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Supporting Information

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A Simple, Reliable Catalytic Asymmetric Allylation of Ketones

Karen M. Waltz, Jason Gavenonis, and Patrick J. Walsh
University of Pennsylvania, Department of Chemistry, 231 South 34th Street
Philadelphia, Pennsylvania 19104-6323

Supporting Information

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General Methods. All reactions were carried out in dry glassware under nitrogen using standard glove box or Schlenk line techniques. All solvents were dried and distilled prior to use. Isopropanol was dried by refluxing over magnesium turnings activated with iodine. Tetraallylstannane was either prepared[1] or purchased from Gelest, Strem, and Aldrich, and if cloudy, distilled prior to use. Titanium tetraisopropoxide and all liquid ketones were distilled prior to use, and solid ketones were recrystallized if necessary before use. NMR spectra were recorded on a Bruker 360 MHz NMR. Chemical shifts are reported relative to residual protiated solvent. Infrared spectra were recorded on a Perkin-Elmer 1600 series spectrometer. High resolution mass spectra were obtained at the University of Pennsylvania Mass Spectrometry Service Center on either a VG Micromass 70/70H or VG ZAB-E spectrometer. Enantiomeric excesses were determined on either a Hewlett-Packard 6890 gas chromatograph with a 30-m Supelco β-DEX™ column, or on a Hewlett-Packard 1050 series HPLC with a Chiralcel OD-H column. Racemates of alcohols were prepared by addition of allylmagnesiumchloride to the appropriate ketone. Compounds previously reported and characterized in the literature include 2-(4-methoxyphenyl)-4-penten-2-ol,[2] 1-allyl-1,2,3,4-tetrahydronaphthalen-1-ol,[2,3] 2-(1-cyclohexenyl)-4-penten-2-ol,[4] (*E*)-3-methyl-1-phenyl-1,5-hexadien-3-ol,[2,3,5,6] 3-methyl-1-phenyl-5-hexen-3-ol,[7] and 1-chloro-3-phenyl-5-hexen-3-ol.[8]

General Procedure for Ketone Allylation Reactions. Titanium isopropoxide [98 μL, 0.332 mmol (20 mol%); or 147 μL, 0.498 mmol (30 mol%)] was added to a solution of (*R*)- or (*S*)-BINOL [95 mg, 0.332 mmol (20 mol%); or 142.5 mg, 0.498 mmol (30 mol%)] in dichloromethane (4.0 mL), and this orange solution was stirred for several minutes at room temperature. Isopropanol (2.54 mL, 33.2 mmol) was added to this solution, followed by ketone substrate (1.66 mmol) and tetraallylstannane (0.6 mL, 2.49 mmol). After an initial induction period, the color of the solution lightened from orange to yellow, indicating the commencement of the reaction. After stirring for 20 h, the reaction was quenched with saturated ammonium chloride, extracted with dichloromethane, dried over magnesium sulfate, and filtered through Celite. After removal of the solvent under reduced pressure, the resulting oily orange residue was extracted with hexanes, filtered through Celite, and chromatographed on silica, starting with hexanes to elute the majority of the tin species, and then with 10-20% ether/hexanes to obtain the alcohol product in yields and ee's reported in Table 1. It is important to use ammonium chloride to quench the reactions instead of dilute hydrochloric acid, which resulted in lower ee's and irreproducible results. It is also best to run the column as quickly as possible, as some of the alcohol products racemize slightly when in contact with the silica for extended periods of time.

The following compounds were prepared according to the general procedure for ketone allylation, and have not been previously characterized in the literature:

2-(3-methylphenyl)-4-penten-2-ol. Prepared using (*R*)-BINOL. White solid. ^{1}H NMR ($CDCl_3$): δ 7.25 (m, 3H), 7.07 (m, 1H), 5.64 (m, 1H), 5.14 (m, 2H), 2.70 (dd, *J* = 13.6, 6.4 Hz, 1H), 2.50 (dd, *J* = 13.7, 8.4 Hz, 1H), 2.38 (s, 3H), 2.08 (s, 1H), 1.54 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$): δ 147.81, 137.92, 133.97, 128.26, 127.53, 125.66, 121.99, 119.60, 73.77, 48.62, 30.13, 21.84; IR (film): 3438, 3074, 3020, 2976, 2926, 2863, 1639, 1607, 1588, 1489, 1451, 1434, 1373, 1343, 1287, 1154, 1109, 1076, 1050, 998, 940, 914, 836, 786, 706 cm^{-1}; HRMS (CI) *m/z* 175.1117 $(M-H)^+$; calcd for $C_{12}H_{15}O$: 175.1122. Resolved by GC at 105°C, 1.0 mL/min, t_r = 67 min (minor), t_r = 69 min (major).

2-(2-methylphenyl)-4-penten-2-ol. Prepared using (*R*)-BINOL. Pale yellow oil. ^{1}H NMR ($CDCl_3$): δ 7.45 (m, 1H), 7.16 (m, 3H), 5.66 (m, 1H), 5.15 (m, 2H), 2.88 (dd, *J* = 13.9, 6.5 Hz, 1H), 2.58 (m, 1H), 2.57 (s, 3H), 1.98 (br s, 1H), 1.62 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$): δ 144.73, 135.51, 134.12, 132.86, 127.18, 126.25, 125.88, 119.58, 74.99, 46.81, 29.18, 22.69; IR (film): 3522, 3423, 3072, 3014, 2976, 2932, 1639, 1486, 1453, 1373, 1341, 1287, 1096, 1054, 997, 916, 866, 762, 729 cm^{-1}; HRMS (CI) *m/z* 177.1283 $(M + H)^+$; calcd for $C_{12}H_{17}O$: 177.1279. Resolved by GC at 95°C, 0.8 mL/min, t_r = 175 min (minor), t_r = 178 min (major).

2-(3-trifluoromethylphenyl)-4-penten-2-ol. Prepared using (*R*)-BINOL. Pale yellow oil ^{1}H NMR ($CDCl_3$): δ 7.73 (s, 1H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.48 (m, 2H), 5.60 (m, 1H), 5.15 (m, 2H), 2.68 (dd, *J* = 13.7, 6.5 Hz, 1H), 2.52 (dd, *J* = 13.7, 8.2 Hz, 1H), 2.14 (br s, 1H), 1.56 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$): δ 148.89, 133.11, 130.71 (q, $^{2}J_{C\text{-}F}$ = 32.0 Hz), 128.83, 128.49, 124.47 (q, $J_{C\text{-}F}$ = 272.3 Hz), 123.72 (q, $^{3}J_{C\text{-}F}$ = 3.6 Hz), 121.92 (q, $^{3}J_{C\text{-}F}$ = 3.7 Hz), 120.44, 73.67, 48.53, 30.11; IR (film): 3430, 3078, 2980, 2933, 1641, 1438, 1377, 1330, 1263, 1166, 1124, 1075, 999, 920, 875, 804, 704 cm^{-1}; HRMS (CI) *m/z* 211.0935 $(M - F)^+$; calcd for $C_{12}H_{13}F_2O$: 211.0916. Resolved by GC at 105°C, 1.0 mL/min, t_r = 36.1 min (minor), t_r = 38.7 min (major).

2-(2-furyl)-4-penten-2-ol.[9] Prepared using (*S*)-BINOL. Pale yellow oil ^{1}H NMR ($CDCl_3$): δ 7.36 (br s, 1H), 6.30 (m, 1H), 6.19 (d, *J* = 3.2 Hz, 1H), 5.67 (m, 1H), 5.13 (m, 2H), 2.68 (dd, *J* = 13.6, 6.8 Hz, 1H), 2.54 (dd, *J* = 13.6, 7.9 Hz, 1H), 2.14 (br s, 1H), 1.53 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$): δ 159.43, 141.72, 133.46, 119.42, 110.22, 104.84, 70.93, 46.34, 26.72; IR (film): 3408, 3118, 3077, 2980, 2934, 1641, 1504, 1435, 1372, 1348, 1290, 1228, 1160, 1125, 1103, 1072, 1013, 920, 884, 808, 736, 598 cm^{-1}; HRMS (CI) *m/z* 135.0805 $(M - OH)^+$; calcd for $C_9H_{11}O$: 135.0810. Resolved by GC at 80°C, 1 mL/min, t_r = 60 min (minor), t_r = 62 min (major).

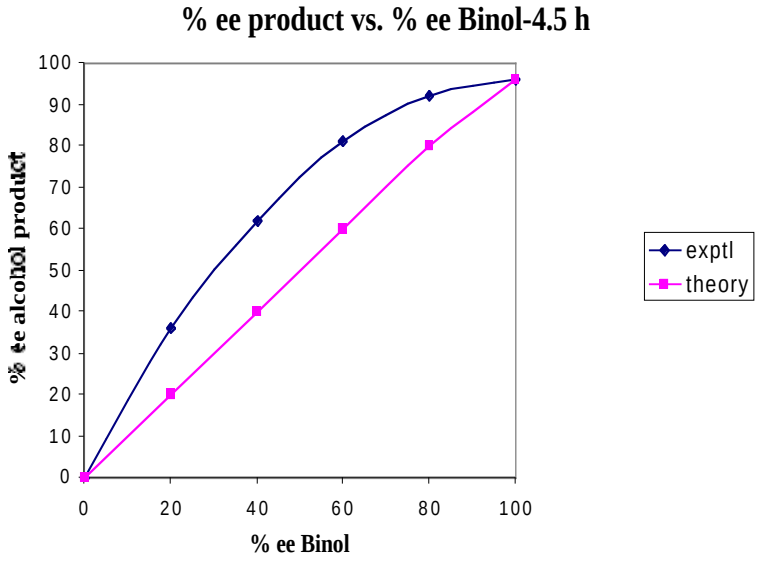
Procedure for Non-Linear Effect Experiments. Stock solutions of 0.083 M (*R*)-BINOL and 0.083 M racemic BINOL were prepared in dichloromethane. The volumes shown in the following table were transferred via syringe to four vials equipped with stir bars to make solutions of 20, 40, 60, and 80%ee of (*R*)-BINOL (0.0332 mmol).

Table S1

% ee BINOL	0.083M (*R*)-BINOL	0.083M (*rac*)-BINOL
20	80 µL	320 µL
40	160 µL	240 µL
60	240 µL	160 µL
80	320 µL	80 µL

Titanium tetraisopropoxide (9.8 µL, 0.0332 mmol) was added to each BINOL solution, and the resulting orange solution was stirred for several minutes. Dry isopropanol (254 µL, 3.32 mmol) was added to each vial, followed by 3-methylacetophenone (22.7 µL, 0.166 mmol), and tetraallylstannane (60 µL, 0.249 mmol). After stirring at room temperature for 4.5 h, samples of each of the four reactions were quenched with saturated ammonium chloride, extracted with dichloromethane, dried over magnesium sulfate, filtered through Celite, and analyzed by chiral GC.

Plot of Data from Non-Linear Effect Experiments



Procedure for Allylation using Different Alcohol Additives. Titanium tetraisopropoxide (9.8 μL, 0.0332 mmol) was added to each of three solutions of (*R*)-BINOL (9.5 mg, 0.0332 mmol) in dichloromethane (0.4 mL), and the resulting orange solutions were stirred for several minutes. Dry alcohol (3.32 mmol) [cycloheptanol (400 μL), cyclohexanol (350 μL), and cyclopentanol (301μL)] was added, followed by 3-methylacetophenone (22.7 μL, 0.166 mmol), and tetraallylstannane (60 μL, 0.249 mmol). After stirring at room temperature for 18 h, the reactions were quenched with saturated ammonium chloride, extracted with dichloromethane, dried over magnesium sulfate, filtered through Celite, and analyzed by chiral GC.

Procedure for Allylation with 0.25 to 1.25 equiv of Tetraallylstannane. Titanium tetraisopropoxide (14.7 μL, 0.0498 mmol) was added to each of five solutions of (*R*)-BINOL (14.2 mg, 0.0498 mmol) in dichloromethane (see Table S2 for volumes), and the resulting orange solutions were stirred for several minutes. Dry isopropanol (254 μL, 3.32 mmol) was added to each vial, followed by 3-trifluoromethylacetophenone (25.3 μL, 0.166 mmol). Tetraallylstannane was then added in amounts ranging from 0.25 to 1.25 equiv (see Table S2 below). After stirring at room temperature for 2 h, samples of each of the five reactions were quenched with saturated ammonium chloride, extracted with dichloromethane, dried over magnesium sulfate, filtered through Celite, and analyzed by chiral GC. All reactions were complete after 2 h, except for the reaction with 0.25 equiv of tetraallylstannane, which required 3 h for >92% conversion.

Table S2

Equiv of Tetraallylstannane	Volume of Tetraallylstannane	Volume of Added Dichloromethane
1.25	50 μL (0.207 mmol)	0.41 mL
1.00	40 μL (0.166 mmol)	0.42 mL
0.75	30 μL (0.124 mmol)	0.43 mL
0.50	20 μL (0.0829 mmol)	0.44 mL
0.25	10 μL (0.0415 mmol)	0.45 mL

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S

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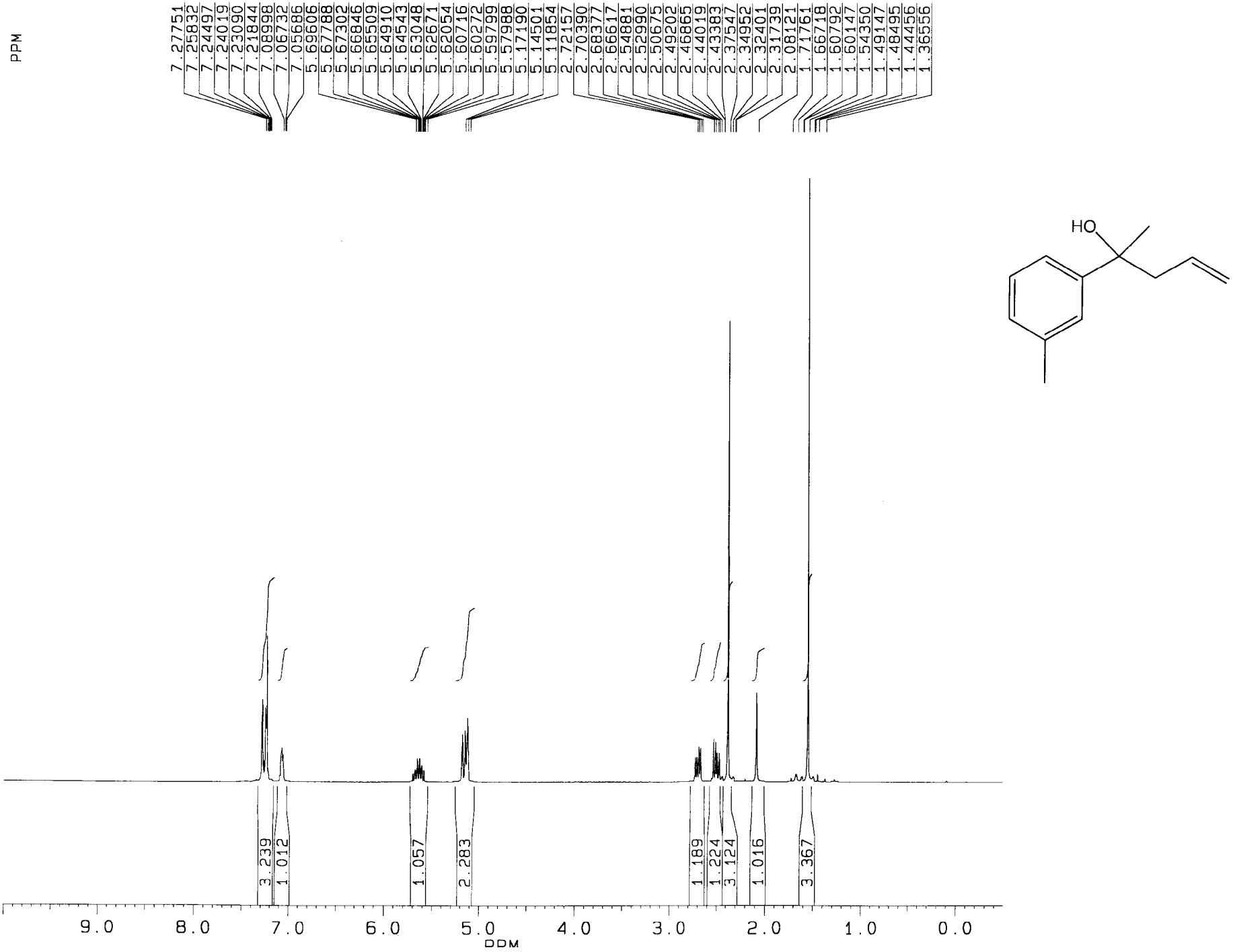

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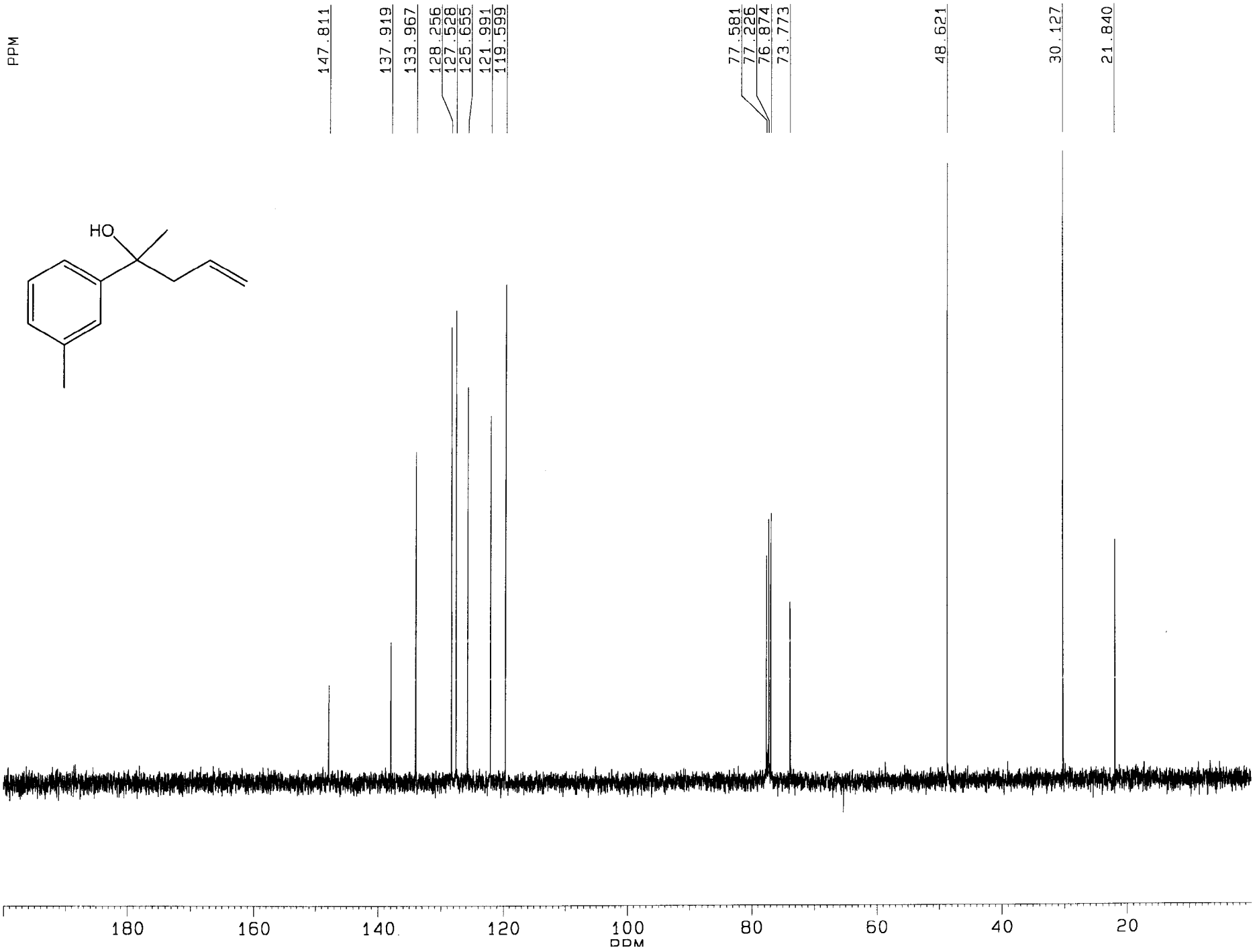

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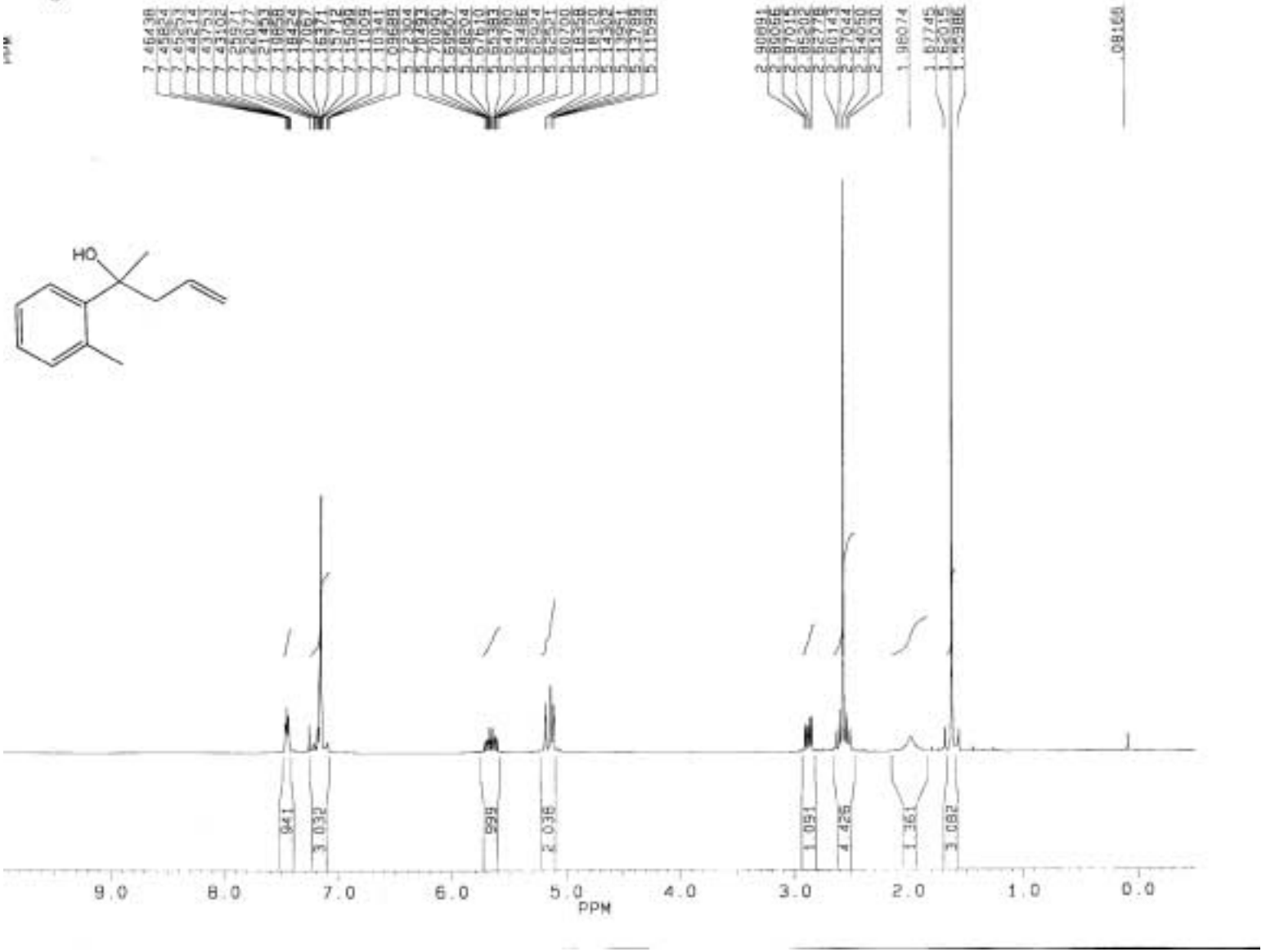

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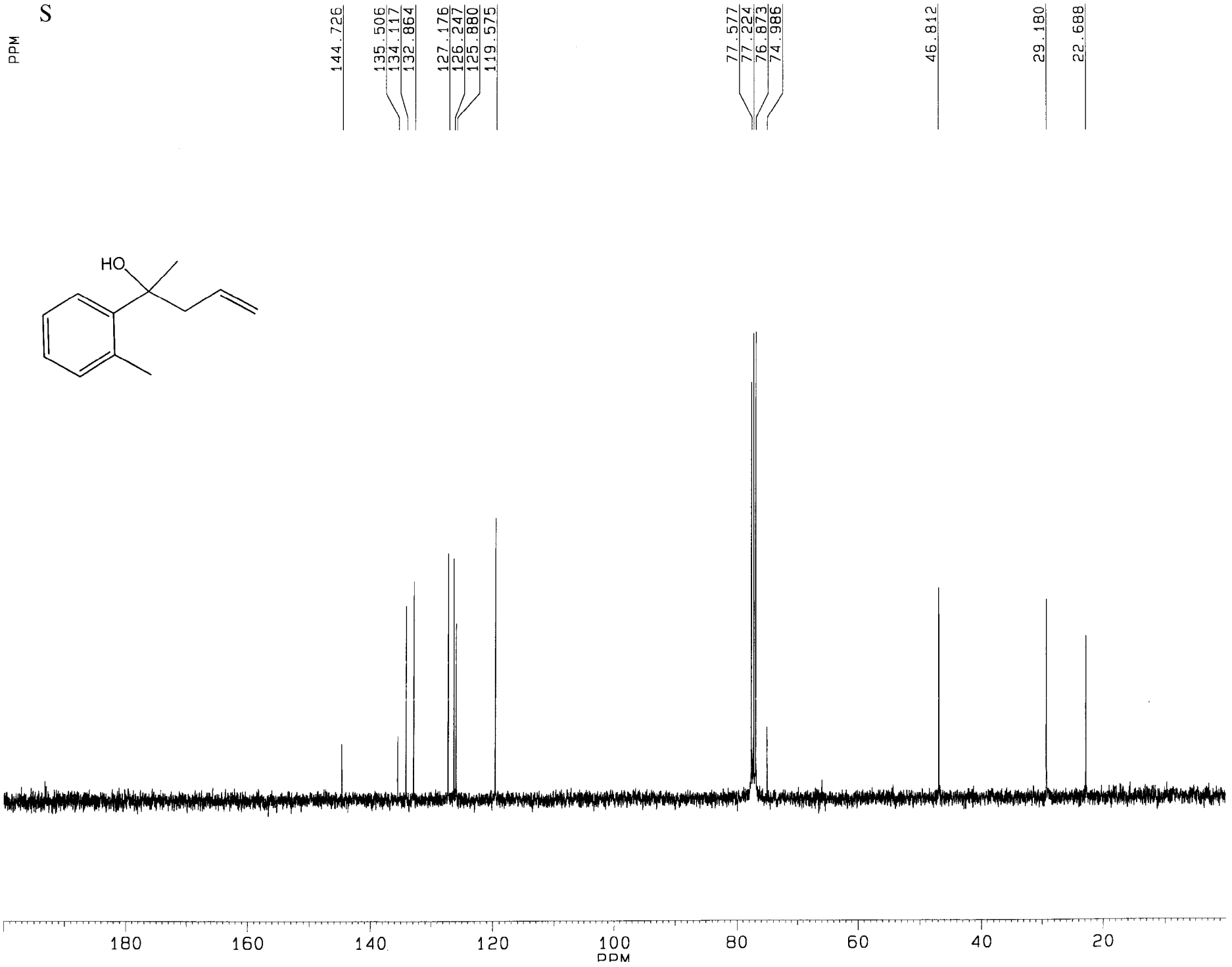
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140
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20
PPM

S

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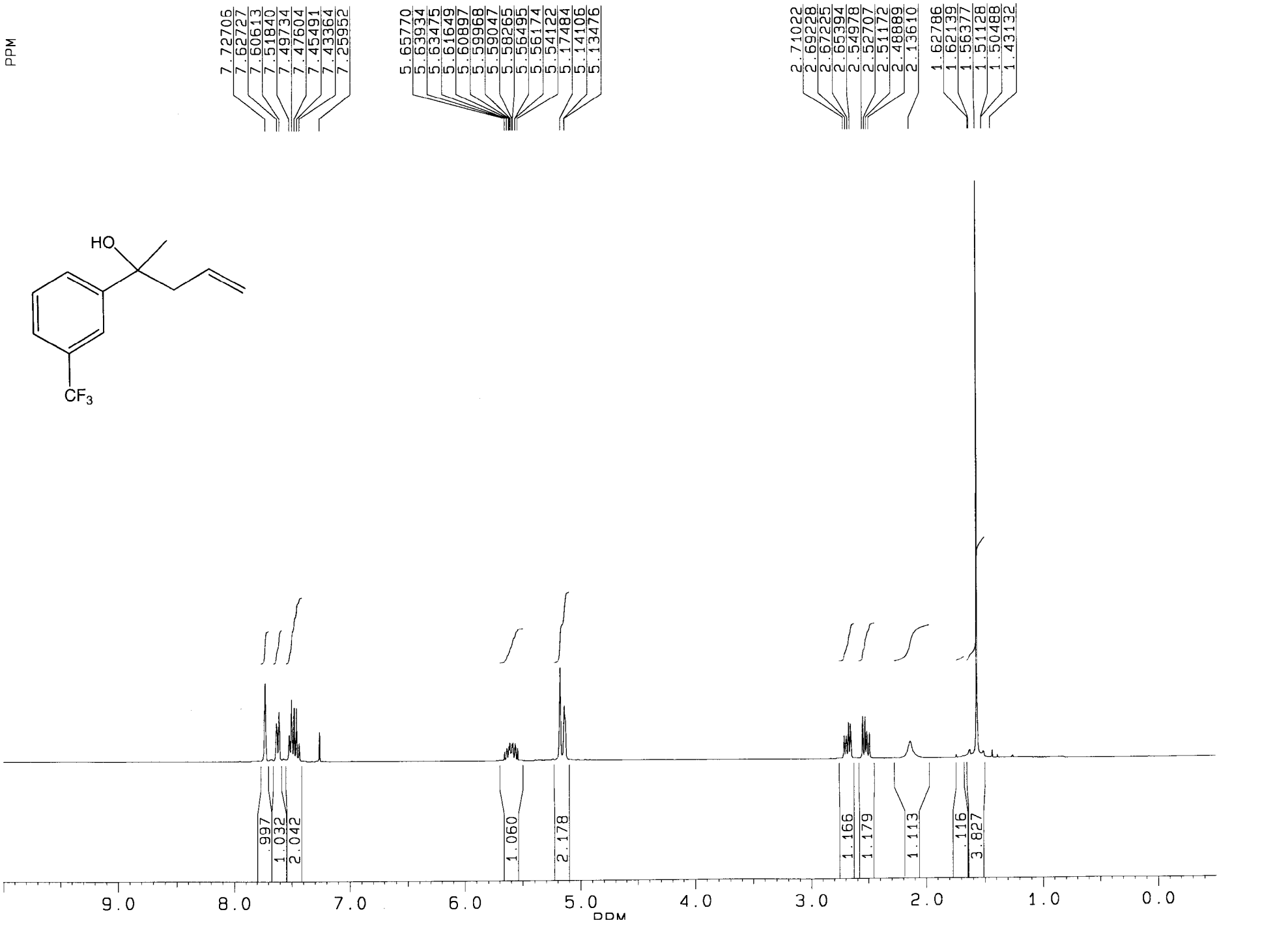

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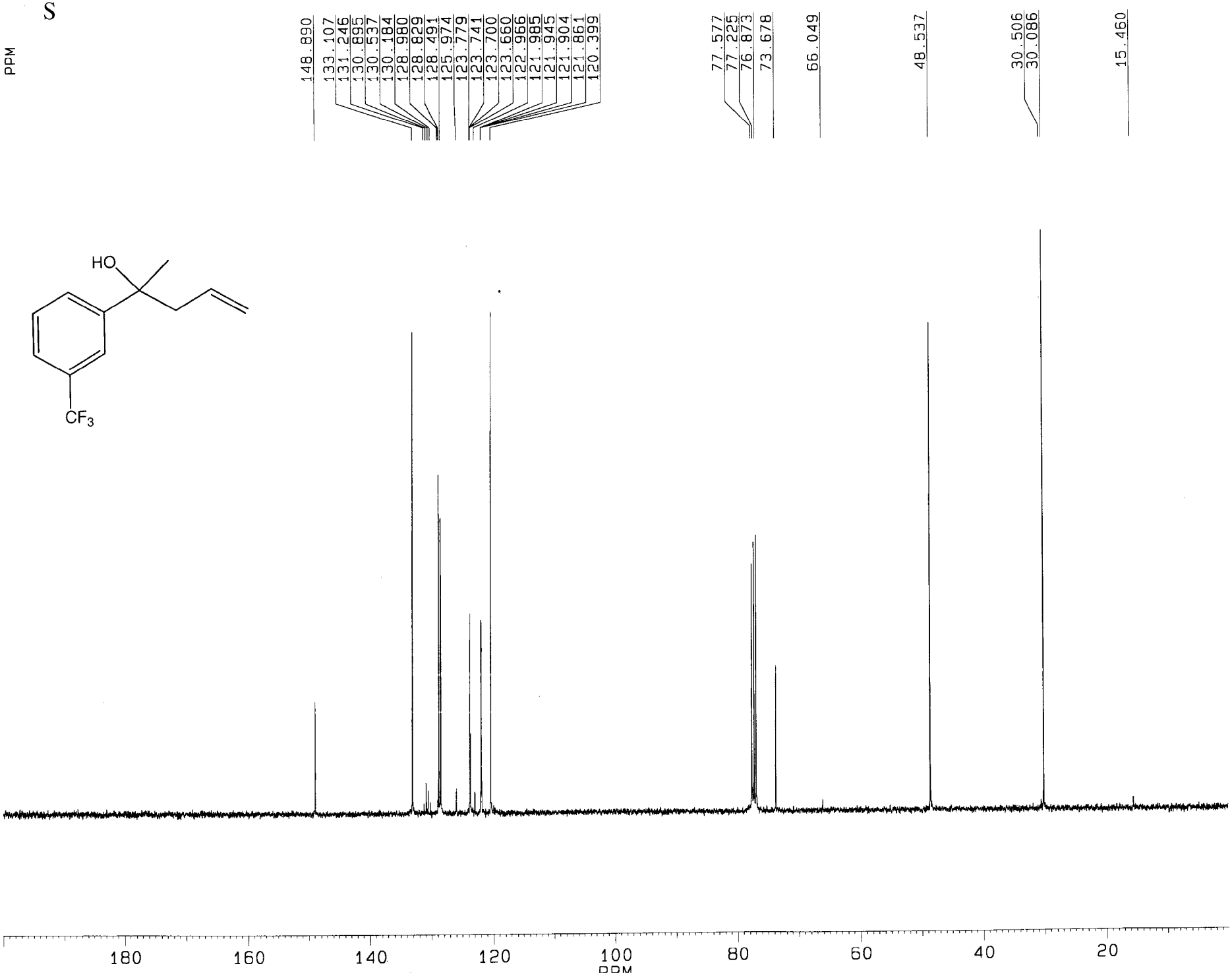
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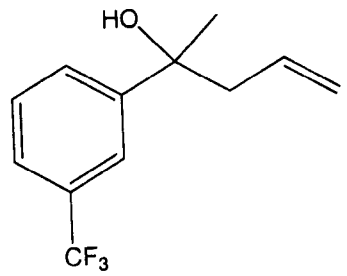
S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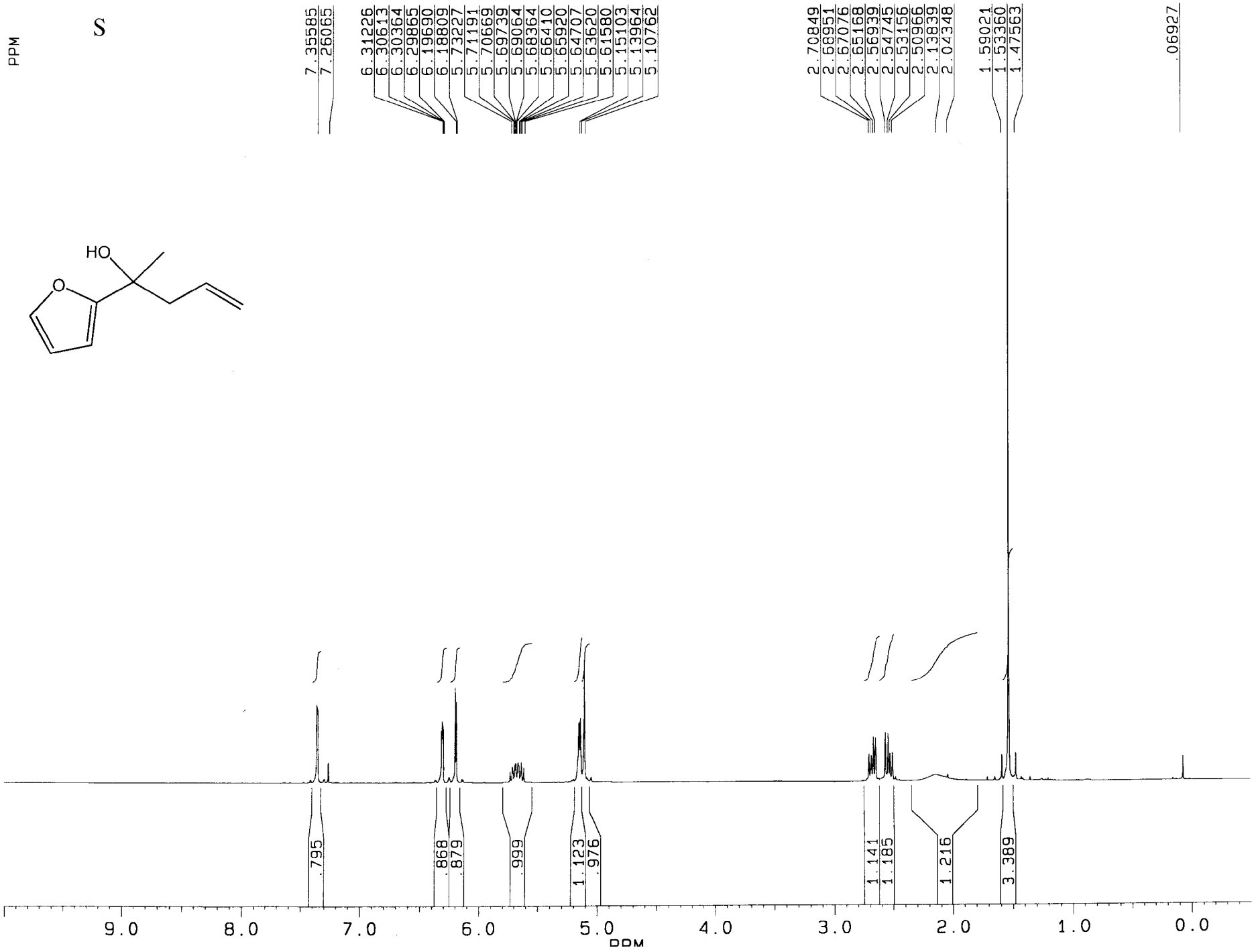
PPM

2-(2-furyl)-4-penten-2-ol



2-(2-furyl)-4-penten-2-ol