Highly Active Chiral Ruthenium Catalysts for Asymmetric Ring-Closing Olefin Metathesis

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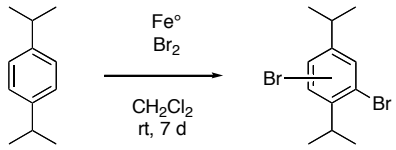
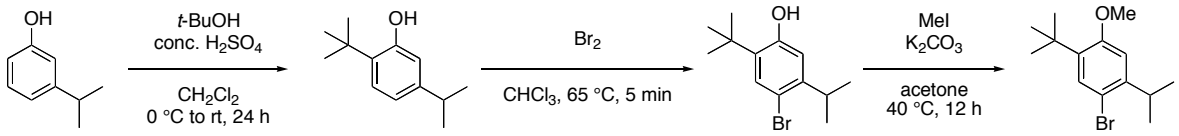
General Information. NMR spectra were recorded on an Oxford 300 MHz NMR spectrometer running Varian VNMR software. Chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane (TMS) with reference to internal solvent for ^{1}H NMR and ^{13}C NMR spectra. Chemical shifts are reported in parts per million (ppm) downfield from H_3PO_4 for ^{31}P NMR spectra. Multiplicities are abbreviated as follows: singlet (s), doublet (d), triplet (t), quartet (q), quintet (quint), septet (sept), multiplet (m), and broad (br). Optical rotations were taken on a Jasco P-1010 polarimeter with a wavelength of 589 nm. The concentration "c" has units of g/100mL (or 10 mg/mL) unless otherwise noted. Analytical thin-layer chromatography (TLC) was performed using silica gel 60 F254 precoated plates (0.25 mm thickness) with a fluorescent indicator. Visualization was performed with standard potassium permanganate stains or UV light. Flash column chromatography of organic compounds was performed using silica gel 60 (230-400 mesh), and flash column chromatography of ruthenium compounds was performed using silica gel 60 (230-400 mesh) from TSI Scientific (Cambridge, MA). All enantiomeric purities were determined by chiral GC (Chiraldex G-TA, 30m×0.25mm or CP Chirasil-Dex-CB, 25m×0.25mm) and were compared to racemic samples. All glassware was either oven dried or flame dried, and reactions were done under an atmosphere of argon unless otherwise noted. All organic solvents were dried by passage through solvent purification columns containing activated alumina. All commercial chemicals were used as obtained, and $(PCy_3)_2Ru(=CHPh)Cl_2$ (**31**) was a gift from Materia, Inc. Compounds **25**, **26**[i], **27**, and **28**[ii] are known compounds.

[i] Zhu, S. S.; Cefalo, D. R.; La, D. S.; Jamieson, J. Y.; Davis, W. M.; Hoveyda, A. H.; Schrock, R. R. *J. Am. Chem. Soc*. **1999**, *121*, 8251–8259.
[ii] Kiely, A. F.; Jernelius, J. A.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc*. **2002**, *124*, 2868–2869.



7b

2-Bromo-1,4-diisopropylbenzene as a mixture (7b). Following a known procedure,[iii] to 1,4-diisopropylbenzene (10 ml, 53 mmol) and Fe (250 mg, 4.5 mmol) in CH_2Cl_2 (10 ml) at 0 °C was added by syringe over 15 min Br_2 (2.67 ml, 52 mmol) in CH_2Cl_2 (10 ml). The red solution was warmed to rt and stirred for 7 days. The reaction was filtered and washed with Na_2SO_3 until it was colorless, and was dried over $MgSO_4$ and concentrated. The oil was purified by column chromatography (100% pentane) to yield 11.35 g (86% yield by weight) of **7b**, which was a 4:1 mixture of brominated products and starting material.

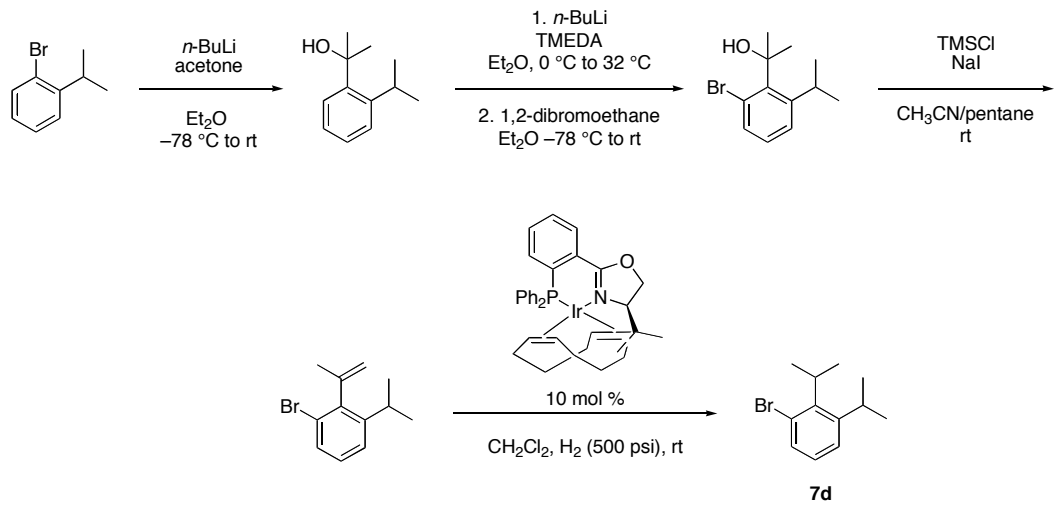


7c

1-Bromo-5-*tert*-butyl-2-isopropyl-4-methoxybenzene (7c). To a solution of 3-isopropyl phenol (10g, 73 mmol) in CH_2Cl_2 at 0 °C was added *tert*-butyl alcohol (7.0 ml, 73 mmol) and conc. H_2SO_4 (3.9 ml, 73 mmol). The reaction was allowed to warm to rt and stirred for 24 h. It was quenched with $NaHCO_3$ and the organic layer was removed. The aqueous layer was extracted 3× with CH_2Cl_2 and the combined organic fractions were dried over $MgSO_4$, concentrated, and purified by column chromatography (5% EtOAc in hexanes) to yield 12.2 g (87%) of the alkylated phenol. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.20 (d, J = 8.1 Hz, 1H), 6.76 (dd, J = 8.1, 1.8 Hz, 1H), 6.54 (d, J = 1.8 Hz, 1H), 4.71 (s, 1H), 2.83 (sept, J = 6.9 Hz, 1H), 1.41 (s, 9H), 1.24 (d, J = 6.9 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 154.2, 148.2, 133.6,

[iii] Patel, B. A.; Ziegler, C. B.; Cortese, N. A.; Plevyak, J. E.; Zebovitz, T. C.; Terpko, M.; Heck, R. F. *J. Org. Chem.* **1977**, *42*, 3903–3907.

127.1, 118.7, 114.9, 34.4, 33.5, 29.9, 24.1. HRMS (EI+) *m/z* calc for $C_{13}H_{20}O$: 192.1514, found 192.1511. Br_2 (980 μl, 19 mmol) in $CHCl_3$ (8 ml) was added dropwise over 20 min from an addition funnel to the alkylated phenol (3.5 g, 19 mmol) in $CHCl_3$ (35 ml) stirring at 65 °C. The reaction stirred for 5 min and was quenched with sat'd $Na_2S_2O_3$ (aq). The organic layer was removed and the aqueous layer was extracted 3× with $CHCl_3$, and the combined organic fractions were dried over $MgSO_4$, concentrated, and purified by column chromatography (5% EtOAc in hexanes) to yield 3.6 g (74%) of the brominated phenol. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.36 (s, 1H), 6.58 (s, 1H), 4.80 (s, 1H), 3.24 (sept, J = 6.9 Hz, 1H), 1.38 (s, 9H), 1.20 (d, J = 6.9 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 153.9, 146.0, 135.9, 131.3, 115.0, 114.8, 34.6, 32.7, 29.7, 23.0. HRMS (EI+) *m/z* calc for $C_{13}H_{19}OBr$: 270.0619, found 270.0617. To a suspension of the brominated phenol (3.55 g, 13 mmol) and K_2CO_3 (5.39 g, 39 mmol) in acetone (100 ml) was added MeI (2.45 ml, 39 mmol). The reaction was heated to 40 °C and stirred for 12 h. It was cooled to rt, filtered through a glass frit, and washed with acetone. The filtrate was concentrated and purified by column chromatography (5% EtOAc in hexanes) to yield 2.93 g (79%) of **7c**. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.36 (s, 1H), 6.76 (s, 1H), 3.83 (s, 3H), 3.30 (sept, J = 6.9 Hz, 1H), 1.34 (s, 9H), 1.24 (d, J = 6.9 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 158.3, 145.7, 138.1, 130.8, 114.7, 110.1, 55.4, 34.8, 33.1, 29.8, 23.1. HRMS (EI+) *m/z* calc for $C_{14}H_{21}OBr$: 284.0776, found 284.0762.



1-Bromo-2,3-diisopropylbenzene (7d). To a solution of 2-isopropylbromobenzene (purchased from Lancaster) (8.6 ml, 56 mmol) in Et_2O (100 ml) at 0 °C was added *n*BuLi (1.4 M in Et_2O, 42 mL, 59 mmol) and the reaction stirred for 5h at 0 °C. The reaction was cooled to –78 °C and acetone (41 ml, 560 mmol) was added in one portion. The reaction was allowed to warm to rt as it stirred for 12h and was quenched with H_2O. The organic layer was removed, washed with sat'd NaCl (aq), dried over $MgSO_4$ and purified by column chromatography (7% EtOAc in pentane) to give 8.82 g (88%) of the desired aromatic alcohol as a white solid. On a larger scale (25 g of 2-isopropylbromobenzene), instead of purifying by column chromatography, the concentrated solution sat at rt for 48h and 13.22 g (59%) of the desired product crystallized. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.45-7.38 (m, 2H), 7.29-7.24 (m, 1H), 7.16-7.11 (m, 1H), 3.91 (sept, J = 6.9 Hz, 1H), 1.79 (br s, 1H), 1.70 (s, 6H), 1.27 (d, J = 6.9 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 148.3, 144.5, 128.0, 127.7, 125.5, 125.1, 73.8, 32.0, 29.5, 25.0. HRMS (EI+) *m/z* calc for $C_{12}H_{18}O$: 178.1350, found 178.1358. This procedure was based on a literature precedent.[iv] This reaction has given variable yields 12% - 25%; what follows is the procedure for the reaction that gave 25% yield. To a solution of the aromatic alcohol (600 mg, 3.4 mmol) and TMEDA (2 ml, 13 mmol) in Et_2O (23 ml) at 0 °C was added *n*BuLi (1.3 M in Et_2O, 10 mL,

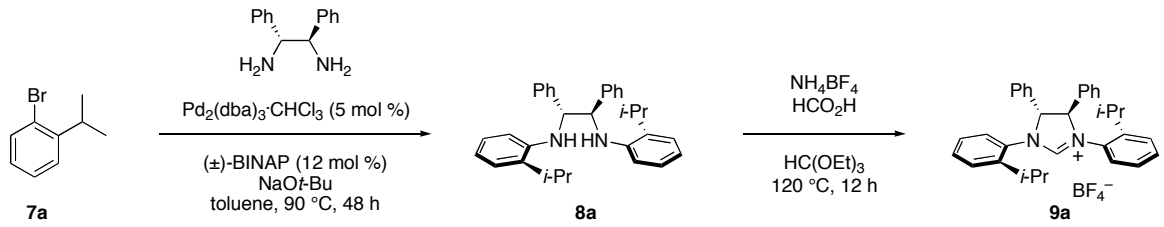
[iv] Taber, D. F.; Dunn, B. S.; Mack, J. F.; Saleh, S. A. *J. Org. Chem.* **1985**, *50*, 1987–1988.

13 mmol). The reaction warmed to rt over 15 min and a reflux condenser was attached, and it was heated to 32 °C for 4h. The reaction was cooled to –78 °C, and 1,2-dibromoethane (1.5 ml, 17 mmol) was added. The reaction was allowed to warm to rt as it stirred for 12h. It was quenched with H_2O, washed with NaCl (aq), dried over Na_2SO_4, and purified by column chromatography (7% EtOAc in pentane) to give 214 mg (25%) of the brominated aromatic alcohol and 232 mg (39%) of unreacted starting material. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.40 (dd, J = 7.8, 1.5 Hz, 1H), 7.31 (dd, J = 7.8, 1.5 Hz, 1H), 7.00 (t, J = 7.8 Hz, 1H), 4.03 (sept, J = 6.9 Hz, 1H), 1.87 (s, 6H), 1.22 (d, J = 6.9 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 151.9, 144.2, 133.2, 127.8, 127.5, 120.2, 76.3, 32.3, 31.4, 25.4. HRMS (EI+) *m/z* calc for $C_{12}H_{17}OBr$: 256.0470, found 256.0463. This procedure was based on a literature precedent.[v] TMSCl (1.5 ml, 11 mmol), NaI (1.7 g, 11 mmol), and CH_3CN (300 μl) were prestirred for 30 min at rt, and the brominated aromatic alcohol (500 mg, 1.9 mmol) was added as a solution in pentane (5 ml) and CH_3CN (200 μl). The reaction stirred for 5h at rt, and Et_2O and H_2O were added to the reaction mixture. The organic layer was removed, dried over $MgSO_4$, concentrated, and the residue was passed through a small plug of silica gel with Et_2O to give 439 mg (96%) of the bromostyrene as an orange oil. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.40 (dd, J = 7.8, 1.5 Hz, 1H), 7.24 (dd, J = 7.8, 1.5 Hz, 1H), 7.10 (t, J = 7.8 Hz, 1H), 5.32-5.30 (m, 1H), 4.84-4.83 (m, 1H), 3.13 (sept, J = 6.9 Hz, 1H), 2.02 (t, J = 1.5 Hz, 3H), 1.22 (d, J = 7.2 Hz, 3H), 1.16 (d, J = 5.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 130.0, 128.6, 124.7, 116.4, 31.0, 25.3, 24.4, 24.2. HRMS (EI+) *m/z* calc for $C_{12}H_{15}Br$: 238.0353, found 238.0357. A solution of the bromostyrene (2.0 g, 8.4 mmol) and (*R*)-[Ir(Ph_2; ^{i}Pr-PHOX)(COD)]BAr_F[vi] (1.3 g, 0.84 mmol) in CH_2Cl_2 (20 ml) was placed in a stainless steel pressure bomb. The bomb was pressurized and

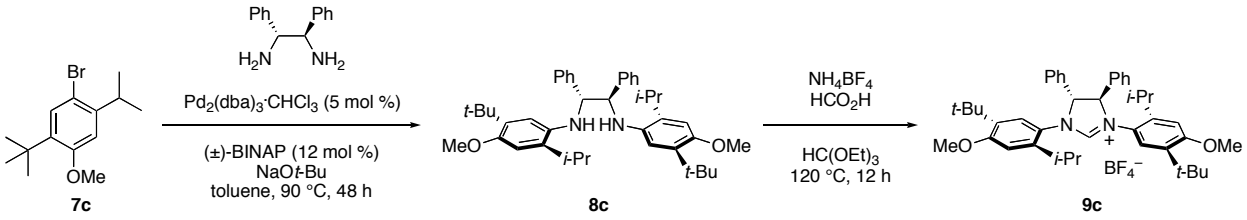
[v] Sakai, T.; Miyata, K.; Utaka, M.; Takeda, A. *Tet. Lett.* **1987**, *28*, 3817–3818.
[vi] a) Pfaltz, P.; Blankenstein, J.; Hörmann, E.; McIntyre, S.; Menges, F.; Hilgraf, R.; Schönleber, M.; Smidt, S. P.; Wüstenberg, B.; Zimmermann, N. *Adv. Synth. Catal.* **2003**, *345*, 33–43. b) Lightfoot, A.; Schnider, P.; Pfaltz, A. *Angew. Chem. Int. Ed. Engl.* **1998**, *37*, 2897–2899.

vented with 3×500 psi H_2 and was sealed at 500 psi H_2. The reaction stirred at rt for 24h and was vented, concentrated, and passed through a short silica gel plug (100% pentane) to yield 1.73 g (87%) of **7d** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.39 (dd, J = 7.8, 1.5 Hz, 1H), 7.23-7.21 (dd, J = 7.8, 1.5 Hz, 1H), 6.99 (t, J = 7.8 Hz, 1H), 3.93-3.28 (m, 2H), 1.47 (br s, 2H), 1.36 (d, J = 6.9 Hz, 4H), 1.24 (d, J = 6.9 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 130.8, 127.6, 127.0, 34.1, 29.8, 24.9, 24.3, 21.9, 20.4. HRMS (EI+) *m/z* calc for $C_{12}H_{17}Br$: 240.0524, found 240.0514.

General 2-Step Procedure for Chiral 4,5-Dihydroimidazolium Salts. A solution of the aryl bromide (2.2 equiv) in toluene in a sealable schlenk tube was freeze/pump/thawed 3 times. After reaching rt, the positive argon pressure was briefly stopped and to this solution was added (1*R*,2*R*)-(+)-1,2-diphenylethylenediamine (1 equiv), $Pd_2(dba)_3$•$CHCl_3$ (0.05 equiv), and (±)-BINAP (0.12 equiv) in one portion. The argon pressure was immediately resumed, and a very brief pump/backfill was performed at rt. NaO*t*-Bu (3 equiv) was added and the reaction was heated to 90 °C and sealed. The reaction mixture stirred for 48 h at 90 °C, and after cooling to rt was quickly passed through a small silica gel column with 5% EtOAc in hexanes. The eluting was stopped when no more UV active material came off the column. The eluent containing partially purified diaryl diamine (**8**) was concentrated and $(EtO)_3CH$ was added. To this solution was added NH_4BF_4 (1 equiv) and 2 drops of formic acid. The reaction was heated to 120 °C and stirred for 12 h. Upon cooling to rt, Et_2O was added and a white precipitate was briefly observed, but ultimately a thick oil formed. Thus, the reaction was concentrated, purified by flash chromatography (MeOH in CH_2Cl_2), and placed under high vacuum for 12 h to yield the desired 4,5-dihydroimidazolium salt (**9**) as a hard foam.



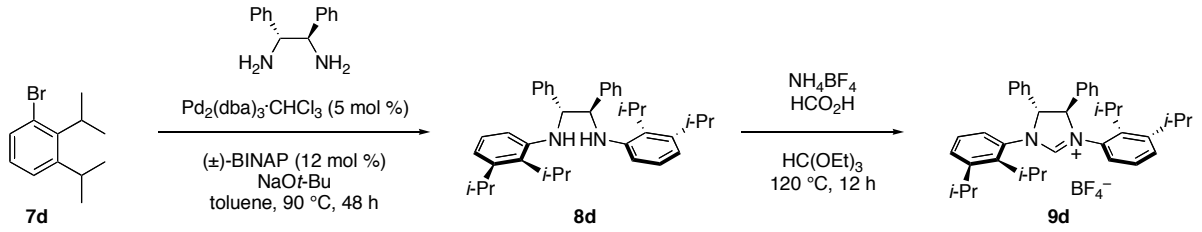
(4*R*,5*R*)-1,3-Bis-(2-isopropylphenyl)-4,5-diphenyl-4,5-dihydro-3*H*-imidazol-1-ium tetrafluoroborate (9a). Using the general procedure above, 2-isopropylbromobenzene (**7a**) (0.55 mL, 3.5 mmol), (1*R*,2*R*)-(+)-1,2-diphenylethylenediamine (351 mg, 1.6 mmol), $Pd_2(dba)_3$•$CHCl_3$ (83 mg, 0.08 mmol), (±)-BINAP (118 mg, 0.19 mmol), and NaO*t*-Bu (461 mg, 4.8 mmol) in 5 mL toluene gave crude **8a**, which was used directly in the next step. Assuming 100% yield in the coupling, **8a**, $(EtO)_3CH$ (2.7 mL, 16 mmol), NH_4BF_4 (168 mg, 1.6 mmol), and 2 drops of formic acid gave crude product that was purified by 5% MeOH in CH_2Cl_2 to give 336 mg (38% over 2 steps) of **9a** as a hard foam. Spectral data matched that previously reported (c values for optical rotations in this reference are in g/10 mL).[vii]



(4*R*,5*R*)-1,3-Bis-(5-*tert*-butyl-2-isopropyl-4-methoxyphenyl)-4,5-diphenyl-4,5-dihydro-3*H*-imidazol-1-ium tetrafluoroborate (9c). Using the general procedure above, **7c** (1.0 g, 3.5 mmol), (1*R*,2*R*)-(+)-1,2-diphenylethylenediamine (351 mg, 1.6 mmol), $Pd_2(dba)_3$•$CHCl_3$ (83 mg, 0.08 mmol), (±)-BINAP (118 mg, 0.19 mmol), and NaO*t*-Bu (461 mg, 4.8 mmol) in 3.5 mL

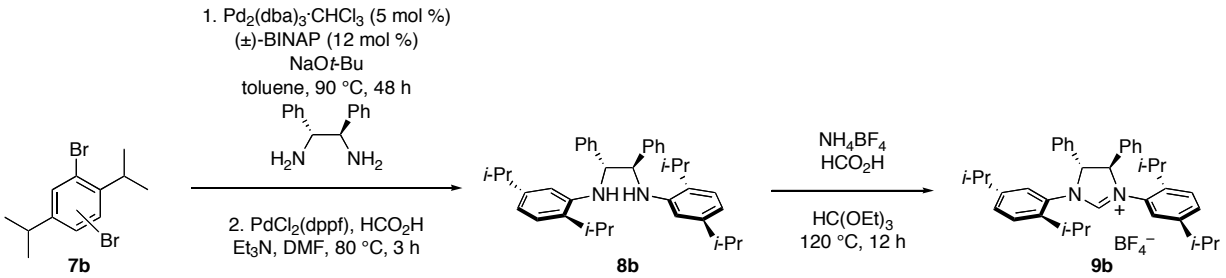
[vii] Seiders, J. T.; Ward, D. W.; Grubbs, R. H. *Org. Lett.* **2001**, *3*, 3225–3228.

toluene gave crude **8c**, which was used directly in the next step. Assuming 100% yield in the coupling, **8c**, $(EtO)_3CH$ (2.7 mL, 16 mmol), NH_4BF_4 (168 mg, 1.6 mmol), and 2 drops of formic acid gave crude product that was purified by 10% MeOH in CH_2Cl_2 to yield a viscous yellow oil. This oil is the desired salt by ^1H NMR, but further purification gives better yields in the catalyst preparation step. Further purification consists of dissolving the yellow oil in copious Et_2O (100 ml) and letting the solution sit at rt for 12 h. At this time, a white precipitate was observed, the rest of the ether was decanted off, the precipitate was washed with a minimal amount of ether and dried to yield 614 mg (53% over 2 steps) of **9c**. The remaining ether can be concentrated to give additional material that can also be used to make catalyst but in a reduced yield. $[\alpha]_D^{22} =$ +191.31 (c 0.53, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$, ppm): δ 8.21 (s, 1H), 7.43-7.39 (m, 10H), 7.18 (s, 2H), 6.66 (s, 2H), 5.64 (s, 2H), 3.81 (s, 6H), 3.11 (sept, J = 7.2 Hz, 2H), 1.36 (d, J = 6.6 Hz, 12H), 1.24 (s, 18H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 161.1, 160.0, 157.6, 151.1, 143.7, 138.0, 133.7, 130.6, 129.9, 129.0, 127.0, 123.2, 108.8, 55.3, 34.9, 29.5, 29.0, 25.0, 24.3. HRMS (FAB+) *m/z* calc for $C_{43}H_{55}N_2O_2$; 631.4264, found 631.4280.



(4*R*,5*R*)-1,3-Bis-(2,3-diisopropylphenyl)-4,5-diphenyl-4,5-dihydro-3*H*-imidazol-1-ium tetrafluoroborate (9d). Using the general procedure above, **7d** (788 mg, 3.3 mmol), (1*R*,2*R*)-(+)-1,2-diphenylethylenediamine (327 mg, 1.5 mmol), $Pd_2(dba)_3$•$CHCl_3$ (78 mg, 0.075 mmol), (±)-BINAP (112 mg, 0.18 mmol), and NaO*t*-Bu (432 mg, 4.5 mmol) in 4 mL toluene gave 444 mg **8d** (21%). **8d** (444 mg, 0.83 mmol), $(EtO)_3CH$ (2.0 mL, 12 mmol), NH_4BF_4 (84 mg, 0.83

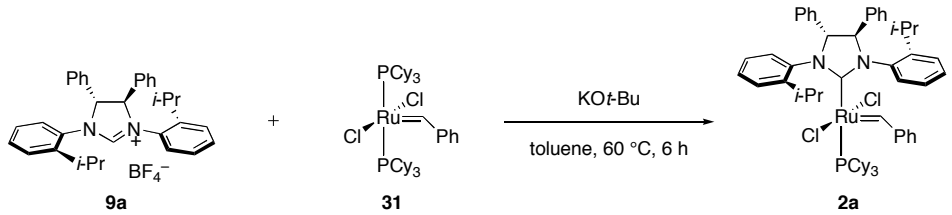
mmol), and 2 drops of formic acid gave crude product that was purified by 10% MeOH in CH_2Cl_2 to give 333 mg (66%) of **9d** as a hard foam. $[\alpha]_D^{22}$ = +209.3 (c 0.82, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 8.12 (br s, 1H), 7.41-7.23 (m, 16H), 5.74 (br s, 2H), 3.36-3.33 (m, 4H), 1.63 (s, 6H), 1.47 (br s, 6H), 1.25-1.18 (m, 12H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 150.1, 140.6, 130.6, 130.2, 130.0, 129.0, 128.2, 29.6, 29.0, 24.8, 24.5, 22.9, 22.6. HRMS (FAB+) *m/z* calc for $C_{39}H_{47}N_2$; 543.3748, found 543.3739.



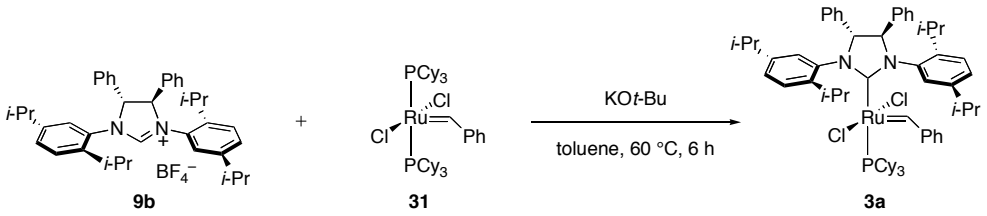
(4*R*,5*R*)-1,3-Bis-(2,5-diisopropylphenyl)-4,5-diphenyl-4,5-dihydro-3*H*-imidazol-1-ium tetrafluoroborate (9b). This is a three step procedure with stable, isolated intermediates. The first and third steps following the general procedure above. A solution of **7b** (1.58 g, 6.6 mmol) in 5 mL toluene in a sealable schlenk tube was freeze/pump/thawed 3 times and warmed to RT. To this solution was added (1*R*,2*R*)-(+)-1,2-diphenylethylenediamine (500 mg, 2.3 mmol), $Pd_2(dba)_3$•$CHCl_3$ (122 mg, 0.12 mmol), and (±)-BINAP (220 mg, 0.36 mmol) in one portion. NaO*t*-Bu (680 mg, 7.1 mmol) was added and the reaction was heated to 90 °C and sealed. It stirred for 48 h and after cooling to rt it was quickly passed through a small silica gel column with 5% EtOAc in hexanes. The eluting was stopped when no more UV active material came off of the column. The eluent was concentrated, and 765 mg of the crude product was isolated as a mixture of mono- and dibrominated arenes. $PdCl_2(dppf)$•CH_2Cl_2 (7.7 mg, 0.0094 mmol) was added to the crude product (576 mg), and the flask was flushed with argon. To this mixture was

added degassed DMF (2.5 ml) and Et_3N (394 μl, 2.8 mmol). The reaction was heated to 80 °C and formic acid (62 μl, 1.7 mmol) was added. It stirred for 3 h at 80 °C, and 10 ml of a 1:1 solution of Hex/Et_2O was added. The reaction was washed with 1N HCl (aq), sat'd $NaHCO_3$ (aq), and sat'd NaCl (aq). The organic layer was dried over Na_2SO_4 and purified by flash chromatography (6:1 pentane in CH_2Cl_2) to give 430 mg of the desired diamine (**8b**). To **8b** (1.32 g, 2.5 mmol) was added $(EtO)_3CH$ (4.1 ml, 25 mmol), NH_4BF_4 (260 mg, 2.5 mmol) and 2 drops of formic acid. The reaction was heated to 120 °C and stirred for 12 h. It was cooled to rt, Et_2O was added, and a yellow solid precipitated. The solid was purified by flash chromatography (10% MeOH in CH_2Cl_2) to yield 1.35 g (86%) of **9b**. $[\alpha]^{22}_D$ +270.78 (c 0.51, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 8.11 (s, 1H), 7.48-7.19 (m, 16H), 5.83 (s, 2H), 3.11 (sept, J = 6.9 Hz, 2H), 2.82 (sept, J = 6.9 Hz, 2H), 1.31 (d, J = 6.9 Hz, 6H), 1.18 (d, J = 6.6 Hz, 6H), 1.13-1.09 (m, 12H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 157.0, 148.9, 142.0, 132.9, 130.9, 130.6, 129.8, 129.1, 126.8, 126.6, 77.1, 33.6, 28.6, 24.9, 24.3, 23.8, 23.5. HRMS (FAB+) *m/z* calc for $C_{39}H_{47}N_2$; 543.3739, found 543.3755.

General Procedure for the Synthesis of Chiral Ruthenium Catalysts 2a–5a. In a drybox, potassium hexafluoro-*t*-butoxide, imidazolium salt, and $(PCy_3)_2Ru(=CHPh)Cl_2$ (**31**) were suspended in toluene. The flask was sealed with a septum and heavy parafilm, removed from the glove box and stirred at 60 °C for 6 hours. The reaction mixture was concentrated and purified by flash chromatography using TSI silica gel (see General Information section) to afford the desired ruthenium catalyst, which was lyophilized from benzene to give a brown powder. Further purification by additional flash chromatography was occasionally necessary due to difficulties in separating unreacted **31**. This further purification resulted in diminished yields.

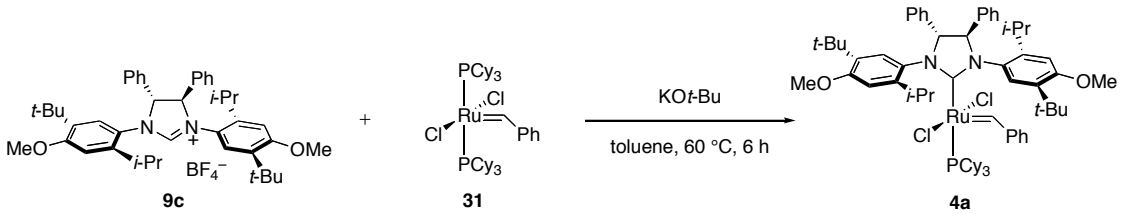


Ruthenium Compound 2a. Following the general procedure above, potassium hexafluoro-*t*-butoxide (134 mg, 0.61 mmol), **9a** (333 mg, 0.61 mmol), and $(PCy_3)_2Ru(=CHPh)Cl_2$ (**31**) (334 mg, 0.41 mmol) in 6 mL toluene gave 398 mg of a brown solid (5% Et_2O in hexanes) that was a 10:1 ratio of **2a**:**31**. Purification by a second flash column (5% Et_2O in hexanes) using TSI silica gel followed by lyophilization from benzene afforded 198 mg (32%) of **2a** as a brown powder. Spectral data matched that previously reported.[vii]

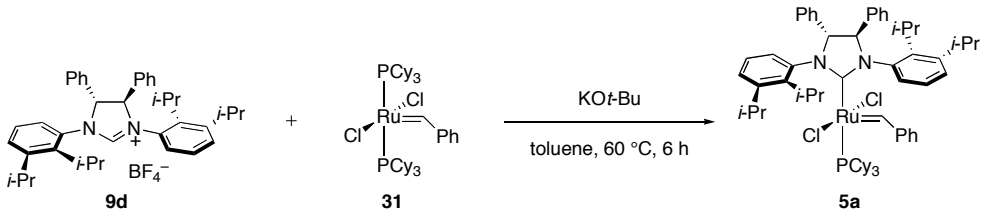


Ruthenium Compound 3a. Following the general procedure above, potassium hexafluoro-*t*-butoxide (140 mg, 0.64 mmol), **9b** (400 mg, 0.64 mmol), and $(PCy_3)_2Ru(=CHPh)Cl_2$ (**31**) (261 mg, 0.32 mmol) in 8 mL toluene afforded 294 mg (85%) of **3a** (10% Et_2O in pentane), which was lyophilized from benzene to give a brown powder. ^1H NMR (300 MHz, C_6D_6, ppm): δ 19.83 (s, 1H), 8.50 (s, 1H), 7.53-7.48 (m, 5H), 7.05-6.89 (m, 15H), 6.67 (d, J = 8.1 Hz, 1H), 6.48 (d, J = 8.4 Hz, 1H), 5.34 (d, J = 4.8 Hz, 1H), 5.10 (d, J = 4.5 Hz, 1H), 4.25 (sept, J = 6.6 Hz, 1H), 3.96 (br s, 1H), 2.87 (sept, J = 6.6 Hz, 1H), 2.36 (sept, J = 6.6 Hz, 1H), 2.06 (q, J = 10.8 Hz, 5H), 1.80-0.85 (m, 52H). $^{31}P\{^1H\}$ NMR (121 MHz, C_6D_6, ppm): δ 25.5 (s). ^{13}C NMR (126 MHz,

C_6D_6, ppm) only diagnostic peaks reported: δ 297.7 (br s), 219.1 (d, J = 78.7 Hz). HRMS (FAB+) *m/z* calc for $C_{64}H_{85}N_2PCl_2Ru$; 1084.487, found 1084.483.

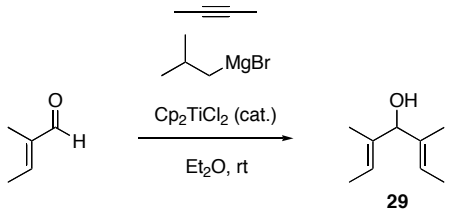


Ruthenium Compound 4a. Following the general procedure above, potassium hexafluoro-*t*-butoxide (60 mg, 0.27 mmol), **9c** (197 mg, 0.27 mmol), and $(PCy_3)_2Ru(=CHPh)Cl_2$ (**31**) (150 mg, 0.18 mmol) in 6 mL toluene afforded 159 mg (75%) of **4a** (10% Et_2O in pentane), which was lyophilized from benzene to give a brown powder. ^1H NMR (300 MHz, C_6D_6, ppm): δ 19.80 (s, 1H), 8.28 (s, 1H), 7.65 (d, J = 7.2 Hz, 2H), 7.57 (d, J = 7.2 Hz, 2H), 7.38 (s, 2H), 7.16-7.00 (m, 10H), 6.74 (s, 1H), 6.09 (s, 1H), 5.35 (d, J = 4.8 Hz, 1H), 5.19 (d, J = 4.8 Hz, 1H), 4.49 (sept, J = 6.6 Hz, 1H), 3.83 (sept, J = 6.9 Hz, 1H), 3.32 (s, 3H), 3.16 (s, 3H), 2.24-1.11 (m, 63H). $^{31}P\{^1H\}$ NMR (121 MHz, C_6D_6, ppm): δ 25.4 (s). ^{13}C NMR (126 MHz, C_6D_6, ppm) only diagnostic peaks reported: δ 296.3 (d, J = 351.0 Hz), 219.9 (d, J = 79.6 Hz). HRMS (FAB+) *m/z* calc for $C_{68}H_{93}N_2PCl_2RuO_2$; 1172.540, found 1172.546.



Ruthenium Compound 5a. Following the general procedure above, potassium hexafluoro-*t*-butoxide (109 mg, 0.50 mmol), **9d** (313 mg, 0.50 mmol), and $(PCy_3)_2Ru(=CHPh)Cl_2$ (**31**) (273

mg, 0.33 mmol) in 6 mL toluene afforded a brown solid (5% Et_2O in pentane), which was a 9:1 ratio of **5a**:**31**. Purification by a second flash column (5% Et_2O in pentane) using TSI silica gel followed by lyophilization from benzene afforded 160 mg (30%) of **5a** as a brown powder. ^1H NMR (300 MHz, C_6D_6, ppm): δ 19.87 (s, 1H), 9.26 (d, J = 6.6 Hz, 1H), 7.75 (d, J = 7.5 Hz, 2H), 7.17-6.89 (m, 16H), 6.39 (d, J = 7.2 Hz, 1H), 6.14 (br s, 1H), 5.28 (d, J = 3.3 Hz, 1H), 4.98 (d, J = 3.3 Hz, 1H), 4.35 (quint, J = 7.2 Hz, 1H), 4.04 (br s, 1H), 3.41 (quint, J = 6.9 Hz, 1H), 3.11 (br s, 1H), 2.21-0.39 (m, 57H). $^{31}P\{^1H\}$ NMR (121 MHz, C_6D_6, ppm): δ 26.2 (s); HRMS (FAB+) *m/z* calc for $C_{64}H_{85}N_2PCl_2Ru$; 1084.487, found 1084.489.

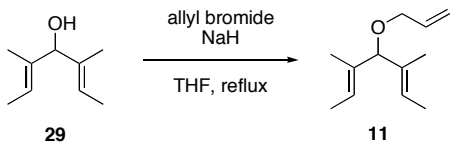


29

(2*E*,5*E*)-3,5-Dimethylhepta-2,5-dien-4-ol (29).[viii] Titanocene dichloride (444 mg, 1.78 mmol) was added to a solution of 2-butyne (5.6 mL, 71 mmol) and isobutylmagnesium bromide (2.0 M in diethyl ether, 33 mL, 66 mmol) in 60 mL Et_2O, and the solution stirred at rt for 1 h. *Trans*-2-methyl-2-butenal (5.7 mL, 59 mmol) in 30 mL Et_2O was added slowly, and the mixture stirred at rt for 3 h. It was quenched with sat'd aqueous NH_4Cl (100 mL), filtered through a pad of Celite, and the organic layer was removed from the filtrate. The aqueous layer was extracted with ether (3×75 mL), and the organic layers were combined, washed with brine, dried over $MgSO_4$, and evaporated to a brown oil. The oil was purified by flash chromatography (10% EtOAc in hexanes) to a yellow oil, which was distilled (Kugelrohr, 1 torr, 120 °C) to give 7.20 g (86%) of **29** as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$, ppm): δ 5.56 (qquint, J = 6.6, 1.4 Hz, 2H), 4.34 (s, 1H), 1.63 (dt, J = 6.9, 1.1 Hz, 6H), 1.47 (t, J = 1.1 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$,

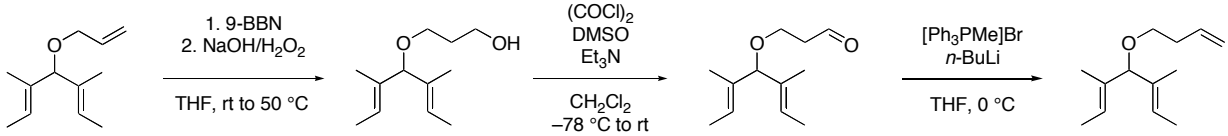
[viii] (a) Garner, C. M.; Prince, M. E. *Tetrahedron Lett*. **1994**, *35*, 2463–2464. (b) Sato, F.; Ishikawa, H.; Sato, M. *Tetrahedron Lett*. **1981**, *22*, 85–88.

ppm): δ 136.1, 120.4, 81.8, 13.3, 12.1. HRMS (EI) *m/z* calc. for $C_9H_{16}O$: 140.1201, found 140.1203.



29 **11**

(2*E*,5*E*)-4-(Allyloxy)-3,5-dimethylhepta-2,5-diene (11). Alcohol **29** (200 mg, 1.43 mmol) was added dropwise to a suspension of NaH (60% in oil, 114 mg, 2.85 mmol) in 6 mL THF. After stirring at reflux for 15 min, the mixture was allowed to cool to rt, and allyl bromide (430 mg, 3.57 mmol) was added. The mixture stirred at reflux for 4 h, was quenched with sat'd aqueous NH_4Cl (10 mL), and was extracted with ether (3×15 mL). The organic layers were combined, dried over $MgSO_4$, and evaporated to an oil which was purified by flash chromatography (1% EtOAc in hexanes) to give 210 mg (82%) of **11** as a colorless oil. Spectral data matched that in the literature.[ix] ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.85-5.98 (m, 1H), 5.55 (qq, J = 6.6, 1.1 Hz, 2H), 5.22-5.29 (m, 1H), 5.10-5.15 (m, 1H), 3.94 (br s, 1H), 3.85 (dq, J = 5.5, 0.8 Hz, 2H), 1.63 (dq, J = 6.6, 1.1 Hz, 6H), 1.46 (d, J = 1.1 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 135.6, 134.2, 121.2, 116.3, 88.3, 68.8, 13.3, 12.3. HRMS (EI) *m/z* calc. for $C_{12}H_{20}O$: 180.15142, found 180.15135.



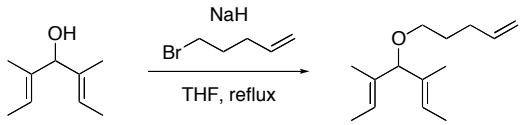
11 **15**

(2*E*,5*E*)-4-(But-3-enyloxy)-3,5-dimethylhepta-2,5-diene (15). **11** (1.07 g, 5.90 mmol) in 3.6 mL THF was added to a solution of 9-BBN (0.5M in THF, 14.2 mL, 7.12 mmol), and the solution stirred at rt. After 5 h 3.6 mL ethanol was added, followed by 1.4 mL 6M $NaOH_{aq}$ and

[ix] La, D. S.; Alexander, J. B.; Cefalo, D. R.; Graf, D. D.; Hoveyda, A. H.; Schrock, R. R. *J. Am. Chem. Soc.* **1998**, *120*, 9720–9721.

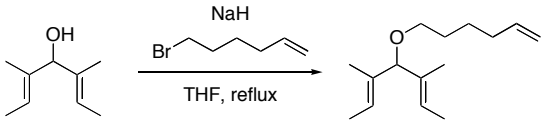
2.8 mL 30% H_2O_2, and the reaction stirred at 50 °C for 1 h. It was diluted with 20 mL sat'd aqueous $NaHCO_3$ and was extracted with ether (3×25 mL). The organic layers were combined, washed with brine, dried over Na_2SO_4, evaporated to an oil, and purified by flash chromatography (20% EtOAc in hexanes) to give 916 mg (83%) of a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.51 (qquint, J = 6.9 Hz, 1.1 Hz, 2H), 3.89 (br s, 1H), 3.79 (t, J = 5.2 Hz, 2H), 3.50 (t, J = 5.5 Hz, 2H), 2.62 (br s, 1H), 1.84 (quint, J = 5.8 Hz, 2H), 1.64 (dt, J = 6.6 Hz, 1.1 Hz, 6H), 1.46 (t, J = 1.4 Hz, 6H). DMSO (0.89 mL, 12.6 mmol) was added slowly to a solution of oxalyl chloride (0.66 mL, 7.56 mmol) in 15 mL CH_2Cl_2 at -78 °C. After 5 min a solution of the alcohol prepared above (500 mg, 2.52 mmol) in 5 mL CH_2Cl_2 was added to the -78 °C reaction solution, and it stirred for 30 min. Triethylamine (2.5 mL, 17.6 mmol) was added, and after 30 min at - 78 °C, the reaction slowly warmed to rt. It was quenched with 40 mL water and extracted with ether (3×50 mL). The organic layers were combined, dried over Na_2SO_4, and evaporated to 448 mg of an orange oil, which was used in the next step without further purification (attempts to purify this aldehyde by silica gel chromatography resulted in product decomposition and low (~30%) isolated yields). To a suspension of triphenylmethylphosphonium bromide (2.15 g, 6.0 mmol) in 20 mL THF at 0 °C was added *n*-butyllithium (2.5 M in hexanes, 2.0 mL, 5.0 mmol). After 20 min a solution of the crude aldehyde (448 mg, 2.3 mmol) in 5 mL THF was added slowly to the orange reaction mixture, and it stirred at 0 °C for 1 h. It was quenched with 30 mL saturated aqueous NH_4Cl and extracted with ether (3×25 mL). The organic layers were combined, dried over $MgSO_4$, and evaporated to an oil, which was purified by flash chromatography (1% EtOAc in hexanes) to give 179 mg of a colorless oil. To a solution of the oil in 10 mL CH_2Cl_2 was added 3% hydrogen peroxide, and the mixture was shaken for 15 minutes. The organic layer was removed, dried over Na_2SO_4, evaporated to an oil, and filtered through a plug of silica gel (1% EtOAc in

hexanes). The filtrate was concentrated to 145 mg (29% over 2 steps) of **15** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.77-5.92 (m, 1H), 5.53 (qquint, J = 6.9, 1.4 Hz, 2H), 4.98-5.11 (m, 2H), 3.88 (s, 1H), 3.33 (t, J = 6.9 Hz, 2H), 2.33 (q, J = 6.9 Hz, 2H), 1.63 (d, J = 6.6 Hz, 6H), 1.46 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 136.0, 134.5, 121.0, 116.2, 89.1, 67.6, 34.7, 13.3, 12.3. HRMS (EI) *m/z* calc. for $C_{13}H_{22}O$: 194.1671, found 194.1679.



29 **17**

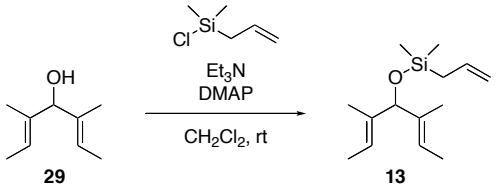
(2*E*,5*E*)-3,5-Dimethyl-4-(pent-4-enyloxy)hepta-2,5-diene (17). **29** (400 mg, 2.9 mmol) was added slowly to a suspension of NaH (60% in oil, 140 mg, 3.4 mmol) in 5 mL THF at rt, and some bubbling occurred. After 2.5 h at rt, 5-bromo-1-pentene (0.68 mL, 5.7 mmol) was added, and the mixture was heated to reflux for 16 h. It was cooled to rt, carefully quenched with 20 mL water, and extracted with ether (3×25 mL). The organic layers were combined, washed with brine, dried over Na_2SO_4, and evaporated to an oil, which was purified by flash chromatography (1% EtOAc in hexanes, then 10% EtOAc in hexanes) to give 130 mg (22%) **17** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.76-5.90 (m, 1H), 5.53 (qquint, J = 6.6, 1.4 Hz, 2H), 4.92-5.04 (m, 2H), 3.86 (s, 1H), 3.29 (t, J = 6.6 Hz, 2H), 2.13 (q, J = 6.9 Hz, 2H), 1.63-1.71 (m, 2H), 1.63 (d, J = 6.6 Hz, 6H), 1.46 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 138.9, 134.6, 120.9, 114.6, 89.1, 67.5, 30.8, 29.4, 13.4, 12.3. HRMS (EI) *m/z* calc. for $C_{14}H_{24}O$: 208.1827, found 208.1828.



29 **19**

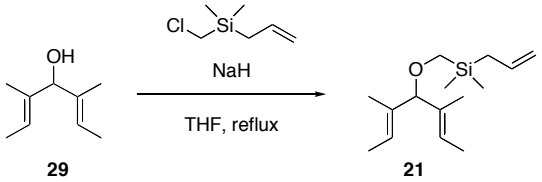
(2*E*,5*E*)-4-(Hex-5-enyloxy)-3,5-dimethylhepta-2,5-diene (19). **29** (500 mg, 3.6 mmol) was added slowly to a suspension of NaH (60% in oil, 285 mg, 7.1 mmol) in 7 mL THF at rt, and

some bubbling occurred. After 15 min at rt, 6-bromo-1-hexene (0.96 mL, 7.1 mmol) was added, the mixture was heated to reflux for 16 h. It was cooled to rt, carefully quenched with 20 mL sat'd aqueous NH_4Cl, and extracted with ether (3×25 mL). The organic layers were combined, washed with brine, dried over $MgSO_4$, and evaporated to an oil, which was purified by flash chromatography (2% EtOAc in hexanes) to give 346 mg (44%) **19** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.74-5.88 (m, 1H), 5.53 (qt, J = 6.6, 1.1 Hz, 2H), 4.91-5.03 (m, 2H), 3.85 (s, 1H), 3.27 (t, J = 6.4 Hz, 2H), 2.06 (q, J = 7.1 Hz, 2H), 1.63 (d, J = 6.9 Hz, 6H), 1.54-1.60 (m, 2H), 1.40-1.52 (m, 2H), 1.45 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 139.2, 134.6, 120.9, 114.5, 89.1, 67.9, 33.9, 29.6, 25.9, 13.3, 12.3. HRMS (EI) *m/z* calc. for $C_{15}H_{26}O$: 222.1984, found 222.1971.



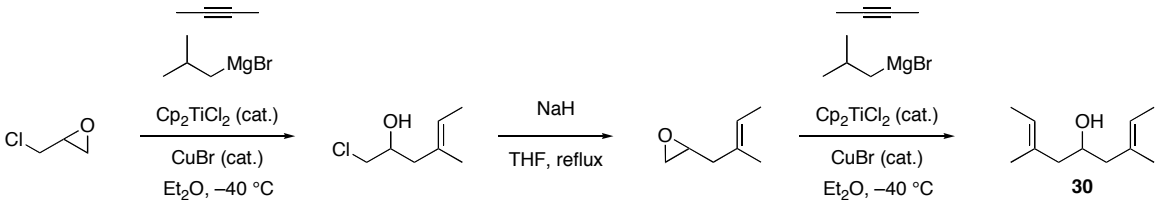
Allyl((2*E*,5*E*)-3,5-dimethylhepta-2,5-dien-4-yloxy)dimethylsilane (13). Allylchlorodimethylsilane (1.1 mL, 7.5 mmol) was added to a solution of **29** (1.0 g, 7.1 mmol), triethylamine (1.2 mL, 8.6 mmol), and *N*,*N*-dimethylaminopyridine (44 mg, 0.4 mmol) in 30 mL CH_2Cl_2 at rt. After 5 h the reaction was quenched with 50 mL water, the organic layer was removed, and the aqueous layer was extracted with ether (3×50 mL). The organic layers were combined, washed with brine, dried over Na_2SO_4, and evaporated to an oil. The oil was redissolved in hexanes and was filtered through a pad of neutral alumina. The filtrate was condensed to give 1.30 g (76%) **13** as a colorless oil. Attempts to purify **13** by silica gel chromatography resulted in inconsistent yields and varying levels of purity due to product decomposition. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.70-5.85 (m, 1H), 5.52 (qquint, J = 6.9, 1.4 Hz, 2H), 4.80-4.90 (m, 2H), 4.30 (s, 1H), 1.61 (dt, J = 6.9, 1.1 Hz, 6H), 1.58-1.63 (m, 2H),

1.43 (t, J = 1.1 Hz, 6H), 0.08 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 136.4, 134.8, 119.9, 113.5, 82.4, 25.1, 13.3, 12.0, –1.9. HRMS (EI) *m/z* calc. for $C_{14}H_{26}OSi$: 238.1753, found 238.1752.



29 **21**

Allyl(((2*E*,5*E*)-3,5-dimethylhepta-2,5-dien-4-yloxy)methyl)dimethylsilane (21). **29** (300 mg, 2.1 mmol) was added to a suspension of NaH (60% in oil, 103 mg, 2.6 mmol) in 3 mL THF and some bubbling occurred. After 30 min at rt, allylchloromethyldimethylsilane (0.70 mL, 4.3 mmol) was added, and the mixture was heated to reflux for 16 h. The reaction mixture was cooled to rt, quenched with 20 mL water, and extracted with ether (3×20 mL). The organic layers were combined, washed with brine, dried over $MgSO_4$, and evaporated to a yellow oil, which was purified by flash chromatography (100% hexanes) to give 349 mg (65%) **21** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.81-5.95 (m, 1H), 5.51 (qquint, J = 6.6, 1.4 Hz, 2H), 4.98 (dq, J = 17.1, 1.7 Hz, 1H), 4.85-4.91 (m, 1H), 4.28 (s, 1H), 2.03-2.12 (m, 2H), 1.61 (dt, J = 6.9, 1.1 Hz, 6H), 1.43 (t, J = 1.1 Hz, 6H), 0.64-0.70 (m, 2H), 0.07 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 142.0, 136.5, 119.8, 112.8, 82.3, 27.6, 16.2, 13.3, 12.1, –1.4. HRMS (FAB) *m/z* calc. for $C_{15}H_{28}OSi$: 252.1910, found 252.1914.

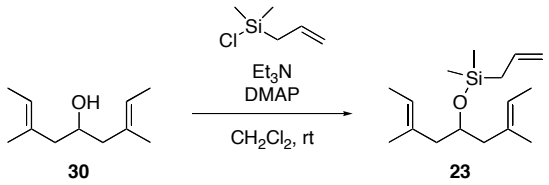


30

(2*E*,7*E*)-3,7-Dimethylnona-2,7-dien-5-ol (30). Titanocene dichloride (212 mg, 0.85 mmol) was added to a solution of 2-butyne (2.4 mL, 30 mmol) and isobutylmagnesium bromide (2.0 M in

diethyl ether, 15 mL, 30 mmol) in 30 mL Et_2O, and the solution stirred at rt for 1 h. This brown solution was slowly transferred via syringe to a suspension of CuBr (397 mg, 2.8 mmol) in Et_2O (75 mL) at –78 °C. After 5 min epichlorohydrin (2.2 mL, 28 mmol) was added slowly to the mixture. It stirred at –78 °C for 3 h, and was allowed to warm to –40 °C where it continued stirring for 48 h. The reaction mixture was poured into 100 mL 1 N $HCl_{(aq)}$ and was extracted with ether (3×100 mL). The organic layers were combined, dried over $MgSO_4$, and evaporated to an oil, which was purified by flash chromatography (10% EtOAc in hexanes) to give 2.83 g of the chlorohydrin as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.36 (qq, J = 6.6, 1.1 Hz, 1H), 3.89-3.97 (m, 1H), 3.61 (dd, J = 11.0, 4.1 Hz , 1H), 3.50 (dd, J = 11.0, 6.3 Hz, 1H), 2.29 (dd, J = 13.5, 5.5 Hz, 1H), 2.20 (dd, J = 13.5, 8.0 Hz, 1H), 2.04 (br s, 1H), 1.66 (t, J = 1.1 Hz, 3H), 1.62 (dt, J = 6.9 Hz, 0.8 Hz, 3H). The chlorohydrin (2.8 g, 19 mmol) was added slowly to a suspension of NaH (60% in oil, 1.13 g, 28 mmol) in 50 mL THF, and the mixture stirred at reflux for 16 h. It was cooled to rt, quenched with sat'd aqueous NH_4Cl until pH = 9 was reached, and was extracted with ether (3×50 mL). The organic layers were combined, dried over $MgSO_4$, and evaporated to a yellow oil, which was purified by flash chromatography (1% Et_2O in pentane) to give 1.08 g of the epoxide as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.34 (qq, J = 6.6, 1.1 Hz, 1H), 2.96-3.02 (m, 1H), 2.77 (dd, J = 4.9, 3.8 Hz, 1H), 2.49 (dd, J = 4.9, 2.7 Hz, 1H), 2.25 (dd, J = 14.8, 6.0 Hz, 1H), 2.16 (dd, J = 14.5, 5.5 Hz, 1H), 1.69 (t, J = 1.1 Hz, 3H), 1.61 (dq, J = 6.6, 1.1 Hz, 3H). Titanocene dichloride (69 mg, 0.28 mmol) was added to a solution of 2-butyne (0.8 mL, 10 mmol) and isobutylmagnesium bromide (2.0 M in diethyl ether, 4.9 mL, 10 mmol) in 10 mL Et_2O, and the solution stirred at rt for 1 h. This brown solution was slowly transferred via syringe to a suspension of CuBr (128 mg, 0.9 mmol) in Et_2O (25 mL) at –78 °C. After 5 min the epoxide (1.0 g, 9 mmol) was added slowly to the mixture. It stirred at –78 °C for 2 h, and was allowed to warm to –40 °C where it continued stirring for 24 h.

The reaction mixture was poured into 75 mL 1 N $HCl_{(aq)}$ and was extracted with ether (3×50 mL). The organic layers were combined, dried over Na_2SO_4, and evaporated to an oil, which was purified by flash chromatography (7% EtOAc in hexanes) to give 894 mg (21% over 3 steps) of **30** as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.30 (q, J = 6.6 Hz, 2H), 3.75-3.82 (m, 1H), 2.01-2.15 (m, 4H), 1.79 (d, J = 1.7 Hz, 1H), 1.62 (s, 6H), 1.59 (d, J = 6.6 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 133.0, 122.2, 66.6, 47.7, 16.0, 13.7. HRMS (EI) *m/z* calc. for $C_{11}H_{20}O$: 168.1514, found 168.1515.



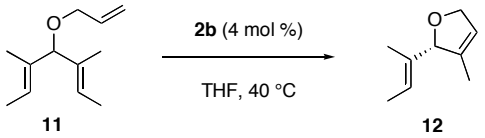
30 **23**

Allyl((2*E*,7*E*)-3,7-dimethylnona-2,7-dien-5-yloxy)dimethylsilane (23). To a solution of **30** (150 mg, 0.9 mmol), triethylamine (0.25 mL, 1.8 mmol), and *N*,*N*-dimethylaminopyridine (5 mg, 0.04 mmol) in 5 mL CH_2Cl_2 was added allylchlorodimethylsilane (0.20 mL, 1.3 mmol). After stirring at rt for 16 h, the reaction was quenched with 10 mL water and extracted with ether (3×20 mL). The organic layers were combined, washed with brine, dried over Na_2SO_4, and evaporated to an oil, which was purified by flash chromatography (1% EtOAc in hexanes) to give 209 mg (88%) of **23** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.70-5.84 (m, 1H), 5.23 (qq, J = 6.6, 1.4 Hz, 2H), 4.81-4.89 (m, 2H), 3.85 (quint, J = 6.3 Hz, 1H), 2.05-2.08 (m, 4H), 1.60 (t, J = 1.1 Hz, 6H), 1.58 (dt, J = 6.6, 0.8 Hz, 6H), 1.54-1.57 (m, 2H), 0.05 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 134.7, 133.0, 121.7, 113.5, 70.5, 48.2, 25.4, 16.5, 13.6, –1.7. HRMS (EI) *m/z* calc. for $C_{16}H_{30}OSi$: 266.2066, found 266.2070.

General Procedure A: Asymmetric Ring-Closing Reactions with 2a-5a. Triene was added to a solution of dichloride catalyst (1-2 mol %) in CH_2Cl_2 (0.055 M), and the reaction stirred at 40

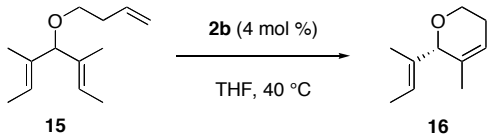
°C for 2 h. The solvent was evaporated, and the remaining residue was purified by flash chromatography to yield the desired cyclic diene.

General Procedure B: Asymmetric Ring-Closing Reactions with 2b-5b. A solution of NaI (25 equiv. relative to catalyst) and dichloride catalyst (4 mol %) in THF were stirred at rt for 1 h. Triene (0.055 M) was added, and the solution stirred at 40 °C for 2 h. The solvent was evaporated, and the remaining residue was purified by flash chromatography to yield the desired cyclic diene.



11 12

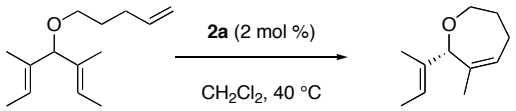
(*S*,*E*)-2-(But-2-en-2-yl)-3-methyl-2,5-dihydrofuran (12). Following general procedure B, **11** (40 mg, 0.22 mmol), **2a** (8.9 mg, 0.0089 mmol), and NaI (33 mg, 0.22 mmol) in 4 mL THF gave 19.8 mg (64%) of **12** as a pale yellow oil (5% Et_2O in pentane) in 90% *ee*. $[\alpha]_D^{25}$ = +116.5 ($CHCl_3$, *c* = 0.55). ^1H NMR (300 MHz, $CDCl_3$, ppm): δ 5.56 (quint, J = 1.6 Hz, 1H), 5.52 (q, J = 6.9 Hz, 1H), 4.88 (br s, 1H), 4.53-4.68 (m, 2H), 1.64 (dq, J = 6.9, 1.1 Hz, 3H), 1.56 (quint, J = 1.4 Hz, 3H), 1.47 (quint, J = 1.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 137.2, 135.6, 123.8, 121.5, 95.0, 75.6, 13.5, 12.4, 10.1. HRMS (EI) *m/z* calc. for $C_9H_{14}O$: 138.1045, found 138.1040.



15 16

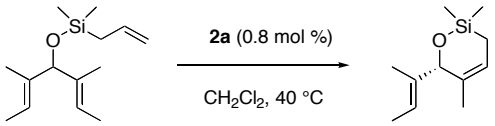
(*S*,*E*)-6-(But-2-en-2-yl)-5-methyl-3,6-dihydro-2*H*-pyran (16). Following general procedure B, **15** (40 mg, 0.21 mmol), **2a** (8.2 mg, 0.0082 mmol), and NaI (31 mg, 0.21 mmol) in 3.8 mL THF gave 22.7 mg (73%) of **16** as a pale yellow oil (3% Et_2O in pentane) in 90% *ee*. $[\alpha]_D^{26}$ = +43.0

($CHCl_3$, *c* = 0.69). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.64-5.68 (m, 1H), 5.53 (q, J = 6.6 Hz, 1H), 4.29 (s, 1H), 3.88-3.94 (m, 1H), 3.53-3.61 (m, 1H), 2.19-2.32 (m, 1H), 1.85-1.96 (m, 1H), 1.64 (dd, J = 6.6, 1.1 Hz, 3H), 1.54 (t, J = 1.4 Hz, 3H), 1.47 (q, J = 1.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 134.9, 134.5, 125.2, 121.5, 84.1, 62.9, 25.8, 19.7, 13.5, 11.5. HRMS (EI) *m/z* calc. for $C_{10}H_{16}O$: 152.1201, found 152.1204.



17 18

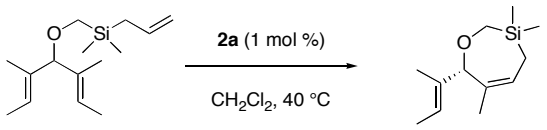
(*S*,*Z*)-7-((*E*)-But-2-en-2-yl)-6-methyl-2,3,4,7-tetrahydrooxepine (18). Following a modified version of general procedure A, **17** (40 mg, 0.19 mmol) was added to a solution of **5a** (2.1 mg, 0.0019 mmol) in 3.5 mL CH_2Cl_2, and the reaction stirred at 40 °C. After 2 h, an additional portion of **5a** (2.1 mg, 0.0019 mmol) was added, and the solution stirred at 40 °C for an additional 2 h. The solvent was removed by evaporation, and the residue was purified by flash chromatography (4% EtOAc in hexanes) to give 29.4 mg (92%) of **18** as a yellow oil in 76% *ee*. $[\alpha]_D^{24}$ = +164.0 ($CHCl_3$, *c* = 0.90). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.57-5.62 (m, 1H), 5.51 (q, J = 6.6 Hz, 1H), 4.26 (s, 1H), 3.85-3.92 (m, 1H), 3.57-3.66 (m, 1H), 2.48-2.59 (m, 1H), 1.87-2.03 (m, 2H), 1.67-1.80 (m, 1H), 1.67 (t, J = 2.2 Hz, 3H), 1.65 (d, J = 6.6 Hz, 3H), 1.50 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 137.2, 134.6, 125.3, 124.0, 91.4, 66.3, 29.2, 23.4, 21.9, 13.5, 12.5. HRMS (EI) *m/z* calc. for $C_{11}H_{18}O$: 166.1358, found 166.1353.



13 14

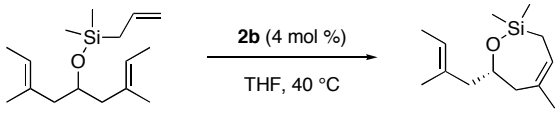
(*S*,*E*)-6-(But-2-en-2-yl)-2,2,5-trimethyl-3,6-dihydro-2*H*-1,2-oxasiline (14). Following general procedure A, **13** (0.95 g, 4.0 mmol) and **5a** (35 mg, 0.032 mmol) in 72 mL CH_2Cl_2 gave 0.60 g (77%) of **14** as a yellow oil (3% EtOAc in hexanes) in 92% *ee*. $[\alpha]_D^{25}$ = +195.4 ($CHCl_3$, *c* =

0.96). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.69 (dquint, J = 7.7, 1.4 Hz, 1H), 5.49 (q, J = 6.6 Hz, 1H), 4.54 (s, 1H), 1.63 (dd, J = 6.6, 1.1 Hz, 3H), 1.54 (t, J = 1.1 Hz, 3H), 1.51 (s, 3H), 1.29-1.39 (m, 1H), 1.12-1.21 (m, 1H), 0.19 (s, 3H), 0.13 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 136.9, 136.0, 122.9, 120.4, 83.4, 22.0, 13.5, 12.5, 10.7, 0.3, –0.6. HRMS (EI) *m/z* calc. for $C_{11}H_{20}OSi$: 196.1284, found 196.1281.



21 **22**

(*S*,*Z*)-7-((*E*)-But-2-en-2-yl)-3,3,6-trimethyl-2,3,4,7-tetrahydro-1,3-oxasilepine (22). Following general procedure A, **21** (40 mg, 0.16 mmol) and **5a** (1.7 mg, 0.0016 mmol) in 2.9 mL CH_2Cl_2 gave 21.7 mg (65%) of **22** as a yellow oil (2% EtOAc in hexanes) in 92% *ee*. $[\alpha]_D^{25}$ = +184.3 ($CHCl_3$, *c* = 0.75). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.66 (t, J = 7.4 Hz, 1H), 5.49 (q, J = 6.9 Hz, 1H), 4.49 (s, 1H), 2.55-2.67 (m, 1H), 2.02-2.12 (m, 1H), 1.68 (t, J = 1.1 Hz, 3H), 1.64 (d, J = 6.9 Hz, 3H), 1.56 (s, 3H), 0.75-0.86 (m, 2H), 0.16 (s, 3H), 0.14 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 137.2, 136.5, 128.8, 121.8, 84.0, 22.6, 21.9, 16.8, 13.5, 11.8, 0.9, –0.3. HRMS (EI) *m/z* calc. for $C_{12}H_{22}OSi$: 210.1440, found 210.1449.

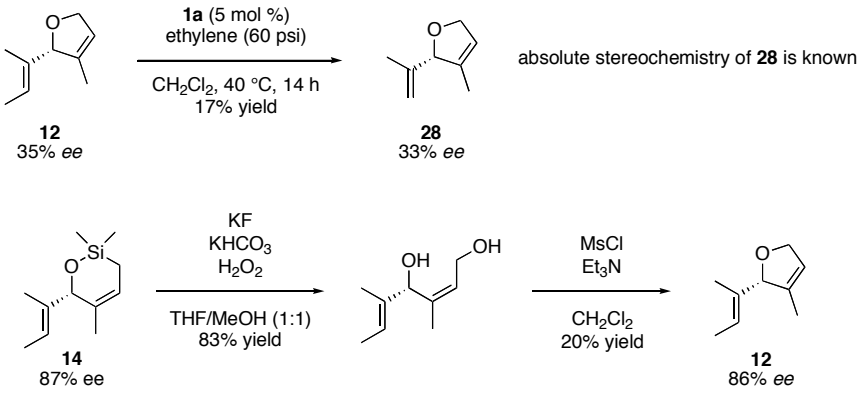


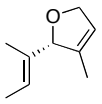
23 **24**

(*S*,*Z*)-2,2,5-Trimethyl-7-((*E*)-2-methylbut-2-enyl)-2,3,6,7-tetrahydro-1,2-oxasilepine (24). Following general procedure B, **23** (40 mg, 0.15 mmol), **2a** (6.0 mg, 0.006 mmol), and NaI (23 mg, 0.15 mmol) in 2.7 mL THF gave 33.1 mg (98%) of **24** as a light yellow oil (2% EtOAc in hexanes) in 78% *ee*. $[\alpha]_D^{24}$ = +8.3 ($CHCl_3$, *c* = 0.99). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.53 (t, J = 7.4 Hz, 1H), 5.24 (qq, J = 6.6, 1.1 Hz, 1H), 3.97-4.05 (m, 1H), 2.21-2.36 (m, 2H), 2.01-2.10 (m, 2H), 1.70 (s, 3H), 1.62 (s, 3H), 1.59 (d, J = 6.6 Hz, 3H), 1.54-1.60 (m, 1H), 1.31-1.39

(m, 1H), 0.11 (s, 3H), 0.08 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 134.3, 133.4, 121.3, 121.2, 71.1, 49.2, 41.3, 25.9, 18.0, 16.2, 13.6, 0.4, –1.4. HRMS (EI) *m/z* calc. for $C_{13}H_{24}OSi$: 224.1597, found 224.1598.

Absolute Stereochemistry Determination. The absolute stereochemistry of **28** has been previously proven.[ix] Compound **12** was transformed into **28** by ethylenolysis, and the chiral GC trace (Chiraldex G-TA, same column used in ref. ix) showed that it was the opposite absolute stereochemistry of that which was proven. Additionally, that same experiment proved the absolute stereochemistry of **12**. The absolute stereochemistry of **14** was determined by oxidizing it to the diol and subsequent mesylation/intramolecular nucleophilic substitution gave **12**. **12** synthesized from **14** had the same absolute stereochemistry as the **12** synthesized by asymmetric ring-closing metathesis. For any given ring-closing substrate in this paper, catalysts **2a** through **5b** all gave products with the same absolute stereochemistry.

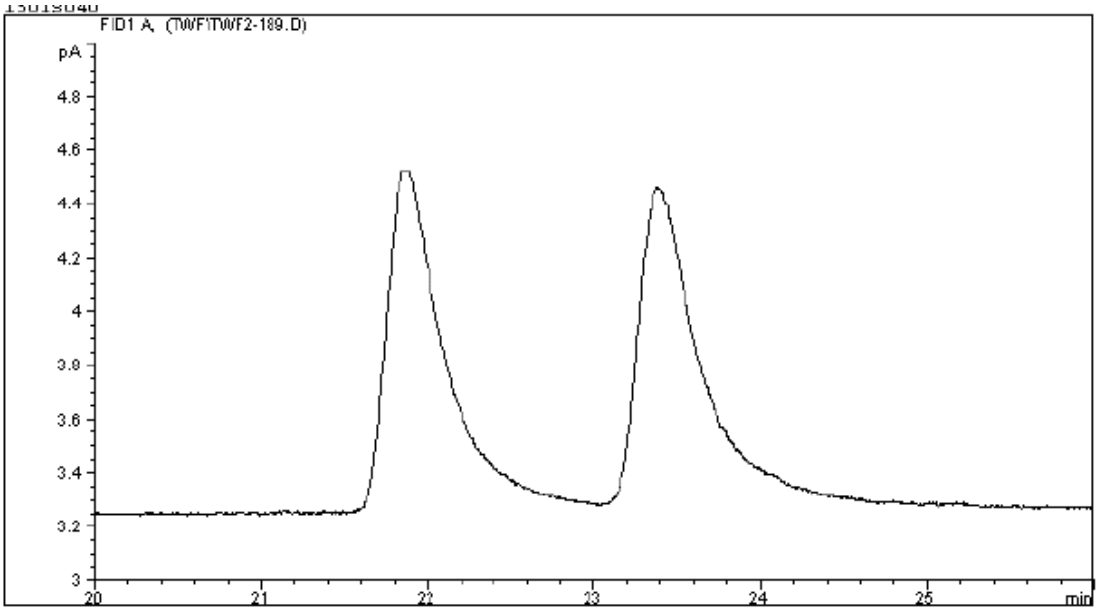




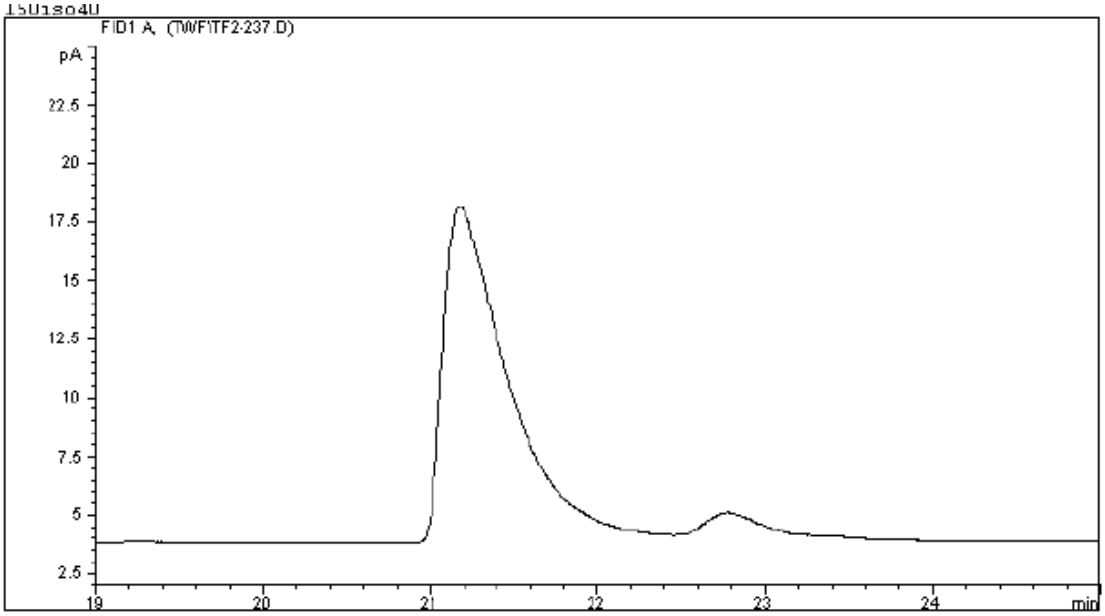
12

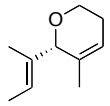
Chiraldex G-TA, 1mL/min, 60 °C for 60 min

Racemic



90% *ee*

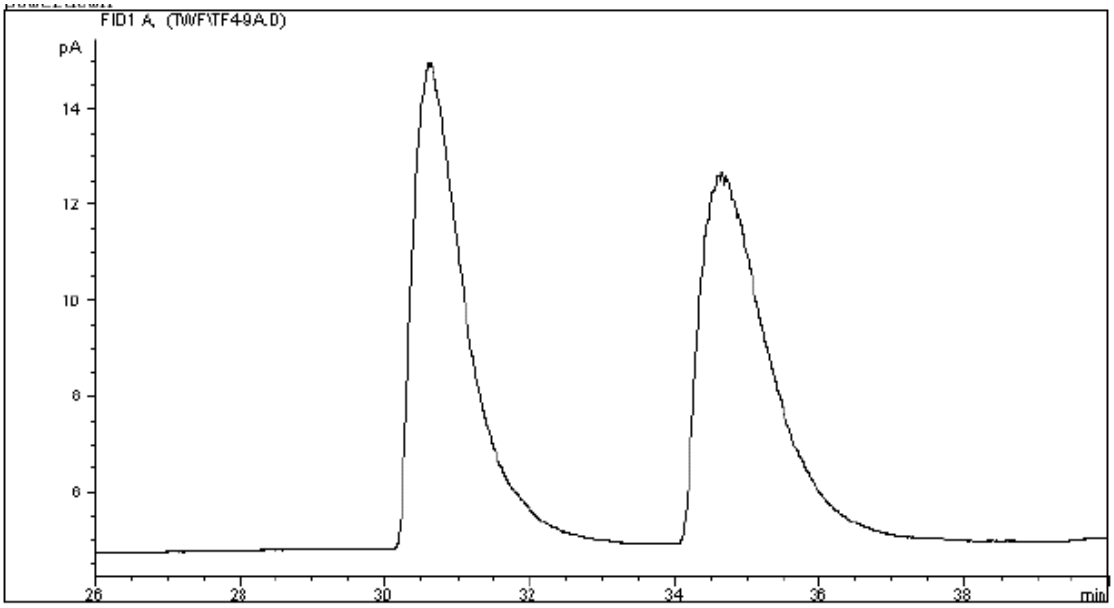




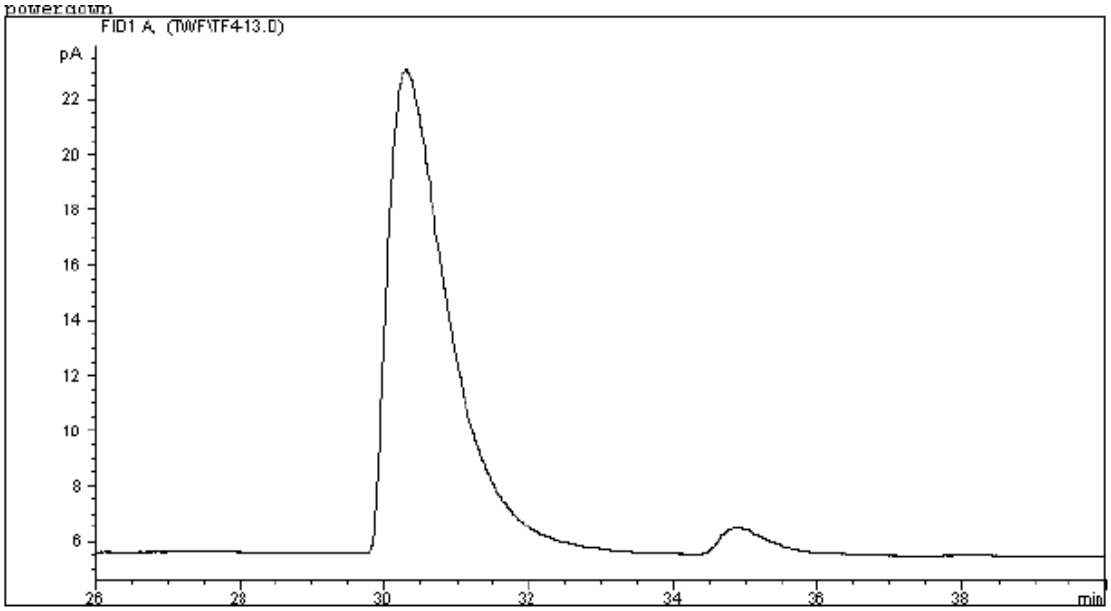
16

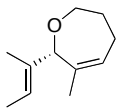
Chiraldex G-TA, 1mL/min, 60 °C for 60 min

Racemic



90% *ee*

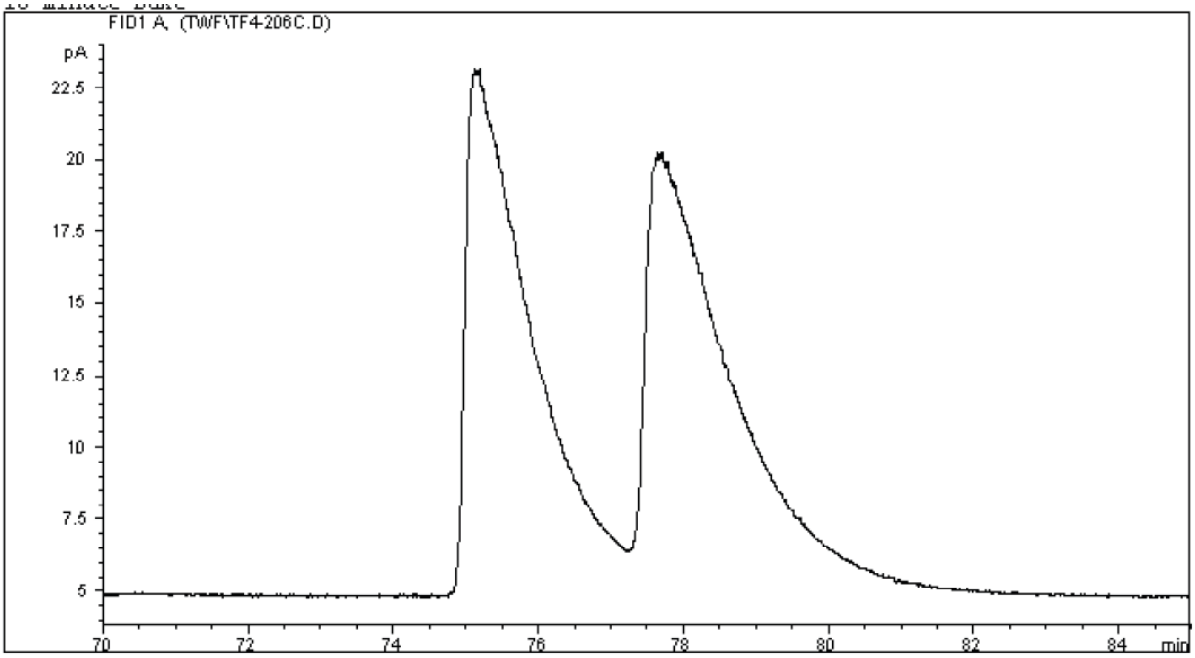




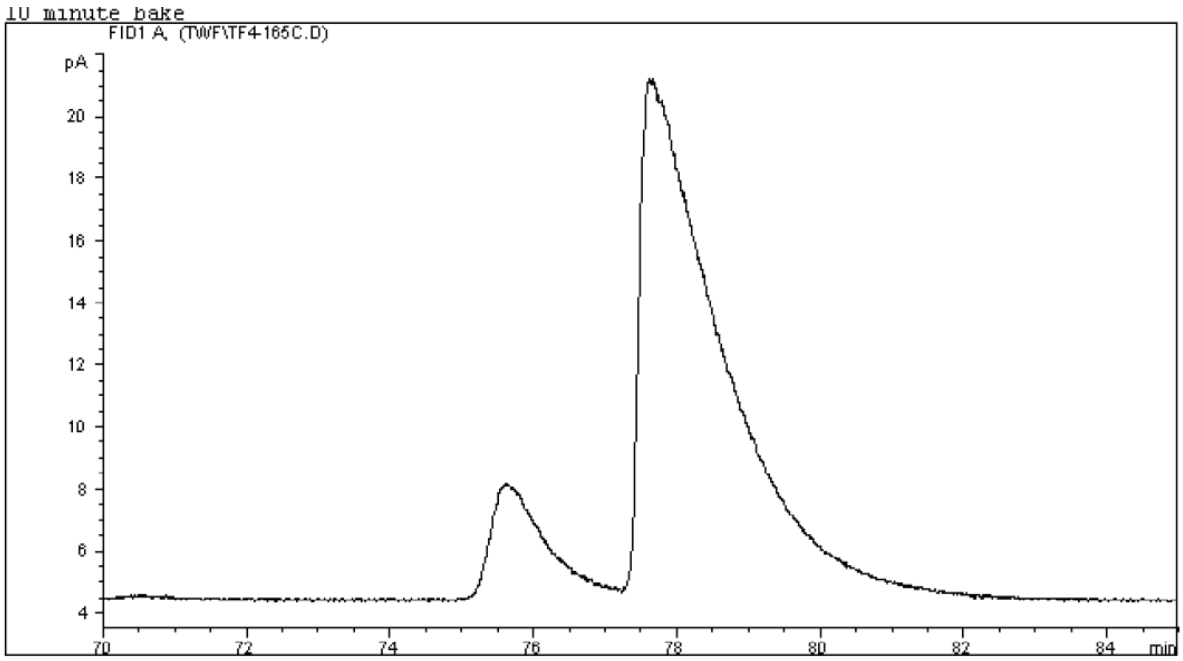
18

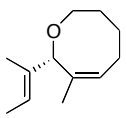
Chiraldex G-TA, 1mL/min, 60 °C for 90 min

Racemic



76% ee

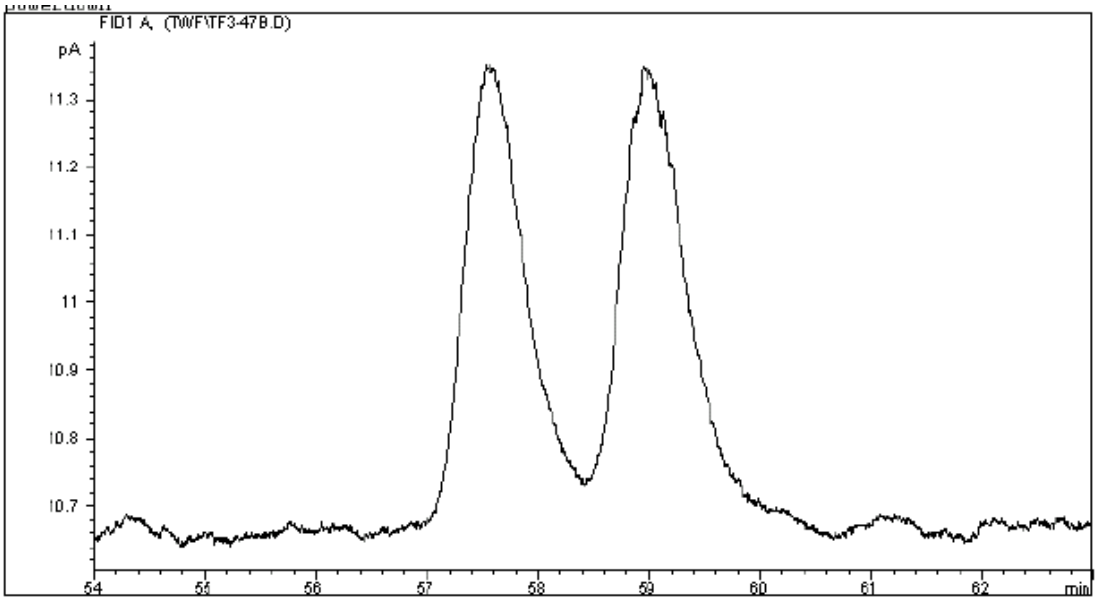




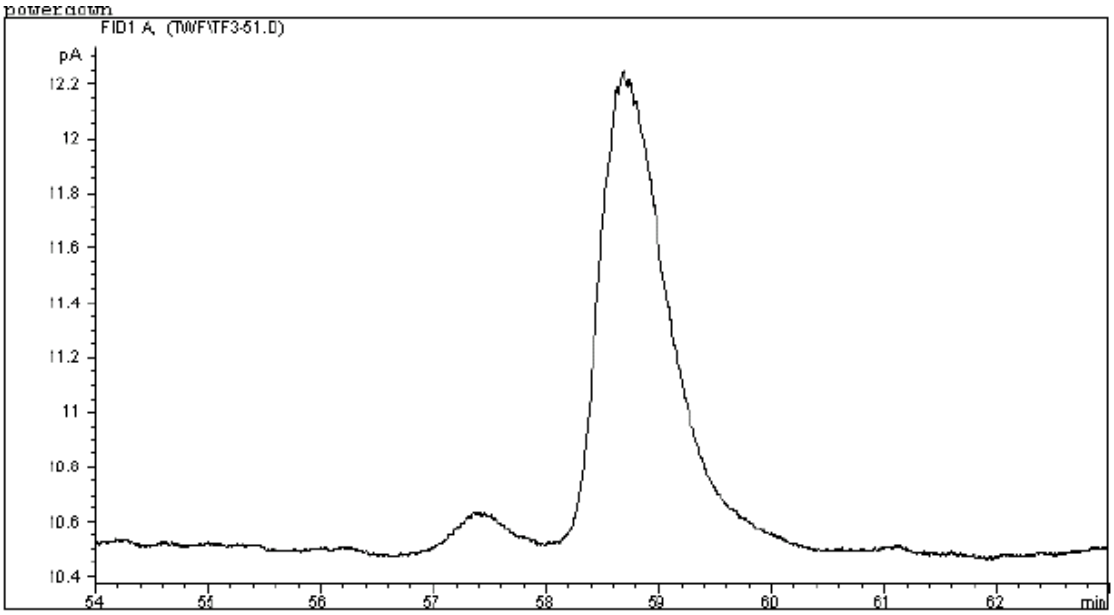
20

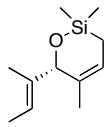
Chiraldex G-TA, 1mL/min, 60 °C for 90 min

Racemic



85% *ee*

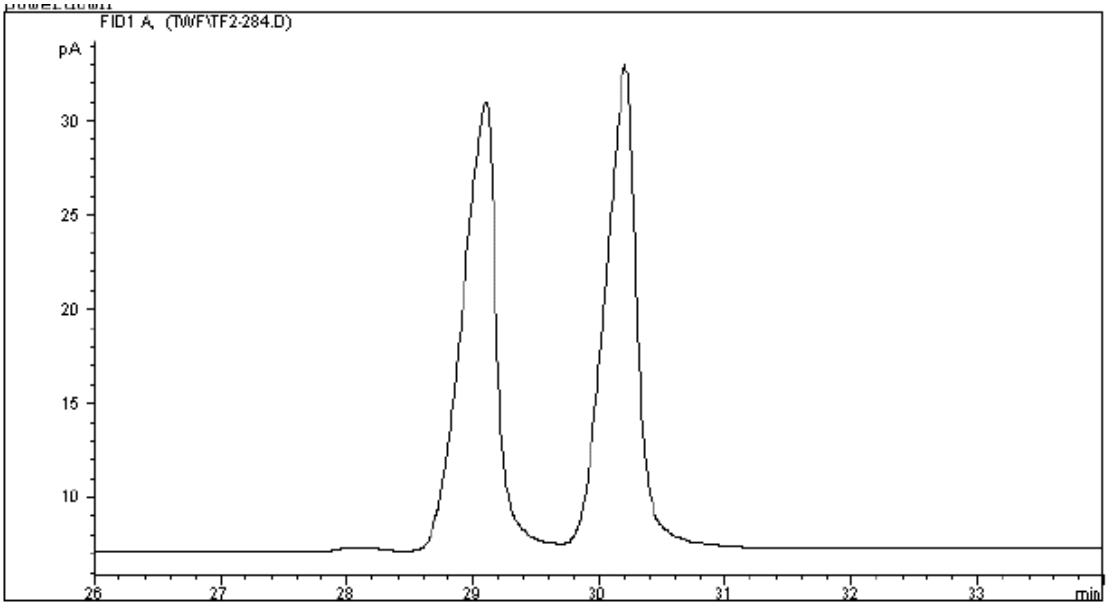




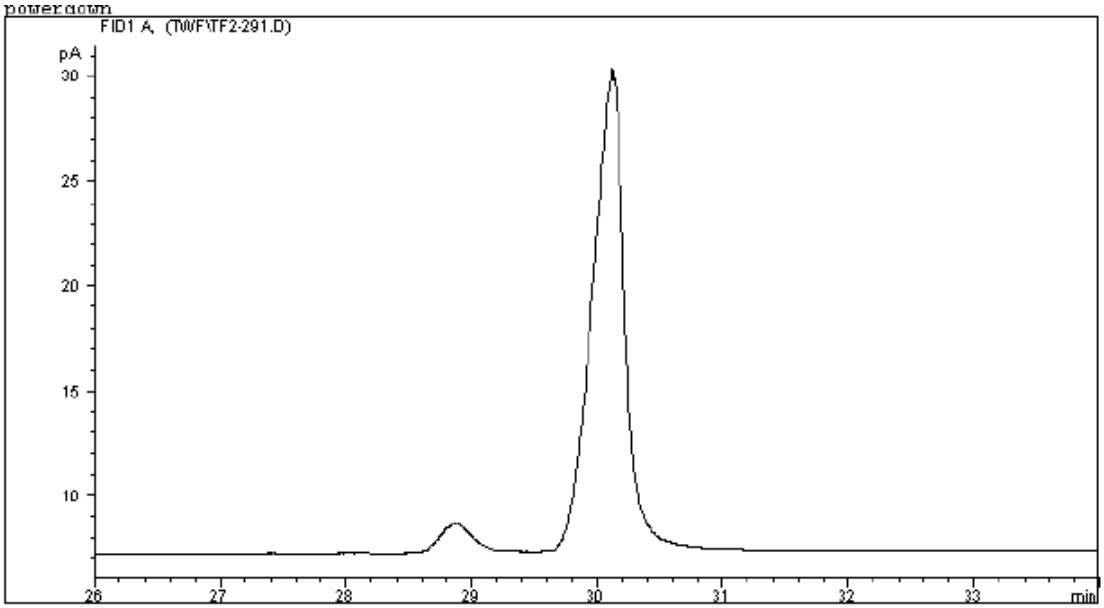
14

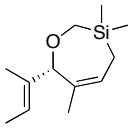
Chiraldex G-TA, 1mL/min, 60 °C for 60 min

Racemic



92% *ee*

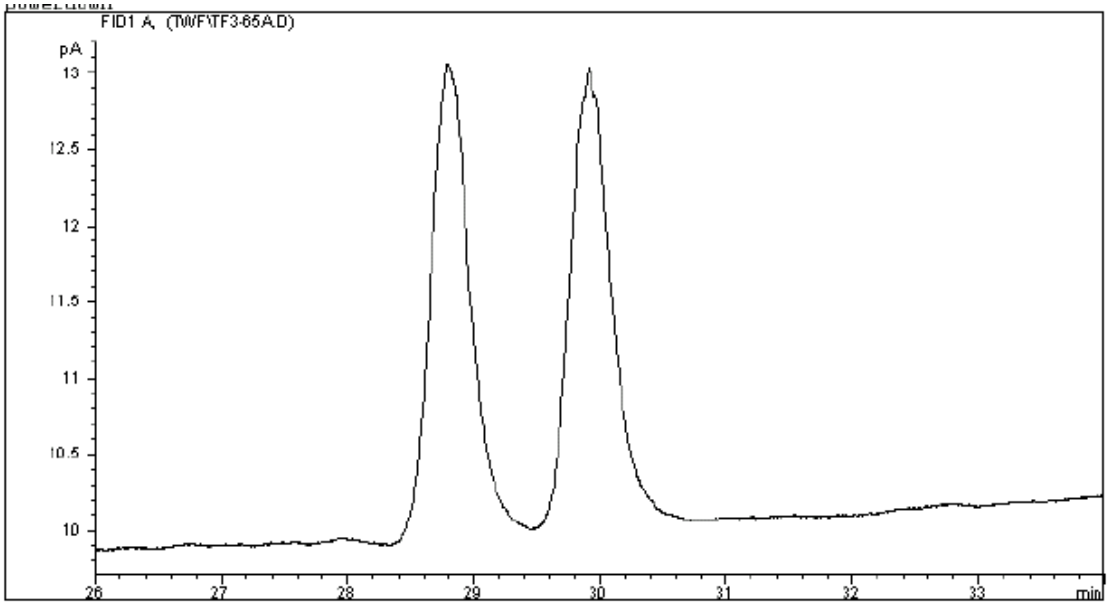




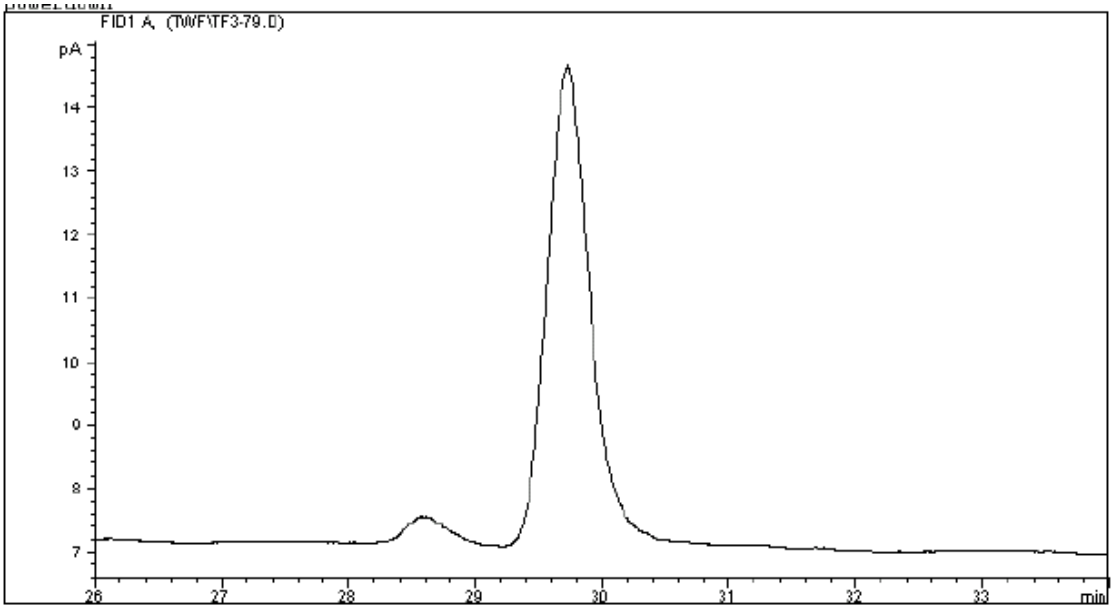
22

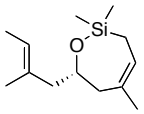
Chiraldex G-TA, 1mL/min, 60 °C for 60 min

Racemic



92% *ee*

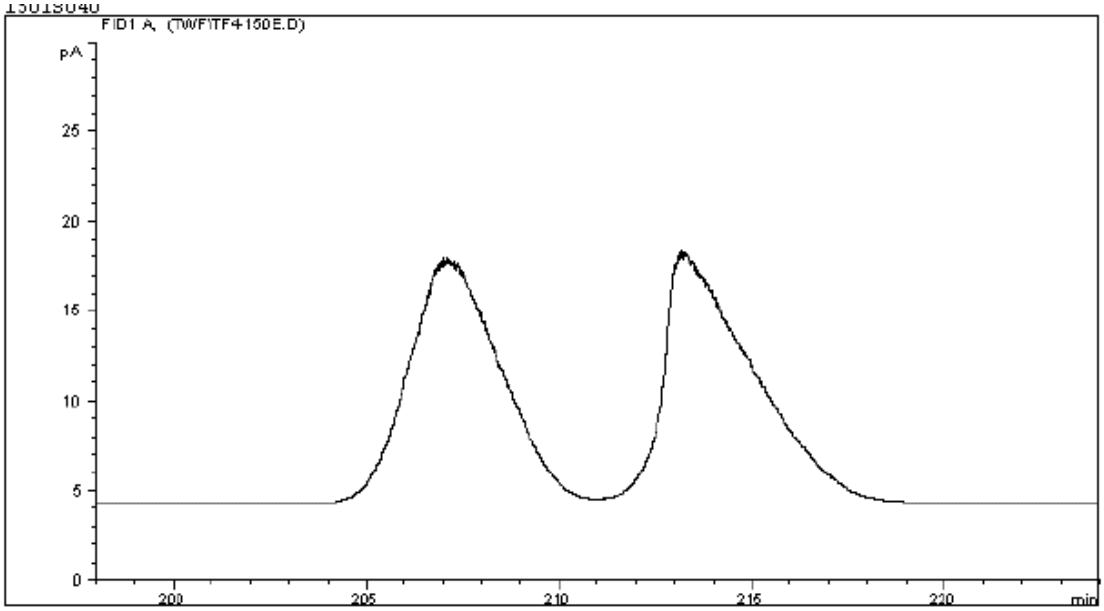




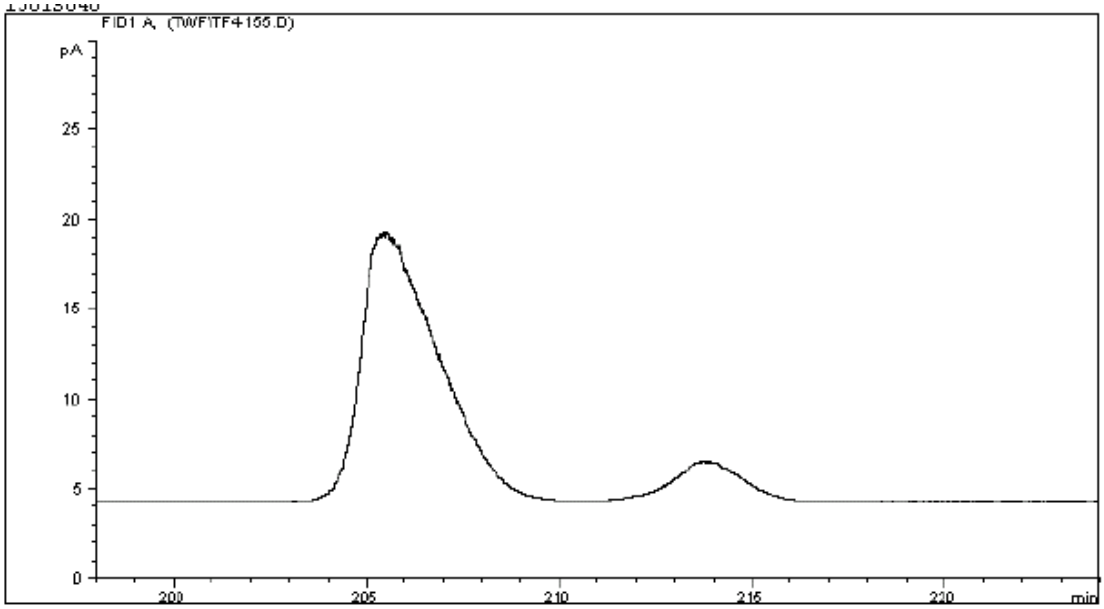
24

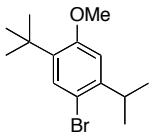
CP Chirasil-Dex-CB, 1 mL/min, 60 °C for 250 min

Racemic

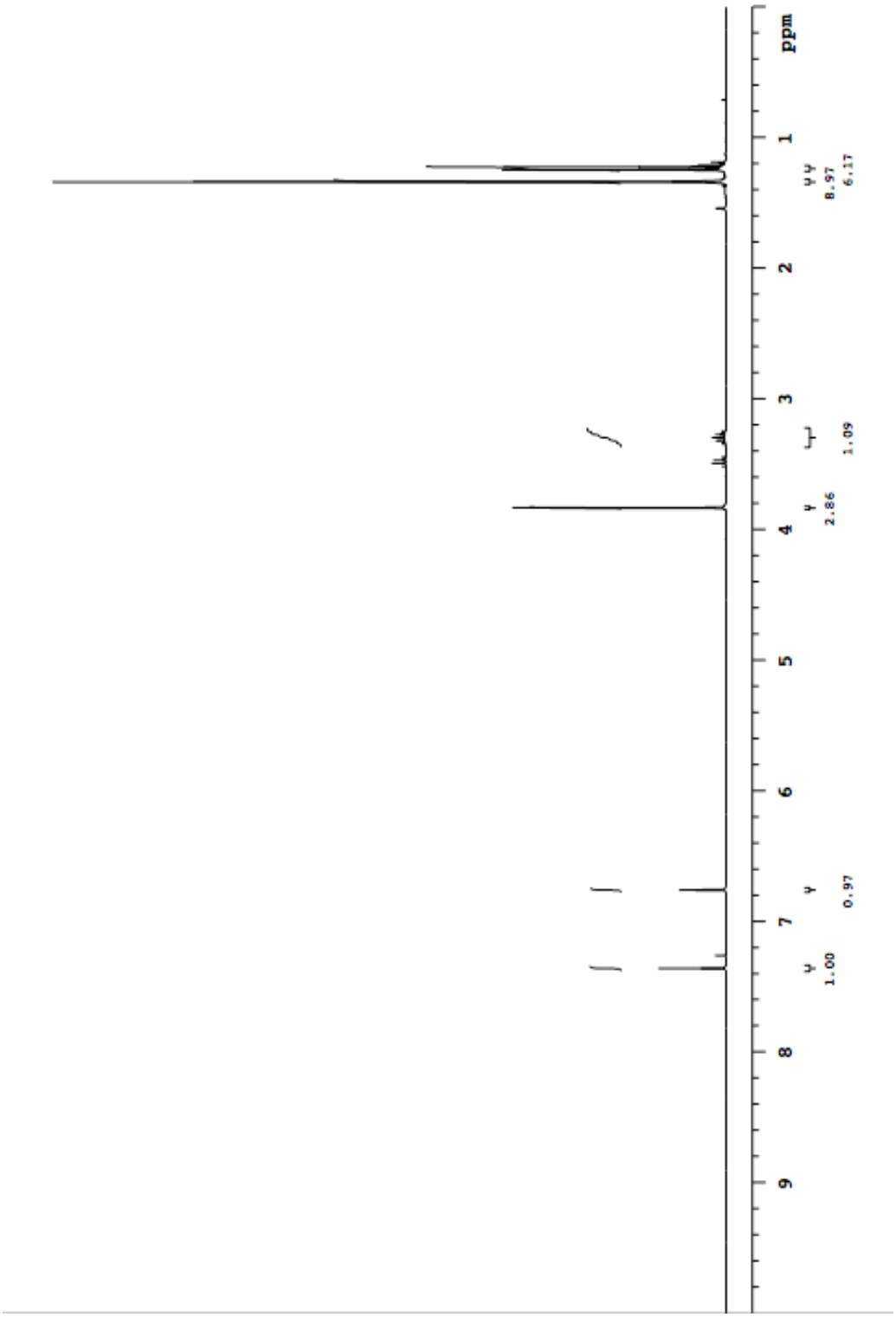


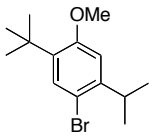
78% *ee*



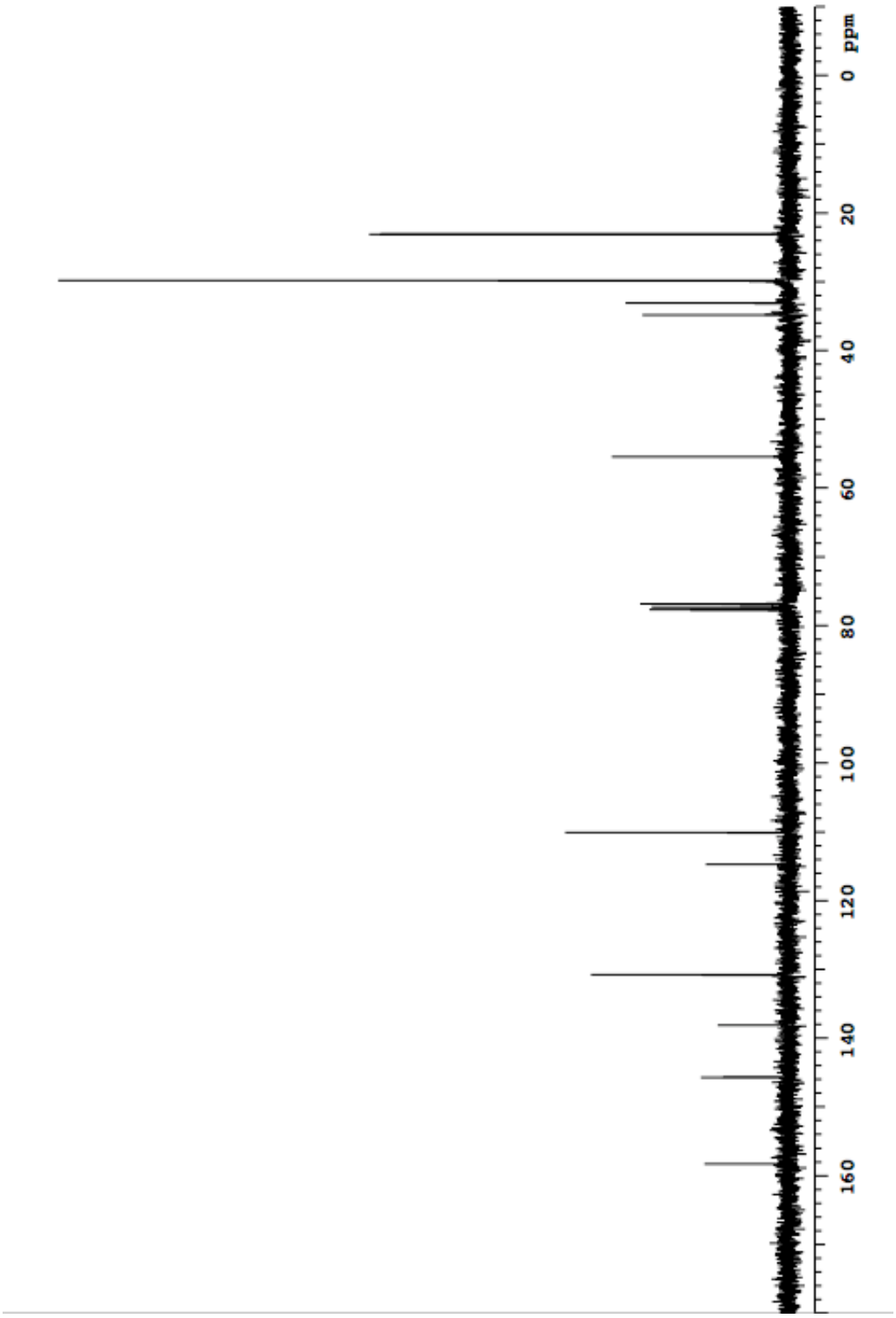


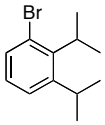
7c



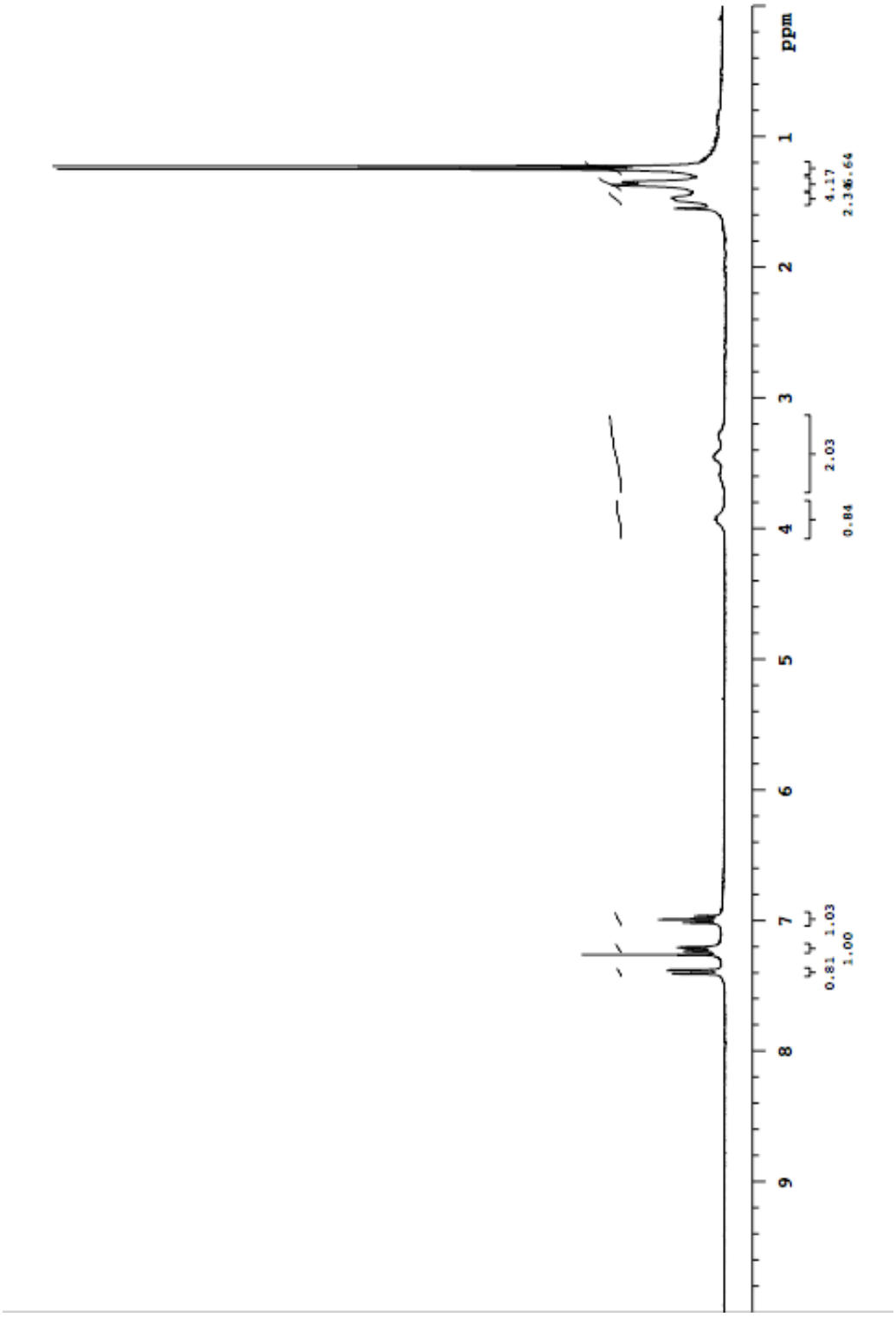


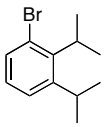
7c



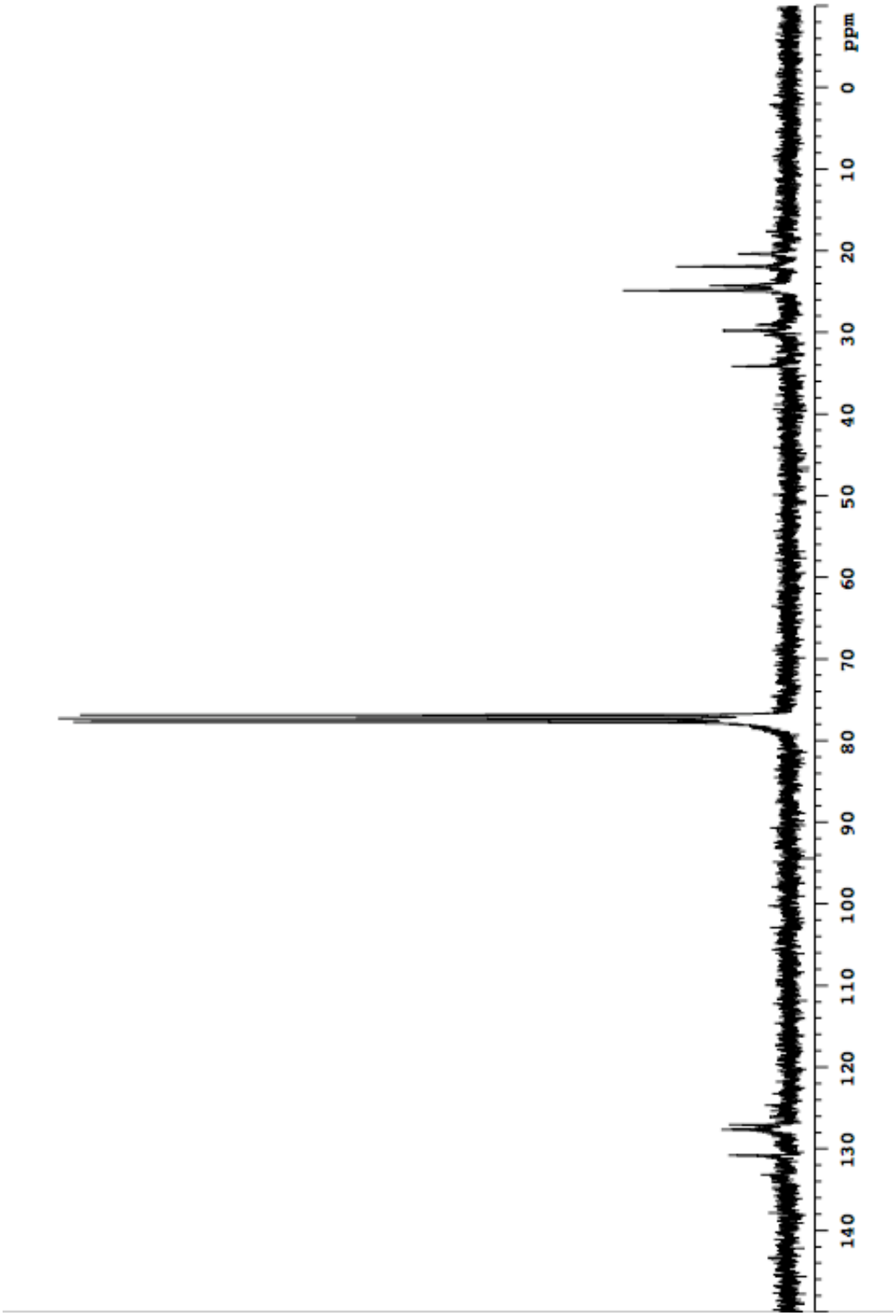


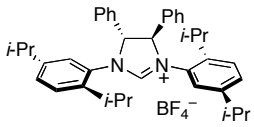
7d



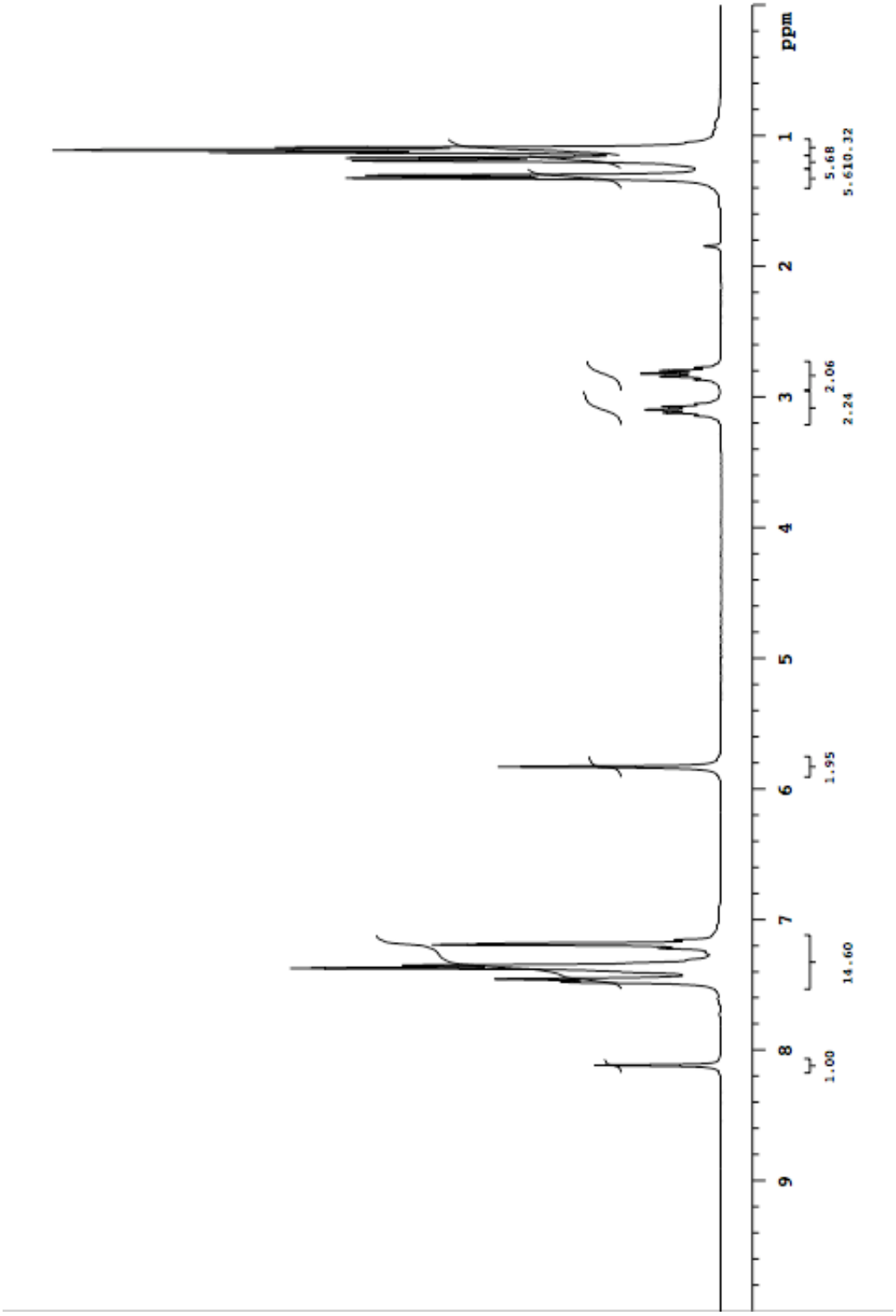


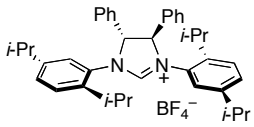
7d



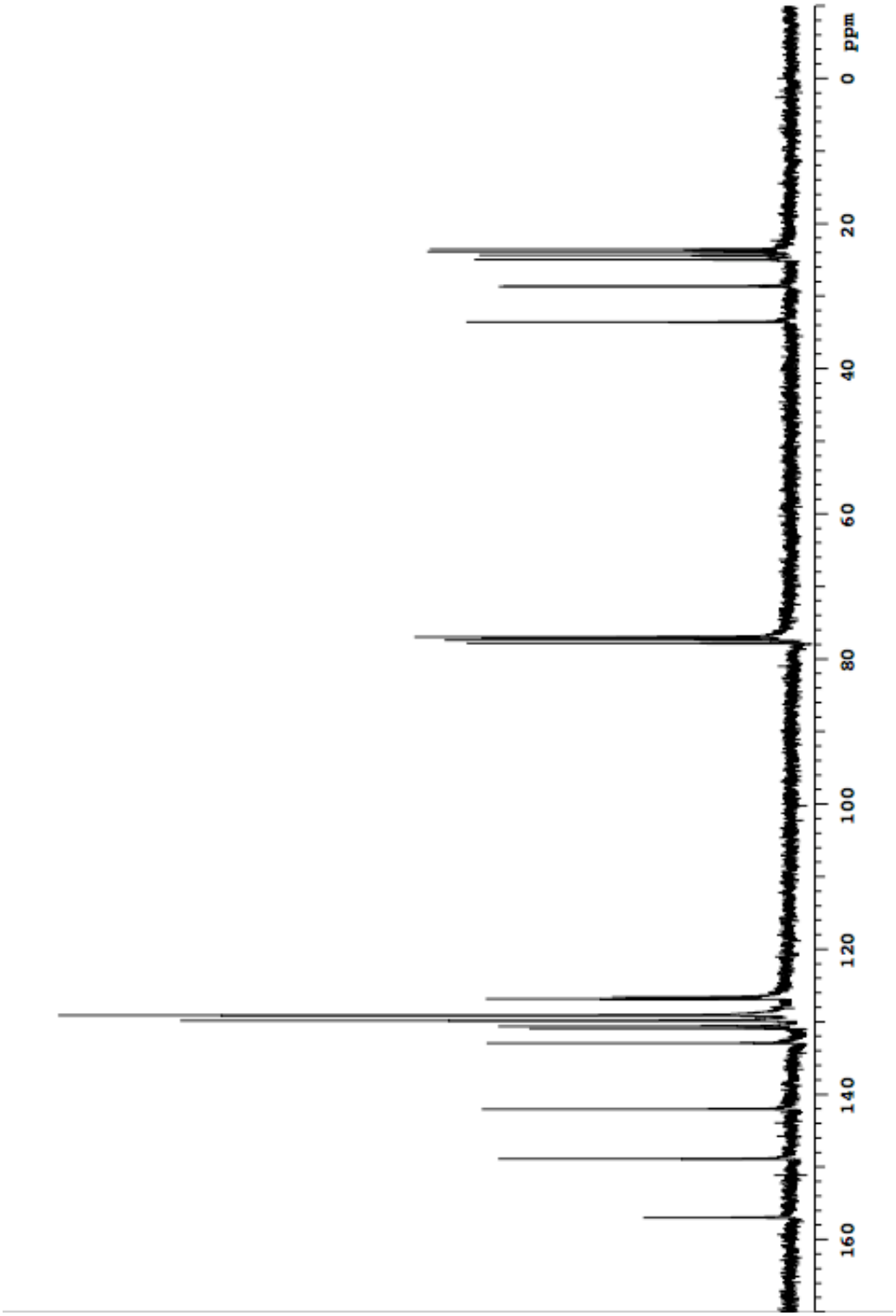

Ph
Ph
i-Pr
i-Pr
N
N
+
i-Pr
BF4−
i-Pr

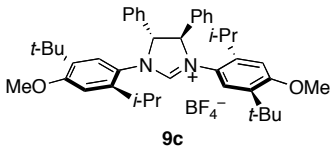
9b


ppm
1
2
3
4
5
6
7
8
9
5.68
5.610.32
2.06
2.24
1.95
14.60
1.00

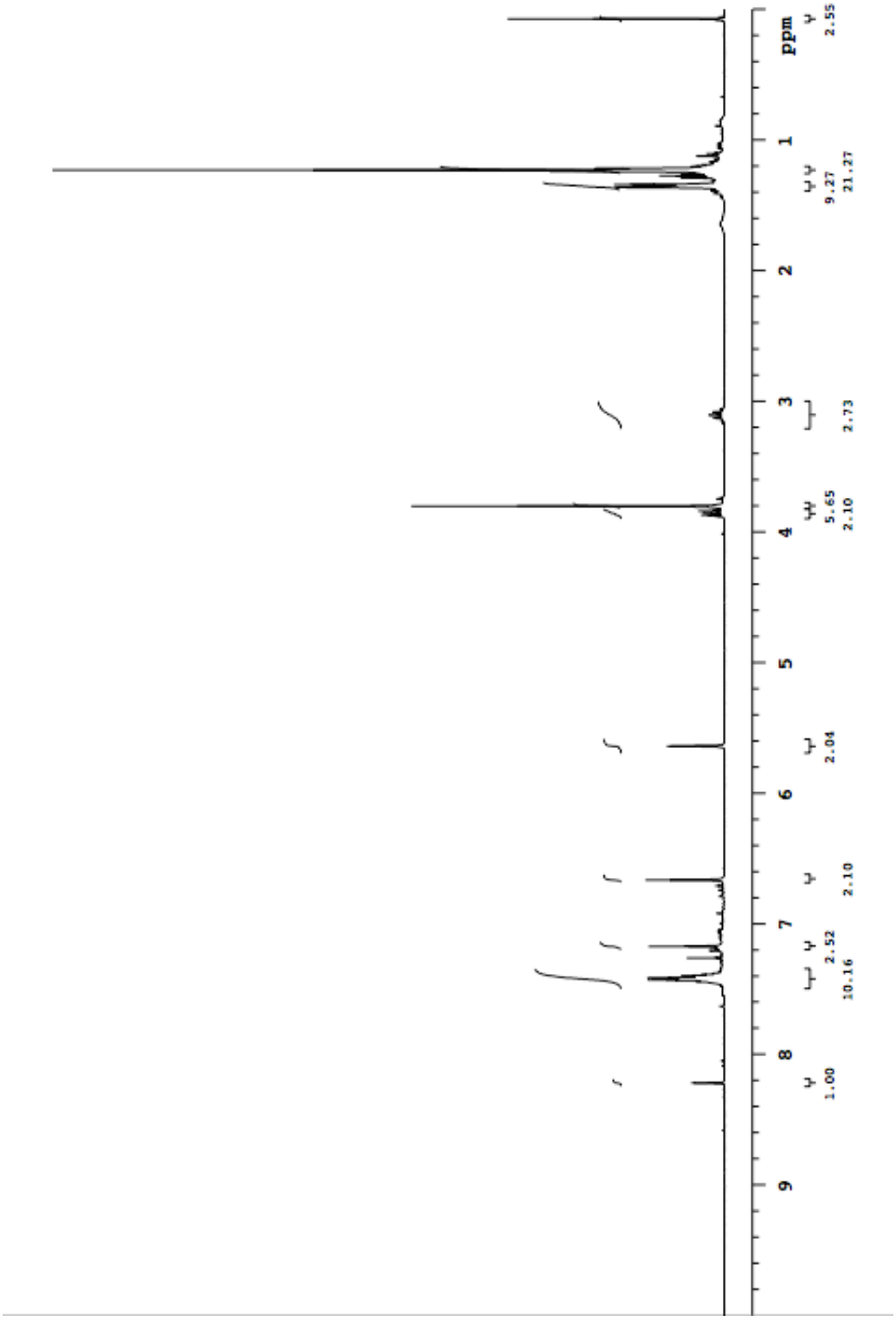


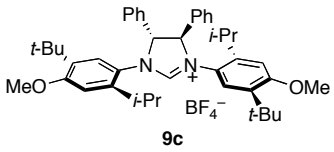
9b



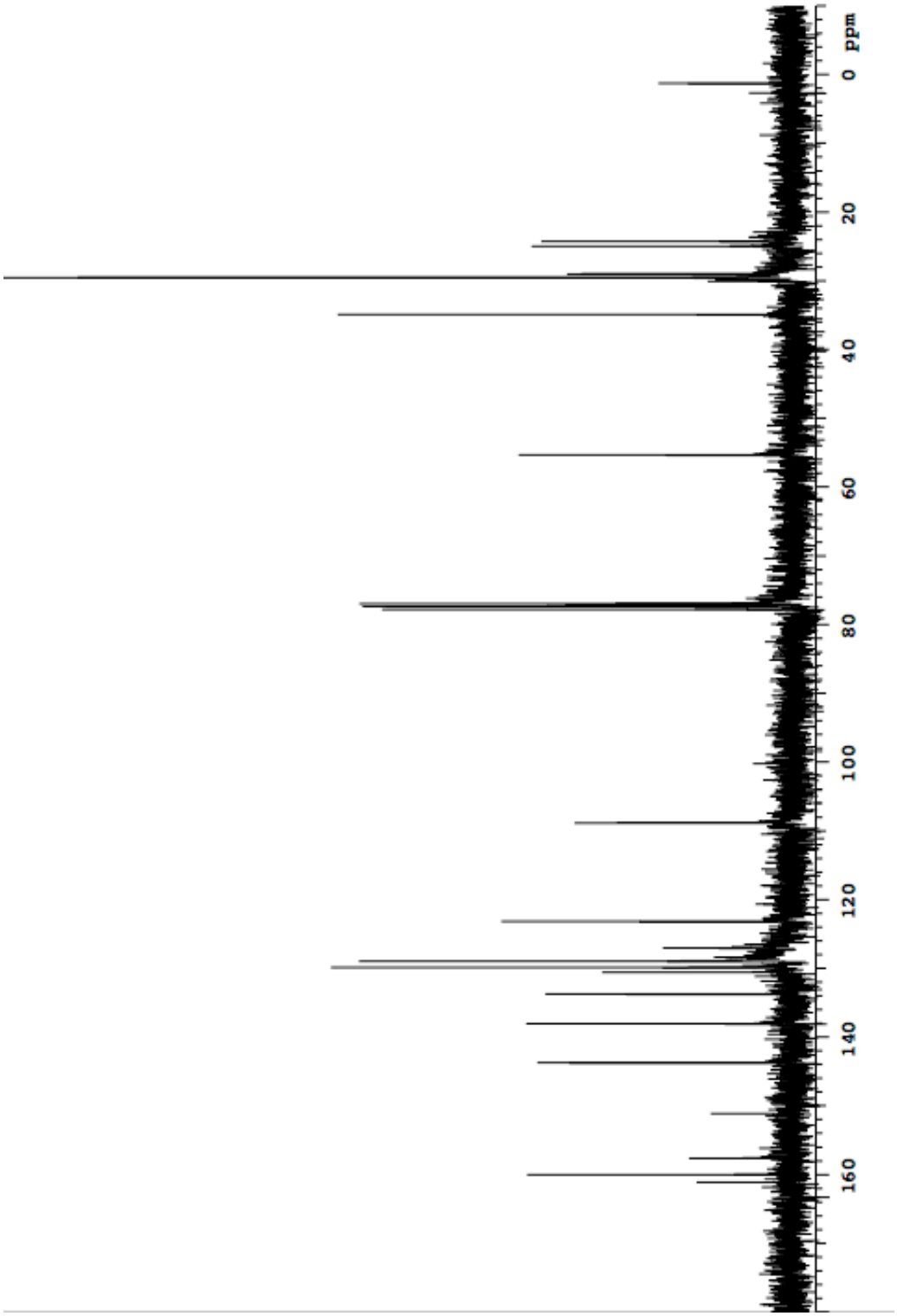

Ph
Ph
t-Bu
i-Pr
MeO
OMe
i-Pr
BF4−
t-Bu

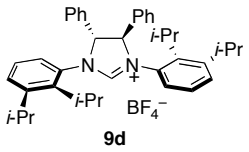
9c


ppm
1
2
3
4
5
6
7
8
9
9.27
21.27
5.65
2.10
2.73
2.04
2.52
10.16
2.10
1.00
2.55

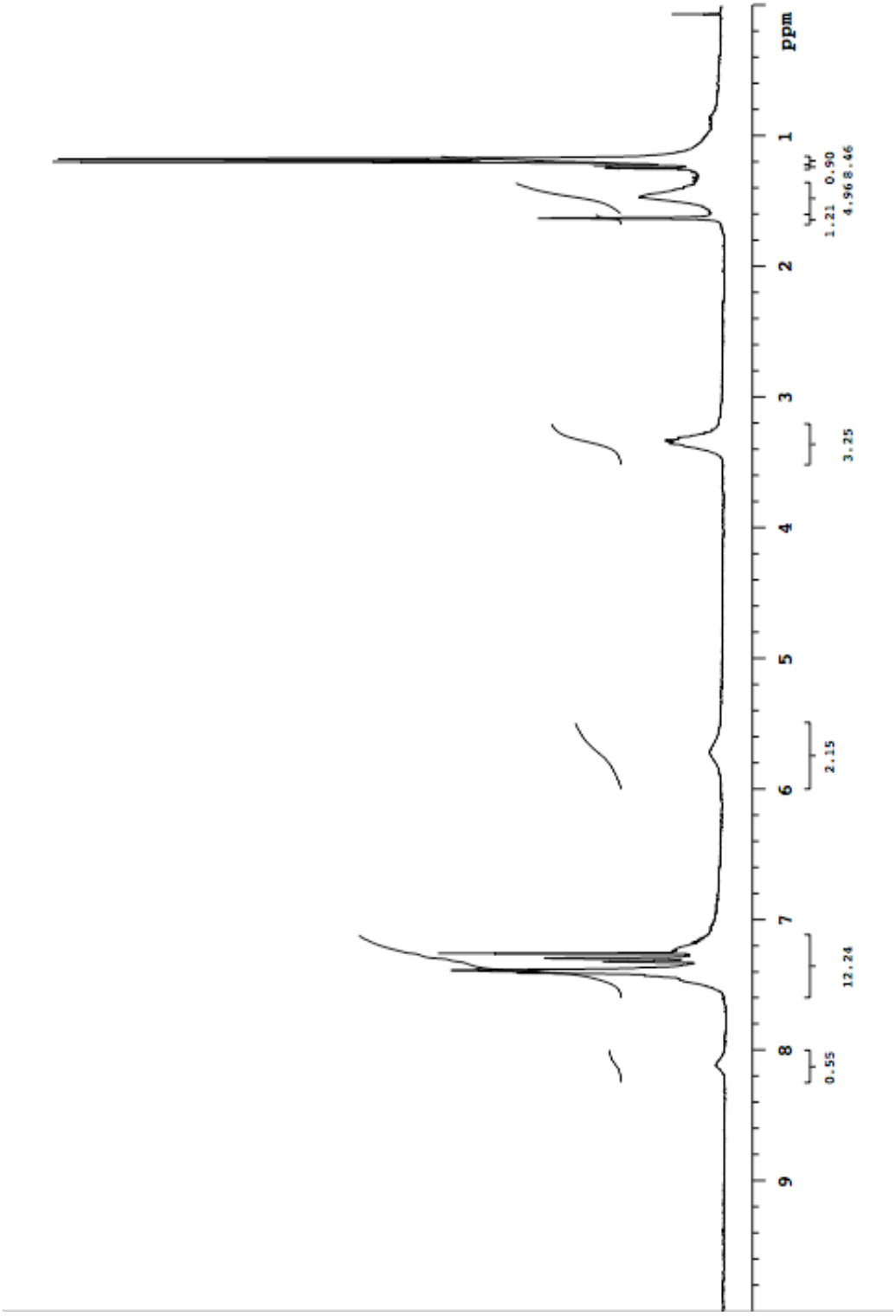

Ph
Ph
t-Bu
i-Pr
MeO
N
N
OMe
i-Pr
BF4−
t-Bu

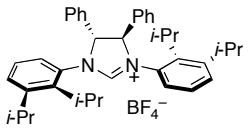
9c


0 ppm
20
40
60
80
100
120
140
160

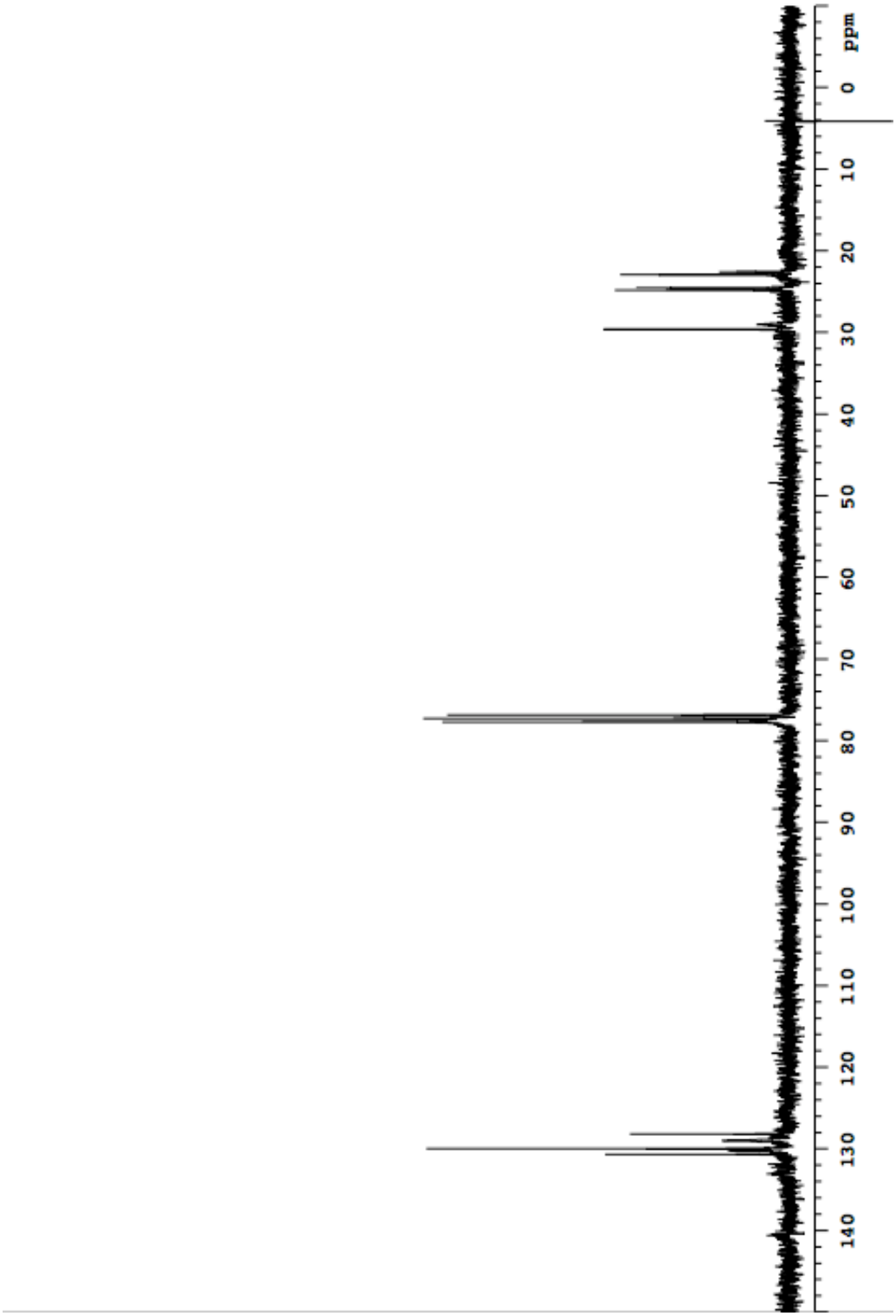

Ph
Ph
i-Pr
i-Pr
i-Pr
i-Pr
BF4−

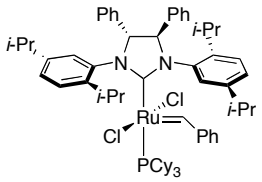
9d


ppm
1
2
3
4
5
6
7
8
9
1.21
0.90
4.96
8.46
3.25
2.15
12.24
0.55

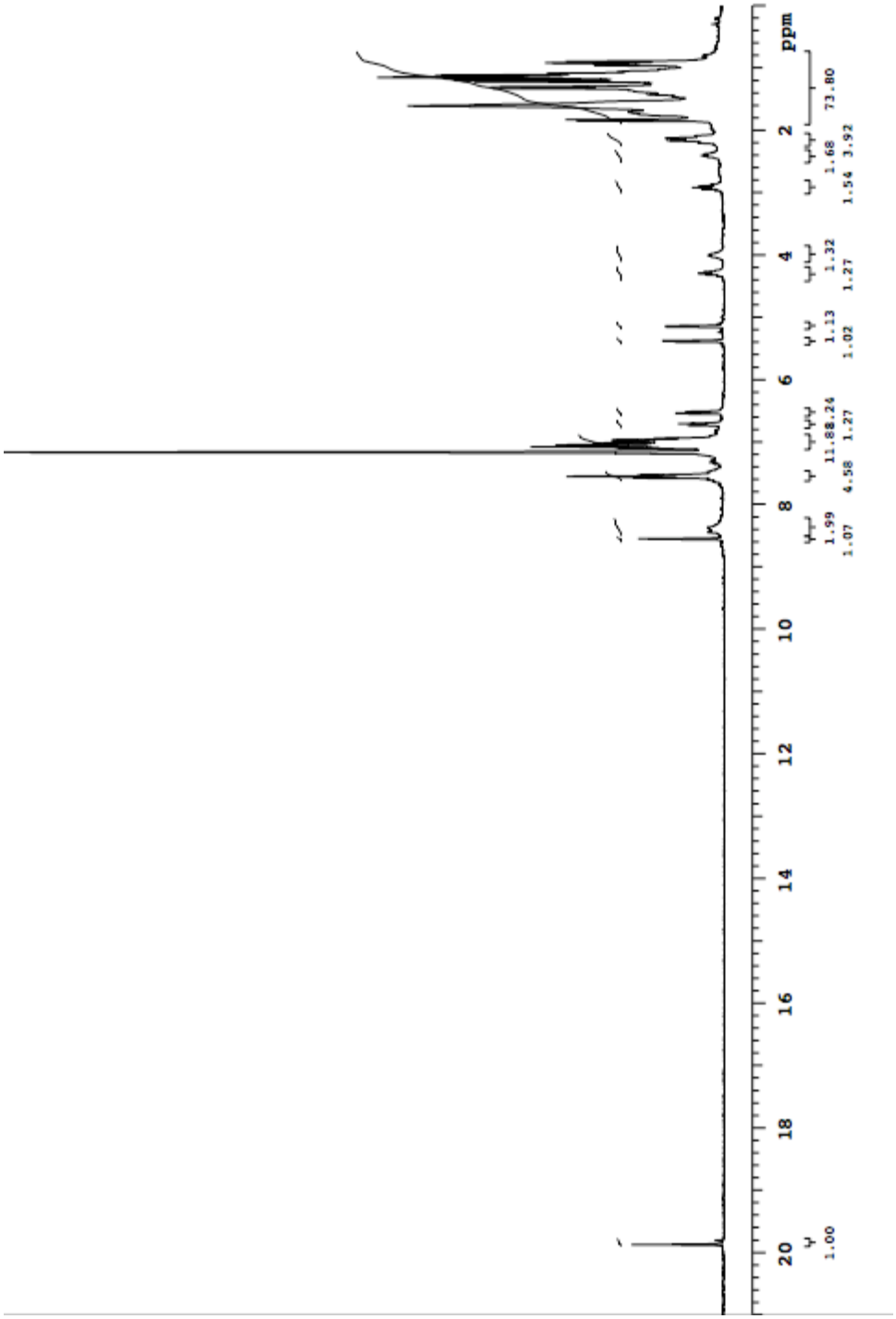

Ph
Ph
i-Pr
i-Pr
N
N
i-Pr
i-Pr
BF4−

9d


ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140


Ph
Ph
i-Pr
i-Pr
N
N
i-Pr
Cl
i-Pr
Ru
Cl
Ph
PCy3

3a


ppm
2
4
6
8
10
12
14
16
18
20
1.00
1.99
1.07
4.58
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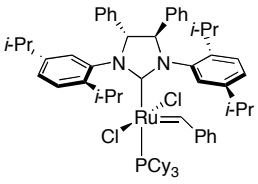
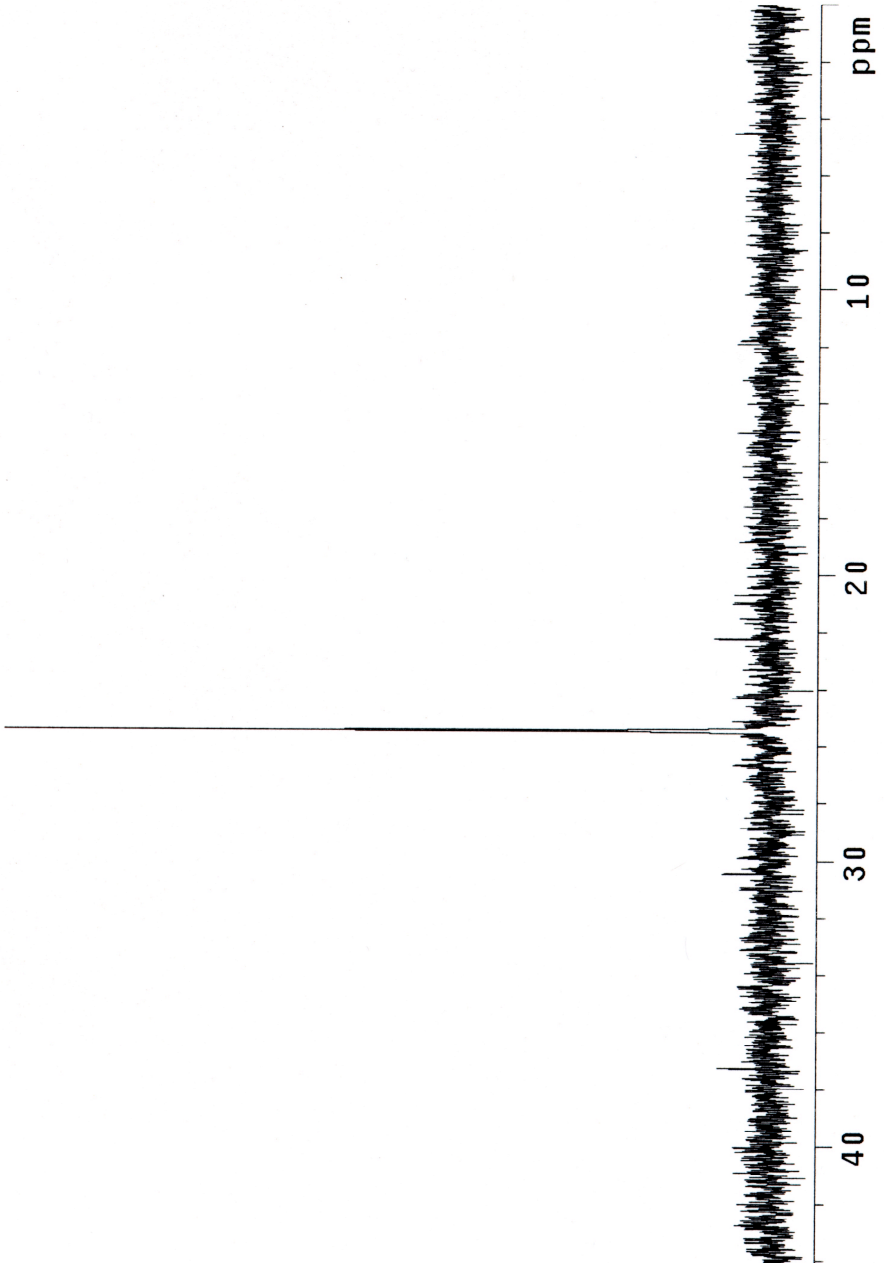
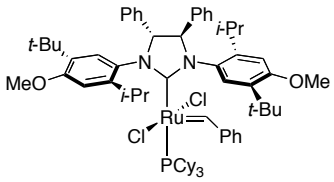
1.27
1.13
1.02
1.32
1.27
1.68
1.54
3.92
73.80



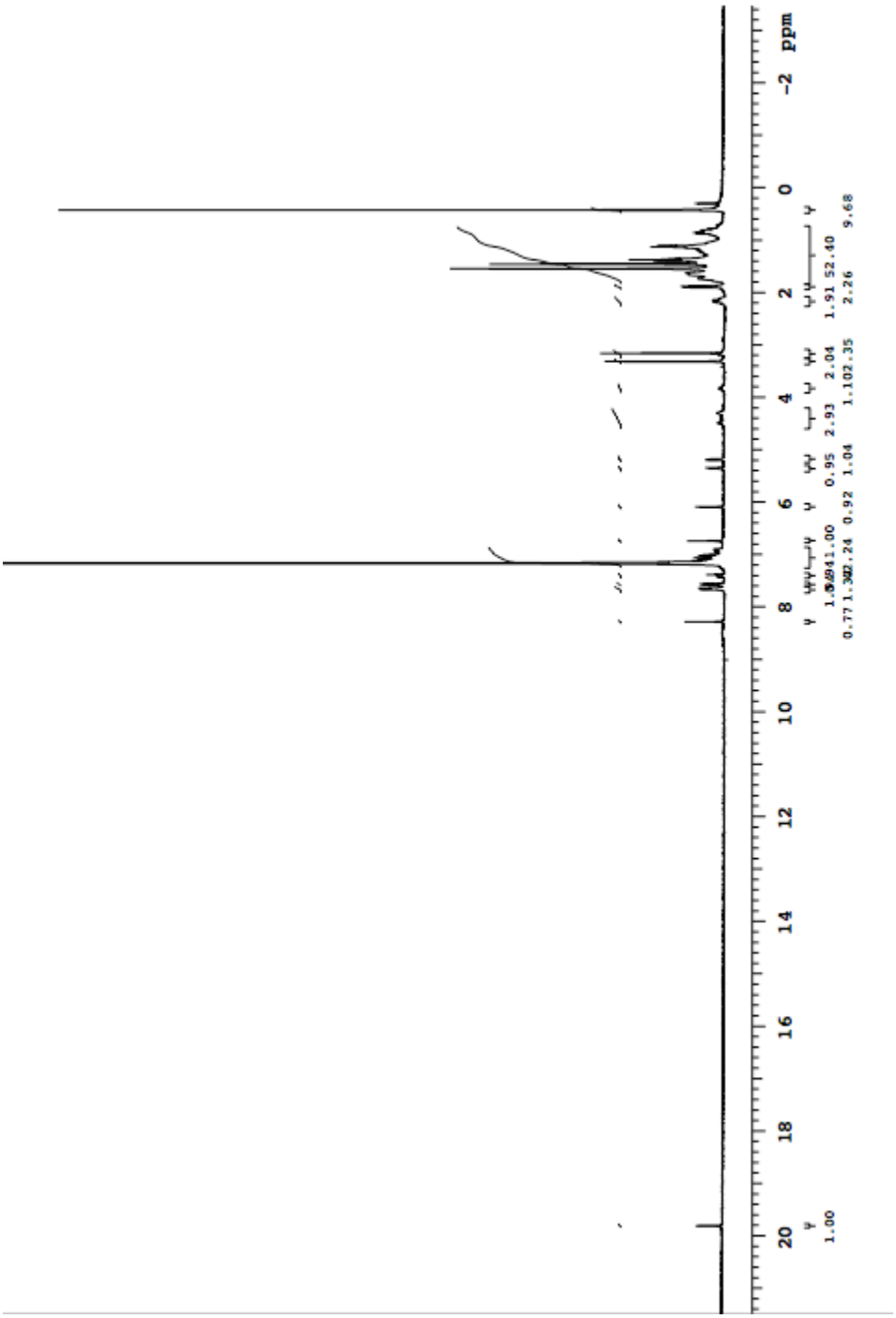
3a

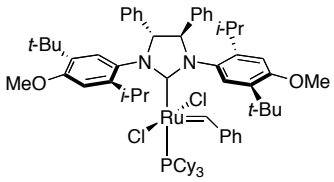
^{31}P NMR




Ph
Ph
i-Pr
t-Bu
MeO
N
N
OMe
i-Pr
Cl
t-Bu
Ru
Cl
Ph
PCy3

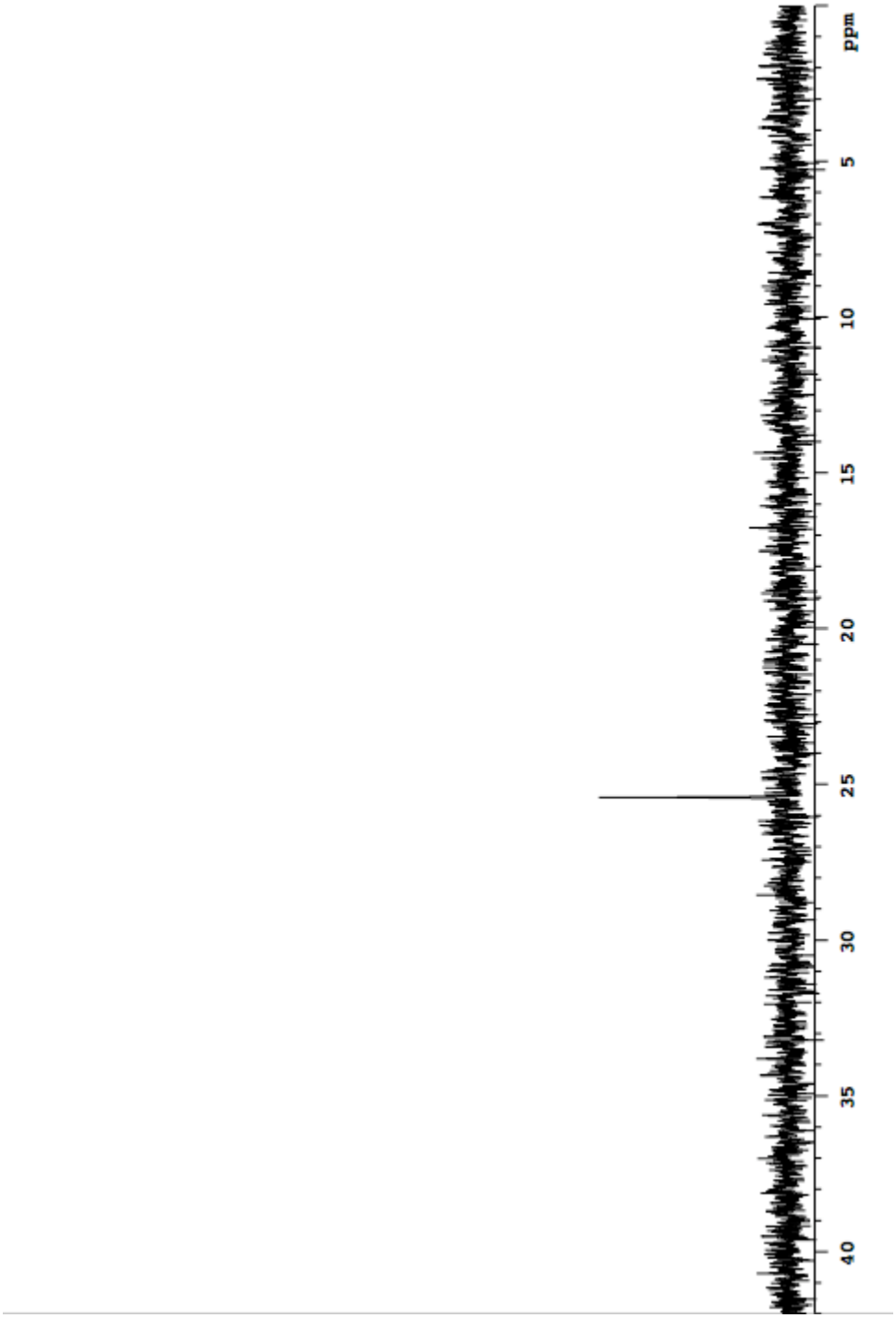
4a

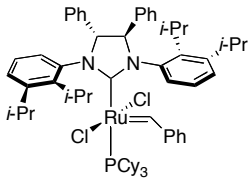

ppm
20
18
16
14
12
10
8
6
4
2
0
-2
1.00
0.77 1.92 0.92 1.04 2.93 2.04 1.91 52.40
1.00 2.24 0.95 1.02.35 2.26
9.68


Ph
Ph
i-Pr
t-Bu
N
N
MeO
OMe
i-Pr
t-Bu
Cl
Ru
Cl
Ph
PCy3

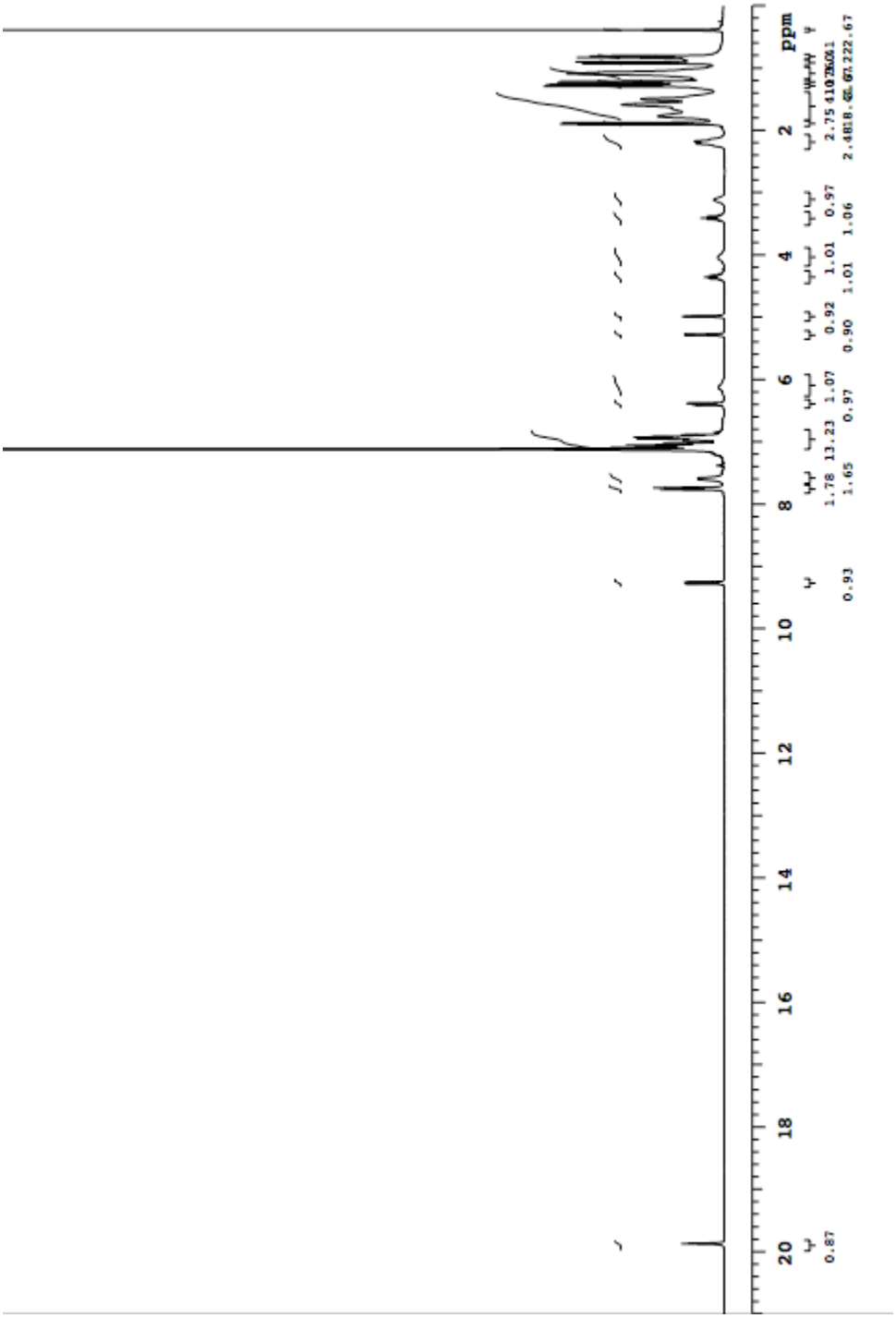
4a

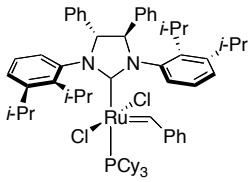
^{31}P NMR


ppm
5
10
15
20
25
30
35
40



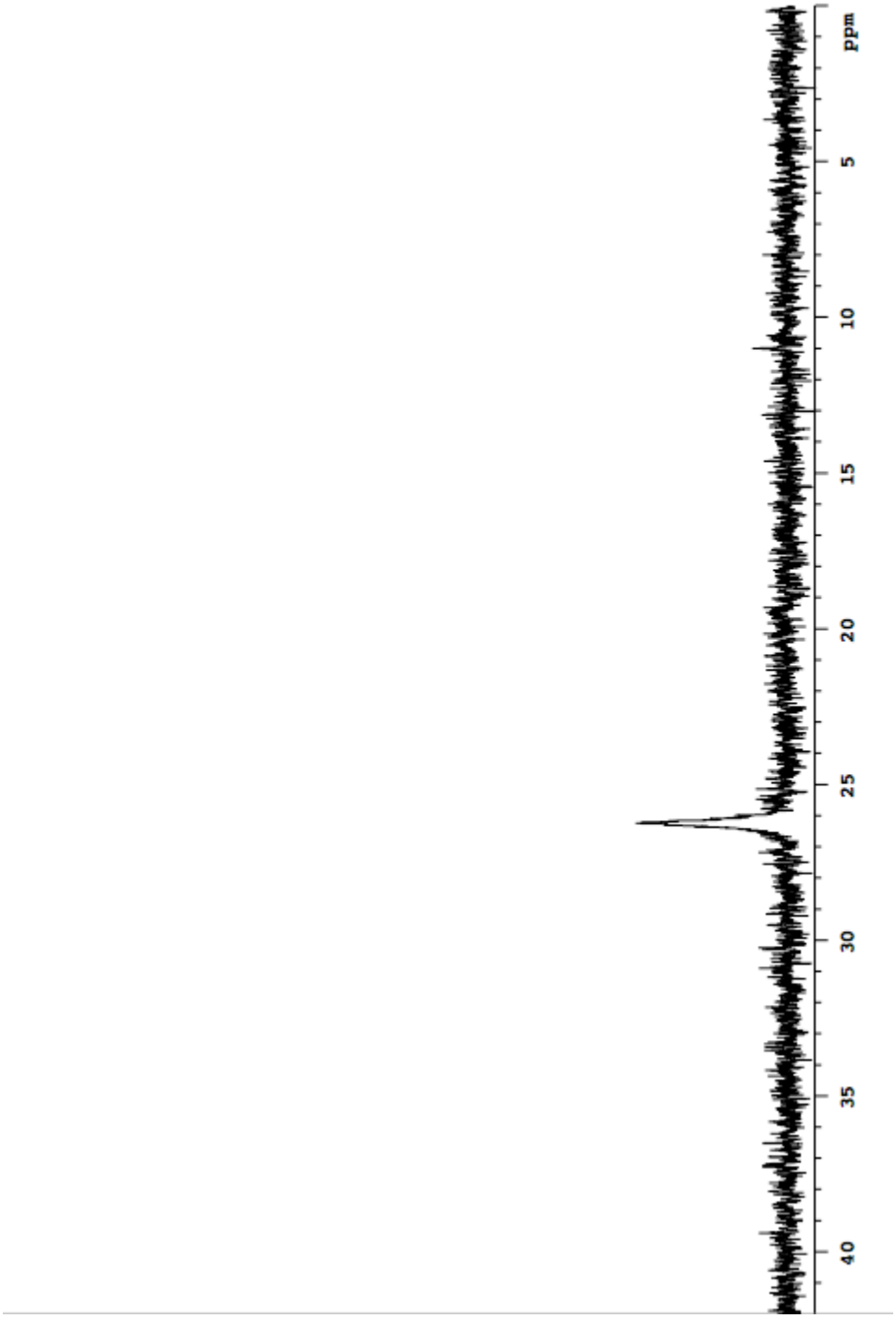
5a

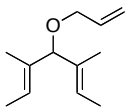




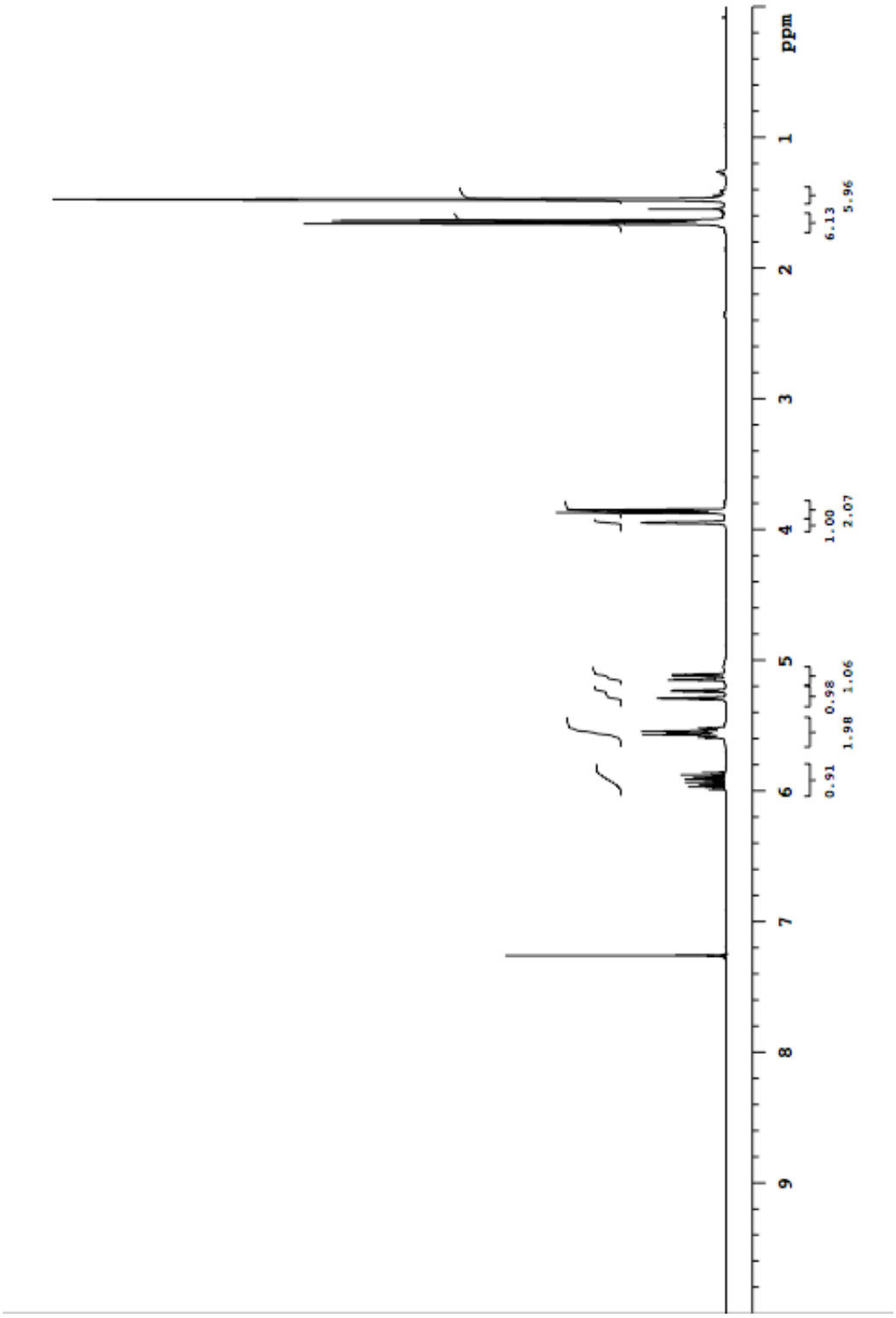
5a

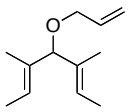
^{31}P NMR



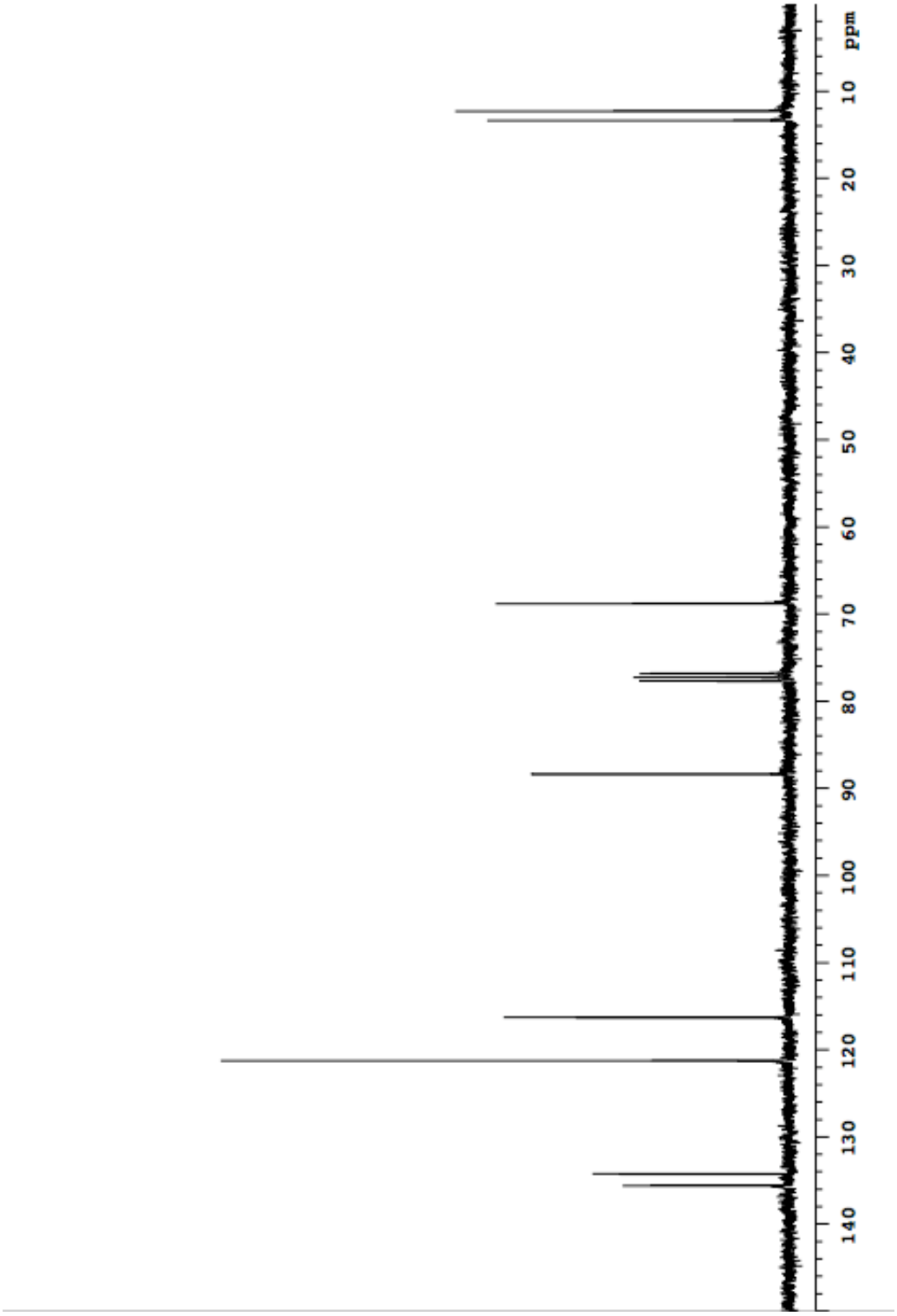


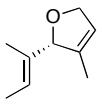
11



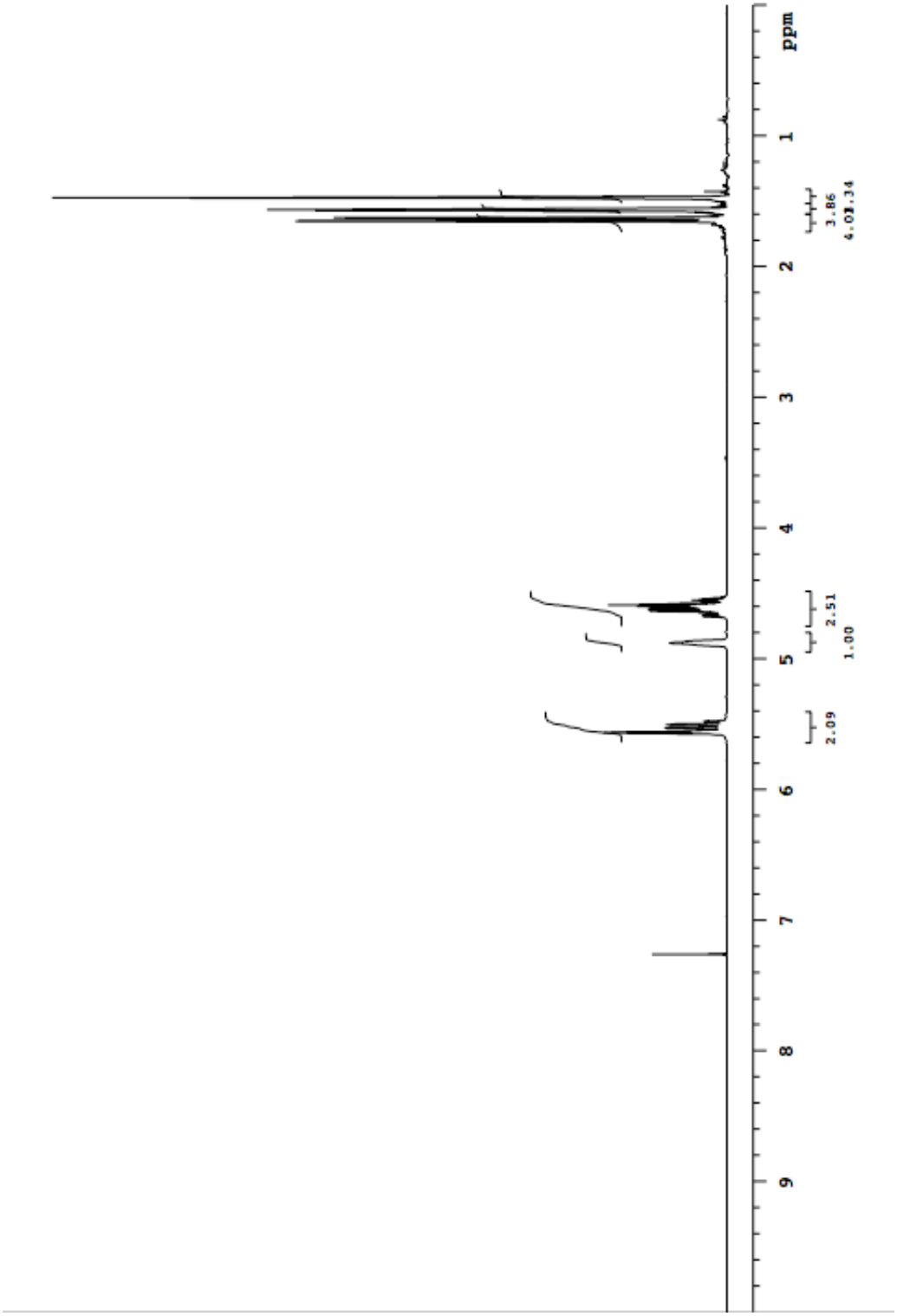


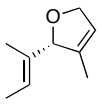
11



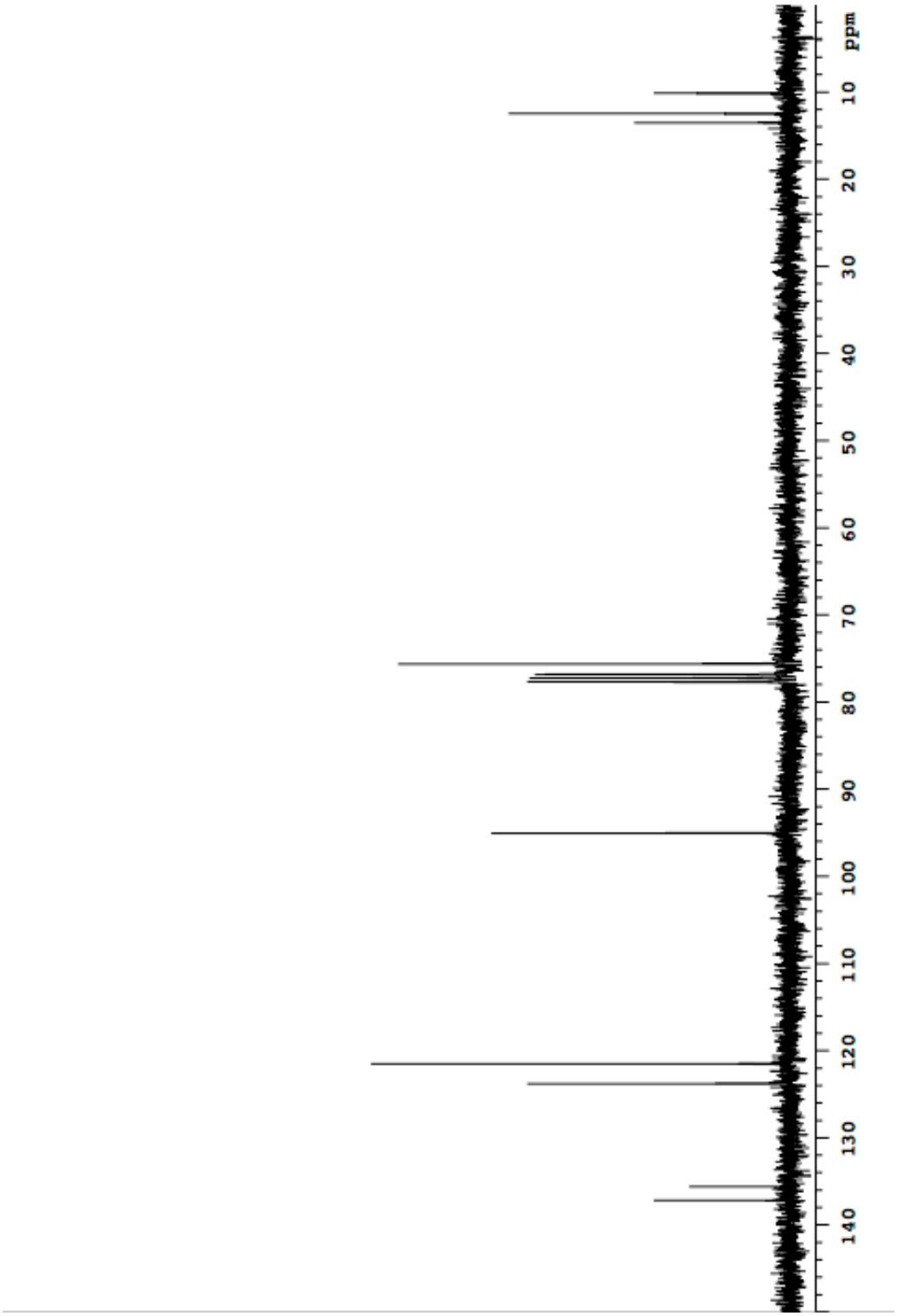


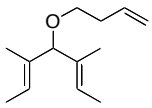
12





12





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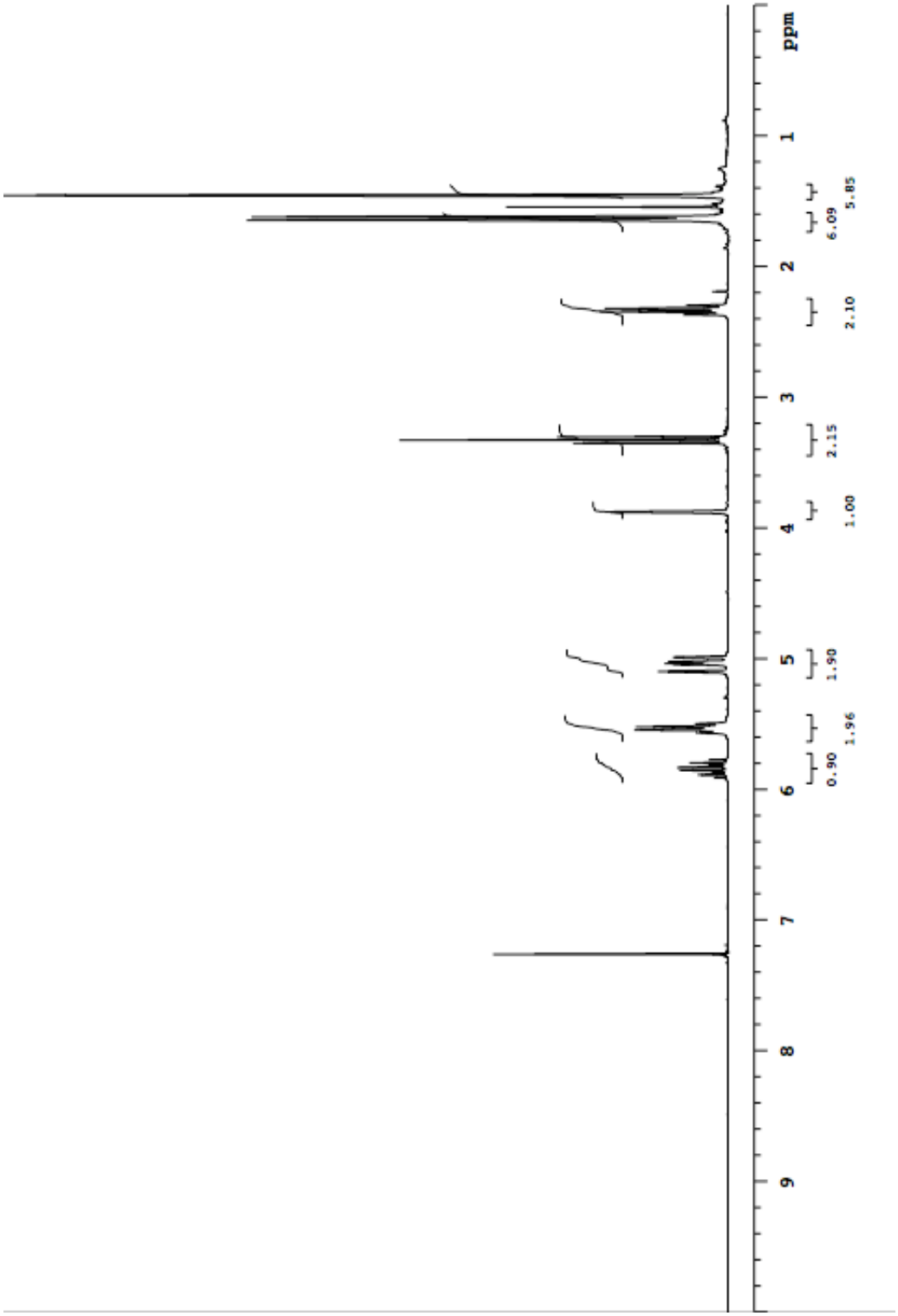

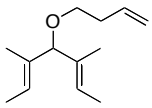

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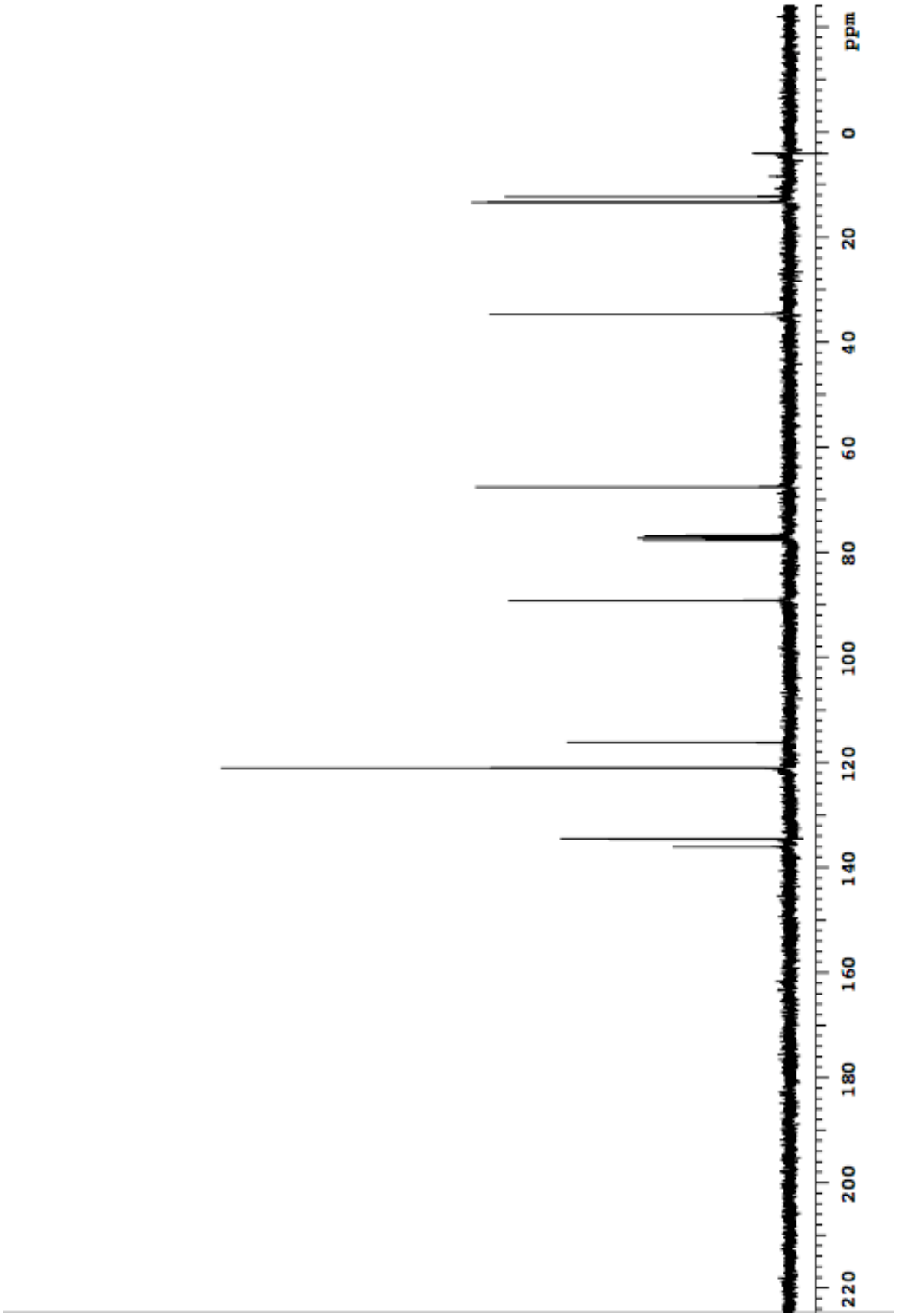
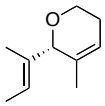
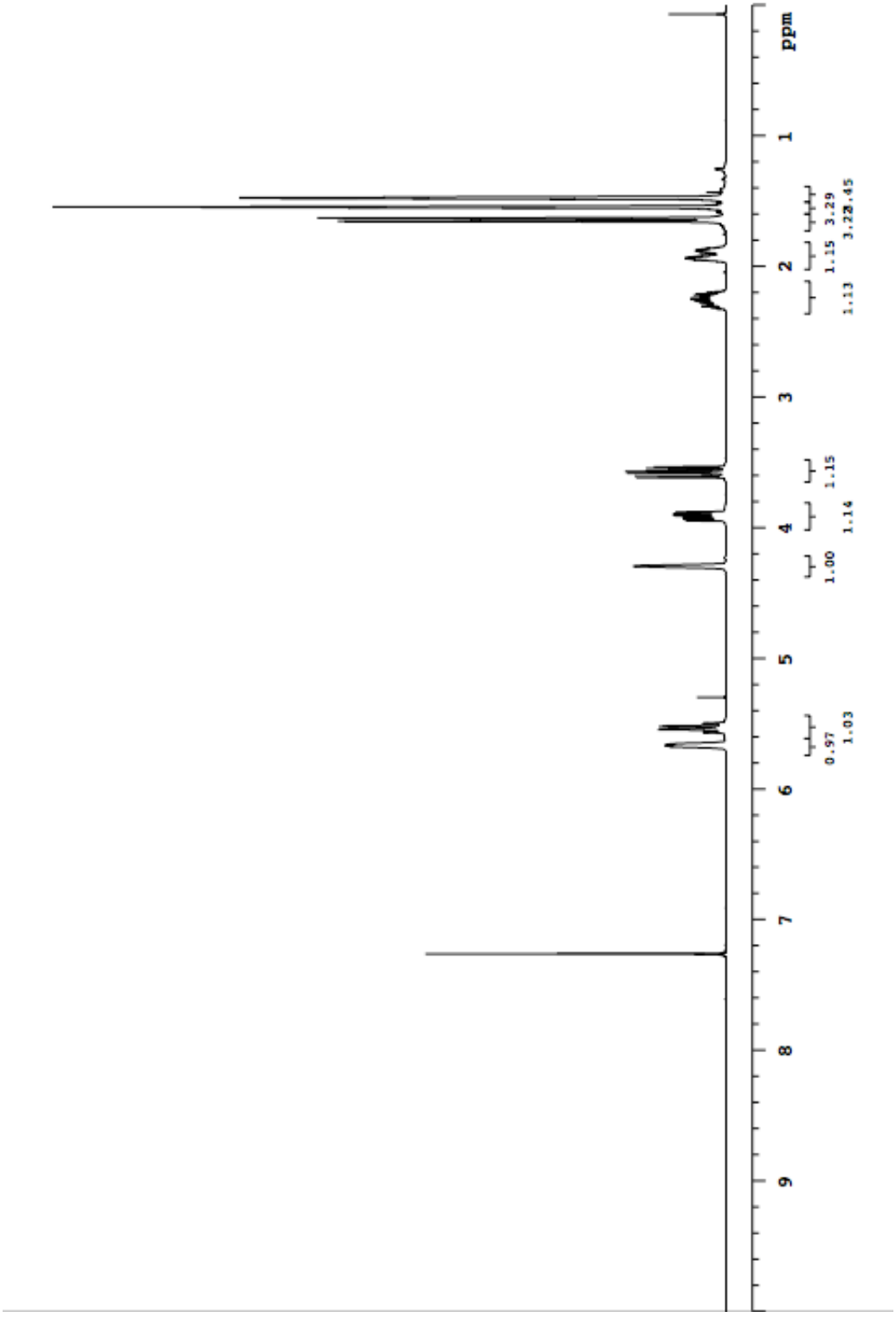
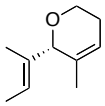


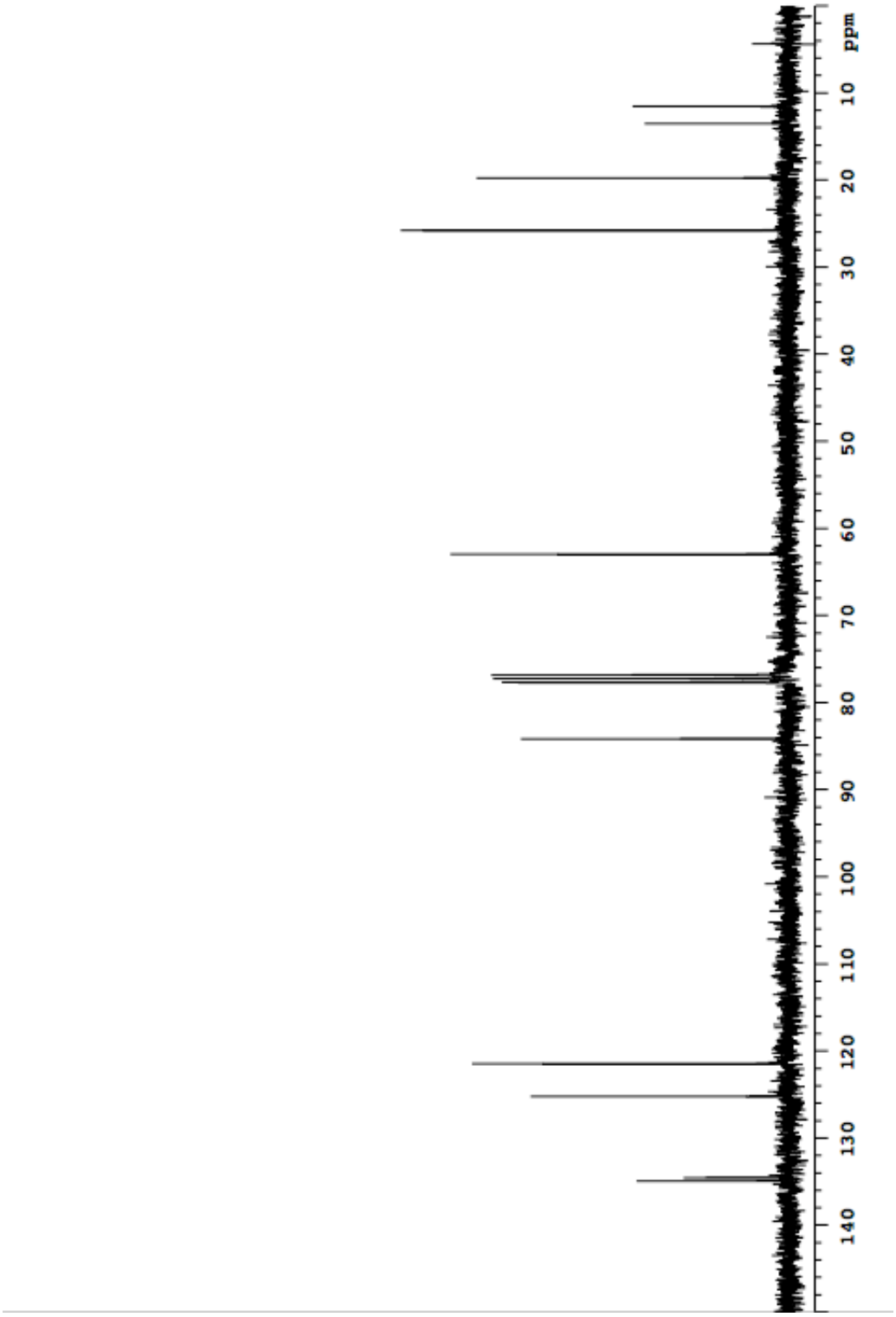


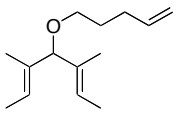
16





16





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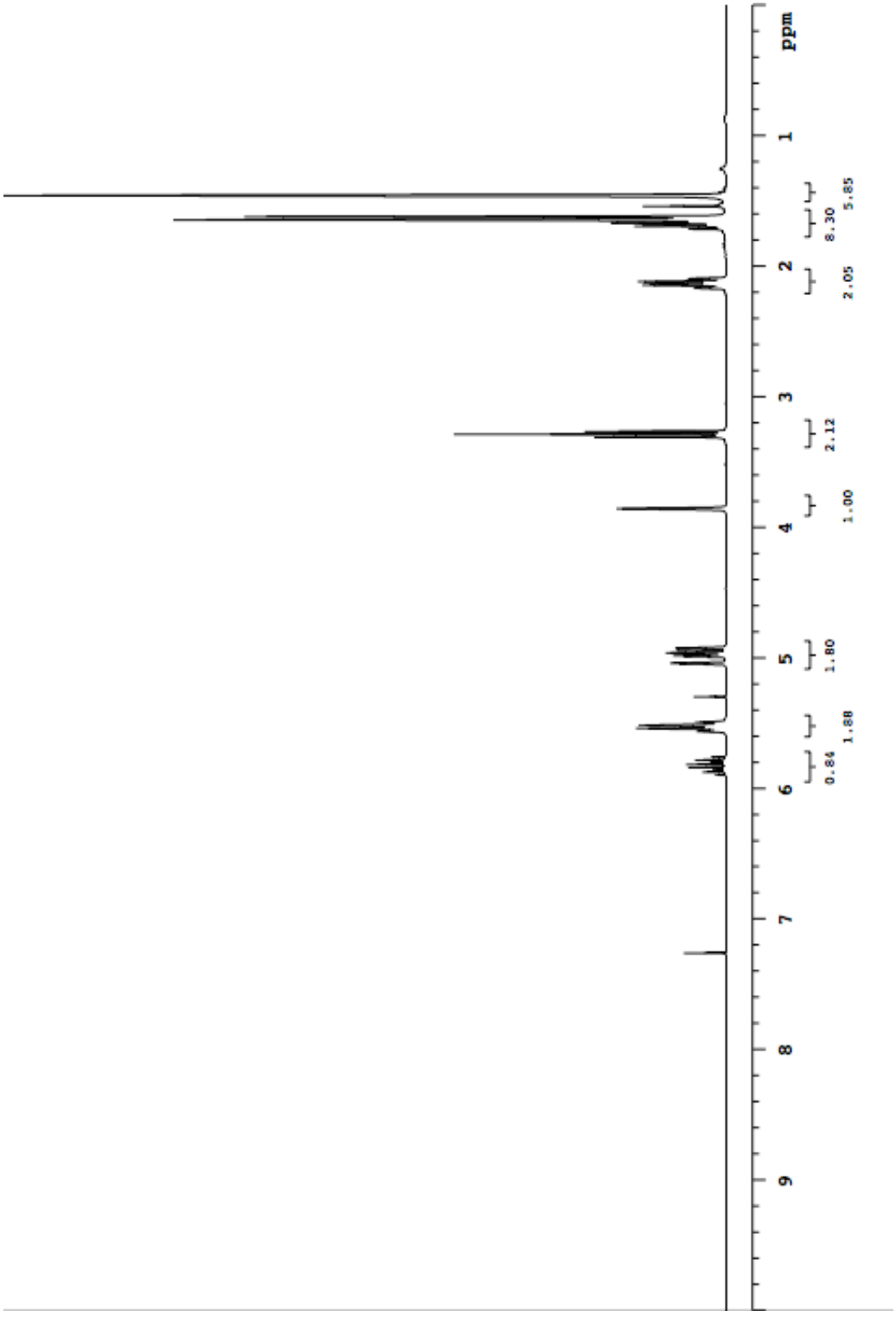

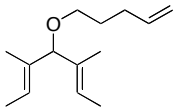

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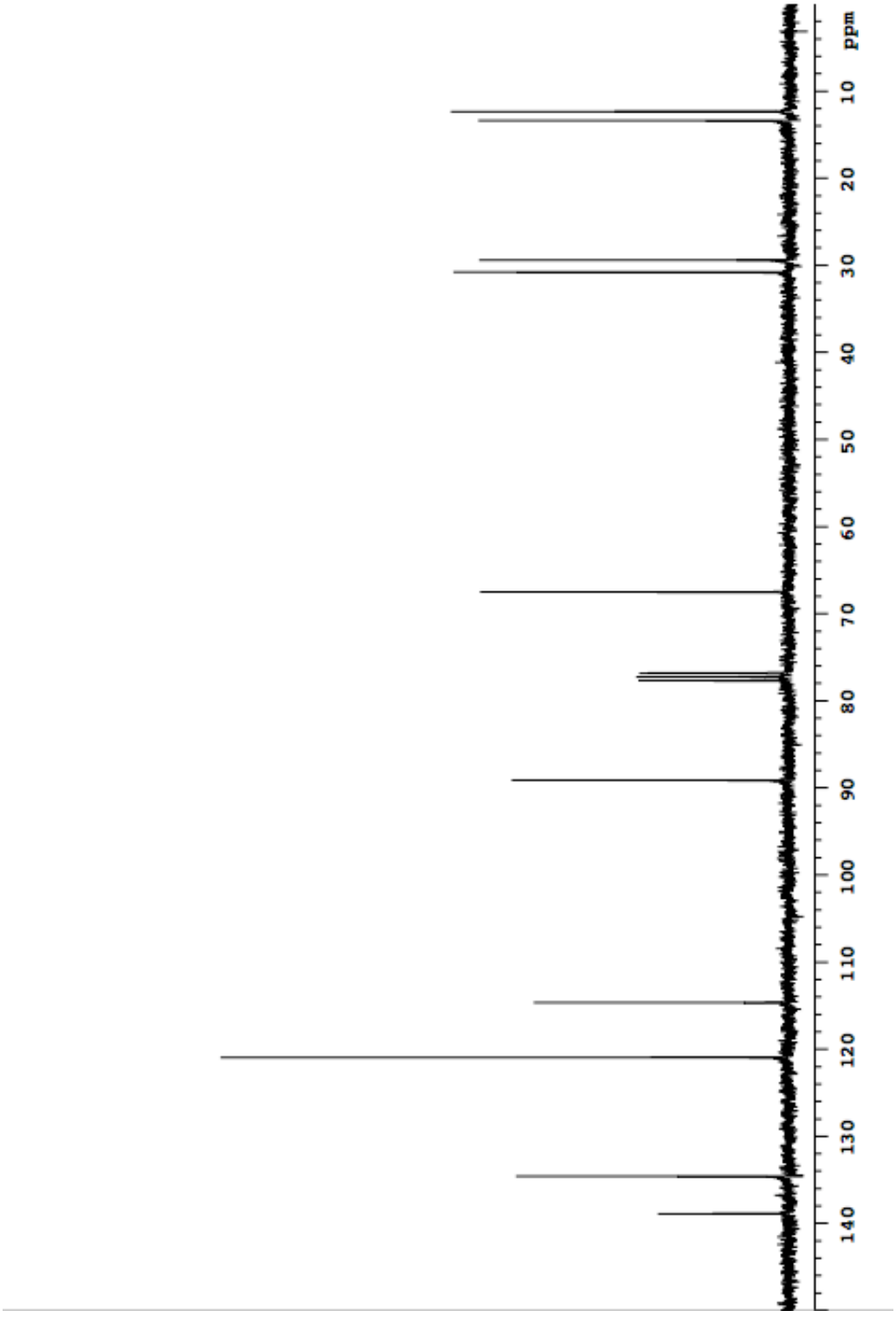

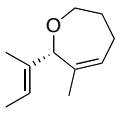

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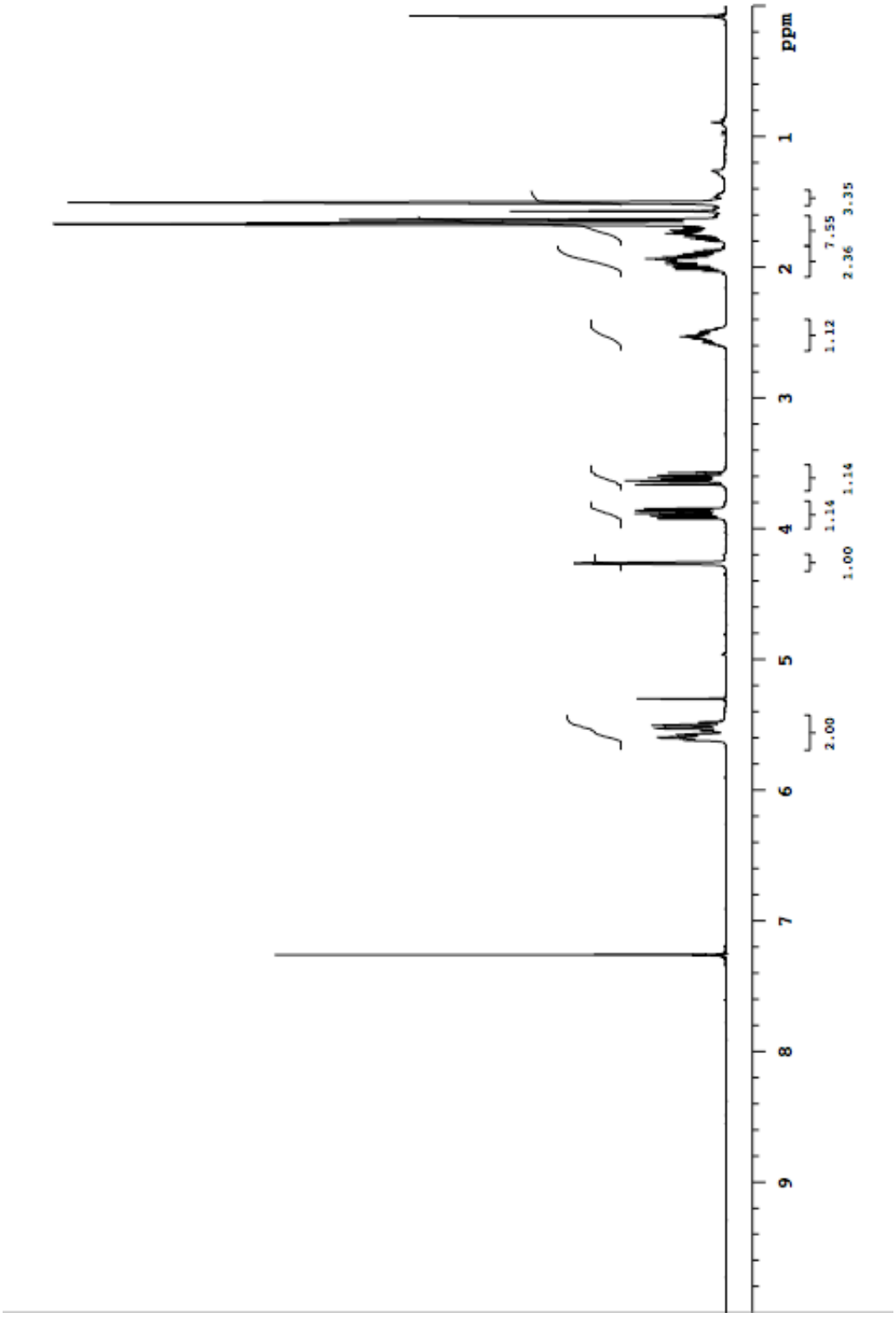

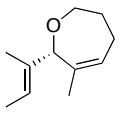

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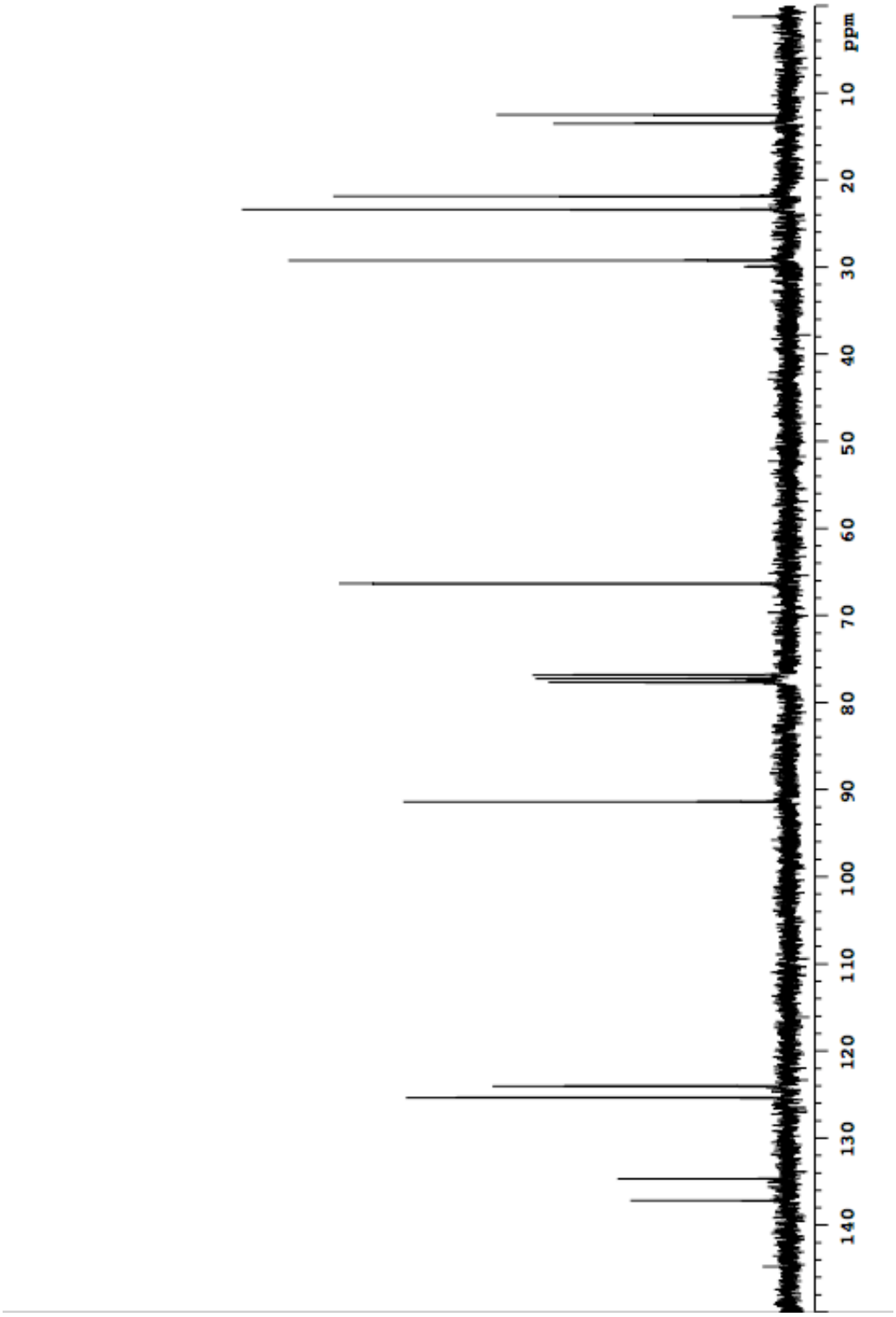

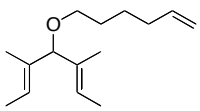

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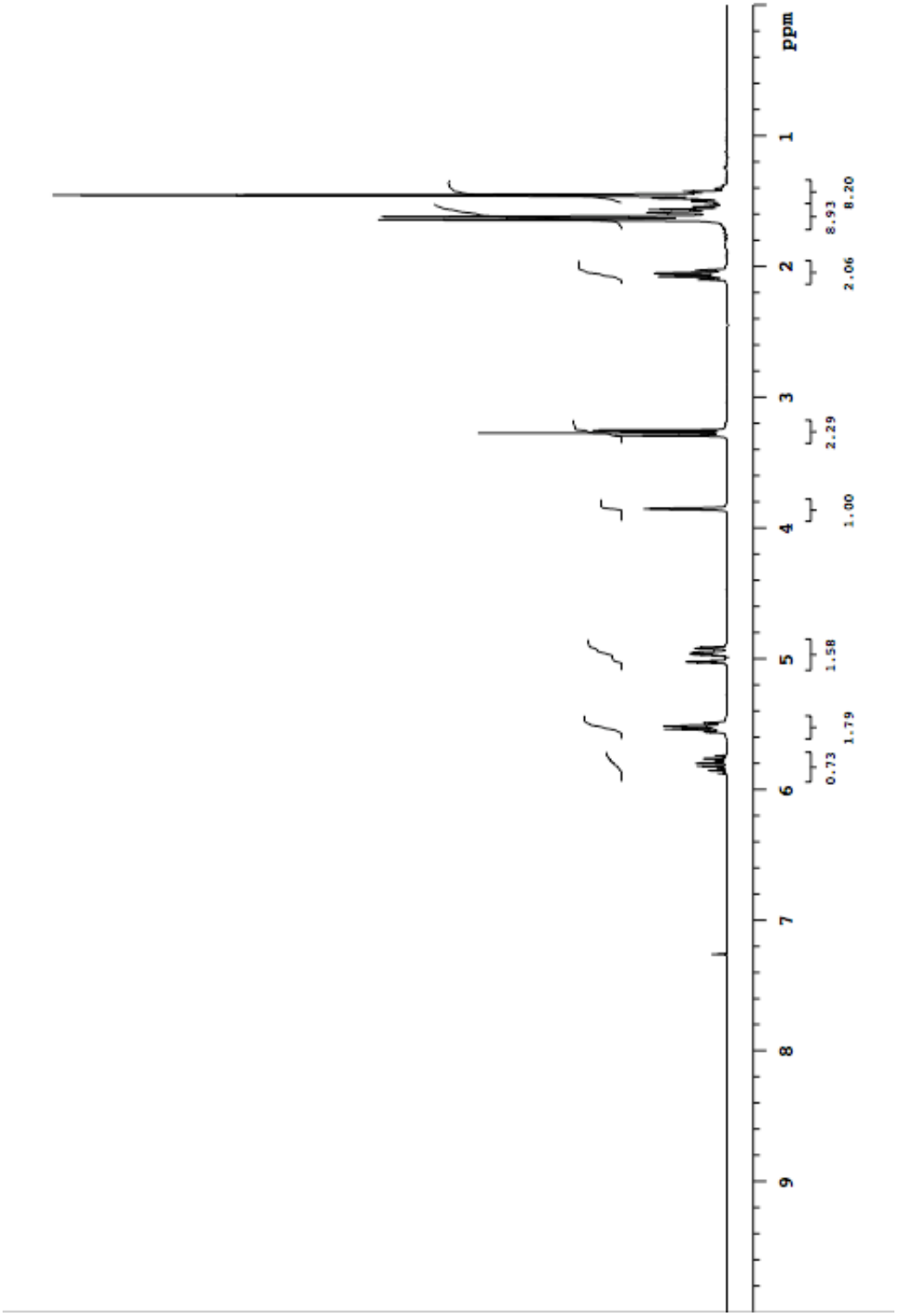

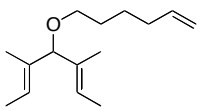

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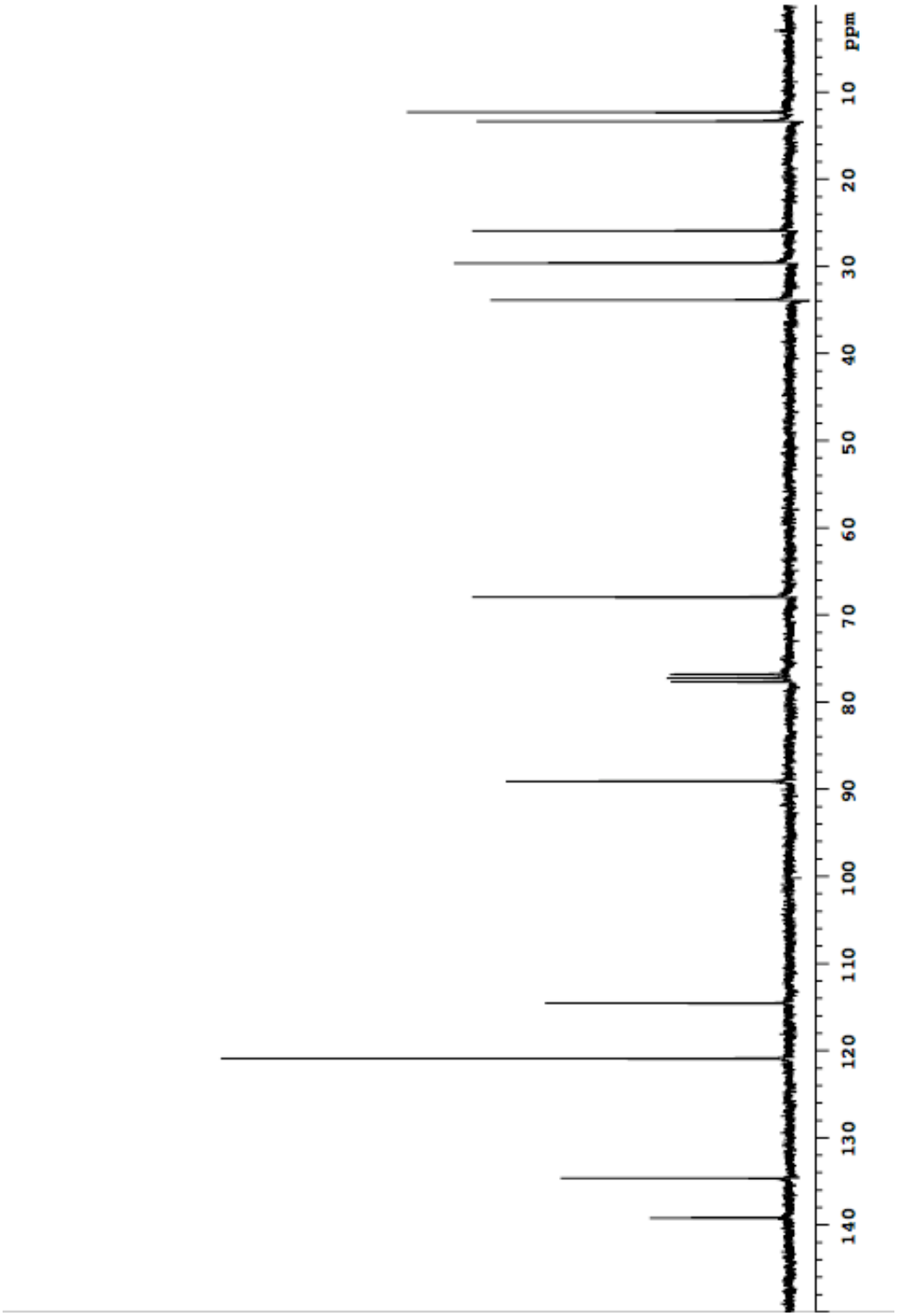

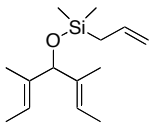

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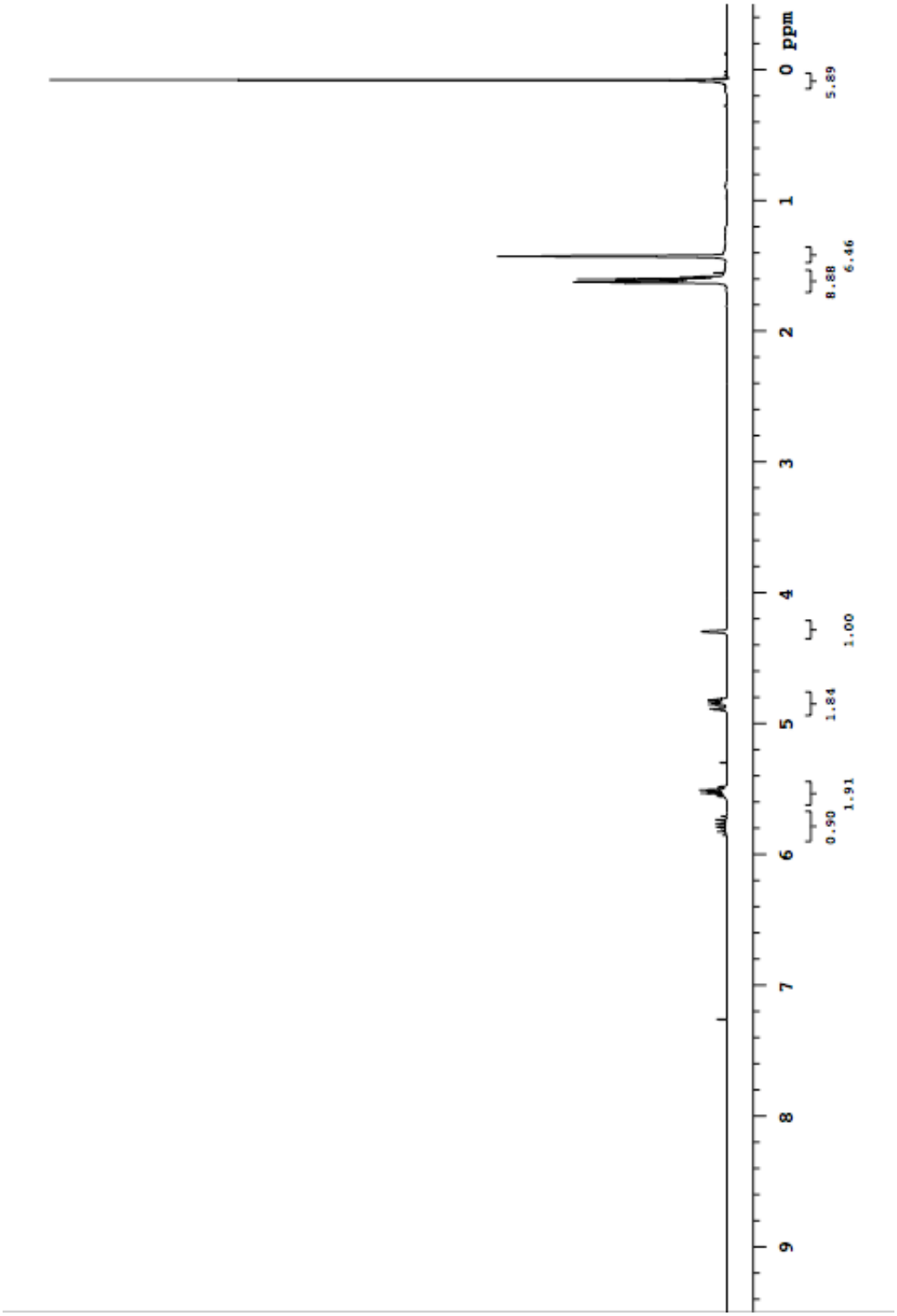

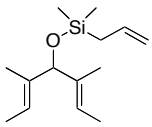

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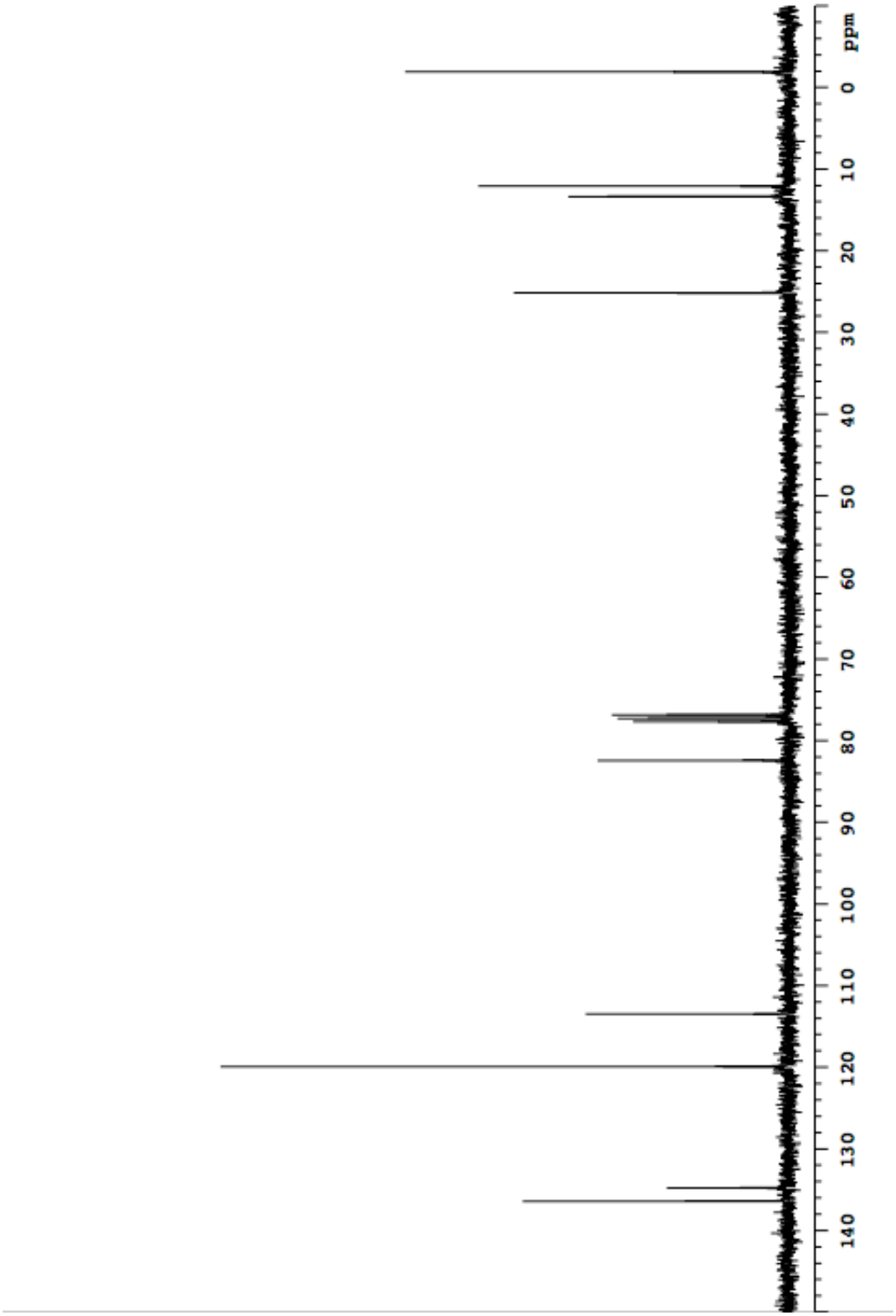

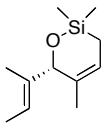

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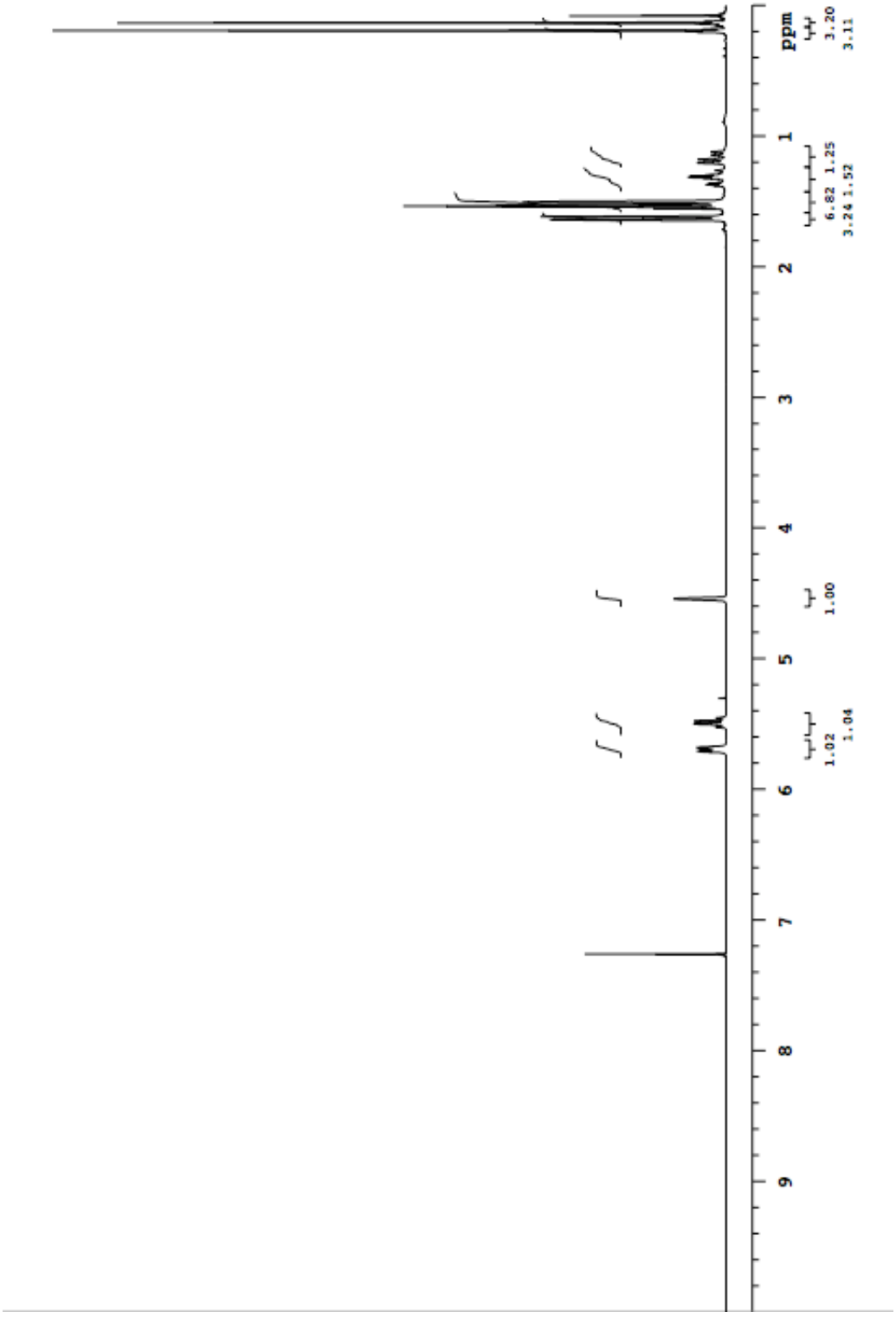

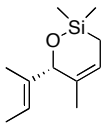

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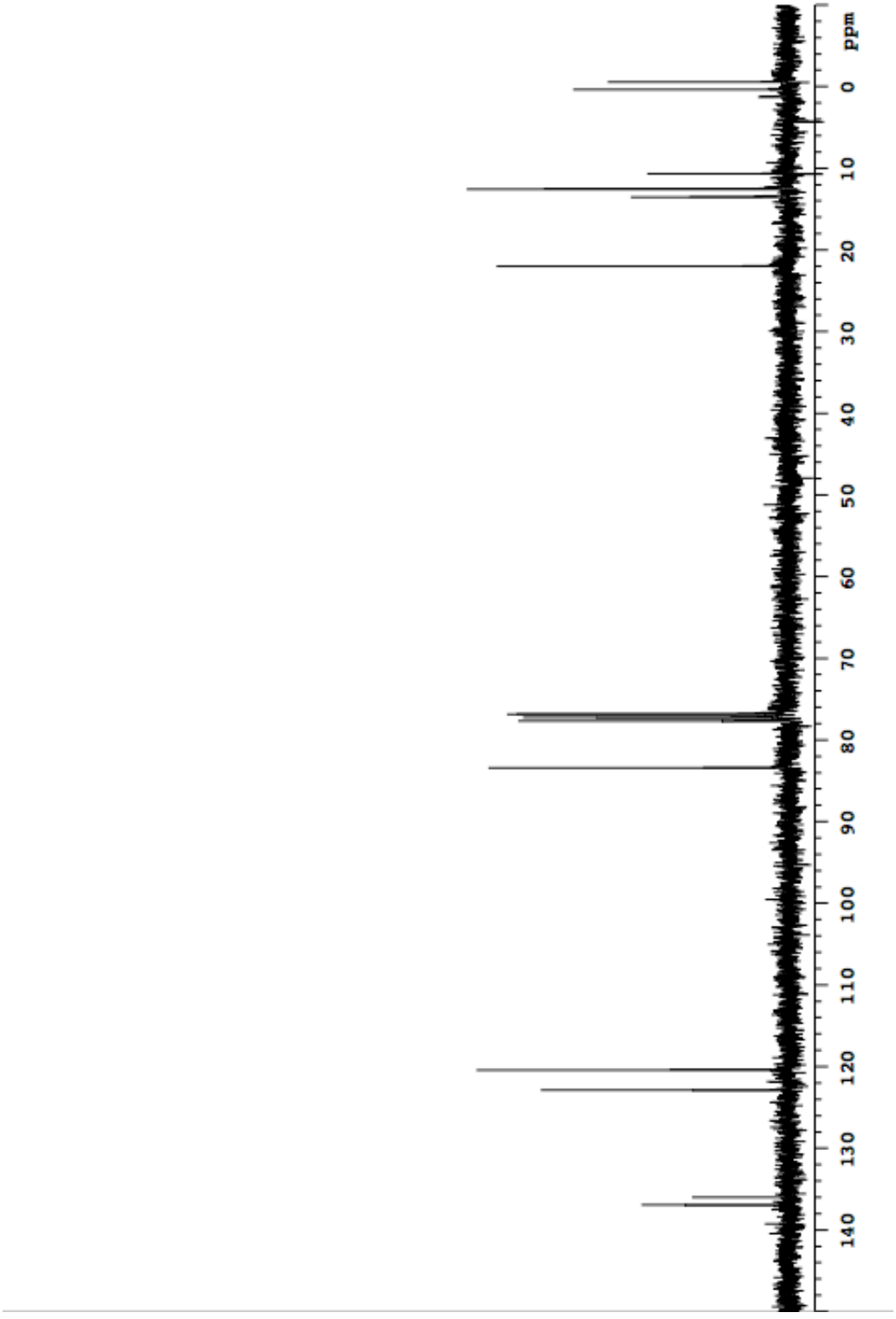

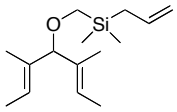

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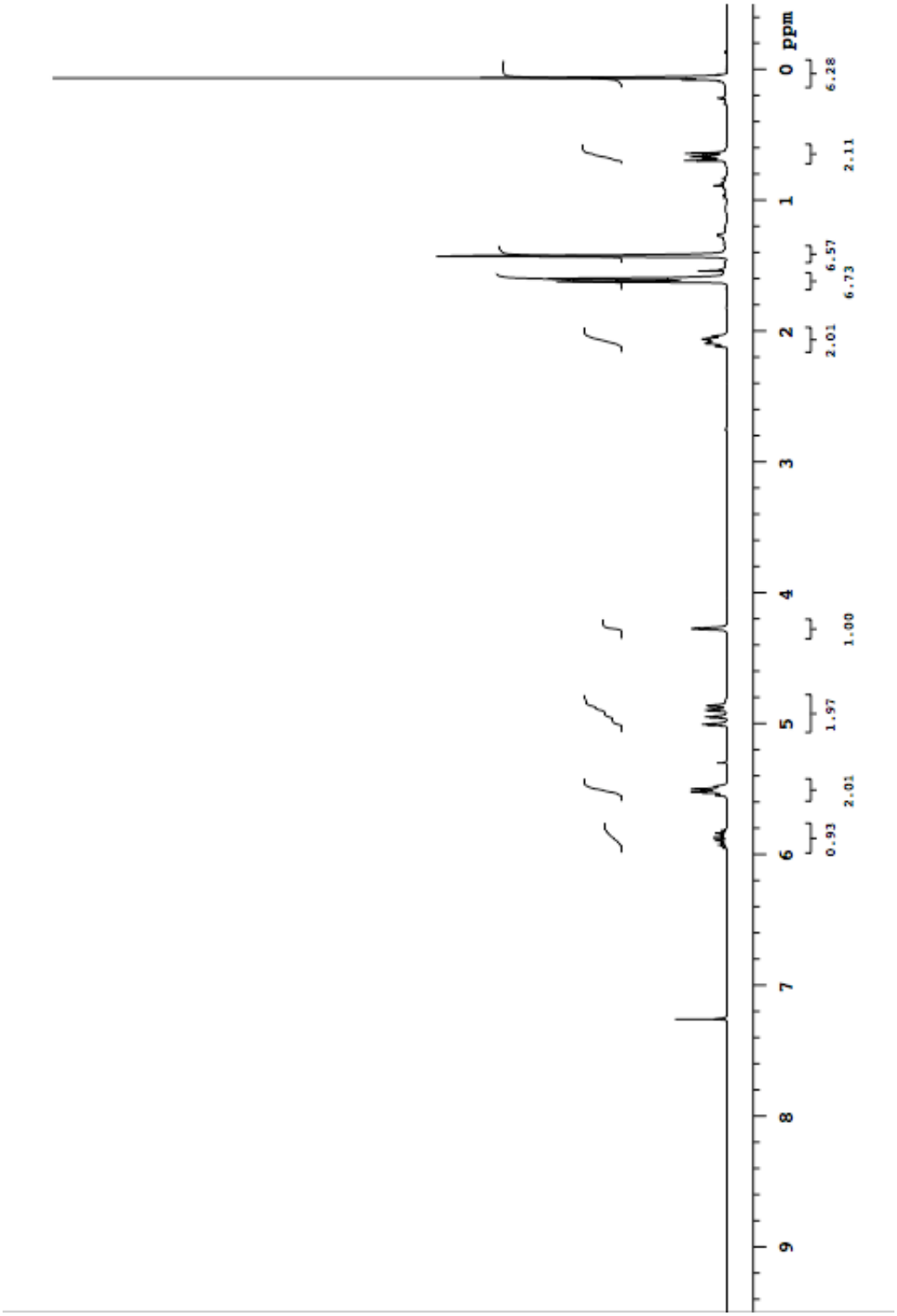

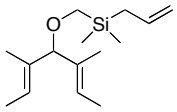

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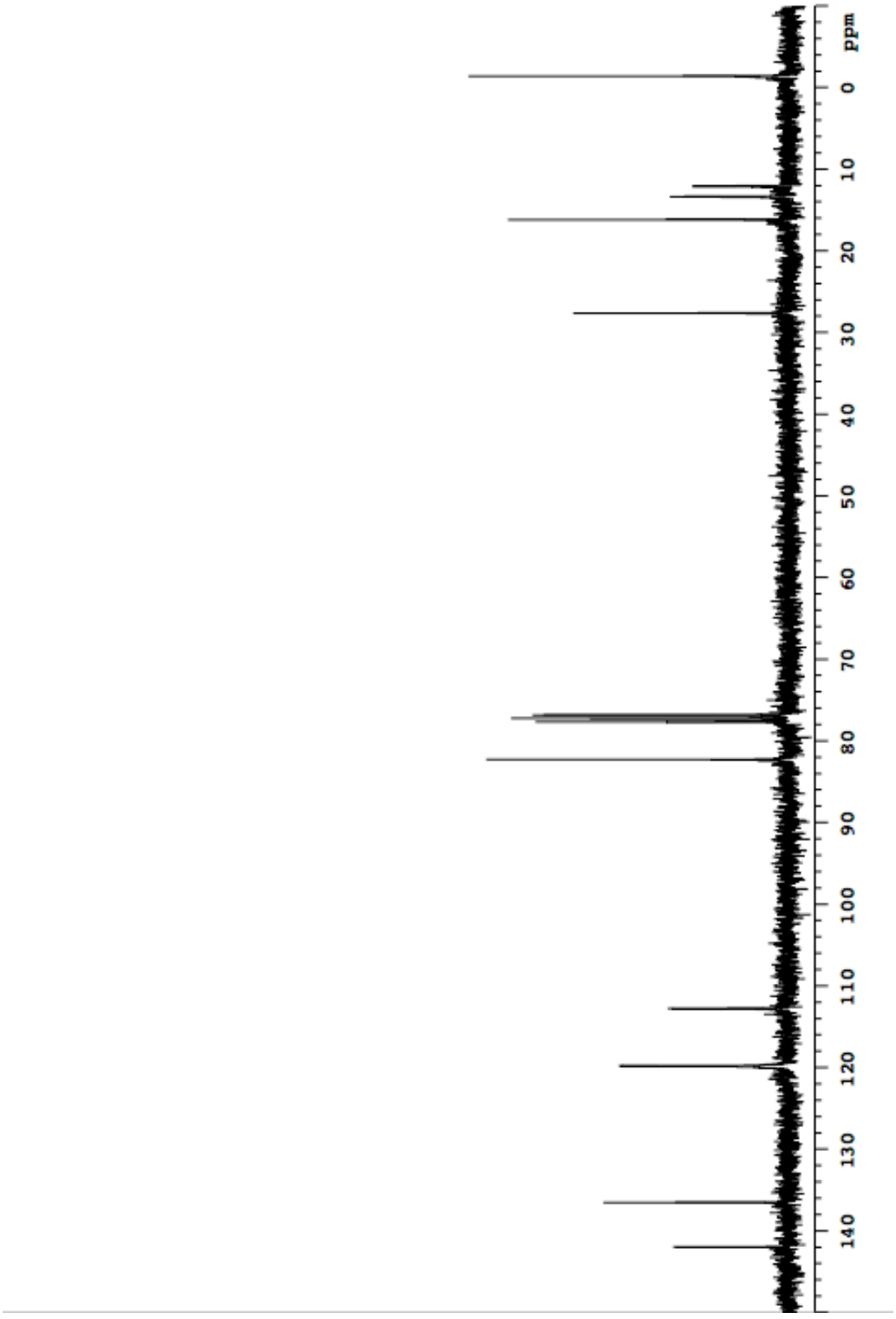

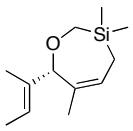

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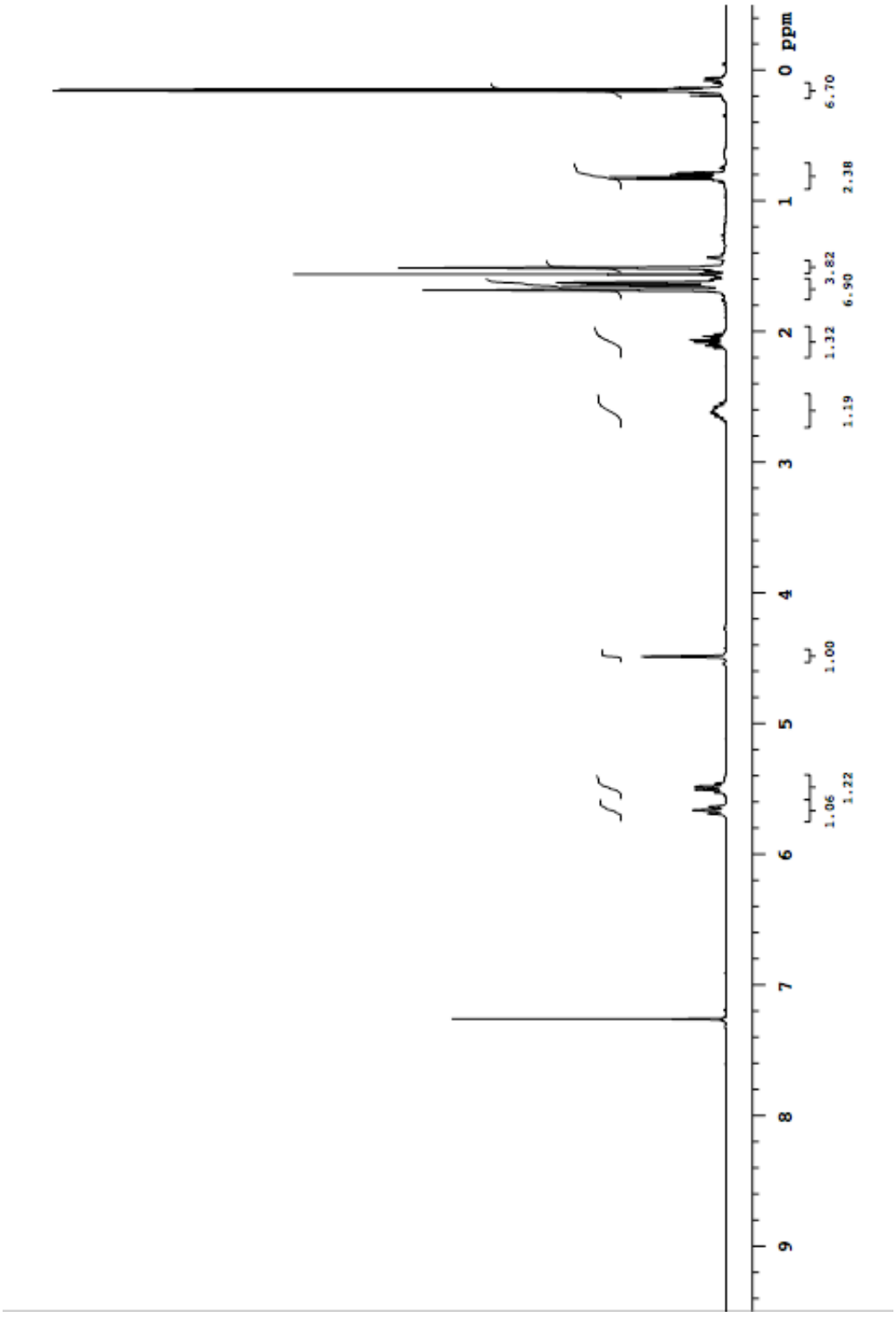

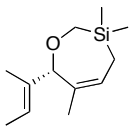

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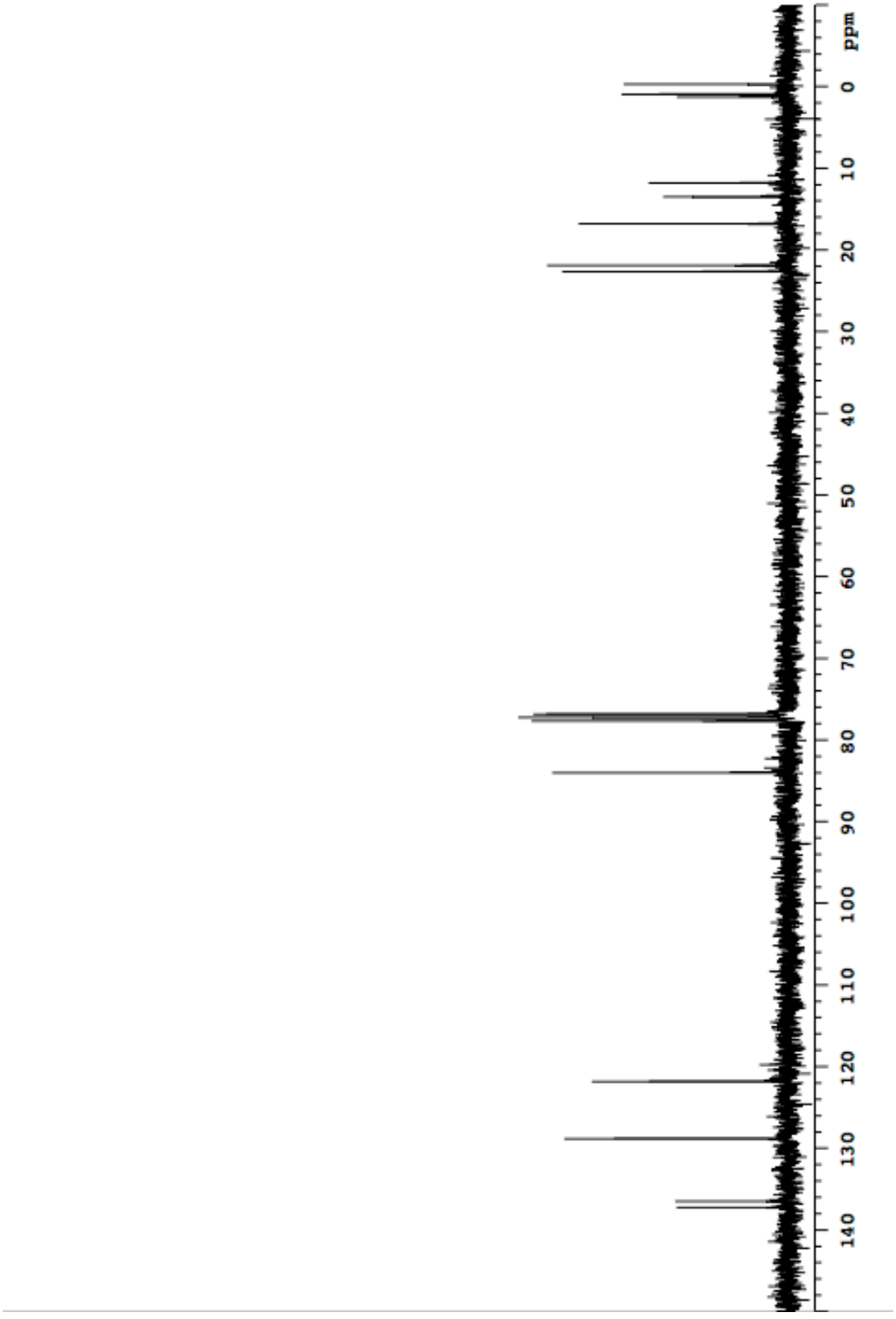

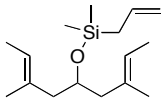

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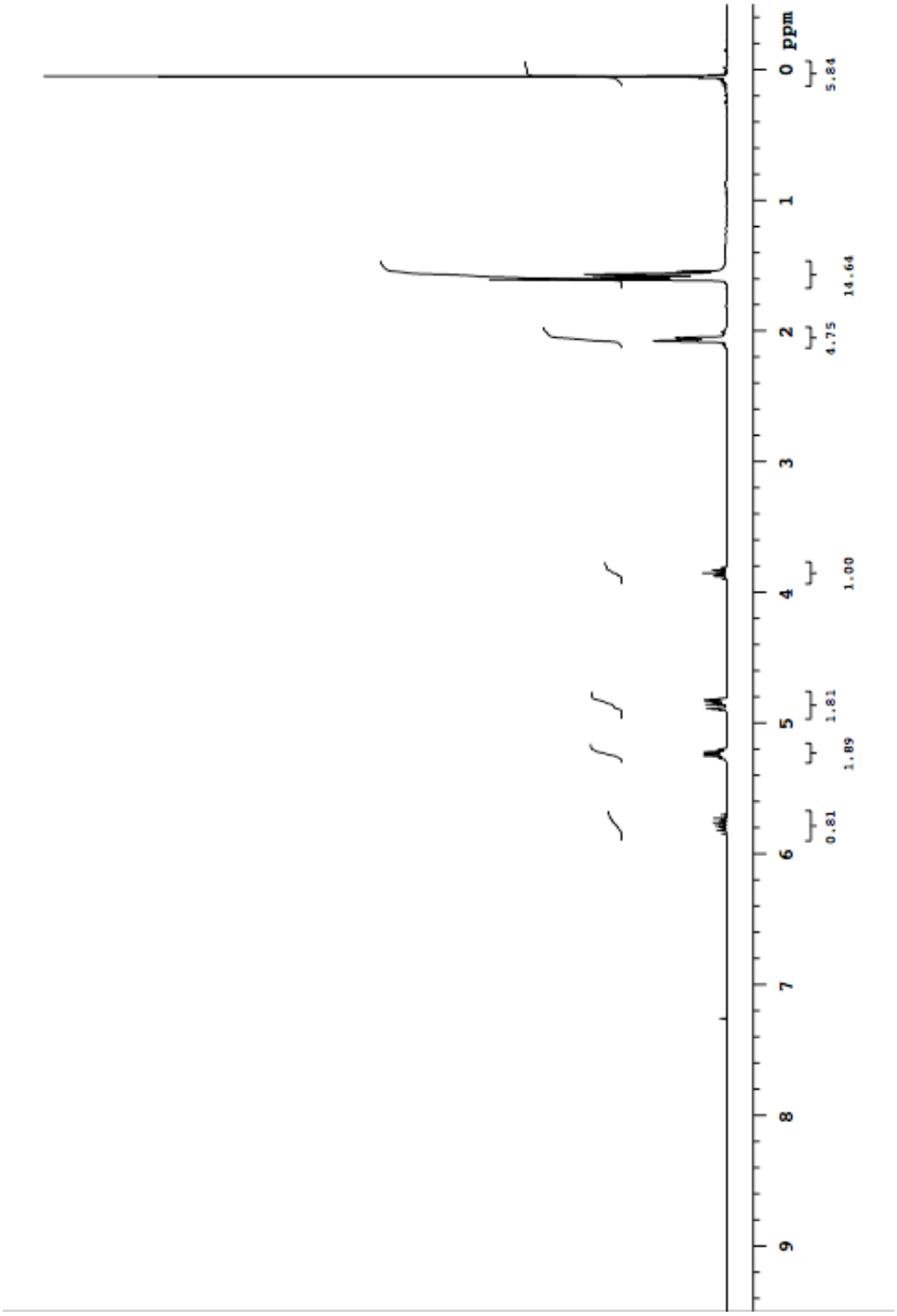

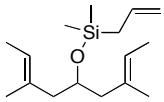

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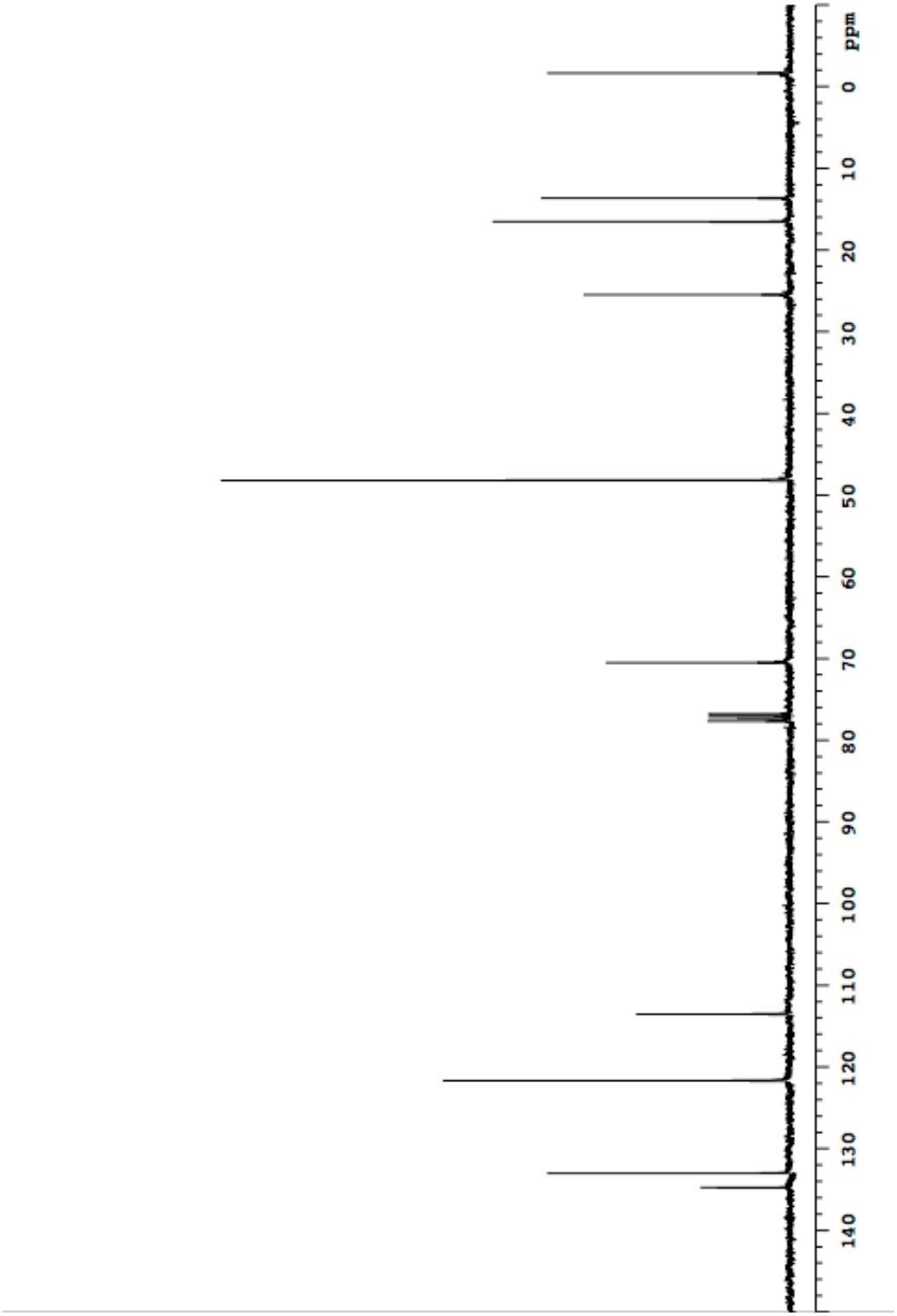

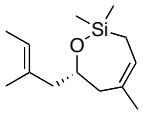

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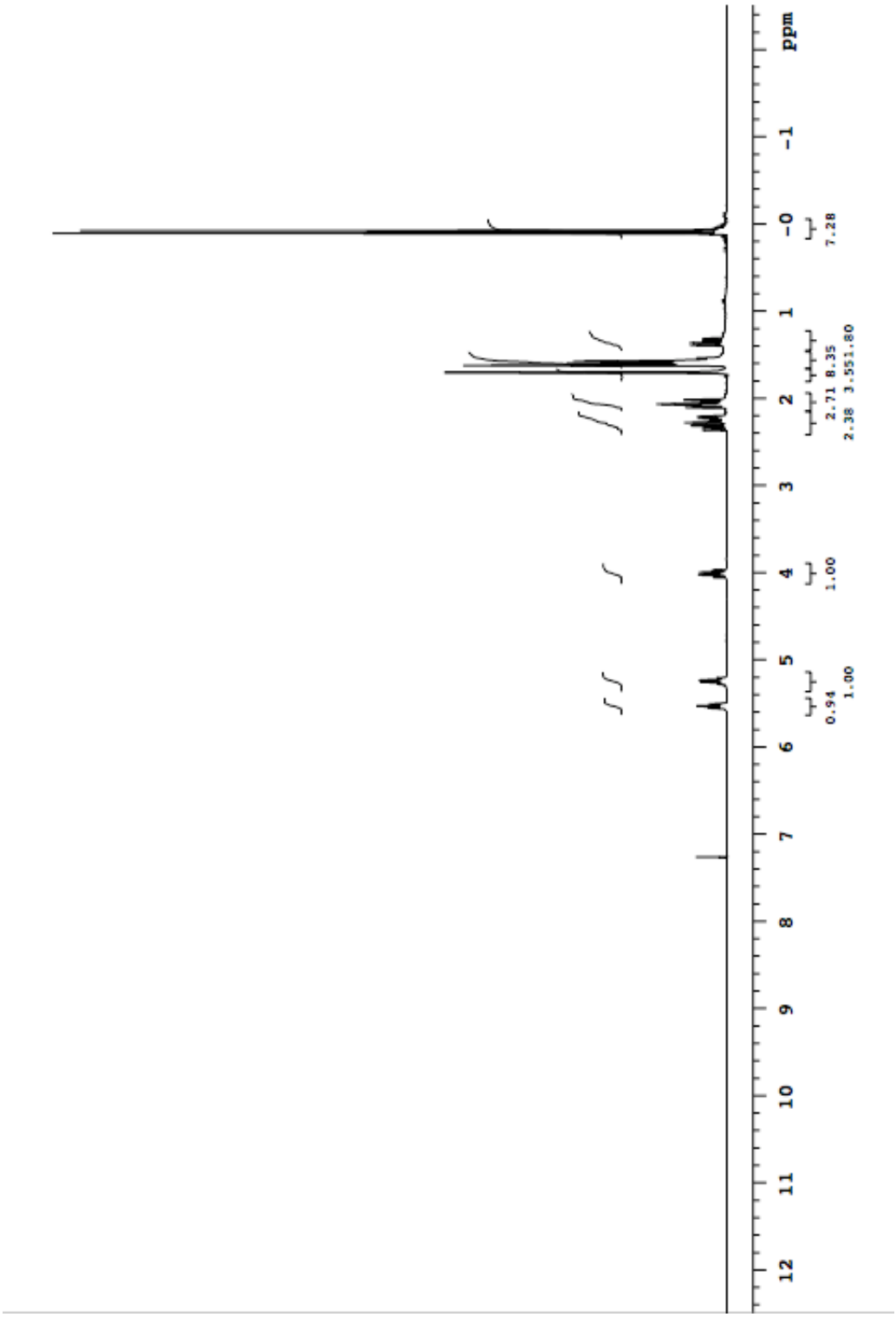

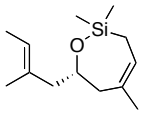

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