4.06 (t, *J* = 6.7 Hz, 2H), 2.30 (t, *J* = 7.5 Hz, 2H), 2.08 (q, *J* = 7.3 Hz, 2H), 2.02 (q, *J* = 7.2 Hz, 2H), 1.74–1.66 (m, 2H), 1.64–1.58 (m, 6H), 1.55 (d, *J* = 5.2 Hz, 2H), 1.38–1.26 (m, 12H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 174.0, 131.0, 129.6, 125.0, 123.8, 64.6, 33.9, 29.7, 29.6, 29.60, 29.4, 28.8, 27.0, 26.3, 26.1, 24.9, 12.9; **HRMS[M+H]$^+$** Calcd for $C_{19}H_{35}O_2$: 295.2637, found: 295.2650.

7. Preparation of compounds 11c **and** 11d

(*Z*)-Dodec-10-en-1-yl hex-5-enoate (11c). In a N_2-filled glove box, a solution of unpurified *Z*-2-butene (**3**) in THF (27 wt %, 10.40 g, 50.10 mmol) was added to an oven-dried vial containing undec-10-en-1-ol (852 mg, 5.00 mmol), followed by a THF solution of **Ru-2a** (38.0 mg, 0.050 mmol in 250 μL THF, 1 mol %). The vessel was sealed and the mixture was allowed to stir for 3 h at 22 °C. The reaction was then quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (1% diethyl ether in hexanes) to afford (*Z*)-dodec-10-en-1-ol (857.0 mg, 4.65 mmol, 93% yield) in 96:4 *Z*:*E* ratio as colorless oil, which was directly used in the next step. *N*-(3-Dimethylaminopropyl)-*N*'-ethylcarbodiimide hydrochloride (307.0 mg, 1.60 mmol) was added to an oven-dried vial containing (*Z*)-dodec-10-en-1-ol (184.0 mg, 1.00 mmol), hex-5-enoic acid (171.0 mg, 1.50 mmol) and DMAP (22.4 mg, 0.20 mmol) in dried CH_2Cl_2 (5 mL) at 0 °C. The vessel was sealed and the mixture was allowed to stir for 3 h at 22 °C. The reaction was then quenched by the addition of water (10 mL) and washed with Et_2O (20 mL×3). The organic layers were combined and washed with aqueous solution of 1N HCl (10 mL), water (10 mL) and brine (10 mL). The organic layers dried over anhydrous $MgSO_4$ and then filtered. The filtrate was concentrated and purified by silica gel chromatography (1% diethyl ether in hexanes) to afford **11c** (267.0 mg, 0.095 mmol, 95% yield) as colorless oil. **IR (neat):** 3013 (m), 2925 (s), 2855 (m), 1736 (s), 1456 (m), 1311 (m), 1239 (m), 1160 (s), 1035 (m), 909 (m), 699 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 5.78 (ddt, *J* = 17.0, 10.3, 6.7 Hz, 1H), 5.50–5.32 (m, 2H), 5.03 (d, *J* = 17.1 Hz, 1H), 4.99 (d, *J* = 10.2 Hz, 1H), 4.06 (t, *J* = 6.7 Hz, 2H), 2.31 (t, *J* = 7.5 Hz, 2H), 2.09 (q, *J*

= 7.2 Hz, 2H), 2.02 (q, *J* = 7.1 Hz, 2H), 1.73 (p, *J* = 7.5 Hz, 2H), 1.65–1.58 (m, 5H), 1.38–1.24 (m, 12H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 173.9, 137.9, 131.0, 123.8, 115.5, 64.6, 33.8, 33.2, 29.7, 29.6, 29.6, 29.4, 29.4, 28.8, 27.0, 26.1, 24.3, 12.9. **HRMS[M+H]$^+$** Calcd for $C_{18}H_{33}O_2$: 281.2481, found: 281.2489.

(*Z*)-Undec-10-en-1-yl hept-5-enoate (11d). *N*-(3-Dimethylaminopropyl)-*N*'-ethylcarbodiimide hydrochloride (307.0 mg, 1.60 mmol) was added to an oven-dried vial containing undec-10-en-1-ol (255.0 mg, 1.50 mmol), *Z*-hept-5-enoic acid (**1b**, prepared through the procedure described above, 128.0 mg, 1.00 mmol) and DMAP (22.4 mg, 0.20 mmol) in dried DCM (5 mL) at 0 °C. The vessel was sealed and the mixture was allowed to stir for 3 h at 22 °C. The reaction was quenched by the addition of water (10 mL) and washed with Et_2O (20 mL × 3). The organic layers were combined and washed with an aqueous solution of 1N HCl (10 mL), water (10 mL) and brine (10 mL). The organic layers dried over anhydrous $MgSO_4$ and then filtered. The filtrate was concentrated *in vacuo* and purified by silica gel chromatography (1% diethyl ether in hexanes) to afford **11d** (237 mg, 0.085 mmol, 85% yield) in 98:2 *Z:E* ratio as colorless oil. **IR (neat):** 3012 (m), 2926 (s), 2855 (m), 1736 (s), 1457 (m), 1310 (m), 1253 (m), 1169 (s), 1024 (m), 912 (m), 702 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 5.81 (ddt, *J* = 17.0, 10.1, 6.6 Hz, 1H), 5.48 (dt, *J* = 13.5, 6.8 Hz, 1H), 5.39–5.32 (m, 1H), 4.99 (d, *J* = 17.1 Hz, 1H), 4.93 (d, *J* = 10.2 Hz, 1H), 4.06 (t, *J* = 6.8 Hz, 2H), 2.30 (t, *J* = 7.5 Hz, 2H), 2.08 (q, *J* = 7.3 Hz, 2H), 2.04 (q, *J* = 7.2 Hz, 2H), 1.69 (p, *J* = 7.4 Hz, 2H), 1.65–1.57 (m, 5H), 1.42–1.24 (m, 12H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 174.0, 139.3, 129.6, 125.0, 114.3, 64.6, 34.0, 33.9, 29.6, 29.5, 29.4, 29.2, 29.1, 28.8, 26.3, 26.1, 24.9, 12.9. **HRMS[M+H]$^+$** Calcd for $C_{18}H_{33}O_2$: 281.2481, found: 281.2476.

8. Macrocyclic ring-closing metathesis with *Z*-butene as the methylene capping agent

General procedure: In a N_2-filled glove box, a solution of unpurified *Z*-butene (**3**) in THF was added to an oven-dried vial containing a bis(α)-olefin substrate (1.0 equiv.), followed by a solution of the appropriate amount of catechothiolate complex **Ru-2a** dissolved in THF. The vessel was sealed and the mixture was allowed to stir for 1–12 h at 22 °C. The reaction was monitored by ^{1}H NMR spectroscopy. After >95% conversion (disappearance of bis(α)-olefin), the volatiles were removed *in vacuo* and the resulting black residue was dissolved in THF and a solution of the appropriate amount of **Ru-2a** in THF was added. The system was placed under 400 torr of vacuum generated from a diaphragm pump. The resulting solution was allowed to stir for 12–48 h at 35 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. Purification was performed by silica gel chromatography.

(*Z*)-Oxacyclohexadec-6-en-2-one (12a). Following the general procedure, in a N_2-filled glove box, a solution of unpurified *Z*-butene (**3**) in THF (27 wt %, 416 mg, 2.01 mmol) was added to an oven-dried vial containing undec-10-en-1-yl hex-5-enoate (**11a**, 26.6 mg, 0.10 mmol), followed by a THF solution of **Ru-2a** (0.76 mg, 0.0010 mmol, 100 μL THF). The vessel was sealed and the mixture was allowed to stir for 1 h at 22 °C. The volatiles were removed *in vacuo* and the resulting green residue was dissolved in THF (19.5 mL) and a solution of **Ru-2a** (3.00 mg, 0.004 mmol, 500 μL THF) was added. The vessel was then connected to a 400 torr vacuum generated from a diaphragm pump. The solution was allowed to stir for 12 h at 35 °C

under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (1% diethyl ether in hexanes) and filtered through a small plug of activated charcoal to afford **12a** (13.4 mg, 0.056 mmol, 56% yield) in 96:4 *Z*:*E* ratio as colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 5.51–5.25 (m, 2H), 4.15 (t, *J* = 5.5 Hz, 2H), 2.38–2.32 (m, 2H), 2.13-2.01 (4H, m), 1.78–1.51 (m, 4H), 1.49–1.24 (m, 12H). **HRMS[M+H]$^+$** Calcd for $C_{15}H_{27}O_2$: 239.2006, found: 239.2011. The characterization data are consistent with those previously reported.[17]

(*Z*)-Oxacyclotetradec-9-en-2-one (12b). Following the general procedure, in a N_2-filled glove box, a solution of unpurified *Z*-butene (**3**) in THF (33 wt %, 342 mg, 2.02 mmol) was added to an oven-dried vial containing hex-5-en-1-yl non-8-enoate (23.8 mg, 0.10 mmol), followed by a THF solution of **Ru-2a** (0.76 mg, 0.0010 mmol, 100 μL THF). The vessel was sealed and the mixture was allowed to stir for 1 h at 22 °C. The volatiles were removed *in vacuo* and the resulting green residue was dissolved in THF (19.5 mL) and a solution of **Ru-2a** (3.00 mg, 0.0040 mmol, 500 μL THF) was added. The vessel was then connected to a 400 torr vacuum generated from a diaphragm pump. The solution was allowed to stir for 12 h at 35 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (1% diethyl ether in hexanes) and filtered through a small plug of activated charcoal to afford **12b** (14.2 mg, 0.067 mmol, 67% yield) in 98:2 *Z*:*E* ratio as colorless oil. **IR (neat):** 3001 (m), 2925 (m), 2858 (m), 1733 (s), 1456 (m), 1249 (s), 1085 (m), 990 (m), 896 (m), 713 (m) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 5.48 (*J* = 10.8, 7.8 Hz, 1H), 5.27 (dt, *J* = 10.8, 7.9 Hz, 1H), 4.14 (t, *J* = 5.8 Hz, 2H), 2.42–2.32 (m, 2H), 2.10–1.93 (m, 4H), 1.81–1.70 (m, 2H), 1.69–1.58 (m, 2H), 1.51–1.36 (m, 4H), 1.33–1.22 (m, 4H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 174.0, 129.9, 129.9, 62.7, 35.5, 27.7, 27.6, 27.2, 26.8, 26.0, 25.7, 25.5, 24.8. **HRMS[M+H]$^+$** Calcd for $C_{13}H_{23}O_2$: 211.1698, found: 211.1699.

(*Z*)-Oxacyclopentadec-7-en-2-one (12c). Following the general procedure, in a N_2-filled glove box, a solution of unpurified *Z*-butene (**3**) in THF (33 wt %, 342 mg, 2.02 mmol) was added to an oven-dried vial containing non-8-en-1-yl hept-6-enoate (25.2 mg, 0.10 mmol), followed by a THF solution of **Ru-2a** (0.76 mg, 0.0010 mmol, 100 μL THF). The vessel was sealed and the mixture was allowed to stir for 1 h at 22 °C. The volatiles were removed *in vacuo* and the resulting green residue was dissolved in THF (19.5 mL) and a solution of **Ru-2a** (3.00 mg, 0.0040 mmol, 500 μL THF) was added. The vessel was then connected to a 400 torr vacuum generated from a diaphragm pump. The solution was allowed to stir for 12 h at 35 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (1% diethyl ether in hexanes) and filtered through a small plug of activated charcoal to afford **12c** (15.1 mg, 0.067 mmol, 67% yield) in 98:2 *Z*:*E* ratio as colorless oil. **IR (neat):** 3005 (m), 2927 (m), 2857 (m), 1732 (s), 1459 (m), 1232 (m), 1144 (m), 1061 (m), 969 (w), 719 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 5.41 (dt, *J* = 10.8, 7.5 Hz, 1H), 5.35 (dt, *J* = 10.8, 7.4 Hz, 1H), 4.14 (t, *J* = 5.3 Hz, 2H), 2.34 (t, *J* = 6.7 Hz, 2H), 2.01 (q, *J* = 7.6 Hz, 4H), 1.75–1.61 (m, 4H), 1.45–1.30 (m, 10H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 174.1,

130.8, 129.2, 64.3, 34.5, 29.4, 28.2, 28.0, 27.2, 27.2, 27.0, 25.6, 25.5, 25.3. **HRMS[M+H]$^+$** Calcd for $C_{14}H_{25}O_2$: 225.1855, found: 225.1866.

(*Z*)-Oxacyclohexadec-11-en-2-one (12d). Following the general procedure, in a N_2-filled glove box, a solution of unpurified *Z*-butene (**3**) in THF (33 wt %, 342 mg, 2.02 mmol) was added to an oven-dried vial containing hex-5-en-1-yl undec-10-enoate (26.6 mg, 0.10 mmol), followed by a THF solution of **Ru-2a** (0.76 mg, 0.0010 mmol, 100 μL THF). The vessel was sealed and the mixture was allowed to stir for 1 h at 22 °C. The volatiles were removed *in vacuo* and the resulting green residue was dissolved in THF (19.5 mL) and a solution of **Ru-2a** (3.00 mg, 0.0040 mmol, 500 μL THF) was added. The vessel was then connected to a 400 torr vacuum generated from a diaphragm pump. The solution was allowed to stir for 12 h at 35 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (1% diethyl ether in hexanes) and filtered through a plug of activated charcoal to afford **12d** (16.6 mg, 0.070 mmol, 70% yield) in 98:2 *Z:E* ratio as colorless oil. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 5.45–5.30 (m, 2H), 4.14 (t, *J* = 6.3 Hz, 2H), 2.41–2.27 (m, 2H), 2.10–2.01 (m, 4H), 1.68–1.63 (m, 4H), 1.46–1.37 (m, 2H), 1.37–1.19 (m, 10H); **HRMS[M+H]$^+$** Calcd for $C_{15}H_{27}O_2$: 239.2011, found: 239.2000. The characterization data are consistent with those reported previously.[18]

(*Z*)-Azacyclohexadec-6-en-2-one (12e). Following the general procedure, in a N_2-filled glove box, a solution of unpurified *Z*-butene (**3**) in THF (33 wt %, 342 mg, 2.02 mmol) was added to an oven-dried vial containing *N*-(undec-10-en-1-yl)hex-5-enamide (25.1 mg, 0.10 mmol), followed by a THF solution of **Ru-2a** (0.76 mg, 0.0010 mmol, 100 μL THF). The vessel was sealed and the mixture was allowed to stir for 1 h at 22 °C. The volatiles were removed *in vacuo* and the resulting green residue was dissolved in THF (19.5 mL) and a solution of **Ru-2a** (3.00 mg, 0.0040 mmol, 500 μL THF) was added. The vessel was then connected to a 400 torr vacuum generated from a diaphragm pump. The solution was allowed to stir for 12 h at 35 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (25% ethyl acetate in hexanes) and filtered through a small plug of activated charcoal to afford **12e** (12.3 mg, 0.055 mmol, 55% yield) in 98:2 *Z:E* selectivity as white solid. **^{1}H NMR (600 MHz, $CDCl_3$):** δ 5.53 (br, 1H), 5.42–5.28 (m, 2H), 3.34 (dt, *J* = 6.0, 5.6 Hz, 2H), 2.22–2.18 (m, 2H), 2.12–2.06 (m, 2H), 2.05–1.98 (m, 2H), 1.77–1.65 (m, 2H), 1.56–1.43 (m, 2H), 1.43–1.25 (m, 12H); **^{13}C NMR (101 MHz, $CDCl_3$):** δ 172.9, 130.9, 129.1, 39.1, 36.5, 29.1, 27.8, 27.5, 27.4, 26.7, 26.6, 26.3, 26.0, 25.9, 25.7; **HRMS[M+H]$^+$** Calcd for $C_{15}H_{28}ON$: 238.2171, found: 238.2174. The characterization data are consistent with those previously reported.[19]

(*Z*)-Cycloheptadec-9-enol (12f). Following the general procedure, in a N_2-filled glove box, a solution of unpurified *Z*-2-butene (**3**) in THF (33 wt %, 342 mg, 2.02 mmol) was added to an oven-dried vial containing nonadeca-1,18-dien-10-ol (29.4 mg, 0.10 mmol), followed by a THF solution of **Ru-2a** (0.76 mg, 0.0010 mmol, 100 μL THF). The vessel was sealed and the mixture was allowed to stir for 1 h at 22 °C. The volatiles were removed *in vacuo* and the resulting green residue was dissolved in THF (19.5 mL) and a solution of **Ru-2a** (4.9 mg, 0.0065 mmol in 500 μL THF) was added. The vessel was then connected to a 400 torr vacuum

generated from a diaphragm pump. The solution was allowed to stir for 12 h at 35 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (20% ethyl acetate in hexanes) and filtered through a small plug of activated charcoal to afford **12f** (14.1 mg, 0.053 mmol, 53% yield) in 96:4 *Z:E* selectivity (determined by quantitative ^{13}C NMR, relaxation time = 13 s) as white solid. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 5.38–5.29 (m, 2H), 3.72 (p, *J* = 6.0 Hz, 1H), 2.15–1.95 (m, 4H), 1.60–1.40 (m, 4H), 1.39–1.22 (m, 21H); **^{13}C NMR (101 MHz, $CDCl_3$):** δ 130.3, 70.6, 35.8, 29.2, 28.3, 28.1, 28.0, 26.9, 23.6. **HRMS[M-H_2O+H]$^+$** Calcd for $C_{17}H_{31}$: 235.2426, found: 235.2424. The characterization data are consistent with those reportedpreviously[7].

(*Z*)-Oxacyclononadec-9-en-2-one (12g). Following the general procedure, in a N_2-filled glove box, a solution of unpurified *Z*-butene (**3**) in THF (33 wt %, 342 mg, 2.02 mmol) was added to an oven-dried vial containing undec-10-en-1-yl non-8-enoate (30.8 mg, 0.10 mmol), followed by a THF solution of **Ru-2a** (0.76 mg, 0.0010 mmol, 100 μL THF). The vessel was sealed and the mixture was allowed to stir for 1 h at 22 °C. The volatiles were removed *in vacuo* and the resulting green residue was dissolved in THF (19.5 mL) and a solution of **Ru-2a** (3.00 mg, 0.0040 mmol in 500 μL THF) was added. The vessel was then connected to a 400 torr vacuum generated from a diaphragm pump. The solution was allowed to stir for 12 h at 35 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (1% diethyl ether in hexanes) and filtered through a small plug of activated charcoal to afford **12g** (18.2 mg, 0.065 mmol, 65% yield) in 96:4 *Z*:*E* ratio as colorless oil. **IR (neat):** 3002 (m), 2927 (s), 2855 (s), 1736 (s), 1461 (m), 1345 (w), 1248 (m), 1081 (m), 718 (m) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 5.44–5.26 (m, 2H), 4.12 (t, *J* = 5.6 Hz, 2H), 2.32 (t, *J* = 6.9 Hz, 2H), 2.05–1.95 (m, 4H), 1.71–1.57 (m, 4H), 1.46–1.22 (m, 18H). **^{13}C NMR (151 MHz, $CDCl_3$):** δ 174.2, 130.3, 130.0, 64.3, 34.8, 29.8, 29.3, 29.2, 29.0, 28.9, 28.7, 28.1, 28.0, 27.3, 26.2, 26.1, 25.5. **HRMS[M+H]$^+$** Calcd for $C_{18}H_{33}O_2$: 281.2481, found: 281.2493.

(*Z*)-Oxacyclohenicos-11-en-2-one (12h). Following the general procedure, in a N_2-filled glove box, a solution of unpurified *Z*-butene (**3**) in THF (33 wt %, 342 mg, 2.02 mmol) was added to an oven-dried vial containing undec-10-en-1-yl undec-10-enoate (33.4 mg, 0.10 mmol), followed by a THF solution of **Ru-2a** (0.76 mg, 0.0010 mmol, 100 μL THF). The vessel was sealed and the mixture was allowed to stir for 1 h at 22 °C. The volatiles were removed *in vacuo* and the resulting green residue was dissolved in THF (19.5 mL) and a solution of **Ru-2a** (3.00 mg, 0.0040 mmol, 500 μL THF) was added. The vessel was then connected to a 400 torr vacuum generated from a diaphragm pump. The solution was allowed to stir for 12 h at 35 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (1% diethyl ether in hexanes) and filtered through a small plug of activated charcoal to afford **12h** (18.3 mg, 0.060 mmol, 60% yield) in 96:4 *Z*:*E* ratio as colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 5.45–5.30 (m, 2H), 4.11 (t, *J* = 5.7 Hz, 2H), 2.31 (t, *J* = 6.9 Hz, 2H), 2.09–1.94 (m, 4H), 1.72–1.58 (m, 4H), 1.43–1.24 (m, 22H);

HRMS[M+H]$^+$ Calcd for $C_{20}H_{37}O_2$: 309.2794, found: 309.2807. The characterization data are consistent with those reported previously.[20]

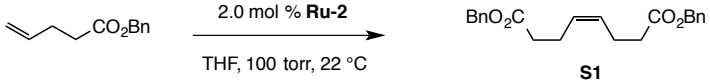
(*Z*)-Azacyclohenicos-11-en-2-one (12i). Following the general procedure, in a N_2-filled glove box, a solution of unpurified *Z*-butene (**3**) in THF (33 wt %, 342 mg, 2.02 mmol) was added to an oven-dried vial containing *N*-(undec-10-en-1-yl)undec-10-enamide (33.5 mg, 0.10 mmol), followed by a THF solution of **Ru-2a** (0.76 mg, 0.0010 mmol, 100 μL THF). The vessel was sealed and the mixture was allowed to stir for 1 h at 22 °C. The volatiles were removed *in vacuo* and the resulting green oil residue was dissolved in THF (19.5 mL) and a solution of **Ru-2a** (3.00 mg, 0.0040 mmol, 500 μL THF) was added. The vessel was then connected to a 400 torr vacuum generated from a diaphragm pump. The solution was allowed to stir for 12 h at 35 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (25% ethyl acetate in hexanes) and filtered through a small plug of activated charcoal to afford **12i** (17.6 mg, 0.057 mmol, 57% yield) in 98:2 *Z*:*E* selectivity as white solid. **IR (neat):** 3287 (br), 3087 (m), 3002 (m), 2922 (s), 2852 (s), 1639 (s), 1556 (s), 1465 (m), 1436 (m), 1355 (m), 1278 (w), 721 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 5.49 (s, 1H), 5.39–5.30 (m, 2H), 3.28 (q, *J* = 5.9 Hz, 2H), 2.16 (t, *J* = 6.6 Hz, 2H), 2.04–1.95 (m, 4H), 1.67–1.59 (m, 2H), 1.50–1.47 (m, 2H), 1.40–1.22 (m, 22H); **^{13}C NMR (101 MHz, $CDCl_3$):** δ 173.3, 130.3, 130.1, 39.4, 37.3, 29.6, 29.5, 29.4, 29.1, 29.1, 29.0, 28.7, 28.7, 28.6, 26.8, 26.7, 26.6, 26.1. **HRMS[M+H]$^+$** Calcd for $C_{20}H_{38}ON$: 308.2953, found: 308.2953.

(*Z*)-2-(2-Oxoazacyclohenicos-11-en-1-yl)acetic acid (12j). Following the general procedure for MRCM reaction, in a N_2-filled glove box, a solution of unpurified *Z*-butene (**3**) in THF (33 wt %, 342 mg, 2.02 mmol) was added to an oven-dried vial containing 2-(*N*-(undec-10-en-1-yl)undec-10-enamido)acetic acid (19.7 mg, 0.050 mmol), followed by a THF solution of **Ru-2a** (0.38 mg, 0.00050 mmol, 100 μL THF). The vessel was sealed and the mixture was allowed to stir for 1 h at 22 °C. The volatiles were removed *in vacuo* and the resulting green residue was dissolved in THF (9.5 mL) and a solution of **Ru-2a** (1.50 mg, 0.0020 mmol, 500 μL THF) was added. The vessel was then connected to a 400 torr vacuum generated from a diaphragm pump. The solution was allowed to stir for 12 h at 35 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (dichloromethane/MeOH/AcOH: 200/4/1) and filtered through a small plug of activated charcoal to afford **12j** (7.5 mg, 0.020 mmol, 40% yield) in 97:3 *Z*:*E* ratio as colorless oil. **IR (neat):** 3000 (m), 2919 (s), 2851 (s), 1723 (m), 1585 (s), 1463 (m), 1251 (s), 1092 (w), 874 (w), 723 (m) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 9.81 (br, 1H), 5.40–5.26 (m, 2H), 4.05 (s, 2H), 3.33 (t, *J* = 7.7 Hz 2H), 2.38 (*J* = 7.6 Hz 2H), 2.03 (q, *J* = 6.1 Hz, 4H), 1.77–1.53 (m, 4H), 1.40–1.20 (m, 22H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 175.3, 172.8, 130.2, 130.2, 49.9, 49.1, 32.6, 29.5, 29.5, 29.5, 29.2, 29.1, 29.0, 28.9, 28.7, 28.3, 27.1, 27.0, 26.3, 25.4; **HRMS[M+H]$^+$** Calcd for $C_{22}H_{40}O_3N$: 366.3008, found: 366.3022.

Macrocyclic ring-closing metathesis of compound 11a **in the presence of 4-acetylbenzaldehyde**: In a N_2-filled glove box, a solution of unpurified *Z*-butene (**3**) in THF (24 wt %, 236 mg, 1.01 mmol) was added to an oven-dried vial containing undec-10-en-1-yl hex-5-enoate (**11a**, 13.3 mg, 0.050 mmol) and 4-acetylbenzaldehyde (7.4 mg, 0.050 mmol),

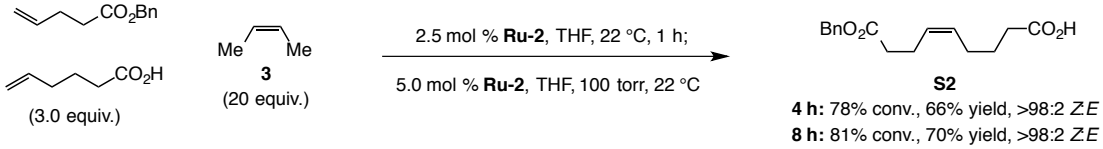
followed by a THF solution of **Ru-2a** (0.38 mg, 0.00050 mmol, 100 μL THF). The vessel was sealed and the mixture was allowed to stir for 1 h at 22 °C. The volatiles were removed *in vacuo* and the resulting green residue was dissolved in THF (9.5 mL) and a solution of **Ru-2a** (1.50 mg, 0.0020 mmol, 500 μL THF) was added. The vessel was then connected to a 400 torr vacuum generated from a diaphragm pump. The solution was allowed to stir for 12 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (1% diethyl ether in hexanes) to afford macrocyclic olefin product **12a** (6.0 mg, 0.025 mmol, 50% yield) in 98:2 *Z*:*E* ratio as colorless oil.

9. Influence of time on *Z* selectivity in homocoupling and cross-metathesis



S1
10 min: 8% conv., 78:22 Z:E
1 h: 14% conv., 13% yield, 78:22 *Z*:*E*
4 h: 15% conv., 14% yield, 77:23 *Z*:*E*

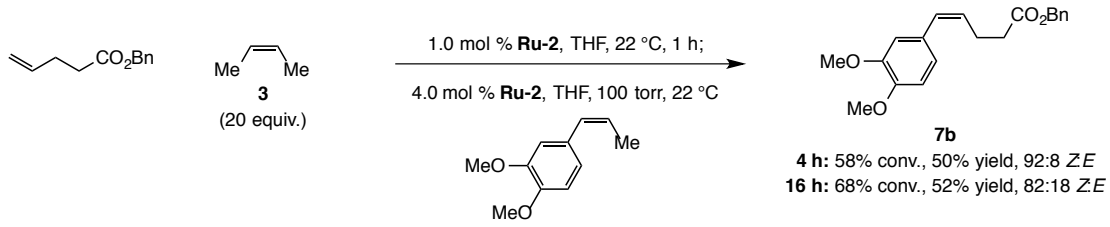
Dibenzyl (*Z*)-dec-5-enedioate (S1). In a N_2-filled glovebox, an oven-dried vial equipped with a magnetic stir bar is charged with benzyl hex-5-enoate (25.9 mg, 0.127 mmol) and a solution of catechothiolate complex **Ru-2a** (2.0 mg, 0.00254 mmol) dissolved in THF (200 μL). The mixture was allowed to stir for 4 hrs at 22 °C, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (20% diethyl ether in hexanes) to afford olefin product (6.3 mg, 0.018 mmol, 14% yield) in 77:23 *Z*:*E* ratio as colorless oil. **IR (neat):** 3063 (w), 3032 (w), 2954 (w), 1735 (s), 1497 (m), 1455 (m), 1235 (m), 1213 (m), 1154 (m), 738 (m), 697 (m); **^{1}H NMR (500 MHz, $CDCl_3$) *Z* isomer:** δ 7.39–7.30 (m, 10H), 5.39 (t, *J* = 4.5 Hz, 2H), 5.11 (s, 4H), 2.41−2.37 (m, 8H); **^{13}C NMR (151 MHz, $CDCl_3$) *Z* isomer:** δ 173.0, 136.1, 129.1, 128.7, 128.4, 128.3, 66.4, 34.3, 22.9. **HRMS[M+H]$^+$:** Calcd for $C_{22}H_{25}O_4$: 352.17; found:352.1755.



S2
4 h: 78% conv., 66% yield, >98:2 *Z*:*E*
8 h: 81% conv., 70% yield, >98:2 *Z*:*E*

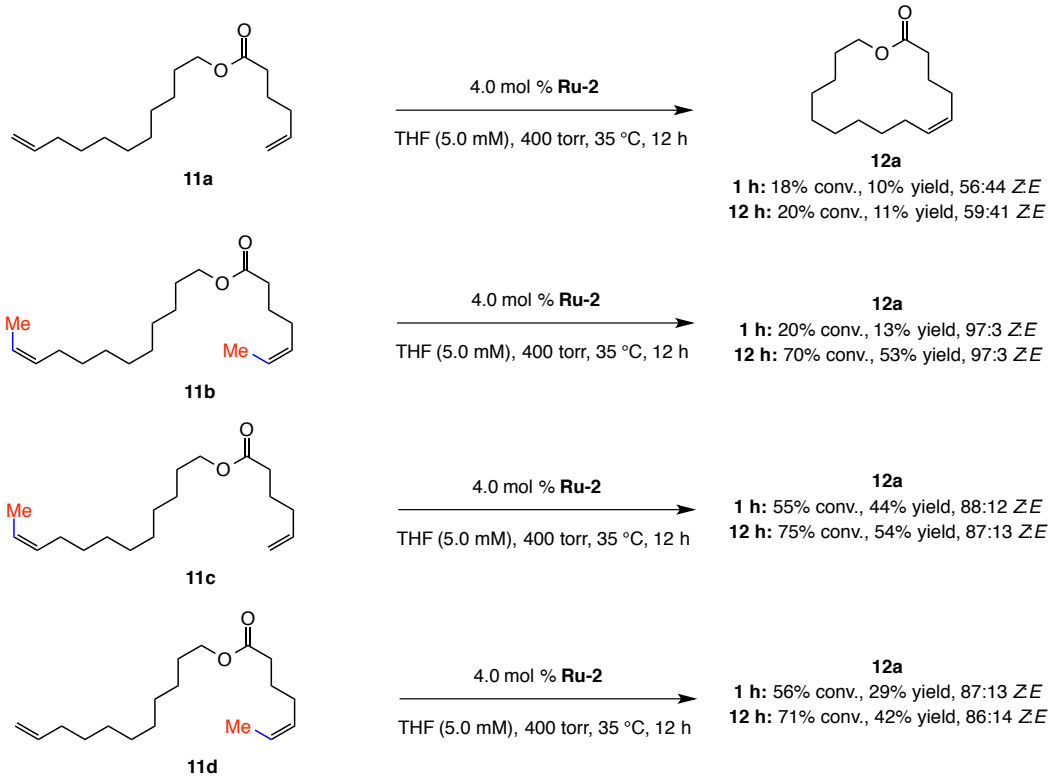
(*Z*)-9-(Benzyloxy)-9-oxonon-5-enoic acid (S2). Following the general procedure A, in a N_2-filled glovebox, an oven-dried vial equipped with a magnetic stir bar was charged with benzyl pent-4-enoate (25.4 mg, 0.127 mmol) and hex-5-enoic acid (43.5 mg, 0.38 mmol), unpurified *Z*-butene in THF (22 wt %, 650 mg, 2.54 mmol) and a THF solution (200 μL) of **Ru-2a** (1.0 mg, 0.00127 mmol). The vessel was sealed. The mixture was allowed to stir at 22 ^{o}C for 1 h, after which the volatiles were removed *in vacuo* (100 torr for 2 mins). The flask containing the residue was then charged with a solution of **Ru-2a** (3.9 mg, 0.00508 mmol) in THF (200 μL) and the system was placed under 100 torr of vacuum generated from a diaphragm pump. The resulting solution was allowed to stir for 8 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (10~20% ethyl acetate in hexanes) and filtered through a small plug of

activated charcoal to afford the desired product (24.6 mg, 0.089 mmol, 70% yield) in >98:2 *Z*:*E* ratio as colorless oil. **IR (neat):** 3009 (m), 2926 (s), 1734 (s), 1703 (s), 1498 (m), 1455 (m), 1381 (m), 1237 (m), 1148 (s), 958 (m), 697 (m) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.45–7.28 (m, 5H), 5.49–5.27 (m, 2H), 5.12 (s, 2H), 2.46–2.29 (m, 6H), 2.14–2.07 (m, 2H), 1.69 (p, *J* = 7.5 Hz, 2H); **^{13}C NMR (101 MHz, $CDCl_3$):** δ 179.7, 173.1, 136.1, 130.1, 128.8, 128.7, 128.4, 128.3, 66.4, 34.4, 33.5, 26.6, 24.6, 22.9; **HRMS[M+H]$^+$:** Calcd for $C_{16}H_{21}O_4$: 277.1440, Found: 277.1452.



(*Z*)-Benzyl 5-(3,4-dimethoxyphenyl)pent-4-enoate (7b). Following the general procedure 2, in a N_2-filled glove box, an oven-dried vial equipped with a magnetic stir bar was charged with benzyl pent-4-enoate (28.5 mg, 0.050 mmol) and *Z*-2-butene (**3**) in THF (24 wt %, 236 mg, 1.01 mmol) and a solution of **Ru-2a** (0.38 mg, 0.0005 mmol in 100 μL THF). The vessel was sealed, and the mixture was allowed to stir at 22 °C for 1 h, after which the volatiles were removed *in vacuo* (100 torr, 2 min). The flask containing the residue was then charged with (*Z*)-1,2-dimethoxy-4-(prop-1-en-1-yl)benzene (8.9 mg, 0.05 mmol), followed by a solution of **Ru-2a** (1.50 mg, 0.002 mmol, 200 μL THF) and the system was placed under 100 torr of vacuum generated from a diaphragm pump. The solution was allowed to stir for 16 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting dark oil residue was purified by silica gel chromatography (5% ethyl acetate in hexanes) and filtered through a small plug of activated charcoal to afford olefin product **7b** (8.5 mg, 0.026 mmol, 52% yield) in 82:18 *Z*:*E* ratio as colorless oil.

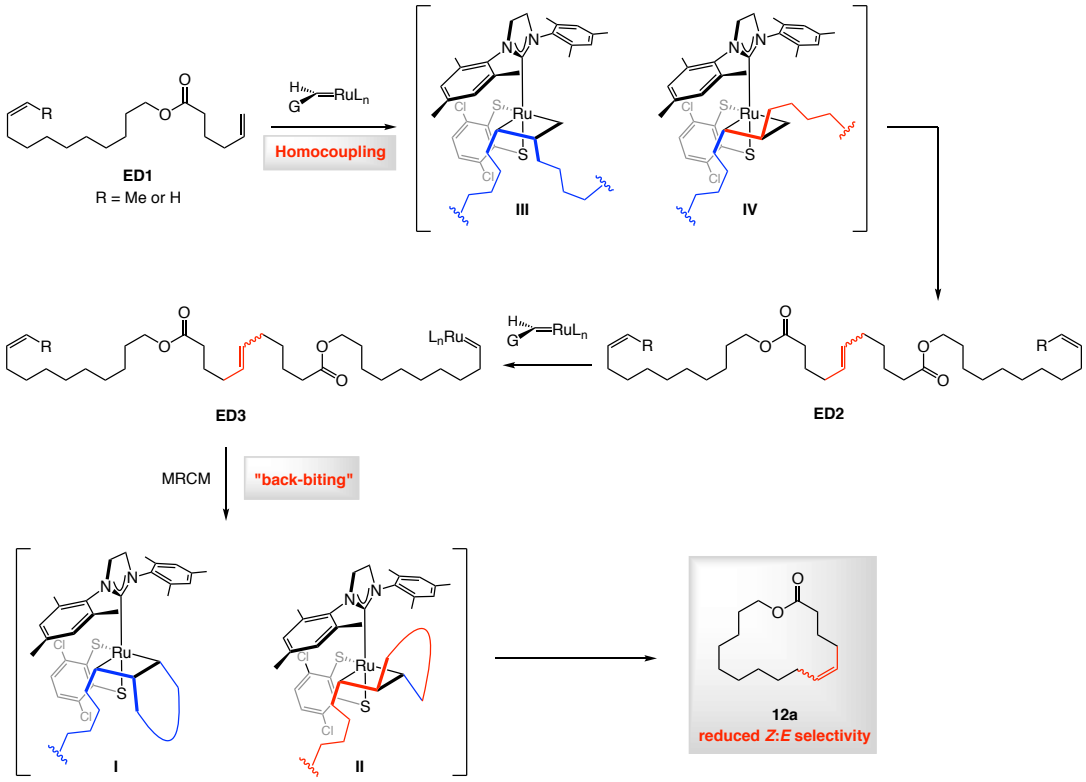
10. Influence of time on *Z* selectivity in macrocyclic ring-closing metathesis



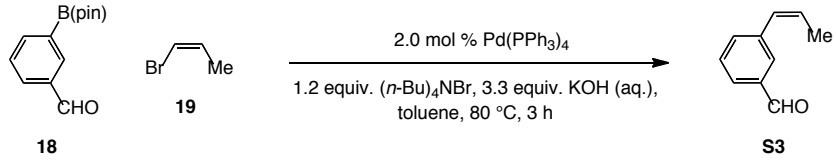
In a N_2-filled glove box, a THF solution of **Ru-2a** (1.50 mg, 0.0020 mmol in 500 μL THF) was added to an oven-dried vial containing **11** (0.05 mmol) and THF (9.50 mL). The vessel was then connected to a 400 torr vacuum generated from a diaphragm pump. The solution was allowed to stir for 12 h at 35 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was dissolved in $CDCl_3$ and subjected to ^1H NMR analysis. Conversion refers to the disappearance of the starting material; yield refers to the conversion to macrocyclic alkene **12a**.

Possible explanation of lowering of Z selectivity MRCM (back-biting):

As shown in the scheme below, when a substrate contains a terminal alkene (e.g., **ED1**), homocoupling can readily occur to afford **ED2**. Reaction via metallacyclobutane **IV**, although less favored than **III**, may generate minor amounts of the *E*-**ED2**. Subsequent reaction would afford Ru carbene **ED3**, which may then undergo MRCM via metallacyclobutane **I** (from *Z*-**ED3**) as well as **II** (from *E*-**ED3**) by a "back-biting" mechanism to afford **12a** as a mixture of stereoisomers. Thus, minimization of homocoupling can lead to higher levels of *Z* selectivity.



11. Stereoselective synthesis of compound 16



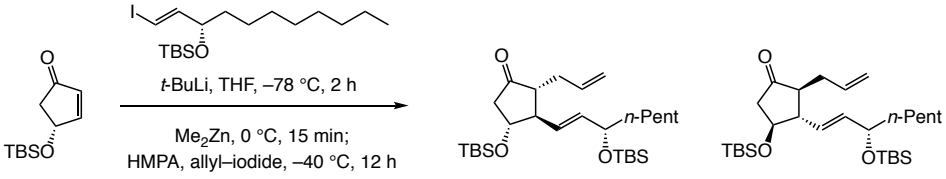
(*Z*)-3-(Prop-1-en-1-yl)benzaldehyde (S3). In a N_2-filled glove box, to a solution of 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde (464.0 mg, 2.00 mmol), was added (*Z*)-1-bromoprop-1-ene (290.0 mg, 2.40 mmol), *tetra*-*n*-butylammonium bromide (TBAB, 772.0 mg, 2.40 mmol, 10 mL toluene) and $Pd(PPh_4)_3$ (46.0 mg, 0.040 mmol), followed by an aqueous solution of KOH (3 M, 2.2 mL, 6.6 mmol) . The vessel was sealed and the mixture was allowed to stir for 3 h at 80 °C in the dark. The solution was passed through a pad of celite with ether as eluent. The filtrate was concentrated *in vacuo* and the resulting brown oil residue was purified by silica gel chromatography (1% diethyl ether in hexanes) to afford (*Z*)-3-(prop-1-en-1-yl)benzaldehyde (**S3**, 234.0 mg, 1.60 mmol, 80% yield) as colorless oil. **IR (neat):** 2981 (m), 2936 (m), 2829 (m), 2732 (m), 1696 (s), 1604 (m), 1483 (m), 1447 (m), 1377 (m), 1275 (m), 1187 (m), 801 (m), 753 (m), 692 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 10.00 (s, 1H), 7.77 (s, 1H), 7.72 (d, *J* = 7.5 Hz, 1H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 1H), 6.46 (d, *J* = 11.6 Hz, 1H), 5.88 (dq, *J* = 11.6, 7.2 Hz, 1H), 1.90 (dd, *J* = 7.2, 1.7 Hz, 3H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 192.4, 138.6, 136.5, 134.8, 129.9, 128.9, 128.6, 128.6, 127.8, 14.66; **HRMS[M+H]$^+$** Calcd for $C_{10}H_{11}O$: 147.0810, found: 147.0808.

(*Z*)-1-(3-(Prop-1-en-1-yl)phenyl)hexan-1-ol (20). Under N_2 protection, a frame-dried flask was charged with Mg turnings (41.0 mg, 1.71 mmol) in THF (5 mL), followed by $BrCH_2CH_2Br$

(13.2 mg, 0.050 mmol). After 2 minutes, *n*-$C_5H_{11}Br$ (211.0 mg, 1.40 mmol) in THF (3 mL) was added slowly via a syringe under reflux. The mixture was refluxed for 2 hours, and then cooled to –78 ºC. (Z)-3-(prop-1-en-1-yl)benzaldehyde **S3** (102.2 mg, 0.70 mmol) in THF (3 mL) was added. The mixture was allowed to warm to 0 °C within 1 h, after which the reaction was quenched with brine and washed with Et_2O (20 mL × 3). The organic layers were dried over anhydrous $MgSO_4$ and then filtered. The filtrate was concentrated and the resulting colorless oil residue and purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford **20** (134.2 mg, 0.62 mmol, 88% yield) as colorless oil. **IR (neat):** 3428 (br), 3016 (s), 2954 (m), 2930 (s), 2858 (m), 1602 (w), 1483 (m), 1402 (m), 1367 (m), 1112 (m), 1054 (m), 897 (s), 804 (m), 702 (s) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.32 (t, *J* = 7.6 Hz, 1H), 7.27 (s, 1H), 7.22 (d, *J* = 7.2 Hz, 1H), 7.20 (d, *J* = 7.3 Hz, 1H), 6.44 (d, *J* = 11.6 Hz, 1H), 5.80 (dq, *J* = 11.6, 7.2 Hz, 1H), 4.67 (t, *J* = 5.5 Hz, 1H), 1.90 (dd, *J* = 7.2, 1.8 Hz, 3H), 1.86–1.64 (m, 3H), 1.47–1.37 (m, 1H), 1.35–1.25 (m, 5H), 0.87 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 145.0, 137.9, 130.0, 128.4, 128.1, 127.1, 126.6, 124.2, 74.9, 39.2, 31.9, 25.7, 22.7, 14.8, 14.2; **HRMS[M-H_2O+H]$^+$** Calcd for $C_{15}H_{21}$: 201.1643, found: 201.1634.

(*Z*)-Methyl 6-(3-(1-hydroxyhexyl)phenyl)hex-5-enoate (16). Following general procedure B (see above), in a N_2-filled glove box, an oven-dried vial equipped with a magnetic stir bar was charged with the methyl hex-5-enoate (19.2 mg, 0.15 mmol), unpurified *Z*-butene (**3**) in THF (17 wt %, 334 mg, 1.01 mmol), followed by a THF solution of **Ru-2a** (0.38 mg, 0.00050 mmol, 100 μL THF). The vessel was sealed and the mixture was allowed to stir for 1 h at 22 °C. The volatiles were removed *in vacuo*, and the vial containing the residue was charged (*Z*)-1-(3-(prop-1-en-1-yl)phenyl)hexan-1-ol (10.9 mg, 0.050 mmol), followed by a THF solution of **Ru-2a** (1.50 mg, 0.00020 mmol, 200 μL THF) and the mixture was placed under 100 torr of vacuum generated from a diaphragm pump. The solution was allowed to stir for 4 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. Purification of the dark oil residue by silica gel chromatography (5% ethyl acetate in hexanes) afford**ed 16** (8.5 mg, 0.028 mmol, 56% yield) in 96:4 *Z*:*E* ratio as colorless oil. **IR (neat):** 3435 (br), 3008 (m), 2952 (m), 2930 (s), 2858 (m), 1737 (s), 1483 (m), 1457 (m), 1367 (m), 1117 (m), 1055 (m), 899 (m), 806 (m), 704 (m) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.30 (t, *J* = 7.6 Hz, 1H), 7.26 (s, 1H), 7.19 (d, *J* = 7.7 Hz, 1H), 7.16 (d, *J* = 7.6 Hz, 1H), 6.46 (d, *J* = 11.7 Hz, 1H), 5.64 (dt, *J* = 11.7, 7.4 Hz, 1H), 4.66 (t, *J* = 5.8 Hz, 1H), 3.64 (s, 3H), 2.36 (t, *J* = 7.4 Hz, 2H), 2.34 (t, *J* = 7.4 Hz, 2H), 2.04 (br, 1H), 1.89–1.63 (m, 4H), 1.48–1.40 (m, 1H), 1.34–1.26 (m, 5H), 0.87 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 174.1, 145.1, 137.7, 131.8, 129.9, 128.4, 127.9, 126.4, 124.4, 74.8, 51.7, 39.2, 33.6, 31.9, 28.1, 25.7, 25.1, 22.7, 14.2; **HRMS[M-H_2O+H]$^+$** Calcd for $C_{19}H_{27}O_2$: 287.2011, found: 287.1999.

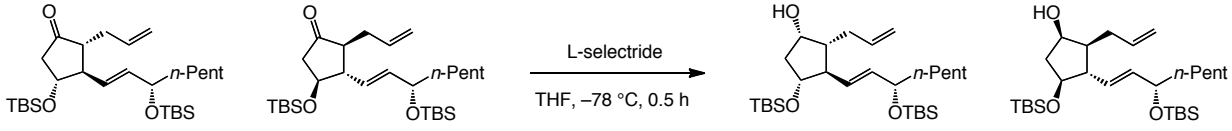
12. Stereoselective synthesis of prostaglandins E_2 and $F_{2\alpha}$



(2*R*,3*R*,4*R*)-2-allyl-4-((*tert*-butyldimethylsilyl)oxy)-3-((*S*,*E*)-3-((*tert*-butyldimethylsilyl)oxy)oct-1-en-1-yl)cyclopentan-1-one & (2*S*,3*S*,4*S*)-2-allyl-4-((*tert*-butyldimethylsilyl)oxy)-3-((*S*,*E*)-3-((*tert*-butyldimethylsilyl)oxy)oct-1-en-1-yl)cyclopentan-1-one (S4). To a solution of (*S*,*E*)-*tert*-butyl((1-iodooct-1-en-3-yl)oxy)dimethylsilane (276.0 mg, 0.75 mmol) in THF (1.2 mL) was added *t*-BuLi (1.7 M, THF, 0.88 mL, 1.50 mmol) at –78 °C. The mixture was allowed to stir for 2 h after which Me_2Zn (2.0 M, toluene, 0.38 mL, 0.76 mmol) was added. The mixture was allowed to warm to and stir at 0 °C for 30 min, after which it was allowed to cool to –78 °C. A solution of *rac*-4-((*tert*-butyldimethylsilyl)oxy)cyclopent-2-en-1-one (106.0 mg, 0.5 mmol) in THF (0.8 mL) was slowly added to the mixture by the use of a syringe pump within an hour (–78 °C). HMPA (0.56 mL) and allyl iodide (0.15 mL) were then added, and the mixture was allowed to stir at –40 °C for an additional 18 h. At this time, the reaction was quenched by addition of a saturated solution of NH_4Cl after which it was washed with ethyl acetate (20 mL × 3). The organic layers were combined and washed with brine, dried over anhydrous $MgSO_4$, concentrated *in vacuo* and the resulting yellow oil purified by silica gel chromatography (1% ethyl acetate in hexanes) to afford **S4** (168.0 mg, 68% yield) as colorless oil (mixture of diastereomers). The isomers were inseparable by silica gel chromatography and used directly in the next step. **IR (neat):** 2955 (m), 2929 (m), 2856 (m), 1746 (m), 1471 (m), 1462 (m), 1361 (m), 1250 (m), 1112 (m), 1004 (m), 967 (m), 937 (m), 877 (s), 733 (s), 668 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 5.79−5.66 (m, 2H), 5.63−5.37 (m, 4H), 5.04−5.00 (m, 4H), 4.14−4.00 (m, 4H), 2.63 (dd, *J* = 18.2, 6.9 Hz, 2H), 2.56−2.40 (m, 4H), 2.33−2.22 (m, 2H), 2.20−2.11 (m, 2H), 2.10−2.00 (m, 2H), 1.58−1.38 (m, 4H), 1.41−1.19 (m, 12H), 0.94−0.83 (m, 42H), 0.05−0.02 (m, 24H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 215.5, 215.4, 137.3, 136.7, 135.2, 135.0, 129.0, 128.6, 117.6, 117.4, 73.5, 73.4, 73.3, 72.9, 53.6, 52.5, 52.4, 47.9, 47.8, 38.7, 38.6, 32.0, 32.0, 32.0, 31.8, 26.0, 25.9, 25.9, 25.9, 25.2, 24.9, 22.8, 18.4, 18.2, 18.1, 14.2, 14.2, −4.1, −4.1, −4.4, −4.5, −4.5, −4.5, −4.6, −4.6; **HRMS[M+NH_4]$^+$** Calcd for $C_{28}H_{58}O_3Si_2N$: 512.3955; found: 512.3968.

(2*R*,3*R*,4*R*)-2-Allyl-4-hydroxy-3-((*S*,*E*)-3-hydroxyoct-1-en-1-yl)cyclopentan-1-one (21a). To the solution of **S4** (32.4 mg, 0.070 mmol) in CH_3CN (1.5 mL) was added hydrogen fluoride pyridine (70%, 0.3 mL) at 22 °C and the mixture was allowed to stir for 15 min. The reaction was quenched by the addition of a saturated solution of $NaHCO_3$ and washed with ethyl acetate (10 mL × 3). The organic layers were combined and washed with brine, dried over anhydrous Na_2SO_4, concentrated and purified by silica gel chromatography (50% ethyl acetate in hexanes) to afford **21a** (8.0 mg, 46% yield) as colorless oil. Note: the two diastereomers were separated by silica gel chromatography at this stage. **$[\alpha]_D^{22}$** –78.3 (*c* 0.59, $CHCl_3$); **IR (neat):** 3374 (br), 2955 (m), 2927 (m), 2857 (m), 1736 (s), 1604 (w), 1458 (m), 1334 (m), 1259 (m), 1160 (m), 1073 (s), 1002 (m), 968 (s), 914 (s) cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 5.77–5.59 (m, 2H), 5.51 (dd, *J* = 15.3, 8.8 Hz, 1H), 5.07–4.98 (m, 2H), 4.18–3.98 (m, 2H), 3.48 (br, 1H), 2.74 (ddd, *J* = 18.5, 7.5, 1.2 Hz, 1H), 2.55–2.35 (m, 3H), 2.34–2.25 (m, 1H), 2.19 (dd, *J* = 18.6, 9.8 Hz, 1H), 2.14–2.06 (m, 1H), 1.67–1.44 (m, 2H), 1.36−1.25 (m, 6H), 0.96–0.85 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR (101 MHz, $CDCl_3$):** δ 213.9, 137.2, 134.8, 131.6, 117.7, 73.3, 72.0, 54.3, 53.8, 46.1, 37.5, 31.8, 31.6, 25.3, 22.8, 14.2; **HRMS[M−H_2O+H]$^+$** Calcd for $C_{16}H_{25}O_2$: 249.1855, found: 249.1865.

Prostaglandin E_2. In a N_2-filled glove box, a solution of unpurified *Z*-butene (**3**) in THF (22 wt %, 184.0 mg, 0.72 mmol) was added to an oven-dried vial containing (2*R*,3*R*,4*R*)-2-allyl-4-hydroxy-3-((*S*,*E*)-3-hydroxyoct-1-en-1-yl)cyclopentanone **21a** (9.6 mg, 0.036 mmol), followed by a THF solution of **Ru-2a** (0.54 mg, 0.00072 mmol in 100 μL THF). The vessel was sealed and the mixture was allowed to stir for 16 h at 22 °C. In another oven-dried vial, a mixture of purified **3** in THF (22 wt %, 184.0 mg, 0.72 mmol), hex-5-enoic acid (**1a**, 12.3 mg, 0.11 mmol) and **Ru-2a** (0.27 mg, 0.00036 mmol, 100 μL THF) was allowed to stir for 1 h at 22 °C. The mixtures were combined and the volatiles were removed *in vacuo*. To the resulting green oil was added a solution of **Ru-2a** (4.1 mg, 0.0054 mmol, 200 μL THF). The vessel was then connected to a 100 torr vacuum generated from a diaphragm pump, and the solution was allowed to stir for 1 h at 22 °C under 100 torr, and then for 7 h under 400 torr. At this time, the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (dichloromethane/MeOH/AcOH (v/v/v 200/2/1)) and filtered through a plug of activated charcoal with ethyl acetate as eluent to afford prostaglandin E_2 (6.4 mg, 0.0182 mmol, 51% yield) in >98:2 *Z:E* ratio as off-white solid. **$[\alpha]_D^{20}$** −60.0 (*c* 0.15, EtOH); **^{1}H NMR (400 MHz, $CDCl_3$):** δ 5.68 (dd, *J* = 15.4, 6.5 Hz, 1H), 5.58 (dd, *J* = 15.3, 8.2 Hz, 1H), 5.47–5.34 (m, 2H), 4.20–4.10 (m, 1H), 4.05 (dd, *J* = 16.7, 9.5 Hz, 1H), 2.75 (dd, *J* = 17.9, 7.3 Hz, 1H), 2.47–1.93 (m, 9H), 1.82–1.43 (m, 4H), 1.40–1.20 (m, 6H), 0.89 (t, *J* = 6.6 Hz, 3H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 214.4, 177.6, 136.7, 130.9, 126.9, 73.2, 72.5, 54.6, 53.6, 46.4, 37.2, 33.2, 31.8, 26.4, 25.4, 25.3, 24.6, 22.8, 14.2; [note: two olefin carbon signals overlap at 130.9 ppm]; **HRMS[M−H_2O+H]$^+$** Calcd for $C_{20}H_{31}O_4$: 335.2222, found: 335.2231. The characterization data are consistent with those of commercially available prostaglandin E_2 (Aldrich) and those reported previously.[21]



S4 **S5**

(1*S*,2*R*,3*R*,4*R*)-2-allyl-4-((*tert*-butyldimethylsilyl)oxy)-3-((*S*,*E*)-3-((*tert*-butyldimethylsilyl)oxy)oct-1-en-1-yl)cyclopentan-1-ol & **(1*R*,2*S*,3*S*,4*S*)-2-allyl-4-((*tert*-butyldimethylsilyl)oxy)-3-((*S*,*E*)-3-((*tert*-butyldimethylsilyl)oxy)oct-1-en-1-yl)cyclopentan-1-ol (S5).** To compound **S4** (40.9 mg, 0.080 mmol) in THF (2.0 mL) was added L-selectride (1M in THF, 0.12 mL) at −78 °C and the resulting mixture was allowed to stir for 30 min. The reaction was quenched by addition of a saturated solution of NH_4Cl and washed with ethyl acetate (10 mL × 3). The organic layers were combined, washed with brine, dried with anhydrous Na_2SO_4, concentrated *in vacuo* and the resulting brown oil residue purified by silica gel chromatography (1% ethyl acetate in hexanes) to afford **S5** (39.0 mg, 95% yield) as a colorless oil (mixture of diastereoisomers). The diastereoisomers could not be separated by silica gel chromatography and were therefore used directly in the next step. **IR (neat):** 2955 (m), 2928 (m), 2856 (m), 1746 (m), 1471 (m), 1462 (m), 1250 (m), 1112 (m), 1004 (m), 966 (m), 912 (m), 877 (m), 833 (s), 773 (s), 668 (m) cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 5.94–5.79 (m, 2H), 5.50–5.41 (m, 2H), 5.39–5.27 (m, 2H), 5.15–5.02 (m, 2H), 5.01–4.93 (m, 2H), 4.18–4.11 (m, 2H), 4.10–3.93 (m, 4H), 2.62 (dd, *J* = 18.2, 6.9 Hz, 2H),

2.42–2.32 (m, 2H), 2.32–2.24 (m, 2H), 2.24–2.13 (m, 2H), 1.95–1.87 (m, 2H), 1.86–1.80 (m, 2H), 1.60–1.38 (m, 2H), 1.36–1.20 (m, 10H), 0.94–0.85 (m, 42H), 0.14–0.02 (m, 24H); **^{13}C NMR (151 MHz, $CDCl_3$):** δ 138.1, 138.0, 135.0, 134.7, 131.1, 130.8, 115.4, 115.4, 80.1, 80.0, 74.7, 74.5, 73.7, 73.4, 56.5, 56.5, 51.6, 51.4, 43.2, 43.1, 38.7, 38.6, 33.5, 33.3, 32.0, 26.1, 26.0, 25.2, 25.1, 22.8, 18.4, 18.0, 18.0, 14.2, 14.2, –4.1, –4.1, –4.4, –4.5, –4.6, –4.6, –4.7, –4.7; **HRMS[M+H]$^+$** Calcd for $C_{28}H_{57}O_3Si_2$: 497.3846, found: 497.3866.

(1*R*,3*S*,4*R*,5*R*)-4-Allyl-5-((*S*,*E*)-3-hydroxyoct-1-en-1-yl)cyclopentane-1,3-diol (21b). To **S5** (35.0 mg, 0.070 mmol) in CH_3CN (1.5 mL) was added HF•pyridine and the solution was allowed to stir for 10 min. The reaction was quenched at this time by addition of a saturated solution of $NaHCO_3$ and resulting mixture was washed with ethyl acetate (10 mL × 3). The organic layers were combined, washed with brine, dried over Na_2SO_4, concentrated *in vacuo* and the yellow oil purified by silica gel chromatography (50% ethyl acetate in hexanes) to afford the desired product **21b** (7.3 mg, 34% yield) as a colorless oil. The diastereomers were separable by silica gel chromatography at this stage. **$[\alpha]_D^{22}$** +10.2 (*c* 0.46, $CHCl_3$); **IR (neat):** 3341 (br), 2956 (m), 2927 (m), 2858 (m), 1727 (s), 1437 (m), 1375 (m), 1245 (m), 1182 (m), 1078 (m), 1045 (m), 1021 (m), 994 (s), 909 (s), 732 (s) cm^{-1}; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 5.90–5.80 (m, 1H), 5.57 (dd, *J* = 15.3, 6.9 Hz, 1H), 5.48 (dd, *J* = 15.3, 8.8 Hz, 1H), 5.10 (dd, *J* = 17.1, 1.7 Hz, 1H), 5.07–4.99 (m, 1H), 4.22 (br, 1H), 4.07 (q, *J*= 6.6 Hz, 1H), 4.00–3.92 (m, 1H), 2.51 (br, 1H), 2.40–2.14 (m, 4H), 1.95 (br, 2H), 1.78 (dd, *J* = 14.8, 2.9 Hz, 1H), 1.66–1.44 (m, 3H), 1.38–1.27 (m, 6H), 0.92–0.87 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR (126 MHz, $CDCl_3$):** δ 137.5, 135.3, 132.4, 116.0, 78.3, 73.3, 73.1, 56.1, 49.9, 42.9, 37.5, 32.6, 31.9, 25.4, 22.8, 14.2; **HRMS[M-H_2O+H]$^+$** Calcd for $C_{16}H_{27}O_2$: 251.2011, found: 251.2024.

Prostaglandin $F_{2\alpha}$. In a N_2-filled glove box, a solution of unpurified *Z*-butene (**3**) in THF (22 wt %, 102.4 mg, 0.40 mmol) was added to an oven-dried vial containing (1*R*,3*S*,4*R*,5*R*)-4-allyl-5-((*S*,*E*)-3-hydroxyoct-1-en-1-yl)cyclopentane-1,3-diol **21b** (5.4 mg, 0.02 mmol), followed by **Ru-2a** (0.30 mg in THF, 0.0004 mmol in 100 μL THF, 2.0 mol %). The vessel was sealed and the mixture was allowed to stir for 4 h at 22 °C. In another oven-dried vial, the mixture of purified **3** in THF (22 wt %, 102.4 mg, 0.40 mmol), hex-5-enoic acid (**1a**, 6.8 mg, 0.060 mmol) and **Ru-2a** (0.15 mg, 0.00020 mmol in 100 μL THF) was allowed to stir for 1 h at 22 °C. The mixtures were combined and the volatiles were removed *in vacuo*. To the resulting green residue was added a solution of **Ru-2a** (2.3 mg, 0.0030 mmol, 200 μL THF). The vessel was then connected to a 100 torr vacuum generated from a diaphragm pump. The solution was allowed to stir for 1 h at 22 °C under 100 torr, and then for 12 h at 22 °C at ambient pressure, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (dichloromethane/MeOH/AcOH (v/v/v 200/2/1)) and filtered through a small plug of activated charcoal with ethyl acetate as eluent to afford prostaglandin $F_{2\alpha}$ (4.2 mg, 0.0119 mmol, 59% yield) in >98:2 *Z:E* ratio as colorless oil. **$[\alpha]_D^{20}$** +24.0 (*c* 0.21, THF); **^{1}H NMR (600 MHz, $CDCl_3$):** δ 5.57 (dd, *J* = 15.3, 6.5 Hz, 1H), 5.51 (dd, *J* = 15.3, 8.5 Hz, 1H), 5.50–5.42 (m, 1H), 5.40–5.32 (m, 1H), 5.10–4.35 (br, 1H), 4.18 (t, *J* = 4.4 Hz, 1H), 4.11 (q, *J* = 6.8 Hz, 2H), 3.98–3.93 (m, 1H), 2.38–2.27 (m, 3H), 2.25–2.17 (m, 2H), 2.16–2.09 (m, 3H), 1.77 (d, *J* = 14.9 Hz, 1H), 1.73–1.62 (m, 2H), 1.62–1.53 (m, 1H), 1.53–1.43 (m, 2H), 1.41–1.25 (m, 6H), 0.88 (t, *J* = 6.7 Hz, 3H); **^{13}C NMR (151 MHz,**

$CDCl_3$): δ 177.2, 134.6, 132.4, 129.6, 129.1, 77.9, 73.0, 72.8, 55.6, 50.5, 42.8, 37.0, 32.9, 31.7, 26.2, 25.3, 25.2, 24.5, 22.6, 14.0; **HRMS[M-H_2O+H]$^+$** Calcd for $C_{20}H_{33}O_4$: 337.2379, found: 337.2391. The characterization data are consistent with those previously reported.[22]

13. Stereoselective synthesis of macrocyclic stapled peptide 23

(5*R*,8*R*,13*R*,*Z*)-Methyl 5-benzyl-13-((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-(4-hydroxyphenyl)propanamido)-3,6,14-trioxo-1,4,7-triazacyclotetradec-10-ene-8-carboxylate (23). In a N_2-filled glove box, a solution of unpurified *Z*-butene in THF (33 wt %, 170.0 mg, 1.00 mmol) was added to an oven-dried vial containing (6*S*,9*R*,15*S*,18*R*)-methyl 9,18-diallyl-15-benzyl-6-(4-hydroxybenzyl)-2,2-dimethyl-4,7,10,13,16-pentaoxo-3-oxa-5,8,11,14,17-pentaazanonadecan-19-oate **22** (34.7 mg, 0.050 mmol), followed by a solution of **Ru-2a** (0.76 mg, 0.0010 mmol in 200 μL THF). The vial was sealed and the mixture was allowed to stir for 12 h at 22 °C. The volatiles were removed *in vacuo* and the green solid was dissolved in THF (800 μL) and a solution of **Ru-2a** (3.78 mg, 0.0050 mmol in 200 μL THF) was added. The mixture was allowed to stir for 48 h at 35 °C, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black solid residue was purified by silica gel chromatography (3% MeOH in CH_2Cl_2) afford **23** (24.0 mg, 0.036 mmol, 72% yield) in >98:2 *Z:E* selectivity as off-white solid. **$[\alpha]_D^{20}$** +34.2 (*c* 0.76, MeOH); **^{1}H NMR (600 MHz, DMSO-d_6 at 37 ° C):** δ 9.08 (s, 1H), 8.84 (d, *J* = 5.5 Hz, 1H), 8.83 (d, *J* = 6.4 Hz, 1H), 8.08 (d, *J* = 7.7 Hz, 1H), 7.27 (d, *J* = 6.8 Hz, 1H), 7.27–7.25 (m, 4H), 7.22–7.13 (m, 1H), 7.01 (d, *J* = 7.4 Hz, 2H), 6.70 (d, *J* = 8.0 Hz, 1H), 6.63 (d, *J* = 8.2 Hz, 2H), 5.29 (t, *J* = 10.8 Hz, 1H), 5.16 (t, *J* = 10.8 Hz, 1H), 4.35–4.27 (m, 2H), 4.24 (ddd, *J* = 11.4, 8.1, 3.3 Hz, 1H), 4.10 (d, *J* = 5.8 Hz, 1H), 3.82 (dd, *J* = 13.3, 5.1 Hz, 1H), 3.67 (s, 3H), 3.18 (d, *J* = 14.6 Hz, 1H), 3.16–3.10 (m, 1H), 2.89–2.71 (m, 3H), 2.67–2.55 (m, 2H), 2.31 (d, *J* = 14.7 Hz, 1H), 1.85 (d, *J* = 10.2 Hz, 1H), 1.31 (s, 9H); **HRMS[M+H]$^+$** Calcd for $C_{34}H_{44}N_5O_9$: 666.3134, found: 666.3131. The characterization data are consistent with those previously reported[11].

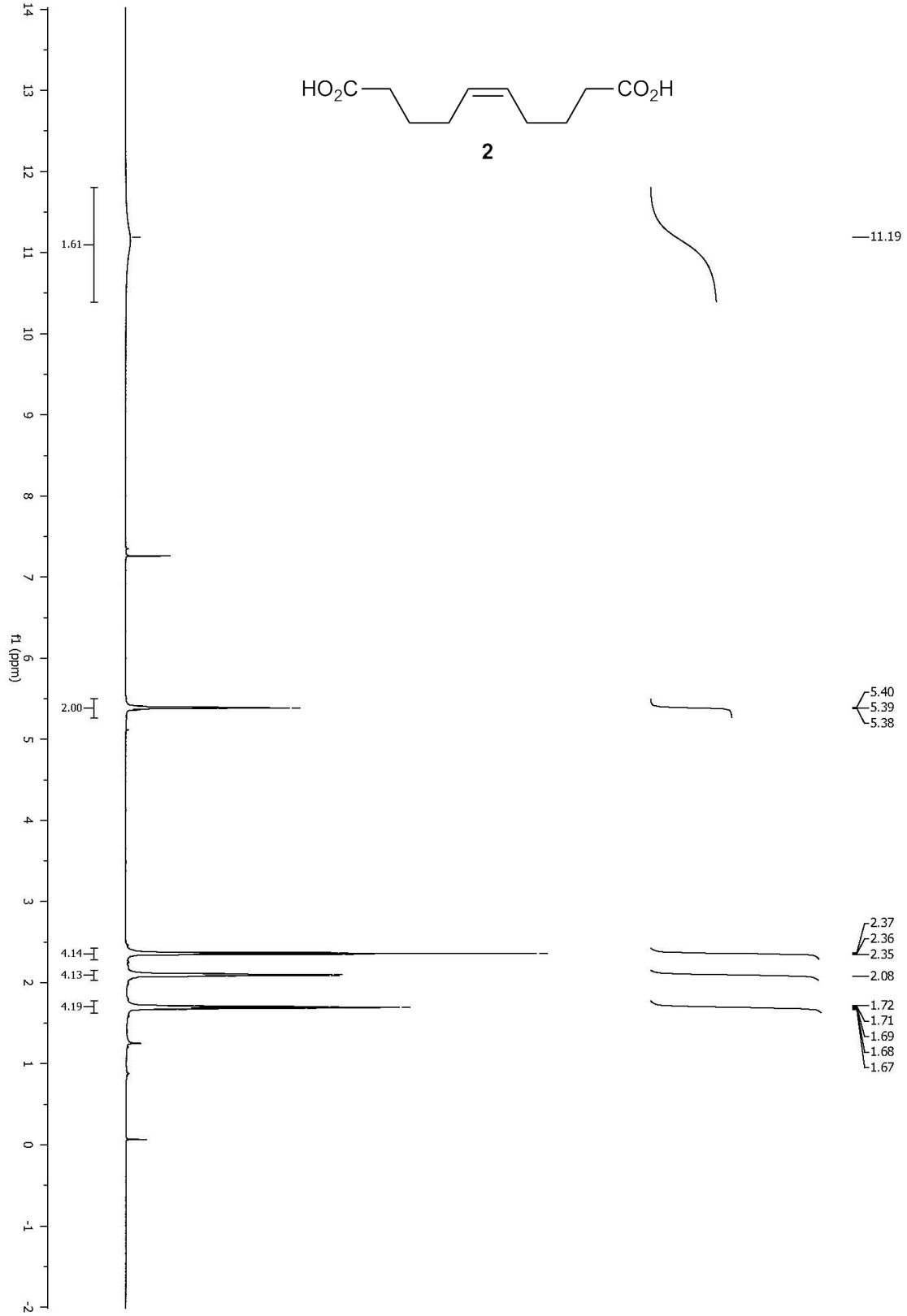
14. Cross-metathesis and macrocyclic ring-closing metathesis with *E*-butene as methylene capping agent

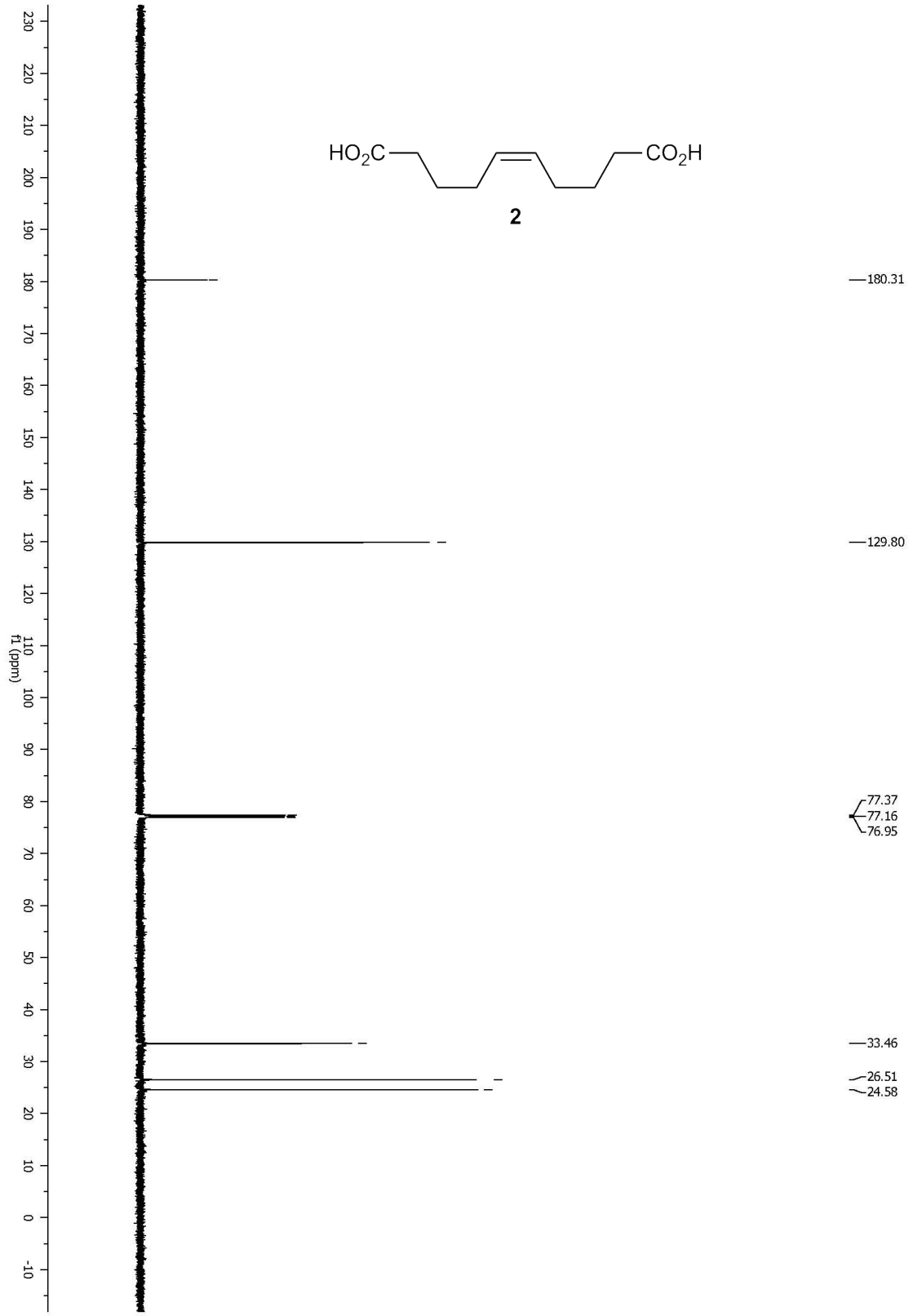
Benzyl (*E*)-12-hydroxydodec-4-enoate (24). In a N_2-filled glovebox, an oven-dried vial equipped with a magnetic stir bar was charged with benzyl pent-4-enoate (28.5 mg, 0.15 mmol) and 8-non-1-ol (7.1 mg, 0.05 mmol), unpurified *E*-2-butene in THF (30 wt %, 698 mg, 3.75 mmol) and a solution of **Ru-2b** (3.0 mg, 0.00375 mmol, 200 μL THF). The vessel was then sealed. The mixture was allowed to stir at 22 °C for 1 h, after which the volatiles were removed *in vacuo* (100 torr, 2 min). The flask containing the residue was then charged with a solution of **Ru-2b** (2.1 mg, 0.0025 mmol in 200 μL THF) and the system was placed under 100 torr of vacuum generated from a diaphragm pump. The resulting solution was allowed to stir for 4 h at 22 °C under vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (10~20% ethyl acetate in hexanes) and filtered through a small plug of activated charcoal to afford **24** (10.0 mg, 0.033 mmol, 66% yield) in 96:4 *E*:*Z* ratio as colorless oil. **IR (neat)**: 3387 (br), 2925 (s), 2853 (m), 1735 (s), 1497 (w), 1455 (m), 1345 (m), 1213 (m), 1158 (s), 1059 (m), 1002 (m), 968 (m), 913 (m), 749 (m), 697 (m) cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43–7.29 (m, 5H), 5.50–5.35 (m, 2H), 5.11 (s, 2H), 3.63 (t, *J* = 6.6 Hz, 2H), 2.67–2.38 (m, 2H), 2.39–2.29 (m, 2H), 1.95 (q, *J* = 6.5 Hz, 2H), 1.61−1.53 (m, 3H), 1.46–1.13 (m, 8H); **^{13}C NMR (126 MHz, $CDCl_3$)**: δ 173.21, 136.23, 132.00, 128.67, 128.30, 128.30, 128.01, 77.41, 77.16, 76.91, 66.26, 63.20, 34.56, 32.93, 32.57, 29.45, 29.38, 29.17, 28.05, 25.83; **HRMS[M+H]$^+$** Calcd for $C_{19}H_{29}O_3$: 305.213, found: 305.2117.

(*E*)-oxacyclohexadec-6-en-2-one (25). In a N_2-filled glove box, a solution of unpurified *E*-butene (**3**) in THF (23 wt %, 608 mg, 2.50 mmol) was added to an oven-dried vial containing undec-10-en-1-yl hex-5-enoate (**11a**, 13.3 mg, 0.05 mmol), followed by a THF solution of **Ru-2b** (1.60 mg, 0.0020 mmol, 100 μL THF). The vessel was sealed and the mixture was allowed to stir for 1 h at 22 °C. The volatiles were removed *in vacuo* and the resulting green residue was dissolved in THF (9.5 mL) and a solution of **Ru-2b** (2.40 mg, 0.0030 mmol, 500 μL THF) was added. The vessel was then connected to a 400 torr vacuum generated from a diaphragm pump. The solution was allowed to stir for 12 h at 35 °C under vacuum and then 12 h at 35 °C without vacuum, after which the reaction was quenched by the addition of wet (undistilled) diethyl ether and the volatiles were removed *in vacuo*. The resulting black oil residue was purified by silica gel chromatography (1% diethyl ether in hexanes) and filtered through a small plug of activated charcoal to afford **25** (6.2 mg, 0.026 mmol, 52% yield) in 95:5 *E*:*Z* ratio as colorless oil. **^{1}H NMR (600 MHz, $CDCl_3$):** δ 5.38–5.28 (m, 2H), 4.12 (t, *J* = 5.3 Hz, 2H), 2.35 (t, *J* = 7.3 Hz, 2H), 2.12–2.00 (m, 4H), 1.77–1.68 (m, 2H), 1.68–1.62 (m, 2H), 1.47–1.21 (m, 12H). The characterization data are consistent with those previously reported[18].

15. NMR spectra

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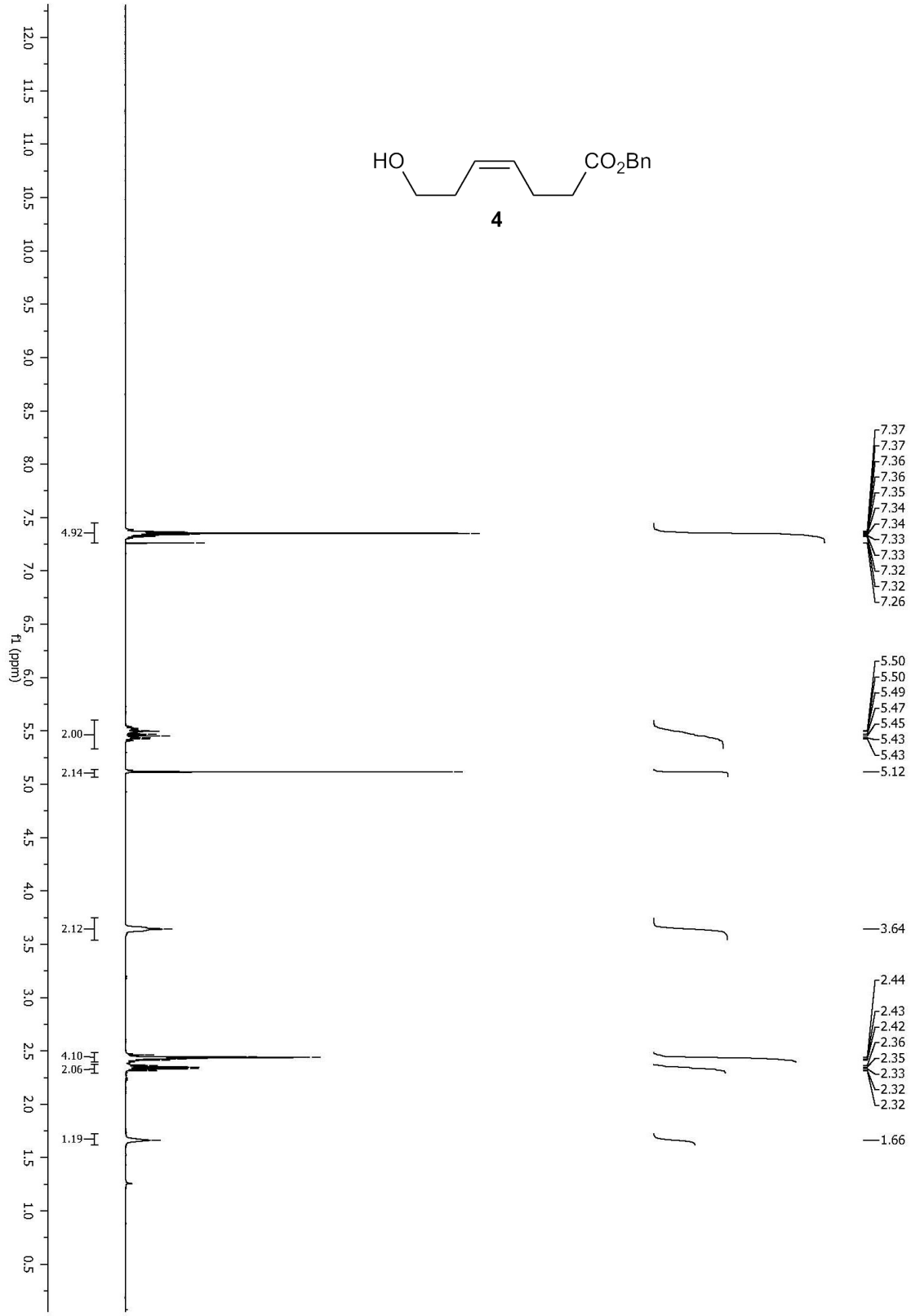
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7.32
7.32
7.26
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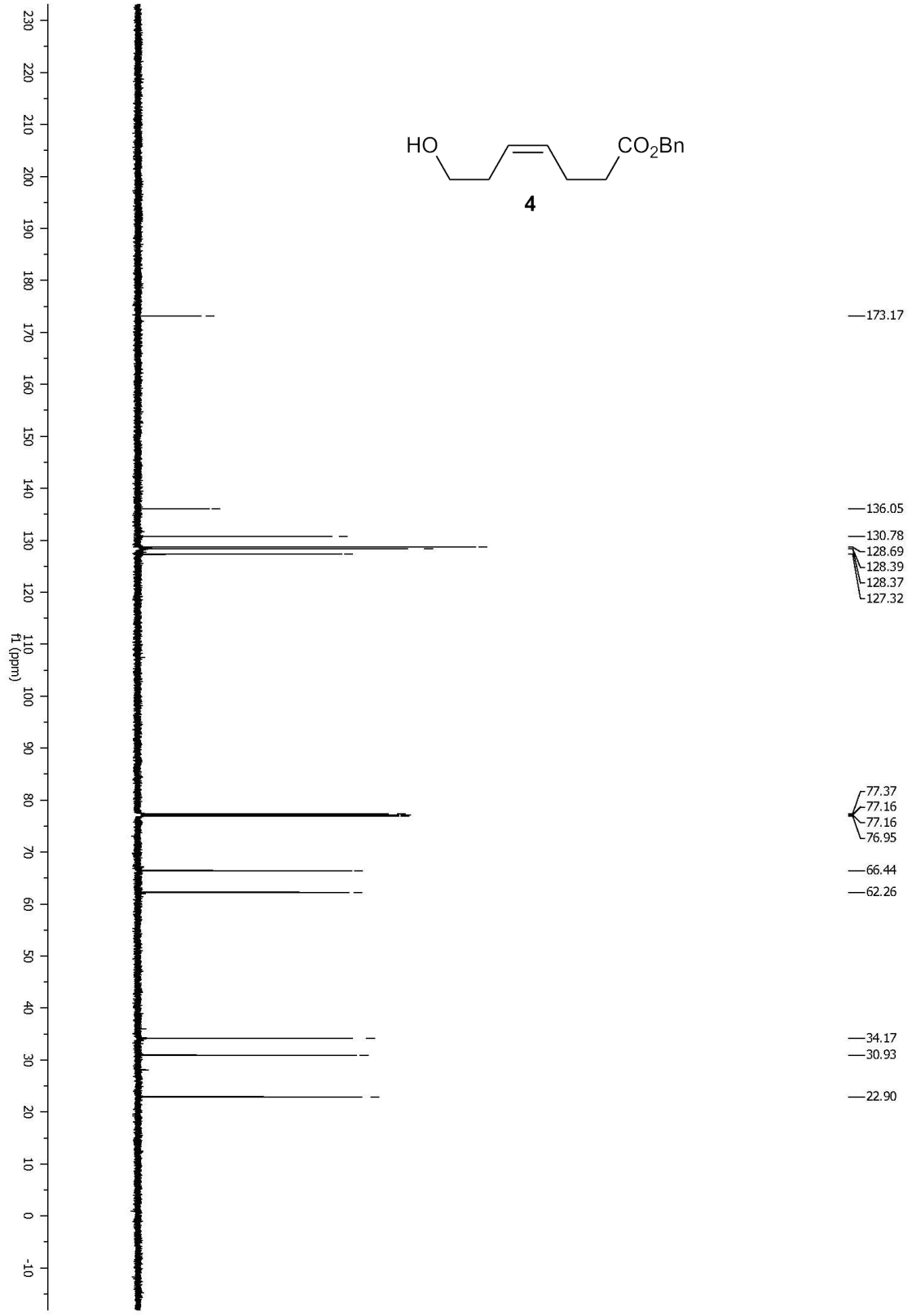
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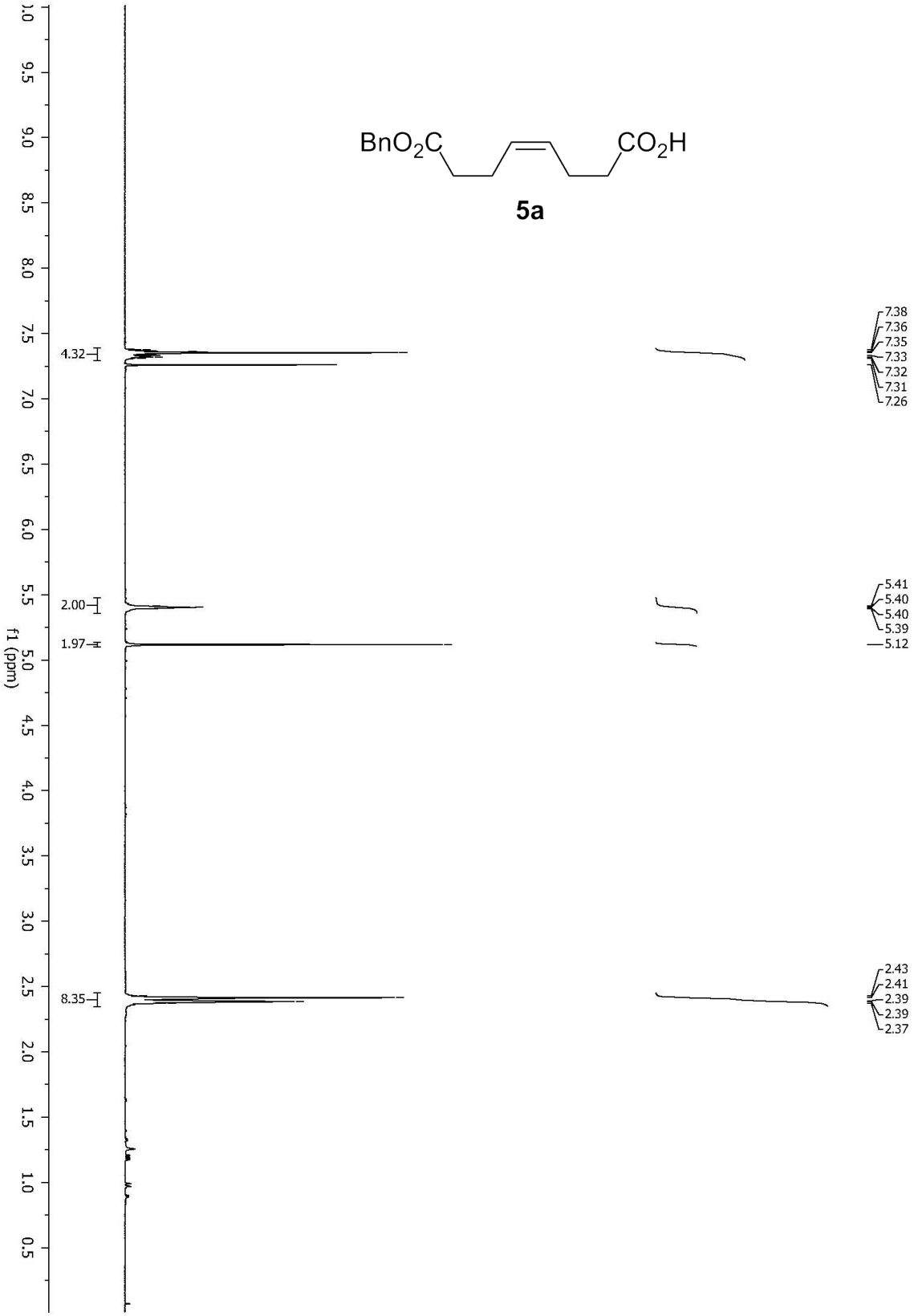
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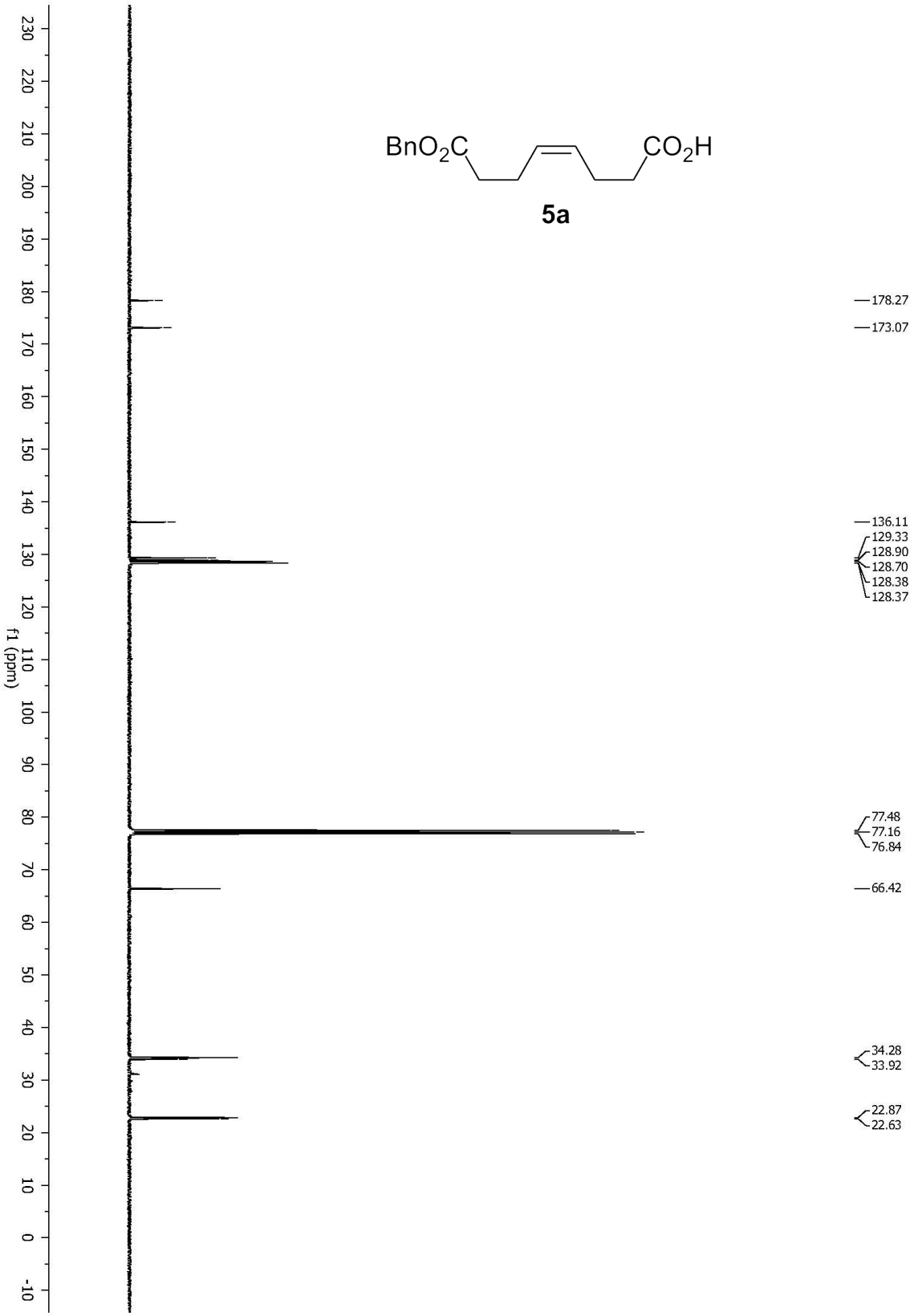
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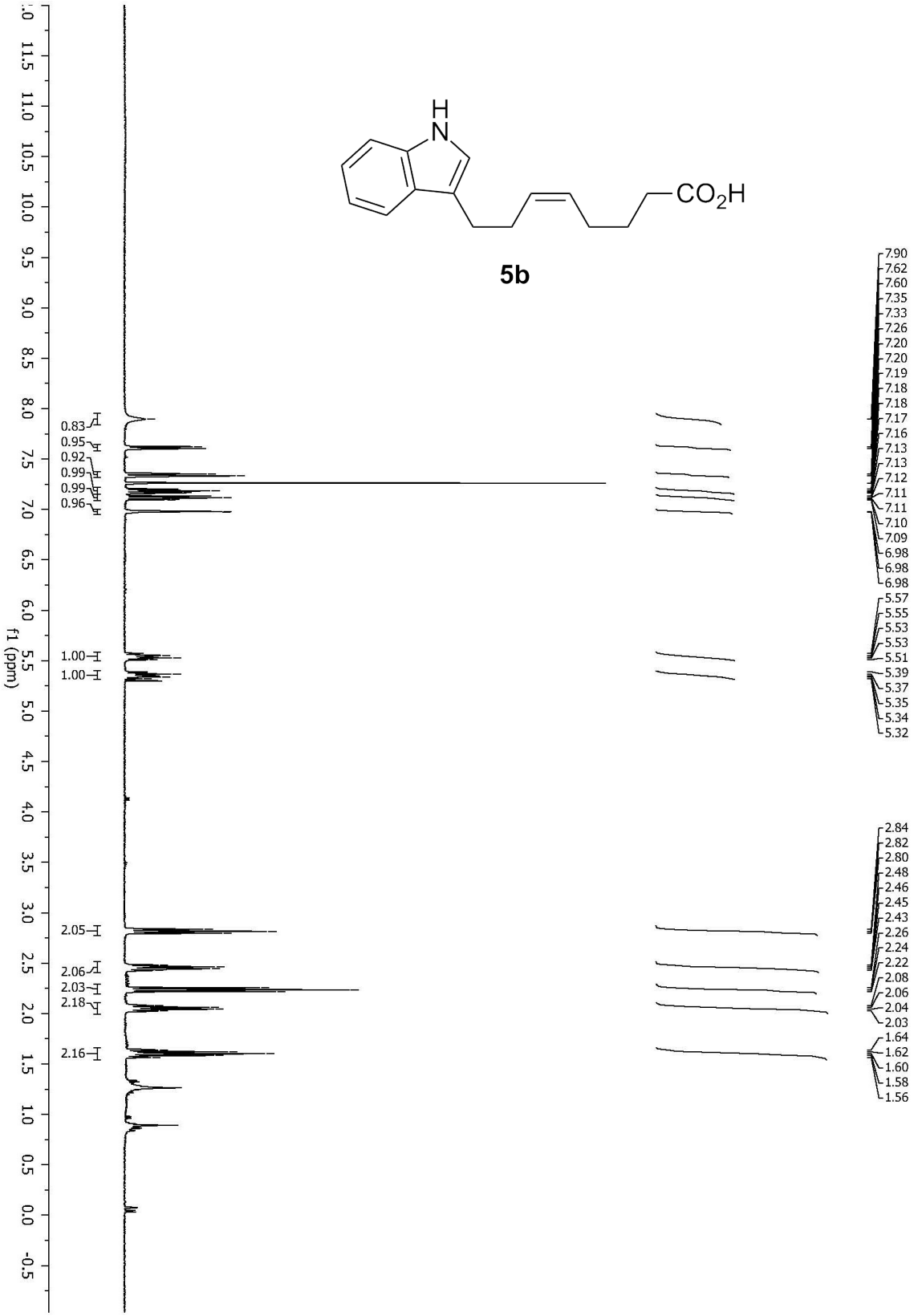
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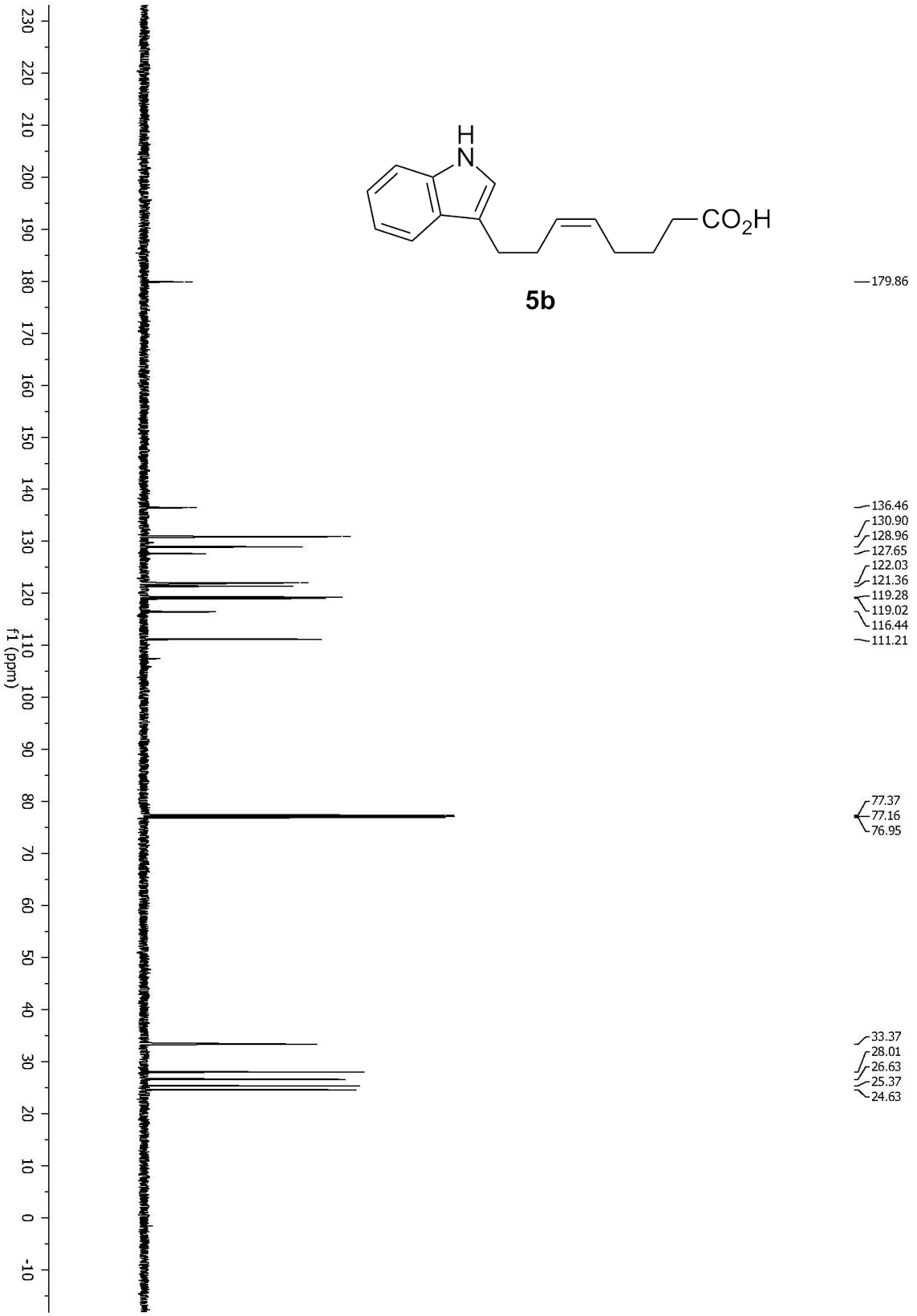
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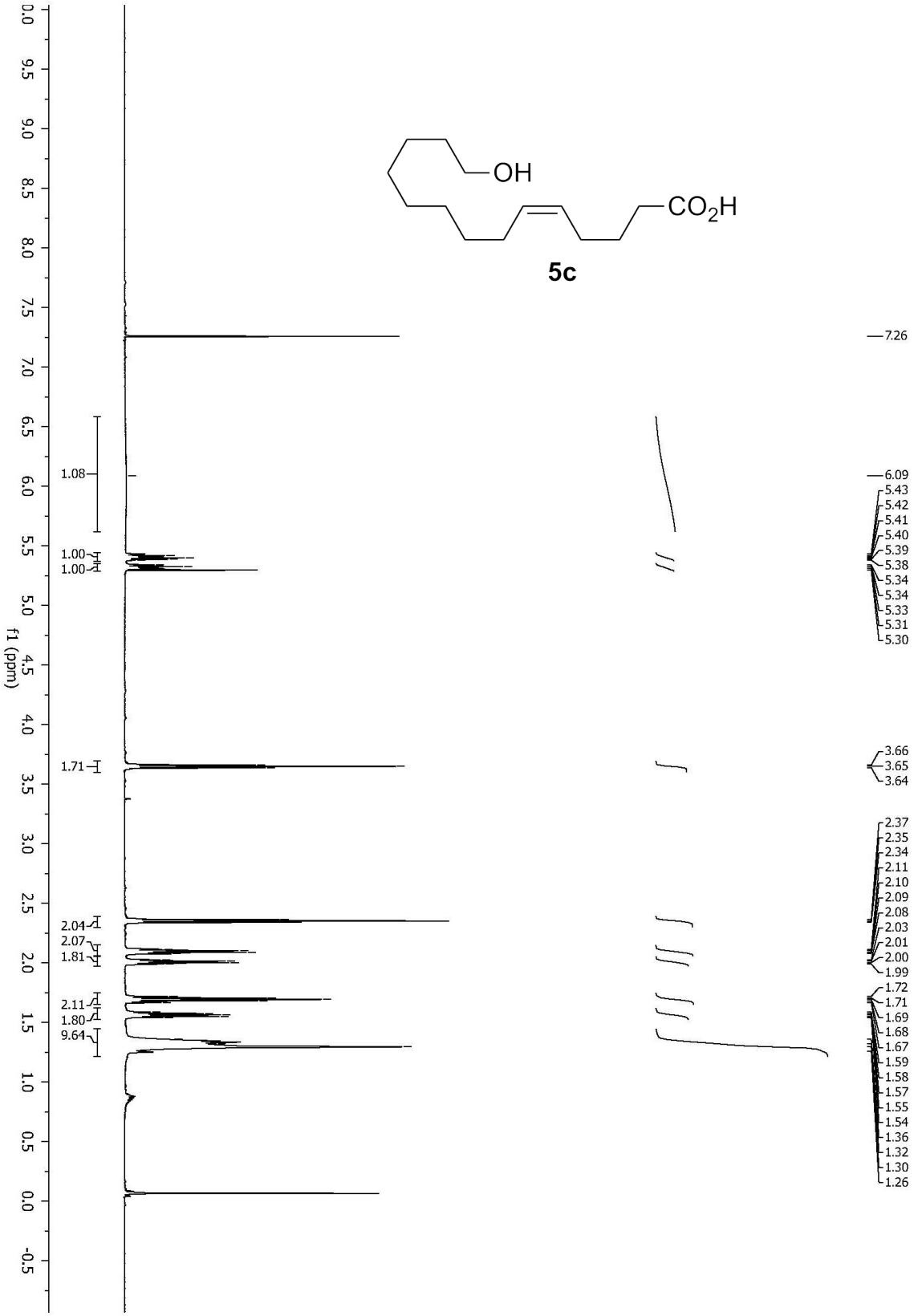
24.63
f1 (ppm)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5.34
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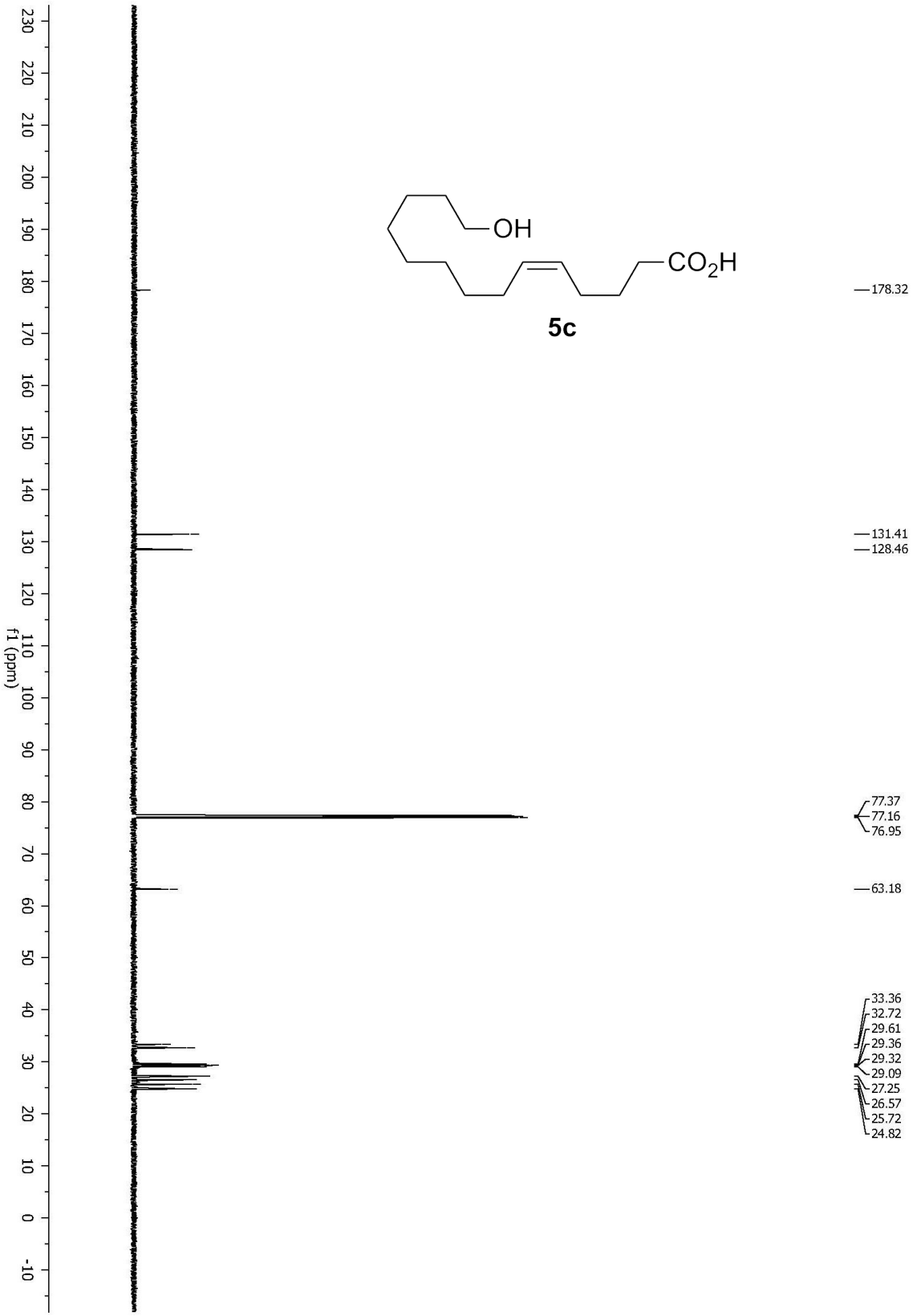
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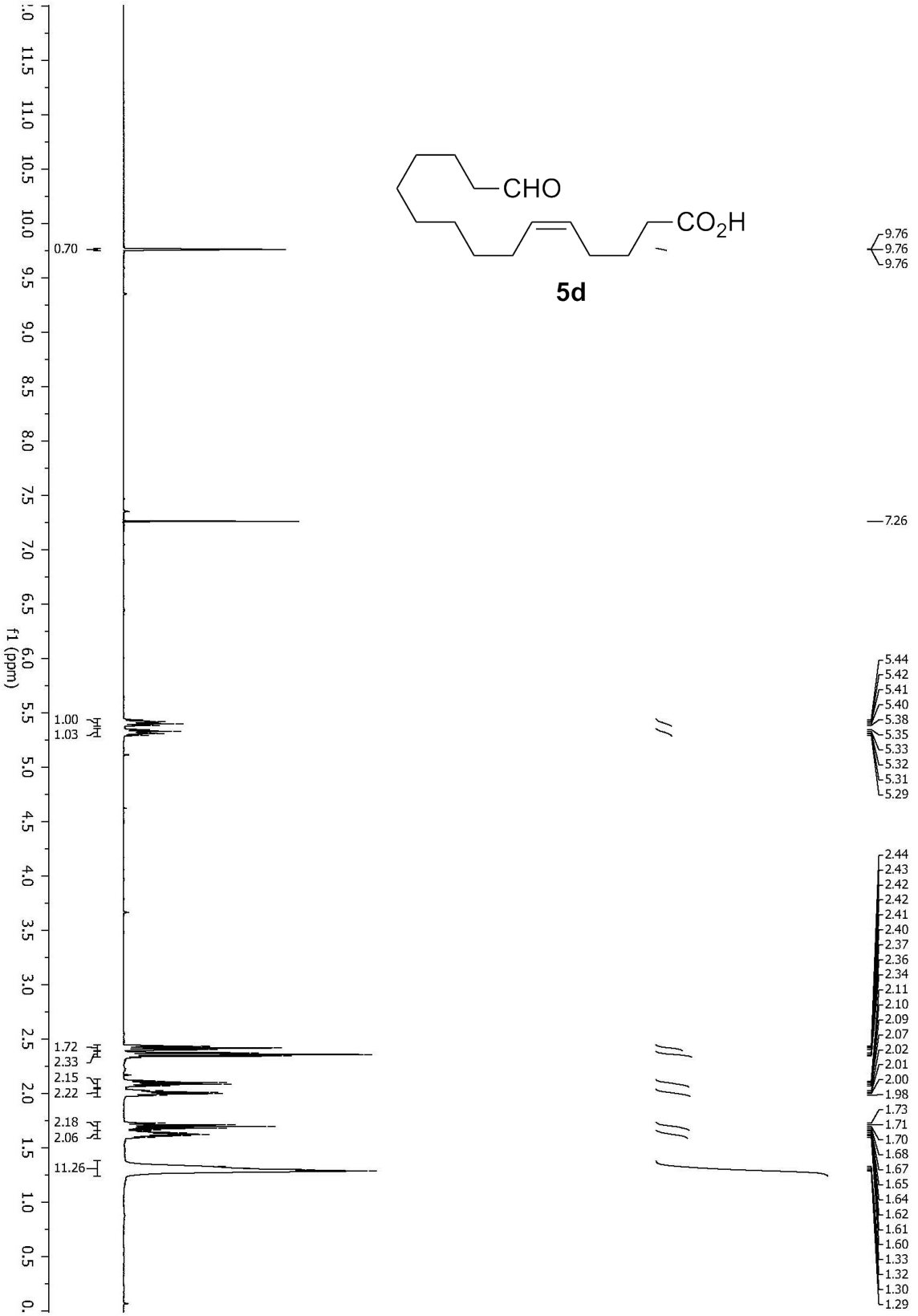
f1 (ppm)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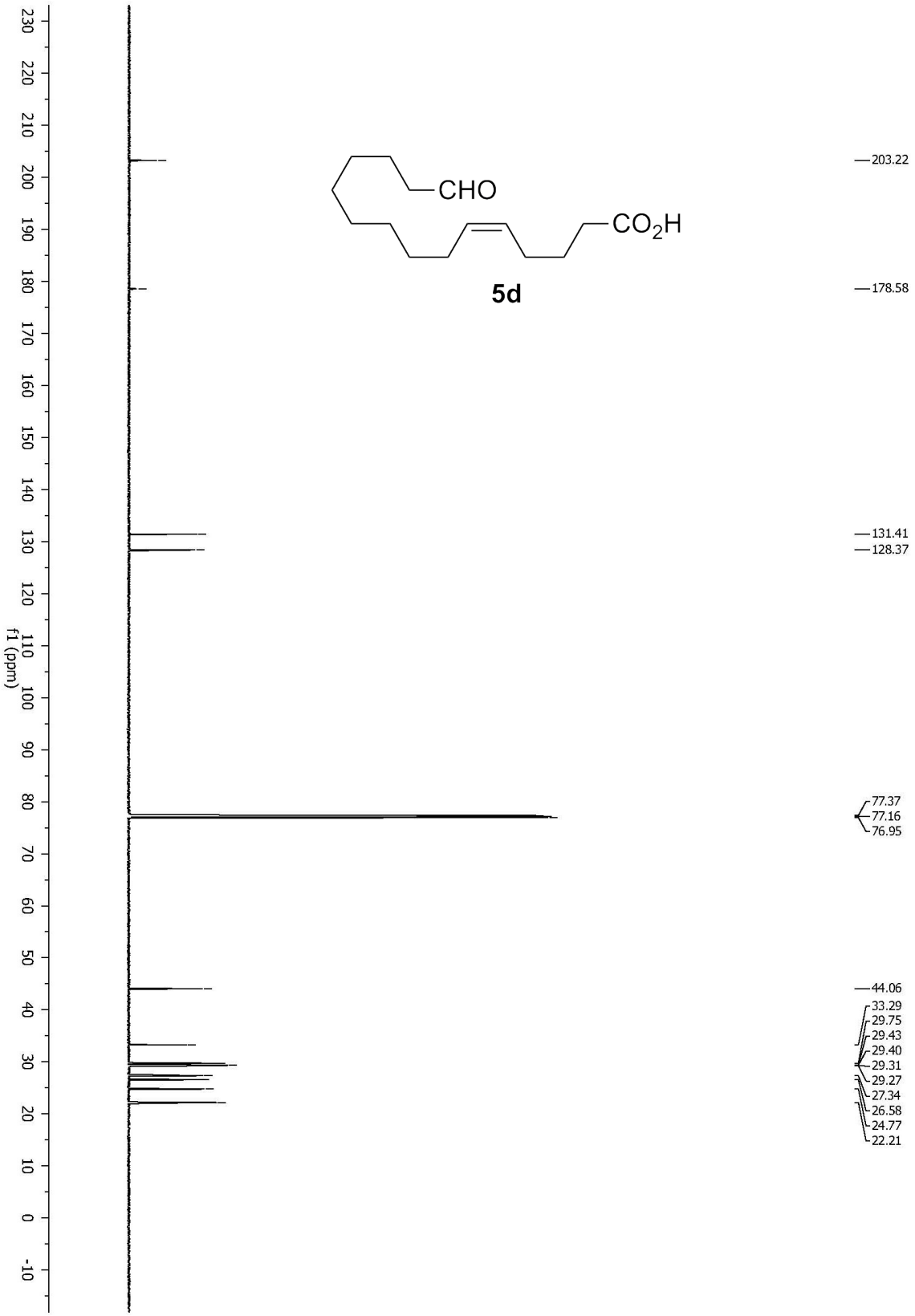
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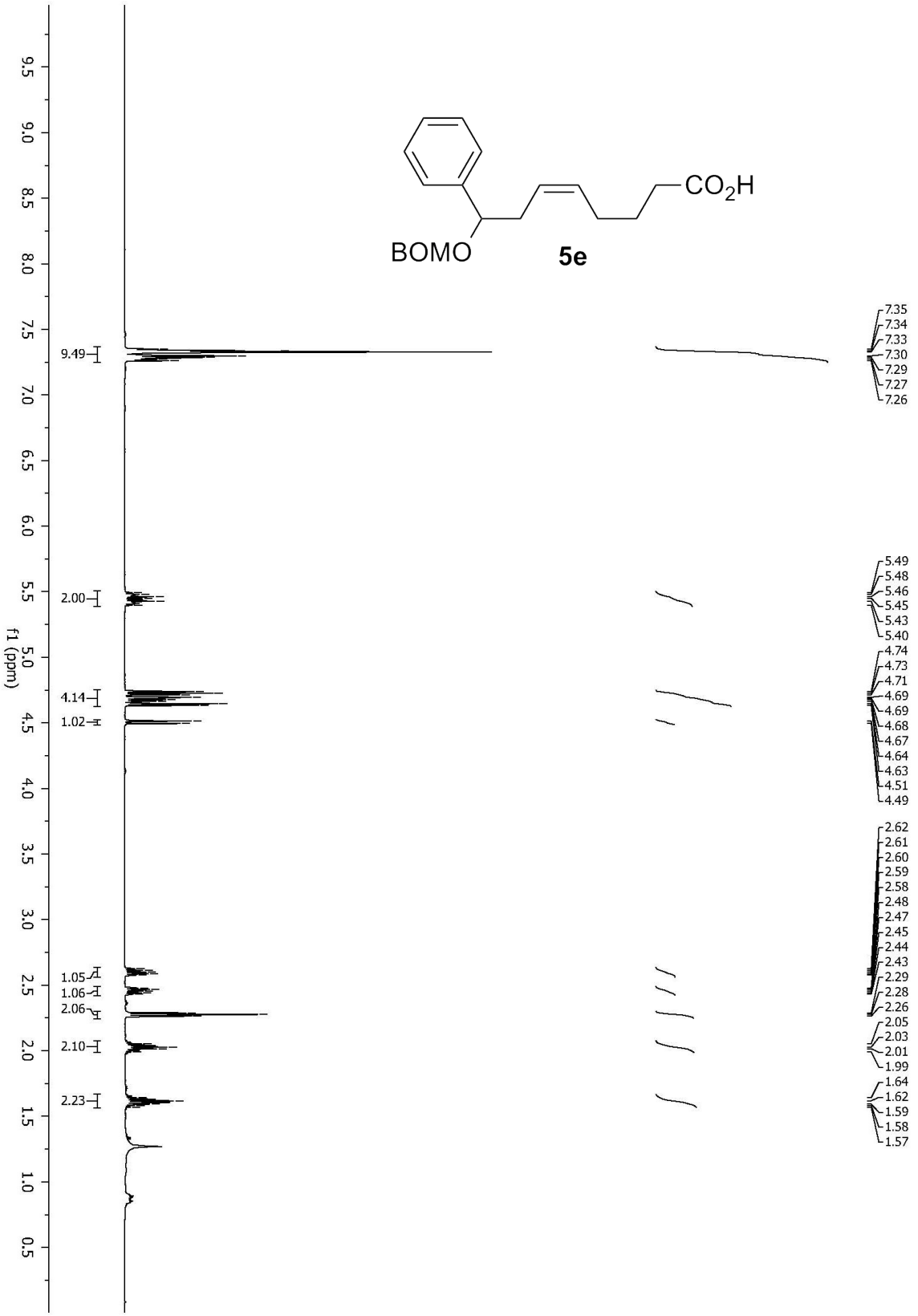
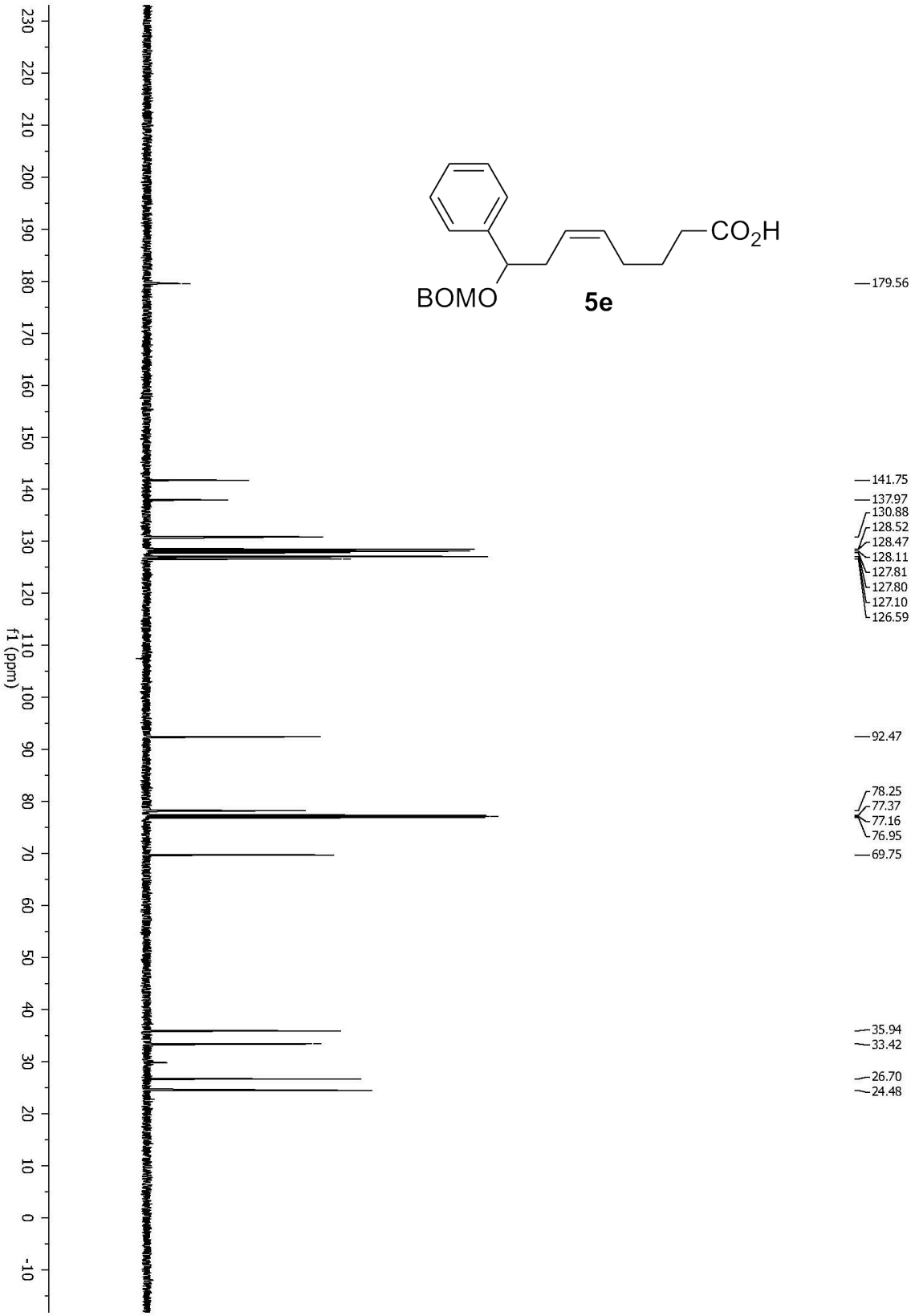
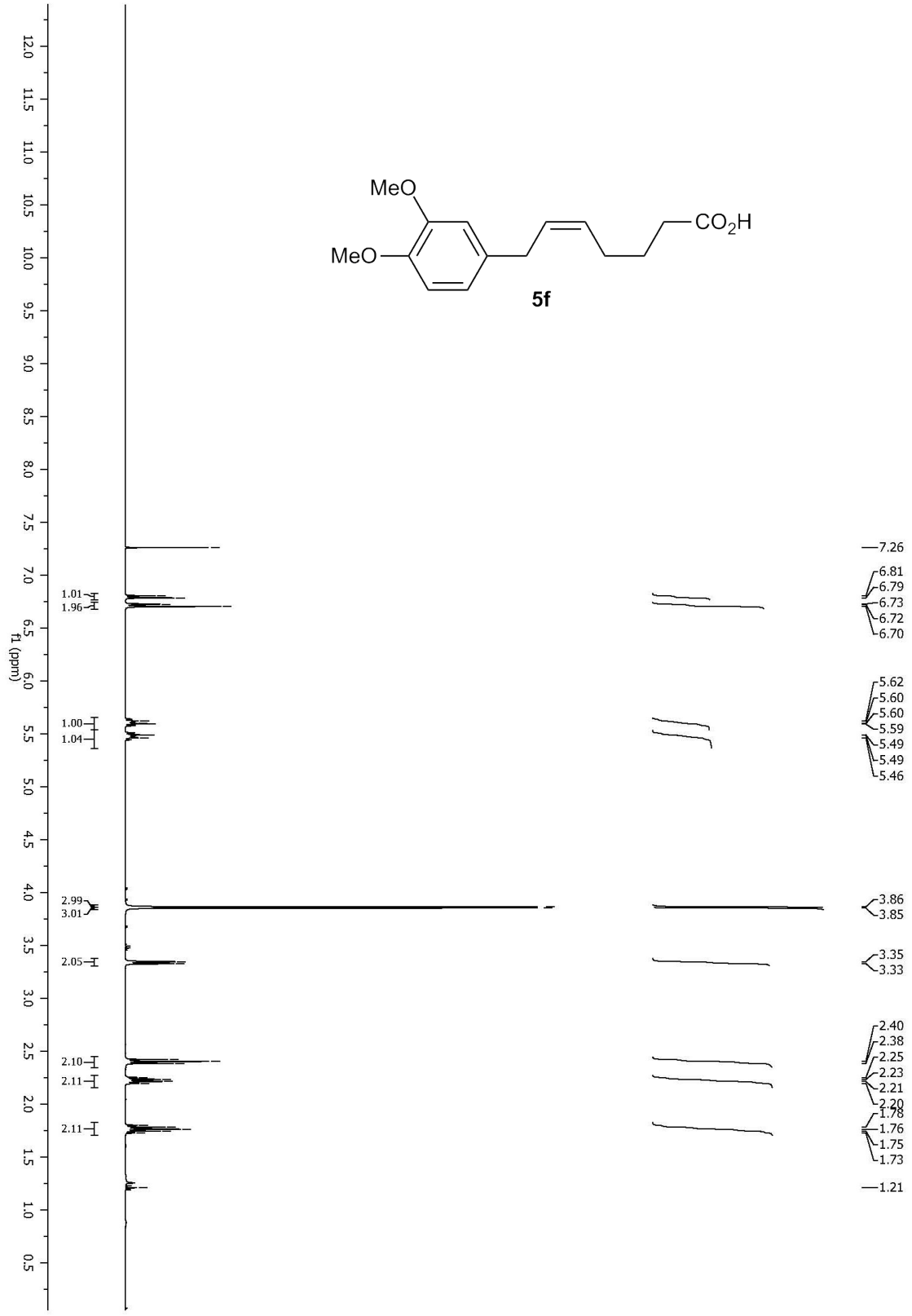
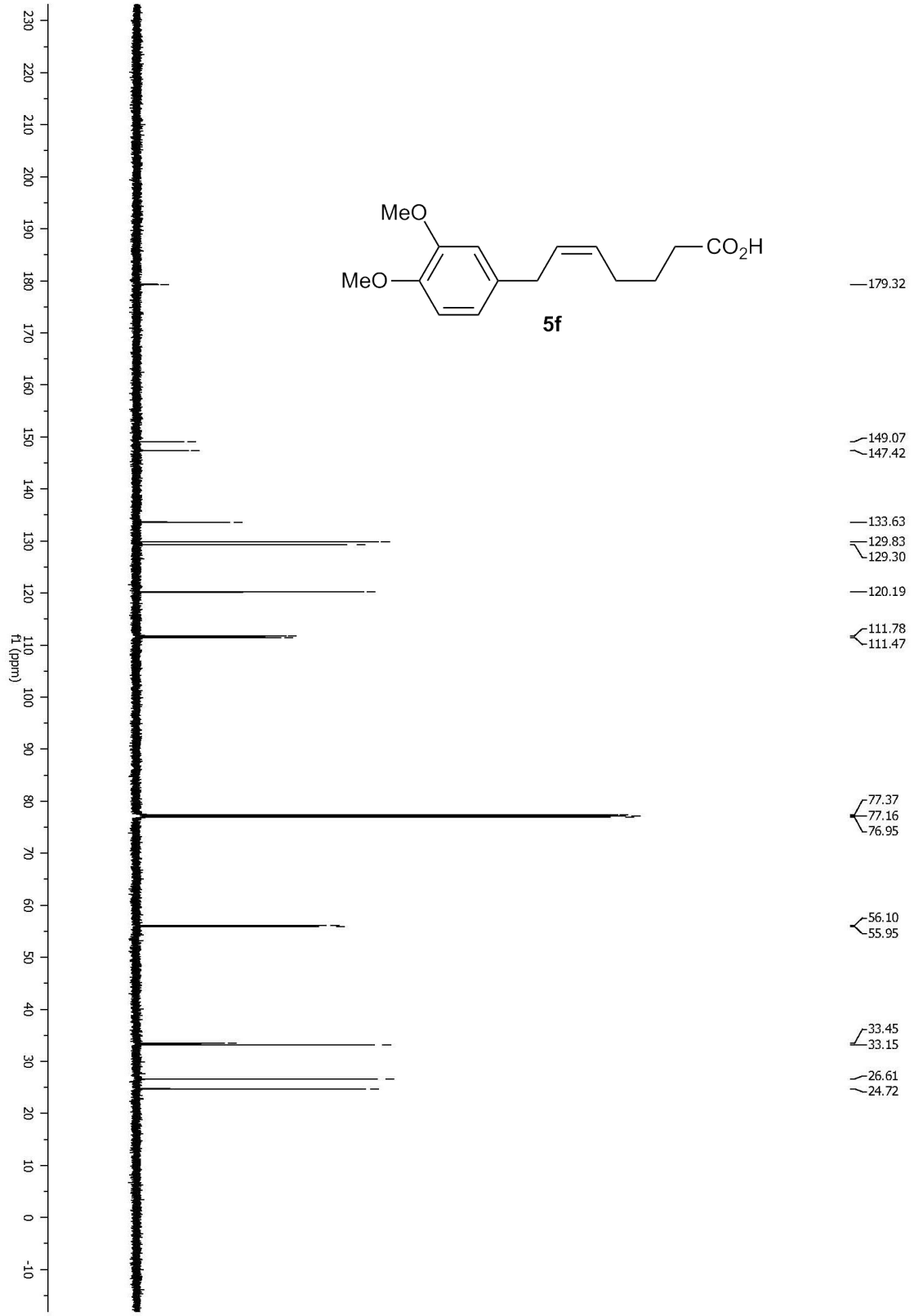
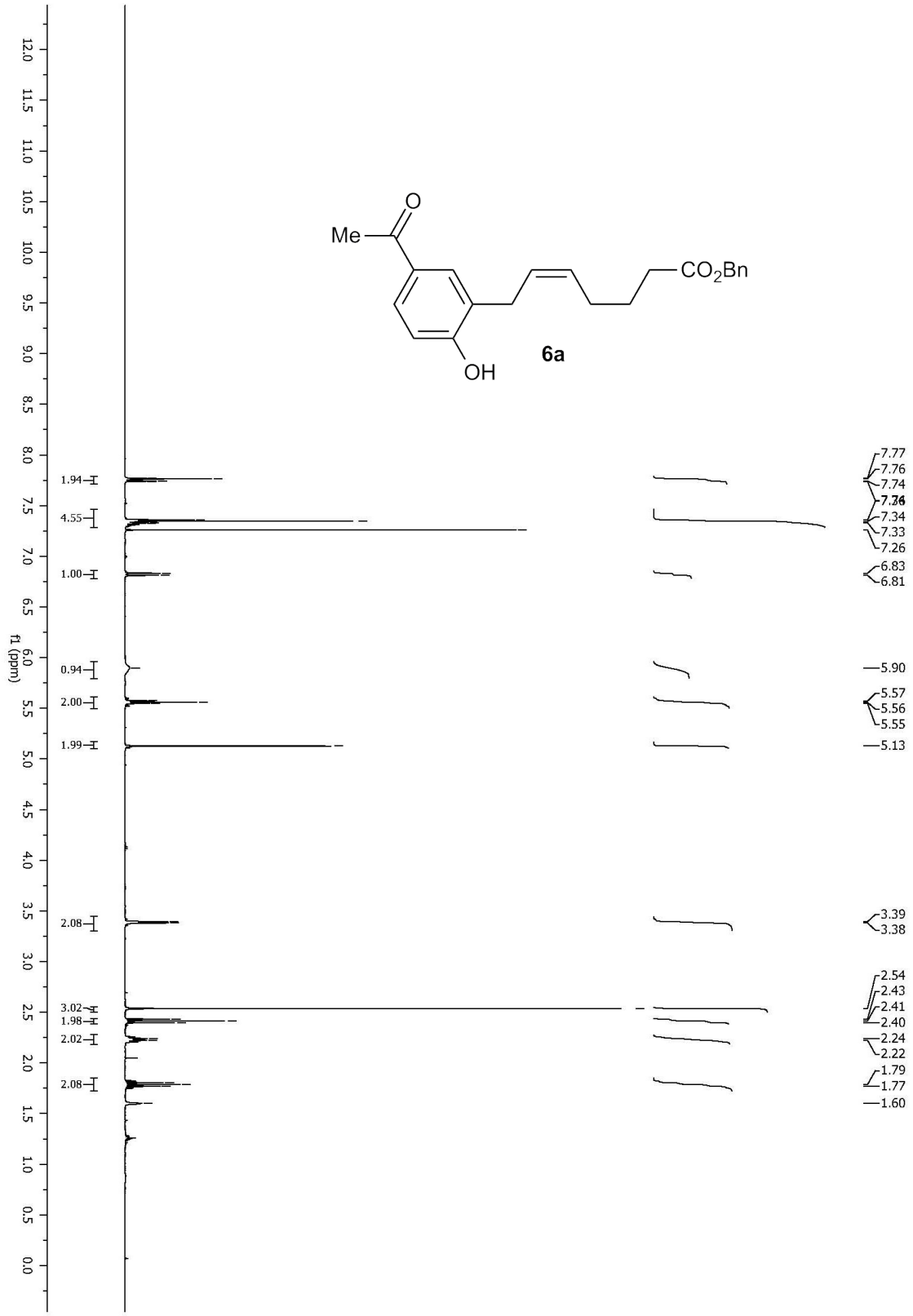
29.43
29.40
29.31
29.27
27.34
26.58
24.77
22.21
f1 (ppm)

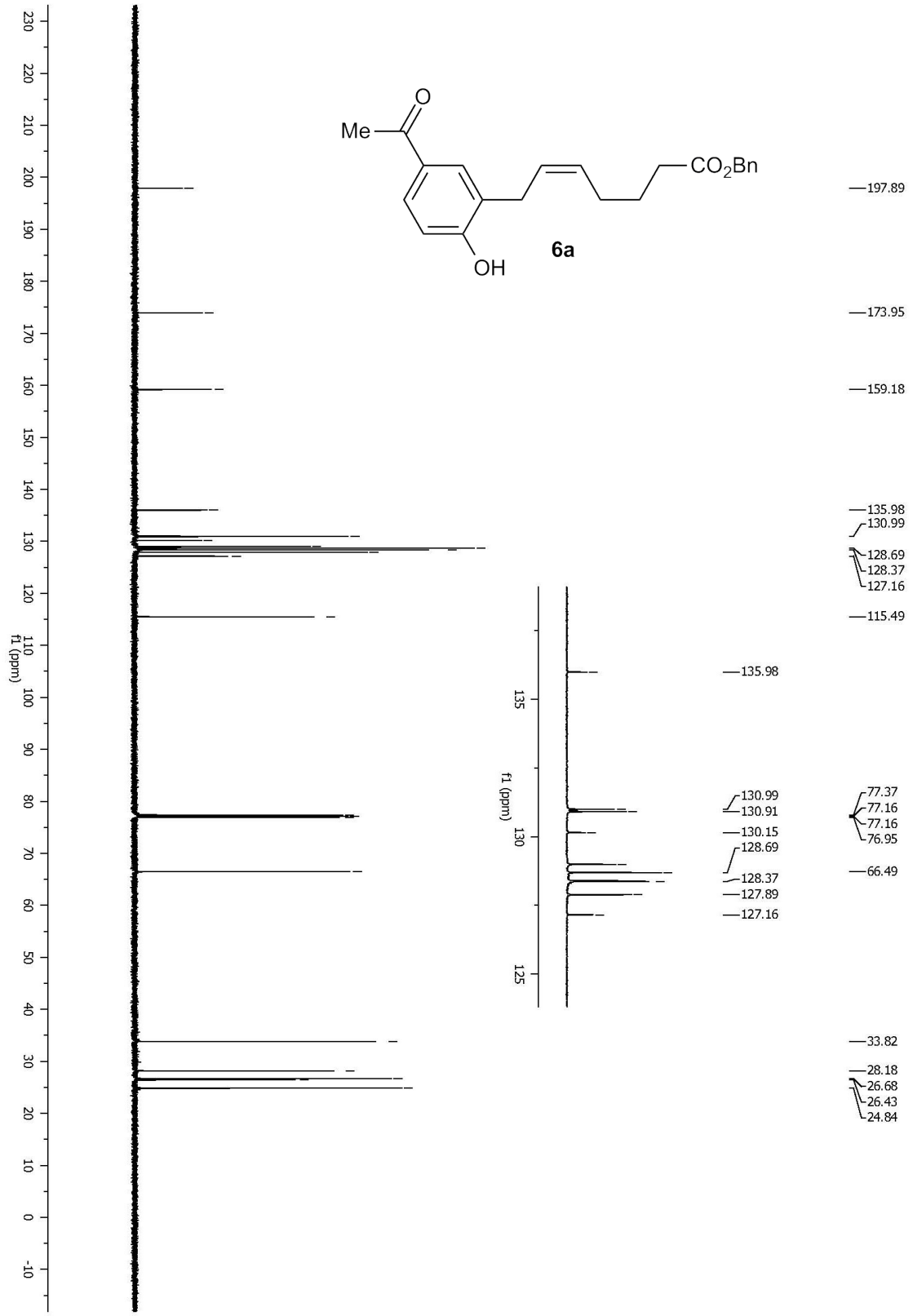

BOMO
CO_2H
5e
f1 (ppm)
9.49
2.00
4.14
1.02
1.05
1.06
2.06
2.10
2.23
7.35
7.34
7.33
7.30
7.29
7.27
7.26
5.49
5.48
5.46
5.45
5.43
5.40
4.74
4.73
4.71
4.69
4.69
4.68
4.67
4.64
4.63
4.51
4.49
2.62
2.61
2.60
2.59
2.58
2.48
2.47
2.45
2.44
2.43
2.29
2.28
2.26
2.05
2.03
2.01
1.99
1.64
1.62
1.59
1.58
1.57

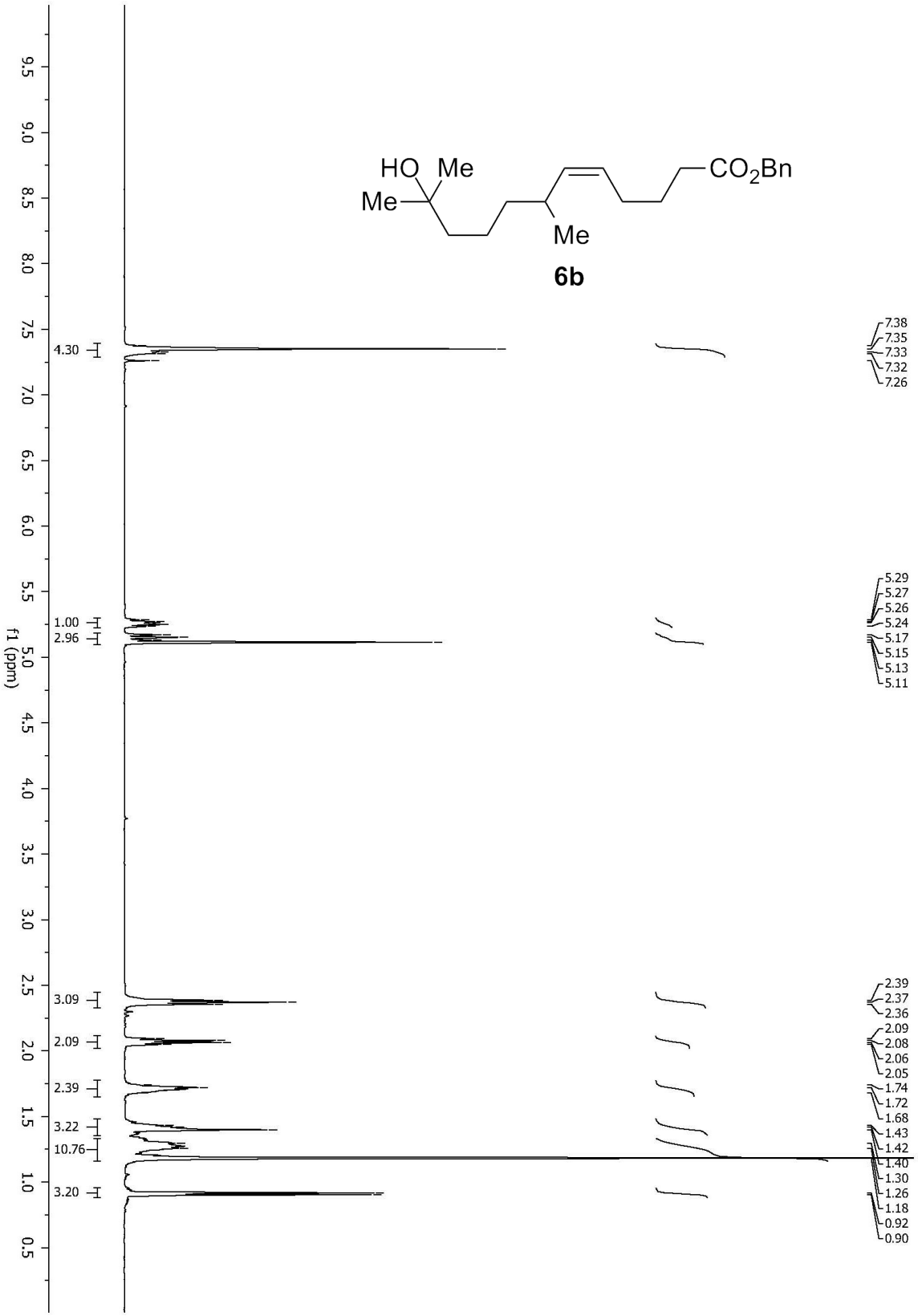

BOMO
CO2H
5e
179.56
141.75
137.97
130.88
128.52
128.47
128.11
127.81
127.80
127.10
126.59
92.47
78.25
77.37
77.16
76.95
69.75
35.94
33.42
26.70
24.48
f1 (ppm)

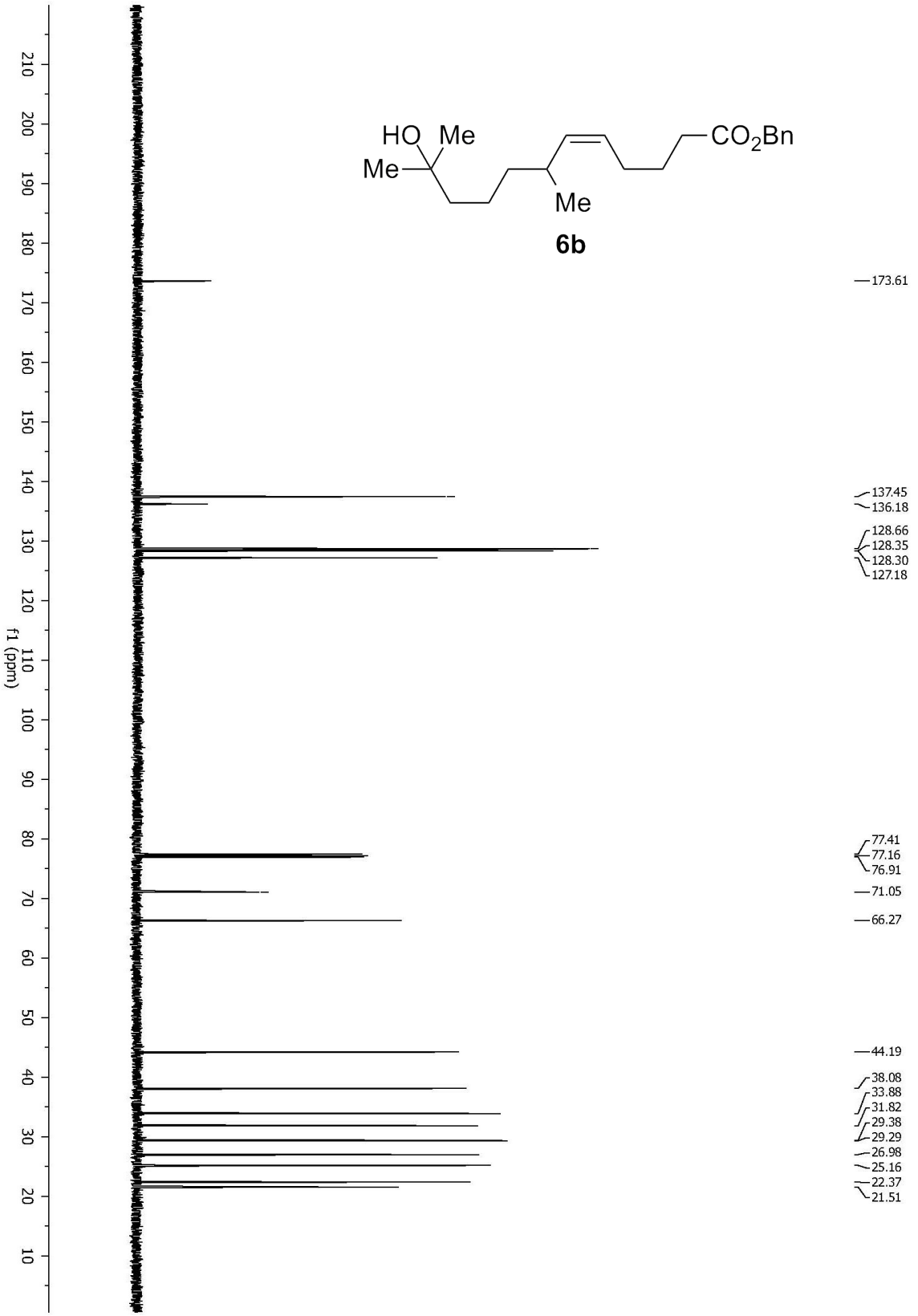

MeO
MeO
CO2H
5f
f1 (ppm)
1.01
1.96
1.00
1.04
2.99
3.01
2.05
2.10
2.11
2.11
7.26
6.81
6.79
6.73
6.72
6.70
5.62
5.60
5.60
5.59
5.49
5.49
5.46
3.86
3.85
3.35
3.33
2.40
2.38
2.25
2.23
2.21
2.20
1.78
1.76
1.75
1.73
1.21

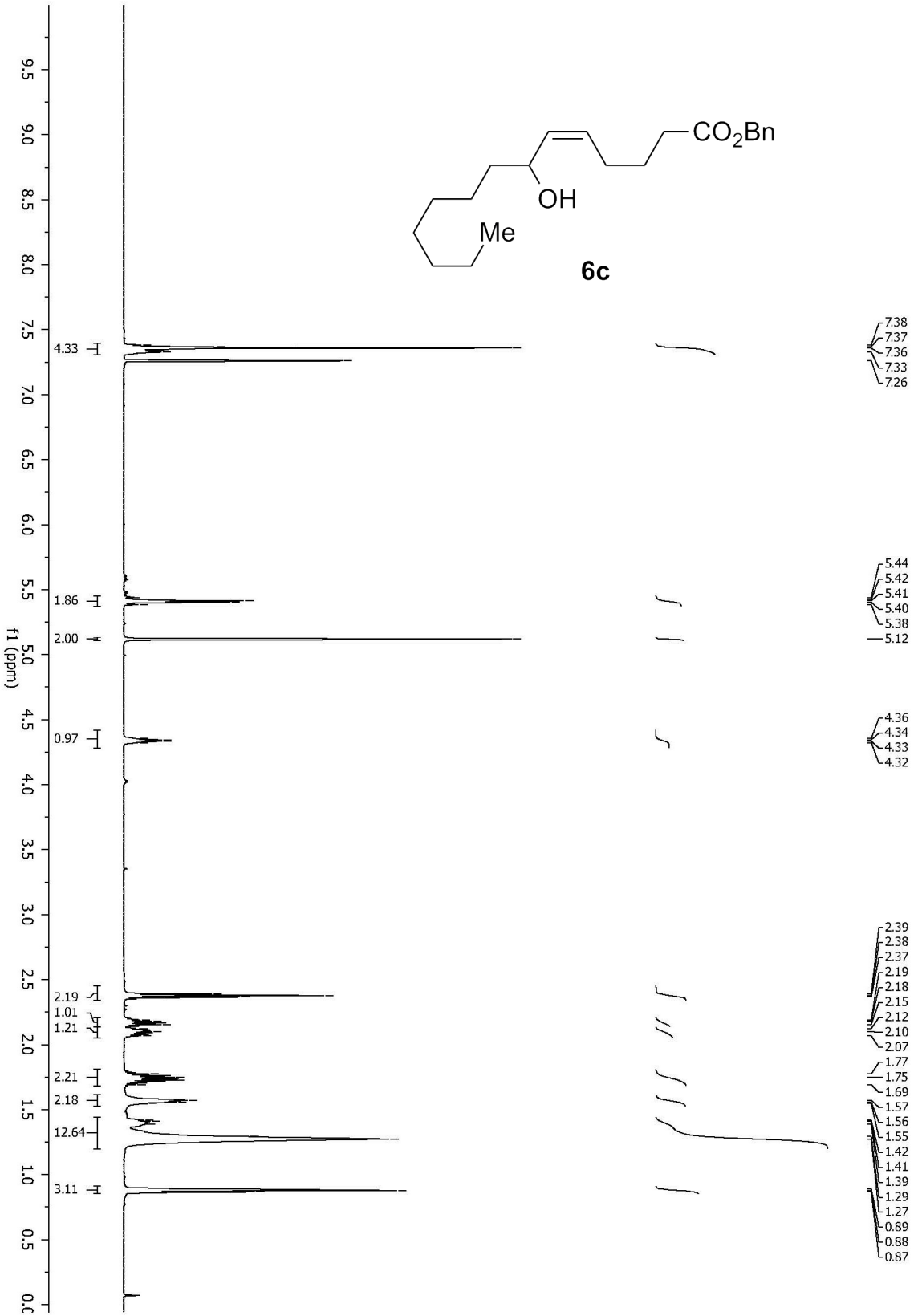

MeO
MeO
CO2H
5f
179.32
149.07
147.42
133.63
129.83
129.30
120.19
111.78
111.47
77.37
77.16
76.95
56.10
55.95
33.45
33.15
26.61
24.72
f1 (ppm)

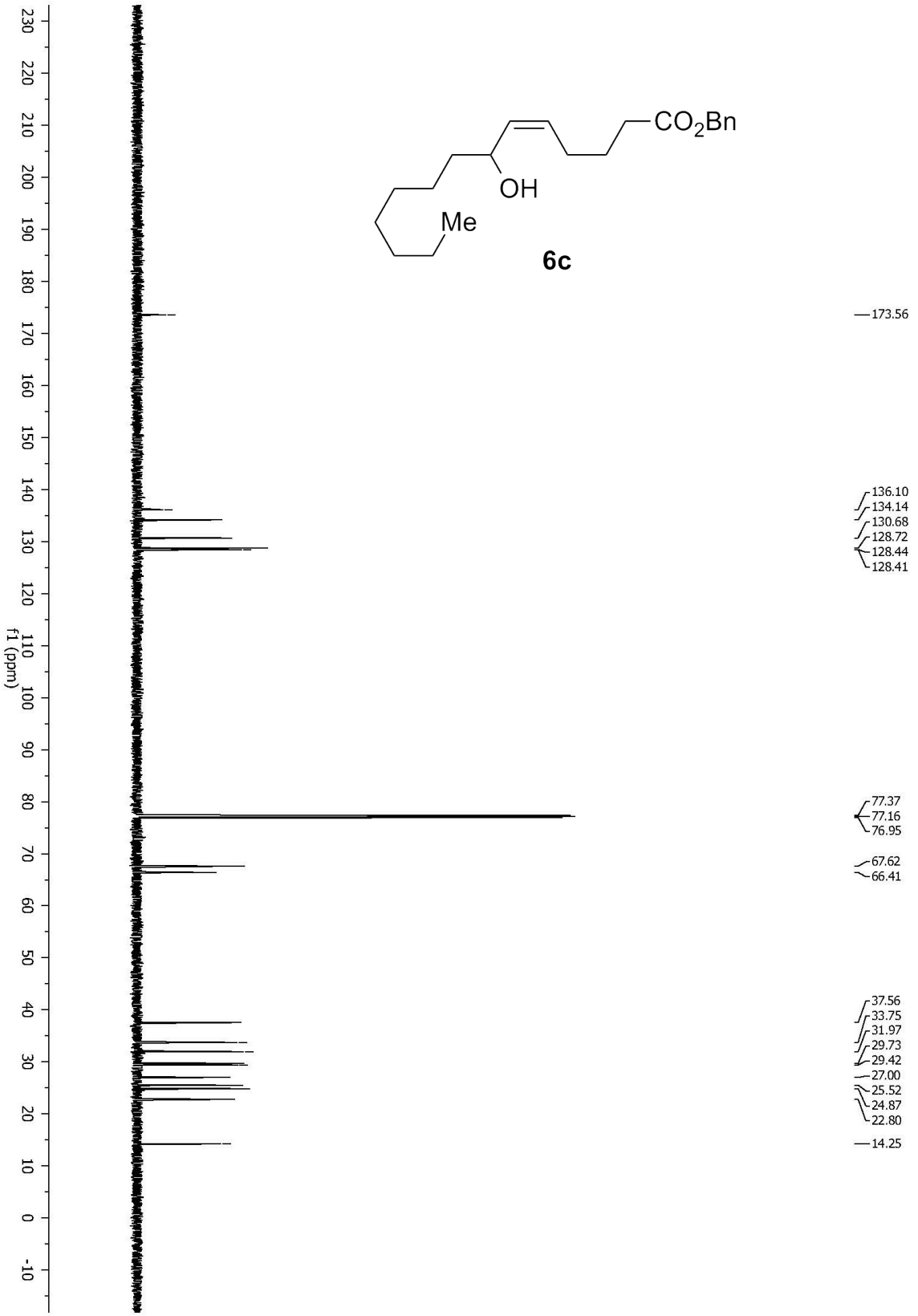

Me
O
CO2Bn
OH
6a
f1 (ppm)
1.94
4.55
1.00
0.94
2.00
1.99
2.08
3.02
1.98
2.02
2.08
7.77
7.76
7.74
7.34
7.33
7.26
6.83
6.81
5.90
5.57
5.56
5.55
5.13
3.39
3.38
2.54
2.43
2.41
2.40
2.24
2.22
1.79
1.77
1.60

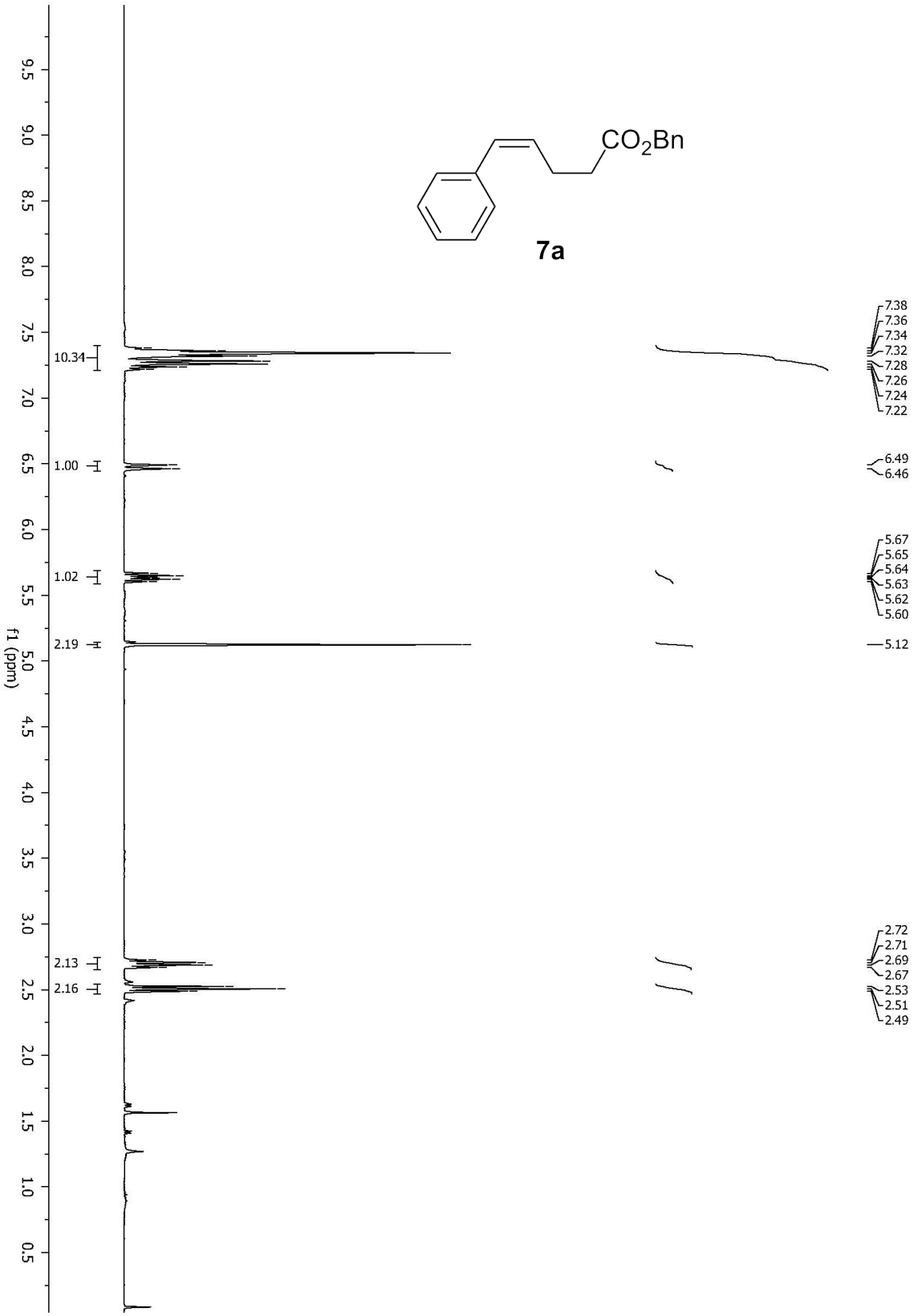

O
Me
CO2Bn
OH
6a
197.89
173.95
159.18
135.98
130.99
128.69
128.37
127.16
115.49
f1 (ppm)
135.98
130.99
130.91
130.15
128.69
128.37
127.89
127.16
77.37
77.16
77.16
76.95
66.49
33.82
28.18
26.68
26.43
24.84

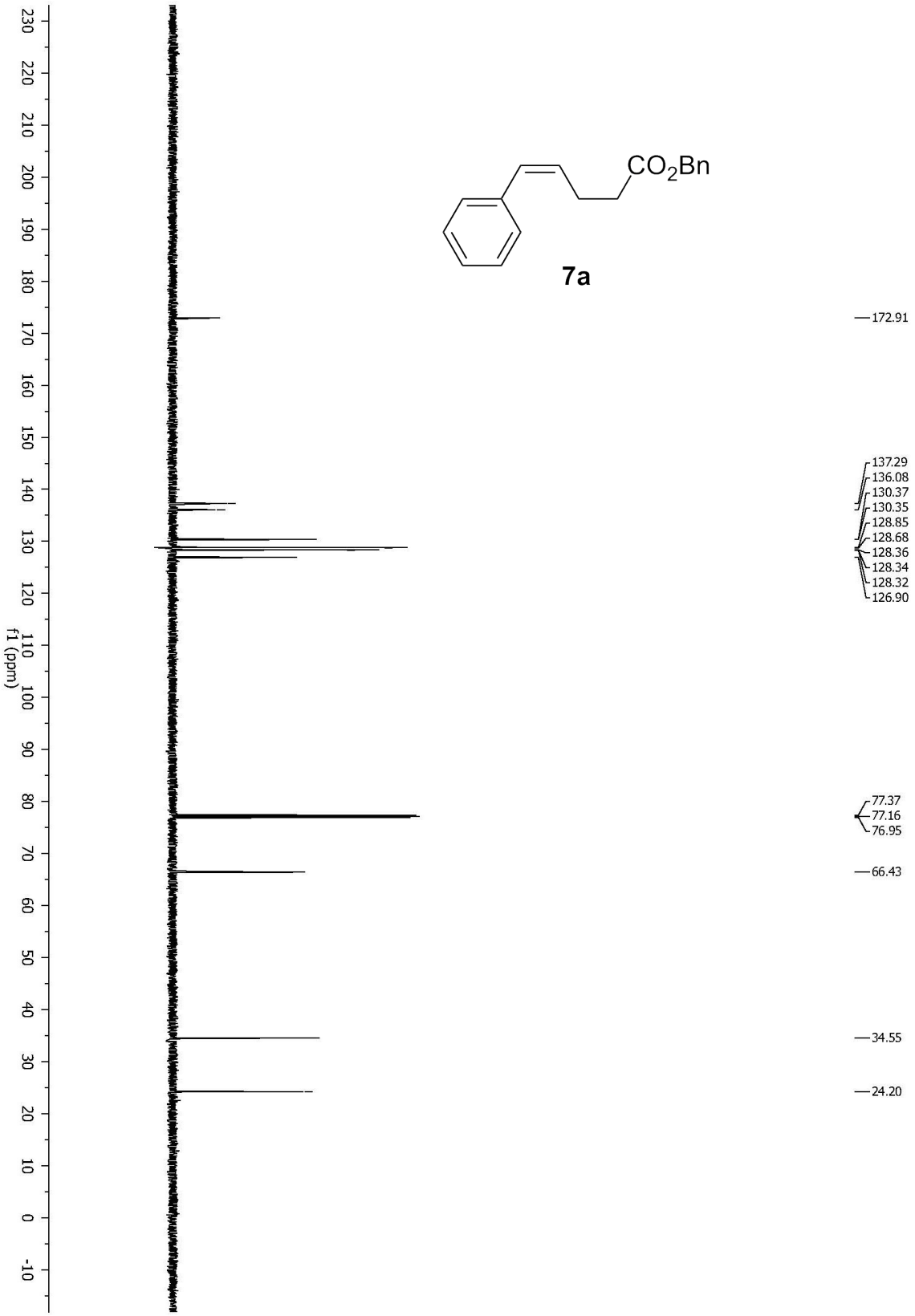

HO Me
Me
Me
CO2Bn
6b
f1 (ppm)
4.30
1.00
2.96
3.09
2.09
2.39
3.22
10.76
3.20
7.38
7.35
7.33
7.32
7.26
5.29
5.27
5.26
5.24
5.17
5.15
5.13
5.11
2.39
2.37
2.36
2.09
2.08
2.06
2.05
1.74
1.72
1.68
1.43
1.42
1.40
1.30
1.26
1.18
0.92
0.90

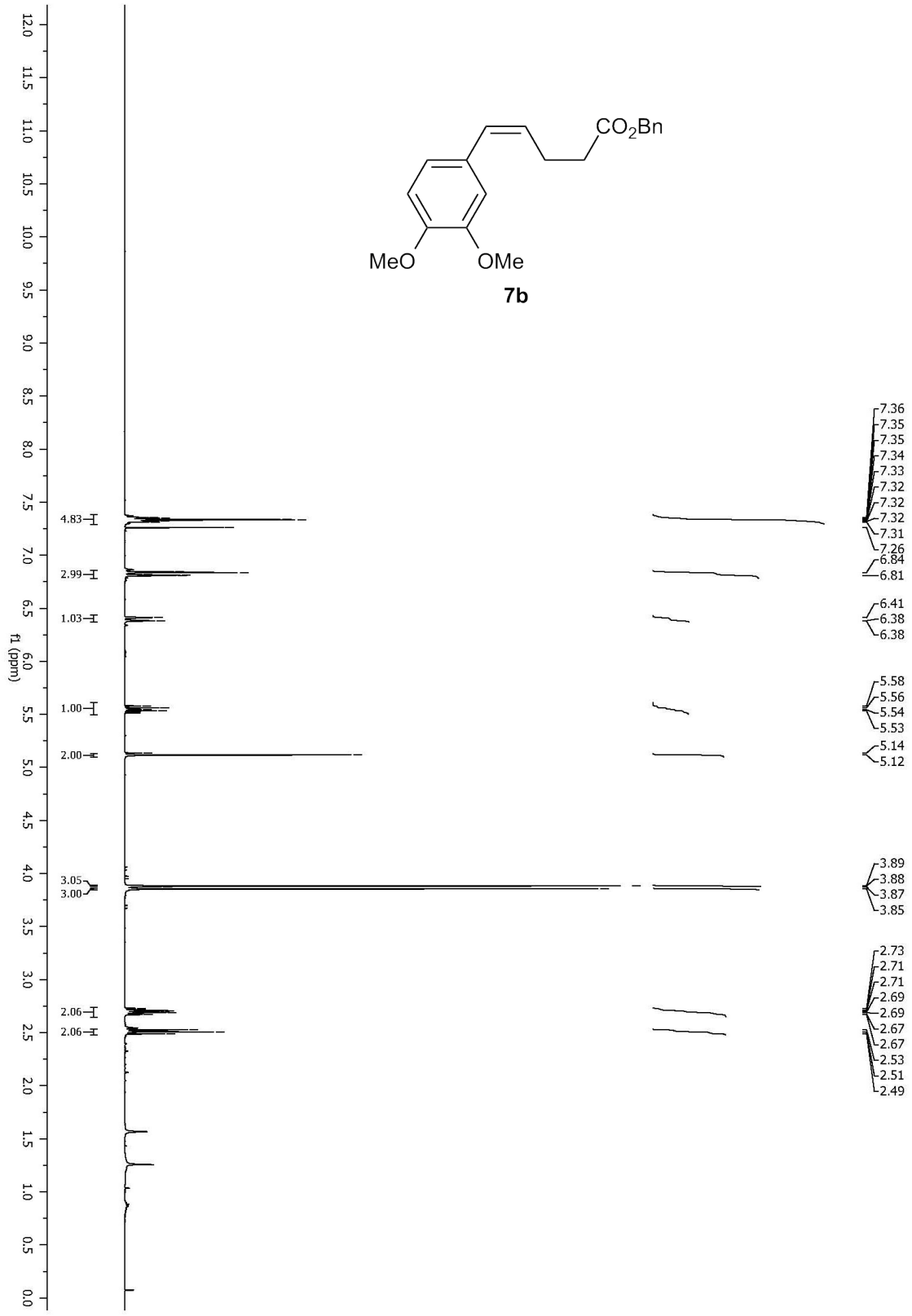

HO Me
Me
Me
CO_2Bn
6b
173.61
137.45
136.18
128.66
128.35
128.30
127.18
77.41
77.16
76.91
71.05
66.27
44.19
38.08
33.88
31.82
29.38
29.29
26.98
25.16
22.37
21.51
f1 (ppm)

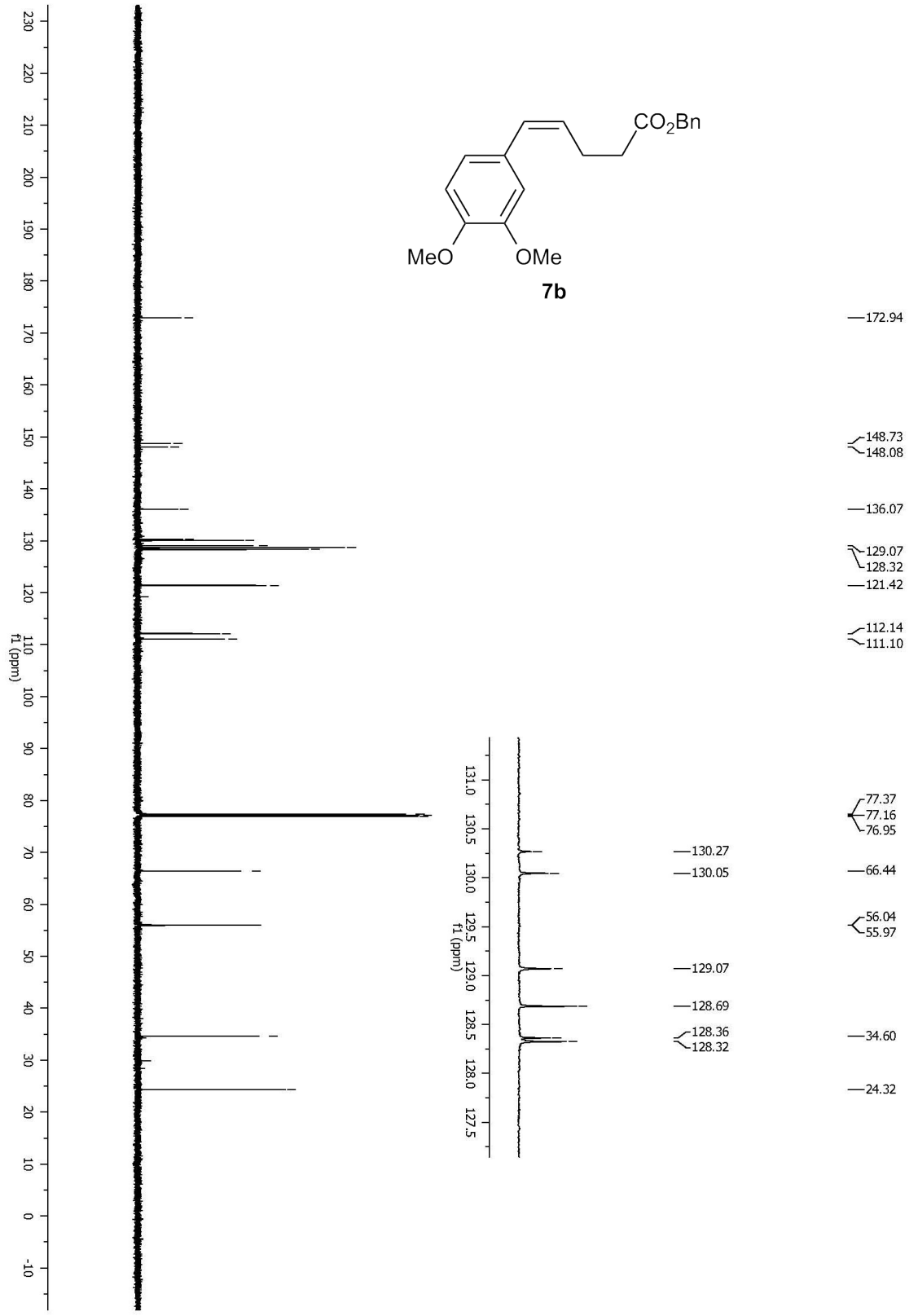

CO2Bn
OH
Me
6c
f1 (ppm)
4.33
1.86
2.00
0.97
2.19
1.01
1.21
2.21
2.18
12.64
3.11
7.38
7.37
7.36
7.33
7.26
5.44
5.42
5.41
5.40
5.38
5.12
4.36
4.34
4.33
4.32
2.39
2.38
2.37
2.19
2.18
2.15
2.12
2.10
2.07
1.77
1.75
1.69
1.57
1.56
1.55
1.42
1.41
1.39
1.29
1.27
0.89
0.88
0.87

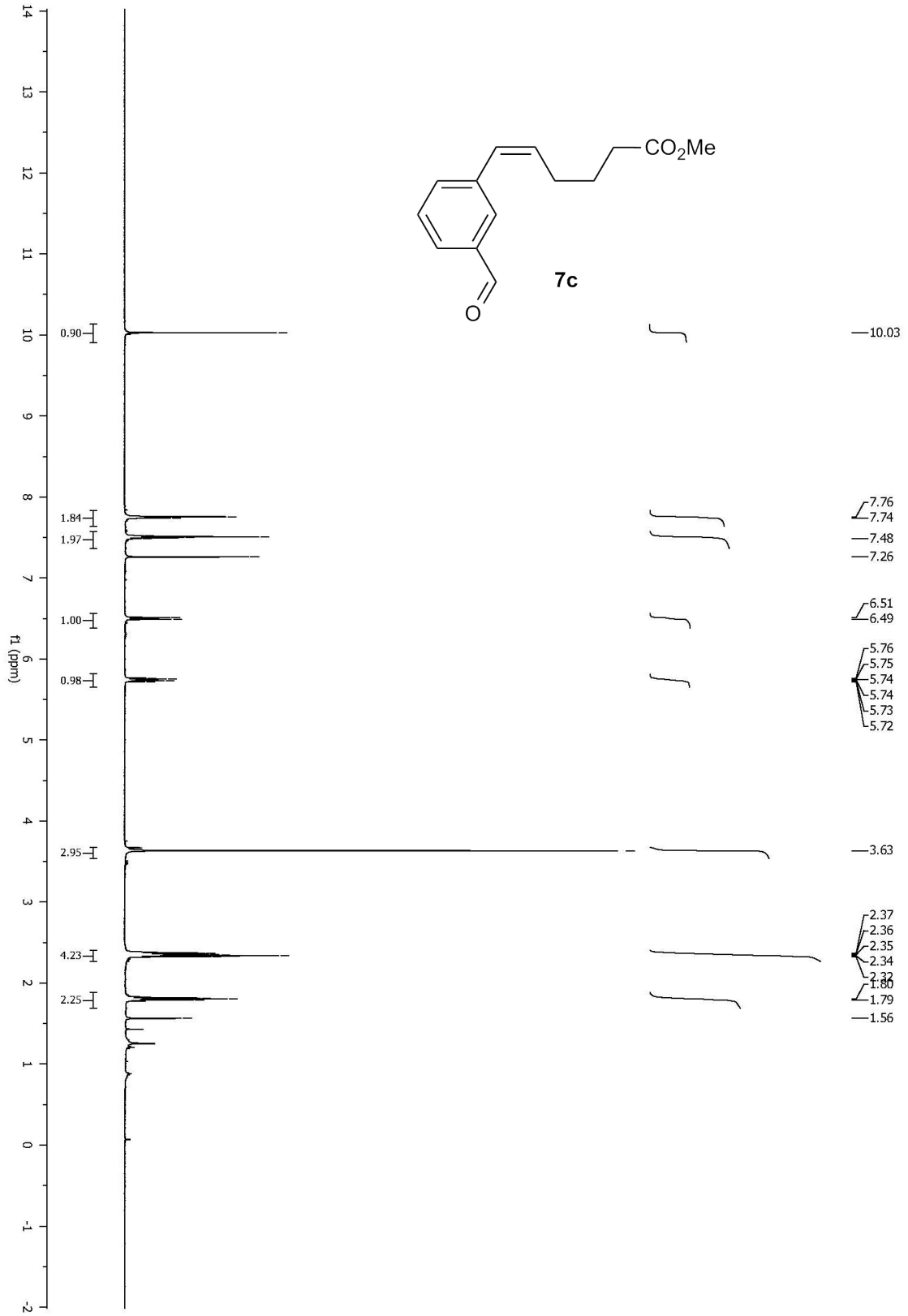

CO2Bn
OH
Me
6c
173.56
136.10
134.14
130.68
128.72
128.44
128.41
77.37
77.16
76.95
67.62
66.41
37.56
33.75
31.97
29.73
29.42
27.00
25.52
24.87
22.80
14.25
f1 (ppm)

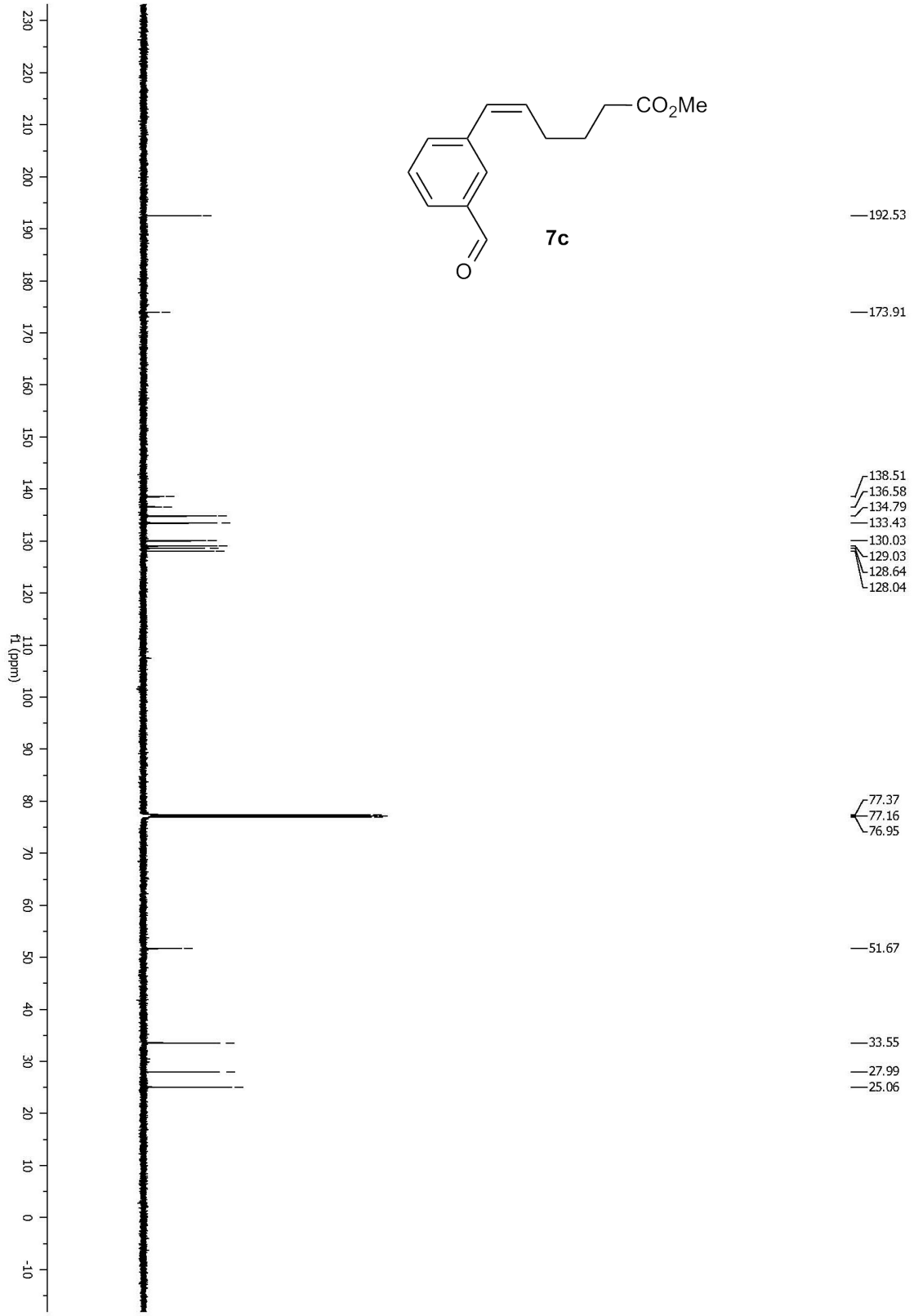

CO2Bn
7a
10.34
1.00
1.02
2.19
2.13
2.16
7.38
7.36
7.34
7.32
7.28
7.26
7.24
7.22
6.49
6.46
5.67
5.65
5.64
5.63
5.62
5.60
5.12
2.72
2.71
2.69
2.67
2.53
2.51
2.49
f1 (ppm)

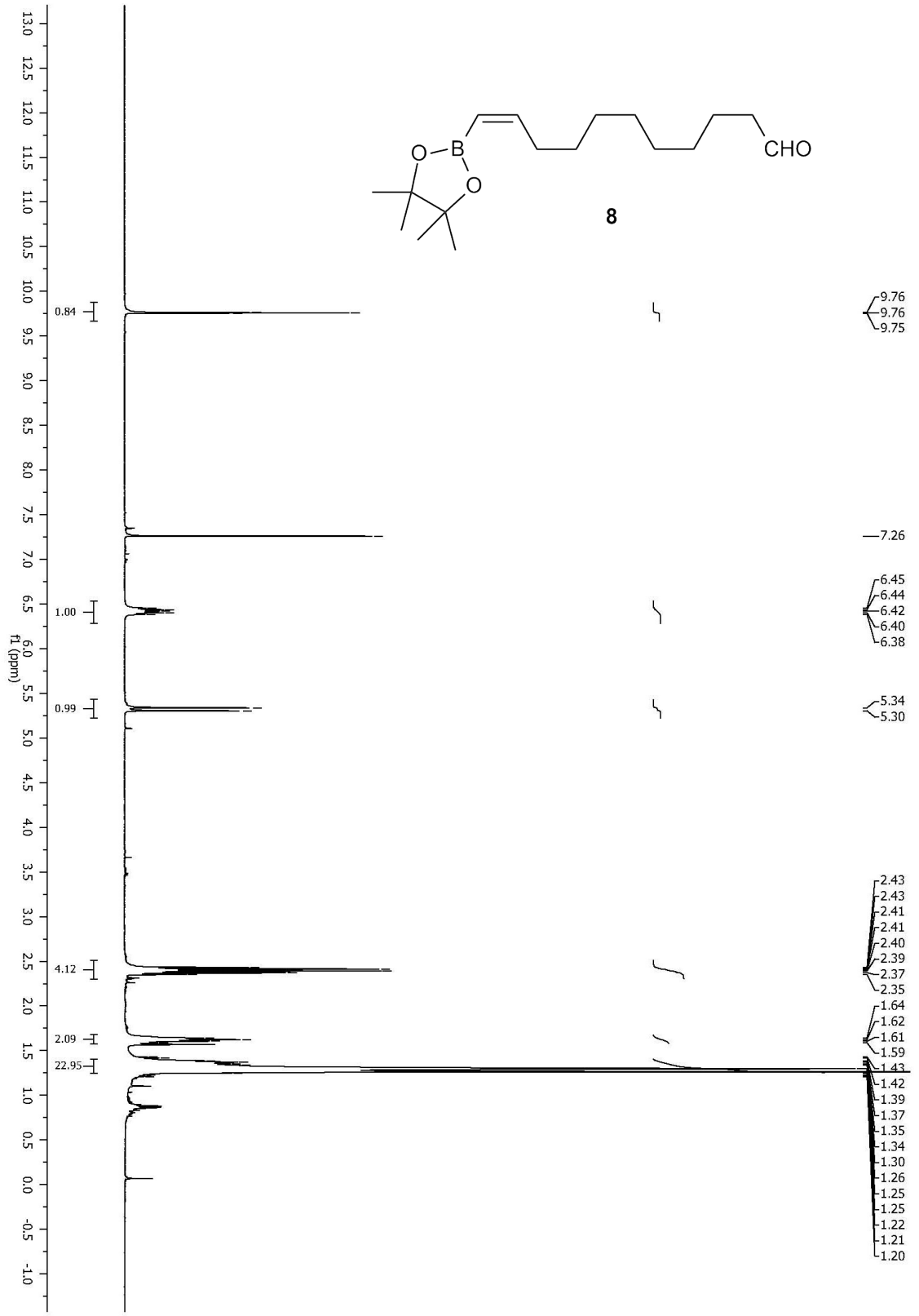

CO2Bn
7a
172.91
137.29
136.08
130.37
130.35
128.85
128.68
128.36
128.34
128.32
126.90
77.37
77.16
76.95
66.43
34.55
24.20
f1 (ppm)

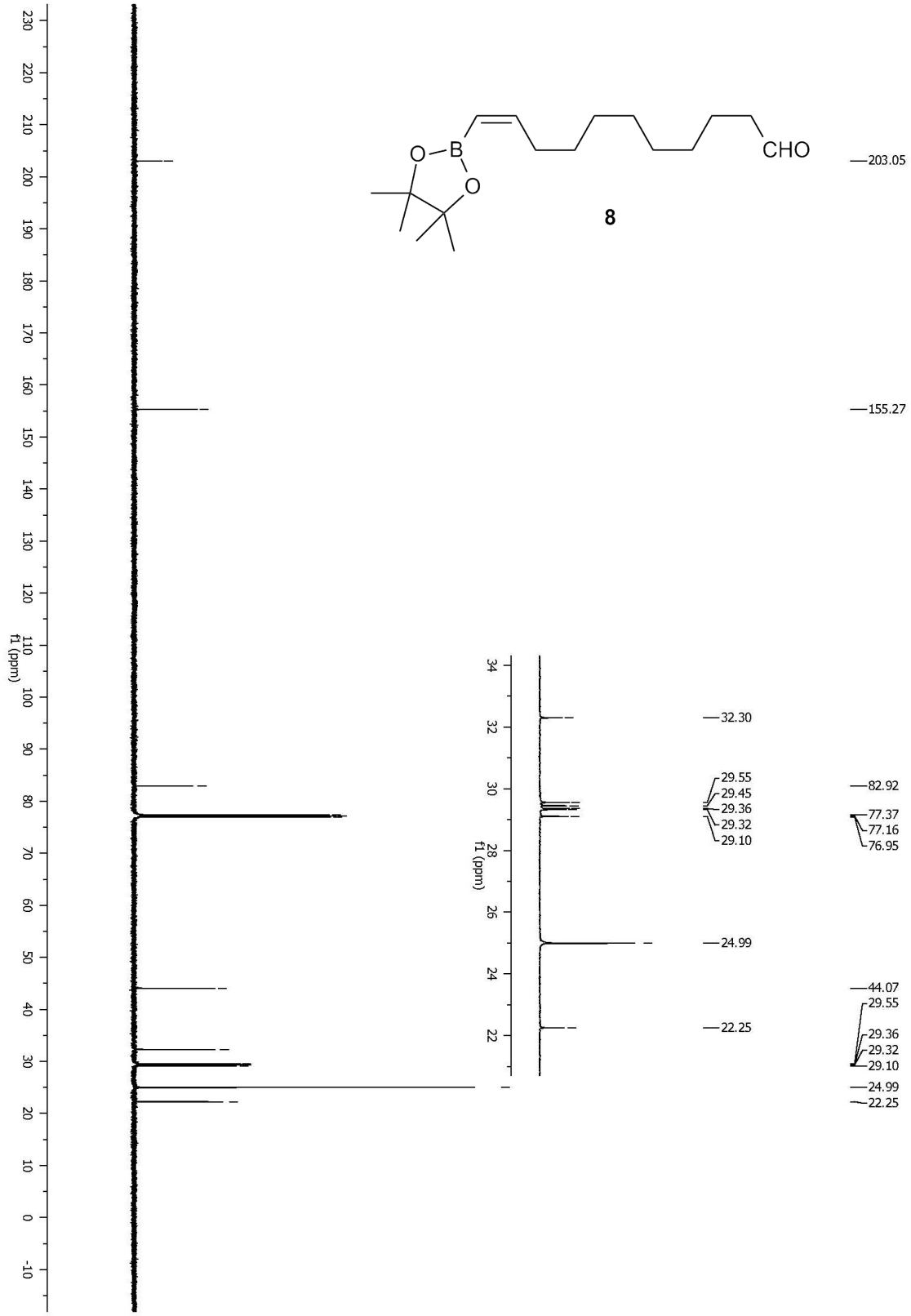

CO2Bn
MeO
OMe
7b
f1 (ppm)
4.83
2.99
1.03
1.00
2.00
3.05
3.00
2.06
2.06
7.36
7.35
7.35
7.34
7.33
7.32
7.32
7.32
7.31
7.26
6.84
6.81
6.41
6.38
6.38
5.58
5.56
5.54
5.53
5.14
5.12
3.89
3.88
3.87
3.85
2.73
2.71
2.71
2.69
2.69
2.67
2.67
2.53
2.51
2.49

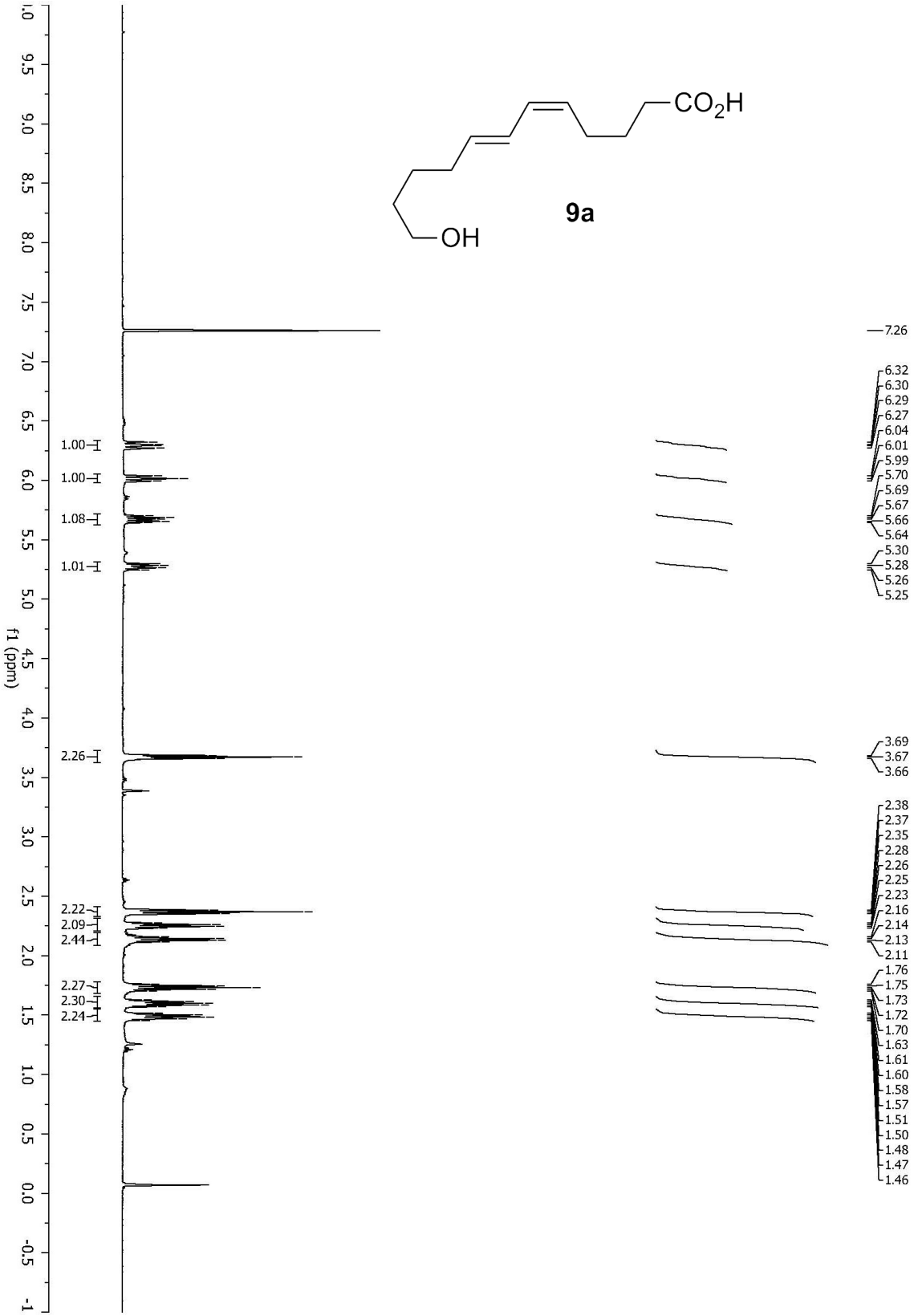

CO2Bn
MeO
OMe
7b
172.94
148.73
148.08
136.07
129.07
128.32
121.42
112.14
111.10
77.37
77.16
76.95
130.27
130.05
66.44
56.04
55.97
129.07
128.69
128.36
128.32
34.60
24.32
f1 (ppm)

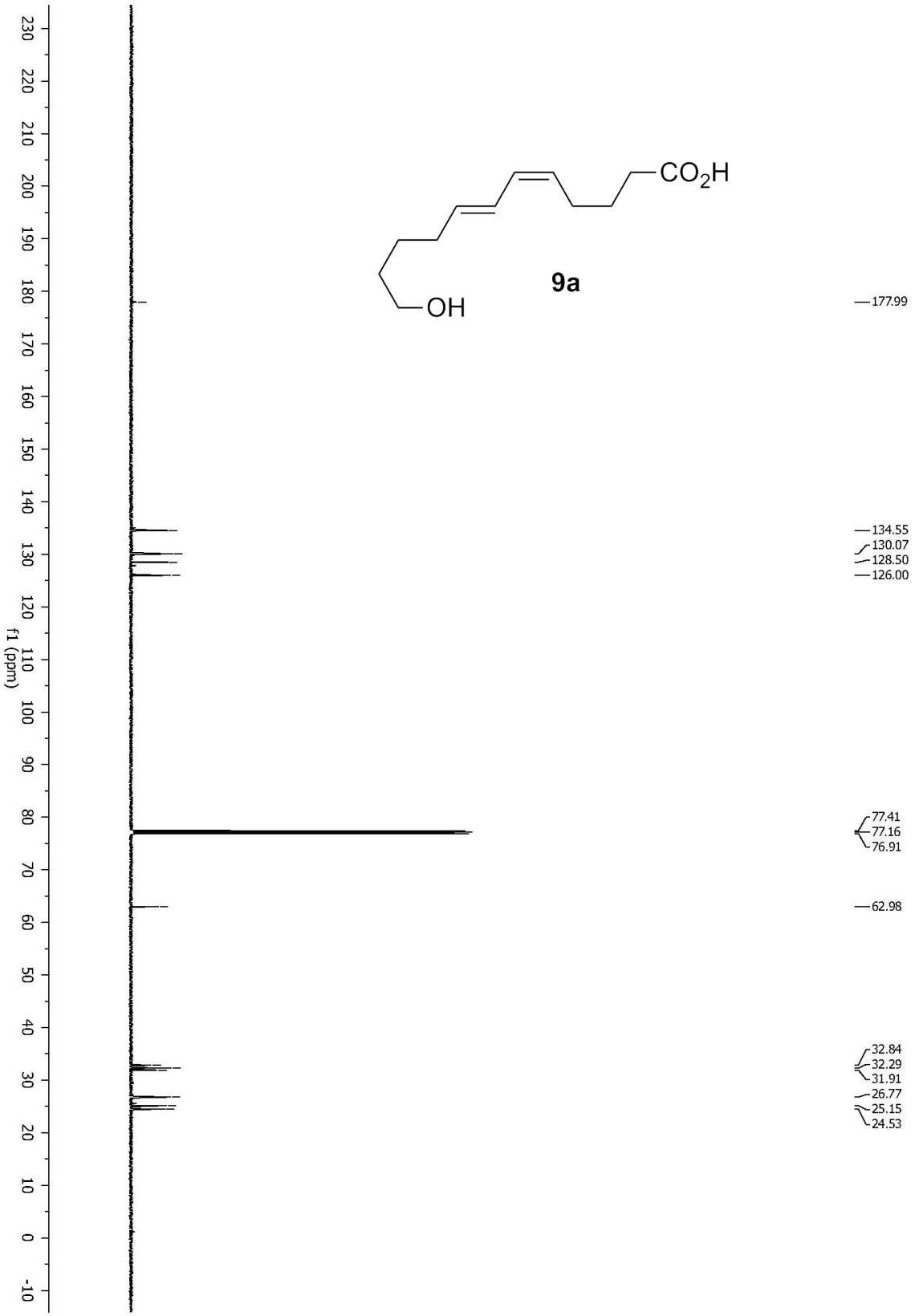

CO2Me
O
7c
f1 (ppm)
0.90
1.84
1.97
1.00
0.98
2.95
4.23
2.25
10.03
7.76
7.74
7.48
7.26
6.51
6.49
5.76
5.75
5.74
5.74
5.73
5.72
3.63
2.37
2.36
2.35
2.34
2.32
1.80
1.79
1.56

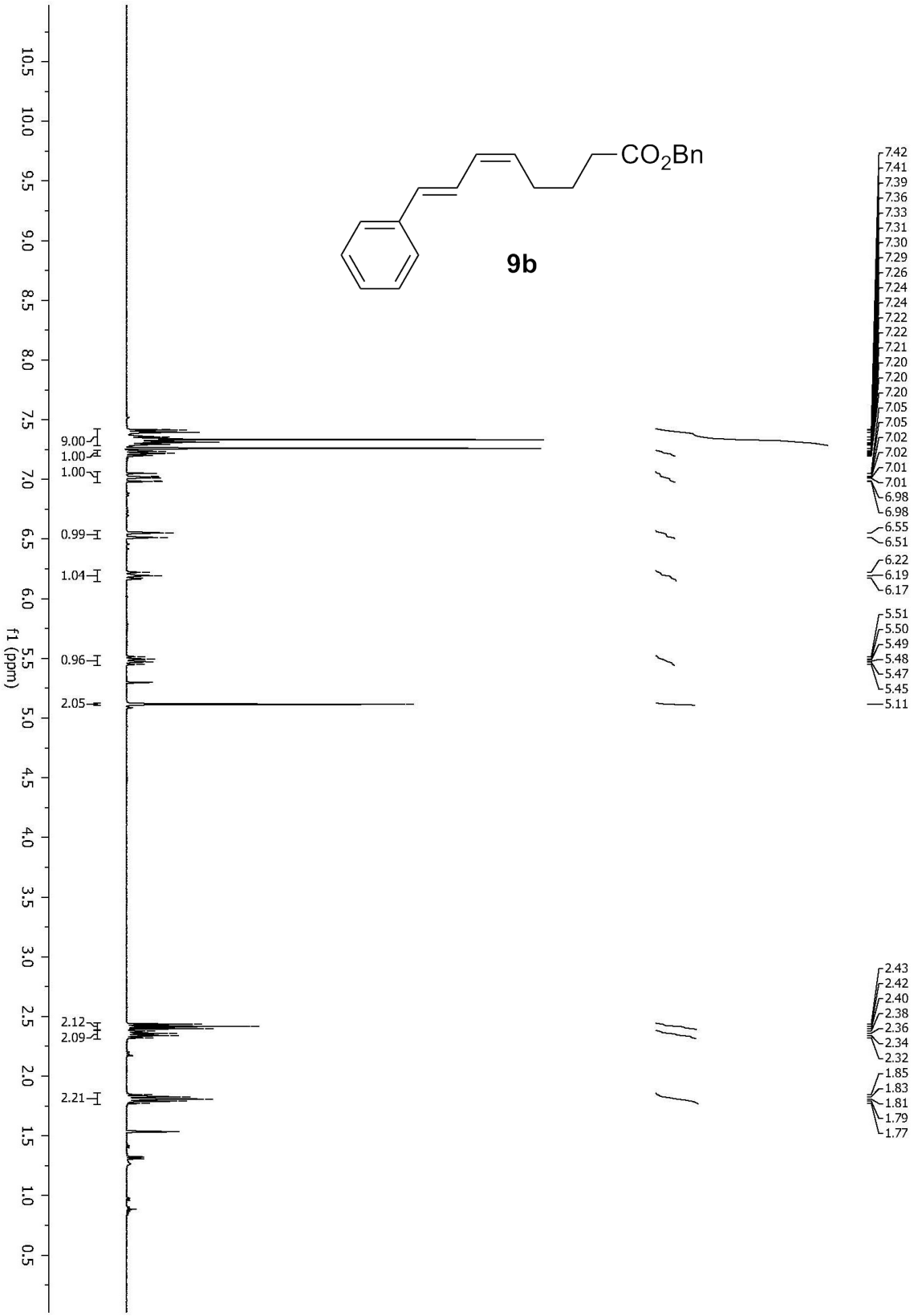

CO2Me
O
7c
192.53
173.91
138.51
136.58
134.79
133.43
130.03
129.03
128.64
128.04
77.37
77.16
76.95
51.67
33.55
27.99
25.06
f1 (ppm)

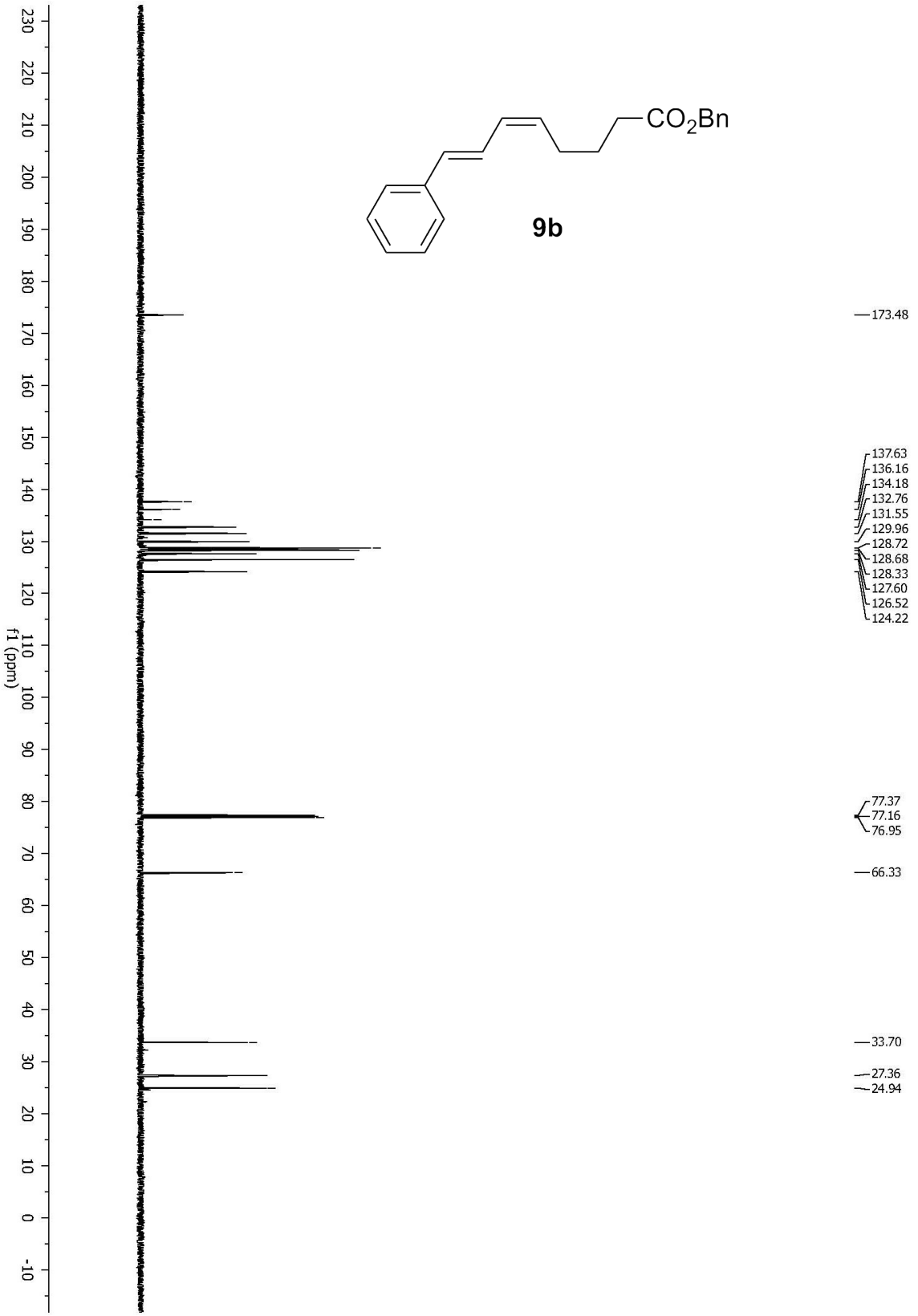

O
B
O
CHO
8
f1 (ppm)
0.84
1.00
0.99
4.12
2.09
22.95
9.76
9.76
9.75
7.26
6.45
6.44
6.42
6.40
6.38
5.34
5.30
2.43
2.43
2.41
2.41
2.40
2.39
2.37
2.35
1.64
1.62
1.61
1.59
1.43
1.42
1.39
1.37
1.35
1.34
1.30
1.26
1.25
1.25
1.22
1.21
1.20

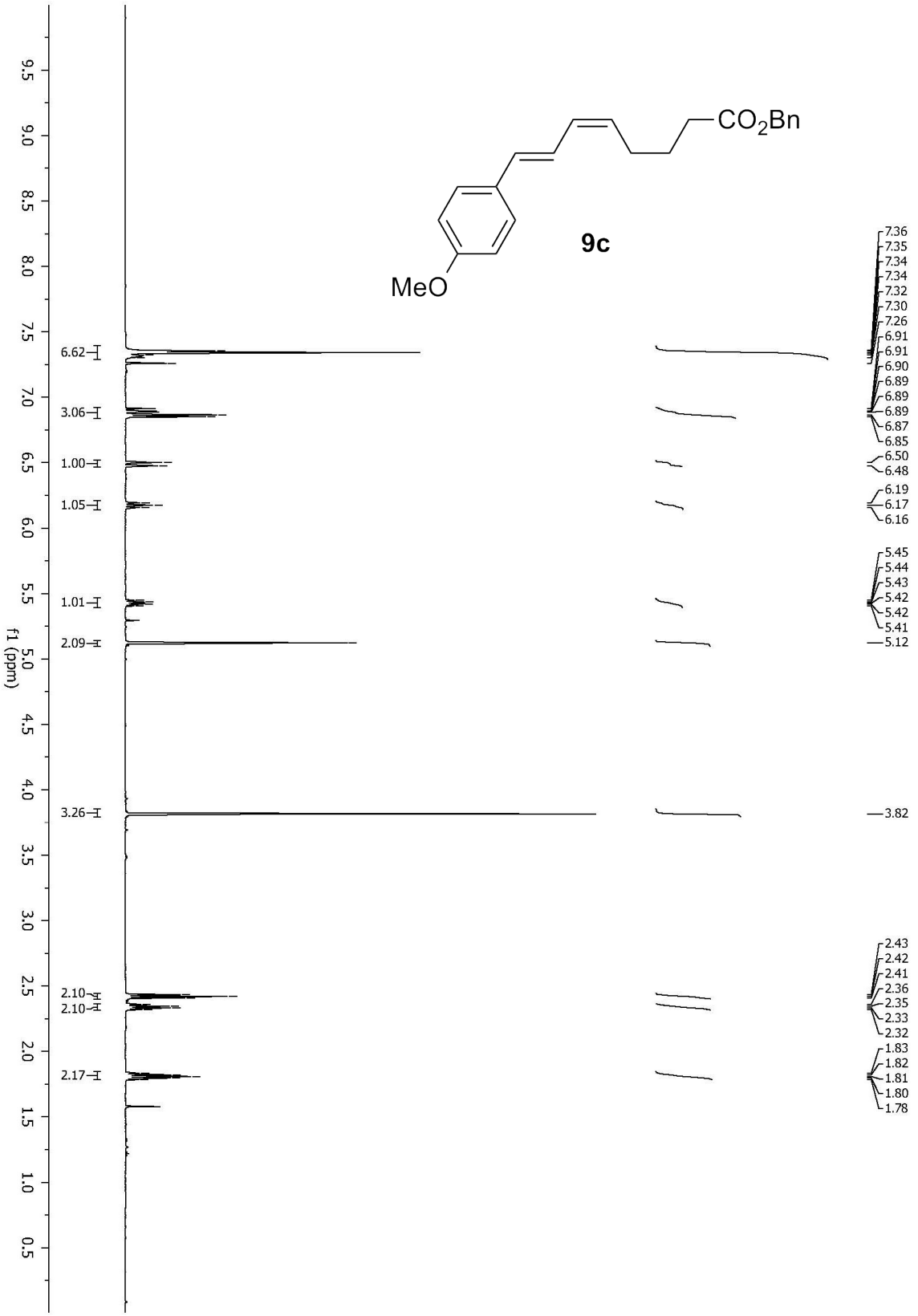

O
B
O
CHO
8
203.05
155.27
82.92
77.37
77.16
76.95
44.07
29.55
29.36
29.32
29.10
24.99
22.25
32.30
29.55
29.45
29.36
29.32
29.10
24.99
22.25
f1 (ppm)
f1 (ppm)

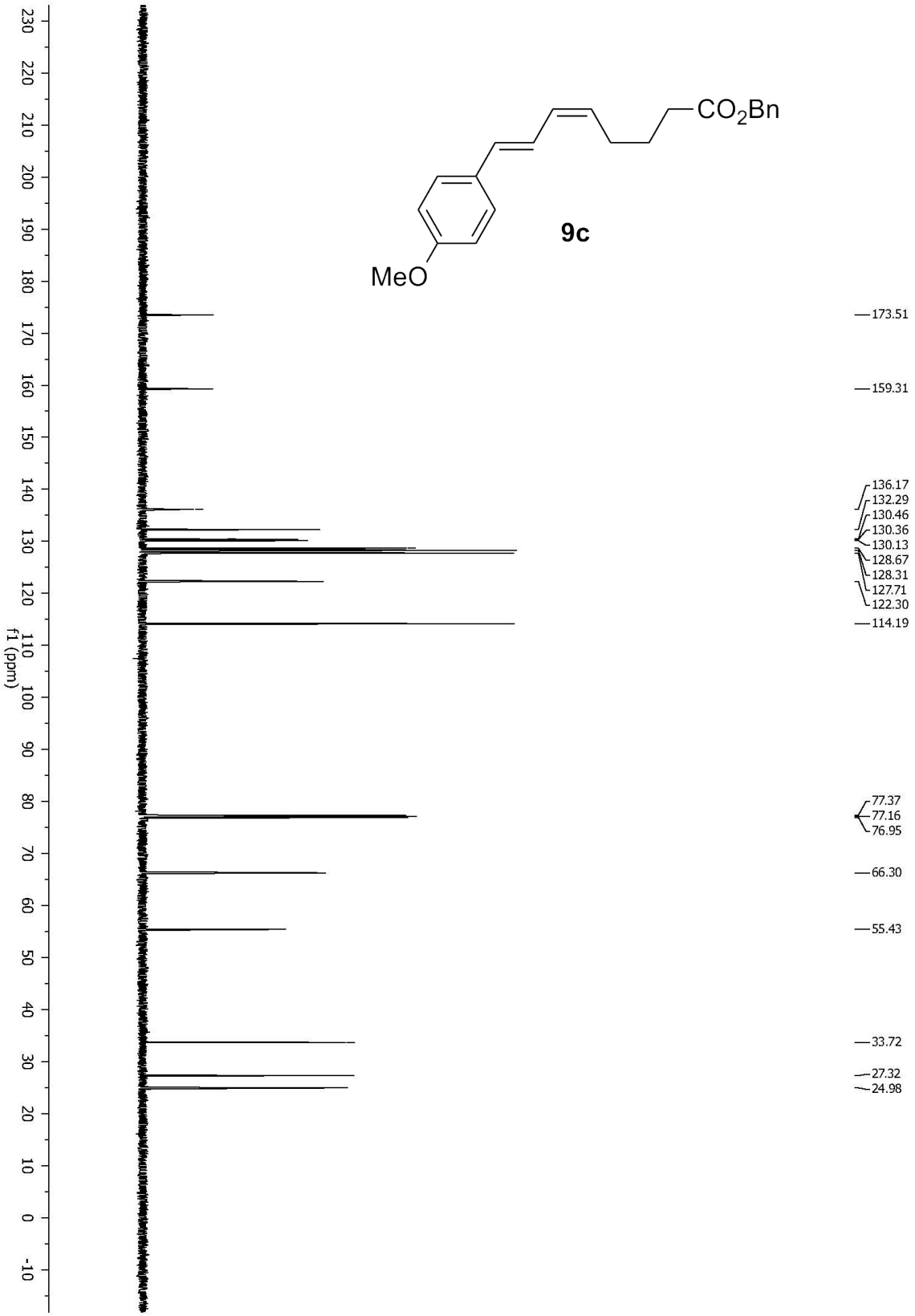

CO2H
OH
9a
f1 (ppm)
1.00
1.00
1.08
1.01
2.26
2.22
2.09
2.44
2.27
2.30
2.24
7.26
6.32
6.30
6.29
6.27
6.04
6.01
5.99
5.70
5.69
5.67
5.66
5.64
5.30
5.28
5.26
5.25
3.69
3.67
3.66
2.38
2.37
2.35
2.28
2.26
2.25
2.23
2.16
2.14
2.13
2.11
1.76
1.75
1.73
1.72
1.70
1.63
1.61
1.60
1.58
1.57
1.51
1.50
1.48
1.47
1.46

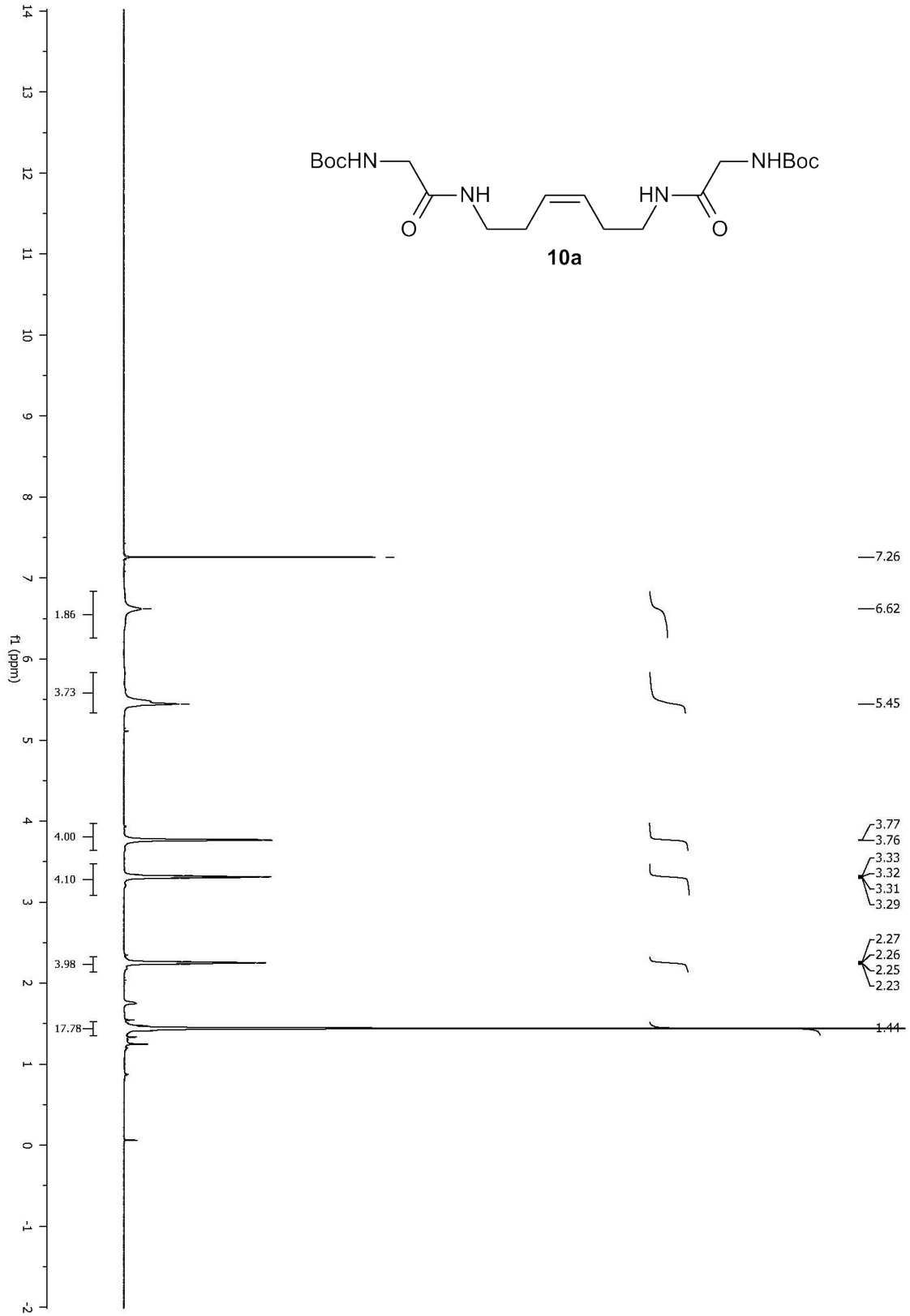

CO2H
OH
9a
177.99
134.55
130.07
128.50
126.00
77.41
77.16
76.91
62.98
32.84
32.29
31.91
26.77
25.15
24.53
f1 (ppm)

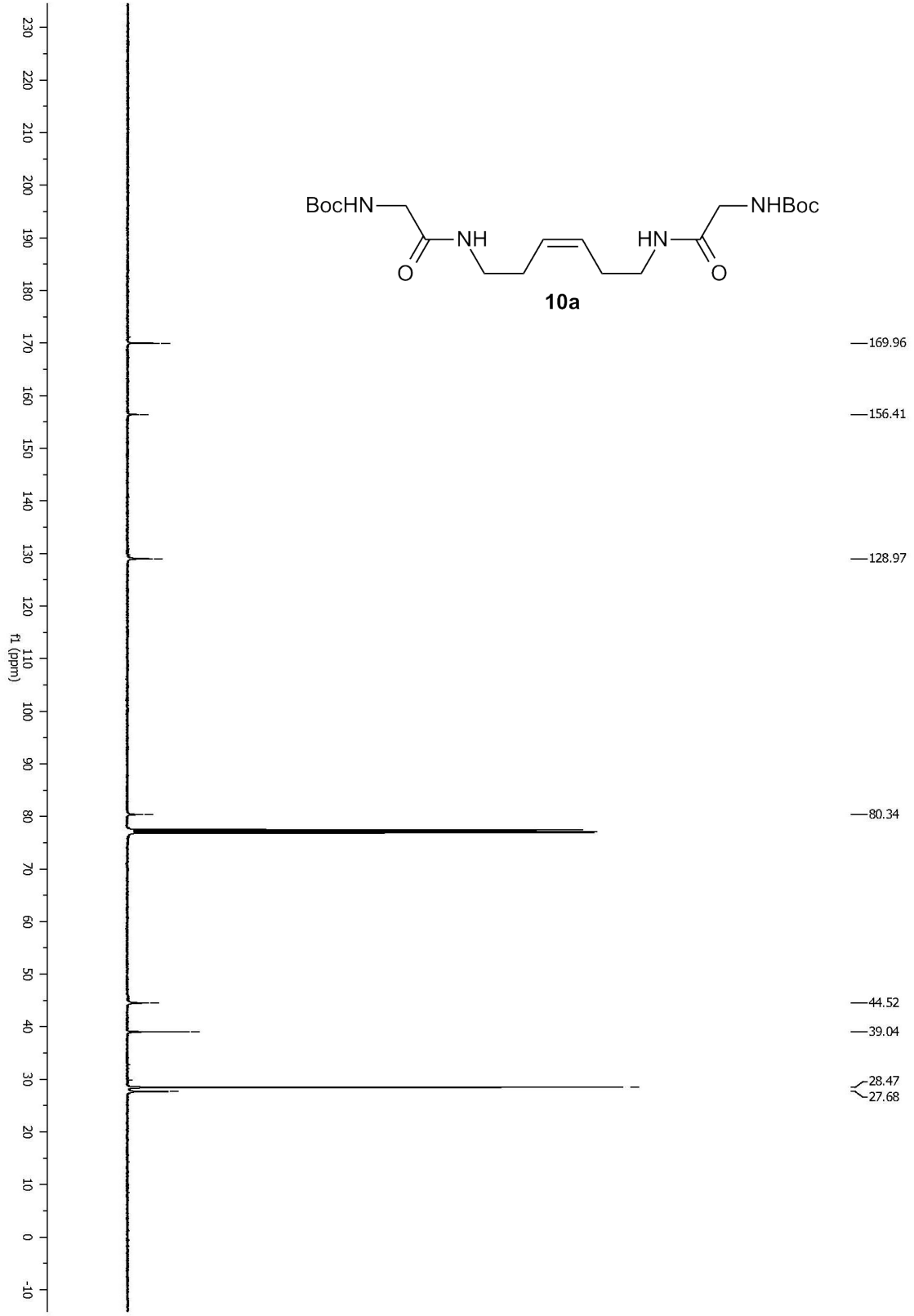

CO2Bn
9b
f1 (ppm)
9.00
1.00
1.00
0.99
1.04
0.96
2.05
2.12
2.09
2.21
7.42
7.41
7.39
7.36
7.33
7.31
7.30
7.29
7.26
7.24
7.24
7.22
7.22
7.21
7.20
7.20
7.20
7.05
7.05
7.02
7.02
7.01
7.01
6.98
6.98
6.55
6.51
6.22
6.19
6.17
5.51
5.50
5.49
5.48
5.47
5.45
5.11
2.43
2.42
2.40
2.38
2.36
2.34
2.32
1.85
1.83
1.81
1.79
1.77

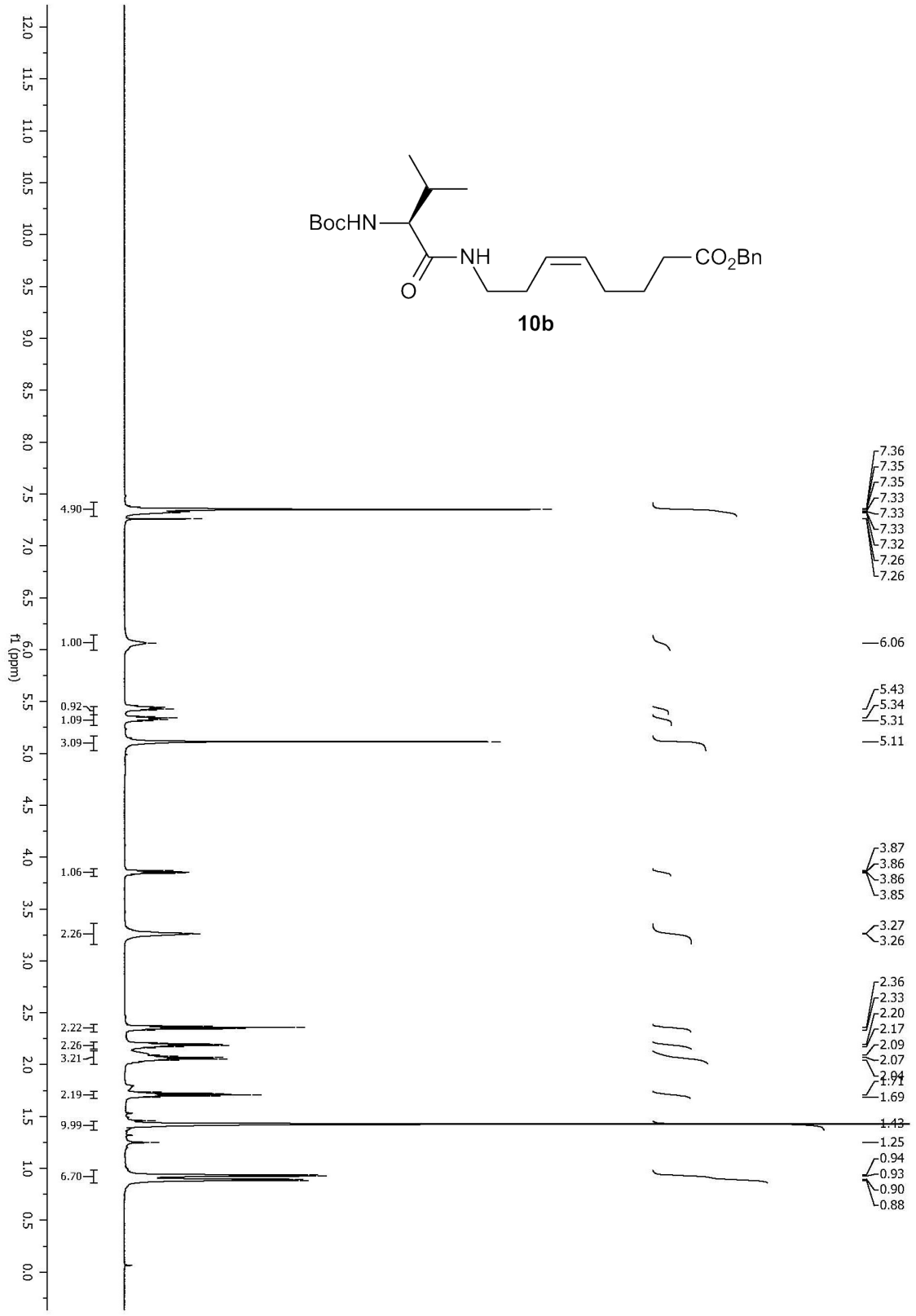

CO2Bn
9b
173.48
137.63
136.16
134.18
132.76
131.55
129.96
128.72
128.68
128.33
127.60
126.52
124.22
77.37
77.16
76.95
66.33
33.70
27.36
24.94
f1 (ppm)

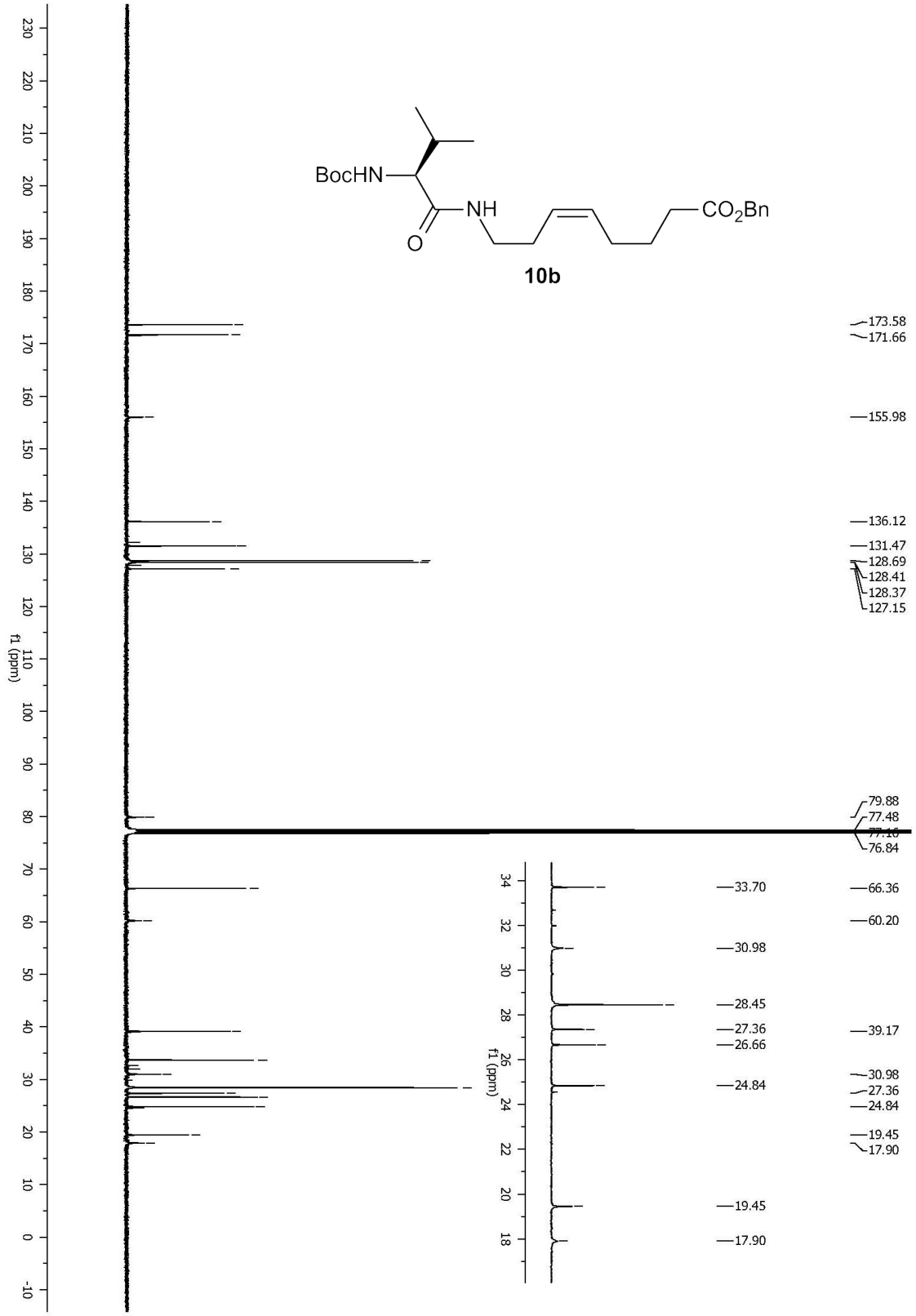

CO2Bn
MeO
9c
f1 (ppm)
6.62
3.06
1.00
1.05
1.01
2.09
3.26
2.10
2.10
2.17
7.36
7.35
7.34
7.34
7.32
7.30
7.26
6.91
6.91
6.90
6.89
6.89
6.89
6.87
6.85
6.50
6.48
6.19
6.17
6.16
5.45
5.44
5.43
5.42
5.42
5.41
5.12
3.82
2.43
2.42
2.41
2.36
2.35
2.33
2.32
1.83
1.82
1.81
1.80
1.78

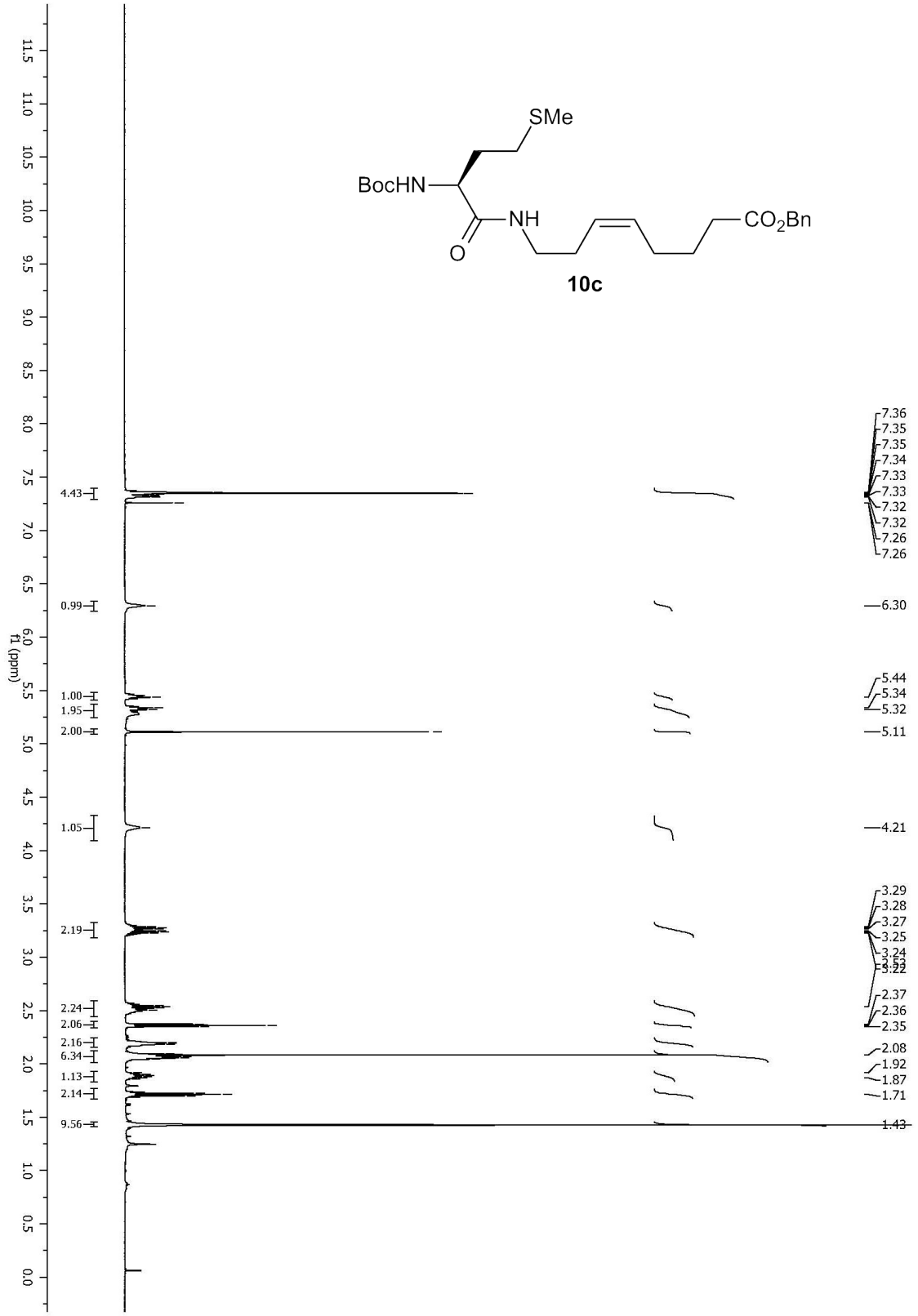

CO2Bn
MeO
9c
173.51
159.31
136.17
132.29
130.46
130.36
130.13
128.67
128.31
127.71
122.30
114.19
77.37
77.16
76.95
66.30
55.43
33.72
27.32
24.98
f1 (ppm)

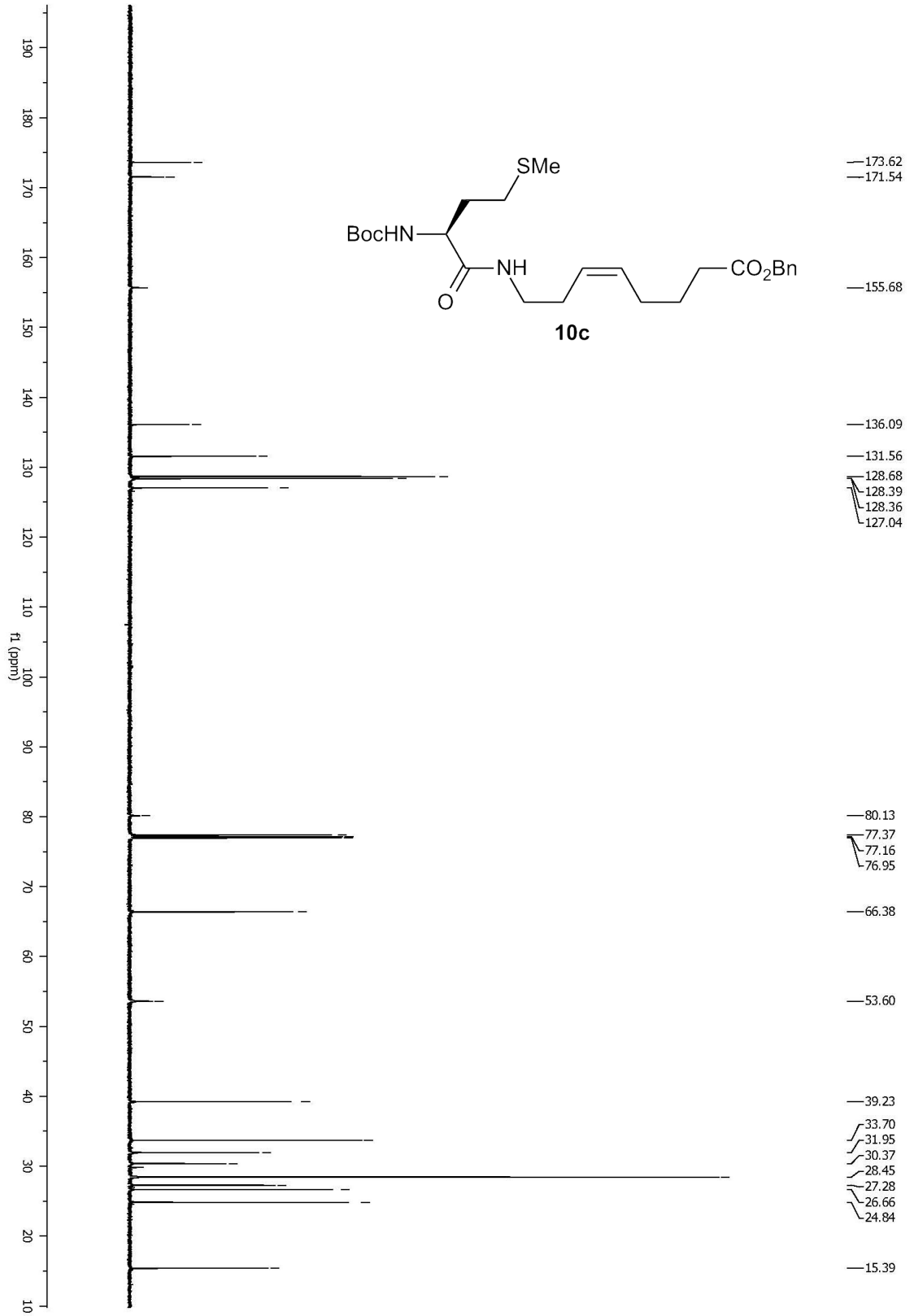

BocHN
NH
HN
NHBoc
O
O
10a
f1 (ppm)
1.86
3.73
4.00
4.10
3.98
17.78
7.26
6.62
5.45
3.77
3.76
3.33
3.32
3.31
3.29
2.27
2.26
2.25
2.23
1.44


BocHN
NH
HN
NHBoc
O
O
10a
169.96
156.41
128.97
80.34
44.52
39.04
28.47
27.68
f1 (ppm)

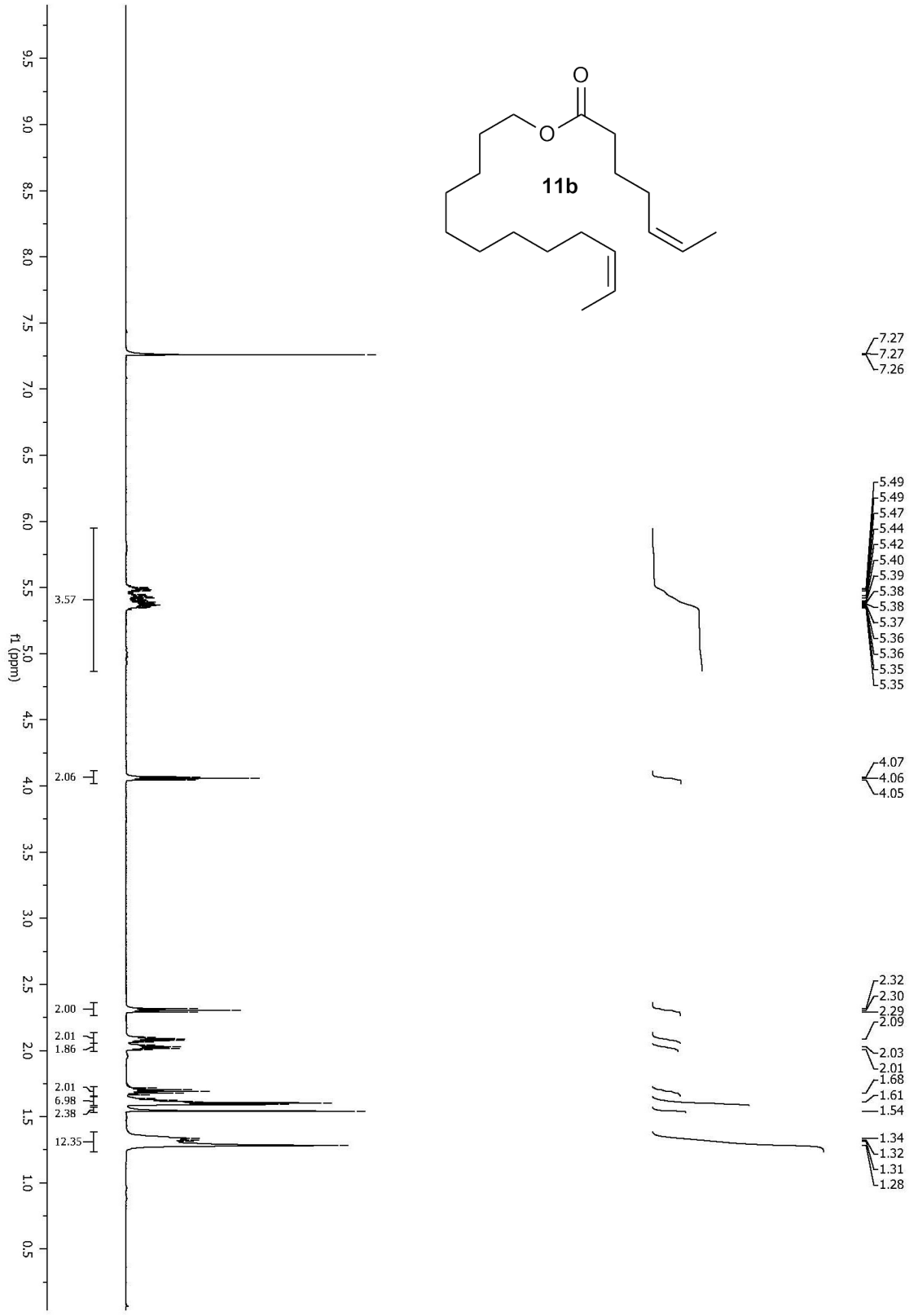

BocHN
NH
O
CO_2Bn
10b
f1 (ppm)
4.90
1.00
0.92
1.09
3.09
1.06
2.26
2.22
2.26
3.21
2.19
9.99
6.70
7.36
7.35
7.35
7.33
7.33
7.33
7.32
7.26
7.26
6.06
5.43
5.34
5.31
5.11
3.87
3.86
3.86
3.85
3.27
3.26
2.36
2.33
2.20
2.17
2.09
2.07
2.04
1.71
1.69
1.43
1.25
0.94
0.93
0.90
0.88

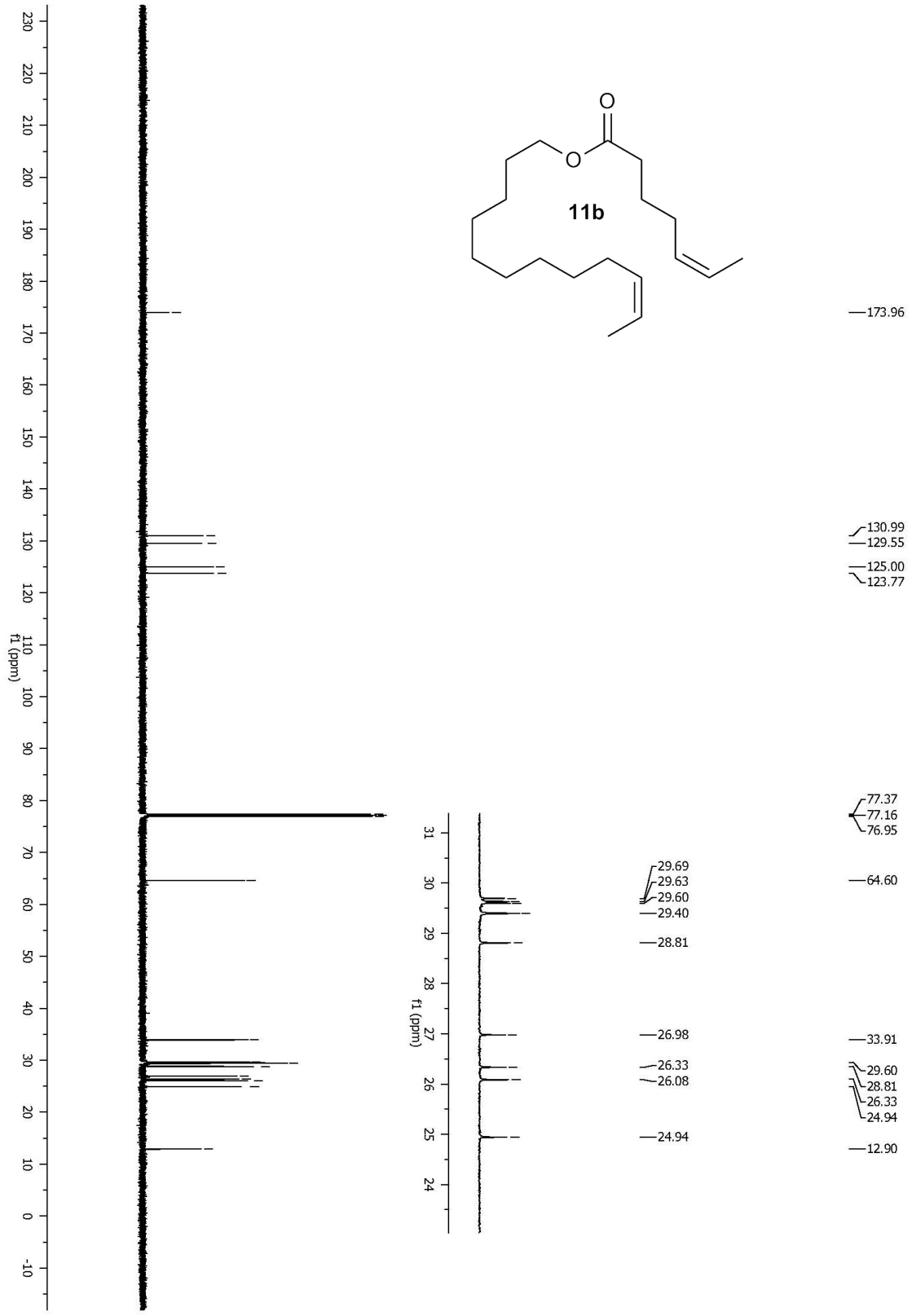

BocHN
NH
O
CO2Bn
10b
f1 (ppm)
173.58
171.66
155.98
136.12
131.47
128.69
128.41
128.37
127.15
79.88
77.48
76.84
66.36
60.20
39.17
33.70
30.98
28.45
27.36
26.66
24.84
19.45
17.90

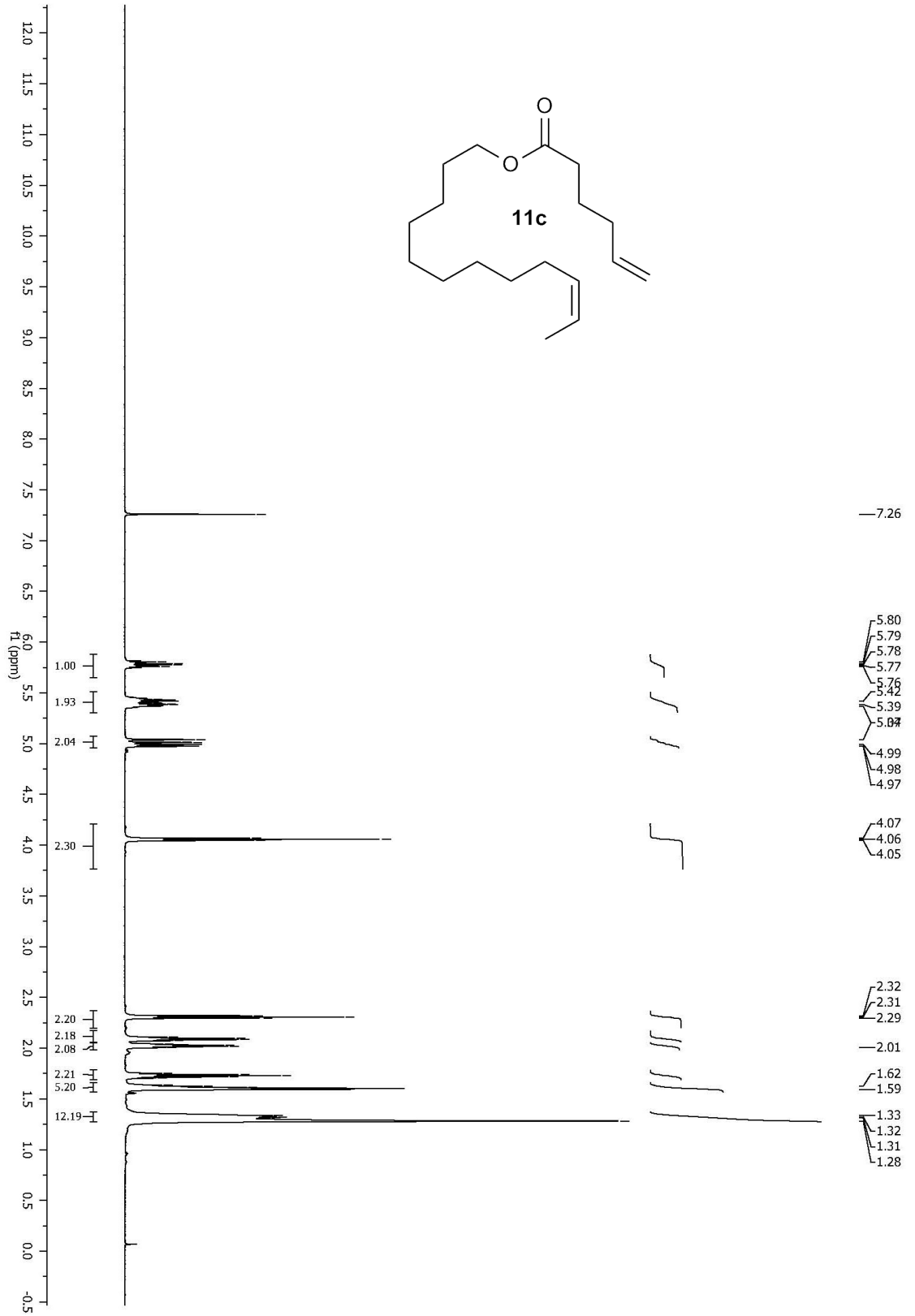

SMe
BocHN
NH
O
CO_2Bn
10c
f1 (ppm)
4.43
0.99
1.00
1.95
2.00
1.05
2.19
2.24
2.06
2.16
6.34
1.13
2.14
9.56
7.36
7.35
7.35
7.34
7.33
7.33
7.32
7.32
7.26
7.26
6.30
5.44
5.34
5.32
5.11
4.21
3.29
3.28
3.27
3.25
3.24
3.22
2.37
2.36
2.35
2.08
1.92
1.87
1.71
1.43

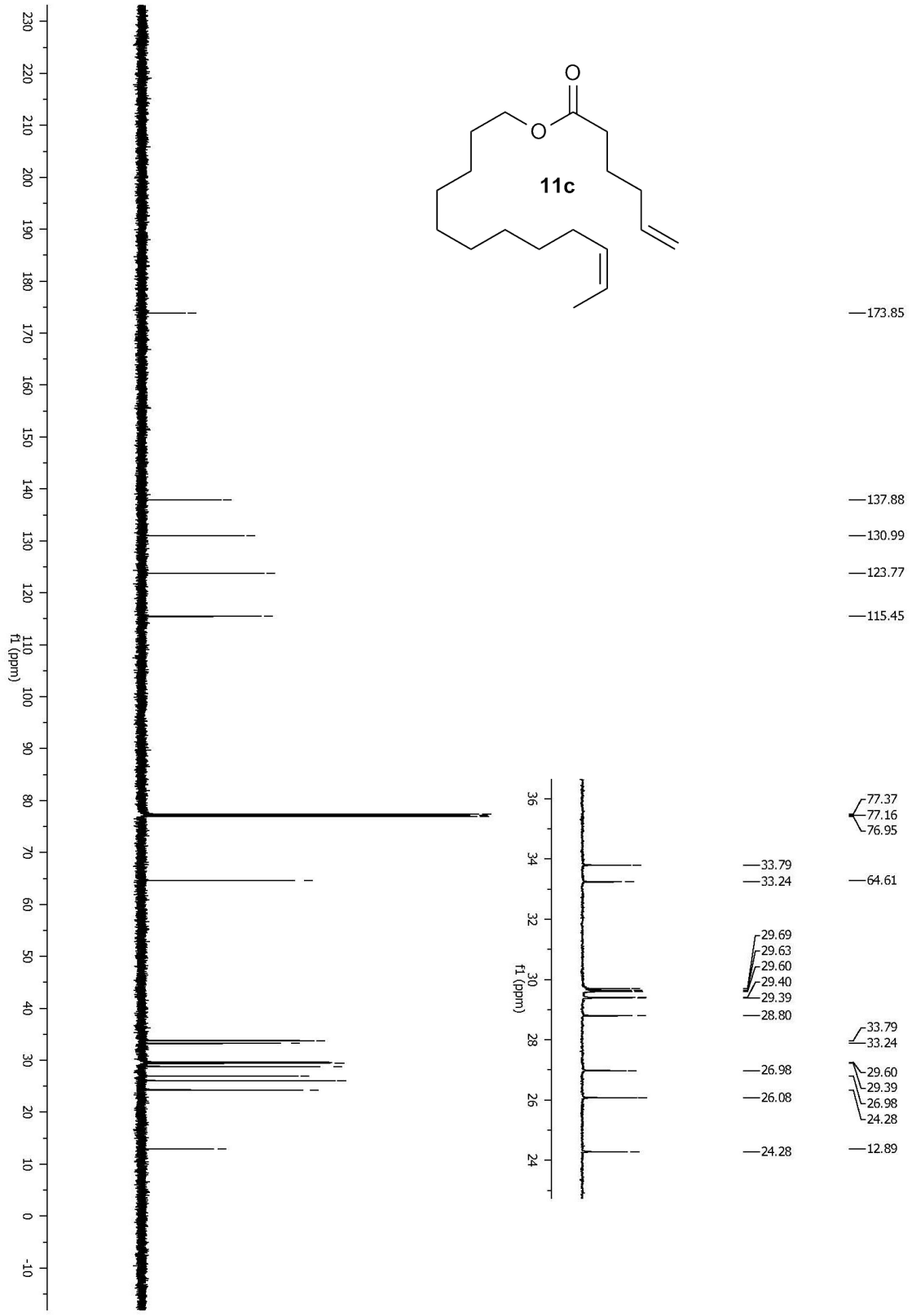

SMe
BocHN
NH
O
CO_2Bn
173.62
171.54
155.68
136.09
131.56
128.68
128.39
128.36
127.04
80.13
77.37
77.16
76.95
66.38
53.60
39.23
33.70
31.95
30.37
28.45
27.28
26.66
24.84
15.39
f1 (ppm)

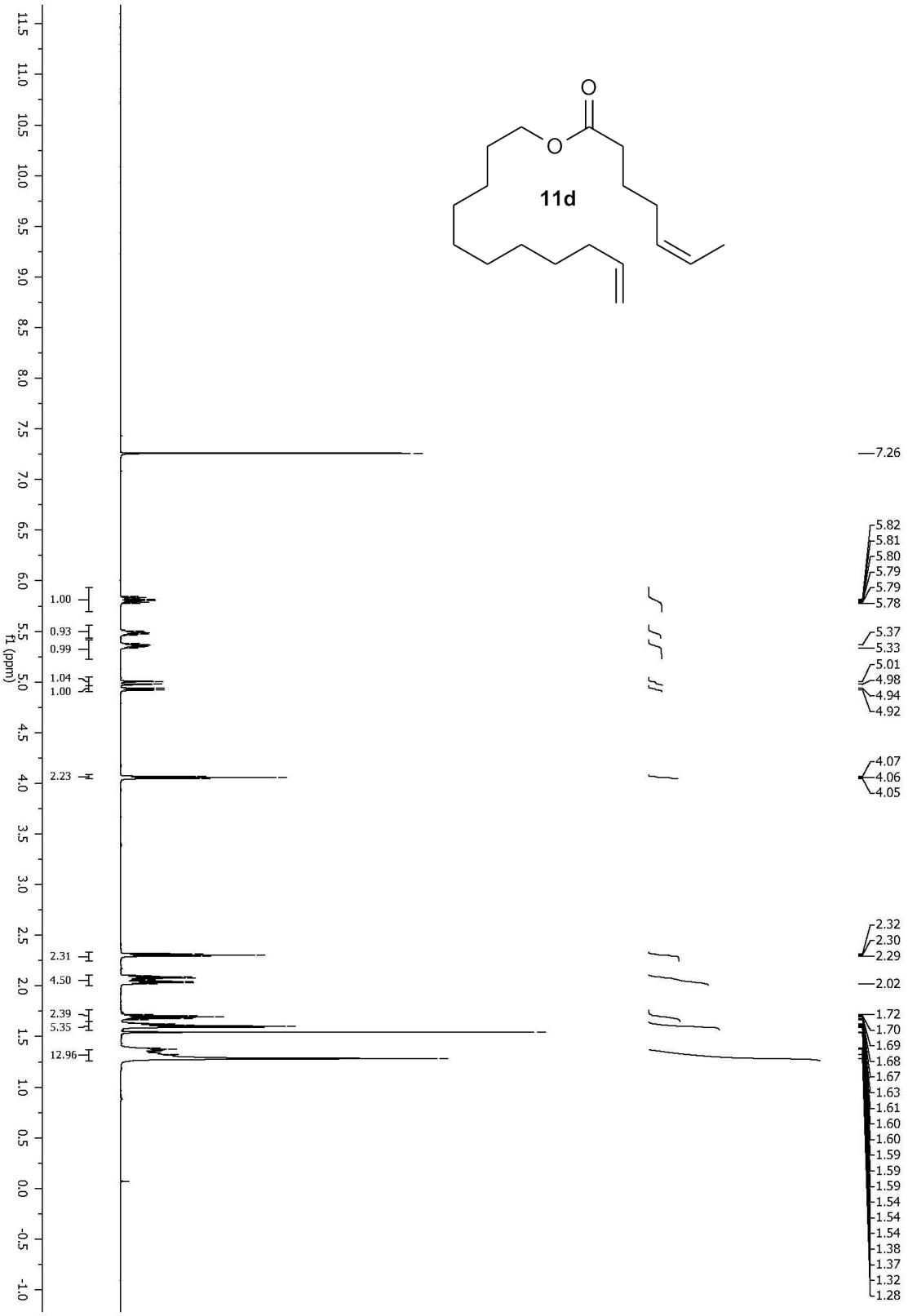
10c

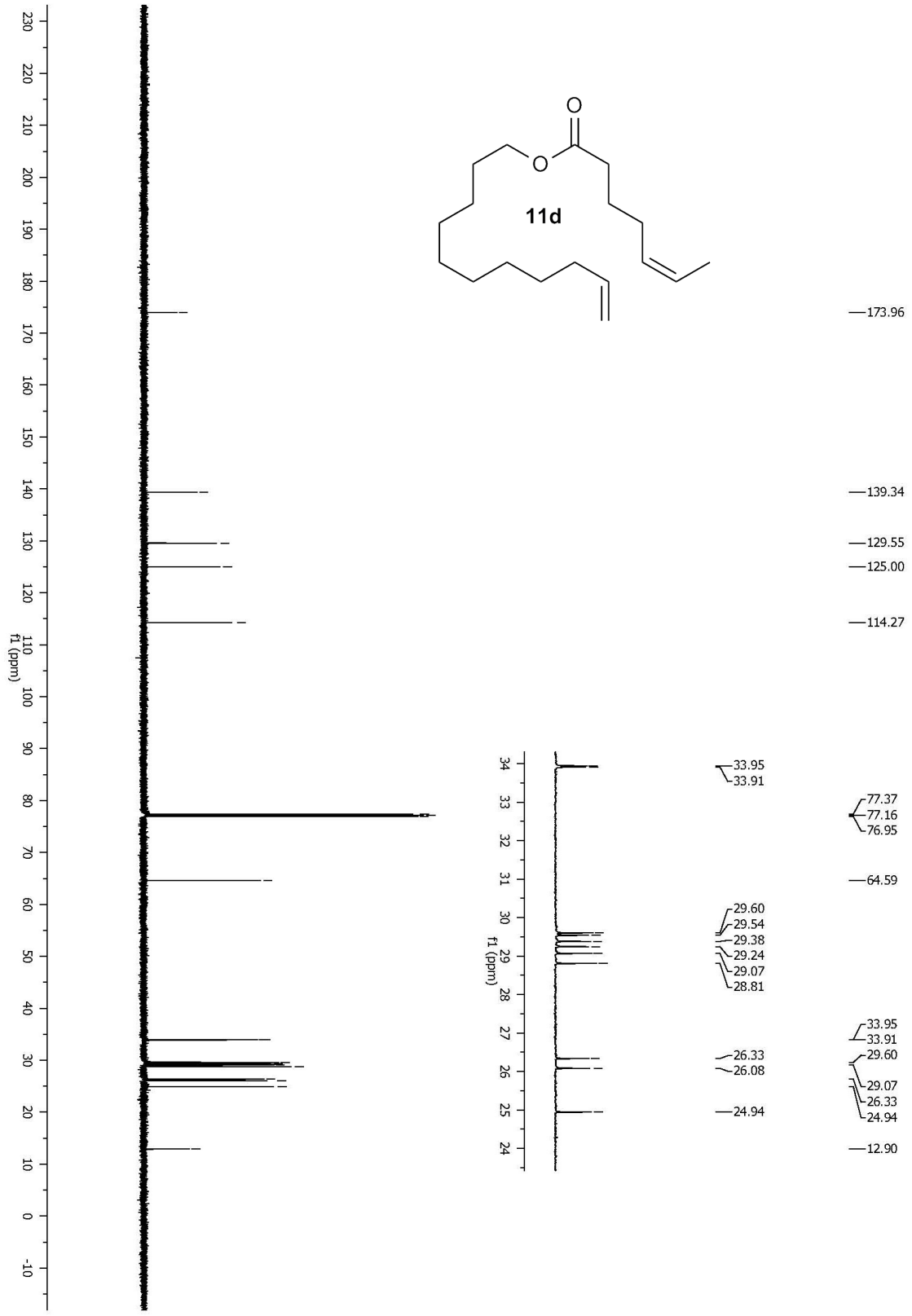

11b
f1 (ppm)
3.57
2.06
2.00
2.01
1.86
2.01
6.98
2.38
12.35
7.27
7.27
7.26
5.49
5.49
5.47
5.44
5.42
5.40
5.39
5.38
5.38
5.37
5.36
5.36
5.35
5.35
4.07
4.06
4.05
2.32
2.30
2.29
2.09
2.03
2.01
1.68
1.61
1.54
1.34
1.32
1.31
1.28

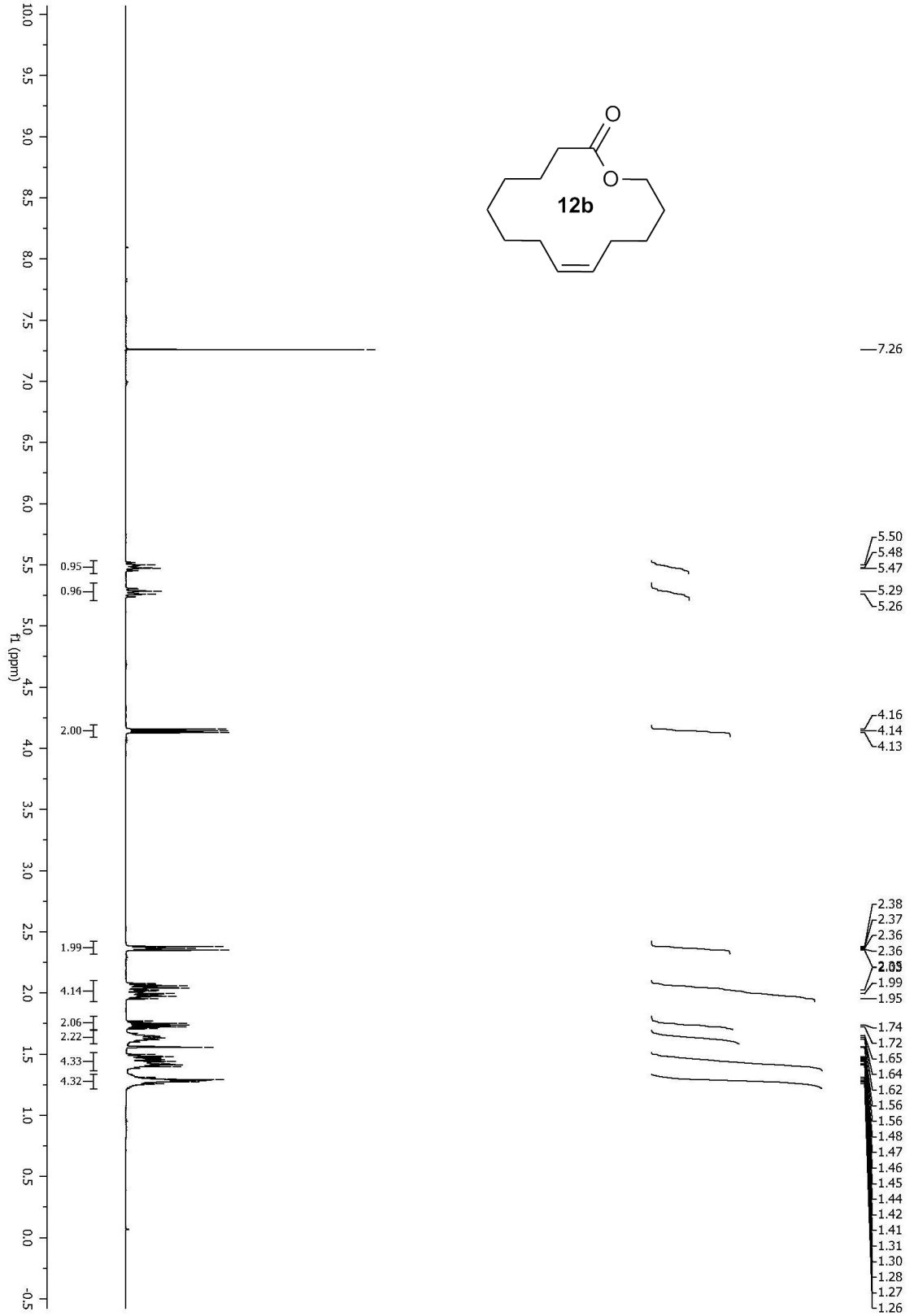

O
O
11b
173.96
130.99
129.55
125.00
123.77
77.37
77.16
76.95
64.60
29.69
29.63
29.60
29.40
28.81
26.98
26.33
26.08
24.94
33.91
29.60
28.81
26.33
24.94
12.90
f1 (ppm)
f1 (ppm)

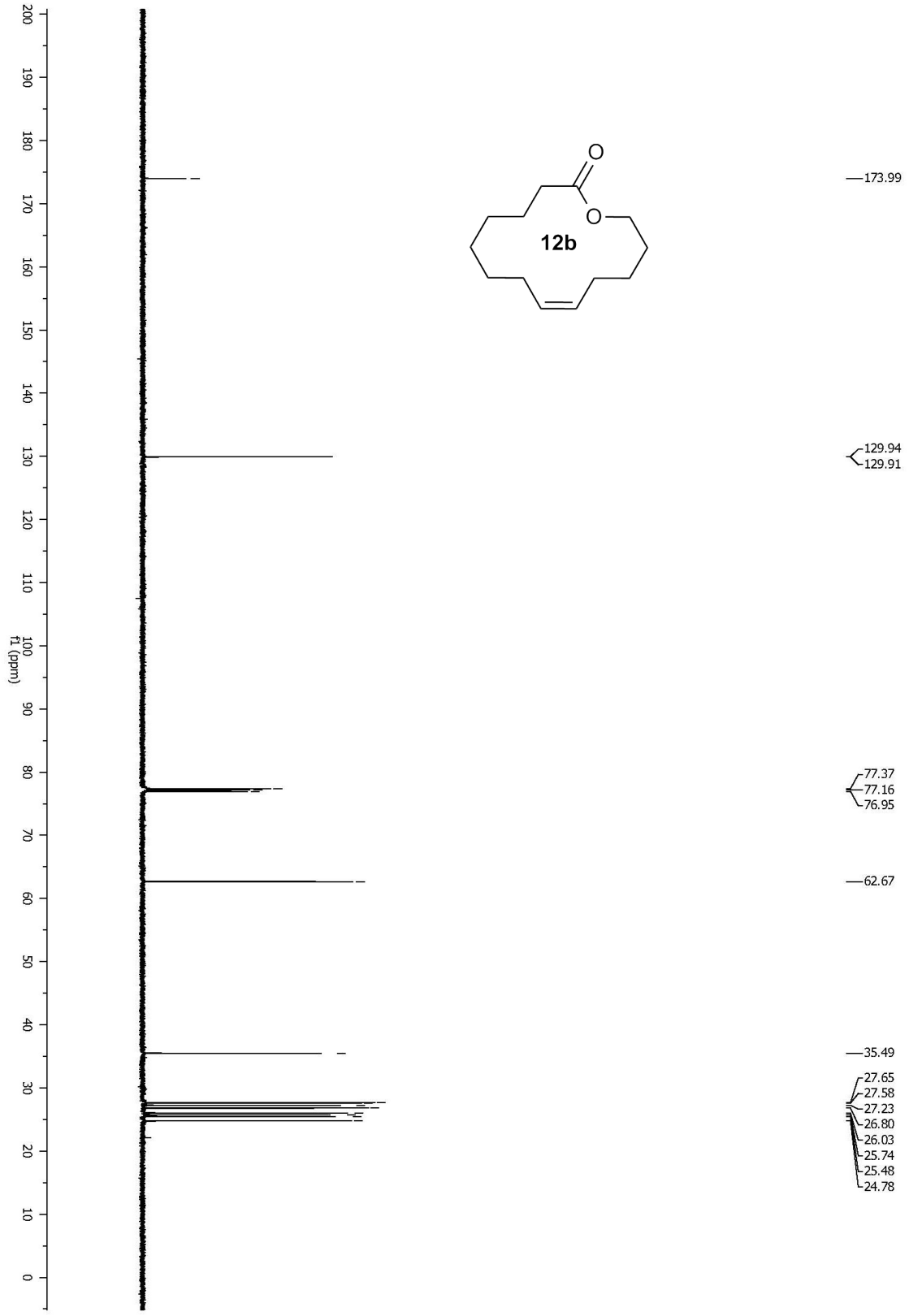

11c
f1 (ppm)
1.00
1.93
2.04
2.30
2.20
2.18
2.08
2.21
5.20
12.19
7.26
5.80
5.79
5.78
5.77
5.76
5.42
5.39
4.99
4.98
4.97
4.07
4.06
4.05
2.32
2.31
2.29
2.01
1.62
1.59
1.33
1.32
1.31
1.28

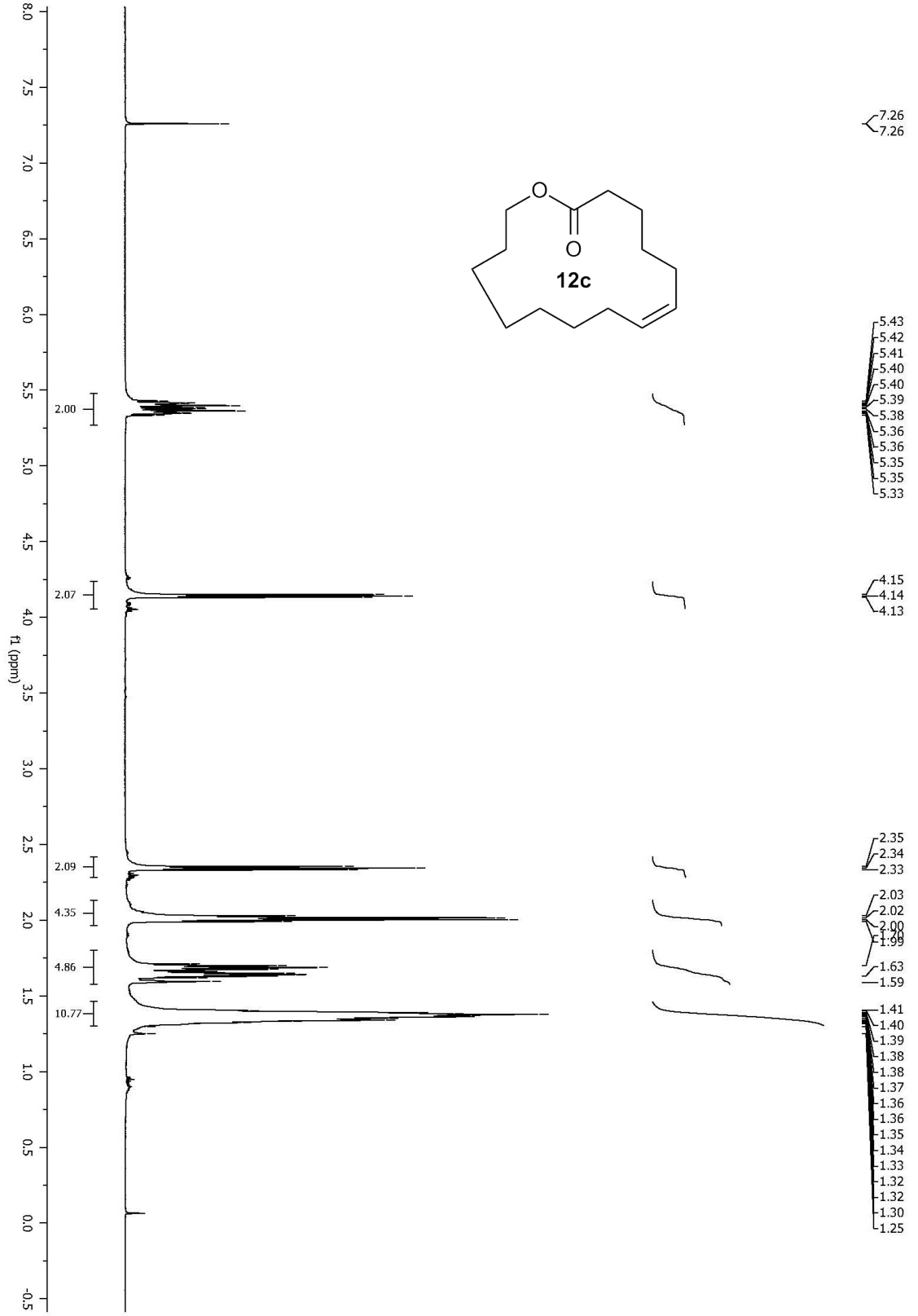

11c
173.85
137.88
130.99
123.77
115.45
77.37
77.16
76.95
33.79
33.24
64.61
29.69
29.63
29.60
29.40
29.39
28.80
26.98
26.08
24.28
12.89
f1 (ppm)


11d
f1 (ppm)
1.00
0.93
0.99
1.04
1.00
2.23
2.31
4.50
2.39
5.35
12.96
7.26
5.82
5.81
5.80
5.79
5.79
5.78
5.37
5.33
5.01
4.98
4.94
4.92
4.07
4.06
4.05
2.32
2.30
2.29
2.02
1.72
1.70
1.69
1.68
1.67
1.63
1.61
1.60
1.60
1.59
1.59
1.59
1.54
1.54
1.54
1.38
1.37
1.32
1.28


11d
173.96
139.34
129.55
125.00
114.27
77.37
77.16
76.95
64.59
33.95
33.91
29.60
29.54
29.38
29.24
29.07
28.81
26.33
26.08
24.94
12.90
f1 (ppm)


12b
f1 (ppm)
0.95
0.96
2.00
1.99
4.14
2.06
2.22
4.33
4.32
7.26
5.50
5.48
5.47
5.29
5.26
4.16
4.14
4.13
2.38
2.37
2.36
2.36
1.99
1.95
1.74
1.72
1.65
1.64
1.62
1.56
1.56
1.48
1.47
1.46
1.45
1.44
1.42
1.41
1.31
1.30
1.28
1.27
1.26


f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
O
O
12b
173.99
129.94
129.91
77.37
77.16
76.95
62.67
35.49
27.65
27.58
27.23
26.80
26.03
25.74
25.48
24.78


12c
f1 (ppm)
2.00
2.07
2.09
4.35
4.86
10.77
7.26
7.26
5.43
5.42
5.41
5.40
5.40
5.39
5.38
5.36
5.36
5.35
5.35
5.33
4.15
4.14
4.13
2.35
2.34
2.33
2.03
2.02
2.00
1.99
1.63
1.59
1.41
1.40
1.39
1.38
1.38
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1.36
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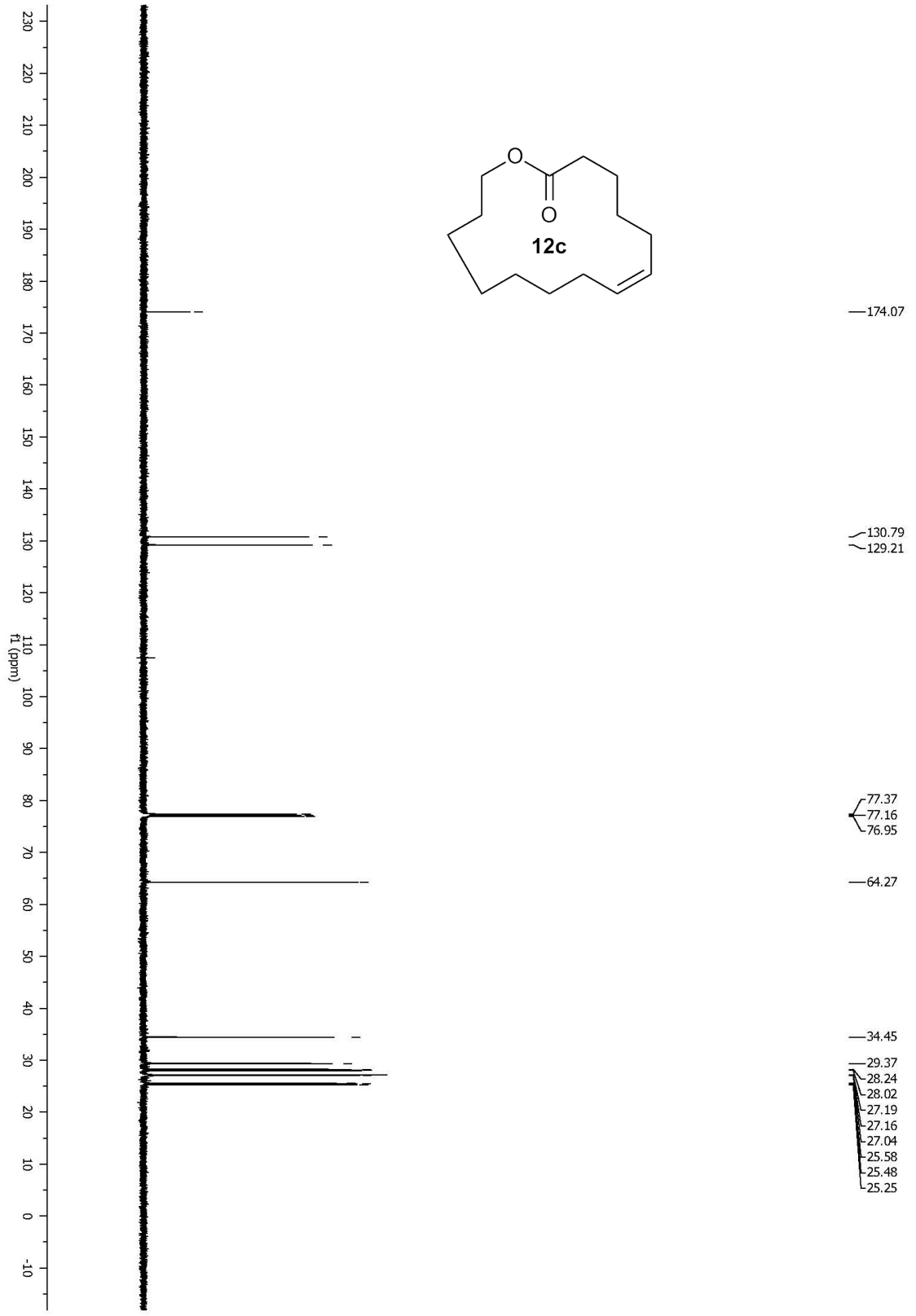
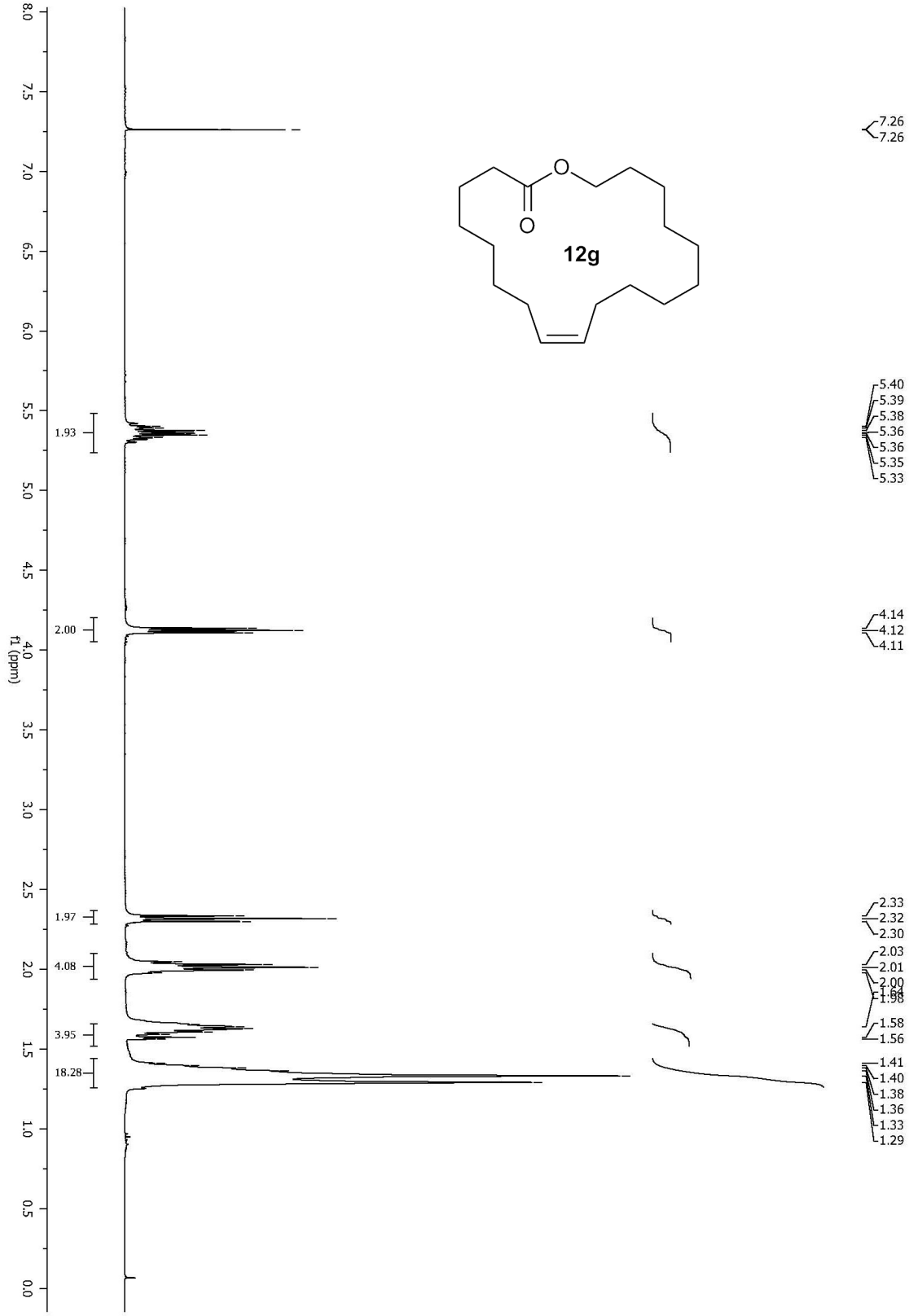
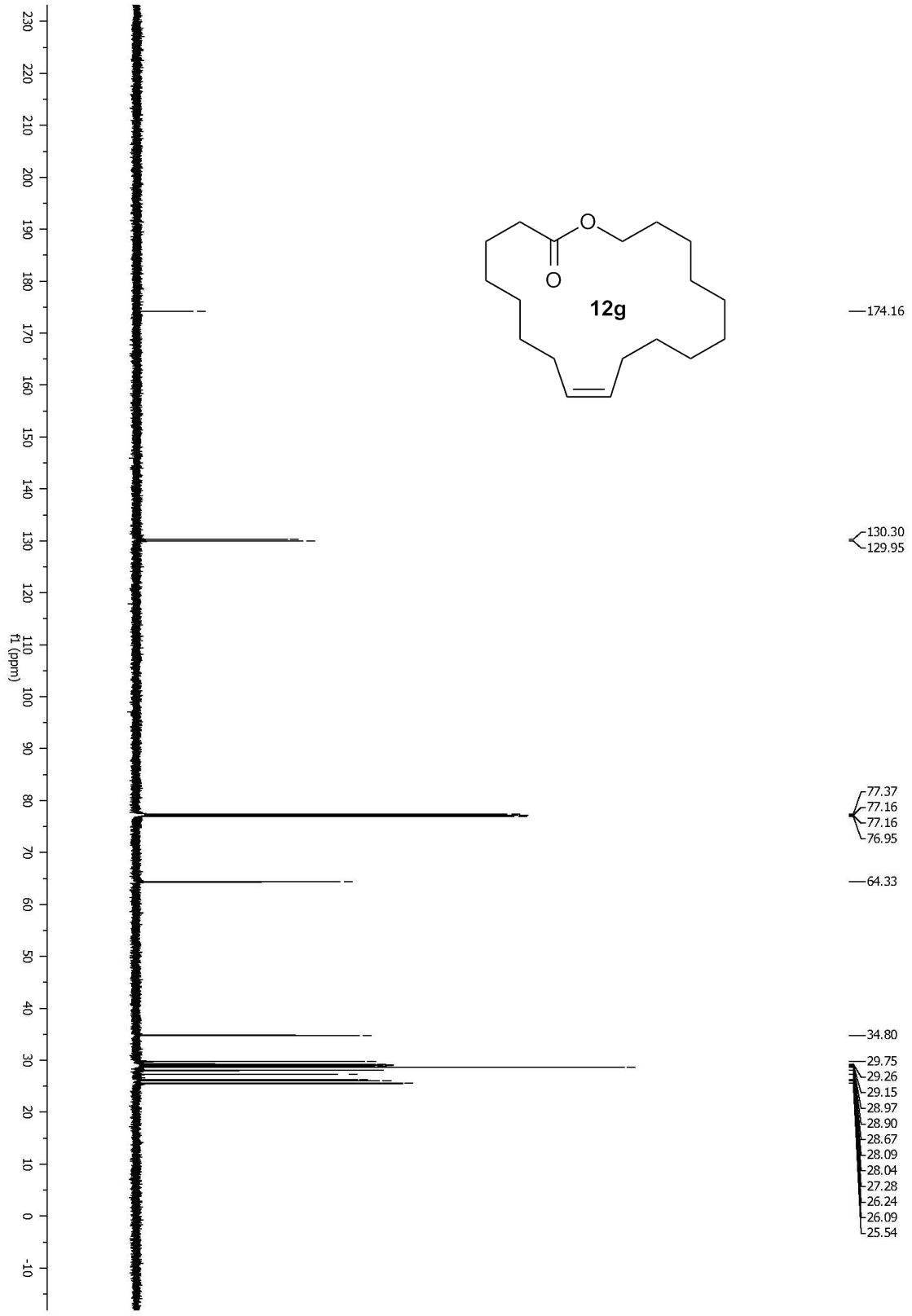
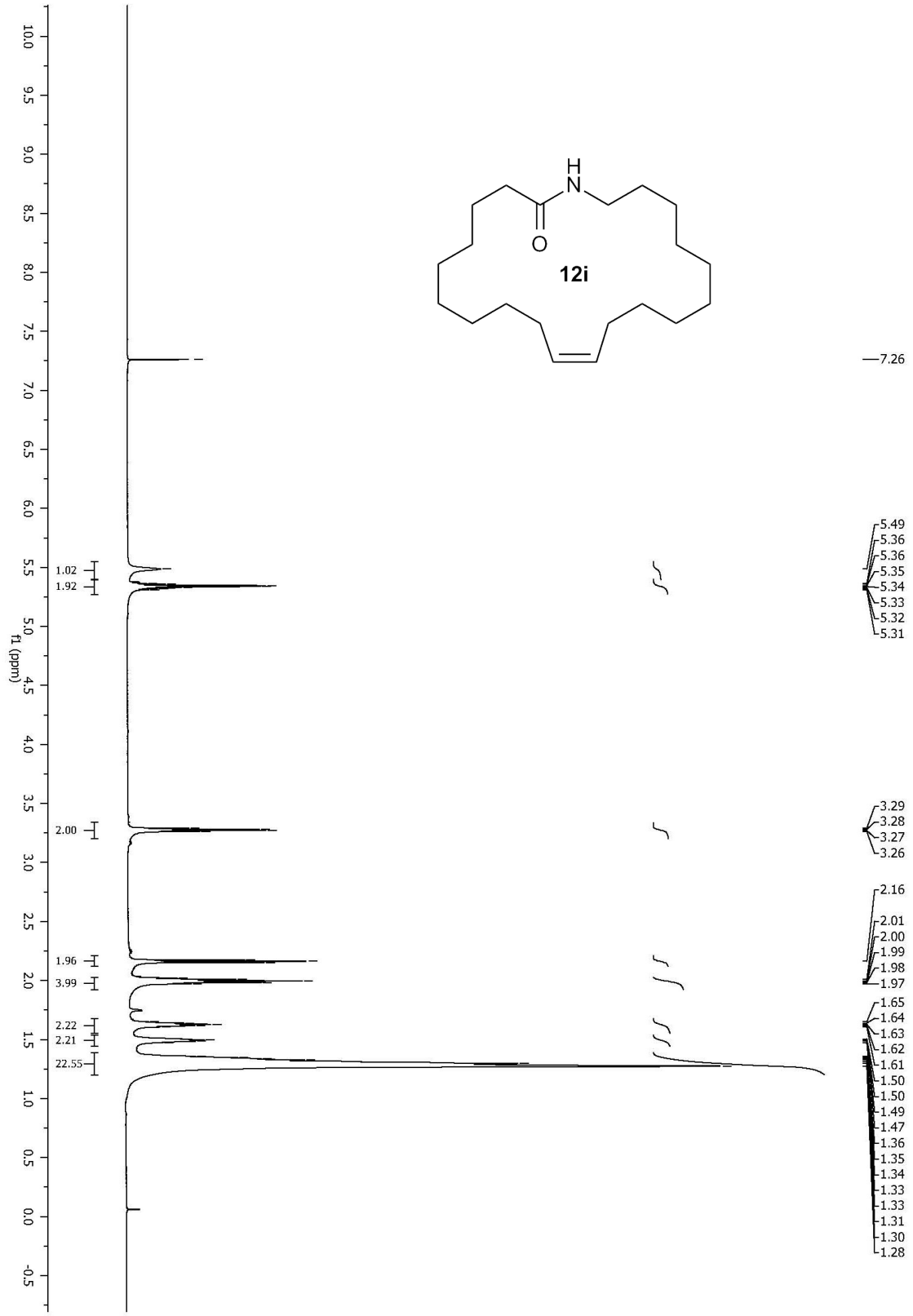
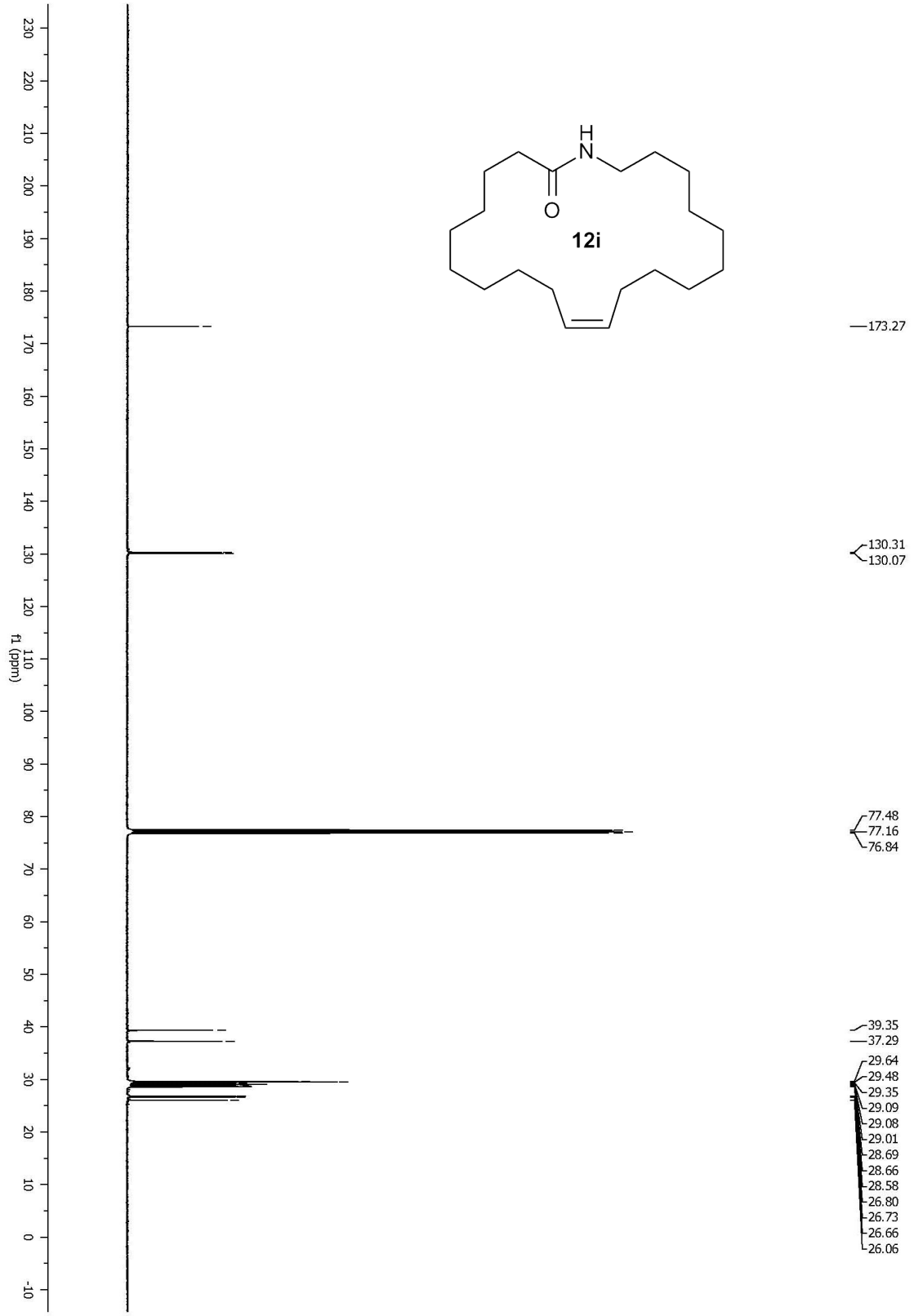
1.35
1.34
1.33
1.32
1.32
1.30
1.25

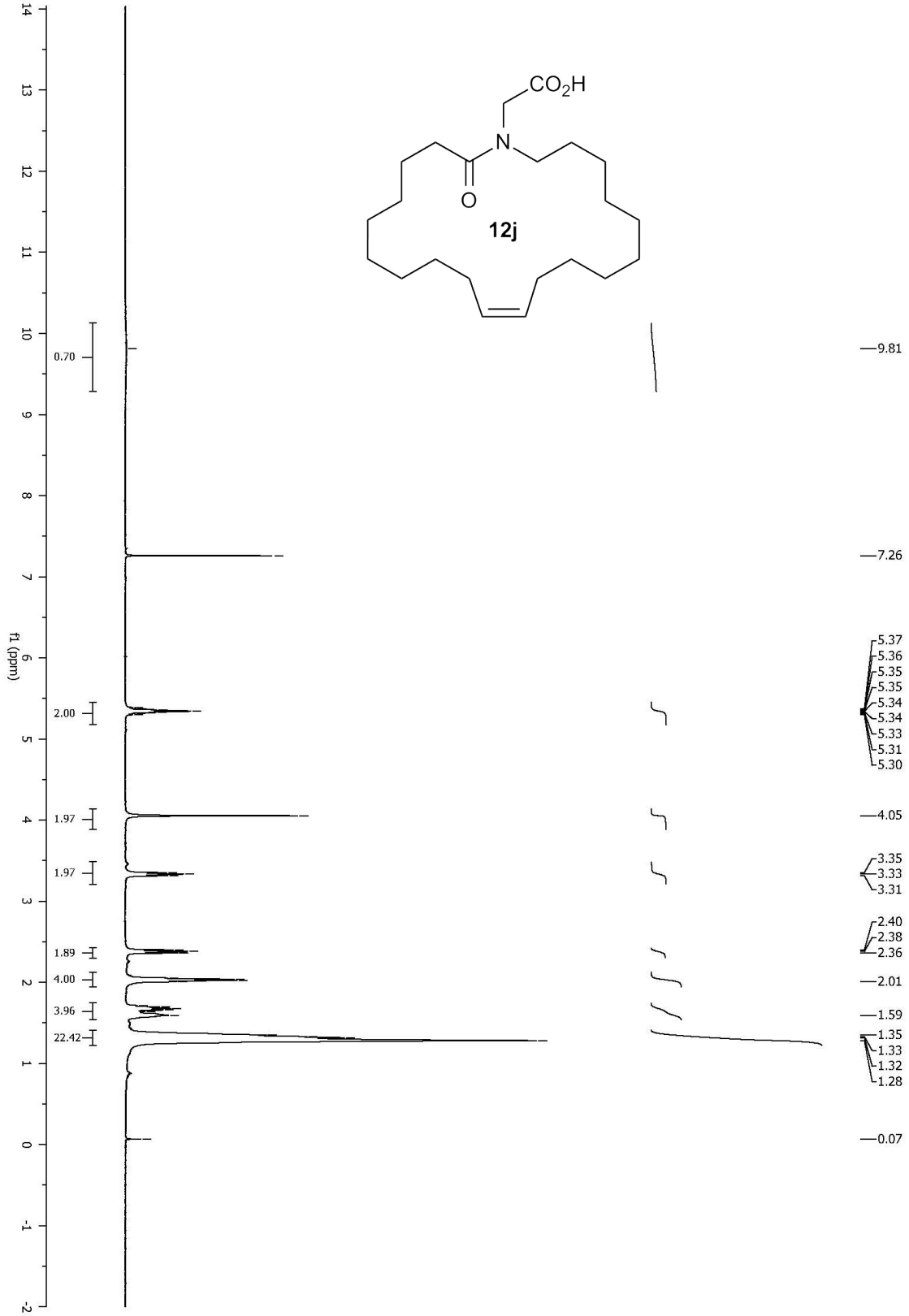

12c
174.07
130.79
129.21
77.37
77.16
76.95
64.27
34.45
29.37
28.24
28.02
27.19
27.16
27.04
25.58
25.48
25.25
f1 (ppm)

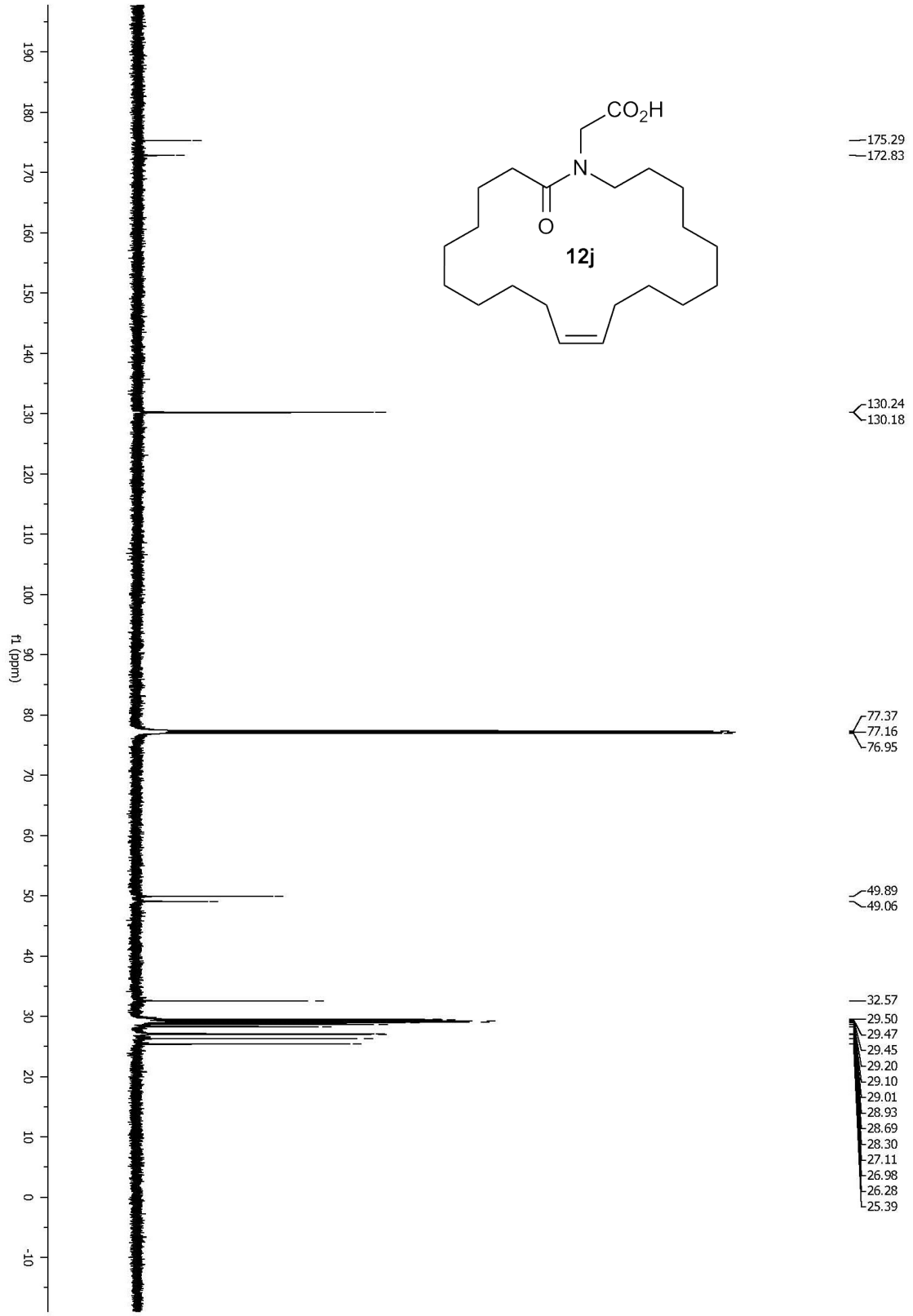

12g
f1 (ppm)
1.93
2.00
1.97
4.08
3.95
18.28
7.26
7.26
5.40
5.39
5.38
5.36
5.36
5.35
5.33
4.14
4.12
4.11
2.33
2.32
2.30
2.03
2.01
2.00
1.58
1.56
1.41
1.40
1.38
1.36
1.33
1.29

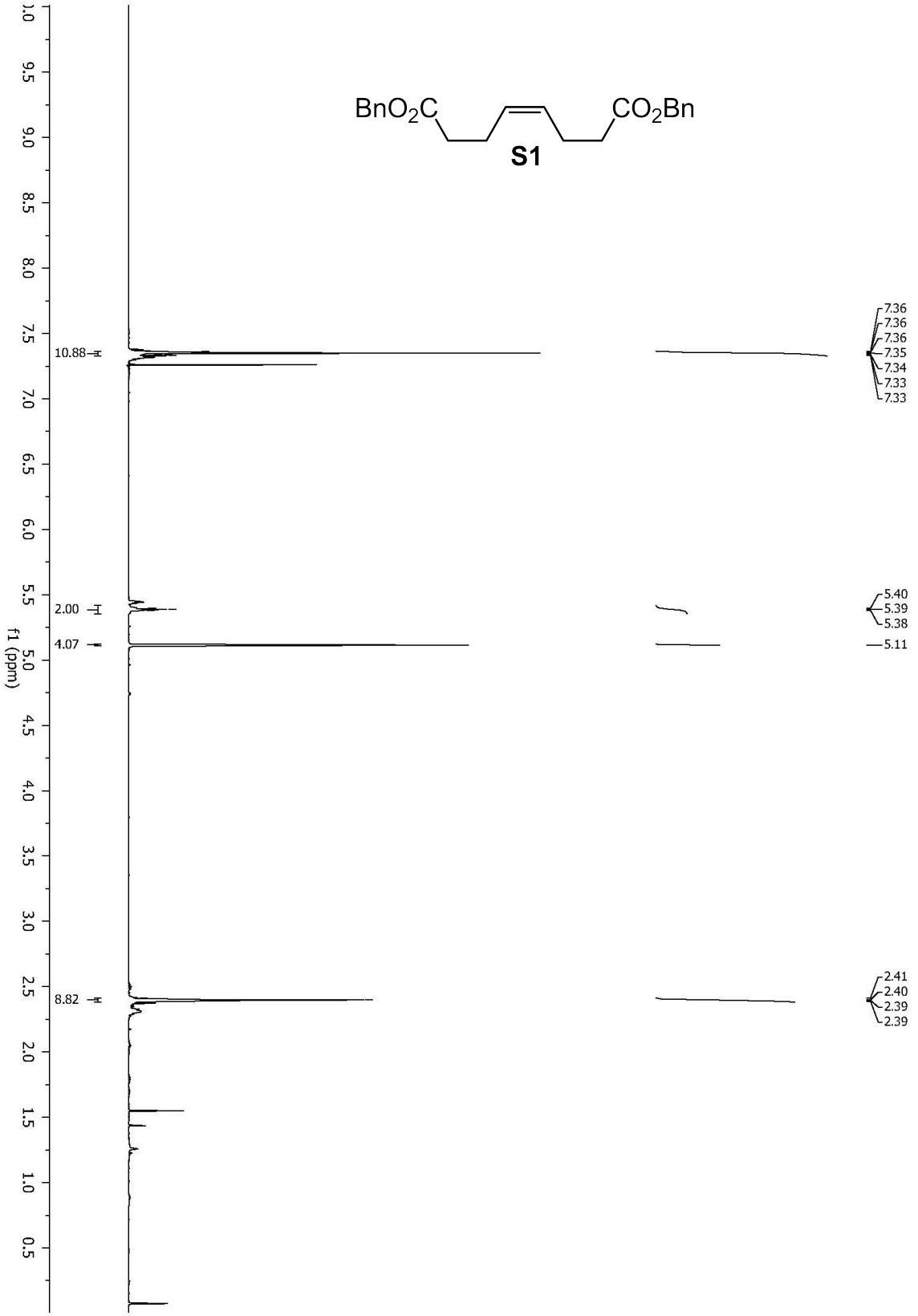

12g
174.16
130.30
129.95
77.37
77.16
77.16
76.95
64.33
34.80
29.75
29.26
29.15
28.97
28.90
28.67
28.09
28.04
27.28
26.24
26.09
25.54
f1 (ppm)

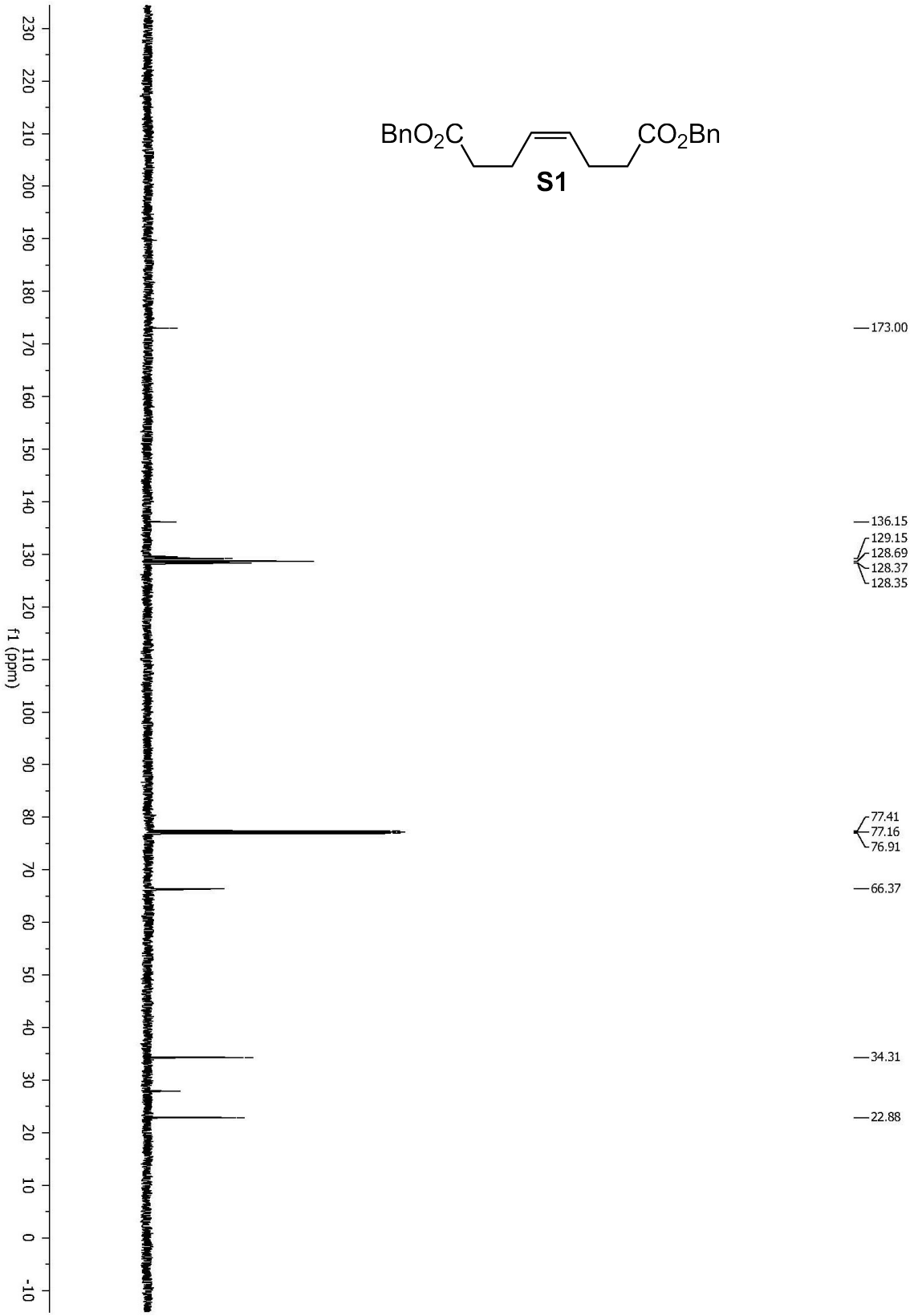

H
N
O
12i
7.26
5.49
5.36
5.36
5.35
5.34
5.33
5.32
5.31
3.29
3.28
3.27
3.26
2.16
2.01
2.00
1.99
1.98
1.97
1.65
1.64
1.63
1.62
1.61
1.50
1.50
1.49
1.47
1.36
1.35
1.34
1.33
1.33
1.31
1.30
1.28
1.02
1.92
2.00
1.96
3.99
2.22
2.21
22.55
f1 (ppm)

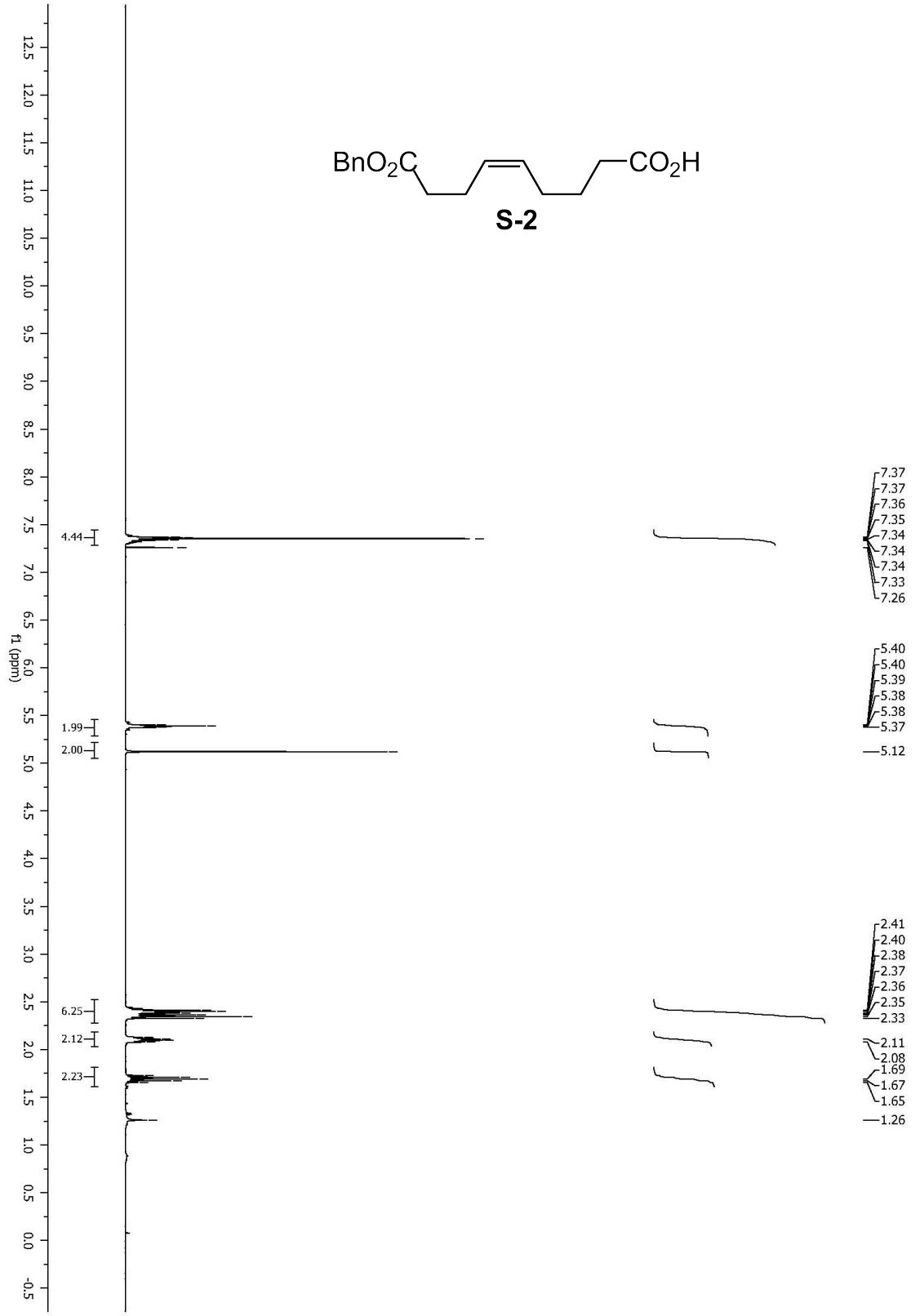

H
N
O
12i
173.27
130.31
130.07
77.48
77.16
76.84
39.35
37.29
29.64
29.48
29.35
29.09
29.08
29.01
28.69
28.66
28.58
26.80
26.73
26.66
26.06
f1 (ppm)

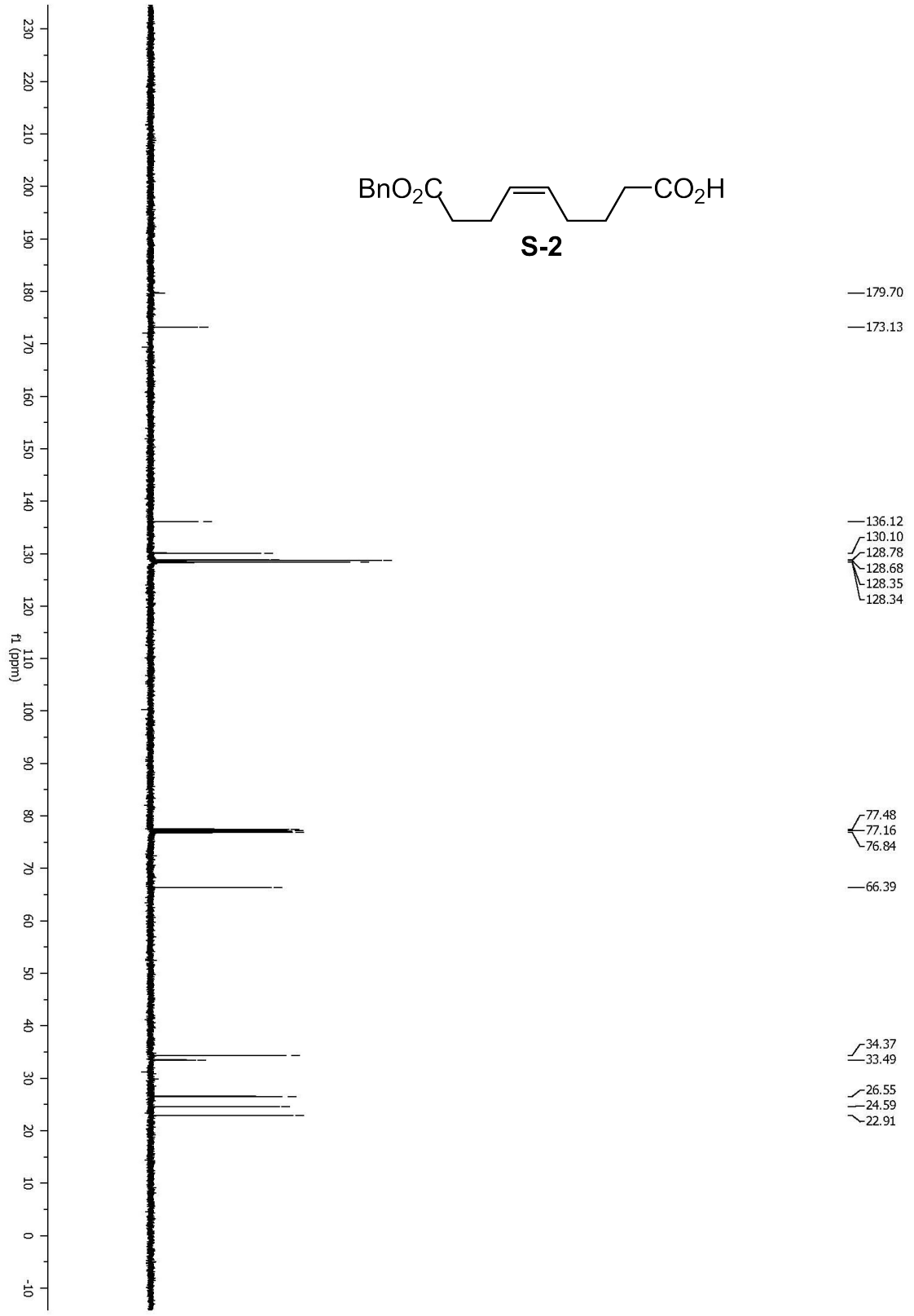

CO2H
N
O
12j
f1 (ppm)
0.70
2.00
1.97
1.97
1.89
4.00
3.96
22.42
9.81
7.26
5.37
5.36
5.35
5.35
5.34
5.34
5.33
5.31
5.30
4.05
3.35
3.33
3.31
2.40
2.38
2.36
2.01
1.59
1.35
1.33
1.32
1.28
0.07

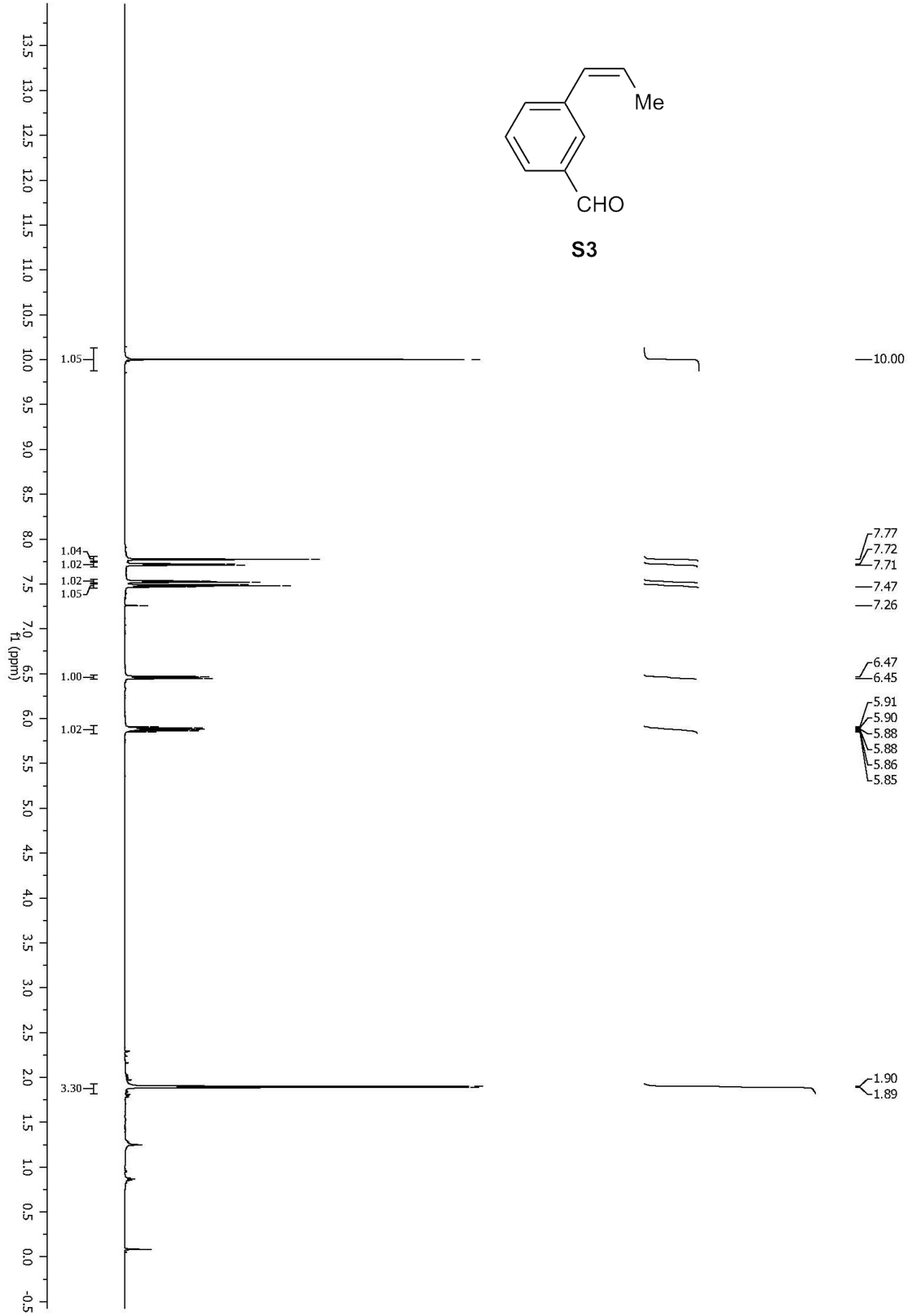

CO2H
N
O
12j
175.29
172.83
130.24
130.18
77.37
77.16
76.95
49.89
49.06
32.57
29.50
29.47
29.45
29.20
29.10
29.01
28.93
28.69
28.30
27.11
26.98
26.28
25.39
f1 (ppm)

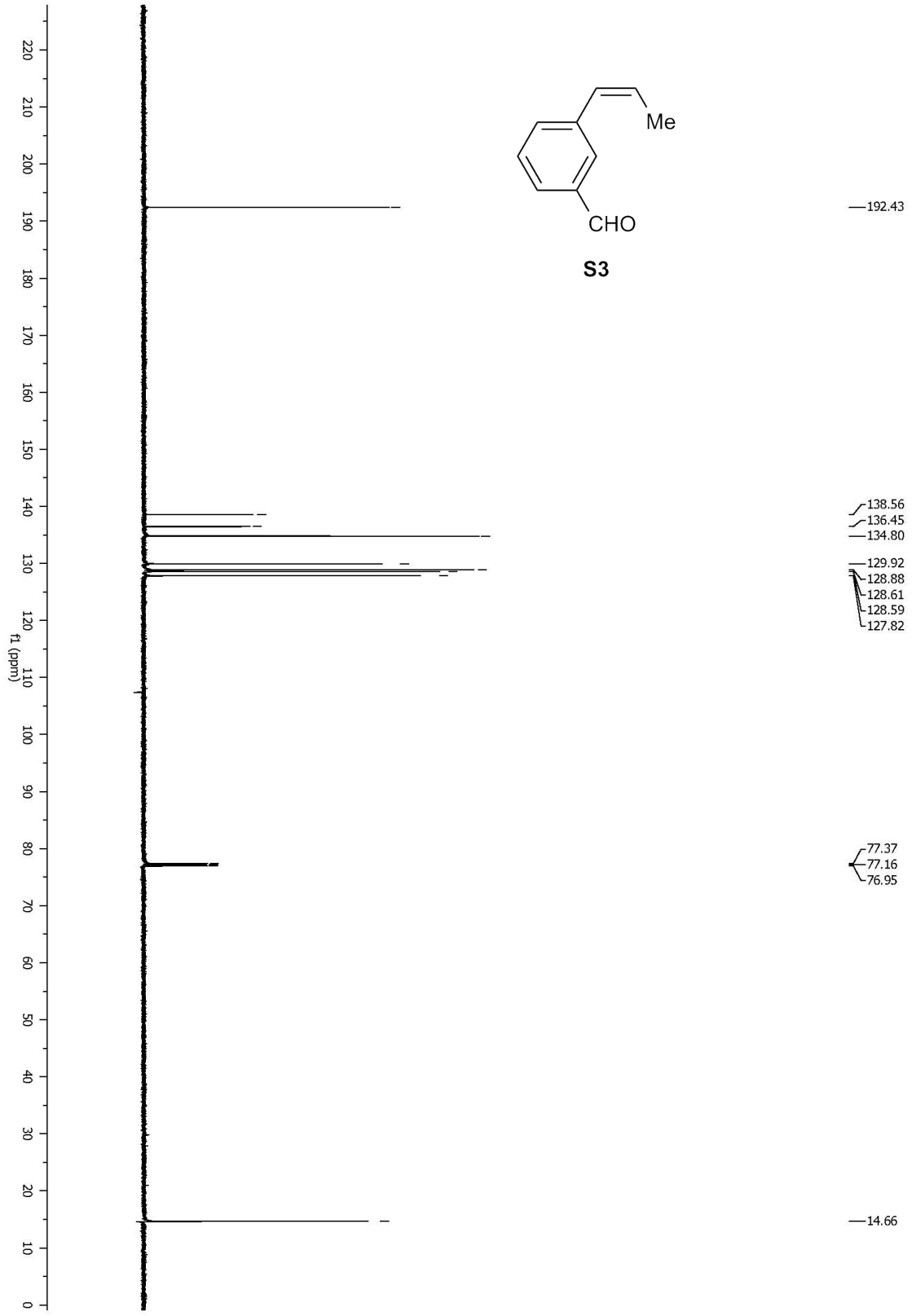

BnO2C
CO2Bn
S1
10.88
2.00
4.07
8.82
7.36
7.36
7.36
7.35
7.34
7.33
7.33
5.40
5.39
5.38
5.11
2.41
2.40
2.39
2.39
f1 (ppm)

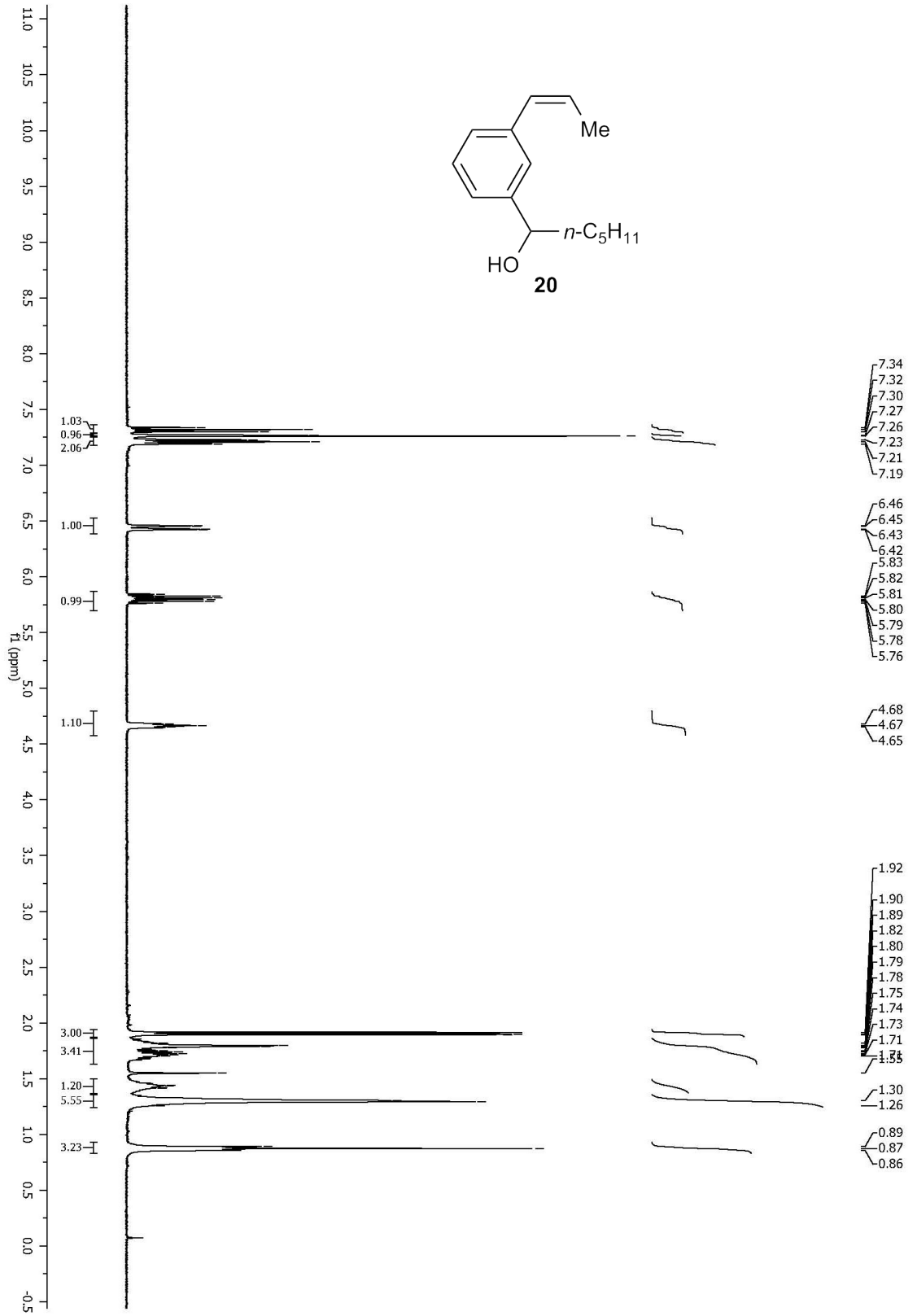

BnO2C
CO2Bn
S1
173.00
136.15
129.15
128.69
128.37
128.35
77.41
77.16
76.91
66.37
34.31
22.88
f1 (ppm)

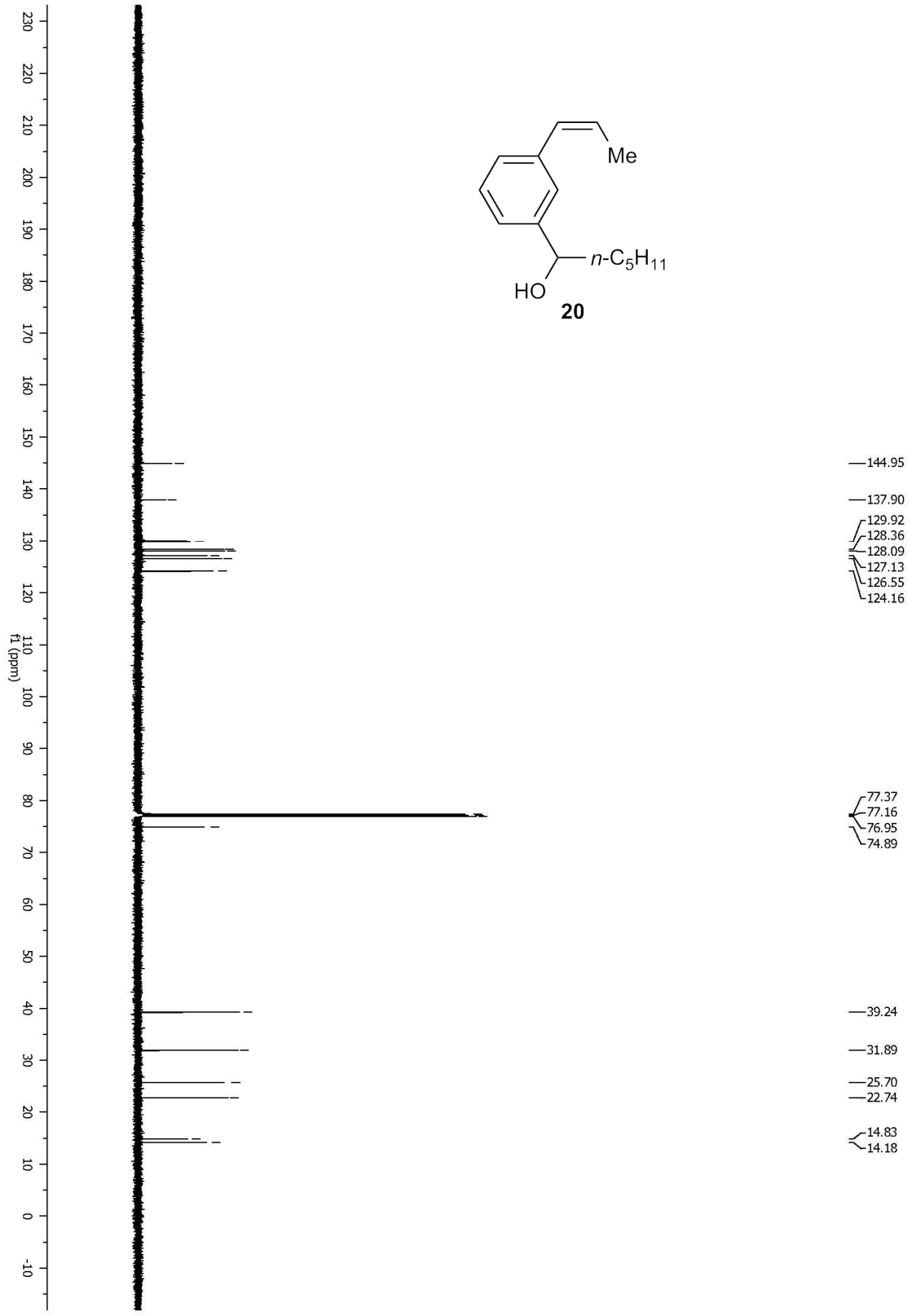

BnO2C
CO2H
S-2
f1 (ppm)
4.44
1.99
2.00
6.25
2.12
2.23
7.37
7.37
7.36
7.35
7.34
7.34
7.34
7.33
7.26
5.40
5.40
5.39
5.38
5.38
5.37
5.12
2.41
2.40
2.38
2.37
2.36
2.35
2.33
2.11
2.08
1.69
1.67
1.65
1.26

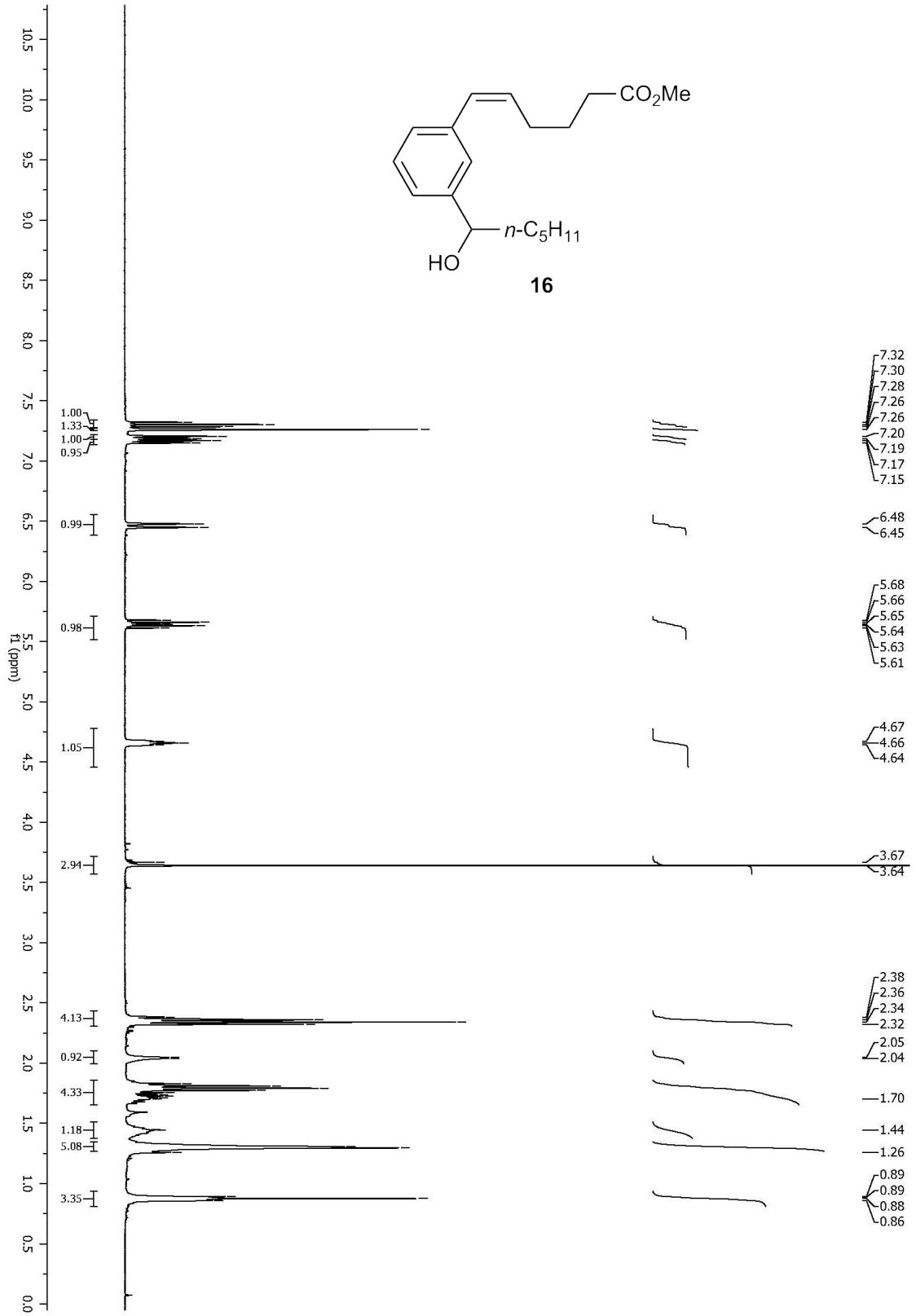

BnO2C
CO2H
S-2
179.70
173.13
136.12
130.10
128.78
128.68
128.35
128.34
77.48
77.16
76.84
66.39
34.37
33.49
26.55
24.59
22.91
f1 (ppm)

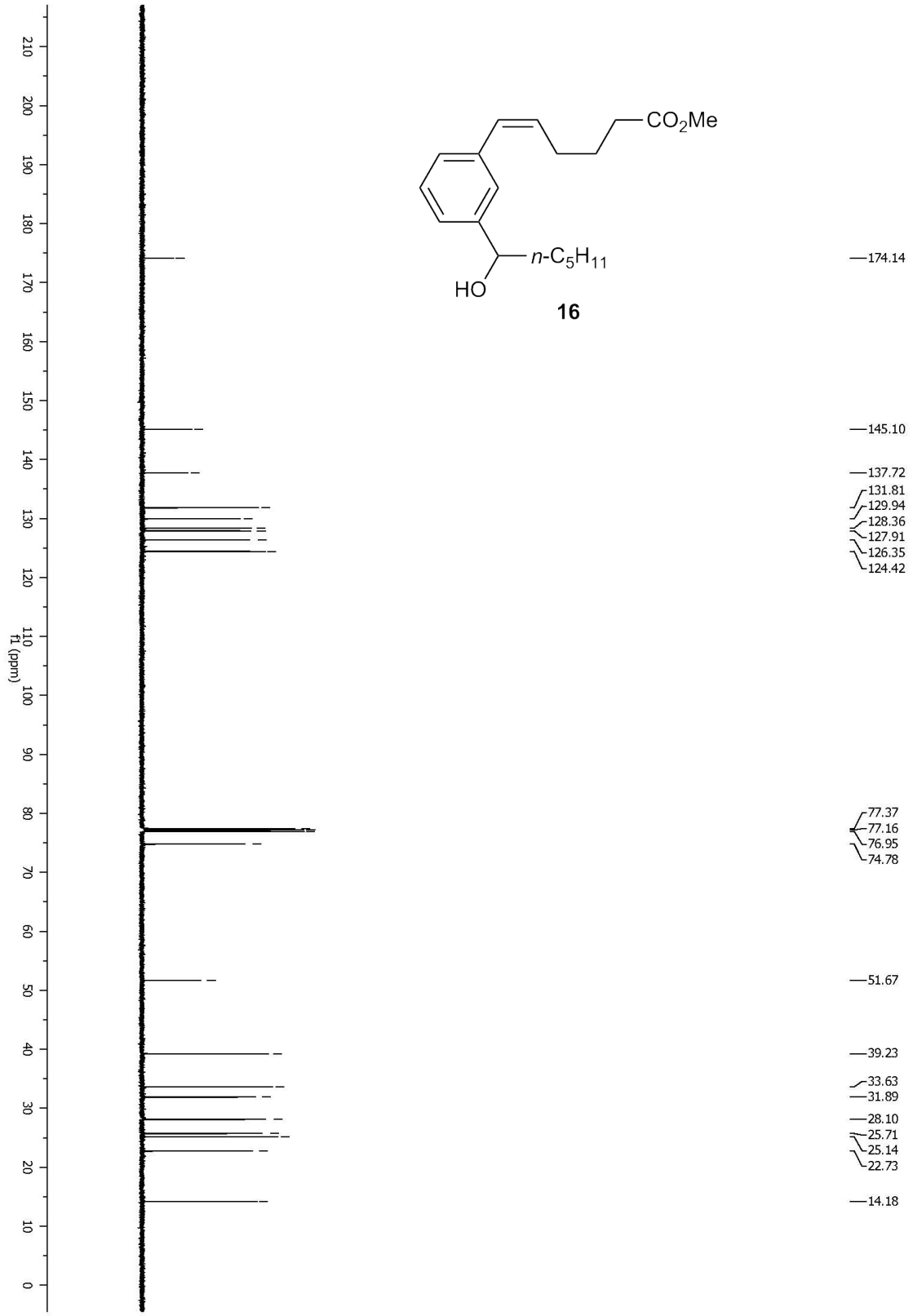

Me
CHO
S3
f1 (ppm)
1.05
1.04
1.02
1.02
1.05
1.00
1.02
3.30
10.00
7.77
7.72
7.71
7.47
7.26
6.47
6.45
5.91
5.90
5.88
5.88
5.86
5.85
1.90
1.89

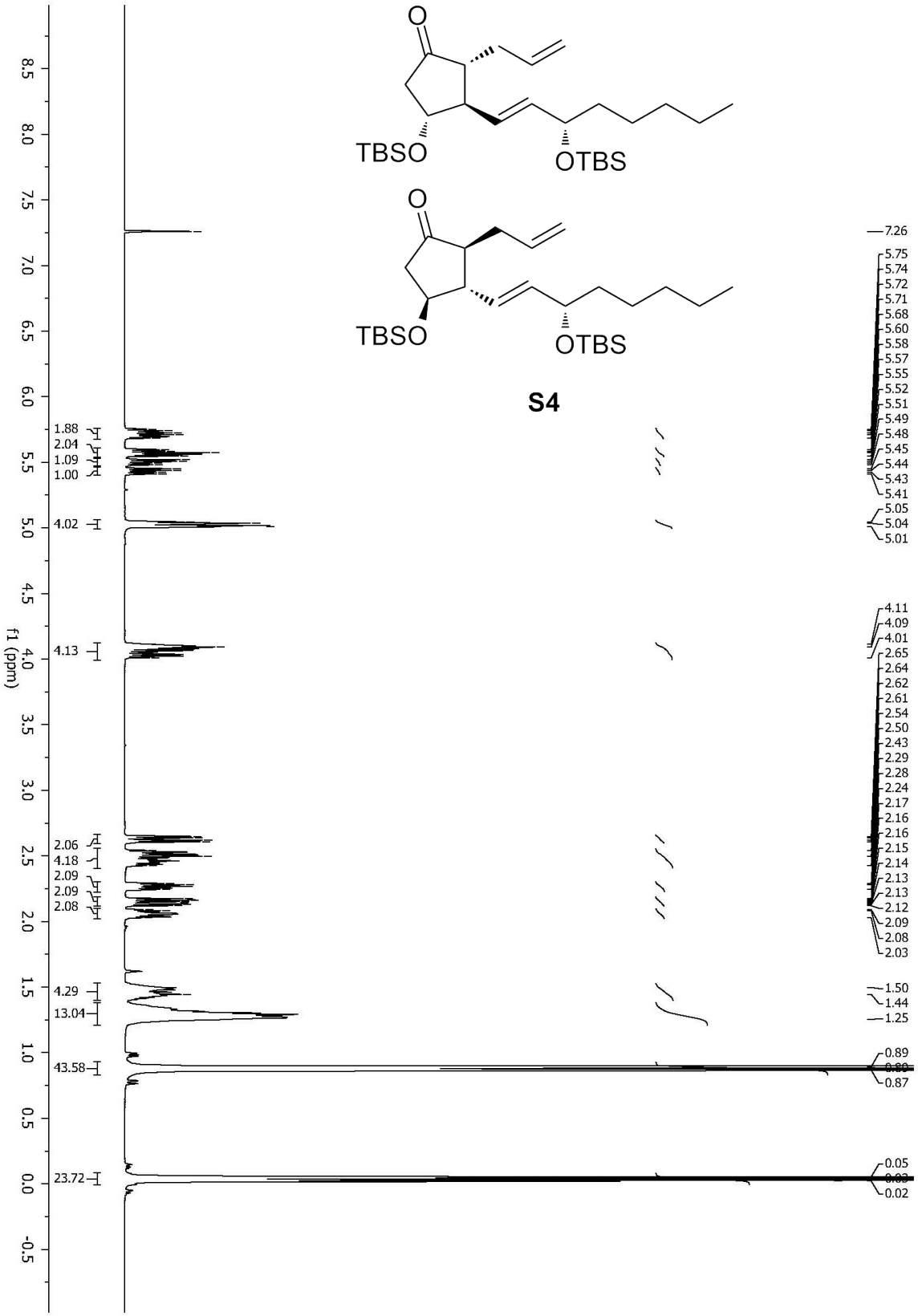

Me
CHO
S3
192.43
138.56
136.45
134.80
129.92
128.88
128.61
128.59
127.82
77.37
77.16
76.95
14.66
f1 (ppm)

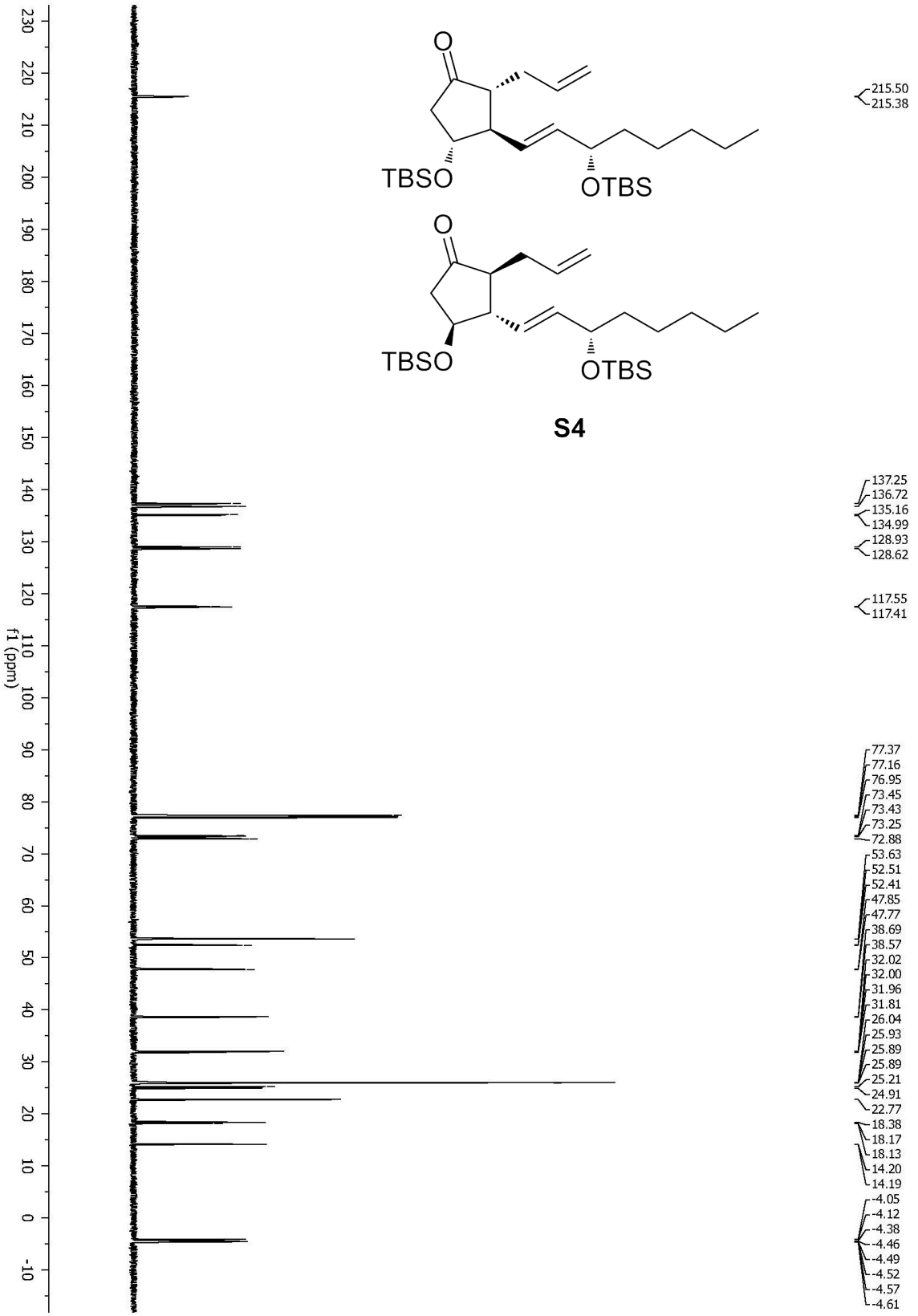

Me
n-C5H11
HO
20
f1 (ppm)
1.03
0.96
2.06
1.00
0.99
1.10
3.00
3.41
1.20
5.55
3.23
7.34
7.32
7.30
7.27
7.26
7.23
7.21
7.19
6.46
6.45
6.43
6.42
5.83
5.82
5.81
5.80
5.79
5.78
5.76
4.68
4.67
4.65
1.92
1.90
1.89
1.82
1.80
1.79
1.78
1.75
1.74
1.73
1.71
1.30
1.26
0.89
0.87
0.86


Me
n-C5H11
HO
20
144.95
137.90
129.92
128.36
128.09
127.13
126.55
124.16
77.37
77.16
76.95
74.89
39.24
31.89
25.70
22.74
14.83
14.18
f1 (ppm)

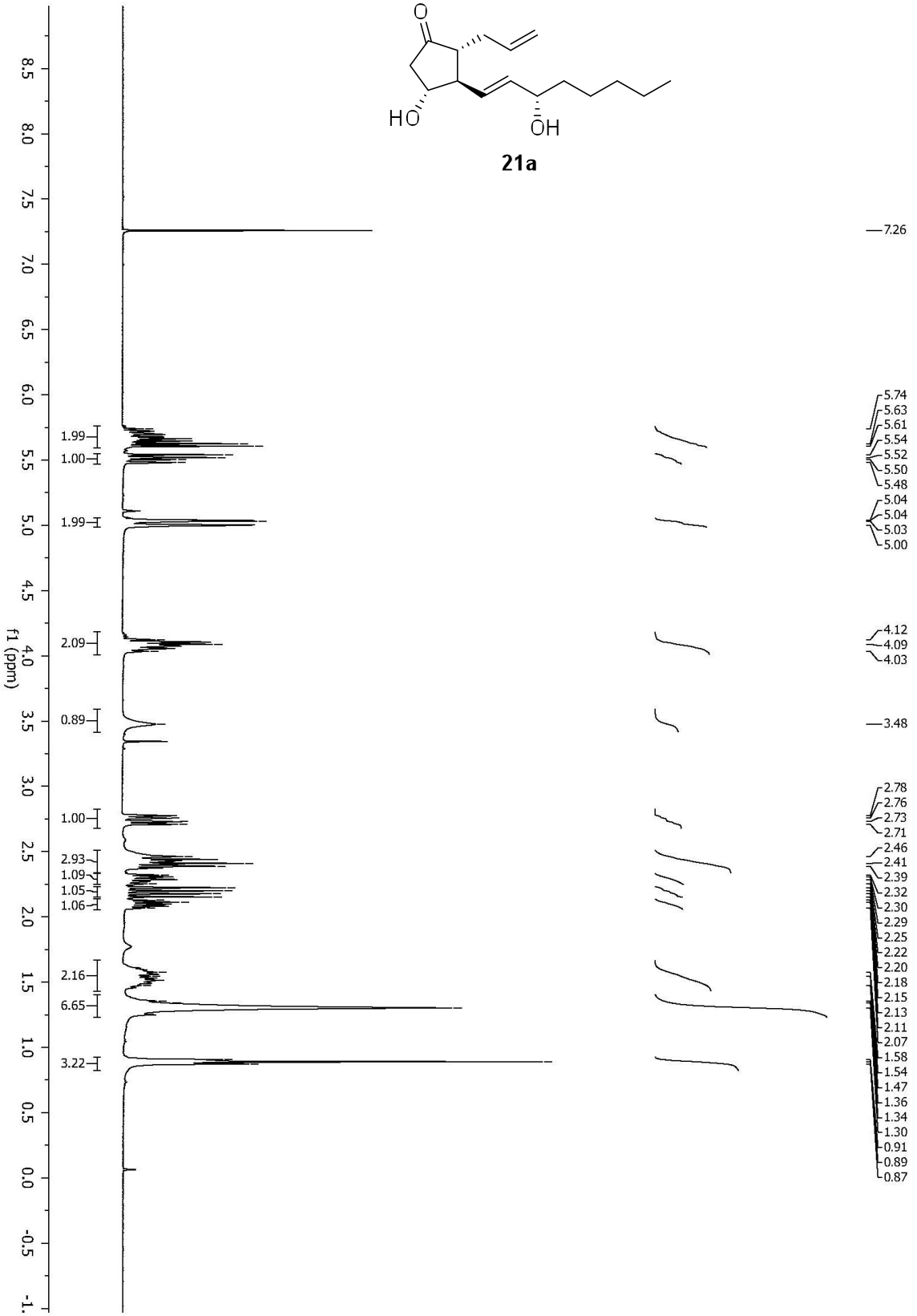

CO2Me
n-C5H11
HO
16
f1 (ppm)
1.00
1.33
1.00
0.95
0.99
0.98
1.05
2.94
4.13
0.92
4.33
1.18
5.08
3.35
7.32
7.30
7.28
7.26
7.26
7.20
7.19
7.17
7.15
6.48
6.45
5.68
5.66
5.65
5.64
5.63
5.61
4.67
4.66
4.64
3.67
3.64
2.38
2.36
2.34
2.32
2.05
2.04
1.70
1.44
1.26
0.89
0.89
0.88
0.86

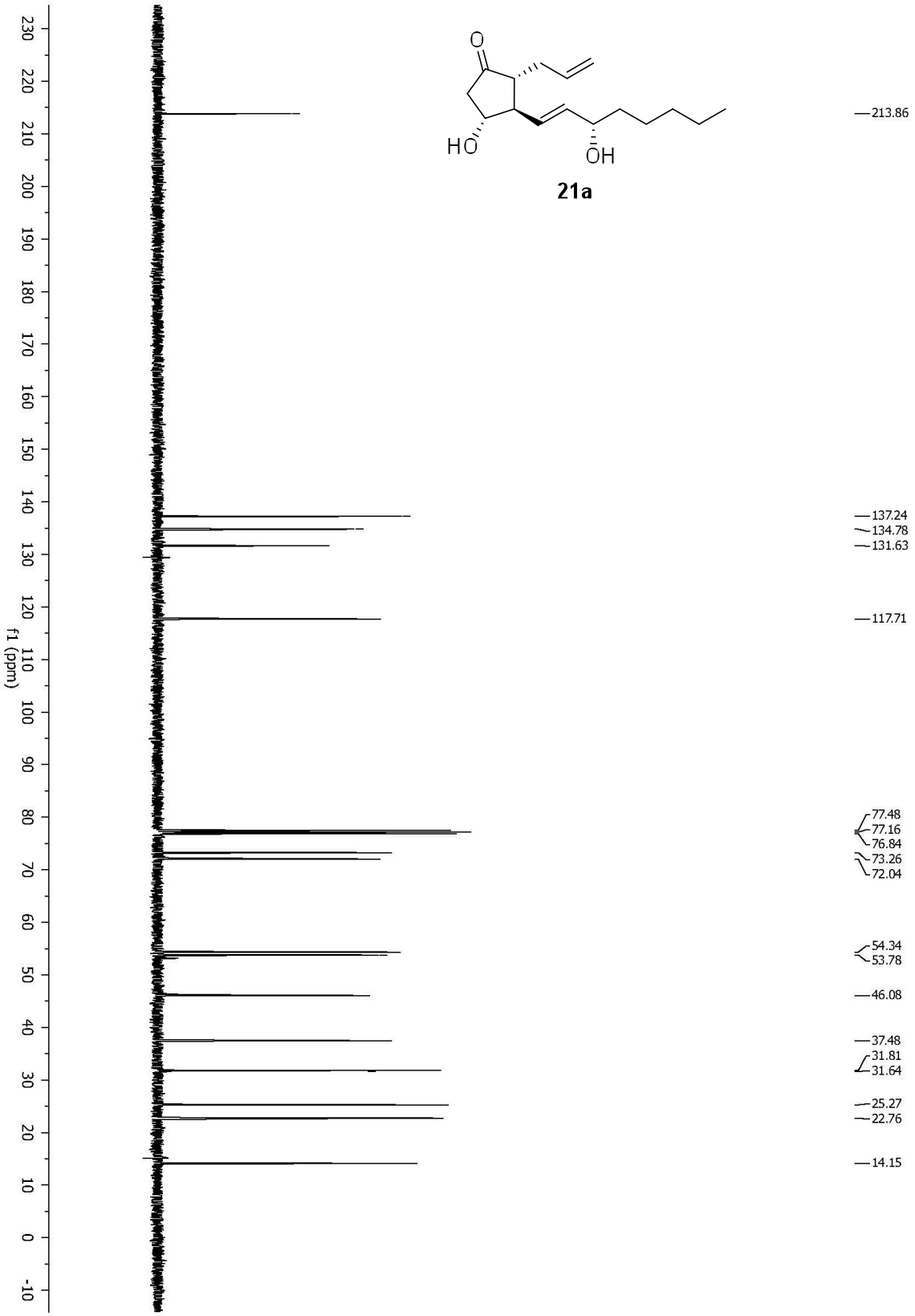

CO2Me
n-C5H11
HO
16
174.14
145.10
137.72
131.81
129.94
128.36
127.91
126.35
124.42
77.37
77.16
76.95
74.78
51.67
39.23
33.63
31.89
28.10
25.71
25.14
22.73
14.18
f1 (ppm)

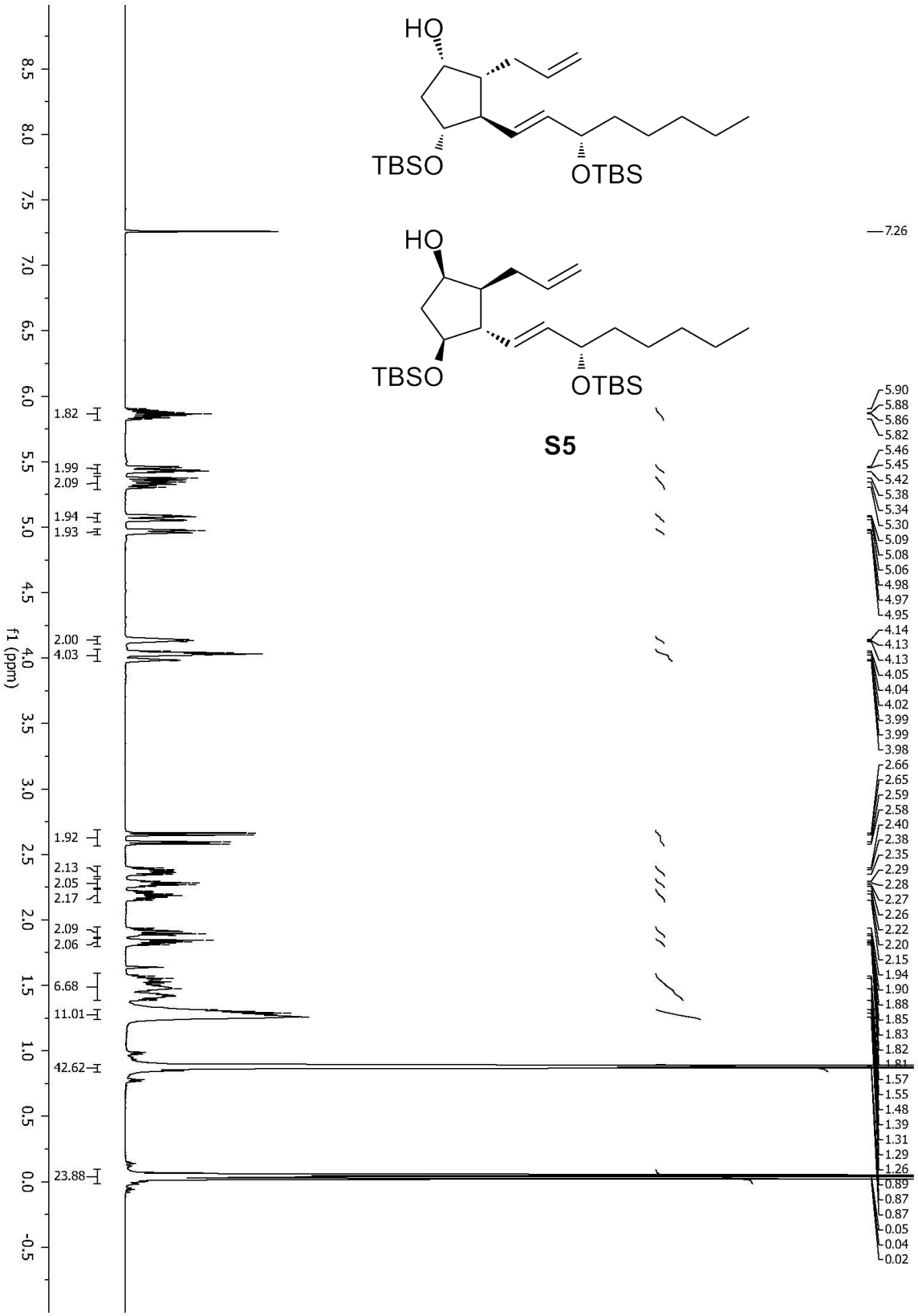

O
TBSO
OTBS
O
TBSO
OTBS
S4
f1 (ppm)
1.88
2.04
1.09
1.00
4.02
4.13
2.06
4.18
2.09
2.09
2.08
4.29
13.04
43.58
23.72
7.26
5.75
5.74
5.72
5.71
5.68
5.60
5.58
5.57
5.55
5.52
5.51
5.49
5.48
5.45
5.44
5.43
5.41
5.05
5.04
5.01
4.11
4.09
4.01
2.65
2.64
2.62
2.61
2.54
2.50
2.43
2.29
2.28
2.24
2.17
2.16
2.16
2.15
2.14
2.13
2.13
2.12
2.09
2.08
2.03
1.50
1.44
1.25
0.89
0.87
0.05
0.02

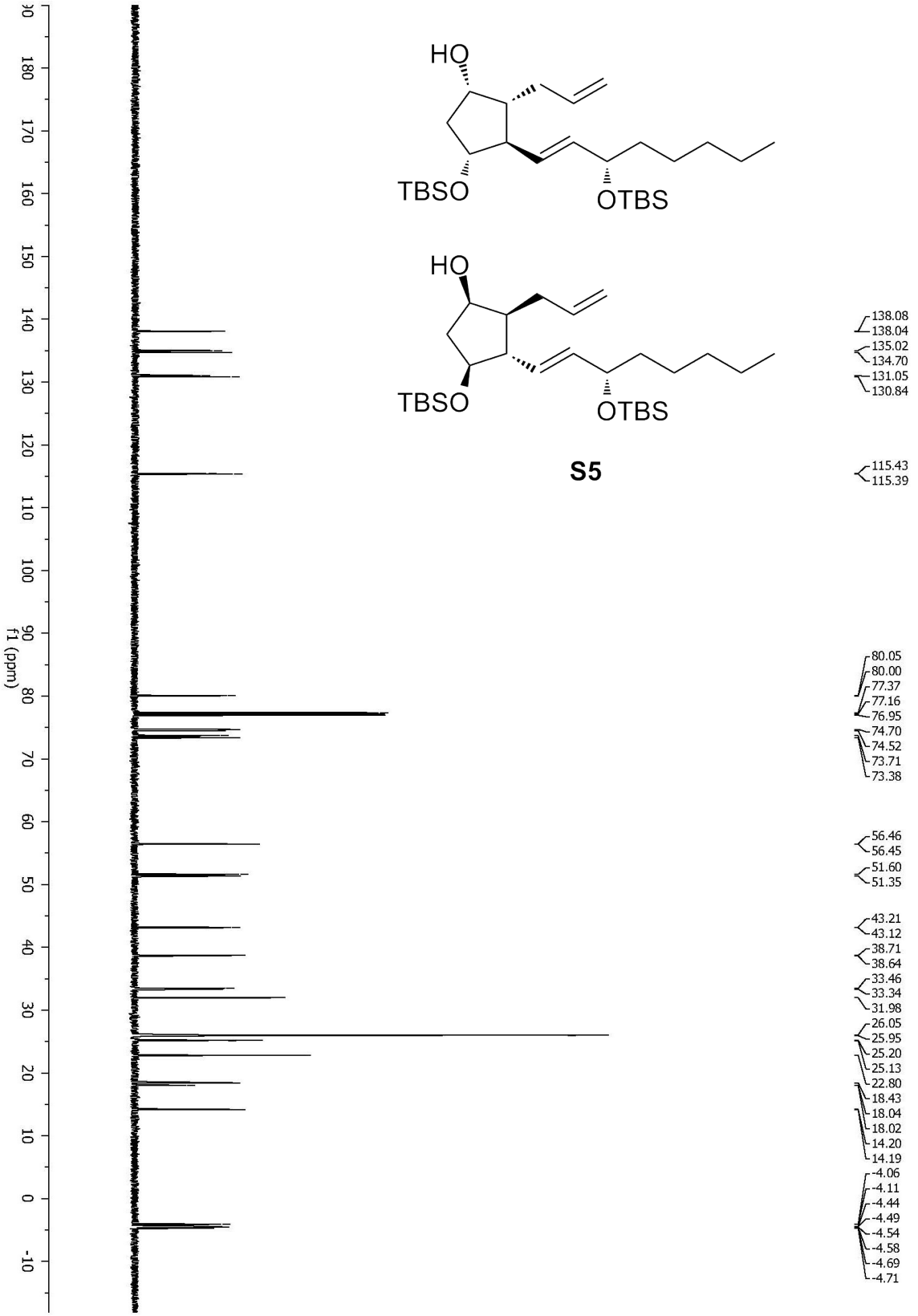

O
TBSO
OTBS
O
TBSO
OTBS
215.50
215.38
137.25
136.72
135.16
134.99
128.93
128.62
117.55
117.41
77.37
77.16
76.95
73.45
73.43
73.25
72.88
53.63
52.51
52.41
47.85
47.77
38.69
38.57
32.02
32.00
31.96
31.81
26.04
25.93
25.89
25.89
25.21
24.91
22.77
18.38
18.17
18.13
14.20
14.19
-4.05
-4.12
-4.38
-4.46
-4.49
-4.52
-4.57
-4.61
f1 (ppm)

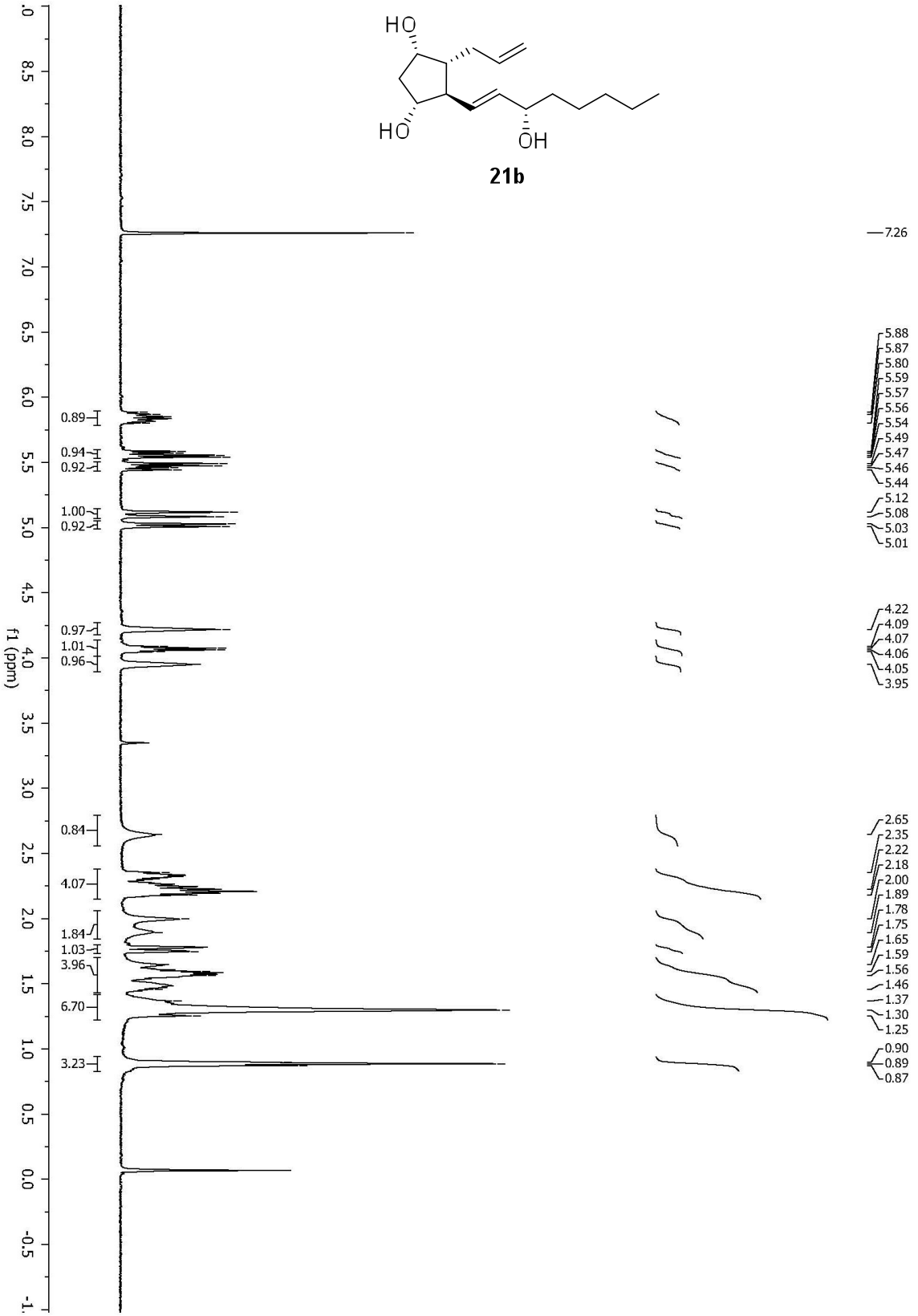
S4

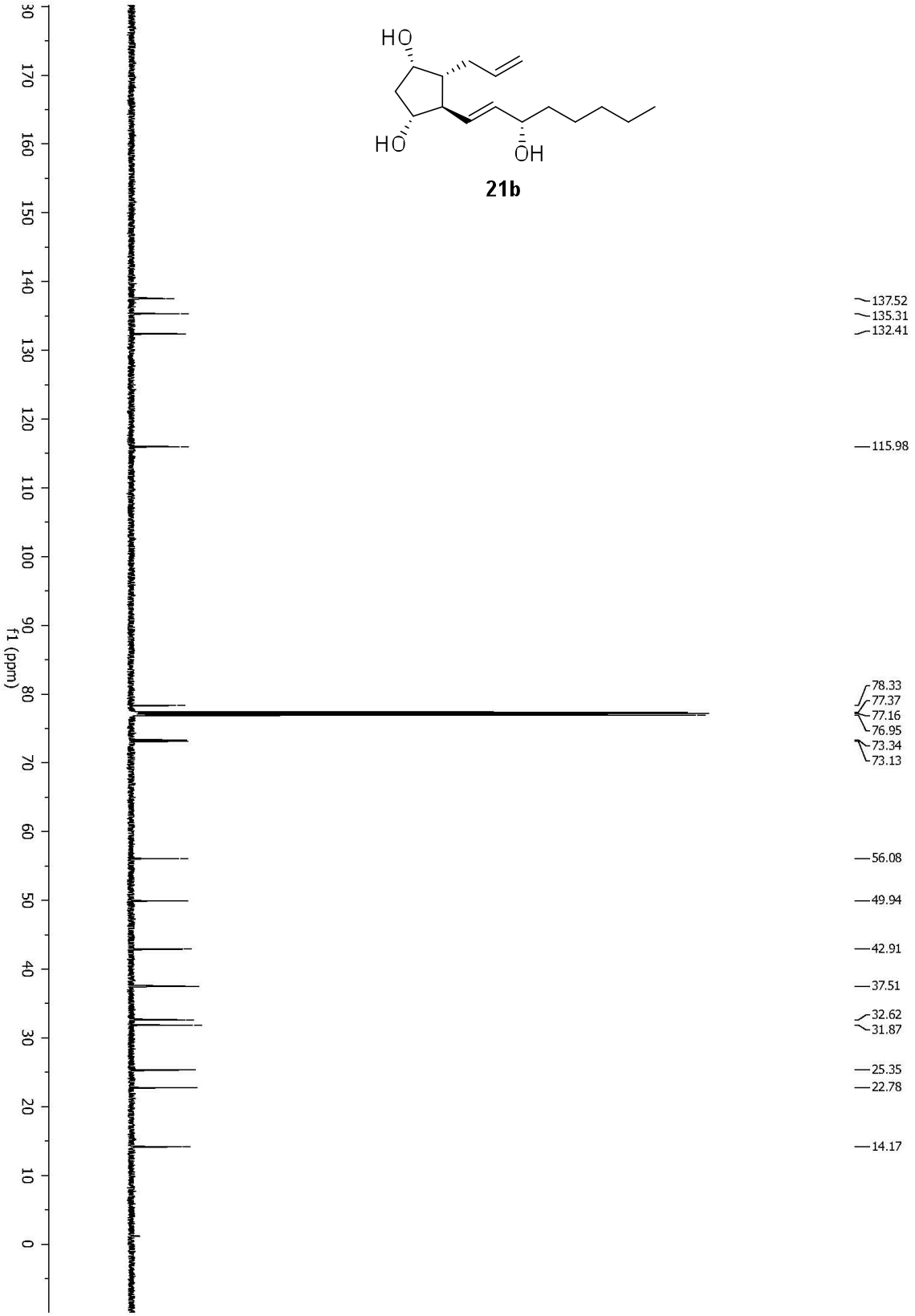

O
HO
OH
21a
f1 (ppm)
1.99
1.00
1.99
2.09
0.89
1.00
2.93
1.09
1.05
1.06
2.16
6.65
3.22
7.26
5.74
5.63
5.61
5.54
5.52
5.50
5.48
5.04
5.04
5.03
5.00
4.12
4.09
4.03
3.48
2.78
2.76
2.73
2.71
2.46
2.41
2.39
2.32
2.30
2.29
2.25
2.22
2.20
2.18
2.15
2.13
2.11
2.07
1.58
1.54
1.47
1.36
1.34
1.30
0.91
0.89
0.87

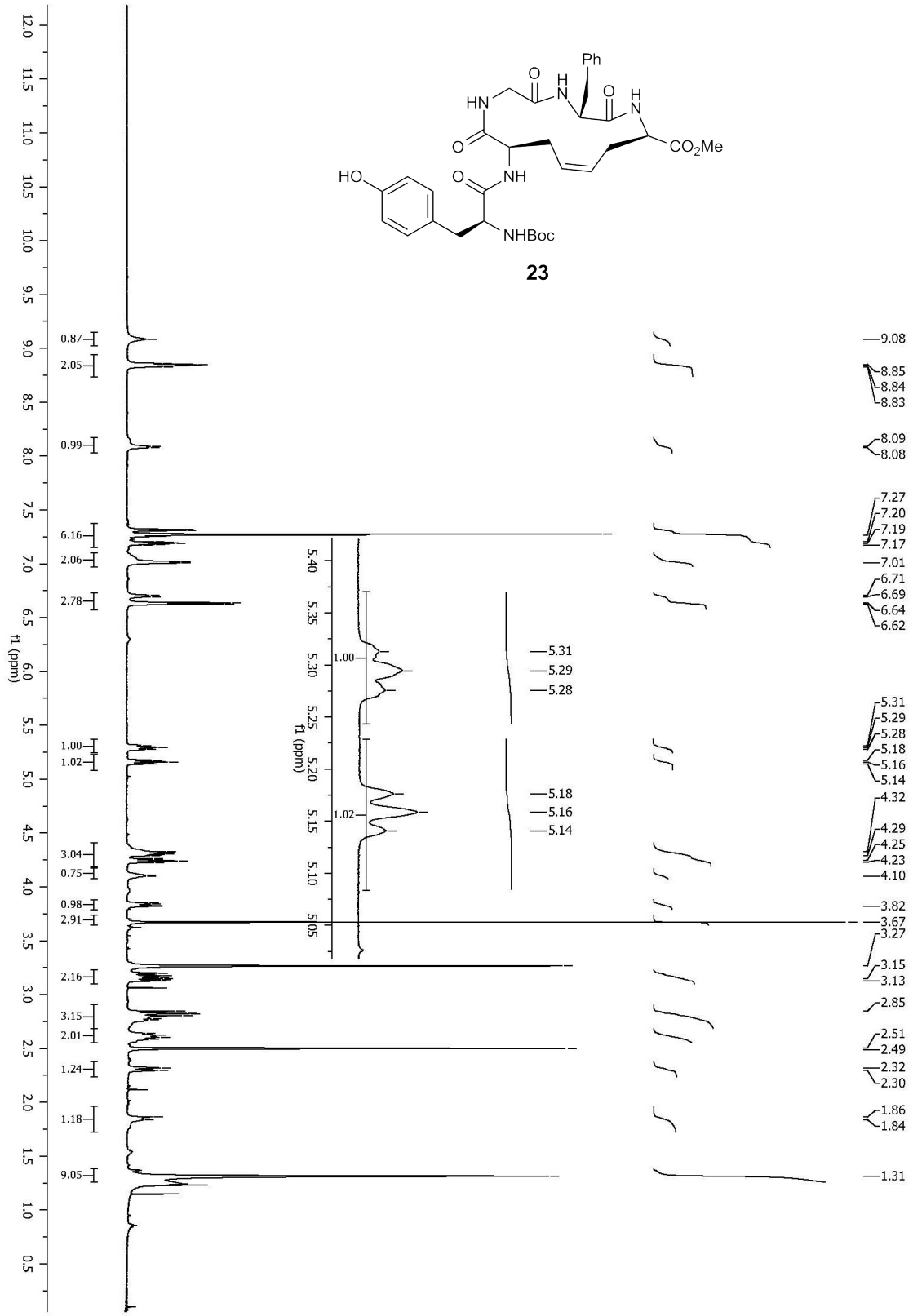

O
HO
OH
21a
213.86
137.24
134.78
131.63
117.71
77.48
77.16
76.84
73.26
72.04
54.34
53.78
46.08
37.48
31.81
31.64
25.27
22.76
14.15
f1 (ppm)

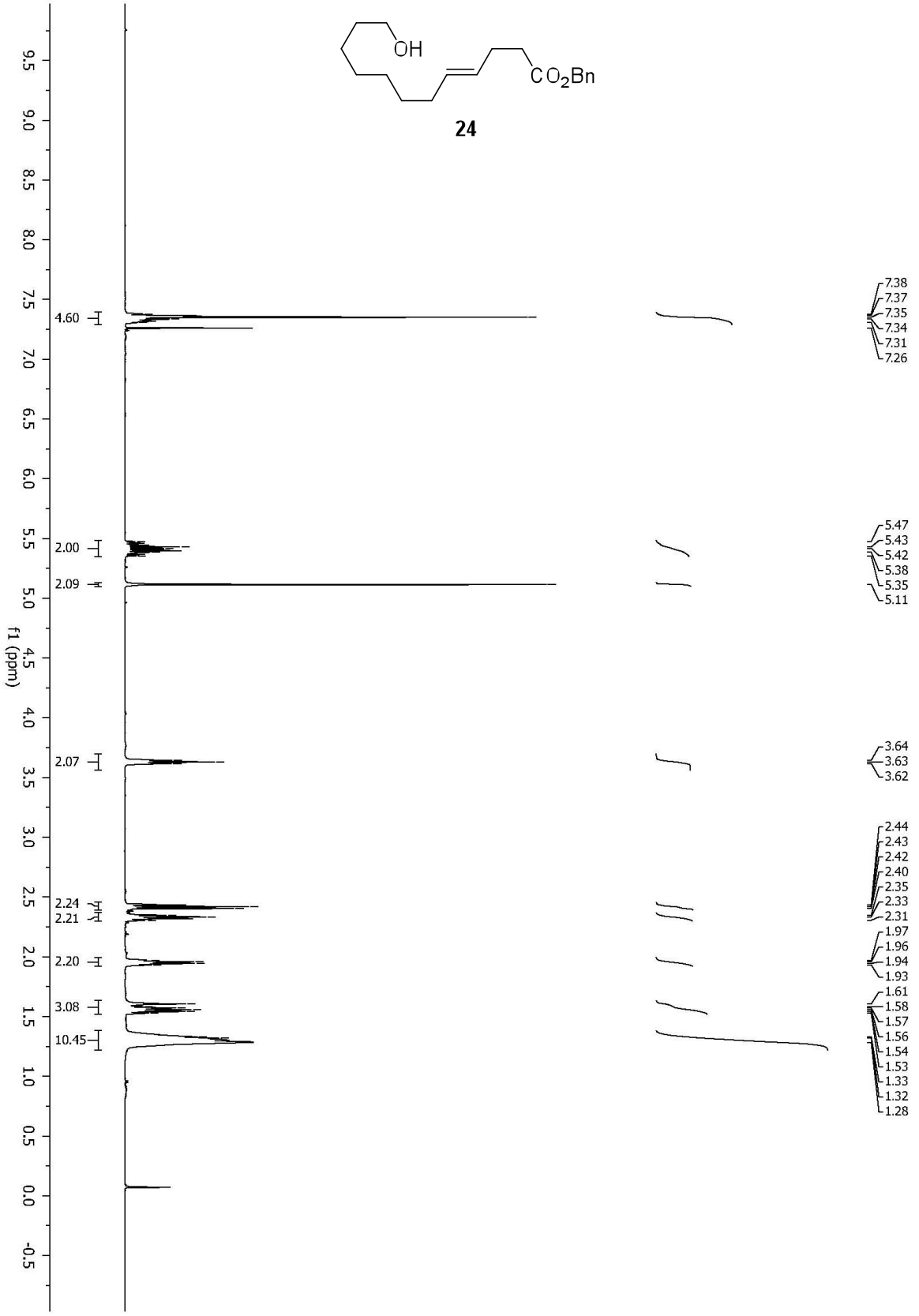

HO
TBSO
OTBS
HO
TBSO
OTBS
S5
f1 (ppm)
1.82
1.99
2.09
1.94
1.93
2.00
4.03
1.92
2.13
2.05
2.17
2.09
2.06
6.68
11.01
42.62
23.88
7.26
5.90
5.88
5.86
5.82
5.46
5.45
5.42
5.38
5.34
5.30
5.09
5.08
5.06
4.98
4.97
4.95
4.14
4.13
4.13
4.05
4.04
4.02
3.99
3.99
3.98
2.66
2.65
2.59
2.58
2.40
2.38
2.35
2.29
2.28
2.27
2.26
2.22
2.20
2.15
1.94
1.90
1.88
1.85
1.83
1.82
1.57
1.55
1.48
1.39
1.31
1.29
1.26
0.89
0.87
0.87
0.05
0.04
0.02

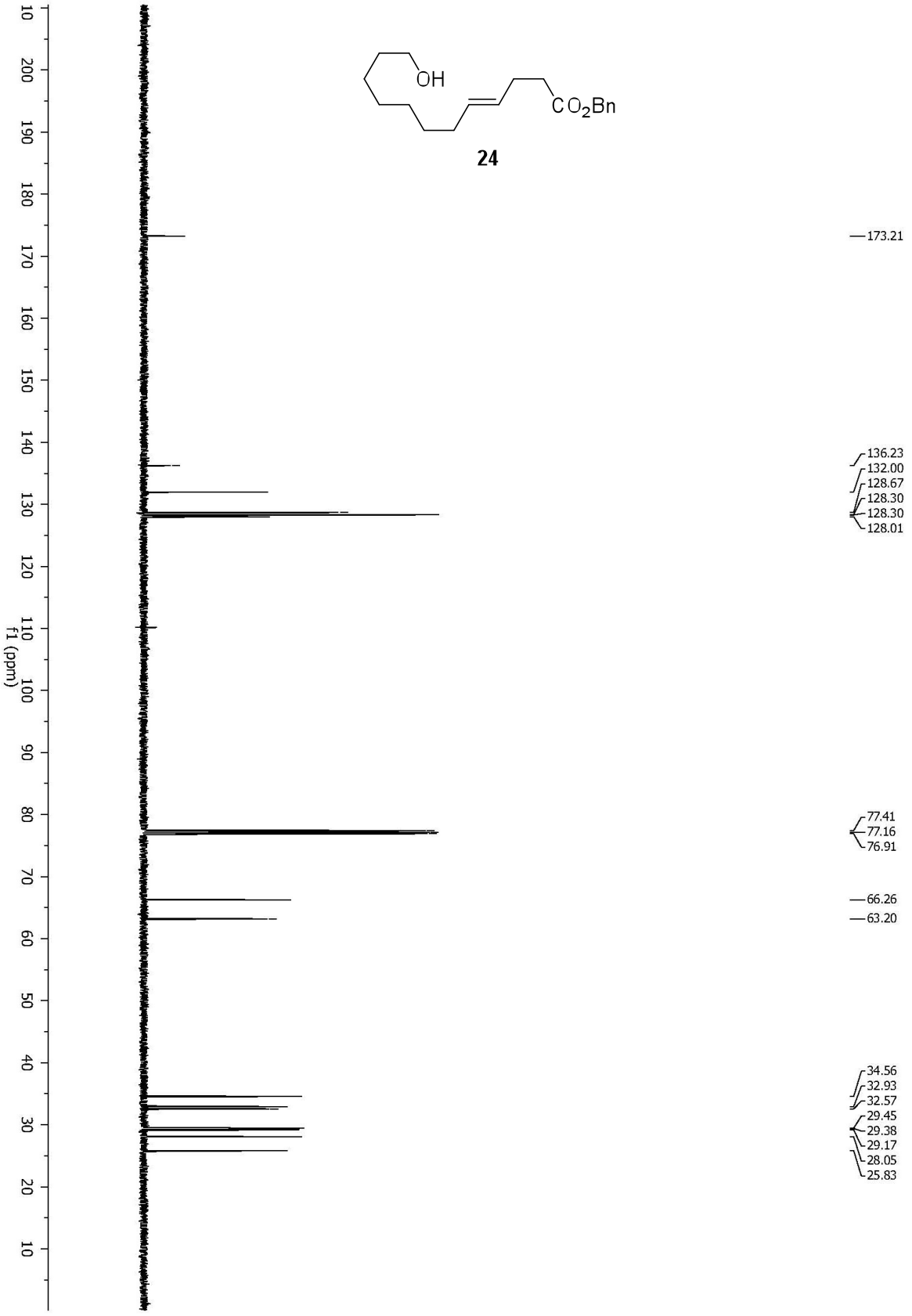

HO
TBSO
OTBS
HO
TBSO
OTBS
S5
138.08
138.04
135.02
134.70
131.05
130.84
115.43
115.39
80.05
80.00
77.37
77.16
76.95
74.70
74.52
73.71
73.38
56.46
56.45
51.60
51.35
43.21
43.12
38.71
38.64
33.46
33.34
31.98
26.05
25.95
25.20
25.13
22.80
18.43
18.04
18.02
14.20
14.19
-4.06
-4.11
-4.44
-4.49
-4.54
-4.58
-4.69
-4.71
f1 (ppm)


HO
HO
OH
21b
f1 (ppm)
0.89
0.94
0.92
1.00
0.92
0.97
1.01
0.96
0.84
4.07
1.84
1.03
3.96
6.70
3.23
7.26
5.88
5.87
5.80
5.59
5.57
5.56
5.54
5.49
5.47
5.46
5.44
5.12
5.08
5.03
5.01
4.22
4.09
4.07
4.06
4.05
3.95
2.65
2.35
2.22
2.18
2.00
1.89
1.78
1.75
1.65
1.59
1.56
1.46
1.37
1.30
1.25
0.90
0.89
0.87


HO
HO
OH
21b
137.52
135.31
132.41
115.98
78.33
77.37
77.16
76.95
73.34
73.13
56.08
49.94
42.91
37.51
32.62
31.87
25.35
22.78
14.17
f1 (ppm)


Ph
O
H
N
HN
O
H
N
O
CO2Me
HO
O
NH
NHBoc
23
f1 (ppm)
0.87
2.05
0.99
6.16
2.06
2.78
1.00
1.02
3.04
0.75
0.98
2.91
2.16
3.15
2.01
1.24
1.18
9.05
1.00
1.02
5.31
5.29
5.28
5.18
5.16
5.14
9.08
8.85
8.84
8.83
8.09
8.08
7.27
7.20
7.19
7.17
7.01
6.71
6.69
6.64
6.62
5.31
5.29
5.28
5.18
5.16
5.14
4.32
4.29
4.25
4.23
4.10
3.82
3.67
3.27
3.15
3.13
2.85
2.51
2.49
2.32
2.30
1.86
1.84
1.31


OH
CO2Bn
24
f1 (ppm)
4.60
2.00
2.09
2.07
2.24
2.21
2.20
3.08
10.45
7.38
7.37
7.35
7.34
7.31
7.26
5.47
5.43
5.42
5.38
5.35
5.11
3.64
3.63
3.62
2.44
2.43
2.42
2.40
2.35
2.33
2.31
1.97
1.96
1.94
1.93
1.61
1.58
1.57
1.56
1.54
1.53
1.33
1.32
1.28


OH
CO2Bn
24
173.21
136.23
132.00
128.67
128.30
128.30
128.01
77.41
77.16
76.91
66.26
63.20
34.56
32.93
32.57
29.45
29.38
29.17
28.05
25.83
f1 (ppm)

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