

Palladium-Catalyzed Ring Opening Reaction of Methyleneaziridines with Carboxylic Acids.

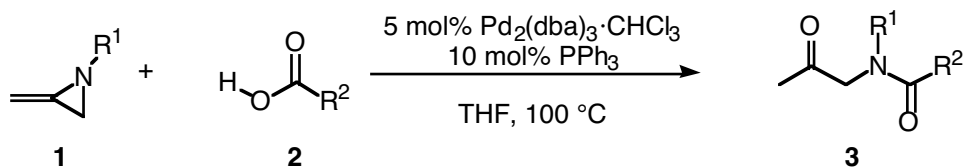
Synthesis of β -Amidoketones

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Japan

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General. Spectroscopic measurements were carried out with the following instrument: JEOL JMMAL-300, JEOL JNM LA-300, JEOL JNM a-500 (^1H and ^{13}C NMR). The α -amido ketone **3** displayed major and minor isomer by ^1H and ^{13}C NMR at room temperature due to slow rotation.¹¹ SHIMADZU FTIR-8200A (FT-IR). Hitachi M-2500S, JEOL JMS-AX500, JEOL JMS-DX303 (high-resolution mass spectra). All methyleneaziridines were prepared following the reported procedure.^{1,2}

General procedure of ring opening reaction of methyleneaziridine **1 with carboxylic acid **2**.**

To a mixture of $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$ (25.9 mg, 0.025 mmol) and triphenylphosphine (13.9 mg, 0.05 mmol) and the carboxylic acid **2** (0.5 mmol) in THF (1 mL) was added methyleneaziridine **1** (0.75 mmol) under Ar atmosphere in a pressure vial. After heating at 100 °C for 2-5 hours, the reaction mixture was filtered through a silica-gel column using ethyl acetate as an eluent. Separation by passing through a silica-gel column and purification by middle-pressure liquid column chromatography (silica gel) and recrystallization afforded β -amidoketone **3**.

N-Benzyl-N-(2-oxo-propyl)-acetamide (3a). White solid: IR (KBr) 3035-2937, 1728, 1633, 1494, 1469, 1454, 1419, 1359, 1247, 1168, 1026, 979, 742, 702, 661 cm^{-1} . ^1H NMR (CDCl_3 , 500 MHz) δ 2.03 (s, 3H, minor), 2.08 (s, 3H, minor), 2.11 (s, 3H, major), 2.22 (s, 3H, major), 4.00 (s, 2H, minor), 4.12 (s, 2H, major), 4.58 (s, 2H, major), 4.60 (s, 2H, minor), 7.17-7.38 (m, 5H, major and m, 5H, minor). ^{13}C NMR (CDCl_3 , 125 MHz, M = major conformer, m = minor conformer) δ 1.10 (M), 21.29 (m), 26.98 (m), 27.22 (M), 49.46 (m), 52.84 (M), 54.79 (M), 57.07 (m), 126.58 (M), 127.55 (m), 127.80 (M), 128.30 (m), 128.58 (m), 128.91 (M), 136.01 (M), 136.69 (m), 170.95 (m), 171.21 (M), 202.67 (m), 203.14 (M). Anal. Calcd for $\text{C}_{12}\text{H}_{15}\text{NO}_2$ (205.25): C, 70.22; H, 7.37; N, 6.82. Found: C, 70.03; H, 7.50; N, 6.56. HRMS (EI) Calcd for $\text{C}_{12}\text{H}_{15}\text{NO}_2$: m/z 205.1103. Found: m/z 205.1104.

N-Benzyl-N-(2-oxo-propyl)-acetamide (3b). Pale yellow solid: IR (KBr) 2916, 1728, 1631, 1496, 1465, 1431, 1398, 1363, 1298, 1257, 1170, 1149, 1049, 1026, 975, 790, 725, 698 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz) δ 1.89 (s, 3H, minor), 2.16 (s, 3H, major), 3.91 (s, 2H, minor), 4.21 (s, 2H, major), 4.58 (s, 2H, major), 4.78 (s, 2H, minor), 7.17-7.54 (m, 10H, major and m, 10H, minor). ^{13}C NMR (CDCl_3 , 75 MHz, M = major conformer, m = minor conformer) δ 26.96 (m), 27.44 (M), 48.88 (m), 53.72 (M), 54.01 (M), 57.44 (m), 126.24 (m), 126.82 (M), 126.87 (M), 127.66 (m), 127.76 (M), 128.37 (m), 128.44 (M), 128.53 (m), 128.71 (m), 128.87 (M), 129.71 (m), 129.88 (M), 135.15 (M), 135.84 (m), 136.12 (M), 136.37 (m), 172.16 (m), 172.32 (M), 202.53 (M), 203.01 (m). Anal. Calcd for $\text{C}_{17}\text{H}_{17}\text{NO}_2$ (267.32): C, 76.38; H, 6.41; N, 5.24. Found: C, 76.09; H, 6.36; N, 5.18. HRMS (EI) Calcd for $\text{C}_{17}\text{H}_{17}\text{NO}_2$: m/z 267.1259. Found: m/z 267.1255.

Pent-2-enoic acid benzyl-(2-oxo-propyl)-amide (3c). Pale yellow oil: IR (neat) 2966, 2933, 1732, 1660, 1622, 1434, 1398, 1359, 1211, 1168, 1082, 700 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz) δ 1.04 (t, $J = 7.5$ Hz, 3H, major and 3H, minor), 2.08 (s, 3H, minor), 2.13 (s, 3H, major), 2.17-2.27 (m, 2H, major and m, 2H, minor), 4.06 (s, 2H, minor), 4.15 (s, 2H, major), 4.66 (s, 2H, major), 4.67 (s, 2H, minor), 5.92 (d, $J = 15$ Hz, 1H, minor), 6.28 (d, $J = 15$ Hz, 1H, major), 6.99-7.39 (m, 6H, major and m, 6H, minor). ^{13}C NMR (CDCl_3 , 75 MHz, M = major conformer, m = minor conformer) δ 12.50 (M and m), 25.63 (M and m), 27.03 (m), 27.33 (M), 50.10 (m), 52.14 (M),

55.47 (M), 56.57 (m), 118.31 (M), 118.38 (m), 126.60 (M), 127.48 (m), 127.65 (M), 128.30 (m), 128.51 (m), 128.77 (M), 136.9 (M), 136.65 (m), 149.27 (m), 149.57 (M), 167.16 (m), 167.35 (M), 203.07 (M and m). HRMS (EI) Calcd for C₁₅H₁₉NO₂: m/z 245.1416. Found: m/z 245.1417.

***N*-[*Benzyl*-(2-oxo-propyl)-carbamoyl]-methyl-benzamide (3d).** Colorless oil: IR (neat) 3400, 3359, 3349, 1732, 1668, 1558, 1361, 1224, 1168, 1058, 731 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz) δ 2.10 (s, 3H, minor), 2.11 (s, 3H, major), 4.09-4.11 (m, 4H, minor), 4.15 (s, 2H, major), 4.44 (d, *J* = 4.2 Hz, 2H), 4.58 (s, 2H, major), 4.63 (s, 2H, minor), 7.18-7.51 (m, 8H, major and m, 8H, minor), 7.81-7.85 (m, 2H, major and m, 2H, minor). ¹³C NMR (CDCl₃, 75 MHz, M = major conformer, m = minor conformer) δ 7.13 (m), 27.20 (M), 41.55 (m), 41.63 (M), 50.16 (m), 51.20 (M), 55.07 (M), 55.31 (m), 126.84 (M and m), 126.90 (M and m), 128.06 (M), 128.17 (m), 128.27 (m), 128.33 (M), 128.64 (m), 128.95 (M), 131.41 (M and m), 133.58 (m), 133.66 (M), 134.71 (M), 135.69 (m), 166.90 (m), 166.93 (M), 168.86 (m), 168.90 (M), 201.63 (m), 201.89 (M). HRMS (EI) Calcd for C₁₉H₂₀N₂O₃: m/z 324.1474. Found: m/z 324.1476.

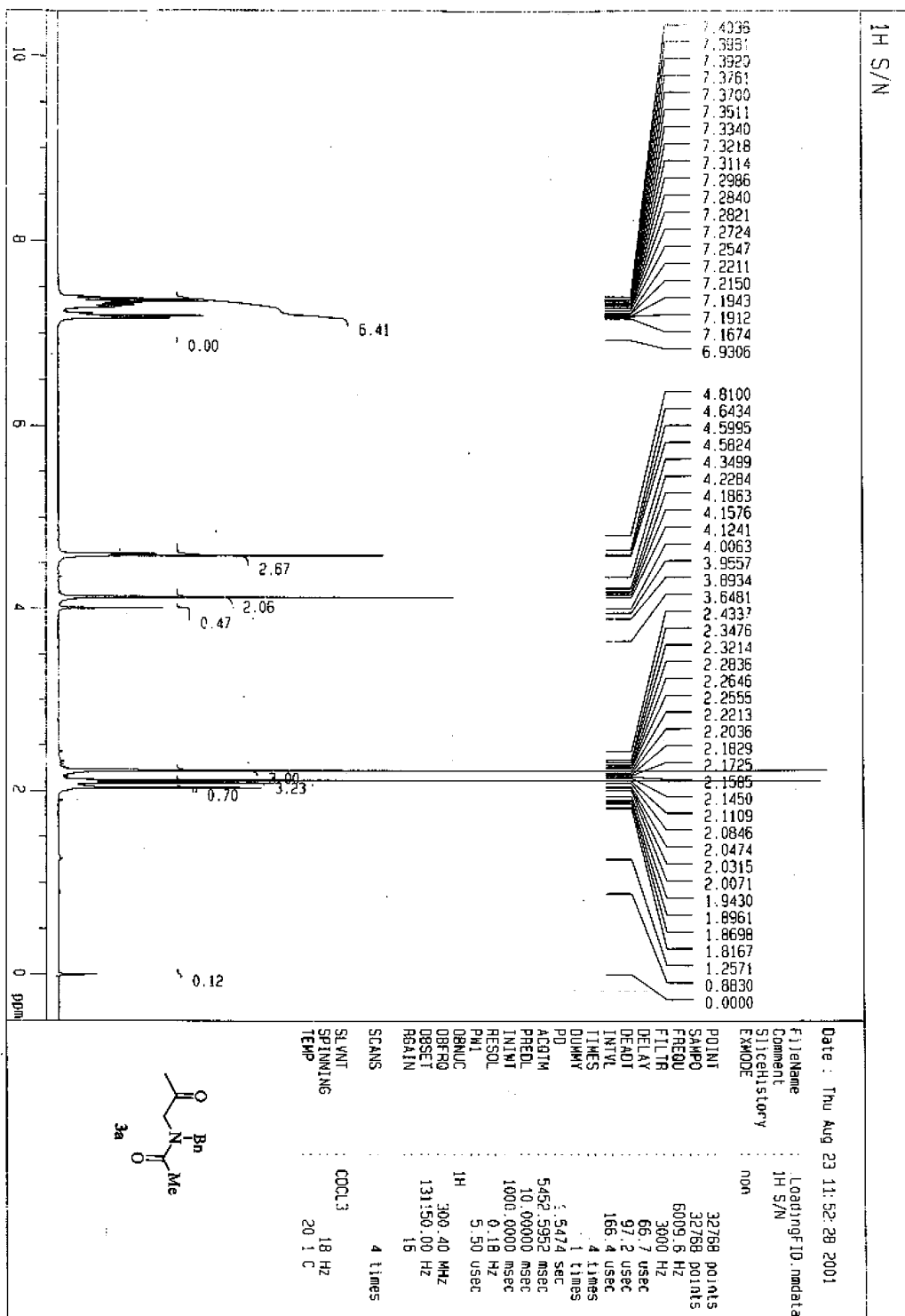
***N*-Hexyl-*N*-(2-oxo-propyl)-benzamide (3e).** Yellow oil: IR (neat) 2929, 2858, 1732, 1638, 1431, 1170, 1110, 702 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz) δ 0.76-0.86 (m, 3H, major and m, 3H, minor), 1.09-1.55 (m, 8H, major and m, 8H, minor), 1.93 (s, 3H, minor), 2.20 (s, 3H, major), 3.20 (t, *J* = 7.8 Hz, 2H, major), 3.43 (t, *J* = 7.8 Hz, 2H, minor), 3.99 (s, 2H, minor), 4.22 (s, 2H, major), 7.24-7.38 (m, 5H, major and m, 5H, minor). ¹³C NMR (CDCl₃, 75 MHz, M = major conformer, m = minor conformer) δ 3.82 (M), 13.93 (m), 22.34 (M), 22.51 (m), 26.02 (M), 26.55 (m), 26.90 (m), 27.12 (m), 27.34 (M), 28.41 (M), 31.12 (M), 31.51 (m), 46.83 (m), 50.31 (M), 54.69 (M), 58.97 (m), 126.16 (m), 126.58 (M), 128.33 (M and m), 129.45 (M and m), 135.92 (M), 136.45 (m), 171.89 (m), 172.03 (M), 202.92 (M), 203.20 (m). HRMS (EI) Calcd for C₁₆H₂₃NO₂: m/z 261.1729. Found: m/z 261.1733.

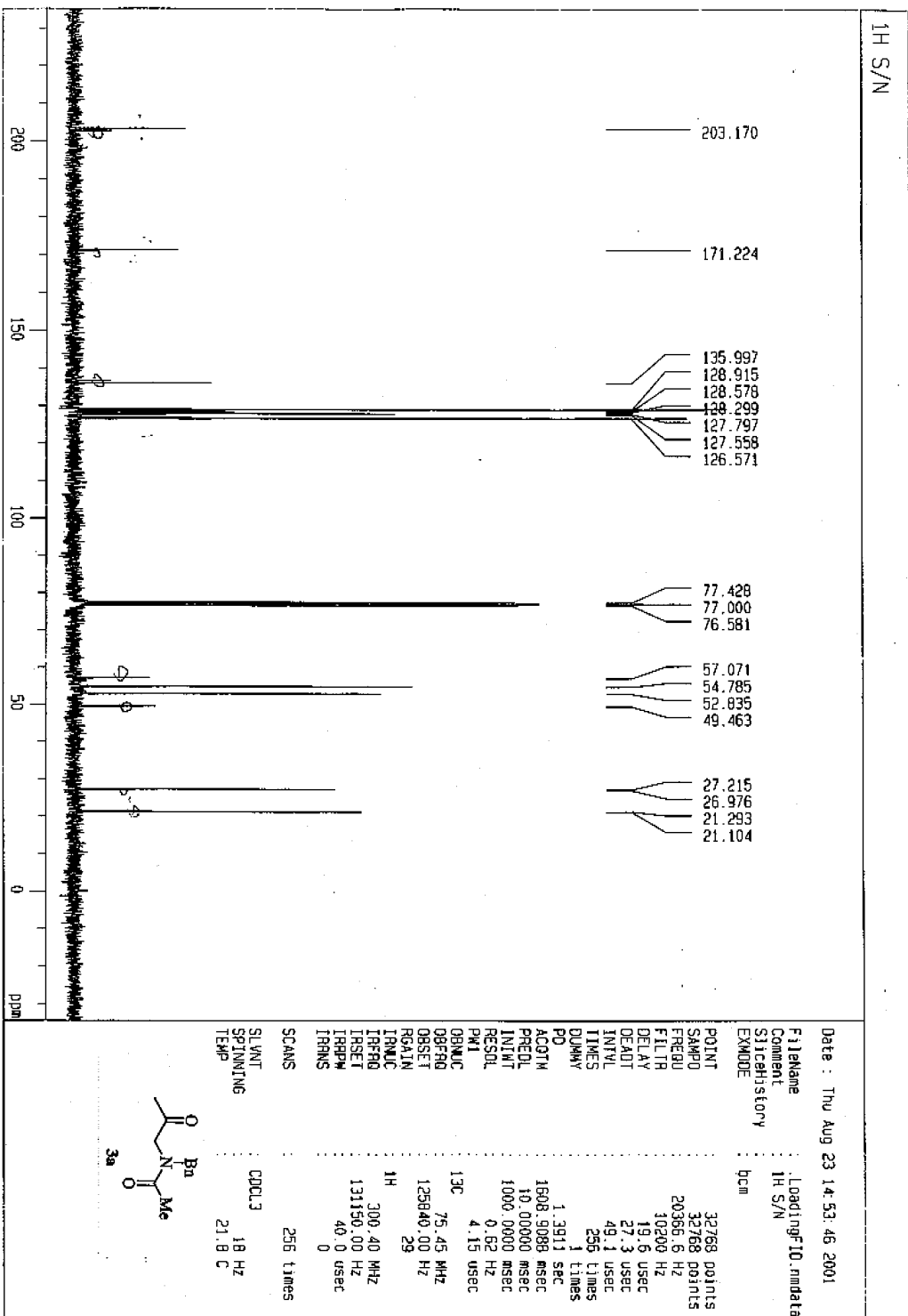
***N*-Hexyl-*N*-(2-oxo-propyl)-benzamide (3f).** Yellow oil: IR (neat) 2958, 2931, 2873, 1732, 1633, 1431, 1172, 1105, 702 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz) δ 0.79 (t, *J* = 7.2 Hz, 3H, major), 0.96 (t, *J* = 7.2 Hz, 3H, minor), 1.11-1.59 (m, 4H, major and m, 4H, minor), 1.97 (s, 3H, minor), 2.24 (s, 3H, major), 3.25 (t, *J* = 7.5 Hz, 2H, major), 3.47 (t, *J* = 7.5 Hz, 2H, minor), 4.04 (s, 2H, minor), 4.26 (s, 2H, major), 7.28-7.41 (m, 5H, major and m, 5H, minor). ¹³C NMR (CDCl₃, 75 MHz, M = major conformer, m = minor conformer) δ 13.57 (M), 13.89 (m), 19.67 (M), 20.21 (m), 26.98 (m), 27.42 (M), 29.32 (m), 30.66 (M), 46.64 (m), 50.16 (M), 54.77 (M), 59.03 (m), 126.22 (m), 126.67 (M), 128.41 (M and m), 129.53 (M and m), 135.99 (M), 136.51 (m), 172.05 (m), 172.10 (M), 202.99 (M), 203.35 (m). HRMS (EI) Calcd for C₁₄H₁₉NO₂: m/z 233.1416. Found: m/z 233.1418.

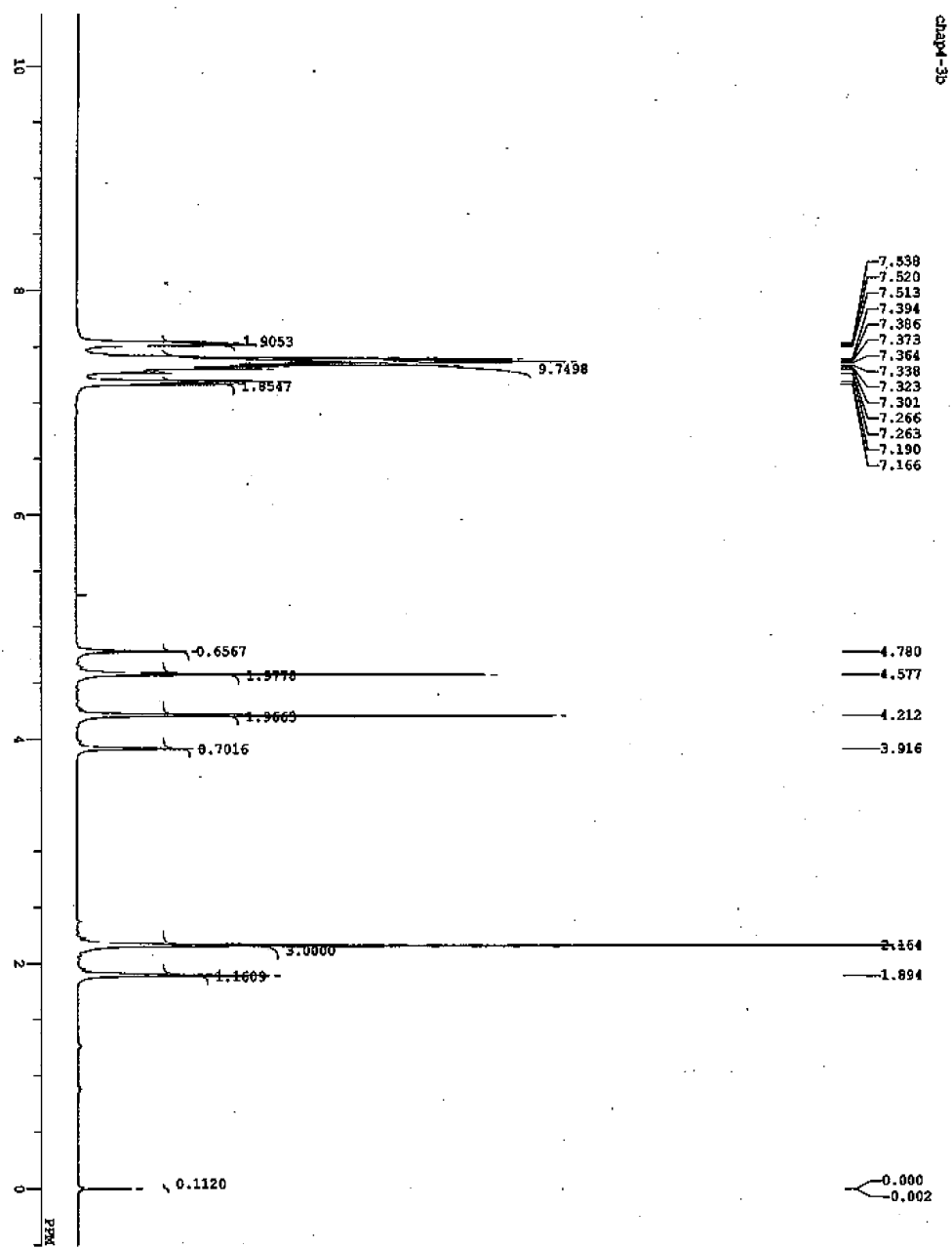
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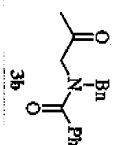
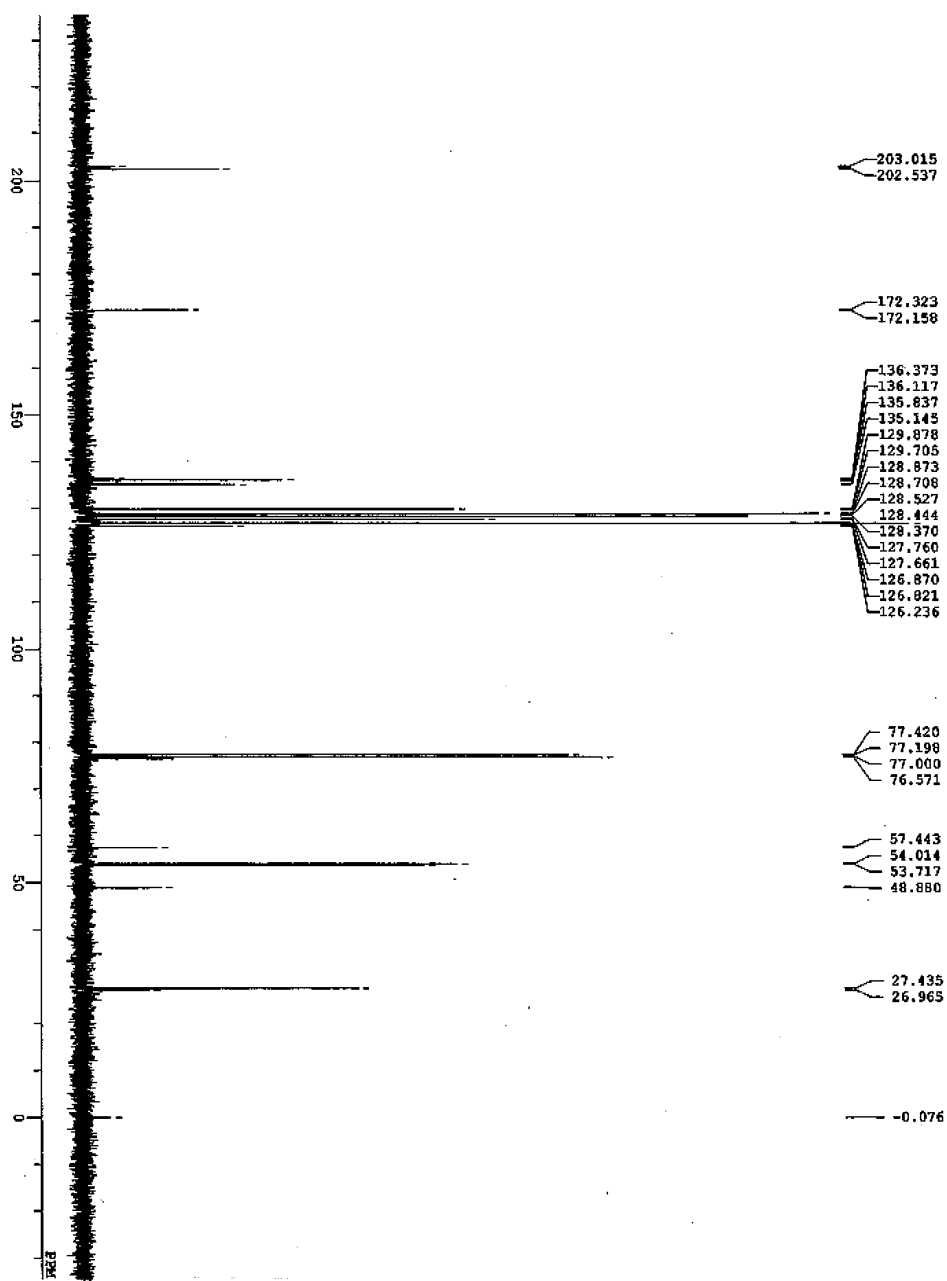
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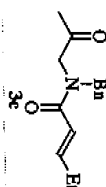
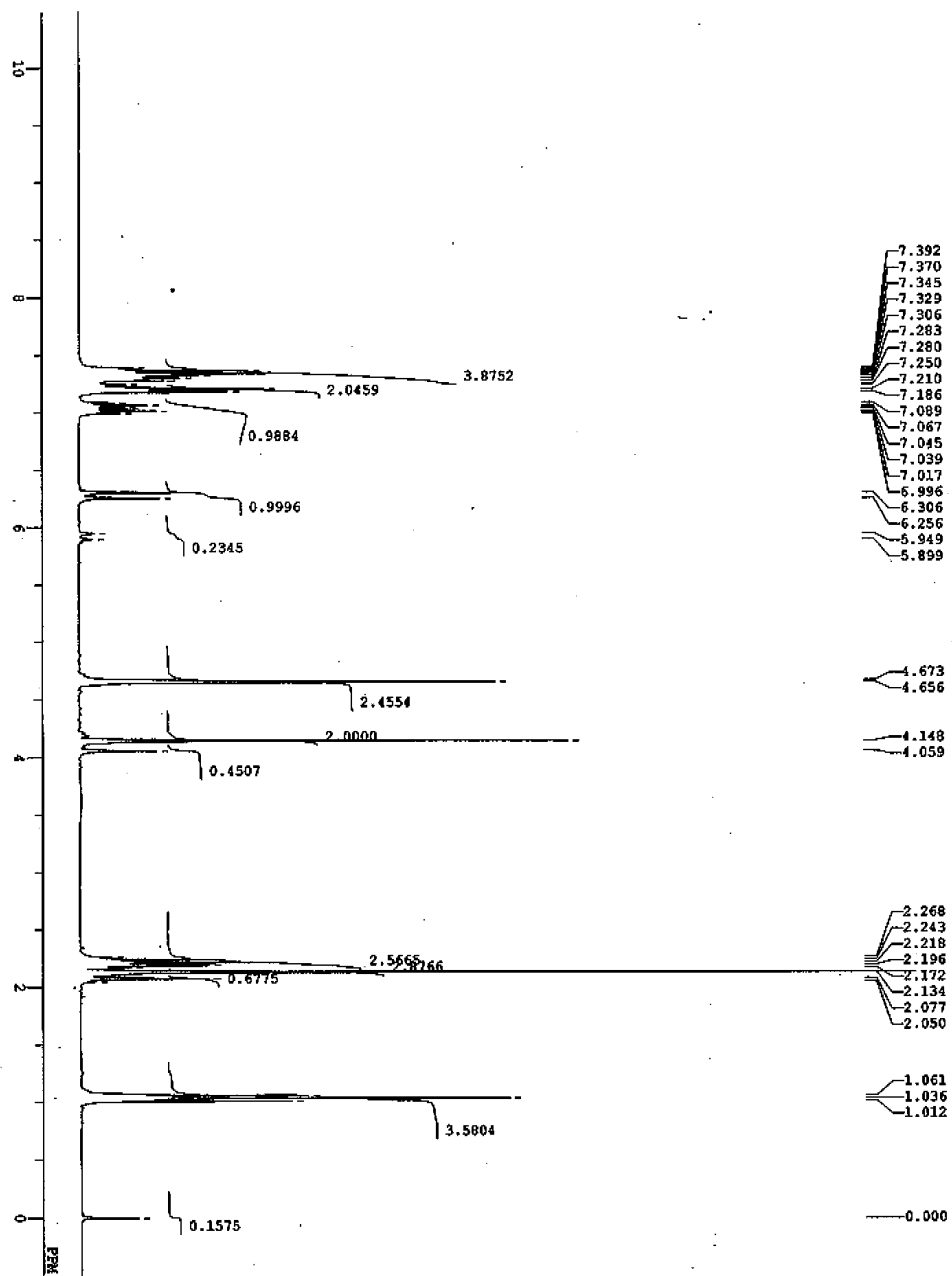
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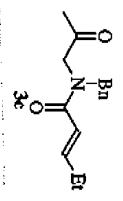
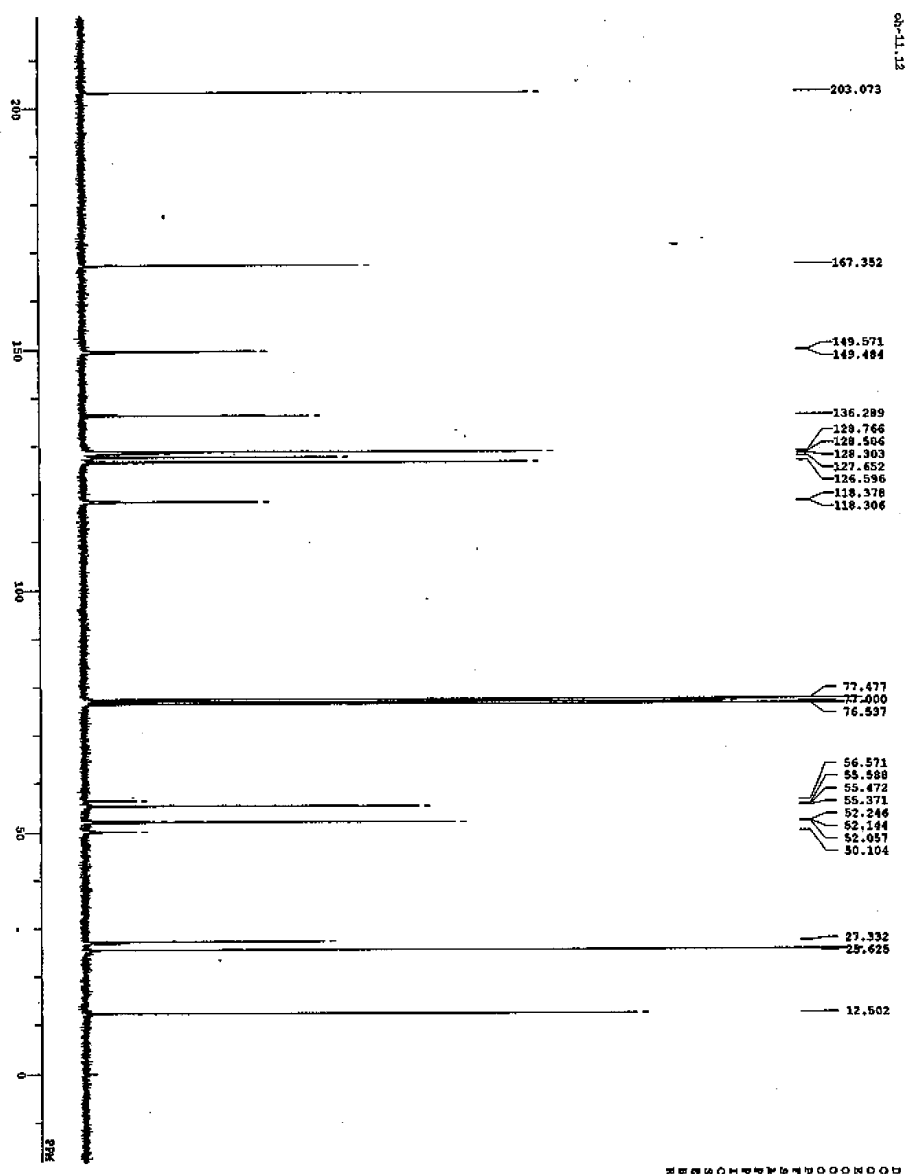






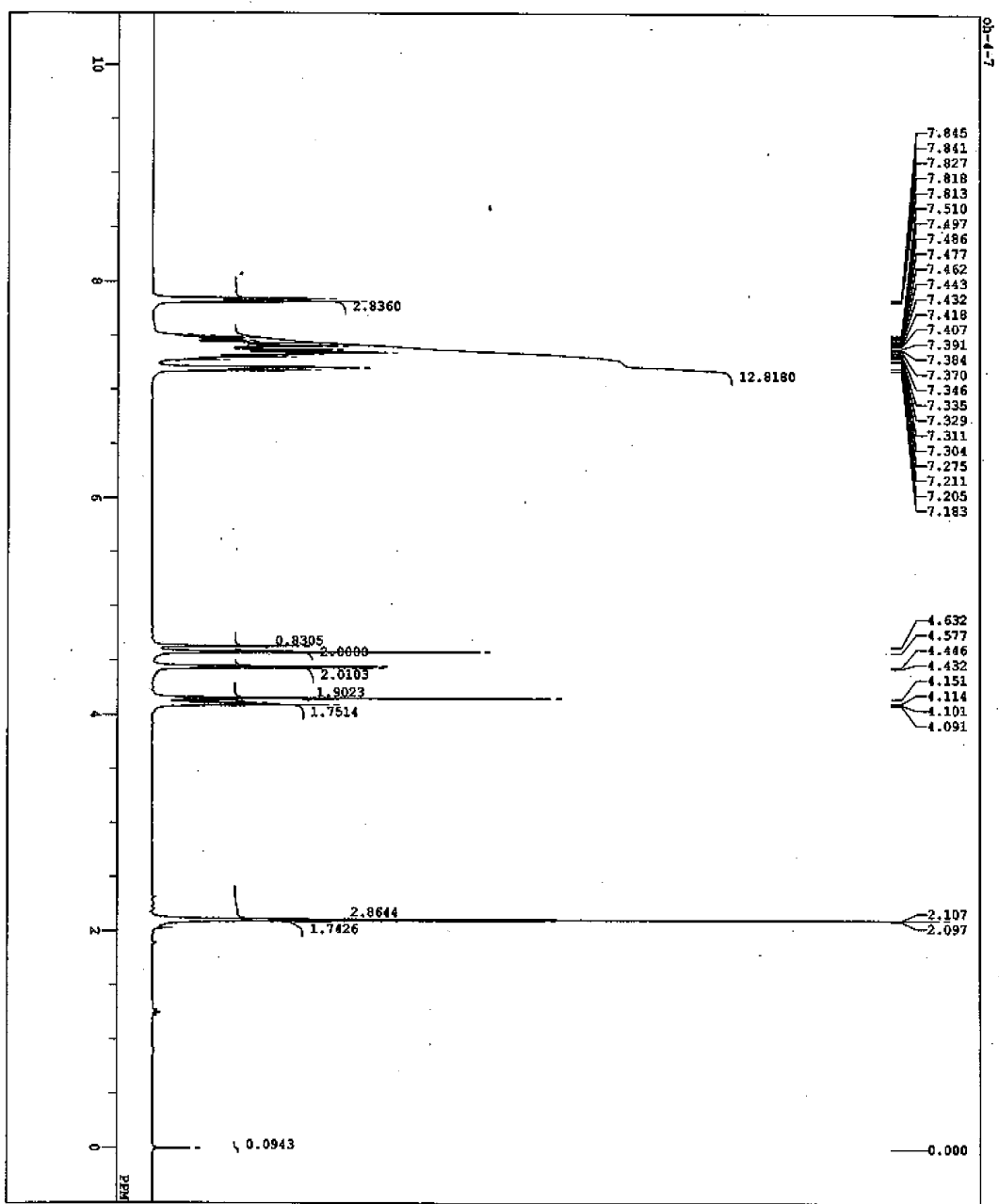




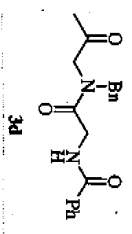


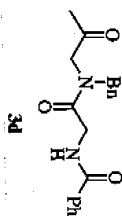
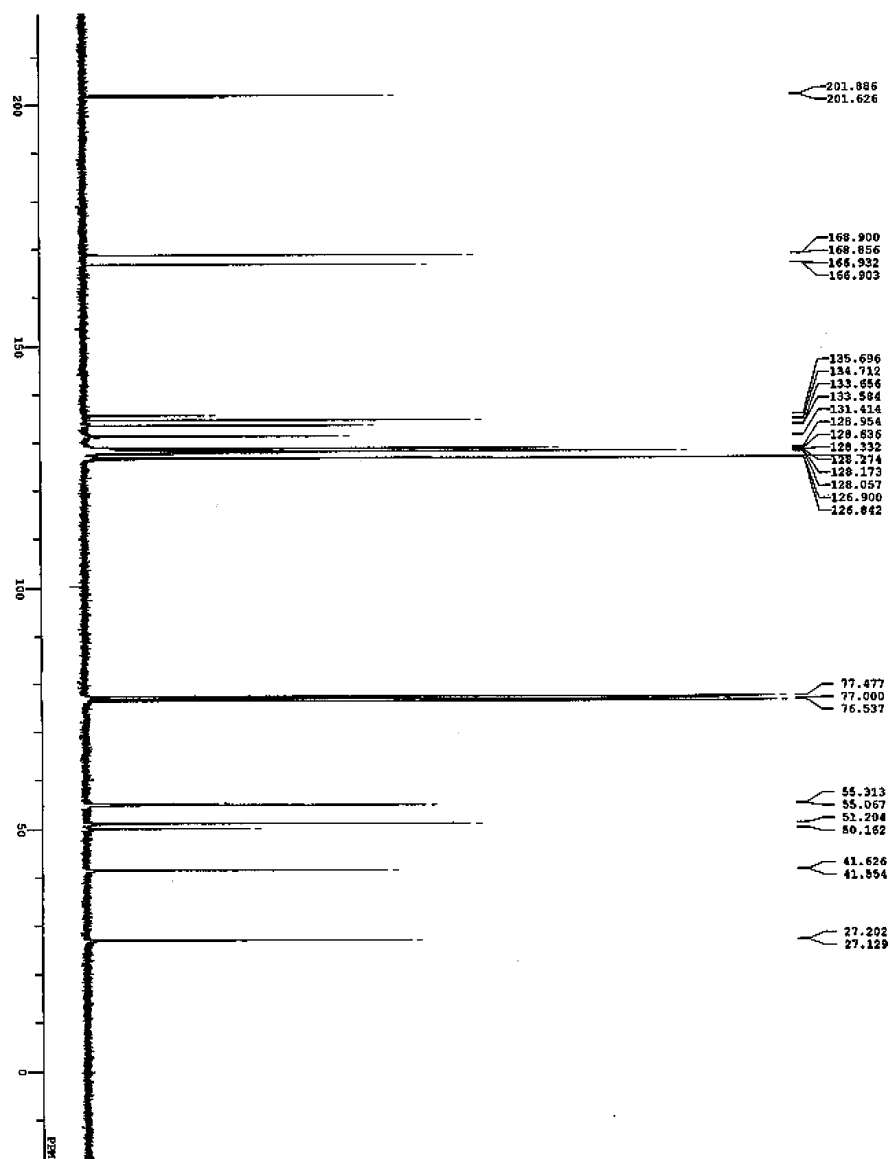
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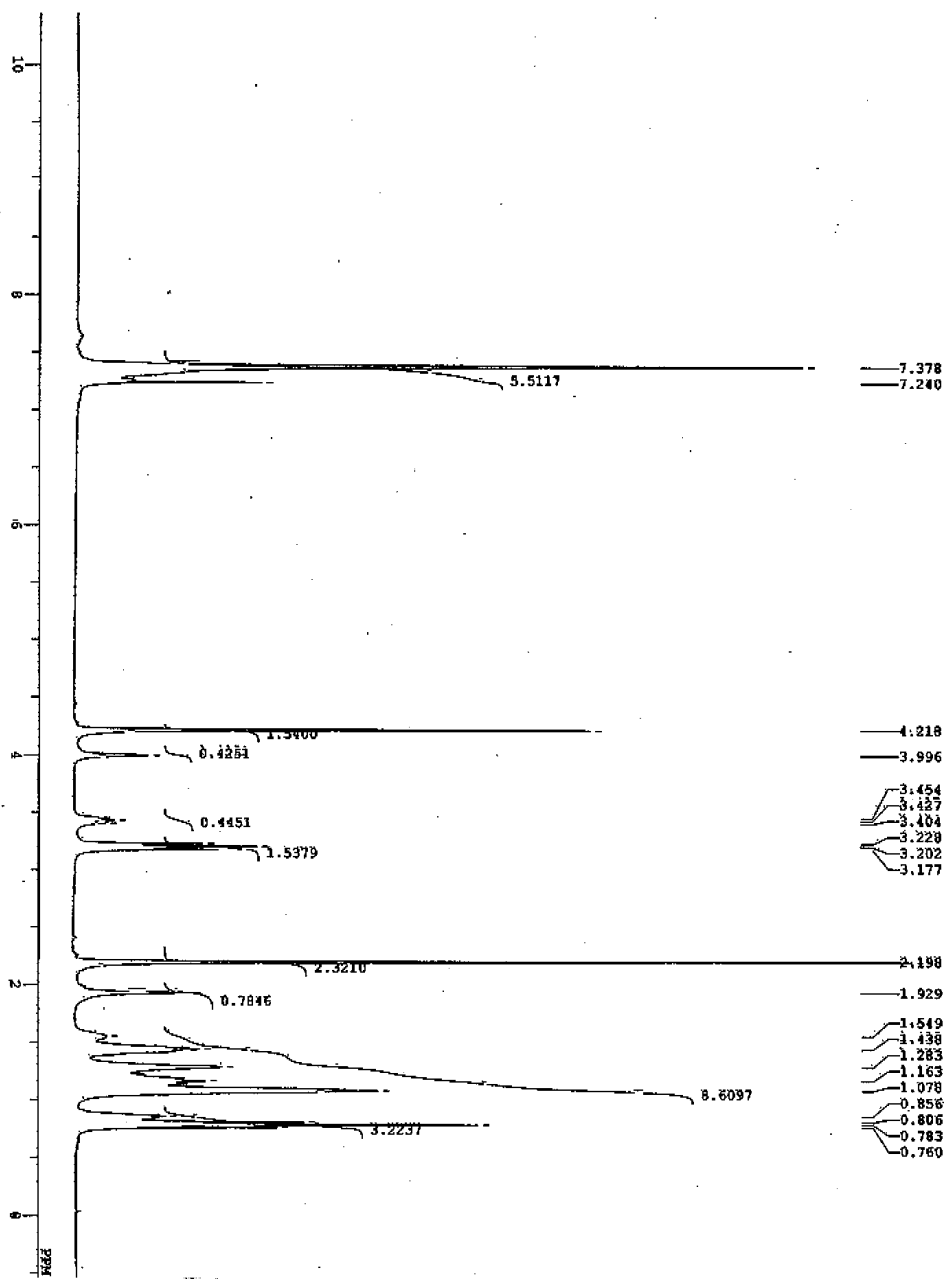
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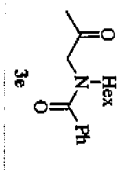
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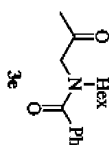
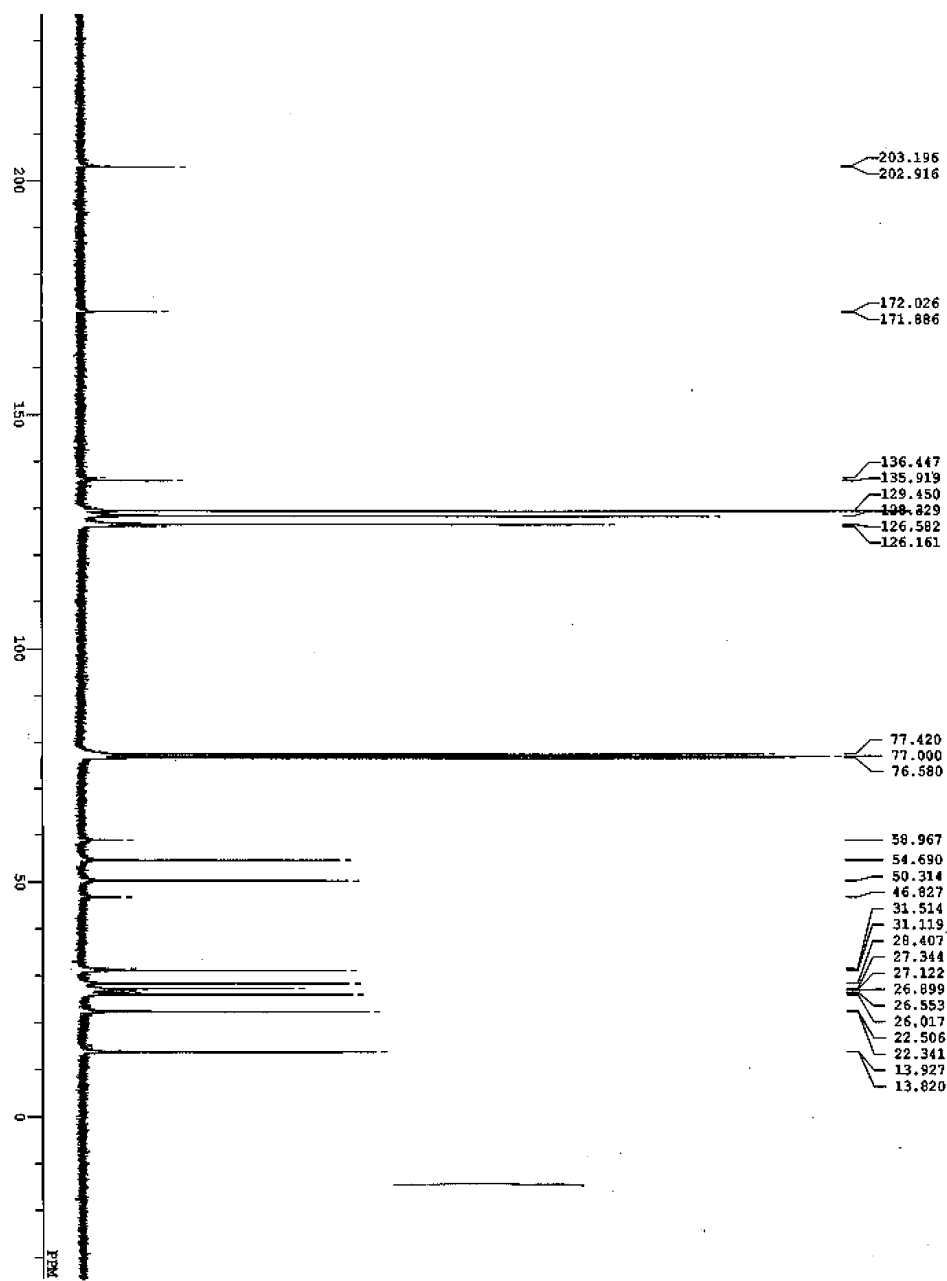


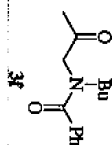
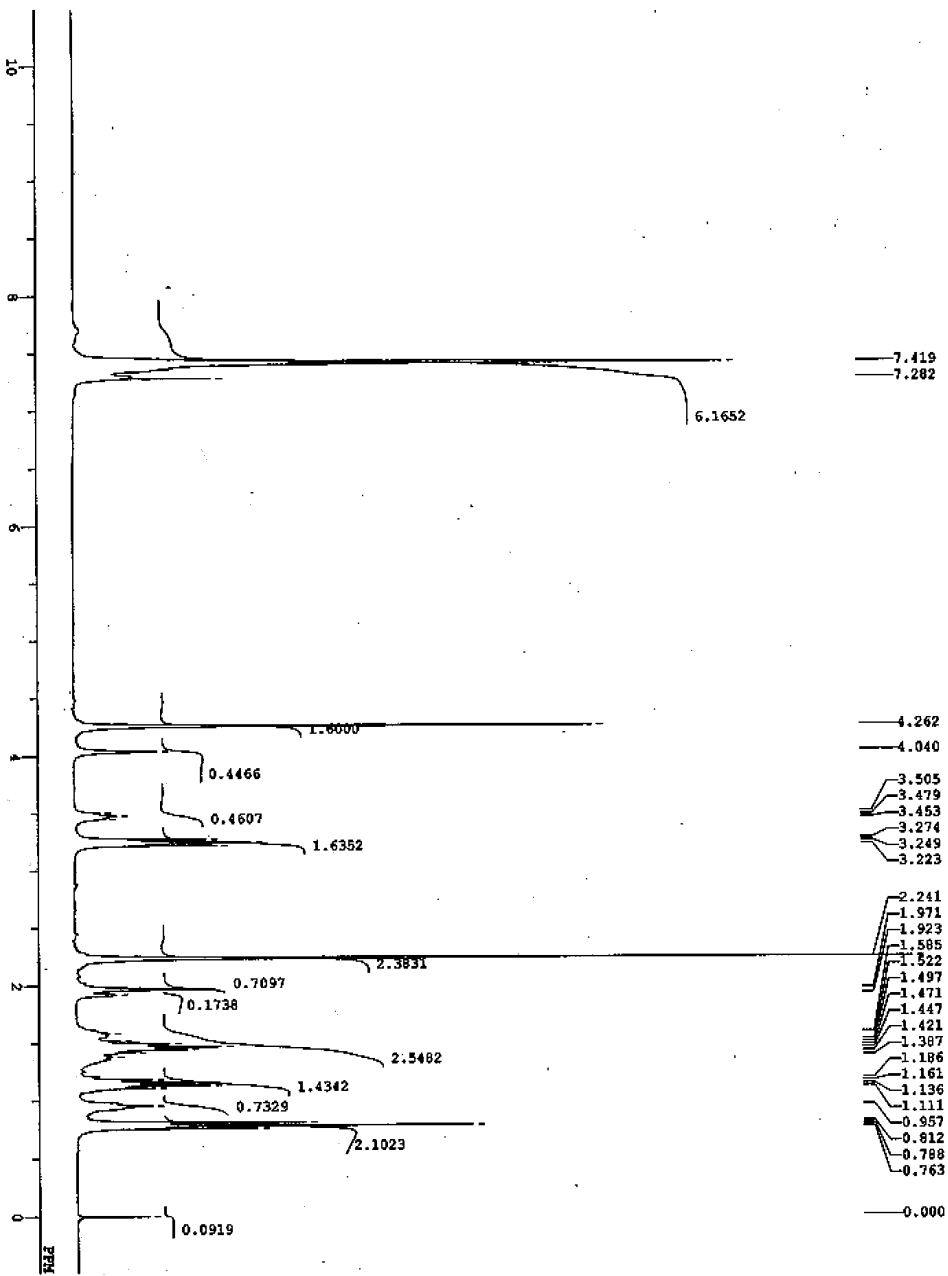




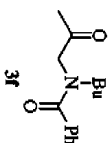
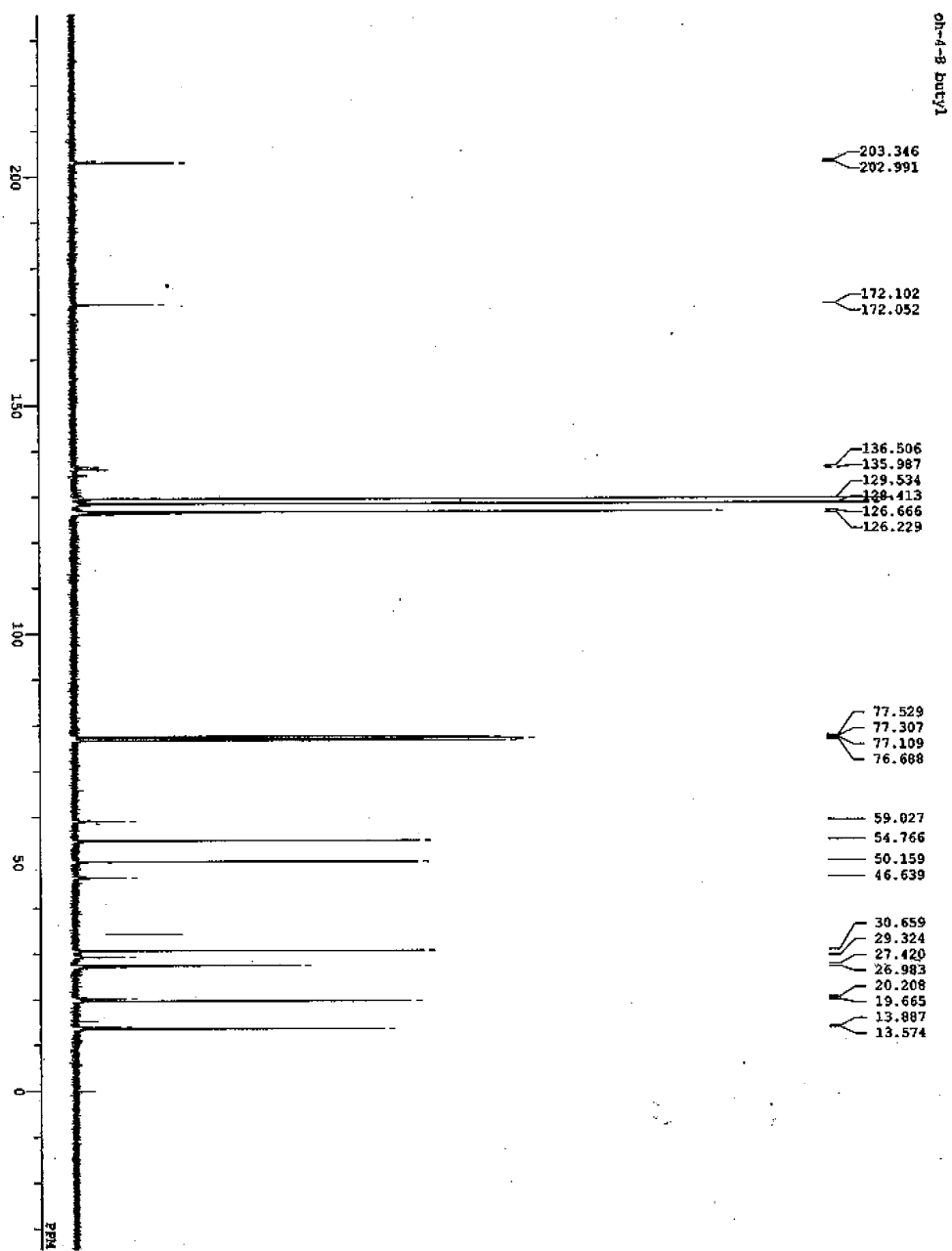
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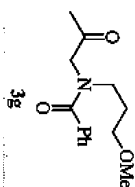
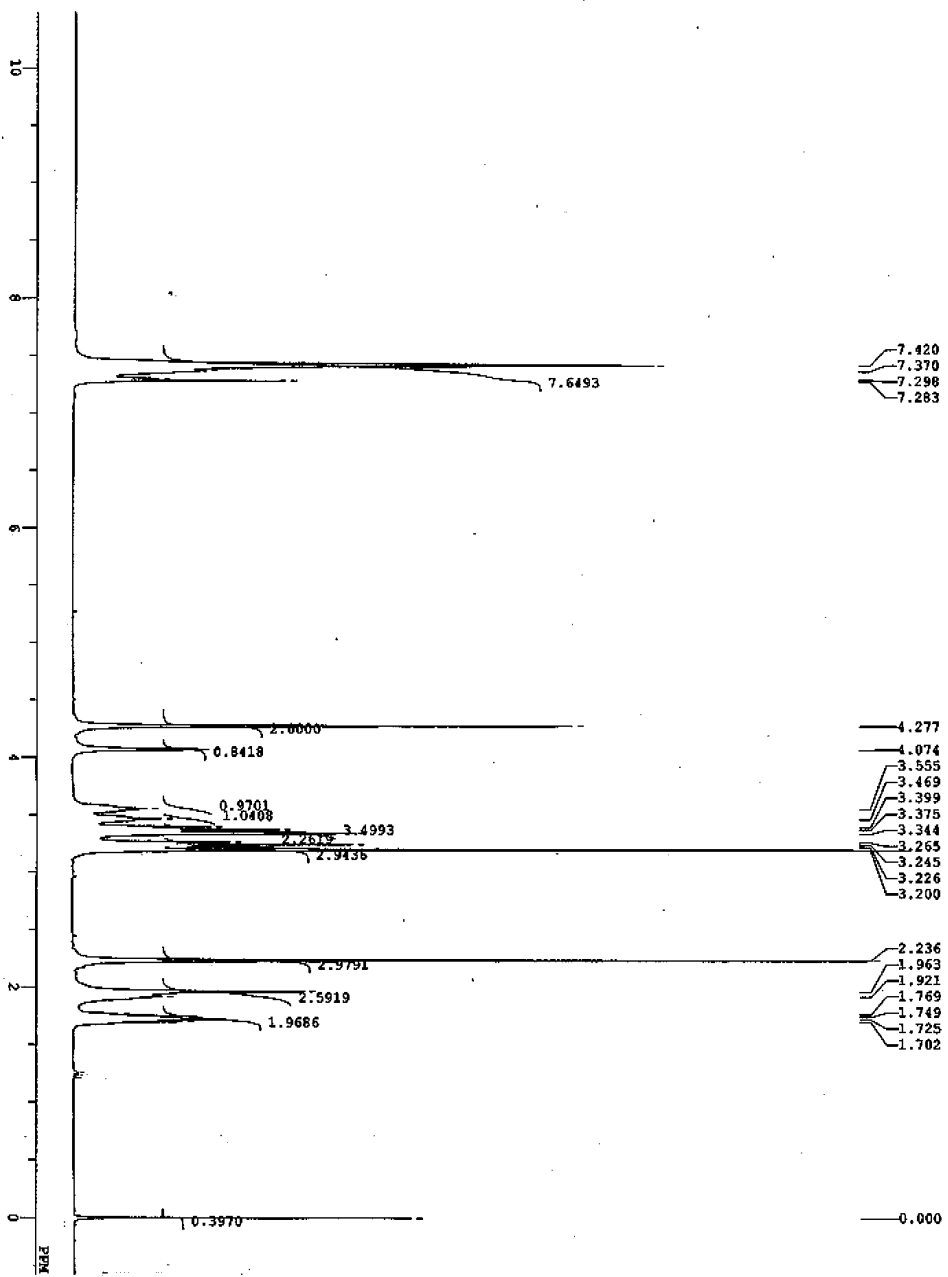






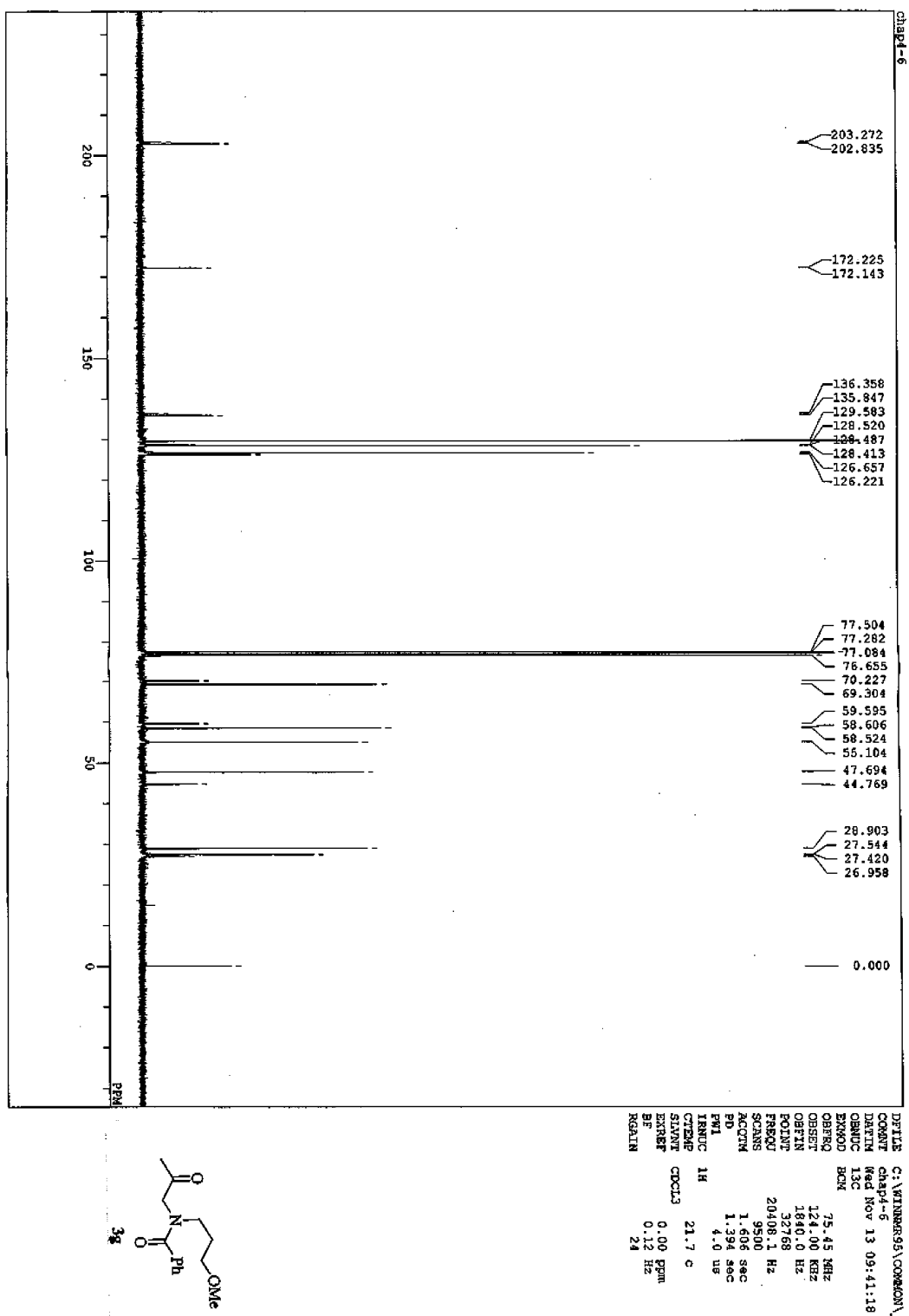
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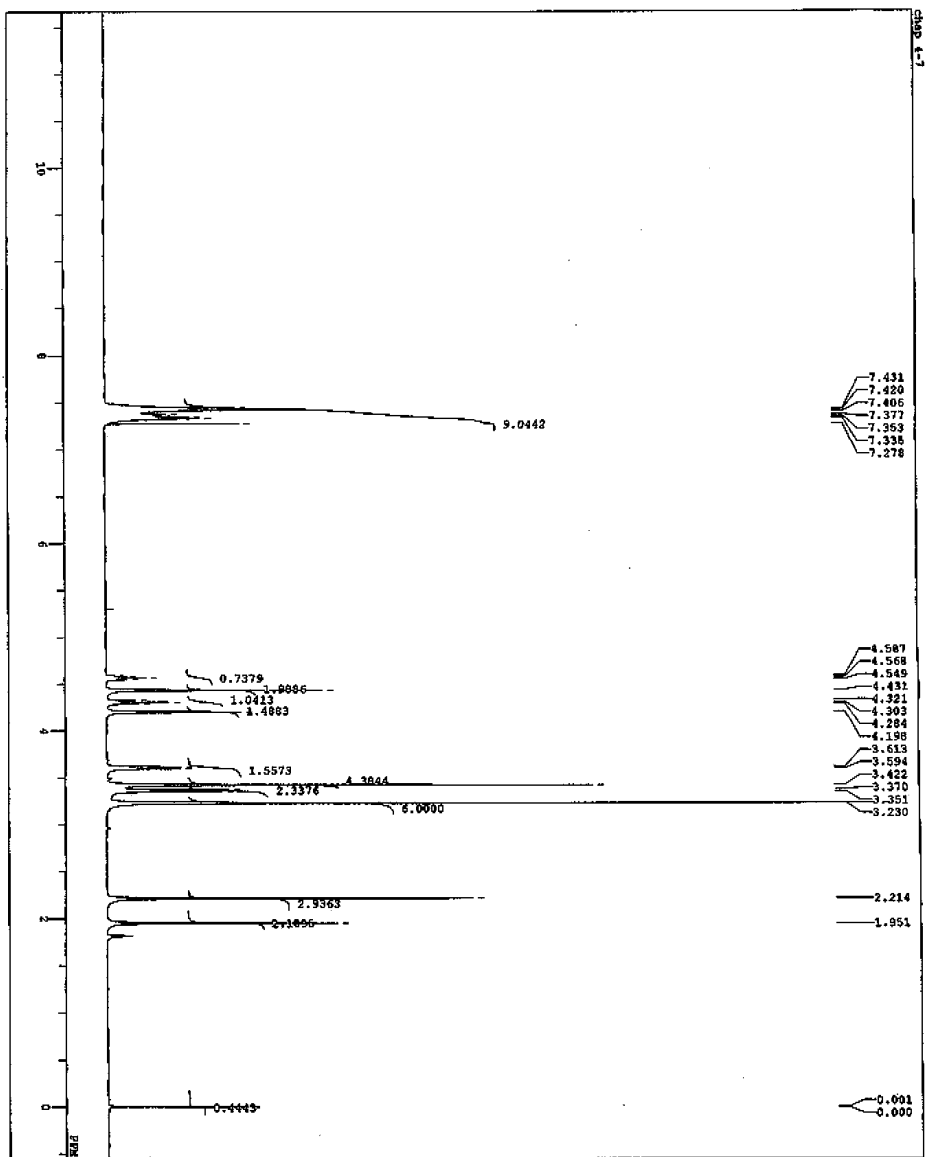




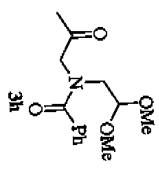
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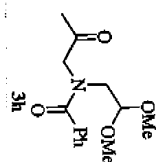
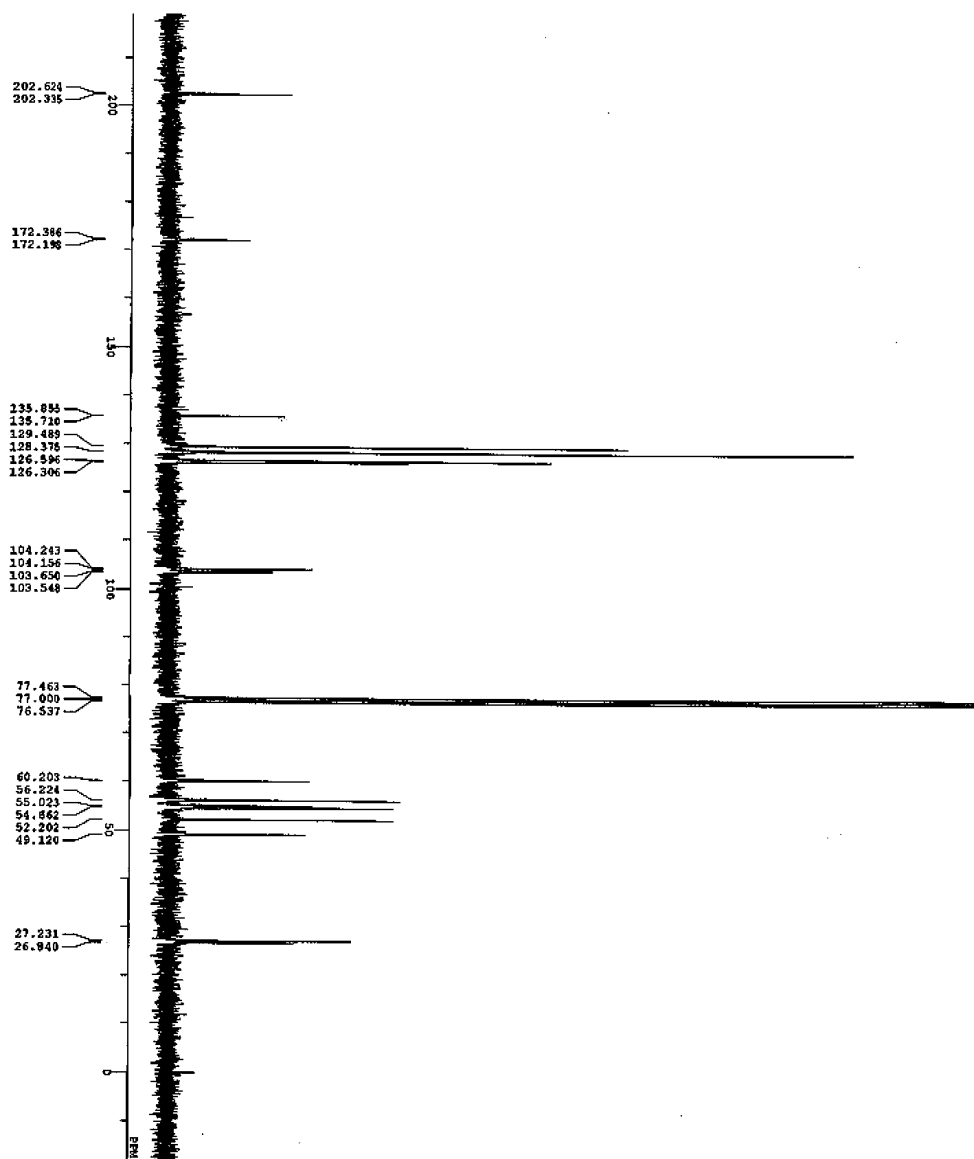
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