

**Synthesis of Cyclic Alkenyl Ethers via Intramolecular Cyclization
of *O*-Alkynylbenzaldehydes. Importance of Combination between CuI catalyst and DMF**

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Contents of Supporting Information

(16 Pages)

Page S-1: Title of the paper, author's name and address along with the contents.

Page S-2: General procedure and characterization data of compounds **3a-d**

Page S-3: Characterization data of compounds **3e-h**

Page S-4: Characterization data of compounds **3i-m**

Page S-5: Characterization data of compounds **3n**

Page S-6: ^1H NMR spectra of compound **3a** (crude)

Page S-7: ^1H NMR spectra of compound **3a** (purified)

Page S-8: ^1H NMR spectra of compound **3b**

Page S-9: ^1H NMR spectra of compound **3c**

Page S-10: ^1H NMR spectra of compound **3d**

Page S-11: ^1H NMR spectra of compound **3e**

Page S-12: ^1H NMR spectra of compound **3g**

Page S-13: ^1H NMR spectra of compound **3h**

Page S-14: ^1H NMR spectra of compound **3i**

Page S-15: ^1H NMR spectra of compound **3m**

Page S-16: ^1H NMR spectra of compound **3n**

Experimental Section. The preparation of **3a** is representative. To a mixture of *O*-alkynylbenzaldehyde **1a** (0.100 g, 0.5813 mmol), MeOH (0.028 g, 0.8720 mmol), Cu(I)I (0.011 g, 0.0581 mmol) was added DMF (0.2 mL) and the mixture was stirred for 8h at 70 °C. Water (20 ml) was added and the product was extracted with ethyl acetate. The extracts were washed with water and dried over anhydrous sodium sulfate. The solvent was removed, and the residue was then filtered through a short silica gel column using hexane/AcOEt, 98:2 as an eluent to give the pure sample of **3a** (0.115 g, 97%). For ¹H NMR spectra of compounds **3f**, **3j**, **3k** and **3l**, see ref 3 in text.

1-Methoxy-3-propyl-1*H*-isochromene (3a**).** oil; IR (neat) 2955, 2930, 2972, 2361, 2341, 1657, 1491, 1078, 999, 964, 752 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 7.25-6.97 (m, 3H), 6.97 (d, *J* = 7.6 Hz, 1H), 5.88 (s, 1H), 5.71 (s, 1H), 3.59 (s, 3H), 2.29-2.14 (m, 2H), 1.59 (quin, *J* = 7.2 Hz, 2H), 0.75 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 153.9, 130.3, 129.1, 126.2, 125.8, 125.7, 123.3, 100.2, 99.6, 54.6, 35.9, 20.4, 13.6; HRMS calcd for C₁₃H₁₆O₂ (M⁺) 204.1150, found 204.1145.

1-Butoxy-3-propyl-1*H*-isochromene (3b**).** oil; IR (neat) 3000, 2930, 2973, 2362, 2341, 1657, 1491, 1078, 1000, 965, 752 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 7.22-7.10 (m, 3H), 6.95 (d, *J* = 7.6 Hz, 1H), 5.96 (s, 1H), 5.69 (s, 1H), 3.80 (dt, *J* = 9.6, 6.4 Hz, 1H), 3.60 (dt, *J* = 9.6, 6.4 Hz, 1H), 2.26-2.12 (m, 2H), 1.61-1.42 (m, 4H), 1.34-1.19 (m, 2H), 0.90 (t, *J* = 7.6 Hz, 3H), 0.84 (t, *J* = 7.6 Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 154.0, 130.4, 128.9, 126.5, 125.7, 125.6, 123.3, 100.1, 98.6, 67.6, 36.0, 31.7, 20.3, 19.3, 13.9, 13.6; HRMS calcd for C₁₆H₂₂O₂ (M⁺) 246.1620, found 246.1614.

1-But-3-enyloxy-3-propyl-1*H*-isochromene (3c**).** oil; IR (neat) 2953, 2940, 2962, 2350, 2340, 1658, 1500, 1070, 999, 964, 754 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 7.24-7.10 (m, 3H), 6.96 (d, *J* = 7.6 Hz, 1H), 5.98 (s, 1H), 5.78-5.70 (m, 2H), 5.05-4.95 (m, 2H), 3.83 (dt, *J* = 10.0, 7.2 Hz, 1H), 3.66 (dt, *J* = 10.0, 7.2 Hz, 1H), 2.40-2.20 (m, 4H), 1.65-2.12 (m, 3H), 0.90 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 153.9, 134.8, 130.4, 129.0, 125.8, 125.7, 123.3, 116.4, 100.1, 98.45, 66.9, 35.9, 34.1, 20.3, 13.6; HRMS calcd for C₁₆H₂₀O₂ (M⁺) 244.1463, found 244.1458.

1-Isopropoxy-3-propyl-1*H*-isochromene (3d**).** oil; IR (neat) 3000, 2950, 2900, 2361, 2341, 1657, 1498, 1078, 995, 964, 753 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) 7.21-7.06 (m, 3H), 6.95 (d, *J* = 8.0 Hz, 1H), 6.04 (s, 1H), 5.70 (m, 1H), 4.17 (sextet, *J* = 6.0 Hz, 1H), 2.25-2.11 (m, 2H), 1.62-1.52 (m, 2H),

1.20 (d, $J = 6$ Hz, 3H), 1.14 (d, $J = 6$ Hz, 3H), 0.91 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 153.9, 130.4, 128.8, 126.7, 125.7, 125.5, 123.4, 100.0, 96.6, 69.5, 36.1, 23.6, 21.9, 20.2, 13.7; HRMS calcd for $\text{C}_{15}\text{H}_{20}\text{O}_2$ (M^+) 232.1463, found 232.1458.

1-Benzylxyloxy-3-propyl-1*H*-isochromene (3e). oil; IR (neat) 3020, 2940, 2900, 2362, 2343, 1657, 1500, 1078, 995, 964, 754 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 7.32-7.05 (m, 3H), 6.98 (d, $J = 7.2$ Hz, 1H), 6.03 (s, 1H), 5.73 (s, 1H), 4.75 (ABq, $J = 12.4$ Hz, 2H), 2.29-2.10 (m, 2H), 1.64-1.53 (m, 2H), 0.91 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 156.4, 129.1, 128.3, 128.0, 127.9, 127.6, 125.7, 123.4, 100.3, 97.3, 68.9, 35.9, 20.3, 13.7; HRMS calcd for $\text{C}_{19}\text{H}_{20}\text{O}_2$ (M^+) 280.1463, found 280.1463.

1-Methoxy-1*H*-isochromene (3f). oil; IR (neat) 3000, 2950, 2901, 2361, 2341, 1657, 1498, 1078, 996, 964, 753 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 7.29-7.05 (m, 4H), 6.57 (d, $J = 5.6$ Hz, 1H), 5.91 (d, $J = 5.6$ Hz, 1H), 5.88 (s, 1H), 3.46 (s, 3H). ^{13}C NMR (CDCl_3 , 100 MHz) δ 141.9, 129.4, 128.9, 127.1, 126.8, 126.1, 123.9, 104.6, 98.9, 55.4; HRMS calcd for $\text{C}_{10}\text{H}_{10}\text{O}_2$ (M^+) 162.0681, found 162.0705.

1-Isopropoxy-1*H*-isochromene (3g). oil; IR (neat) 3010, 2945, 2900, 2364, 2331, 1657, 1500, 1078, 996, 964, 758 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 7.25-7.14 (m, 2H), 7.09 (d, $J = 7.2$ Hz, 1H), 7.01 (d, $J = 8.0$ Hz, 1H), 6.53 (d, $J = 5.6$ Hz, 1H), 6.04 (s, 1H), 5.89 (d, $J = 5.6$ Hz, 1H), 4.12 (sextet, $J = 6.4$ Hz, 1H), 1.18 (d, $J = 6.4$ Hz, 3H), 1.15 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 142.6, 129.7, 129.6, 128.4, 127.2, 126.4, 124.4, 105.0, 96.8, 70.4, 23.4, 22.2; HRMS calcd for $\text{C}_{12}\text{H}_{14}\text{O}_2$ (M^+) 190.0994, found 190.0988.

1-Methoxy-3-propyl-7-trifluoromethyl-1*H*-isochromene (3h). oil; IR (neat) 3009, 2900, 2384, 2331, 1660, 1499, 1078, 996, 964, 758 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 7.45 (d, $J = 8.8$ Hz, 1H), 7.38 (s, 1H), 7.05 (d, $J = 8.8$ Hz, 1H), 5.91 (s, 1H), 5.76 (s, 1H), 3.49 (s, 3H), 2.37-2.16 (m, 2H), 1.65-1.51 (m, 2H), 0.92 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 156.5, 133.8, 126.1, 126.0, 123.5, 123.0, 122.9, 99.6, 99.1, 55.3, 36.0, 20.3, 13.5; HRMS calcd for $\text{C}_{14}\text{H}_{15}\text{F}_3\text{O}_2$ (M^+) 272.1024, found 272.1019.

1-Isopropoxy-3-propyl-7-trifluoromethyl-1*H*-isochromene (3i). oil; IR (neat) 3000, 2945, 2902, 2364, 2335, 1657, 1504, 1078, 997, 964, 760 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) 7.42 (d, *J* = 8.4 Hz, 1H), 7.30 (s, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 6.07 (s, 1H), 5.74 (s, 1H), 4.18 (sextet, *J* = 6 Hz, 1H), 2.27-2.09 (m, 2H), 1.62-1.53 (m, 2H), 1.21 (d, *J* = 6.0 Hz, 3H), 1.15 (d, *J* = 6.0 Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 156.5, 133.7, 126.7, 125.8, 125.7, 123.5, 122.7, 99.5, 96.1, 70.0, 36.2, 23.5, 21.8, 20.1, 13.7; HRMS calcd for C₁₆H₁₉F₃O₂ (M⁺) 300.1337, found 300.1340.

3-Butyl-1-methoxy-1*H*-isochromene (3j). oil; IR (neat) 2955, 2930, 2972, 2361, 2341, 1657, 1491, 1078, 999, 964, 752 cm⁻¹; ¹H-NMR (CDCl₃, 400 MHz) δ 7.31-7.15 (m, 3H), 7.04 (d, *J* = 7.5 Hz, 1H), 5.94 (s, 1H), 5.78 (s, 1H), 3.53 (s, 1H), 2.30 (ddd, *J* = 4.0, 7.3, 7.3 Hz, 2H), 1.60 (quin, *J* = 7.5 Hz, 2H), 1.46-1.33 (m, 2H), 0.94 (t, *J* = 7.5 Hz, 3H); ¹³C-NMR (CDCl₃, 100 MHz) δ 154.2, 130.4, 129.3, 126.2, 125.9, 125.8, 123.4, 100.2, 99.6, 55.0, 33.6, 29.2, 22.1, 13.9; HRMS calcd for C₁₄H₁₈O₂ (M⁺) 218.1306, found 218.1328.

1-Methoxy-3-phenyl-1*H*-isochromene (3k). oil; IR (neat) 3059, 2930, 2907, 2360, 2341, 1634, 1493, 1457, 1086, 1040, 1022, 957, 766, 691 cm⁻¹; ¹H-NMR (CDCl₃, 400 MHz) δ 7.85 (d, *J* = 6.9 Hz, 2H), 7.44-7.19 (m, 7H), 6.62 (s, 1H), 6.15 (s, 1H), 3.61 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 149.4, 134.4, 130.2, 129.4, 128.7, 128.4, 127.0, 126.6, 125.7, 124.8, 124.5, 100.3, 99.7, 55.1; HRMS calcd for C₁₆H₁₄O₂ (M⁺) 238.0994, found 238.0993.

1-Isopropoxy-3-phenyl-1*H*-isochromene (3l). Solid; mp 92.5 °C; IR (KBr) 2970, 2930, 2917, 2866, 1628, 1609, 1493, 1456, 1379, 1328, 1117, 1070, 1035, 1014, 961, 764, 687, 517 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 7.80 (d, *J* = 6.84 Hz, 2H), 7.44-7.20 (m, 7H), 6.61 (s, 1H), 6.32 (s, 1H), 4.38 (tt, *J* = 6.0, 6.2 Hz, 1H), 1.32 (d, *J* = 6.0 Hz, 3H), 1.18 (t, *J* = 6.2 Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 149.5, 134.8, 130.4, 129.1, 128.6, 128.4, 127.6, 1266.6, 125.5, 124.8, 124.6, 100.4, 96.9, 69.8, 23.6, 22.0; HRMS calcd for C₁₈H₁₈O₂ (M⁺) 266.0306, found 266.1299.

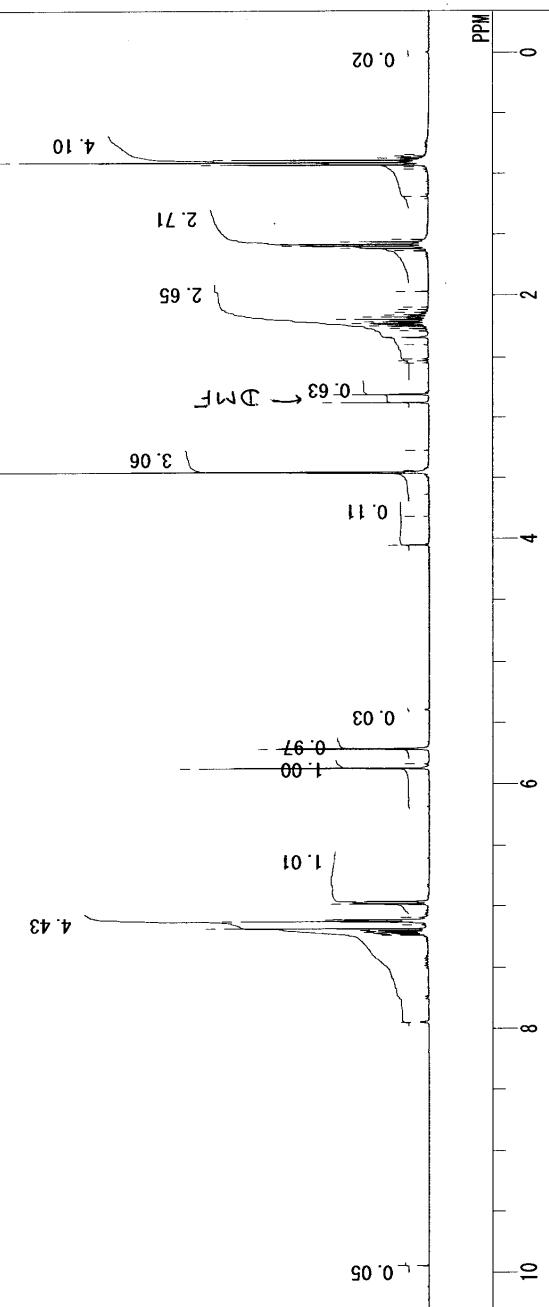
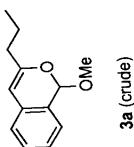
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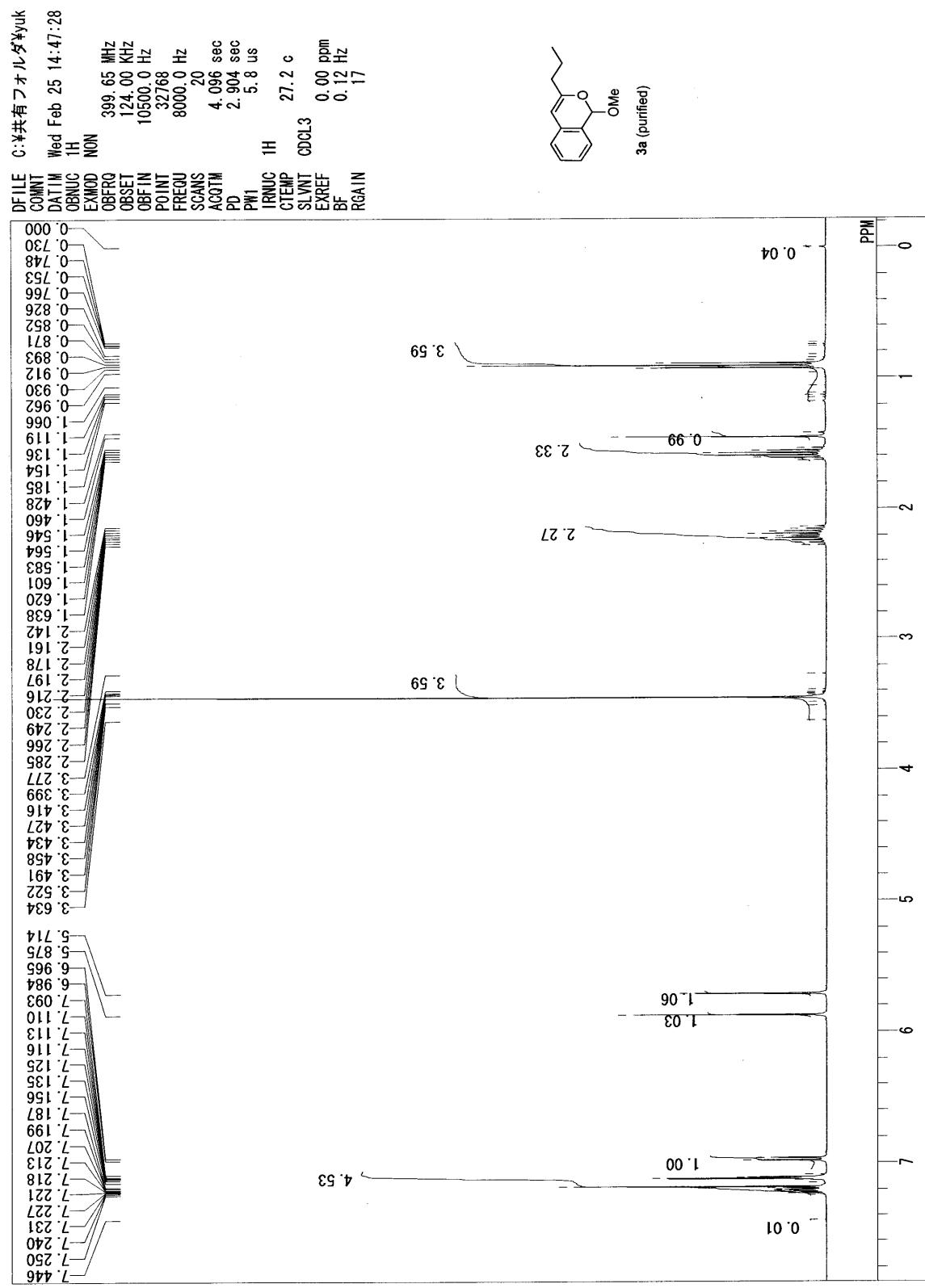
3H), 3.40 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 149.0, 129.3, 129.2, 126.9, 126.8, 125.8, 124.1, 103.2, 99.5, 71.9, 57.9, 55.0; HRMS calcd for $\text{C}_{12}\text{H}_{14}\text{O}_3$ (M^+) 206.0943, found 206.0937.

1-Isopropoxy-3-methoxymethyl-1*H*-isochromene (3n). oil; IR (neat) 3010, 2944, 2902, 2365, 2329, 1658, 1499, 1075, 997, 968, 753 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 7.30-7.14 (m, 3H), 7.08 (d, $J = 7.2$ Hz, 1H), 6.15 (s, 1H), 6.03 (s, 1H), 4.25 (sep, $J = 6$ Hz, 1H), 4.09 (d, $J = 12.8$ Hz, 1H), 3.99 (d, $J = 12.8$ Hz, 1H), 3.40 (s, 3H), 1.25 (d, $J = 6.4$ Hz, 3H), 1.21 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 149.0, 129.3, 128.9, 127.4, 126.7, 125.6, 124.1, 102.8, 96.8, 72.0, 69.9, 58.1, 23.5, 21.9; HRMS calcd for $\text{C}_{14}\text{H}_{18}\text{O}_3$ (M^+) 234.1256, found 234.1250.

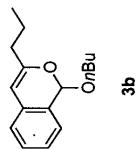
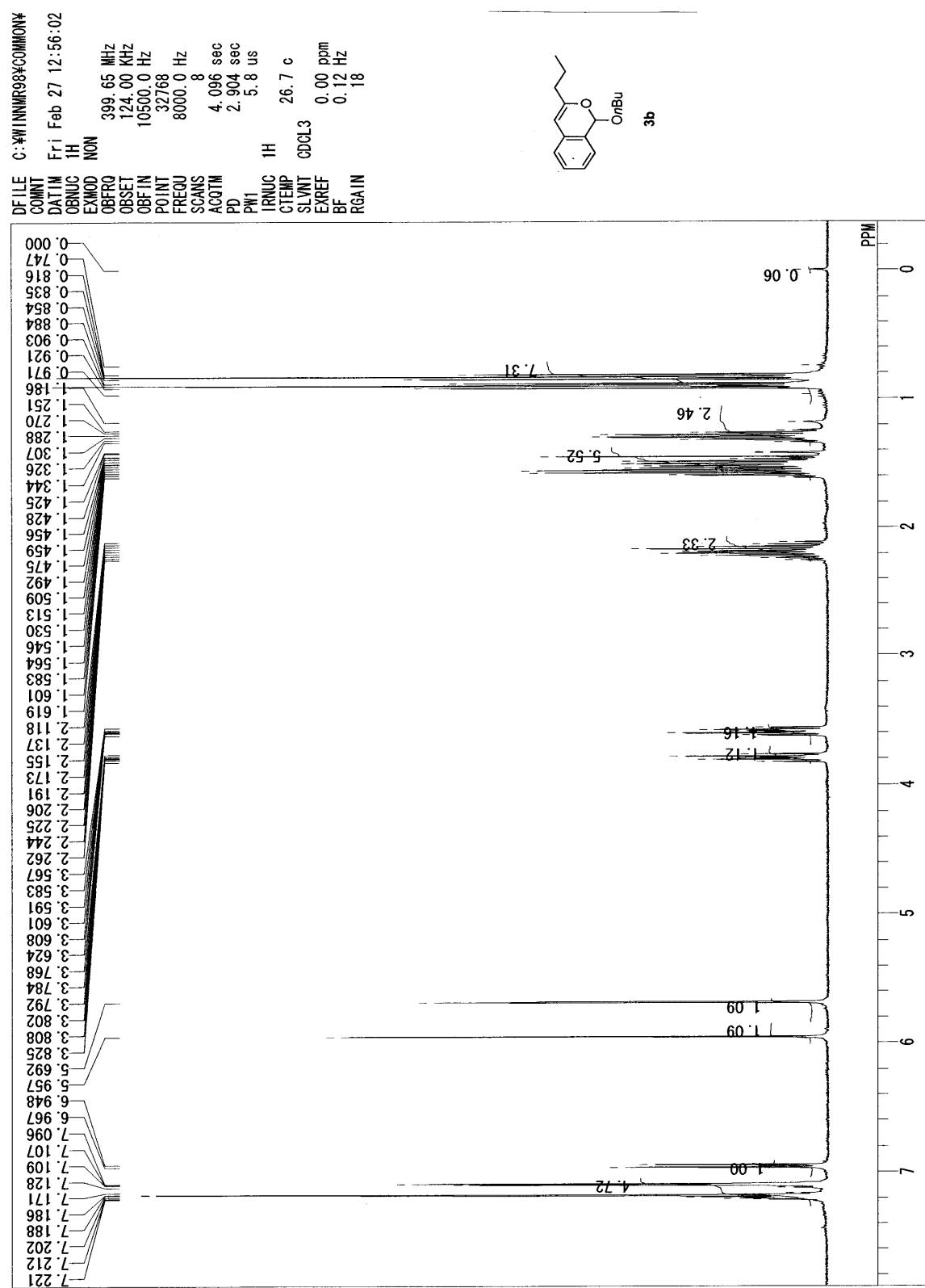
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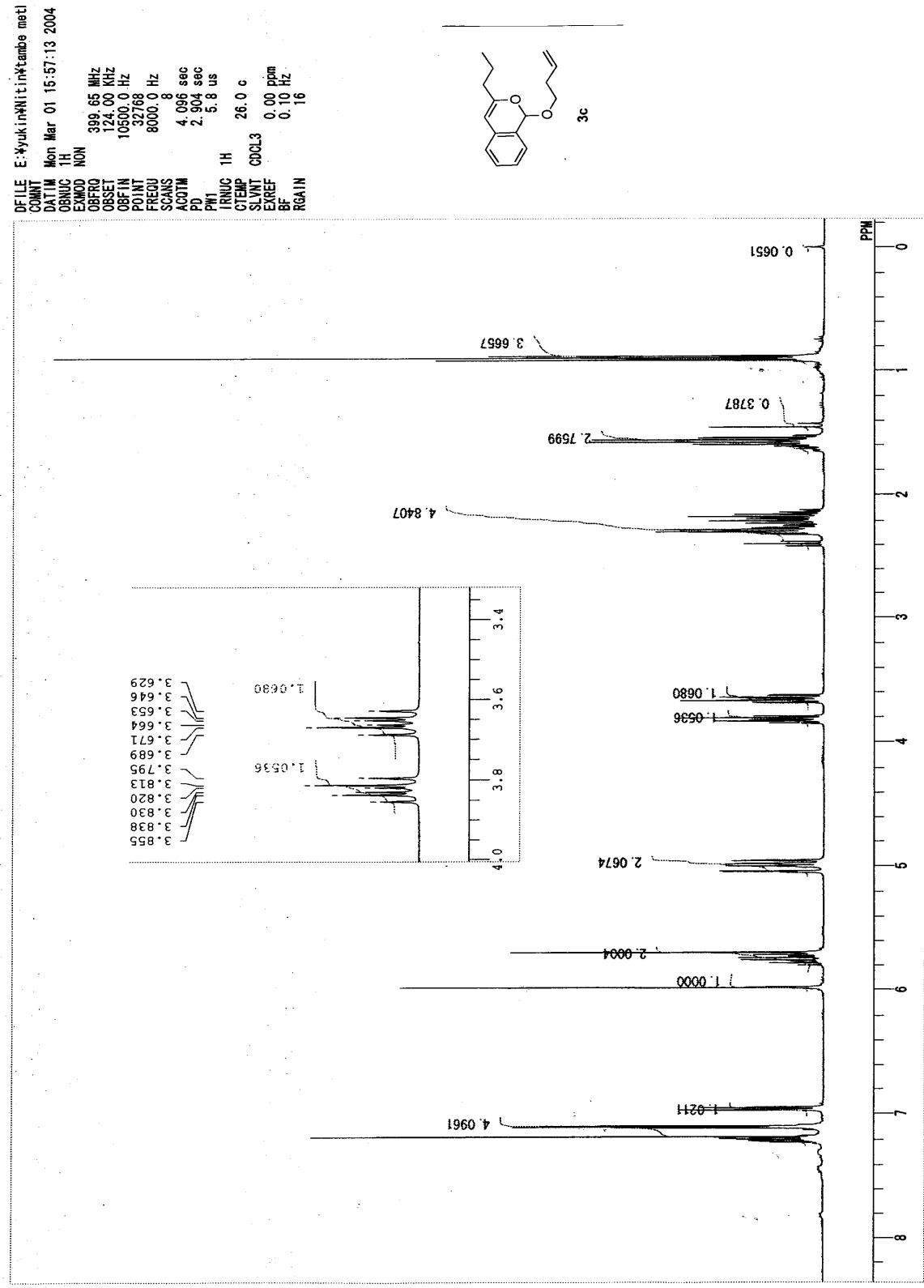




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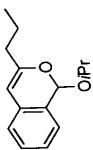
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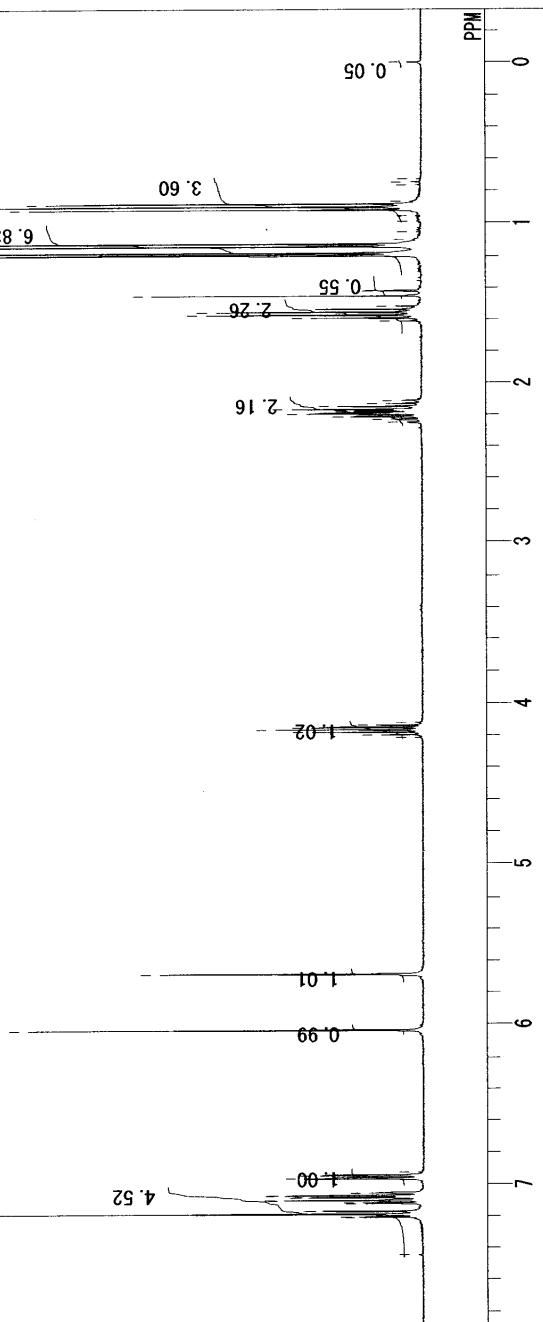
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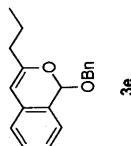
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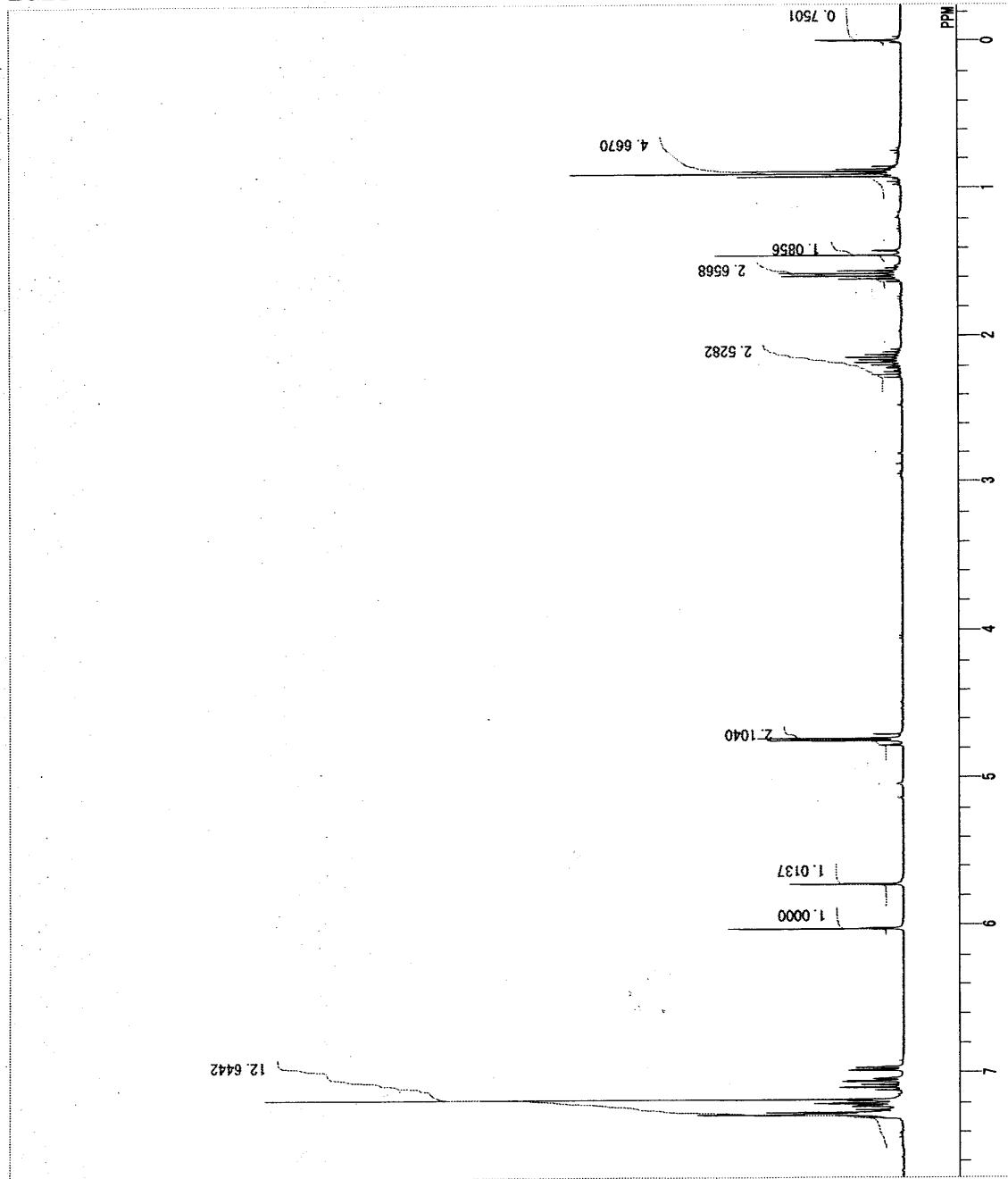
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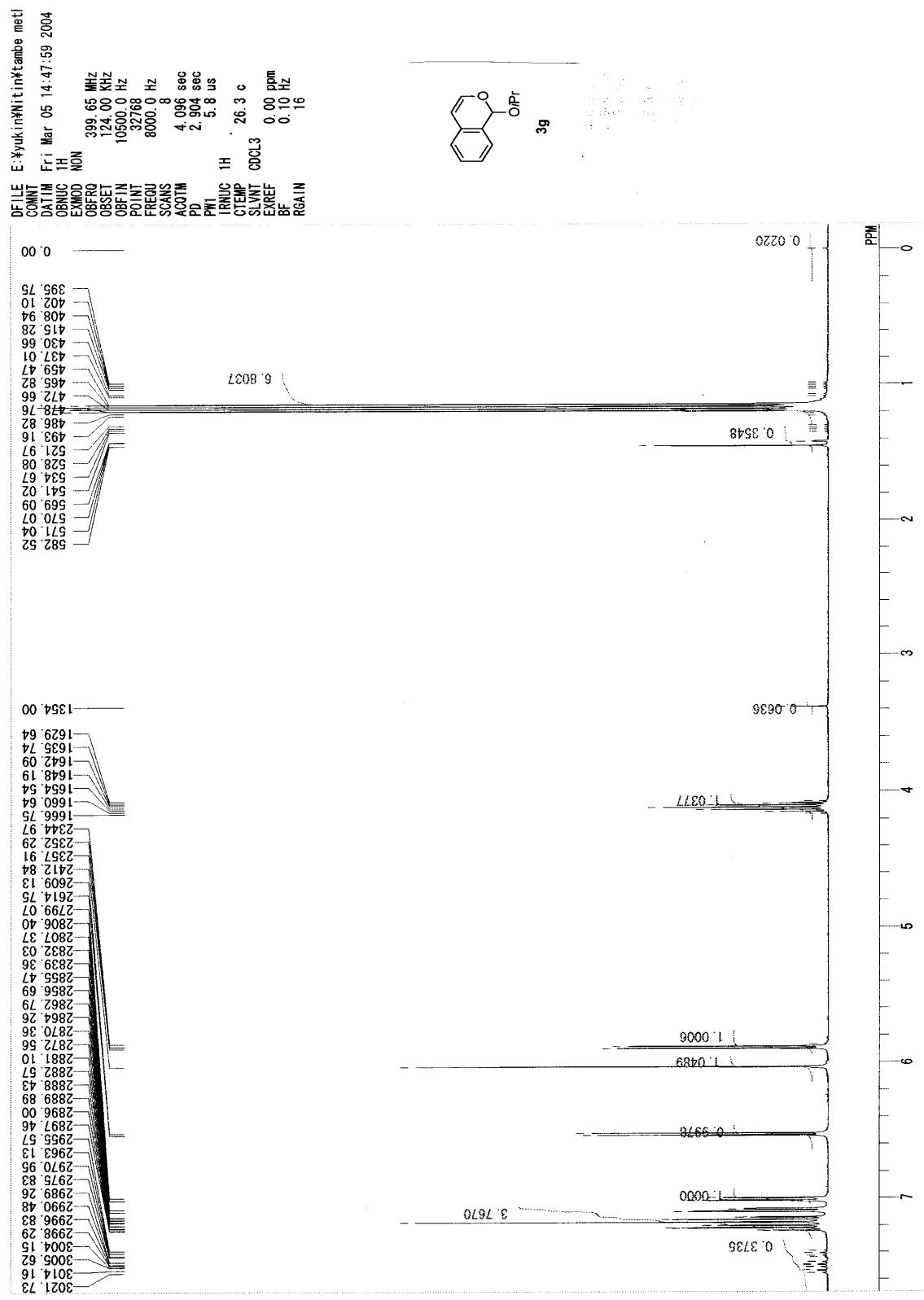
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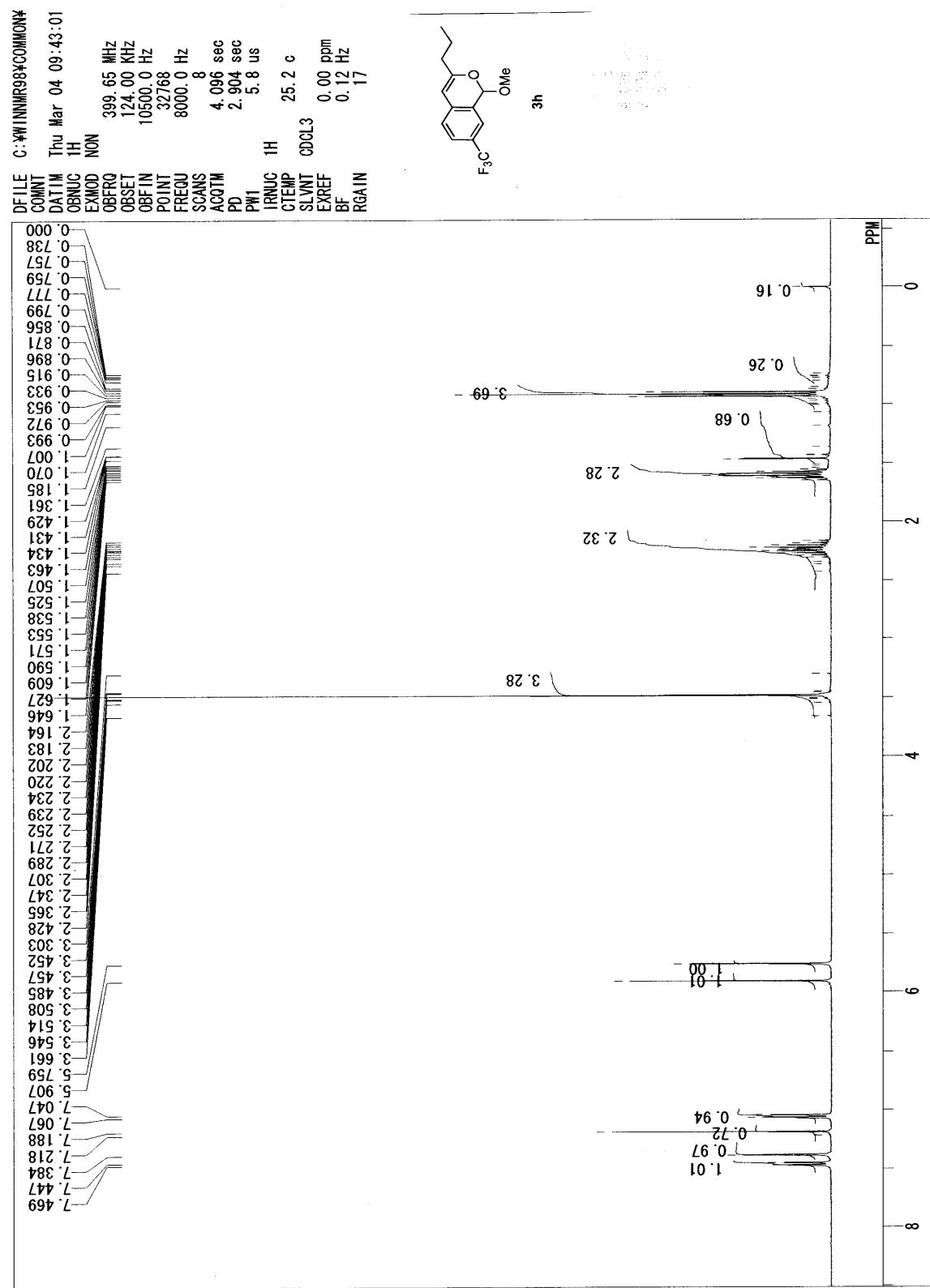
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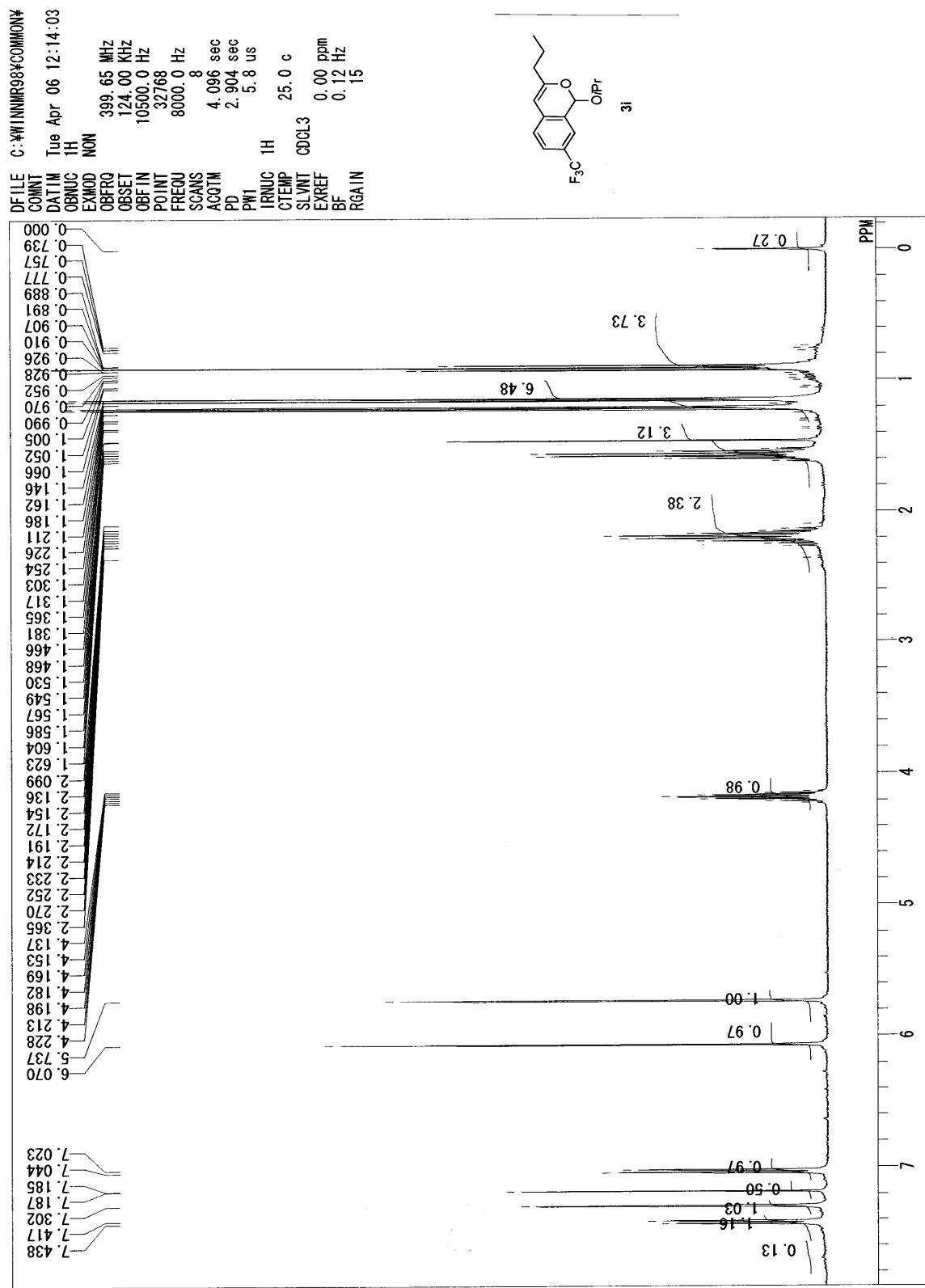
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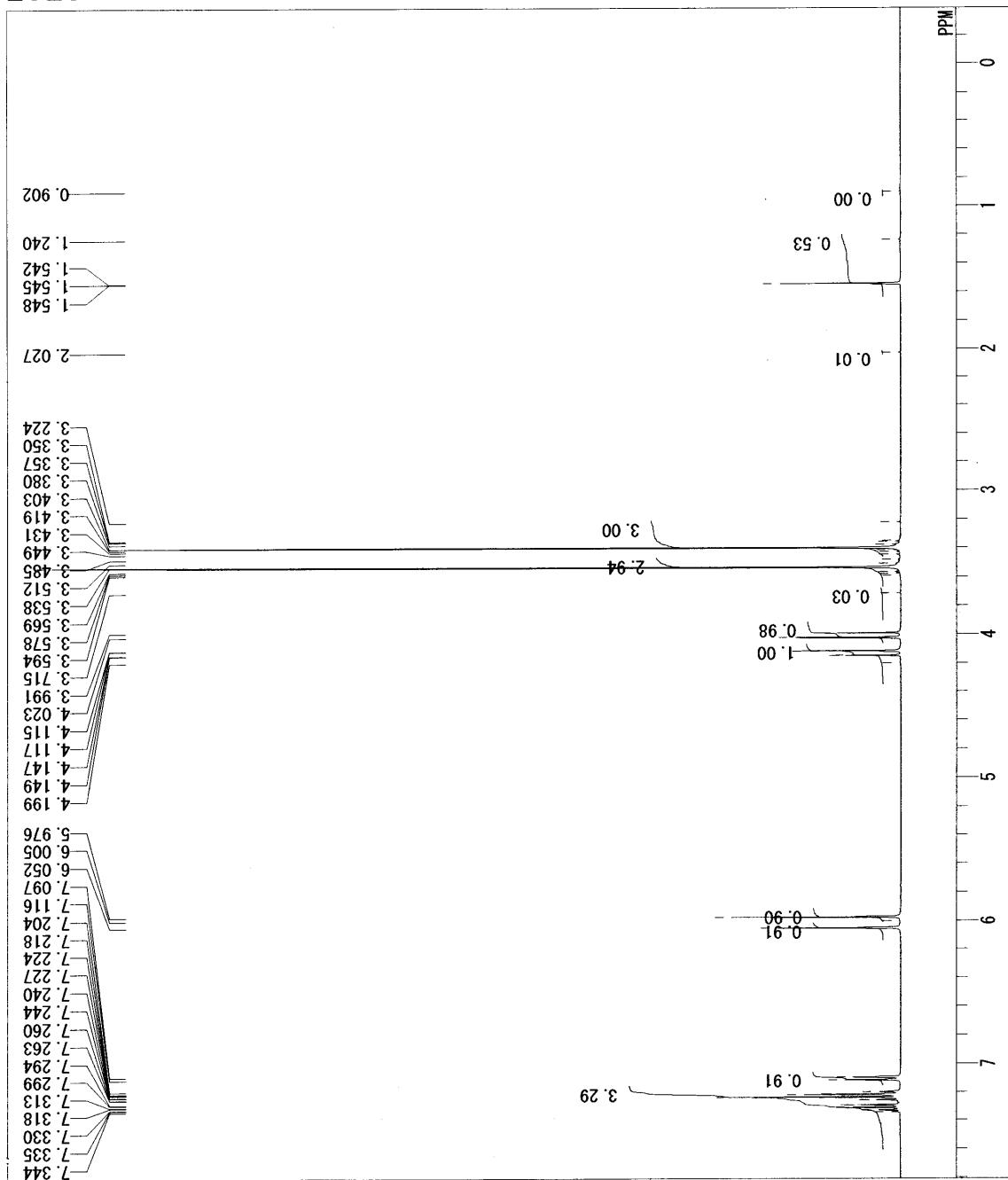
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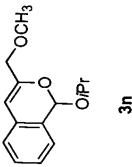
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Chemical structure of compound 3n: 2-methoxy-3-(isopropylidene)cyclohexen-1-one. It features a cyclohexene ring substituted at the 2-position with a methoxy group (-OCH₃) and at the 3-position with an isopropylidene group (-CH=CH-C(CH₃)₂).



3n

