Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

Iridium-Catalyzed Asymmetric Allylic Etherification Using Aliphatic Alcohols

Satoshi Ueno and John F. Hartwig*

Department of Chemistry, University of Illinois, 600 South Mathews Avenue,

Urbana, Illinois 61801

jhartwig@uiuc.edu

Table of Contents

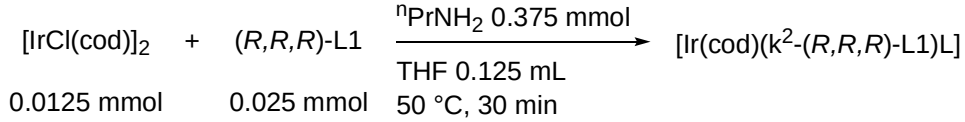
1. General Experimental Details.

All reagents were purchased from Aldrich Chemical Company, except for $IrCl_3$ which was obtained as a gift from Johnson-Matthey. n-Propyl amine was stored over KOH. THF, pentane, benzene, ether, toluene, and CH_2Cl_2 were purified by passing deoxygenated solvent (Ar) through a column of activated alumina (Solvent purification system purchased from Innovative Technologies of Newburyport, MA). All allylic alcohols were synthesized according to literature procedures.[1] All allylic acetates were synthesized by the reaction of the allyl alcohols (1.0 equiv) with acetic anhydride (1.5 equiv) in the presence of pyridine (3.0 equiv) in CH_2Cl_2 (1.0 M) solvent at 0 °C to room temperature. The complex $[IrCl(cod)]_2$ was synthesized according to the procedure of Crabtree.[2] Phosphoramidite ligands were synthesized according to the published procedures.[3]

GCMS analyses were performed on an Agilent 6890N GC equipped with a 5973 MS and an HP-5ms column (30 m x 0.25 mm ID x 0.25 μm film). GC analyses were obtained on an Agilent 6890 GC equipped with an HP-5 column (25 m x 0.20 mm ID x 0.33 μm film) and an FID detector. In both cases, the temperature program was 100 °C for 2 min, followed by a ramp from 100 - 260 °C at 30 °/min and a constant temperature of 260 °C for 3 min. Optical rotations were measured on a JASCO DIP-360. IR spectra were obtained of thin films on NaCl plates using a Perkin-Elmer Spectrum BX FT-IR instrument. NMR spectra were acquired on 400 MHz Varian Unity or Innova instruments (University of Illinois VOICE NMR facility). Chemical shifts are reported in ppm relative to internal standard or residual solvent peak (tetramethylsilane δ 0.00 ppm for ^1H NMR spectra, and $CDCl_3$ δ 77.00 ppm for ^{13}C NMR spectra). ^1H NMR data are reported as chemical shifts in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad), coupling constants (Hz), relative intensity. HPLC analyses were carried out on a Waters chromatography system (1525 binary pump, 717+ autosampler, 2487 dual wavelength detector). Chromatography was conducted on Silicycle Siala-P Silica gel using hexanes/ether as eluent. While many products were only weakly visible on TLC by UV (256 nm) irradiation, all products were easily identified by strong staining with P/Mo/Ce. Elemental Analyses were performed by Robertson Microlit Laboratories, Inc. (Madison, NJ).

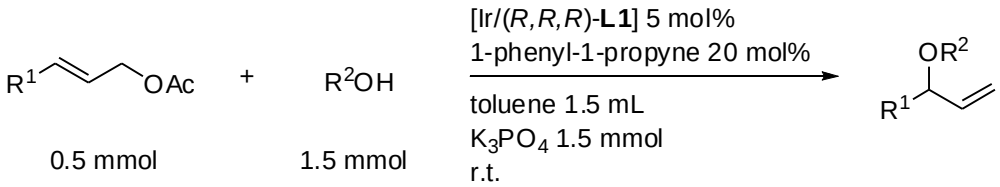
2. General Procedures

Procedure for Activation of the $[IrCl(cod)]_2$/(R,R,R)-L1 Catalyst System



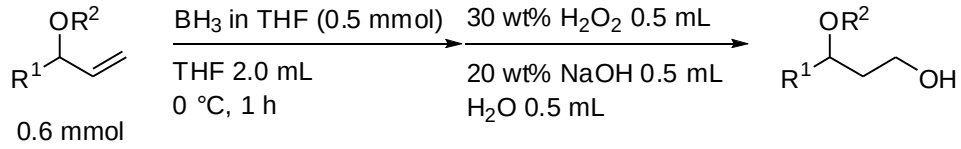
The activated, cyclometalated catalyst was prepared by a procedure our group reported recently.[4] In a drybox, $[IrCl(cod)]_2$ (MW: 671.70, 0.013 mmol = 8.4 mg) and (*R*,*R*,*R*)-L1 (MW: 539.60, 0.0250 mmol = 13.5 mg) were mixed in a screw-capped vial. THF (0.125 mL), $^{n}PrNH_2$ (MW: 59.11, 0.375 mmol = 22.2 mg) and a magnetic stirrer bar was added, and the vial was sealed with a cap containing a PTFE septum and removed from the drybox. The vial was heated in a 50 °C-oil bath for 30 min. The vial of the resulting yellow-colored solution was returned to the drybox. Ether (1.0 mL) was added to precipitate the n-propylamine hydrochloride. The solution was then filtered through a syringe tip filter (0.25 μm), and the solvent was removed under vacuum. Toluene (1 mL) was added to this vial, and the yellow solution was directly used without further purification.

Procedure for Iridium-Catalyzed Allylic Etherification



In a drybox, into a screw-capped vial was added 0.5 mL of toluene solution and K_3PO_4 (MW: 212.27, 1.500 mmol = 318.4 mg). To these materials were added the activated catalyst (0.025 mmol, generated in situ by the method shown above) dissolved in toluene (1.0 mL) and alcohol (1.5 mmol). A magnetic stir bar was added, and the vial was sealed with a cap containing a PTFE septum and removed from the drybox. 1-Phenyl-1-propyne (MW: 116.16, 0.100 mmol = 12.5 μL) and allyl acetate (0.50 mmol) were added by syringe, and the resulting suspension was stirred vigorously at room temperature (23 °C). When the reaction was complete, as determined by GC, the crude mixture was passed through a pad of silica gel, eluting with 100 mL of ether. The resulting solutions were evaporated. The ratio of regioisomers was determined by ^1H NMR spectroscopy (usually based on integration of the olefinic protons). The mixture was then purified by flash column chromatography on silica gel to give the desired product.

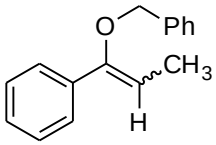
Procedure for Hydroboration and Oxidation.



To measure the ee of some allylic ethers, it was necessary to convert the products to the corresponding terminal alcohol. This conversion was accomplished by hydroboration and oxidation following literature procedures.[5] A portion of the product (0.6 mmol) was dissolved in THF (2.0 mL), cooled to 0 °C, and treated with 0.5 mL of a solution of BH_3 in THF (1.0 M, 0.5 mmol). After 1 h, H_2O (0.5 mmol) was added, and the reaction was stirred for another 30 min before adding aqueous NaOH (20 wt% in H_2O, 0.5 mL) and H_2O_2 (30 wt%, 0.5 mL). The reaction was then warmed to room temperature over 1 h. To this warmed solution was added saturated aqueous K_2CO_3 (25 mL) and water (50 mL). The resulting aqueous solution was washed with CH_2Cl_2 (2 x 50 mL), and the combined organic layers were dried over $MgSO_4$, evaporated, and purified by flash column chromatography on silica gel to give the final alcohol.

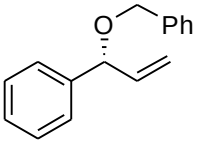
3. Characterization of reaction products

1-Phenyl-1-benzyloxy-1-propene.



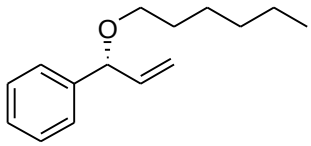
Following the general allylic etherification procedure in the absence of 1-phenyl-1-propyne at 40 °C for 20 h, the enol ether product was mainly obtained as a mixture with the saturated product (1-phenyl-1-benzyloxy-1-propane) after column chromatography (SiO_2, hexane/ether = 50/1) in ~65% combined yield. Bp 155 °C/80 mmHg. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.72 (d, *J* = 7.2 Hz, 3H), 4.67 (s, 2H), 5.40 (q, *J* = 6.8 Hz, 1H), 7.23-7.50 (m, 10H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 11.2, 72.1, 110.1, 125.9, 127.7, 127.8, 128.1, 128.3, 128.4, 136.3, 137.7, 153.8. IR (Neat) 3059 w, 3030 w, 2913 w, 2858 w, 1657 w, 1493 w, 1449 w, 1314 m, 1262 w, 1057 s, 1027 m, 761 m, 735 s, 696 s cm^{-1}. Anal. Calcd for $C_{16}H_{16}O$: C, 85.68; H, 7.19. Found: C, 85.82; H, 7.40.

(+)-1-Benzyloxy-1-allylbenzene.

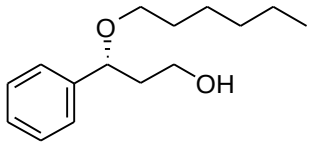


Following the general procedure for allylic etherification, the product was obtained after column chromatography (SiO_2, hexane/ether = 60/1) as a colorless oil in 68% yield. ^{1}H NMR analysis of the crude product mixture showed a branched to linear ratio of 99:1. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.52 (s, 2H), 4.83 (d, *J* = 6.80 Hz, 1H), 5.23 (dt, *J* = 10.4 Hz, *J* = 1.4 Hz, 1H), 5.29 (dt, *J* = 17.2 Hz, *J* = 1.4 Hz, 1H), 5.99 (ddd, *J* = 16.8 Hz, *J* = 10.0 Hz, *J* = 6.8 Hz, 1H), 7.25-7.39 (m, 10H). HPLC analysis indicated that the enantiomeric excess of the product was 93% [Daicel Chiralcel OJ (0.46 cm x 0.25 cm), hexanes:2-propanol = 99.8:0.2, v = 0.5 mL/min, λ = 220 nm, ~25 °C, t_R [min] = 32.8 (minor), 37.9 (major)]. $[\alpha]_D^{24}$ + 8.53 (*c* = 0.77, $CHCl_3$).

(-)-1-Hexyloxyallylbenzene.



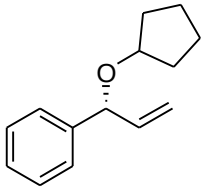
Following the general procedure for allylic etherification, the product was obtained after column chromatography (SiO_2, hexane/ether = 70/1) as a colorless oil in 71% yield. R_f = 0.74 (hexane/ether = 5/1). ^{1}H NMR analysis of the crude product mixture showed a branched to linear ratio of 99:1. Bp. 159 °C/80 mmHg. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.88 (t, *J* = 13.6 Hz, 3H), 1.23-1.39 (m, 6H), 1.57-1.65 (m, 2H), 3.33-3.39 (m, 1H), 3.42-3.49 (m, 1H), 4.72 (d, *J* = 6.4 Hz, 1H), 5.18 (dd, *J* = 10.4 Hz, *J* = 6.4 Hz, 1H), 5.25 (d, *J* = 17.2 Hz, 1H), 5.94 (ddd, *J* = 16.8 Hz, *J* = 10.0 Hz, *J* = 6.8 Hz, 1H), 7.24-7.25 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.1, 22.6, 25.9, 29.8, 31.7, 68.7, 82.9, 115.9, 126.7, 127.5, 128.4, 139.3, 141.4. IR (Neat) 3028 w, 2955 s, 2931 s, 2858 s, 1453 m, 1304 w, 1095 s, 1029 w, 990 m, 923 m, 758 m, 700 s cm^{-1}. Anal. Calcd for $C_{15}H_{22}O$: C, 82.52; H, 10.16. Found: C, 82.37; H, 10.53 $[\alpha]_D^{24}$ – 1.18 (*c* = 0.90, $CHCl_3$)..



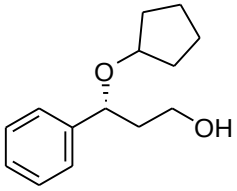
To measure the ee of 1-hexyloxyallylbenzene, it was converted to (-)-3-hexyloxy-3-phenylpropan-1-ol using the general procedure for hydroboration and oxidation. The product was isolated by column chromatography (SiO_2, hexane/ether = 1/1) as a clear oil. HPLC analysis indicated that the enantiomeric excess of the product was 91% [Daicel Chiralcel OJ (0.46 cm x 0.25 cm), hexanes:2-propanol = 97:3, v = 1.0 mL/min, λ = 210 nm, ~25 °C, t_R [min] = 4.8 (major), 5.4 (minor)]. Bp. 210 °C/80 mmHg. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.87 (t, *J* = 14.0 Hz, 3H), 1.20-1.35 (m, 6H), 1.43-1.60 (m, 2H), 1.83-1.89 (m, 1H), 1.89-2.05 (m, 1H), 2.96 (dd, *J* = 6.8 Hz, *J* = 4.0 Hz, 1H), 3.24-3.37 (m, 2H), 3.77-3.85 (m, 2H), 4.50 (dd, *J*

= 9.2 Hz, *J* = 3.6 Hz, 1H), 7.26-7.38 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.0, 22.6, 25.8, 29.8, 31.6, 40.4, 61.6, 69.1, 82.8, 126.3, 127.6, 128.5, 142.1. IR (Neat) 3391 brm, 3062 w, 3029 w, 2930 s, 2859 s, 1492 w, 1349 w, 1308 w, 1101 s, 1054 s, 758 m, 701 s cm^{-1}. Anal. Calcd for $C_{15}H_{24}O_2$: C, 76.23; H, 10.24. Found: C, 76.04; H, 10.52. $[\alpha]_D^{24}$ – 46.02 (*c* = 0.76, $CHCl_3$).

(-)-1-Cyclopentyloxyallylbenzene.

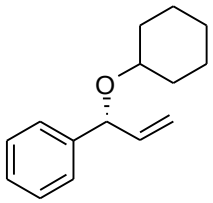


Following the general procedure for allylic etherification, but using 5 equiv of cyclopentanol and 5 equiv of K_3PO_4, the product was obtained after column chromatography (SiO_2, hexane/ether = 60/1) as a colorless oil in 72% yield. ^{1}H NMR analysis of the crude product mixture showed a branched to linear ratio of 89:11. Bp. 150 °C/80 mmHg. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.43-1.55 (m, 2H), 1.64-1.79 (m, 6H), 3.96-4.02 (m, 1H), 4.80 (d, *J* = 6.8 Hz, 1H), 5.17 (dt, *J* = 10.4 Hz, *J* = 1.0 Hz, 1H), 5.24 (dt, *J* = 17.2 Hz, *J* = 1.2 Hz, 1H), 5.94 (ddd, *J* = 16.8 Hz, *J* = 10.0 Hz, *J* = 6.4 Hz, 1H), 7.24-7.35 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.5, 23.6, 32.3, 32.5, 78.7, 80.5, 115.7, 126.8, 127.3, 128.3, 139.6, 141.7. IR (Neat) 3062 w, 3027 w, 2958 s, 2870 m, 1491 w, 1451 m, 1340 w, 1325 w, 1305 w, 1196 w, 1176 w, 1124 m, 1087 s, 1057 s, 1029 m, 991 m, 923 s, 756 m, 700 s cm^{-1}. Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 83.51; H, 8.75. $[\alpha]_D^{24}$ – 3.24 (*c* = 0.29, $CHCl_3$).

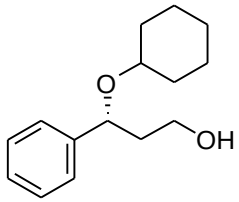


To measure the ee of 1-cyclopentyloxyallylbenzene, it was converted to (+)-3-cyclopentyloxy-3-phenylpropan-1-ol using the general procedure for hydroboration and oxidation. The product was isolated by column chromatography (SiO_2, hexane/ether = 1/1) as a clear oil. HPLC analysis indicated that the enantiomeric excess of the product was 95% [Daicel Chiralcel OJ (0.46 cm x 0.25 cm), hexanes/2-propanol = 90/10, v = 1.0 mL/min, λ = 210 nm, ~25 °C, t_R [min] = 4.55 (major), 6.49 (minor)]. Bp. 210 °C/80 mmHg. $[\alpha]_D^{24}$ + 60.72 (*c* = 0.45, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.43-1.77 (m, 8H), 1.80-1.88 (m, 1H), 1.93-2.03 (m, 1H), 3.03 (brs, 1H), 3.75-3.85 (m, 3H), 4.58 (dd, *J* = 9.6 Hz, *J* = 4.0 Hz, 1H), 7.26-7.38 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.4, 23.4, 31.5, 33.3, 40.5, 61.7, 78.9, 80.2, 126.4, 127.5, 128.4, 142.4. IR (Neat) 3399 brm, 3061 w, 3027 w, 2955 s, 2870 s, 1492 w, 1452 m, 1345 m, 1173 w, 1054 s, 756 m, 701 s cm^{-1}. Anal. Calcd for $C_{14}H_2O_2$: C, 76.33; H, 9.15. Found: C, 76.18; H, 9.43.

(+)-1-Cyclohexyloxyallylbenzene.

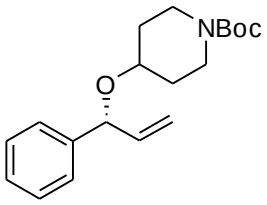


Following the general procedure for allylic etherification, but using 5 equiv of cyclo-hexanol and 5 equiv of K_3PO_4, the product was obtained after column chromatography (SiO_2, hexane/ether = 70/1) as a colorless oil in 68% yield. ^{1}H NMR analysis of the crude product mixture showed a branched to linear ratio of 99:1. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.17-1.43 (m, 5H), 1.50-1.52 (m, 1H), 1.67-1.77 (m, 2H), 1.84 (d, *J* = 11.2 Hz, 1H), 1.94 (d, *J* = 11.2 Hz, 1H), 3.34 (ddd, *J* = 13.2 Hz, *J* = 9.2 Hz, *J* = 4.0 Hz, 1H), 4.92 (d, *J* = 6.8 Hz, 1H), 5.15 (dt, *J* = 10.4 Hz, *J* = 1.2 Hz, 1H), 5.23 (dt, *J* = 17.2 Hz, *J* = 1.4 Hz, 1H), 5.94 (ddd, *J* = 17.2 Hz, *J* = 10.4 Hz, *J* = 6.4 Hz, 1H), 7.23-7.37 (m, 5H). $[\alpha]_D^{24}$ + 5.13 (*c* = 0.70, $CHCl_3$).



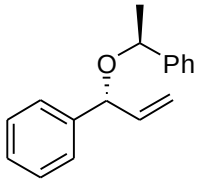
To measure the ee of 1-cyclohexyloxyallylbenzene, the allylic ether was converted to (+)-3-Cyclohexyloxy-3-phenylpropan-1-ol using the general procedure for hydroboration and oxidation. The product was isolated by column chromatography (SiO_2, hexane/ether = 1/1) as a clear oil. HPLC analysis indicated that the enantiomeric excess of the product was 93% [Daicel Chiralcel OJ (0.46 cm x 0.25 cm), hexanes:2-propanol = 95:5, v = 1.0 mL/min, λ = 210 nm, ~25 °C, t_R [min] = 5.01 (major), 6.48 (minor)]. Bp. 220 °C/80 mmHg. $[\alpha]_D^{24}$ + 155.41 (*c* = 0.53, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.12-1.36 (m, 5H), 1.46-1.50 (m, 1H), 1.62-1.73 (m, 3H), 1.81-1.88 (m, 1H), 1.94-2.03 (m, 2H), 3.17-3.23 (m, 2H), 3.76-3.81 (m, 2H), 4.71 (dd, *J* = 9.2 Hz, *J* = 4.0 Hz, 1H), 7.26-7.37 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.8, 24.1, 25.6, 31.1, 33.4, 40.6, 61.5, 74.9, 79.0, 126.3, 127.4, 128.3, 142.8. IR (Neat) 3411 brs, 2931 s, 2856 m, 1451 w, 1058 m, 1026 w, 657 w, 701 m cm^{-1}. Anal. Calcd for $C_{15}H_{22}O$: C, 76.88; H, 9.46. Found: C, 76.76; H, 9.71.

(+)-4-(1-Phenylallyloxy)piperidine-1-carboxylic acid tert-butyl ester.



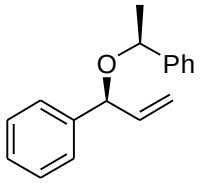
Following the general procedure for allylic etherification, the product was obtained after column chromatography (SiO_2, hexane/ether = 3/1) as a colorless oil in 66% yield. ^{1}H NMR analysis of the crude product mixture showed a branched to linear ratio of 99:1. $[\alpha]_D^{24}$ + 10.18 (*c* = 0.14, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.44 (s, 9H), 1.53-1.64 (m, 2H), 1.70-1.79 (m, 1H), 1.80-1.88 (m, 1H), 3.04-3.15 (m, 2H), 3.57 (sept, *J* = 3.9 Hz, 1H), 3.75 (m, 3.65-3.85 (m, 2H), 4.91 (d, *J* = 6.4 Hz, 1H), 5.17 (d, *J* = 10.4 Hz, 1H), 5.25 (d, *J* = 17.6 Hz, 1H), 5.93 (ddd, *J* = 17.2 Hz, *J* = 10.4 Hz, *J* = 6.4 Hz, 1H), 7.23-7.32 (m, 1H), 7.34 (d, *J* = 4.4 Hz, 4H). HPLC analysis indicated that the enantiomeric excess of the product was 90% [Daicel Chiralcel OD-H (0.46 cm x 0.25 cm), hexanes:2-propanol = 97:3, v = 0.6 mL/min, λ = 220 nm, ~25 °C, t_R [min] = 8.3 (major), 9.1 (minor)].

(-)-1-Phenylethoxy-1-allylbenzene.



Following the general procedure for allylic etherification, the product was obtained as a mixture of diastereomers by column chromatography (SiO_2, hexane/ether = 60/1) as a colorless oil in 67% yield and 88% de. R_f = 0.61 (hexane/ether = 5/1). ^{1}H NMR analysis of the crude product mixture showed a branched to linear ratio of >99:1. Bp. 190 °C/80 mmHg. $[\alpha]_D^{24}$ – 31.13 (*c* = 0.67, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.49 (d, *J* =6.8 Hz, 3H), 4.63-4.71 (m, 2H), 5.25 (d, *J* =18.4 Hz, 1H), 5.28 (d, *J* =10.8 Hz, 1H), 5.91 (ddd, *J* = 18.0 Hz, 10.0 Hz, 8.0 Hz, 1H), 7.22-7.34 (m, 10H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.2, 74.5, 79.5, 117.2, 126.4, 126.6, 127.3, 127.4, 128.3, 128.4, 138.4, 141.4, 143.8. IR (Neat) 3062 w, 3028 w, 2975 m, 1492 w, 1451 m, 1371 w, 1303 w, 1283 w, 1208 w, 1088 s, 1046 m, 1029 m, 991 m, 927 m, 761 m, 700 s cm^{-1}. Anal. Calcd for $C_{17}H_{18}O$: C, 85.67; H, 7.61. Found: C, 85.96; H, 7.91.

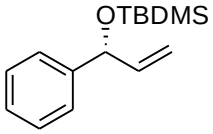
(-)-1-Phenylethoxy-1-allylbenzene.



Following the general procedure for allylic etherification, the diastereomeric mixture of products was obtained as a colorless oil after column chromatography (SiO_2, hexane/ether = 60/1) in 63% yield and 90% de. R_f = 0.61 (hexane/ether = 5/1). ^{1}H NMR analysis of the crude product mixture showed a branched to linear ratio of >99:1. Bp. 190 °C/80 mmHg. $[\alpha]_D^{24}$ – 86.56 (*c* = 0.67, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.41 (d, *J* = 6.8 Hz, 3H), 4.37 (q, *J* =

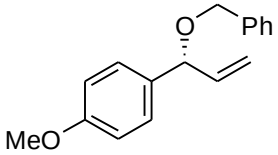
6.4 Hz, 1H), 4.65 (d, *J* = 6.0 Hz, 1H), 5.06-5.16 (m, 2H), 5.96 (ddd, *J* = 17.2 Hz, *J* = 10.4 Hz, *J* = 6.0 Hz, 1H), 7.25-7.38 (m, 10H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.4, 74.5, 79.5, 115.3, 126.3, 127.2, 127.4, 127.6, 128.4, 128.5, 139.4, 141.0, 143.8. IR (Neat) 3062 w, 3028 w, 2976 m, 2875 w, 1491 w, 1451 m, 1370 w, 1301 w, 1088 s, 1031 m, 991 m, 923 m, 761 s, 701 s cm^{-1}. Anal. Calcd for $C_{17}H_{18}O$: C, 85.67; H, 7.61. Found: C, 85.72; H, 7.93.

(+)-tert-Butyldimethyl(1-phenylallyloxy)silane.



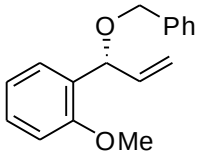
Following the general procedure for allylic etherification, the product was obtained after column chromatography (SiO_2, hexane/ether = 60/1) as a colorless oil in 85% yield. ^{1}H NMR analysis of the crude product mixture showed a branched to linear ratio of 98:2. $[\alpha]_D^{24}$ + 5.36 (*c* = 0.16, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.00 (s, 3H), 0.08 (s, 3H), 0.92 (s, 9H), 5.07 (dt, *J* = 10.0 Hz, *J* = 1.6 Hz, 1H), 5.17 (d, *J* = 5.6 Hz, 1H), 5.29 (dt, *J* = 17.2 Hz, *J* = 1.6 Hz, 1H), 5.92 (ddd, *J* = 16.0 Hz, *J* = 10.4 Hz, *J* = 6.0 Hz, 1H), 7.20-7.27 (m, 1H), 7.30-7.36 (m, 4H).

(-)-1-(1-Benzyloxyallyl)-4-methoxybenzene.



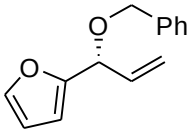
Following the general procedure for allylic etherification, the product was obtained after column chromatography (SiO_2, hexane/ether = 30/1) as a colorless oil in 82% yield. R_f = 0.43 (hexane/ether = 5/1). ^{1}H NMR analysis of the crude product mixture showed a branched to linear ratio of >99:1. Bp. 190 °C/80 mmHg. $[\alpha]_D^{24}$ – 60.72 (*c* = 0.45, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.37 (s, 3H), 4.49 (s, 2H), 4.78 (d, *J* = 6.8 Hz, 1H), 5.20 (d, *J* = 10.0 Hz, 1H), 5.26 (d, *J* = 17.6 Hz, 1H), 5.98 (ddd, *J* = 17.2 Hz, *J* = 10.4 Hz, *J* = 6.4 Hz, 1H), 6.89 (d, *J* =8.8 Hz, 2H), 7.25-7.34 (m, 7H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 55.2, 69.8, 81.4, 113.8, 116.1, 127.4, 127.6, 128.2, 128.3, 132.9, 138.5, 139.0 159.0. IR (Neat) 3063 w, 3030 w, 2953 w, 2933 w, 2906 w, 2859 w, 2835 m, 1610 s, 1585 w, 1511 s, 1497 m, 1464 m, 1454 m, 1442 w, 1419 w, 1388 w, 1335 w, 1303 m, 1248 s, 1201 s, 1173 s, 1106 s, 1088 s, 1066 s, 1035 s, 991 m, 926 m, 849 w, 830 s, 736 m, 698 s, 614 w cm^{-1}. Anal. Calcd for $C_{17}H_{18}O$: C, 80.28; H, 7.13. Found: C, 80.43; H, 7.35. HPLC analysis of the purified product indicated that the enantiomeric excess was 92% [Daicel Chiralcel OJ (0.46 cm x 0.25 cm), hexanes:2-propanol = 99.7:0.3, v = 1.0 mL/min, λ = 220 nm, ~25 °C, t_R [min] = 38.9 (major), 45.9 (minor)].

(+)-1-(1-Benzyloxyallyl)-2-methoxybenzene.



Following the general procedure for allylic etherification, the product was obtained after column chromatography (SiO_2, hexane/ether = 30/1) as a colorless oil in 77% yield. R_f = 0.45 (hexane/ether = 5/1). ^{1}H NMR analysis of the crude product mixture showed a branched to linear ratio of >99:1. Bp. 180 °C/80 mmHg. $[\alpha]_D^{24}$ + 11.62 (*c* = 0.88, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.81 (s, 3H), 4.52 (s, 2H), 5.15 (dt, *J* = 10.4 Hz, *J* = 1.4 Hz, 1H), 5.27-5.34 (m, 2H), 5.99 (ddd, *J* = 16.8 Hz, *J* = 10.0 Hz, *J* = 5.6 Hz, 1H), 6.88 (d, *J* = 4.8 Hz, 1H), 6.99 (dt, *J* = 7.4 Hz, *J* = 0.8 Hz, 1H), 7.23-7.38 (m, 6H), 7.49 (dd, *J* = 7.2 Hz, *J* = 1.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 55.3, 70.3, 75.5, 110.4, 115.3, 120.8, 127.2, 127.3, 127.6, 128.2, 128.5, 129.2, 138.2, 138.7, 156.8. IR (Neat) 3063 w, 3030 w, 3005 w, 2937 w, 2861 w, 2836 w, 1600 m, 1588 m, 1490 s, 1464 s, 1454 s, 1438 m, 1404 w, 1389 w, 1343 w, 1285 m, 1267 m, 1242 s, 1190 w, 1173 w, 1161 w, 1096 s, 1066 s, 1050 s, 1028 s, 990 m, 923 m, 788 w, 754 s, 736 s, 713 w, 698 s, 677 w cm^{-1}. Anal. Calcd for $C_{17}H_{18}O$: C, 80.28; H, 7.13. Found: C, 80.27; H, 7.35. HPLC analysis of the purified product indicated that the enantiomeric excess was 72% [Daicel Chiralcel OJ (0.46 cm x 0.25 cm), hexanes:2-propanol = 99.7:0.3, v = 1.0 mL/min, λ = 220 nm, ~25 °C, t_R [min] = 19.7 (minor), 28.8 (major)].

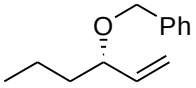
(-)-2-(1-Benzyloxyallyl)furan.



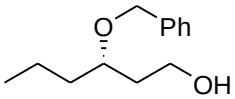
Following the general procedure for allylic etherification, the product was obtained after column chromatography (SiO_2, hexane/ether = 40/1) as a colorless oil in 67% yield. R_f = 0.52 (hexane/ether = 5/1). ^{1}H NMR analysis of the crude product mixture showed a branched to linear ratio of 96:4. Bp. 150 °C/80 mmHg. $[\alpha]_D^{24}$ – 18.24 (*c* = 0.49, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.55 (s, 2H), 4.89 (d, *J* = 6.4 Hz, 1H), 5.32 (dt, *J* = 10.4 Hz, *J* = 1.6 Hz, 1H), 5.38 (d, *J* = 15.6 Hz, *J* = 1.6 Hz, 1H), 6.08 (ddd, *J* = 17.2 Hz, *J* = 10.4 Hz, *J* = 6.8 Hz, 1H), 6.30 (d, *J* = 3.2 Hz, 1H), 6.35 (dd, *J* = 3.2 Hz, *J* = 2.0 Hz, 1H), 7.27-7.36 (m, 5H), 7.42 (dd, *J* = 1.6 Hz, *J* = 0.4 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 70.0, 74.8, 108.0, 110.1, 117.9, 127.6, 127.8, 128.3, 135.2, 138.0, 142.6, 153.4. IR (Neat) 3030 w, 2861 w, 1497 m, 1453 m, 1306 w, 1271 w, 1227 w, 1205 w, 1150 s, 1107 m, 1084 s, 1064 s, 1028 s, 1012 s, 990 s, 932 m, 918 m, 814 w, 796 m, 737 s, 698 s cm^{-1}. Anal. Calcd for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59. Found: C, 78.58; H, 6.89. HPLC analysis of the purified product indicated that the enantiomeric excess was 93% [HPLC (Daicel Chiralcel OD-H (0.46 cm x 0.25 cm),

hexanes/2-propanol = 99.5/0.5, v = 0.6 mL/min, λ = 220 nm, ~25 °C, t_R [min] = 39.4 (minor), 40.6 (major)].

(-)-1-Vinylbutoxymethyl-benzene.

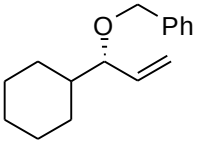


Following the general procedure for allylic etherification, the product was obtained after column chromatography (SiO_2, hexane/ether = 60/1) as a colorless oil in 68% yield. ^{1}H NMR analysis of the crude product mixture showed a branched to linear ratio of 99:1. $[\alpha]_D^{24}$ – 18.70 (*c* = 0.72, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.89 (t, *J* = 7.2 Hz, 3H), 1.33-1.49 (m, 3H), 1.57-1.66 (m, 1H), 3.73 (q, *J* = 6.7 Hz, 1H), 4.35 (d, *J* = 12.0 Hz, 1H), 4.59 (d, *J* = 12.0 Hz, 1H), 5.17-5.24 (m, 2H), 5.73 (ddd, *J* = 16.8 Hz, *J* = 10.4 Hz, *J* = 7.6 Hz, 1H), 7.24-7.45 (m, 5H).



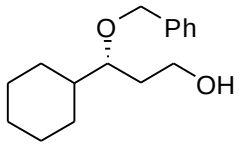
To measure the ee of 1-vinylbutoxymethylbenzene, it was converted to (+)-3-Benzyloxyhexan-1-ol using the general procedure for hydroboration and oxidation. The product was isolated by column chromatography (SiO_2, hexane/ether = 1/1) as a clear oil. Bp. 150 °C/80 mmHg. $[\alpha]_D^{24}$ + 28.00 (*c* = 0.10, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.94 (t, *J* = 7.2 Hz, 3H), 1.35-1.43 (m, 2H), 1.50-1.56 (m, 1H), 1.62-.1.84 (m, 3H), 2.47 (brs, 1H), 3.64-3.82 (m, 3H), 4.49 (d, *J* = 11.2 Hz, 1H), 4.60 (d, *J* = 11.2 Hz, 1H), 7.27-7.35 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.3, 18.4, 35.6, 35.8, 60.8, 70.9, 78.5, 127.7, 127.8, 128.4, 138.3. IR (Neat) 3400 brm, 3030 w, 2957 s, 2932 s, 2871 s, 1497 w, 1464 w, 1455 m, 1435 w, 1379 w, 1360 m, 1067 s, 1028 s, 735 s, 697 s, 609 w cm^{-1}. Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.69; H, 9.96. HPLC analysis indicated that the enantiomeric excess of the product was 84% [Daicel Chiralcel OJ (0.46 cm x 0.25 cm), hexanes:2-propanol = 97:3, v = 0.5 mL/min, λ = 210 nm, ~25 °C, t_R [min] = 17.6 (minor), 19.9 (major)].

(-)-1-Cyclohexylallyloxymethylbenzene.



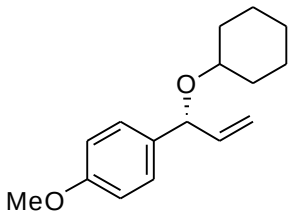
Following the general procedure for allylic etherification, the product was obtained after column chromatography (SiO_2, hexane/ether = 60/1) as a colorless oil in 57% yield. ^{1}H NMR analysis of the crude product mixture showed a branched to linear ratio of 82/18. $[\alpha]_D^{24}$ – 17.71 (*c* = 0.58, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.91-1.02 (m, 2H), 1.07-1.26 (m,

3H), 1.43-1.53 (m, 1H), 1.65-1.74 (m, 4H), 1.98 (d, *J* = 12.8 Hz, 1H), 3.42 (t, *J* = 7.6 Hz, 1H), 4.32 (d, *J* = 12.0 Hz, 1H), 4.59 (d, *J* = 12.0 Hz, 1H), 5.16 (dd, *J* = 17.2 Hz, *J* = 2.0 Hz, 1H), 5.27 (dd, *J* = 2.0 Hz, *J* = 10.0 Hz, 1H), 5.71 (ddd, *J* = 17.6 Hz, *J* = 10.4 Hz, *J* = 8.0 Hz, 1H), 7.24-7.34 (m, 5H).



To measure the ee of 1-cyclohexylallyloxymethylbenzene, the allylic ether was converted to (+)-3-Benzyloxy-3-cyclohexyl-propan-1-ol by the general procedure for hydroboration and oxidation that make the alcohol. The product was isolated by column chromatography (SiO_2, hexane/ether = 1/1) as a clear oil. Bp. 160 °C/80 mmHg. $[\alpha]_D^{24}$ + 9.96 (*c* = 0.75, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.99-1.28 (m, 5H), 1.64-1.83 (m, 8H), 2.51 (brs, 1H), 3.40-3.45 (m, 1H), 3.70-3.79 (m, 2H), 4.49 (d, *J* = 11.2 Hz, 1H), 4.59 (d, *J* = 11.2 Hz, 1H), 7.25-7.35 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 26.3, 26.4, 26.6, 27.8, 29.3, 32.3, 40.4, 61.0, 71.7, 83.0, 127.6, 127.8, 128.4, 138.4. IR (Neat) 3390 brw, 2925 s, 2852 s, 1451 m, 1090 m, 1059 m, 1028 m, 734 w, 696 m cm^{-1}. Anal. Calcd for $C_{16}H_{24}O_2$: C, 77.38; H, 9.74. Found: C, 77.17; H, 9.80. HPLC analysis indicated that the enantiomeric excess of the product was 93% [Daicel Chiralcel OJ-H (0.46 cm x 0.25 cm), hexanes:2-propanol = 98.8:1.2, v = 1.0 mL/min, λ = 210 nm, ~25 °C, t_R [min] = 12.9 (minor), 13.8 (major)].

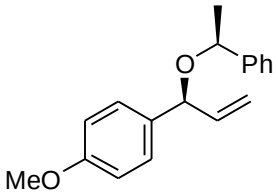
(-)-1-(1-Cyclohexyloxyallyl)-4-methoxybenzene.



Following the general procedure for allylic etherification, using 5 equiv of cyclohexanol and 5 equiv of K_3PO_4, the product was obtained after column chromatography (SiO_2, hexane/ether = 60/1) as a colorless oil in 75% yield. ^1H NMR analysis of the crude product mixture showed a branched to linear ratio of 99:1. $[\alpha]_D^{24}$ + 6.81 (*c* = 0.58, $CHCl_3$). (Although the optical rotation of this compounds was – 11.1 (*c* = 2.57, $CHCl_3$) in our previous report, the opposite rotation of the same magnitude was observed in the current work.) ^1H NMR ($CDCl_3$, 400 MHz) δ 1.16-1.40 (m, 5H), 1.49-1.51 (m, 1H), 1.69-1.76 (m, 2H), 1.81-1.84 (m, 1H), 1.91-1.95 (m, 1H), 3.28-3.35 (m, 1H), 3.80 (s, 3H), 4.88 (d, *J* = 6.9 Hz, 1H), 5.13 (dt, *J* = 10.0 Hz, *J* = 1.6 Hz, 1H), 5.20 (dt, *J* = 17.2 Hz, *J* = 1.4 Hz, 1H), 5.94 (ddd, *J* = 17.2 Hz, *J* = 10.4 Hz, *J* = 6.8 Hz, 1H), 6.87 (dt, *J* = 8.4 Hz, *J* = 5.2 Hz, 2H), 7.27 (dt, *J* = 8.4 Hz, *J* = 2.6 Hz, 2H). HPLC analysis indicated that the enantiomeric excess of the product was 94%

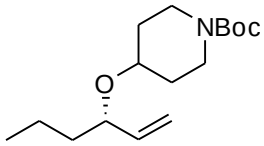
[Daicel Chiralcel OD-H (0.46 cm x 0.25 cm), hexanes:2-propanol = 99.95:0.05, v = 0.7 mL/min, λ = 220 nm, ~25 °C, t_R [min] = 13.1 (minor), 14.3 (major)].

(-)-1-Methoxy-4-[1-(1-phenylethoxy)allyl]benzene.



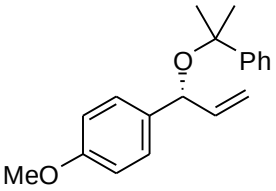
Following the general procedure for allylic etherification, the diastereomeric mixture of products were obtained by column chromatography (SiO_2, hexane/ether = 35/1) as a colorless oil in 83% yield and 96% de. R_f = 0.68 (hexane/ether = 5/1). ^{1}H NMR analysis of the crude product mixture showed a branched to linear ratio of >99:1. Bp. 190 °C/80 mmHg. $[\alpha]_D^{24}$ – 97.06 (*c* = 1.27, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.40 (d, *J* = 6.4 Hz, 3H), 3.82 (s, 3H), 4.35 (q, *J* = 6.5 Hz, 1H), 4.60 (d, *J* = 5.6 Hz, 1H), 5.05-5.14 (m, 2H), 5.96 (ddd, *J* = 17.2 Hz, *J* = 10.4 Hz, *J* = 5.6 Hz, 1H), 6.90 (dt, *J* = 6.9 Hz, *J* = 2.4 Hz, 2H), 7.18-7.22 (m, 2H), 7.26-7.38 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.5, 55.2, 74.2, 78.9, 113.8, 115.1, 126.3, 127.3, 128.4, 128.5, 133.0, 139.6, 143.9, 159.1. IR (Neat) 3061 w, 2973 m, 2929 w, 2834 w, 1609 s, 1585 w, 1510 s, 1492 w, 1452 m, 1370 w, 1302 m, 1281 w, 1246 s, 1202 w, 1172 s, 1087 s, 1035 s, 990 w, 924 w, 830 m, 761 w, 701 s cm^{-1}. Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.84; H, 7.69.

(-)-4-(1-Vinylbutoxy)piperidine-1-carboxylic acid tert-butyl ester.



Following the general procedure for allylic etherification, using 5 equiv of 4-vinylbutoxypiperidine-1-carboxylic acid tert-butyl ester and 5 equiv of K_3PO_4, the product was obtained after column chromatography (SiO_2, hexane/ether = 60/1) as a colorless oil in 40% yield. ^{1}H NMR analysis of the crude product mixture showed a branched to linear ratio of 99:1. $[\alpha]_D^{24}$ – 14.65 (*c* = 0.58, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.91 (t, *J* = 6.8 Hz, 3H), 1.29-1.61 (m, 6H), 1.45 (s, 9H), 1.76 (brs, 2H), 3.08 (m, 2H), 3.51 (sept, *J* = 3.9 Hz, 1H), 3.65-3.83 (m, 3H), 5.10-5.20 (m, 2H), 5.70 (ddd, *J* = 17.6 Hz, *J* = 10.4 Hz, *J* = 7.6 Hz, 1H). HPLC analysis indicated that the enantiomeric excess of the product was 94% [Daicel Chiralcel OD-H (0.46 cm x 0.25 cm), hexanes:2-propanol = 99.75:0.25, v = 0.6 mL/min, λ = 210 nm, ~25 °C, t_R [min] = 12.0 (minor), 13.6 (major)].

(+)-1-Methoxy-4-[1-(1-methyl-1-phenylethoxy)allyl]benzene.



Following the general procedure for allylic etherification, using 5 equiv of 2-phenyl-2-propanol and 5 equiv of K_3PO_4 at 40 °C, the product was obtained by column chromatography (SiO_2, hexane/ether = 40/1) as a colorless oil in 56% yield. R_f = 0.64 (hexane/ether = 5/1). ^{1}H NMR analysis of the crude product mixture showed a branched to linear ratio of >99:1. HPLC analysis of the purified product indicated that the enantiomeric excess was 97%. [Daicel Chiralcel OD-H (0.46 cm x 0.25 cm), hexanes:2-propanol = 99.9:0.1, v = 1.0 mL/min, λ = 220 nm, ~25 °C, t_R [min] = 8.22 (minor), 9.88 (major)]. Bp. 200 °C/80 mmHg. $[\alpha]_D^{24}$ + 62.26 (*c* = 0.58, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.43 (s, 3H), 1.56 (s, 3H), 3.79 (s, 3H), 4.63 (d, *J* = 5.6 Hz, 1H), 4.98 (dt, *J* = 4.4 Hz, *J* = 1.6 Hz, 1H), 5.01 (dt, *J* = 11.6 Hz, *J* = 1.6 Hz, 1H), 5.91 (ddd, *J* = 17.2 Hz, *J* = 10.4 Hz, *J* = 5.6 Hz, 1H), 6.82 (dt, *J* = 8.8 Hz, *J* = 2.8 Hz, 2H), 7.14-7.17 (m, 2H), 7.22-7.27 (m, 1H), 7.28-7.33 (m, 2H), 7.42-7.46 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 28.4, 30.5, 55.2, 76.2, 78.5, 113.5, 113.7, 126.2, 126.9, 127.7, 127.9, 135.8, 141.5, 146.5, 158.5. IR (Neat) 3059 w, 2978 m, 2932 w, 2834 w, 1610 m, 1585 w, 1510 s, 1463 m, 1381 w, 1363 w, 1301 m, 1246 s, 1156 s, 1101 m, 1074 w, 1036 s, 992 w, 921 w, 853 w, 826 m, 765 m, 700 s cm-^{1}. Anal. Calcd for $C_{19}H_{22}O_2$: C, 80.82; H, 7.85. Found: C, 81.11; H, 8.04.

5. References.

(1) Blanchette, M. A.; Choy, W.; Davis, J. T.; Essenfeld, A. P; Masamune, S.; Roush, W. R.; Sakai, T. *Tetrahedron Lett.* **1984**, *25*, 2183-2186.

(2) Crabtree, R. H.; Quirk, J. M.; Felkin, H.; Fillebeen-khan, T. *Synth. React. Inorg. Met.-Org. Chem.* **1982**, *12*, 407-413.

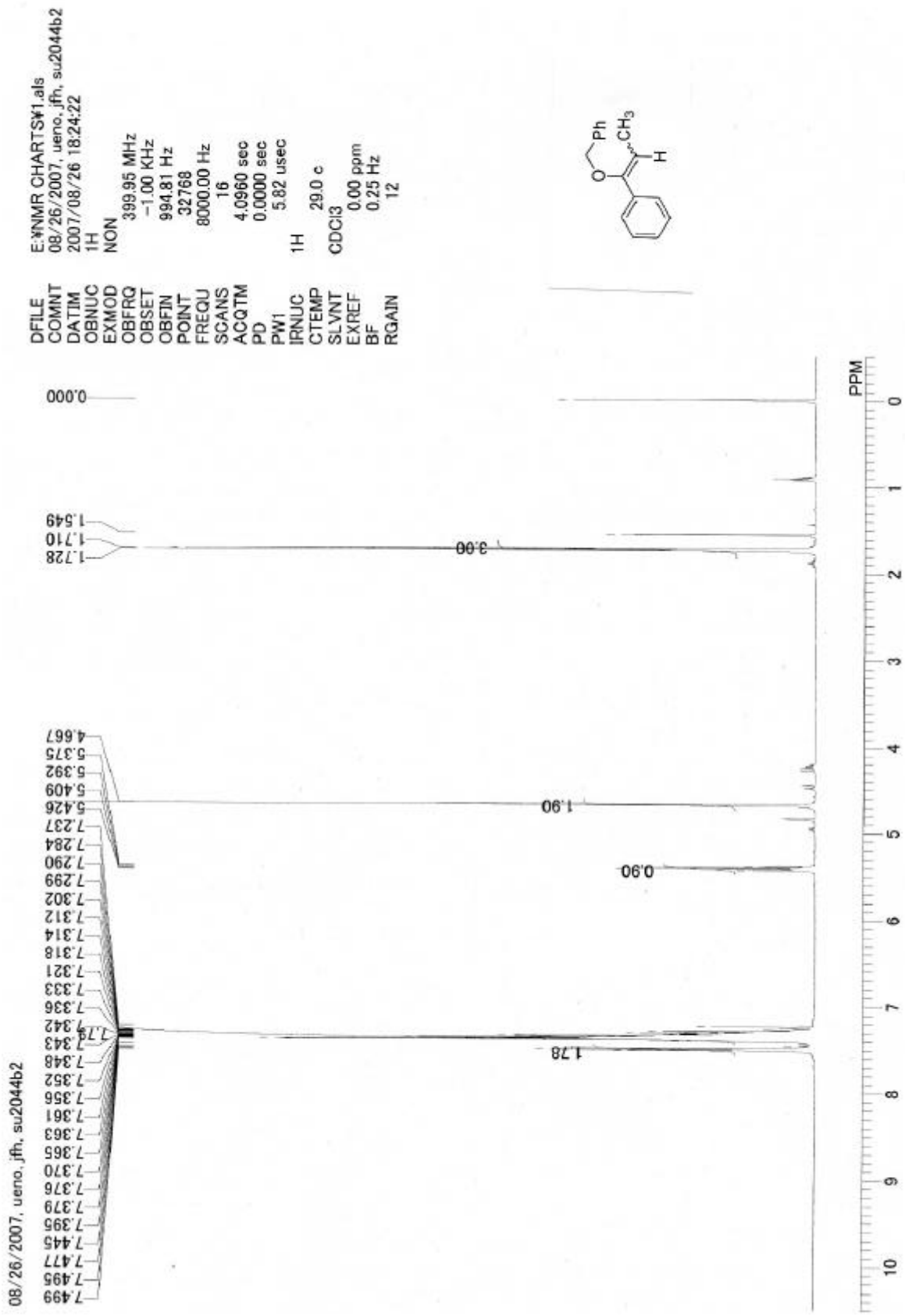
(3) (a) Polet, D.; Alexakis, A. *Org. Lett.* **2005**, *7*, 1621-1624. (b) Polet, D.; Alexakis, A.; Tissot-Croset, K.; Corminboeuf, C.; Ditrich, K. *Chem. Eur. J.* **2006**, *12*, 3596-3609.

(4) Weix, D. J.; Hartwig, J. F. *J. Am. Chem. Soc*. **2007**, *129*, 7720-7721.

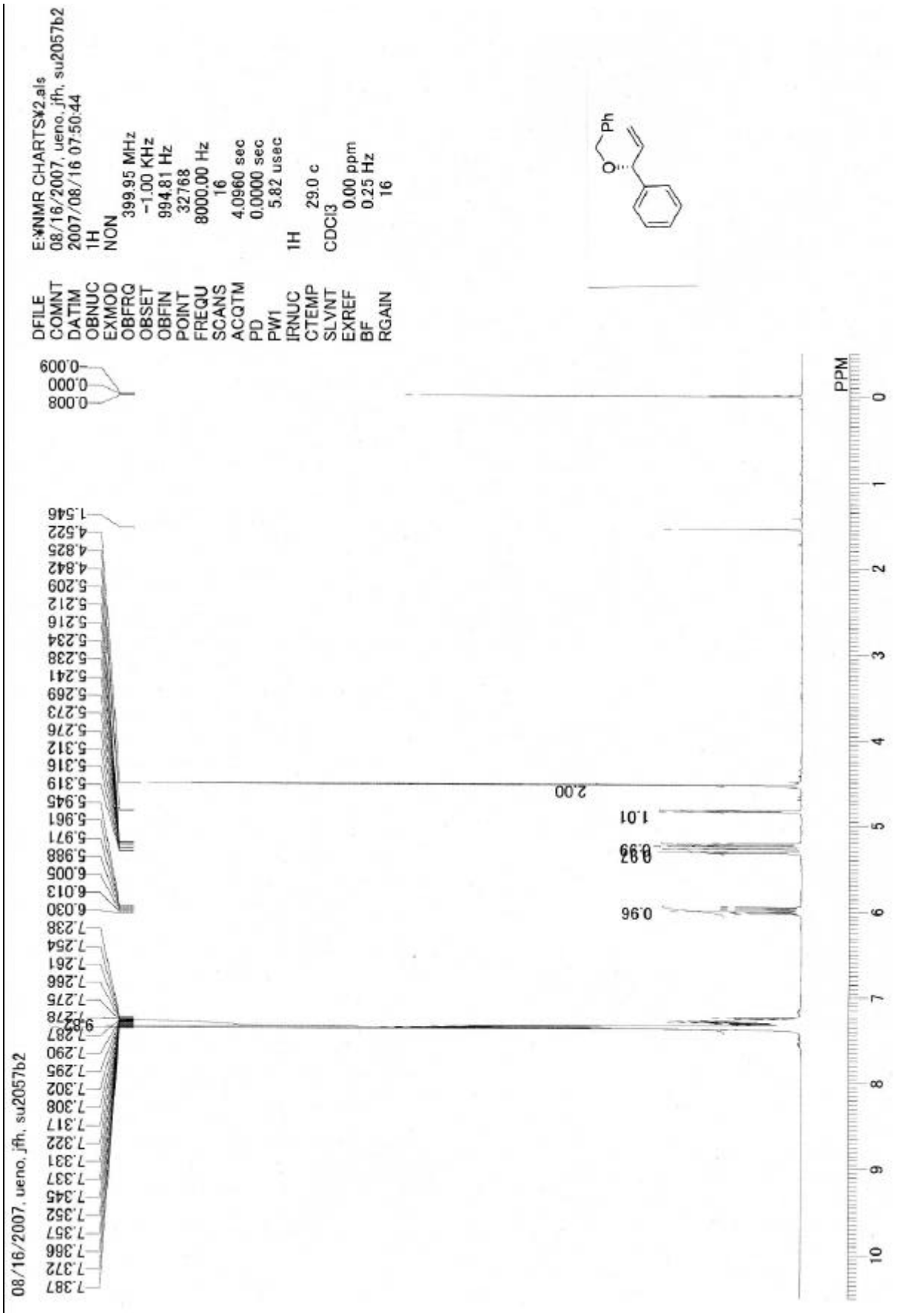
(5) Shu, C.; Hartwig, J. F. *Angew. Chem. Int. Ed.* **2004**, *43*, 4794-4797.

6. ^{1}H NMR spectra of reaction products.

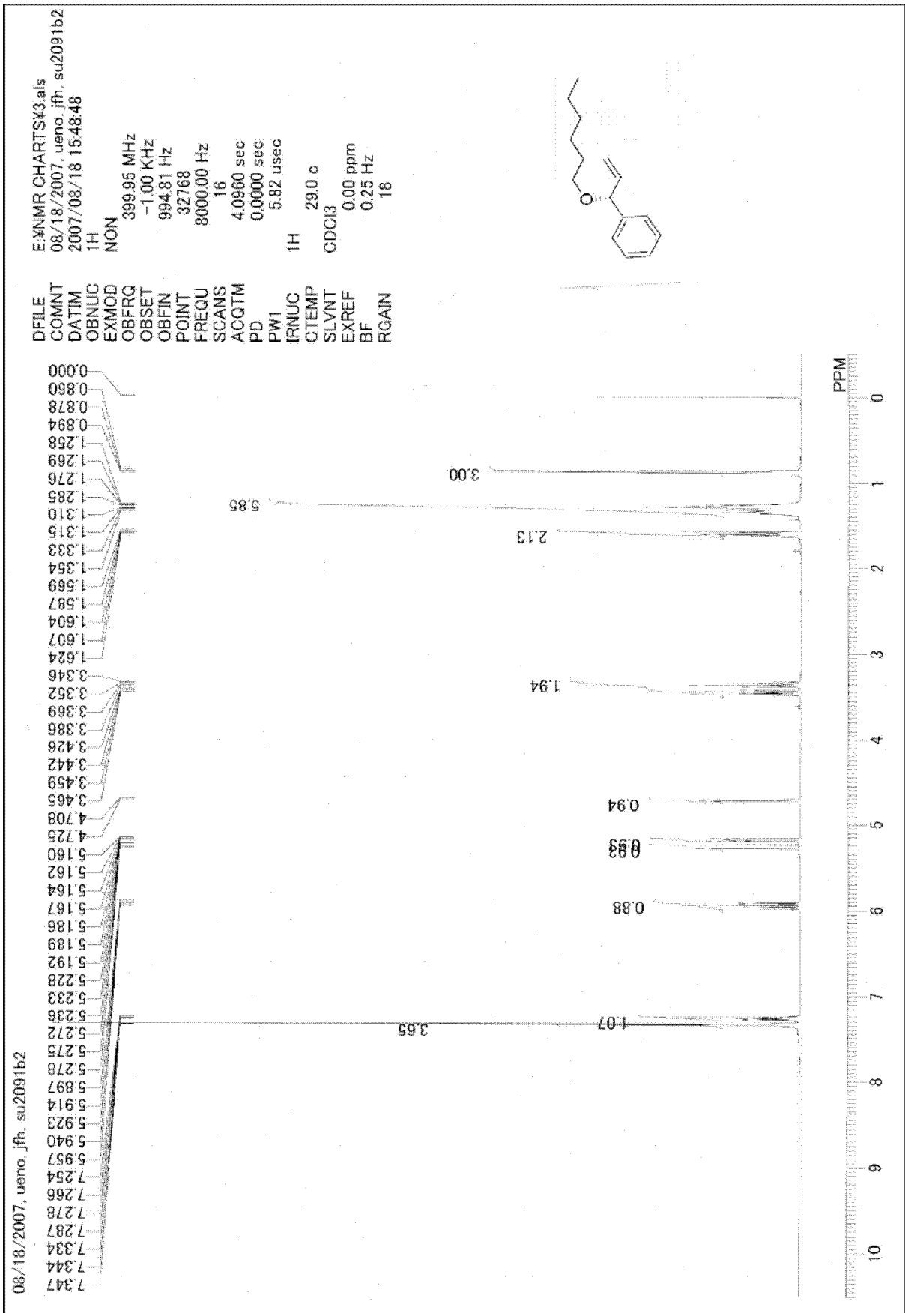
1-Phenyl-1-benzyloxy-1-propene.



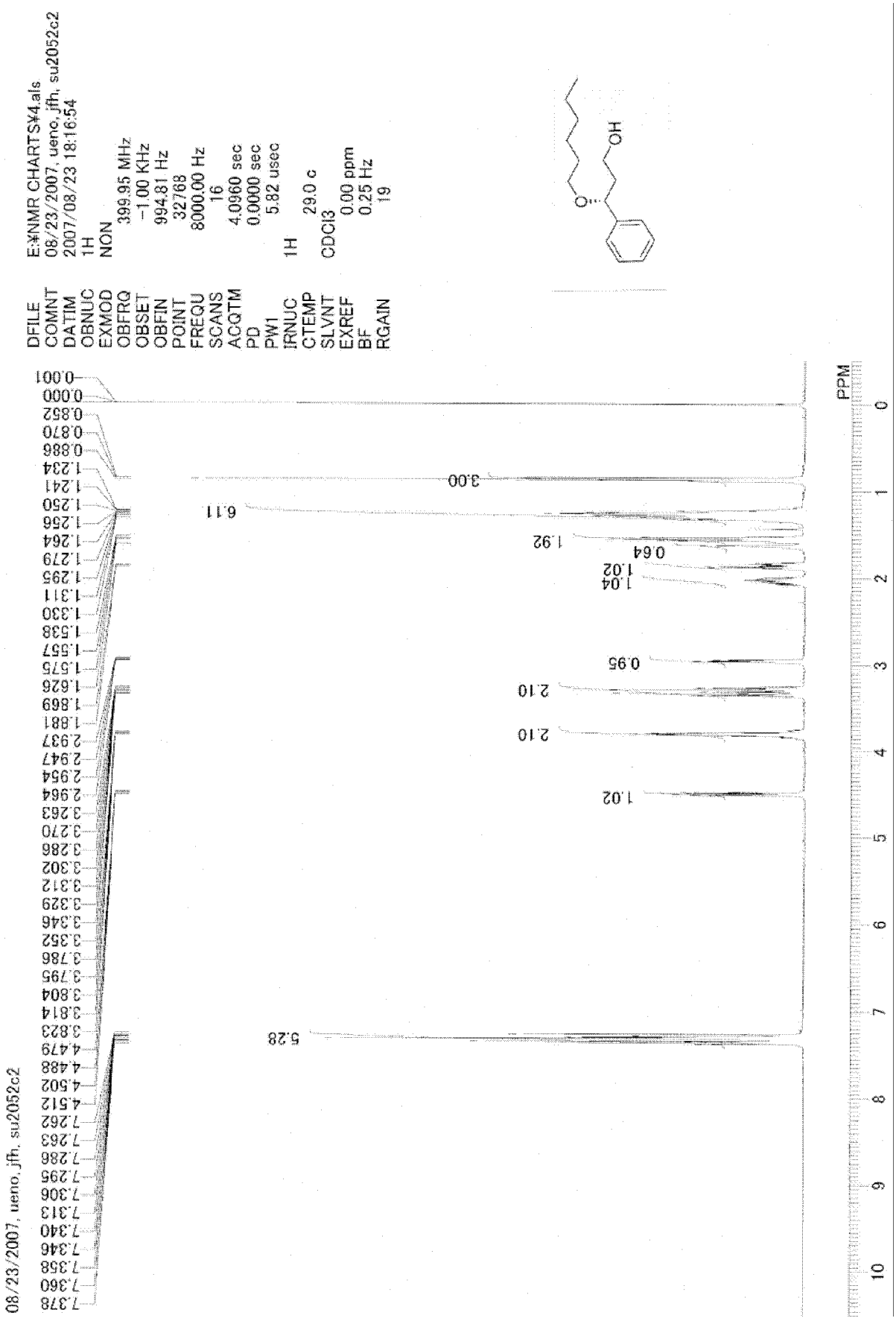
1-Benzyloxy-1-allylbenzene.



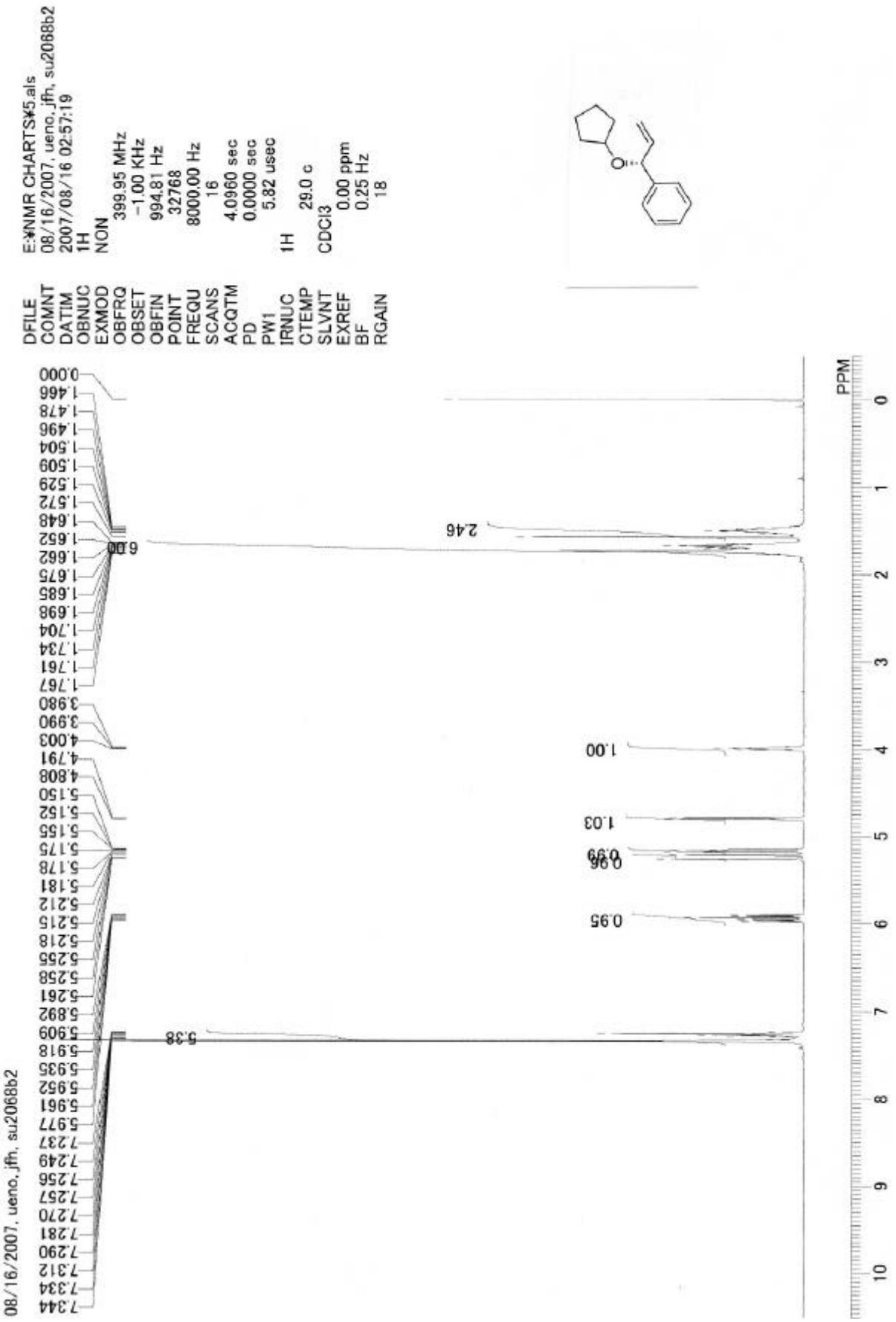
1-Hexyloxyallylbenzene.



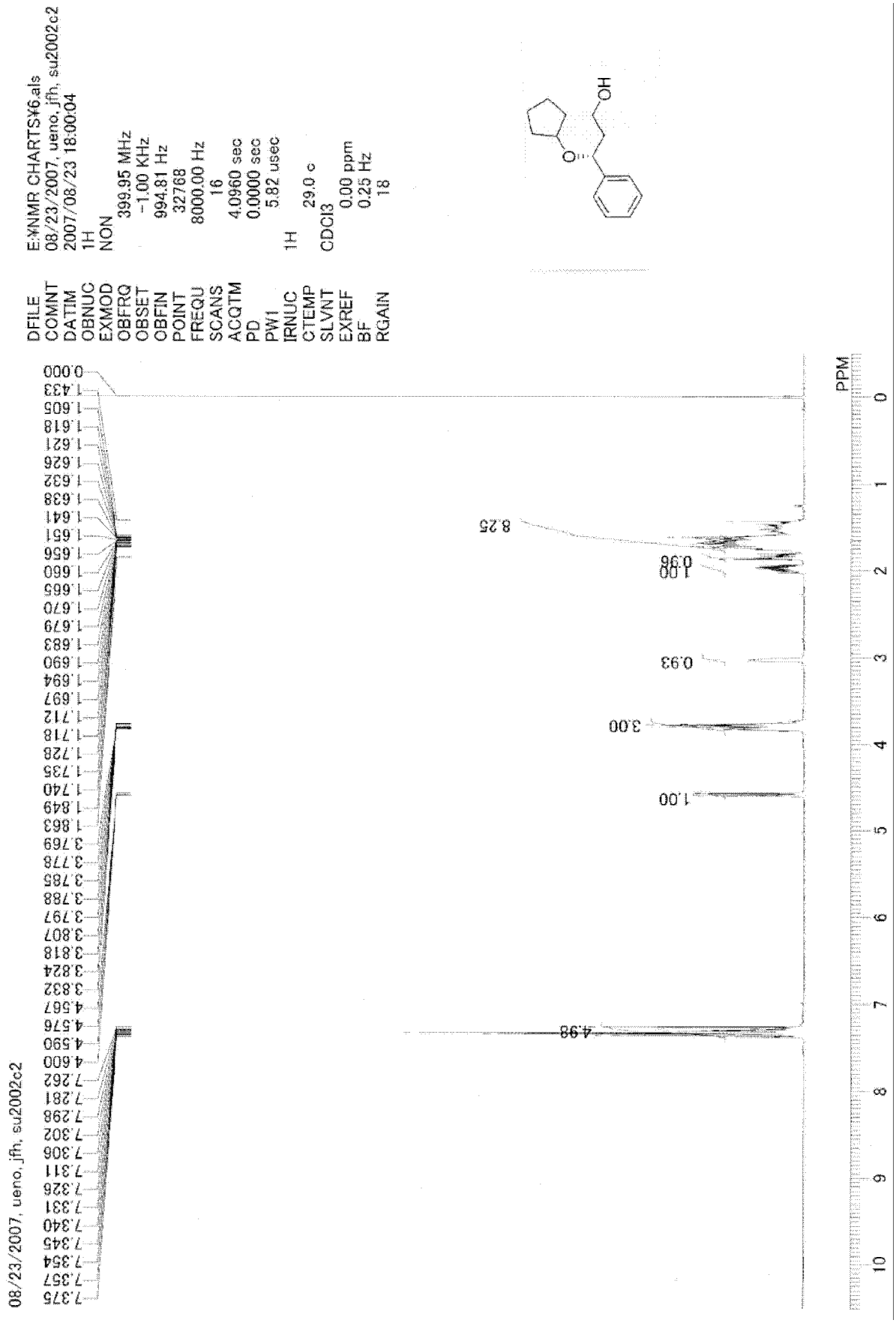
3-Hexyloxy-3-phenyl-propan-1-ol.



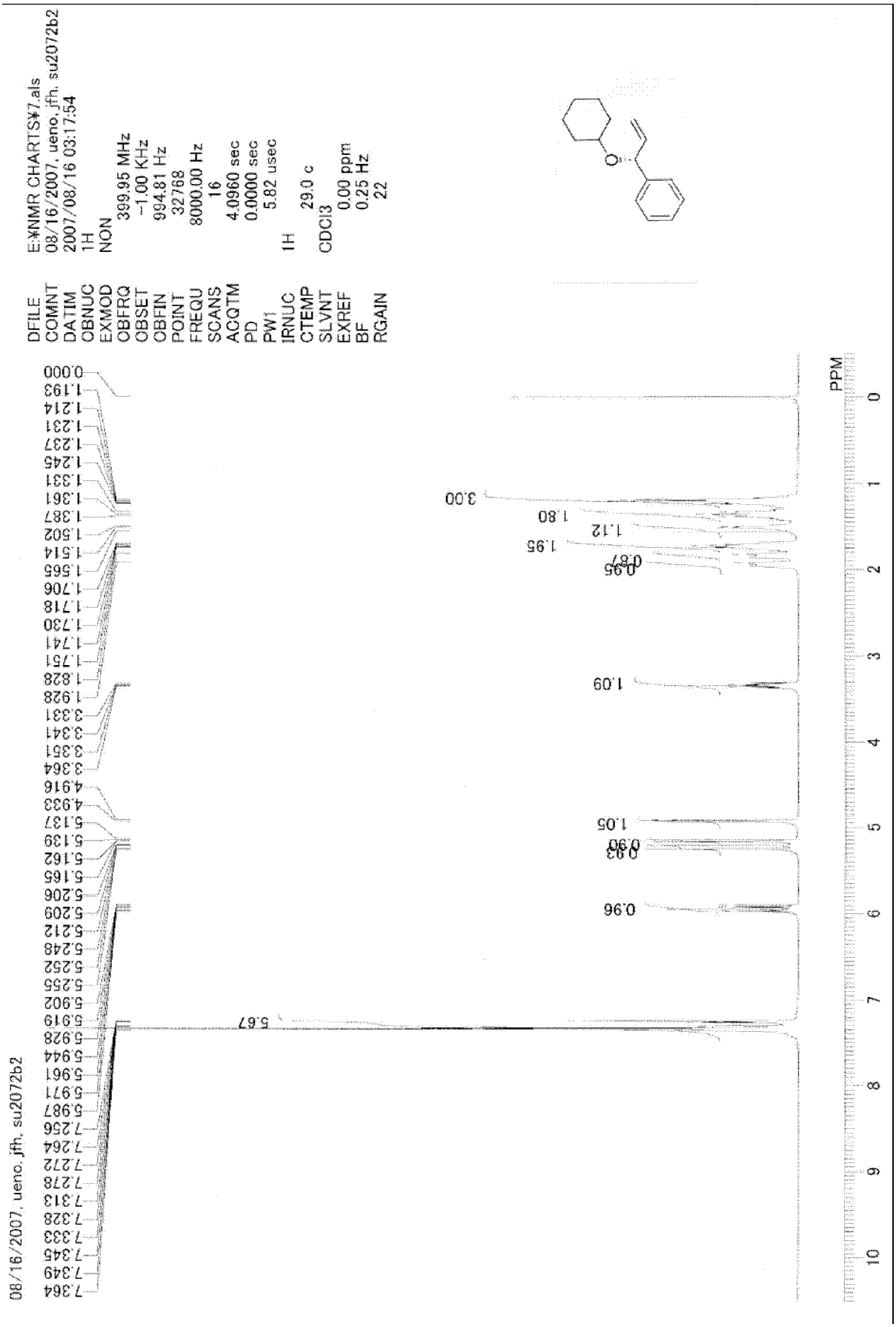
1-Cyclopentyloxyallylbenzene.



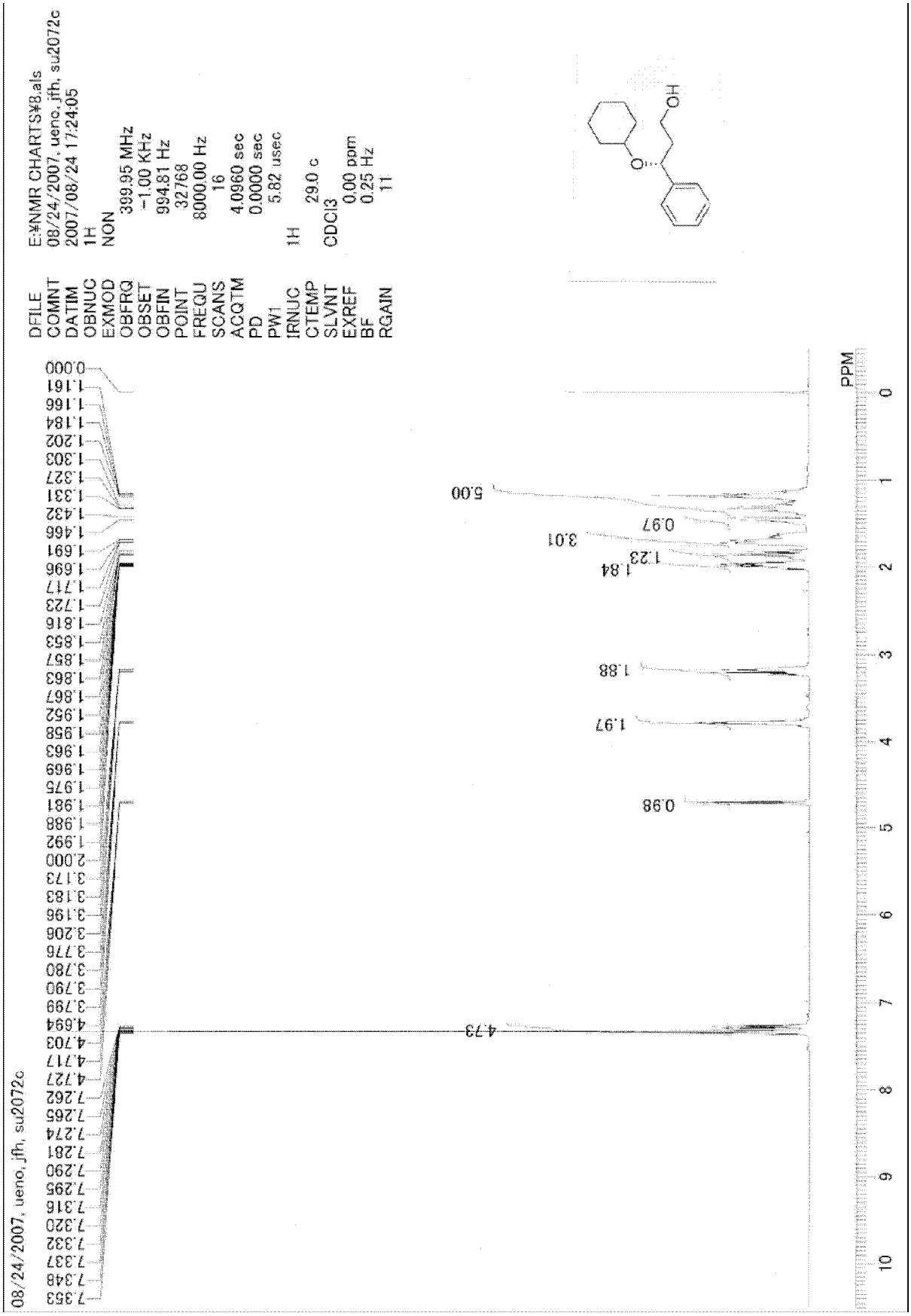
3-Cyclopentyloxy-3-phenyl-propan-1-ol.



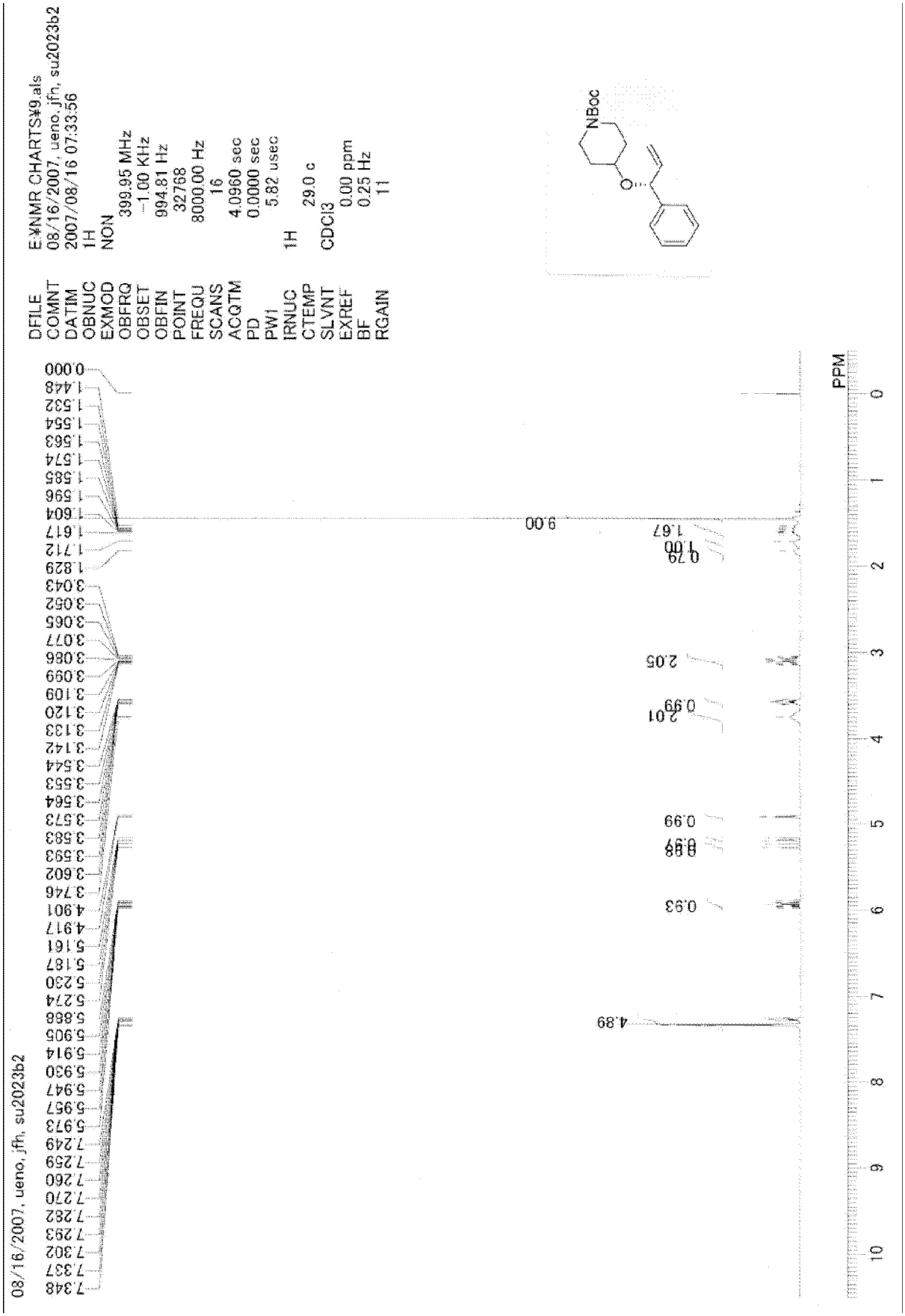
1-Cyclohexyloxyallylbenzene.



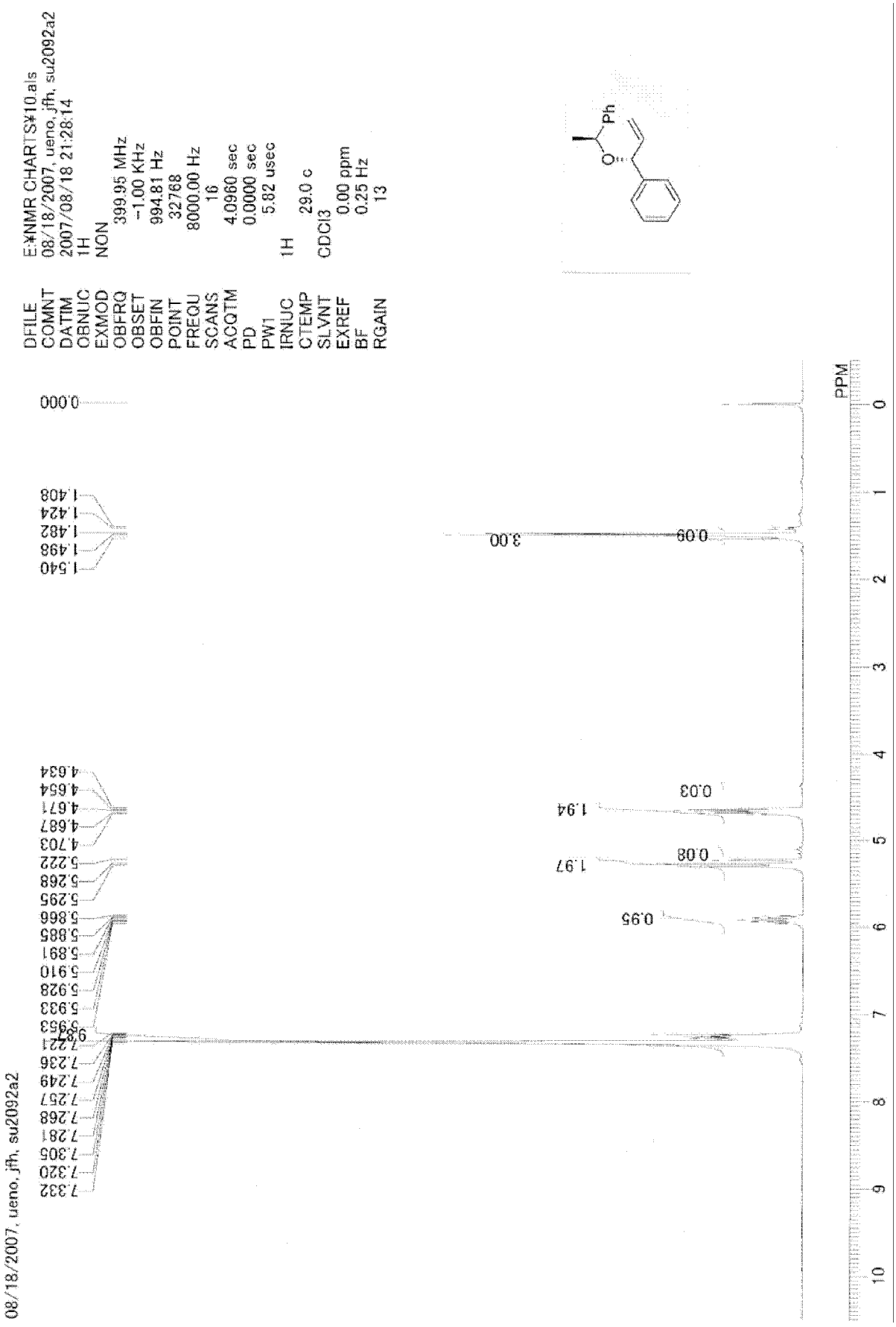
3-Cyclohexyloxy-3-phenylpropan-1-ol.



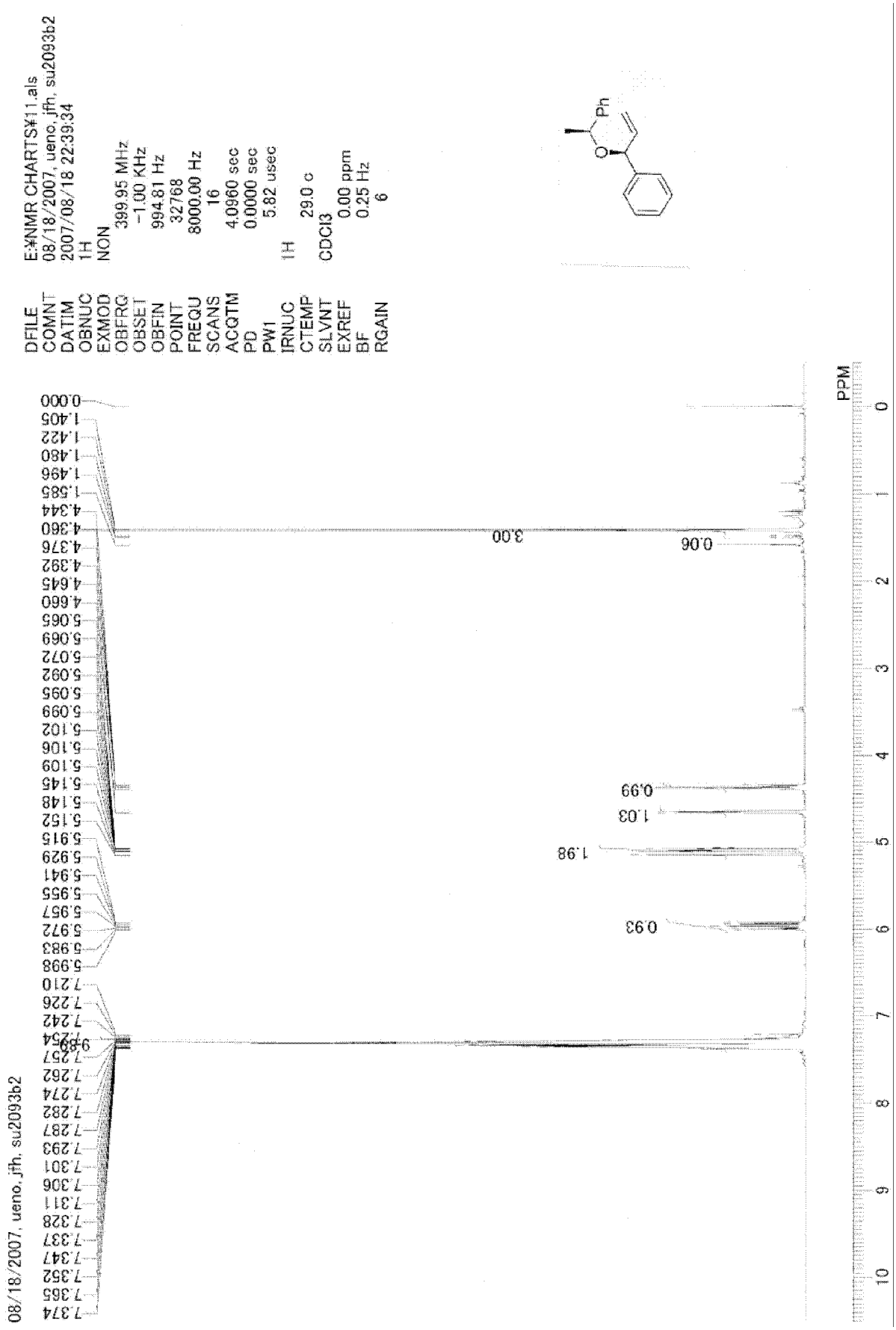
4-(1-Phenylallyloxy)piperidine-1-carboxylic acid tert-butyl ester.



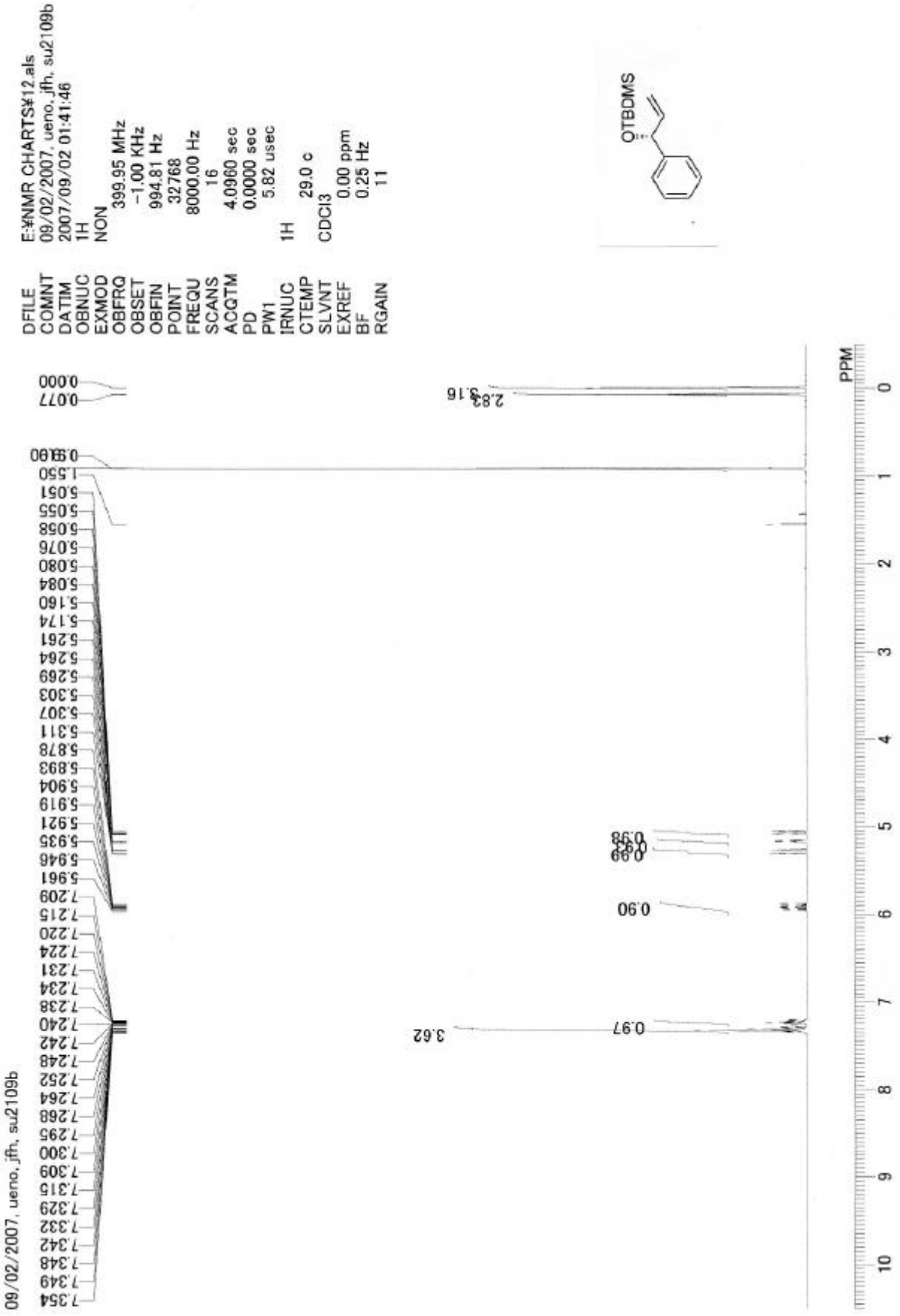
1-Phenylethoxy-1-allylbenzene. (From (*R*,*R*,*R*)-L1)



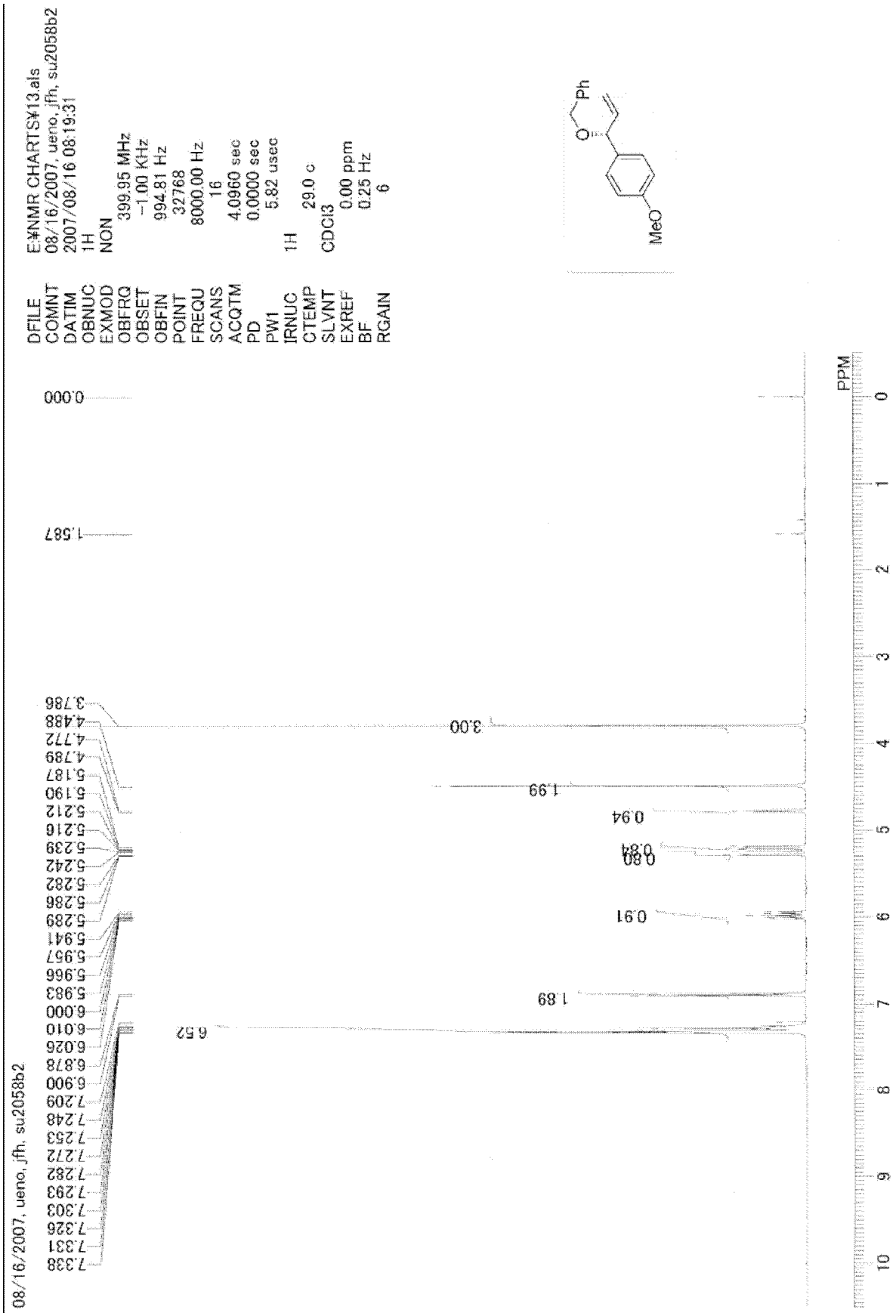
1-Phenylethoxy-1-allylbenzene. (From (*S*,*S*,*S*)-L1)



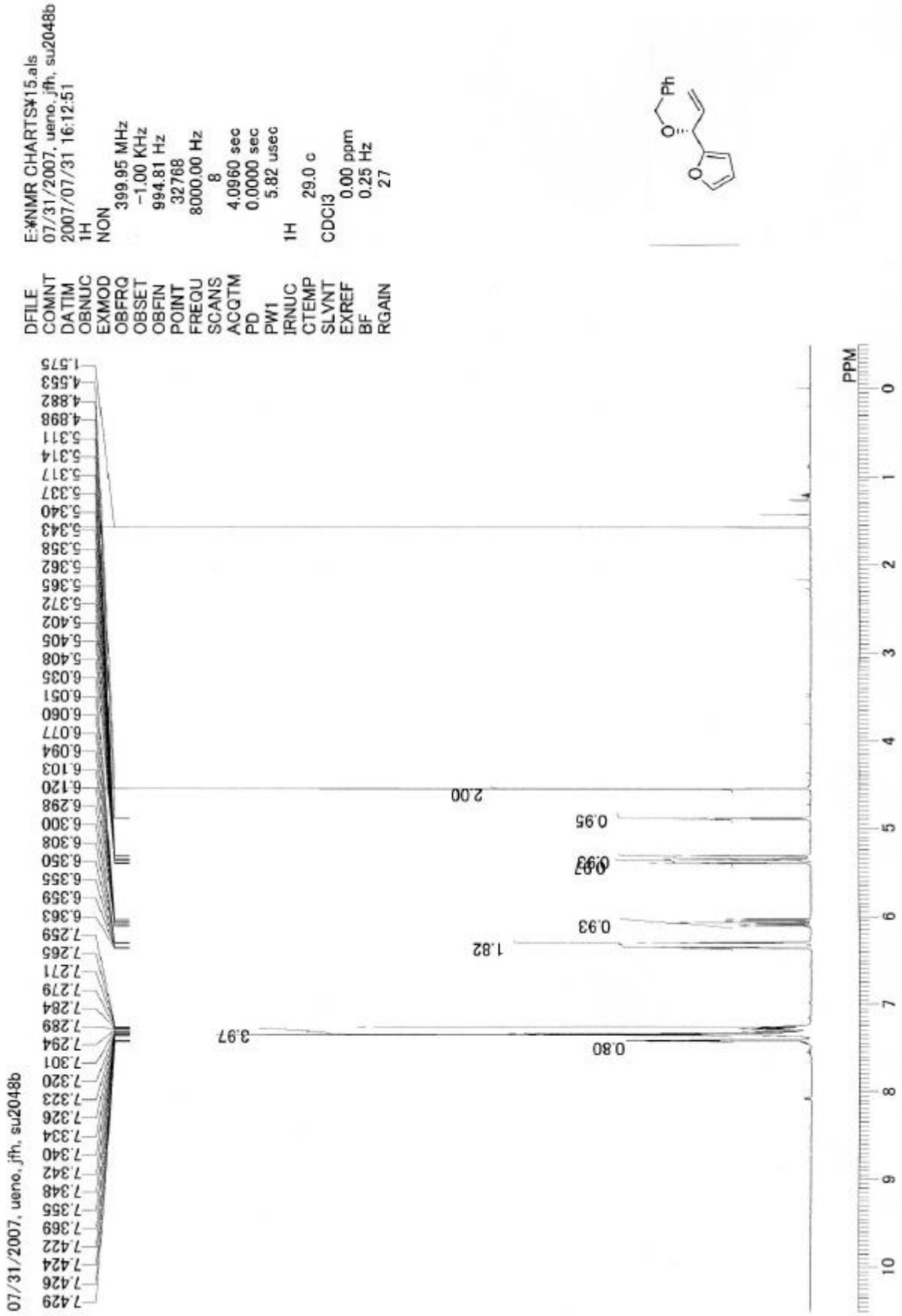
tert-Butyldimethyl(1-phenylallyloxy)silane.



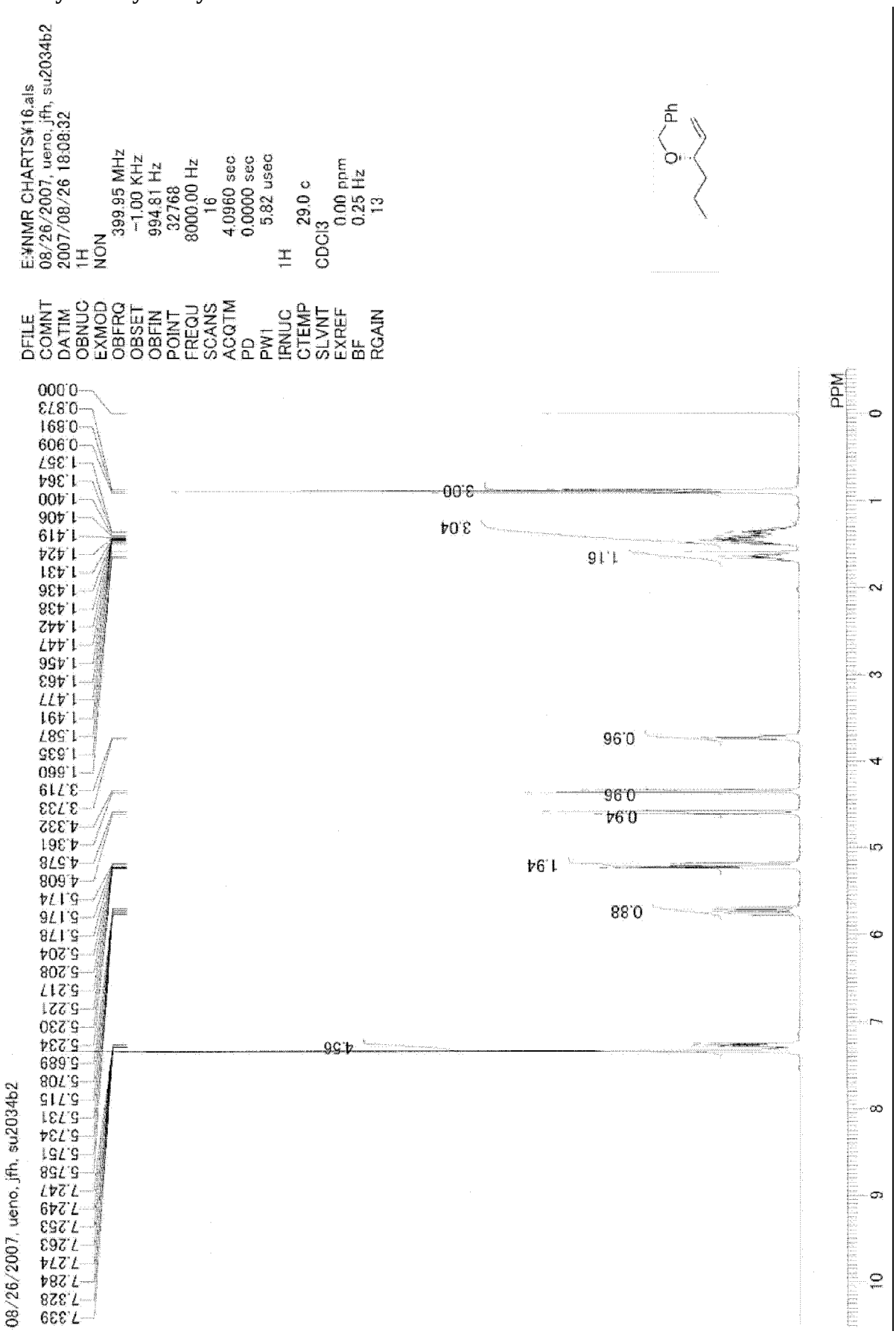
1-(1-Benzyloxyallyl)-4-methoxybenzene.



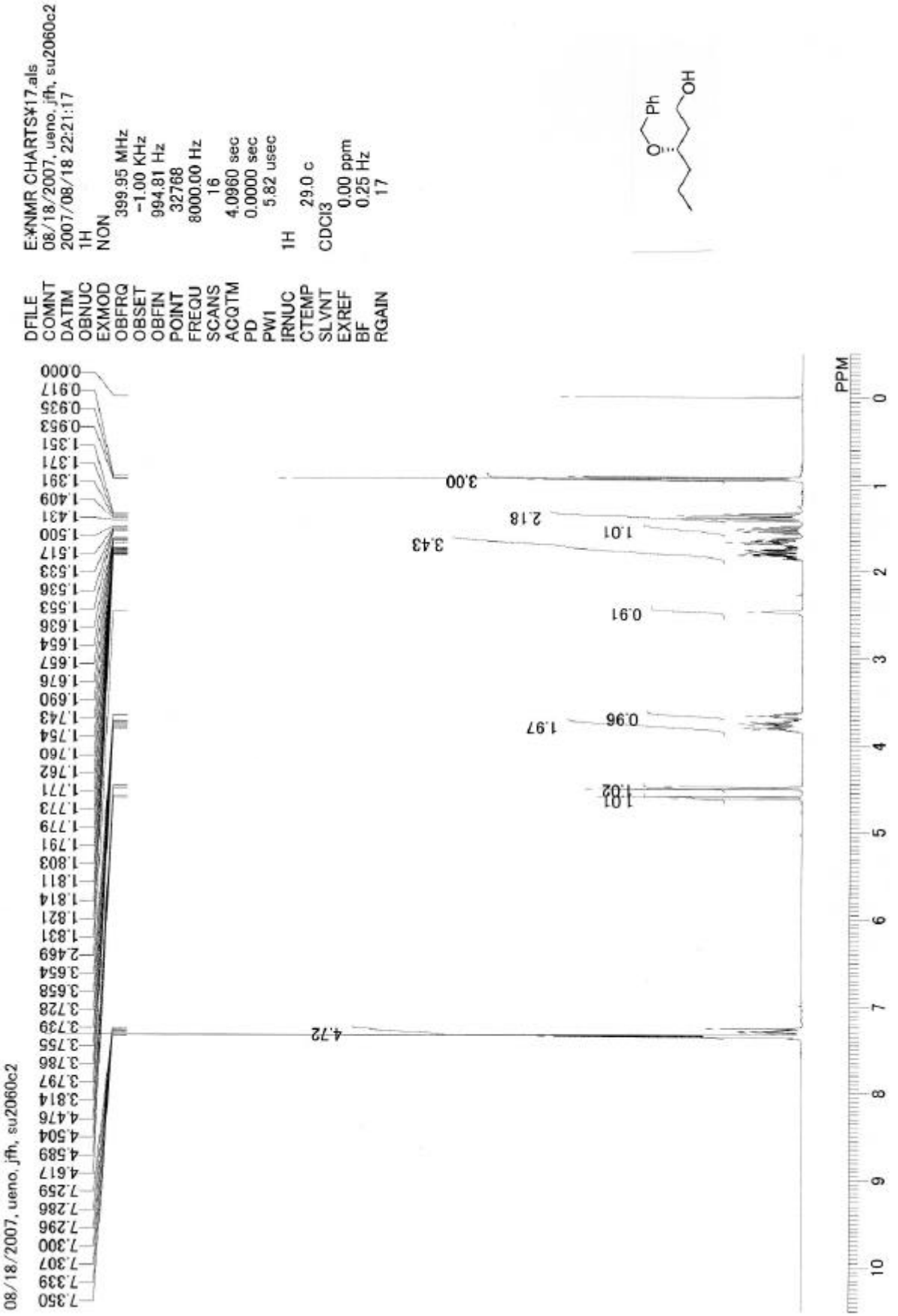
2-(1-Benzyloxyallyl)furan.



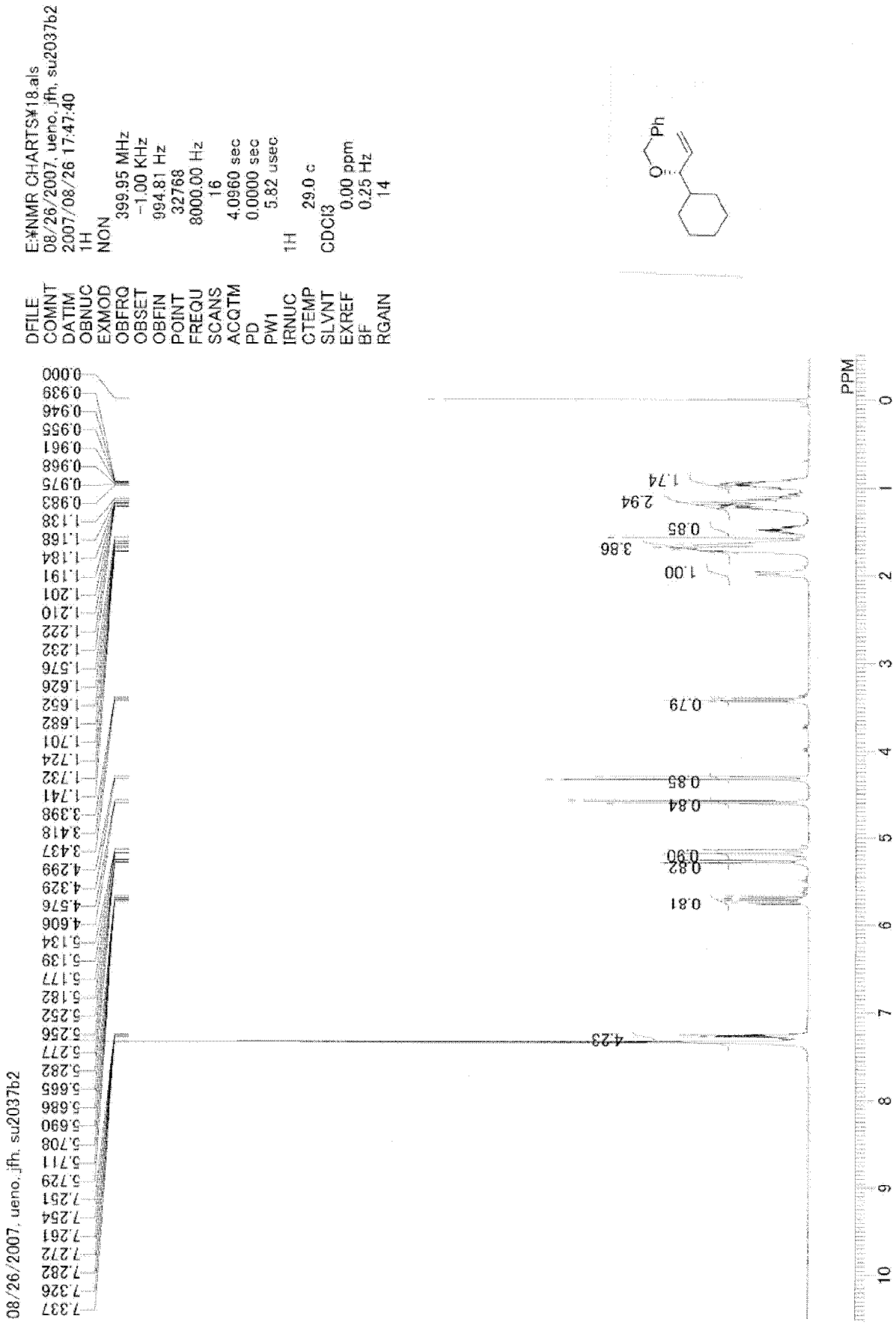
1-Vinylbutoxymethyl-benzene.



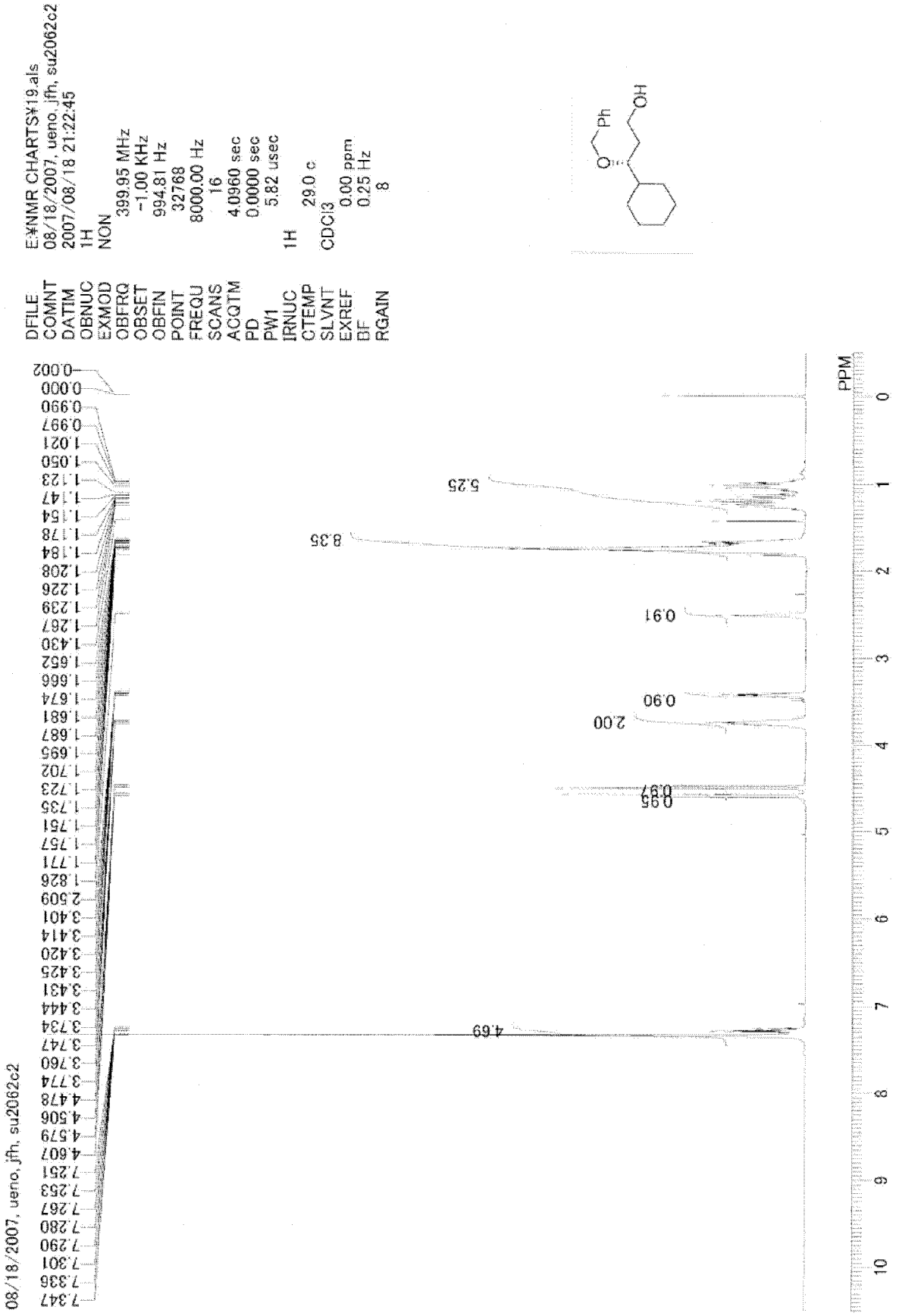
3-Benzyloxyhexan-1-ol.



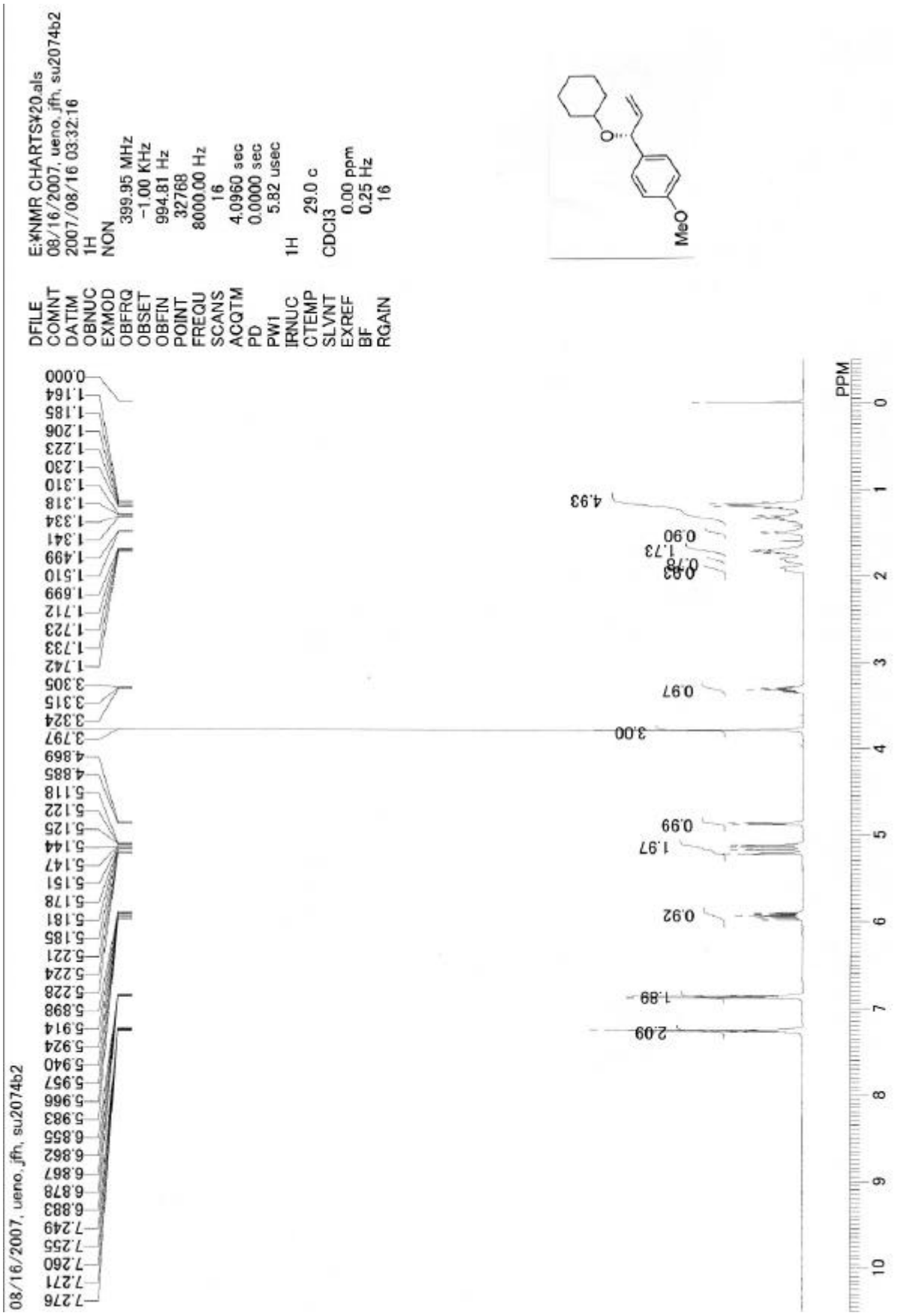
1-Cyclohexylallyloxymethylbenzene



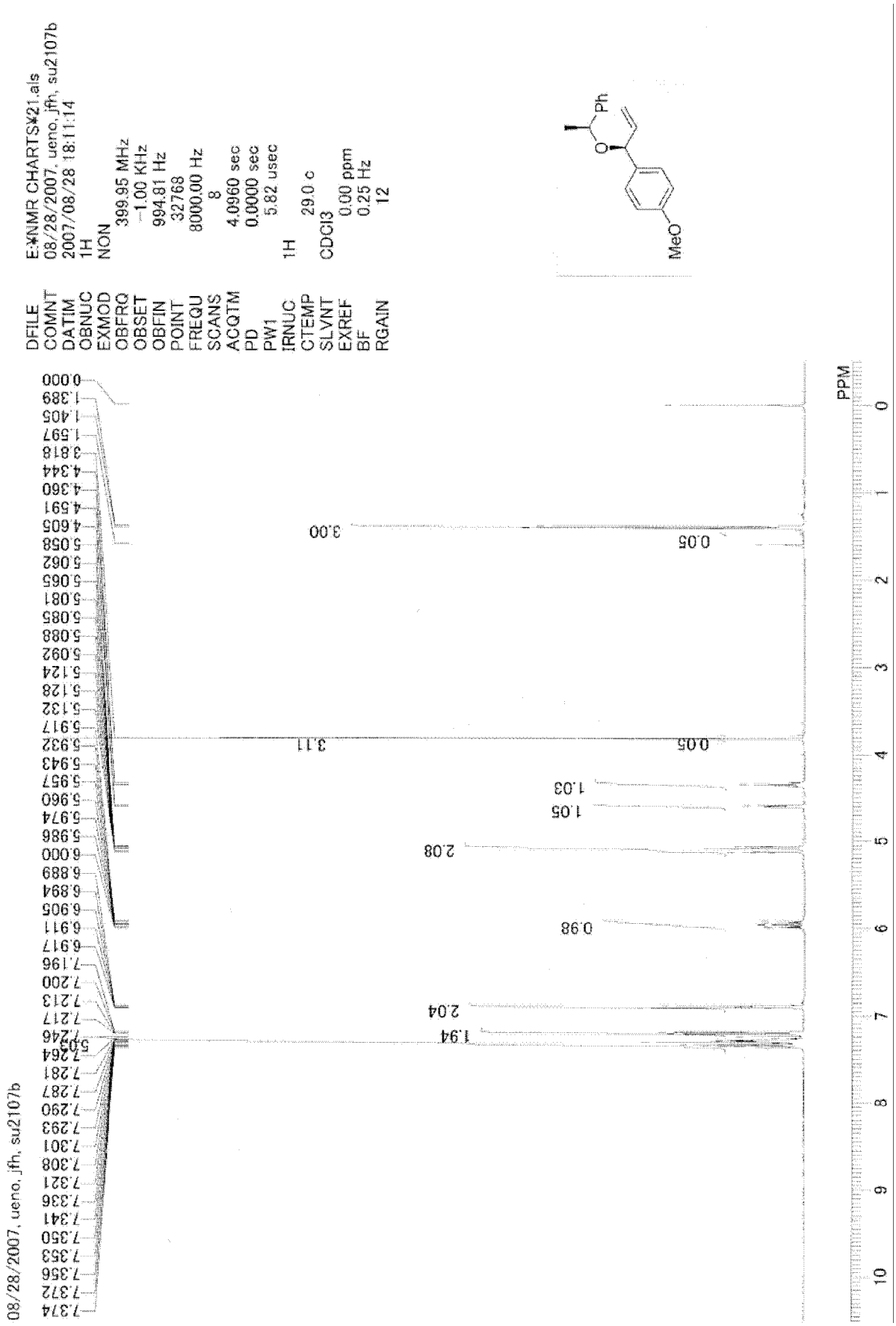
3-Benzyloxy-3-cyclohexyl-propan-1-ol.



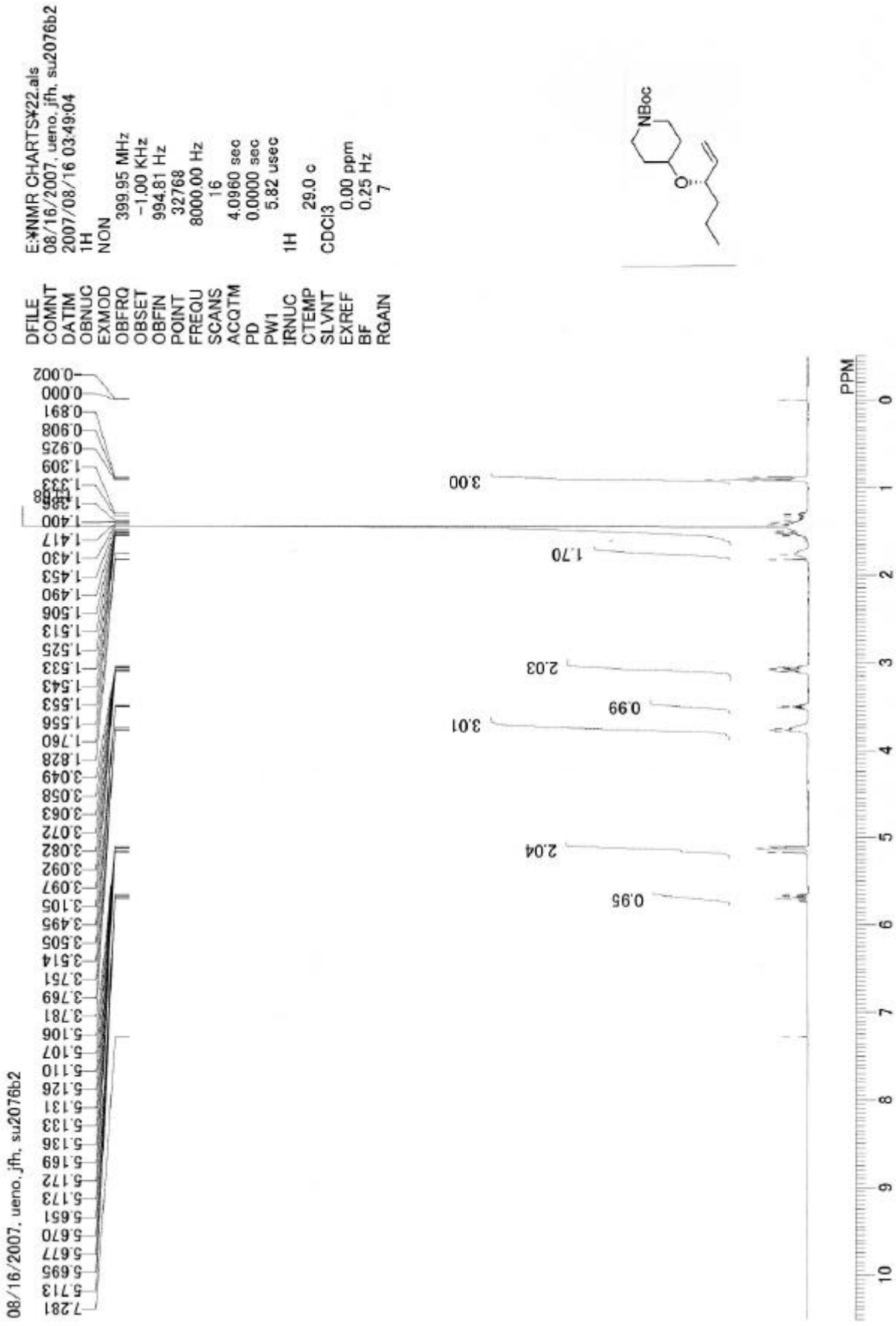
1-(1-Cyclohexyloxyallyl)-4-methoxybenzene.



1-Methoxy-4-[1-(1-phenylethoxy)allyl]benzene. (from (*S*,*S*,*S*)-L1)



4-(1-Vinylbutoxy)piperidine-1-carboxylic acid tert-butyl ester.



1-Methoxy-4-[1-(1-methyl-1-phenylethoxy)allyl]benzene.