

Supporting Information

Enantioselective Conjugate Hydrocyanation of α,β -Unsaturated *N*-Acylpyrroles Catalyzed by Chiral Lithium(I) Phosphoryl Phenoxide

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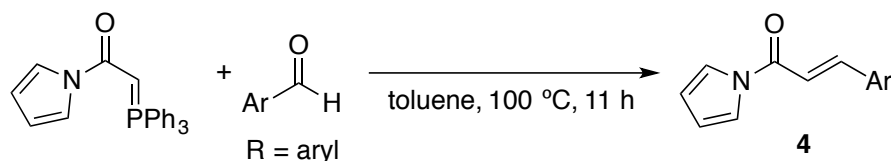
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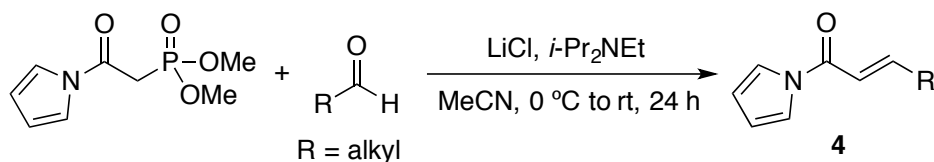
1. General methods.

¹H NMR spectra were measured on a JEOL ECS400 (400 MHz) spectrometer at ambient temperature. Data were recorded as follows: chemical shift in ppm from internal tetramethylsilane on the δ scale, multiplicity (s = singlet; d = doublet; t = triplet; q = quartet, m = multiplet, br = broad), coupling constant (Hz), integration, and assignment. ¹³C NMR spectra were measured on a JEOL ECS400 (100 MHz) spectrometer. Chemical shifts were recorded in ppm from the solvent resonance employed as the internal standard (deuteriochloroform at 77.00 ppm). ¹⁹F NMR spectra were measured on a JEOL ECS-400 (376 MHz) spectrometer. Chemical shifts were recorded in ppm from the solvent resonance employed as the external standard (CFCl₃ at 0 ppm). Optical rotations were measured on Rudolph Autopol IV digital polarimeter. The products were purified by column chromatography on silica gel (E. Merck Art. 9385; Kanto Chemical Co., Inc. 37560). High resolution mass spectral analyses were performed at Chemical Instrument Center, Nagoya University (JEOL JMS-T100GCV (EI), Bruker Daltonics micrOTOF-QII (ESI)). Infrared (IR) spectra were recorded on a JASCO FT/IR 460 plus spectrometer. X-ray analysis was performed by Rigaku PILATUS-200K. High performance liquid chromatography (HPLC) analysis was conducted using Shimadzu LC-10 AD coupled diode array-detector SPD-M20A and chiral column of Daicel CHIRALCEL, CHIRALPAK; AD-3, AS-3, OD-3, OJ-H, and IA-3. Gas-liquid-phase chromatography (GC) was performed with Shimadzu GC-2010 instrument with a flame-ionization detector and a capillary column of CHIRALDEX B-DM and G-TA (i.d., 0.25 mm \times 20 m; Tokyo Kasei Kogyo Co., LTD). For thin-layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60GF254 0.25 mm) were used. Visualization was accomplished by UV light (254 nm), anisaldehyde, KMnO₄, and phosphomolybdic acid. In experiments that required dry solvents such as toluene, diethyl ether, dichloromethane, and trimethylsilyl cyanide [**Caution!** Highly toxic] were distilled in prior to use.

2. Preparation of α,β -unsaturated *N*-acylpyrroles **4**.

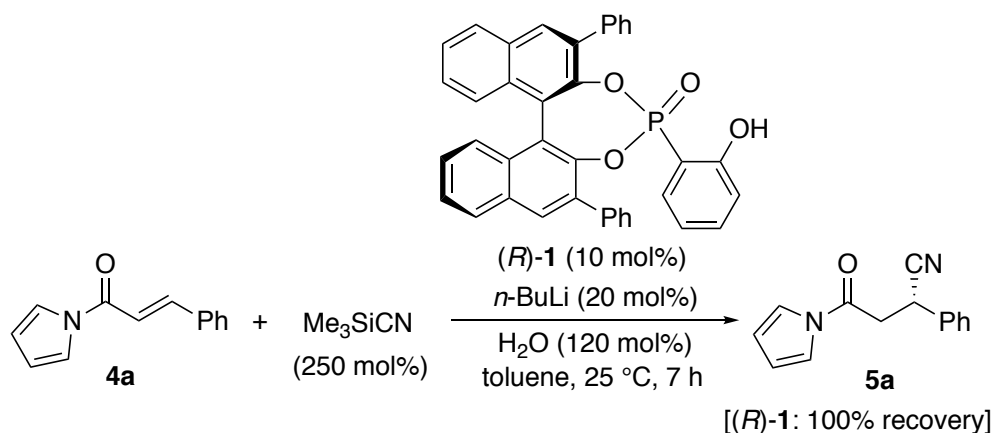


Compounds **4** (Ar = aryl) were prepared on the basis of a literature procedure.¹ To a solution of ylide¹ (960 mg, 2.6 mmol) in toluene (5 mL) was added aromatic aldehyde (2.0 mmol). The mixture was heated to 100 °C and stirred for 11 h. After cooling to room temperature, volatiles were removed under reduced pressure. The resultant residue was purified by neutral silica gel column chromatography (eluent: *n*-hexane:EtOAc = 10:1 to 6:1) to give the desired products **4** in 31–99% yields (Colorless solid for **4a–i** and **4u**; yellow solid for **4j**).

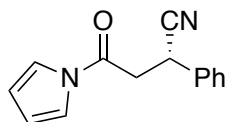


Compounds **4** (R = alkyl) were prepared on the basis of a literature procedure.² Lithium chloride (170 mg, 4.0 mmol) in a 50 mL flask was dried by a heat gun under reduced pressure. Phosphonate² (478 mg, 2.2 mmol) in acetonitrile (13 mL) and *N,N*-diisopropylethylamine (686 μ L, 4.0 mmol) were added at 0 °C. The mixture was stirred at 0 °C for 20 min, and then aliphatic aldehyde (2.0 mmol) was added. The mixture was stirred at room temperature for 24 h, and water (10 mL) was added. The mixture was extracted with ethyl acetate (10 mL \times 3), and washed with brine (10 mL). The combined extracts were dried over Na₂SO₄. The organic phase was concentrated under reduced pressure, and the resultant residue was purified by neutral silica gel column chromatography (eluent: *n*-hexane:EtOAc = 10:1) to give the desired products **4** in 90–99% yields (Colorless oil for **4k–m** and **4v**; pale yellow solid for **4n** and **4q**; colorless solid for **4r**; pale yellow oil for **4o**, **4p**, **4s**, and **4t**).

3. Representative procedure for catalytic enantioselective conjugate hydrocyanation of α,β -unsaturated *N*-acylpyrroles (Schemes 1 and 2).

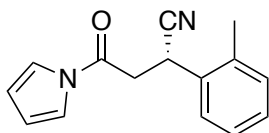


Chiral ligand (*R*)-**1**³ (17.3 mg, 0.030 mmol, 10 mol%) and water (6.5 μ L, 0.36 mmol) were placed in a Schlenk tube under a nitrogen atmosphere and dissolved in dry toluene (1.2 mL). To a stirred solution was added *n*-BuLi (1.63 *M* in *n*-hexane, 36.8 μ L, 0.060 mmol, 20 mol%) at 25 $^\circ$ C, and the solution was stirred for 1 h. Substrate **4a** (59.2 mg, 0.30 mmol) was then added at 25 $^\circ$ C. Trimethylsilyl cyanide (93.8 μ L, 0.75 mmol) was added dropwise at 25 $^\circ$ C, and the mixture was stirred for 7 h. The resulting mixture was quenched with water (2 mL), extracted with ethyl acetate (5 mL \times 2), and washed with brine (10 mL). The combined extracts were dried over Na₂SO₄. The organic phase was concentrated under reduced pressure, and the resultant residue was purified by neutral silica gel column chromatography (eluent: *n*-hexane:EtOAc = 10:1 to 5:1) to give the desired product **5a** in 90% yield (60.7 mg) as colorless solid. The enantiomeric purity of **5a** was determined by HPLC analysis. Chiral ligand (*R*)-**1** could be recovered as some metal salts of (*R*)-**1** through the same silica gel column chromatography (eluent: CHCl₃:MeOH = 10:1) quantitatively. When the recovered ligand would be reused for the catalysis, the further purification with washing 1 *M* HCl aq. is necessary in toluene solution. The organic phase was then concentrated under reduced pressure, and ligand (*R*)-**1** was fully recovered (>99% purity) as colorless solid.

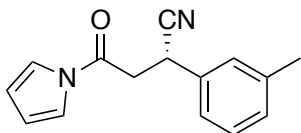


(*S*)-4-Oxo-2-phenyl-4-(1*H*-pyrrol-1-yl)butanenitrile (5a**):**⁴ 90%, 91% ee (TMSCN 250 mol%, 25 $^\circ$ C, 7 h). Column chromatography (eluent: *n*-hexane:EtOAc = 10:1 to 5:1). *R*_f = 0.33 (*n*-hexane:EtOAc = 4:1). Colorless solid. Compound **5a** was recrystallized from *i*-PrOH/*n*-hexane at room temperature (68%, >99% ee). ¹H NMR (400 MHz, CDCl₃) δ 3.35 (dd, *J* = 17.4, 6.4 Hz, 1H), 3.57 (dd, *J* = 17.4, 8.2 Hz, 1H), 4.55 (dd, *J* = 7.8, 6.0 Hz, 1H), 6.32 (t, *J* = 2.3 Hz, 2H), 7.26 (br, 2H), 7.34-7.47 (m, 5H). ¹³C NMR (100 MHz, CDCl₃) δ 32.3, 40.5, 113.9

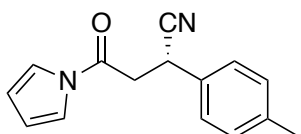
(2C), 118.8 (2C), 119.9, 127.4 (2C), 128.7, 129.3 (2C), 134.3, 165.9. IR (KBr) 3141, 2244, 1715, 1473, 1282, 1128 cm^{-1} . M.p. 154-155 °C. $[\alpha]_{\text{D}}^{26} = -19.6$ (c 1.00, CHCl_3 , 91% ee) [lit.⁴ $[\alpha]_{\text{D}}^{23} = -19.9$ (c 0.985, CHCl_3 , for *S* enantiomer with 92% ee)]. HPLC analysis; OD-3, *n*-hexane/*i*-PrOH = 9/1, 240 nm, 1.0 mL/min, $t_{\text{R}} = 28.6$ min (major), 38.4 min (minor). HRMS (ESI+) calcd for $\text{C}_{14}\text{H}_{12}\text{N}_2\text{NaO}$ $[\text{M}+\text{Na}]^+$ 247.0842, found 247.0840.



(*S*)-4-Oxo-4-(1*H*-pyrrol-1-yl)-2-(*o*-tolyl)butanenitrile (5b): 59%, 71% ee (TMSCN 250 mol%, 25 °C, 18 h). Column chromatography (eluent: *n*-hexane:EtOAc = 10:1 to 5:1). $R_{\text{f}} = 0.30$ (*n*-hexane:EtOAc = 4:1). Colorless solid. ^1H NMR (400 MHz, CDCl_3) δ 2.42 (s, 3H), 3.28 (dd, $J = 17.4, 5.5$ Hz, 1H), 3.55 (dd, $J = 17.4, 9.2$ Hz, 1H), 4.69 (dd, $J = 9.2, 5.5$ Hz, 1H), 6.33 (t, $J = 2.3$ Hz, 2H), 7.22-7.30 (m, 5H), 7.49 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 19.3, 29.4, 39.3, 114.1 (2C), 119.0 (2C), 120.2, 127.3, 127.6, 128.9, 131.6, 132.6, 135.4, 166.2. IR (KBr) 2928, 2244, 1717, 1471, 1407, 1369, 1280, 1122 cm^{-1} . M.p. 76-78 °C. $[\alpha]_{\text{D}}^{26} = -38.0$ (c 1.00, CHCl_3 , 71% ee). HPLC analysis; OD-3, *n*-hexane/*i*-PrOH = 4/1, 240 nm, 1.0 mL/min, $t_{\text{R}} = 17.0$ min (major), 26.1 min (minor). HRMS (ESI+) calcd for $\text{C}_{15}\text{H}_{14}\text{N}_2\text{NaO}$ $[\text{M}+\text{Na}]^+$ 261.0998, found 261.0997.

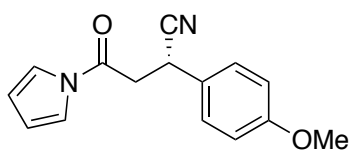


(*S*)-4-Oxo-4-(1*H*-pyrrol-1-yl)-2-(*m*-tolyl)butanenitrile (5c): 76%, 92% ee (TMSCN 250 mol%, 25 °C, 26 h). Column chromatography (eluent: *n*-hexane:EtOAc = 10:1 to 5:1). $R_{\text{f}} = 0.31$ (*n*-hexane:EtOAc = 4:1). Colorless solid. ^1H NMR (400 MHz, CDCl_3) δ 2.38 (s, 3H), 3.33 (dd, $J = 17.4, 6.4$ Hz, 1H), 3.55 (dd, $J = 17.4, 8.2$ Hz, 1H), 4.50 (dd, $J = 8.2, 6.0$ Hz, 1H), 6.31 (t, $J = 2.8$ Hz, 2H), 7.17 (d, $J = 7.8$ Hz, 1H), 7.19-7.32 (m, 5H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.5, 32.4, 40.7, 114.1 (2C), 119.0 (2C), 120.2, 124.6, 128.2, 129.4, 129.5, 134.3, 139.4, 166.2. IR (KBr) 2930, 2245, 1716, 1473, 1403, 1374, 1296, 1279, 1129, 1068, 1130 cm^{-1} . M.p. 140-143 °C. $[\alpha]_{\text{D}}^{26} = -19.6$ (c 1.00, CHCl_3 , 92% ee). HPLC analysis; OD-3, *n*-hexane/*i*-PrOH = 4/1, 240 nm, 1.0 mL/min, $t_{\text{R}} = 13.0$ min (major), 15.0 min (minor). HRMS (ESI+) calcd for $\text{C}_{15}\text{H}_{14}\text{N}_2\text{NaO}$ $[\text{M}+\text{Na}]^+$ 261.0998, found 261.0998.

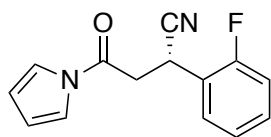


(*S*)-4-Oxo-4-(1*H*-pyrrol-1-yl)-2-(*p*-tolyl)butanenitrile (5d): 94%, 93% ee (TMSCN 250 mol%, 25 °C, 16 h). Column chromatography (eluent: *n*-hexane:EtOAc = 10:1 to 5:1). $R_{\text{f}} = 0.31$

(*n*-hexane:EtOAc = 4:1). Colorless solid. ^1H NMR (400 MHz, CDCl_3) δ 2.36 (s, 3H), 3.33 (dd, $J = 17.4, 6.4$ Hz, 1H), 3.54 (dd, $J = 17.4, 8.2$ Hz, 1H), 4.50 (dd, $J = 7.8, 6.4$ Hz, 1H), 6.31 (t, $J = 2.3$ Hz, 2H), 7.21 (d, $J = 7.8$ Hz, 2H), 7.26 (br, 2H), 7.32 (d, $J = 8.2$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.1, 32.0, 40.6, 114.0 (2C), 118.8 (2C), 120.1, 127.3 (2C), 130.0 (2C), 131.3, 138.7, 166.0. IR (KBr) 2931, 2245, 1716, 1474, 1293, 1281 1129 cm^{-1} . M.p. 166-170 $^\circ\text{C}$. $[\alpha]_{\text{D}}^{26} = -20.8$ (c 1.00, CHCl_3 , 93% ee). HPLC analysis; OD-3, *n*-hexane/*i*-PrOH = 4/1, 240 nm, 1.0 mL/min, $t_{\text{R}} = 13.5$ min (major), 14.9 min (minor). HRMS (ESI+) calcd for $\text{C}_{15}\text{H}_{14}\text{N}_2\text{NaO}$ $[\text{M}+\text{Na}]^+$ 261.0998, found 261.0998.

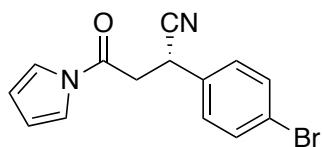


(*S*)-2-(4-Methoxyphenyl)-4-oxo-4-(1*H*-pyrrol-1-yl)butanenitrile (5e):⁴ 85%, 90% ee (TMSCN 300 mol%, 25 $^\circ\text{C}$, 17 h). Column chromatography (eluent: *n*-hexane:EtOAc = 7:1 to 2:1). $R_{\text{f}} = 0.23$ (*n*-hexane:EtOAc = 4:1). Colorless solid. ^1H NMR (400 MHz, CDCl_3) δ 3.32 (dd, $J = 17.4, 6.4$ Hz, 1H), 3.53 (dd, $J = 17.4, 7.8$ Hz, 1H), 3.81 (s, 3H), 4.49 (t, $J = 6.9$ Hz, 1H), 6.31 (t, $J = 2.3$ Hz, 2H), 6.92 (d, $J = 8.7$ Hz, 2H), 7.26 (br, 2H), 7.35 (d, $J = 8.7$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 31.6, 40.6, 55.3, 113.9 (2C), 114.7 (2C), 118.8 (2C), 120.2, 126.2, 128.6 (2C), 159.7, 166.0. IR (KBr) 3140, 2245, 1711, 1511, 1474, 1406, 1373, 1286, 1253, 1032 cm^{-1} . M.p. 116-118 $^\circ\text{C}$. $[\alpha]_{\text{D}}^{26} = -22.5$ (c 1.00, CHCl_3 , 90% ee) [lit.⁴ $[\alpha]_{\text{D}}^{25} = -16.5$ (c 1.080, CHCl_3 , for *S* enantiomer with 90% ee)] HPLC analysis; AD-3, *n*-hexane/*i*-PrOH = 9/1, 230 nm, 1.0 mL/min, $t_{\text{R}} = 25.7$ min (minor), 27.4 min (major). HRMS (ESI+) calcd for $\text{C}_{15}\text{H}_{14}\text{N}_2\text{NaO}_2$ $[\text{M}+\text{Na}]^+$ 277.0947, found 277.0944.



(*S*)-2-(2-Fluorophenyl)-4-oxo-4-(1*H*-pyrrol-1-yl)butanenitrile (5f): 84%, 71% ee (TMSCN 250 mol%, 25 $^\circ\text{C}$, 7 h). Column chromatography (eluent: *n*-hexane:EtOAc = 10:1 to 5:1). $R_{\text{f}} = 0.29$ (*n*-hexane:EtOAc = 4:1). Colorless solid. Compound **5f** was recrystallized from EtOAc/*n*-hexane at room temperature (46%, 94% ee). ^1H NMR (400 MHz, CDCl_3) δ 3.41 (dd, $J = 17.4, 5.9$ Hz, 1H), 3.55 (dd, $J = 17.4, 8.7$ Hz, 1H), 4.73 (dd, $J = 8.3, 5.5$ Hz, 1H), 6.32 (t, $J = 2.3$ Hz, 2H), 7.26 (br, 2H), 7.14 (m, 1H), 7.22 (td, $J = 6.4, 1.3$ Hz, 1H), 7.38 (m, 1H), 7.56 (td, $J = 7.8, 1.8$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 27.3, 38.5, 114.1 (2C), 116.2 (d, $J_{\text{C-F}} = 21.0$ Hz), 118.8, 118.9 (2C), 121.3 (d, $J_{\text{C-F}} = 15.3$ Hz), 125.1 (d, $J_{\text{C-F}} = 2.9$ Hz), 129.7 (d, $J_{\text{C-F}} = 2.9$ Hz), 130.9 (d, $J_{\text{C-F}} = 8.6$ Hz), 160.0 (d, $J_{\text{C-F}} = 250$ Hz), 165.8. ^{19}F NMR (376 MHz, CDCl_3) δ -117.6. IR (KBr) 3141, 2940, 2243, 1713, 1493, 1472, 1405, 1372, 1320, 1274, 1240, 1121, 1067 cm^{-1} . M.p. 121-127 $^\circ\text{C}$ (decomposition). $[\alpha]_{\text{D}}^{23} = -26.7$ (c 1.00, CHCl_3 , 71% ee). HPLC analysis;

OD-3, *n*-hexane/*i*-PrOH = 4/1, 240 nm, 1.0 mL/min, t_R = 13.1 min (major), 15.9 min (minor). HRMS (ESI+) calcd for $C_{14}H_{11}FN_2NaO$ $[M+Na]^+$ 265.0748, found 265.0748.



(S)-2-(4-Bromophenyl)-4-oxo-4-(1H-pyrrol-1-yl)butanenitrile (5g): 85%, 73% ee (TMSCN 250 mol%, 25 °C, 8 h). Column chromatography (eluent: *n*-hexane:EtOAc = 7:1 to 2:1). R_f = 0.25 (*n*-hexane:EtOAc = 4:1). Colorless solid. Compound **5g** was recrystallized from *i*-PrOH/ CH_2Cl_2 at room temperature (55%, >99% ee). 1H NMR (400 MHz, $CDCl_3$) δ 3.37 (dd, J = 16.9, 6.4 Hz, 1H), 3.55 (dd, J = 17.4, 7.3 Hz, 1H), 4.52 (t, J = 6.9 Hz, 1H), 6.32 (t, J = 2.3 Hz, 2H), 7.24 (br, 2H), 7.33 (d, J = 8.2 Hz, 2H), 7.55 (d, J = 8.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.8, 40.2, 114.1 (2C), 118.8 (2C), 119.5, 122.8, 129.2 (2C), 132.5 (2C), 133.3, 165.7. IR (KBr) 2933, 2246, 1708, 1473, 1290, 1129 cm^{-1} . M.p. 134–137 °C. $[\alpha]_D^{27} = -21.2$ (c 1.00, $CHCl_3$, 73% ee). HPLC analysis; AD-3, *n*-hexane/*i*-PrOH = 4/1, 230 nm, 1.0 mL/min, t_R = 14.6 min (minor), 17.2 min (major). HRMS (ESI+) calcd for $C_{14}H_{11}BrN_2NaO$ $[M+Na]^+$ 324.9947, found 324.9942.

Crystal data of 5g (Figure S1): Compound **5g** was recrystallized from *i*-PrOH/ CH_2Cl_2 at room temperature for 1 day. Formula $C_{14}H_{11}BrN_2O$, colorless, crystal dimensions $0.35 \times 0.25 \times 0.20$ mm³, orthorhombic, space group $P2_12_12_1$ (#19), a = 5.1494(9) Å, b = 10.5103(18) Å, c = 23.635(4) Å, α = 90.00°, β = 90.00°, γ = 90.00°, V = 838.5(6) Å³, Z = 4, ρ_{calc} = 1.574 g cm⁻³, $F(000)$ = 608, $\mu(MoK\alpha)$ = 3.202 mm⁻¹, T = 93 K. 10436 reflections collected, 2875 independent reflections with $I > 2\sigma(I)$ ($2\theta_{max}$ = 27.495°), and 203 parameters were used for the solution of the structure.

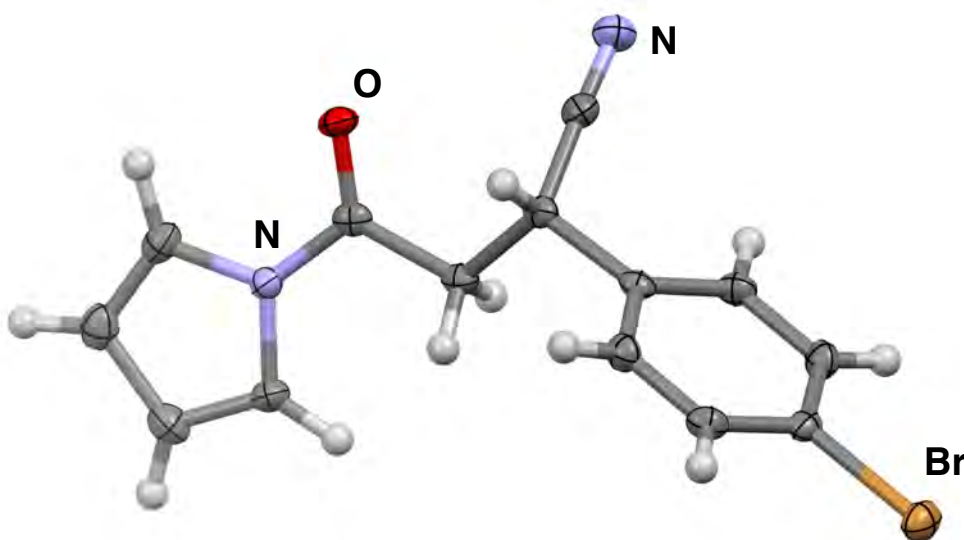
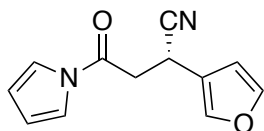
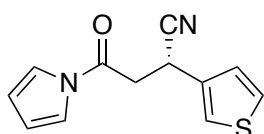


Figure S1. ORTEP drawing of **5g**.

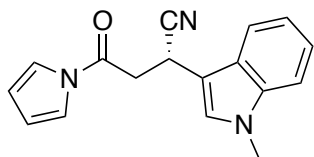
The non-hydrogen atoms were refined anisotropically. $R_1 = 0.0188$ and $wR_2 = 0.0391$. GOF = 0.967. Flack x parameter = 0.002(4). Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 1522874. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: int. code + 44(1223)336-033; E-mail: deposit@ccdc.cam.ac.uk; Web page: <http://www.ccdc.cam.ac.uk/pages/Home.aspx>].



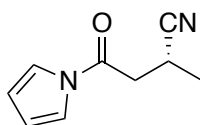
(S)-2-(Furan-3-yl)-4-oxo-4-(1H-pyrrol-1-yl)butanenitrile (5h): 70%, 94% ee (TMSCN 250 mol%, 25 °C, 19 h). Column chromatography (eluent: *n*-hexane:EtOAc = 10:1 to 5:1). R_f = 0.32 (*n*-hexane:EtOAc = 4:1). Colorless solid. ^1H NMR (400 MHz, CDCl_3) δ 3.33 (dd, J = 17.0, 6.9 Hz, 1H), 3.50 (dd, J = 17.4, 6.9 Hz, 1H), 4.50 (t, J = 6.9 Hz, 1H), 6.34 (t, J = 2.3 Hz, 2H), 6.45 (d, J = 0.9 Hz, 1H), 7.26 (br, 2H), 7.44 (t, J = 1.8 Hz, 1H), 7.54 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 23.6, 39.3, 109.3, 114.2 (2C), 119.0 (2C), 119.4, 119.5, 140.6, 144.4, 166.1. IR (KBr) 2904, 2249, 1707, 1472, 1413, 1376, 1302, 1263, 1122, 1027 cm^{-1} . M.p. 90-92 °C. $[\alpha]_D^{26} = +10.0$ (c 1.00, CHCl_3 , 94% ee). HPLC analysis; AS-3, *n*-hexane/*i*-PrOH = 4/1, 240 nm, 1.0 mL/min, t_R = 26.7 min (major), 32.9 min (minor). HRMS (ESI+) calcd for $\text{C}_{12}\text{H}_{10}\text{N}_2\text{NaO}_2$ $[\text{M}+\text{Na}]^+$ 237.0634, found 237.0632.



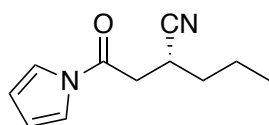
(S)-4-Oxo-4-(1H-pyrrol-1-yl)-2-(thiophen-3-yl)butanenitrile (5i): 62%, 90% ee (TMSCN 250 mol%, 25 °C, 16 h). Column chromatography (eluent: *n*-hexane:EtOAc = 10:1 to 5:1). R_f = 0.29 (*n*-hexane:EtOAc = 4:1). Colorless solid. ^1H NMR (400 MHz, CDCl_3) δ 3.38 (dd, J = 17.4, 6.4 Hz, 1H), 3.54 (dd, J = 16.9, 7.3 Hz, 1H), 4.66 (t, J = 6.9 Hz, 1H), 6.33 (t, J = 2.3 Hz, 2H), 7.12 (dd, J = 4.1, 2.3 Hz, 1H), 7.26 (br, 2H), 7.38 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 27.7, 39.7, 114.0 (2C), 118.8 (2C), 119.7, 123.5, 126.2, 127.6, 134.0, 165.9. IR (KBr) 2938, 2237, 1707, 1471, 1405, 1372, 1291, 1122, 1067 cm^{-1} . M.p. 109-111 °C. $[\alpha]_D^{24} = -5.6$ (c 1.00, CHCl_3 , 90% ee). HPLC analysis; AD-3, *n*-hexane/*i*-PrOH = 4/1, 240 nm, 1.0 mL/min, t_R = 12.8 min (minor), 15.1 min (major). HRMS (ESI+) calcd for $\text{C}_{12}\text{H}_{10}\text{N}_2\text{NaOS}$ $[\text{M}+\text{Na}]^+$ 253.0406, found 253.0405.



(S)-2-(1-Methyl-1H-indol-3-yl)-4-oxo-4-(1H-pyrrol-1-yl)butanenitrile (5j): 73%, 85% ee (TMSCN 250 mol%, 60 °C, 12 h). Column chromatography (eluent: *n*-hexane:EtOAc = 3:1 to 1:1). *R*_f = 0.32 (*n*-hexane:EtOAc = 1:1). Yellow solid. Compound **5j** was recrystallized from CH₂Cl₂/*n*-hexane at room temperature (55%, 99% ee). ¹H NMR (400 MHz, CDCl₃) δ 3.51 (dd, *J* = 17.4, 6.4 Hz, 1H), 3.59 (dd, *J* = 17.4, 7.8 Hz, 1H), 3.79 (s, 3H), 4.81 (dd, *J* = 7.3, 6.4 Hz, 1H), 6.30 (t, *J* = 2.3 Hz, 2H), 7.17-7.22 (m, 2H), 7.26 (br, 2H), 7.30 (m, 1H), 7.36 (d, *J* = 8.3 Hz, 1H), 7.67 (d, *J* = 7.8 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 24.2, 32.9, 39.3, 107.1, 109.9 (2C), 113.8 (2C), 118.2, 118.8, 120.0, 120.1, 122.5, 125.2, 127.6, 137.2, 166.4. IR (KBr) 2930, 2240, 1721, 1474, 1408, 1373, 1322, 1285, 1256, 1129, 1071 cm⁻¹. M.p. 122-126 °C (decomposition). [α]_D²⁷ = -32.8 (*c* 1.00, CHCl₃, 85% ee). HPLC analysis; IA-3, *n*-hexane/*i*-PrOH = 1/1, 240 nm, 0.5 mL/min, *t*_R = 14.7 min (minor), 15.7 min (major). HRMS (ESI+) calcd for C₁₇H₁₅N₃NaO [M+Na]⁺ 300.1107, found 300.1106

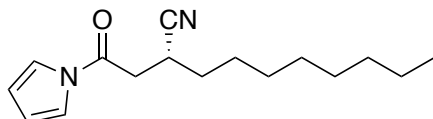


(R)-2-Methyl-4-oxo-4-(1H-pyrrol-1-yl)butanenitrile (5k):⁵ 97%, 90% ee (10 mol%-catalysts: TMSCN 250 mol%, 25 °C, 3 h), 92%, 90% ee (2.5 mol%-catalysts: TMSCN 350 mol%, 25 °C, 22 h). Column chromatography (eluent: *n*-hexane:EtOAc = 10:1 to 5:1). *R*_f = 0.33 (*n*-hexane:EtOAc = 4:1). Colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 1.48 (d, *J* = 6.9 Hz, 3H), 3.06 (dd, *J* = 17.0, 6.9 Hz, 1H), 3.24-3.40 (m, 2H), 6.34 (t, *J* = 2.3 Hz, 2H), 7.29 (br, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 17.7, 21.0, 38.2, 113.9 (2C), 118.8 (2C), 121.8, 166.3. IR (neat) 3417, 2939, 2244, 1717, 1471, 1407, 1372, 1293, 1115, 1047 cm⁻¹. [α]_D²⁷ = +8.3 (*c* 1.00, CHCl₃, 90% ee) [lit.⁵ [α]_D²³ = -8.94 (*c* 0.57, CHCl₃, for *S* enantiomer with 97% ee)]. HPLC analysis; OJ-H, *n*-hexane/*i*-PrOH = 4/1, 240 nm, 1.0 mL/min, *t*_R = 31.7 min (major), 42.0 min (minor). HRMS (ESI+) calcd for C₉H₁₀N₂NaO [M+Na]⁺ 185.0685, found 185.0687.

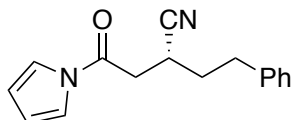


(R)-2-(2-Oxo-2-(1H-pyrrol-1-yl)ethyl)pentanenitrile (5l):⁴ 99%, 92% ee (TMSCN 250 mol%, 0 °C, 6 h). Column chromatography (eluent: *n*-hexane:EtOAc = 10:1 to 5:1). *R*_f = 0.35 (*n*-hexane:EtOAc = 4:1). Colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 1.00 (t, *J* = 7.3 Hz, 3H), 1.47-1.76 (m, 4H), 3.08 (dd, *J* = 19.3, 9.2 Hz, 1H), 3.22-3.32 (m, 2H), 6.34 (t, *J* = 2.3 Hz, 2H), 7.29 (br, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 13.3, 20.3, 26.6, 33.7, 36.9, 113.8 (2C), 118.8 (2C),

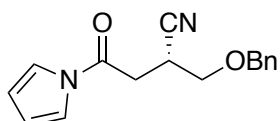
121.0, 166.5. IR (neat) 3147, 2962, 2242, 1716, 1471, 1408, 1374, 1285, 1120, 1074 cm^{-1} . $[\alpha]_{\text{D}}^{26} = +16.4$ (c 1.00, CHCl_3 , 92% ee) [lit.⁴ $[\alpha]_{\text{D}}^{24} = +19.1$ (c 0.858, CHCl_3 , for *R* enantiomer with 98% ee)]. HPLC analysis; OD-3, *n*-hexane/*i*-PrOH = 4/1, 240 nm, 1.0 mL/min, $t_{\text{R}} = 9.1$ min (major), 10.2 min (minor). HRMS (ESI+) calcd for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{NaO}$ $[\text{M}+\text{Na}]^+$ 213.0998, found 213.1004.



(*R*)-2-(2-Oxo-2-(1*H*-pyrrol-1-yl)ethyl)decanenitrile (5m): 86%, 94% ee (TMSCN 250 mol%, -20 °C, 7 h). Column chromatography (eluent: *n*-hexane:EtOAc = 10:1 to 5:1). $R_{\text{f}} = 0.38$ (*n*-hexane:EtOAc = 4:1). Colorless solid. ^1H NMR (400 MHz, CDCl_3) δ 0.89 (t, $J = 6.8$ Hz, 3H), 1.20-1.42 (m, 10H), 1.44-1.66 (m, 2H), 1.71 (q, $J = 7.3$ Hz, 2H), 3.02-3.12 (m, 1H), 3.21-3.30 (m, 2H), 6.34 (t, $J = 2.3$ Hz, 2H), 7.29 (br, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 14.0, 22.6, 26.8, 27.0, 28.9, 29.1, 29.2, 31.7, 31.8, 36.9, 113.8 (2C), 118.8 (2C), 121.1, 166.5. IR (KBr) 3146, 2924, 2851, 2243, 1720, 1471, 1406, 1373, 1321, 1276, 1113, 1071 cm^{-1} . M.p. 56-60 °C. $[\alpha]_{\text{D}}^{27} = +14.2$ (c 1.00, CHCl_3 , 85% ee). HPLC analysis; OD-3, *n*-hexane/*i*-PrOH = 9/1, 240 nm, 1.0 mL/min, $t_{\text{R}} = 10.6$ min (major), 12.6 min (minor). HRMS (ESI+) calcd for $\text{C}_{16}\text{H}_{24}\text{N}_2\text{NaO}$ $[\text{M}+\text{Na}]^+$ 283.1781, found 283.1776.

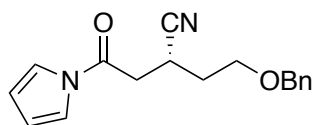


(*R*)-4-Oxo-2-phenethyl-4-(1*H*-pyrrol-1-yl)butanenitrile (5n):⁶ 94%, 95% ee (TMSCN 250 mol%, 0 °C, 4 h). Column chromatography (eluent: *n*-hexane:EtOAc = 10:1 to 5:1). $R_{\text{f}} = 0.31$ (*n*-hexane:EtOAc = 4:1). Colorless solid. ^1H NMR (400 MHz, CDCl_3) δ 2.04 (q, $J = 7.3$ Hz, 2H), 2.79-2.88 (m, 1H), 2.93-3.12 (m, 2H), 3.19-3.30 (m, 2H), 6.32 (t, $J = 1.8$ Hz, 2H), 7.20-7.35 (m, 7H). ^{13}C NMR (100 MHz, CDCl_3) δ 26.3, 33.1, 33.3, 36.8, 113.9 (2C), 118.8 (2C), 120.7, 126.5, 128.3 (2C), 128.7 (2C), 139.5, 166.3. IR (KBr) 2920, 2244, 1710, 1471, 1402, 1376, 1277, 1122, 1072 cm^{-1} . M.p. 92-94 °C. $[\alpha]_{\text{D}}^{26} = +23.0$ (c 1.00, CHCl_3 , 95% ee) [lit.⁶ $[\alpha]_{\text{D}}^{23} = -21.7$ (c 0.88, CHCl_3 , for *S* enantiomer with 95% ee)]. HPLC analysis; OD-3, *n*-hexane/*i*-PrOH = 4/1, 240 nm, 1.0 mL/min, $t_{\text{R}} = 22.9$ min (major), 25.6 min (minor). HRMS (ESI+) calcd for $\text{C}_{16}\text{H}_{16}\text{N}_2\text{NaO}$ $[\text{M}+\text{Na}]^+$ 275.1155, found 275.1150.

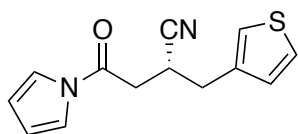


(*R*)-2-((Benzyloxy)methyl)-4-oxo-4-(1*H*-pyrrol-1-yl)butanenitrile (5o):⁶ 90%, 97% ee (TMSCN 250 mol%, -20 °C, 16 h). Column chromatography (eluent: *n*-hexane:EtOAc = 10:1 to

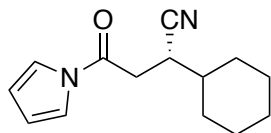
3:1). $R_f = 0.24$ (n -hexane:EtOAc = 4:1). Colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 3.24 (dd, $J = 17.4, 6.9$ Hz, 1H), 3.33 (dd, $J = 17.4, 6.4$ Hz, 1H), 3.50 (m, 1H), 3.69-3.78 (m, 2H), 4.57 (d, $J = 11.9$ Hz, 1H), 4.61 (d, $J = 11.9$ Hz, 1H), 6.33 (t, $J = 2.3$ Hz, 2H), 7.24-7.38 (m, 7H). ^{13}C NMR (100 MHz, CDCl_3) δ 27.7, 33.6, 67.8, 73.4, 113.9 (2C), 118.9 (2C), 119.5, 127.7 (2C), 128.1, 128.5 (2C), 136.9, 166.5. IR (neat) 2870, 2248, 1717, 1471, 1408, 1372, 1319, 1291, 1110 cm^{-1} . $[\alpha]_{\text{D}}^{25} = -8.8$ (c 1.00, CHCl_3 , 97% ee) [lit.⁶ $[\alpha]_{\text{D}}^{22} = +7.87$ (c 0.34, CHCl_3 , 92% ee)]. HPLC analysis; IA-3, n -hexane/ i -PrOH = 4/1, 240 nm, 1.0 mL/min, $t_{\text{R}} = 10.4$ min (major), 12.0 min (minor). HRMS (ESI+) calcd for $\text{C}_{16}\text{H}_{16}\text{N}_2\text{NaO}_2$ $[\text{M}+\text{Na}]^+$ 291.1104, found 291.1100.



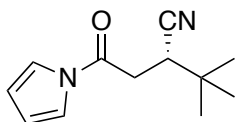
(R)-2-(2-(Benzyloxy)ethyl)-4-oxo-4-(1H-pyrrol-1-yl)butanenitrile (5p): 73%, 96% ee (TMSCN 250 mol%, -20 °C, 11 h). Column chromatography (eluent: n -hexane:EtOAc = 10:1 to 3:1). $R_f = 0.24$ (n -hexane:EtOAc = 4:1). Colorless solid. ^1H NMR (400 MHz, CDCl_3) δ 2.04 (q, $J = 6.0$ Hz, 2H), 3.18 (dd, $J = 17.4, 6.4$ Hz, 1H), 3.25 (dd, $J = 17.4, 6.8$ Hz, 1H), 3.52 (quint, $J = 6.8$ Hz, 1H), 3.65-3.75 (m, 2H), 4.52 (s, 2H), 6.31 (t, $J = 2.8$ Hz, 2H), 7.24 (br, 2H), 7.27-7.37 (m, 5H). ^{13}C NMR (100 MHz, CDCl_3) δ 24.4, 31.5, 36.6, 66.7, 73.2, 113.7 (2C), 118.8 (2C), 120.7, 127.7 (2C), 127.8, 128.4 (2C), 137.7, 166.5. IR (KBr) 2865, 2241, 1703, 1474, 1409, 1375, 1298, 1273, 1092 cm^{-1} . M.p. 64-67 °C. $[\alpha]_{\text{D}}^{27} = +7.8$ (c 1.00, CHCl_3 , 75% ee). HPLC analysis; OD-3, n -hexane/ i -PrOH = 4/1, 240 nm, 1.0 mL/min, $t_{\text{R}} = 17.6$ min (minor), 38.5 min (major). HRMS (ESI+) calcd for $\text{C}_{17}\text{H}_{18}\text{N}_2\text{NaO}_2$ $[\text{M}+\text{Na}]^+$ 305.1260, found 305.1259.



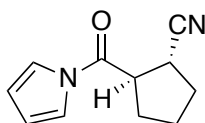
(R)-4-Oxo-4-(1H-pyrrol-1-yl)-2-(thiophen-3-ylmethyl)butanenitrile (5q): 91%, 95% ee (TMSCN 250 mol%, 0 °C, 18 h). Column chromatography (eluent: n -hexane:EtOAc = 10:1 to 5:1). $R_f = 0.32$ (n -hexane:EtOAc = 4:1). Colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 3.07 (dd, $J = 17.9, 6.9$ Hz, 1H), 3.11 (d, $J = 6.9$ Hz, 2H), 3.19 (dd, $J = 17.4, 6.9$ Hz, 1H), 3.53 (quin, $J = 6.8$ Hz, 1H), 6.33 (t, $J = 2.3$ Hz, 2H), 7.05 (dd, $J = 5.0, 1.4$ Hz, 1H), 7.16 (dd, $J = 2.3, 0.9$ Hz, 1H), 7.26 (br, 2H), 7.34 (dd, $J = 5.0, 3.2$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 28.0, 31.7, 35.7, 114.0 (2C), 118.8 (2C), 120.8, 123.4, 126.7, 127.9, 135.9, 166.3. IR (neat) 3146, 3105, 2927, 2244, 1713, 1470, 1408, 1372, 1328, 1289, 1121, 1075, 1049 cm^{-1} . $[\alpha]_{\text{D}}^{27} = -4.4$ (c 1.00, CHCl_3 , 94% ee). HPLC analysis; AS-3, n -hexane/ i -PrOH = 4/1, 240 nm, 1.0 mL/min, $t_{\text{R}} = 25.5$ min (major), 30.5 min (minor). HRMS (ESI+) calcd for $\text{C}_{13}\text{H}_{12}\text{N}_2\text{NaOS}$ $[\text{M}+\text{Na}]^+$ 267.0563, found 267.0562.



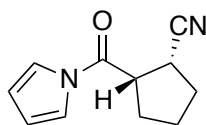
(S)-2-Cyclohexyl-4-oxo-4-(1H-pyrrol-1-yl)butanenitrile (5r):⁶ 98%, 91% ee (TMSCN 250 mol%, 0 °C, 7 h). Column chromatography (eluent: *n*-hexane:EtOAc = 10:1 to 5:1). *R*_f = 0.30 (*n*-hexane:EtOAc = 4:1). Colorless solid. ¹H NMR (400 MHz, CDCl₃) δ 1.13-1.36 (m, 5H), 1.58-1.73 (m, 2H), 1.74-1.93 (m, 4H), 3.11 (m, 1H), 3.17-3.27 (m, 2H), 6.34 (t, *J* = 2.3 Hz, 2H), 7.30 (br, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 25.6, 25.7, 25.8, 28.9, 31.3, 33.0, 34.5, 38.7, 113.8 (2C), 118.8 (2C), 120.2, 166.8. IR (KBr) 2931, 2238, 1713, 1472, 1405, 1373, 1321, 1285, 1114 cm⁻¹. M.p. 110-112 °C. [α]_D²⁸ = -2.8 (*c* 1.00, CHCl₃, 91% ee). HPLC analysis; OD-3, *n*-hexane/*i*-PrOH = 9/1, 240 nm, 1.0 mL/min, *t*_R = 12.2 min (major), 14.0 min (minor). HRMS (ESI⁺) calcd for C₁₄H₁₈N₂NaO [M+Na]⁺ 253.1311, found 253.1313.



(S)-2-(tert-Butyl)-4-oxo-4-(1H-pyrrol-1-yl)butanenitrile (5s):⁴ 93%, 92% ee (TMSCN 250 mol%, 0 °C, 7 h). Column chromatography (eluent: *n*-hexane:EtOAc = 10:1 to 5:1). *R*_f = 0.32 (*n*-hexane:EtOAc = 4:1). Colorless solid. ¹H NMR (400 MHz, CDCl₃) δ 1.14 (s, 9H), 3.02-3.21 (m, 3H), 6.34 (t, *J* = 2.3 Hz, 2H), 7.32 (br, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 27.2 (3C), 32.9, 33.1, 38.4, 113.8 (2C), 118.9 (2C), 120.4, 167.1. IR (KBr) 2972, 2239, 1714, 1470, 1407, 1375, 1328, 1293, 1270, 1122, 1073 cm⁻¹. M.p. 125-129 °C. [α]_D²⁷ = -38.4 (*c* 1.00, CHCl₃, 92% ee) [lit.⁴ [α]_D²⁵ = -34.5 (*c* 1.048, CHCl₃, for *S* enantiomer with 90% ee)]. HPLC analysis; OD-3, *n*-hexane/*i*-PrOH = 9/1, 240 nm, 1.0 mL/min, *t*_R = 9.5 min (minor), 12.0 min (major). HRMS (ESI⁺) calcd for C₁₂H₁₆N₂NaO [M+Na]⁺ 227.1155, found 227.1149.

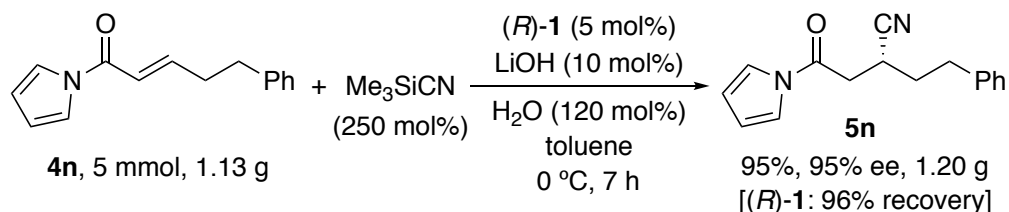


(1R,2R)-2-(1H-Pyrrole-1-carbonyl)cyclopentane-1-carbonitrile (trans-5t):⁴ 56%, 93% ee (TMSCN 250 mol%, 25 °C, 7 h). Column chromatography (eluent: *n*-hexane:EtOAc = 10:1 to 5:1). *R*_f = 0.38 (*n*-hexane:EtOAc = 4:1). Colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 1.80-1.99 (m, 3H), 2.06 (m, 1H), 2.23-2.39 (m, 2H), 3.52 (q, *J* = 6.8 Hz, 1H), 3.71 (td, *J* = 9.6, 6.4 Hz, 1H), 6.35 (t, *J* = 2.8 Hz, 2H), 7.32 (br, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 25.4, 30.7, 31.5, 31.7, 48.2, 113.9 (2C), 119.2 (2C), 121.7, 170.1. IR (neat) 3147, 2967, 2877, 2241, 1711, 1599, 1470, 1375, 1292, 1121, 1074 cm⁻¹. [α]_D²⁶ = -123.6 (*c* 1.00, CHCl₃, 93% ee) [lit.⁴ [α]_D²⁵ = -119.8 (*c* 1.595, CHCl₃, for (1R,2R)-enantiomer with 86% ee)]. HPLC analysis; OD-3, *n*-hexane/*i*-PrOH = 4/1, 240 nm, 1.0 mL/min, *t*_R = 7.6 min (major), 8.4 min (minor). HRMS (ESI⁺) calcd for C₁₁H₁₂N₂NaO [M+Na]⁺ 211.0842, found 211.0840.



(1*R*,2*S*)-2-(1*H*-Pyrrole-1-carbonyl)cyclopentane-1-carbonitrile (*cis*-5*t*):⁴ 34%, 84% ee (TMSCN 250 mol%, 25 °C, 7 h). Column chromatography (eluent: *n*-hexane:EtOAc = 10:1 to 5:1). *R*_f = 0.29 (*n*-hexane:EtOAc = 4:1). Colorless solid. ¹H NMR (400 MHz, CDCl₃) δ 1.81 (m, 1H), 2.00-2.38 (m, 5H), 3.10 (q, *J* = 7.8 Hz, 1H), 3.73 (q, *J* = 7.8 Hz, 1H), 6.34 (t, *J* = 2.8 Hz, 2H), 7.32 (br, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 23.8, 29.5, 30.9, 32.5, 45.8, 113.8 (2C), 119.1 (2C), 119.6, 169.2. IR (KBr) 2957, 2240, 1713, 1470, 1375, 1279, 1126, 1076 cm⁻¹. M.p. 54-65 °C (decomposition). [α]_D²⁶ = +23.6 (*c* 1.00, CHCl₃, 84% ee) [lit.⁴ [α]_D²⁶ = +21.1 (*c* 1.265, CHCl₃, for (1*R*,2*S*)-enantiomer with 84% ee)]. HPLC analysis; OD-3, *n*-hexane/*i*-PrOH = 4/1, 240 nm 1.0 mL/min, *t*_R = 8.5 min (minor), 9.6 min (major). HRMS (ESI+) calcd for C₁₁H₁₂N₂NaO [M+Na]⁺ 211.0842, found 211.0841.

4. Gram scale synthesis of **5n** (Eq. 1).

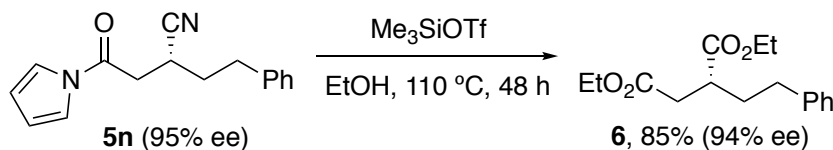


Chiral ligand $(R)\text{-1}$ (144.1 mg, 0.25 mmol, 5 mol%) and lithium hydroxide monohydrate (21.0 mg, 0.50 mmol, 10 mol%) dissolved in water (108 μL , 6.0 mmol) were placed in a Schlenk tube under a nitrogen atmosphere and dissolved in dry toluene (20 mL), and the solution was stirred for 2 h. Substrate **4n** (1.13 g, 5.0 mmol) was then added at $25\text{ }^\circ\text{C}$ and the mixture was stirred at $0\text{ }^\circ\text{C}$ for 20 min. Trimethylsilyl cyanide (1.56 mL, 12.5 mmol) was added dropwise at $0\text{ }^\circ\text{C}$, and the mixture was stirred at $0\text{ }^\circ\text{C}$ for 7 h. The resulting mixture was quenched with water (10 mL) at $0\text{ }^\circ\text{C}$ extracted with ethyl acetate (10 mL \times 3), and washed with brine (10 mL). The combined extracts were dried over Na_2SO_4 . The organic phase was concentrated under reduced pressure, and the resultant residue was purified by neutral silica gel column chromatography (eluent: *n*-hexane:EtOAc = 10:1 to 4:1) to give the desired product **5n** in 95% yield (1.20 g). The enantiomeric purity of **5n** was determined by HPLC analysis. Chiral ligand $(R)\text{-1}$ could be recovered as some metal salts of $(R)\text{-1}$ through the same silica gel column chromatography (eluent: $\text{CHCl}_3\text{:MeOH}$ = 10:1) almost quantitatively. When the recovered ligand would be reused for the catalysis, the further purification with washing 1 M HCl aq. is necessary in toluene solution. The organic phase was then concentrated under reduced pressure, and ligand $(R)\text{-1}$ was obtained (138.8 mg, 96%, >99% purity) as colorless solid (Figure S2).



Figure S2. Gram scale synthesis of **5n**.

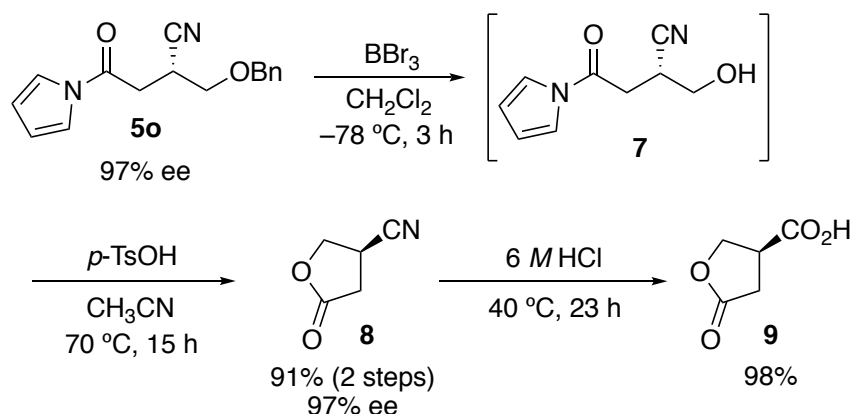
5. Transformation of products **5n** to optically active succinic acid diester **6** (Eq. 2).



On the basis of a literature procedure.⁷ To a suspension of **5n** (37.8 mg, 0.15 mmol) in ethanol (1.5 mL), trimethylsilyl triflate (136 μL , 0.75 mmol) was added dropwise at room temperature. The mixture was then allowed to heat at 110 $^\circ\text{C}$ and stirred for 10 h. Monitoring the reaction by TLC, the mixture was cooled to room temperature, and trimethylsilyl triflate (136 μL , 0.75 mmol) was added dropwise. The mixture was then allowed to heat at 110 $^\circ\text{C}$ and stirred for 30 h. Monitoring the reaction by TLC, the mixture was cooled to room temperature, and trimethylsilyl triflate (136 μL , 0.75 mmol) was added dropwise. The mixture was then allowed to heat at 110 $^\circ\text{C}$ and stirred for 8 h. Monitoring the reaction by TLC, the resulting mixture was quenched with water (5 mL) at 0 $^\circ\text{C}$, filtered through celite pad, extracted with ethyl acetate (10 mL \times 3), and washed with brine (10 mL). The combined extracts were dried over Na_2SO_4 . The organic phase was concentrated under reduced pressure, and the resultant residue was purified by neutral silica gel column chromatography (eluent: *n*-hexane:EtOAc = 10:1) to give the desired product **6** as pale brown oil in 85% yield (35.3 mg). The enantiomeric purity of **6** was determined by HPLC analysis.

Diethyl (*R*)-2-phenethylsuccinate (6**):**⁸ Pale brown oil. ^1H NMR (400 MHz, CDCl_3) δ 1.24 (t, J = 6.9 Hz, 3H), 1.28 (t, J = 6.9 Hz, 3H), 1.82 (m, 1H), 1.99 (m, 1H), 2.47 (dd, J = 16.5, 5.5 Hz, 1H), 2.57-2.69 (m, 2H), 2.75 (dd, J = 16.0, 9.2 Hz, 1H), 2.88 (m, 1H), 4.12 (q, J = 6.9 Hz, 2H), 4.17 (qd, J = 6.9, 2.3 Hz, 2H), 7.15-7.24 (m, 3H), 7.25-7.30 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 14.1, 14.2, 33.2, 33.6, 36.2, 40.9, 60.6, 60.7, 126.0, 128.3 (2C), 128.4 (2C), 141.2, 171.8, 174.7. IR (neat) 2981, 1733, 1455, 1374, 1259, 1175, 1031 cm^{-1} . $[\alpha]_{\text{D}}^{27} = +29.7$ (c 1.00, CHCl_3 , 94% ee). HPLC analysis; OD-3, *n*-hexane/*i*-PrOH = 95/5, 210 nm, 1.0 mL/min, t_{R} = 8.1 min (major), 10.3 min (minor). HRMS (ESI+) calcd for $\text{C}_{16}\text{H}_{22}\text{NaO}_4$ $[\text{M}+\text{Na}]^+$ 301.1410, found 301.1410.

6. Transformation of products **5o** to optically active (*S*)-(-)-paraconic acid **9** (Eq. 3).

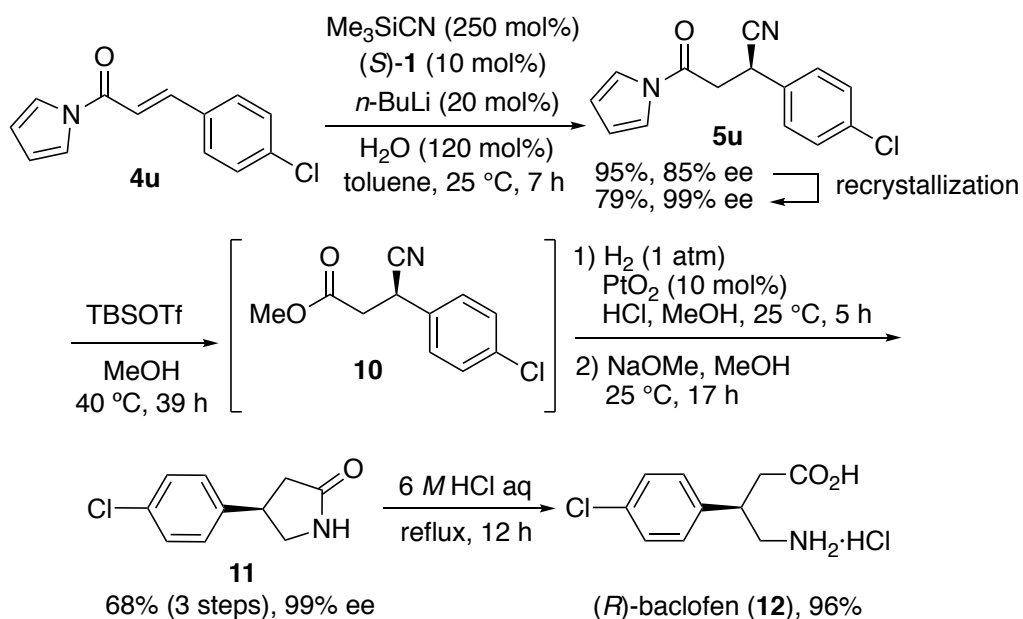


(*R*)-5-Oxotetrahydrofuran-3-carbonitrile (8**):** To a solution of **5o** (61.0 mg, 0.23 mmol, 97% ee) in dichloromethane (2.3 mL), boron tribromide (1 M in dichloromethane, 340 μL , 0.34 mmol) was added at $-78\text{ }^\circ\text{C}$.⁹ The mixture was stirred at $-78\text{ }^\circ\text{C}$ for 3 h, and then purified by flash neutral silica gel column chromatography (eluent: $\text{CHCl}_3\text{:EtOAc} = 3\text{:}1$) to give the desired compound **7**. Compound **7** was immediately used without further purification. To a solution of **7** in acetonitrile (5 mL), *p*-toluenesulfonic acid anhydrate (58.7 mg, 0.34 mmol) was added, and the mixture was stirred at $70\text{ }^\circ\text{C}$ for 12 h. Monitoring the reaction by TLC, *p*-toluenesulfonic acid anhydrate (58.7 mg, 0.34 mmol) was added, and the mixture was stirred at $70\text{ }^\circ\text{C}$ for additional 3 h. The mixture was allowed to cool to room temperature, and diluted with water (10 mL). The mixture was extracted with ethyl acetate (10 mL \times 3). The combined extracts were dried over Na_2SO_4 . The organic phase was concentrated under reduced pressure, and the resultant residue was purified by neutral silica gel column chromatography (eluent: $\text{CHCl}_3\text{:EtOAc} = 3\text{:}1$) to give the desired product **8** as colorless oil in 91% yield (23.4 mg). The enantiomeric purity of **8** was determined by chiral GC analysis. ^1H NMR (400 MHz, CDCl_3) δ 2.87 (dd, $J = 17.9, 8.3\text{ Hz}$, 1H), 2.95 (dd, $J = 17.9, 9.2\text{ Hz}$, 1H), 3.55 (quintet, $J = 7.8\text{ Hz}$, 1H), 4.47 (dd, $J = 9.6, 6.9\text{ Hz}$, 1H), 4.60 (dd, $J = 9.2, 7.8\text{ Hz}$, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 25.4, 31.7, 68.3, 117.7, 172.4. IR (neat) 3544, 2957, 2251, 1790, 1416, 1382, 1335, 1170, 1040 cm^{-1} . $[\alpha]_{\text{D}}^{22} = -26.8$ (c 1.00, CHCl_3 , 97% ee). GC analysis; CHIRALDEX G-TA, $100\text{ }^\circ\text{C}$ to $115\text{ }^\circ\text{C}$ ($+5\text{ }^\circ\text{C/min}$), 110 kPa, $t_{\text{R}} = 37.6\text{ min}$ (major), 43.3 min (minor). HRMS (EI) calcd for $\text{C}_5\text{H}_5\text{NO}_2$ $[\text{M}]^+$ 111.0320, found 111.0317.

(*S*)-(-)-Paraconic acid (9**):**¹⁰ A solution of **8** (14.0 mg, 0.126 mmol) in 6 M HCl (1 mL) was allowed to heat at $40\text{ }^\circ\text{C}$ and stirred for 23 h. The resulting mixture was allowed to cool to room temperature, and then concentrated under reduced pressure. The resultant residue was diluted with chloroform (10 mL), and was dried over MgSO_4 , and then was concentrated under reduced pressure to give the desired product **9** as colorless viscous oil in 98% yield (16.1 mg). ^1H NMR (400 MHz, CDCl_3) δ 2.80 (dd, $J = 17.8, 9.6\text{ Hz}$, 1H), 2.91 (dd, $J = 17.9, 6.9\text{ Hz}$, 1H), 3.52 (m, 1H), 4.50 (dd, $J = 9.2, 6.4\text{ Hz}$, 1H), 4.54 (dd, $J = 9.2, 8.2\text{ Hz}$, 1H) [CO_2H was not observed]. ^{13}C NMR

(100 MHz, CDCl₃) δ 30.7, 39.7, 68.9, 175.4, 176.4. IR (neat) 3500, 2923, 1770, 1732, 1384, 1193, 1032 cm⁻¹. $[\alpha]_D^{24} = -49.2$ (*c* 1.00, MeOH, 97% ee (*S*)) [lit.¹¹ $[\alpha]_D^{25} = -35$ (*c* 0.002, MeOH, for *S* enantiomer), $[\alpha]_D^{25} = +40.0$ (*c* 0.001, MeOH, for *R* enantiomer)]. HRMS (ESI⁻) calcd for C₅H₅NaO₄ [M-H]⁻ 129.0193, found 129.0189.

7. Synthesis of (*R*)-(-)-baclofen **12** (Eq. 4).



(*R*)-2-(4-Chlorophenyl)-4-oxo-4-(1*H*-pyrrol-1-yl)butanenitrile (5u**):**⁶ 95%, 85% ee (TMSCN 250 mol%, 25 °C, 18 h). Column chromatography (eluent: *n*-hexane:EtOAc = 10:1 to 5:1). *R_f* = 0.31 (*n*-hexane:EtOAc = 4:1). Compound **5u** was recrystallized from dichloromethane/*n*-hexane at room temperature (99% ee). Colorless solid. ¹H NMR (400 MHz, CDCl₃) δ 3.34 (dd, *J* = 17.4, 6.9 Hz, 1H), 3.55 (dd, *J* = 17.4, 7.3 Hz, 1H), 4.53 (t, *J* = 6.9 Hz, 1H), 6.32 (t, *J* = 2.3 Hz, 2H), 7.24 (br, 2H), 7.39 (s, 4H). ¹³C NMR (100 MHz, CDCl₃) δ 31.8, 40.4, 114.2 (2C), 118.8 (2C), 119.5, 128.9 (2C), 129.6 (2C), 132.8, 134.8, 165.7. IR (KBr) 2934, 2245, 1710, 1473, 1406, 1374, 1315, 1290, 1130, 1094 cm⁻¹. M.p. 145-150 °C. $[\alpha]_D^{22} = +18.4$ (*c* 1.00, CHCl₃, 99% ee) [lit.⁶ $[\alpha]_D^{22} = +8.50$ (*c* 0.39, CHCl₃, for *S* enantiomer with 41% ee)]. HPLC analysis; AS-3, *n*-hexane/*i*-PrOH = 4/1, 240 nm, 1.0 mL/min, *t_R* = 22.4 min (minor), 27.5 min (major). HRMS (ESI⁺) calcd for C₁₄H₁₁ClN₂NaO [M+Na]⁺ 281.0452, found 281.0457.

(*R*)-4-(4-Chlorophenyl)pyrrolidin-2-one (11**):**¹² To a suspension of **5u** (37.0 mg, 0.145 mmol) in methanol (0.75 mL), *t*-BuMe₂SiOTf (TBSOTf) (333 μ L, 1.45 mmol) was added at 25 °C.⁷ The mixture was stirred at 40 °C for 39 h, and then directly purified by flash neutral silica gel column chromatography (eluent: *n*-hexane:EtOAc = 2:1) to give the desired compound **10**, which involved

impurities such as an diester via overreaction of the CN moiety. The mixture of **10** was subsequently used without further purification. To a solution of **10** in methanol (1.2 mL), platinum(IV) oxide (3.3 mg, 0.0145 mmol) and 3 M HCl in methanol (290 μ L, 0.87 mmol) were added, and the mixture was stirred at 25 °C under a hydrogen atmosphere (760 Torr, balloon) for 5 h.¹³ Platinum(IV) oxide was removed by filtration, and then the filtrate was concentrated under reduced pressure. To a solution of crude material in methanol (1.5 mL), sodium methoxide (157 mg, 2.9 mmol) was added, and the mixture was stirred at 25 °C for 17 h, and saturated aqueous NH₄Cl solution (5 mL) was added. The mixture was extracted with ethyl acetate (10 mL \times 3). The combined extracts were dried over MgSO₄. The organic phase was concentrated under reduced pressure, and the resultant residue was purified by neutral silica gel column chromatography (eluent: *n*-hexane:EtOAc = 3:1 to CHCl₃:MeOH = 12:1) to give the desired product **11** (19.3 mg, 68% yield in 3 steps). The enantiomeric purity of **11** was determined by HPLC analysis. ¹H NMR (400 MHz, CDCl₃) δ 2.46 (dd, *J* = 17.0, 8.7 Hz, 1H), 2.74 (dd, *J* = 16.9, 8.7 Hz, 1H), 3.38 (dd, *J* = 7.3, 9.2 Hz, 1H), 3.68 (quint, *J* = 8.2 Hz, 1H), 3.79 (t, *J* = 8.3 Hz, 1H), 6.03 (br, 1H), 7.19 (d, *J* = 8.2 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 37.9, 39.6, 49.4, 128.1 (2C), 129.0 (2C), 132.9, 140.6, 177.6. IR (KBr) 3197, 1688, 1492, 1346, 1259, 1090, 1013 cm⁻¹. M.p. 105-110 °C. $[\alpha]_D^{26} = -28.2$ (*c* 0.78, EtOH, 99% ee) [lit.¹⁴ $[\alpha]_D^{30} = -39.7$ (*c* 1.00, CHCl₃, for *S* enantiomer with >99% ee)]. HPLC analysis; AD-3, *n*-hexane/*i*-PrOH = 9/1, 220 nm, 1.0 mL/min, *t*_R = 10.1 min (major), 11.8 min (minor). HRMS (ESI+) calcd for C₁₀H₁₁ClNO [M+H]⁺ 196.0524, found 196.0520.

(R)-(-)-Baclofen (12):¹⁴ A suspension of **11** (23.7 mg, 0.121 mmol) in 6 M HCl aqueous solution (1 mL) was allowed to heat at 100 °C and stirred for 24 h. The resulting mixture was filtered through celite pad, and concentrated under reduced pressure to give the desired product **12** in 96% yield (29.1 mg). ¹H NMR (400 MHz, D₂O) δ 2.73 (m, 1H), 2.83 (dd, *J* = 16.0, 3.7 Hz, 1H), 3.22 (m, 1H), 3.30-3.46 (m, 2H), 7.27-7.38 (m, 2H), 7.41 (d, *J* = 6.9 Hz, 2H) [NH₂·HCl and CO₂H were not observed.]. ¹³C NMR (100 MHz, D₂O) δ 38.5, 39.8, 44.0, 129.5 (2C), 129.7 (2C), 133.6, 138.3, 175.7. IR (KBr) 2915, 1718, 1495, 1413, 1198, 1094 cm⁻¹. M.p. 185-189 °C $[\alpha]_D^{25} = -3.1$ (*c* 0.65, H₂O, 99% ee) [lit.¹⁴ $[\alpha]_D^{30} = -3.79$ (*c* 0.65, H₂O, for *R* enantiomer with >99% ee)]. HRMS (ESI+) calcd for C₁₀H₁₃ClNO₂ [M+H]⁺ 214.0629, found 214.0639.

We summarized the transformation of **5u** to **10** or **11** in Eqs. S1–S5 and Table S1. Compound **5u** was easily epimerized under basic conditions. Therefore, regarded reaction conditions with *n*-Bu₄CN¹⁵ and NaOMe gave the corresponding racemic product **10** (Eqs. S1 and S2). CoCl₂ or NiCl₂ with NaBH₄^{12,16} gave the corresponding product **11** with a significant loss of enantio-purity (Eqs. S3 and S4). Moreover, common reduction process with H₂ on Pd/C gave an unexpected Cl-reduced product **S1** (Eq. S5). In contrast, acid-treatment to **5u** in methanol generally worked

well, and **10** was obtained without epimerization (Table S1). In particular, TBSOTf was better than TMSOTf,¹⁷ **10** was ultimately obtained in 76% yield when 10 equiv of TBSOTf was used (entry 4). In all cases, the generation of undesired diester **S2** (22–32% yields) could not be avoided.

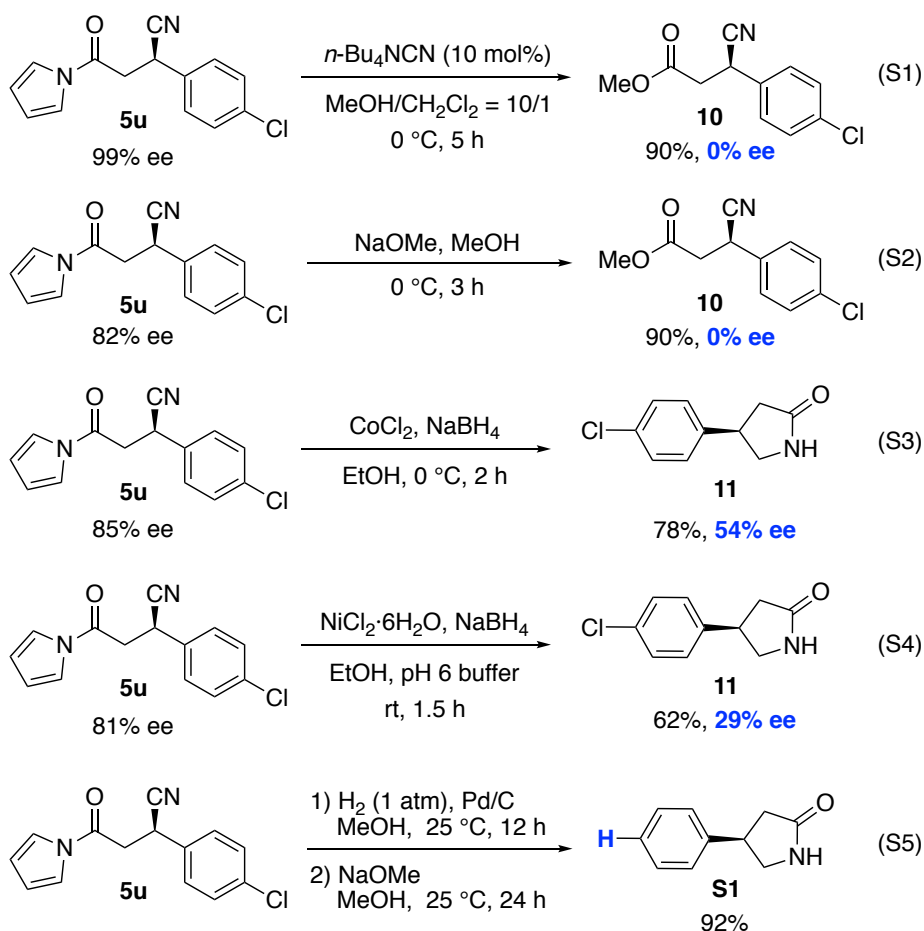
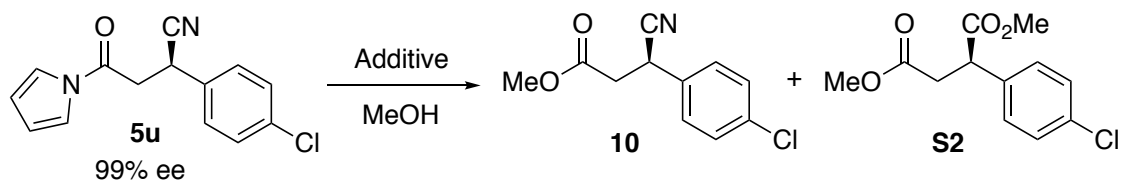
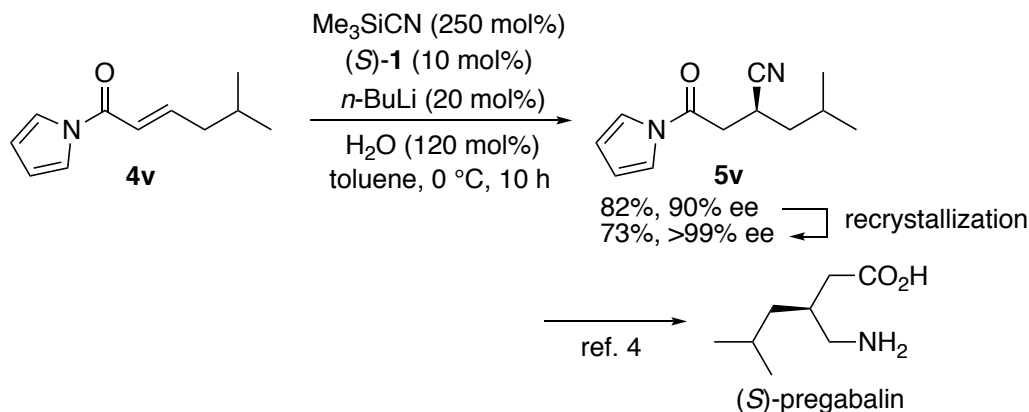


Table S1. Screening of reaction conditions of **5u**.



entry	Additive (equiv)	Conditions	yield (%) of 10	yield (%) of S2
1	TMSOTf (7.5)	60 °C, 25 h	58 (99% ee)	22
2	TMSOTf (15)	60 °C, 31 h	54 (99% ee)	23
3	TBSOTf (7.5)	60 °C, 21 h	64 (99% ee)	32
4	TBSOTf (10)	40 °C, 39 h	76 (99% ee)	24

8. Synthesis of (*S*)-pregabalin (Eq. 5).

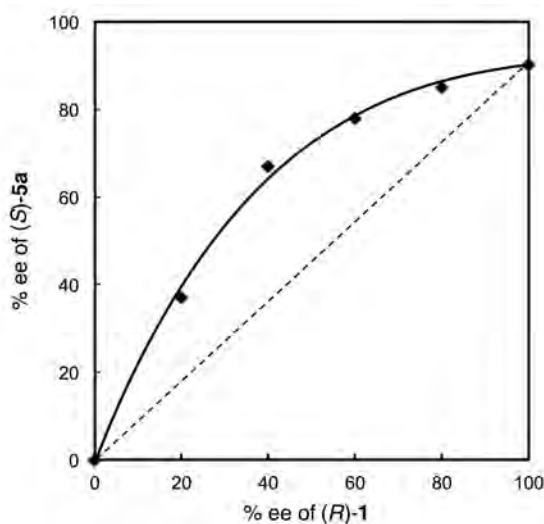
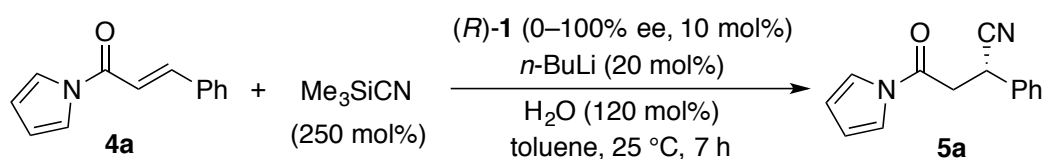


(*S*)-4-Methyl-2-(2-oxo-2-(1*H*-pyrrol-1-yl)ethyl)pentanenitrile (5v**):**⁴ 82%, 90% ee (TMSCN 250 mol%, $0\text{ }^\circ\text{C}$, 10 h). Column chromatography (eluent: *n*-hexane:EtOAc = 10:1 to 5:1). R_f = 0.36 (*n*-hexane:EtOAc = 4:1). Compound **5v** was recrystallized from dichloromethane/*n*-hexane at room temperature (>99% ee). Colorless solid. ^1H NMR (400 MHz, CDCl_3) δ 1.00 (d, J = 6.4 Hz, 3H), 1.01 (d, J = 6.4 Hz, 3H), 1.45 (m, 1H), 1.71 (m, 1H), 1.92 (m, 1H), 3.05 (m, 1H), 3.22 (d, J = 6.9 Hz, 1H), 3.30 (m, 1H), 6.34 (t, J = 2.3 Hz, 2H), 7.29 (brs, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 21.1, 22.8, 25.0, 26.1, 37.3, 40.7, 113.8 (2C), 118.8 (2C), 121.1, 166.5. IR (KBr) 2967, 2240, 1727, 1473, 1378, 1290, 1072 cm^{-1} . M.p. 64-67 $^\circ\text{C}$. $[\alpha]_D^{22} = -26.2$ (c 1.00, CHCl_3 , 90% ee). [lit.⁴ $[\alpha]_D^{22} = +26.2$ (c 0.940, CHCl_3 , for *R* enantiomer with 97% ee)]. HPLC analysis; OD-3, *n*-hexane/*i*-PrOH = 9/1, 240 nm, 1.0 mL/min, t_R = 10.6 min (minor), 13.0 min (major). HRMS (ESI+) calcd for $\text{C}_{12}\text{H}_{16}\text{N}_2\text{NaO}$ $[\text{M}+\text{Na}]^+$ 227.1155, found 227.1153.

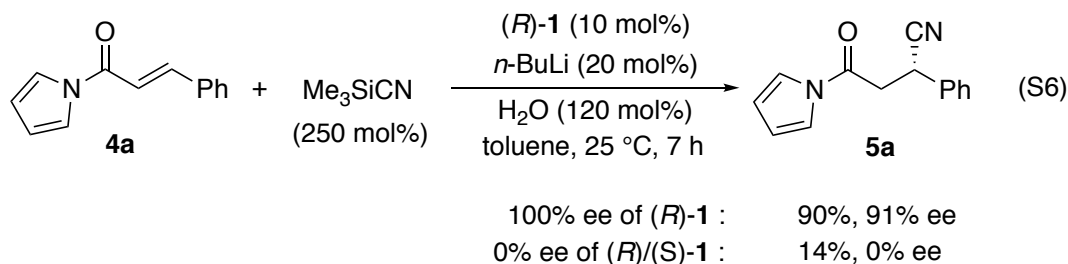
9. Non-linear effect between the ee (%) of (*R*)-1 and the ee (%) of (*S*)-5a.

As shown in Scheme S1, a non-linear effect was examined in the reaction of *N*-acetylpyrrole **4a** (0.30 mmol) with trimethylsilyl cyanide (250 mol%) in the presence of (*R*)-1 (10 mol%, 0% ee to 100% ee), *n*-BuLi (20 mol%), and water (120 mol%) in toluene at 25 °C for 7 h. This non-linear relationship strongly suggests that inactive hetero-(*R*)_n/(*S*)_m oligomeric lithium(I) complexes might be involved under these reaction conditions with the use of <100% ee of (*R*)-1.

Scheme S1. Plot of ee of (*S*)-5a vs. ee of (*R*)-1.



As expected, a 1:1 ratio of (*R*)/(*S*)-1-derived catalyst (i.e., 0% ee catalyst) showed low catalytic activity (14% yield, 0% ee), while (*R*)-100% ee catalyst showed higher catalytic activity (90%, 90% ee) (Eq. S6). These results strongly suggest that hetero-(*R*)/(*S*)-1-derived Li(I)-dimer (or oligomers) might be stable and inactive. Overall, the remaining (*R*)-enriched monomeric lithium(I) complexes should be the active species and promote the reaction. These observations can clearly explain the strong positive non-linear effect.



10. Possible transition states.

Plausible transition states for α,β -unsaturated *N*-acylpyrroles are shown in Figure S3. In this reaction, α,β -unsaturated *N*-acylpyrrole **4a** can be activated at the Lewis acidic Li(I) center in TS-13 or TS-13'. TS-13 shows favored *trans*-coordination of amide to an acid center (i.e., *trans*-N-C=O \cdots Li), whereas TS-13' shows disfavored *cis*-coordination (i.e., *cis*-N-C=O \cdots Li).

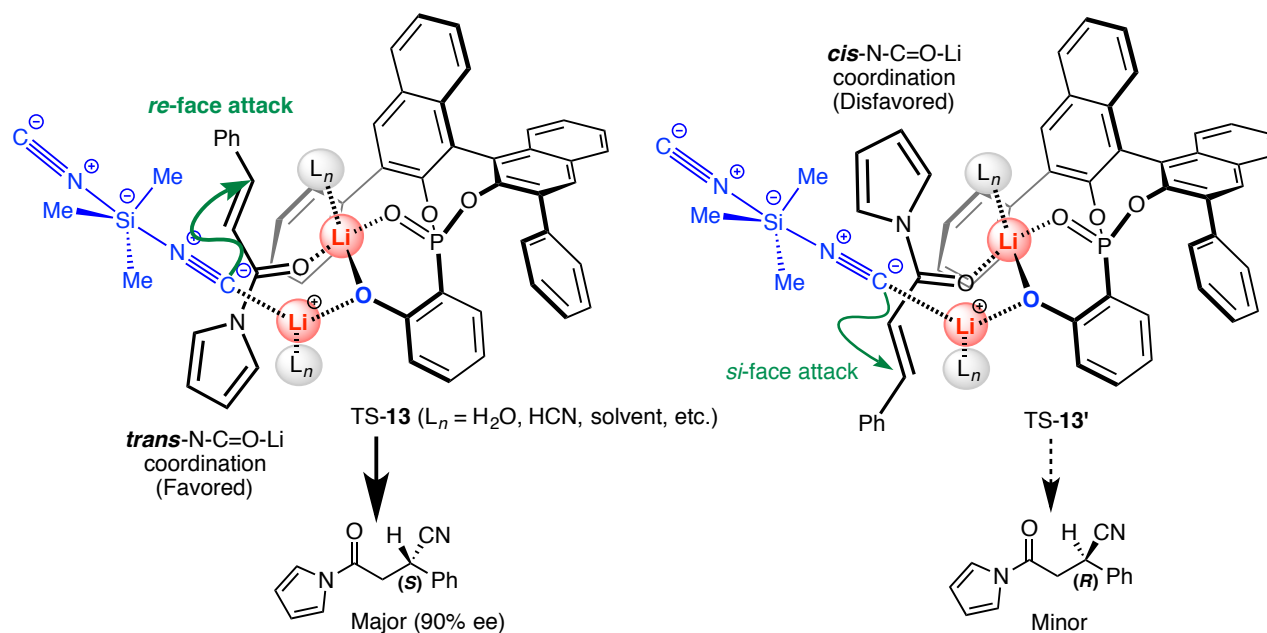


Figure S3. Possible transition states for *N*-cinnamoylpyrrole **4a**.

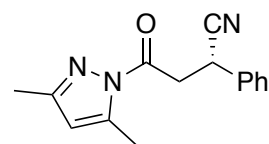
11. Optimization of the substrates.

Optimization of the substrates are summarized in Table S2. In our catalysis, the *N*-acylpyrrole moiety was essential both to promote the reaction and to induce the enantioselectivity.

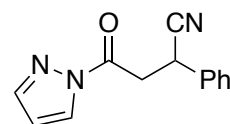
Table S2. Optimization of the substrates.^a

Product, yield, enantioselectivity, and reaction time: ^a	
 5a 90%, 90% ee (7 h)	 S3 38%, 70% ee (6 h) ^[b]
 S4 32%, 0% ee (12 h)	 S5 0% (12 h)
 S6 24%, 1% ee	 S7 70%, 58% ee (20 h)
 S8 98%, 0% ee (9 h)	 S9 0% (14 h)
 S10 98%, 0% ee (7 h)	 S11 0% (19 h)
 S12 40%, 19% ee (8 h)	

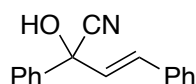
^a The reaction was carried out with substrate (0.30 mmol), Me₃SiCN (250 mol%), (*R*)-**1** (10 mol%), *n*-BuLi (20 mol%), and H₂O (120 mol%) in toluene at 25 °C unless otherwise noted. ^b 15 mol of *n*-BuLi was used.



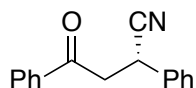
(S)-4-(3,5-Dimethyl-1H-pyrazol-1-yl)-4-oxo-2-phenylbutanenitrile (S3):¹⁸ Column chromatography (eluent: *n*-hexane:EtOAc = 10:1 to 5:1). R_f = 0.38 (*n*-hexane:EtOAc = 4:1). Colorless solid. ¹H NMR and ¹³C NMR data were consistent with previously reported values.¹⁸ HPLC analysis; OD-H, *n*-hexane/*i*-PrOH = 9/1, 1.0 mL/min, *t*_R = 31.3 min (major), 39.6 min (minor).



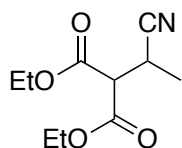
Oxo-2-phenyl-4-(1*H*-pyrazol-1-yl)butanenitrile (S4): Column chromatography (eluent: *n*-hexane:EtOAc = 10:1 to 5:1). *R*_f = 0.31 (*n*-hexane:EtOAc = 4:1). Colorless solid. ¹H NMR (400 MHz, CDCl₃) δ 3.70 (dd, *J* = 17.9, 6.4 Hz, 1H), 3.89 (dd, *J* = 17.9, 8.7 Hz, 1H), 4.52 (dd, *J* = 8.2, 6.4 Hz, 1H), 6.47 (dd, *J* = 2.7, 1.4 Hz, 1H), 7.34-7.46 (m, 5H), 7.70 (s, 1H), 8.25 (d, *J* = 3.2 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 32.4, 40.0, 110.3, 119.8, 127.5 (2C), 128.5, 128.6, 129.3 (2C), 134.3, 144.7, 167.7. IR (KBr) 3130, 2246, 1732, 1422, 1389, 1321, 1255, 1203, 1095, 1035 cm⁻¹. M.p. 93-96 °C. HPLC analysis; OD-3, *n*-hexane/*i*-PrOH = 9/1, 1.0 mL/min, *t*_R = 16.4 min and 18.0 min. HRMS (ESI+) calcd for C₁₃H₁₁N₃NaO [M+Na]⁺ 248.0794, found 248.0791.



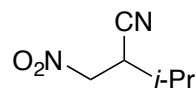
2-Hydroxy-2,4-diphenylbut-3-enenitrile (S6):¹⁹ Column chromatography (eluent: *n*-hexane:EtOAc = 10:1 to 5:1). *R*_f = 0.36 (*n*-hexane:EtOAc = 4:1). Colorless oil. ¹H NMR and ¹³C NMR data were consistent with previously reported values.¹⁹ HPLC analysis; IA-3, *n*-hexane/*i*-PrOH = 95/5, 1.0 mL/min, *t*_R = 8.5 min (major), 10.9 min (minor).



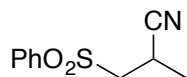
(*S*)-4-Oxo-2,4-diphenylbutanenitrile (S7):¹⁸ Column chromatography (eluent: *n*-hexane:EtOAc = 10:1 to 5:1). *R*_f = 0.28 (*n*-hexane:EtOAc = 4:1). Colorless solid. ¹H NMR and ¹³C NMR data were consistent with previously reported values.¹⁸ HPLC analysis; OD-3, *n*-hexane/*i*-PrOH = 7/3, 1.0 mL/min, *t*_R = 12.8 min (major, *S*), 15.6 min (minor, *R*).



Diethyl 2-(1-cyanoethyl)malonate (S8):²⁰ Column chromatography (eluent: *n*-hexane:EtOAc = 15:1). *R*_f = 0.42 (*n*-hexane:EtOAc = 9:1). Colorless oil. ¹H NMR and ¹³C NMR data were consistent with previously reported values.²⁰ GC analysis; CHIRALDEX B-DM, 100 °C, 100 kPa, *t*_R = 17.4 min, 18.7 min.



3-Nethyl-2-(nitromethyl)butanenitrile (S10):²¹ Column chromatography (eluent: *n*-hexane:EtOAc = 15:1). *R*_f = 0.45 (*n*-hexane:EtOAc = 9:1). Colorless oil. ¹H NMR and ¹³C NMR data were consistent with previously reported values.²¹ HPLC analysis; AD-3, *n*-hexane/*i*-PrOH = 98/2, 1.0 mL/min, *t*_R = 22.0 min, 25.6 min.

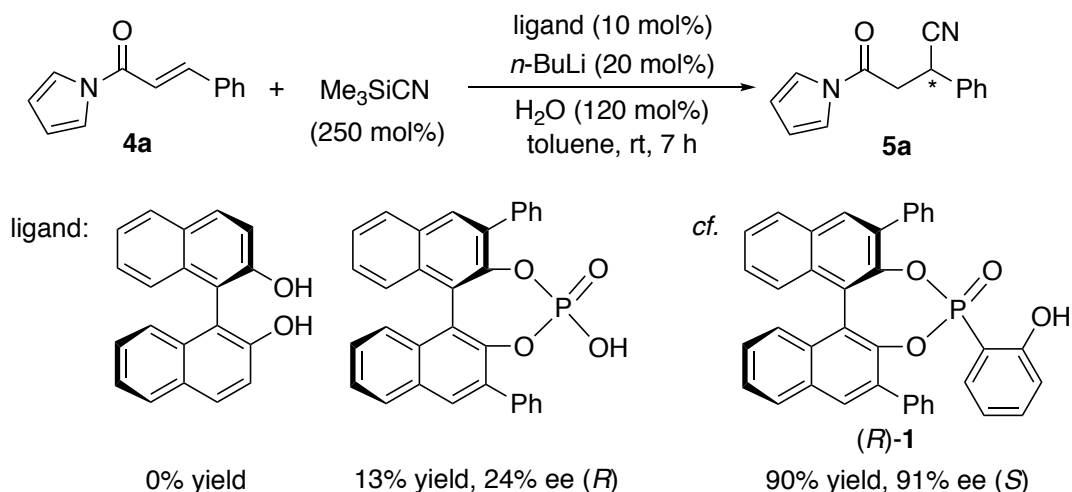


2-Phenyl-3,3-bis(phenylsulfonyl)propanenitrile (S12):²² Column chromatography (eluent: *n*-hexane:EtOAc = 3:1 to 1:1). *R*_f = 0.28 (*n*-hexane:EtOAc = 2:1). Colorless solid. ¹H NMR (400 MHz, CDCl₃) δ 1.52 (d, *J* = 7.3 Hz, 3H), 3.17-3.30 (m, 2H), 3.47 (dd, *J* = 13.3, 6.4 Hz, 1H), 7.63 (t, *J* = 8.2 Hz, 2H), 7.73 (t, *J* = 7.3 Hz, 1H), 7.96 (d, *J* = 7.3 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 18.3, 20.8, 58.3, 119.7, 128.2 (2C), 129.7 (2C), 134.6, 138.3. IR (KBr) 2994, 2939, 2243, 1450, 1315, 1293, 1183, 1147 cm⁻¹. M.p. 76–77 °C. [α]_D²⁷ = –2.4 (*c* 1.00, CHCl₃, 23% ee). HPLC analysis; AD-3, *n*-hexane/*i*-PrOH = 1/1, 0.7 mL/min, *t*_R = 14.3 min (minor), 15.6 min (major). HRMS (ESI+) calcd for C₁₀H₁₁NNaO₂S [M+Na]⁺ 232.0403, found 232.0398.

12. Control experiments with our previous catalysts.

We examined a probe reaction with the use of our previous catalysts such as a chiral lithium(I) binaphtholate aqua complex²³ and a chiral lithium(I) phosphate²⁴ (Scheme S2). However, the reactions scarcely proceeded with these catalysts (<15% yield) under the same optimal conditions as in entry 5 of Table 1. Therefore, this catalytic system with silicate [Li]⁺[Me₃Si(CN)₂]⁻ **3** turned out to be different from our previous catalytic systems with Me₃SiCN.

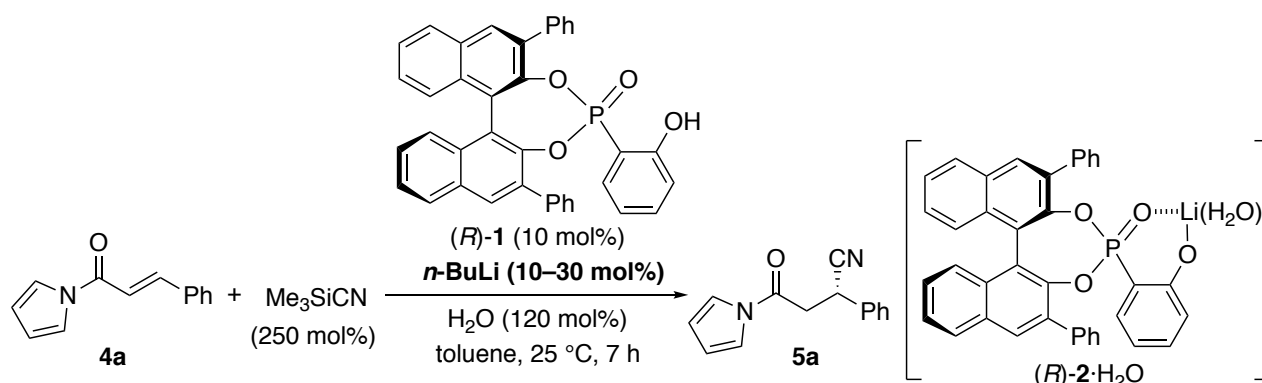
Scheme S2. Control experiments with previous catalysts.



13. Control experiments of cyanation of *N*-acetylpyrrole **4a** and acetophenone **S13**.

To confirm lithium(I) dicyanotrimethylsilicate(IV), $[\text{Li}]^+[\text{Me}_3\text{Si}(\text{CN})_2]^-$ **3**, would be essential or not, a present probe reaction was carried out in the absence or presence of **3** (i.e., 0, 5, 10, and 20 mol% of LiCN) (Table S3, also see Table 1 in the paper). As a result, in the absence of **3**, the reaction itself hardly proceeded (entry 1). This result strongly suggests that Me_3SiCN , HCN, and/or the combined reagent $\text{Me}_3\text{SiCN}/\text{HCN}$ would not be effective in this present reaction. Moreover, we have already confirmed that the combined use of Me_3SiCN and HCN in the absence of Li(I)^+ almost did not provide the corresponding silicate(IV), such as $[\text{H}]^+[\text{Me}_3\text{Si}(\text{CN})_2]^-$.³ In contrast, the reaction was facilitated more smoothly in the presence of 10 mol% of **3** (entry 3) than 5 mol% of **3** (entry 2). However, 20 mol% of **3** provided an insoluble black material probably due to undesired side reactions, and the yield and enantioselectivity were decreased (entry 4).

Table S3. Conjugate hydrocyanation to *N*-acetylpyrrole **4a**.^a

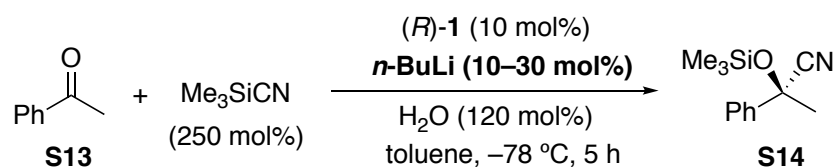


entry	<i>n</i> -BuLi (mol%)	Theoretical amount (mol%) of					5a yield (%)	5a ee (%)
		(R) - 2 · H_2O	LiCN	Me_3SiCN	HCN	Me_3SiOH		
1	10	10	0	140	110	110	7	53
2	15	10	5	140	105	110	67	91
3	20	10	10	140	100	110	90	91
4	30	10	20	140	90	110	65	60

^a The reaction was carried out with **4a** (0.30 mmol), Me_3SiCN (250 mol%), (R) -**1** (10 mol%), $n\text{-BuLi}$ (10–30 mol%), and H_2O (120 mol%) in toluene at 25 °C for 7 h.

Next, to consider the cyanation of *N*-acylpyrrole **4a**, and we carried out the cyanosilylation of acetophenone **S13** according to the previous report (Table S4).³ As a result, in the absence of **3**, the reaction proceeded, and **S14** was obtained in 68% yield with 90% ee (entry 1). Since acetophenone **S13** is much more reactive (reaction temperature is –78 °C) than *N*-acylpyrrole **4a** (reaction temperature is 25 °C), we cannot completely deny the participation of Me₃SiCN, HCN, and/or the combined reagent Me₃SiCN/HCN. However, in the presence of only 5 mol% of **3**, the reaction was greatly promoted, and **S14** was obtained in more improved yield (94%) with 91% ee (entry 2). The reaction was also greatly promoted in the presence of 10 mol% and 20 mol% of **3**, although the enantioselectivity was gradually decreased (entries 3 and 4).

Table S4. Cyanosilylation to acetophenone **S13**.^a



entry	<i>n</i> -BuLi (mol%)	Theoretical amount (mol%) of					S14 yield (%)	S14 ee (%)
		(<i>R</i>)- 2 ·H ₂ O	LiCN	Me ₃ SiCN	HCN	Me ₃ SiOH		
1	10	10	0	140	110	110	68	90
2	15	10	5	140	105	110	94	91
3	20	10	10	140	100	110	93	89
4	30	10	20	140	90	110	97	84

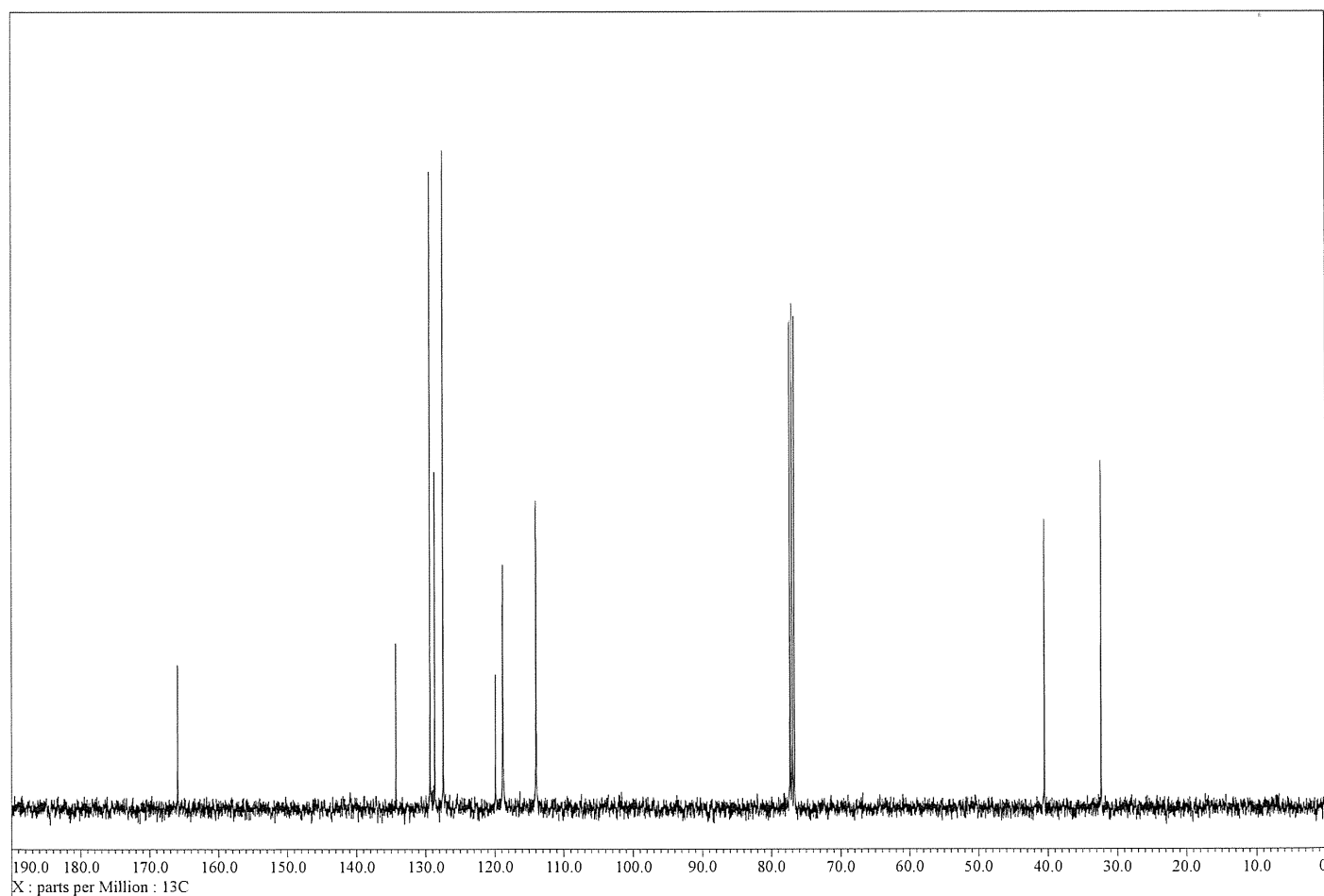
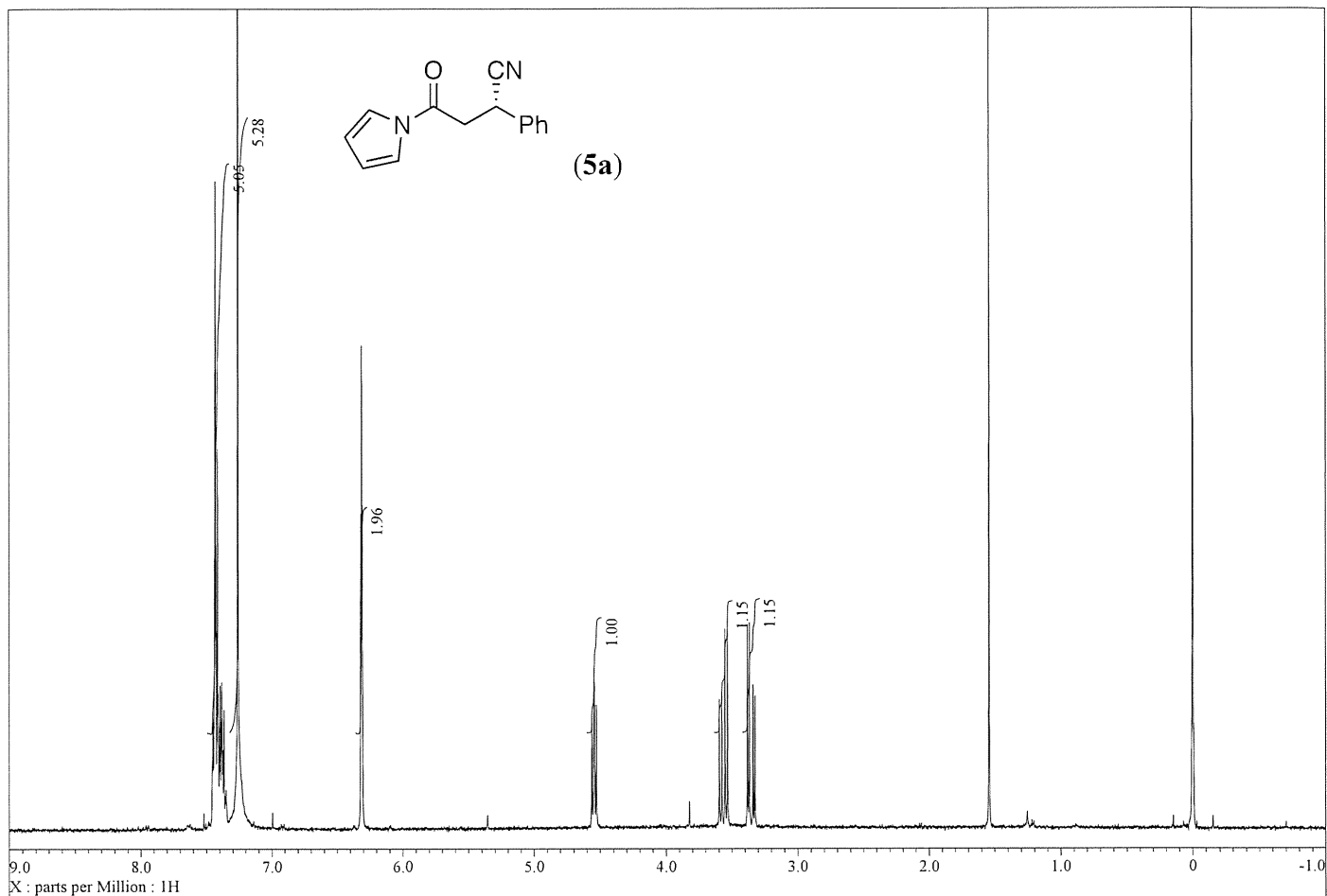
^a The reaction was carried out with **S13** (0.30 mmol), Me₃SiCN (250 mol%), (*R*)-**1** (10 mol%), *n*-BuLi (10–30 mol%), and H₂O (120 mol%) in toluene at –78 °C for 5 h.

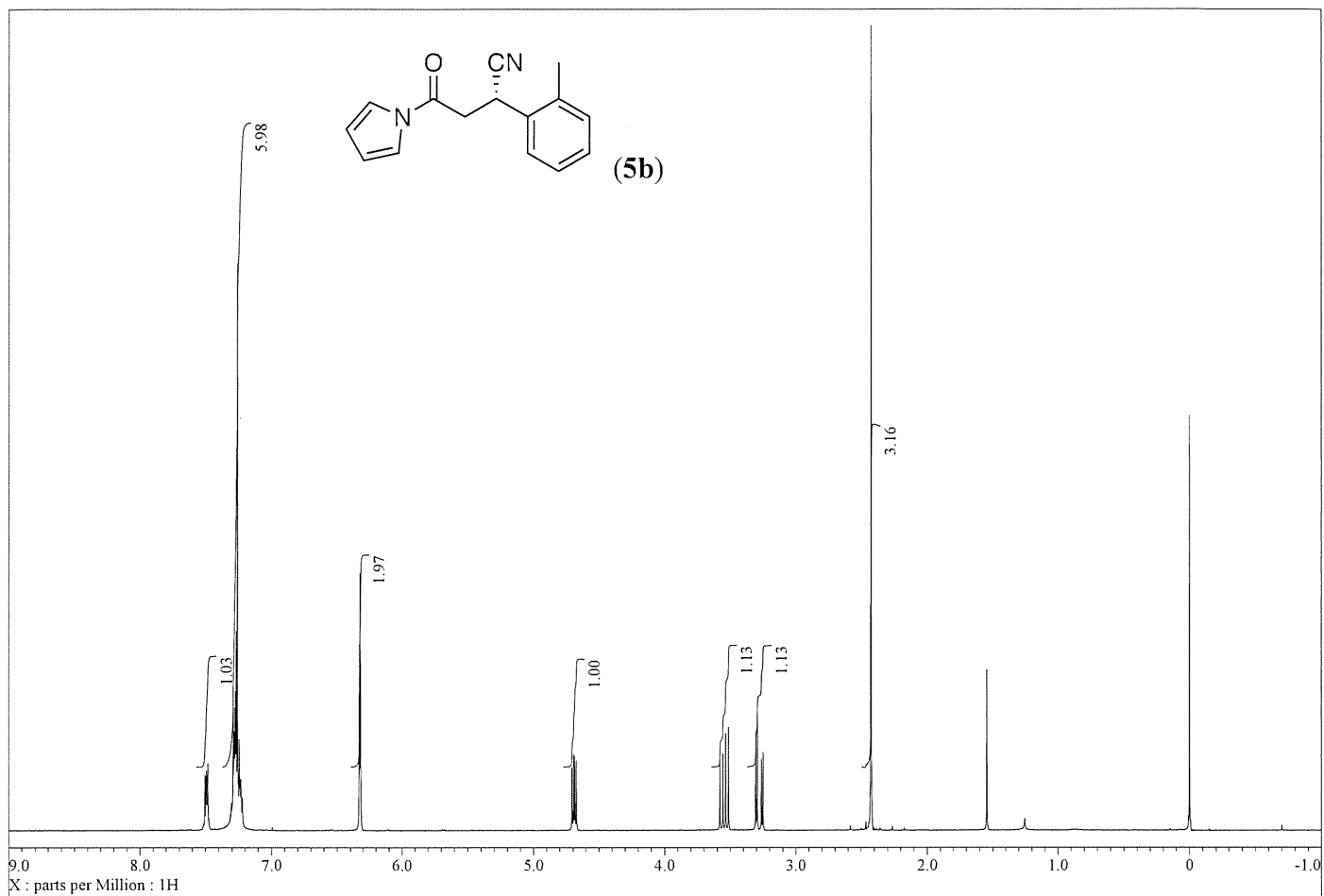
Overall, between the conjugate hydrocyanation to *N*-acylpyrrole **4a** and the previous cyanosilylation of acetophenone **S13**, the optimum reaction conditions were practically same except for the reaction temperature. In both reactions, the use of lithium(I) dicyanotrimethylsilicate(IV), [Li]⁺[Me₃Si(CN)₂][–] **3** was quite effective. In particular, shortage or lack of **3** decreased the yield. Moreover, the use of the more than optimal amount of **3** decreased the enantioselectivity.

14. References.

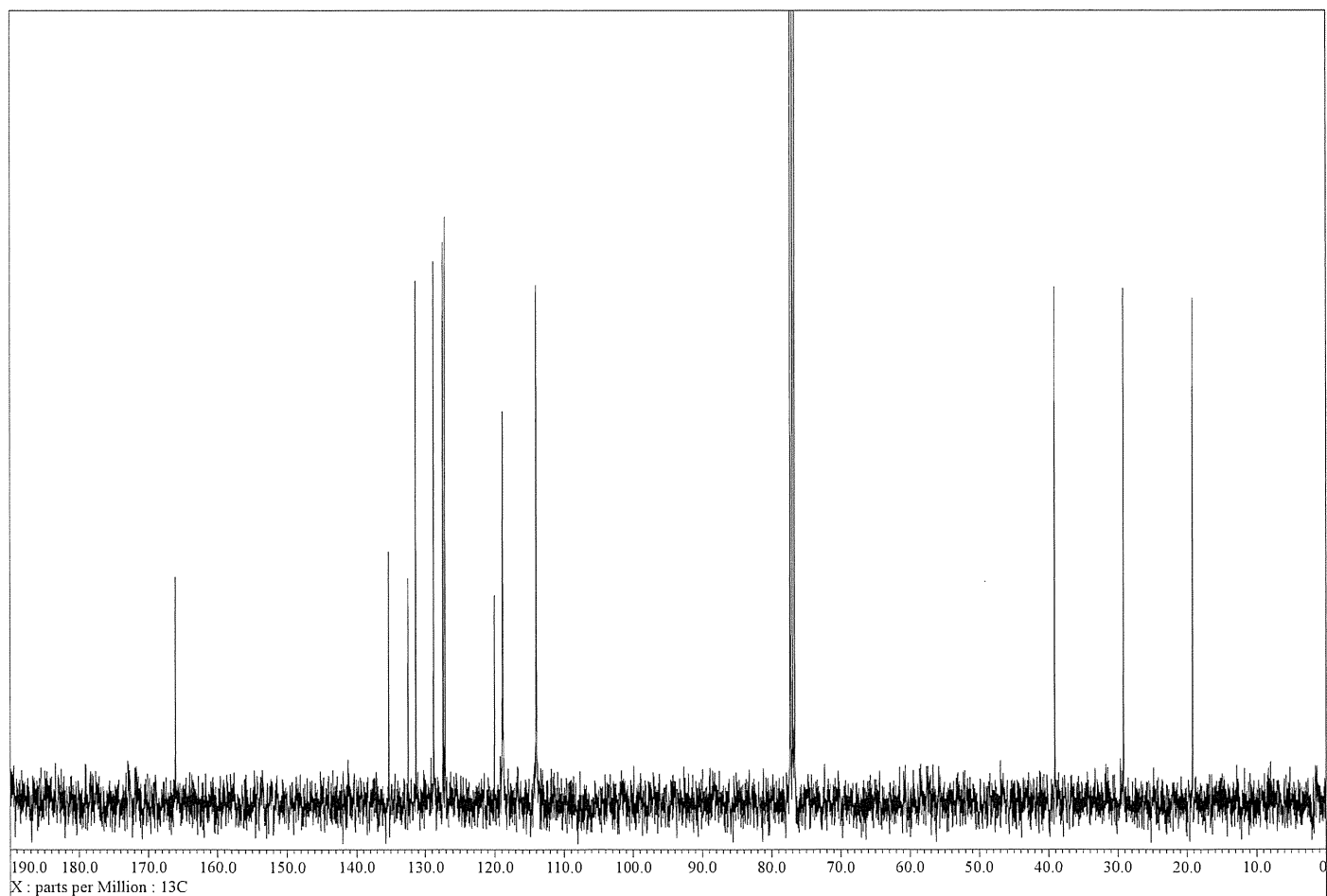
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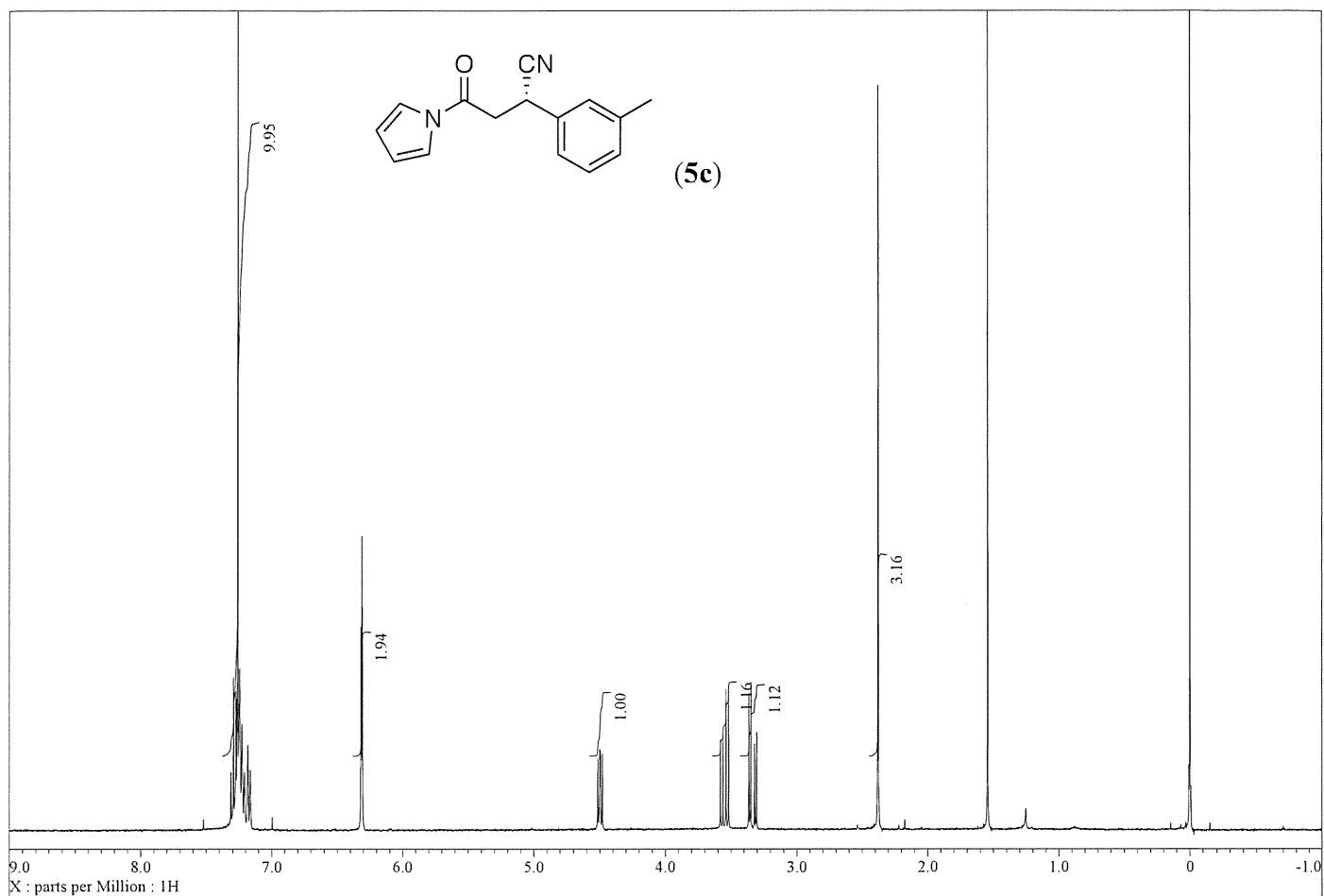




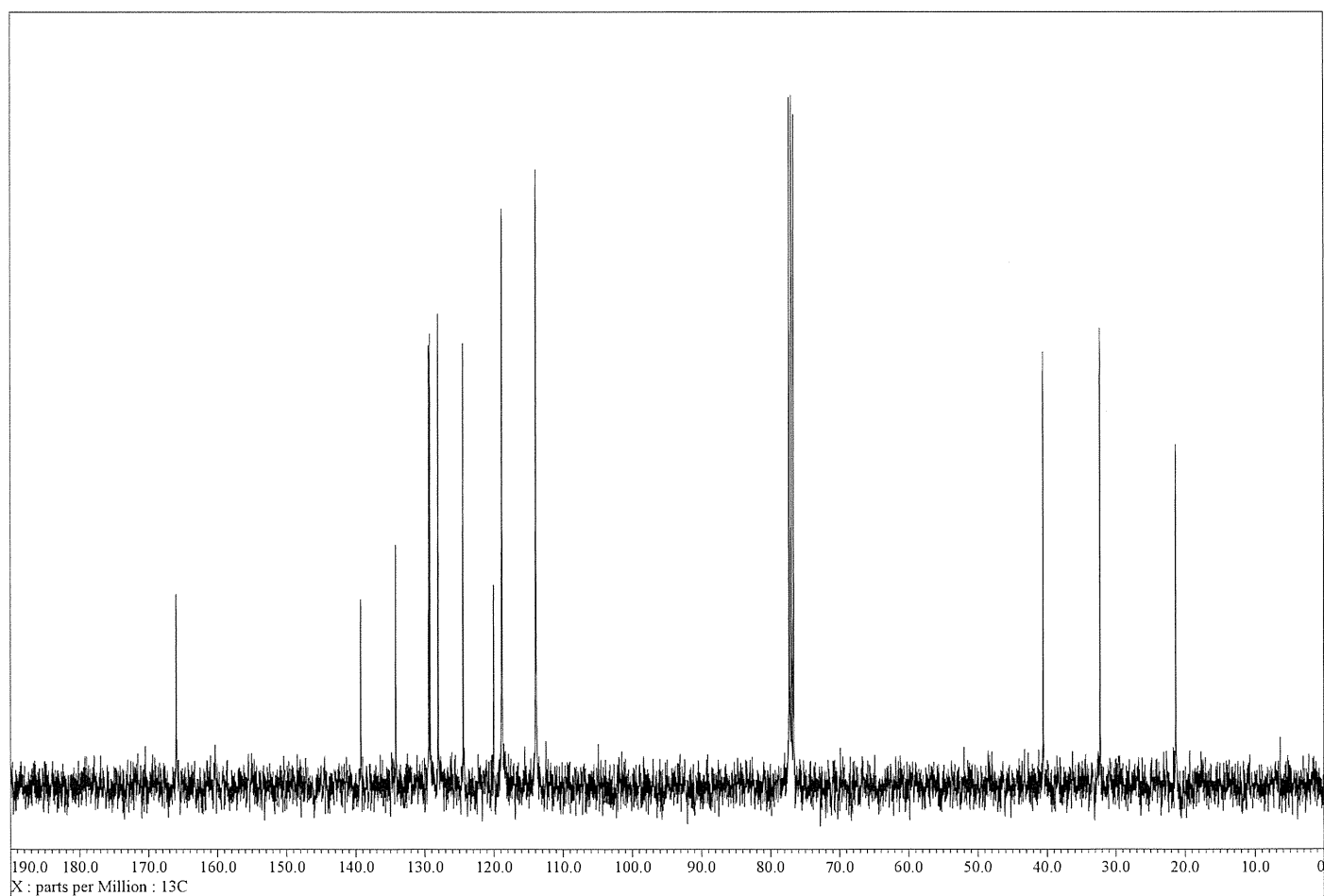
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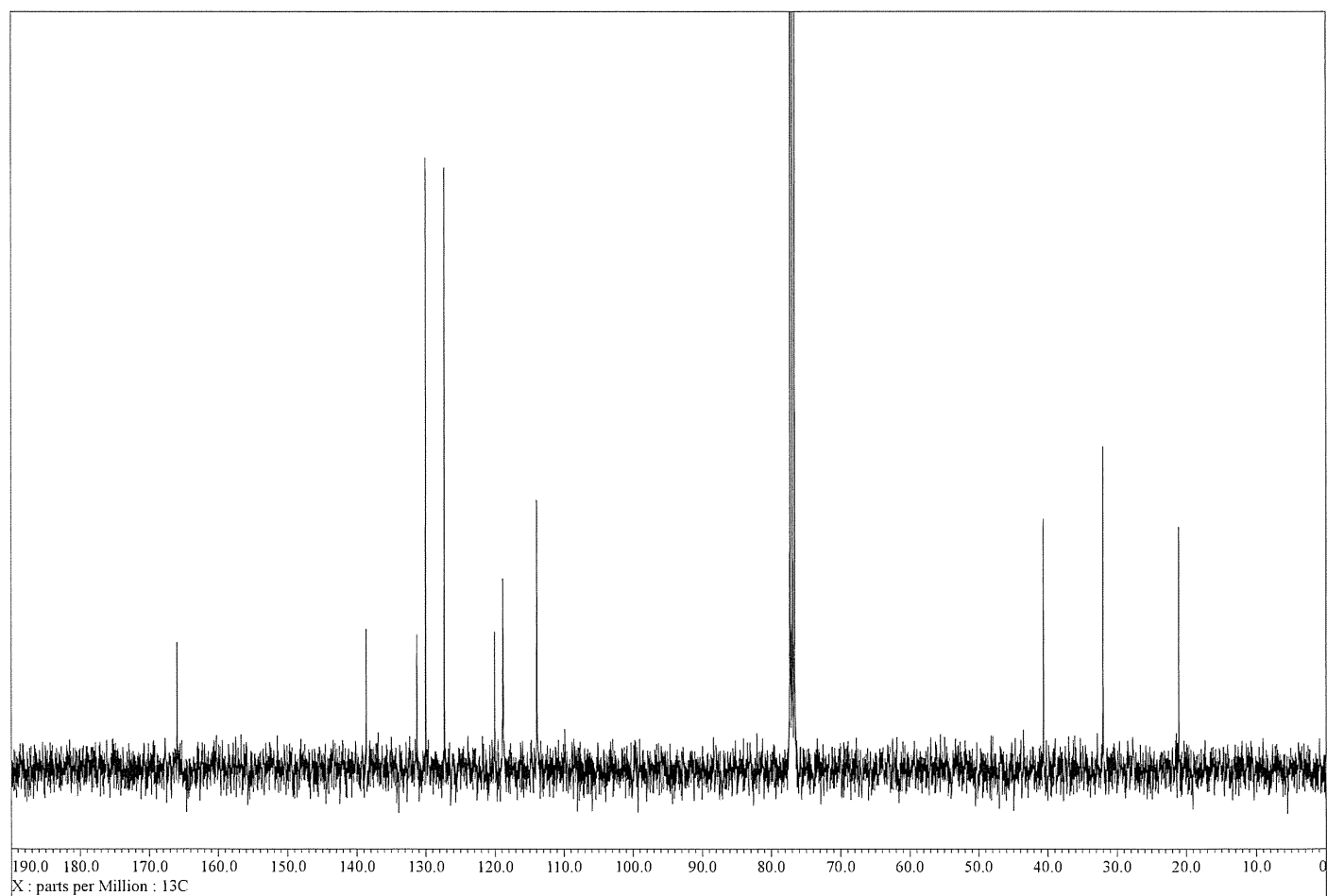
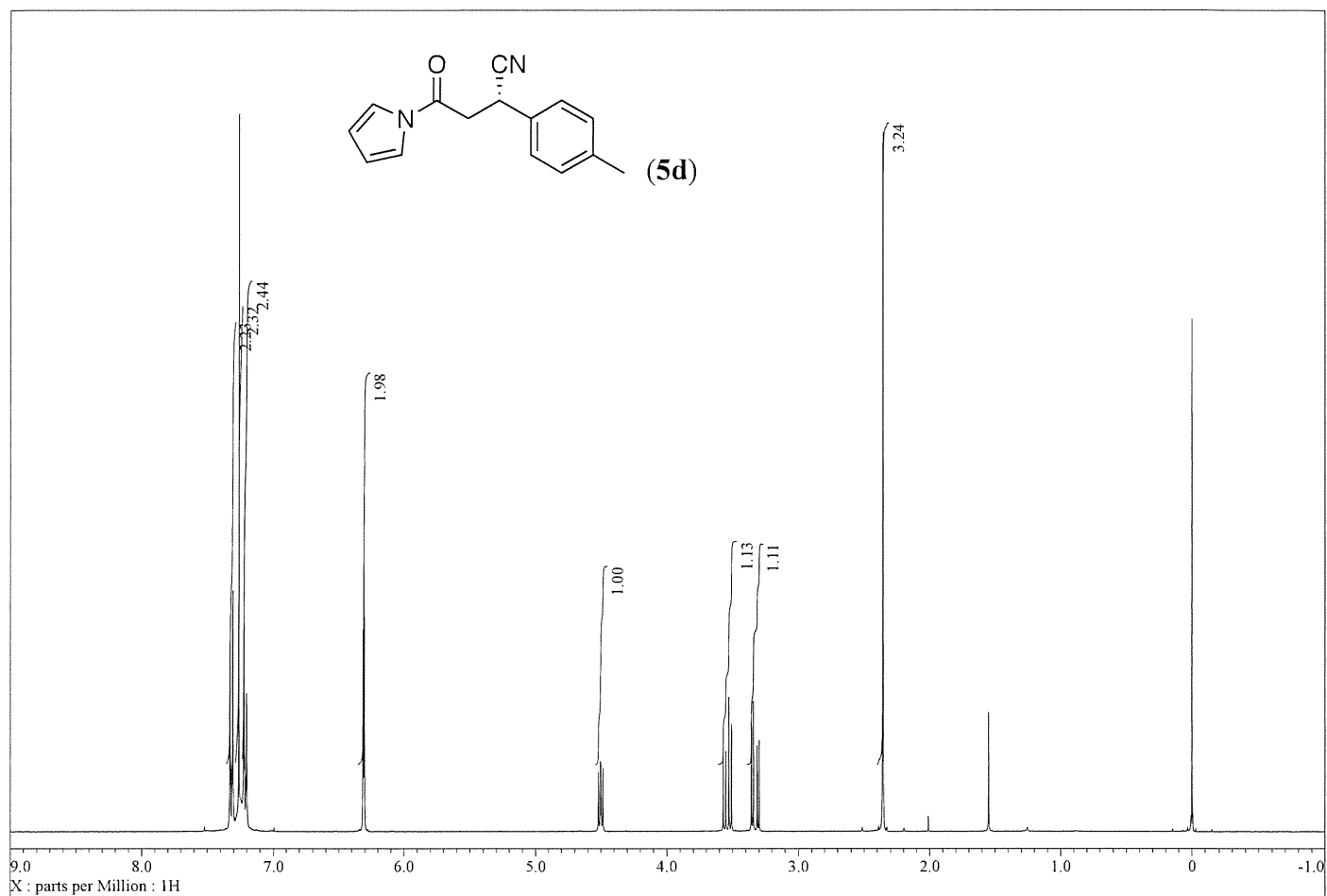
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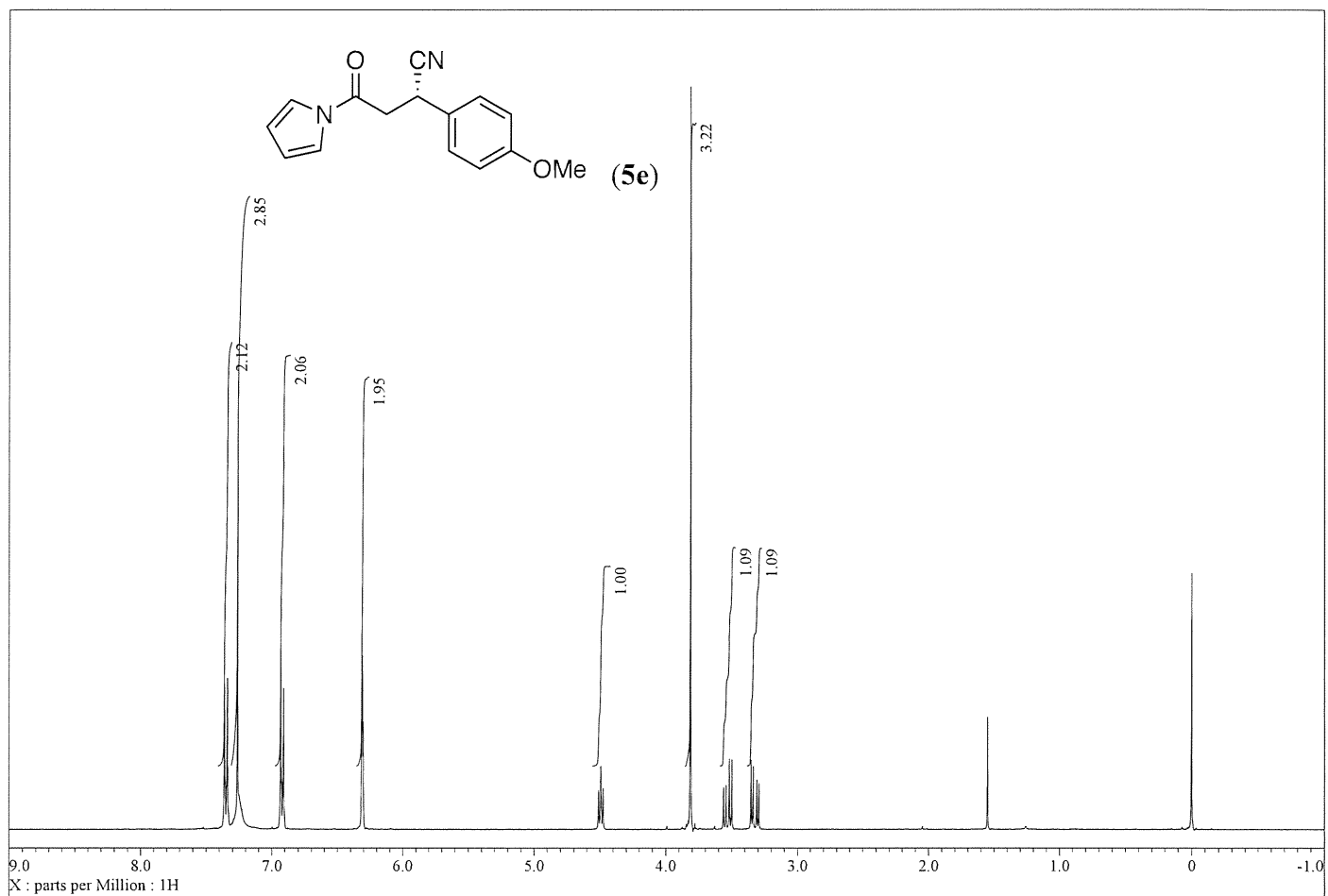
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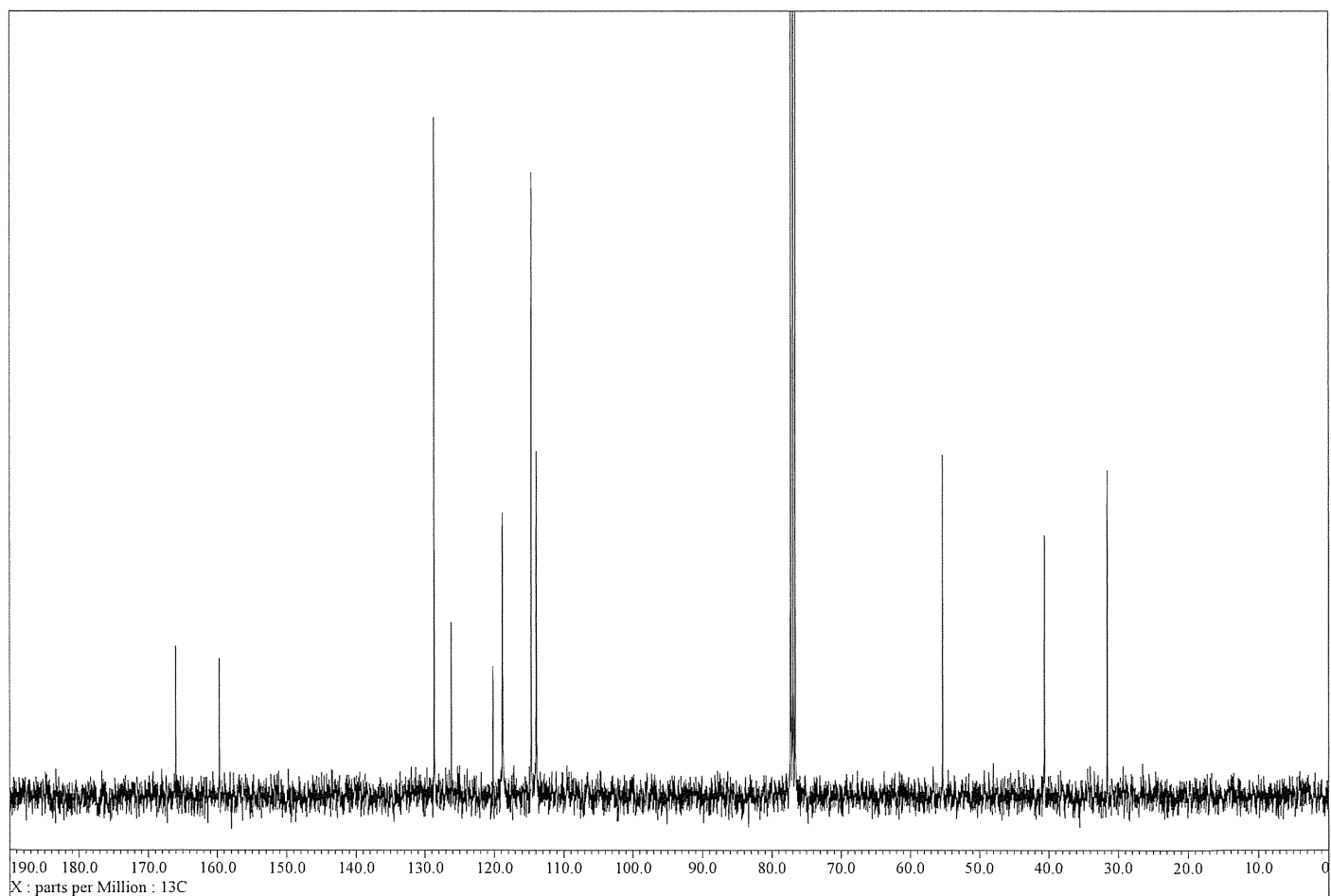
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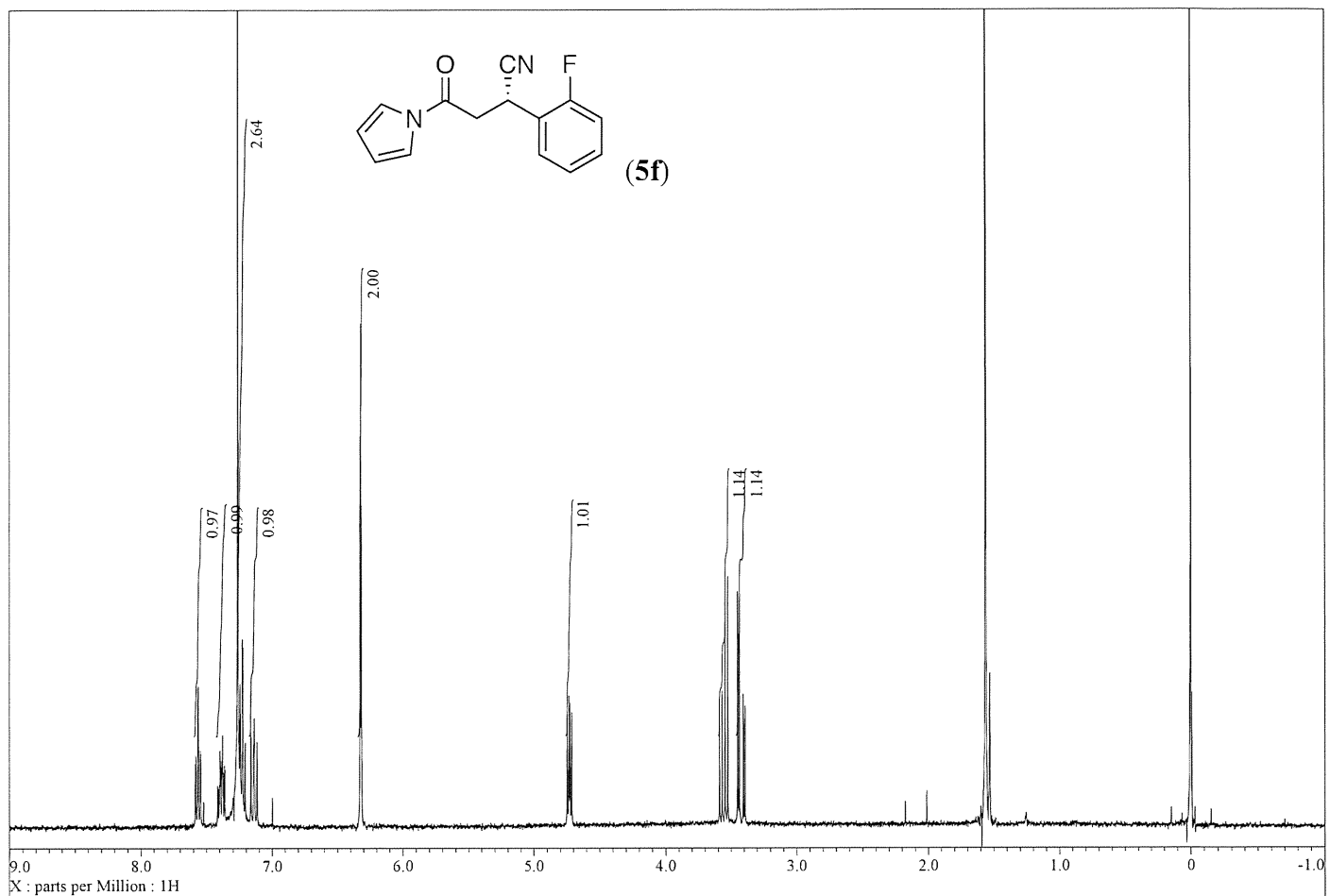
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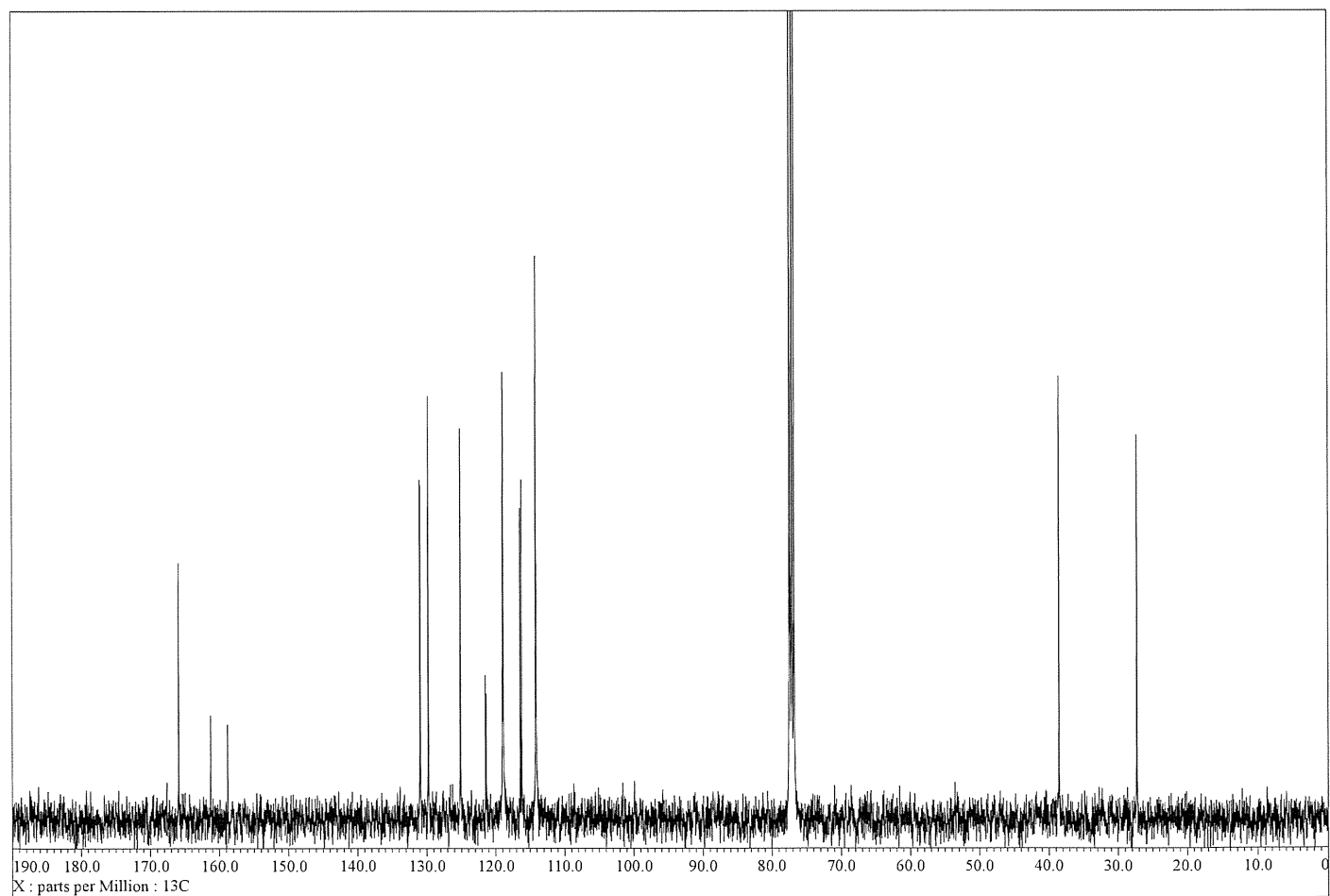
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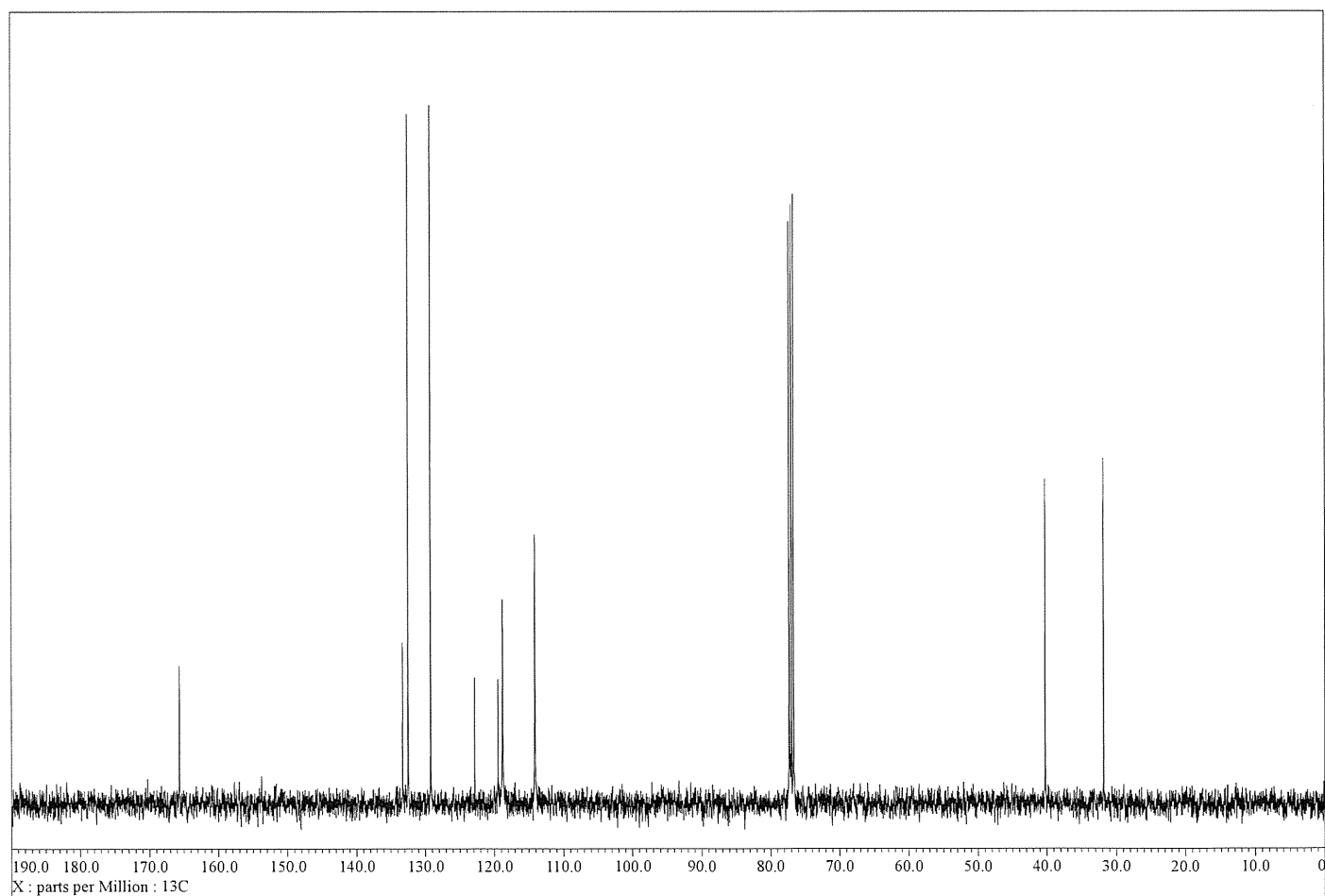
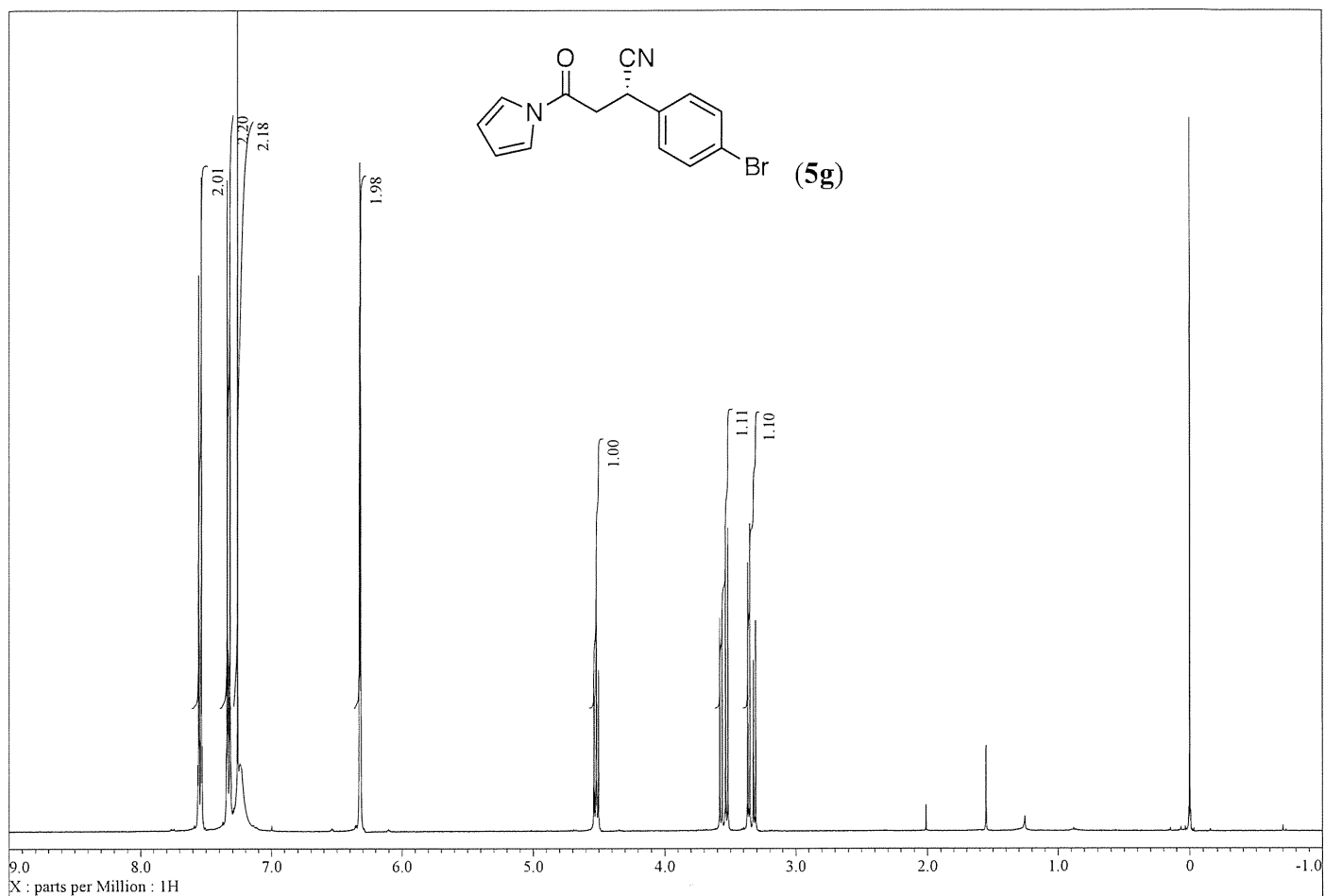
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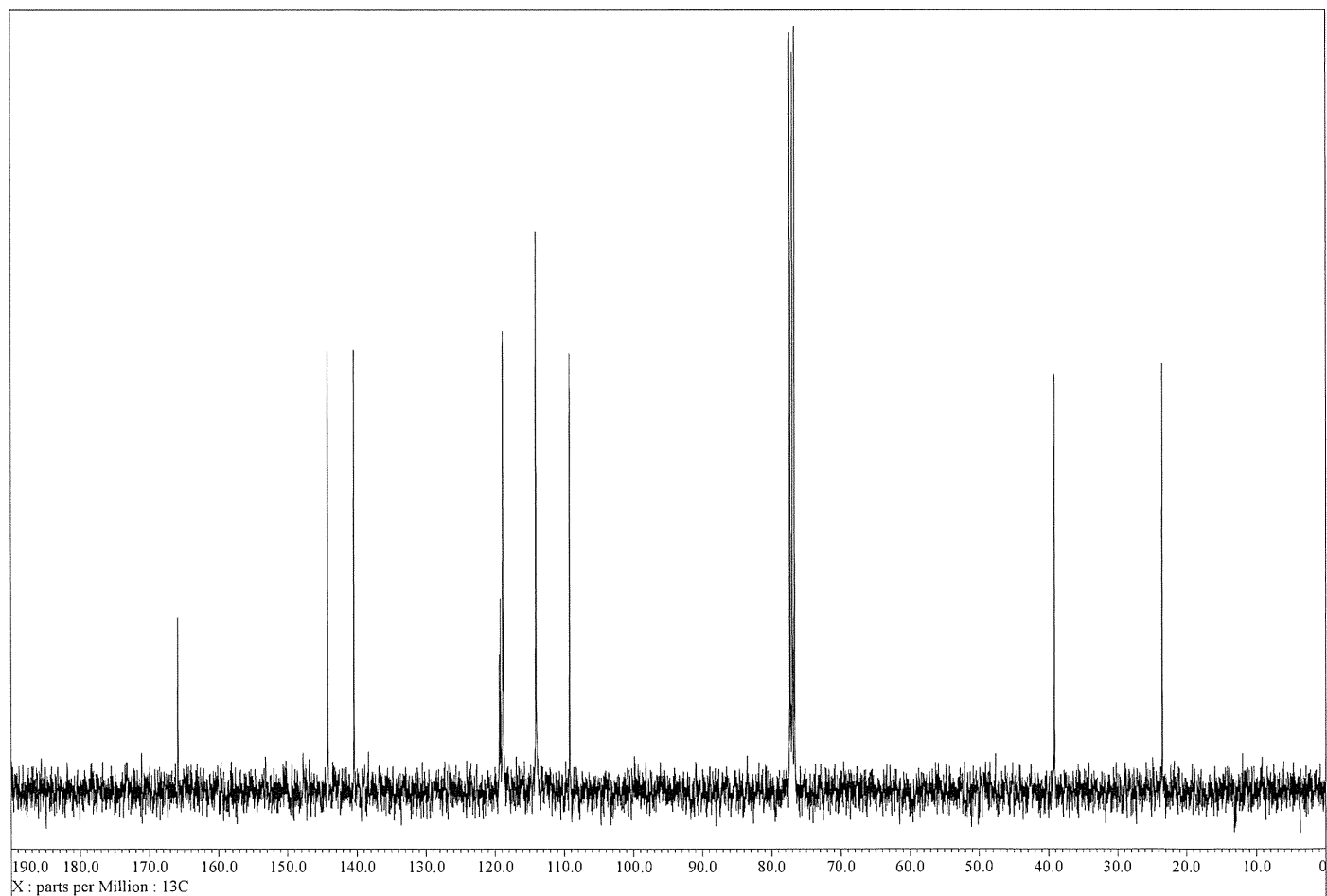
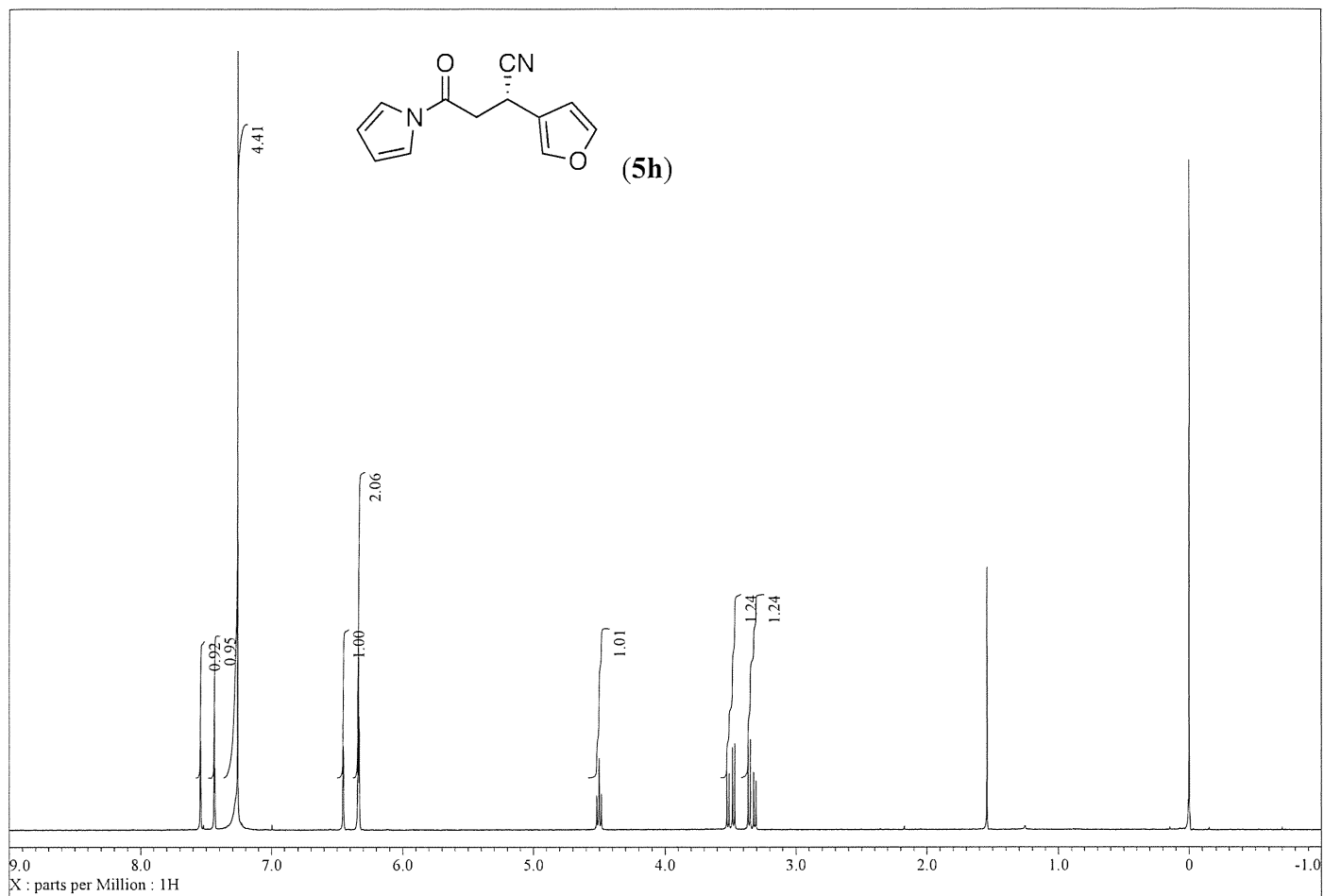


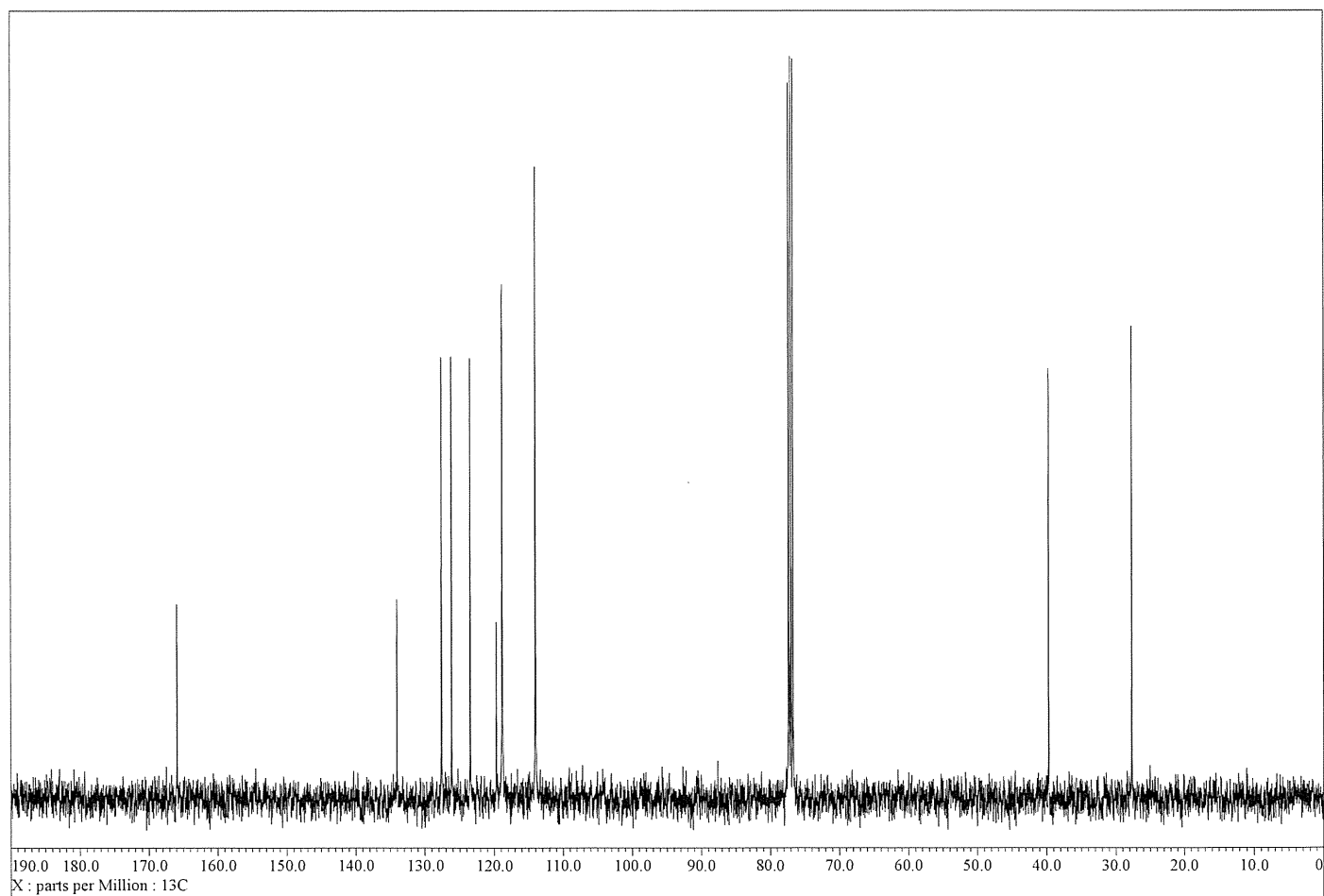
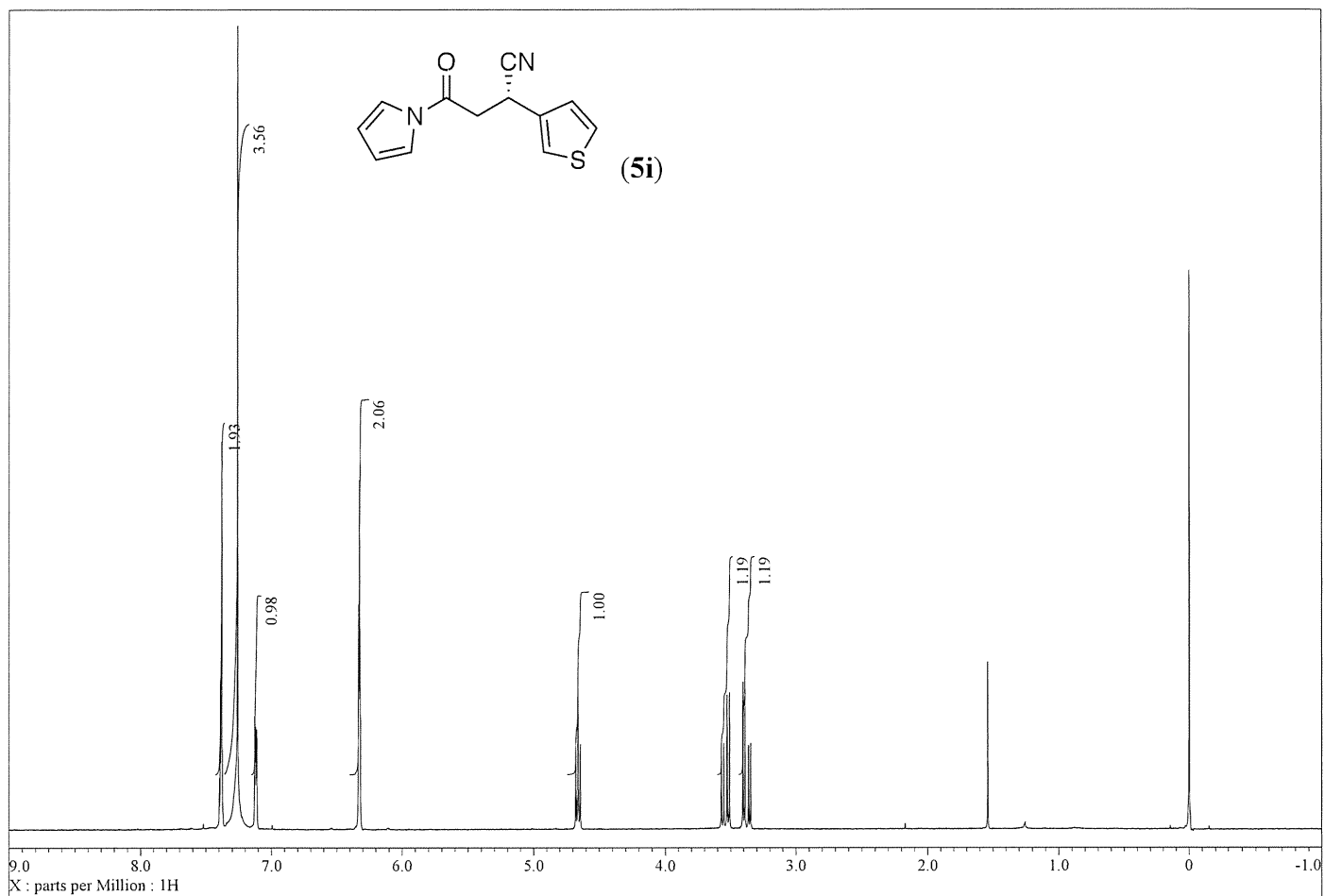
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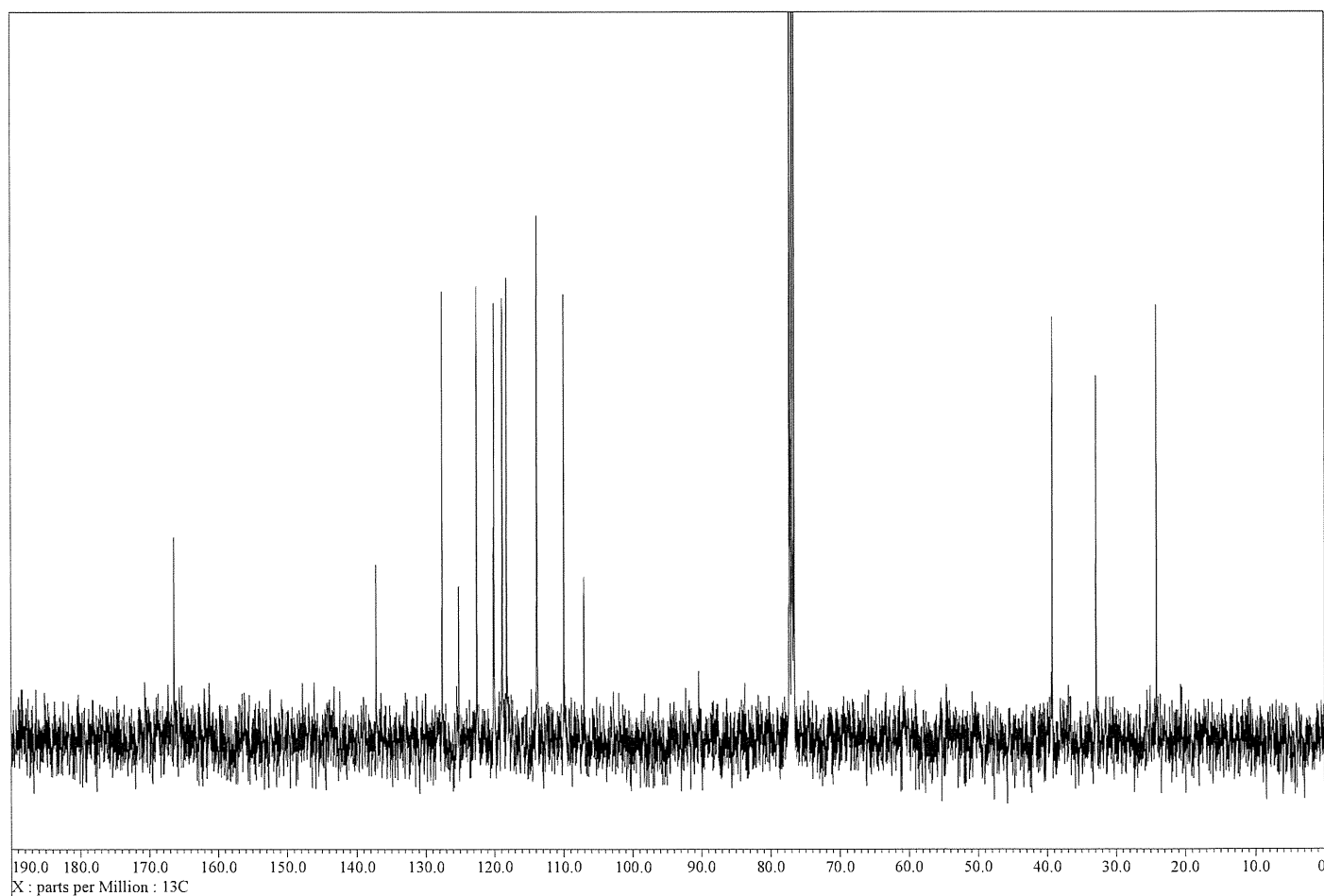
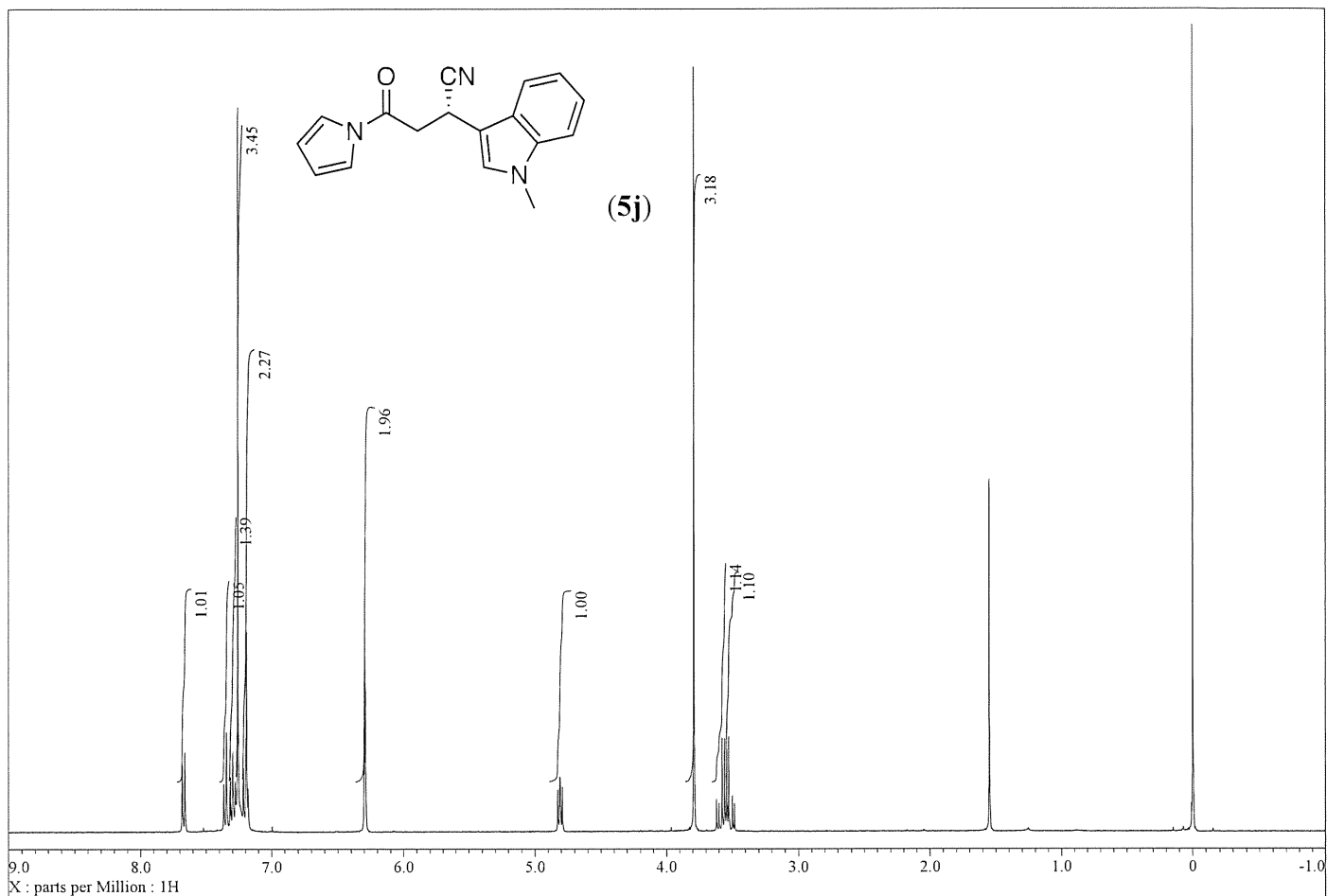
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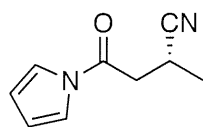




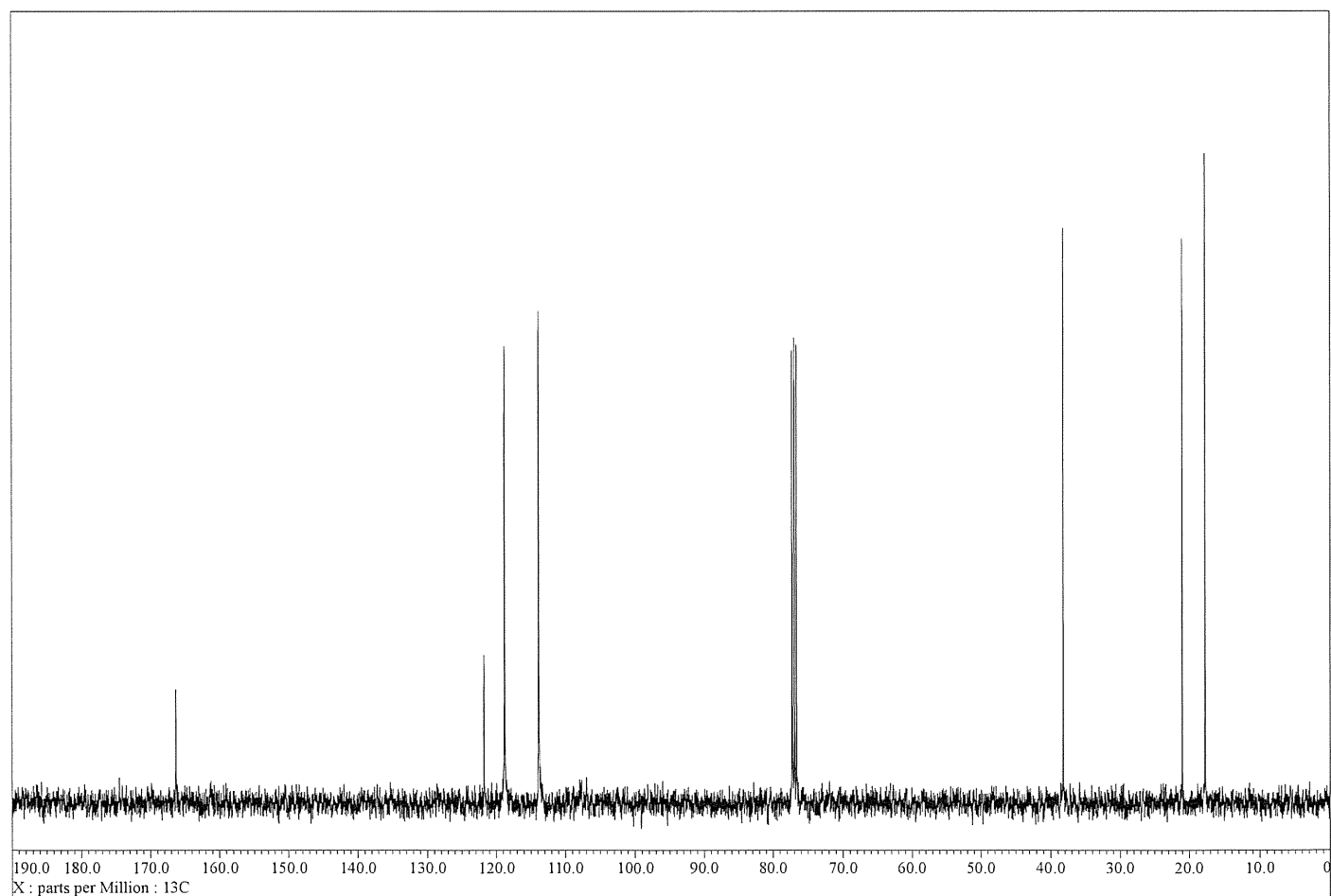
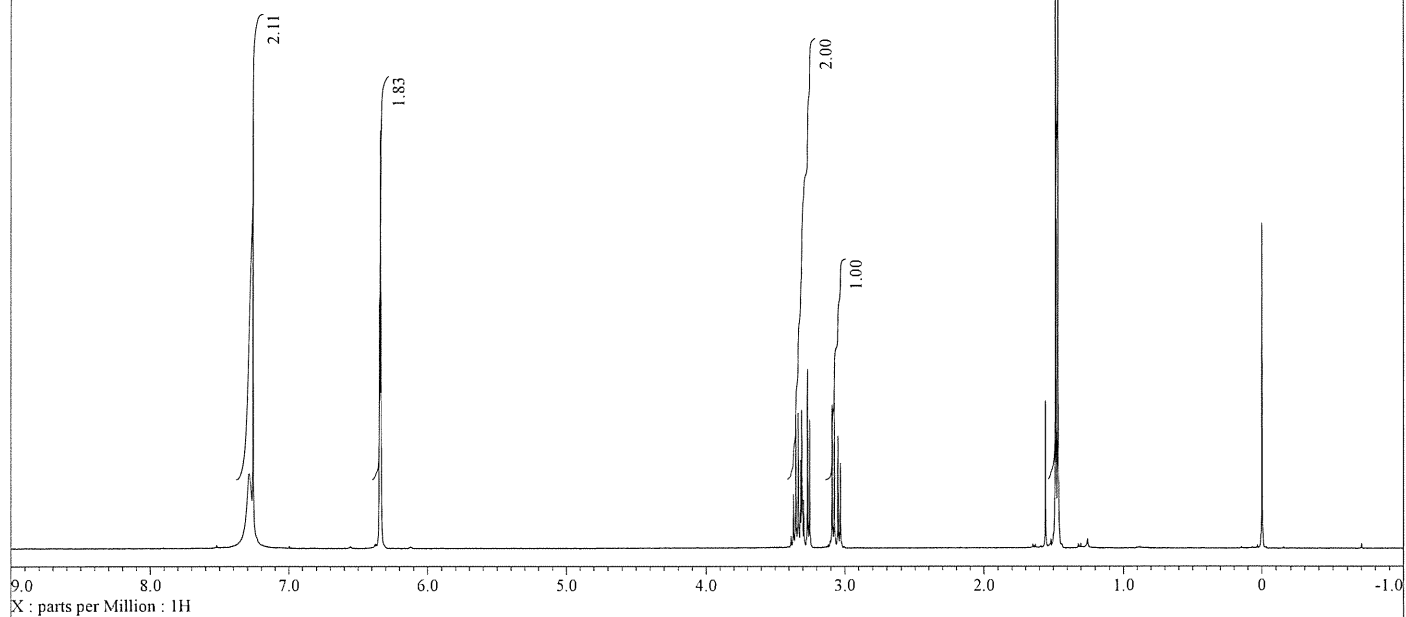
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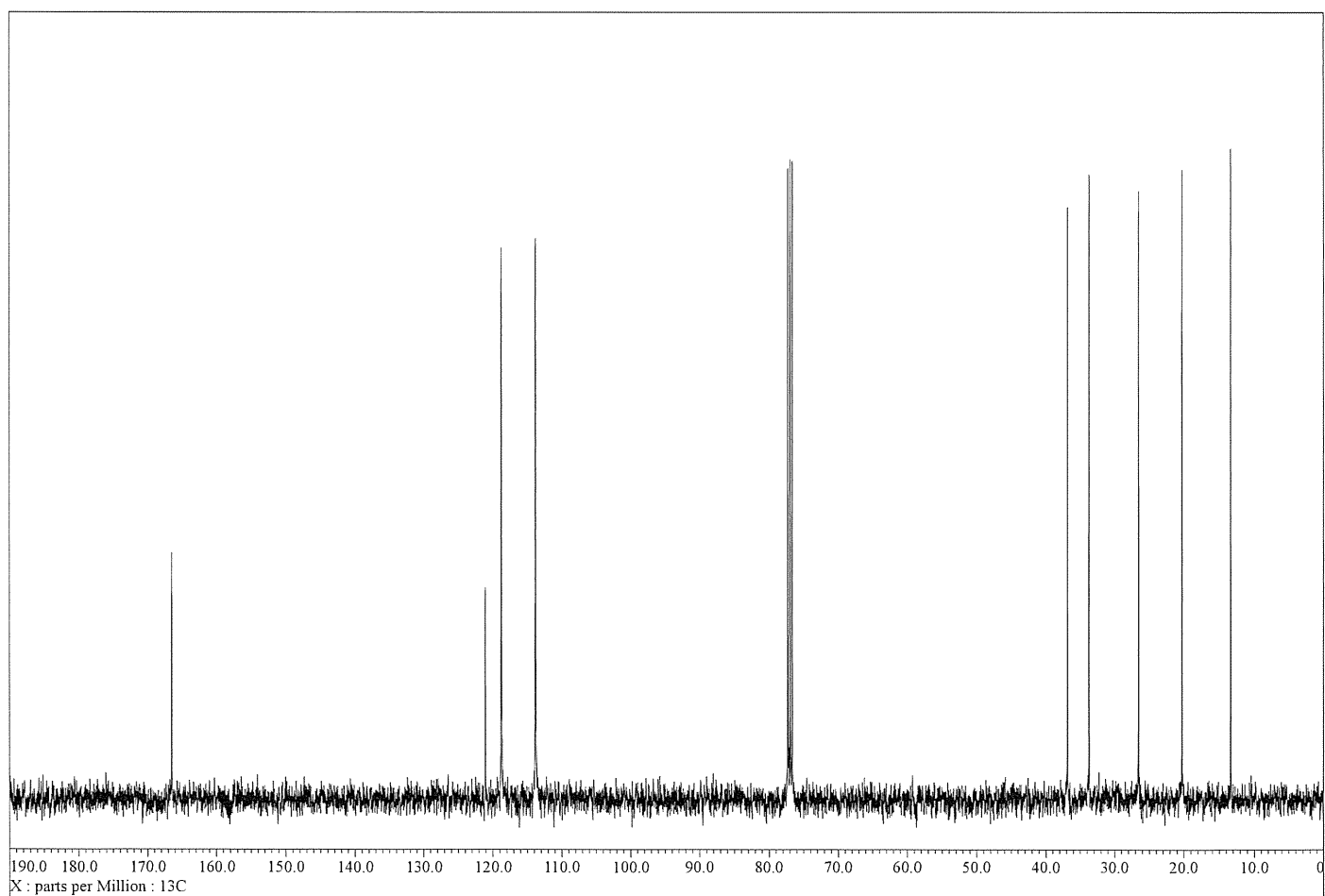
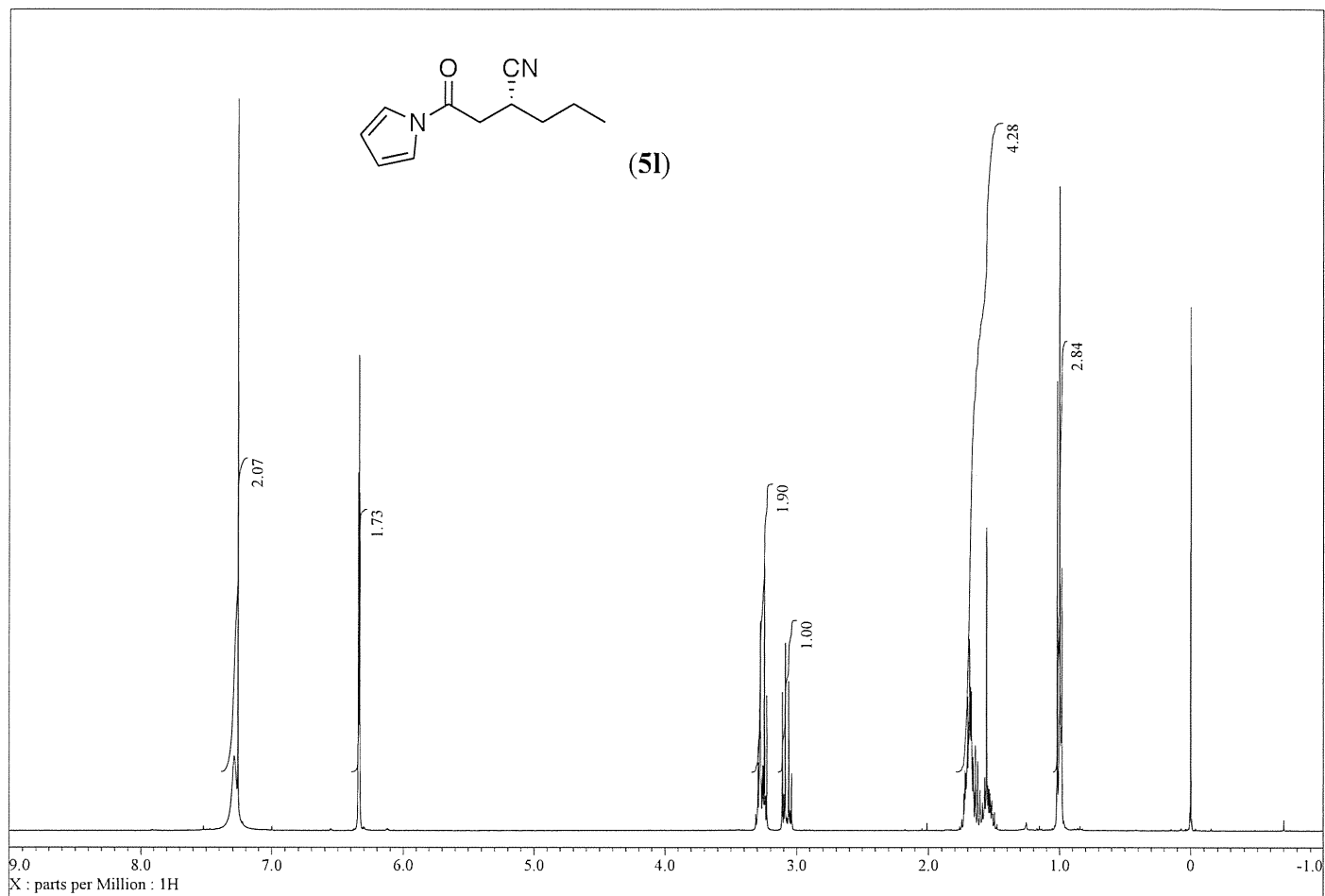
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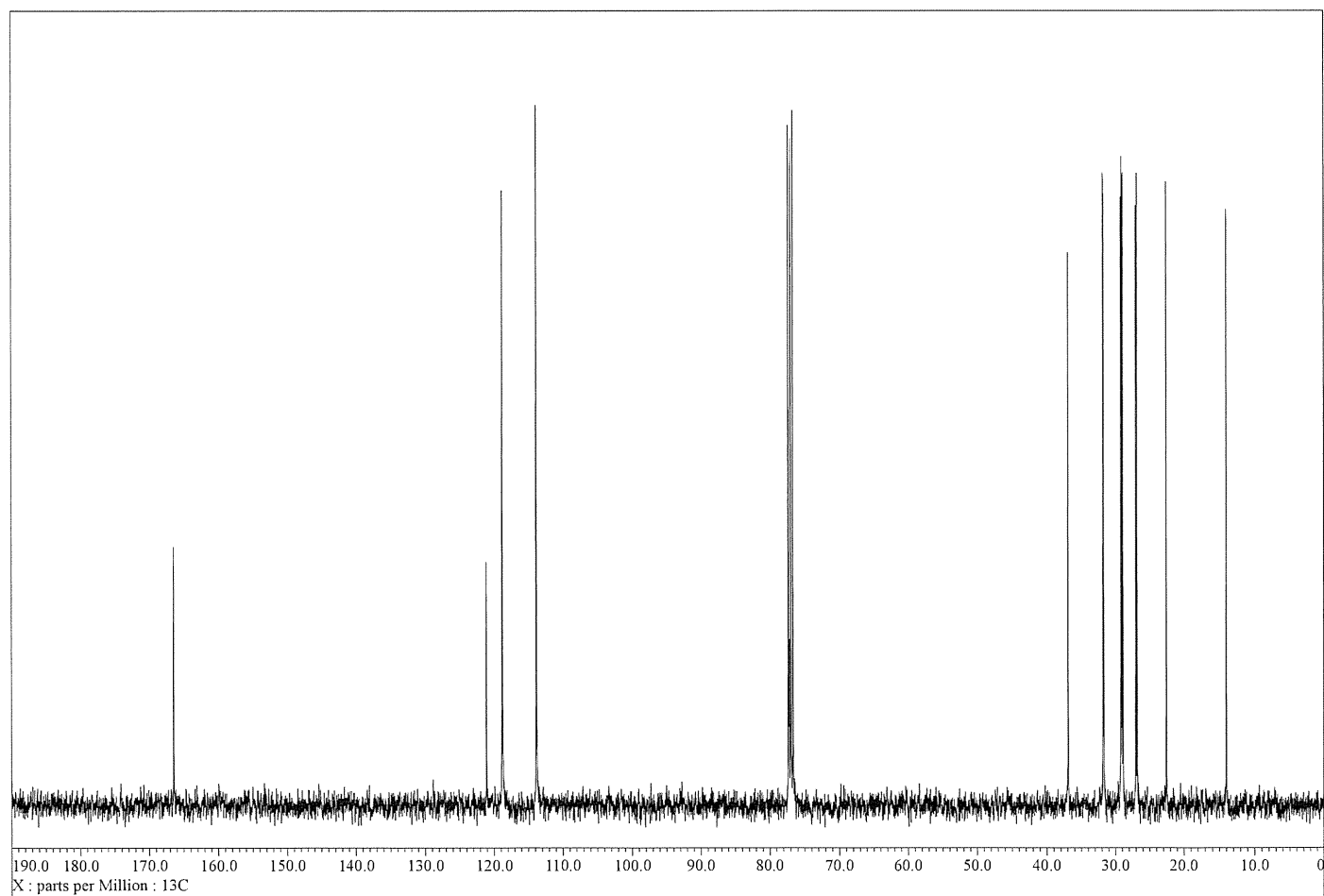
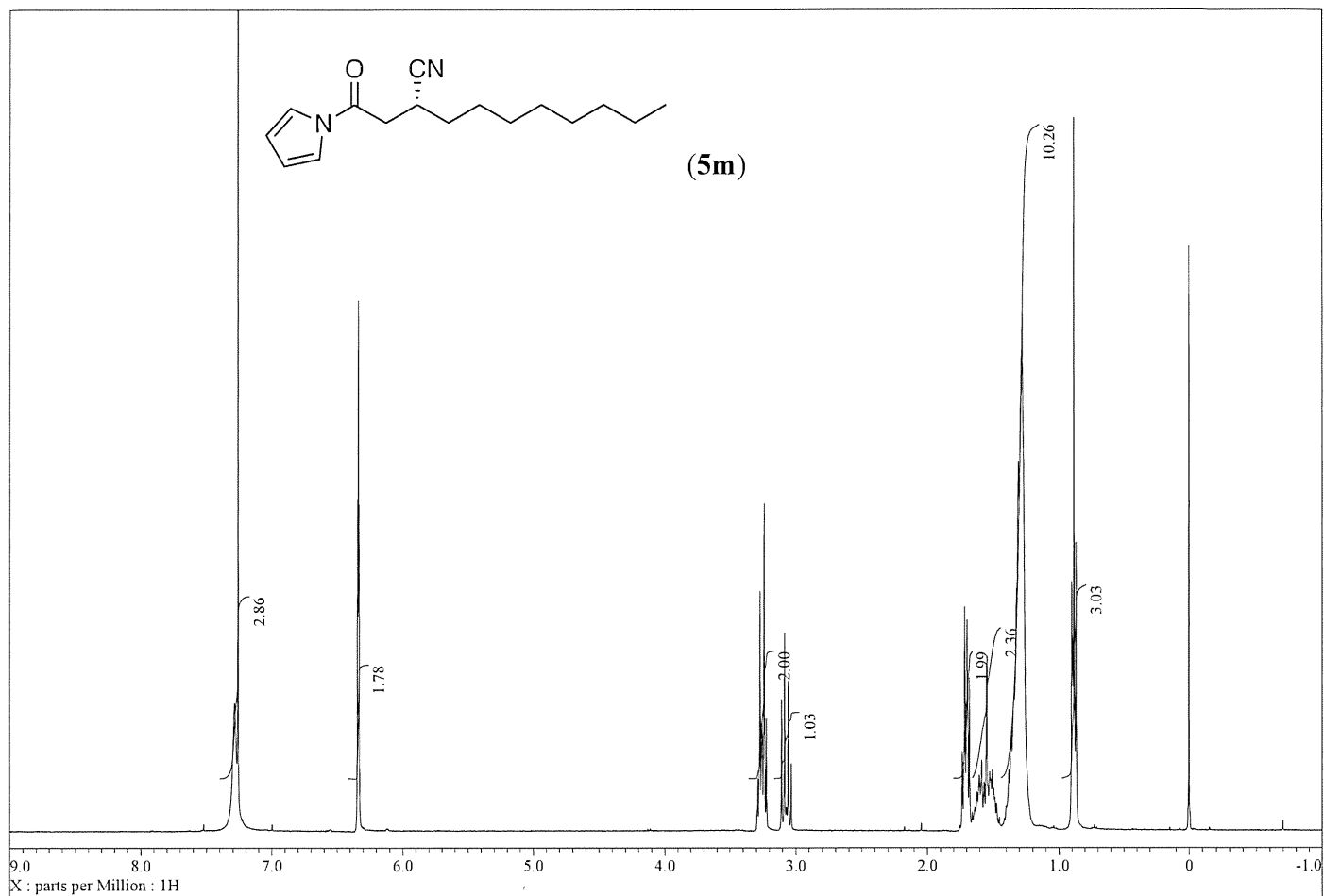


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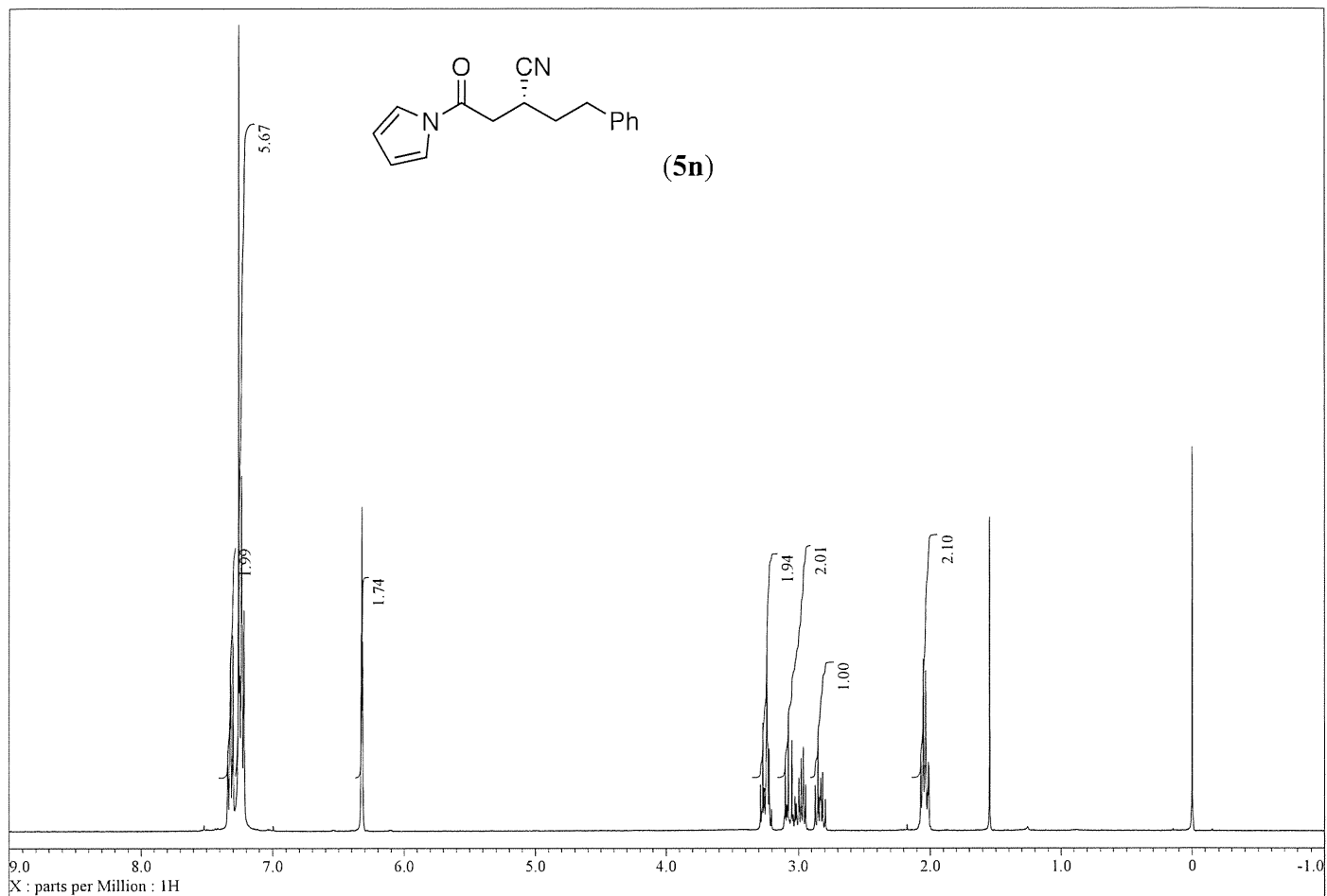


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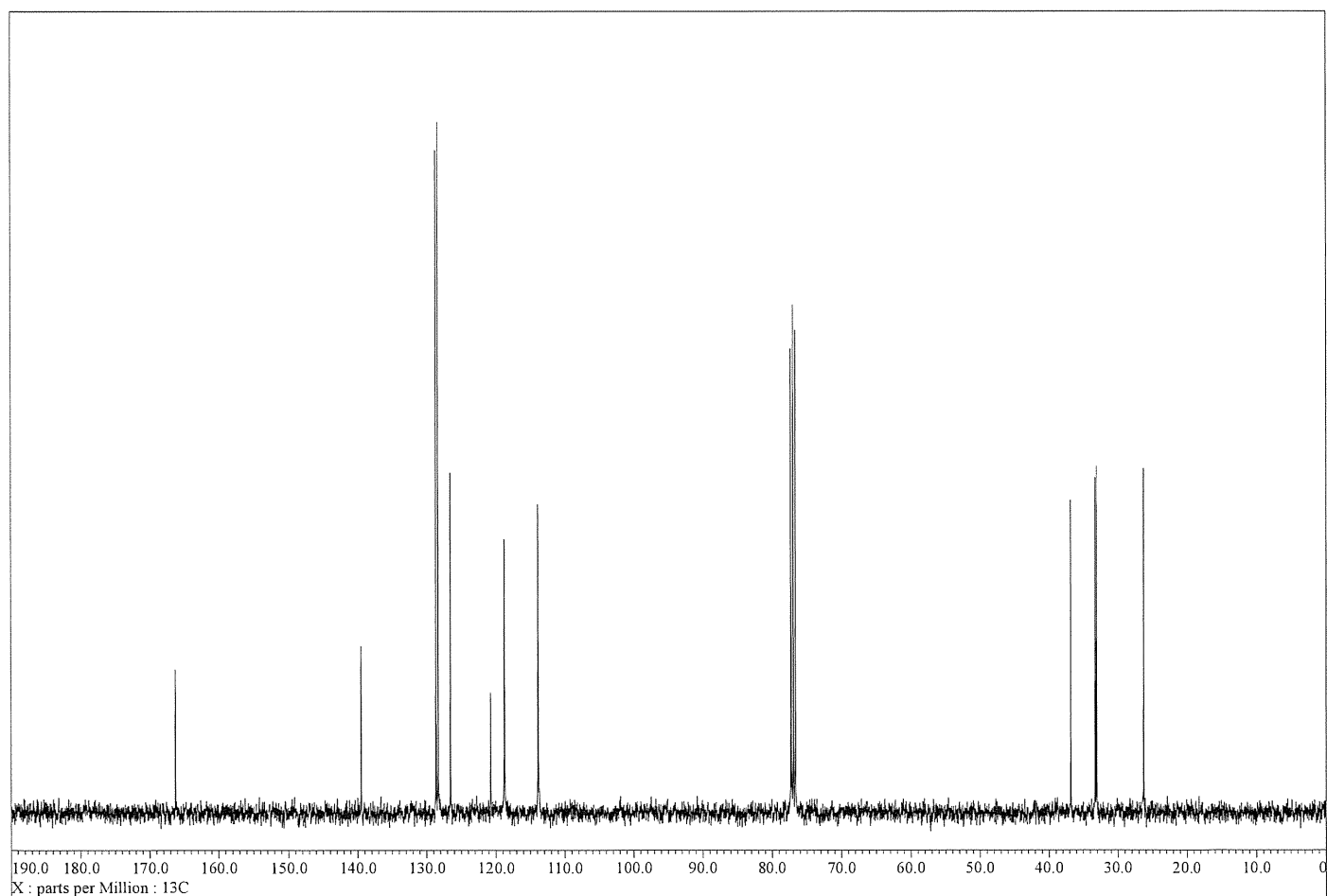




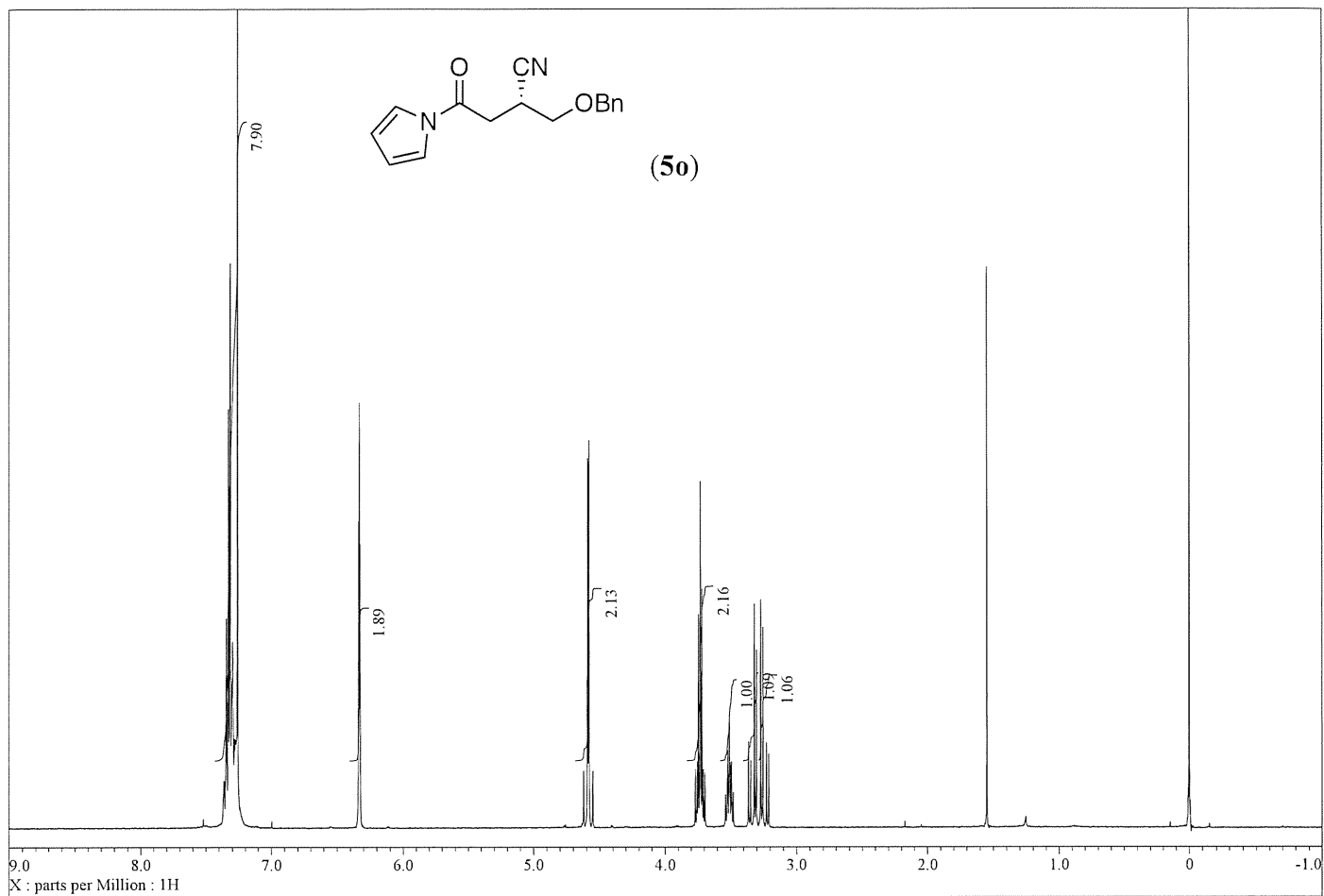
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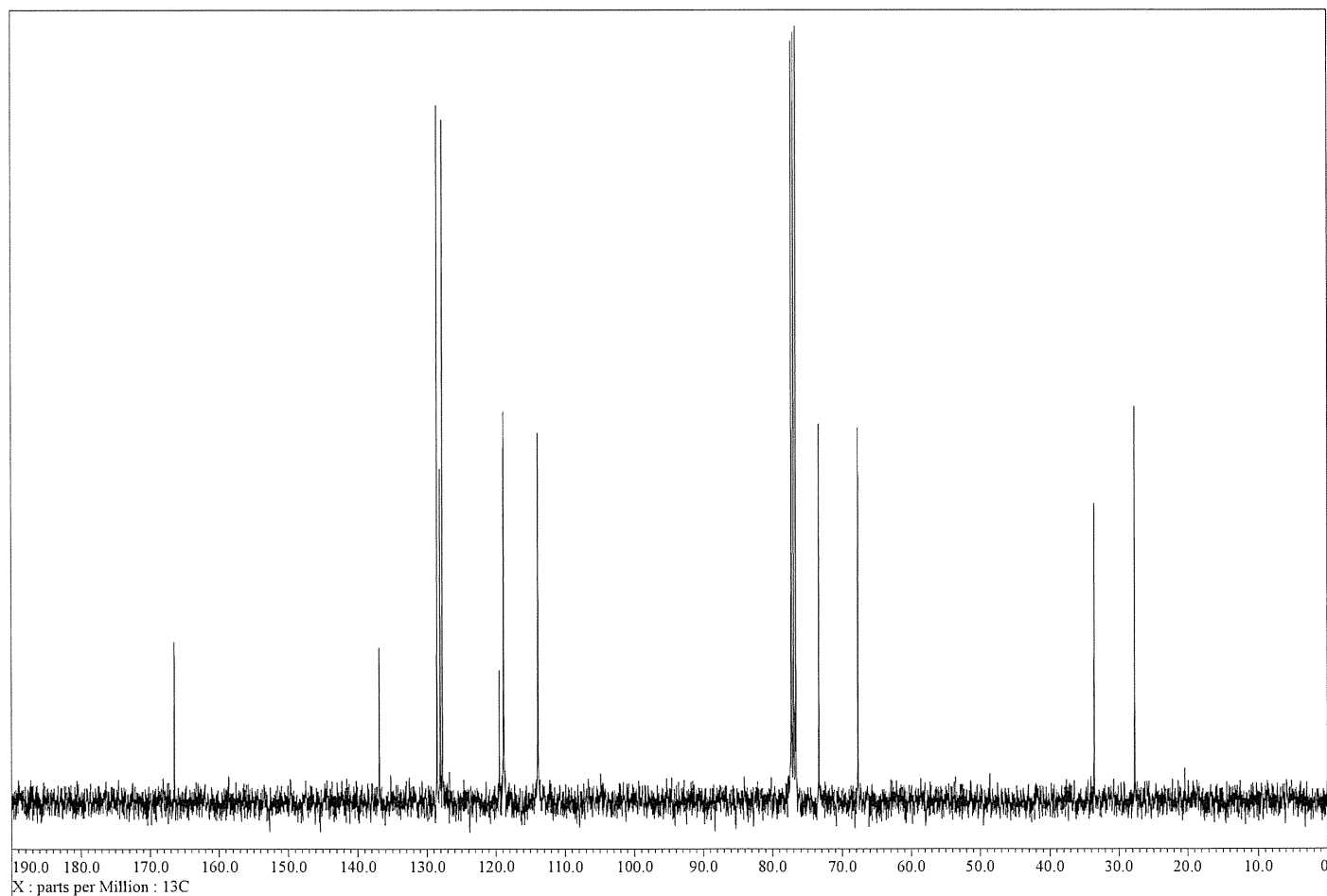
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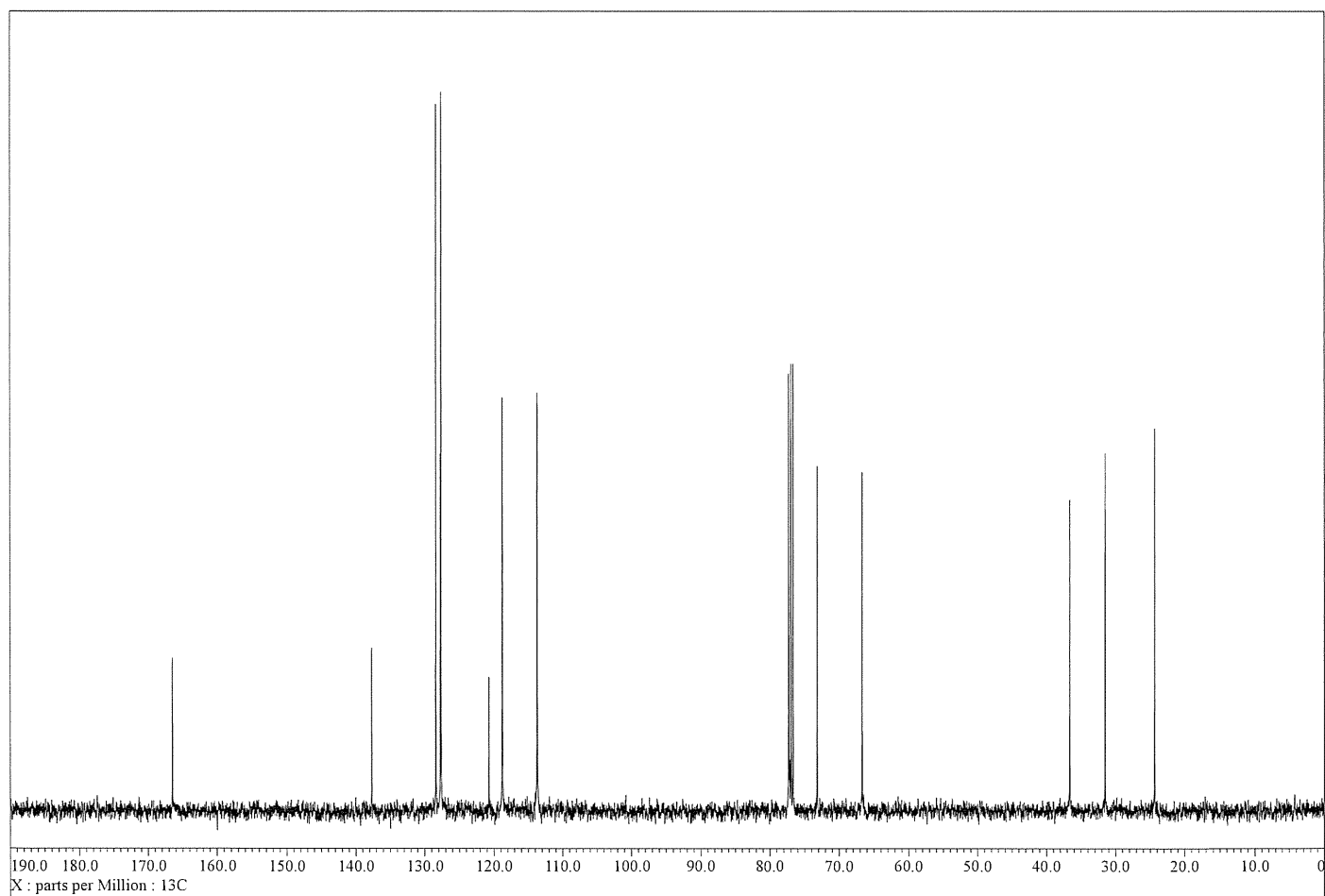
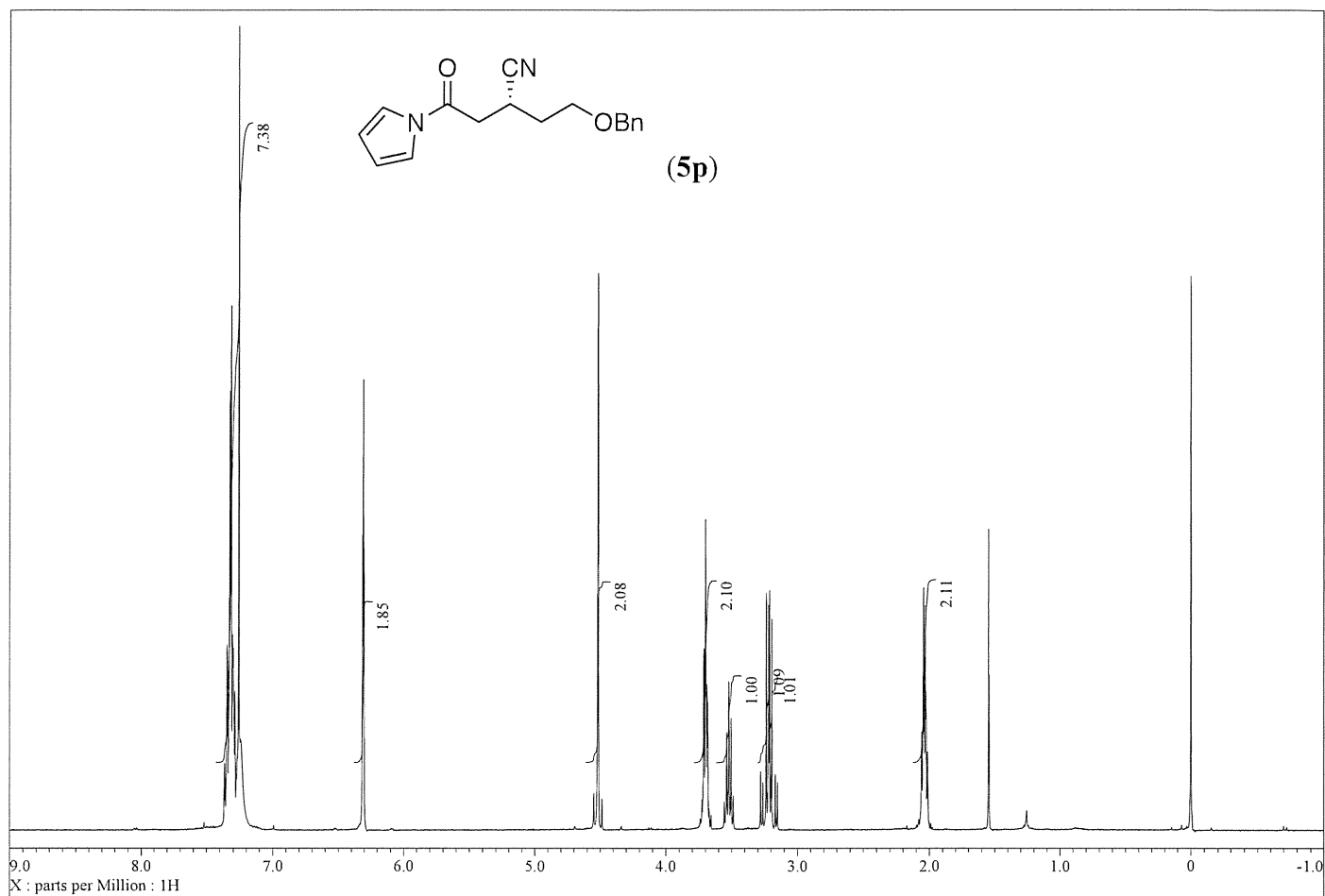
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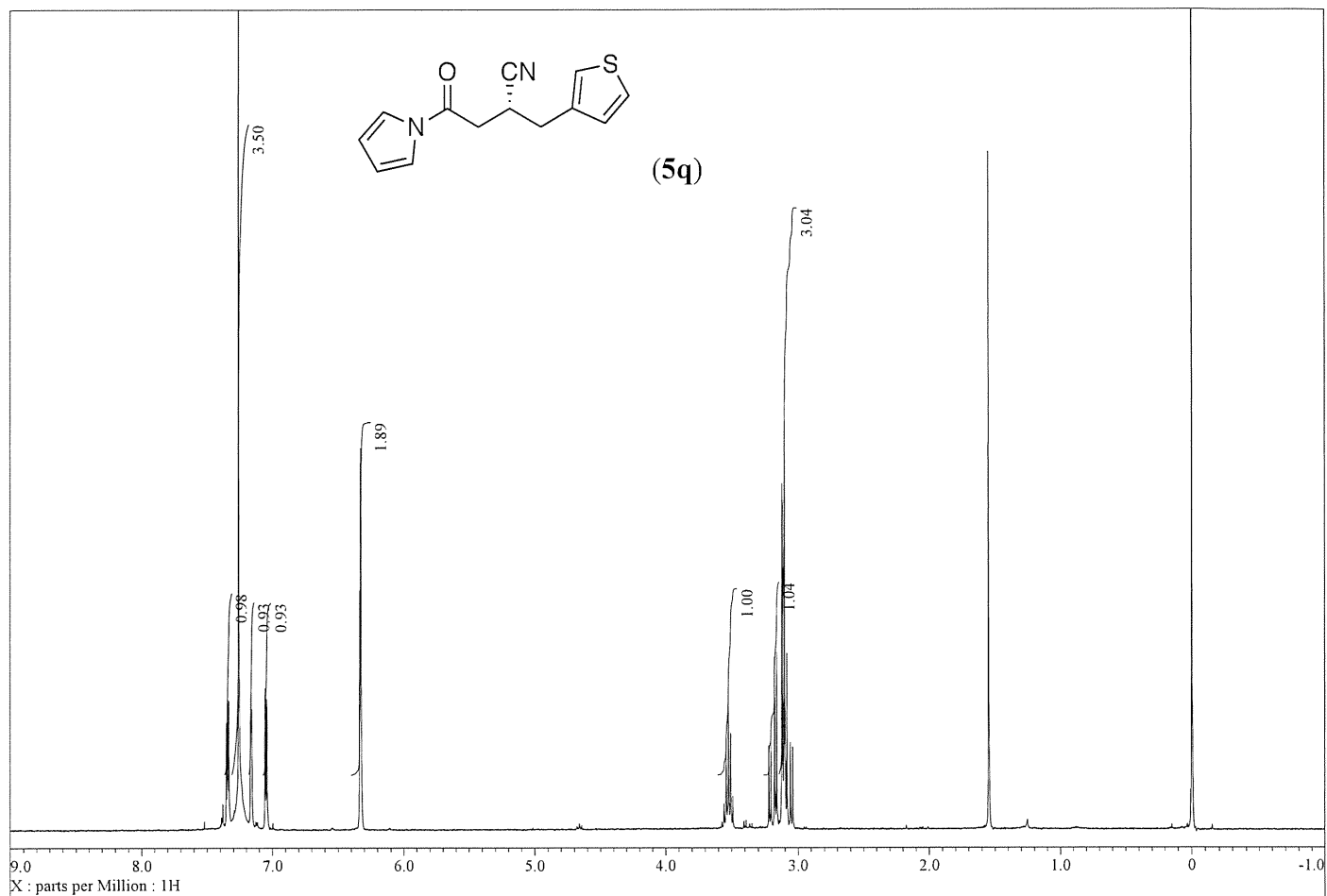


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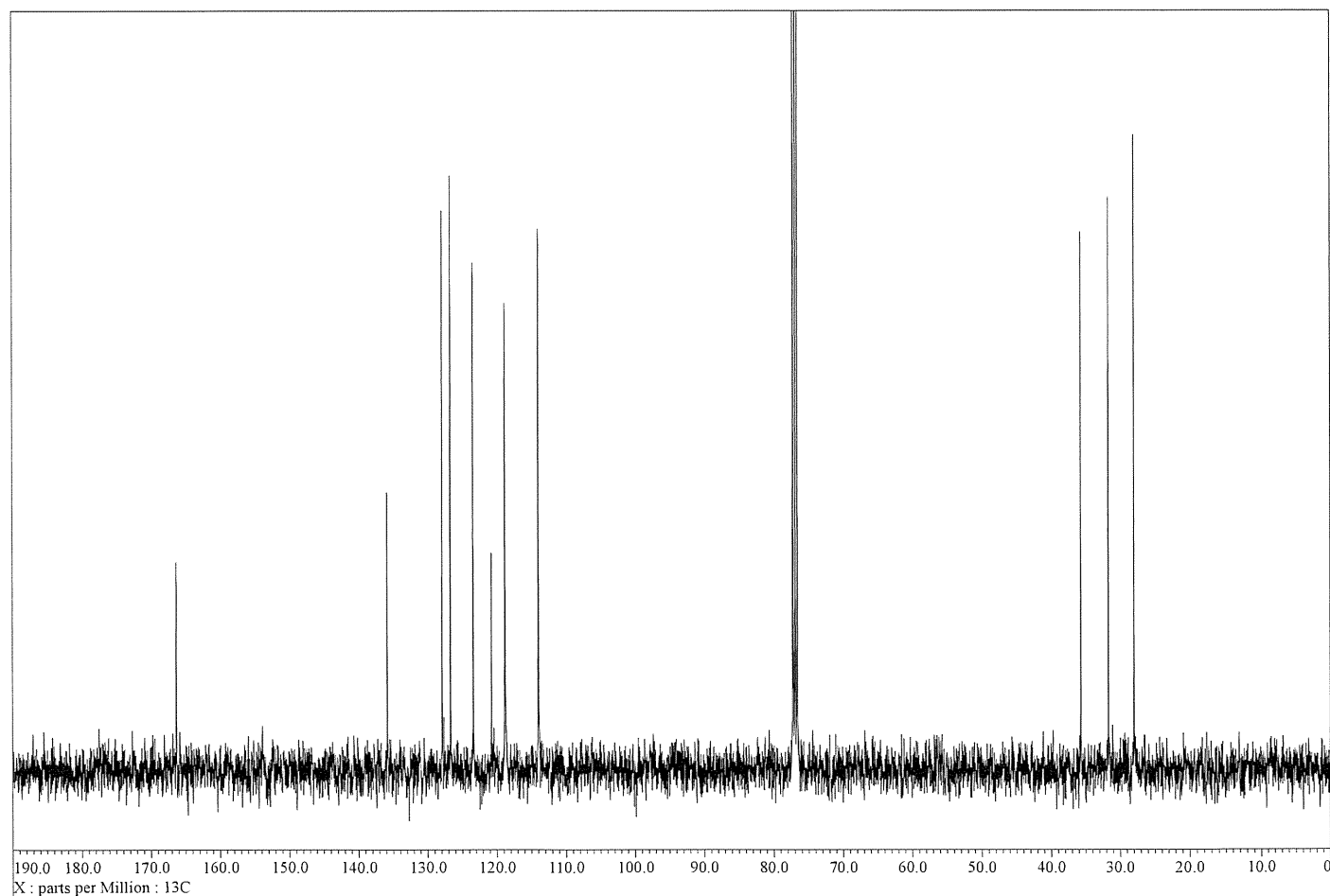


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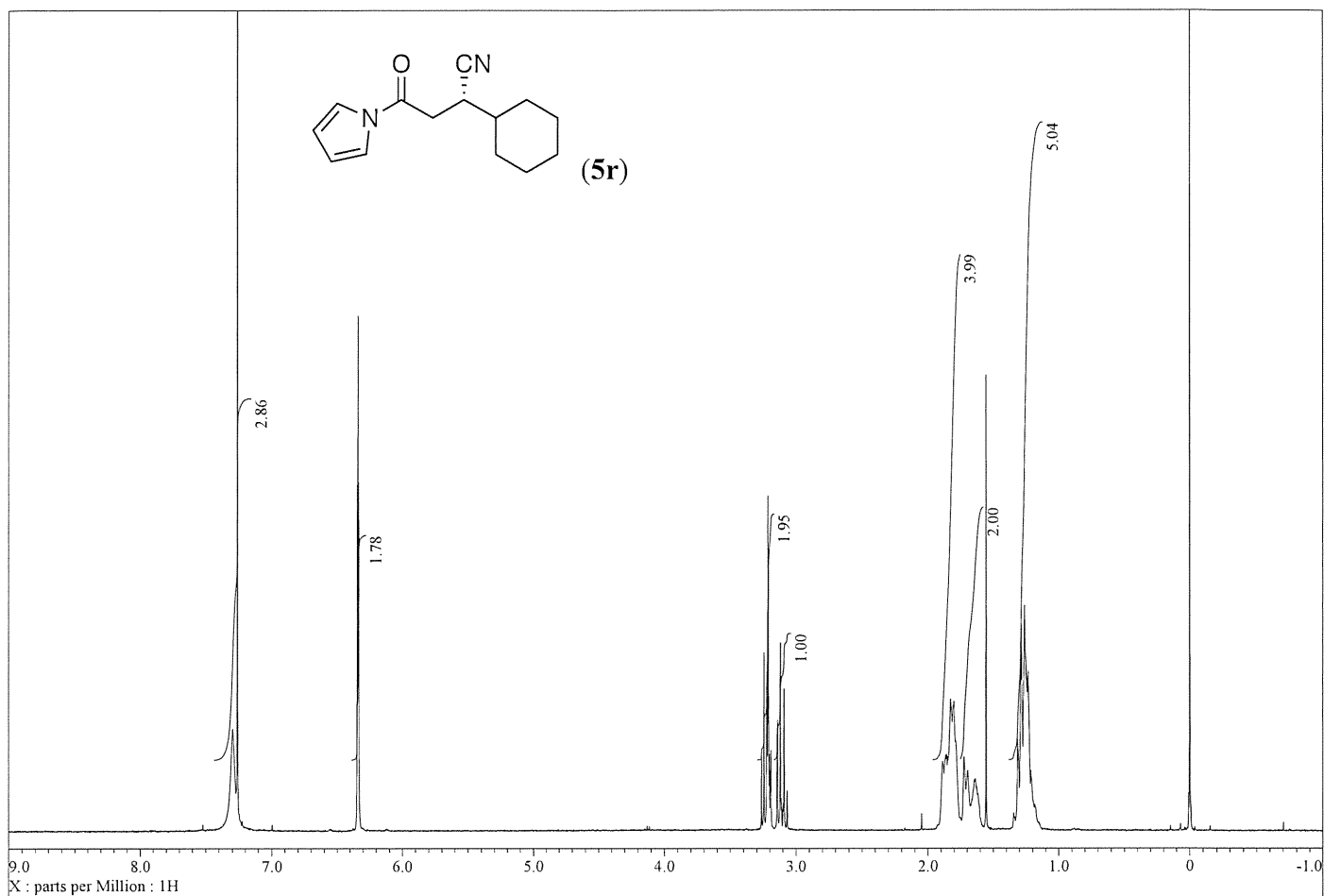




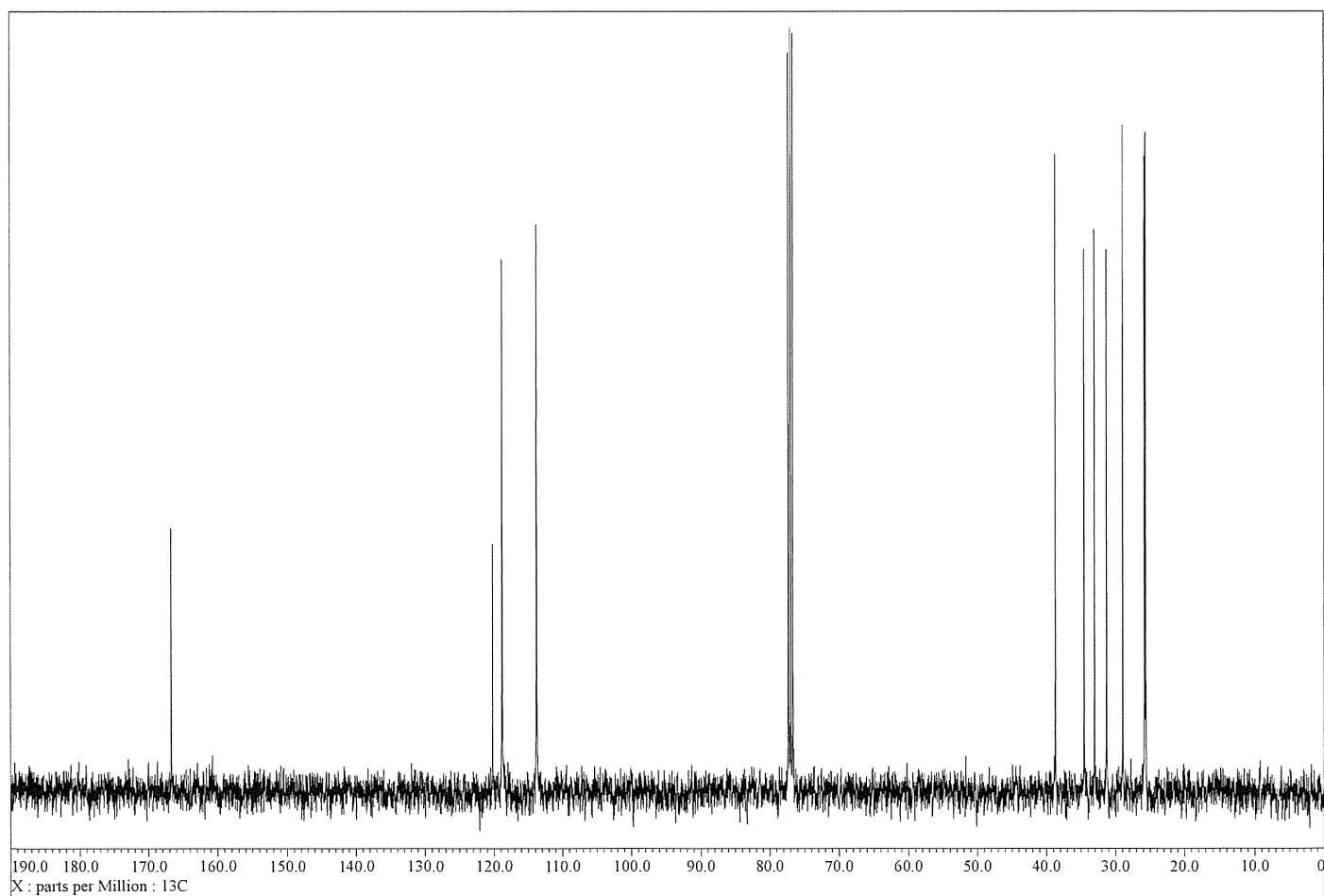
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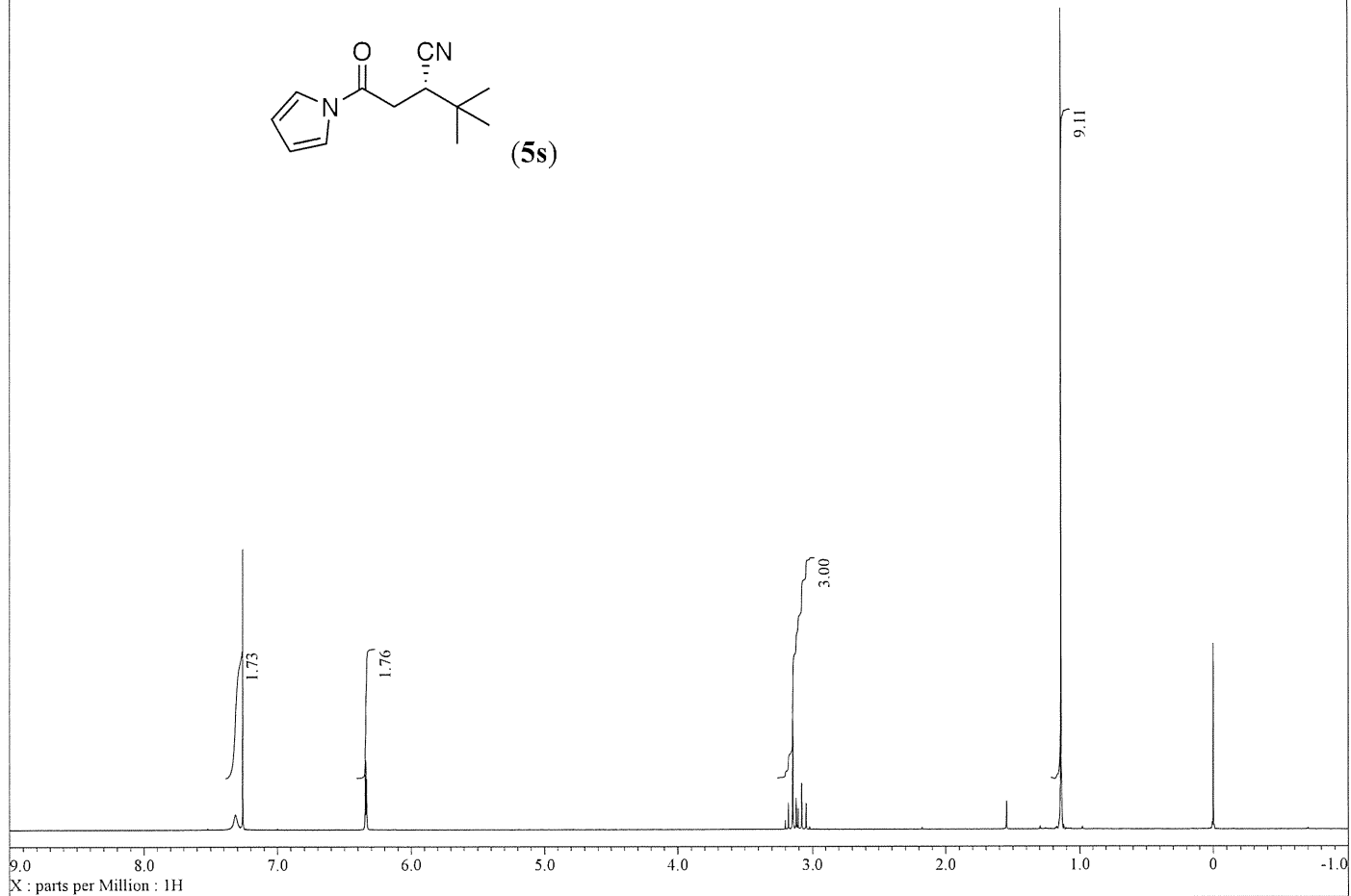
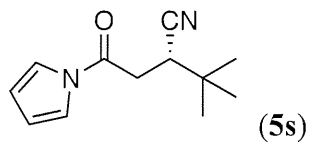
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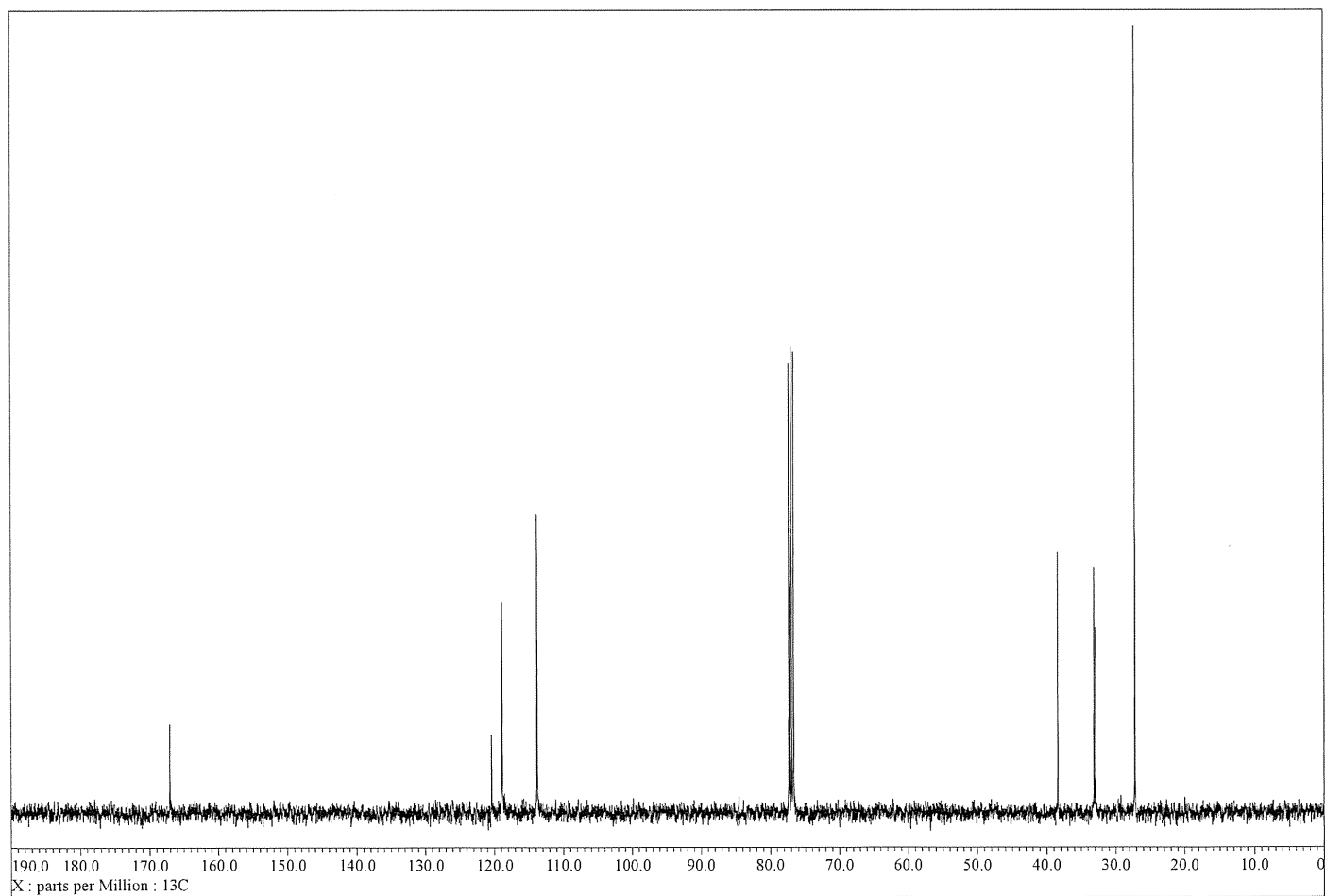
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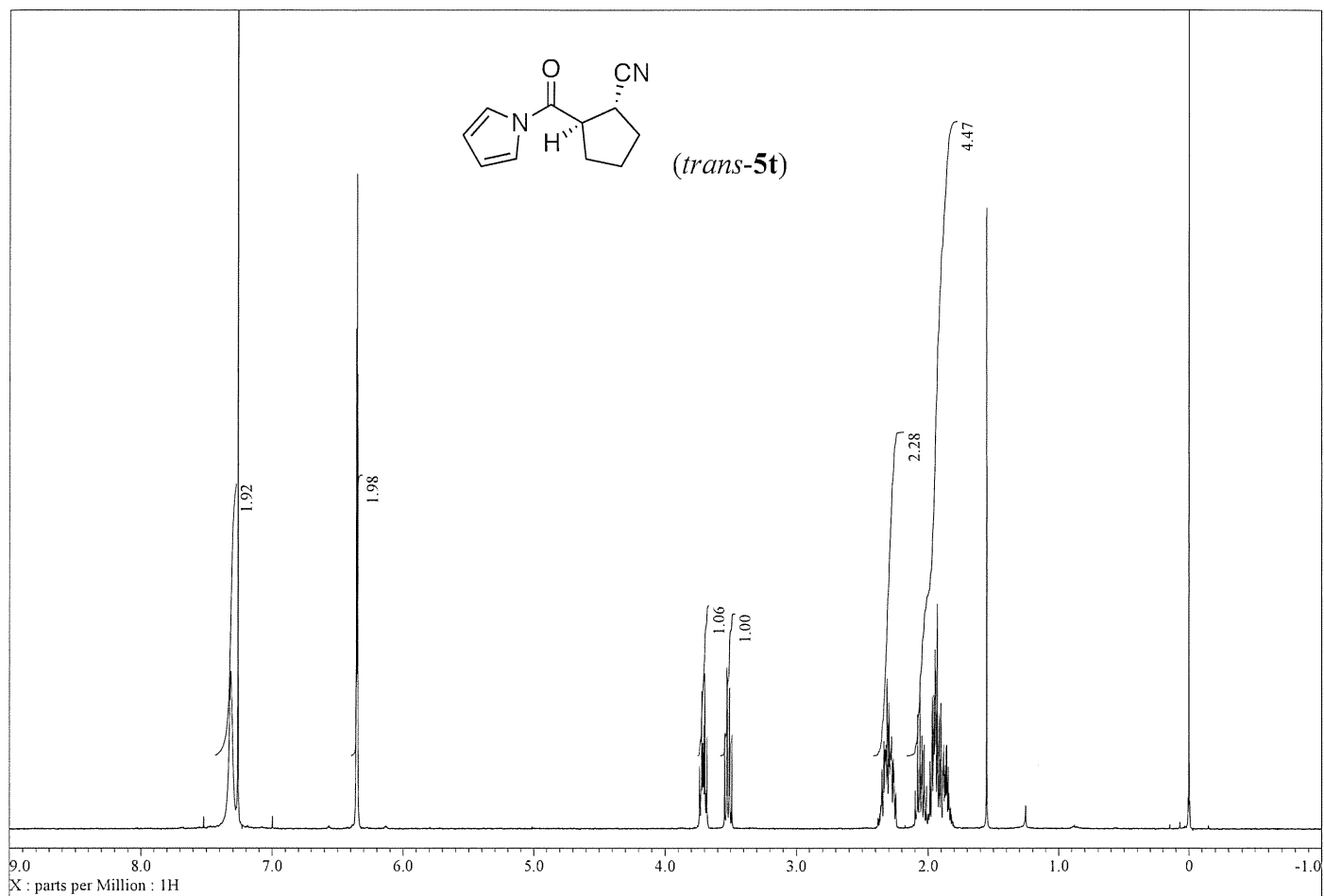
¹³C NMR, 100 MHz, CDCl₃



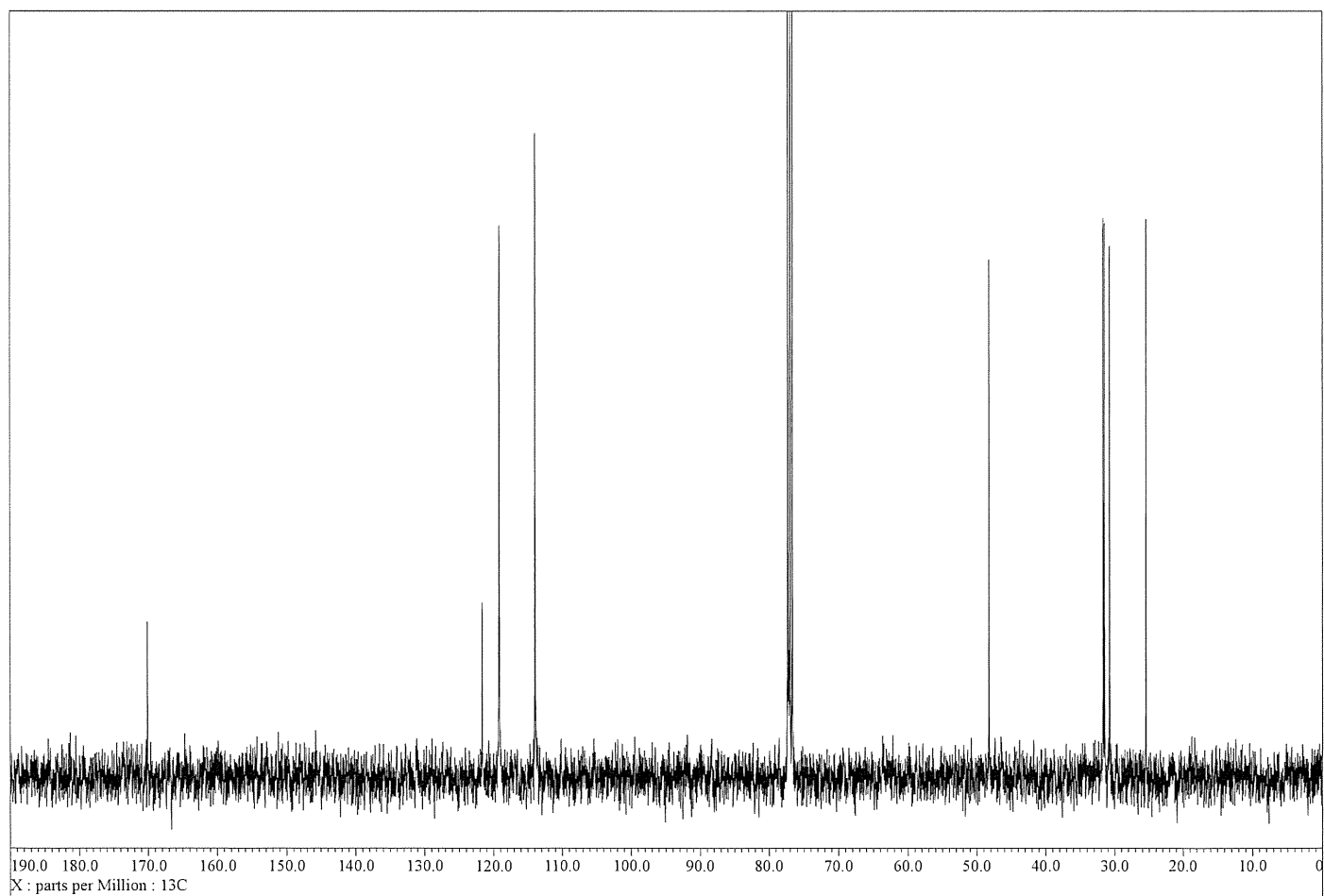
^1H NMR, 400 MHz, CDCl_3



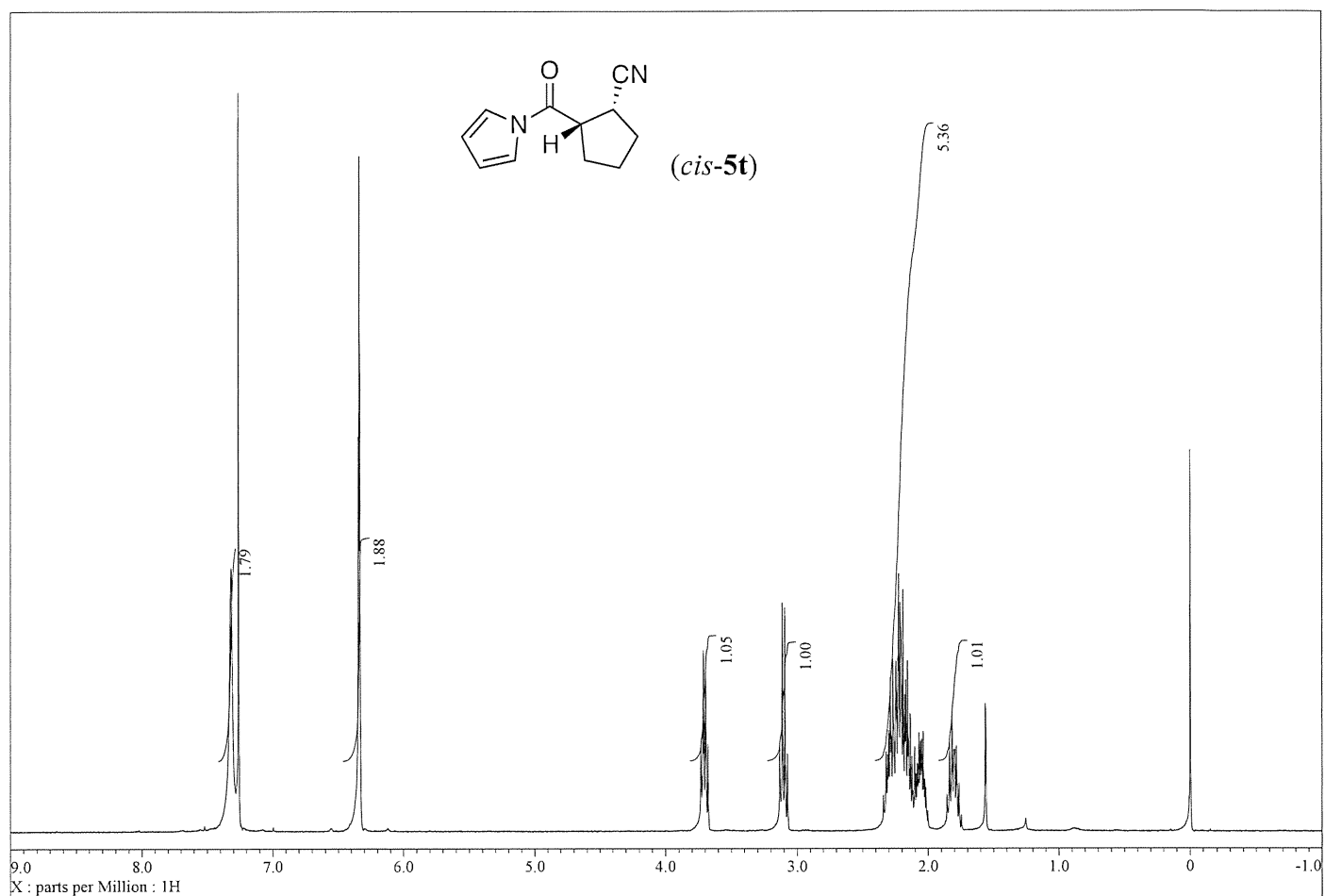
^{13}C NMR, 100 MHz, CDCl_3



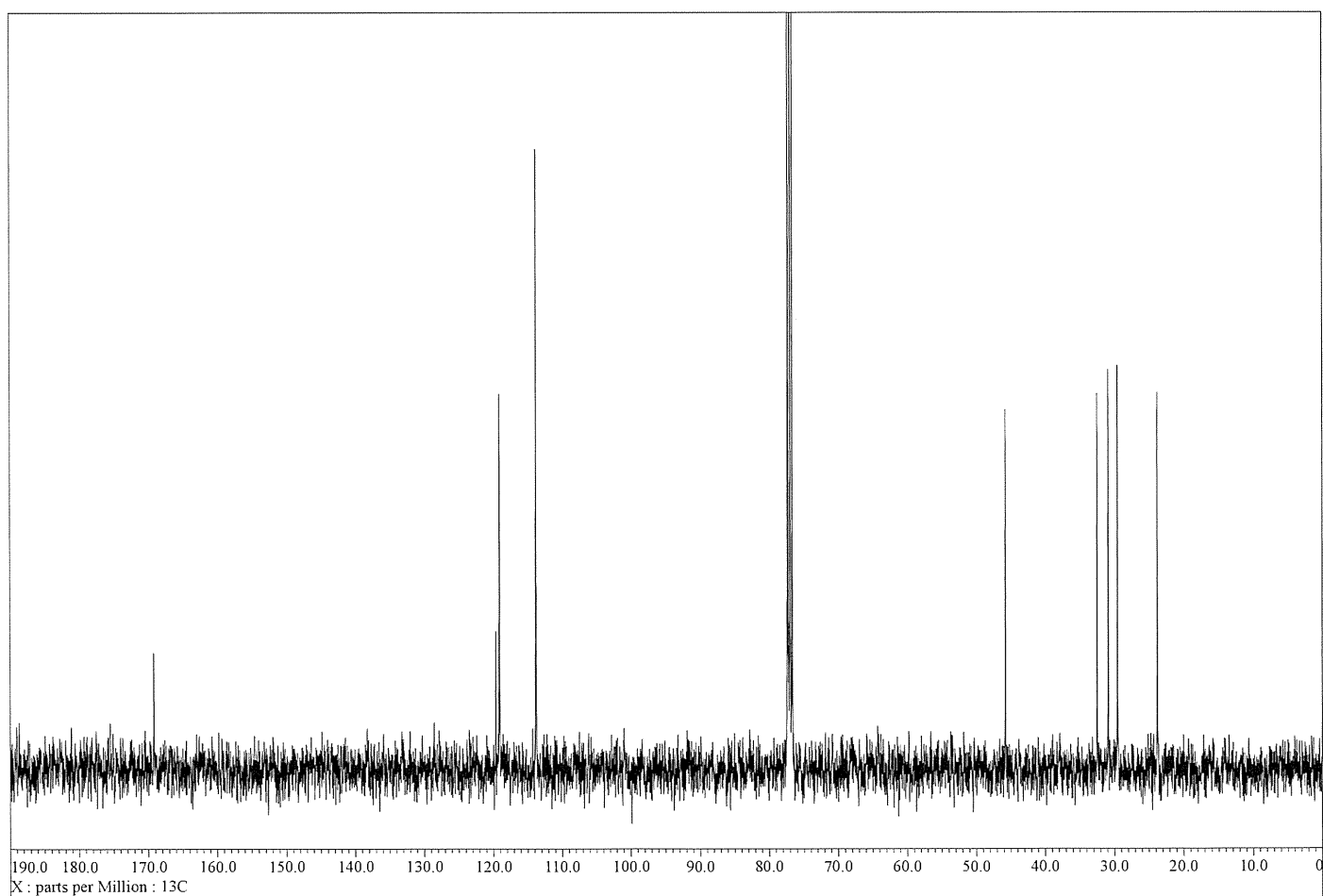
¹H NMR, 400 MHz, CDCl₃



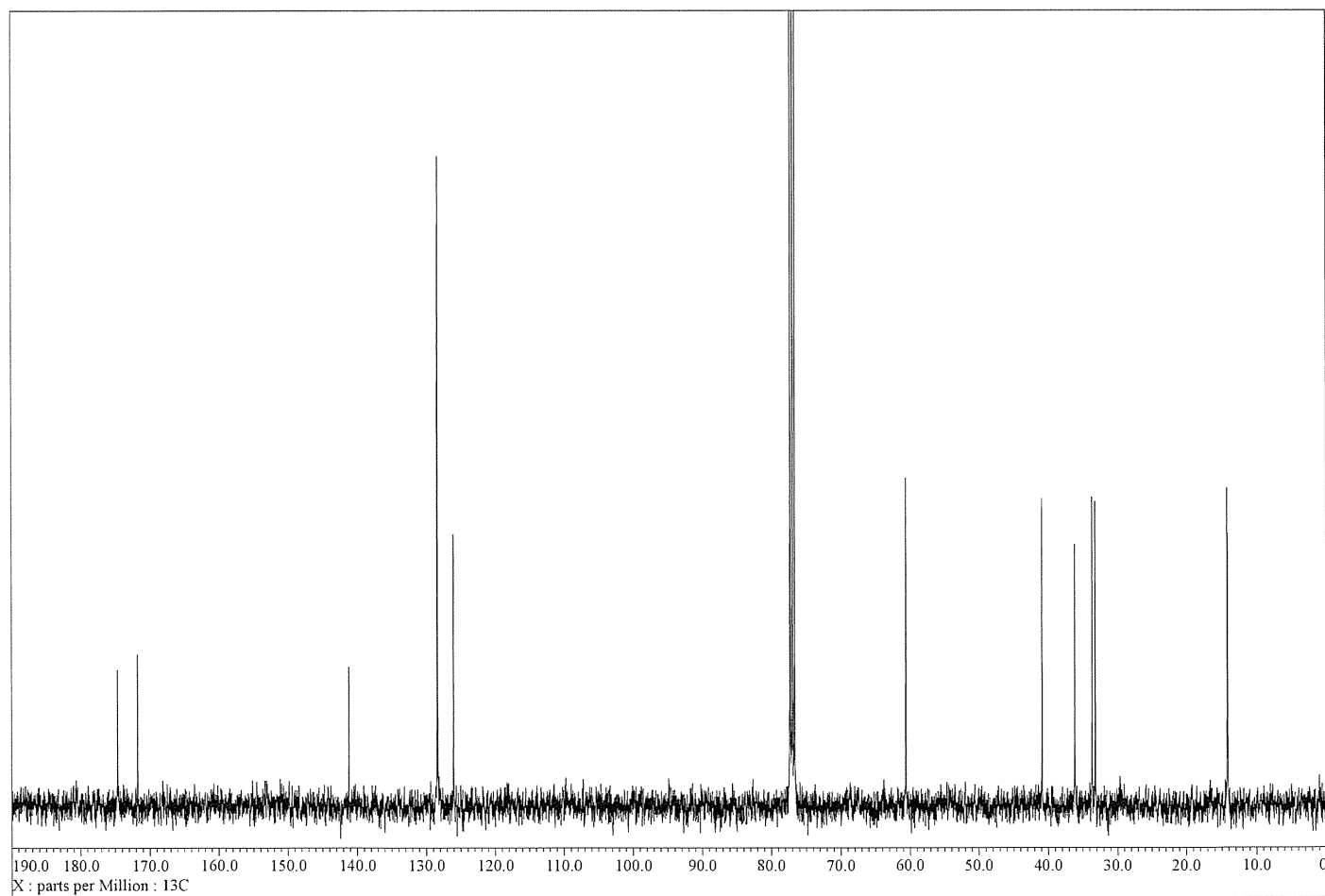
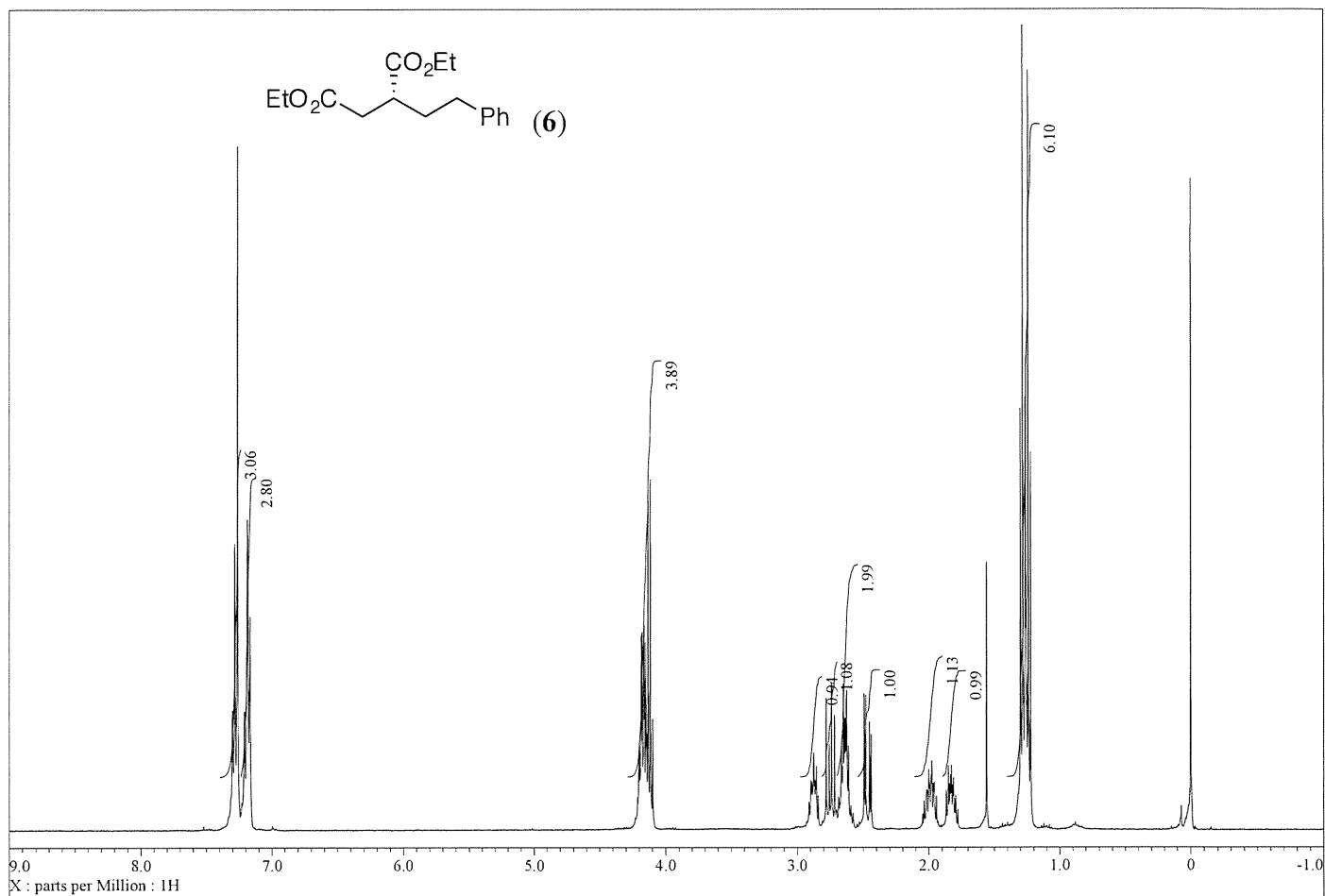
¹³C NMR, 100 MHz, CDCl₃

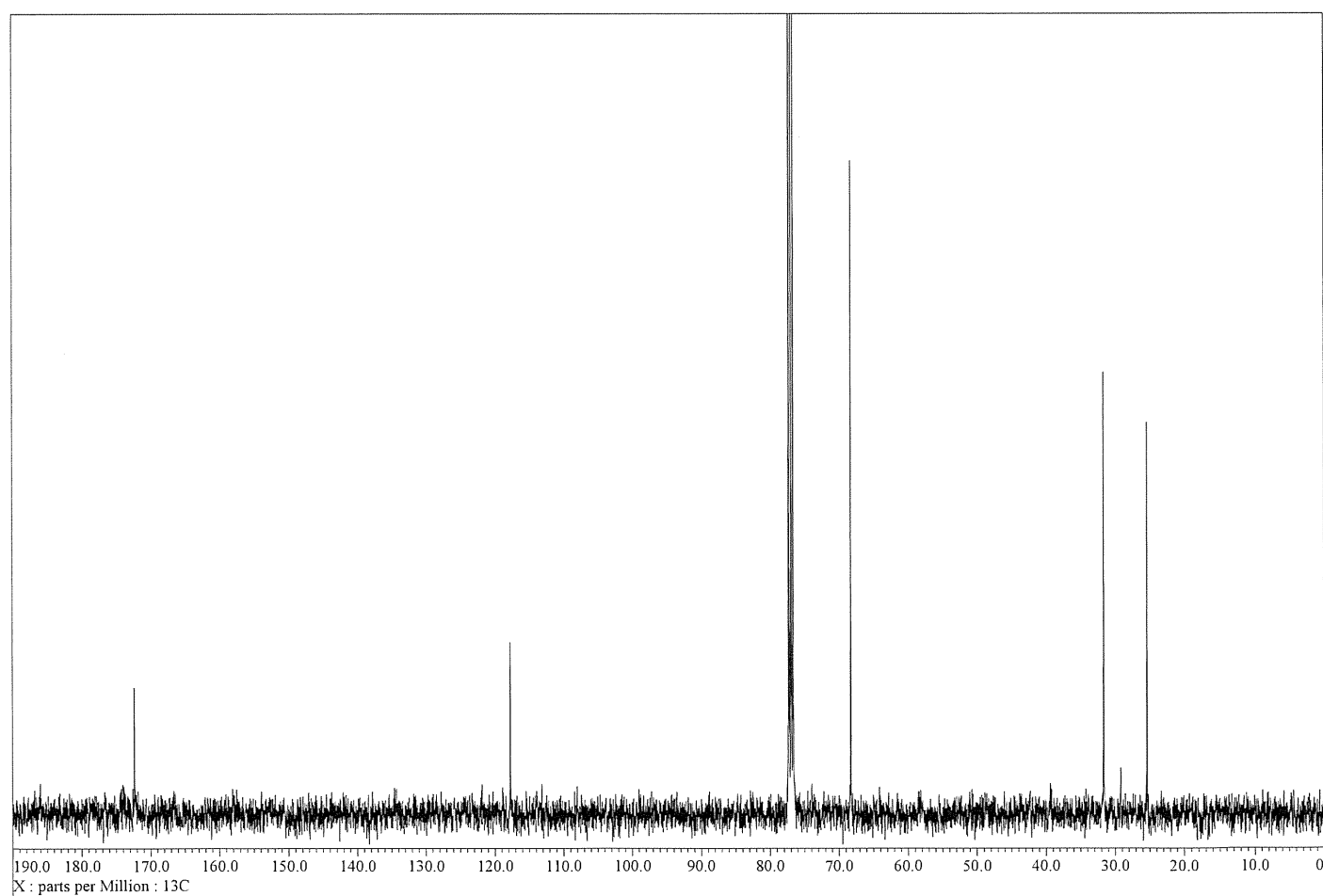
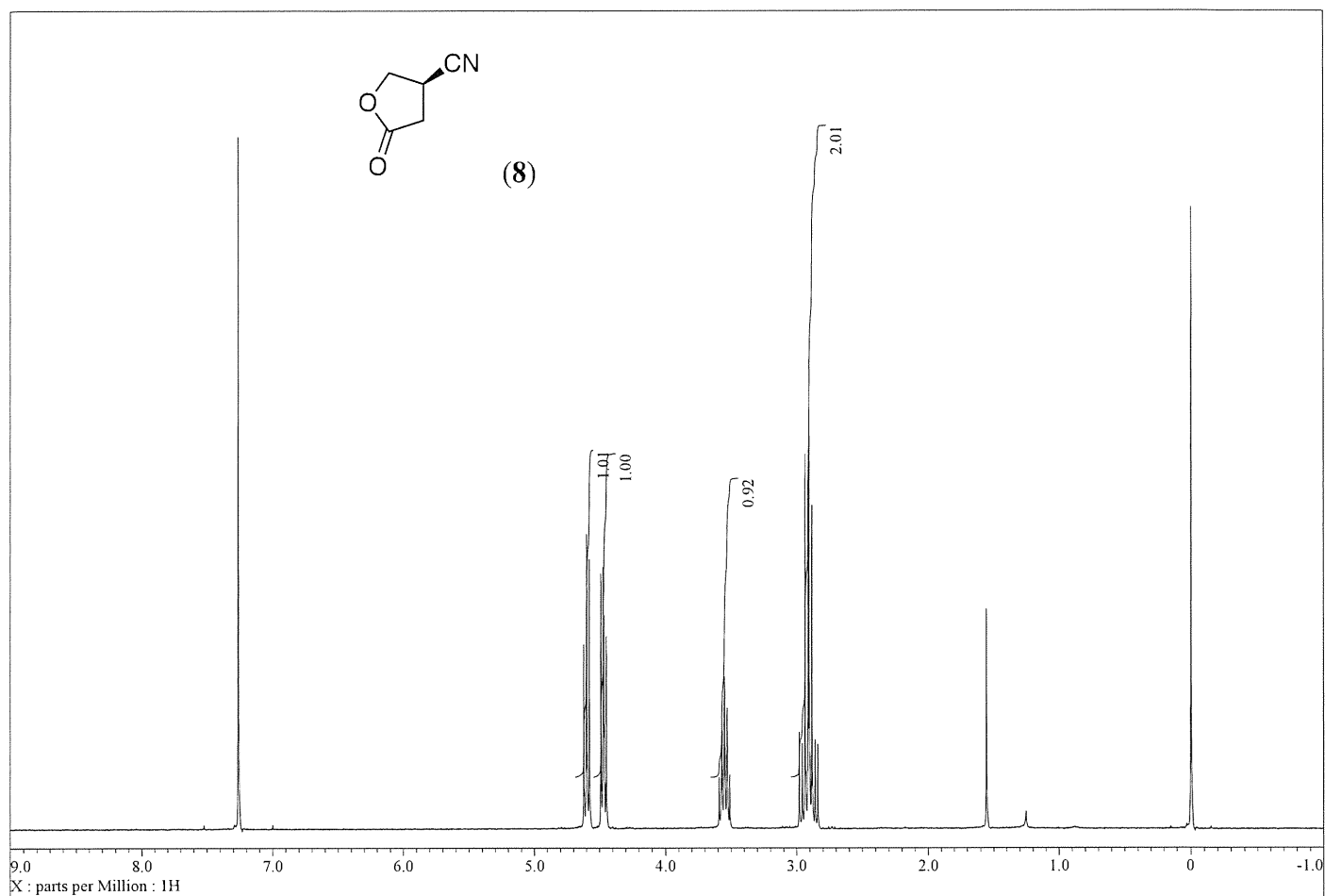


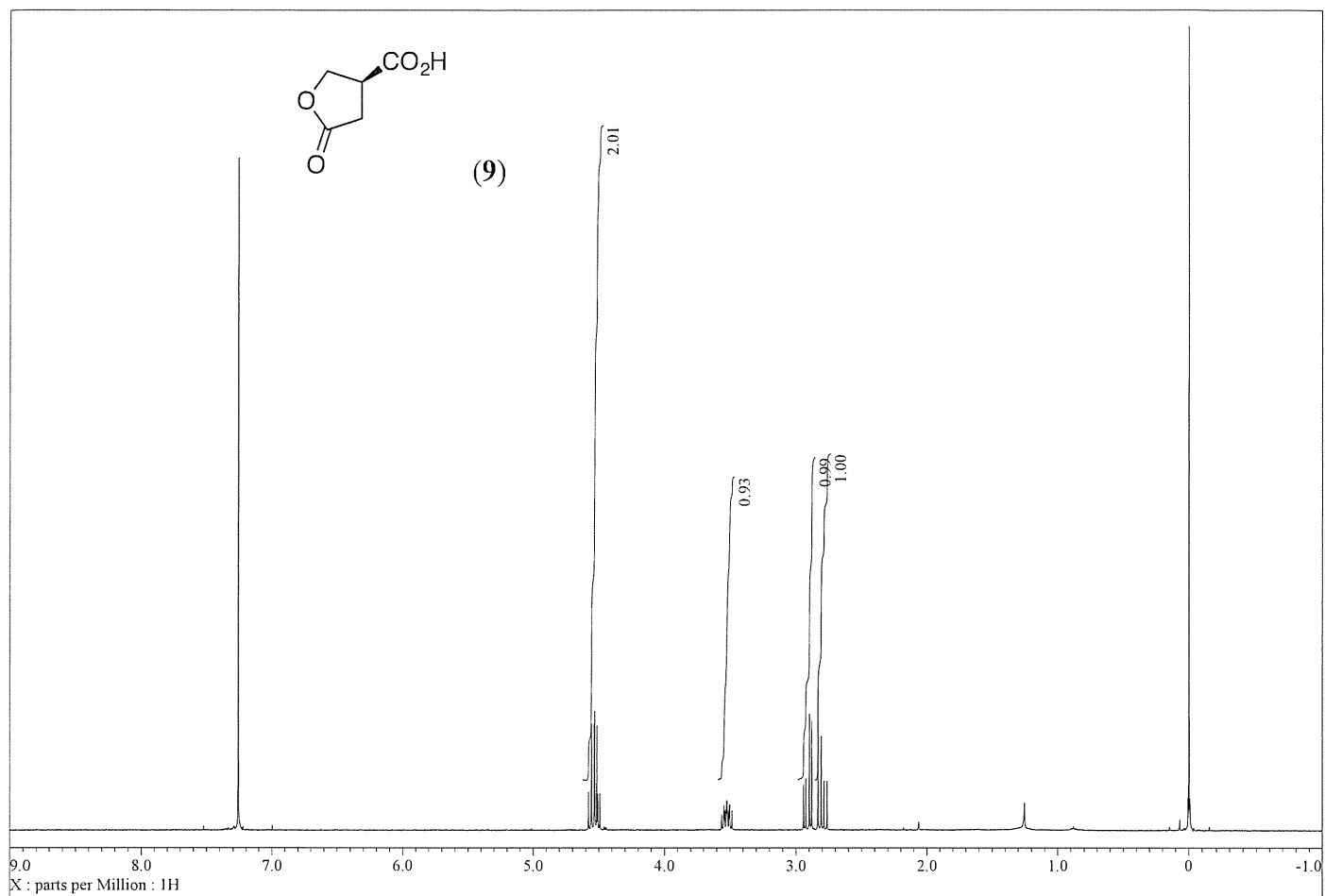
^1H NMR, 400 MHz, CDCl_3



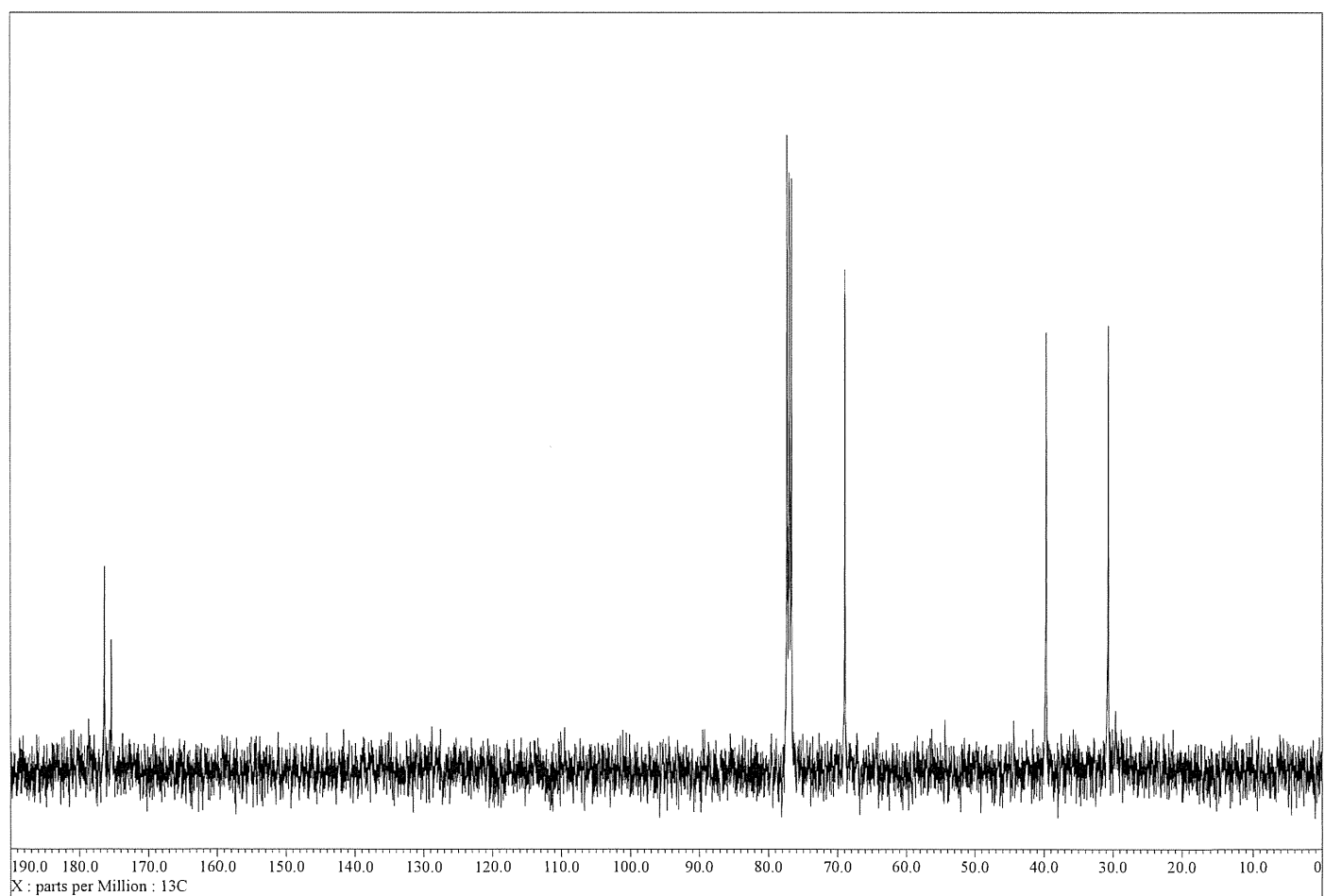
^{13}C NMR, 100 MHz, CDCl_3



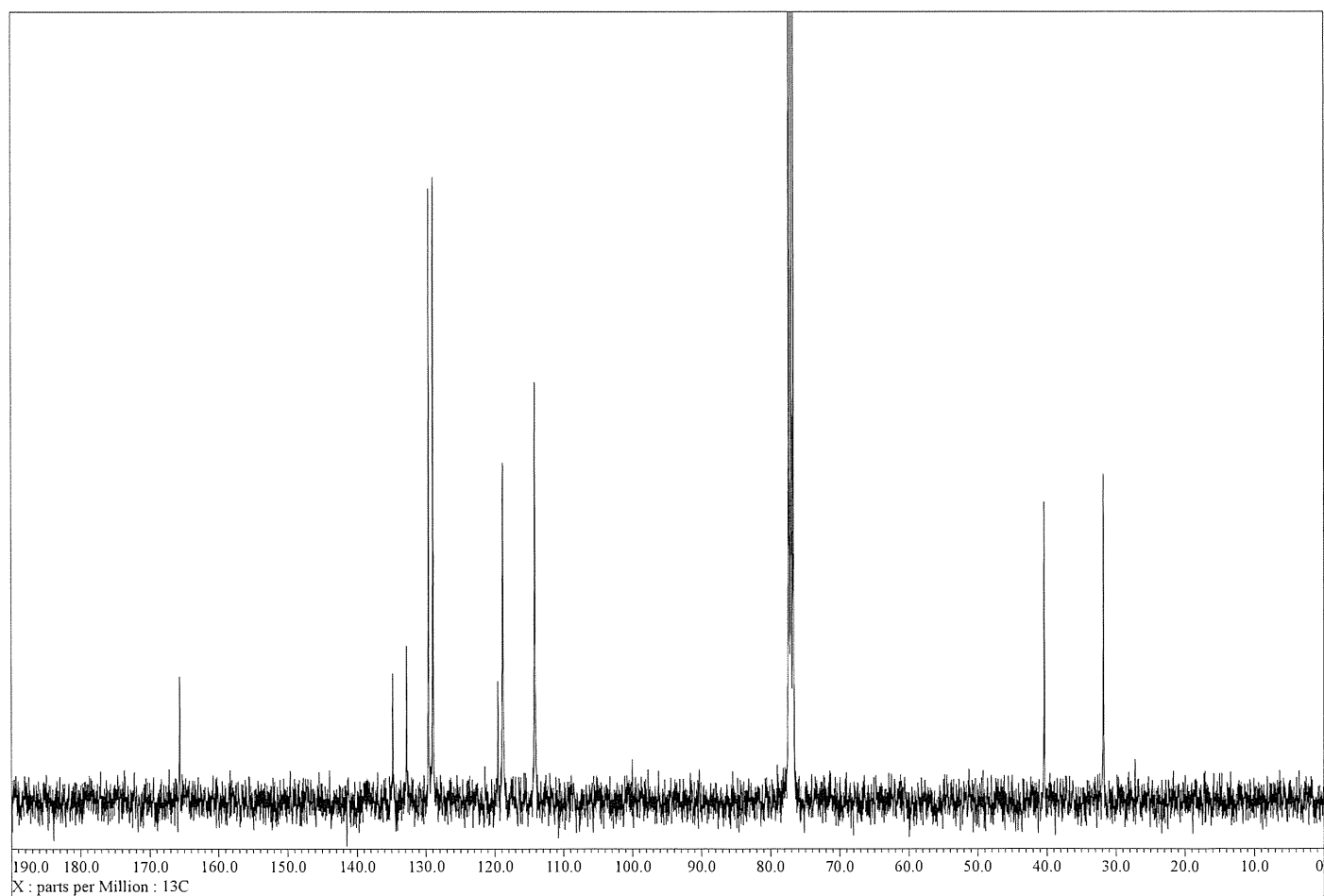
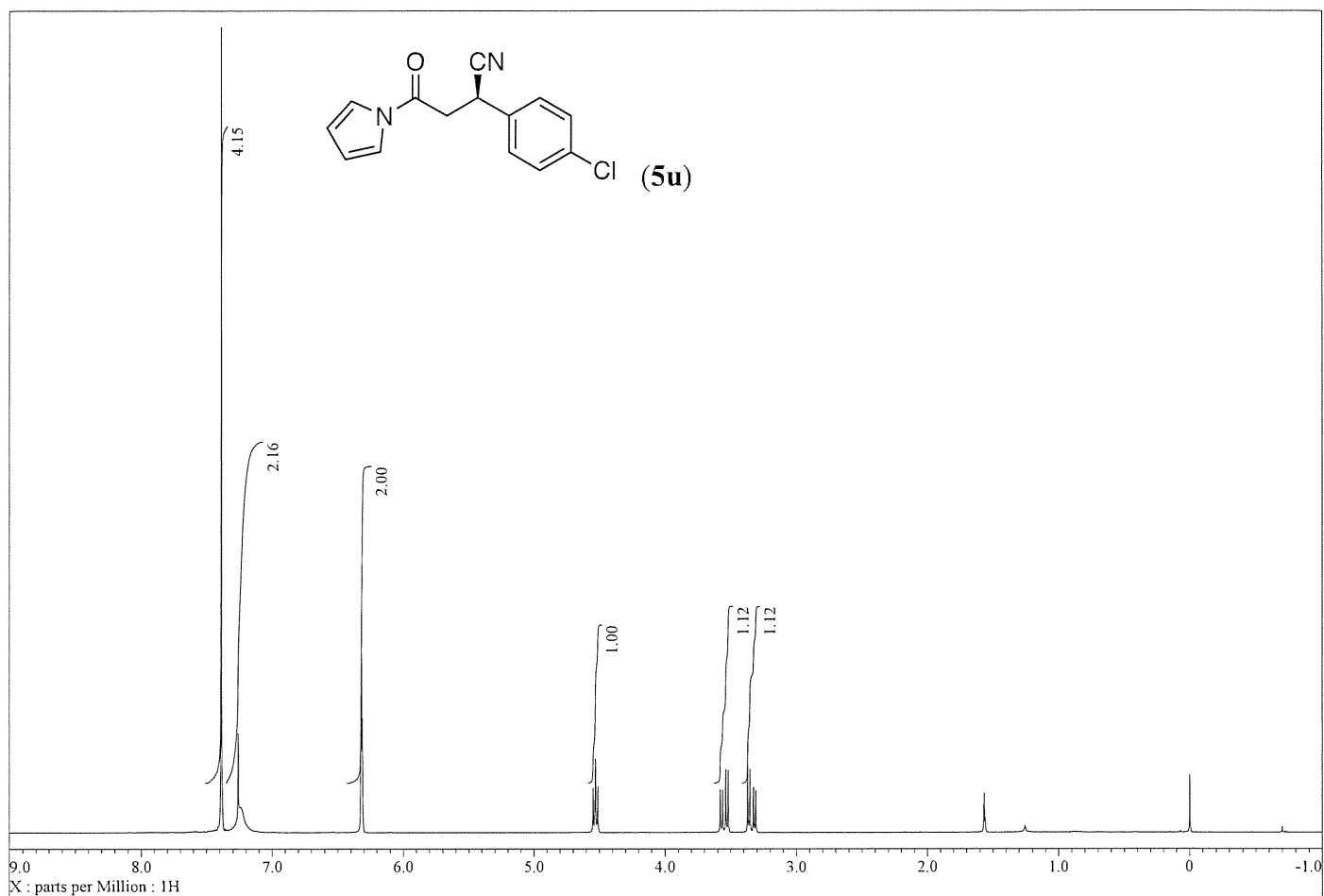


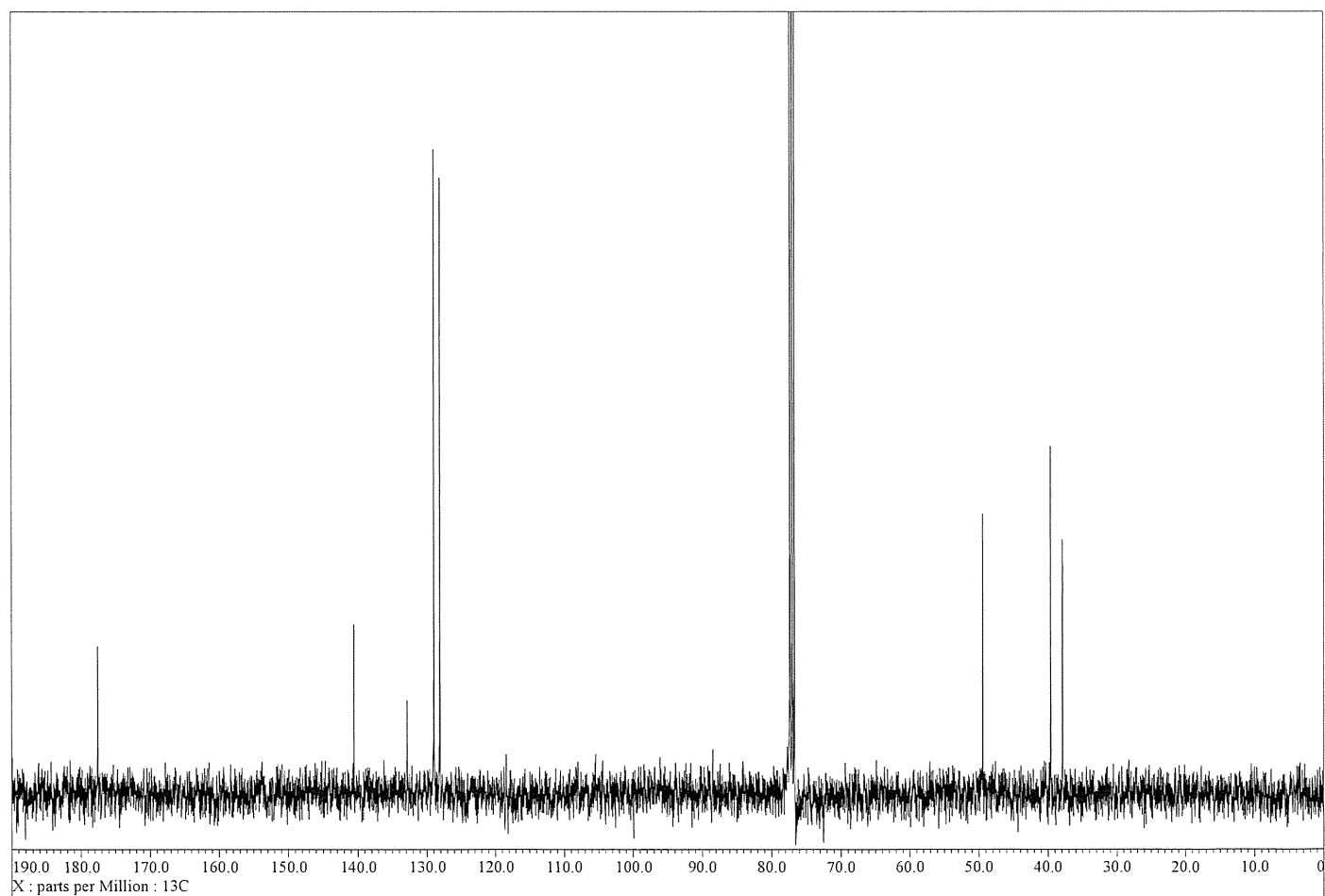
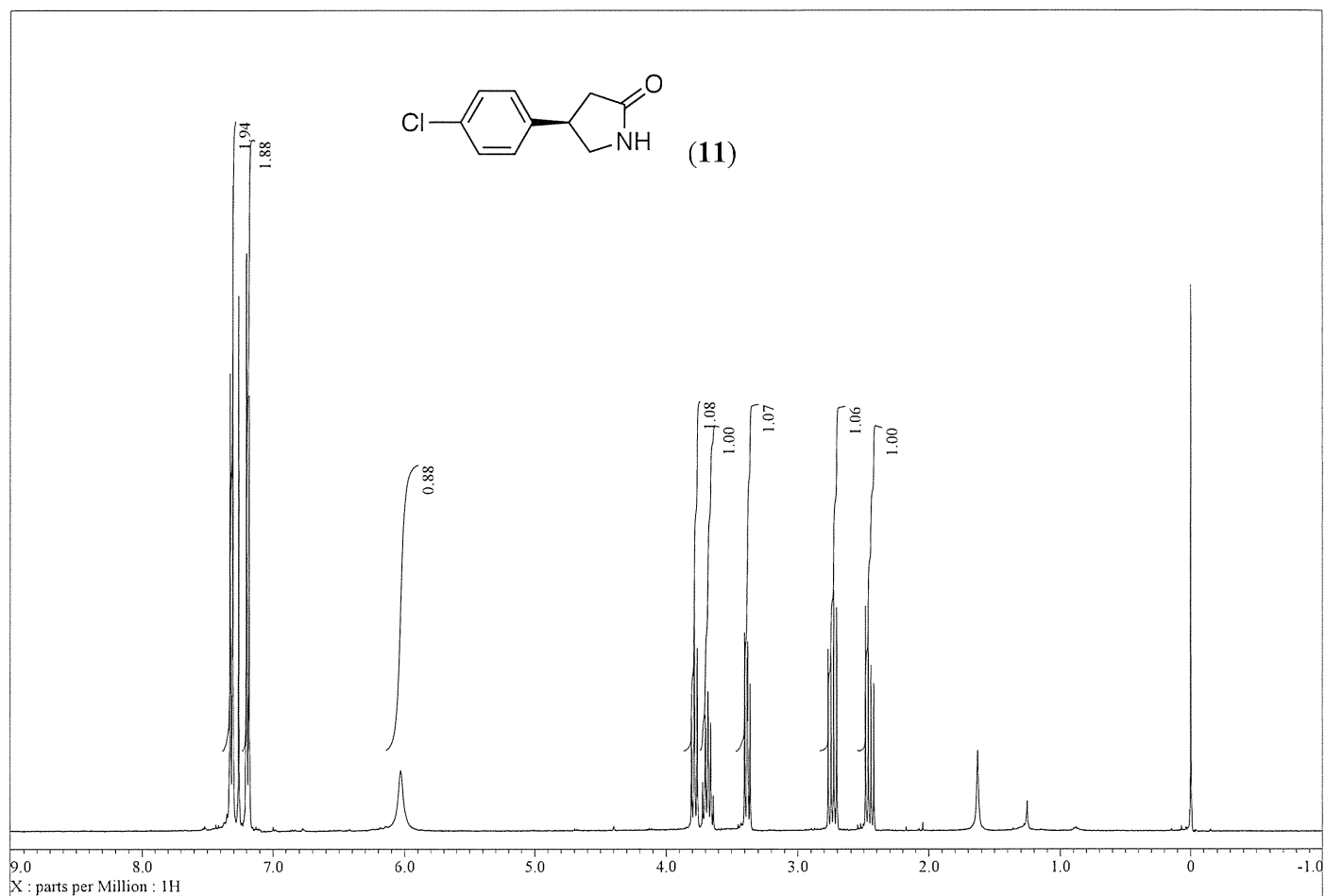


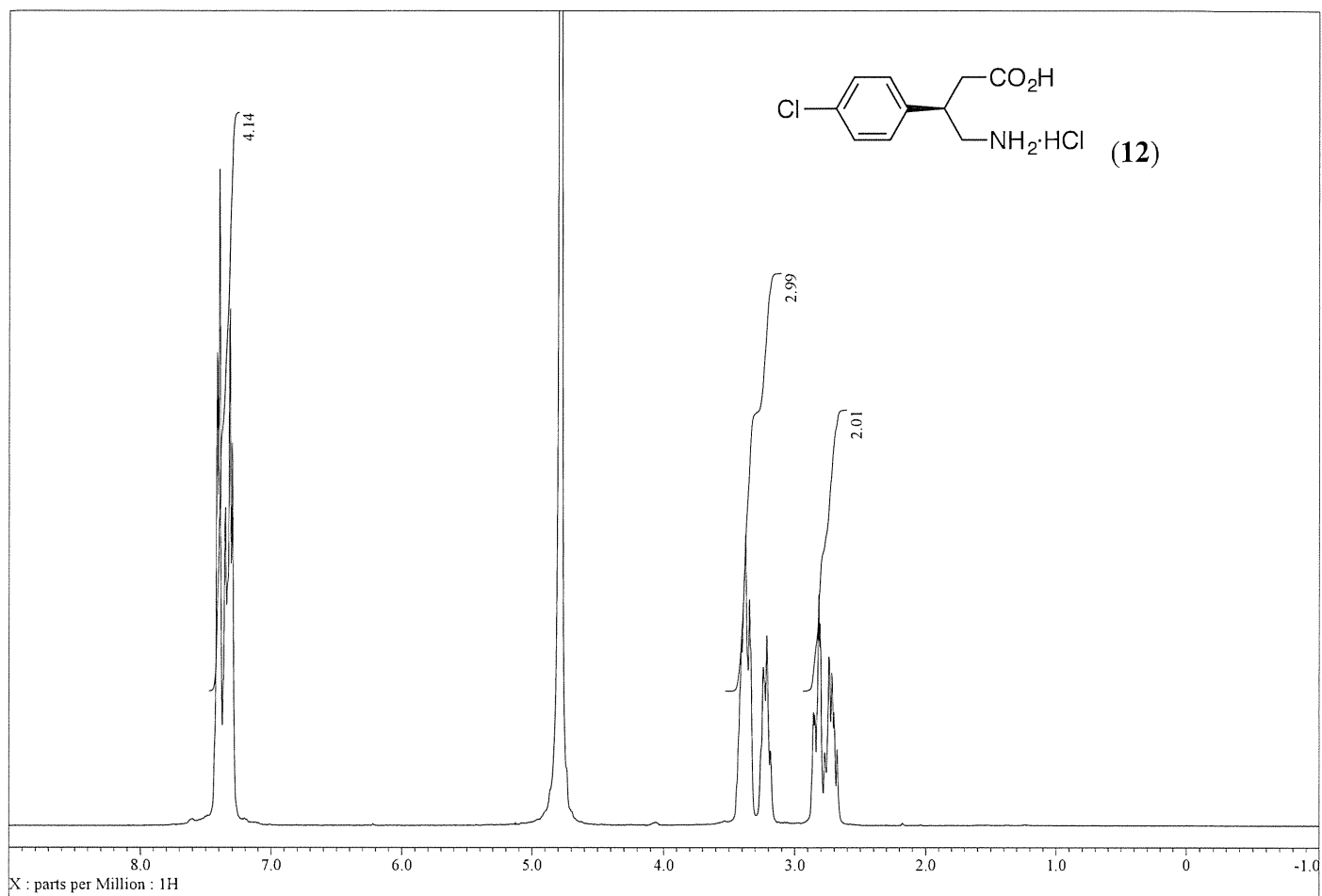
¹H NMR, 400 MHz, CDCl₃



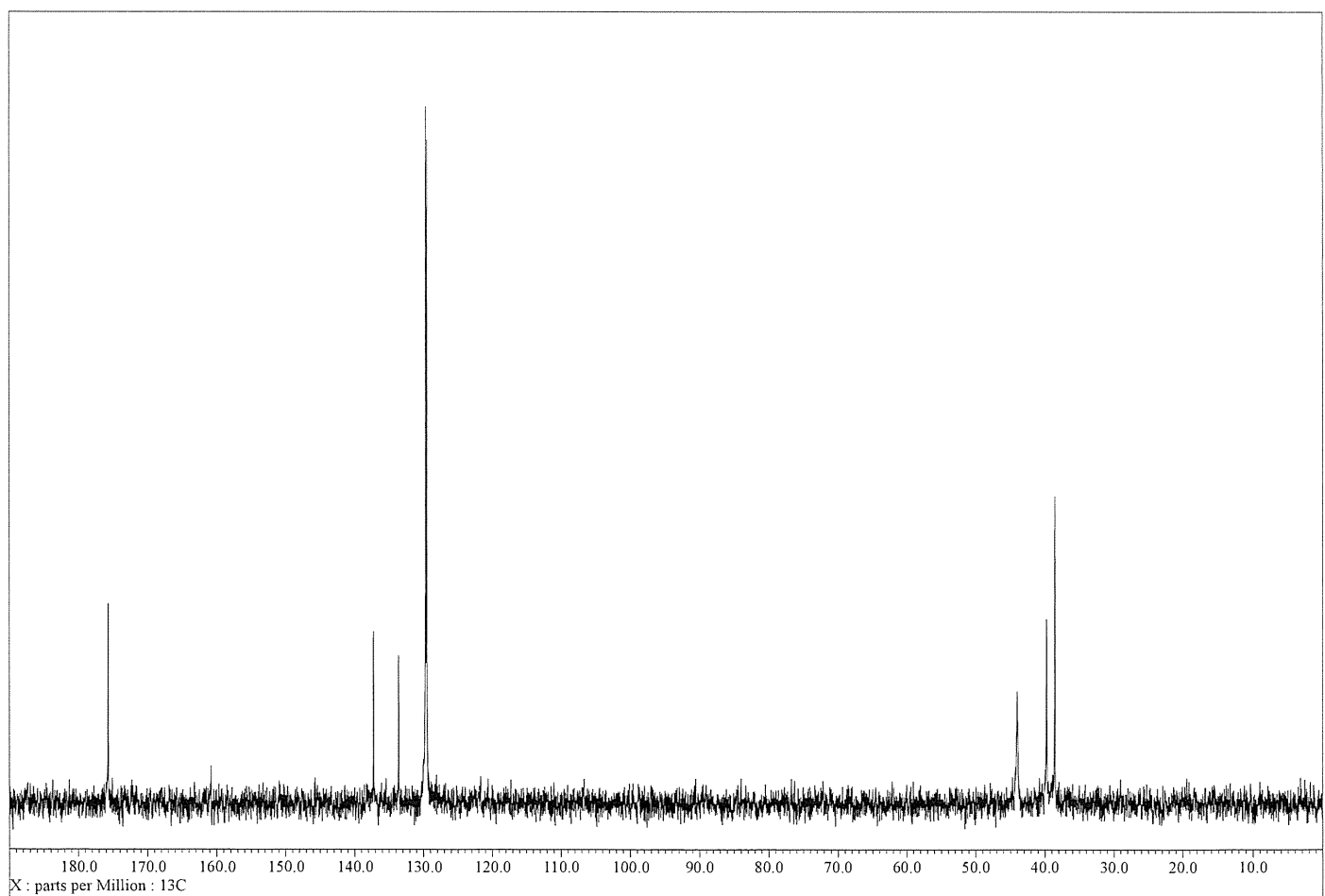
¹³C NMR, 100 MHz, CDCl₃



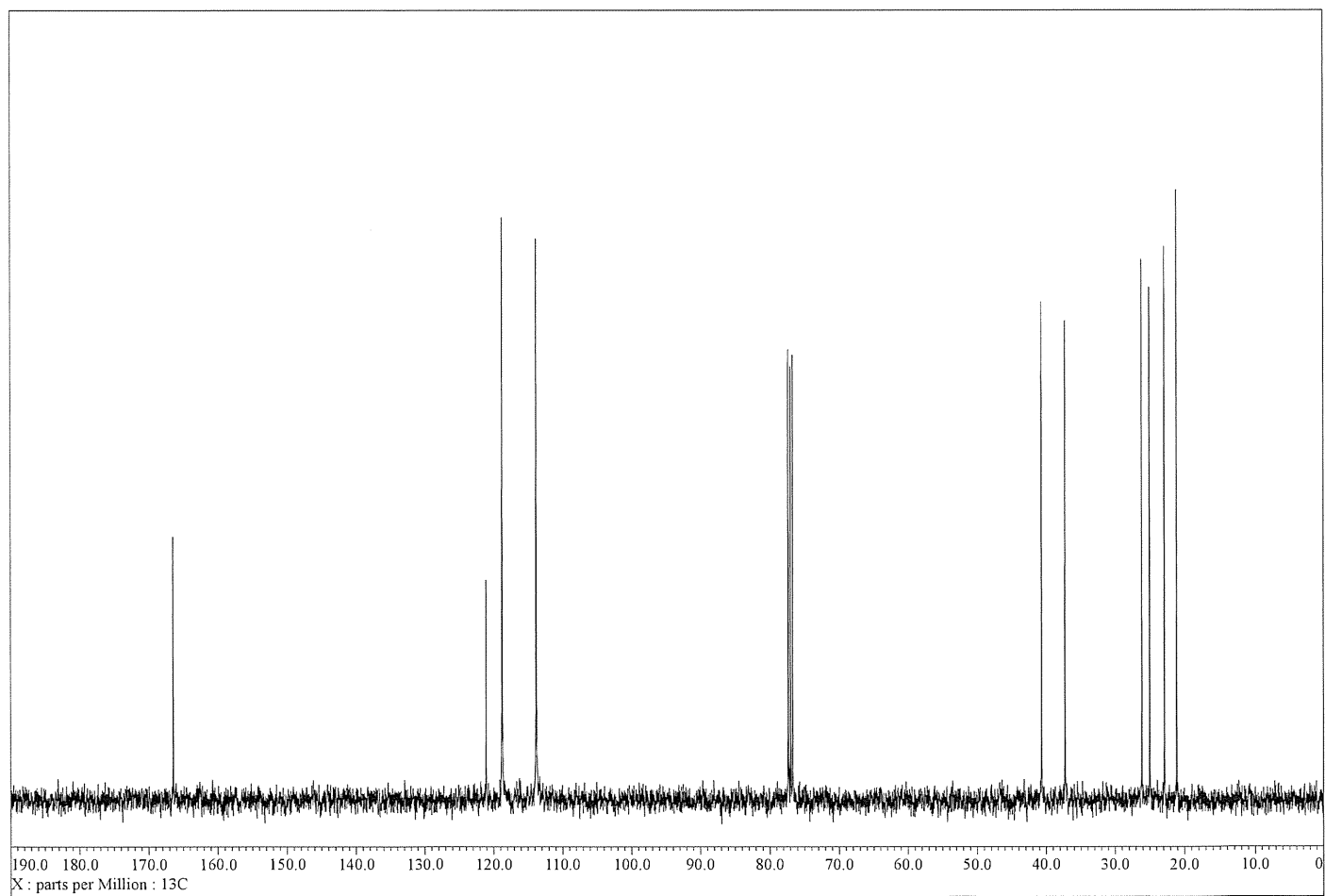
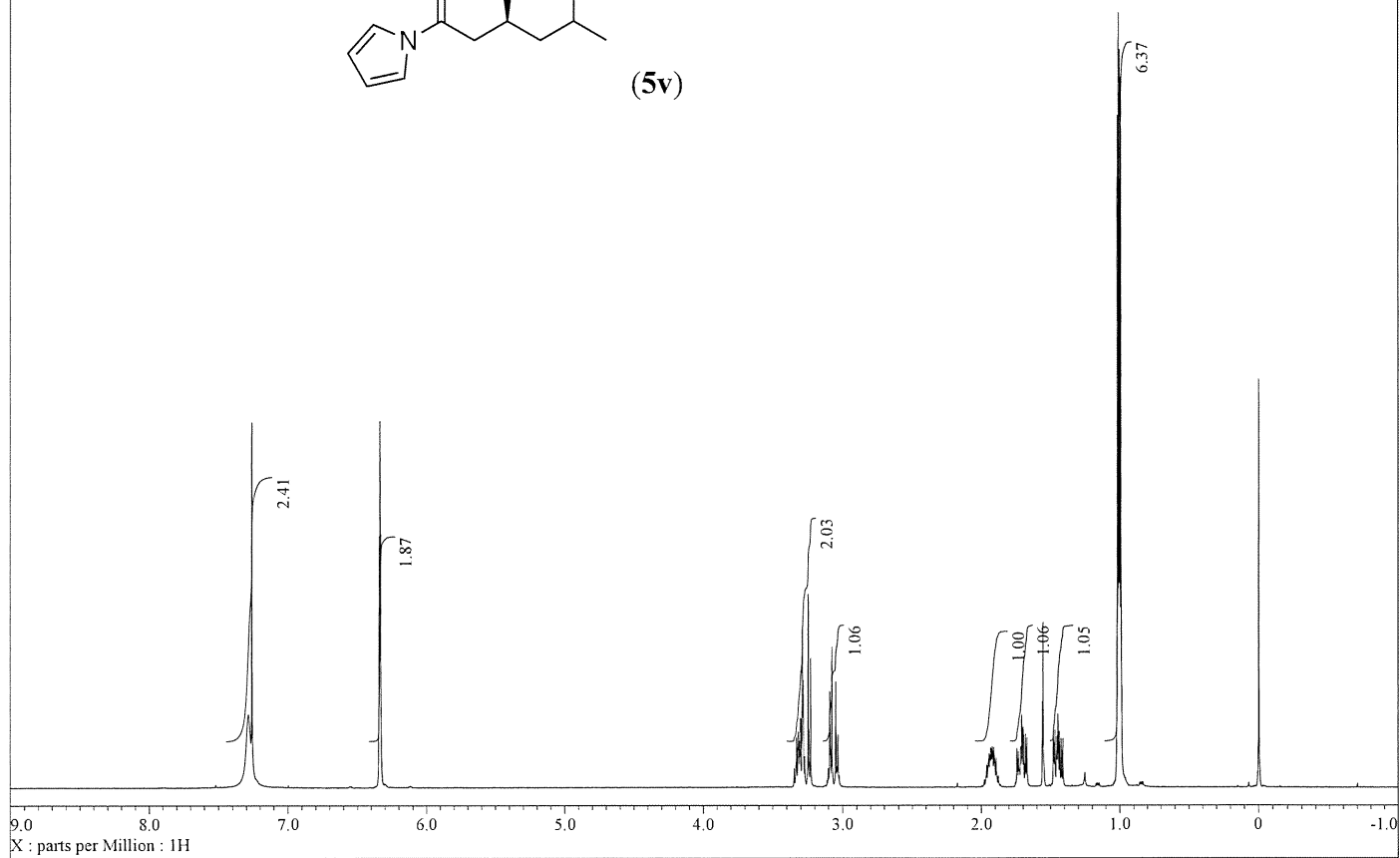
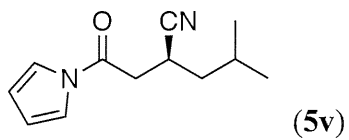


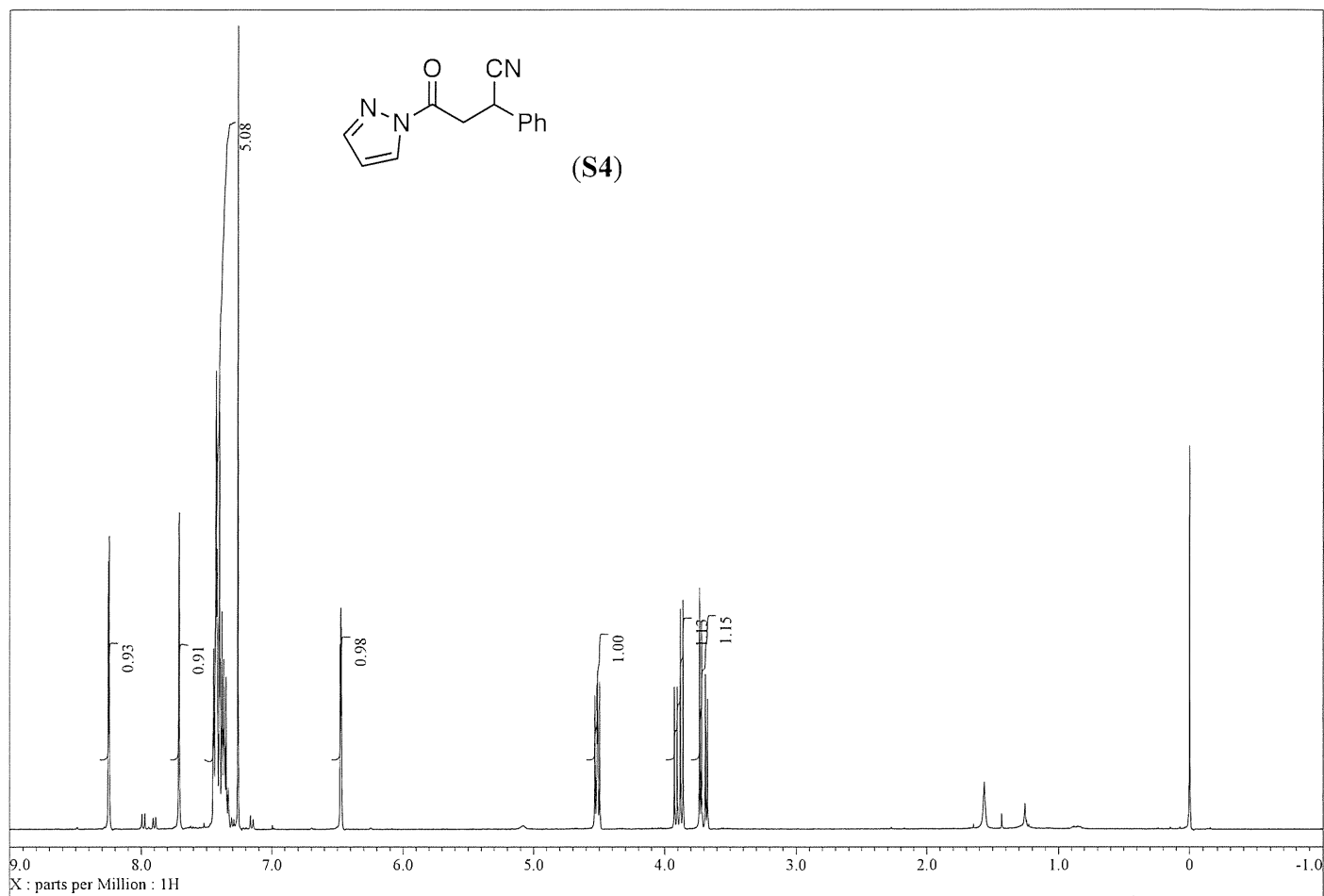


^1H NMR, 400 MHz, D_2O

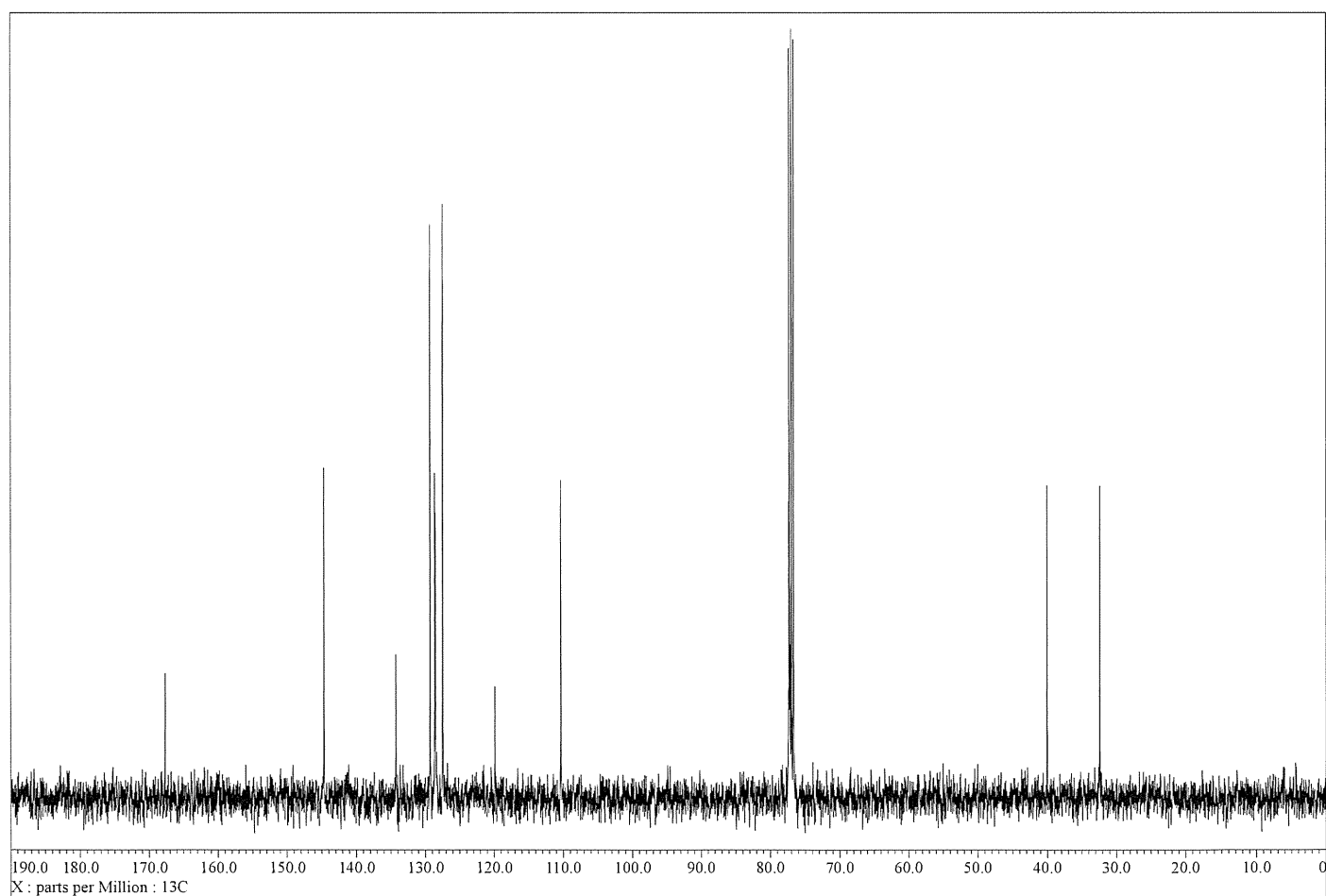


^{13}C NMR, 100 MHz, D_2O

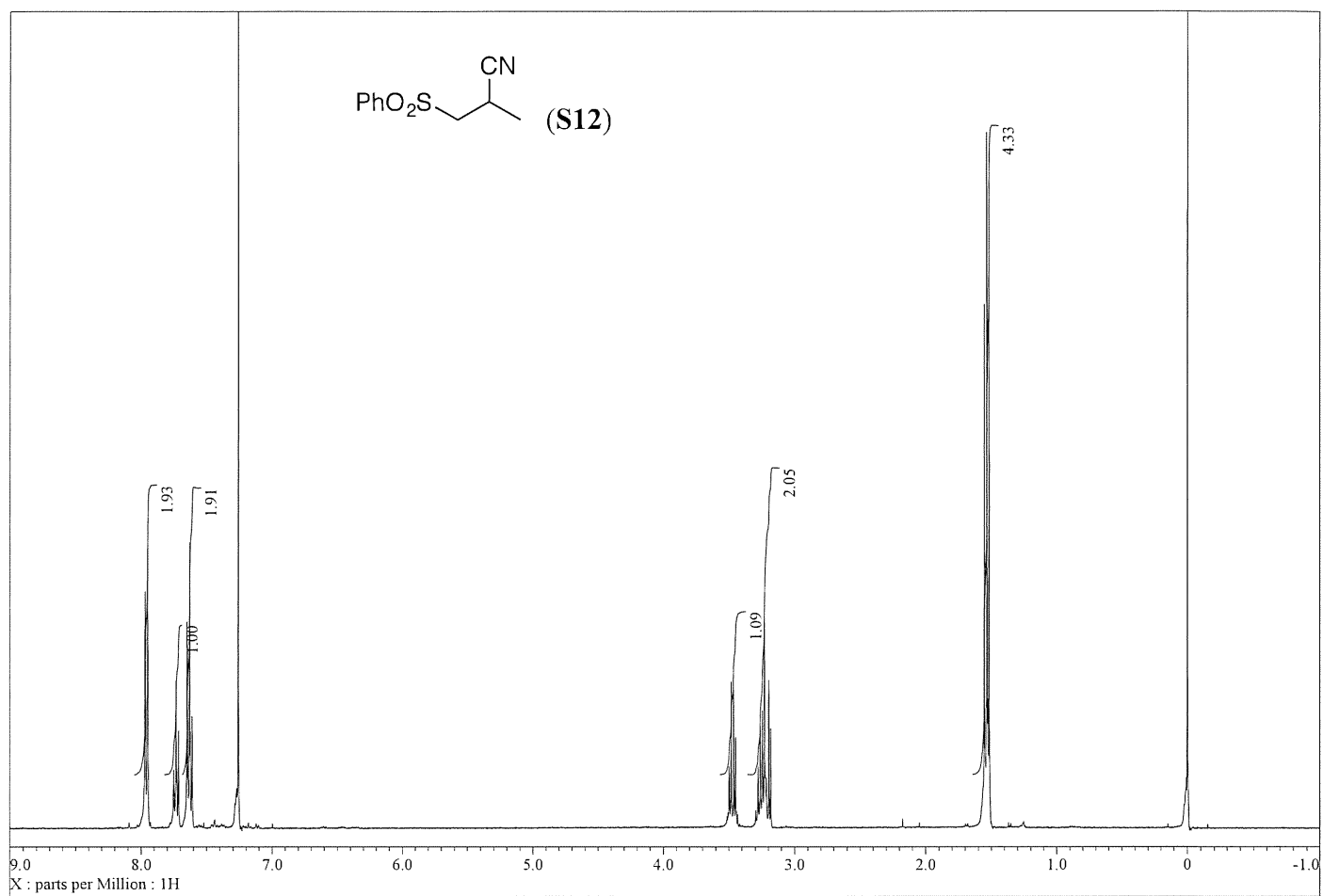
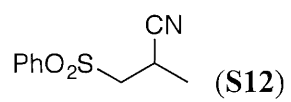




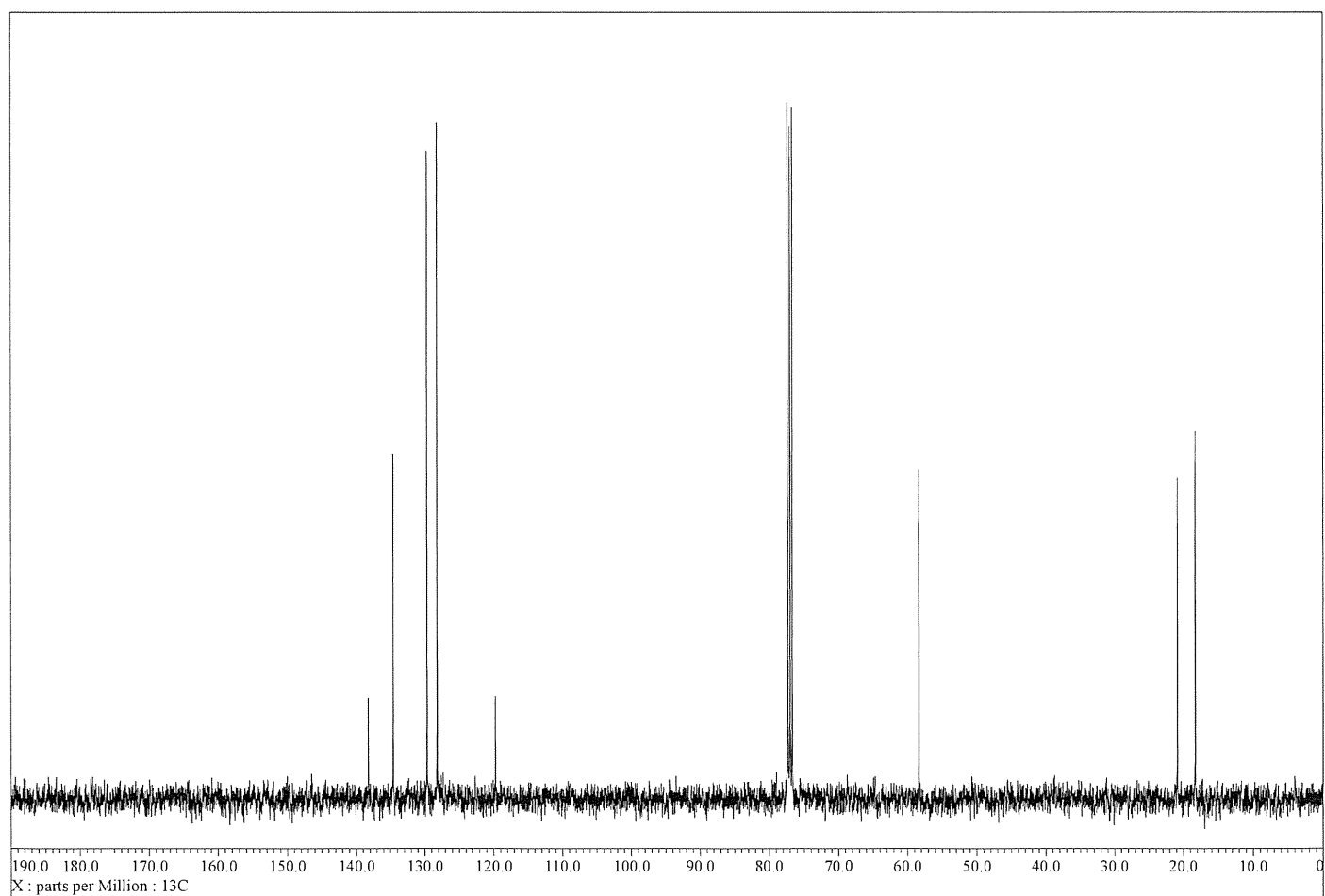
¹H NMR, 400 MHz, CDCl₃



¹³C NMR, 100 MHz, CDCl₃



¹H NMR, 400 MHz, CDCl₃



¹³C NMR, 100 MHz, CDCl₃