PQS: A New Platform for Micellar Catalysis. RCM Reactions in Water, with Catalyst Recycling

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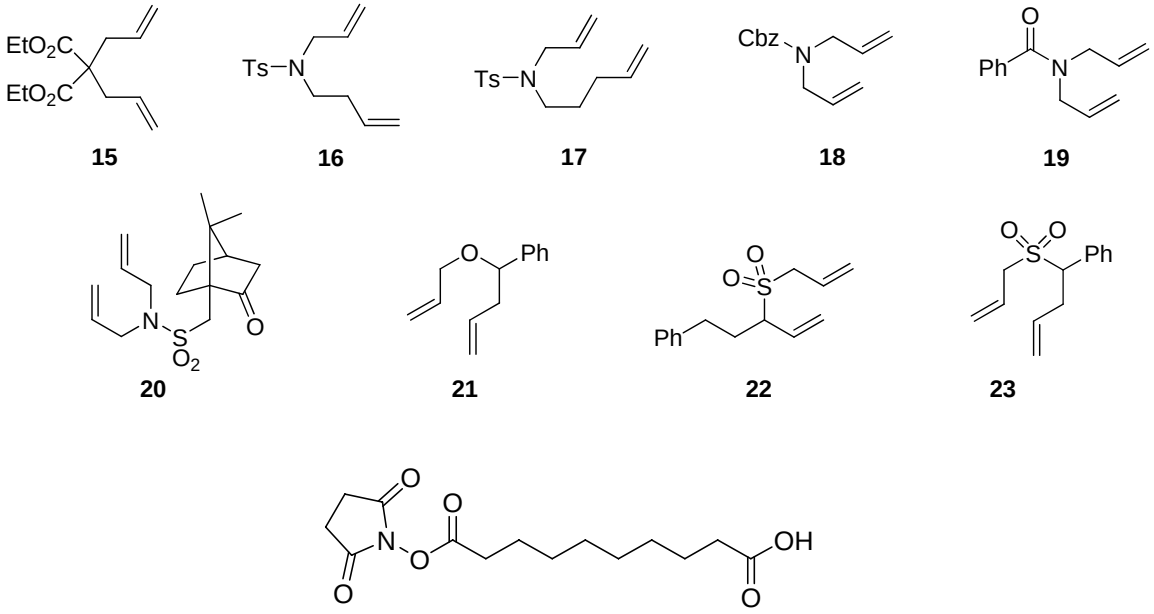
Supporting Information

General Considerations: All reactions were preformed in Biotage 2-5 mL microwave reactor vials containing a Teflon-coated stir bar. Column chromatography was preformed using Silicycle Silia-P 60 Å flash silica gel. Thin-Layer-Chromatography analysis was conducted using commercially available EMD silica gel 60 F_{254} plates. Nuclear Magnetic Resonance spectra were obtained on a Varian Inova system, in $CDCl_3$, with proton and carbon resonances at 400 and 100 MHz, respectively, and are referenced to the residual solvent signal at δ 7.27 ppm for ^1H and δ 77.23 ppm for ^{13}C. Data for ^1H are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, sep = septet), coupling constant and integration. Data for ^{13}C NMR are reported in terms of chemical shift. Infrared spectra were obtained either, neat or by thin-flim, on NaCl plates using a JASCO FT/IR-430 series spectrometer and are reported as cm^{-1}. Mass spectral data were acquired on either a VF Autospec or an analytical VG-70-250 HF spectrometer. Solvents and reagents were all obtained from commercial vendors and used with no further purification. Compounds **7**[1], **12**[2], **15**[3], **16**[2], **17**[4], **18**[5], **19**[2], **20**[6], **21**[7], **22**[8] and **23**[8] were all synthesized and characterized according to known procedures and data.

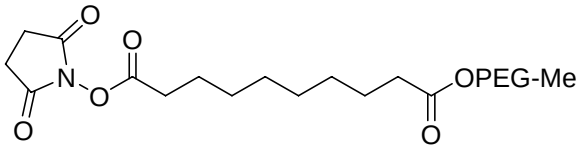


15 **16** **17** **18** **19**

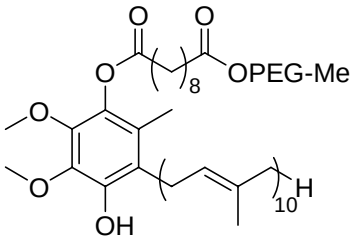
20 **21** **22** **23**

10-(2,5-dioxopyrrolidin-1-yloxy)-10-oxodecanoic acid (4): Trimethylacetyl chloride (5.48 mL, 44.50 mmol) was added to a stirred solution of sebacic acid (36.00 g, 178.00 mmol) in CH_2Cl_2 (180 mL) at 0 °C. Then Et_3N (6.52 mL, 46.78 mmol) was added, and the solution was stirred at 0 °C for 2.5 h. A suspended solution of *N*-hydroxysuccinimide (5.12 g, 44.5 mmol) in THF (90 mL) was added to the mixture at 0 °C, and the stirring was continued for 10 min. Then Et_3N (6.52 mL, 46.78 mmol) was added, and the solution was stirred at 0 °C for another 2.5 h. Water was added to the reaction mixture and extracted with CH_2Cl_2. The combined organic layers were washed with water, dried and concentrated *in vacuo* affording a white solid material, which was purified by flash column chromatography on silica gel,

eluting with CH_2Cl_2 to 1:99 MeOH/CH_2Cl_2 gradient afforded the title compound **4** (5.99 g, 45%) as a white solid. IR (thin-film): 2933, 2855, 1818, 1788, 1729, 1712, 1469, 1429, 1409, 1370, 1299, 1269, 1210, 1071 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.85 (br d, *J* = 4.4 Hz, 4H), 2.61 (t, *J* = 7.2 Hz, 2H), 2.35 (t, *J* = 7.2 Hz, 2H), 1.74 (quintet, *J* = 7.2 Hz, 2H), 1.64 (quintet, *J* = 7.2 Hz, 2H), 1.43-1.38 (m, 2H), 1.37-1.33 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.0, 169.5, 168.9, 34.2, 31.1, 29.08, 29.05, 29.0, 28.8, 25.8, 24.8, 24.7; MS (ESI): *m/z* 322 (M + Na).

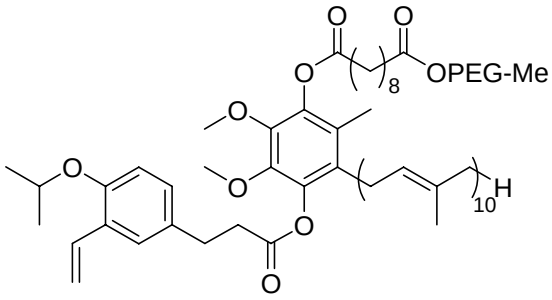


Compound 5: To a solution of PEG-OMe-2000 (**3**) (10.00 g, 5.00 mmol), **4** (1.65 g, 5.50 mmol) and DMAP (0.09 g, 0.74 mmol) in CH_2Cl_2 (60 mL), DCC (1.55 g, 7.50 mmol) was added at 0 °C with stirring, and the stirring was continued at 22 °C for 20 h. The mixture was then filtered and washed with CH_2Cl_2. The organic layer was washed with water, brine, dried and concentrated *in vacuo* affording a colorless liquid, which was purified by flash column chromatography on silica gel, eluting with CH_2Cl_2 to 1:24 MeOH/CH_2Cl_2 gradient afforded the title compound **5** (7.41 g, 65%) as a white waxy solid. IR (thin-film): 2871, 1813, 1783, 1739, 1646, 1466, 1349, 1286, 1250, 1203, 1111, 994, 949, 923 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.22-4.20 (m, 2H), 3.82-3.44 (m, PEG), 3.37 (s, 3H), 2.83 (br d, *J* = 3.6 Hz, 4H), 2.59 (t, *J* = 7.6 Hz, 2H), 2.31 (t, *J* = 7.6 Hz, 2H), 1.73 (quintet, *J* = 7.6 Hz, 2H), 1.63-1.57 (m, 2H), 1.41-1.35 (m, 2H), 1.30 (br s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.4, 168.8, 167.7, 71.0, 69.7-69.2 (m, PEG), 68.2, 62.4, 58.0, 33.1, 29.9, 28.1, 28.0, 27.98, 27.7, 24.7, 23.9, 23.7; MS (ESI): *m/3z* ~ 788 $(M + 3Na)^{+3}$.



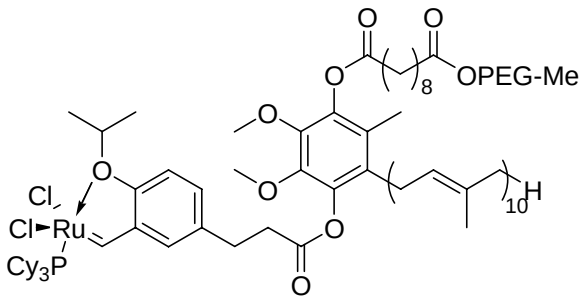
PQS (1): NaH (0.06 g, 2.37 mmol, 95% suspension in mineral oil) was added to a stirred solution of **6** (1.90 g, 2.20 mmol) in THF (25 mL) at 0 °C. After the addition was over, the reaction mixture was stirred at 22 °C for 1 h. A solution of **5** (4.18 g, 1.83 mmol) in THF (20 mL) was added to the mixture at 0 °C, and the stirring was continued for 30 min. The mixture was then stirred for another 6 h at 22 °C. It was

then cooled to 0 °C and saturated aqueous NH_4Cl was added to the reaction mixture and extracted with CH_2Cl_2. The combined organic layers were washed with water, brine, dried and concentrated *in vacuo* affording a yellowish liquid, which was purified by flash column chromatography on silica gel, eluting with CH_2Cl_2 to 1:19 MeOH/CH_2Cl_2 gradient afforded the compound **1** (3.35 g, 60%, mixture of two regioisomers) as a white waxy solid. IR (thin-film): 3506, 2882, 2741, 1758, 1736, 1650, 1468, 1359, 1345, 1280, 1242, 1110, 1062, 949, 843 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.76 (s, 0.3H), 5.72 (s, 0.7H), 5.12-5.09 (m, 9H), 4.98-4.95 (m, 1H), 4.23-4.20 (m, 2H), 3.90 (s, 3H), 3.79 (s, 3H), 3.70-3.45 (m, PEG), 3.37 (s, 3H), 3.32 (d, *J* = 6.4 Hz, 1.4H), 3.15 (d, *J* = 6.4 Hz, 0.6H), 2.59-2.53 (m, 2H), 2.32 (t, *J* = 7.6 Hz, 2H), 2.14-1.96 (m, 39H), 1.81-1.67 (m, 8H), 1.63-1.57 (m, 29H), 1.42-1.32 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.7, 172.3, 172.1, 145.2, 144.9, 142.1, 141.9, 137.8, 137.7, 135.3, 135.2, 135.0, 134.9, 134.8, 131.2, 128.5, 124.8, 124.4, 124.2, 124.1, 124.0, 121.9, 121.7, 121.6, 117.8, 77.4, 71.9, 70.7-70.1 (m, PEG), 69.2, 63.3, 60.9, 60.8, 60.5, 60.4, 59.0, 39.7, 39.6, 34.1, 33.9, 29.1, 26.7, 26.6, 26.0, 25.7, 25.3, 25.1, 24.8, 17.7, 16.3, 16.2, 16.0, 12.0, 11.3; MS (ESI): *m/3z* ~ 1038 $(M + 3Na)^{+3}$.

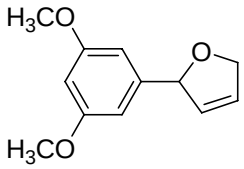


Compound 8: **1** (1.47 g, 0.48 mmol) was dissolved in CH_2Cl_2 (6 mL) and cooled to 0 °C. 1-(p-Isopropoxy-m-vinylphenyl)propionic acid (**7**)[1] (0.15 g, 0.64 mmol), 1-(3-dimethylaminopropyl)-3-ethyl carbodiimide (EDCI) (0.14 g, 0.73 mmol), and DMAP (0.024 g, 0.20 mmol) were then directly added in succession to the mixture as solids. Et_3N (0.12 mL, 0.86 mmol) was added through a syringe. The resulting mixture was stirred at 22 °C for 20 h. Water was added to the reaction mixture and extracted with CH_2Cl_2. The combined organic layers were washed with saturated $NaHCO_3$, water, brine, dried and concentrated *in vacuo* affording a colorless liquid, which was purified by flash column chromatography on silica gel, eluting with Et_2O, followed by CH_2Cl_2 to 1:16 MeOH/CH_2Cl_2 gradient afforded the compound **8** (1.49 g, 95%, mixture of two regioisomers) as a white foam. IR (thin-film): 2882, 1763, 1736, 1650, 1468, 1359, 1345, 1280, 1245, 1146, 1114, 1062, 948, 843 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.38-7.36 (m, 1H), 7.11-7.08 (m, 1H), 7.03 (dd, *J* = 18.0, 11.2 Hz, 1H), 6.83-6.80 (m, 1H), 5.76-5.70 (m, 1H), 5.24-5.21 (m, 1H), 5.12-5.05 (m, 9H), 4.97-4.94 (m, 1H), 4.49 (sep, *J* = 6.4 Hz, 1H), 4.22 (t, *J* = 4.8 Hz, 2H), 3.80 (s, 3H), 3.74 (s, 3H), 3.70-3.45 (m, PEG), 3.38 (s, 3H), 3.20-3.13 (m, 2H),

3.06-3.00 (m, 2H), 2.94-2.86 (m, 2H), 2.61-2.54 (m, 2H), 2.35-2.30 (m, 2H), 2.09-1.93 (m, 39H), 1.81-1.73 (m, 2H), 1.70-1.57 (m, 35H), 1.43-1.32 (m, 14H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.4, 171.5, 171.3, 170.8, 170.6, 153.5, 143.3, 143.2, 143.1, 143.0, 140.5, 140.4, 140.2, 140.1, 135.4, 134.8, 134.6, 132.0, 131.6, 130.9, 128.4, 128.3, 128.2, 127.7, 127.6, 126.21, 126.16, 124.7, 124.2, 124.1, 123.8, 121.1, 114.4, 114.3, 113.8, 71.7, 70.7-69.6 (m, PEG), 69.0, 63.1, 60.3, 58.8, 39.5, 39.4, 35.5, 33.9, 33,7, 30.0, 28.9, 28.86, 26.54, 26.45, 26.0, 25.5, 24.8, 24.6, 22.0, 17.5, 16.1, 15.8, 12.0, 11.8; MS (ESI): *m/3z* ~ 1110 $(M + 3Na)^{+3}$.



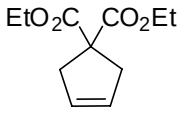
Catalyst 2: **8** (1.26 g, 0.39 mmol) was weighed into a 50 mL round-bottom flask and dissolved in 18 mL of CH_2Cl_2. $(PCy_3)_2Cl_2Ru$=CHPh (**9**) (0.40 g, 0.48 mmol) and CuCl (0.052 g, 0.53 mmol) were added directly to this solution as solids. The mixture was stirred for a period of 4 h at 22 °C, during which time the original purple solution turned dark brown. The following workup procedures were conducted in air with reagent grade solvents. The mixture was concentrated at reduced pressure and passed through a short column of silica gel eluting with CH_2Cl_2 followed by Et_2O. Finally, the column was flushed with 6% MeOH/CH_2Cl_2, at which point the product elutes (brown band). Solvent removal afforded the catalyst **2** (1.42 g, 99%, mixture of two regioisomers) as dark brown foam. IR (thin-film): 2920, 2868, 1763, 1736, 1645, 1451, 1351, 1298, 1250, 1108, 950, 850 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 17.39 (d, J_{PH} = 4.8 Hz, 1H), 7.61-7.59 (m, 1H), 7.56-7.52 (m, 1H), 7.04-7.01 (m, 1H), 5.26 (sep, *J* = 6.4 Hz, 1H), 5.13-5.10 (m, 9H), 5.00-4.95 (m, 1H), 4.23-4.20 (m, 2H), 3.81 (s, 3H), 3.77 (s, 3H), 3.70-3.45 (m, PEG), 3.37 (s, 3H), 3.19-3.15 (m, 4H), 2.97-2.89 (m, 2H), 2.61-2.54 (m, 2H), 2.34-2.26 (m, 5H), 2.08-1.96 (m, 39H), 1.82-1.58 (m, 67H), 1.43-1.24 (m, 14H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.6, 171.5, 171.4, 170.7, 170.6, 151.4, 143.8, 143.3, 143.2, 143.1, 143.05, 140.6, 140.4, 140.3, 140.1, 135.7, 135.6, 134.94, 134.89, 134.7, 134.34, 134.30, 131.0, 129.4, 129.3, 128.3, 128.2, 124.77, 124.72, 124.3, 124.1, 123.8, 122.4, 121.1, 113.2, 75.4, 71.8, 70.4-69.2 (m, PEG), 69.0, 63.2, 60.5, 60.4, 58.9, 39.6, 39.5, 35.8, 35.7, 35.6, 35.5, 35.4, 34.9, 34.0, 33.8, 30.0, 29.6, 29.0, 28.9, 27.7, 27.6, 26.8, 26.7, 26.6, 26.5, 26.2, 26.0, 25.6, 24.9, 24.7, 21.9, 17.6, 16.2, 15.95, 15.91, 12.1; MS (ESI): *m/3z* ~ 1256 $(M + 3Na)^{+3}$.



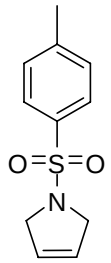
Representative Ring-Closing Metathesis Procedure; 2-(3,5-dimethoxyphenyl)-2,5-dihydrofuran (11). Precursor diene **26** (24 mg, 0.10 mmol) and catalyst **2** (7.5 mg, 0.002 mmol) were both added into a Teflon-coated-stir-bar-containing Biotage 2-5 mL microwave reactor vial at room temperature, and sealed with a septum. H_2O (1.0 mL; all RCM reaction were conducted at 0.1 M unless stated otherwise) was added, via syringe, and the resulting solution was allowed to stir at room temperature for 3 hours. The homogeneous reaction mixture was then diluted with EtOAc (2 mL), filtered through a bed of silica gel layered over Celite, and the bed further washed (2 x 4 mL) with EtOAc to collect all of the cyclized material. The volatiles were removed *in vacuo* to afford the crude product which was subsequently purified by flash chromatography using silica gel (4% EtOAc/Hexanes) to afford the title compound as a colorless liquid (19 mg, 92%). IR (neat): 3085, 3001, 2940, 2840, 1598, 1463, 1428, 1349, 1295, 1242, 1204, 1155, 1054, 1020, 930 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.48 (d, J = 2.4 Hz, 2H), 6.39 (t, J = 2.4 Hz, 1H), 6.04-6.02 (m, 1H), 5.90-5.87 (m, 1H), 5.75-5.72 (m, 1H), 4.90-4.84 (m, 1H), 4.80-4.74 (m, 1H), 3.79 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.1, 144.7, 130.0, 126.9, 104.3, 99.9, 88.0, 76.1, 55.5; EI-MS *m/z* (%): 206 (100), 177 (30), 175 (35), 165 (57), 138 (48), 137 (19); HRMS (EI) calcd for $C_{12}H_{14}O_3$ $[M]^+$ = 206.0943, found 206.0952.

Notes:

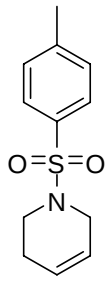
- Reaction mixtures can be analyzed via TLC directly from the reaction solution with no "mini work-up" needed.
- Thorough stirring of the reaction mixture is needed for the success of the reported reactions, especially when using solid substrates.
- Reactions can be preformed either under an blanket of Ar, in an open system (ie., a vent needle is placed through the septum), or in a closed system. All conditions yield similar results at the reaction scale mentioned.



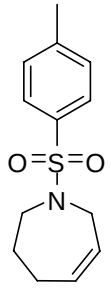
Diethyl cyclopent-3-ene-1,1-dicarboxylate: The representative procedure was followed using **15** (30 mg, 0.125 mmol) and catalyst **2** (9.2 mg, 0.0025 mmol). Column chromatography using silica gel (eluting with 16% EtOAc/Hexane) afforded the product as a colorless oil (24 mg, 91%). The ^{1}H-NMR obtained was in accord to the data previously reported for this compound.[9]



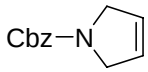
***N*-Tosyl-2,5-dihydro-1*H*-pyrrole:** The representative procedure was followed using **12** (30 mg, 0.12 mmol) and catalyst **2** (8.8 mg, 0.0024 mmol). Column chromatography using silica gel (eluting with 5% EtOAc/Hexane) afforded the product as a white solid (26.5 mg, 99%). The ^{1}H-NMR obtained was in accord to the data previously reported for this compound.[9]



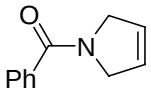
***N*-Tosyl-1,2,3,6-tetrahydropyridine:** The representative procedure was followed using **16** (33 mg, 0.124 mmol) and catalyst **2** (9.2 mg, 0.0025 mmol). Column chromatography using silica gel (eluting with 4% EtOAc/Hexane) afforded the product as a white solid (29 mg, 99%). The ^{1}H-NMR obtained was in accord to the data previously reported for this compound.[9]



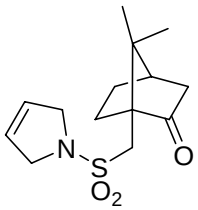
(*Z*)-*N*-Tosyl-2,3,4,7-tetrahydro-1*H*-azepine: The representative procedure was followed using **17** (35 mg, 0.125 mmol) and catalyst **2** (9.2 mg, 0.0025 mmol). Column chromatography using silica gel (eluting with 4% EtOAc/Hexane) afforded the product as a colorless oil (26 mg, 82%). The ^{1}H-NMR obtained was in accord to the data previously reported for this compound.[4]



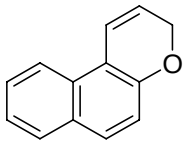
Benzyl 2,5-dihydro-1H-pyrrole-1-carboxylate: The representative procedure was followed using **18** (29 mg, 0.125 mmol) and catalyst **2** (9.2 mg, 0.0025 mmol). Column chromatography using silica gel (eluting with 5% EtOAc/Hexane) afforded the product as a colorless oil (25 mg, 99%). The ^{1}H-NMR obtained was in accord to the data previously reported for this compound.[10]



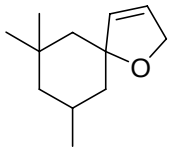
***N*-Benzoyl-3-pyrroline:** The representative procedure was followed using **19** (20 mg, 0.10 mmol) and catalyst **2** (7.5 mg, 0.002 mmol). Column chromatography using silica gel (eluting with 15% EtOAc/Hexane) afforded the product as a colorless liquid (16 mg, 94%). The ^{1}H-NMR obtained was in accord to the data previously reported for this compound.[11]



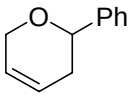
1-((2,5-Dihydro-1*H*-pyrrol-1-ylsulfonyl)methyl)-7,7-dimethylbicyclo[2.2.1]heptan-2-one: The representative procedure was followed using **20** (39 mg, 0.125 mmol) and catalyst **2** (9.2 mg, 0.0025 mmol). Column chromatography using silica gel (eluting with 12% EtOAc/Hexane) afforded the product as a white solid (32.5 mg, 92%). The ^{1}H-NMR obtained was in accord to the data previously reported for this compound.[6]



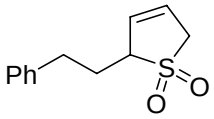
3H-Benzo[*f*]chromene: The representative procedure was followed using **25** (21 mg, 0.10 mmol) and catalyst **2** (7.6 mg, 0.002 mmol). Column chromatography using silica gel (eluting with 1% EtOAc/Hexane) afforded the product as a colorless liquid (16 mg, 89%). The ^{1}H-NMR obtained was in accord to the data previously reported for this compound.[12]



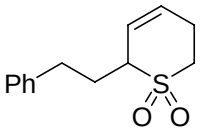
7,7,9-Trimethyl-1-oxaspiro[4.5]dec-3-ene: The representative procedure was followed using **27** (21 mg, 0.10 mmol) and catalyst **2** (7.5 mg, 0.002 mmol). Column chromatography using silica gel (eluting with 1% EtOAc/Hexane) afforded the product as a colorless liquid (16 mg, 90%). IR (neat): 3077, 2994, 2950, 2911, 2869, 2835, 1455, 1422, 1386, 1362, 1349, 1250, 1210, 1193, 1086, 1048, 1019 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.77 (dt, *J* = 6.0, 1.6 Hz, 1H), 5.55 (dt, *J* = 6.0, 2.4 Hz, 1H), 4.59 (dd, *J* = 2.4, 1.6 Hz, 2H), 1.96-1.87 (m, 1H), 1.64-1.59 (m, 1H), 1.44-1.37 (m, 2H), 1.17 (d, *J* = 14.0 Hz, 1H), 1.07 (s, 3H), 0.95 (dd, *J* = 13.2, 12.4 Hz, 1H), 0.874 (s, 3H), 0.872 (d, *J* = 6.4 Hz, 3H), 0.75 (dd, *J* = 13.2, 12.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.3, 125.1, 90.2, 74.3, 48.2, 47.0, 44.7, 34.3, 31.5, 27.1, 24.9, 22.8; GC-MS *m/z*: 180 (M^+);



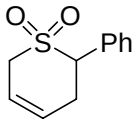
2-Phenyl-3,6-dihydro-2H-pyran: The representative procedure was followed using **21** (19 mg, 0.10 mmol) and catalyst **2** (7.5 mg, 0.002 mmol). Column chromatography using silica gel (eluting with 2% EtOAc/Hexane) afforded the product as a colorless liquid (15 mg, 95%). The ^1H-NMR obtained was in accord to the data previously reported for this compound.[7]



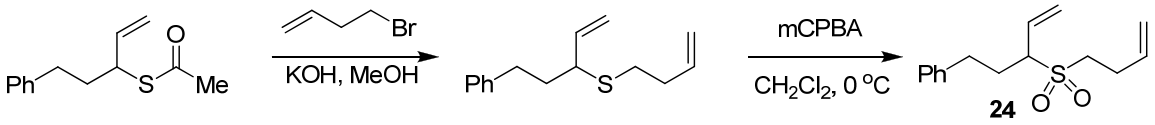
2-Phenethyl-1,1-dioxo-2,5-dihydrothiophene: The representative procedure was followed using **22** (25 mg, 0.10 mmol) and catalyst **2** (11.0 mg, 0.003 mmol). Resulting solution was allowed to stir at 50 °C for 4 hours. Column chromatography using silica gel (eluting with 4:1 CH_2Cl_2/hexanes to CH_2Cl_2 gradient) afforded the product as a colorless liquid (21 mg, 96%). The ^1H-NMR obtained was in accord to the data previously reported for this compound.[8]



6-Phenethyl-1,1-dioxo-3,6-dihydro-2H-thiopyran: The representative procedure was followed using **24** (26.5 mg, 0.10 mmol) and catalyst **2** (11.0 mg, 0.003 mmol). Resulting solution was allowed to stir at 50 °C for 4 hours. Column chromatography using silica gel (eluting with 4:1 CH_2Cl_2/hexanes to CH_2Cl_2 gradient) afforded the product as a colorless liquid (22 mg, 94%). IR (neat): 3028, 2926, 1603, 1496, 1454, 1431, 1311, 1282, 1231, 1152, 1119, 1029, 907 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.33-7.30 (m, 2H), 7.24-7.20 (m, 3H), 5.87-5.82 (m, 1H), 5.63-5.58 (m, 1H), 3.52 (br s, 1H), 3.13-3.02 (m, 2H), 2.98-2.83 (m, 2H), 2.81-2.64 (m, 2H), 2.51-2.42 (m, 1H), 1.97-1.88 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.4, 128.8, 128.7, 126.6, 126.4, 124.9, 58.1, 46.6, 32.6, 30.8, 25.7; EI-MS *m/z* (%): 236 (36), 170 (15), 145 (13), 132 (50), 105 (16), 92 (38), 91 (100), 81 (45); HRMS (EI) calcd for $C_{13}H_{16}O_2S$ $[M]^+$ = 236.0871, found 236.0874.

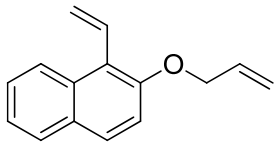


2-Phenyl-1,1-dioxo-3,6-dihydro-2H-thiopyran: The representative procedure was followed using **23** (24 mg, 0.10 mmol) and catalyst **2** (11.0 mg, 0.003 mmol). Resulting solution was allowed to stir at 50 °C for 4 hours. Column chromatography using silica gel (eluting with 4:1 CH_2Cl_2/hexanes to CH_2Cl_2 gradient) afforded the product as a colorless liquid (18.7 mg, 90%). The ^1H-NMR obtained was in accord to the data previously reported for this compound.[8]



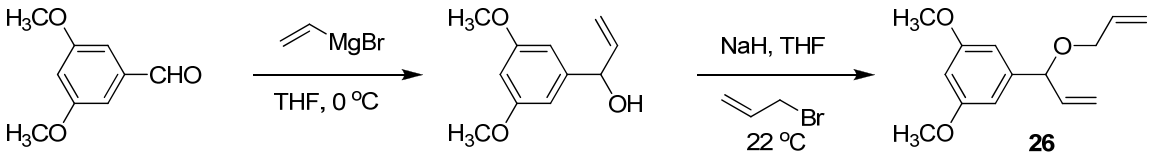
Solution of the thiolester[8] (0.20 g, 0.91 mmol) in degassed MeOH (5 mL) was treated with KOH (0.26 g, 4.62 mmol) and 4-bromobut-1-ene (0.14 mL, 1.36 mmol) and the reaction mixture was stirred at 22 °C under Ar for 30 min. Water (50 mL) was then added and the mixture was extracted with EtOAc. The combined organic layer was washed with water, brine, dried, and concentrated *in vacuo* gave the crude product which was subsequently purified by flash chromatography using silica gel (20% CH_2Cl_2/Hexanes) to afford the sulfide (0.18 g, 81%) as a colorless oil. The sulfide (0.18 g, 0.73 mmol) was then taken up with CH_2Cl_2 (15 mL) and treated with mCPBA (0.44 g, 2.57 mmol) at 0 °C. After stirring at 0 °C for 1 h, the reaction was quenched with 10% aqueous $Na_2S_2O_4$. The reaction mixture was then poured into sat. $NaHCO_3$, followed by extracted with CH_2Cl_2. The combined organic layer was

washed with water, brine, dried, and concentrated *in vacuo* to give pale yellow liquid, which was subsequently purified by flash chromatography using silica gel (eluting with 4:1 CH_2Cl_2/hexanes to CH_2Cl_2 gradient) to afford the sulfone **24** (0.10 g, 49%) as a colorless oil. IR (neat): 3085, 3064, 3027, 2982, 2930, 2864, 1687, 1641, 1604, 1496, 1454, 1417, 1308, 1234, 1180, 1129, 1079, 996, 923 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.30-7.25 (m, 2H), 7.22-7.15 (m, 3H), 5.88-5.70 (m, 2H), 5.54 (dd, *J* = 10.0, 1.2 Hz, 1H), 5.40 (d, *J* = 17.2 Hz, 1H), 5.11-5.03 (m, 2H), 3.44 (td, *J* = 10.0, 2.8 Hz, 1H), 3.01-2.96 (m, 2H), 2.87-2.80 (m, 1H), 2.60-2.42 (m, 4H), 2.08-1.99 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.0, 134.2, 131.4, 128.7, 128.6, 126.5, 124.1, 117.5, 66.5, 49.3, 32.2, 27.0, 25.7; EI-MS *m/z* (%): 264 (3), 145 (20), 144 (46), 129 (18), 91 (100); HRMS (EI) calcd for $C_{15}H_{20}O_2S$ $[M]^+$ = 264. 1184, found 264.1194.

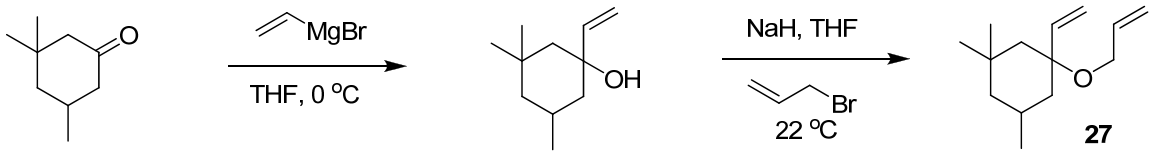


25

2-(Allyloxy)-1-vinylnaphthalene (**25**)**:** A 100 mL round-bottom flask equipped with a magnetic stir bar and charged with $MePPh_3Br$ (1.04 g, 2.92 mmol) and THF (25 mL) are allowed to cool to -40 °C for five min prior to addition of *n*-BuLi (2.55 M solution in hexanes, 1.17 mL, 2.92 mmol). The reaction mixture was allowed to warm to -10 °C and stirred for 30 min. Then again it was cooled down to -30 °C and 2-(allyloxy)-1-naphthaldehyde (0.50 g, 2.34 mmol) in THF (5 mL) was added dropwise to the solution. The solution was allowed to warm to room temperature and stirred for 10 h. The reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with CH_2Cl_2. The combined organic layer was washed with water, brine, dried, and concentrated *in vacuo* gave the crude product which was subsequently purified by flash chromatography using silica gel (4% EtOAc/Hexanes) to afford the product **25** as a yellowish liquid (0.48 g, 98%). IR (neat): 3081, 3016, 2921, 2866, 1647, 1626, 1591, 1512, 1464, 1422, 1367, 1334, 1302, 1265, 1243, 1221, 1182, 1148, 1105, 1066, 1042, 993, 923 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.29 (dd, *J* = 8.4, 0.4 Hz, 1H), 7.84 (dd, *J* = 8.4, 0.4 Hz, 1H), 7.79 (d, *J* = 9.2 Hz, 1H), 7.53 (ddd, *J* = 8.4, 6.8, 1.2 Hz, 1H), 7.42 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1H), 7.29 (d, *J* = 9.2, 1H), 7.22 (dd, *J* = 18.0, 12.0 Hz, 1H), 6.16 (ddt, *J* = 17.2, 10.0, 4.8 Hz, 1H), 5.87 (dd, *J* = 18.0, 2.0 Hz, 1H), 5.83 (dd, *J* = 12.0, 2.0 Hz, 1H), 5.52 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.35 (dq, *J* = 10.0, 1.6 Hz, 1H), 4.73 (dt, *J* = 4.8, 1.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.5, 133.7, 132.6, 130.5, 129.5, 128.9, 128.4, 126.6, 124.5, 123.8, 122.0, 121.0, 117.5, 114.9, 70.2; EI-MS *m/z* (%): 210 (40), 169 (58), 141 (100), 115 (34); HRMS (EI) calcd for $C_{15}H_{14}O$ $[M]^+$ = 210.1045, found 210.1042.



To a solution of 3,5-dimethoxybenzaldehyde (1.62 g, 9.77 mmol) in dry THF (17 mL) was dropwise added vinylmagnesium bromide (1.0 M in THF, 12.5 mL, 12.5 mmol) at 0 °C. The solution was allowed to warm to room temperature and stirred for 2 h. The reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with CH_2Cl_2. The combined organic layer was washed with water, dried, and concentrated *in vacuo* gave the brown liquid which was subsequently purified by flash chromatography using silica gel (14% EtOAc/Hexanes) to afford the alcohol (1.60 g, 84%) as a light yellowish liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.54 (d, *J* = 2.4 Hz, 2H), 6.38 (t, *J* = 2.4 Hz, 1H), 6.02 (ddd, *J* = 17.2, 10.4, 6.0 Hz, 1H), 5.36 (dt, *J* = 17.2, 1.2 Hz, 1H), 5.20 (dt, *J* = 10.4, 1.2 Hz, 1H), 5.14 (br t, *J* = 4.8 Hz, 1H), 3.79 (s, 6H), 1.99-1.97 (m, 1H); A solution of the above alcohol (0.26 g, 1.33 mmol) in THF (2 mL) was added to a stirred suspension of NaH (0.072 g, 3.01 mmol, 60% suspension in mineral oil) in THF (4 mL) at 0 °C. After H_2 evolution ceased, the mixture was stirred at 22 °C for 30 min. To this mixture allyl bromide (0.15 mL, 1.72 mmol) was added dropwise via syringe at 0 °C and the solution was allowed to warm to room temperature and stirred for 6 h. Then the reaction mixture was quenched with water and extracted with CH_2Cl_2. The combined organic layer was washed with water, dried, and concentrated *in vacuo* gave yellow liquid which was subsequently purified by flash chromatography using silica gel (3% EtOAc/Hexanes) to afford the product **26** (0.28 g, 91%) as a colorless liquid. IR (neat): 3080, 3002, 2932, 2839, 1644, 1607, 1461, 1428, 1347, 1294, 1242, 1205, 1153, 1065, 991, 926 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.51 (d, *J* = 2.4 Hz, 2H), 6.38 (t, *J* = 2.4 Hz, 1H), 5.99-5.89 (m, 2H), 5.32-5.26 (m, 2H), 5.21-5.17 (m, 2H), 4.73 (d, *J* = 6.8 Hz, 1H), 4.00-3.98 (m, 2H), 3.79 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.0, 143.6, 138.7, 134.9, 116.9, 116.4, 104.7, 99.6, 82.1, 69.3, 55.3; EI-MS *m/z* (%): 234 (7), 178 (100), 177 (26), 165 (12), 147 (20); HRMS (EI) calcd for $C_{14}H_{18}O_3$ $[M]^+$ = 234.1256, found 234.1260.



To a solution of 3,3′,5-trimethylcyclohexanone (1.29 g, 9.22 mmol) in dry THF (17 mL) was dropwise added vinylmagnesium bromide (1.0 M in THF, 12.0 mL, 12.0 mmol) at -78 °C. After strirred at -78 °C

for 1 h, the solution was allowed to warm to room temperature and stirred for another 2 h. The reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with CH_2Cl_2. The combined organic layer was washed with water, dried, and concentrated *in vacuo* gave the brown liquid which was subsequently purified by flash chromatography using silica gel (6% EtOAc/Hexanes) to afford the alcohol (1.24 g, 80%) as a light yellowish liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ 5.88 (dd, *J* = 17.2, 10.6 Hz, 1H), 5.20 (dd, *J* = 17.2, 1.2 Hz, 1H), 4.97 (dd, *J* = 10.6, 1.2 Hz, 1H), 2.09-1.91 (m, 1H), 1.60-1.20 (m, 3H), 1.13 (s, 3H), 1.10-1.00 (m, 1H), 0.93-0.88 (7H), 0.78 (t, *J* = 12.8 Hz, 1H); A solution of the above alcohol (0.325 g, 1.93 mmol) in THF (2 mL) was added to a stirred suspension of NaH (0.069 g, 2.64 mmol, 95% suspension in mineral oil) in THF (4 mL) at 0 °C. After H_2 evolution ceased, the mixture was stirred at 22 °C for 30 min. To this mixture allyl bromide (0.20 mL, 2.29 mmol) was added dropwise via syringe at 0 °C and the solution was allowed to warm to room temperature and stirred for 6 h. Then the reaction mixture was quenched with water and extracted with CH_2Cl_2. The combined organic layer was washed with water, dried, and concentrated *in vacuo* gave yellow liquid which was subsequently purified by flash chromatography using silica gel (Hexanes) to afford the product **27** (0.26 g, 65%) as a colorless liquid. IR (neat): 3084, 2997, 2980, 2951, 2923, 2868, 2837, 1646, 1457, 1421, 1414, 1385, 1375, 1362, 1341, 1288, 1251, 1223, 1188, 1159, 1130, 1056, 994, 919 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.95-5.86 (ddt, *J* = 17.2, 10.8, 5.2 Hz, 1H), 5.74 (dd, *J* = 17.6, 10.8 Hz, 1H), 5.26 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.12-5.06 (m, 3H), 3.77 (dt, *J* = 5.2, 1.6 Hz, 2H), 1.98-1.90 (m, 1H), 1.87 (dq, *J* = 13.6, 2.4 Hz, 1H), 1.70 (dt, *J* = 14.4, 2.4 Hz, 1H), 1.44-1.39 (m, 1H), 1.11 (s, 3H), 1.10 (d, *J* = 14.4 Hz, 1H), 0.91-0.88 (m, 7H), 0.77 (t, *J* = 12.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.6, 136.0, 115.6, 113.5, 77.8, 63.5, 48.9, 44.3, 43.1, 34.7, 31.6, 27.2, 24.1, 22.7; EI-MS *m/z* (%): 208 (3), 193 (11), 181 (17), 151 (31), 137 (54), 110 (37), 95 (35), 83 (39), 69 (35), 55 (100); HRMS (EI) calcd for $C_{14}H_{24}O$ $[M]^+$ = 208.1827, found 208.1829.

General Procedure for Catalyst Recycling

Diene **12** (24 mg, 0.10 mmol) and catalyst **2** (7.5 mg, 0.002 mmol) were both added into a Teflon-coated-stir-bar-containing Biotage 2-5 mL microwave reactor vial at room temperature, and sealed with a septum. H_2O (1.0 mL) was added, via syringe, and the resulting solution was allowed to stir at room temperature for 2 hours. Then Et_2O (3 mL) was added to the reaction mixture and stirred for 10 sec. The reaction mixture was then allowed to separate and the upper (Et_2O) layer was removed by pippet. The aqueous layer was successively washed with Et_2O (3 x 3 mL). The combined Et_2O extracts layers were evaporated to afforded the crude product, which was examined by 400 MHz ^{1}H NMR spectroscopy to reveal complete conversion of diene and clean formation of the corresponding cyclized product. Then for the second run, diene **12** (24 mg, 0.10 mmol) was added again to the same reaction vessel and stirred at

room temperature for another 2 hours. The work up was conducted in exactly the same way as described for the first cycle. This reaction was repeated eight more times, each using the diene **12** (24 mg, 0.10 mmol).

Reaction in Seawater: Diene **17** (35 mg, 0.125 mmol) and catalyst **2** (9.2 mg, 0.0025 mmol) were both added into a Teflon-coated-stir-bar-containing Biotage 2-5 mL microwave reactor vial at room temperature, and sealed with a septum. Seawater (1.25 mL) was added, via syringe, and the resulting solution was allowed to stir at room temperature for 3 hours. The homogeneous reaction mixture was then diluted with EtOAc (2 mL), filtered through a bed of silica gel layered over Celite, and the bed further washed (2 x 4 mL) with EtOAc to collect all of the cyclized material. The volatiles were removed *in vacuo* to afford the crude product which was subsequently purified by flash chromatography using silica gel (4% EtOAc/Hexanes) to afford the product as a colorless oil (25 mg, 79%). The ^{1}H-NMR obtained was in accord to the data previously reported for this compound.[4]

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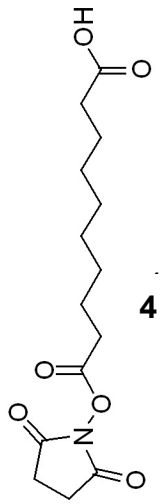

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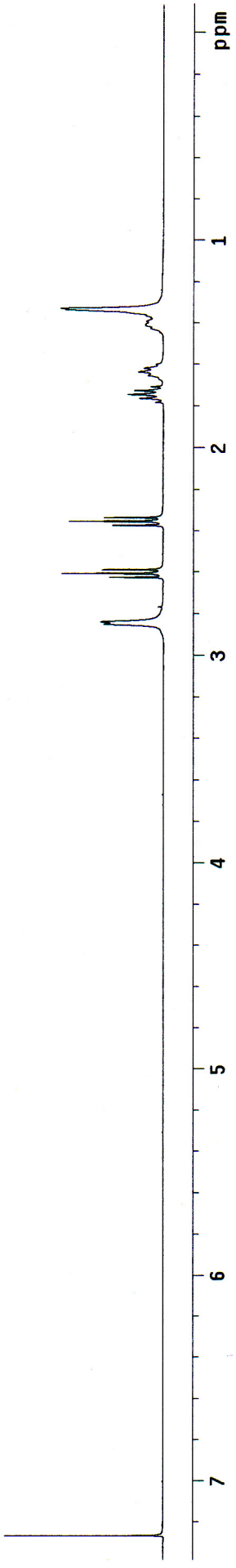

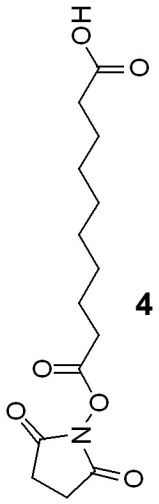

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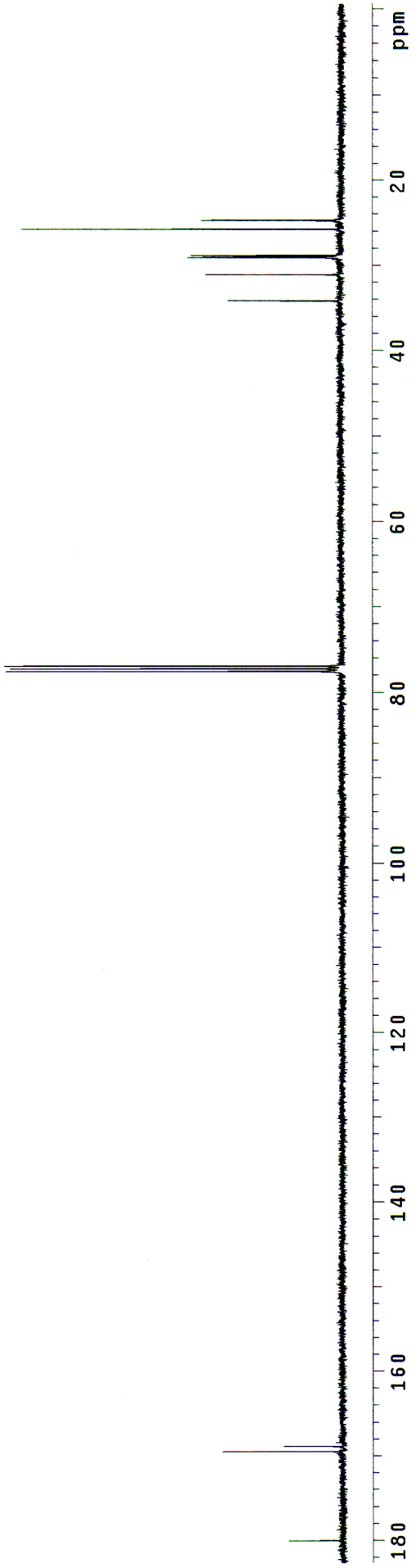

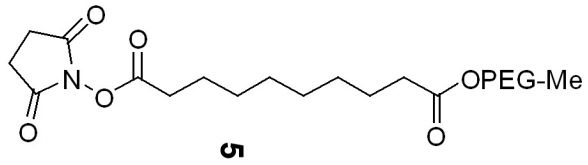

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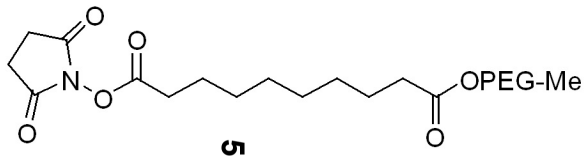

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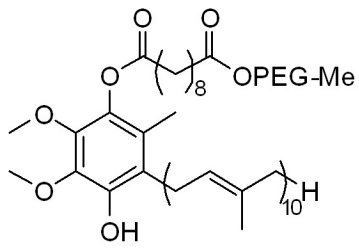

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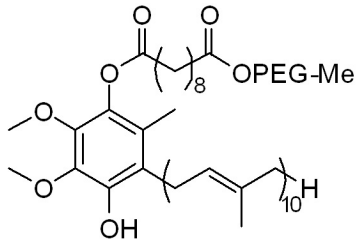

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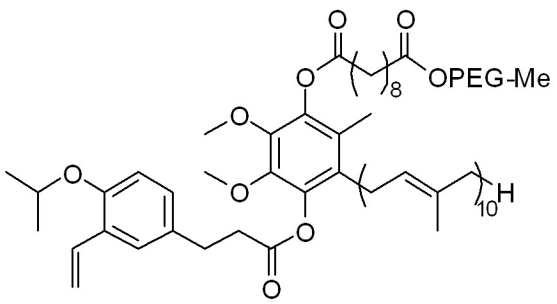

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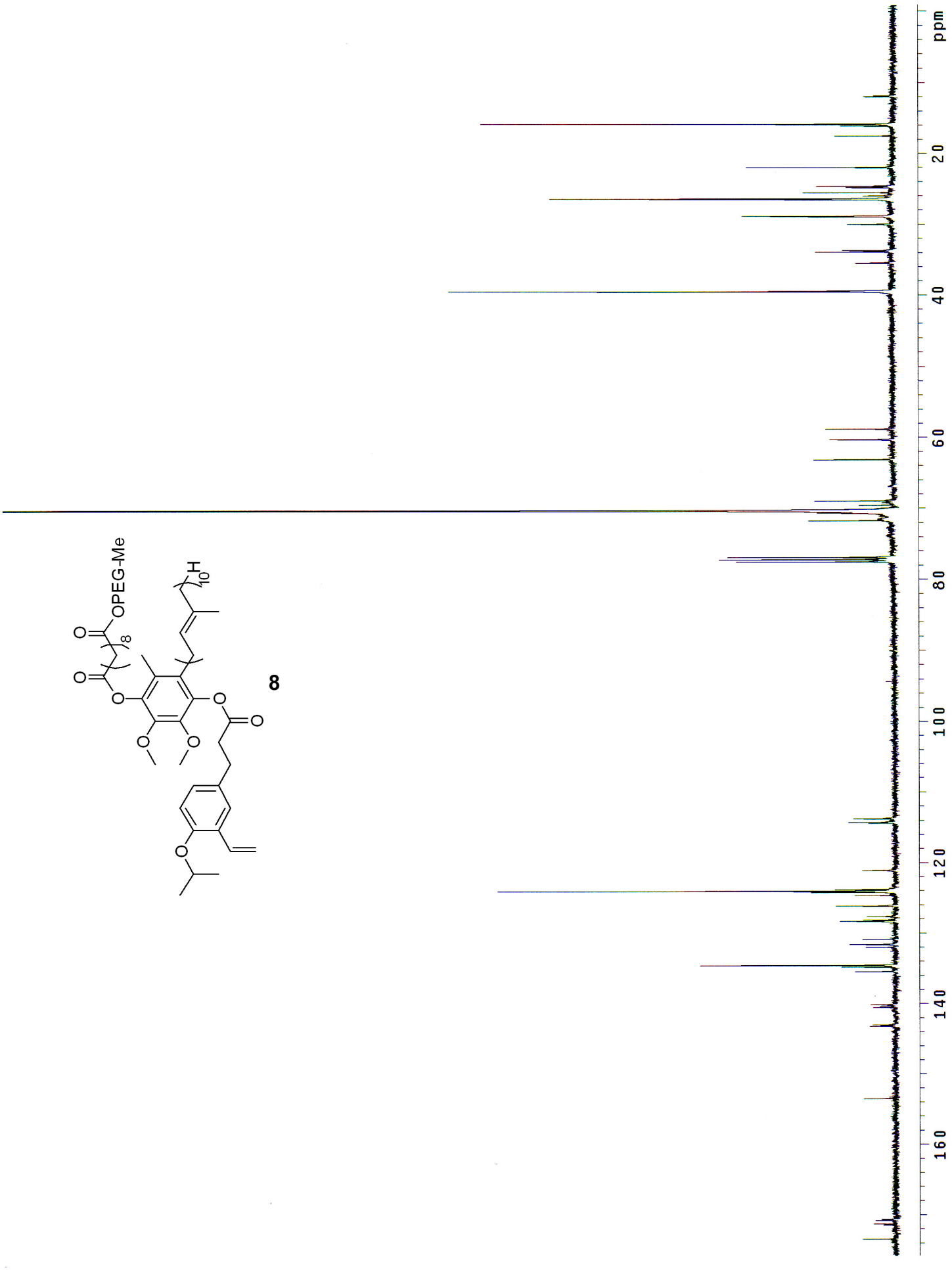
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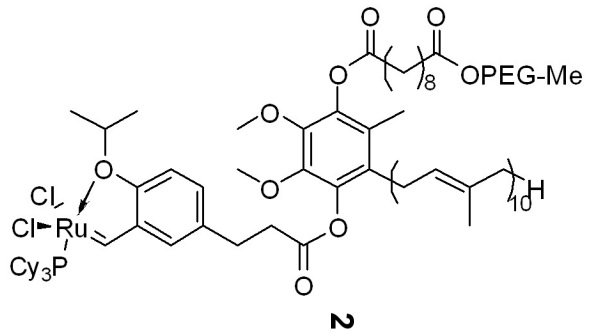

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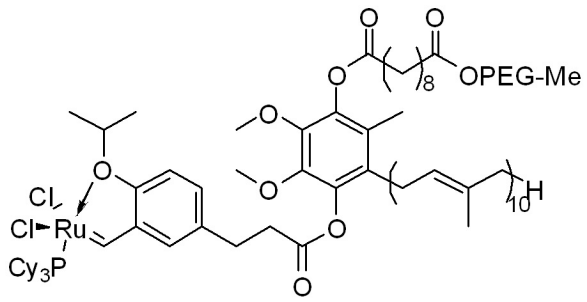

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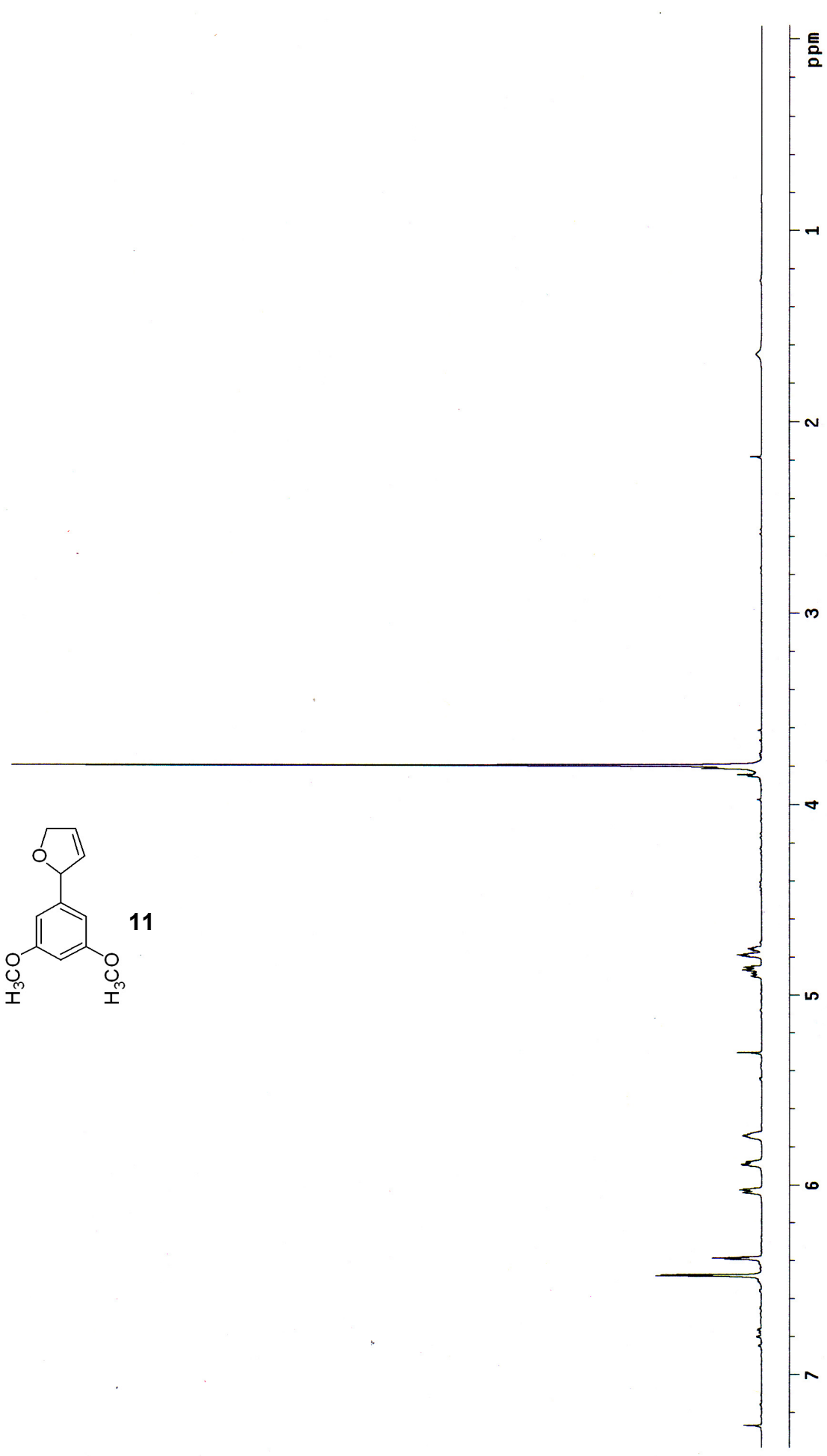
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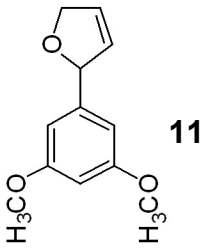

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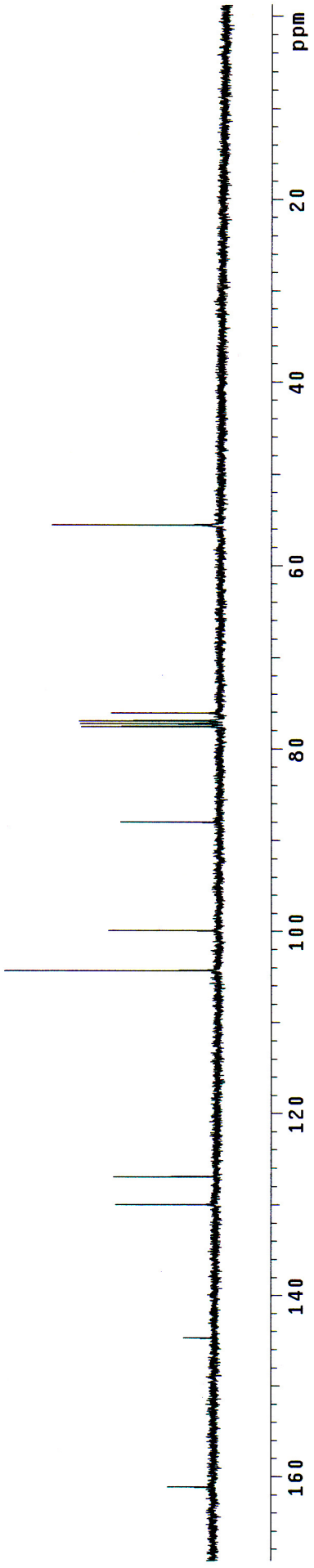

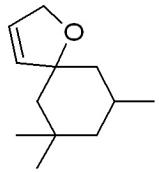

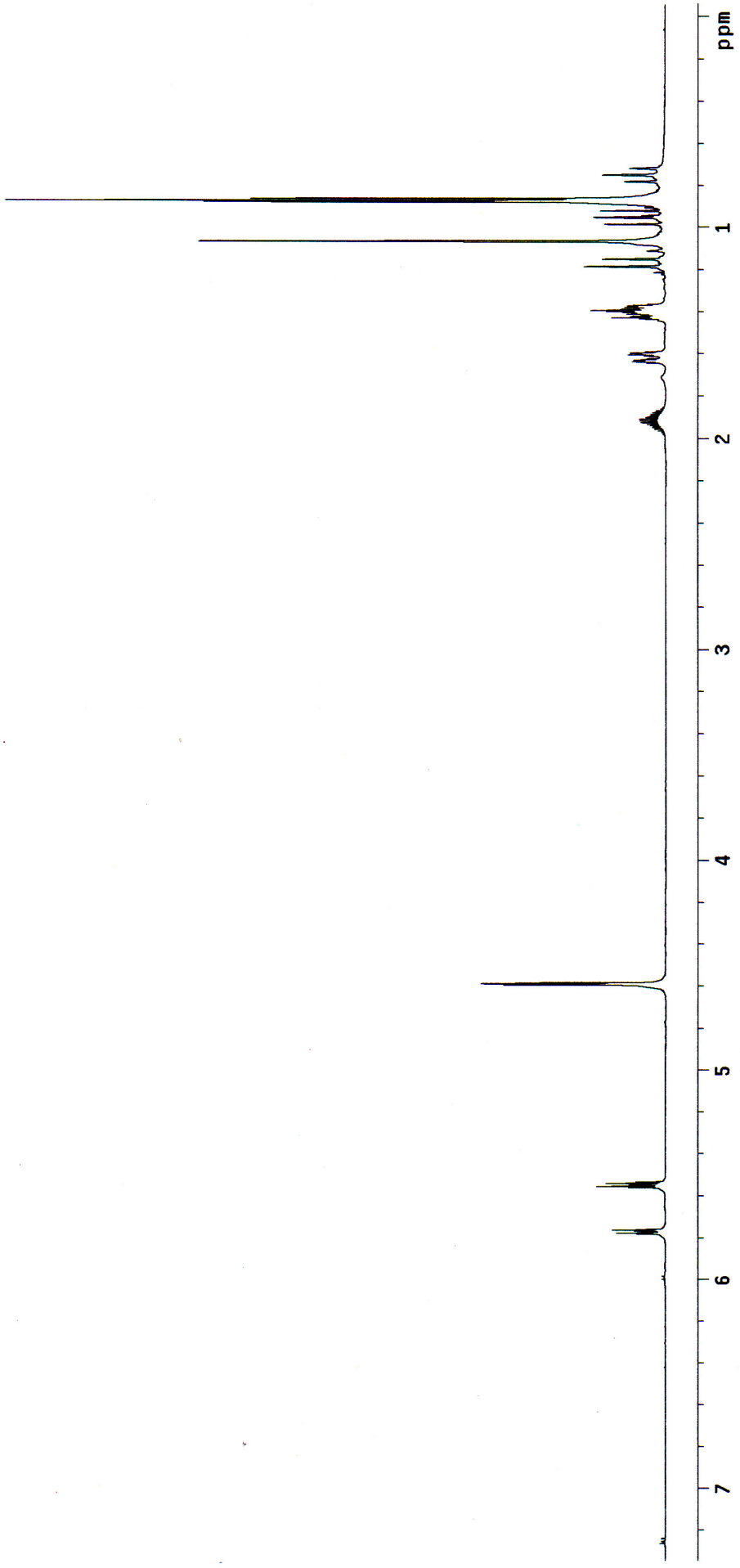
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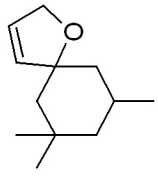

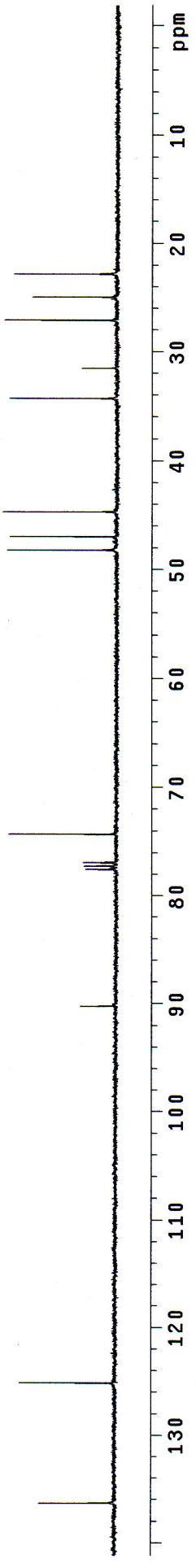
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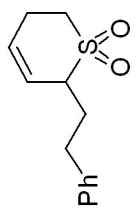
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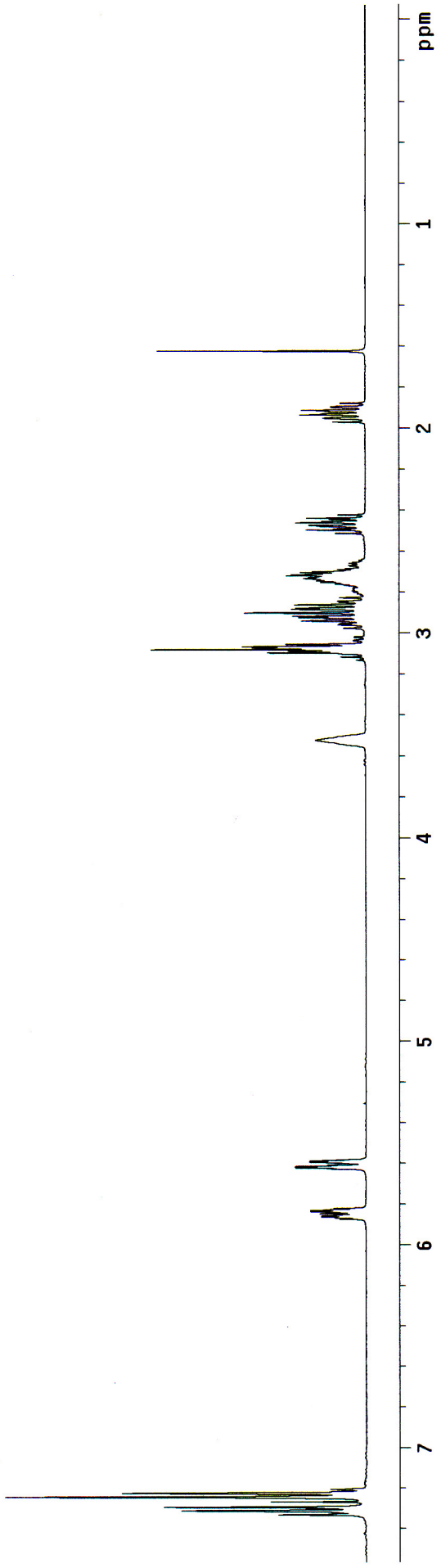
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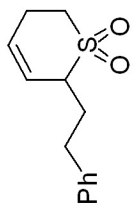
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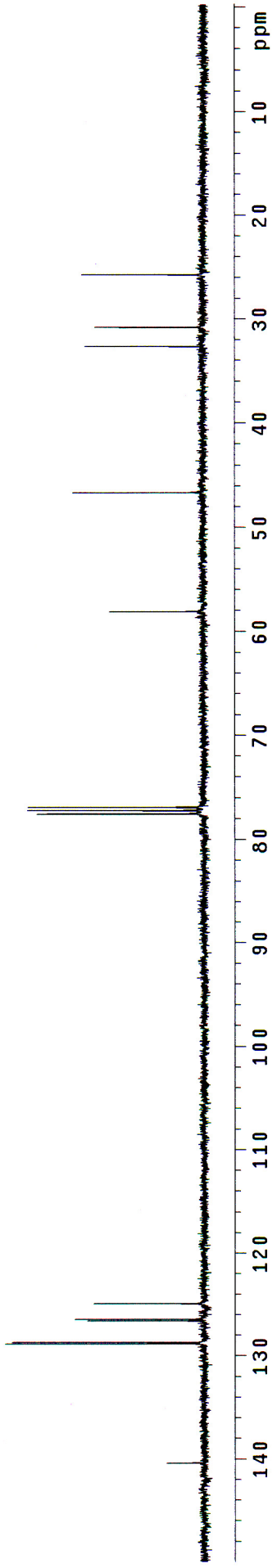
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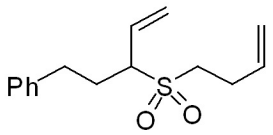
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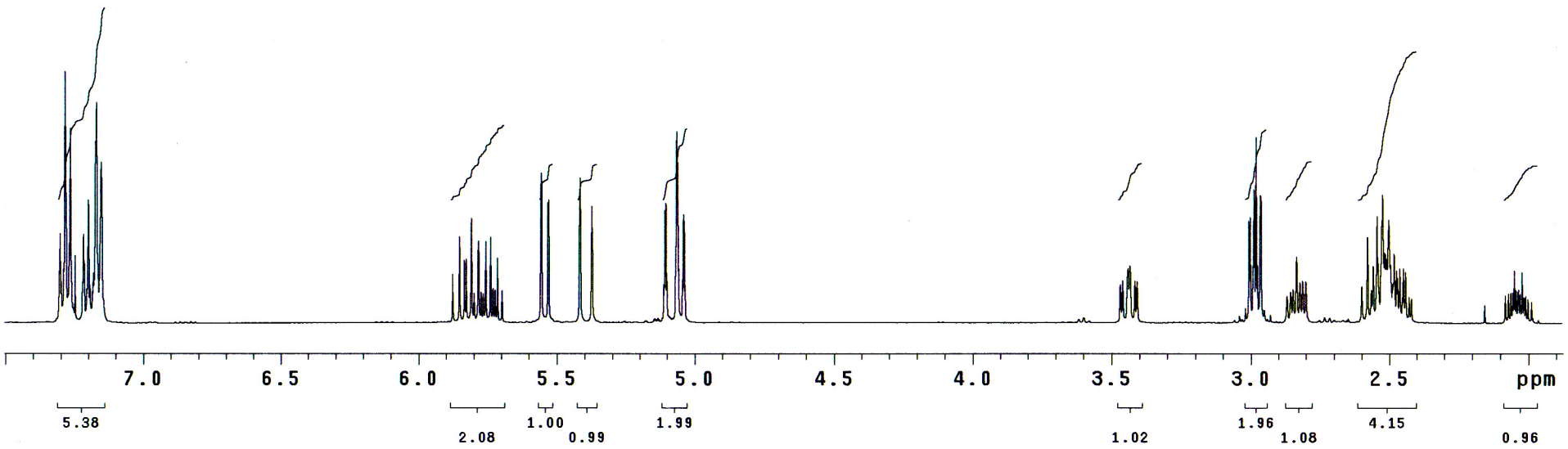
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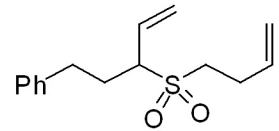

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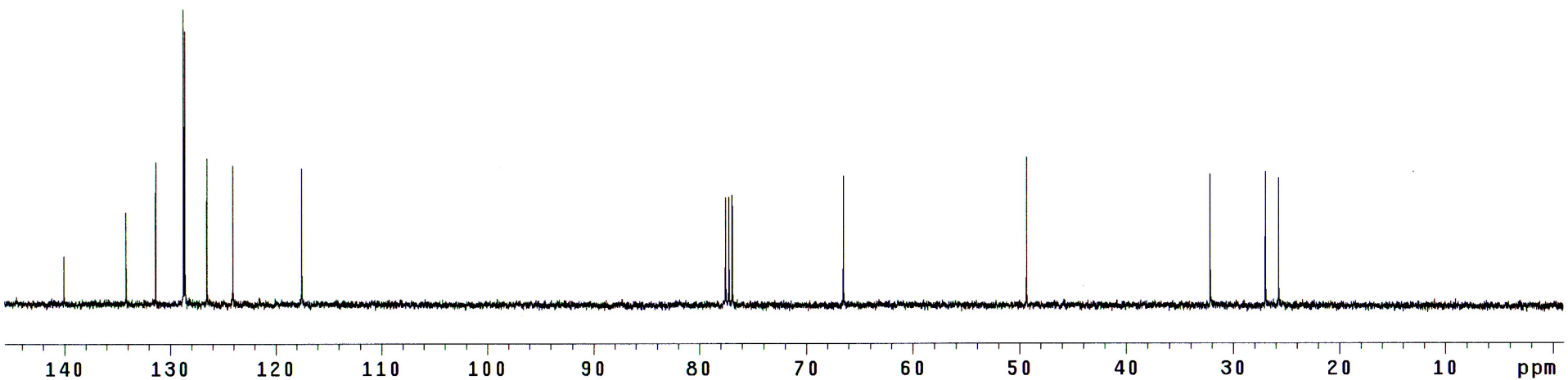

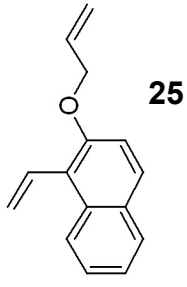

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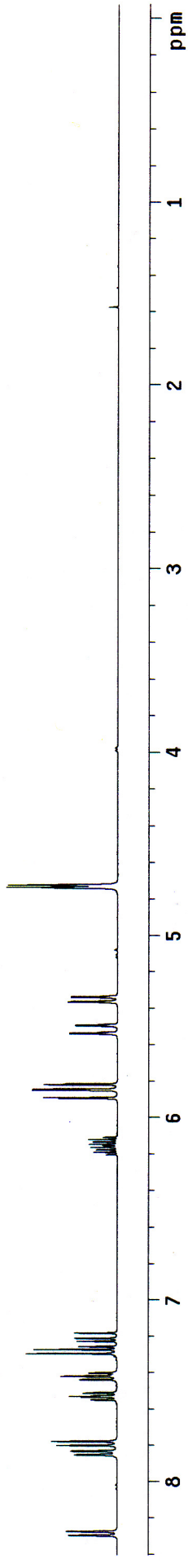

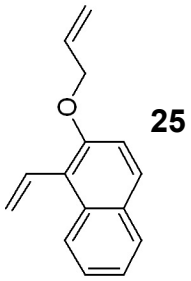

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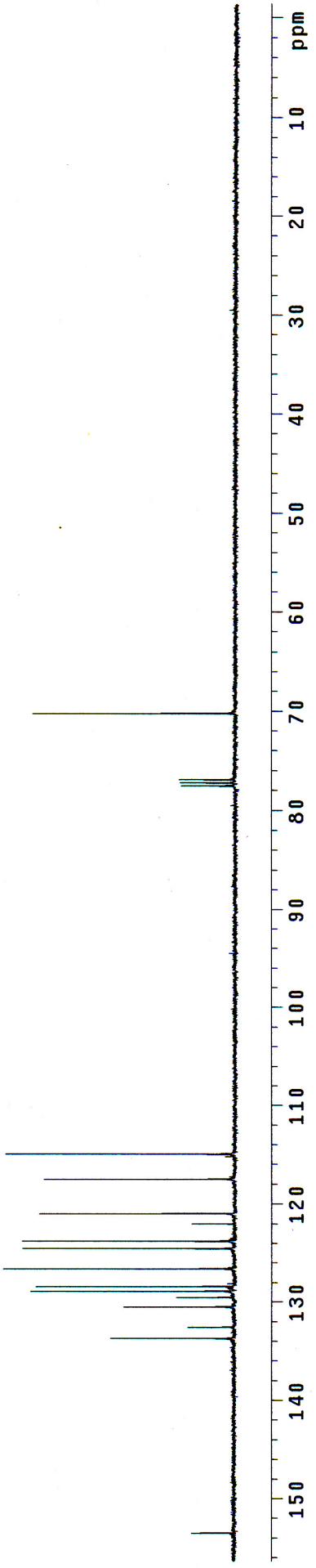

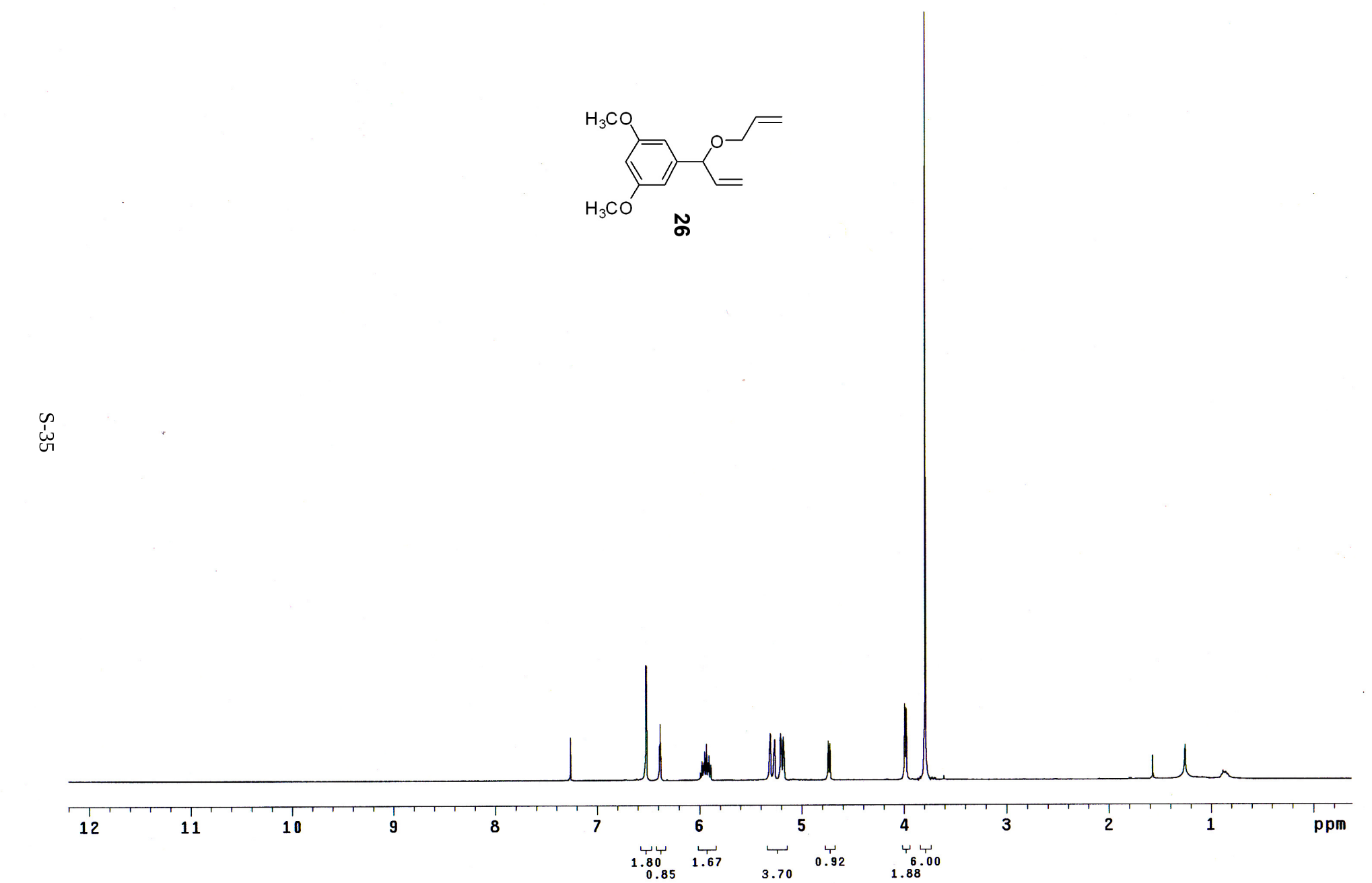
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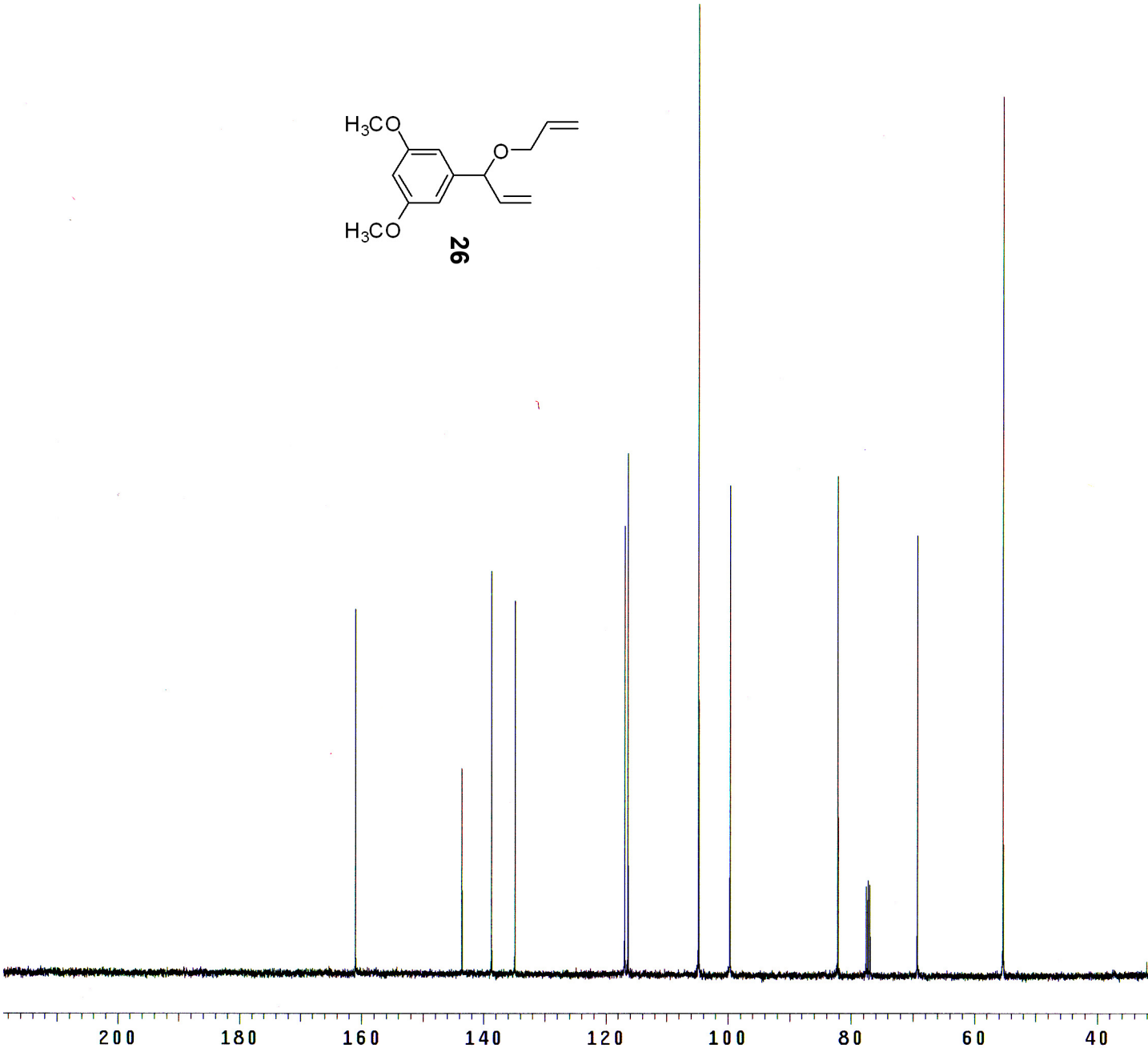
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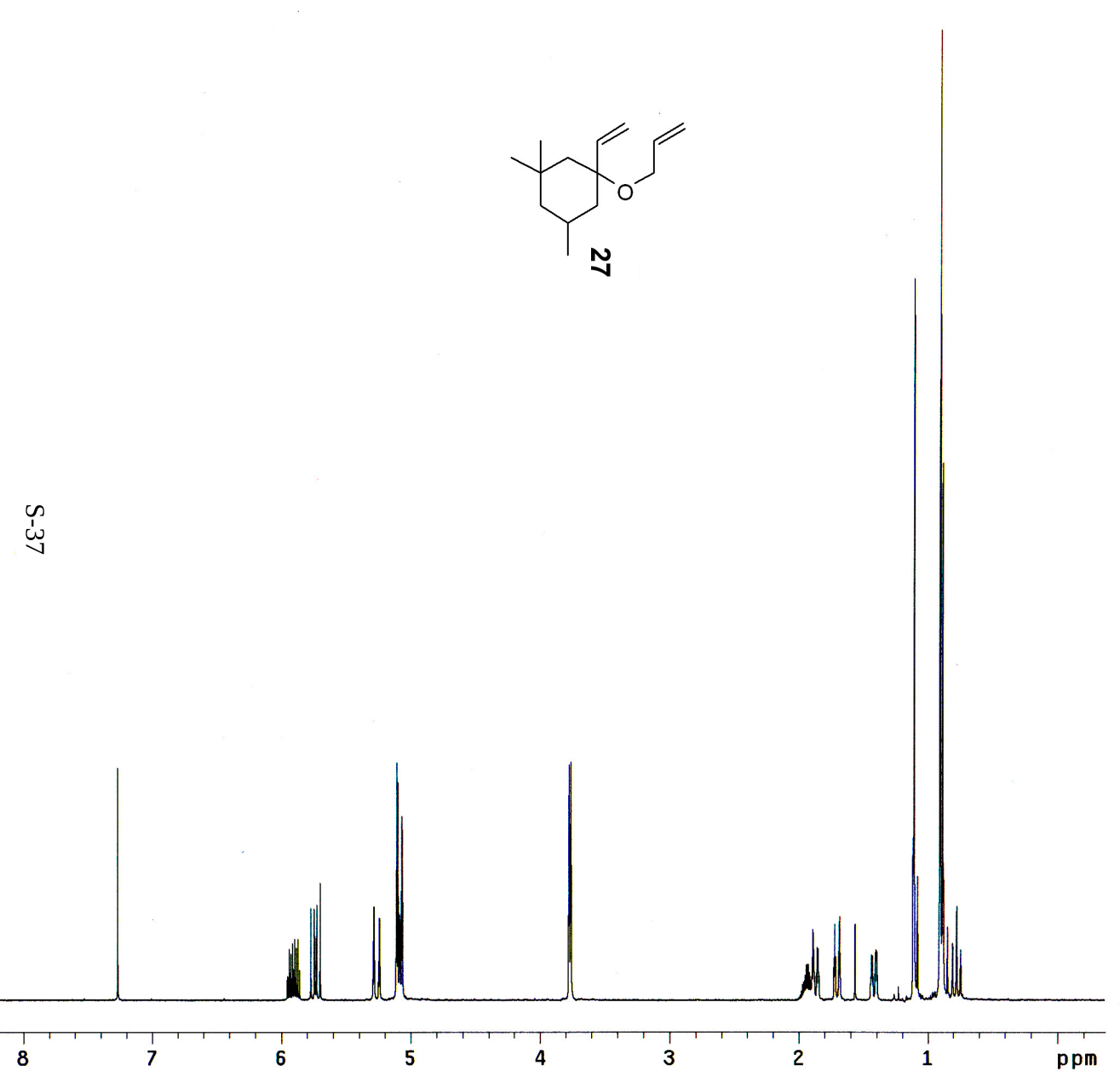
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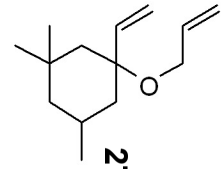

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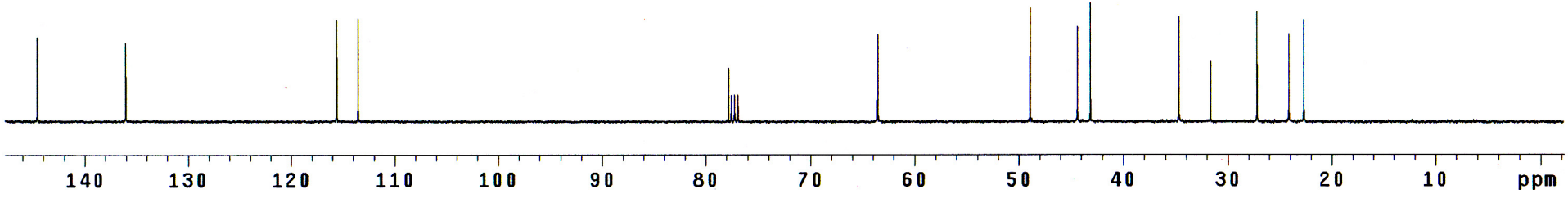


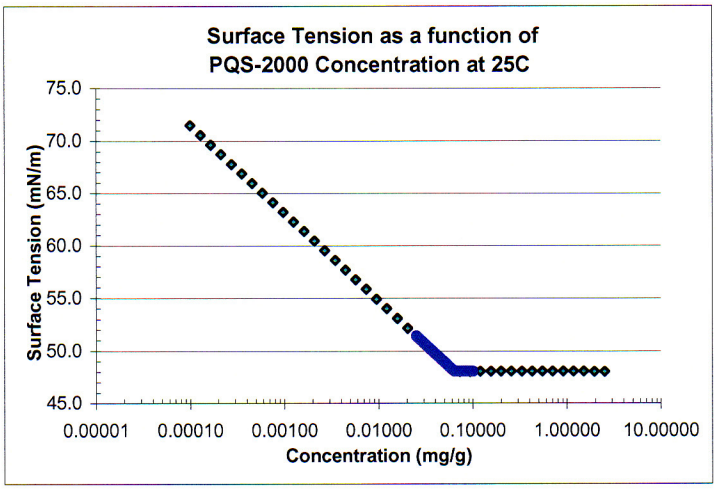
Critical Micelle Determination Study for PQS-2000 in RO Water at 25C

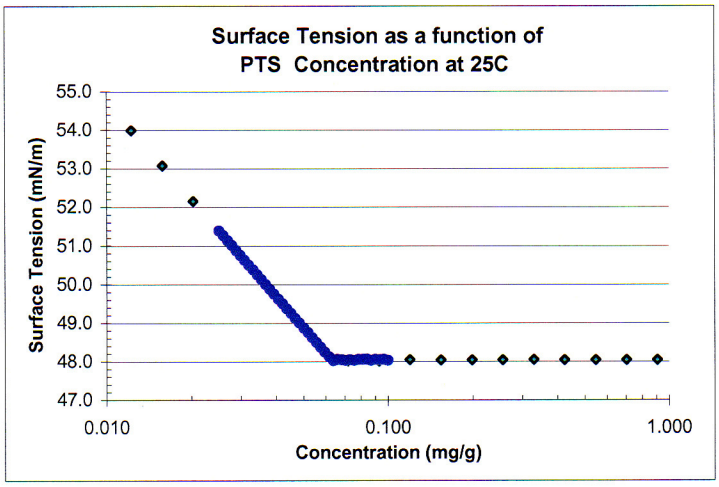
Performed 9/27/07 by Augustine Scientific using Wilhelmy Plate Method on a Kruss K100 Tensiometer

Run #1: PQS-2000 concentration is augmented lograthmically by successive dosing of a 5.0 mg/g stock solution into initially pure water at 25 +/- 0.2 deg C - followed by surface tension measurement at each new concentration.
Run #2: Experiment is repeated with prepared 0.2 mg/g stock solution

Concentration (mg/g)	Run #1 Surface Tension (mN/m)	Concentration (mg/g)	Run #2 Surface Tension (mN/m)
0.00010	71.49	0.0251	51.38
0.00013	70.57	0.0260	51.26
0.00017	69.65	0.0269	51.13
0.00021	68.73	0.0279	51.01
0.00027	67.80	0.0288	50.88
0.00035	66.88	0.0299	50.75
0.00045	65.96	0.0309	50.63
0.00059	65.04	0.0320	50.50
0.00075	64.12	0.0331	50.38
0.00097	63.20	0.0343	50.25
0.00125	62.28	0.0355	50.13
0.00161	61.36	0.0367	50.00
0.00208	60.44	0.0380	49.88
0.00268	59.52	0.0394	49.75
0.00345	58.60	0.0407	49.62
0.00445	57.68	0.0422	49.50
0.00573	56.76	0.0437	49.37
0.00738	55.84	0.0452	49.25
0.00950	54.91	0.0468	49.12
0.01224	53.99	0.0484	49.00
0.01577	53.07	0.0501	48.87
0.02032	52.15	0.0519	48.75
0.02618	51.23	0.0537	48.62
0.03372	50.31	0.0556	48.49
0.04345	49.39	0.0575	48.37
0.05597	48.47	0.0596	48.24
0.07210	48.03	0.0617	48.12
0.09288	48.02	0.0638	48.02
0.11966	48.05	0.0661	48.05
0.15415	48.04	0.0684	48.04
0.19858	48.04	0.0708	48.03
0.25582	48.04	0.0733	48.04
0.32956	48.05	0.0759	48.03
0.42456	48.04	0.0785	48.05
0.54694	48.04	0.0813	48.05
0.70460	48.04	0.0841	48.06
0.90770	48.04	0.0871	48.03
1.16934	48.04	0.0902	48.05
1.50640	48.05	0.0933	48.04
1.94062	48.02	0.0966	48.05
2.50000	48.03	0.1000	48.03

Determined CMC = 0.063 mg/g





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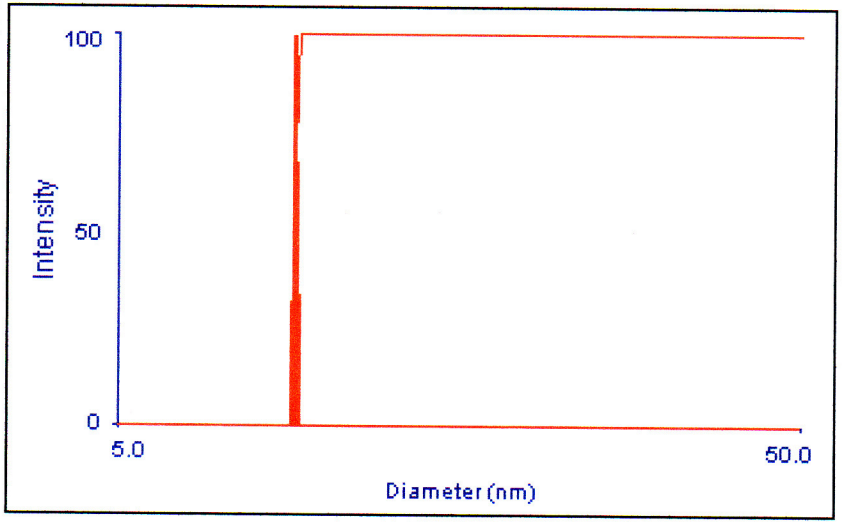
Skew	0.003
RMS Error	6.2950e-003



NNLS

d	G(d)	C(d)	d	G(d)	C(d)	d	G(d)	C(d)
8.46	0	0	9.09	100	66	9.76	0	100
8.51	0	0	9.15	68	89	9.82	0	100
8.57	0	0	9.21	34	100	9.89	0	100
8.63	0	0	9.27	0	100	9.95	0	100
8.68	0	0	9.33	0	100	10.02	0	100
8.74	0	0	9.39	0	100	10.08	0	100
8.80	0	0	9.45	0	100	10.15	0	100
8.85	0	0	9.51	0	100	10.22	0	100
8.91	0	0	9.57	0	100	10.28	0	100
8.97	33	11	9.63	0	100	10.35	0	100
9.03	66	33	9.70	0	100	10.42	0	100

Elapsed Time	00:05:11
Mean Diam.	44.1 nm
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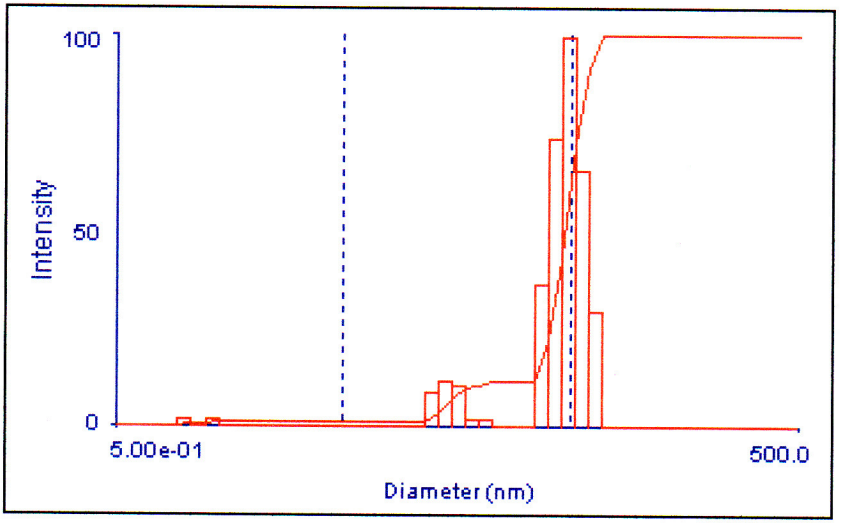

NNLS

d	G(d)	C(d)	d	G(d)	C(d)	d	G(d)	C(d)
1.00	2	1	4.58	0	1	20.96	2	12
1.15	0	1	5.26	0	1	24.07	0	12
1.32	2	1	6.04	0	1	27.64	0	12
1.51	0	1	6.93	0	1	31.74	0	12
1.74	0	1	7.96	0	1	36.44	37	22
2.00	0	1	9.14	0	1	41.85	74	44
2.29	0	1	10.50	0	1	48.05	100	72
2.63	0	1	12.05	9	4	55.18	66	91
3.02	0	1	13.84	12	7	63.37	30	100
3.47	0	1	15.89	11	10	72.76	0	100
3.99	0	1	18.25	2	11	83.56	0	100