Site- and Chemoselective C–H Functionalization for the Synthesis of Spiroaminals *via* Silver-catalyzed Nitrene Transfer Reaction

Shingo Harada,*[a] Mayu Kobayashi,[a] Masato Kono,[a] and Tetsuhiro Nemoto*[a,b]

[a] Graduate School of Pharmaceutical Sciences, Chiba University, 1-8-1, Inohana, Chuo-ku, Chiba 260-8675, Japan

Tel/Fax : 81-43-226-2920.

E-mail : Sharada@chiba-u.jp, tnemoto@faculty.chiba-u.jp

[b] Molecular Chirality Research Center, Chiba University, 1-33, Yayoi-cho, Inage-ku, Chiba 263-8522, Japan

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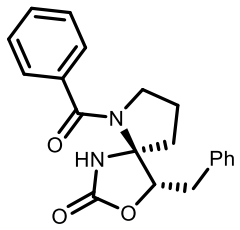
1. General information

NMR spectra were recorded on a JEOL ecs 400 spectrometer, JEOL ecz 400 spectrometer and JEOL ecz 600 spectrometer. For ^{1}H NMR, chemical shifts are reported relative to residual protiated solvent peaks (δ 7.26 and 3.31 ppm for $CDCl_3$ and CD_3OD respectively). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad), integration and coupling constants in Hz. For ^{13}C NMR, chemical shifts were again reported in accordance to residual protiated solvent peaks (δ 77.2, 49.0 and 118.3 ppm for $CDCl_3$, CD_3OD, CD_3CN respectively). ESI mass spectra were measured on JEOL AccuTOF LC-plus JMS-T100LP. Optical rotations were measured on a JASCO P-1020 polarimeter. The enantiomeric excess (ee) was determined by HPLC analysis. HPLC was performed on JASCO HPLC systems consisting of the following: pump, PU-980; detector, UV-970; column DAICEL CHIRALPAK AS-H; mobile phase, *n*-hexane/*i*-PrOH. Melting points were measured with a SIBATA NEL-270 melting point apparatus. Analytical thin layer chromatography was performed on Kieselgel 60F254, 0.25 mm thickness plates. Column chromatography was performed with silica gel 60 N (spherical, neutral 40-50 mesh). Reactions were conducted in dry solvent. Other reagents were purified by the usual methods.

2. Characterization of C-H insertion products

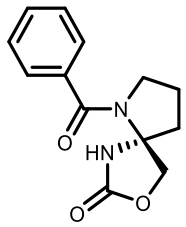
General procedure A for the Ag-catalyzed C–H insertion reaction

To a pre-dried 50 mL flask were added $AgClO_4 \cdot H_2O$ (4.5 mg, 10 mol %, 0.02 mmol) and 2,2'-(propane-2,2-diyl)bis(4,4-dimethyl-4,5-dihydrooxazole) (6.0 mg, 12.5 mol%, 0.025 mmol), and the flask was filled with argon gas. After CH_2Cl_2 (10 mL) was injected into the flask, wrapped with aluminium foil to avoid light, the solution was stirred at room temperature for 30 min under the argon atmosphere. A solution of the carbamate substrate (0.2 mmol, 1 eq) in CH_2Cl_2 (10 mL) was added to the reaction flask, followed by 4Å molecular sieves (1 mmol substrate/g of sieves). Iodosobenzene (88.0 mg, 0.4 mmol, 2.0 eq) was added in one portion and the reaction mixture was continually stirred at room temperature for 1 day. The reaction mixture was filtered through celite and the filtrate was concentrated under reduced pressure. The reaction mixture was diluted with CH_2Cl_2, and washed with 0.2 M aqueous $KHSO_4$. The aqueous phase was then extracted with CH_2Cl_2, and the combined organics were dried over Na_2SO_4, concentrated under reduced pressure. The obtained crude mixture was purified by flash chromatography on silica gel (column condition; gradient elution: *n*-hexane/EtOAc → EtOAc → EtOAc/MeOH) to afford C-H insertion product.



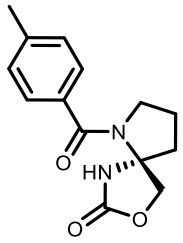
(4*S*,5*S*)-6-benzoyl-4-benzyl-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3a)

Prepared according to the general procedure A using **1a** (67.7 mg, 0.2 mmol), and isolated as white powder. (53.8 mg, 80% yield) : TLC R_f = 0.4 (EtOAc), mp: 151-153 ºC, ^{1}H NMR (400 MHz, CD_3OD) δ 7.53-7.42 (m, 5H), 7.34-7.21 (m, 5H), 5.16 (dd, *J* = 10.5, 3.7 Hz, 1H), 3.53-3.42 (m, 2H), 3.21 (dd, *J* = 14.2, 3.7 Hz, 1H), 3.00 (dd, *J* = 14.2, 10.5 Hz, 1H), 2.57-2.50 (m, 1H), 2.11 (m, 1H), 1.93-1.78 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 159.0, 137.3, 136.6, 130.1, 129.4, 128.6, 128.3, 127.0, 126.9, 82.3, 81.9, 50.5, 37.9, 35.3, 23.4; IR (ATR) ν 3255, 2925, 2358, 1748, 1634, 1385, 1032, 700, 654, 631 cm^{-1}; HRMS (ESI-TOF) [M + Na]$^+$ calcd for $C_{20}H_{20}N_2NaO_3^+$ m/z 359.1372, found 359.1380.



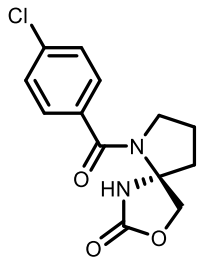
(*S*)-6-benzoyl-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3b)

Prepared according to the general procedure A using **1b** (49.6 mg, 0.2 mmol), and isolated as white powder (33.0 mg, 67% yield): ^{1}H and ^{13}C NMR, IR, and MS data were identical to those reported.[1] : $[\alpha]^{24}_D$ –72.4 (*c* 0.5, MeOH) The enantiomeric excess was determined to be >99% by analytical chiral HPLC. Retention time: 9.9 min (major isomer), 12.0 min (minor isomer) (AS-H column, 80/20 *n*-hexane/*i*-PrOH, 1 mL/min, 216 nm).



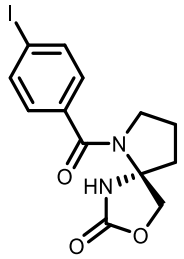
(*S*)-6-(4-methylbenzoyl)-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3c)

Prepared according to the general procedure A using **1c** (52.5 mg, 0.2 mmol), and isolated as white amorpous (39.0 mg, 75% yield) : TLC R_f = 0.2 (EtOAc), ^{1}H NMR (400 MHz, CD_3OD) δ 7.42 (d, *J* = 8.0 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 4.72 (d, *J* = 9.4 Hz, 1H), 4.40 (d, *J* = 9.4 Hz, 1H), 3.58-3.49 (m, 2H), 2.38 (s, 3H), 2.23 (dd, *J* = 8.2, 6.2 Hz, 2H), 1.96-1.82 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 160.0, 140.4, 134.0, 128.9, 127.2, 78.7, 73.3, 50.5, 40.2, 23.2, 21.5; IR (ATR) ν 3263, 2924, 1739, 1612, 1385, 1069, 1037, 942, 830, 754, 712 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{14}H_{16}N_2NaO_3^+$ m/z 283.1059, found 283.1055.



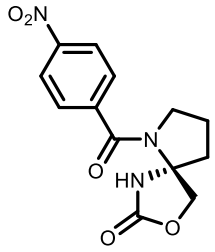
(*S*)-6-(4-chlorobenzoyl)-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3d)

Prepared according to the general procedure A using **1d** (52.5 mg, 0.2 mmol), and isolated as white powder (33.0 mg, 67% yield) : TLC R_f = 0.2 (EtOAc), mp: 142-144 ºC, ^{1}H NMR (400 MHz, CD_3OD) δ 7.52 (d, *J* = 8.7 Hz, 2H), 7.45 (d, *J* = 8.7 Hz, 2H), 4.72 (d, *J* = 9.4 Hz, 1H), 4.40 (d, *J* = 9.4 Hz, 1H), 3.53-3.47 (m, 2H), 2.26-2.21 (m, 2H), 1.96-1.83 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 159.9, 136.4, 135.2, 128.7, 128.6, 79.0, 73.4, 50.5, 40.1, 23.2; IR (ATR) ν 3264, 2956, 1747, 1633, 1404, 1218, 1135, 1068, 1014, 839, 760 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{13}H_{13}ClN_2NaO_3^+$ m/z 303.0512, found 303.0502.



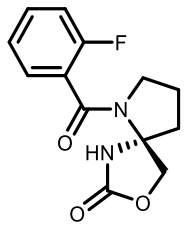
(*S*)-6-(4-iodobenzoyl)-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3e)

Prepared according to the general procedure A using **1e** (74.8 mg, 0.2 mmol), and isolated as white powder (51.3 mg, 69% yield) : TLC R_f = 0.2 (EtOAc), mp: 154-156 ºC, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.0 Hz, 2H), 7.26 (s, 1H), 7.18 (d, *J* = 8.0 Hz, 2H), 4.73 (d, *J* = 9.1 Hz, 1H), 4.32 (d, *J* = 9.1 Hz, 1H), 3.55-3.49 (m, 1H), 3.41-3.34 (m, 1H), 2.35-2.29 (m, 1H), 2.12-1.93 (m, 2H), 1.81 (ddd, *J* = 11.4, 11.4, 5.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 159.5, 137.7, 136.0, 128.8, 97.0, 78.8, 73.4, 50.5, 40.2, 23.3; IR (ATR) ν 3289, 2952, 1744, 1632, 1586, 1414, 1336, 1295, 1145, 1006 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{13}H_{13}IN_2NaO_3^+$ m/z 394.9869, found 394.9883.



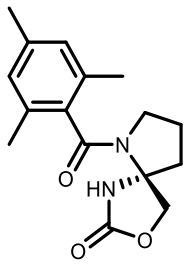
(*S*)-6-(4-nitrobenzoyl)-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3f)

Prepared according to the general procedure A using **1f** (58.6 mg, 0.2 mmol), and isolated as white powder (39.0 mg, 67% yield) : TLC R_f = 0.2 (EtOAc), mp: 156-158 ºC, ^{1}H NMR (400 MHz, CD_3OD) δ 8.27 (d, *J* = 8.8 Hz, 2H), 7.70 (d, *J* = 8.8 Hz, 2H), 4.72 (d, *J* = 9.6 Hz, 1H), 4.38 (d, *J* = 9.6 Hz, 1H), 3.44-3.39 (m, 2H), 2.22-2.18 (m, 2H), 1.91-1.81 (m, 2H); ^{13}C NMR (100 MHz, CD_3CN) δ 168.7, 159.3, 149.5, 144.3, 128.7, 124.7, 79.5, 73.6, 51.0, 40.4, 23.5; IR (ATR) ν 3247, 2924, 1747, 1635, 1600, 1522, 1391, 1347, 1052, 942, 862, 703 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{13}H_{13}N_3NaO_5^+$ m/z 314.0753, found 314.0748.



(*S*)-6-(2-fluorobenzoyl)-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3g)

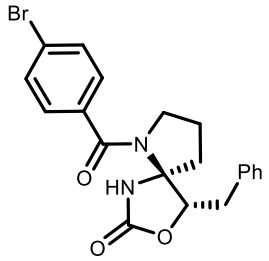
Prepared according to the general procedure A using **1g** (53.3 mg, 0.2 mmol), and isolated as white powder (37.1 mg, 70% yield) : TLC R_f = 0.2 (EtOAc), mp: 151-153 ºC, ^{1}H NMR (400 MHz, CD_3OD) δ 7.54-7.41 (m, 2H), 7.30-7.19 (m, 2H), 4.74 (d, *J* = 9.6 Hz, 1H), 4.43 (d, *J* = 9.6 Hz, 1H), 3.41-3.38 (m, 2H), 2.27-2.23 (m, 2H), 1.99-1.83 (m, 2H); ^{13}C NMR (150 MHz, CD_3OD) δ 168.0, 161.4, 159.5 (d, *J* = 247.1 Hz), 133.2 (d, *J* = 8.7 Hz), 129.4 (d, *J* = 2.9 Hz), 126.5 (d, *J* = 17.3 Hz), 126.0 (d, *J* = 2.9 Hz), 117.1 (d, *J* = 21.7 Hz), 80.3, 74.2, 50.2, 40.8, 23.5; IR (ATR) ν 3241, 2928, 1739, 1631, 1454, 1390, 1212, 1133, 1067, 942, 756 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{13}H_{13}FN_2NaO_3^+$ m/z 287.0808, found 287.0808.



(*S*)-6-(2,4,6-trimethylbenzoyl)-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3h)

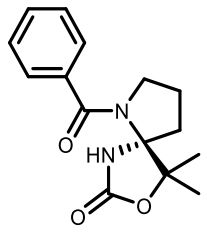
Prepared according to the general procedure A using **1h** (58.1 mg, 0.2 mmol), and isolated as white powder (54.0 mg, 94% yield) : TLC R_f = 0.3 (EtOAc), mp: 183-185 ºC, ^{1}H NMR (400 MHz, CD_3OD) δ 6.90 (s, 2H), 4.78 (d, *J* = 9.4 Hz, 1H), 4.43 (d, *J* = 9.4 Hz, 1H), 3.18-3.09 (m, 2H), 2.27-2.22 (m, 11H), 1.97-1.82 (m, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 171.8, 160.0, 138.7, 134.3, 132.8, 132.6, 128.1, 128.0, 78.4, 72.8, 48.6, 39.5, 22.2, 19.9, 17.44, 17.38; IR (ATR) ν 3355,

2921, 1738, 1626, 1385, 1290, 1219, 1173, 1137, 1067, 1036, 941, 857 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{16}H_{20}N_2NaO_3^+$ m/z 311.1372, found 311.1366.



(4*S*,5*S*)-4-benzyl-6-(4-bromobenzoyl)-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3i)

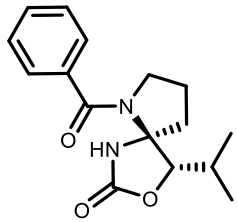
Prepared according to the general procedure A using **1i** (83.7 mg, 0.2 mmol), and isolated as white powder (52.5 mg, 63% yield) : TLC R_f = 0.3 (EtOAc), mp: 139-141 ºC, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.40 (d, *J* = 8.7 Hz, 2H), 7.32-7.21 (m, 7H), 5.16 (t, *J* = 7.3 Hz, 1H), 3.47-3.41 (m, 1H), 3.26 (ddd, *J* = 10.1, 6.9, 6.9 Hz, 1H), 3.03 (d, *J* = 7.3 Hz, 2H), 2.37-2.30 (m, 1H), 2.20-2.14 (m, 1H), 1.92-1.85 (m, 1H), 1.68-1.62 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 159.2, 136.5, 136.0, 131.6, 129.3, 128.8, 128.6, 126.9, 124.5, 82.6, 82.0, 50.4, 37.9, 35.1, 23.4; IR (ATR) ν 3260, 2923, 1746, 1634, 1380, 1258, 1070, 1011, 756, 699 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{20}H_{19}BrN_2NaO_3^+$ m/z 437.0477, found 437.0490.



(*S*)-6-benzoyl-4,4-dimethyl-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3j)

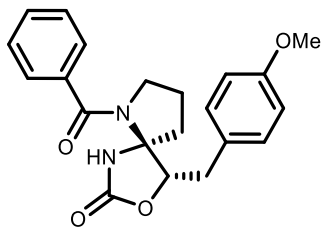
Prepared according to the general procedure A using **1j** (55.3 mg, 0.2 mmol), and isolated as white amorphous (46.6 mg, 85% yield) : TLC R_f = 0.2 (EtOAc), ^{1}H

NMR (400 MHz, $CDCl_3$) δ 7.48-7.43 (m, 3H), 7.39-7.27 (m, 3H), 3.57-3.52 (m, 1H), 3.31 (ddd, *J* = 9.8, 6.1 Hz, 1H), 2.28-2.23 (m, 1H), 2.16-2.09 (m, 1H), 1.98-1.90 (m, 1H), 1.77-1.71 (m, 1H), 1.51 (s, 3H), 1.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 159.6, 138.0, 129.9, 128.4, 126.8, 85.1, 52.3, 35.6, 26.3, 23.3, 21.6; IR (ATR) ν 3251, 2922, 1743, 1635, 1377, 1231, 1128, 1000, 886, 737, 701 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{15}H_{18}N_2NaO_3^+$ m/z 297.1215, found 297.1216.



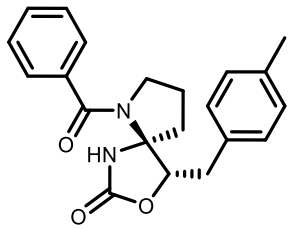
(4*S*,5*S*)-6-benzoyl-4-isopropyl-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3k)

Prepared according to the general procedure A using **1k** (58.1 mg, 0.2 mmol), and isolated as white amorphous (33.4 mg, 58% yield) : TLC R_f = 0.4 (EtOAc), ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (br s, 1H), 7.48 (d, *J* = 7.3 Hz, 2H), 7.39-7.31 (m, 3H), 4.81 (d, *J* = 3.2 Hz, 1H), 3.48 (ddd, *J* = 9.6, 9.6, 2.8 Hz, 1H), 3.37 (dd, *J* = 16.0, 9.6 Hz, 1H), 2.32-2.21 (m, 2H), 2.11-1.99 (m, 2H), 1.84-1.82 (m, 1H), 1.11 (d, *J* = 6.4 Hz, 3H), 1.05 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 159.8, 137.5, 130.1, 128.3, 127.0, 86.5, 81.9, 50.5, 34.9, 29.4, 23.5, 21.1, 16.6; IR (ATR) ν 3263, 2965, 1744, 1624, 1380, 1222, 1132, 1036, 727, 700 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{16}H_{20}N_2NaO_3^+$ m/z 311.1372, found 311.1382.



(4*S*,5*S*)-6-benzoyl-4-(4-methoxybenzyl)-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3l)

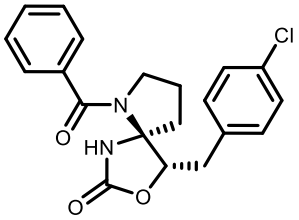
Prepared according to the general procedure A using **1l** (64.0 mg, 0.17 mmol), and isolated as white powder (46.1 mg, 74% yield) : TLC R_f = 0.3 (EtOAc), mp: 144-146 ºC, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.46-7.44 (m, 2H), 7.37-7.28 (m, 3H), 7.21 (d, *J* = 8.2 Hz, 2H), 6.84 (d, *J* = 8.2 Hz, 2H), 5.20 (dd, *J* = 8.2, 5.9 Hz, 1H), 3.78 (s, 3H), 3.48-3.43 (m, 1H), 3.36-3.30 (m, 1H), 3.02-3.00 (m, 2H), 2.39-2.31 (m, 1H), 2.19-2.13 (m, 1H), 1.94-1.87 (m, 1H), 1.74-1.68 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.8, 159.0, 158.6, 137.3, 130.4, 130.1, 128.6, 128.3, 127.1, 114.1, 82.5, 81.9, 55.4, 50.6, 37.1, 35.4, 23.5; IR (ATR) ν 3260, 2963, 1747, 1634, 1513, 1385, 1247, 1030, 728, 701 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{21}H_{22}N_2NaO_4^+$ m/z 389.1480, found 389.1477.



(4*S*,5*S*)-6-benzoyl-4-(4-methylbenzyl)-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3m)

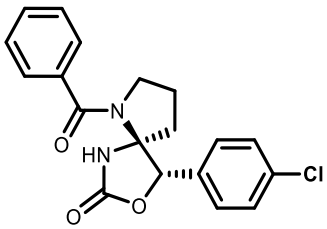
Prepared according to the general procedure A using **1m** (70.2 mg, 0.2 mmol), and isolated as white powder (42.7 mg, 61% yield) : TLC R_f = 0.4 (EtOAc), mp: 137-139 ºC, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.42 (d, *J* = 7.8 Hz, 2H), 7.34-7.25 (m, 3H), 7.16 (d, *J* = 7.8 Hz, 2H), 7.08 (d, *J* = 7.8 Hz, 2H), 5.21 (t, *J* = 7.1 Hz, 1H), 3.45-3.39 (m, 1H), 3.28 (dd, *J* = 16.2, 7.8 Hz, 1H), 3.02-2.99 (m, 2 H), 2.35-2.30 (m, 4H), 2.17-2.11 (m, 1H), 1.91-1.84 (m, 1H), 1.67-1.63 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 159.0, 137.3, 136.3, 133.5, 130.0, 129.3, 129.2, 128.3, 127.0, 82.4, 81.9, 50.5, 37.5, 35.3, 23.4, 21.1; IR (ATR) ν 3252, 2980, 1743, 1632, 1378, 1081, 1056, 907, 789, 724, 698 cm^{-1}; HRMS (ESI-TOF)

$[M + Na]^+$ calcd for $C_{21}H_{22}N_2NaO_3^+$ m/z 373.1528, found 373.1525.



(4*S*,5*S*)-6-benzoyl-4-(4-chlorobenzyl)-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3n)

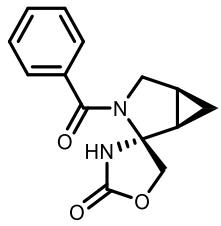
Prepared according to the general procedure A using **1n** (47.0 mg, 0.13 mmol), and isolated as white amorphous (38.7 mg, 80% yield) : TLC R_f = 0.3 (EtOAc), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (s, 1H), 7.43 (d, *J* = 6.4 Hz, 2H), 7.35-7.20 (m, 7H), 5.16 (t, *J* = 7.1 Hz, 1H), 3.48-3.34 (m, 2H), 3.00 (d, *J* = 6.9 Hz, 2H), 2.32-2.13 (m, 2H), 1.97-1.88 (m, 1H), 1.76-1.72 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.9, 158.8, 137.1, 135.1, 132.8, 130.8, 130.2, 128.7, 128.4, 127.0, 82.2, 81.7, 50.5, 37.3, 35.3, 23.5; IR (ATR) ν 3258, 1745, 1632, 1492, 1382, 1081, 1014, 908, 729, 700 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{20}H_{19}ClN_2NaO_3^+$ m/z 393.0982, found 393.0984.



(4*S*,5*S*)-6-benzoyl-4-(4-chlorophenyl)-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3o)

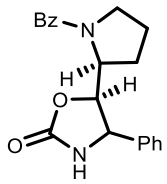
Prepared according to the general procedure A using **1o** (71.8 mg, 0.2 mmol), and isolated as pale yellow powder (47.6 mg, 67% yield) : TLC R_f = 0.3 (EtOAc), mp: 126-128 ºC, ^{1}H NMR (400 MHz, CD_3OD) δ 7.58-7.56 (m, 2H), 7.48-7.44 (m, 5H), 7.37 (d, *J* = 8.2 Hz, 2H), 5.87 (s, 1H), 3.50-3.43 (m, 2H), 1.72-1.57 (m, 4H);

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 159.4, 137.0, 135.1, 135.0, 130.5, 129.1, 128.5, 128.4, 127.2, 84.0, 82.8, 50.8, 37.3, 23.2; IR (ATR) ν 3262, 2956, 1752, 1634, 1382, 1221, 1142, 1054, 1025, 733, 700 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{19}H_{17}ClN_2NaO_3^+$ m/z 379.0825, found 379.0825.



(1*R*,2*S*,5*S*)-3-benzoyl-3-azaspiro[bicyclo[3.1.0]hexane-2,4'-oxazolidin]-2'-one (3p)

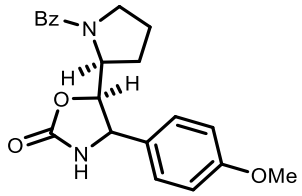
Prepared according to the general procedure A using **1p** (52.1 mg, 0.2 mmol), and isolated as white powder (26.6 mg, 54% yield) : TLC R_f = 0.3 (EtOAc), mp: 168-170 ºC, ^{1}H NMR (400 MHz, CD_3OD) δ 7.47-7.42 (m, 5H), 4.60 (m, 2H), 3.59 (d, *J* = 3.7 Hz, 2H), 1.88-1.84 (m, 1H), 1.68-1.65 (m, 1H), 0.92-0.87 (m, 1H), 0.73 (dd, *J* = 5.2, 4.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO) δ 170.7, 158.1, 137.6, 129.6, 128.4, 126.4, 126.3, 80.2, 73.2, 51.2, 25.5, 13.2, 7.7; IR (ATR) ν 3295, 2916, 2359, 1758, 1617, 1388, 1027, 741, 706, 654 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{14}H_{14}N_2NaO_3^+$ m/z 281.0902, found 281.0896.



(5*R*)-5-((*S*)-1-benzoylpyrrolidin-2-yl)-4-phenyloxazolidin-2-one (5a)

Prepared according to the general procedure A using **1a** (33.8 mg, 0.1 mmol), CH_2Cl_2 (20 mL, 0.05 M), $AgNTf_2$ (7.8 mg, 20 mol%, 0.02 mmol) and 1,10-phenanthroline (10.8 mg, 60 mol%, 0.06 mmol) instead of $AgClO_4 \cdot H_2O$ and 2,2'-

(propane-2,2-diyl)bis(4,4-dimethyl-4,5-dihydrooxazole), and isolated as pale yellow oil (5.7 mg, 54% yield) : TLC R_f = 0.3 (*n*-hexane/EtOAc = 1/2, v/v), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56-7.30 (m, 10H), 5.46 (s, 1H), 5.19 (d, *J* = 5.9 Hz, 1H), 4.95-4.92 (m, 1H), 4.50 (d, *J* = 5.9Hz, 1H), 3.70-3.64 (m, 1H), 3.54-3.49 (m, 1H), 2.18-1.95 (m, 3H), 1.76-1.71 (m, 1H); ^{13}C NMR (100 MHz,$CDCl_3$) δ 172.9, 158.7, 139.8, 136.4, 130.9, 129.3, 128.8, 128.6, 127.8, 126.5, 88.3, 58.6, 56.6, 52.1, 28.1, 25.2; IR (ATR) ν 3284, 1754, 1621, 1576, 1495, 1395, 1227, 1068, 1036, 975 cm^{-1}; HRMS (ESI-TOF) [M + Na]$^+$ calcd for $C_{20}H_{20}N_2NaO_3^+$ m/z 359.1372, found 359.1364.



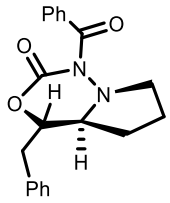
(5*R*)-5-((*S*)-1-benzoylpyrrolidin-2-yl)-4-(4-methoxyphenyl)oxazolidin-2-one (5l)

Prepared according to the general procedure A using **1l** (64.0 mg, 0.17 mmol), and isolated as pale yellow oil (9.4 mg, 15% yield) : TLC R_f = 0.3 (*n*-hexane/EtOAc = 1/2, v/v), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 6.9 Hz, 2H), 7.46-7.41 (m, 5H), 6.91 (d, *J* = 8.7 Hz, 2H), 5.33 (s, 1H), 5.14 (d, *J* = 6.0 Hz, 1H), 4.94-4.91 (m, 1H), 4.50 (d, *J* = 6.0 Hz, 1H), 3.80 (s, 3H), 3.72-3.65 (m, 1H), 3.55-3.48 (m, 1H), 2.18-1.97 (m, 3H), 1.78-1.71 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.8, 160.0, 158.7, 136.4, 131.6, 130.8, 128.6, 127.9, 114.6, 88.6, 58.1, 56.4, 55.5, 52.0, 28.1, 25.2; IR (ATR) ν 3277, 2954, 2363, 1758, 1614, 1513, 1403, 1247, 1029, 654 cm^{-1}; HRMS (ESI-TOF) [M + Na]$^+$ calcd for $C_{21}H_{22}N_2NaO_4^+$ m/z 389.1477, found 389.1476.

3. Characterization of amide insertion products

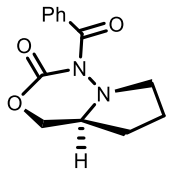
General procedure B for the Rh-catalyzed amide insertion reaction

To a pre-dried test tube were added carbamate substrate (0.2 mmol), $PhI(OAc)_2$ (0.28 mmol, 1.4 eq, 90.2 mg), MgO (0.46 mmol, 2.3 eq, 18.5 mg), and $Rh_2(esp\text{-}OMe)_2(acetone)_2$[1](4 μmol, 2 mol%, 3.7 mg), and the tube was filled with argon gas. Then $PhCF_3$ (0.05 M, 4 mL) was added via a syringe at room temperature, and the reaction mixture was stirred for 1-2 h at 80 °C. After complete consumption of the starting material, the reaction mixture was concentrated under reduced pressure. The obtained crude mixture was purified by flash chromatography on silica gel (*n*-hexane/EtOAc) to afford amide insertion product.



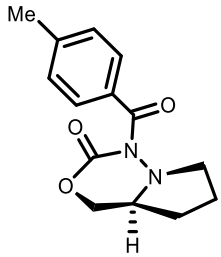
(4*S*)-1-benzoyl-4-benzyltetrahydro-4*H*-pyrrolo[1,2-*d*][1,3,4]oxadiazin-2(1*H*)-one (2a)

Prepared according to the general procedure B using **1a** (67.7 mg, 0.2 mmol), and isolated as yellow oil (26.6 mg, 54% yield) : TLC R_f = 0.5 (*n*-hexane/EtOAc = 1/2, v/v), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49-7.45 (m, 3H), 7.38-7.26 (m, 7H), 4.61 (dt, *J* = 8.4, 5.6 Hz, 1H), 3.66-3.61 (m, 1H), 3.55-3.51 (m, 1H), 3.12 (dd, *J* = 14.2, 5.6 Hz, 1H), 3.01 (dd, *J* = 14.2, 5.6 Hz, 1H), 2.85 (dd, *J* = 8.8, 8.8 Hz, 1H), 2.16 (ddd, *J* = 20.9, 7.8, 7.8 Hz, 1H), 2.03-1.95 (m, 2H), 1.69-1.61 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 149.5, 135.2, 134.7, 132.1, 130.0, 128.9, 128.4, 128.2, 127.4, 80.4, 58.1, 52.4, 39.3, 26.3, 20.8; IR (ATR) ν 2952, 1729, 1699, 1600, 1496, 1449, 1375, 1282, 1229, 1177, 1131, 1036, 1000, 698 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{20}H_{20}N_2NaO_3^+$ m/z 359.1372, found 359.1361.



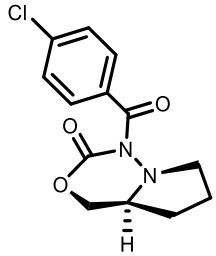
1-benzoyltetrahydro-4*H*-pyrrolo[1,2-*d*][1,3,4]oxadiazin-2(1*H*)-one (2b)

Prepared according to the general procedure A using **1b** (49.6 mg, 0.2 mmol), and isolated as white powder (4.9 mg, 10% yield): ^{1}H and ^{13}C NMR, IR, and MS data were identical to those reported.[1]



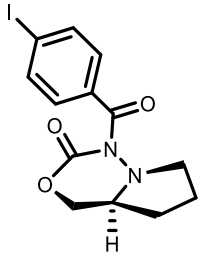
1-(4-methylbenzoyl)tetrahydro-4*H*-pyrrolo[1,2-*d*][1,3,4]oxadiazin-2(1*H*)-one (2c)

Prepared according to the general procedure A using **1c** (52.5 mg, 0.2 mmol), and isolated as pale brown powder (5.2 mg, 10% yield): ^{1}H and ^{13}C NMR, IR, and MS data were identical to those reported.[1]



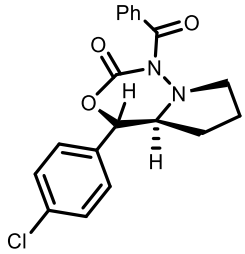
1-(4-chlorobenzoyl)tetrahydro-4*H*-pyrrolo[1,2-*d*][1,3,4]oxadiazin-2(1*H*)-one (2d)

Prepared according to the general procedure A using **1d** (56.5 mg, 0.2 mmol), and isolated as white powder (4.5 mg, 8% yield): ^{1}H and ^{13}C NMR, IR, and MS data were identical to those reported.[1]



1-(4-iodobenzoyl)tetrahydro-4*H*-pyrrolo[1,2-*d*][1,3,4]oxadiazin-2(1*H*)-one (2e)

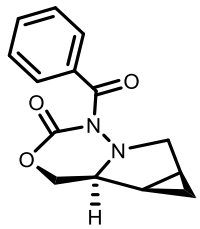
Prepared according to the general procedure A using **1e** (74.8 mg, 0.2 mmol), and isolated as white powder (5.2 mg, 7% yield) : TLC R_f = 0.5 (*n*-hexane/EtOAc = 1/2, v/v), mp: 147-149 ºC, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 8.3 Hz, 2H), 4.43 (dd, *J* = 11.4, 4.5 Hz, 1H), 4.34 (dd, *J* = 11.4, 2.4 Hz, 1H), 3.96-3.95 (m, 1H), 3.75-3.71 (m, 1H), 2.76-2.72 (m, 1H), 2.17-2.15 (m, 1H), 1.98-1.96 (m, 1H), 1.92-1.85 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.5, 153.9, 137.7, 133.5, 129.8, 99.5, 69.3, 57.5, 56.3, 28.1, 22.6; IR (ATR) ν 2949, 1755, 1698, 1583, 1479, 1390, 1288, 1215, 1131, 1058, 1029, 1006, 957 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{13}H_{13}IN_2NaO_3^+$ m/z 394.9869, found 394.9864.



(4*S*)-1-benzoyl-4-(4-chlorophenyl)tetrahydro-4*H*-pyrrolo[1,2-*d*][1,3,4]oxadiazin-2(1*H*)-one (2o)

Prepared according to the general procedure B using **1o** (71.8 mg, 0.2 mmol) and $Rh_2(OAc)_2$ instead of $Rh_2(esp\text{-}OMe)_2(acetone)_2$, and isolated as yellow oil (6.3 mg, 9% yield) : TLC R_f = 0.5 (*n*-hexane/EtOAc = 1/1, v/v), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.51-7.36 (m, 9H), 5.34 (d, *J* = 7.6 Hz, 1H), 3.87-3.77 (m, 2H), 2.98 (dd,

J = 18.0, 7.6 Hz, 1H), 2.17-2.04 (m, 3H), 1.77-1.74 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.2, 150.1, 135.7, 134.6, 134.2, 132.3, 129.4, 129.0, 128.4, 128.3, 79.8, 60.2, 53.5, 25.6, 20.9; IR (ATR) ν 2924, 1703, 1492, 1449, 1232, 1090, 1014, 827, 696, 665 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{19}H_{17}ClN_2NaO_3^+$ m/z 379.0825, found 379.0822.



(4b*R*,5a*S*)-1-benzoylhexahydrocyclopropa[3,4]pyrrolo[1,2-*d*][1,3,4]oxadiazin-2(1*H*)-one (2p)

Prepared according to the general procedure A using **1p** (52.1 mg, 0.2 mmol), and isolated as colorless oil (5.0 mg, 10% yield) : TLC R_f = 0.7 (EtOAc), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 8.2, 1.4 Hz, 2H), 7.51-7.47 (m, 1H), 7.39 (dd, *J* = 8.2, 8.2 Hz, 2H), 4.48 (dd, *J* = 11.2, 5.6 Hz, 1H), 4.39 (dd, *J* = 11.2, 6.6 Hz, 1H), 3.79 (dd, *J* = 6.6, 5.6 Hz, 1H), 3.55 (d, *J* = 8.7 Hz, 1H), 3.01 (dd, *J* = 8.7, 4.4 Hz, 1H), 1.61-1.56 (m, 1H), 1.43-1.38 (m, 1H), 0.72 (dd, *J* = 8.7, 4.4 Hz, 1H), 0.65-0.60 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 151.1, 134.3, 132.2, 128.4, 128.2, 69.5, 56.7, 54.8, 17.5, 14.4, 8.1; IR (ATR) ν 2921, 1759, 1702, 1599, 1448, 1398, 1280, 1238, 1129, 1039, 987 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{14}H_{14}N_2NaO_3^+$ m/z 281.0902, found 281.0897.

4. Synthesis and characterization of substrates and catalysts

4-1. Synthesis and characterization of **1a** and **1i**

General procedure C for acylation of methyl prolinate hydrochloride

To a stirred solution of methyl prolinate hydrochloride, Et_3N (3 eq), and DMAP (10 mol%) in CH_2Cl_2 (0.2 M) was added acyl chloride (1 eq) at 0 °C, and the reaction mixture was stirred at room temperature (reaction time is given below). The reaction was quenched with saturated aqueous NH_4Cl, extracted with CH_2Cl_2, washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash chromatography on silica gel (conditions are given below).

General procedure D for benzylation

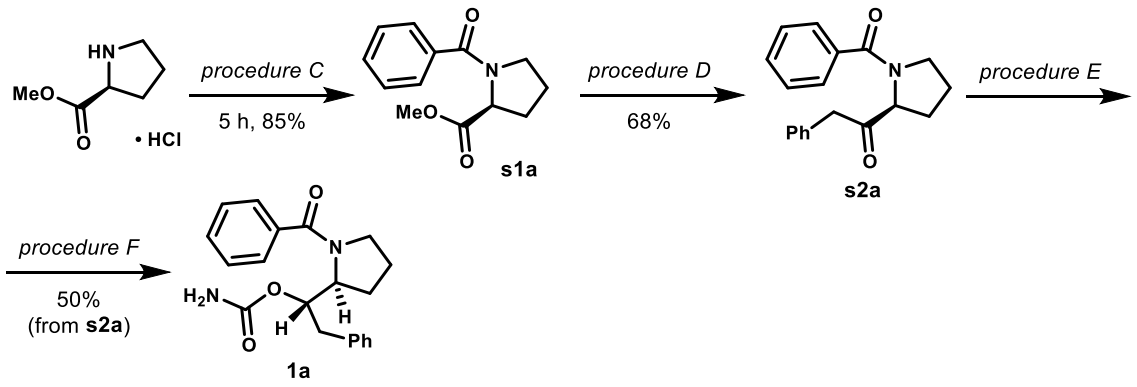
To a stirred solution of ester substrate in THF (0.1 M) was slowly added BnMgBr (0.9 M in THF) (5 eq) dropwise at -78 °C. After being stirred for 3 h, the reaction was quenched with 1N HCl, extracted with EtOAc, washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash chromatography on silica gel (conditions are given below).

General procedure E for reduction of ketones

To a stirred solution of ketone substrate in MeOH (0.04 M) was added $NaBH_4$ (1.5 eq) at 0 °C. After being stirred for 2 h, the reaction was quenched with saturated aqueous NH_4Cl, extracted with CH_2Cl_2, washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure.

General procedure F for carbamoylation of alcohols

To a stirred solution of alcohol substrate in CH_2Cl_2 (0.1 M) was added $Cl_3CCONCO$ (1.2 eq) at 0 °C. After being stirred for 2 h, the reaction mixture was concentrated under reduced pressure, and used for the next step without further purification. The solution of the crude residue and K_2CO_3 (0.2 eq) in MeOH (0.1 M) was stirred at room temperature for 3-7 h. The reaction was quenched with saturated aqueous NH_4Cl, extracted with CH_2Cl_2, washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash chromatography on silica gel (conditions are given below) to afford carbamate compound.



Methyl benzoyl-*L*-prolinate (s1a)

Prepared according to the general procedure C (reaction time 5 h) using *L*-methyl prolinate hydrochloride (5.0 g, 30 mmol) and benzoyl chloride (3.2 mL, 1 eq, 30 mmol) in 85% yield (6.0 g) (column condition; *n*-hexane/EtOAc, 1/1).

^1H and ^{13}C NMR, IR, and MS were identical to those reported.[2]

(*S*)-1-(1-benzoylpyrrolidin-2-yl)-2-phenylethan-1-one (s2a)

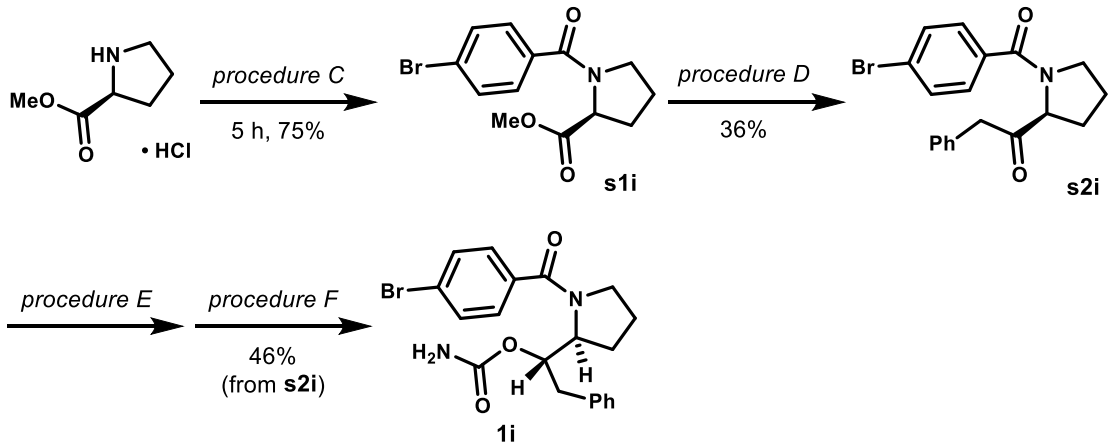
Prepared according to the general procedure D using **s1a** (933.1 mg, 4 mmol) as white powder in 68% yield (787.0 mg) (column condition; *n*-hexane/EtOAc, 2/1) : TLC R_f = 0.3 (*n*-hexane/EtOAc = 1/1, v/v), mp: 89-91 ºC, ^1H NMR (400 MHz, $CDCl_3$) (mixture of rotamers) δ 7.54 (dd, *J* = 7.3, 0.9 Hz, 1.8H), 7.43-7.20 (m, 8.0H), 6.83 (s, 0.2H), 4.82 (t, *J* = 5.9 Hz, 0.9H), 4.53 (d, *J* = 9.1 Hz, 0.1H), 3.94 (s, 1.8H), 3.75 (s, 0.2H), 3.59-3.48 (m, 1.8H), 3.35 (d, *J* = 16.0 Hz, 0.1H), 3.24 (d,

J = 16.0 Hz, 0.1H), 2.13-1.74 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) (major rotamer) δ 205.6, 168.6, 135.4, 133.4, 129.6, 129.2, 127.9, 127.6, 126.7, 126.2, 64.2, 49.6, 46.5, 28.0, 24.9; IR (ATR) ν 1720, 1621, 1574, 1495, 1446, 1406, 1060, 1025, 790, 697 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{19}H_{19}NNaO_2^+$ m/z 316.1314, found 316.1317.

(*S*)-1-((*S*)-1-benzoylpyrrolidin-2-yl)-2-phenylethyl carbamate (1a)

Compound **s2a** (787.0 mg, 2.7 mmol) was reduced to alcohol substrate according to the general procedure E, which was used for the next step without purification by column chromatography.

The crude alcohol was converted to **1a** according to the general procedure F, and isolated as white amorphous in 50% yield (3 steps, 456.9 mg) (column condition; *n*-hexane/EtOAc, 1.5/1): TLC R_f = 0.2 (*n*-hexane/EtOAc = 1/2, v/v), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 6.9 Hz, 2H), 7.42-7.35 (m, 3H), 7.27-7.21 (m, 5H), 5.06 (dd, *J* = 12.3, 7.8 Hz, 1H), 4.78-4.65 (m, 3H), 3.59-3.53 (m, 1H), 3.35 (br s, 1H), 2.97 (d, *J* = 7.8 Hz, 2H), 2.05-1.78 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 156.8, 137.6, 137.0, 130.1, 129.3, 128.4, 128.2, 127.6, 126.5, 76.4, 58.5, 49.9, 38.1, 27.3, 24.8; IR (ATR) ν 3341, 2970, 1713, 1615, 1389, 1321, 1075, 1053, 908, 724, 697 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{20}H_{22}N_2NaO_3^+$ m/z 361.1528, found 361.1527.



Methyl (4-bromobenzoyl)-*L*-prolinate (s1i)

Prepared according to the general procedure C (reaction time 5 h) using methyl prolinate hydrochloride (828.4 mg, 5 mmol) and 4-bromobenzoyl chloride (1.1 g,

1 eq, 5 mmol) in 75% yield (1.2 g, 3.7 mmol) (column condition; *n*-hexane/EtOAc, 1/1).

^{1}H and ^{13}C NMR, IR, and MS were identical to those reported.[3]

(*S*)-1-(1-(4-bromobenzoyl)pyrrolidin-2-yl)-2-phenylethan-1-one (s2i)

Prepared according to the general procedure D using **s1i** (1.1 g, 3.5 mmol) as colorless oil in 36% yield (469.0 mg) (column condition; gradient elution: *n*-hexane/EtOAc, 6/1 → 1/1): TLC R_f = 0.2 (*n*-hexane/EtOAc = 1/1, v/v), ^{1}H NMR (400 MHz, $CDCl_3$) (major rotamer) δ 7.53 (d, *J* = 8.6 Hz, 2H), 7.42 (d, *J* = 8.6 Hz, 2H), 7.34-7.24 (m, 5H), 4.81 (dd, *J* = 7.1, 7.1 Hz, 1H), 3.93 (s, 2H), 3.57-3.44 (m, 2H), 2.07-1.89 (m, 2H), 1.87-1.72 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) (major rotamer) δ 206.3, 168.5, 134.8, 133.7, 131.6, 129.8, 129.1, 128.7, 127.2, 124.8, 64.5, 50.3, 48.0, 28.8, 25.7; IR (ATR) ν 2973.7, 1719.2, 1621.8, 1495.5, 1412.6, 1177.3, 1066.4, 1010.5, 910.2, 836.9 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{19}H_{18}BrNNaO_2^+$ m/z 394.0419, found 394.0432.

(*S*)-1-((*S*)-1-(4-bromobenzoyl)pyrrolidin-2-yl)-2-phenylethyl carbamate (1i)

Compound **s2i** (362.8 mg, 1.0 mmol) was reduced to alcohol substrate according to the general procedure E, which was used for the next step without purification by column chromatography.

The crude alcohol was converted to **1i** according to the general procedure F, and isolated as white amorphous in 46% yield (3 steps, 192.0 mg) (column condition; gradient elution: *n*-hexane/EtOAc, 2/1 → 1/1): TLC R_f = 0.3 (*n*-hexane/EtOAc = 1/2, v/v), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.2 Hz, 2H), 7.38 (d, *J* = 8.2 Hz, 2H), 7.29-7.21 (m, 5H), 5.04 (dd, *J* = 12.8, 8.0 Hz, 1H), 4.75-4.61 (m, 3H), 3.58-3.51 (m, 1H), 3.32 (br s, 1H), 2.97 (d, *J* = 8.0 Hz, 2H), 2.06-2.02 (m, 2H), 1.80-1.79 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 156.8, 137.5, 135.8, 131.6, 129.4, 129.3, 128.5, 126.6, 124.6, 76.3, 58.8, 49.9, 38.2, 27.4, 25.0; IR (ATR) ν 3339, 2960, 1714, 1620, 1416, 1321, 1068, 1011, 910, 837 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{20}H_{21}BrN_2NaO_3^+$ m/z 439.0633, found 439.0640.

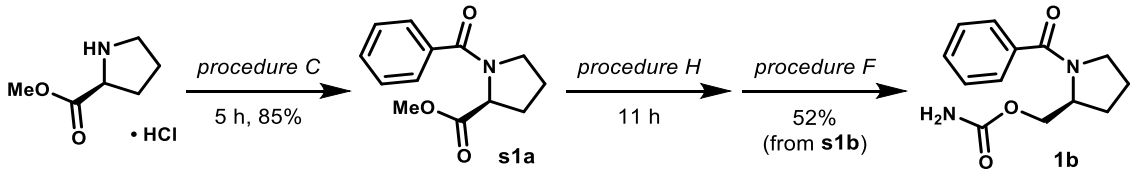
4-2. Synthesis and characterization of **1b-1h**

General procedure G for acylation of methyl prolinate hydrochloride

To a stirred solution of carboxylic acid, methyl prolinate hydrochloride (1.2 eq), and Et_3N (1.5 eq) in CH_2Cl_2 (0.2 M) were added EDCI hydrochloride (1.5 eq) and HOBt (1.3 eq) at 0 °C. Et_3N (1.2 eq) was added dropwise, and the stirring was continued for 2 h at 0 °C. After being stirred at room temperature (reaction time is given below), the reaction was quenched with H_2O, extracted with CH_2Cl_2, washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash chromatography on silica gel (conditions are given below).

General procedure H for reduction of esters

To a stirred solution of ester substrate in THF (0.2 M) was added $LiBH_4$ (2.5 eq) at 0 °C. After being stirred at room temperature (reaction time is given below), the reaction was quenched with saturated aqueous NH_4Cl, extracted with EtOAc, washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure.



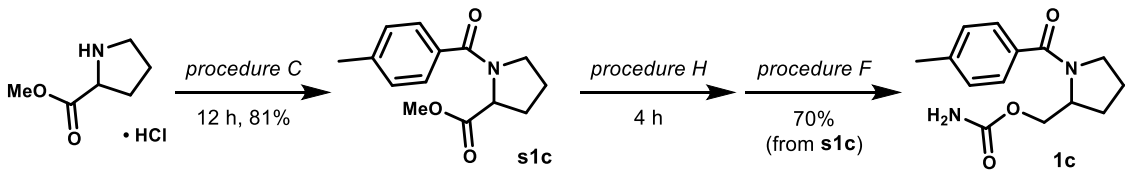
(*S*)-(1-Benzoylpyrrolidin-2-yl)methyl carbamate (1b)

Compound **s1a** (373.4 mg, 1.6 mmol) was reduced to alcohol substrate according to the general procedure H (reaction time 11 h), which was used for the next step without purification by column chromatography.

The crude alcohol was converted to **1b** according to the general procedure F, and isolated in 52% yield (3 steps, 206.6 mg) (column condition; gradient elution: *n*-hexane/EtOAc, 1/2 → EtOAc).

^1H and ^{13}C NMR, IR, and MS were identical to those reported.[1]

The enantiomeric excess was determined to be >99% by analytical chiral HPLC. Retention time: 12.3 min (major isomer), 15.8 min (minor isomer) (AS-H column, 85/15 *n*-hexane/*i*-PrOH, 1 mL/min, 216 nm).



Methyl (4-methylbenzoyl)prolinate (s1c)

Prepared according to the general procedure C (reaction time 12 h) using methyl prolinate hydrochloride (828.4 mg, 5 mmol) and 4-methylbenzoyl chloride (0.66 mL, 1 eq, 5 mmol) in 81% yield (1.0 g, 4.1 mmol) (column condition; *n*-hexane/EtOAc, 1/1).

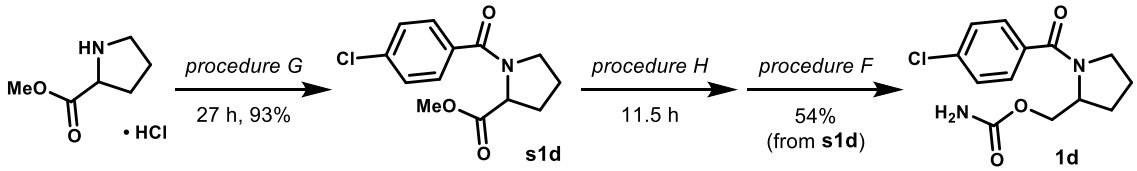
^{1}H and ^{13}C NMR, IR, and MS were identical to those reported.[1]

(1-(4-Methylbenzoyl)pyrrolidin-2-yl)methyl carbamate (1c)

Compound **s1c** (670.7 mg, 2.7 mmol) was reduced to alcohol substrate according to the general procedure H (reaction time 4 h), which was used for the next step without purification by column chromatography.

The crude alcohol was converted to **1c** according to the general procedure F, and isolated in 70% yield (3 steps, 559.4 mg) (column condition; gradient elution: *n*-hexane/EtOAc, 1/2 → EtOAc).

^{1}H and ^{13}C NMR, IR, and MS were identical to those reported.[1]



Methyl (4-chlorobenzoyl)prolinate (s1d)

Prepared according to the general procedure G (reaction time, 27 h) using 4-chlorobenzoic acid (782.9 mg, 5.0 mmol) and methyl prolinate hydrochloride (993.7 mg, 1.2 eq, 6.0 mmol) in 93% yield (1.3 g) (column condition; *n*-hexane/EtOAc, 1/1).

^{1}H and ^{13}C NMR, IR, and MS were identical to those reported.[4]

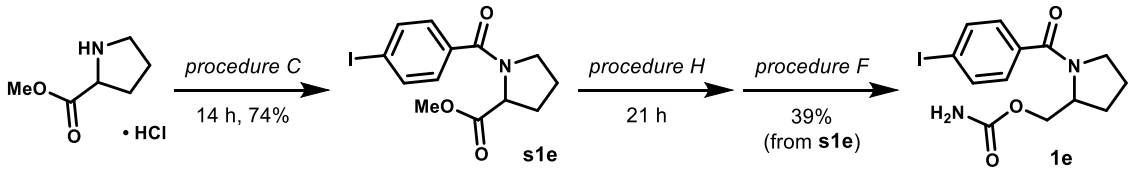
(1-(4-Chlorobenzoyl)pyrrolidin-2-yl)methyl carbamate (1d)

Compound **s1d** (863.1 mg, 3.0 mmol) was reduced to the corresponding alcohol

according to the general procedure H (reaction time 11.5 h), which was used for the next step without purification by column chromatography.

The crude alcohol was converted to **1d** according to the general procedure F, and isolated in 54% yield (3 steps, 491.8 mg) (column condition; gradient elution: *n*-hexane/EtOAc, 1/2 → EtOAc).

^{1}H and ^{13}C NMR, IR, and MS were identical to those reported.[1]



Methyl (4-iodobenzoyl)prolinate (s1e)

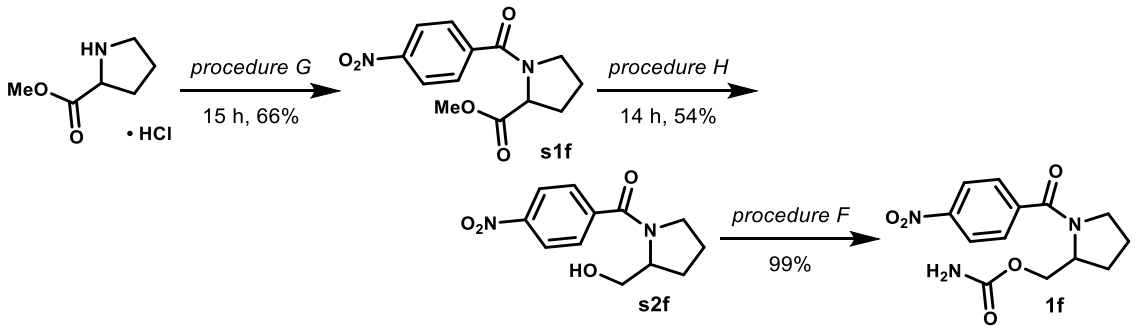
Prepared according to the general procedure C (reaction time 14 h) using methyl prolinate hydrochloride (828.4 mg, 5 mmol) and 4-iodobenzoyl chloride (1.3 g, 1 eq, 5 mmol) in 74% yield (1.3 g, 3.7 mmol) (column condition; *n*-hexane/EtOAc, 1/1).

^{1}H and ^{13}C NMR, IR, and MS were identical to those reported.[5]

(1-(4-iodobenzoyl)pyrrolidin-2-yl)methyl carbamate (1e)

Compound **s1e** (1.3 g, 3.7 mmol) was reduced to alcohol substrate according to the general procedure H (reaction time 21 h), which was used for the next step without purification by column chromatography.

The crude alcohol was converted to **1e** according to the general procedure F, and isolated as white powder in 39% yield (3 steps, 539.9 mg) (column condition; EtOAc): TLC R_f = 0.2 (*n*-hexane/EtOAc = 1/2, v/v), mp: 140-142 ºC, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.0 Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 4.81 (br s, 2H), 4.57 (br s, 1H), 4.30 (br s, 2H), 3.47-3.40 (m, 2H), 2.12-1.84 (m, 4H); ^{13}C NMR (100 MHz, CD_3OD) δ 171.4, 159.7, 138.8, 137.6, 130.0, 97.2, 64.9, 57.9, 51.6, 28.3, 25.8; IR (ATR) ν 3328, 2949, 1715, 1614, 1423, 1328, 1006, 829, 752, 627 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{13}H_{15}IN_2NaO_3^+$ m/z 397.0025, found 397.0027.



Methyl (4-nitrobenzoyl)prolinate (s1f)

Prepared according to the general procedure G (reaction time, 15 h) using 4-nitrobenzoic acid (668.5 mg, 4.0 mmol) and methyl prolinate hydrochloride (797.3 mg, 1.2 eq, 4.8 mmol) in 66% yield (731.5 mg) after recrystallization from EtOAc instead of column chromatography.

^{1}H and ^{13}C NMR, IR, and MS were identical to those reported.[6]

(2-(Hydroxymethyl)pyrrolidin-1-yl)(4-nitrophenyl)methanone (s2f)

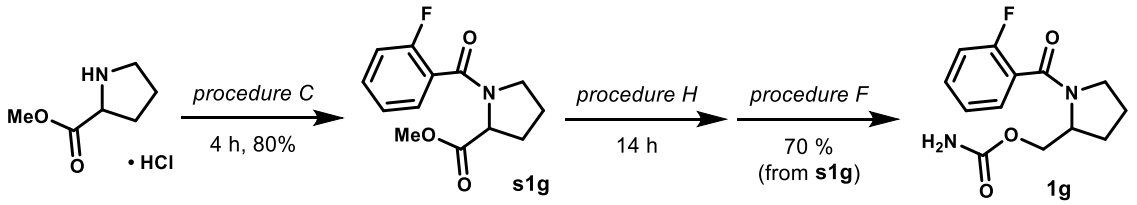
Prepared according to the general procedure H (reaction time 14 h) using **s1f** (556.5 mg, 2.0 mmol) in 54% yield (270.3 mg) (column condition; gradient elution: EtOAc → EtOAc/MeOH, 10/1).

^{1}H and ^{13}C NMR, IR, and MS were identical to those reported.[7]

(1-(4-Nitrobenzoyl)pyrrolidin-2-yl)methyl carbamate (1f)

Prepared according to the general procedure F using **s2f** (270.3 mg, 1.1 mmol), and isolated in 99% yield (2 steps, 314.2 mg) (column condition; gradient elution: EtOAc → EtOAc/MeOH, 10/1).

^{1}H and ^{13}C NMR, IR, and MS were identical to those reported.[1]



Methyl (2-fluorobenzoyl)prolinate (s1g)

Prepared according to the general procedure C (reaction time 4 h) using methyl

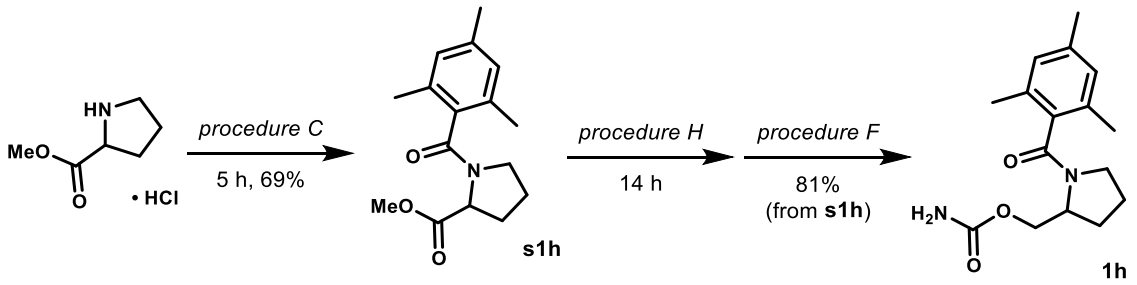
prolinate hydrochloride (828.1 mg, 5 mmol) and 2-fluorobenzoyl chloride (0.60 mL, 1 eq, 5 mmol) in 80% yield (993.0 mg, 4.0 mmol) (column condition; *n*-hexane/EtOAc, 1/1).

^{1}H and ^{13}C NMR, IR, and MS were identical to those reported.[4]

(1-(2-fluorobenzoyl)pyrrolidin-2-yl)methyl carbamate (1g)

Compound **s1g** (993.0 mg, 4.0 mmol) was reduced to alcohol substrate according to the general procedure H (reaction time 14 h), which was used for the next step without purification by column chromatography.

The crude alcohol was converted to **1g** according to the general procedure F, and isolated as white powder in 70% yield (3 steps, 745.6 mg) (column condition; gradient elution: *n*-hexane/EtOAc, 1/2 →EtOAc): TLC R_f = 0.3 (EtOAc), mp: 97-99 ºC, ^{1}H NMR (400 MHz, $CDCl_3$) (mixture of rotamers) δ 7.43-7.36 (m, 2H), 7.24-7.17 (m, 1H), 7.10 (dd, *J* = 17.2, 8.4 Hz, 1H), 4.94-4.77 (m, 2H), 4.54 (td, *J* = 8.9, 4.4 Hz, 0.8H), 4.36-4.29 (m, 1.6H), 4.03-3.98 (m, 0.2H), 3.87-3.76 (m, 0.6H), 3.66-3.61 (m, 0.2H), 3.42-3.27 (m, 1.6H), 2.15-1.78 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) (major rotamer) δ 165.6, 158.3 (d, *J* = 247.1 Hz), 157.1, 131.4 (d, *J* = 8.7 Hz), 129.0 (d, *J* = 2.9 Hz), 125.5 (d, *J* = 18.6 Hz), 124.6 (d, *J* = 2.9 Hz), 115.9 (d, *J* = 21.6 Hz), 64.4, 55.9, 48.5, 27.6, 24.3; IR (ATR) ν 3345, 2971, 1714, 1613, 1455, 1400, 1326, 1224, 1068, 908, 755, 725, 645.072 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{13}H_{15}FN_2NaO_3^+$ m/z 289.0964, found 289.0959.



Methyl (2,4,6-trimethylbenzoyl)prolinate (s1h)

Prepared according to the general procedure C (reaction time 5 h) using methyl

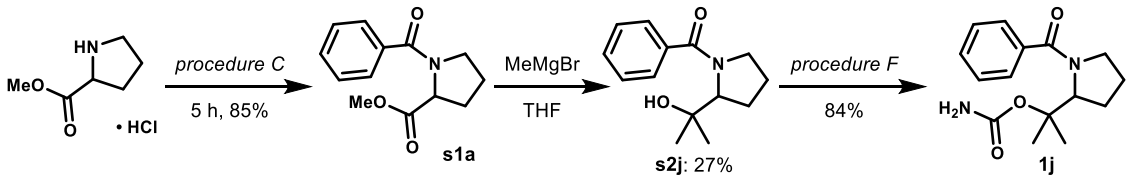
prolinate hydrochloride (828.1 mg, 5 mmol) and 2,4,6-trimethylbenzoyl chloride (0.83 mL, 1 eq, 5 mmol) in 69% yield (950.0 mg, 3.4 mmol) as colorless oil (column condition; *n*-hexane/EtOAc, 1/1): TLC R_f = 0.3 (*n*-hexane/EtOAc = 1/1, v/v), ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84 (d, *J* = 11.0 Hz, 2H), 4.69 (dd, *J* = 8.8, 4.6 Hz, 1H), 3.79 (s, 3H), 3.28-3.22 (m, 1H), 3.15-3.09 (m, 1H), 2.33-2.16 (m, 10H), 2.08-1.95 (m, 2H), 1.90-1.85 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 170.2, 138.2, 134.2, 134.2, 132.8, 128.5, 128.1, 57.9, 52.2, 47.9, 29.8, 24.8, 21.5, 18.9, 18.6; IR (ATR) ν 2951, 1743, 1632, 1434, 1402, 1278, 1170, 1090, 1036, 850 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{16}H_{21}NNaO_3^+$ m/z 298.1419, found 298.1420.

(1-(2,4,6-trimethylbenzoyl)pyrrolidin-2-yl)methyl carbamate (1h)

Compound **s1h** (950.0 mg, 3.4 mmol) was reduced to alcohol substrate according to the general procedure H (reaction time 14 h), which was used for the next step without purification by column chromatography.

The crude alcohol was converted to **1h** according to the general procedure F, and isolated as white powder in 81% yield (3 steps, 804.3 mg) (column condition; *n*-hexane/EtOAc, 1/2): TLC R_f = 0.2 (*n*-hexane/EtOAc = 1/2, v/v), mp: 145-147 ºC, ^{1}H NMR (400 MHz, $CDCl_3$) (mixture of rotamers) δ 6.85-6.82 (m, 2H), 4.89-4.75 (m, 2H), 4.55 (td, *J* = 8.4, 5.2 Hz, 0.8H), 4.34-4.33 (m, 1.7H), 3.86-3.83 (m, 0.2H), 3.78-3.59 (m, 0.6H), 3.05 (ddd, *J* = 6.7, 6.7, 2.3 Hz, 1.7H), 2.25-2.15 (m, 9H), 2.07-1.75 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) (major rotamer) δ 170.4, 157.1, 138.0, 135.0, 133.1, 132.7, 128.3, 128.2, 64.4, 55.2, 48.0, 27.7, 24.2, 21.1, 19.0, 18.6; IR (ATR) ν 3345, 2957, 1712, 1606, 1440, 1398, 1324, 1062, 911, 850, 727 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{16}H_{22}N_2NaO_3^+$ m/z 313.1528, found 313.1533.

4-3. Synthesis and characterization of **1j-1p**

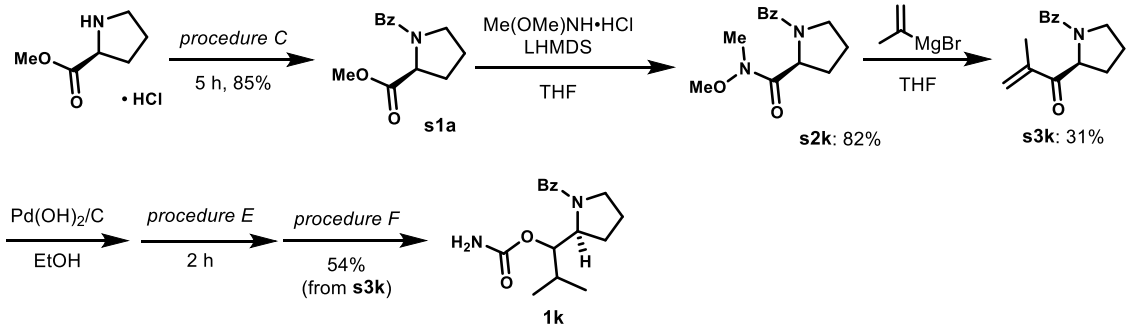


(2-(2-hydroxypropan-2-yl)pyrrolidin-1-yl)(phenyl)methanone (s2j)

To a stirred solution of **s1a** (233.3 mg, 1 mmol) in THF (7 mL, 0.1 M) was slowly added MeMgBr (1.0 M in THF) (3 mL, 3 eq, 3 mmol) dropwise at -78 °C. After being stirred for 5 h, the reaction was quenched with 1N HCl, extracted with EtOAc, washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash chromatography on silica gel (column condition; *n*-hexane/EtOAc, 1/1) to afford **s2j** in 27% yield (62.2 mg). ^{1}H and ^{13}C NMR, IR, and MS were identical to those reported.[8]

2-(1-benzoylpyrrolidin-2-yl)propan-2-yl carbamate (1j)

Compound **s2j** (233.3 mg, 1.0 mmol) was converted to **1j** according to the general procedure F, and isolated as white powder in 84% yield (2 steps, 231.5 mg) (column condition; gradient elution: *n*-hexane/EtOAc, 1/1 → 1/2): TLC R_f = 0.3 (*n*-hexane/EtOAc = 1/2, v/v), mp: 147-149 ºC, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 6.9 Hz, 2H), 7.42-7.34 (m, 3H), 4.82 (br s, 1H), 4.65 (br s, 2H), 3.49-3.41 (m, 2H), 2.06-1.84 (m, 3H), 1.65-1.53 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 156.2, 137.1, 130.4, 128.3, 127.9, 84.9, 62.7, 51.8, 25.7, 23.5, 23.5; IR (ATR) ν 3347, 2951, 1708, 1613, 1364, 1147, 1078, 1025, 789, 699, 659 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{15}H_{20}N_2NaO_3^+$ m/z 299.1371, found 299.1369.



(*S*)-1-benzoyl-*N*-methoxy-*N*-methylpyrrolidine-2-carboxamide (s2k)

To a stirred solution of **s1a** (1.9 g, 8.0 mmol) and Me(OMe)NH・HCl (2.3 g, 3 eq, 24 mmol) in THF (61.5 mL, 0.1 M) was slowly added LHMDS (1.3 M in THF) (18.5 mL, 3 eq, 24 mmol) dropwise at -10 °C, and the stirring was continued for 15 min at -10 °C. After being stirred for 5 h at room temperature, the reaction was quenched with saturated aqueous NH_4Cl, extracted with CH_2Cl_2, washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash chromatography on silica gel (column condition; gradient elution: *n*-hexane/EtOAc, 1/2 → EtOAc) to afford **s2k** as pale yellow oil in 82% yield (1.7 g): TLC R_f = 0.2 (EtOAc), ^{1}H NMR (400 MHz, $CDCl_3$) (mixture of rotamers) δ 7.58-7.55 (m, 1.6H), 7.41-7.33 (m, 3.4H), 5.09 (dd, *J* = 6.4, 6.8 Hz, 0.8H), 4.52 (d, *J* = 8.2 Hz, 0.2H), 3.87 (s, 2.4H), 3.83-3.78 (m, 0.4H), 3.70-3.64 (m, 0.8H), 3.56-3.50 (m, 0.8H), 3.23 (s, 2.4H), 3.10 (s, 0.6H), 3.01 (s, 0.6H), 2.33-2.24 (m, 0.8H), 2.21-2.16 (m, 0.2H), 2.09-1.79 (m, 3.0H); ^{13}C NMR (100 MHz, $CDCl_3$) (mixture of rotamers) δ 172.5, 169.6, 137.8, 136.5, 130.1, 129.4, 128.4, 128.2, 127.4, 126.6, 61.4, 60.8, 59.7, 56.8, 50.3, 46.9, 32.2, 30.9, 29.2, 25.5, 22.6; IR (ATR) ν 3503, 2972, 1664, 1624, 1576, 1445, 1409, 1176, 997, 719, 701 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{14}H_{18}N_2NaO_3^+$ m/z 285.1215, found 285.1213.

(*S*)-1-(1-benzoylpyrrolidin-2-yl)-2-methylprop-2-en-1-one (s3k)

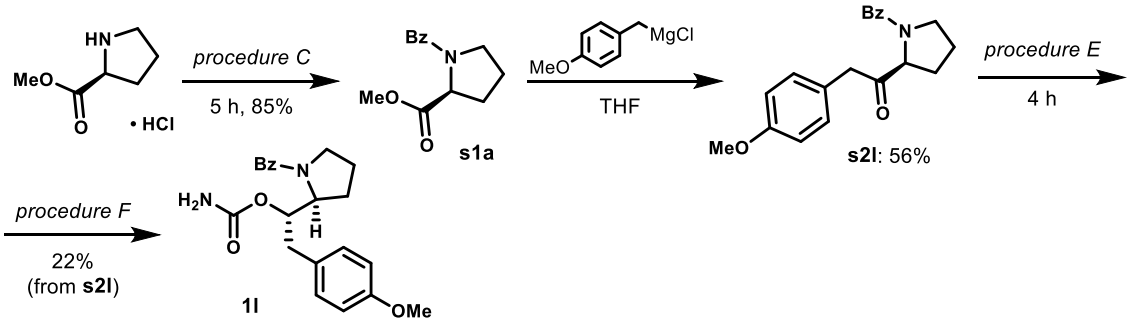
To a stirred solution of **s2k** (918.1 mg, 3.5 mmol) in THF (14 mL, 0.1 M) was slowly added isopropenylmagnesium bromide (0.5 M in THF) (21 mL, 3 eq, 10.5 mmol) at -10 °C. After being stirred for 3 h at -10 °C, the reaction was quenched with saturated aqueous NH_4Cl, extracted with EtOAc, washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash chromatography on silica gel (column condition: *n*-hexane/EtOAc, 1/1.5) to afford **s3k** as pale yellow oil in 31% yield (266.4 mg): TLC R_f = 0.5 (*n*-hexane/EtOAc = 1/2, v/v), ^{1}H NMR (400 MHz, $CDCl_3$) (major rotamer) δ 7.55 (dd, *J* = 7.5, 2.1 Hz, 2H), 7.40-7.36 (m, 3H), 6.09 (s, 1H), 5.87 (s, 1H), 5.44-5.39 (m, 1H), 3.67-3.50 (m, 2H) , 1.96-1.80 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) (major rotamer) δ 199.2, 169.3, 143.0, 136.5, 130.1, 128.3, 127.4, 125.4, 60.7, 50.2, 29.8, 25.5, 18.1; IR (ATR) ν 2975, 2372, 2350, 1682, 1624, 1575, 1446, 1414, 1072, 934 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{15}H_{17}NNaO_2^+$ m/z

266.1157, found 266.1149.

1-((*S*)-1-benzoylpyrrolidin-2-yl)-2-methylpropyl carbamate (1k)

To a stirred solution of **s3k** (266.4 mg, 1.1 mmol) in EtOH (2.2 mL, 0.5 M) was added 20% $Pd(OH)_2$ (26.6 mg, 10 %w/w). After being stirred under a hydrogen balloon for 3 h at room temperature, the Pd/C was removed by filtration through celite, washing with MeOH. The filtrate was concentrated under reduced pressure, which was used for the next step without purification by column chromatography. The crude mixture was reduced to alcohol substrate according to the general procedure E, which was used for the next step without purification by column chromatography.

The crude alcohol was converted to **1k** according to the general procedure F, and isolated as white amorphous in 54% yield (4 steps, 173.8 mg) (column condition: *n*-hexane/EtOAc, 1/1.5): TLC R_f = 0.3 (*n*-hexane/EtOAc = 1/2, v/v), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.3 Hz, 2H), 7.42-7.33 (m, 3H), 4.86-4.81 (m, 1H), 4.59 (dd, *J* = 9.1, 3.7 Hz, 1H), 3.60-3.53 (m, 1H), 3.35-3.29 (m, 1H), 2.03 -1.90 (m, 3H), 1.82-1.68 (m, 2H), 1.04 (d, *J* = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, CD_3OD) (major rotamer) δ 173.2, 160.1, 138.2, 131.4, 129.4, 128.4, 80.5, 58.2, 50.9, 30,7, 28.3, 25.3, 20.5, 16.8; IR (ATR) ν 3350, 2958, 1708, 1592, 1573, 1426, 1320, 1051, 782, 701 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{16}H_{22}N_2NaO_3^+$ m/z 313.1528, found 313.1519.



(*S*)-1-(1-benzoylpyrrolidin-2-yl)-2-(4-methoxyphenyl)ethan-1-one (s2l)

To a suspension of magnesium (303.8 mg, 6.3 eq, 12.5 mmol) in THF (17 mL, 0.4 M) was added dibromoethane (2 drops), and the stirring was continued for 15

min at room temperature. To the suspension was slowly added a solution of 4-methoxybenzyl chloride (1.4 mL, 5 eq, 10 mmol) in THF (8mL) at 0 °C. On completion of addition, the mixture was allowed to warm to room temperature. Stirring was continued for 2 h, and the reaction was then cooled to 0 °C.

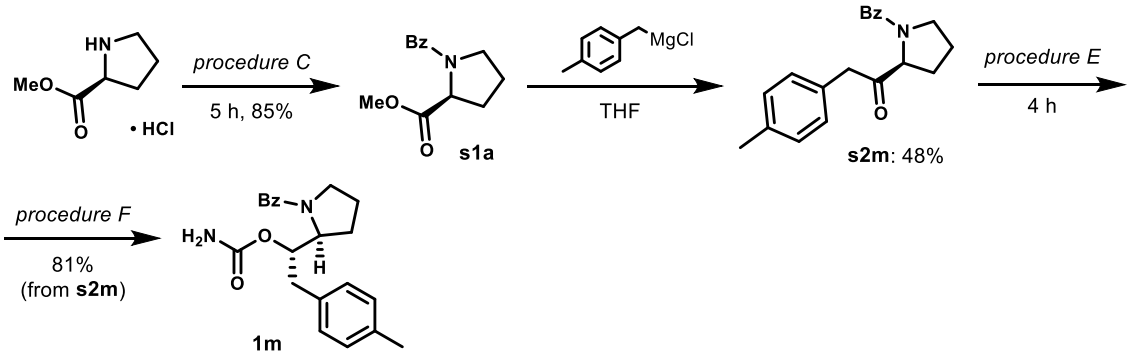
To a stirred solution of **s1a** (466.7 mg, 2.0 mmol) in THF (20 mL, 0.1 M) was slowly added the solution of (4-methoxybenzyl)magnesium chloride at -78 °C. After being stirred for 2 h at -78 °C, the reaction was quenched with 1N HCl, extracted with EtOAc, washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash chromatography on silica gel (column condition; gradient elution: *n*-hexane/EtOAc, 1.5/1 → 1/1) to afford **s2l** as colorless oil in 56% yield (362.6 mg): TLC R_f = 0.2 (*n*-hexane/EtOAc = 1/1, v/v), ^{1}H NMR (400 MHz, $CDCl_3$) (major rotamer) δ 7.58-7.55 (m, 2H), 7.45-7.36 (m, 3H), 7.19 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 4.82 (dd, *J* = 7.3, 7.3 Hz, 1H), 3.90 (s, 2H), 3.80-3.78 (m, 3H), 3.67-3.49 (m, 2H), 2.06-1.76 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) (major rotamer) δ 207.1, 169.7, 158.8, 136.1, 130.9, 130.4, 128.4, 127.4, 125.8, 114.2, 64.4, 55.4, 50.4, 47.1, 29.0, 25.7; IR (ATR) ν 2953, 1721, 1622, 1575, 1511, 1446, 1409, 1299, 1245, 1177, 1062, 1028 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{20}H_{21}NNaO_3^+$ m/z 346.1419, found 346.1427.

(*S*)-1-((*S*)-1-benzoylpyrrolidin-2-yl)-2-(4-methoxyphenyl)ethyl carbamate (1l)

Compound **s1l** (279.1 mg, 0.86 mmol) was reduced to alcohol substrate according to the general procedure E (reaction time 15 h), which was used for the next step without purification by column chromatography.

The crude alcohol was converted to **1h** according to the general procedure F, and isolated as white powder in 22% yield (3 steps, 70.2 mg) (column condition; *n*-hexane/EtOAc, 1/1.5): TLC R_f = 0.2 (*n*-hexane/EtOAc = 1/1, v/v), mp: 128-130 ºC, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 6.9 Hz, 2H), 7.42-7.34 (m, 3H), 7.18

(d, *J* = 8.0 Hz, 2H), 6.82 (d, *J* = 8.0 Hz, 2H), 5.01 (dd, *J* = 12.1, 8.0 Hz,1H), 4.74-4.67 (m, 3H), 3.77 (s, 3H), 3.58-3.52 (m, 1H), 3.34 (br s, 1H), 2.95-2.86 (m, 2H), 2.04-1.76 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 158.3, 156.9, 137.0, 130.3, 130.1, 129.6, 128.3, 127.6, 113.9, 76.6, 58.5, 55.3, 49.9, 37.3, 27.4, 24.9; IR (ATR) ν 3347, 2954, 1715, 1613, 1512, 1415, 1323, 1246, 1178, 1036, 727 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{21}H_{24}N_2NaO_4^+$ m/z 391.1634, found 391.1629.



(*S*)-1-(1-benzoylpyrrolidin-2-yl)-2-(*p*-tolyl)ethan-1-one (s2m)

To a suspension of magnesium (121.5 mg, 6.3 eq, 5.0 mmol) in THF (6.5 mL, 0.4 M) was added dibromoethane (2 drops), and the stirring was continued for 15 min at room temperature. To this was slowly added a solution of 4-methylbenzyl chloride (0.53 mL, 5 eq, 4.0 mmol) in THF (3.5 mL) at 0 °C. On completion of addition, the mixture was allowed to warm to room temperature. Stirring was continued for 1 h, and the reaction was then cooled to 0 °C.

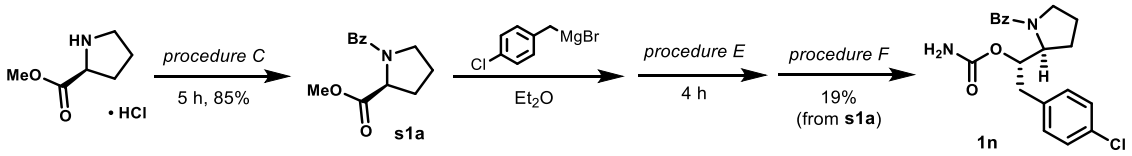
To a stirred solution of **s1a** (187.0 mg, 0.8 mmol) in THF (8 mL, 0.1 M) was slowly added the solution of (4-methylbenzyl)magnesium chloride at -78 °C. After being stirred for 2 h at -78 °C, the reaction was quenched with 1N HCl, extracted with EtOAc, washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash chromatography on silica gel (column condition; gradient elution: *n*-hexane/EtOAc, 2/1 → 1.5/1) to afford **s2m** as colorless oil in 48% yield (117.5 mg): TLC R_f = 0.4 (*n*-hexane/EtOAc = 1/1,

v/v), ^{1}H NMR (400 MHz, $CDCl_3$) (major rotamer) δ 7.54 (d, *J* = 7.8 Hz, 2H), 7.43-7.33 (m, 3H), 7.30-7.11 (m, 4H), 4.81 (dd, *J* = 7.1, 7.1 Hz, 1H), 3.90 (s, 2H), 3.59-3.46 (m, 2H), 2.32 (s, 3H), 2.06-1.73 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) (major rotamer) δ 206.9, 169.6, 136.7, 136.1, 130.7, 130.3, 129.7, 129.4 (2C), 128.3, 127.4, 64.5, 50.3, 47.6, 29.0, 25.7, 21.2; IR (ATR) ν 2976, 1719, 1623, 1575, 1514, 1446, 1410, 1214, 1062, 1024 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{20}H_{21}NNaO_2^+$ m/z 330.1470, found 330.1467.

(*S*)-1-((*S*)-1-benzoylpyrrolidin-2-yl)-2-(*p*-tolyl)ethyl carbamate (1m)

Compound **s2m** (117.5 mg, 0.38 mmol) was reduced to alcohol substrate according to the general procedure E (reaction time 16 h), which was used for the next step without purification by column chromatography.

The crude alcohol was converted to **1m** according to the general procedure F, and isolated as white amorphous in 81% yield (3 steps, 114.7 mg) (column condition; *n*-hexane/EtOAc, 1/1.5): TLC R_f = 0.4 (*n*-hexane/EtOAc = 1/2, v/v), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 6.4 Hz, 2H), 7.42-7.34 (m, 3H), 7.15 (d, *J* = 7.8 Hz, 2H), 7.08 (d, *J* = 7.8 Hz, 2H), 5.04 (dd, *J* = 12.1, 8.0 Hz, 1H), 4.77-4.66 (m, 3H), 3.58-3.52 (m, 1H), 3.34 (s, 1H), 2.94 (d, *J* = 8.0 Hz, 2H), 2.31 (s, 3H), 2.04-1.78 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 156.9, 137.1, 136.1, 134.4, 130.2, 129.2, 128.3, 127.7, 76.6, 58.6, 49.9, 37.8, 27.4, 25.0, 21.2; IR (ATR) ν 3342, 2954, 2923, 2855, 1722, 1623, 1575, 1448, 1415, 1323, 1051 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{21}H_{24}N_2NaO_3^+$ m/z 375.1685, found 375.1672.



(*S*)-1-((*S*)-1-benzoylpyrrolidin-2-yl)-2-(4-chlorophenyl)ethyl carbamate (1n)

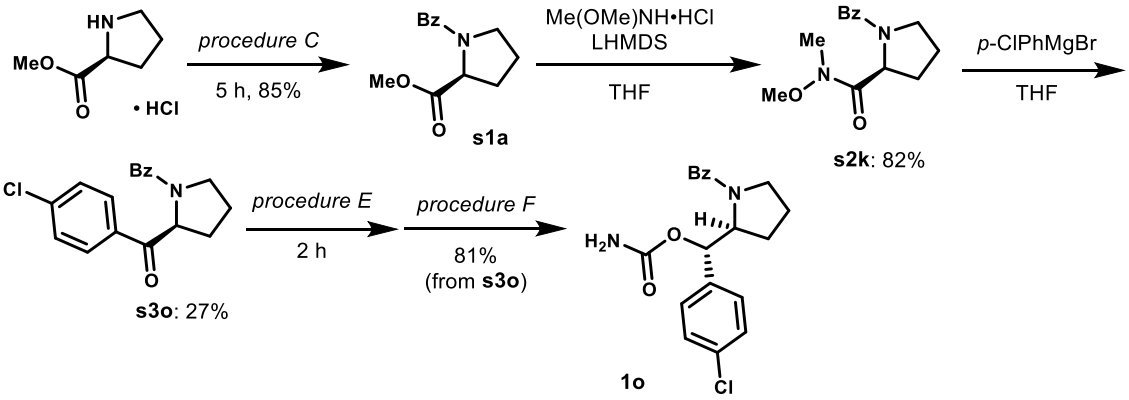
To a suspension of magnesium (267.3 mg, 3.7 eq, 11 mmol) in Et_2O (6.5 mL, 0.4

M) was added Iodine (1.4 mg, 1.9 mol %, 0.056 mmol), and the stirring was continued for 15 min at room temperature. To this was slowly added a solution of 4-chlorobenzyl bromide (2.1 g, 3.3 eq, 10 mmol) in Et_2O (18.5 mL) at room temperature. On completion of addition, the mixture was refluxed for 30 min, and the reaction was then cooled to 0 °C.

To a stirred solution of **s1a** (786.9 mg, 3.0 mmol) in Et_2O (30 mL, 0.1 M) was slowly added the solution of (4-chlorobenzyl)magnesium bromide at -78 °C. After being stirred for 2 h at 0 °C, the reaction was quenched with 1N HCl, extracted with EtOAc, washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The obtained mixture was passed through a short pad of silica (hexane/EtOAc = 1/1) to give crude corresponding ketone substrate.

The crude ketone was reduced to alcohol substrate according to the general procedure E (reaction time 15 h), which was used for the next step without purification by column chromatography.

The crude alcohol was converted to **1n** according to the general procedure F, and isolated as colorless oil in 19% yield (4 steps, 212.5 mg) (column condition; *n*-hexane/EtOAc, 1/1.5): TLC R_f = 0.2 (*n*-hexane/EtOAc = 1/2, v/v), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 6.4 Hz, 2H), 7.42-7.35 (m, 3H), 7.30-7.20 (m, 4H), 5.03 (s, 1H), 4.80-4.74 (m, 3H), 3.56-3.52 (m, 1H), 3.36 (s, 1H), 2.98-2.86 (m, 2H), 2.14-1.77 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 156.7, 136.9, 136.1, 132.4, 130.7, 130.3, 128.6, 128.3, 127.6, 76.3, 58.5, 50.0, 37.5, 27.4, 25.0; IR (ATR) ν 3345, 2966, 1713, 1614, 1575, 1491, 1408, 1321, 1053, 1015 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{20}H_{21}ClN_2NaO_3^+$ m/z 395.1138, found 395.1123.



(*S*)-(1-benzoylpyrrolidin-2-yl)(4-chlorophenyl)methanone (s3o)

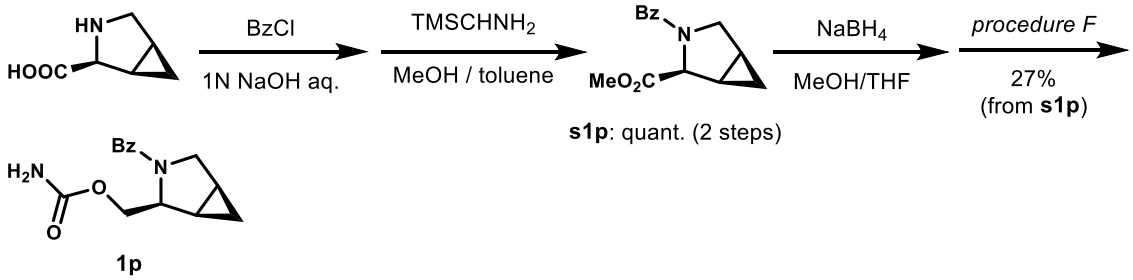
To a stirred solution of **s2k** (1.8 g, 4.4 mmol) in THF (26.4 mL, 0.17 M) was slowly added 4-chlorophenylmagnesium bromide solution (1.0 M in 2-methyltetrahydrofuran) (17.6 mL, 4 eq, 17.6 mmol) dropwise at -10 °C. After being stirred for 4 h at -10 °C, the reaction was quenched with 1N HCl, extracted with EtOAc, washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash chromatography on silica gel (column condition; gradient elution: *n*-hexane/EtOAc, 1.5/1 → 1/1) to afford **s3o** as yellow oil in 27% yield (372.5 mg): TLC R_f = 0.3 (*n*-hexane/EtOAc = 1/1, v/v), ^{1}H NMR (400 MHz, $CDCl_3$) (major rotamer) δ 8.00 (dd, *J* = 8.7, 1.8 Hz, 2H), 7.60 (dd, *J* = 5.6, 1.6 Hz, 2H), 7.47-7.38 (m, 5H), 5.65-5.62 (m, 1H), 3.75-3.60 (m, 2H), 2.42-2.32 (m, 1H), 2.04-1.91 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (major rotamer) δ 196.9, 169.4, 139.8, 136.2, 133.9, 130.3, 130.0, 129.1, 128.3, 127.4, 61.3, 50.2, 29.5, 25.5; IR (ATR) ν 2966, 1693, 1624, 1587, 1416, 1221, 1090, 1006, 841, 700 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{18}H_{16}ClNNaO_2^+$ m/z 336.0767, found 336.0771.

(*S*)-((*S*)-1-benzoylpyrrolidin-2-yl)(4-chlorophenyl)methyl carbamate (1o)

Compound **s3o** (344.3 mg, 1.2 mmol) was reduced to alcohol substrate according to the general procedure E, which was used for the next step without purification by column chromatography.

The crude alcohol was converted to **1o** according to the general procedure F, and isolated as white amorphous in 81% yield (3 steps, 357.5 mg) (column condition; gradient elution: *n*-hexane/EtOAc, 1/1.5 → EtOAc): TLC R_f = 0.2 (*n*-hexane/EtOAc = 1/2, v/v), ^{1}H NMR (400 MHz, $CDCl_3$) (major rotamer) δ 7.50 (d,

J = 5.5 Hz, 2H), 7.44-7.35 (m, 7H), 5.88 (d, *J* = 7.3Hz, 1H), 4.92-4.65 (m, 3H), 3.43-3.33 (m, 2H), 1.88-1.66 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) (major rotamer) δ 170.9, 156.3, 136.8, 136.2, 134.2, 130.2, 128.9, 128.6, 128.3, 127.4, 75.1, 59.5, 50.0, 25.8, 24.4; IR (ATR) ν 3354, 2958, 1714, 1612, 1491, 1414, 1326, 1057, 1013, 790 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{19}H_{19}ClN_2NaO_3^+$ m/z 381.0982, found 381.0974.



Methyl (1*R*, 2*S*, 5*S*)-3-benzoyl-3-azabicyclo[3.1.0]hexane-2-carboxylate (s1p)

To a stirred solution of (1*R*, 2*S*, 5*S*)-3-azabicyclo[3.1.0]hexane-2-carboxylic acid (196.5 mg, 1.6 mmol) in 1N NaOH (4.3 mL, 0.36 M) was added benzoyl chloride (0.2 mL, 1.1 eq, 1.7 mmol) at 0 °C. After being stirred for 15 h at room temperature, the reaction was quenched with 1N HCl. The water layer was acidified with 1N aqueous HCl., extracted with CH_2Cl_2, washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was used for the next step without purification by column chromatography.

A solution of the crude mixture in MeOH/toluene (22 mL, 0.07 M, 1/1) was slowly added trimethylsilyldiazomethane (2.0 M in hexane) (2.7 mL, 3.5 eq, 5.4 mmol). After being stirred for 2 h at room temperature, the reaction was quenched with acetic acid, extracted with CH_2Cl_2, washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was purified by flash chromatography on silica gel (column condition; *n*-hexane/EtOAc, 1/1) to afford **s1p** as colorless oil in quantitative yield (2 steps, 413.6 mg): TLC R_f = 0.3 (*n*-hexane/EtOAc = 1/1, v/v), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.39 (m, 5H), 4.70 (s, 1H), 3.78-3.71 (m, 4H), 3.58 (s, 1H), 2.00-1.94 (m, 1H), 1.69 (s, 1H), 0.86-0.71 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 170.5, 136.1, 130.0, 128.2, 126.9, 60.6, 52.2, 52.0, 19.2, 17.1, 8.6; IR (ATR) ν 2951, 1746, 1633, 1400, 1361,

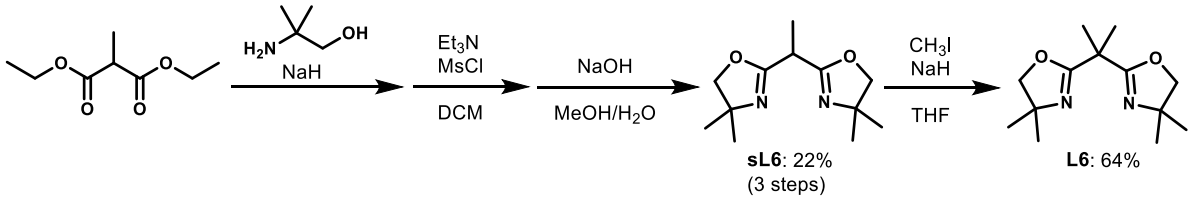
1269, 1196, 1174, 1017, 919 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{14}H_{15}NNaO_3^+$ m/z 268.0950, found 268.0947.

((1*R*,2*S*,5*S*)-3-benzoyl-3-azabicyclo[3.1.0]hexan-2-yl)methyl carbamate (1p)

To a stirred solution of **s1p** (245.4 mg, 1.0 mmol) in MeOH/THF (5.0 mL, 0.2 M, 1/5) was added $NaBH_4$ (94.6 mg, 2.5 eq, 2.5 mmol). After being refluxed for 2.5 h, the reaction was quenched with saturated aqueous NH_4Cl, extracted with CH_2Cl_2, washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude mixture was used for the next step without purification by column chromatography.

The crude alcohol was converted to **1p** according to the general procedure F, and isolated as white amorphous in 27% yield (3 steps, 70.3 mg) (column condition; *n*-hexane/EtOAc, 1/5): TLC R_f = 0.3 (EtOAc), mp: 150-152 ºC, ^{1}H NMR (400 MHz, $CDCl_3$) (major rotamer) δ 7.46-7.35 (m, 5H), 4.92-4.74 (m, 3H), 4.37 (dd, *J* = 10.8, 6.0 Hz, 1H), 4.25 (dd, *J* = 10.8, 6.0 Hz, 1H), 3.73 (dd, *J* = 10.5, 3.2 Hz, 1H), 3.37 (d, *J* = 10.5 Hz, 1H), 1.50-1.39 (m, 2H), 0.67 (ddd, *J* = 7.5, 7.5, 5.5 Hz, 1H), 0.16 (dd, *J* = 9.4, 3.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (major rotamer) δ 171.1, 157.1, 136.9, 130.2, 128.4, 127.3, 65.4, 57.6, 51.3, 16.4, 15.3, 7.4; IR (ATR) ν 3351, 1714, 1613, 1575, 1496, 1416, 1372, 1325, 1070, 1045 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{14}H_{16}N_2NaO_3^+$ m/z 283.1059, found 283.1056.

4-4. Synthesis and characterization of BOX ligand



2,2'-(ethane-1,1-diyl)bis(4,4-dimethyl-4,5-dihydrooxazole) (sL6)

To a stirred mixture of diethyl 2-methylmalonate (2.7 mL, 16 mmol), 2-amino-2-methylpropan-1-ol (3.1 mL, 2 eq, 32 mmol) and NaH (25.6 mg, 0.04 eq, 0.64 mmol) was heated to 140 °C for 3.5 h. The malonamide was obtained after removal of ethanol in vacuo, and used for the next step without further purification. A solution of the crude malonamide and Et_3N (11.3 mL, 5 eq, 80 mmol) in CH_2Cl_2

(100 mL, 0.16 M) was added methanesulfonyl chloride (3.1 mL, 2.5 eq, 40 mmol) at 0 °C, and the reaction mixture was stirred for 1.5 h at room temperature. The reaction was quenched with saturated aqueous NH_4Cl, extracted with CH_2Cl_2, washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure, and used for the next step without further purification.

A solution of the crude mesylate and NaOH (2.8 g, 4.3 eq, 68.8 mmol) in MeOH/H_2O (106 mL, 0.15 M, 1/1) was refluxed for 5 h, concentrated under reduced pressure. The reaction mixture was extracted with CH_2Cl_2, washed with brine, dried over Na_2SO_4, concentrated under reduced pressure, and purified by flash chromatography on silica gel (column condition; CH_2Cl_2/MeOH, 30/1) to afford **sL6** in 25% yield (3 steps, 897.3 mg).

^1H and ^{13}C NMR, IR, and MS were identical to those reported.[9]

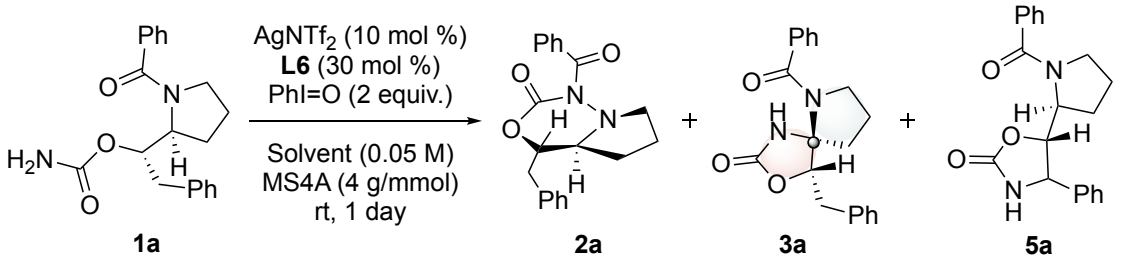
2,2'-(propane-2,2-diyl)bis(4,4-dimethyl-4,5-dihydrooxazole) (L6)

A solution of **sL6** (897.3 mg, 4.0 mmol) and NaH (560 mg, 3.5 eq, 14 mmol) in THF (89 mL, 0.045 M) was stirred for 20 min at room temperature and added CH_3I (0.37 mL, 1.5 eq, 6.0 mmol). After being stirred for 6 h at room temperature, the reaction mixture was concentrated under reduced pressure. The reaction mixture was diluted with EtOAc, and washed with saturated aqueous $Na_2S_2O_3$. The aqueous phase was then extracted with EtOAc, and the combined organics dried over Na_2SO_4, concentrated under reduced pressure. The crude mixture was purified by flash chromatography on silica gel (column condition; *n*-hexane/EtOAc, 1/2.5) to afford **L6** in 55% yield (525.9 mg).

^1H and ^{13}C NMR, IR, and MS were identical to those reported.[10]

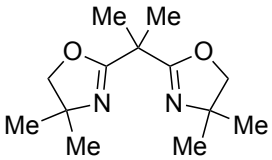
5. Additional studies

Table S1. Solvent effect.



1a **2a** **3a** **5a**

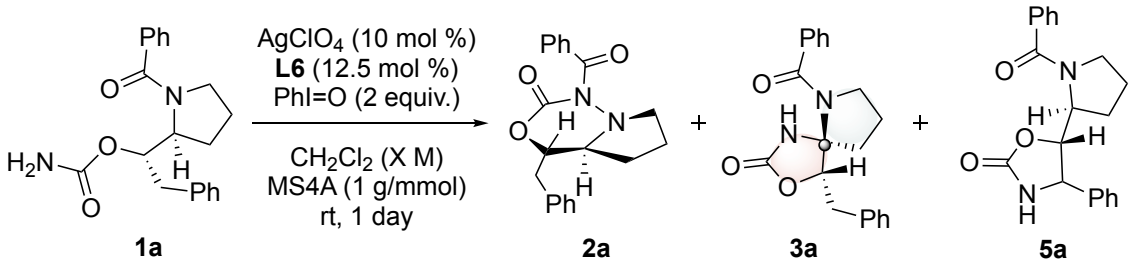
entry	Solvent	yield (%)[a] 2a	3a	5a
1	CH_2Cl_2	6	77	trace
2	$CHCl_3$	trace	31	trace
3	CH_3CN	trace	40	trace
4	benzene/toluene (=3/1)	trace	61	trace



L6

[a] NMR yields using Ph_3CH as an internal standard.

Table S2. Optimization of solvent volume.

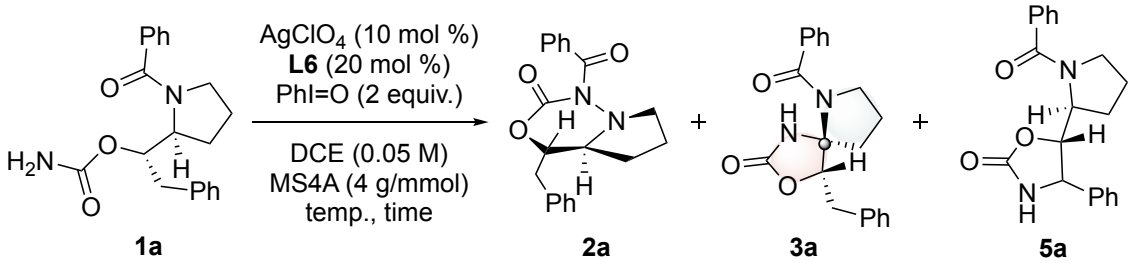


1a **2a** **3a** **5a**

entry	X	yield (%)[a] 2a	3a	5a
1	0.05	trace	70	trace
2	0.02	trace	79	trace
3	0.01	trace	80	trace

[a] NMR yields using Ph_3CH as an internal standard.

Table S3. Temperature effect.



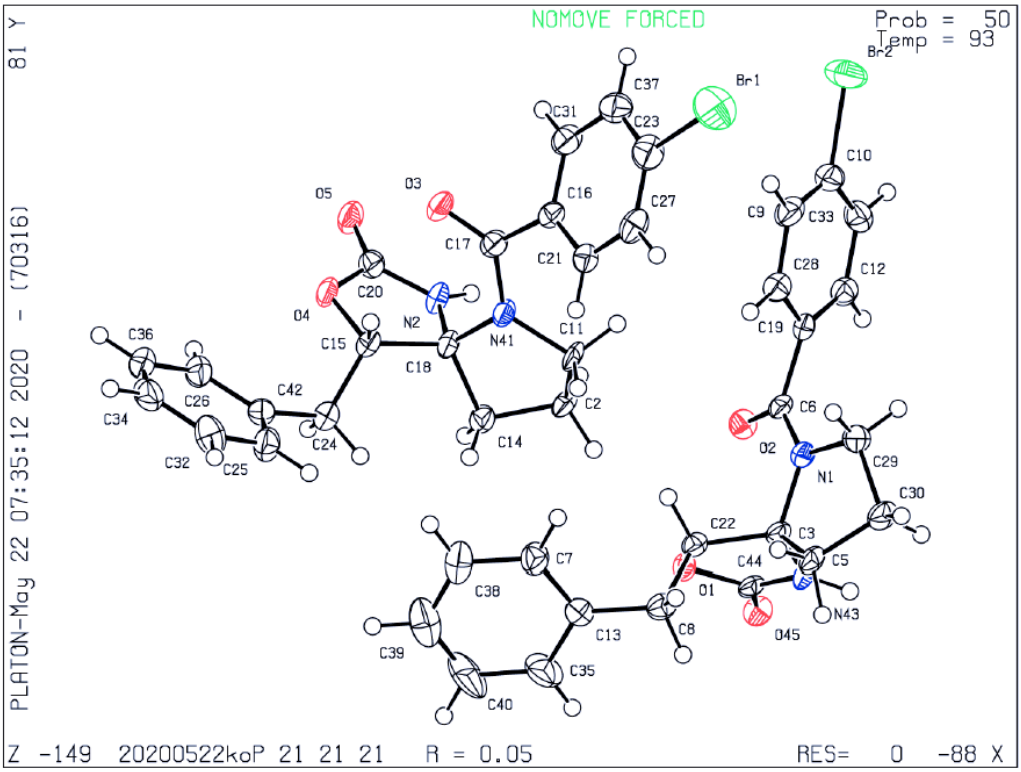
1a **2a** **3a** **5a**

entry	temp.	time	yield (%)[a]		
			2a	**3a**	**5a**
1	rt	27 h	trace	82	trace
2	60 °C	5 h	trace	68	trace

[a] NMR yields using Ph_3CH as an internal standard.

6. X-ray crystallographic analysis

ORTEP of **3i**, CCDC No. 2005342



The ellipsoid contour probability level in the ORTEP is 50%.

EXPERIMENTAL DETAILS

A. Crystal Data

Empirical Formula	$C_{20}H_{19}BrN_2O_3$
Formula Weight	415.29
Crystal Color, Habit	colorless, block
Crystal Dimensions	0.200 X 0.100 X 0.100 mm

Crystal System	orthorhombic
Lattice Type	Primitive
Lattice Parameters	a = 11.3768(2) Å b = 13.3425(2) Å c = 24.5874(5) Å V = 3732.26(12) Å^3
Space Group	$P2_12_12_1$ (#19)
Z value	8
D_{calc}	1.478 g/cm^3
F_{000}	1696.00
m(CuKa)	31.899 cm^{-1}

B. Intensity Measurements

Diffractometer	R-AXIS RAPID
Radiation monochromated	CuKa (l = 1.54187 Å) multi-layer mirror
Voltage, Current	40kV, 30mA
Temperature	-180.0°C
Detector Aperture	460.0 x 256.0 mm
Data Images	45 exposures
w oscillation Range (c=54.0, f=0.0)	80.0 - 260.0°
Exposure Rate	3.0 sec./°
w oscillation Range (c=54.0, f=90.0)	80.0 - 260.0°
Exposure Rate	3.0 sec./°
w oscillation Range (c=54.0, f=180.0)	80.0 - 260.0°
Exposure Rate	3.0 sec./°
w oscillation Range (c=54.0, f=270.0)	80.0 - 260.0°
Exposure Rate	3.0 sec./°
w oscillation Range (c=0.0, f=0.0)	80.0 - 260.0°

Exposure Rate	3.0 sec./^{o}
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2q_{max}$	136.4^{o}
No. of Reflections Measured	Total: 41269 Unique: 6810 (R_{int} = 0.0621) Friedel pairs: 2990
Corrections	Lorentz-polarization Absorption (trans. factors: 0.499 - 0.727)

C. Structure Solution and Refinement

Structure Solution	Direct Methods (SIR2008)
Refinement	Full-matrix least-squares on F^2
Function Minimized	$S\ w\ (Fo^2 - Fc^2)^2$
Least Squares Weights	$w = 1/[\ s^2(Fo^2) + (0.0238 \cdot P)^2 + 1.6837 \cdot P\ ]$ where $P = (Max(Fo^2,0) + 2Fc^2)/3$
$2q_{max}$ cutoff	136.4^o
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (All reflections)	6810
No. Variables	469
Reflection/Parameter Ratio	14.52
Residuals: R1 (I>2.00s(I))	0.0462
Residuals: R (All reflections)	0.0673
Residuals: wR2 (All reflections)	0.0817
Goodness of Fit Indicator	1.023
Flack Parameter (Friedel pairs = 2990)	0.006(14)
Max Shift/Error in Final Cycle	0.001

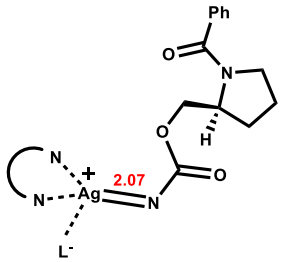
Maximum peak in Final Diff. Map	0.44 $e^-/Å^3$
Minimum peak in Final Diff. Map	-0.39 $e^-/Å^3$

7. Computational details

All DFT calculations were performed with Gaussian 16 program.[11] The molecular structure optimizations were carried out using the hybrid density functional method based on Becke's three-parameter exchange function and the Lee-Yang-Parr nonlocal correlation functional (B3LYP)[12] and the LANL2DZ basis set for Ag, and the 6-31G* basis set for H, C, N, O and Cl. The vibrational frequencies were computed at the same level to check whether each optimized structure is an energy minimum (no imaginary frequency) or a transition state (one imaginary frequency) and to evaluate its zero-point vibrational energy (ZPVE) and thermal corrections at 298.15 K. The intrinsic reaction coordinate (IRC) method was used to track minimum energy paths from transition structures to the corresponding local minima.[13] Single point energies were calculated at the ωb97xd level using SDD basis set for Ag and 6-311++G** basis set for H, C, N, O and Cl.

	E(rB3LYP/LANL2DZ/6-31G*) (A.U.)	E(rωb97xd/SDD/6-311++G**) (A.U.)
^{1}CP1	-2514.007180	-2515.218536
^{1}TS1$_{Amide}$	-2513.998458	-2515.205113
^{1}TS2$_{Amide}$	-2514.045957	-2515.263293
^{1}TS1$_{C\text{-}H}$	-2513.995622	-2515.204594
^{1}INT1$_{Amide}$	-2514.057627	-2515.276510
^{1}PRO$_{Amide}$	-838.961417	-838.917660
^{1}PRO$_{C\text{-}H}$	-839.008705	-838.974007
Cat.	-1675.123667	-1676.357606

	E(uB3LYP/LanL2DZ/6-31G*) (A.U.)	E(uωb97xd/SDD/6-311++G**) (A.U.)
^{3}CP2	-2514.022740	-2515.232843
^{3}TS1$_{C\text{-}H}$	-2513.993822	-2515.208916
^{3}TS2$_{C\text{-}H}$	-2513.986310	-2515.215371
^{3}INT$_{C\text{-}H}$	-2514.027805	-2515.249163



^{1}CP1

Zero-point correction= 0.617892 (Hartree/Particle)

Thermal correction to Energy= 0.661663

Thermal correction to Enthalpy= 0.662607

Thermal correction to Gibbs Free Energy= 0.533205

Sum of electronic and zero-point Energies= -2513.389287

Sum of electronic and thermal Energies= -2513.345517

Sum of electronic and thermal Enthalpies= -2513.344573

Sum of electronic and thermal Free Energies= -2513.473975

Cartesian Coordinates

Atom	X	Y	Z
C	-3.72755400	-1.14990400	-1.00641600
C	-5.90112500	-0.31909300	-1.77663600
C	-5.05662700	-0.75353200	-2.98338200
C	-4.05112000	-1.74954600	-2.38509600
H	-3.52208800	-1.91163800	-0.25002200

H	-6.76192500	-0.98518900	-1.63074900
H	-6.28520600	0.69720500	-1.88752800
H	-5.67092200	-1.18448900	-3.77959000
H	-4.52788300	0.10877400	-3.40572300
H	-4.52141400	-2.73161500	-2.25364800
H	-3.16140100	-1.87622200	-3.00647500
N	-4.96686400	-0.43412100	-0.63396300
C	-5.33648100	-0.42449300	0.69430800
C	-2.56342800	-0.15045900	-0.99392300
H	-2.62102600	0.55980600	-1.82196800
H	-2.52785500	0.39203900	-0.04927500
O	-1.28765700	-0.85555700	-1.06151900
C	-0.62789300	-0.85513400	-2.21388600
N	0.65671400	-1.12875800	-2.27544400
O	-1.09019100	-0.66863400	-3.36061500
O	-4.63745800	-0.94120800	1.56391800
Ag	2.06639100	-0.23790600	-1.05003400
C	4.50476700	2.08754500	-1.10811800
C	4.98847800	2.88260300	0.12070100
H	5.94395300	3.39152700	-0.01621100
H	4.22835400	3.57664500	0.49182300
C	2.13273500	-3.10546500	0.67869500
C	3.03087100	-3.68281400	1.80358500
H	2.47169900	-4.11034100	2.63791700
H	3.76135500	-4.41201000	1.43683600
C	3.57942800	-1.53096900	1.42116400
C	4.42923400	0.80436200	0.74111700
C	4.37801400	-0.29119100	1.79272300

O	5.17522500	1.85805500	1.13673400
O	3.76778700	-2.53900300	2.30360600
N	2.75104700	-1.76238900	0.47079800
N	3.94563300	0.86127300	-0.44652400
Cl	0.46053500	2.04976800	0.67161300
O	0.58751400	1.64876400	-0.80779900
O	0.90763100	0.87313600	1.49028500
O	1.35630600	3.21271700	0.92375300
O	-0.95528800	2.38132100	0.94434300
C	3.75580800	0.29310200	3.09661600
H	2.73444700	0.63702400	2.91512200
H	3.75075900	-0.47545400	3.87369200
H	4.36078200	1.13664000	3.43682200
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H	6.43666800	0.14598900	2.36520500
H	5.87637300	-1.46753200	2.85944000
H	6.30656400	-1.15724000	1.16502500
C	-6.62834600	0.25323900	1.06194200
C	-7.45301300	-0.37778900	2.00364900
C	-6.98062000	1.52274700	0.58431000
C	-8.63387600	0.22996600	2.42574200
H	-7.14959200	-1.34083200	2.40225800
C	-8.15186500	2.14076300	1.02502600
H	-6.32135300	2.04361100	-0.10378600
C	-8.98650500	1.49066600	1.93613400
H	-9.27382300	-0.27342600	3.14549500
H	-8.40804200	3.13231300	0.66158200
H	-9.90216200	1.96944900	2.27297400

C	5.67703700	1.63449500	-1.99555500
H	5.32866400	0.92704300	-2.75509600
H	6.12115400	2.49599700	-2.50730500
H	6.45823000	1.14496800	-1.40275600
C	3.45728600	2.84485400	-1.92255000
H	3.90626200	3.75281500	-2.34295900
H	3.10208100	2.23322300	-2.75973100
H	2.59865700	3.12309100	-1.30943000
C	2.20026000	-3.93032000	-0.60881200
H	1.79456500	-4.93409100	-0.43639300
H	1.61120100	-3.45343000	-1.39875600
H	3.23392000	-4.03086100	-0.95819100
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H	0.08183300	-2.40550100	0.40189300
H	0.23073600	-3.89737300	1.35206400
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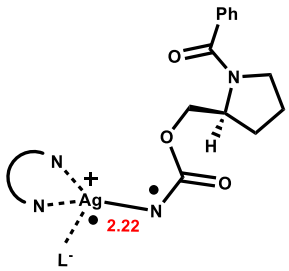

^{3}CP2

Zero-point correction=	0.616928 (Hartree/Particle)
Thermal correction to Energy=	0.661123
Thermal correction to Enthalpy=	0.662067
Thermal correction to Gibbs Free Energy=	0.529270
Sum of electronic and zero-point Energies=	-2513.405812
Sum of electronic and thermal Energies=	-2513.361617

Sum of electronic and thermal Enthalpies= -2513.360673

Sum of electronic and thermal Free Energies= -2513.493470

Cartesian Coordinates

Atom	X	Y	Z
C	-4.11006100	1.26244100	-1.01736900
C	-5.87636900	1.86009300	0.57560700
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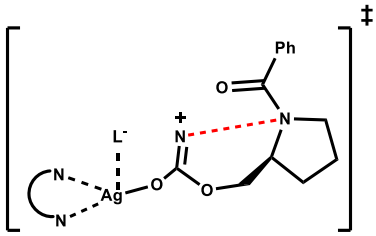
C	-3.95259400	2.73270000	-0.59273000
H	-4.18984100	1.14329000	-2.10097500
H	-6.74211800	2.39747700	0.16569900
H	-6.18793000	1.39854200	1.51475100
H	-4.98219400	3.80848200	1.04120700
H	-4.01770300	2.41856800	1.55408900
H	-4.45817800	3.37593900	-1.32324700
H	-2.90831000	3.04416400	-0.52766500
N	-5.39033800	0.85682300	-0.39708800
C	-6.17143500	-0.06576000	-1.05491500
C	-3.01109800	0.31375100	-0.51828200
H	-2.80936000	0.42747800	0.54778100
H	-3.29412200	-0.71720500	-0.73182700
O	-1.77731600	0.51366400	-1.26020600
C	-0.79581600	1.19524700	-0.67281000
N	0.40354600	1.11805100	-1.36662800
O	-0.87950800	1.87493300	0.34741900
O	-5.80174300	-0.59438700	-2.10259700
Ag	1.95638000	-0.09639500	-0.34919300
C	3.22005700	2.66185100	1.27118100
C	4.64648700	3.27115000	1.42717700
H	4.71479300	4.30631600	1.08023200
H	5.04367400	3.19988400	2.44281300
C	4.19656400	-2.77782700	-0.21484600

C	5.65198400	-2.96430500	-0.72758200
H	6.30494300	-3.48721400	-0.02592300
H	5.70319200	-3.44847100	-1.70857900
C	5.09792100	-0.78979500	-0.76688800
C	4.69082600	1.58239600	-0.05830000
C	5.36960200	0.68062500	-1.08905600
O	5.49699400	2.46599100	0.56620200
O	6.16333200	-1.61163300	-0.88280900
N	3.97637500	-1.32152700	-0.45798500
N	3.44629500	1.61526100	0.23463500
Cl	0.08852500	-1.93272300	1.43169500
O	0.26157100	-1.65245700	-0.08581500
O	1.09087100	-1.06106600	2.13708500
O	-1.29480600	-1.57600500	1.81572400
O	0.38325600	-3.36393300	1.67085200
C	6.88782400	0.95430100	-1.13538400
H	7.37043400	0.73941500	-0.17927200
H	7.35101600	0.32997000	-1.90182700
H	7.06530800	2.00408500	-1.37931000
C	4.75216600	0.98350500	-2.48458100
H	4.95070400	2.02474300	-2.75846700
H	5.21015700	0.33546800	-3.23884300
H	3.67146700	0.82314500	-2.49034000
C	-7.50172300	-0.42822200	-0.45143000
C	-8.60284900	-0.53297800	-1.31264500
C	-7.65495900	-0.76490500	0.90027500
C	-9.84739400	-0.92252000	-0.82119900
H	-8.46510800	-0.31433200	-2.36701300
C	-8.89651700	-1.17724000	1.38688300
H	-6.79662000	-0.73947500	1.56524800
C	-9.99718300	-1.24447500	0.53056400
H	-10.69831500	-0.98682000	-1.49409100
H	-9.00137900	-1.45166100	2.43311900

H	-10.96528100	-1.55811600	0.91205700
C	2.73124800	2.00236400	2.56790900
H	2.58500500	2.76409800	3.34303000
H	1.78053200	1.48501000	2.41114200
H	3.45896900	1.27053700	2.93546400
C	2.20597700	3.69291400	0.76074400
H	1.22504300	3.23226100	0.61515800
H	2.09980700	4.50377500	1.49161300
H	2.53504800	4.12731500	-0.19001000
C	4.08725900	-3.05001200	1.29345500
H	3.09497300	-2.78854200	1.66828100
H	4.26057000	-4.11376100	1.49438500
H	4.83341500	-2.46853900	1.84777800
C	3.18744000	-3.61390600	-1.00739500
H	3.40227800	-4.68152000	-0.88082000
H	2.16918100	-3.42879200	-0.65495900
H	3.23748700	-3.37712400	-2.07634900



^{1}TS1*Amide*

Zero-point correction=	0.616139 (Hartree/Particle)
Thermal correction to Energy=	0.660015
Thermal correction to Enthalpy=	0.660959
Thermal correction to Gibbs Free Energy=	0.530386
Sum of electronic and zero-point Energies=	-2513.382319
Sum of electronic and thermal Energies=	-2513.338444
Sum of electronic and thermal Enthalpies=	-2513.337499
Sum of electronic and thermal Free Energies=	-2513.468072

Cartesian Coordinates

Atom	X	Y	Z
C	3.69679700	-1.88480200	-1.08590300
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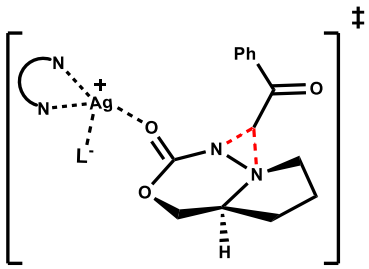
C	4.50892800	-3.13065100	-1.52667100
H	3.29306600	-1.32799500	-1.93591100
H	6.30787200	-2.16863600	-2.29074000
H	6.65755300	-3.54564600	-1.22975100
H	4.24236400	-3.44736700	-2.53825200
H	4.30158900	-3.97598500	-0.85767600
C	2.54629400	-2.29985200	-0.17947900
H	1.86755300	-2.99847700	-0.67413500
H	2.92027600	-2.74133400	0.75019000
O	1.73285700	-1.12855600	0.14092700
C	1.46528600	-0.91213200	1.39052700
N	1.76963000	-1.30731500	2.56568400
O	0.64334500	-0.02762600	1.86181500
Ag	-1.53539200	-0.18351700	0.52748800
C	-0.65168500	2.88516100	-0.65732800
C	-1.40363800	4.06777900	-1.33616600
H	-1.44580700	4.96854800	-0.71672700
H	-1.00851600	4.32444900	-2.32290900
C	-4.78611300	-0.51291400	1.81215800
C	-6.13755200	-0.45788900	1.04762200
H	-6.39051700	-1.40630200	0.56253900
H	-6.97986000	-0.12226700	1.65731900
C	-4.59203600	0.78946400	-0.00789200
C	-2.81794900	2.34467700	-0.99370300
C	-4.16430900	1.65141100	-1.19163400
O	-2.76169700	3.59435100	-1.51513700
O	-5.92471900	0.52727600	0.00556300
N	-3.88205100	0.24892400	0.90679700
N	-1.73368800	1.87528300	-0.50338300

C	5.94617700	-1.73211200	-0.20275200
H	6.78312700	-1.03371100	-0.18595300
H	5.94506100	-2.28226600	0.74865800
N	4.66980900	-1.01530700	-0.38887800
C	4.55517100	0.35530200	-0.53867500
O	3.65854200	0.86488800	-1.20809900
Cl	-1.35313000	-3.05117500	-0.82273800
O	-0.18688800	-3.83841400	-1.30628400
O	-2.56587600	-3.89628600	-0.71003900
O	-1.60774400	-1.87890100	-1.72873100
O	-1.01028000	-2.48378200	0.56428100
C	5.54447900	1.22229100	0.18910900
C	6.00489100	0.92564700	1.47973000
C	5.93586200	2.42258200	-0.42072800
C	6.85933700	1.80848000	2.14177900
H	5.67113400	0.01977600	1.97734300
C	6.80520300	3.29313800	0.23299500
H	5.54349000	2.65894700	-1.40471800
C	7.26889700	2.98756200	1.51596200
H	7.19930800	1.57785100	3.14767400
H	7.11540200	4.21428500	-0.25291300
H	7.93975000	3.67106700	2.02954400
C	-5.26385400	2.70437000	-1.47629300
H	-5.00003900	3.28720000	-2.36011000
H	-6.21534700	2.20127100	-1.65204300
H	-5.38712100	3.39542800	-0.63645300
C	-4.02275600	0.70536500	-2.42436600
H	-4.98800800	0.23338200	-2.63130100
H	-3.72843800	1.29017100	-3.30211000
H	-3.27755600	-0.07510300	-2.24856900
C	-0.09978200	3.26962800	0.72149800
H	0.35408700	2.40262300	1.21121400
H	0.66970200	4.04392800	0.61818200

H	-0.89578200	3.65617800	1.36817400
C	0.45464200	2.31672300	-1.55618800
H	1.23268000	3.07058100	-1.72271200
H	0.93548400	1.44715700	-1.10058100
H	0.04910900	2.01570700	-2.52848300
C	-4.85513200	0.22691200	3.15732700
H	-5.50971700	-0.30727300	3.85610700
H	-3.85821600	0.29546400	3.60428200
H	-5.24329300	1.24376800	3.02806300
C	-4.28452600	-1.94837800	1.99683300
H	-3.31402200	-1.95941300	2.50298200
H	-4.99336100	-2.51751300	2.61086000
H	-4.16379300	-2.46146900	1.03808200



^{1}TS2*Amide*

Zero-point correction=	0.618454 (Hartree/Particle)
Thermal correction to Energy=	0.661022
Thermal correction to Enthalpy=	0.661966
Thermal correction to Gibbs Free Energy=	0.534372
Sum of electronic and zero-point Energies=	-2513.427504
Sum of electronic and thermal Energies=	-2513.384936
Sum of electronic and thermal Enthalpies=	-2513.383992
Sum of electronic and thermal Free Energies=	-2513.511585

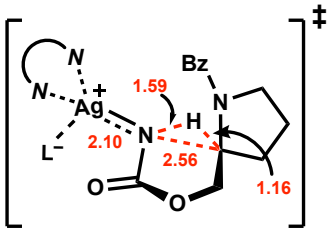
Cartesian Coordinates

Atom	X	Y	Z
C	3.95095600	1.60124700	-1.68771100

C	5.57434000	-0.21251500	-2.01536200
C	4.98347200	1.04400600	-2.69261700
H	4.26057200	2.52901200	-1.19857900
H	6.44645900	0.04947600	-1.40526600
H	5.88330500	-0.97322400	-2.73681400
H	5.74670300	1.78742300	-2.93685900
H	4.47959100	0.76505600	-3.62493900
C	2.55332000	1.75604600	-2.27108800
H	2.51688300	2.59360400	-2.97122900
H	2.22653300	0.84333600	-2.77951200
O	1.61239900	2.07120500	-1.23589200
C	1.58758600	1.27779200	-0.14154800
N	2.62862000	0.43202200	0.15790500
O	0.60638800	1.33246100	0.60016600
Ag	-1.32236000	0.06143300	-0.34921200
C	-2.77743500	3.06136700	0.71692800
C	-4.23283900	3.58169100	0.89958400
H	-4.41515700	4.05130000	1.86901400
H	-4.55065700	4.25968600	0.10022500
C	-2.70582400	-2.72952600	1.18843200
C	-4.00568900	-2.92679400	2.01895300
H	-4.47362200	-3.90429600	1.88197500
H	-3.86567300	-2.73471800	3.08828400
C	-4.18666800	-1.10727900	0.71500100
C	-4.24620000	1.38765800	0.41870300
C	-4.94276400	0.06658900	0.09048800
O	-5.06264000	2.39242700	0.82061700
O	-4.92237000	-1.92163400	1.51046100
N	-2.96835200	-1.43220100	0.50916600
N	-3.00348100	1.65320600	0.29555900
C	4.43526300	-0.70482300	-1.12539500
H	4.74514800	-1.33107200	-0.28985300
H	3.64111900	-1.20863700	-1.68603800

N	3.87018200	0.57356300	-0.60448500
C	4.06512100	1.13356300	0.91533500
O	4.17238100	2.34007900	1.02443800
Cl	0.45241900	-1.74041400	-2.47643200
O	1.84570500	-1.64879800	-3.01461600
O	-0.42263100	-2.49623000	-3.39991200
O	-0.07777900	-0.30894000	-2.33192500
O	0.46343700	-2.36765000	-1.11570400
C	4.62509700	0.13640800	1.88353300
C	4.02929200	-1.09377700	2.19065700
C	5.80475100	0.51949400	2.54019000
C	4.62417300	-1.93842200	3.12915200
H	3.09918600	-1.36669000	1.70552000
C	6.39655900	-0.33108800	3.47221700
H	6.23759000	1.48984700	2.31963700
C	5.80878300	-1.56370600	3.76671200
H	4.15428800	-2.88875900	3.36706500
H	7.31171600	-0.02813300	3.97362000
H	6.26727000	-2.22509100	4.49708200
C	-6.40825300	0.08873800	0.57248600
H	-6.94362300	0.90710200	0.08667200
H	-6.89511200	-0.85445000	0.31423900
H	-6.48052700	0.22527900	1.65390600
C	-4.91052600	-0.10902600	-1.45478700
H	-5.41493300	-1.04035600	-1.73239800
H	-5.43686800	0.72382000	-1.93287300
H	-3.88523700	-0.14272800	-1.82969600
C	-1.99271300	3.06702100	2.03792100
H	-1.01769700	2.59270900	1.89897500
H	-1.83518900	4.09765000	2.37877000
H	-2.54121700	2.52741300	2.81906300
C	-2.01311900	3.81799500	-0.37476300
H	-1.89548300	4.87226700	-0.09619200

H	-1.01779300	3.38356100	-0.50692300
H	-2.54654400	3.77070500	-1.33081100
C	-1.45558100	-2.62750600	2.06730800
H	-1.29227800	-3.56712400	2.60883000
H	-0.57477400	-2.43400600	1.44715100
H	-1.55381000	-1.81865300	2.79996100
C	-2.53581900	-3.81495400	0.11387000
H	-1.68978200	-3.57706500	-0.53667800
H	-2.35173400	-4.78769300	0.58623600
H	-3.43844100	-3.89753900	-0.50252900



^{1}TS1$_{C\text{-}H}$

Zero-point correction=	0.615646 (Hartree/Particle)
Thermal correction to Energy=	0.658365
Thermal correction to Enthalpy=	0.659309
Thermal correction to Gibbs Free Energy=	0.534392
Sum of electronic and zero-point Energies=	-2513.379976
Sum of electronic and thermal Energies=	-2513.337257
Sum of electronic and thermal Enthalpies=	-2513.336312
Sum of electronic and thermal Free Energies=	-2513.461230

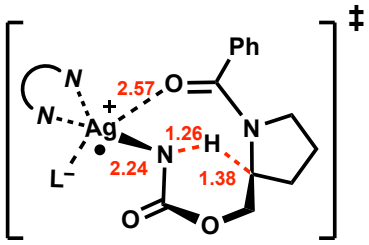
Cartesian Coordinates

Atom	X	Y	Z
C	-3.65635100	2.05641000	0.13670600
C	-5.88603500	1.35927000	-0.54577900
C	-5.85653600	2.88324800	-0.39082300
C	-4.36676900	3.21615600	-0.57808200
H	-2.68048600	1.79800300	-0.36276500

H	-5.95403600	1.08403400	-1.60411700
H	-6.70517000	0.87573900	-0.00950600
H	-6.49959600	3.38209900	-1.12012900
H	-6.19437700	3.17015000	0.61128400
H	-4.10706500	3.21064900	-1.64253100
H	-4.07845400	4.18659900	-0.16657500
N	-4.58139100	0.93778600	0.01716700
C	-4.19625300	-0.33088300	0.37832800
C	-3.25929600	2.36808800	1.58782100
H	-4.09604600	2.78352700	2.15251400
H	-2.87574000	1.47629900	2.08346600
O	-2.24783900	3.40089500	1.61468500
C	-1.10135100	3.21596900	0.94269600
N	-0.96038300	2.32995100	-0.03620700
O	-0.11267900	3.93141200	1.17608400
O	-3.07377900	-0.53341700	0.85668700
Ag	0.45712900	0.90019400	-0.35965000
C	3.40289200	2.47485300	0.10153600
C	4.86671400	2.06169600	-0.20907400
H	5.48073500	2.87070100	-0.60731200
H	5.36312900	1.58926800	0.64172200
C	0.37359300	-2.42847600	-0.55971700
C	1.44563000	-3.48521900	-0.93476300
H	1.97309700	-3.87988600	-0.06412300
H	1.06975400	-4.29610500	-1.56033500
C	2.16057000	-1.44574200	-1.54272700
C	3.46286700	0.67666300	-1.27444000
C	3.12714700	-0.47542800	-2.21577100
O	4.74858500	1.04430000	-1.24475200
O	2.42865000	-2.74400600	-1.71834900
N	1.08316300	-1.15760100	-0.90369500
N	2.64636100	1.37687900	-0.57215500
Cl	4.13414300	-1.88411200	2.03428500

O	3.01994700	-1.07905400	2.63453400
O	3.63488400	-3.25719300	1.70479600
O	4.61119300	-1.21182800	0.77825300
O	5.26290300	-1.98056400	3.00658100
C	2.42088600	0.11469900	-3.47204000
H	2.16395800	-0.69416600	-4.16283900
H	1.50873300	0.65405200	-3.20544800
H	3.09960000	0.80312300	-3.98475100
C	4.41278000	-1.21024200	-2.64954100
H	5.08387800	-0.50975800	-3.15052900
H	4.92920100	-1.64062500	-1.78981500
H	4.15914400	-2.01060800	-3.34758200
C	-5.16311900	-1.46943000	0.22222700
C	-5.27016200	-2.36451500	1.29890100
C	-5.87190200	-1.73019300	-0.95948100
C	-6.10368400	-3.47760100	1.21008900
H	-4.69724000	-2.17688800	2.20143100
C	-6.68772400	-2.85940100	-1.05404100
H	-5.76996200	-1.07598500	-1.81877500
C	-6.81415800	-3.72779700	0.03215900
H	-6.19263800	-4.15387800	2.05540200
H	-7.22170700	-3.05993700	-1.97840400
H	-7.45740800	-4.60016600	-0.04084200
C	-0.88368200	-2.54312900	-1.43425600
H	-1.39090500	-3.49400800	-1.23523900
H	-1.58320600	-1.73329400	-1.20479100
H	-0.62979600	-2.50431700	-2.49963200
C	0.01848400	-2.47220500	0.92893700
H	-0.74535100	-1.72375300	1.16248700
H	-0.39261700	-3.45687900	1.18128300
H	0.90411400	-2.29589100	1.54535900
C	3.11751800	2.48616700	1.60573000
H	3.77148600	3.21311300	2.10190100

H	2.08088000	2.78225600	1.79428500
H	3.29529300	1.49850100	2.04159700
C	3.02798300	3.81216000	-0.55303000
H	1.96556100	4.02292900	-0.40253400
H	3.60672900	4.62463300	-0.09888000
H	3.24157900	3.79709800	-1.62787400



^{3}TS1$_{C\text{-}H}$

Zero-point correction=	0.611513 (Hartree/Particle)
Thermal correction to Energy=	0.654700
Thermal correction to Enthalpy=	0.655644
Thermal correction to Gibbs Free Energy=	0.530199
Sum of electronic and zero-point Energies=	-2513.382310
Sum of electronic and thermal Energies=	-2513.339122
Sum of electronic and thermal Enthalpies=	-2513.338178
Sum of electronic and thermal Free Energies=	-2513.463624

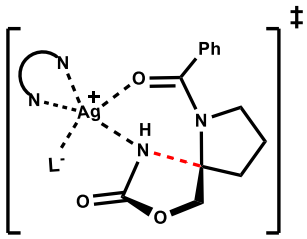
Cartesian Coordinates

Atom	X	Y	Z
C	2.69431600	-2.33476200	-0.20123500
C	4.85690200	-1.58289000	-0.99157700
C	4.90862700	-3.09111500	-0.70943400
C	3.43260800	-3.52901500	-0.78859100
H	1.42098300	-2.23350900	-0.71037700
H	4.93528500	-1.36674500	-2.06401700
H	5.64394300	-1.02885100	-0.47797000
H	5.55514100	-3.61688000	-1.41776700
H	5.29988800	-3.27015300	0.29843600

H	3.13884200	-3.68518300	-1.83500500
H	3.21967400	-4.45170800	-0.24223500
N	3.50891300	-1.18364700	-0.49627400
C	2.95761600	0.05054300	-0.73782500
C	2.22417300	-2.45307800	1.24493800
H	3.01670300	-2.84022500	1.89546300
H	1.88229500	-1.49246900	1.63609400
O	1.17312700	-3.43057500	1.33260800
C	0.11128300	-3.31462000	0.49242400
N	0.18543700	-2.39246900	-0.55379200
O	-0.83756900	-4.07251300	0.60924100
O	1.73452800	0.23022900	-0.80550100
Ag	-0.67653500	-0.37169700	-0.13161200
C	-3.40484900	-1.84082300	-1.95101400
C	-4.75448300	-1.23274500	-2.42439500
H	-4.69325300	-0.76967400	-3.41587100
H	-5.58828400	-1.93781600	-2.40180600
C	-0.78707200	3.06674300	-0.41780000
C	-1.86497300	4.13993100	-0.09873000
H	-1.68730500	4.64747800	0.85409600
H	-2.00142300	4.88131700	-0.89019500
C	-2.77064300	2.08689700	0.01056700
C	-3.89586200	-0.00502000	-0.75341600
C	-3.92807300	1.12463500	0.27352600
O	-5.03516500	-0.18043500	-1.46673400
O	-3.10312100	3.39564900	0.02617700
N	-1.53946600	1.79829500	-0.19039300
N	-2.93638200	-0.82119300	-0.97123400
Cl	0.13019400	0.23809500	3.17621500
O	-0.49980000	-0.79173100	2.21451700
O	1.47700700	0.59330600	2.63196200
O	-0.74794000	1.44041500	3.21743600
O	0.23954900	-0.39616200	4.50619600

C	3.89871800	1.19945700	-0.93722800
C	3.70981700	2.04761600	-2.03687100
C	4.90367800	1.48929300	-0.00328600
C	4.53914000	3.15335400	-2.21865700
H	2.91522900	1.83172500	-2.74460000
C	5.71582400	2.61013300	-0.17541400
H	5.02299000	0.85891000	0.87331100
C	5.54200100	3.43673600	-1.28790200
H	4.39836200	3.79828000	-3.08158800
H	6.47940100	2.84072700	0.56198800
H	6.18099000	4.30480200	-1.42462700
C	-3.75027000	0.51496700	1.69414400
H	-2.81482800	-0.03621700	1.79643300
H	-3.75349500	1.31481100	2.44043700
H	-4.58757500	-0.15993200	1.90188100
C	-5.27662800	1.87384500	0.21143200
H	-5.44677700	2.33877200	-0.76247400
H	-6.09210500	1.17278900	0.40305300
H	-5.29751300	2.65410300	0.97470900
C	-2.39904900	-1.99016800	-3.09602100
H	-1.44573200	-2.36450300	-2.71241100
H	-2.77532100	-2.69889500	-3.84369600
H	-2.22334400	-1.02804600	-3.59125700
C	-3.61315200	-3.17257800	-1.21382800
H	-3.95784700	-3.94086700	-1.91734700
H	-2.68526900	-3.51228600	-0.74627900
H	-4.37065200	-3.06371200	-0.42887200
C	-0.34648300	3.10922000	-1.88906200
H	0.19130200	4.04180500	-2.09839800
H	0.32328200	2.27036500	-2.09987500
H	-1.20906100	3.04848200	-2.56331800
C	0.41443700	3.17542500	0.52433200
H	1.14026800	2.38753200	0.31323400

H	0.90517700	4.14707400	0.38410600
H	0.10378200	3.07659400	1.56701100



^{3}TS2$_{C\text{-}H}$

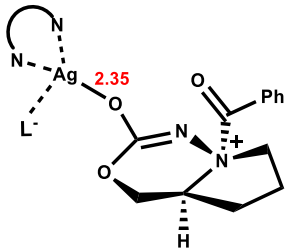
Zero-point correction=	0.617104 (Hartree/Particle)
Thermal correction to Energy=	0.659199
Thermal correction to Enthalpy=	0.660143
Thermal correction to Gibbs Free Energy=	0.538409
Sum of electronic and zero-point Energies=	-2513.369206
Sum of electronic and thermal Energies=	-2513.327111
Sum of electronic and thermal Enthalpies=	-2513.326167
Sum of electronic and thermal Free Energies=	-2513.447901

Cartesian Coordinates

Atom	X	Y	Z
C	2.44115100	2.54653200	-0.15348800
C	4.38447300	1.66897600	0.86404300
C	4.43412100	3.19051500	1.01776300
C	2.97086700	3.59928800	0.81762600
H	0.36748100	1.99272500	1.37742000
H	4.19268000	1.16130600	1.81861400
H	5.30284400	1.27110000	0.43450000
H	4.83953000	3.49536500	1.98688500
H	5.06584200	3.62461200	0.23518500
H	2.42526900	3.54790000	1.76807300
H	2.84363500	4.61347300	0.42803500
N	3.26475400	1.44205500	-0.08089200
C	2.95175500	0.19663200	-0.66661400

C	1.87857700	3.05446600	-1.47176600
H	2.56077700	3.78180400	-1.92486200
H	1.68780600	2.23644500	-2.16341700
O	0.66001700	3.77513800	-1.18951700
C	0.00908300	3.31016400	-0.08543300
N	0.64179600	2.17339900	0.40930000
O	-0.96409600	3.87939600	0.36416400
O	1.88577100	0.19383200	-1.43952900
Ag	-0.09968800	0.24287100	-0.52382800
C	-2.91145600	1.07200900	-2.03959500
C	-4.30541000	0.43072100	-1.90106500
H	-5.11839700	1.03062800	-2.31312700
H	-4.33880500	-0.59130500	-2.28833600
C	-0.00090600	-1.06172700	2.85777900
C	-1.05929500	-2.08890600	3.33212500
H	-1.01230000	-3.02929300	2.77684000
H	-1.04672600	-2.28165000	4.40749700
C	-2.03686600	-0.45862400	2.15087900
C	-3.27360200	0.40729500	0.08829300
C	-3.26658300	0.26961400	1.60986200
O	-4.50154300	0.35319000	-0.46072600
O	-2.32261300	-1.46103700	3.00870700
N	-0.80159600	-0.16570300	1.96915500
N	-2.31180100	0.70985000	-0.70899600
Cl	-1.49521300	-2.86677700	-1.08775800
O	-2.55738100	-2.56301500	-2.08257900
O	-0.30650400	-1.89160000	-1.31959800
O	-2.01116400	-2.65370000	0.29608600
O	-0.95723700	-4.22901600	-1.25911400
C	3.75491200	-1.00998300	-0.59950500
C	4.87666400	-1.29371100	0.23494900
C	3.31899000	-2.07285700	-1.45143900
C	5.51787900	-2.52596200	0.18843500

H	5.23911400	-0.58264300	0.96162100
C	3.97280500	-3.29442000	-1.48800800
H	2.44583200	-1.90686400	-2.06803800
C	5.08701300	-3.53777300	-0.67603300
H	6.36370000	-2.70065900	0.84921100
H	3.60287900	-4.06993900	-2.15349200
H	5.59703800	-4.49629500	-0.70338300
C	-4.55293900	-0.44914200	2.07565200
H	-4.60331000	-1.46637300	1.68112500
H	-4.56987500	-0.50138800	3.16612000
H	-5.42977100	0.10391300	1.73541600
C	-3.25019900	1.72345500	2.17387600
H	-2.38748700	2.28812000	1.81381600
H	-4.16128900	2.24594800	1.86404900
H	-3.23320300	1.68967700	3.26843600
C	-3.00568900	2.60586300	-2.11885000
H	-2.01404000	3.06407300	-2.08570900
H	-3.48792100	2.89747100	-3.05963100
H	-3.59010800	3.01366500	-1.28769700
C	-2.11232600	0.51457200	-3.21755900
H	-2.62161100	0.76031000	-4.15717700
H	-1.11696600	0.97323800	-3.25774500
H	-2.00125100	-0.56880800	-3.14979600
C	0.53361600	-0.21659000	4.02670800
H	1.12860900	-0.83426900	4.71002300
H	1.17399200	0.59165000	3.65534300
H	-0.28722900	0.23421300	4.59596500
C	1.14508900	-1.73127900	2.09779300
H	1.87397300	-0.99031900	1.75283300
H	1.67348000	-2.43786300	2.74940500
H	0.77537800	-2.27719000	1.22611400



[1]INT1*Amide*

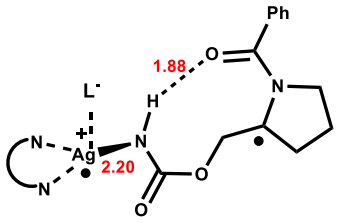
Zero-point correction=	0.619917 (Hartree/Particle)
Thermal correction to Energy=	0.663105
Thermal correction to Enthalpy=	0.664049
Thermal correction to Gibbs Free Energy=	0.534273
Sum of electronic and zero-point Energies=	-2513.437710
Sum of electronic and thermal Energies=	-2513.394521
Sum of electronic and thermal Enthalpies=	-2513.393577
Sum of electronic and thermal Free Energies=	-2513.523354

Cartesian Coordinates

Atom	X	Y	Z
C	3.47594000	2.25141200	-0.79784700
C	4.51938400	0.78798400	-2.49880800
C	4.24493200	2.27413400	-2.13081000
H	3.85540800	2.95686400	-0.06168000
H	5.59135000	0.57005700	-2.44660000
H	4.17862800	0.54071700	-3.50684300
H	5.17669800	2.83470700	-2.02573000
H	3.64317000	2.77107500	-2.89820900
C	1.97755100	2.42078200	-0.96611900
H	1.76644300	3.45863900	-1.23816600
H	1.57307000	1.77185000	-1.74913600
O	1.30868700	2.18313400	0.26789000
C	1.62785100	1.02551800	0.94814500
N	2.76718500	0.35430000	0.76922600
O	0.77951000	0.64209800	1.77880500
Ag	-1.14752100	-0.09150000	0.64409000

C	-2.95997900	2.66329100	1.52879300
C	-4.45790300	3.07919200	1.60144600
H	-4.84512400	3.11580900	2.62511600
H	-4.67546200	4.02503800	1.09828600
C	-2.73145800	-3.15074500	0.45446800
C	-3.91080500	-3.61898500	-0.43615100
H	-3.60095800	-3.84571500	-1.46179100
H	-4.47244600	-4.46168000	-0.02605200
C	-4.08839500	-1.41962000	0.00052800
C	-4.24876800	1.06985900	0.60117700
C	-4.83093700	-0.10085100	-0.18004500
O	-5.16707000	2.02975400	0.89929600
O	-4.79721400	-2.47558500	-0.48400200
N	-2.93535700	-1.67429900	0.49154500
N	-3.03710700	1.31268800	0.91722900
C	3.74131400	-0.03118100	-1.46967700
H	4.18792300	-0.98766800	-1.20773200
H	2.69883200	-0.19214000	-1.74725200
N	3.70666100	0.85472700	-0.22989300
C	5.04420400	0.81686300	0.54950100
O	5.61063700	1.86565000	0.72590500
Cl	-0.23432300	-0.33338100	-2.66990500
O	0.88407600	0.26044900	-3.46991800
O	-0.74488500	-1.57352100	-3.30949200
O	-1.33230900	0.66833900	-2.50165300
O	0.32269800	-0.67343400	-1.29092800
C	5.58968700	-0.49767200	0.97835500
C	4.84203500	-1.66981900	1.19589500
C	6.98254000	-0.51588600	1.18852400
C	5.49022500	-2.83620900	1.59725100
H	3.76473000	-1.63618500	1.09253800
C	7.61981300	-1.68793000	1.58275500
H	7.54933100	0.39608300	1.03520300

C	6.87428300	-2.85219000	1.78568500
H	4.90622000	-3.73473600	1.77380300
H	8.69539400	-1.69266000	1.73370300
H	7.37028700	-3.76758900	2.09694100
C	-6.31233100	-0.31224900	0.22951800
H	-6.88051600	0.60120400	0.04865200
H	-6.74433800	-1.12448300	-0.35627300
H	-6.40041800	-0.56501200	1.29173000
C	-4.75404600	0.27650600	-1.69177300
H	-5.22493700	-0.51014700	-2.28822100
H	-5.29495400	1.21324600	-1.86021000
H	-3.71631700	0.39711800	-2.01553900
C	-2.30315500	2.57146800	2.91164700
H	-1.27874200	2.19569000	2.82063500
H	-2.26938300	3.56048300	3.38488400
H	-2.86432000	1.89491700	3.56623300
C	-2.15006200	3.58153400	0.60073800
H	-2.11306700	4.59711000	1.01429800
H	-1.12591800	3.21114500	0.49711100
H	-2.60374000	3.62805400	-0.39535200
C	-2.84883900	-3.68212000	1.89215300
H	-2.69461200	-4.76754300	1.91442700
H	-2.09458900	-3.21312300	2.53224400
H	-3.83738900	-3.46450500	2.31267600
C	-1.37323900	-3.50387500	-0.15672100
H	-0.55857300	-3.12499700	0.46970000
H	-1.26770900	-4.59376700	-0.22818400
H	-1.25875500	-3.07211900	-1.15480100



^{3}INT$_{C\text{-}H}$

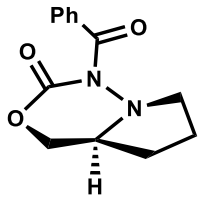
Zero-point correction=	0.614736 (Hartree/Particle)
Thermal correction to Energy=	0.659341
Thermal correction to Enthalpy=	0.660285
Thermal correction to Gibbs Free Energy=	0.527653
Sum of electronic and zero-point Energies=	-2513.413070
Sum of electronic and thermal Energies=	-2513.368464
Sum of electronic and thermal Enthalpies=	-2513.367520
Sum of electronic and thermal Free Energies=	-2513.500152

Cartesian Coordinates

Atom	X	Y	Z
C	3.25674200	-2.41728600	0.65591900
C	5.30129900	-1.41382400	1.32520400
C	4.92337900	-2.49305300	2.34830700
C	3.92843400	-3.38900500	1.57991600
H	1.43744500	-0.61184700	-1.90723400
H	6.15919700	-1.71551400	0.71140400
H	5.52856400	-0.45087400	1.78033800
H	5.80112300	-3.03062300	2.71770300
H	4.41781300	-2.03017400	3.20217900
H	4.46528200	-4.17169100	1.01876500
H	3.21608300	-3.90062900	2.23592600
N	4.09473200	-1.31805100	0.45722800
C	3.99579600	-0.44491900	-0.61177900
C	1.81087000	-2.38812400	0.34887900
H	1.25396200	-2.90027600	1.13782900
H	1.44233900	-1.36783200	0.27274900

O	1.44816400	-3.14524900	-0.87557200
C	0.83948400	-2.52612800	-1.88360000
N	0.56506600	-1.15263800	-1.78431600
O	0.46880700	-3.11597000	-2.88063500
O	3.28656500	-0.71046800	-1.59111100
Ag	-1.23495800	-0.22829800	-0.91334600
C	-3.60365100	-2.64343400	-0.26001300
C	-5.03797700	-2.66767000	0.34130700
H	-5.81752700	-2.80427900	-0.41550800
H	-5.17039800	-3.40715000	1.13502700
C	-2.22105300	3.04011600	-1.19725600
C	-2.52386200	3.88110300	0.06014600
H	-1.64944100	3.99047400	0.70851100
H	-2.97971200	4.85185900	-0.14369400
C	-3.35403100	1.81592700	0.30142600
C	-4.13772700	-0.61257700	0.55021900
C	-4.16638800	0.80567000	1.09970000
O	-5.21380700	-1.35418600	0.92344900
O	-3.49901900	3.07613200	0.77619500
N	-2.61248500	1.66925400	-0.73544100
N	-3.22667900	-1.21425600	-0.11343700
Cl	0.63287800	1.01132500	1.71823400
O	-0.38119900	-0.11716000	1.65796200
O	1.27063400	1.11395000	0.35463700
O	-0.06675000	2.28421000	2.04747700
O	1.67348300	0.68828400	2.73156500
C	4.77856400	0.82574800	-0.54694300
C	5.52098700	1.21447200	-1.67049800
C	4.70138500	1.67707100	0.56619700
C	6.22060300	2.42013000	-1.66382500
H	5.54190100	0.56603900	-2.54135000
C	5.38797800	2.89128900	0.55923100
H	4.06525300	1.41076600	1.40568500

C	6.15731400	3.25862800	-0.54771900
H	6.80742700	2.70972200	-2.53135500
H	5.31143900	3.55606200	1.41518700
H	6.69581000	4.20268400	-0.54620700
C	-3.59951100	0.74607300	2.55037700
H	-2.55237900	0.43294100	2.54611200
H	-3.66947000	1.73565500	3.00863100
H	-4.19136200	0.04037300	3.14175500
C	-5.63369200	1.31642000	1.13304500
H	-6.06860400	1.34415300	0.12785200
H	-6.24313000	0.65605200	1.75180400
H	-5.65996700	2.32376000	1.55133400
C	-3.58155900	-3.04854700	-1.73856300
H	-2.56726500	-2.97853100	-2.14606300
H	-3.92064800	-4.08468200	-1.85638500
H	-4.23671000	-2.40058600	-2.33090800
C	-2.62700400	-3.50250200	0.55826000
H	-2.90465500	-4.56125400	0.49223200
H	-1.60634700	-3.39523700	0.17748800
H	-2.63134100	-3.20501500	1.61228000
C	-3.14409700	3.41128300	-2.37074300
H	-2.88659300	4.40244500	-2.76234000
H	-3.03881300	2.68243600	-3.18092300
H	-4.19444000	3.42640800	-2.05781000
C	-0.75210600	3.10738000	-1.61228400
H	-0.57509300	2.47919600	-2.49317600
H	-0.48542600	4.13697900	-1.88093600
H	-0.09076200	2.77371400	-0.80907700



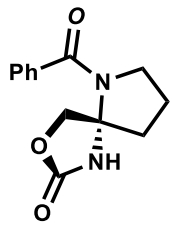
^{1}PRO*Amide*

Zero-point correction=	0.259852 (Hartree/Particle)
Thermal correction to Energy=	0.274533
Thermal correction to Enthalpy=	0.275477
Thermal correction to Gibbs Free Energy=	0.216780
Sum of electronic and zero-point Energies=	-838.701565
Sum of electronic and thermal Energies=	-838.686884
Sum of electronic and thermal Enthalpies=	-838.685940
Sum of electronic and thermal Free Energies=	-838.744637

Cartesian Coordinates

Atom	X	Y	Z
C	-2.90122200	0.33758400	-0.43814900
C	-3.47415000	-1.74739700	0.74128600
C	-4.09508200	-0.45990500	0.14211100
H	-3.02363500	0.56789500	-1.50339700
H	-3.55807800	-2.57552500	0.03174300
H	-3.95188100	-2.05152100	1.67659400
H	-4.83831300	-0.68207600	-0.62746400
H	-4.60018100	0.13024500	0.91598900
C	-2.63362000	1.63749800	0.30566700
H	-3.42879200	2.37440800	0.16577700
H	-2.50588700	1.45900300	1.38168400
O	-1.44978400	2.24198400	-0.22821000
C	-0.36390000	1.47884000	-0.49858100
N	-0.48653700	0.09454800	-0.25972000
O	0.63959000	1.99432300	-0.93070400
C	-2.00117900	-1.38221600	0.93065700
H	-1.33253400	-2.24586700	0.92719800

H	-1.83994300	-0.81605200	1.86471000
N	-1.75685800	-0.56766700	-0.27004400
C	0.60580200	-0.79365100	-0.55602700
O	0.37800400	-1.89144900	-1.02472700
C	1.97875700	-0.39462400	-0.12886900
C	2.22871400	0.39255100	1.00355300
C	3.05479300	-0.95391400	-0.83124000
C	3.53762400	0.62627500	1.41716400
H	1.40162400	0.80981800	1.56824900
C	4.36363100	-0.70021100	-0.42873200
H	2.84808800	-1.58419400	-1.68988400
C	4.60752600	0.08891100	0.69742200
H	3.72350000	1.23087000	2.30050200
H	5.19282800	-1.12356700	-0.98874500
H	5.62833200	0.28107400	1.01694400



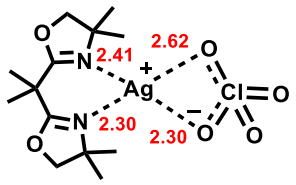
^{1}PRO$_{C\text{-}H}$

Zero-point correction=	0.260625 (Hartree/Particle)
Thermal correction to Energy=	0.275393
Thermal correction to Enthalpy=	0.276338
Thermal correction to Gibbs Free Energy=	0.217583
Sum of electronic and zero-point Energies=	-838.748080
Sum of electronic and thermal Energies=	-838.733312
Sum of electronic and thermal Enthalpies=	-838.732368
Sum of electronic and thermal Free Energies=	-838.791122

Cartesian Coordinates

Atom	X	Y	Z

C	-1.62142400	-0.00839800	-0.31215300
C	0.00571900	1.70378400	-0.44280200
C	-1.02868100	1.95982100	-1.58479200
C	-1.82557000	0.64069100	-1.69629400
H	-2.58874300	1.60012100	0.77206700
H	-0.17225900	2.36789300	0.41064300
H	1.03523700	1.85298500	-0.76620800
H	-1.68082000	2.80235800	-1.33181900
H	-0.53190800	2.21364100	-2.52501700
H	-2.88153100	0.78566200	-1.94225000
H	-1.38376900	-0.01852800	-2.45173000
N	-0.19932800	0.29214300	-0.03868400
C	0.77554600	-0.66445200	-0.30031000
C	-2.07388500	-1.47697400	-0.13911400
H	-2.08755000	-2.03965200	-1.06990500
H	-1.46390000	-2.00173500	0.59650500
O	-3.42328000	-1.38132400	0.36228200
C	-3.61804200	-0.15195100	0.91665000
N	-2.46793000	0.59743200	0.71636300
O	-4.62889000	0.19015100	1.47776700
O	0.50677700	-1.77483700	-0.75210500
C	2.18931800	-0.30472200	0.05040500
C	3.21952800	-0.93139700	-0.66521200
C	2.51118400	0.55769000	1.10834500
C	4.55115100	-0.67495000	-0.34853800
H	2.95616300	-1.62120900	-1.46051100
C	3.84537500	0.80111100	1.43386900
H	1.71687100	1.01381700	1.69144500
C	4.86630500	0.19236500	0.70117800
H	5.34421900	-1.15617400	-0.91413400
H	4.08729900	1.45990000	2.26330300
H	5.90550500	0.38627100	0.95292400



Cat.

Zero-point correction=	0.358666 (Hartree/Particle)
Thermal correction to Energy=	0.385124
Thermal correction to Enthalpy=	0.386069
Thermal correction to Gibbs Free Energy=	0.297906
Sum of electronic and zero-point Energies=	-1674.765001
Sum of electronic and thermal Energies=	-1674.738543
Sum of electronic and thermal Enthalpies=	-1674.737599
Sum of electronic and thermal Free Energies=	-1674.825761

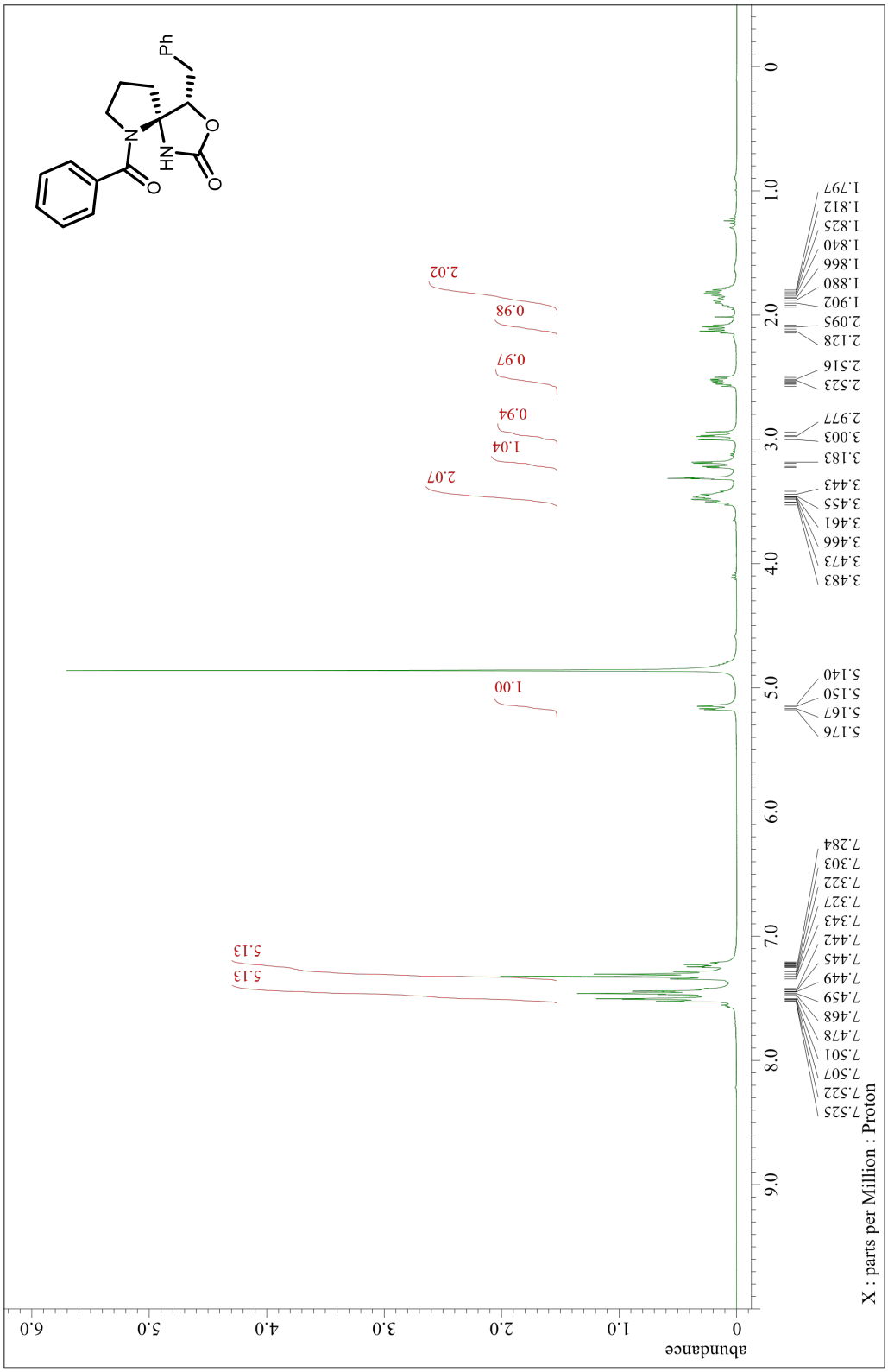
Cartesian Coordinates

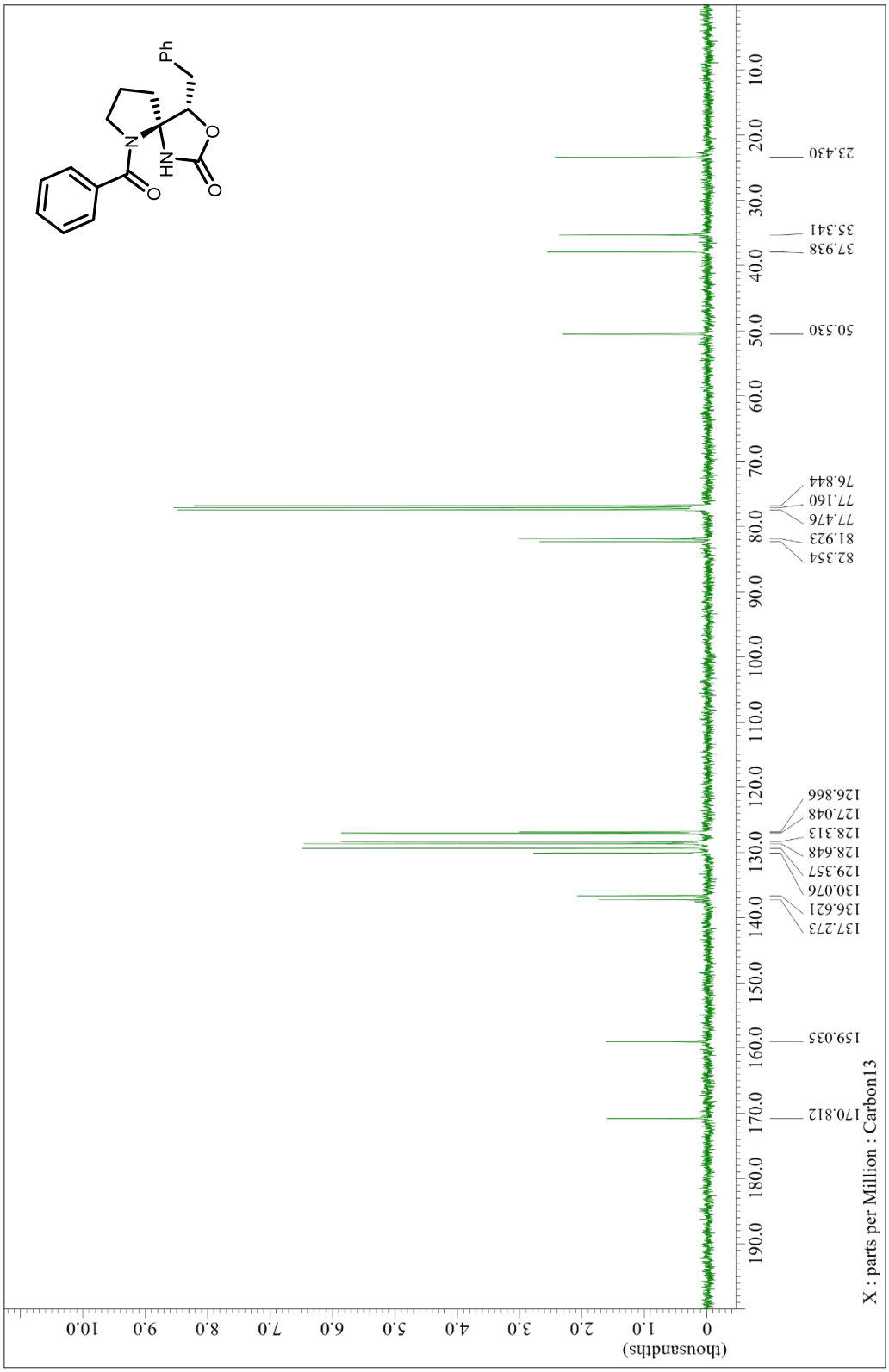
Atom	X	Y	Z
C	0.19487700	2.77640900	0.59566400
C	-1.02023900	3.74583300	0.70898100
H	-1.18525800	4.12907700	1.71869300
H	-0.97131500	4.58209900	0.00440600
C	-1.75129500	-2.62686600	0.57550500
C	-3.27090600	-2.50959600	0.89387600
H	-3.89045700	-3.18811900	0.29943600
H	-3.50933900	-2.63332100	1.95280900
C	-2.53529700	-0.61417100	-0.07099600
C	-1.68909000	1.75209200	-0.07987600
C	-2.72235700	0.78380000	-0.66247700
O	-2.17632800	2.93933400	0.34921200
O	-3.62500700	-1.15230700	0.51756400
N	-1.48033000	-1.33898100	-0.11840800
N	-0.42743800	1.57252200	-0.01876100
C	-1.44115100	-3.79700100	-0.36490200
H	-0.37794300	-3.80682900	-0.62601100

H	-1.68173100	-4.75097300	0.11853300
H	-2.02161300	-3.72138600	-1.29069900
C	-0.89970100	-2.70292100	1.85137800
H	-1.08876200	-3.64458000	2.37997500
H	0.16777700	-2.65431400	1.61088800
H	-1.13294500	-1.87369800	2.52825600
C	1.29561800	3.32377200	-0.32057400
H	1.69638300	4.25840700	0.08981000
H	2.12222300	2.61127900	-0.40442100
H	0.90413400	3.52844100	-1.32338800
C	0.76522300	2.39820300	1.97085500
H	1.53295300	1.62531900	1.86880900
H	1.21958600	3.27618100	2.44516500
H	-0.02475900	2.02115500	2.63119000
Ag	0.64139400	-0.53421200	-0.51083200
Cl	3.64198000	-0.48628000	-0.03212400
O	2.79094400	-0.73216100	-1.29628700
O	2.68442300	-0.61984200	1.13682000
O	4.18873800	0.89192400	-0.08392300
O	4.70489200	-1.50606500	0.03979600
C	-4.15544400	1.29510900	-0.40736900
H	-4.87899200	0.60662100	-0.85002700
H	-4.37401600	1.38290800	0.65912900
H	-4.27968000	2.27911700	-0.86390500
C	-2.47240900	0.69435200	-2.19477600
H	-2.59441000	1.68442200	-2.64561900
H	-1.46532900	0.33145000	-2.41236900
H	-3.19959200	0.01552800	-2.65243800

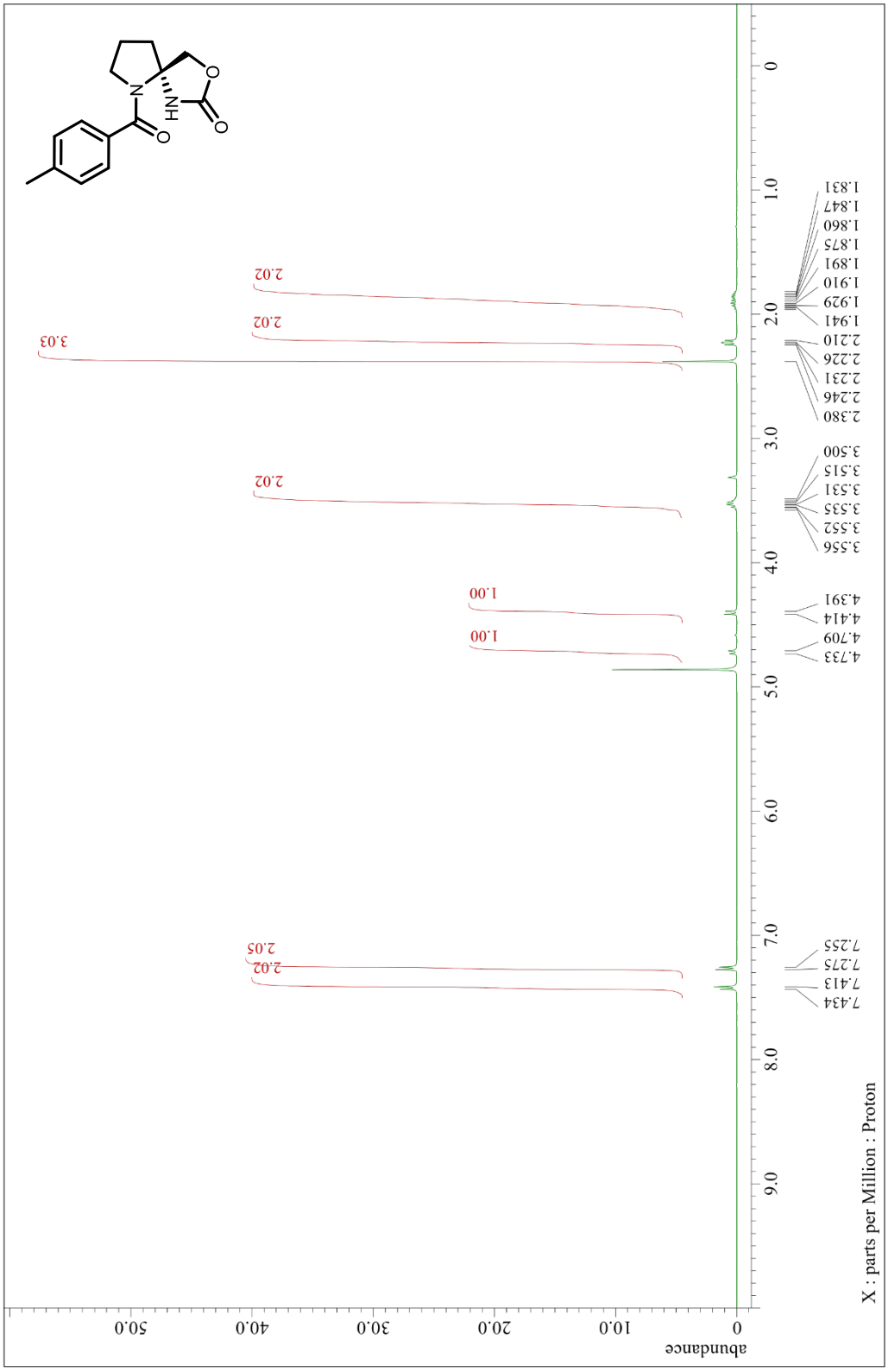
8. Charts of ^{1}H- and ^{13}C-NMR spectra

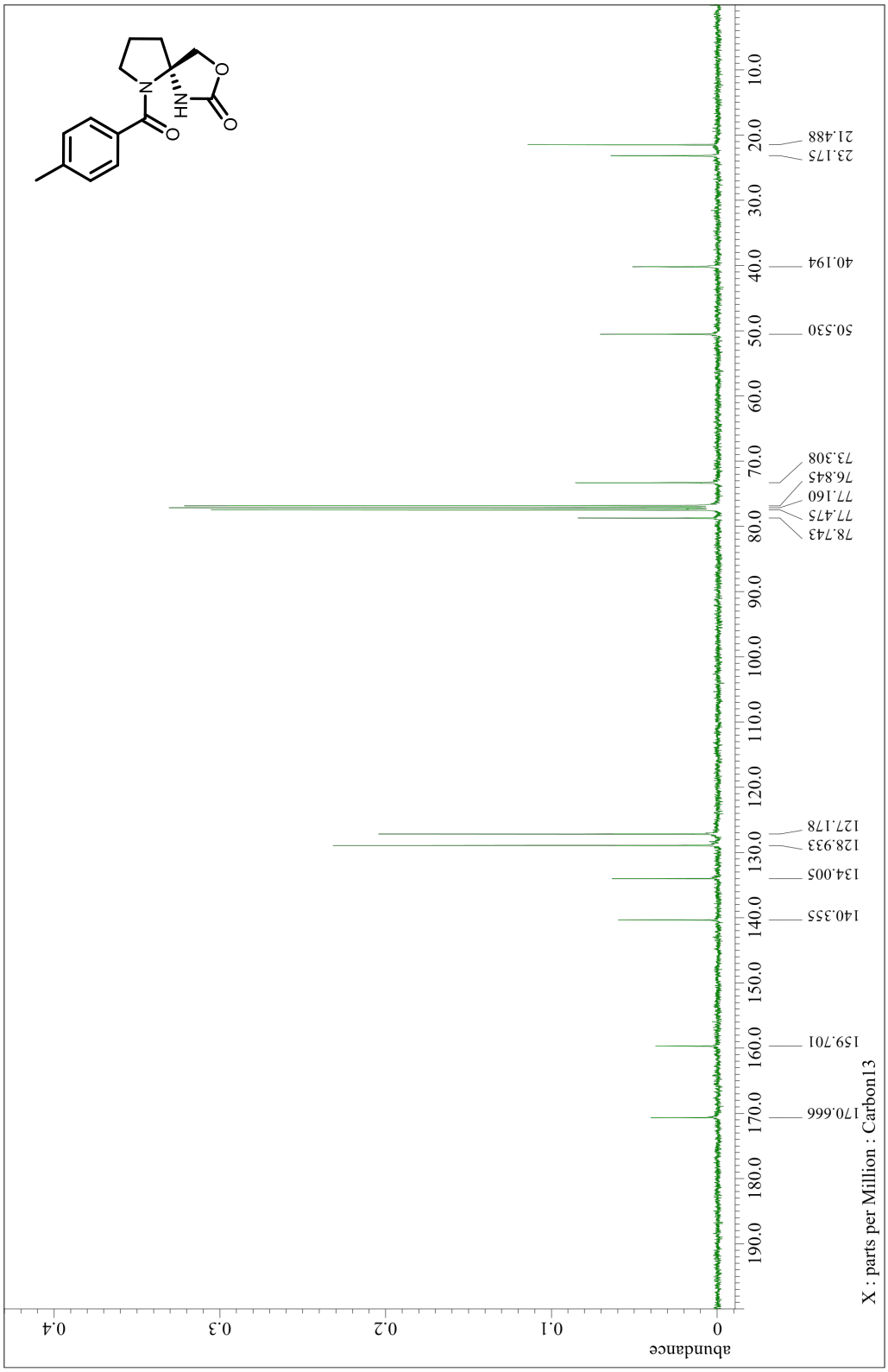
(4*S*,5*S*)-6-benzoyl-4-benzyl-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3a)



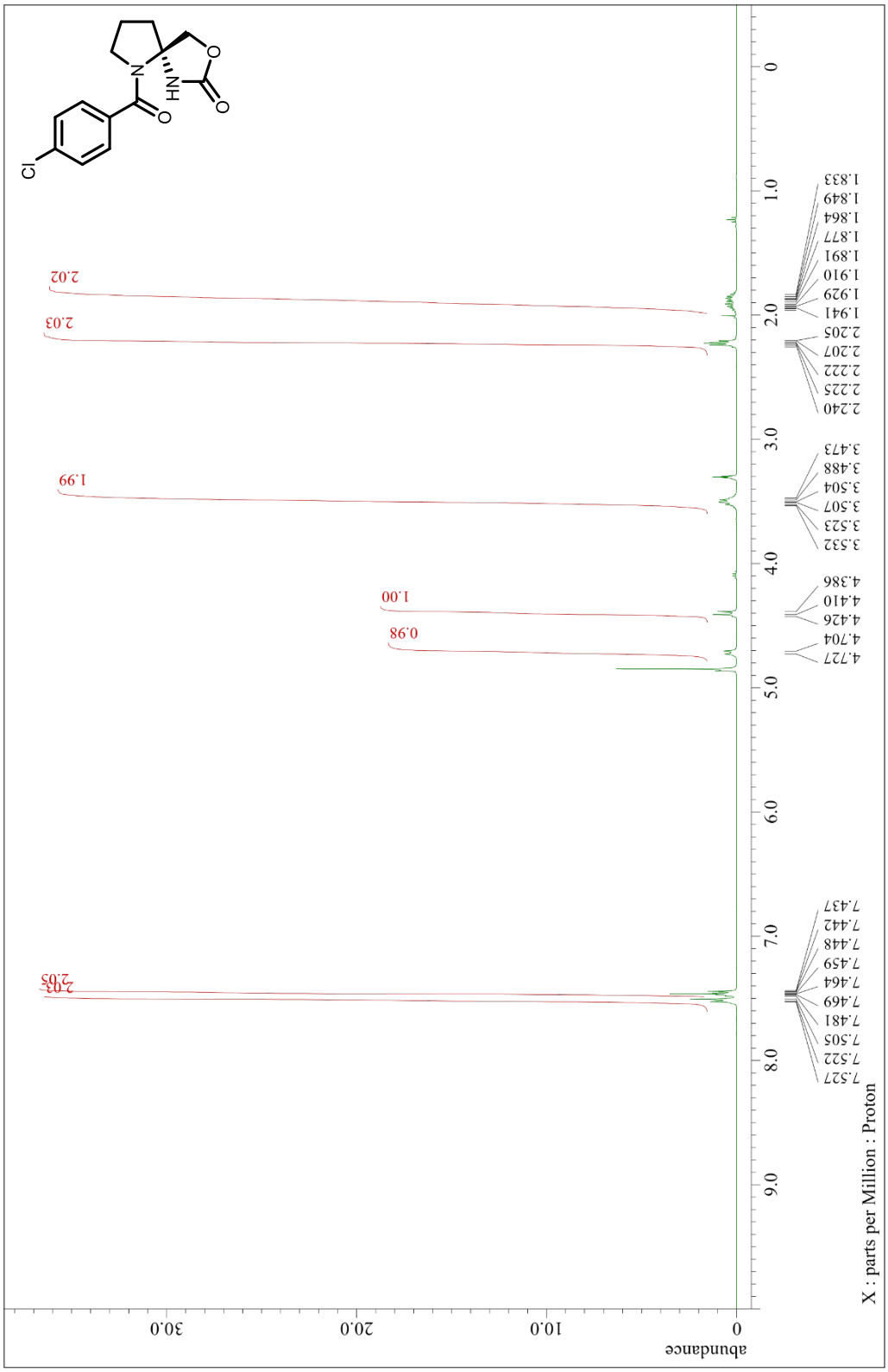

Ph
N
HN
O
O
O
23.430
35.341
37.938
50.530
76.844
77.160
77.476
81.923
82.354
126.866
127.048
128.313
128.648
129.357
130.076
136.621
137.273
159.035
170.812
X : parts per Million : Carbon13
(thousandths)

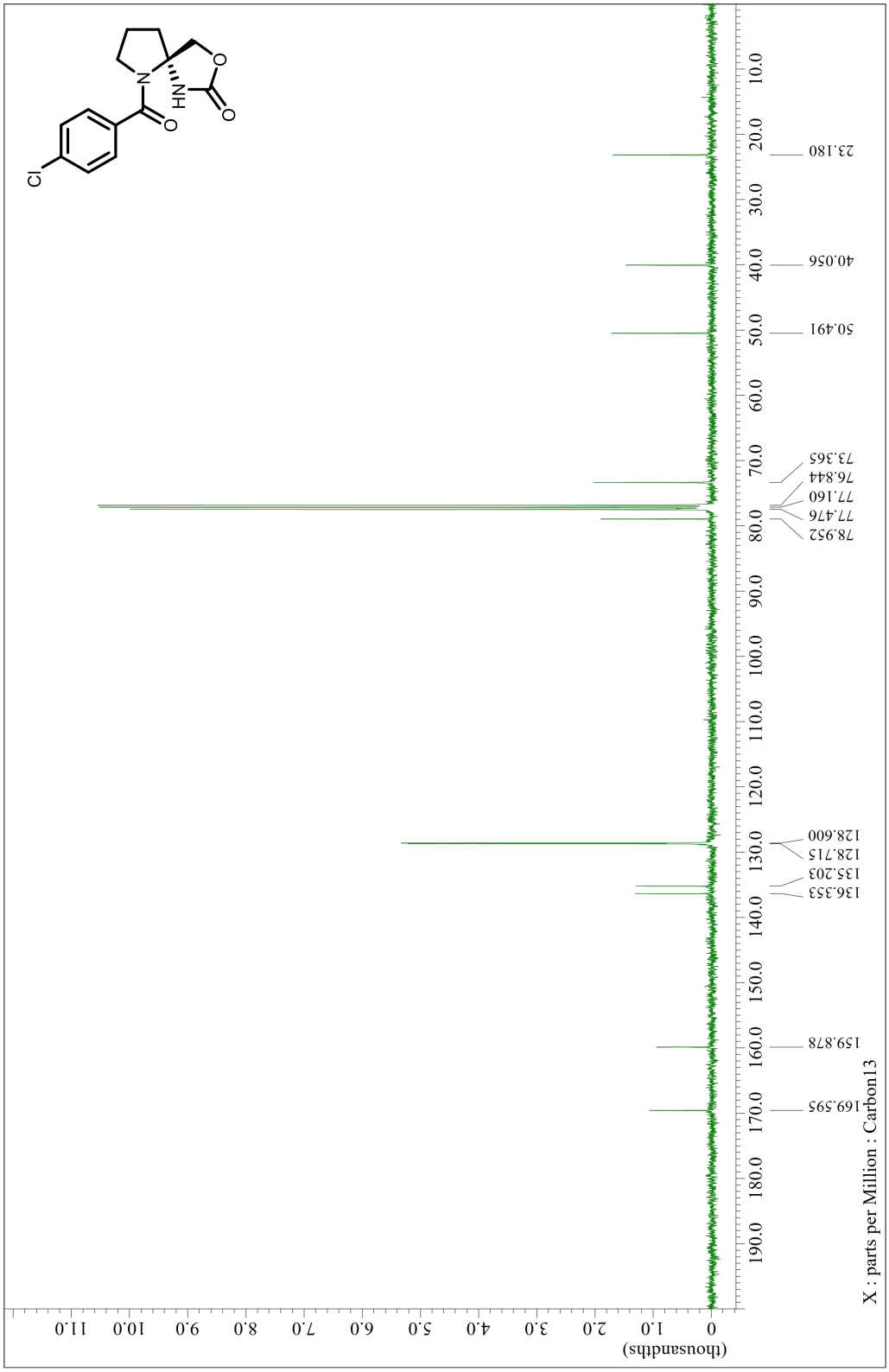
(*S*)-6-(4-methylbenzoyl)-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3c)



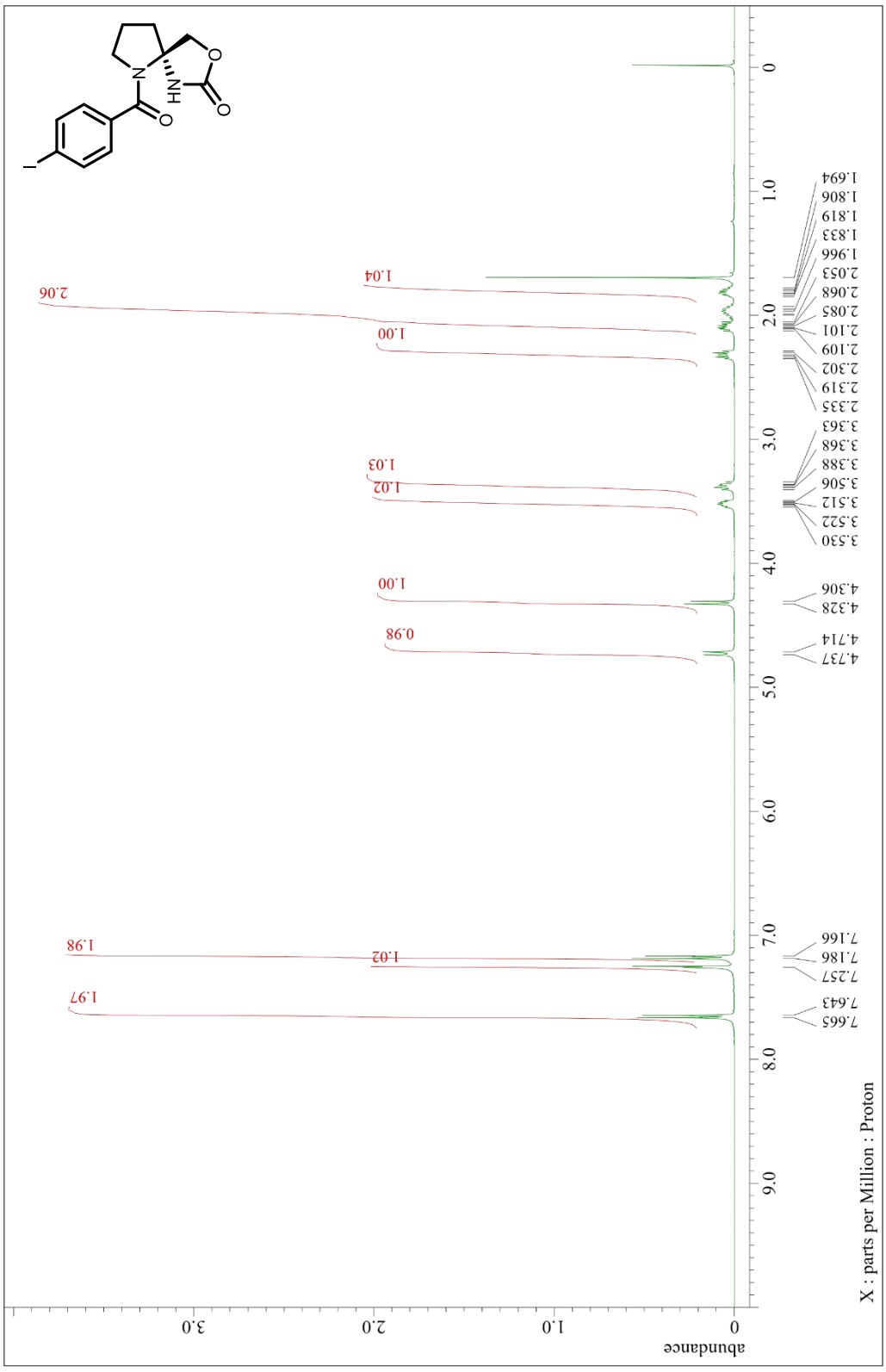

abundance
0
0.1
0.2
0.3
0.4
X : parts per Million : Carbon13
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
170.666
159.701
140.355
134.005
128.933
127.178
78.743
77.475
77.160
76.845
73.308
50.530
40.194
23.175
21.488
O
HN
O
O
N

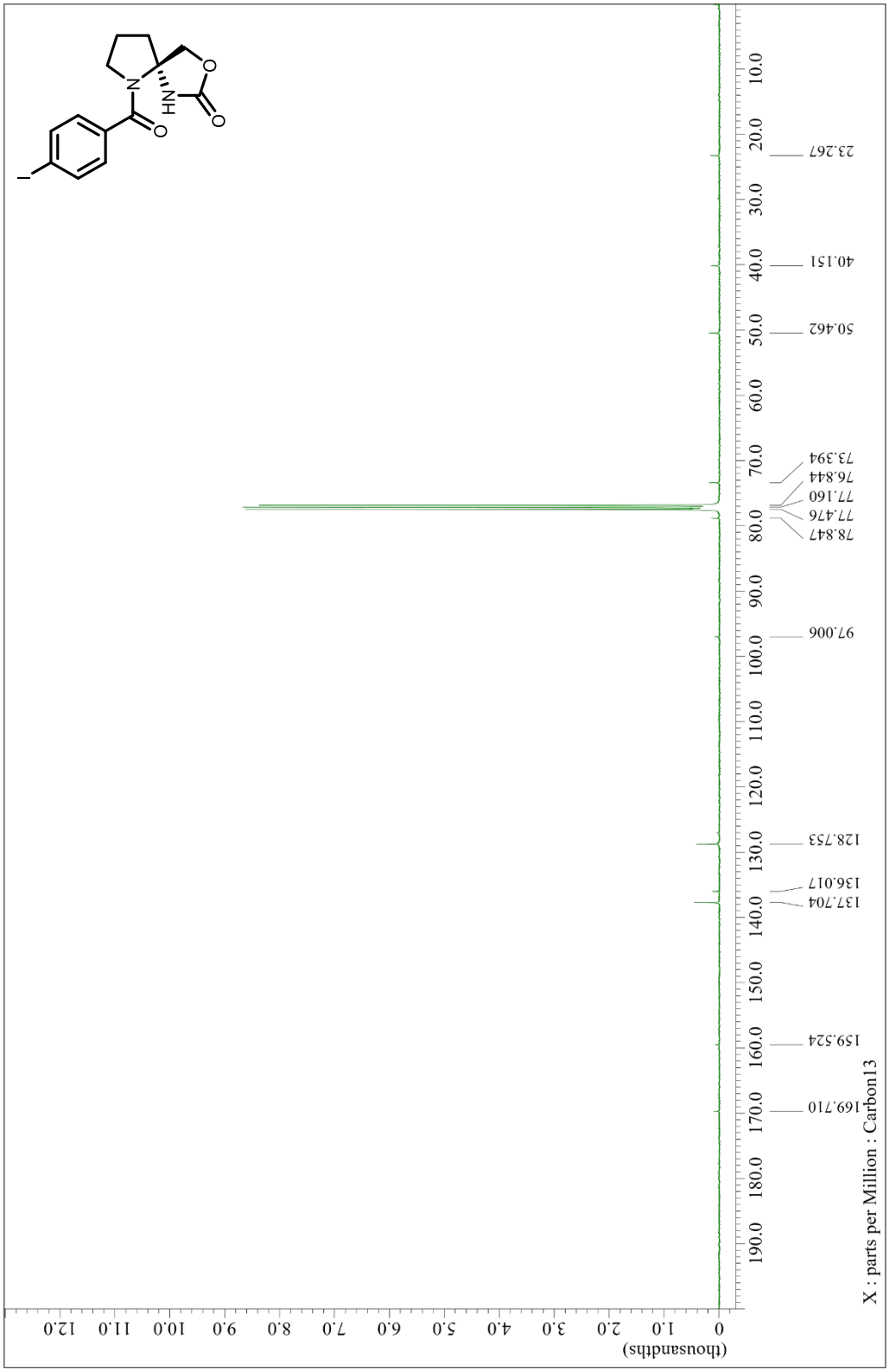
(*S*)-6-(4-chlorobenzoyl)-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3d)



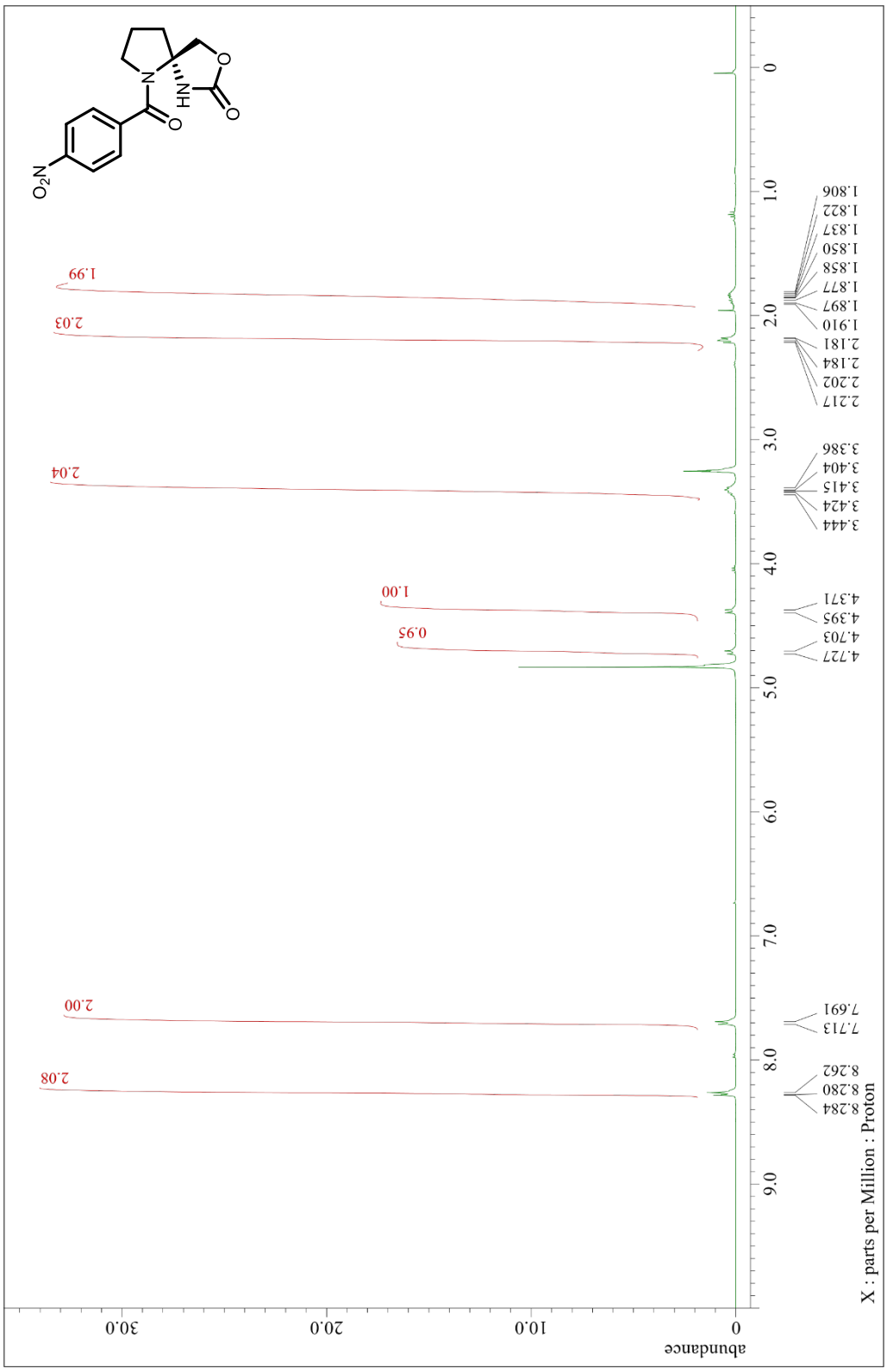

Cl
N
O
NH
O
O
23.180
40.056
50.491
73.365
76.844
77.160
77.476
78.952
128.600
128.715
135.203
136.353
159.878
169.595
X : parts per Million : Carbon13
(thousandths)

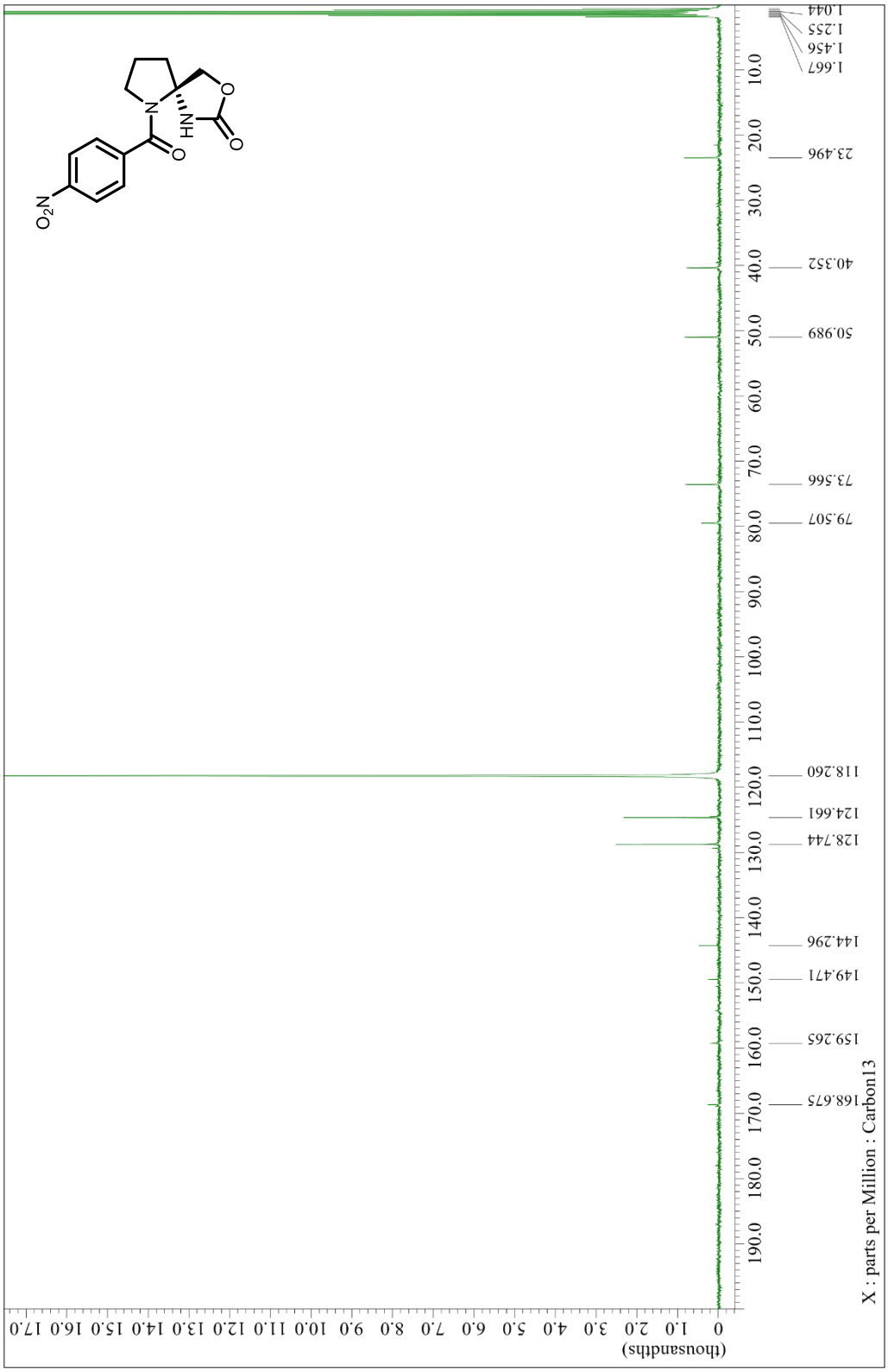
(*S*)-6-(4-iodobenzoyl)-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3e)



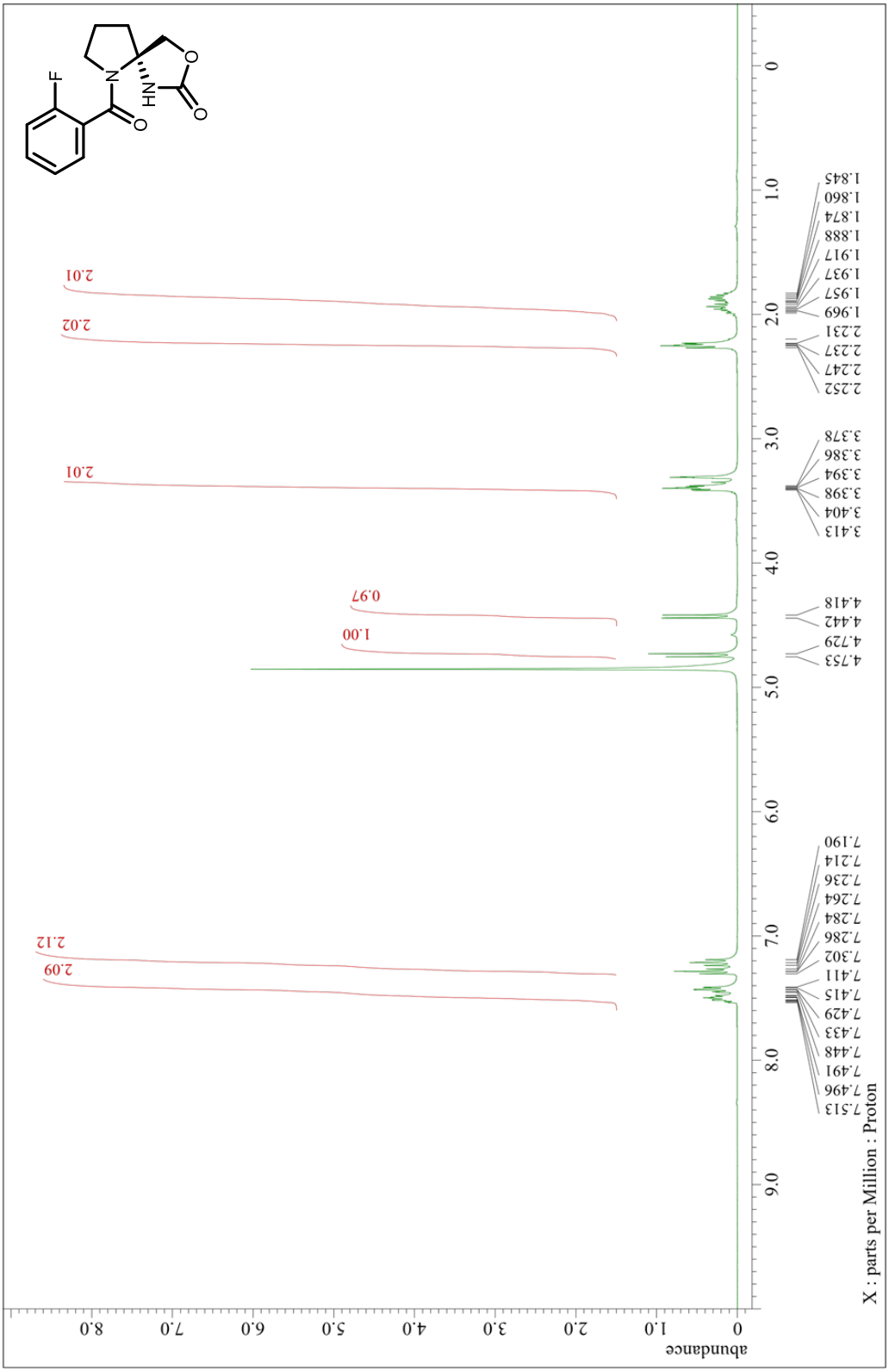

23.267
40.151
50.462
73.394
76.844
77.160
77.476
78.847
97.006
128.753
136.017
137.704
159.524
169.710
X : parts per Million : Carbon13
(thousandths)

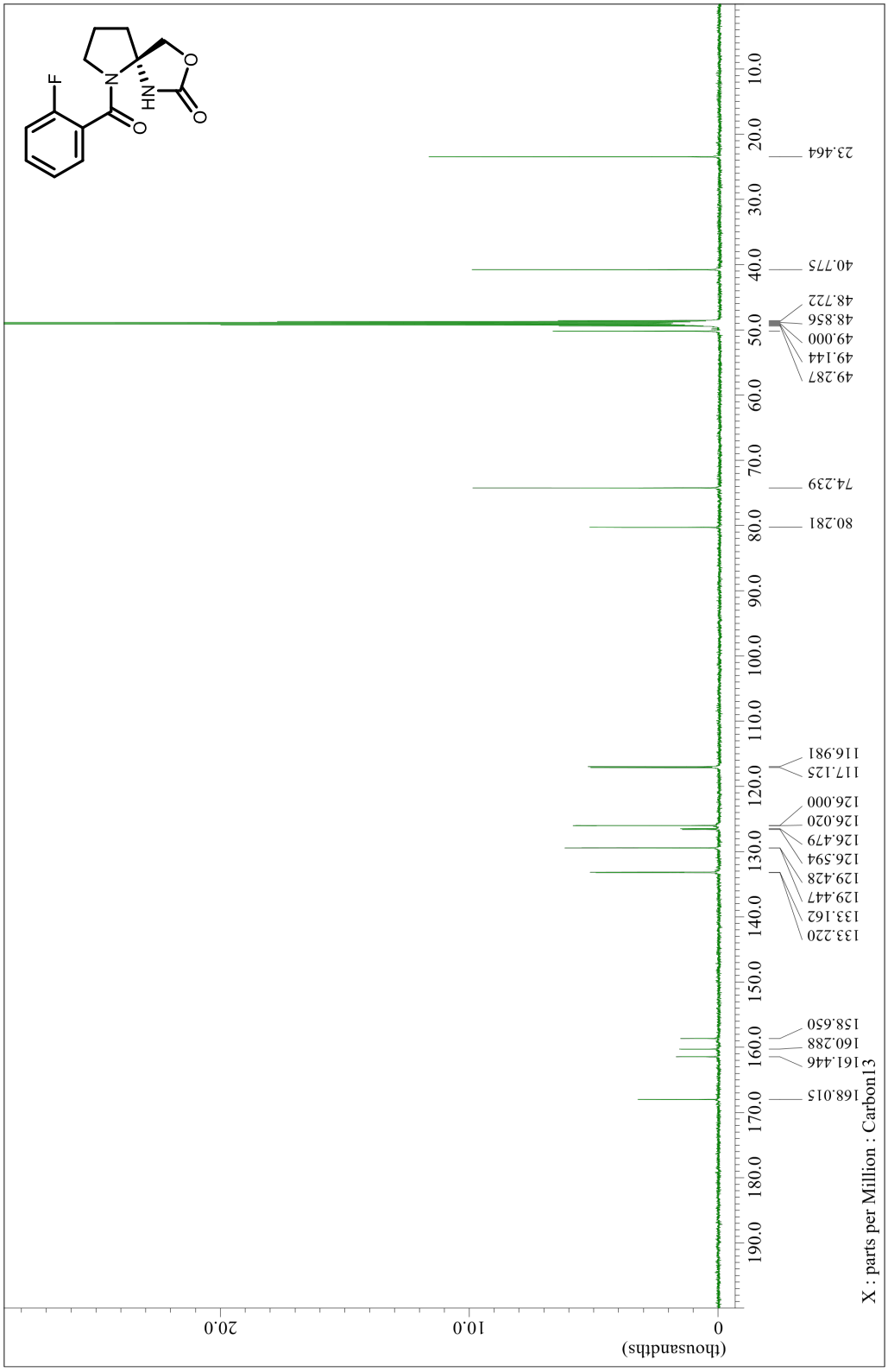
(*S*)-6-(4-nitrobenzoyl)-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3f)



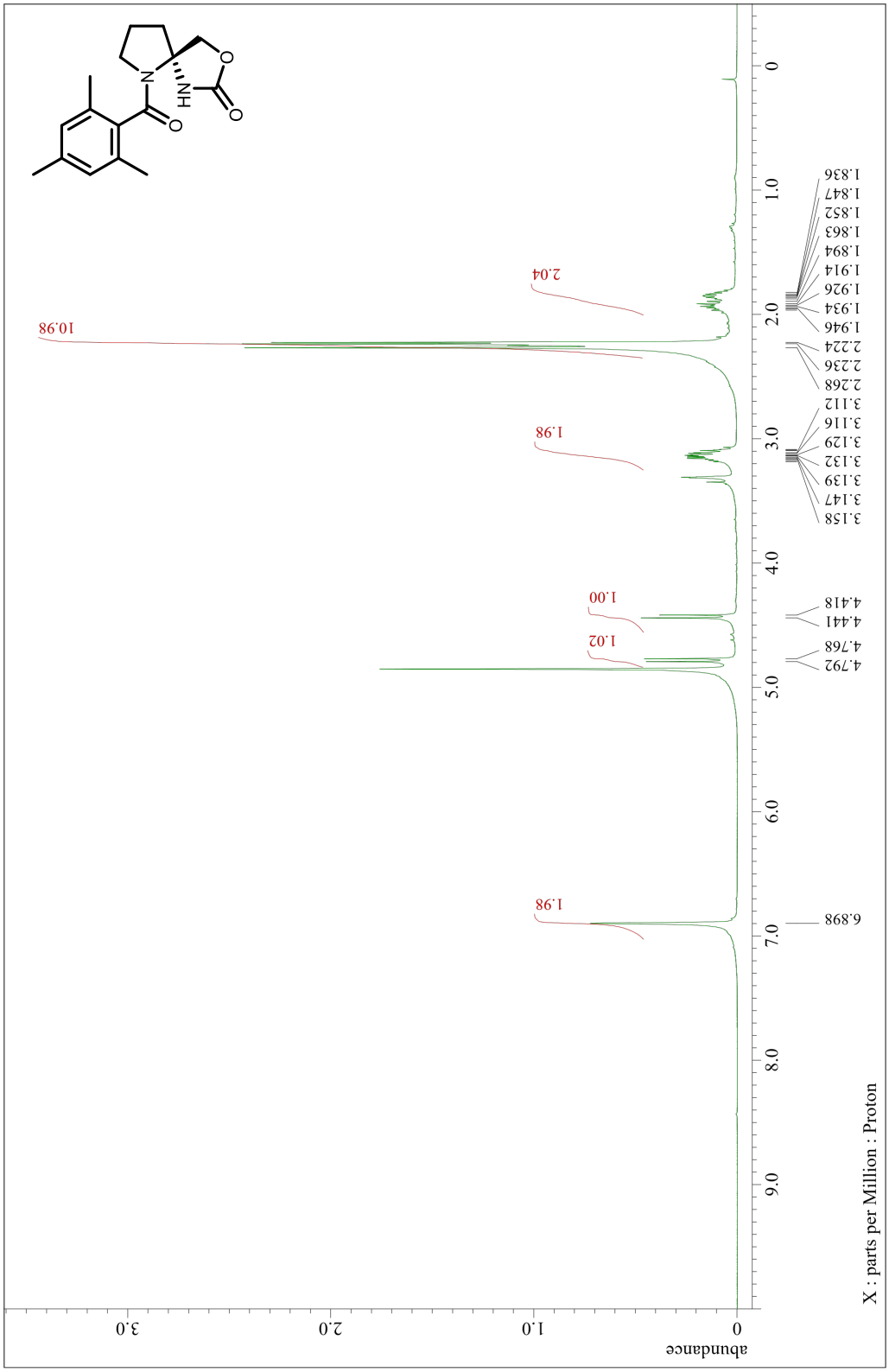

1.044
1.255
1.456
1.667
23.496
40.352
50.989
73.566
79.507
118.260
124.661
128.744
144.296
149.471
159.265
168.675
X : parts per Million : Carbon13
(thousandths)

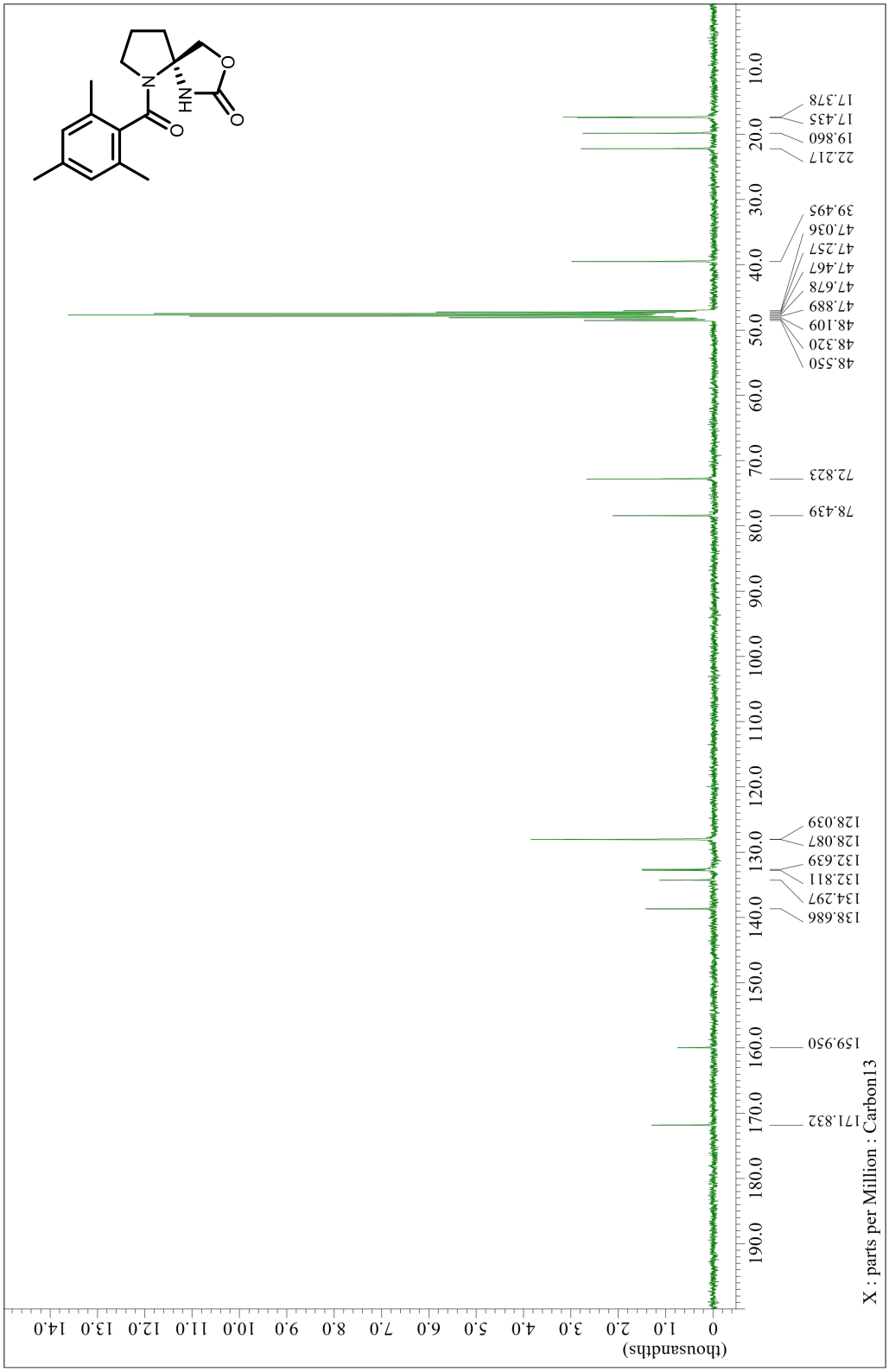
(*S*)-6-(2-fluorobenzoyl)-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3g)



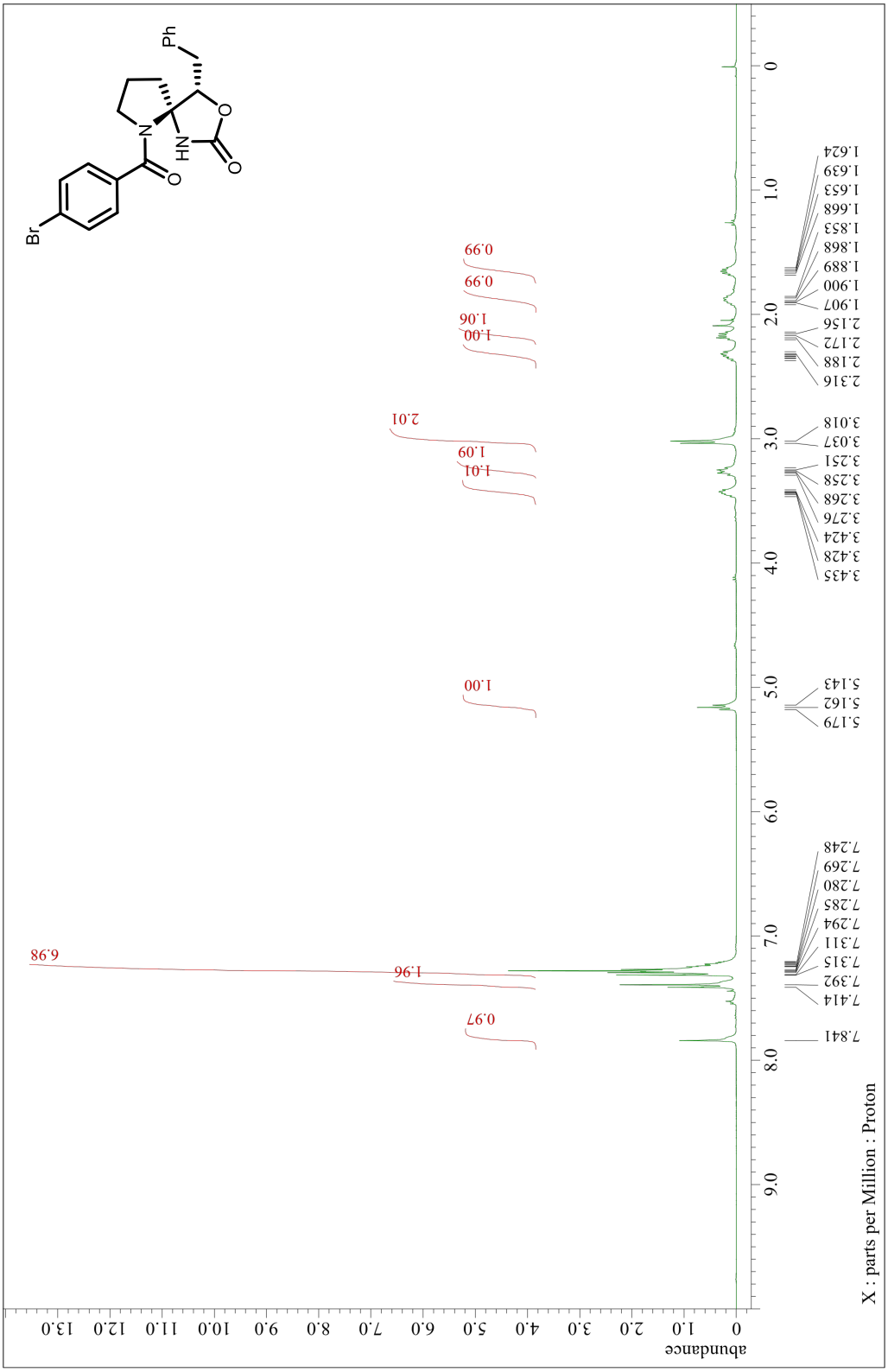

F
N
O
HN
O
O
23.464
40.775
48.722
48.856
49.000
49.144
49.287
74.239
80.281
116.981
117.125
126.000
126.020
126.479
126.594
129.428
129.447
133.162
133.220
158.650
160.288
161.446
168.015
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0
X : parts per Million : Carbon13
0
10.0
20.0
(thousandths)

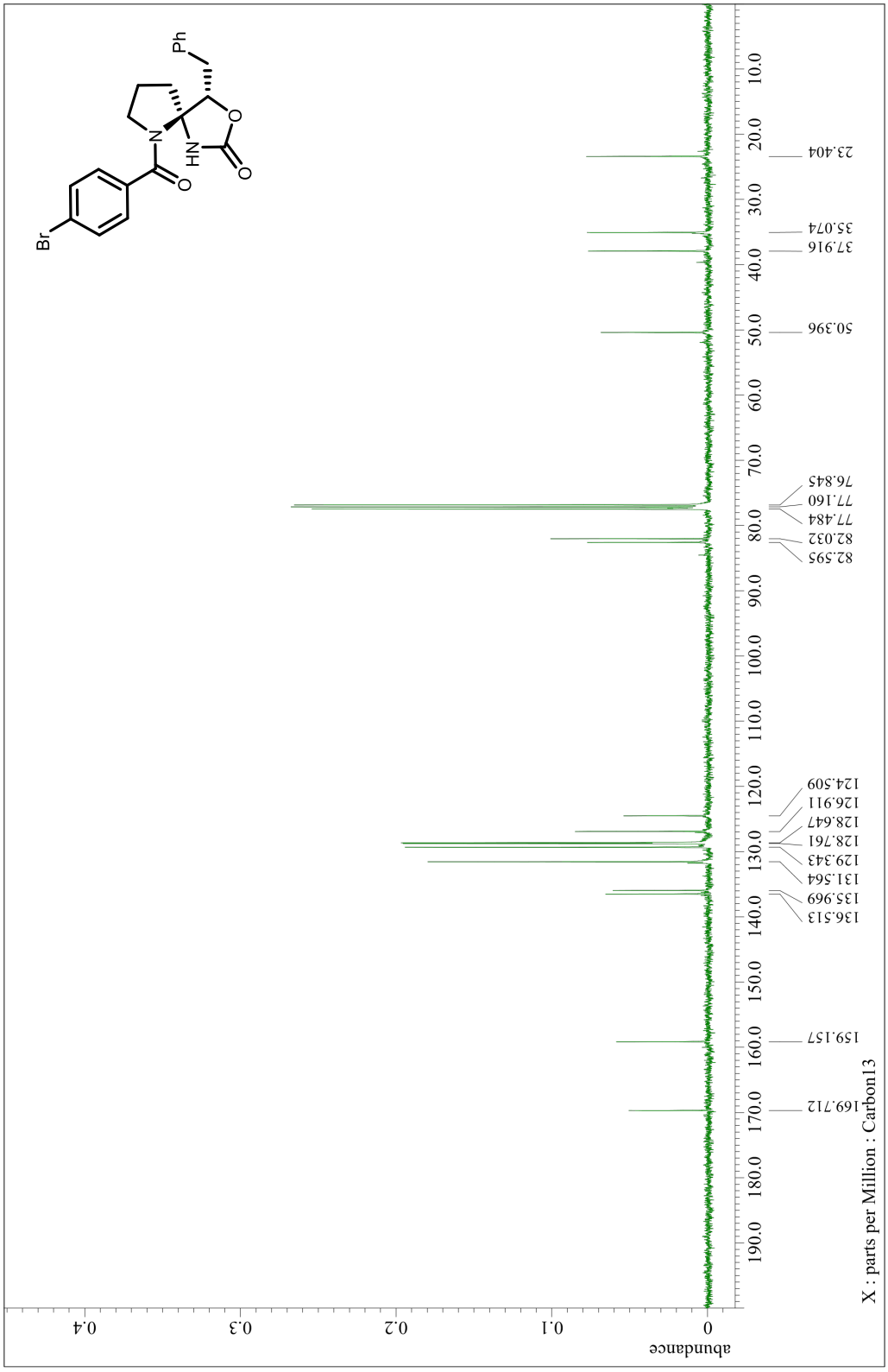
(*S*)-6-(2,4,6-trimethylbenzoyl)-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3h)



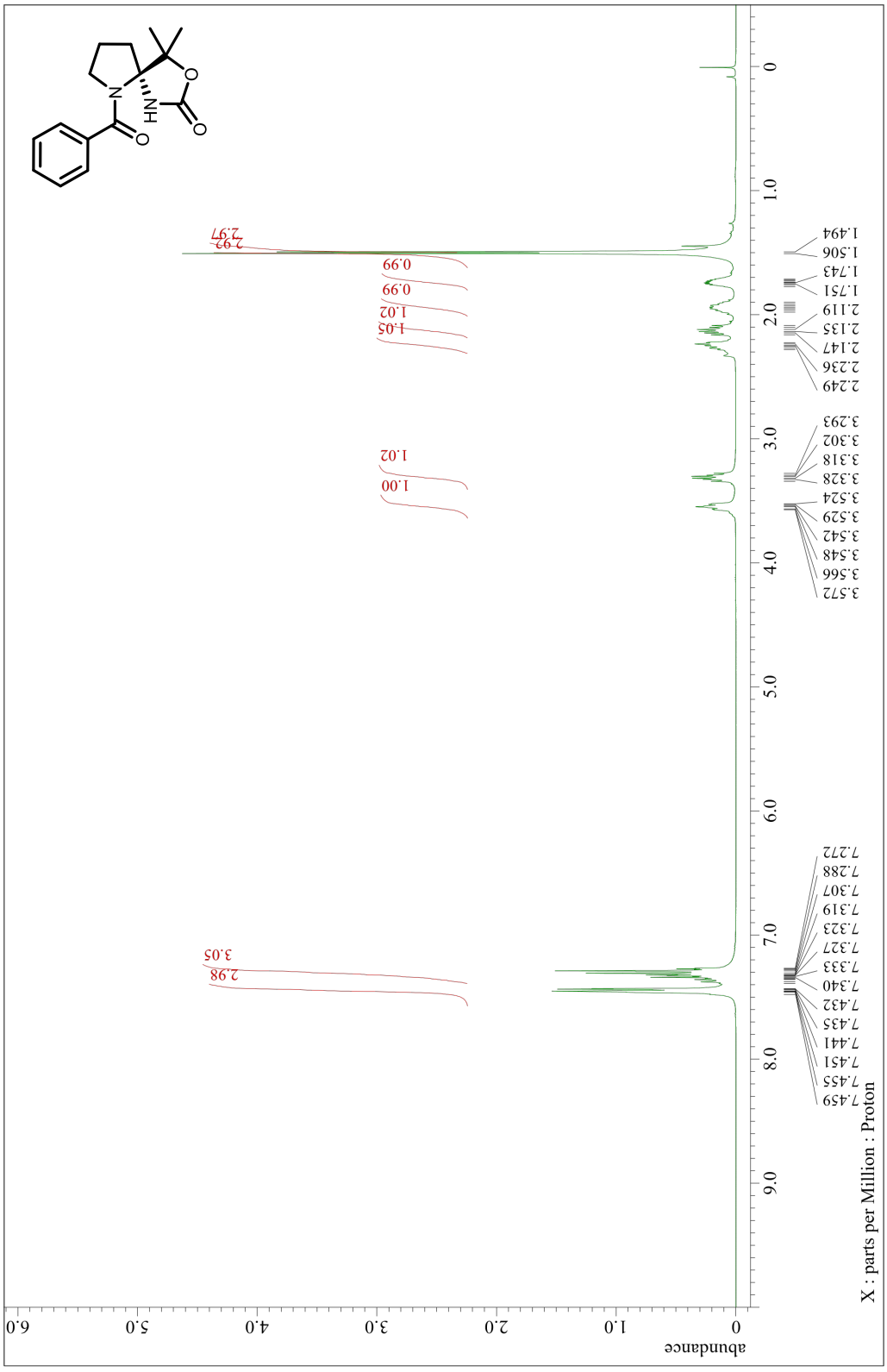

X : parts per Million : Carbon13
(thousandths)
17.378
17.435
19.860
22.217
39.495
47.036
47.257
47.467
47.678
47.889
48.109
48.320
48.550
72.823
78.439
128.039
128.087
132.639
132.811
134.297
138.686
159.950
171.832

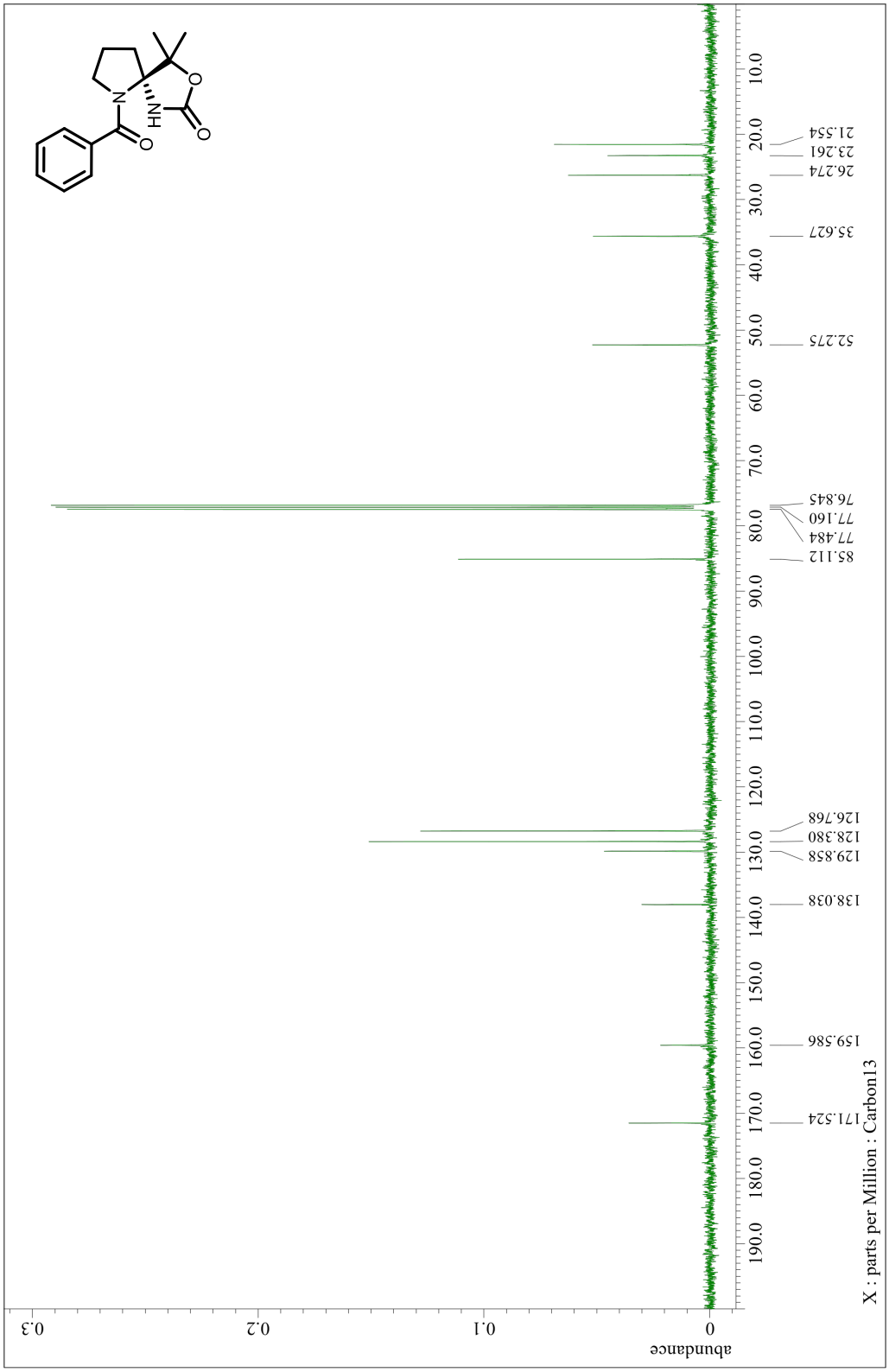
(4*S*,5*S*)-4-benzyl-6-(4-bromobenzoyl)-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3i)



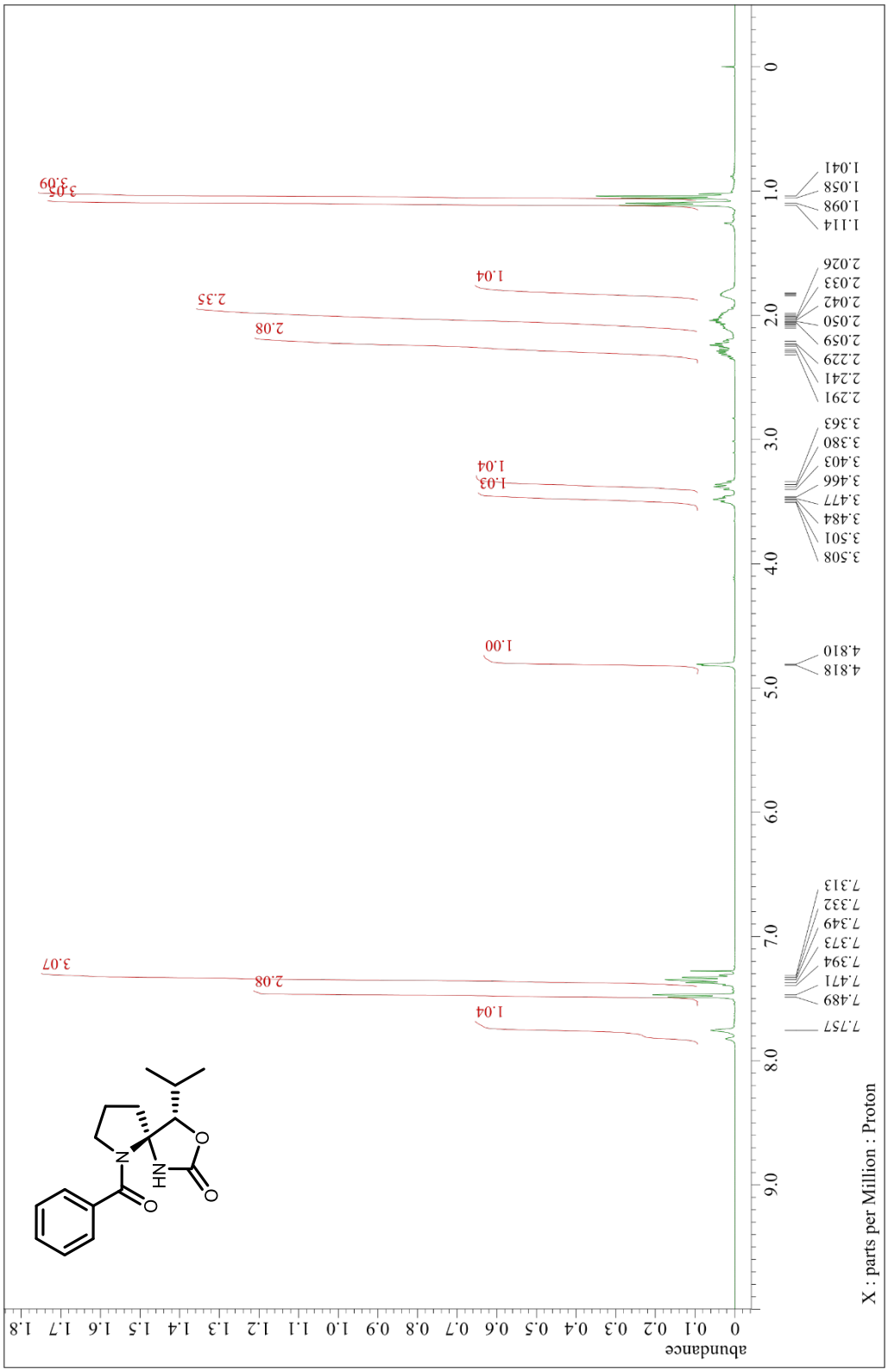

Ph
O
N
HN
O
O
Br
23.404
35.074
37.916
50.396
76.845
77.160
77.484
82.032
82.595
124.509
126.911
128.647
128.761
129.343
131.564
135.969
136.513
159.157
169.712
X : parts per Million : Carbon13
abundance

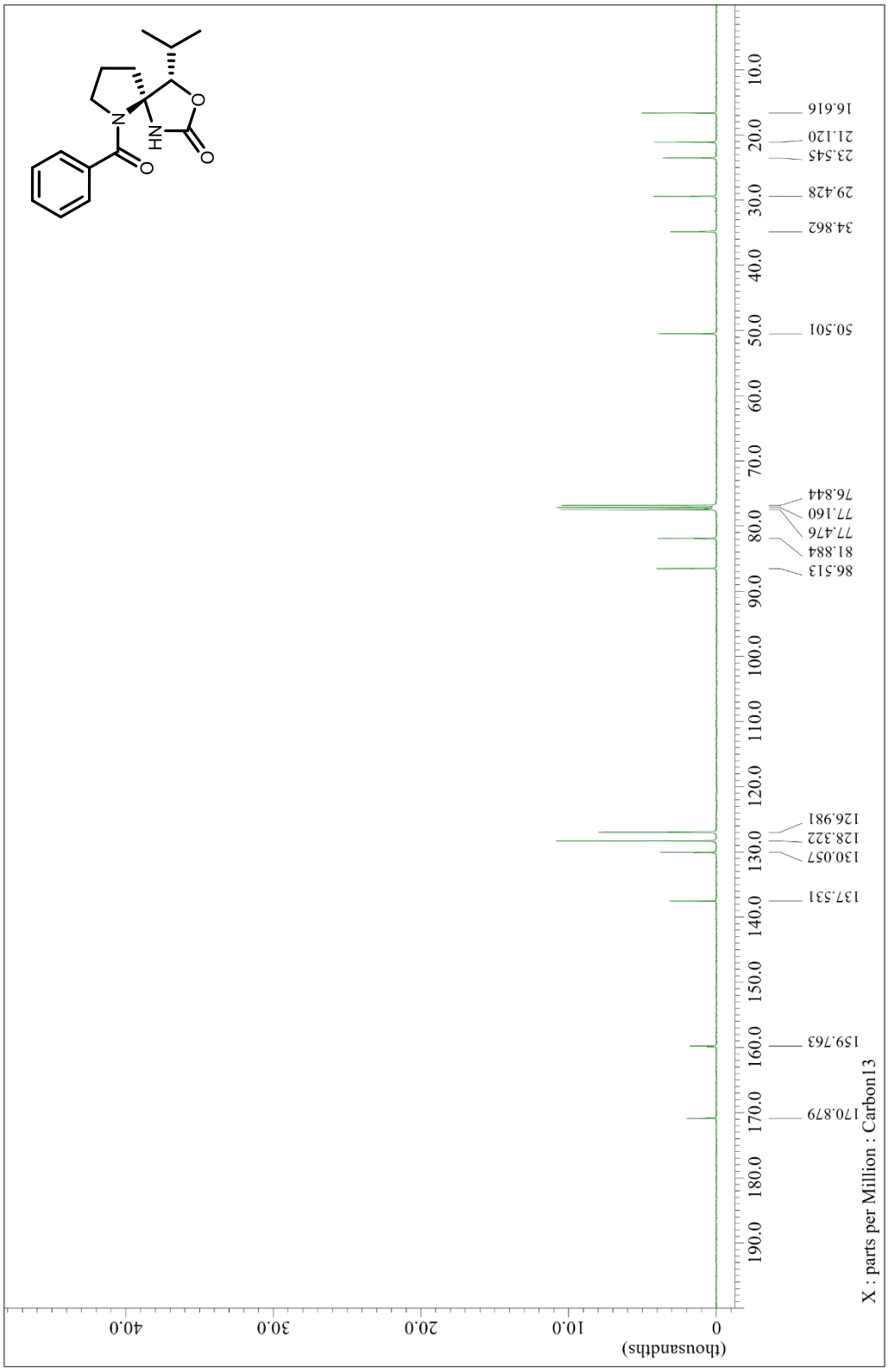
(*S*)-6-benzoyl-4,4-dimethyl-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3j)



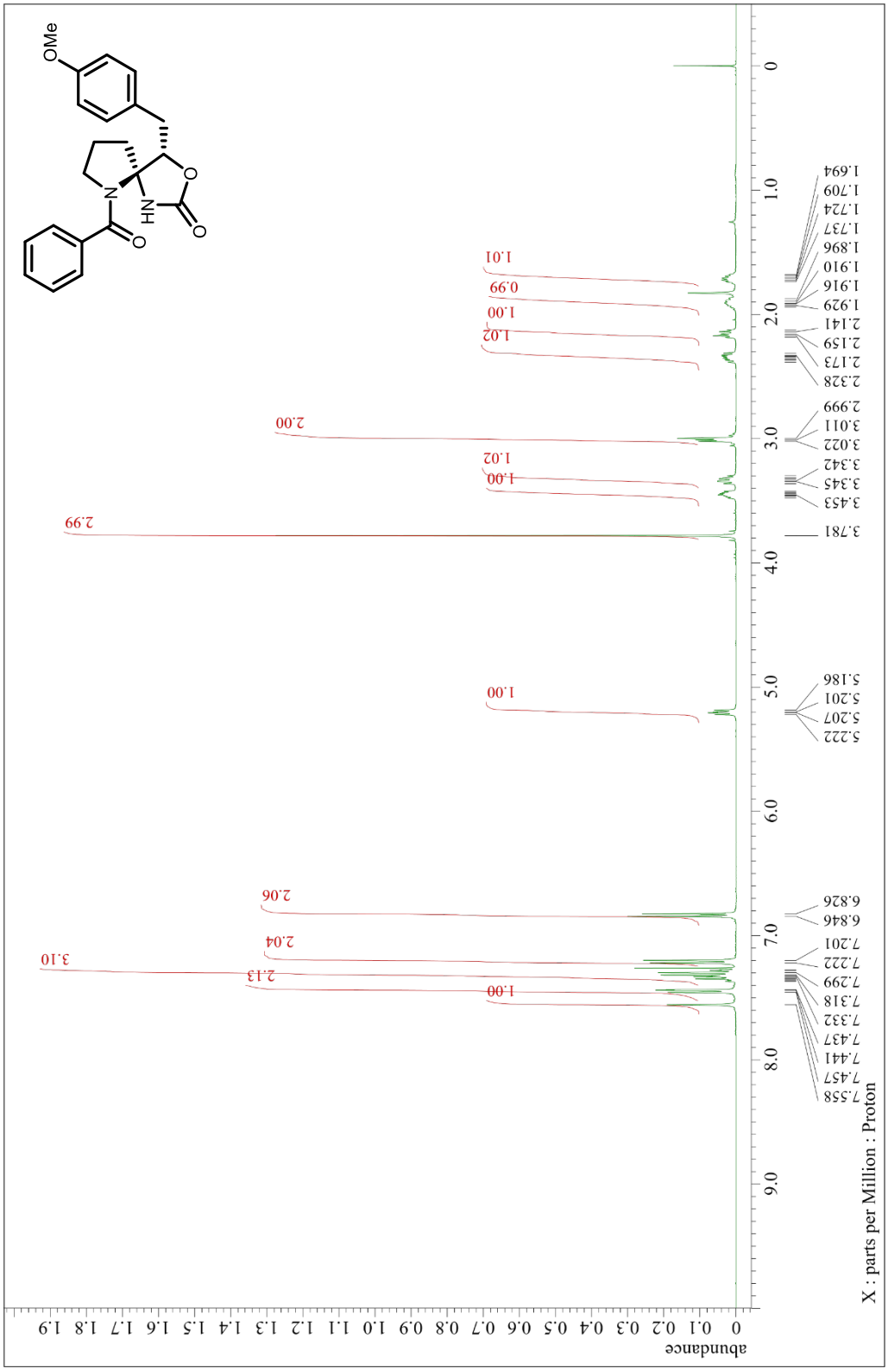

21.554
23.261
26.274
35.627
52.275
76.845
77.160
77.484
85.112
126.768
128.380
129.858
138.038
159.586
171.524
X : parts per Million : Carbon13
abundance

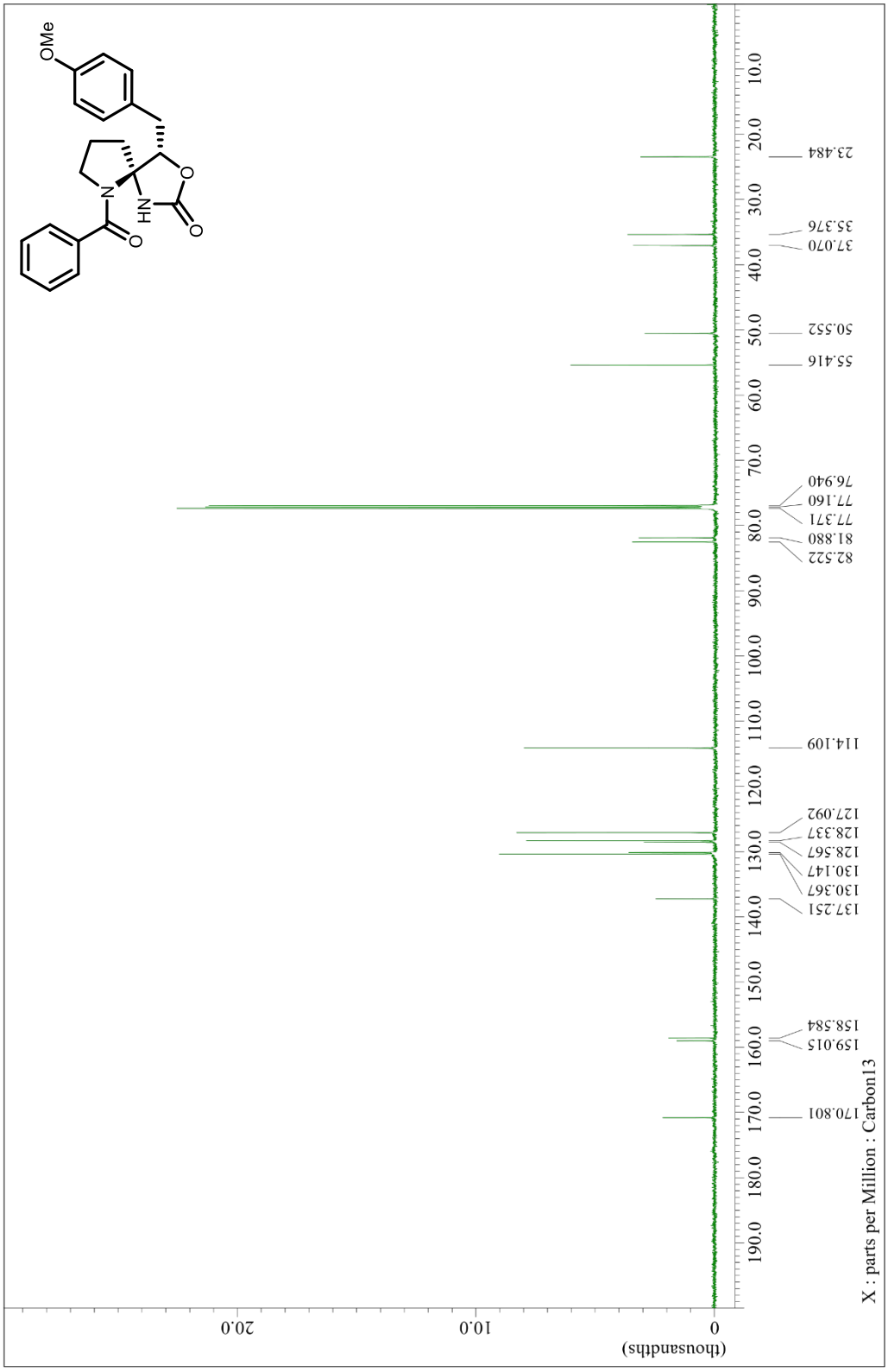
(4*S*,5*S*)-6-benzoyl-4-isopropyl-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3k)



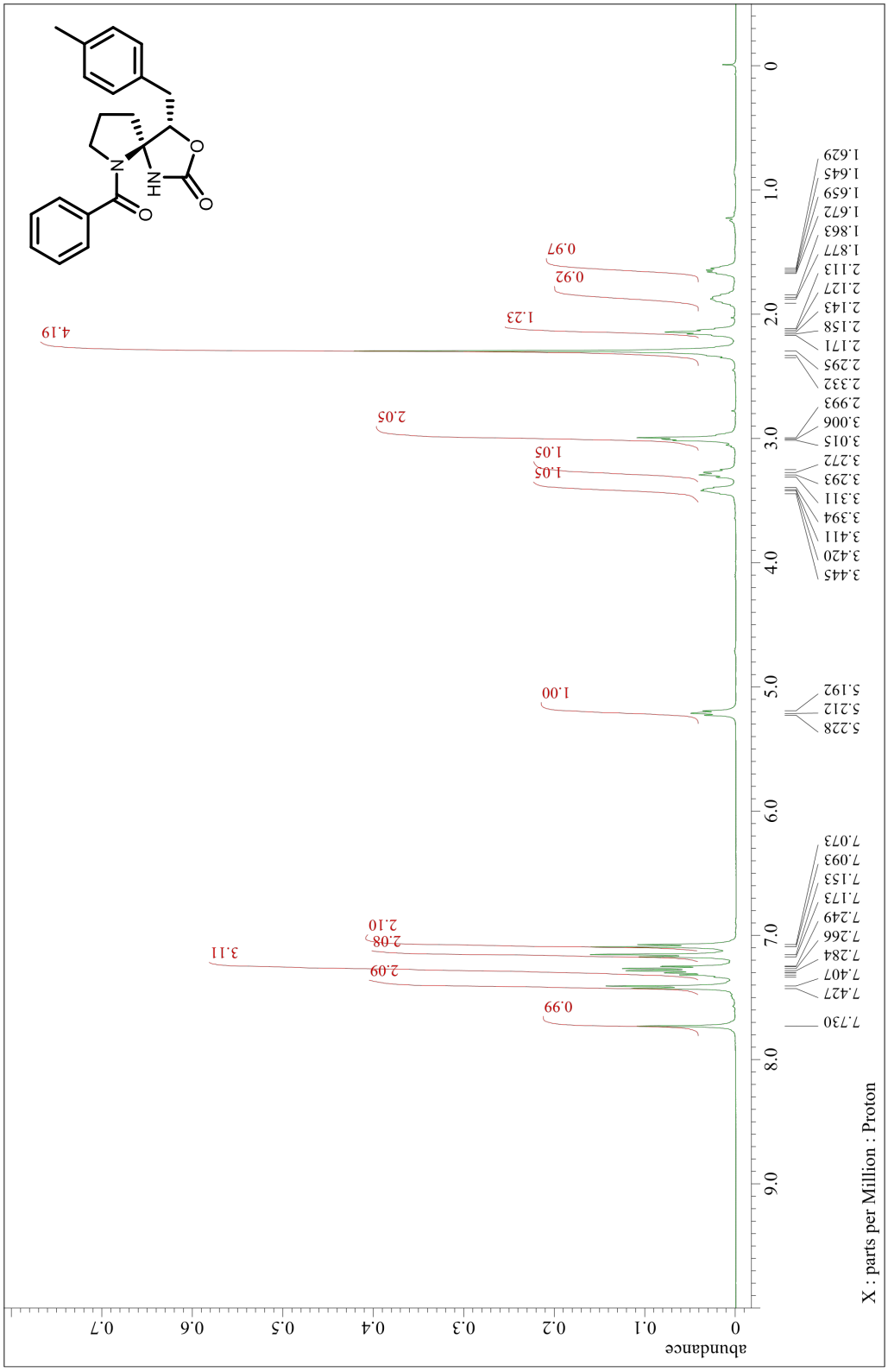

16.616
21.120
23.545
29.428
34.862
50.501
76.844
77.160
77.476
81.884
86.513
126.981
128.322
130.057
137.531
159.763
170.879
X : parts per Million : Carbon13
(thousandths)

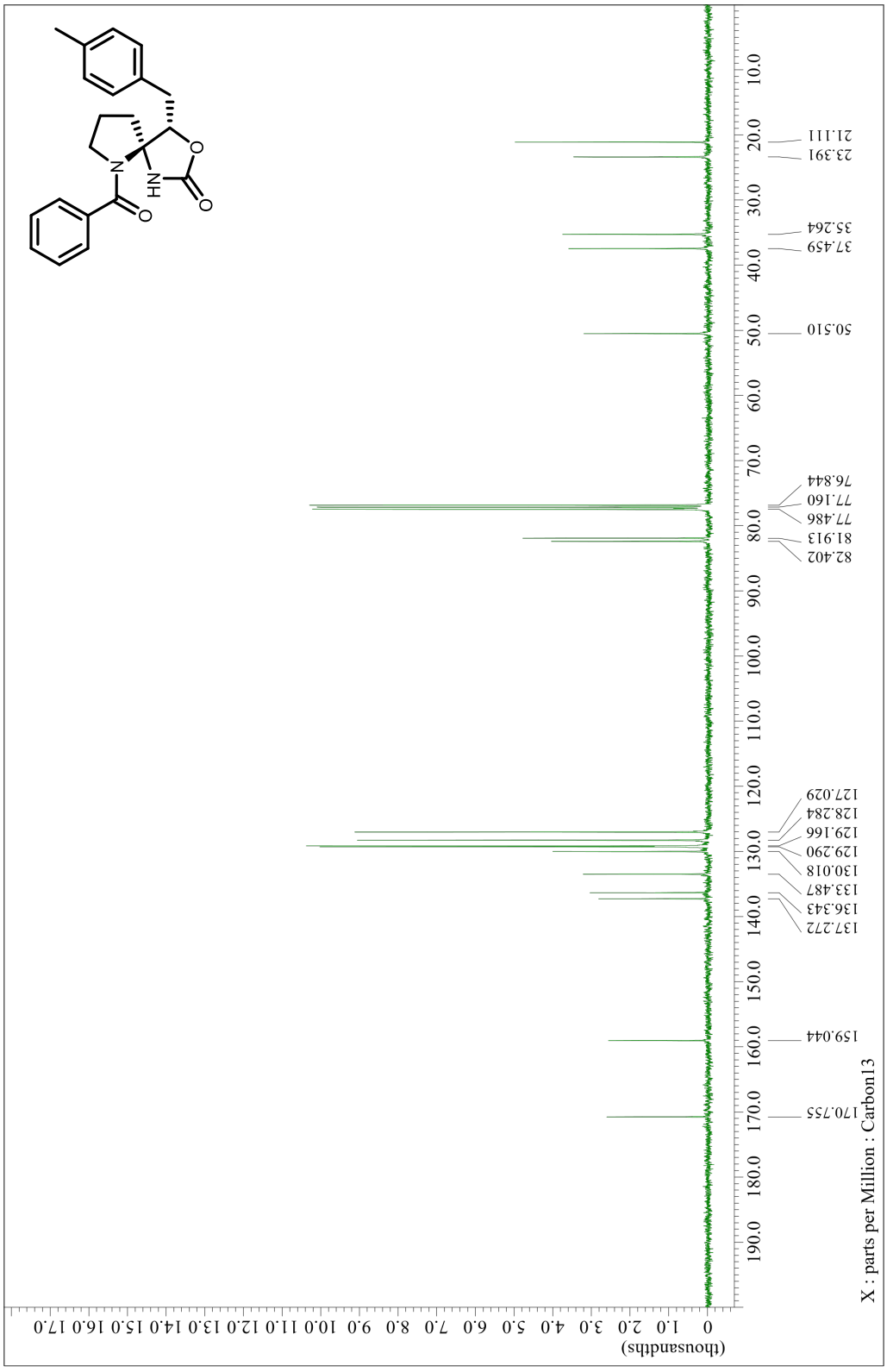
(4*S*,5*S*)-6-benzoyl-4-(4-methoxybenzyl)-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3l)



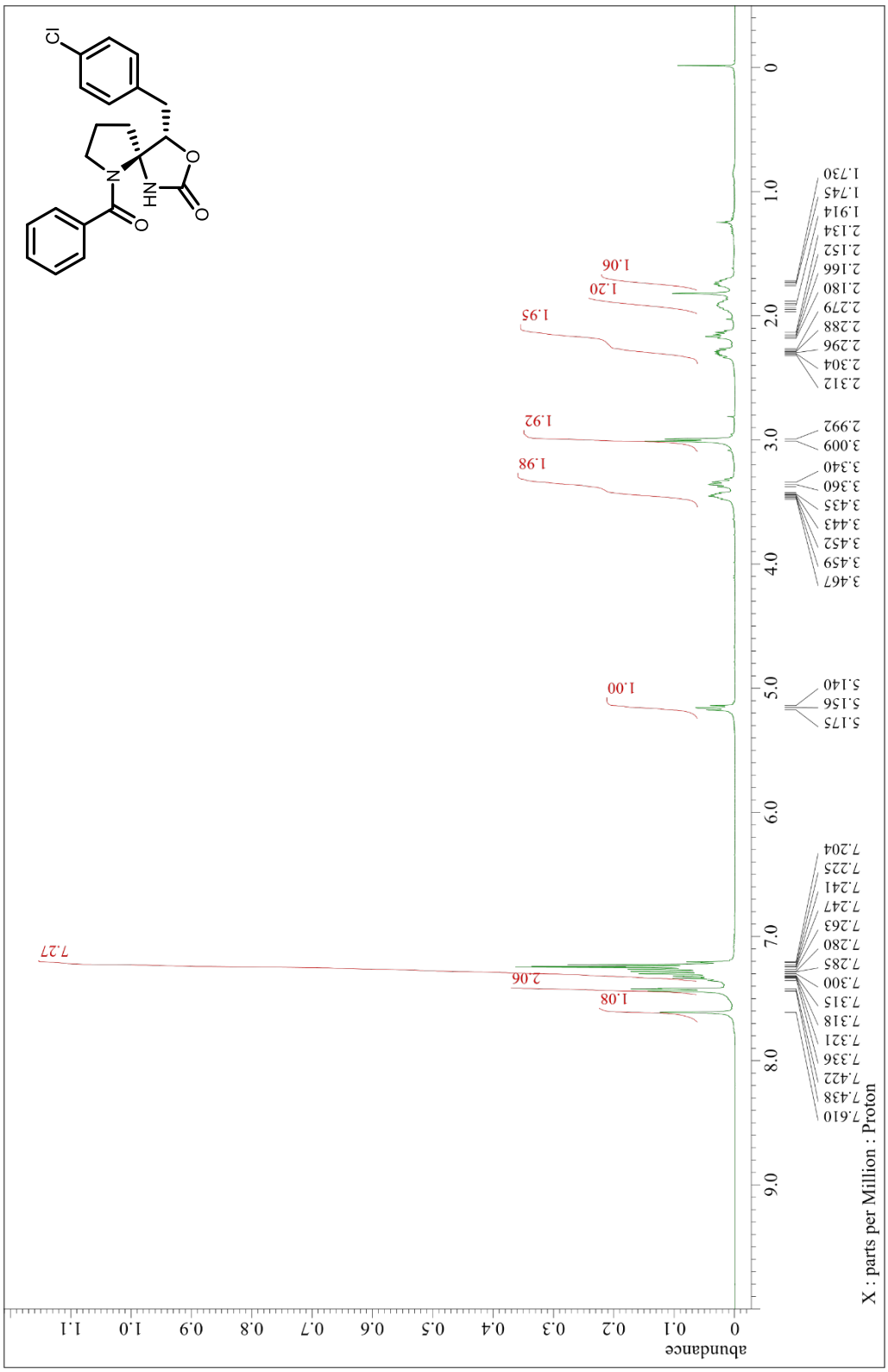

OMe
O
HN
O
N
O
23.484
35.376
37.070
50.552
55.416
76.940
77.160
77.371
81.880
82.522
114.109
127.092
128.337
128.567
130.147
130.367
137.251
158.584
159.015
170.801
X : parts per Million : Carbon13
(thousandths)
0
10.0
20.0

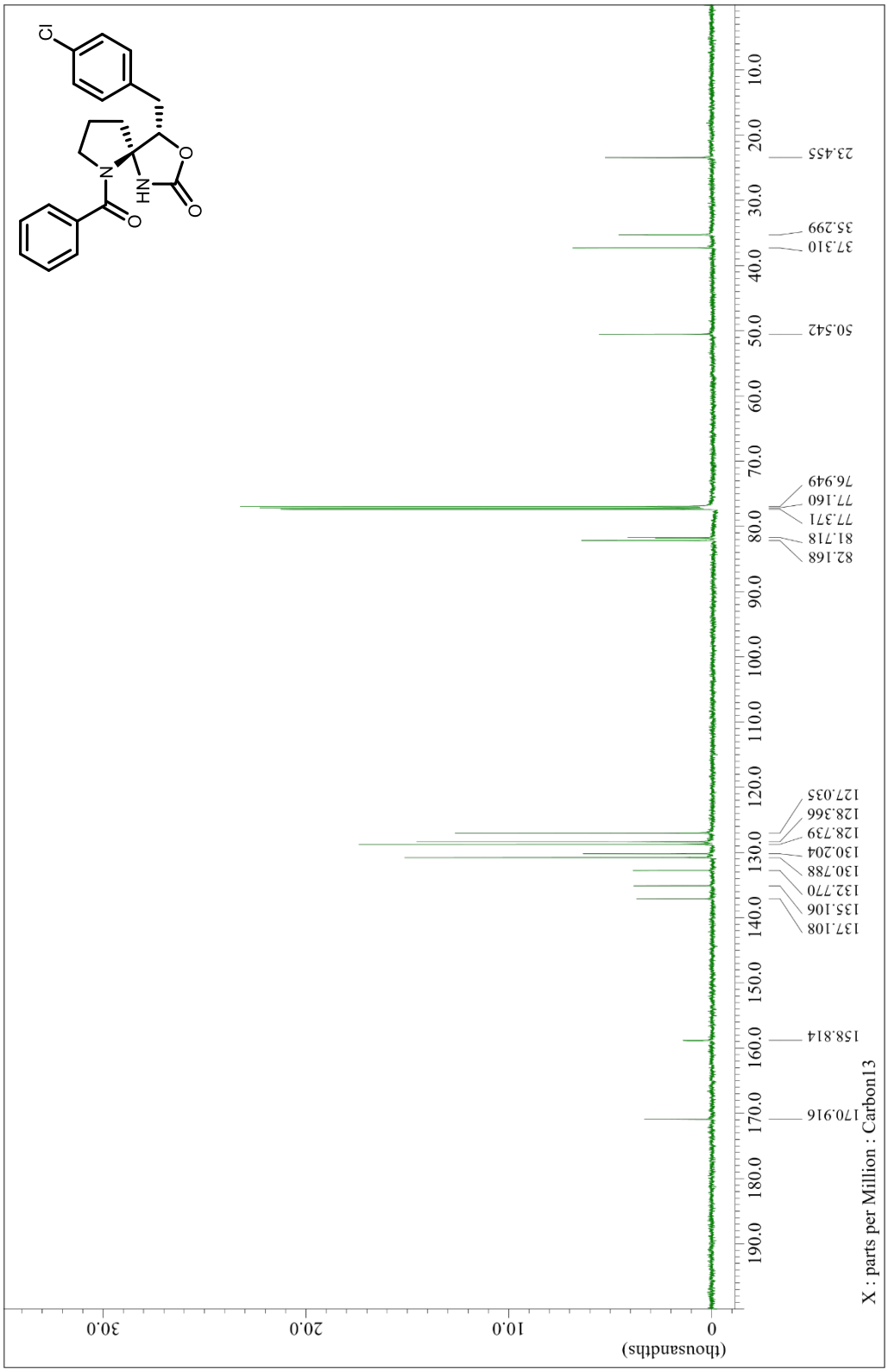
(4*S*,5*S*)-6-benzoyl-4-(4-methylbenzyl)-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3m)



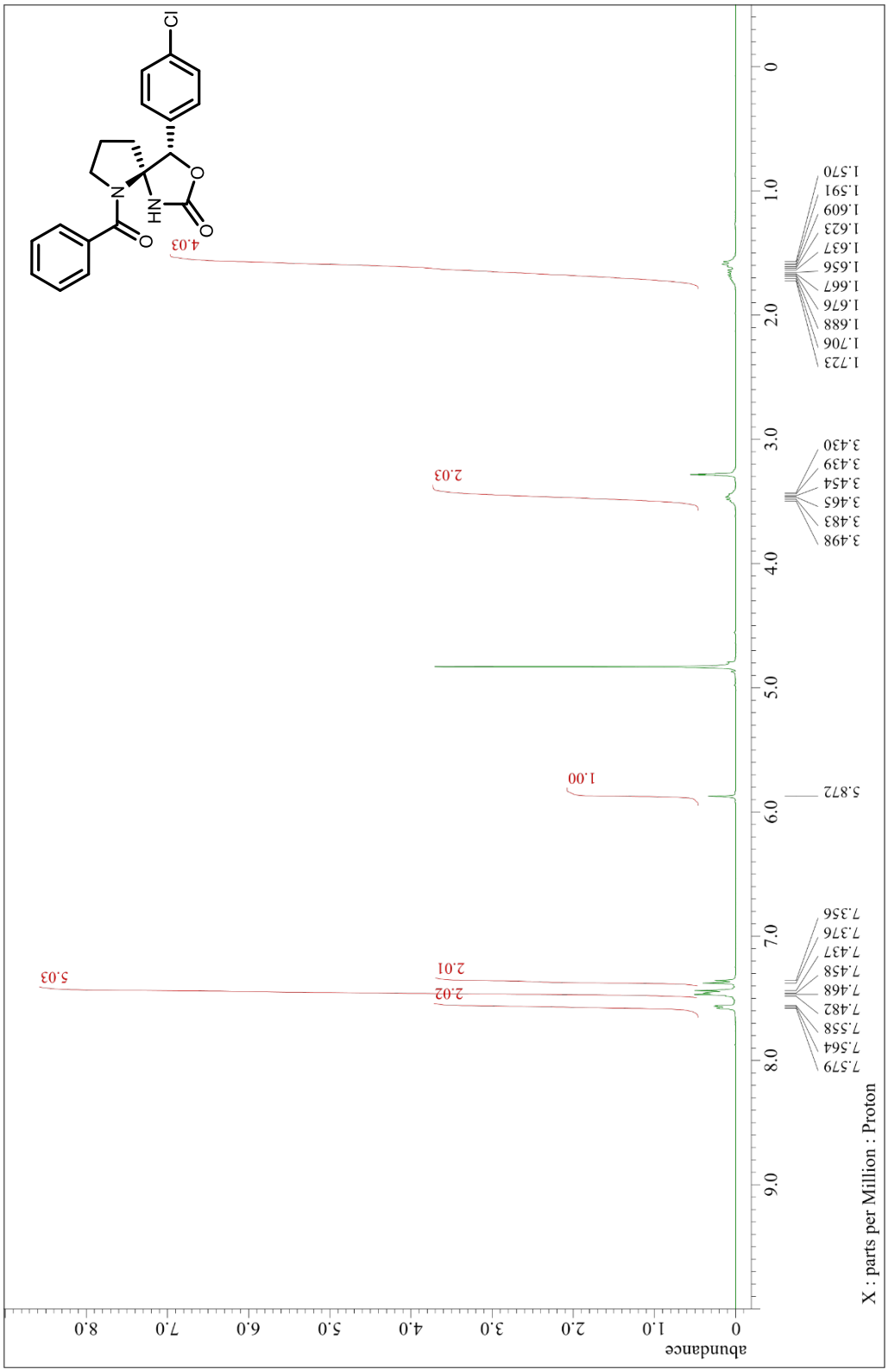

21.111
23.391
35.264
37.459
50.510
76.844
77.160
77.486
81.913
82.402
127.029
128.284
129.166
129.290
130.018
133.487
136.343
137.272
159.044
170.755
X : parts per Million : Carbon13
(thousandths)

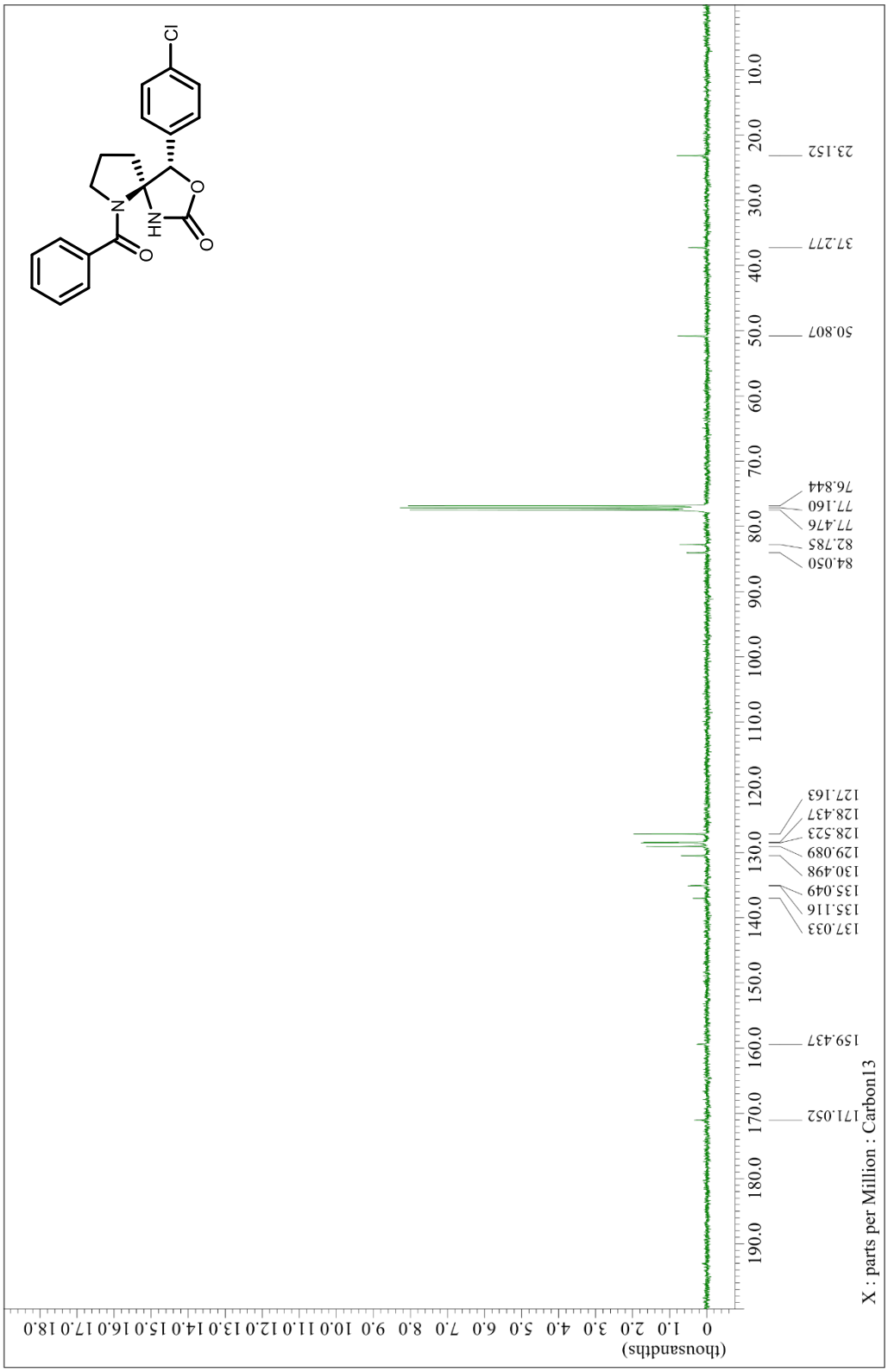
(4*S*,5*S*)-6-benzoyl-4-(4-chlorobenzyl)-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3n)



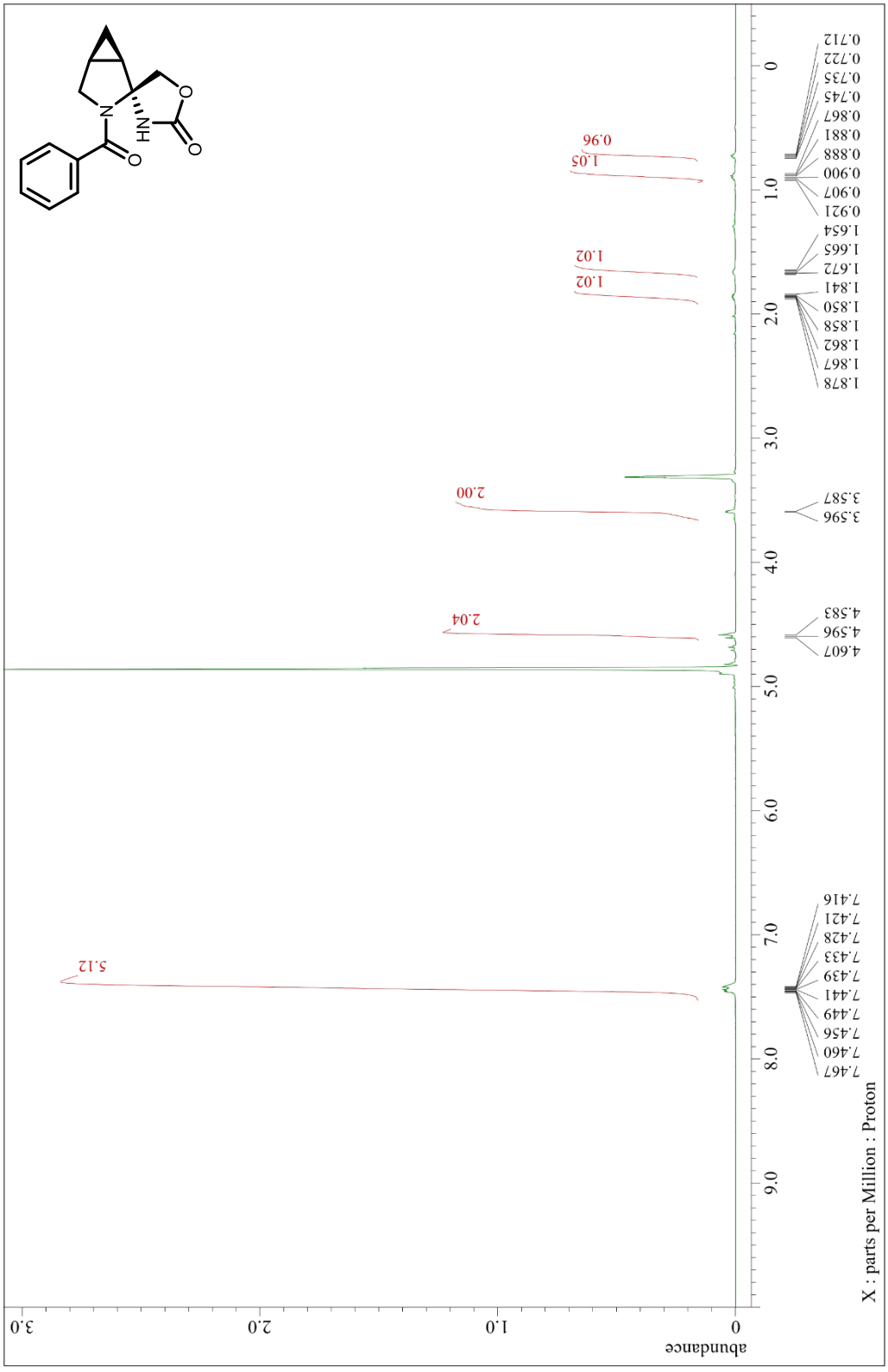

Cl
N
HN
O
O
O
23.455
35.299
37.310
50.542
76.949
77.160
77.371
81.718
82.168
127.035
128.366
128.739
130.204
130.788
132.770
135.106
137.108
158.814
170.916
X : parts per Million : Carbon13
(thousandths)

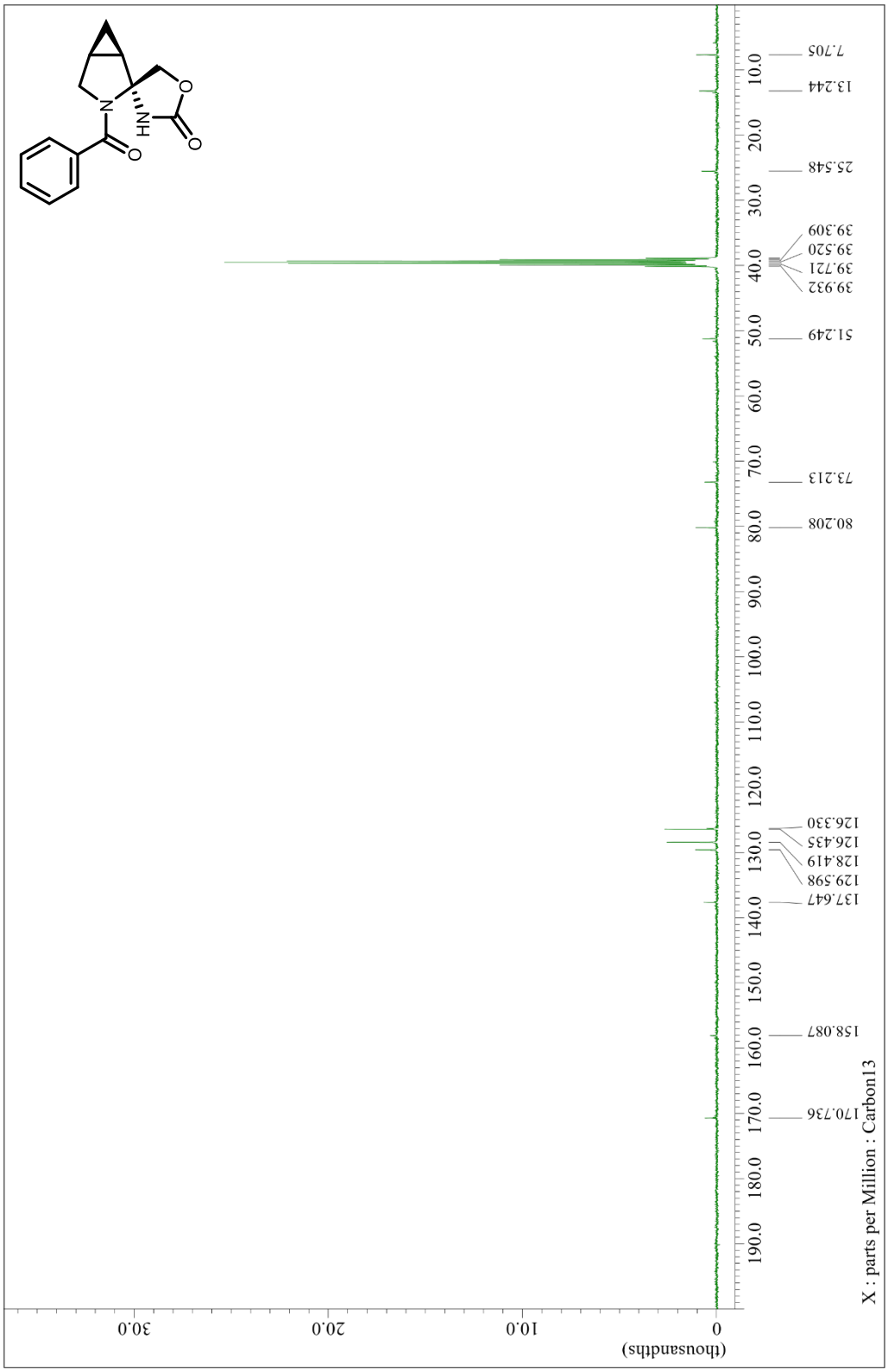
(4*S*,5*S*)-6-benzoyl-4-(4-chlorophenyl)-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3o)



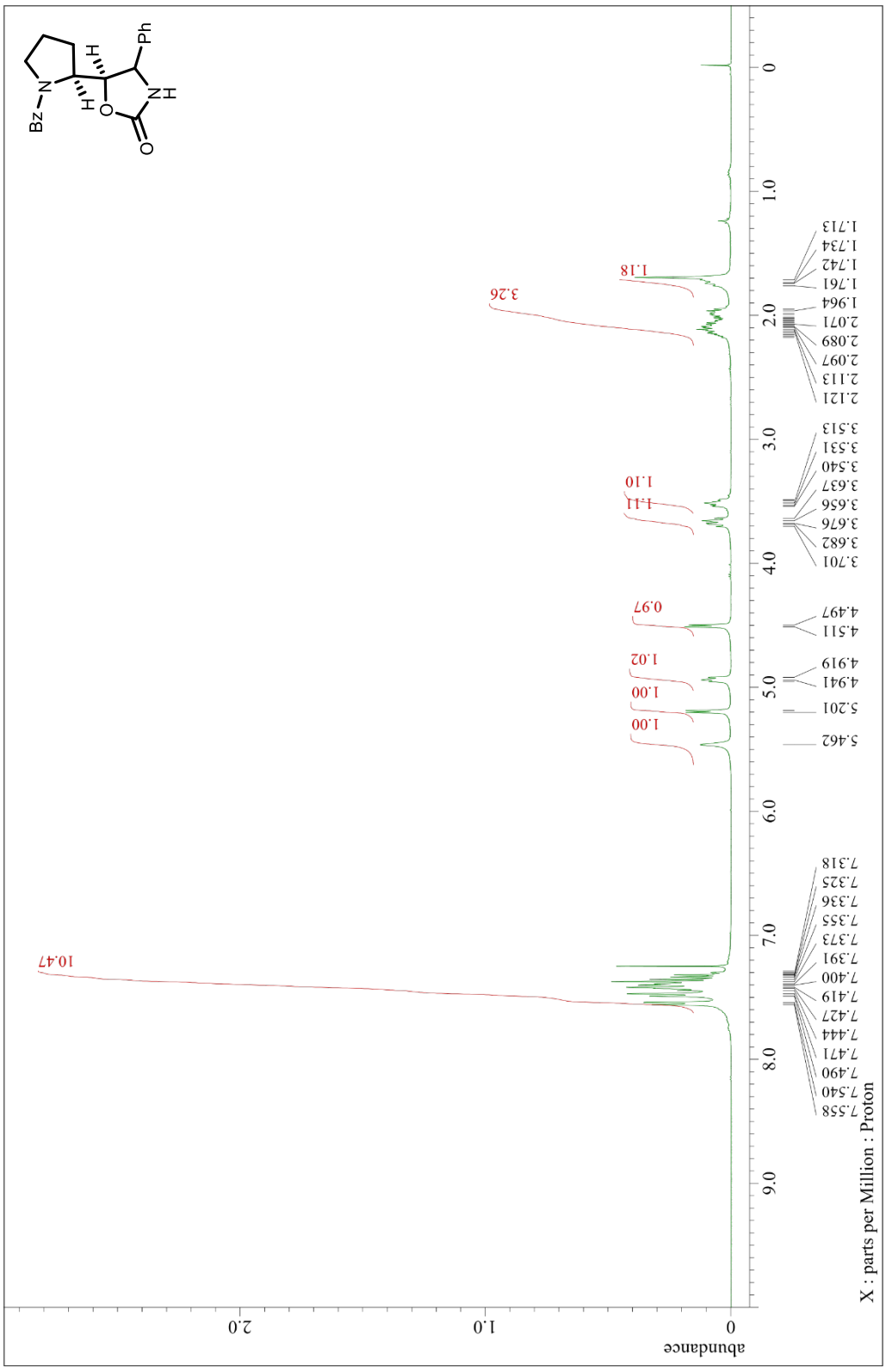

Cl
N
HN
O
O
O
23.152
37.277
50.807
76.844
77.160
77.476
82.785
84.050
127.163
128.437
128.523
129.089
130.498
135.049
135.116
137.033
159.437
171.052
X : parts per Million : Carbon13
(thousandths)

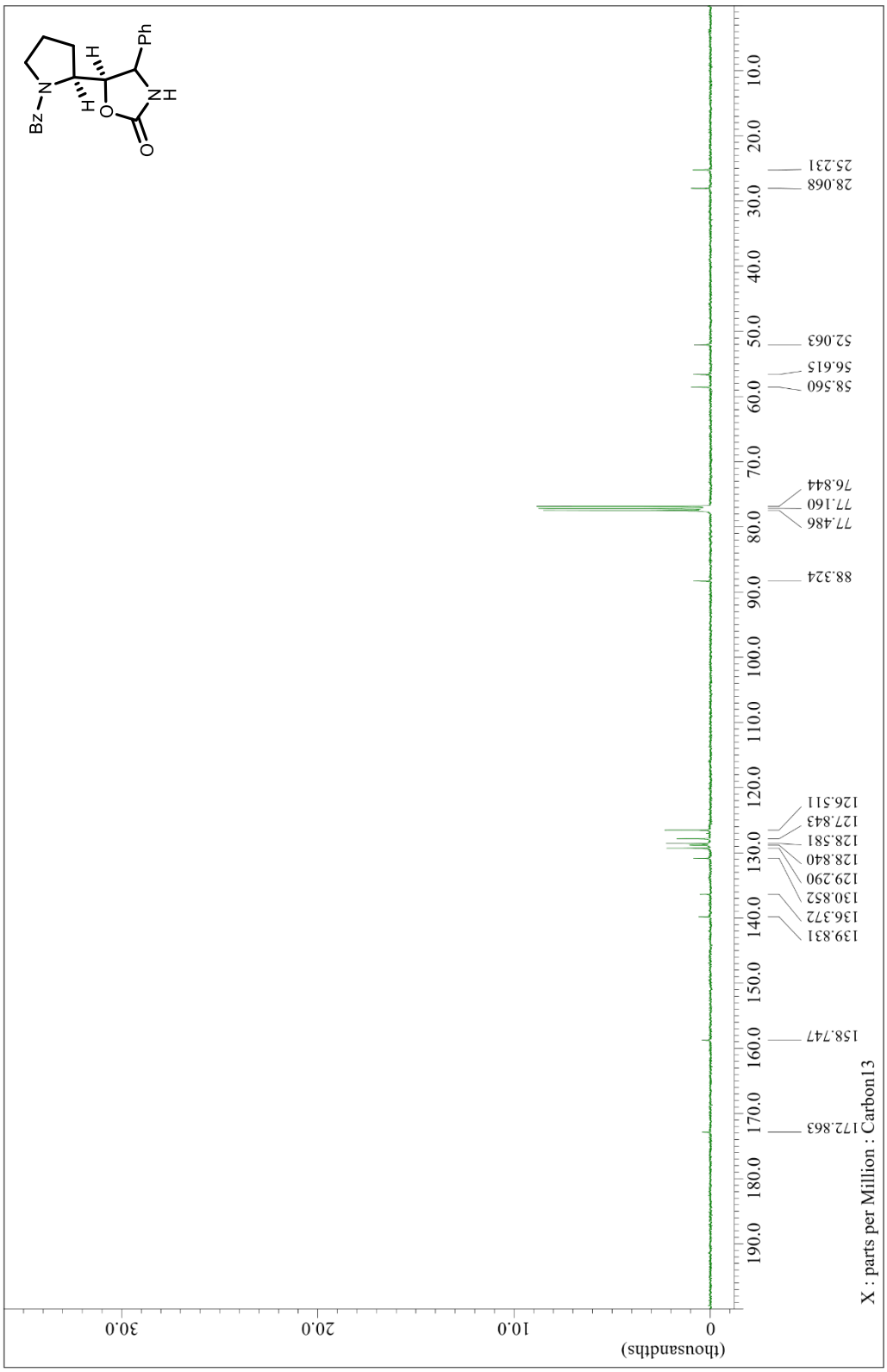
(1*R*,2*S*,5*S*)-3-benzoyl-3-azaspiro[bicyclo[3.1.0]hexane-2,4'-oxazolidin]-2'-one (3p)



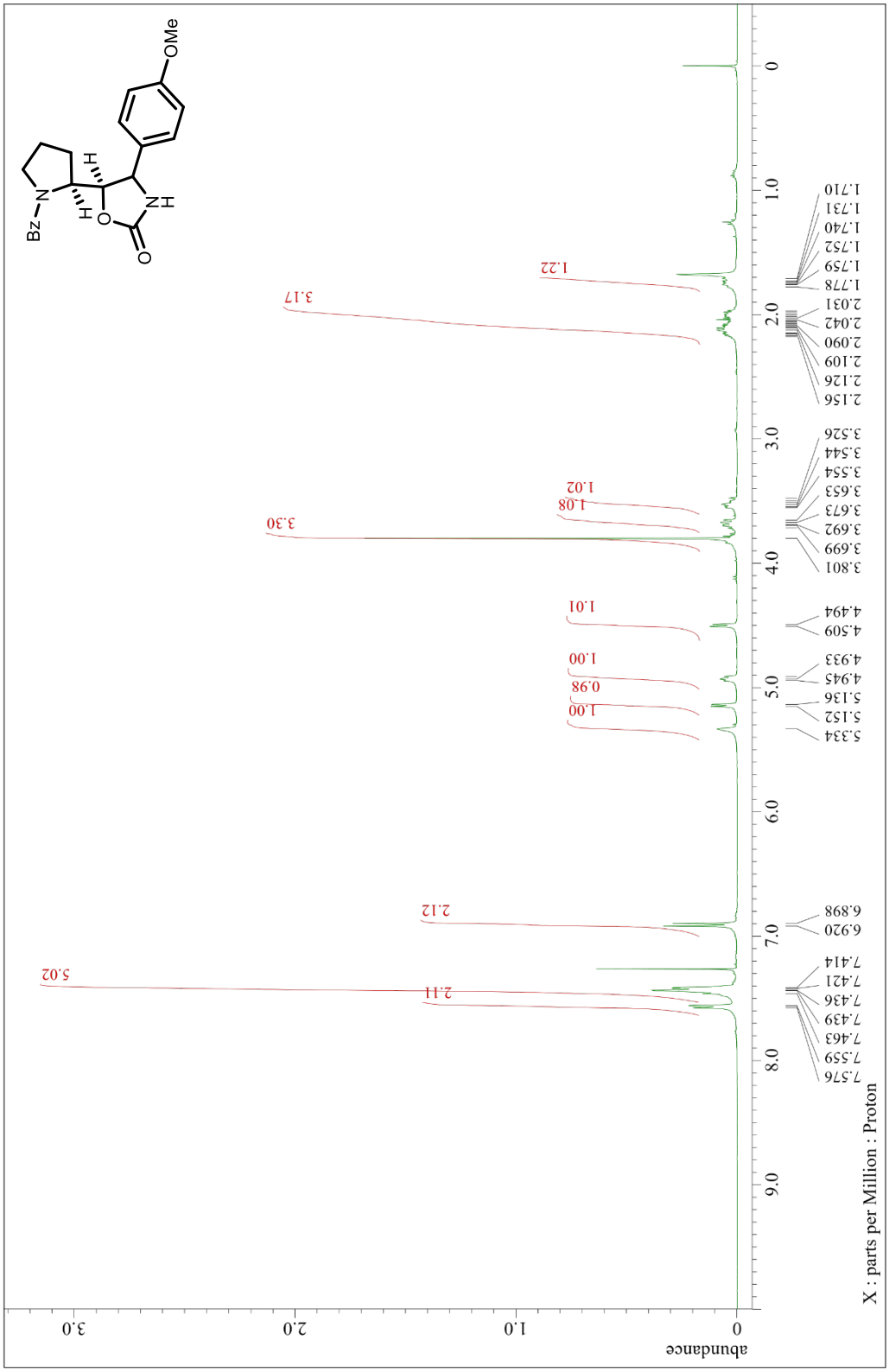

7.705
13.244
25.548
39.309
39.520
39.721
39.932
51.249
73.213
80.208
126.330
126.435
128.419
129.598
137.647
158.087
170.736
X : parts per Million : Carbon13
(thousandths)

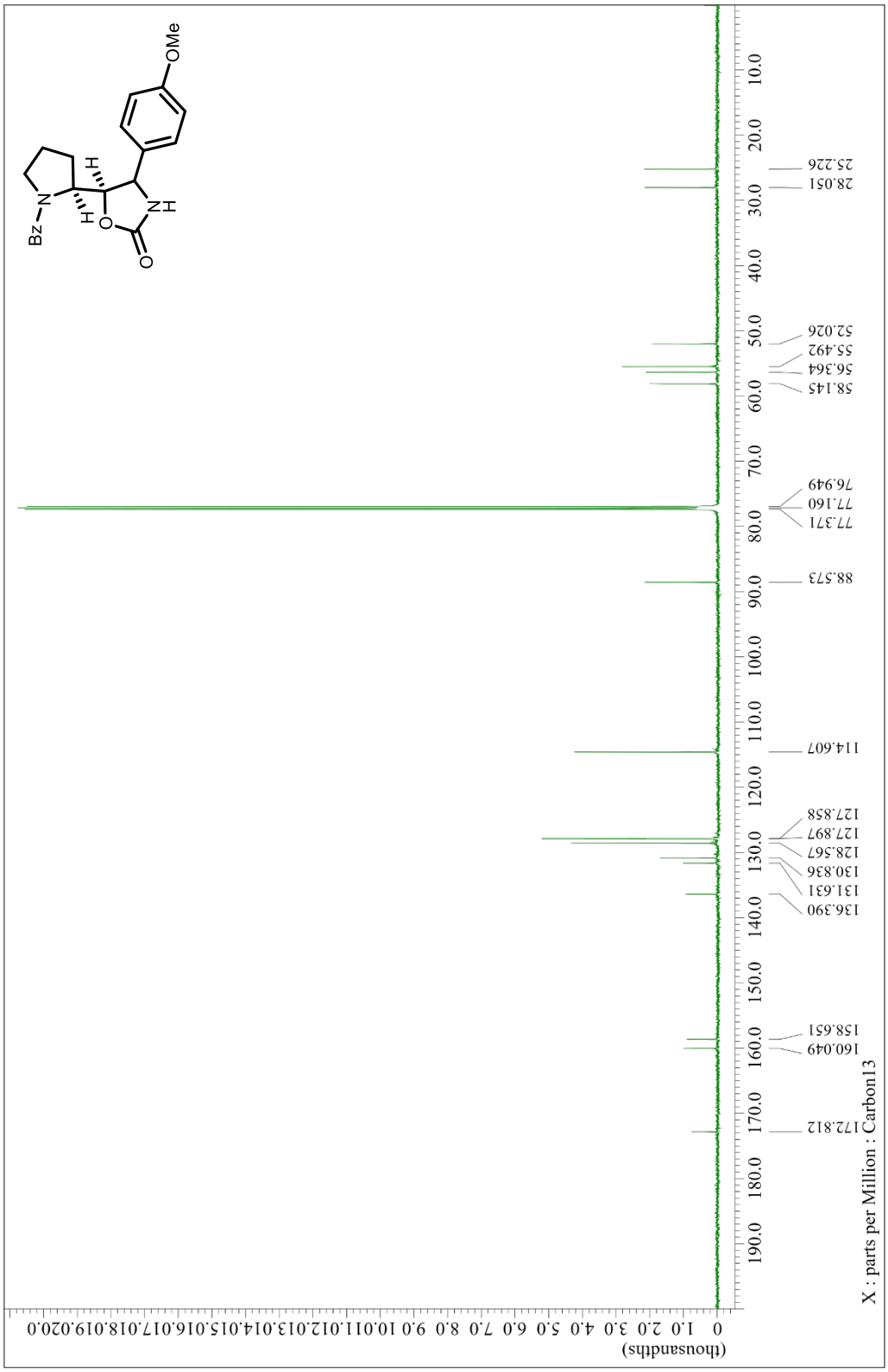
(5*R*)-5-((*S*)-1-benzoylpyrrolidin-2-yl)-4-phenyloxazolidin-2-one (5a)



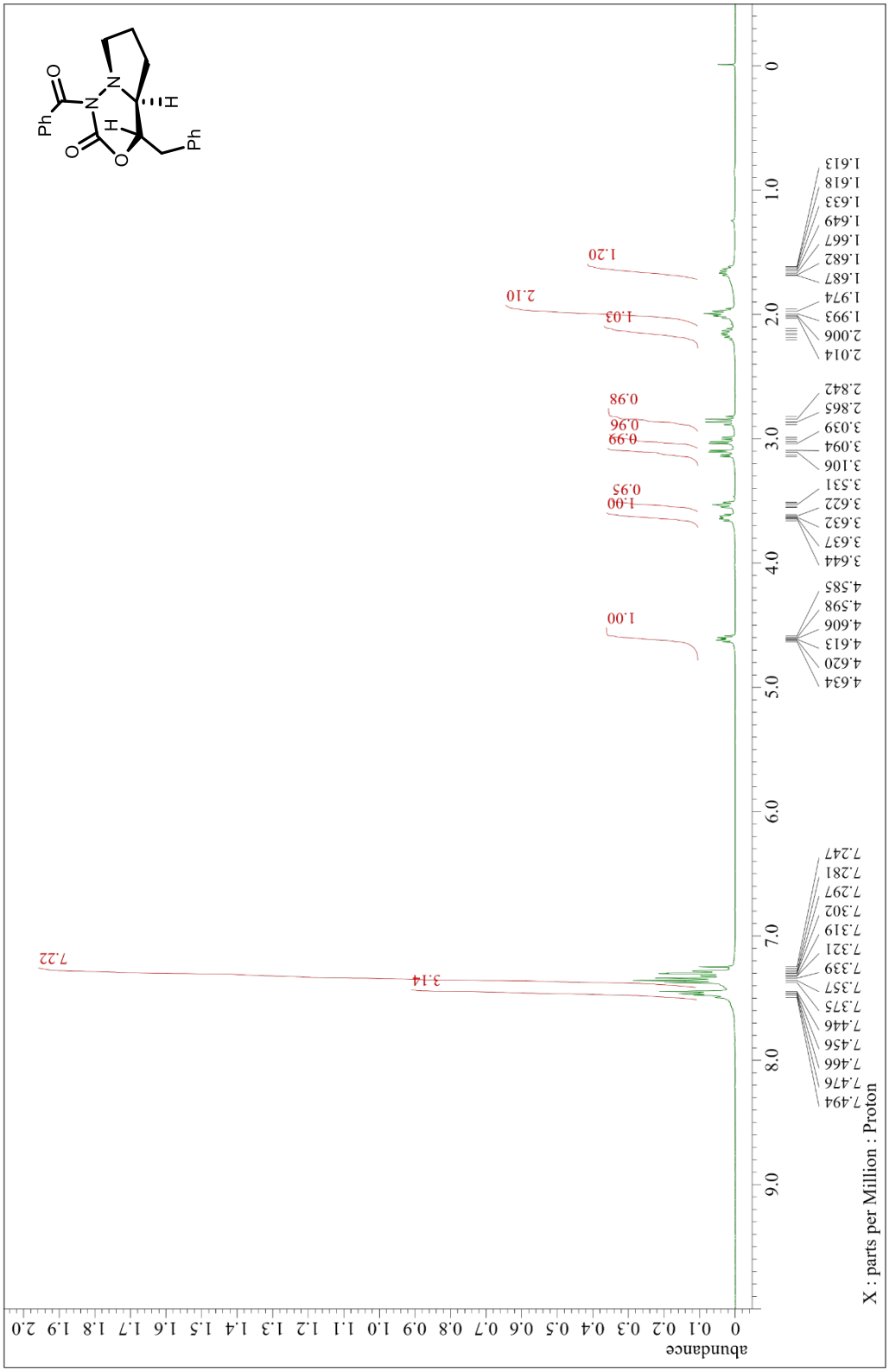

Ph
H
H
N
Bz
O
O
N
H
(thousandths)
0
10.0
20.0
30.0
X : parts per Million : Carbon13
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0
25.231
28.068
52.063
56.615
58.560
76.844
77.160
77.486
88.324
126.511
127.843
128.581
128.840
129.290
130.852
136.372
139.831
158.747
172.863

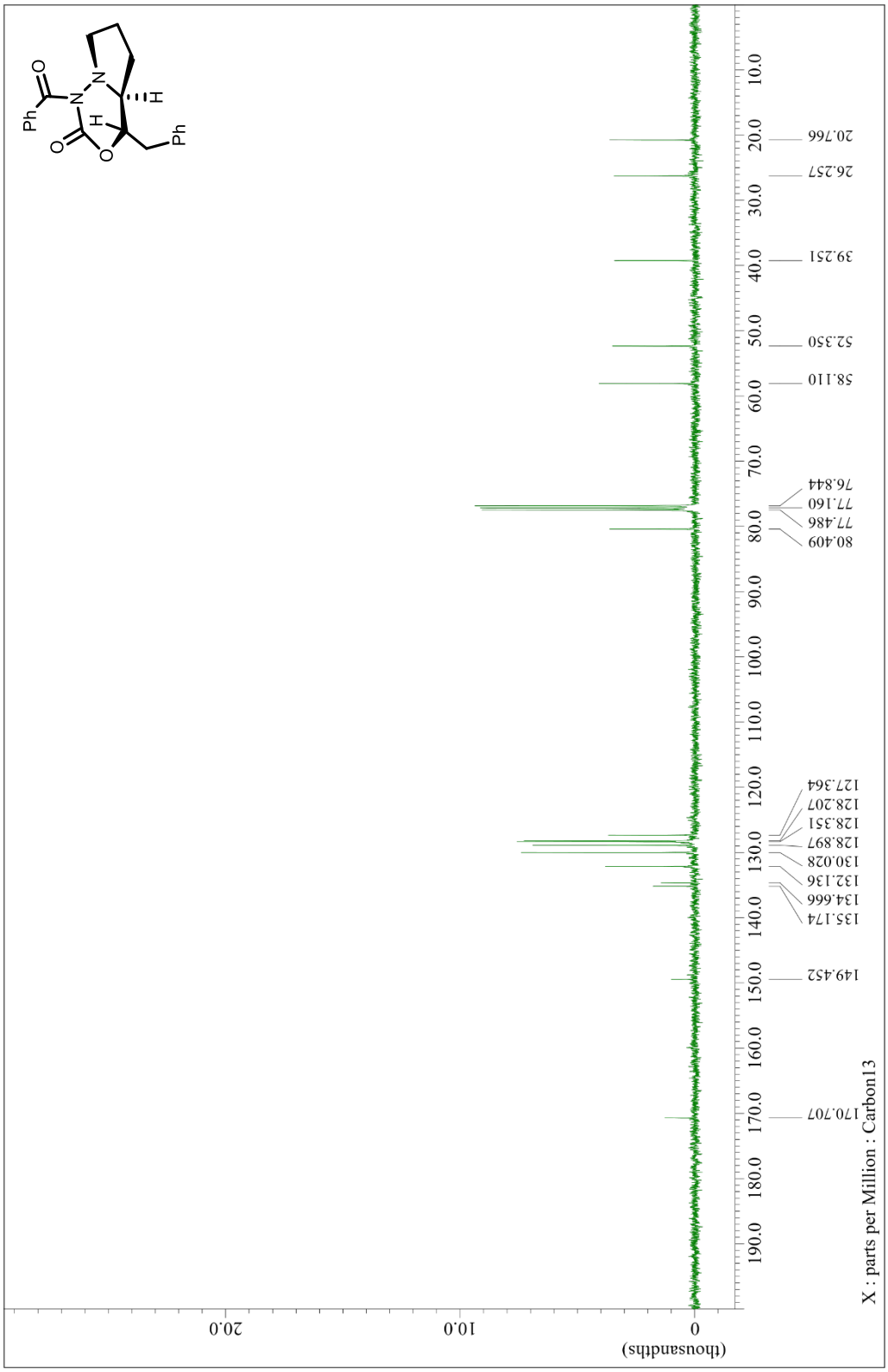
(5*R*)-5-((*S*)-1-benzoylpyrrolidin-2-yl)-4-(4-methoxyphenyl)oxazolidin-2-one (5l)



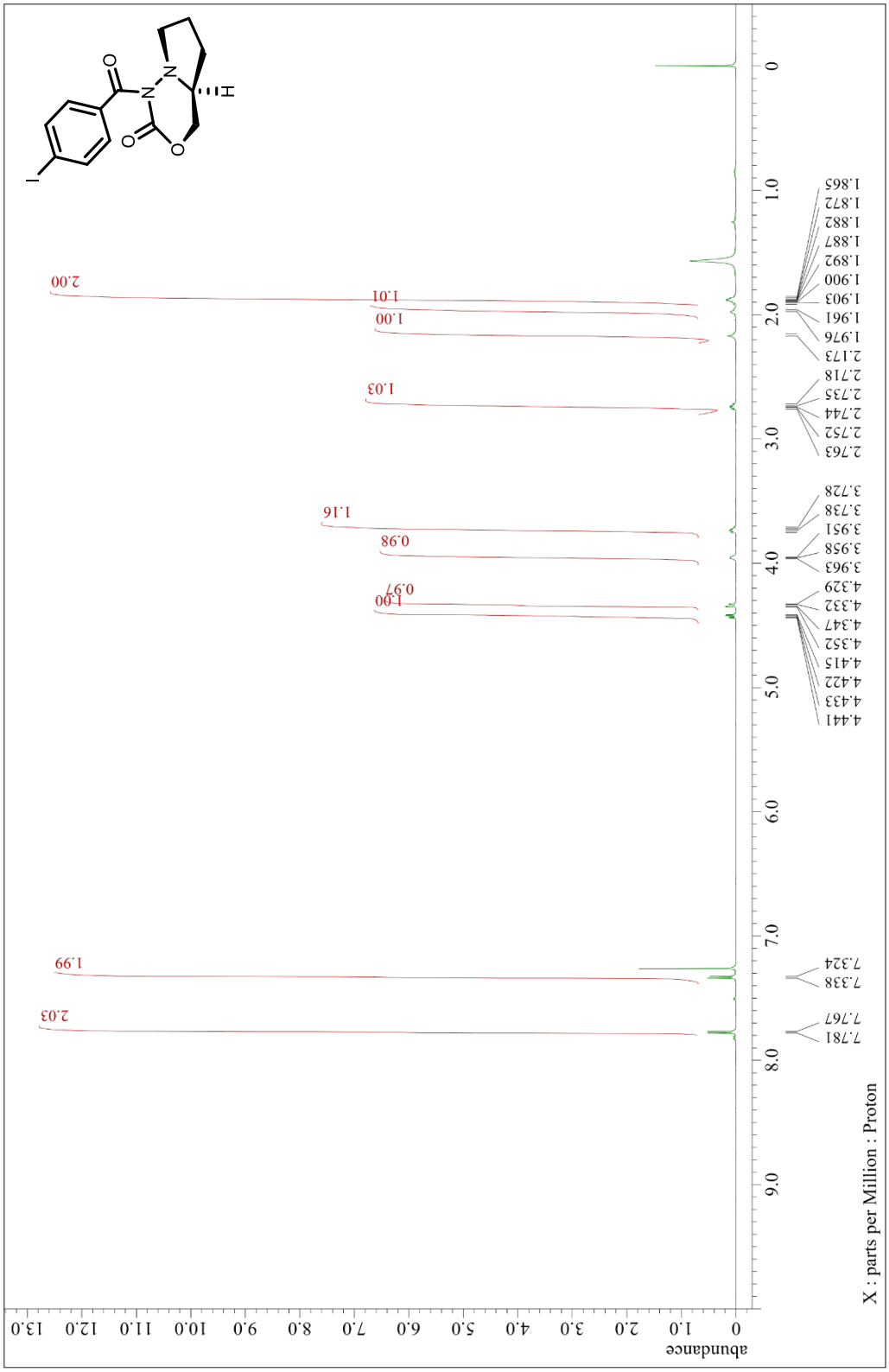

OMe
H
H
N
Bz
O
N
H
O
25.226
28.051
52.026
55.492
56.364
58.145
76.949
77.160
77.371
88.573
114.607
127.858
127.897
128.567
130.836
131.631
136.390
158.651
160.049
172.812
X : parts per Million : Carbon13
(thousandths)

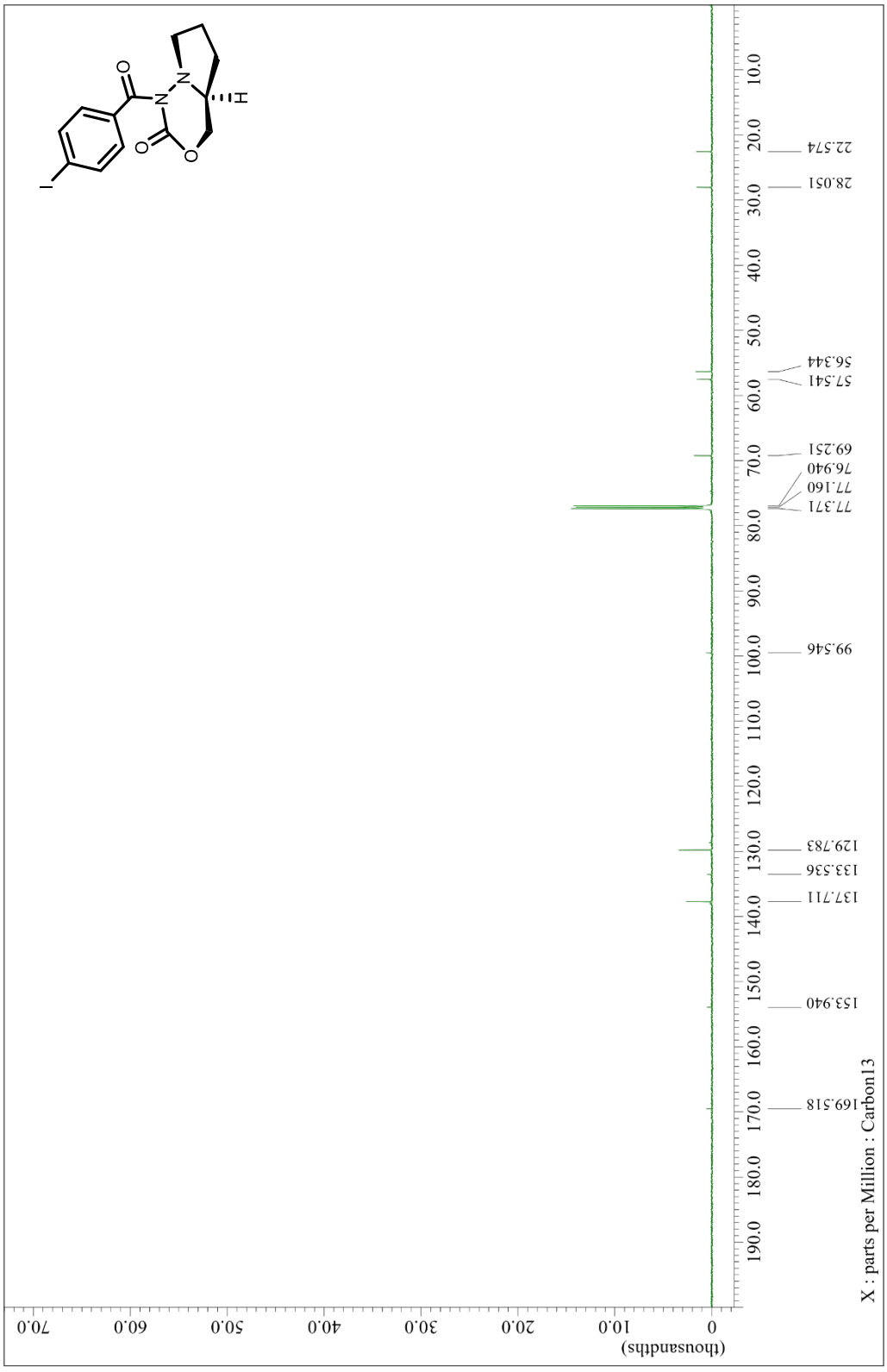
(4*S*)-1-benzoyl-4-benzyltetrahydro-4*H*-pyrrolo[1,2-*d*][1,3,4]oxadiazin-2(1*H*)-one (2a)



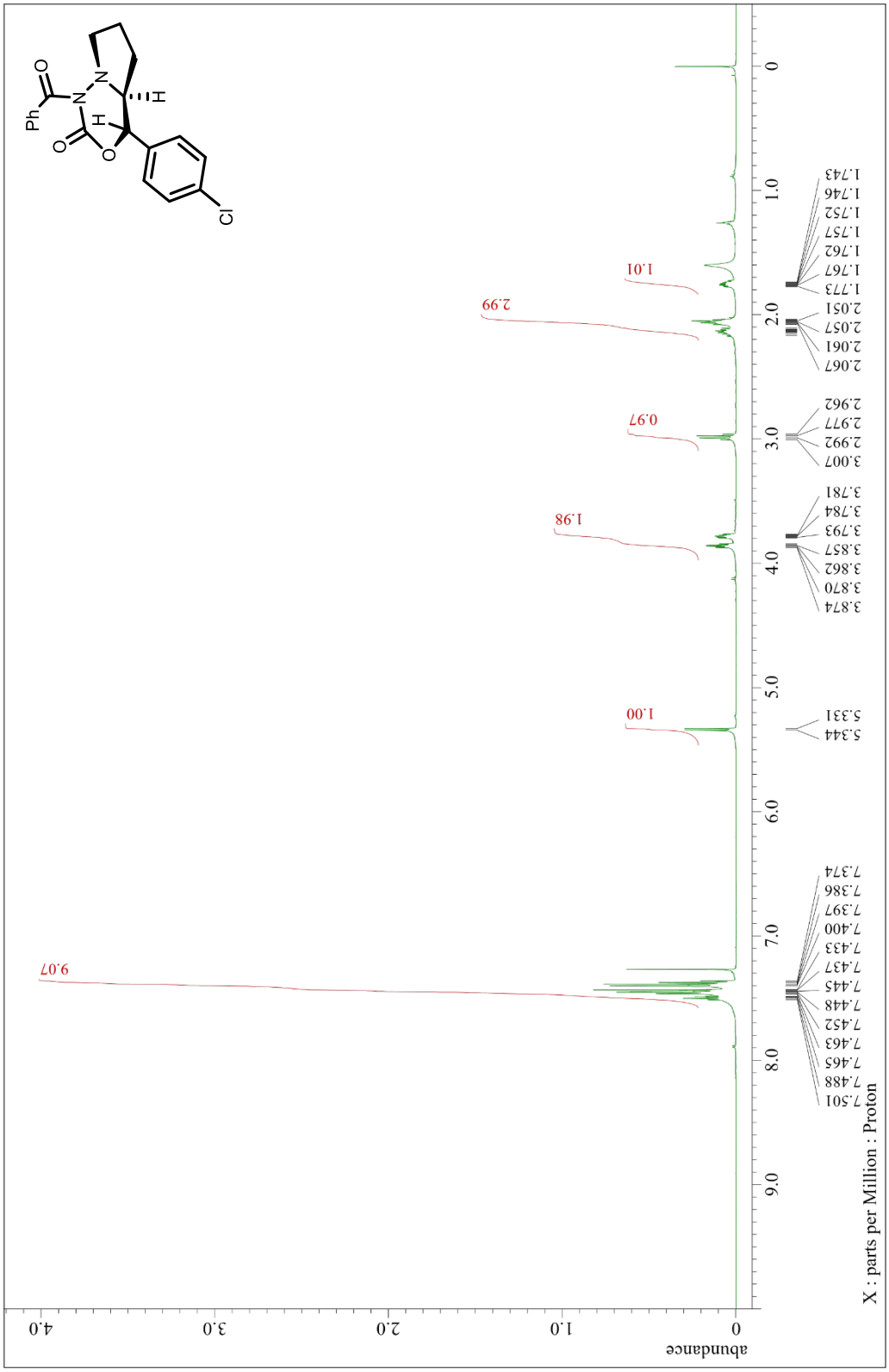

Ph
O
N
N
H
O
H
O
Ph
(thousandths)
0
10.0
20.0
X : parts per Million : Carbon13
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0
20.766
26.257
39.251
52.350
58.110
76.844
77.160
77.486
80.409
127.364
128.207
128.351
128.897
130.028
132.136
134.666
135.174
149.452
170.707

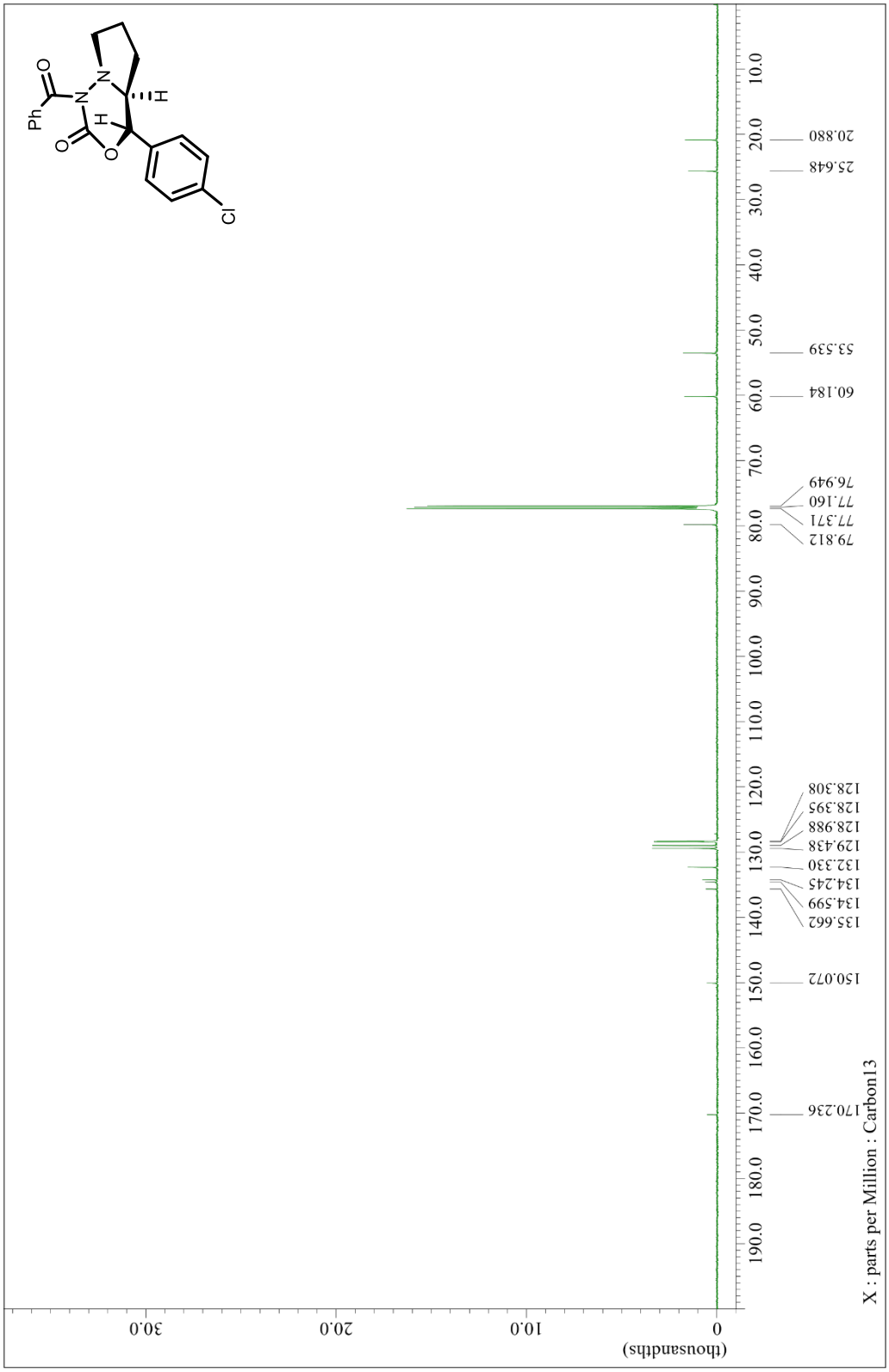
1-(4-iodobenzoyl)tetrahydro-4*H*-pyrrolo[1,2-*d*][1,3,4]oxadiazin-2(1*H*)-one (2e)



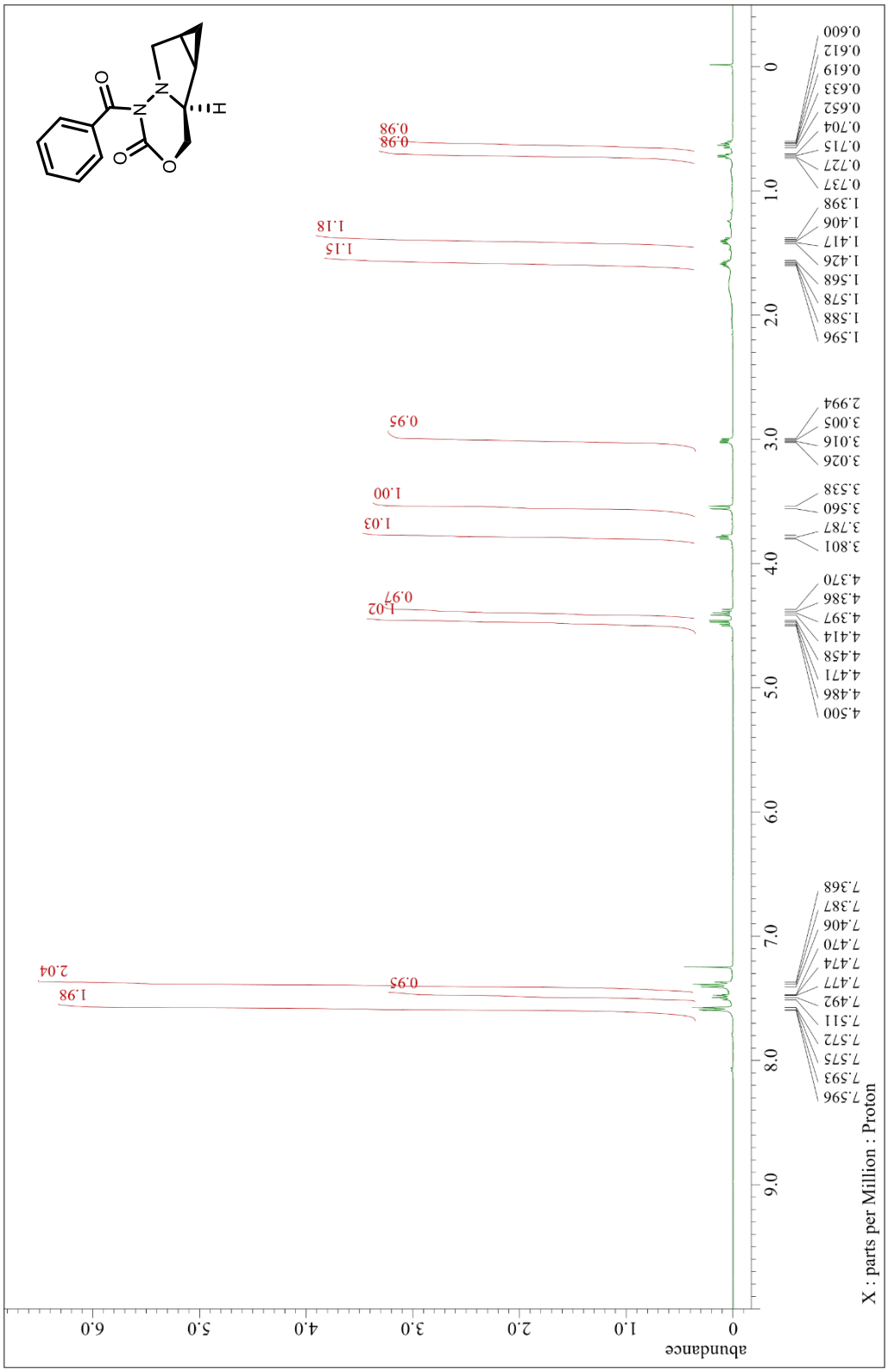

22.574
28.051
56.344
57.541
69.251
76.940
77.160
77.371
99.546
129.783
133.536
137.711
153.940
169.518
X : parts per Million : Carbon13
(thousandths)

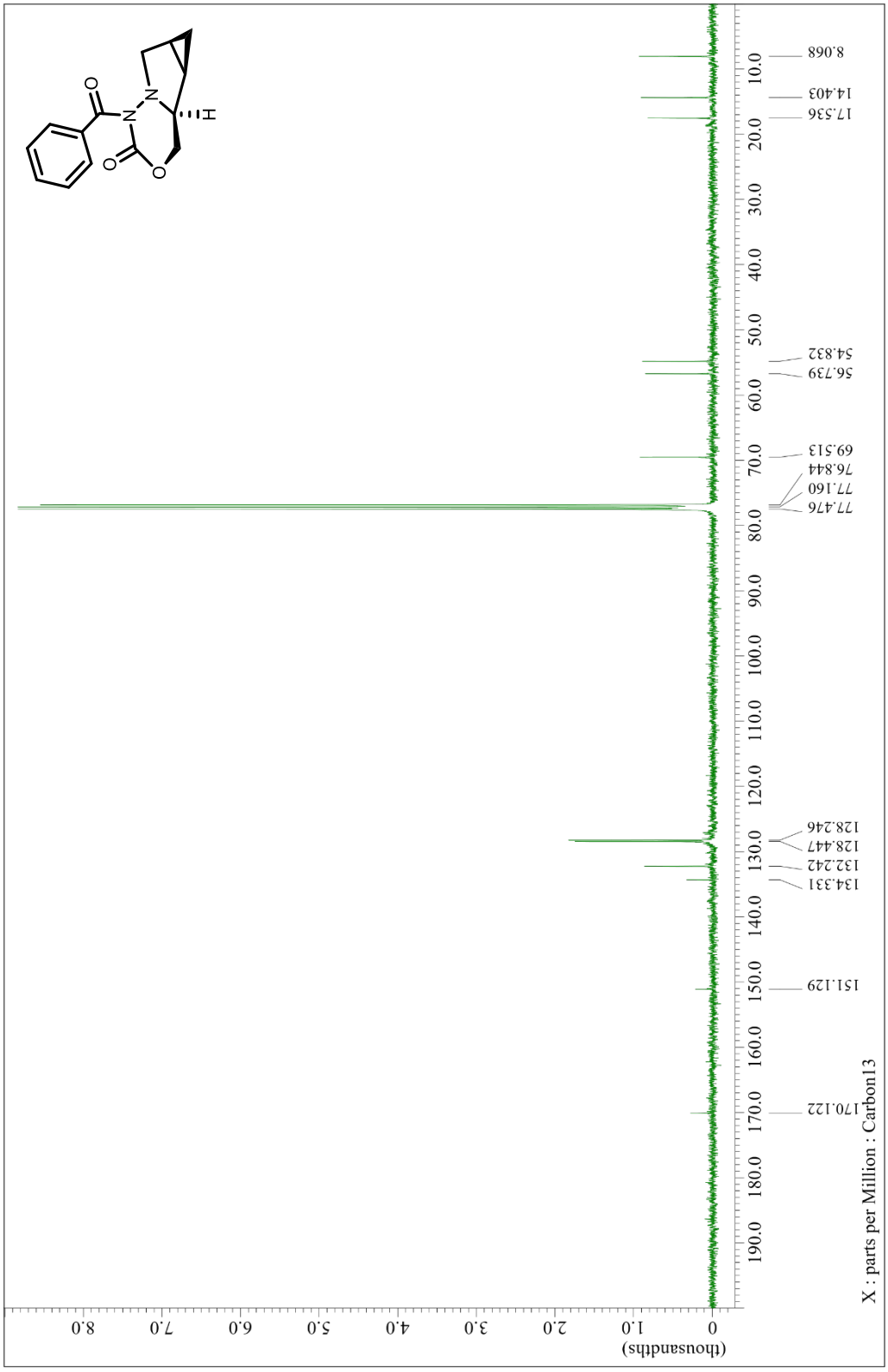
(4*S*)-1-benzoyl-4-(4-chlorophenyl)tetrahydro-4*H*-pyrrolo[1,2-*d*][1,3,4]oxadiazin-2(1*H*)-one (2o)



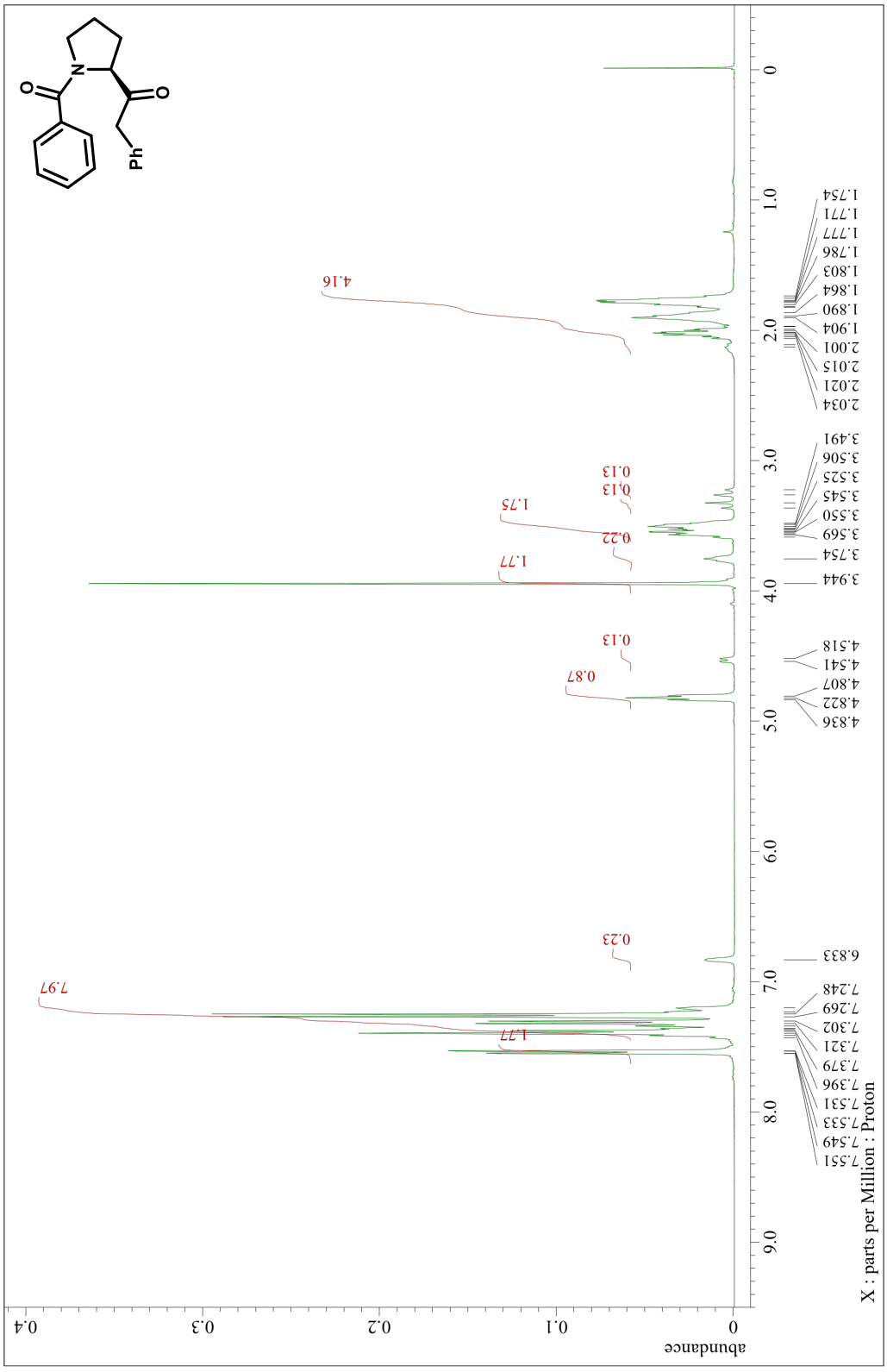

Ph
O
N
N
H
H
O
O
Cl
20.880
25.648
53.539
60.184
76.949
77.160
77.371
79.812
128.308
128.395
128.988
129.438
132.330
134.245
134.599
135.662
150.072
170.236
X : parts per Million : Carbon13
(thousandths)

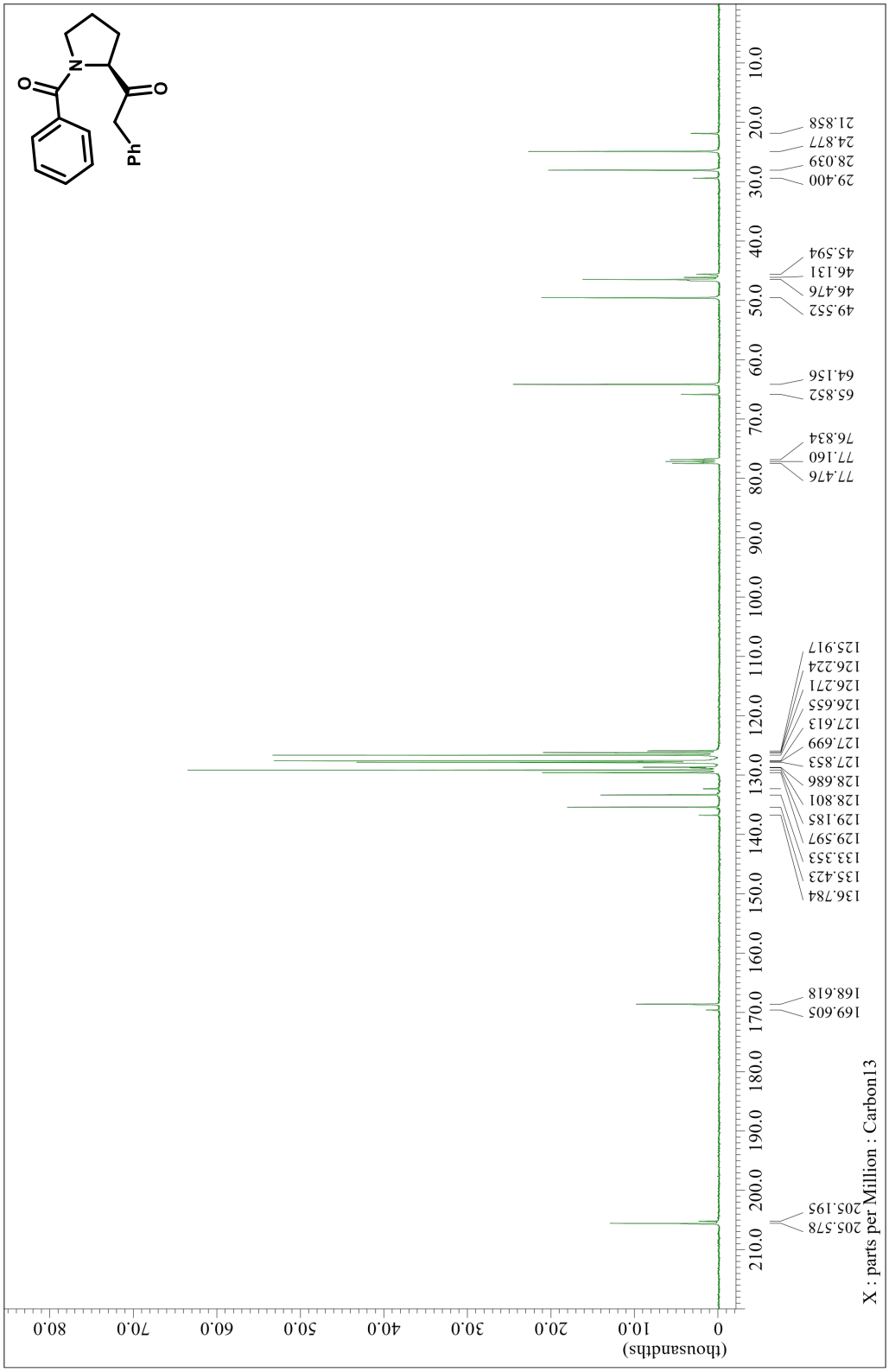
(4b*R*,5a*S*)-1-benzoylhexahydrocyclopropa[3,4]pyrrolo[1,2-*d*][1,3,4]oxadiazin-2(1*H*)-one (2p)



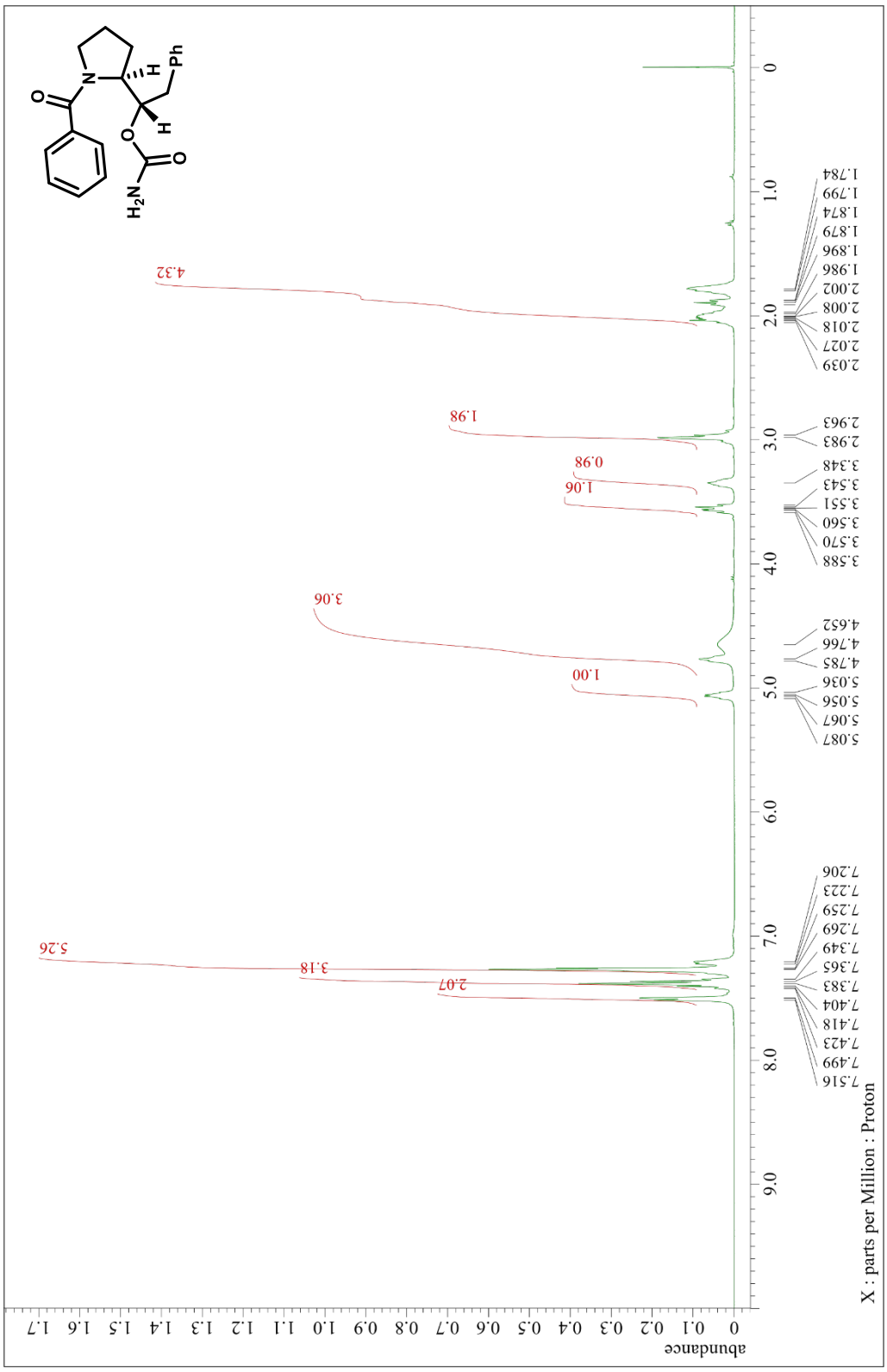

8.068
14.403
17.536
54.832
56.739
69.513
76.844
77.160
77.476
128.246
128.447
132.242
134.331
151.129
170.122
X : parts per Million : Carbon13
(thousandths)

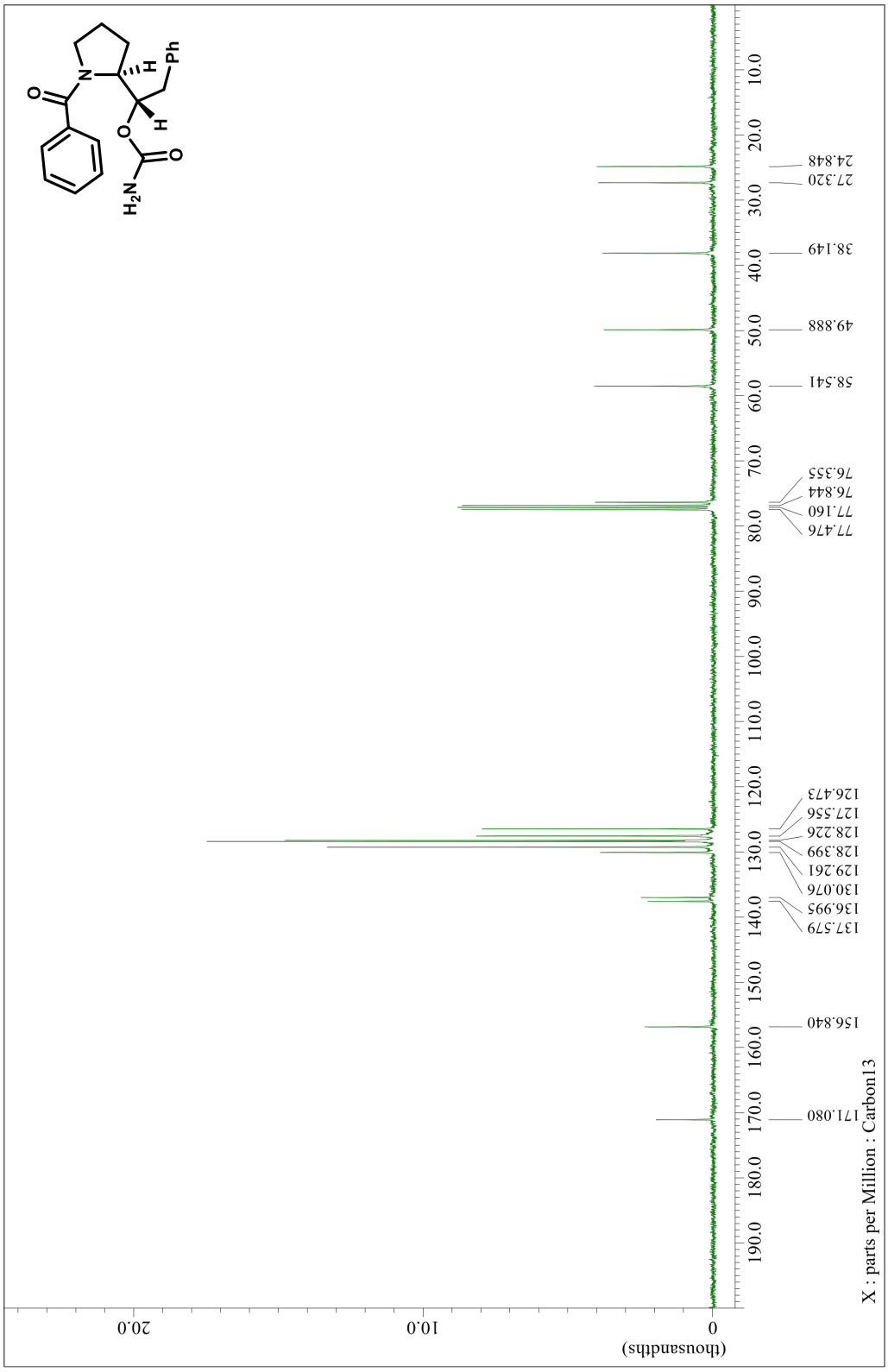
(*S*)-1-(1-benzoylpyrrolidin-2-yl)-2-phenylethan-1-one (s2a)



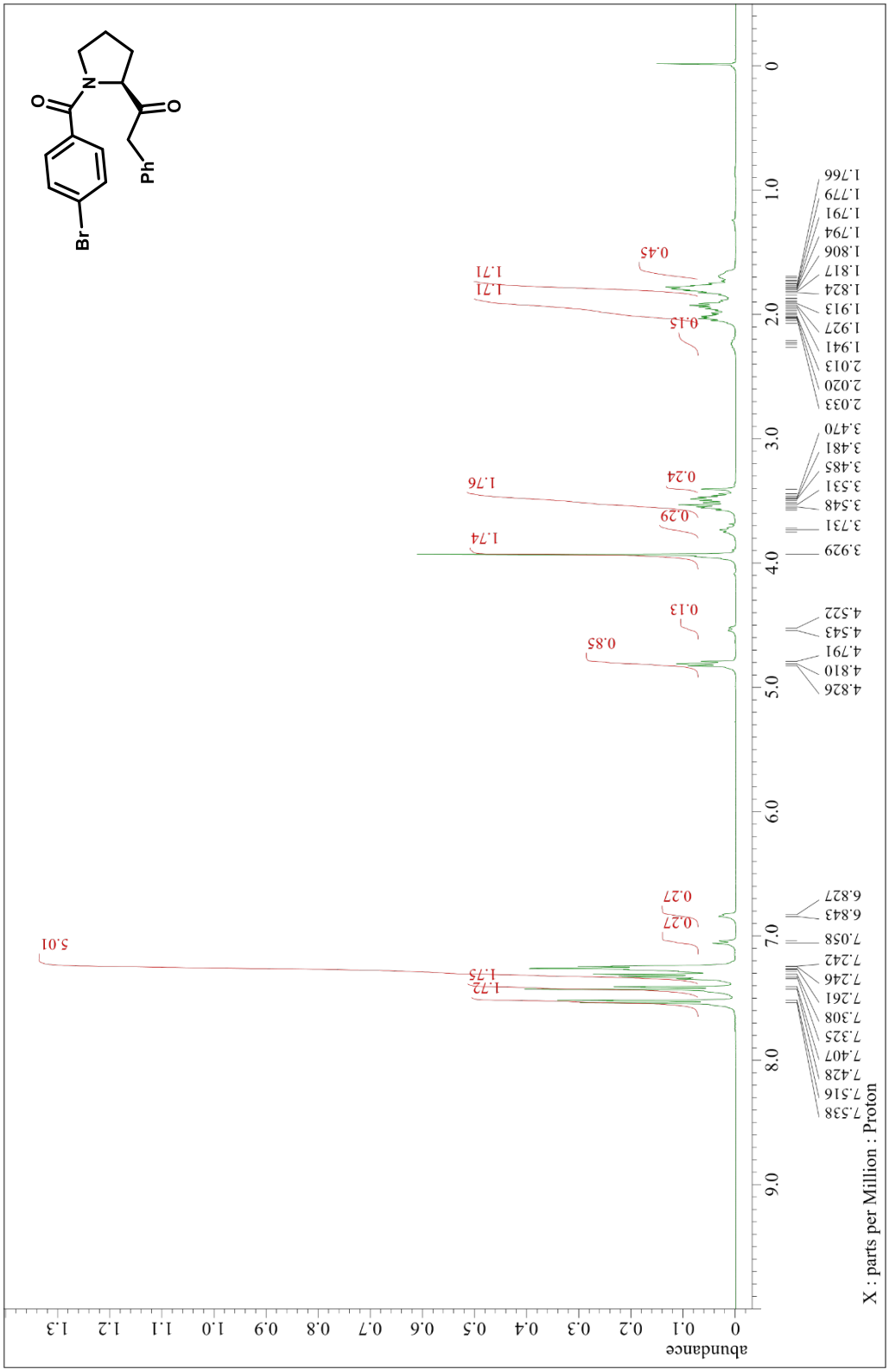

O
N
O
Ph
205.578
205.195
169.605
168.618
136.784
135.423
133.353
129.597
129.185
128.801
128.686
127.853
127.699
127.613
126.655
126.271
126.224
125.917
77.476
77.160
76.834
65.852
64.156
49.552
46.476
46.131
45.594
29.400
28.039
24.877
21.858
X : parts per Million : Carbon13
(thousandths)

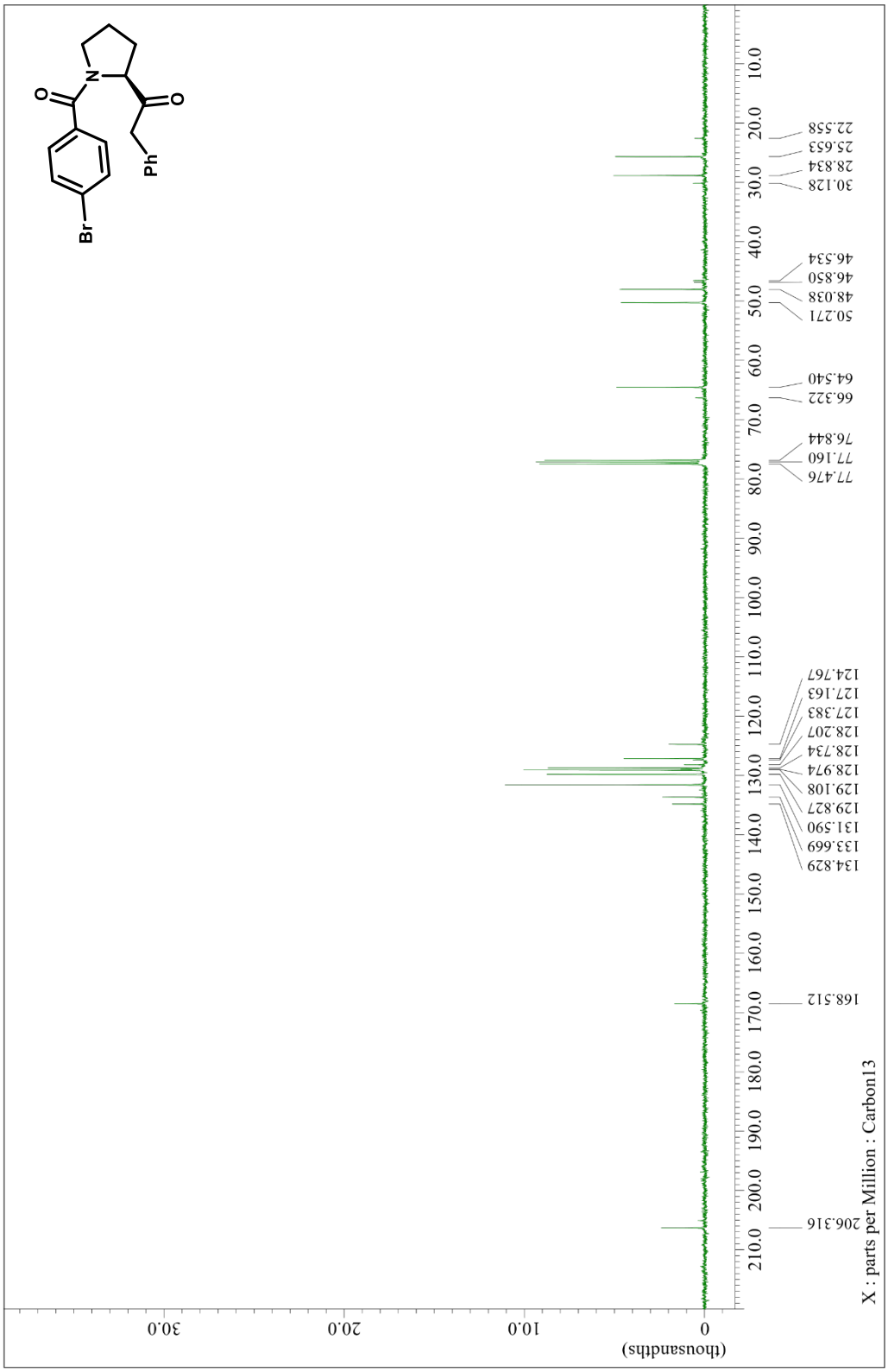
(*S*)-1-((*S*)-1-benzoylpyrrolidin-2-yl)-2-phenylethyl carbamate (1a)



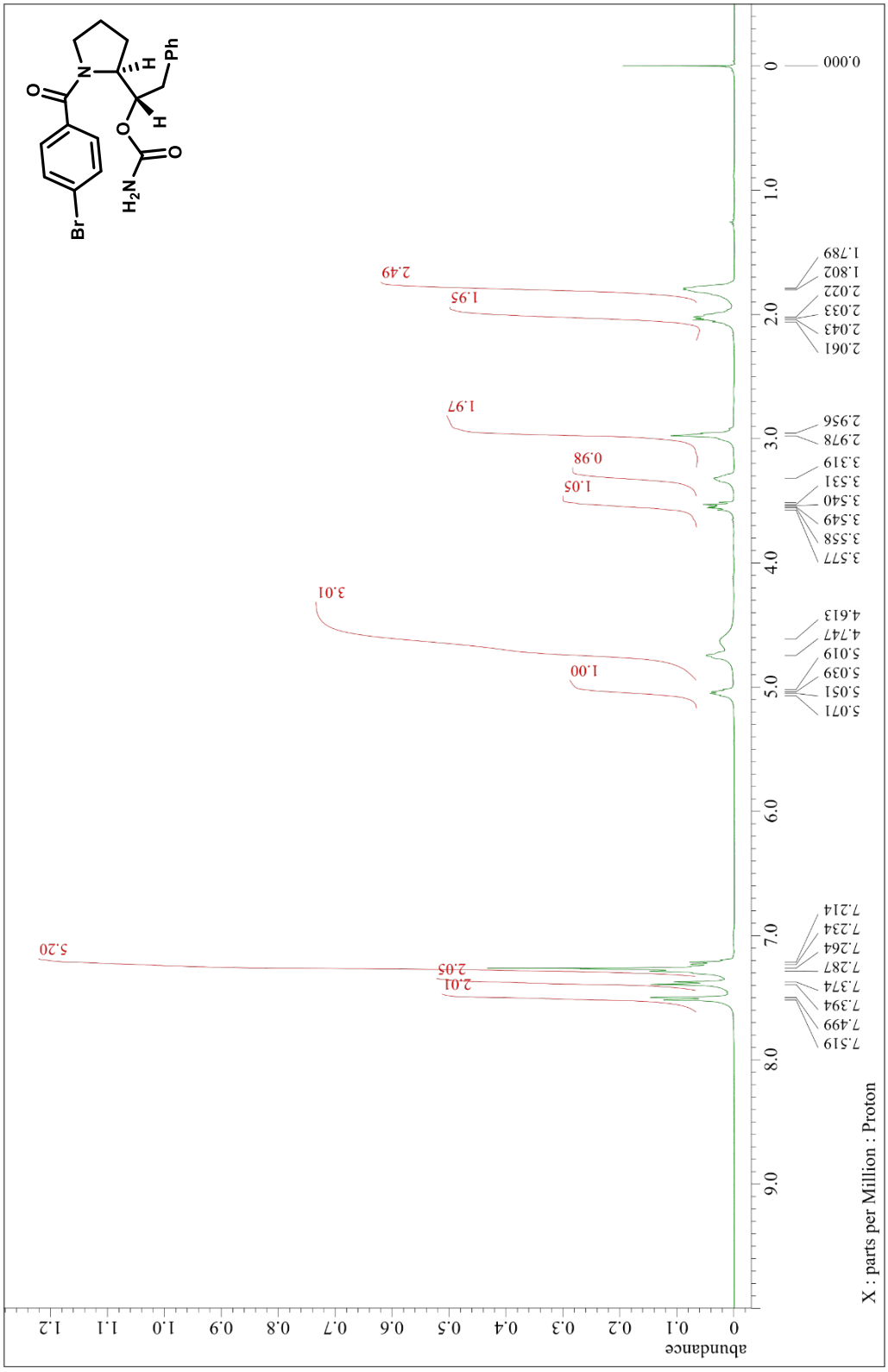

(thousandths)
0
10.0
20.0
X : parts per Million : Carbon13
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0
24.848
27.320
38.149
49.888
58.541
76.355
76.844
77.160
77.476
126.473
127.556
128.226
128.399
129.261
130.076
136.995
137.579
156.840
171.080
Ph
H
H
O
O
N
O
H_2N

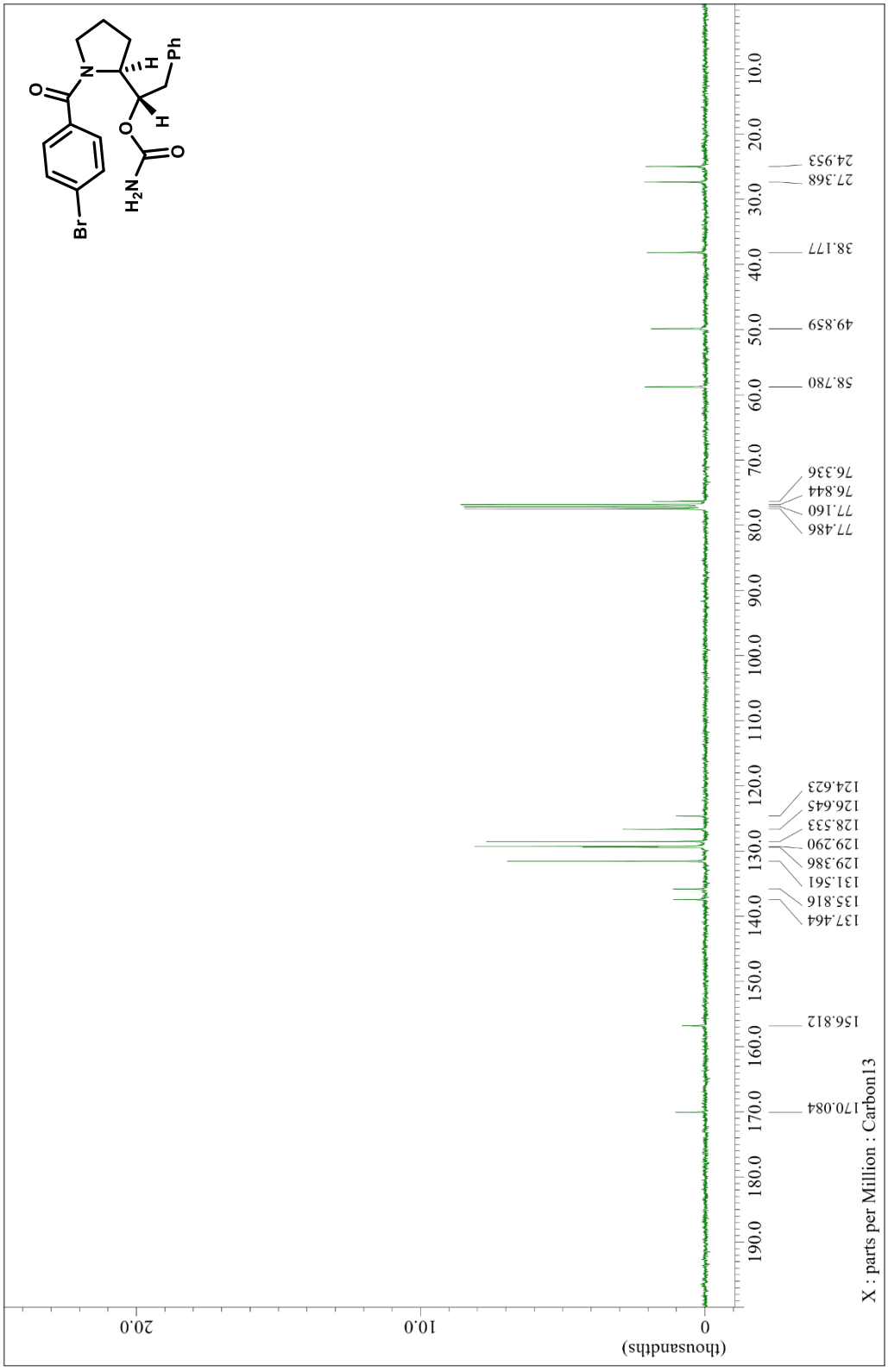
(*S*)-1-(1-(4-bromobenzoyl)pyrrolidin-2-yl)-2-phenylethan-1-one (s2i)



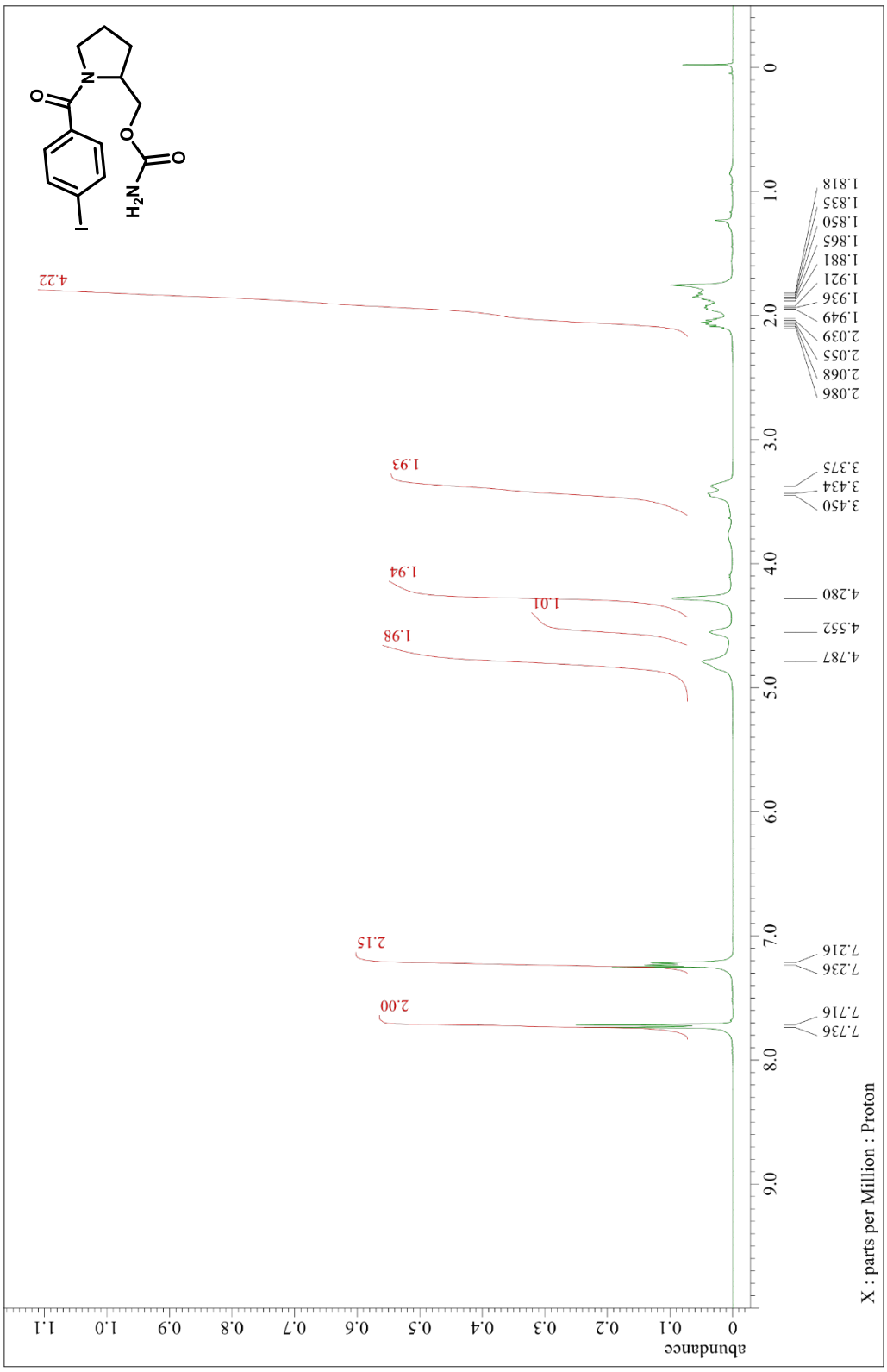

Br
Ph
(thousandths)
X : parts per Million : Carbon13
206.316
168.512
134.829
133.669
131.590
129.827
129.108
128.974
128.734
128.207
127.383
127.163
124.767
77.476
77.160
76.844
66.322
64.540
50.271
48.038
46.850
46.534
30.128
28.834
25.653
22.558

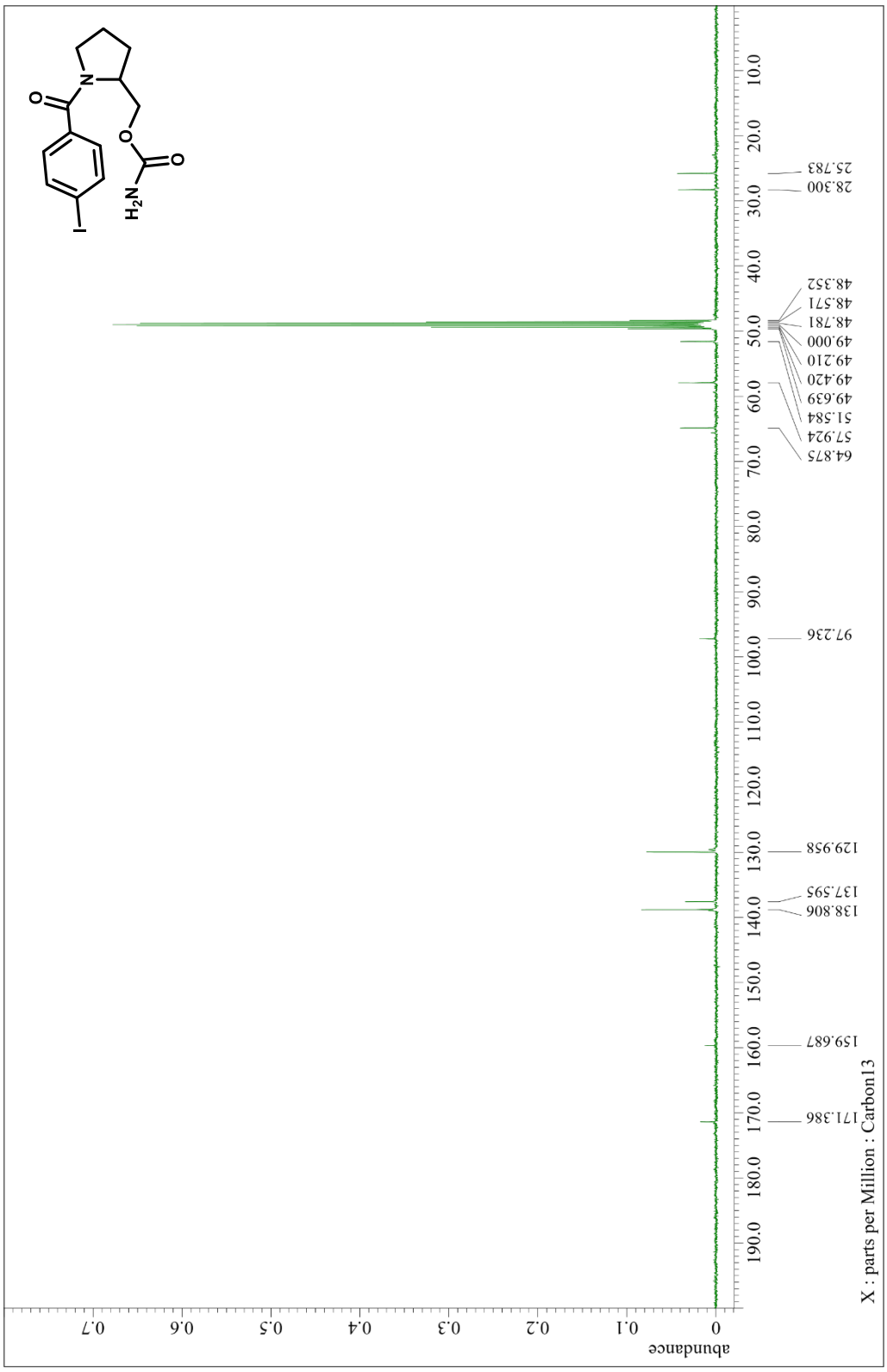
(*S*)-1-((*S*)-1-(4-bromobenzoyl)pyrrolidin-2-yl)-2-phenylethyl carbamate (1i)



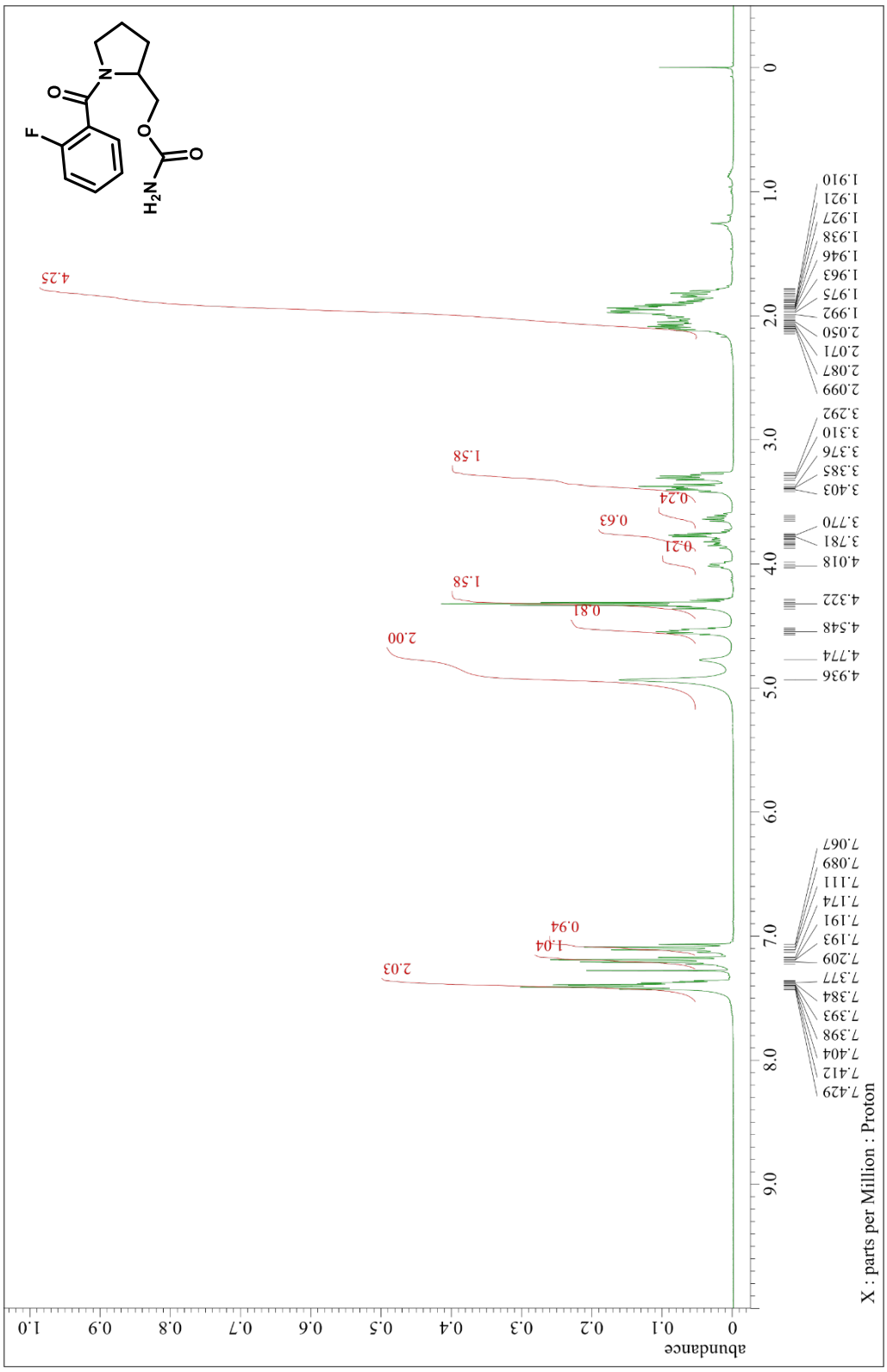

Br
O
N
O
O
H
Ph
H
H_2N
O
(thousandths)
0
10.0
20.0
X : parts per Million : Carbon13
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0
24.953
27.368
38.177
49.859
58.780
76.336
76.844
77.160
77.486
124.623
126.645
128.533
129.290
129.386
131.561
135.816
137.464
156.812
170.084

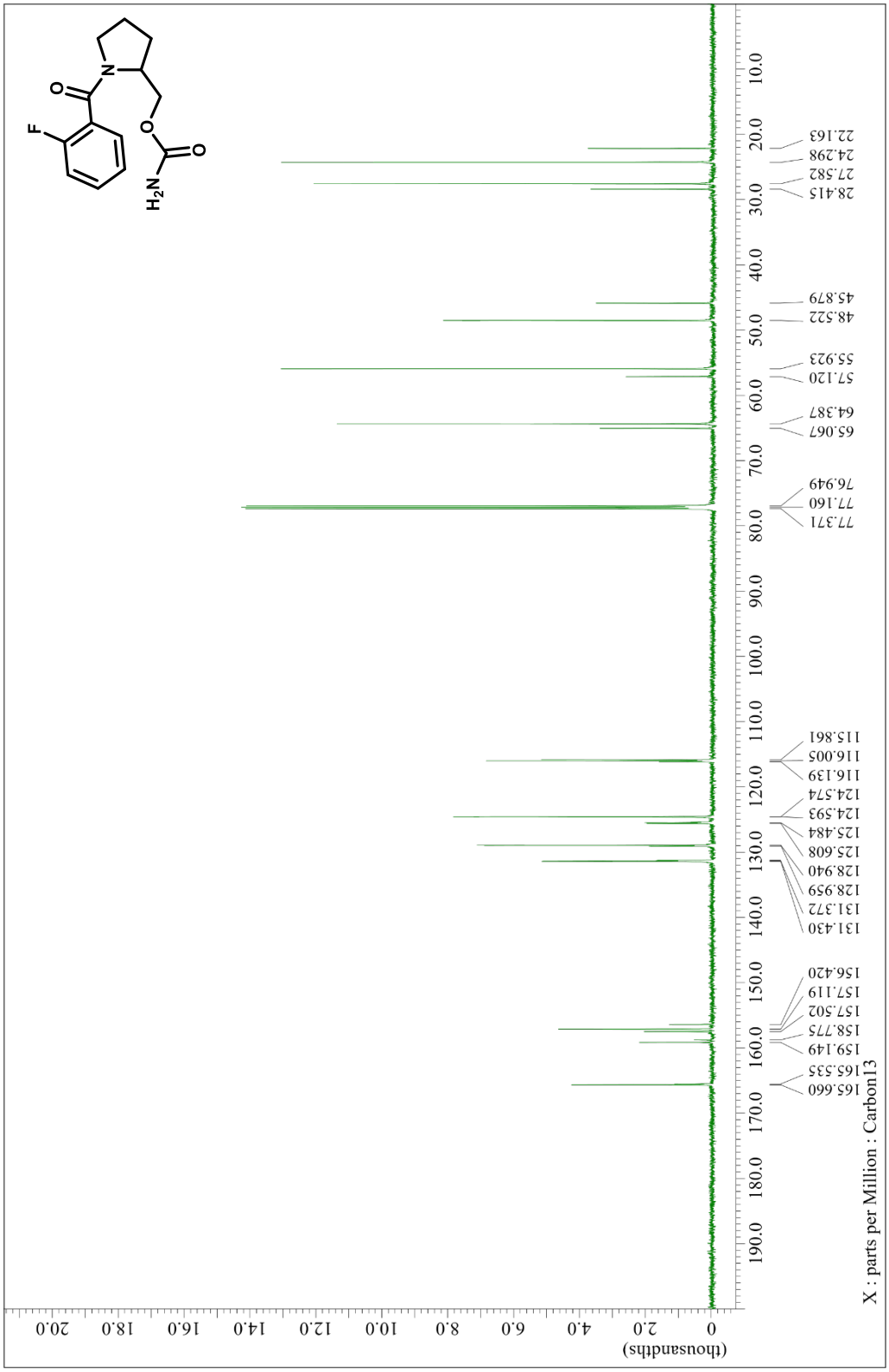
(1-(4-iodobenzoyl)pyrrolidin-2-yl)methyl carbamate (1e)



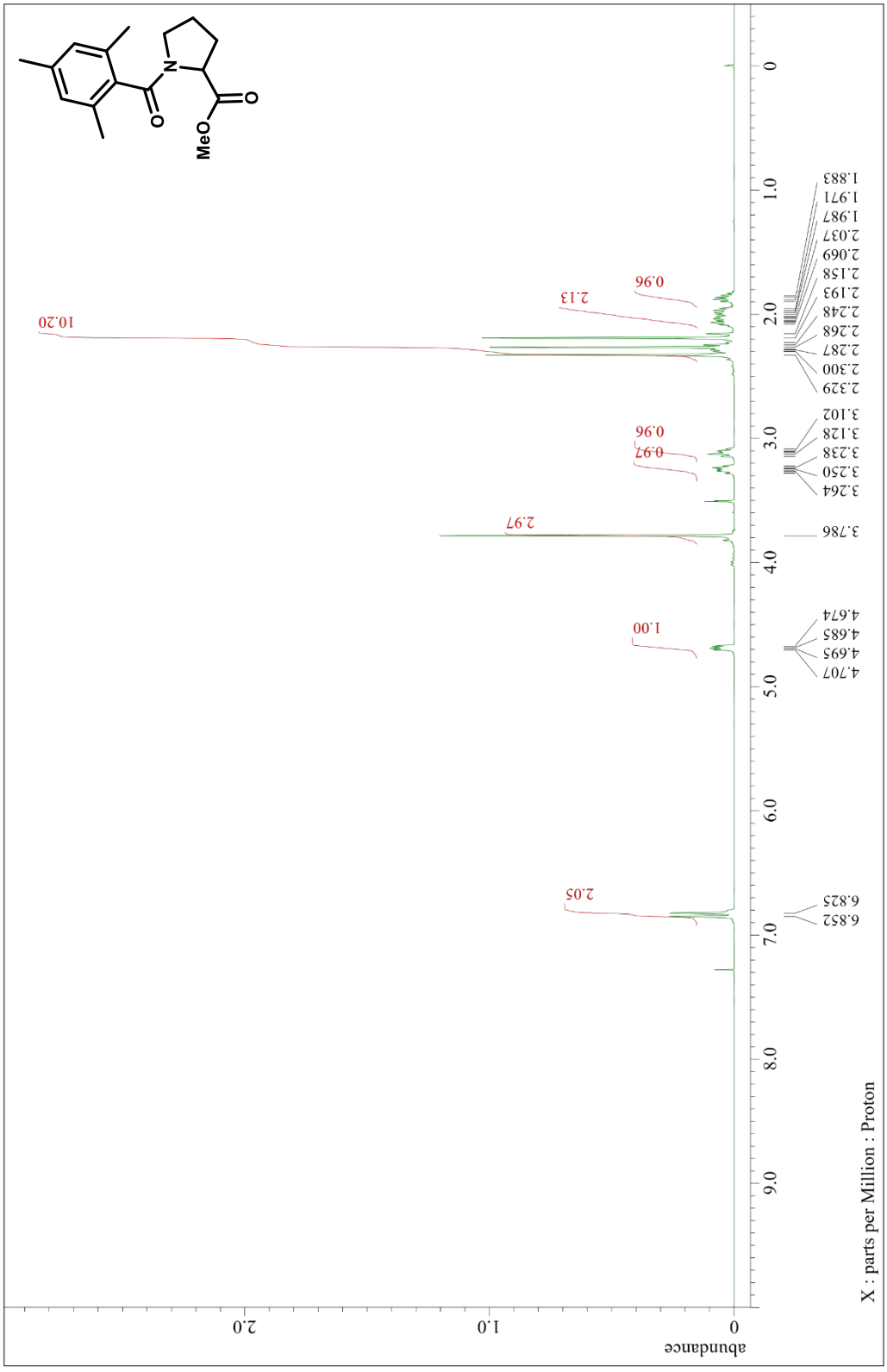

X : parts per Million : Carbon13
abundance
25.783
28.300
48.352
48.571
48.781
49.000
49.210
49.420
49.639
51.584
57.924
64.875
97.236
129.958
137.595
138.806
159.687
171.386

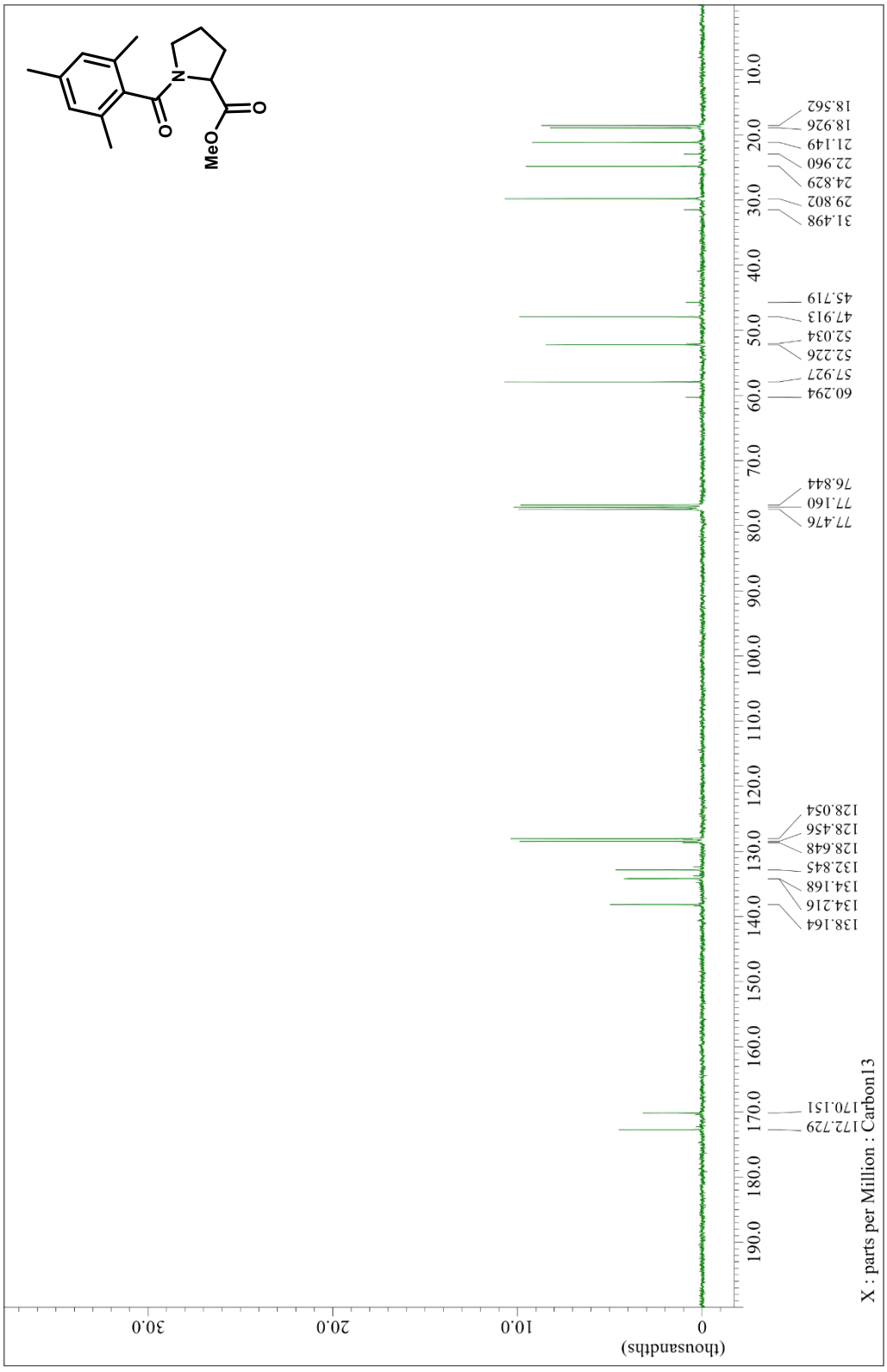
(1-(2-fluorobenzoyl)pyrrolidin-2-yl)methyl carbamate (1g)



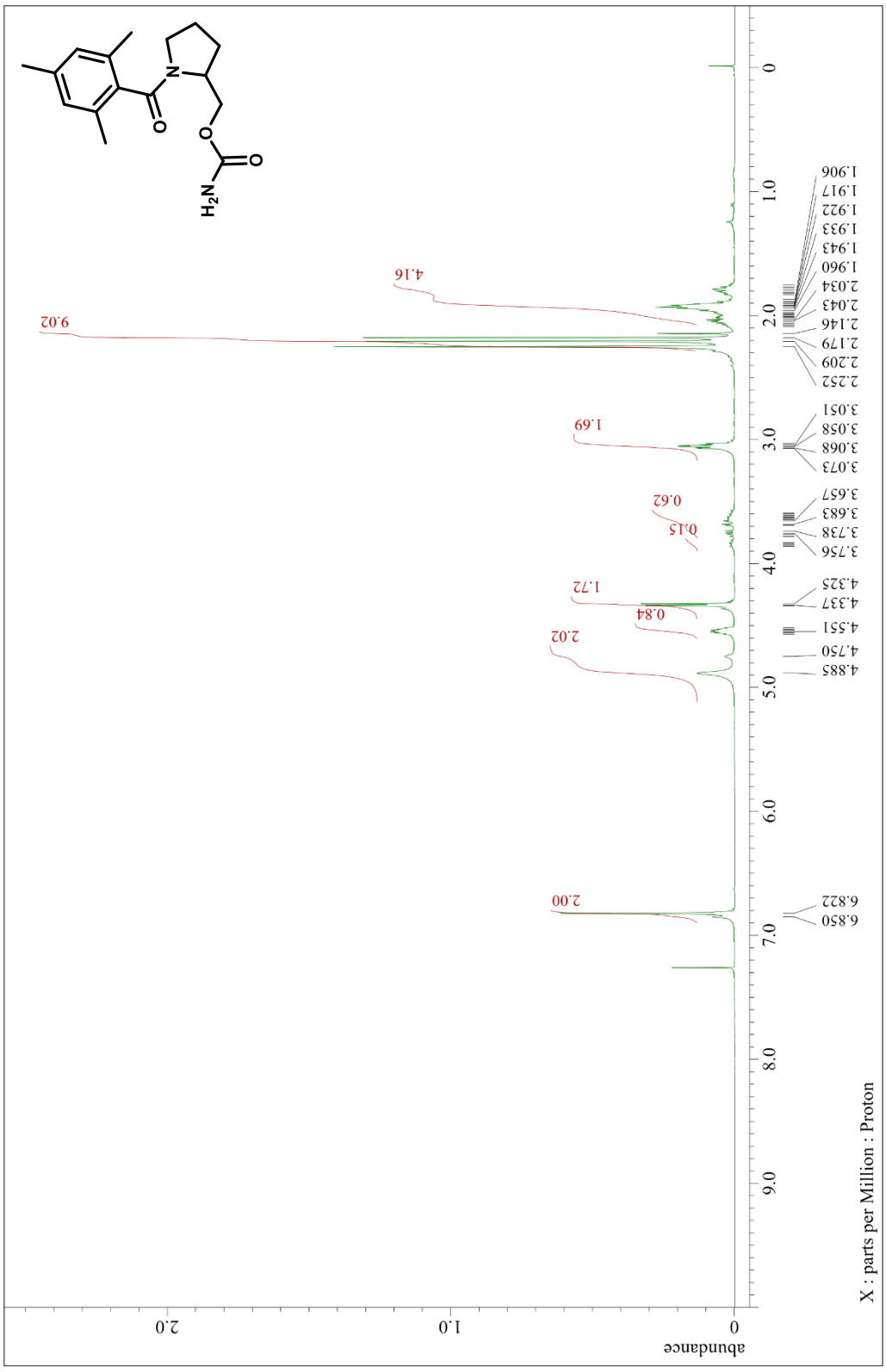

F
O
N
O
O
H_2N
O
(thousandths)
0
2.0
4.0
6.0
8.0
10.0
12.0
14.0
16.0
18.0
20.0
X : parts per Million : Carbon13
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0
22.163
24.298
27.582
28.415
45.879
48.522
55.923
57.120
64.387
65.067
76.949
77.160
77.371
115.861
116.005
116.139
124.574
124.593
125.484
125.608
128.940
128.959
131.372
131.430
156.420
157.119
157.502
158.775
159.149
165.535
165.660

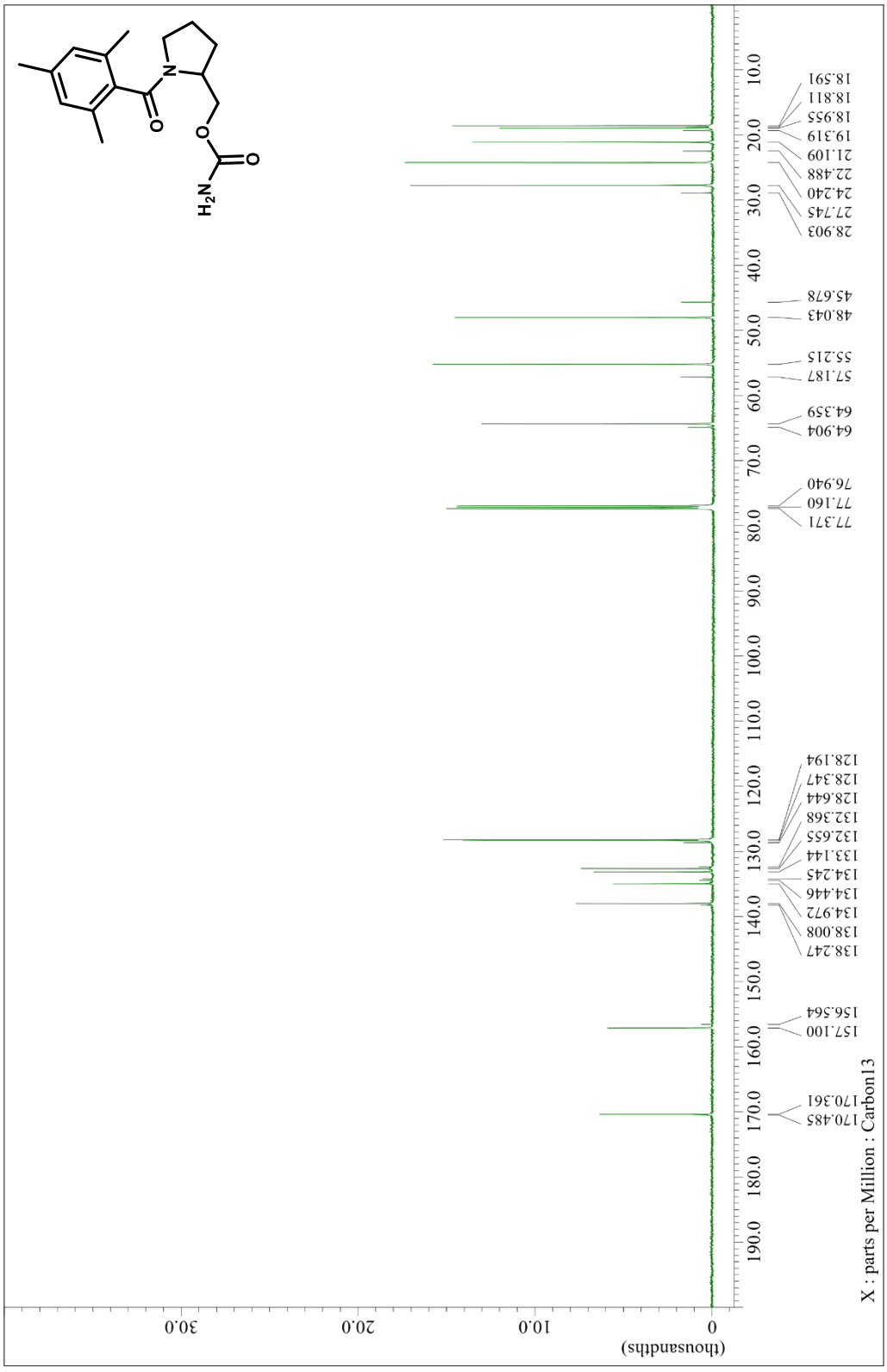
Methyl (2,4,6-trimethylbenzoyl)prolinate (s1h)



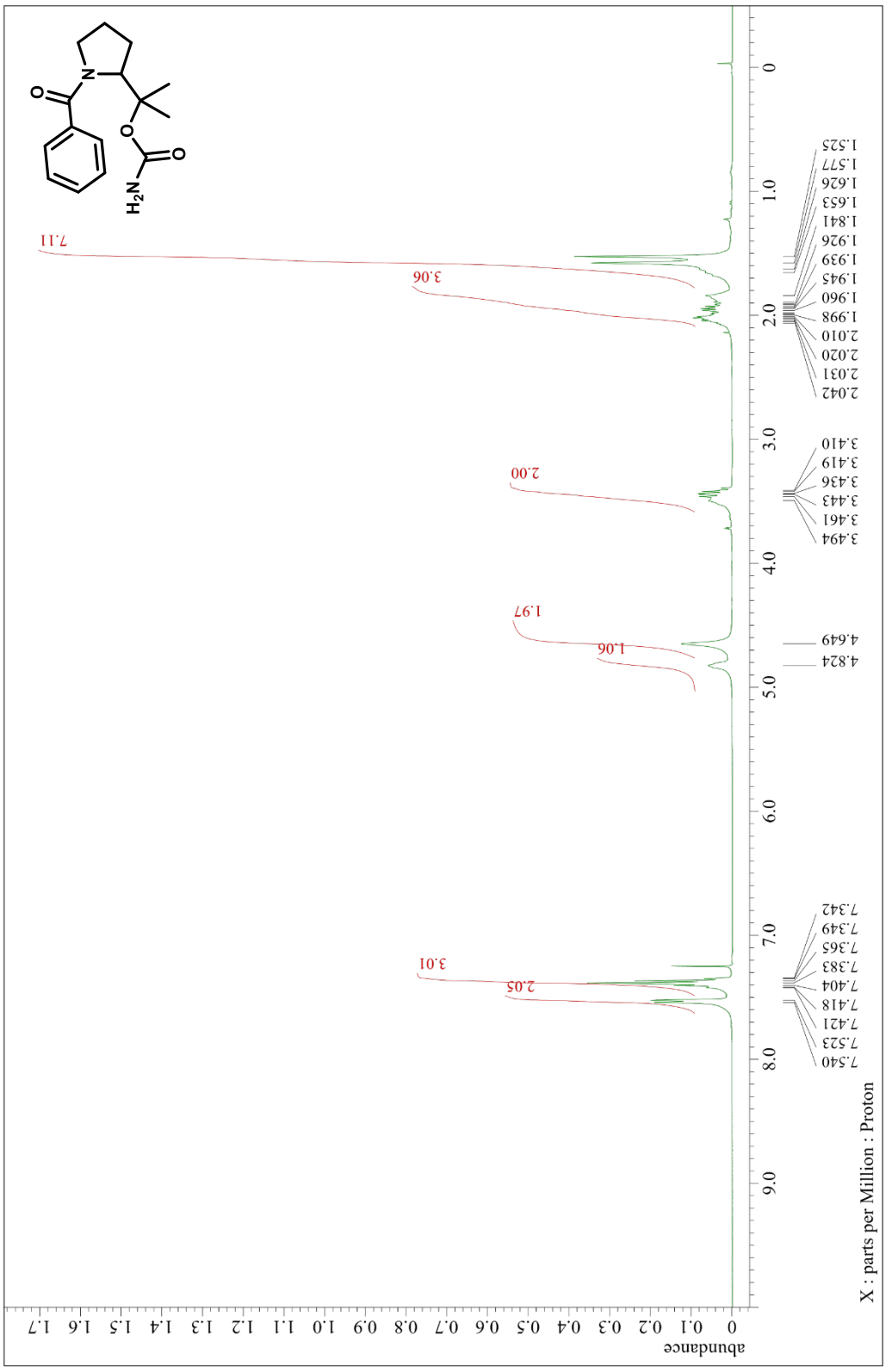

MeO
(thousandths)
X : parts per Million : Carbon13
18.562
18.926
21.149
22.960
24.829
29.802
31.498
45.719
47.913
52.034
52.226
57.927
60.294
76.844
77.160
77.476
128.054
128.456
128.648
132.845
134.168
134.216
138.164
170.151
172.729

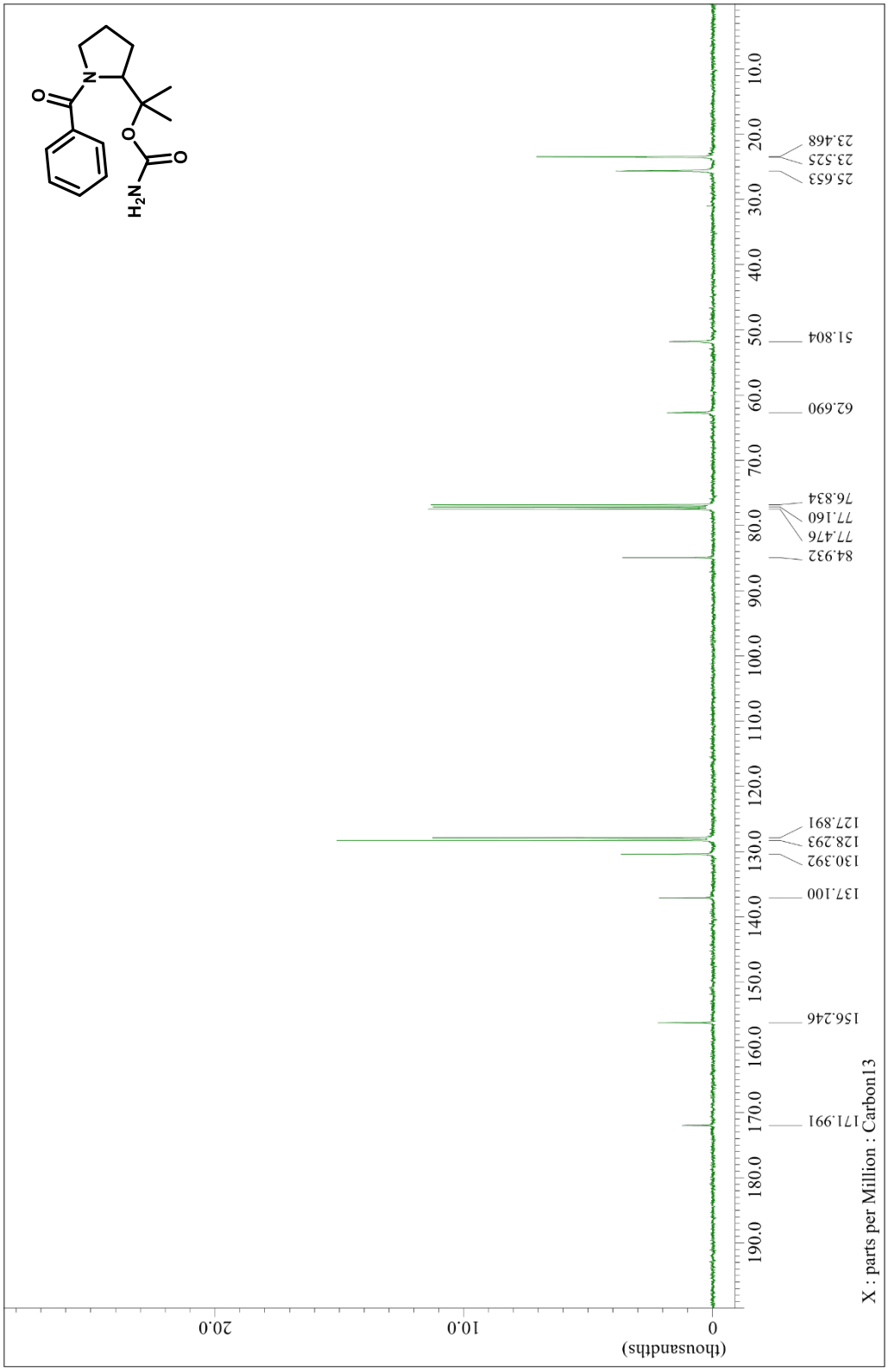
(1-(2,4,6-trimethylbenzoyl)pyrrolidin-2-yl)methyl carbamate (1h)



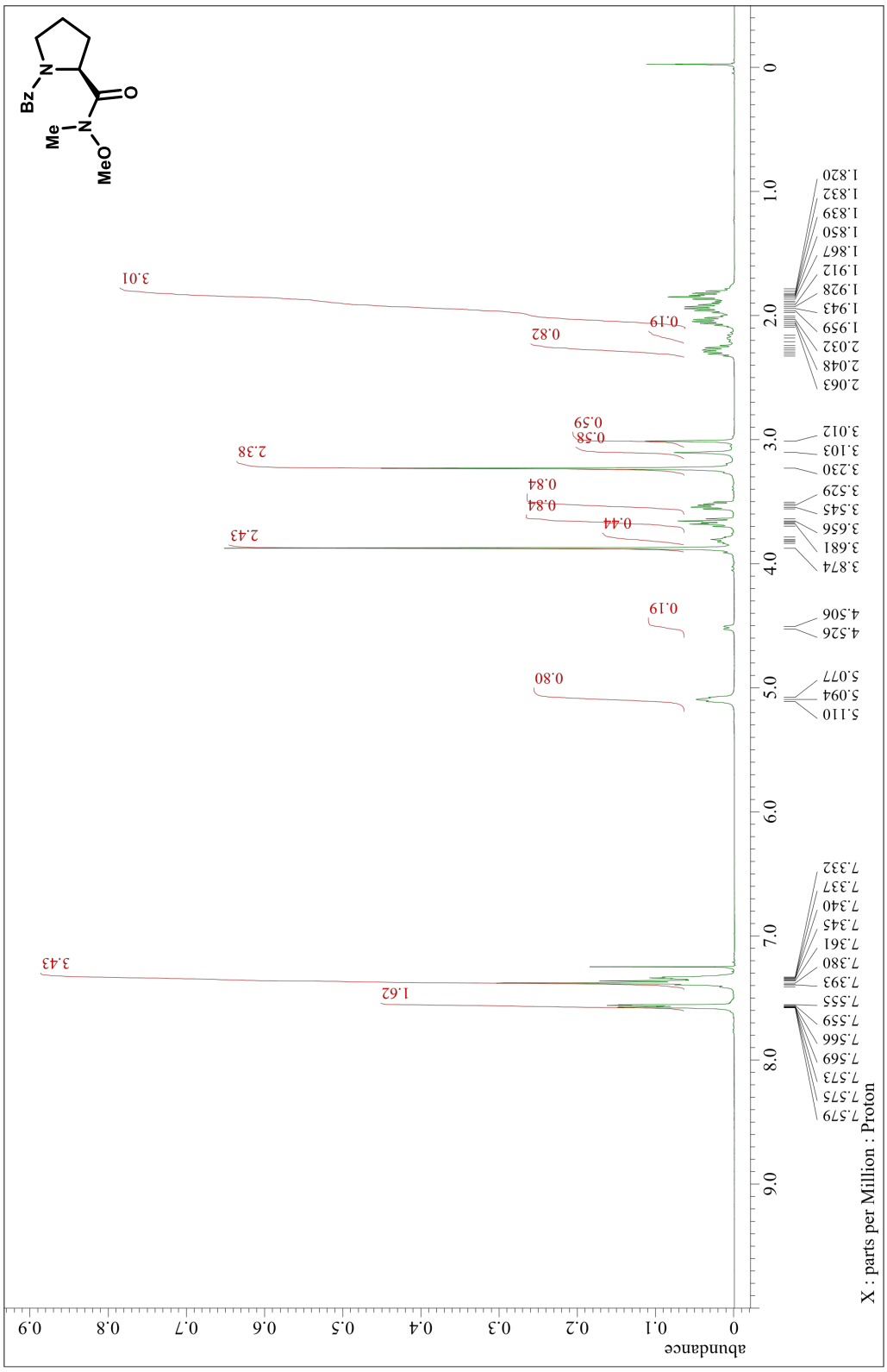

O
N
O
O
H_2N
(thousandths)
0
10.0
20.0
30.0
X : parts per Million : Carbon13
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0
18.591
18.811
18.955
19.319
21.109
22.488
24.240
27.745
28.903
45.678
48.043
55.215
57.187
64.359
64.904
76.940
77.160
77.371
128.194
128.347
128.644
132.368
132.655
133.144
134.245
134.446
134.972
138.008
138.247
156.564
157.100
170.361
170.485

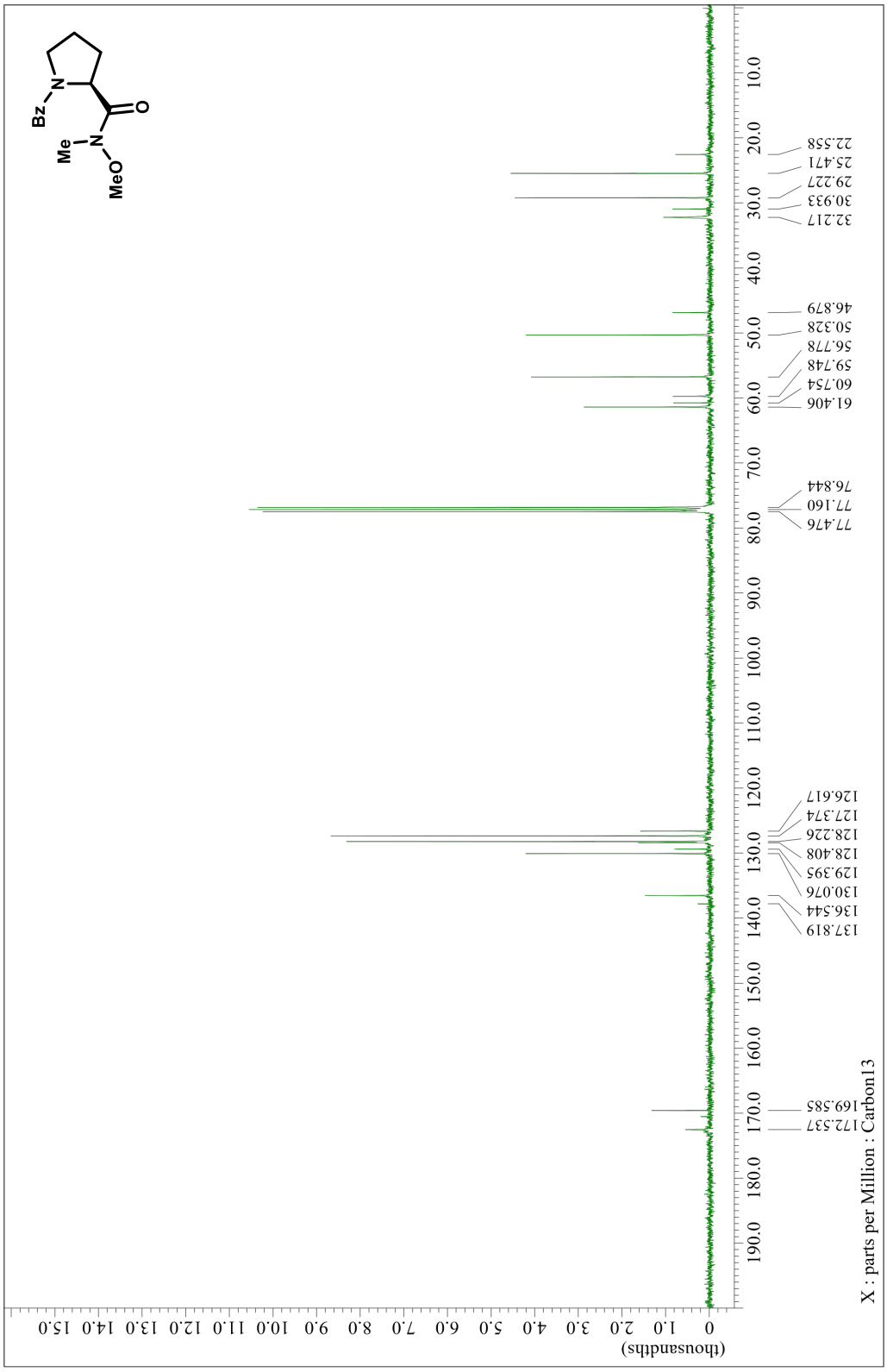
2-(1-benzoylpyrrolidin-2-yl)propan-2-yl carbamate (1j)



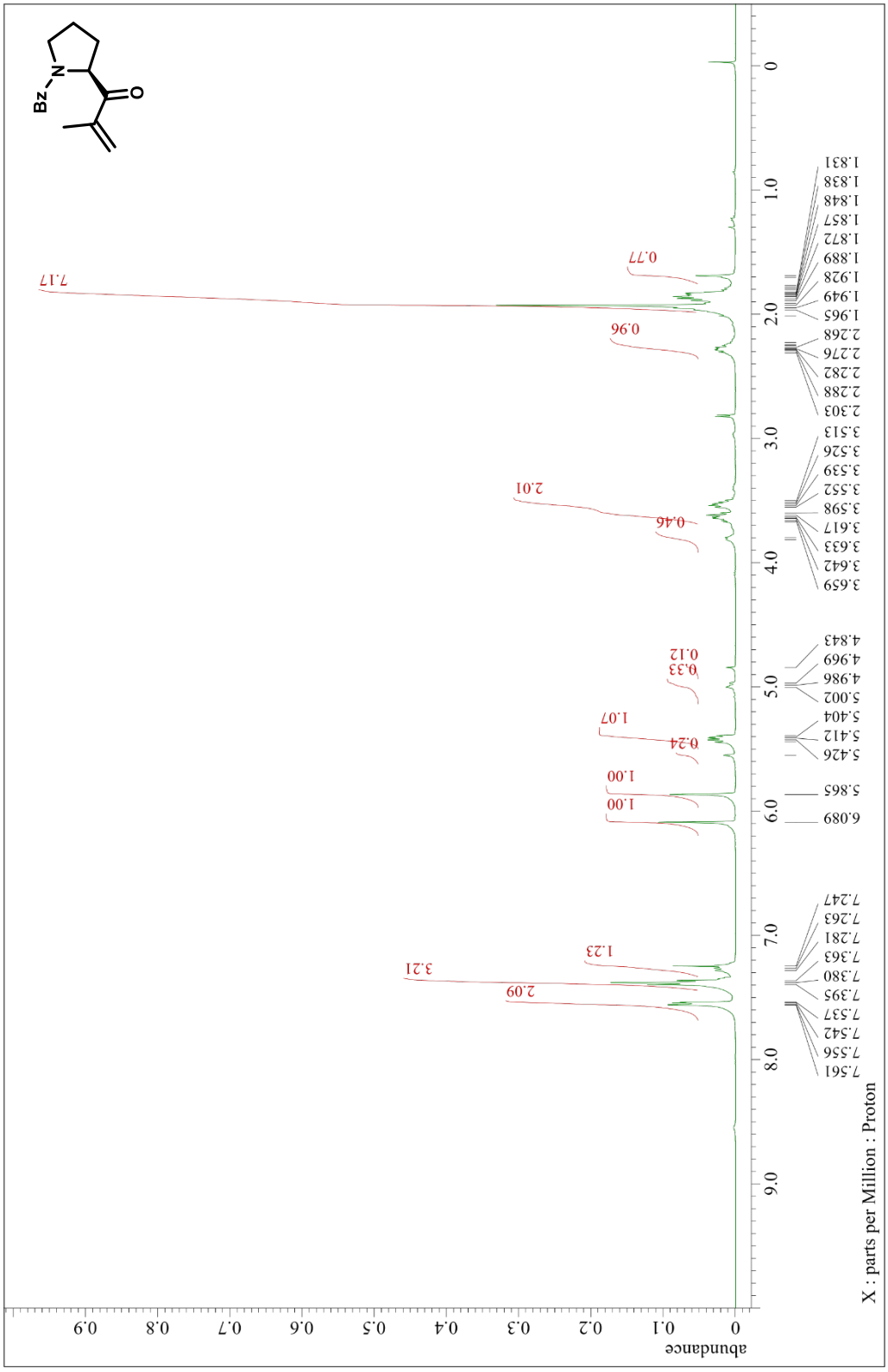

O
N
O
O
H_2N
23.468
23.525
25.653
51.804
62.690
76.834
77.160
77.476
84.932
127.891
128.293
130.392
137.100
156.246
171.991
X : parts per Million : Carbon13
(thousandths)

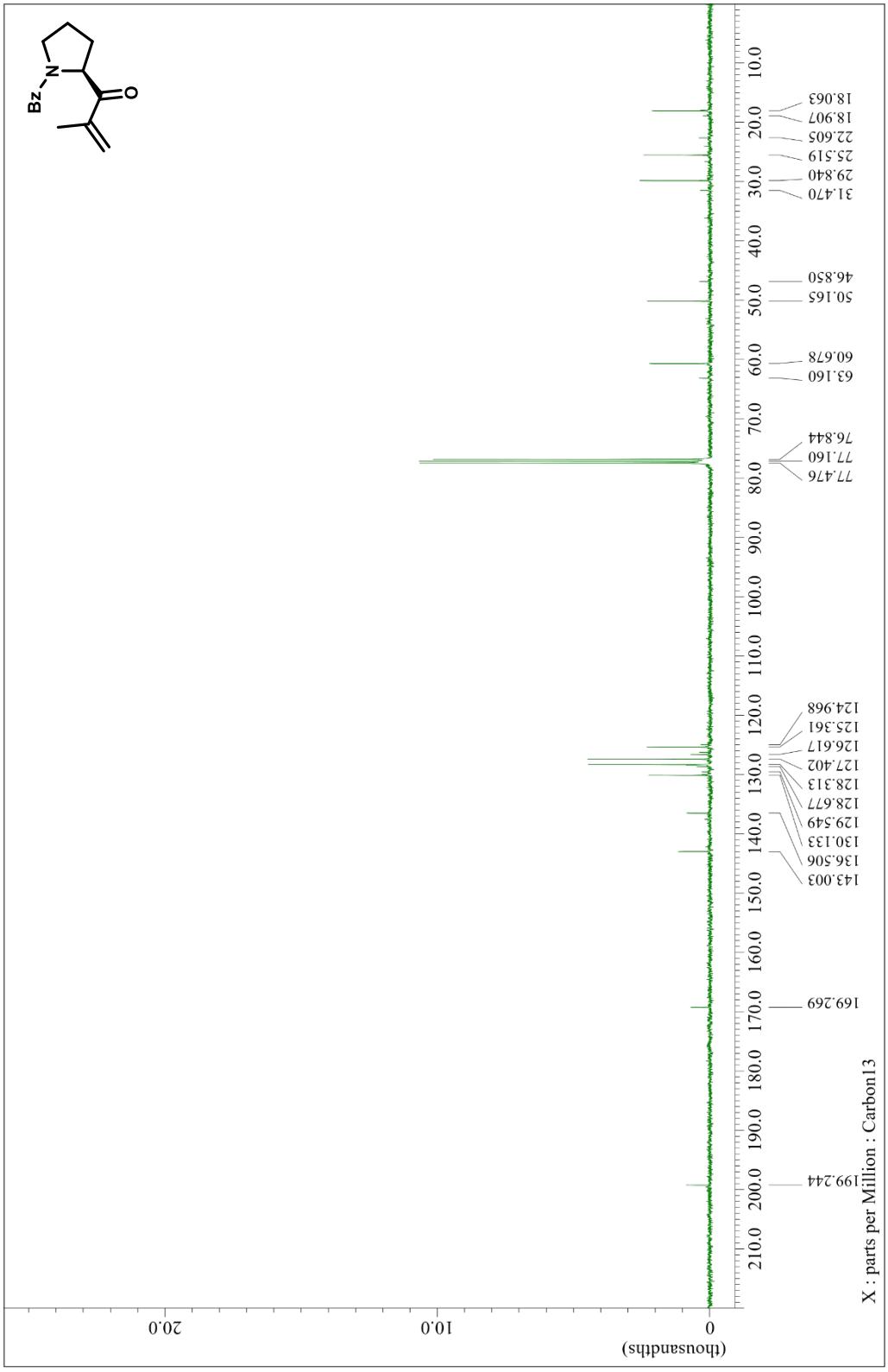
(*S*)-1-benzoyl-*N*-methoxy-*N*-methylpyrrolidine-2-carboxamide (s2k)



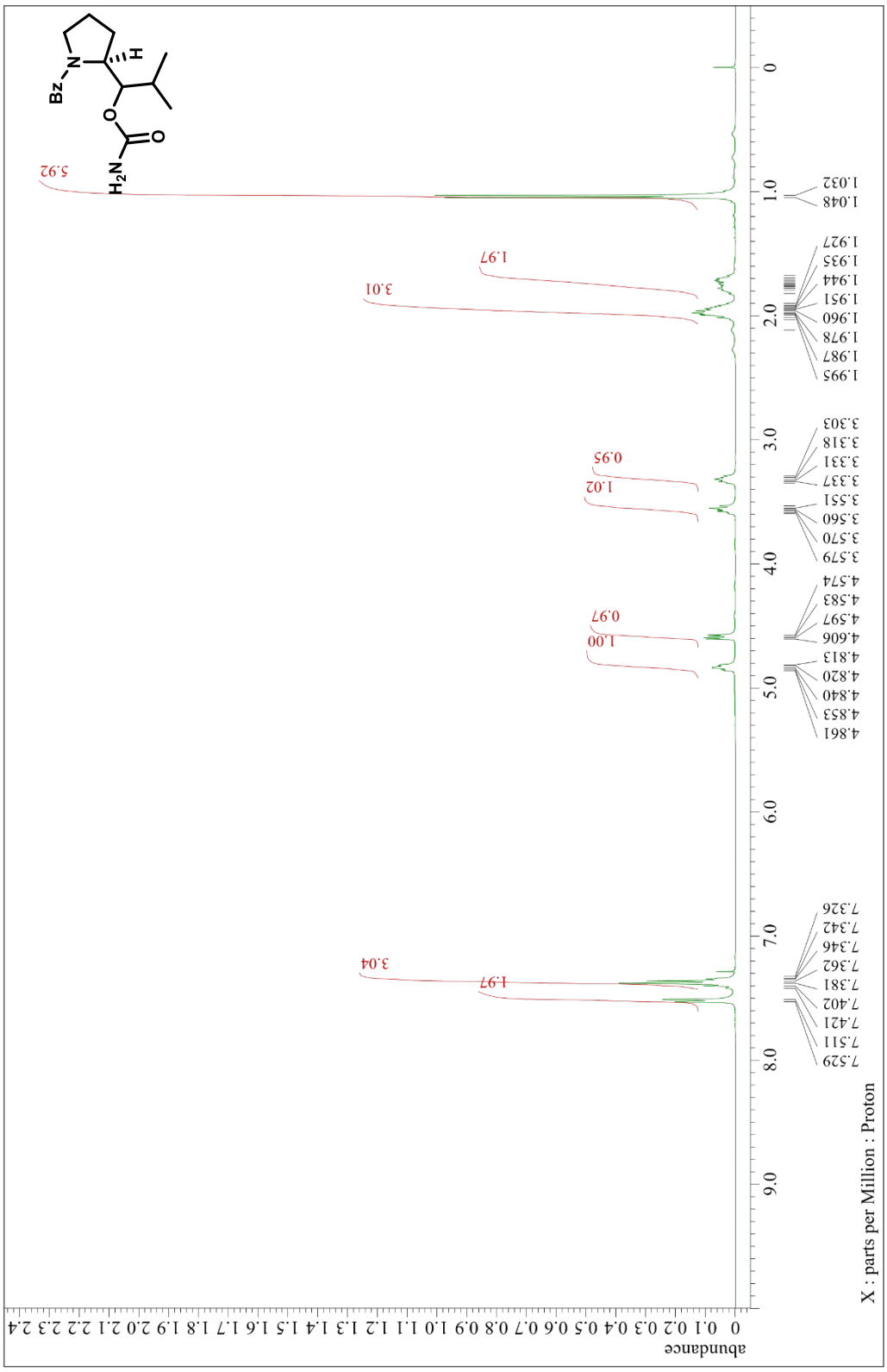

Bz
N
Me
N
O
MeO
O
(thousandths)
X : parts per Million : Carbon13
22.558
25.471
29.227
30.933
32.217
46.879
50.328
56.778
59.748
60.754
61.406
76.844
77.160
77.476
126.617
127.374
128.226
128.408
129.395
130.076
136.544
137.819
169.585
172.537

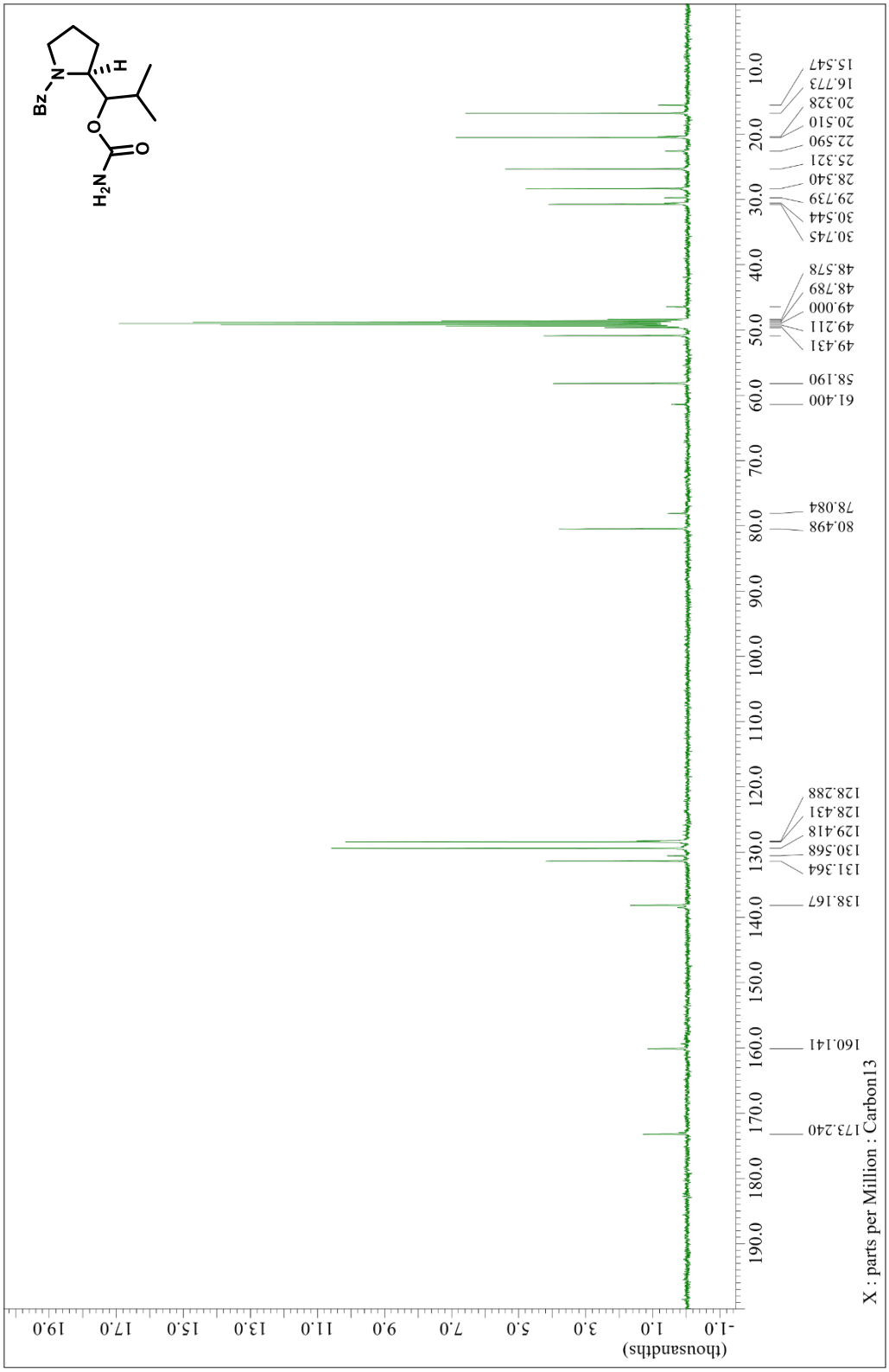
(*S*)-1-(1-benzoylpyrrolidin-2-yl)-2-methylprop-2-en-1-one (s3k)



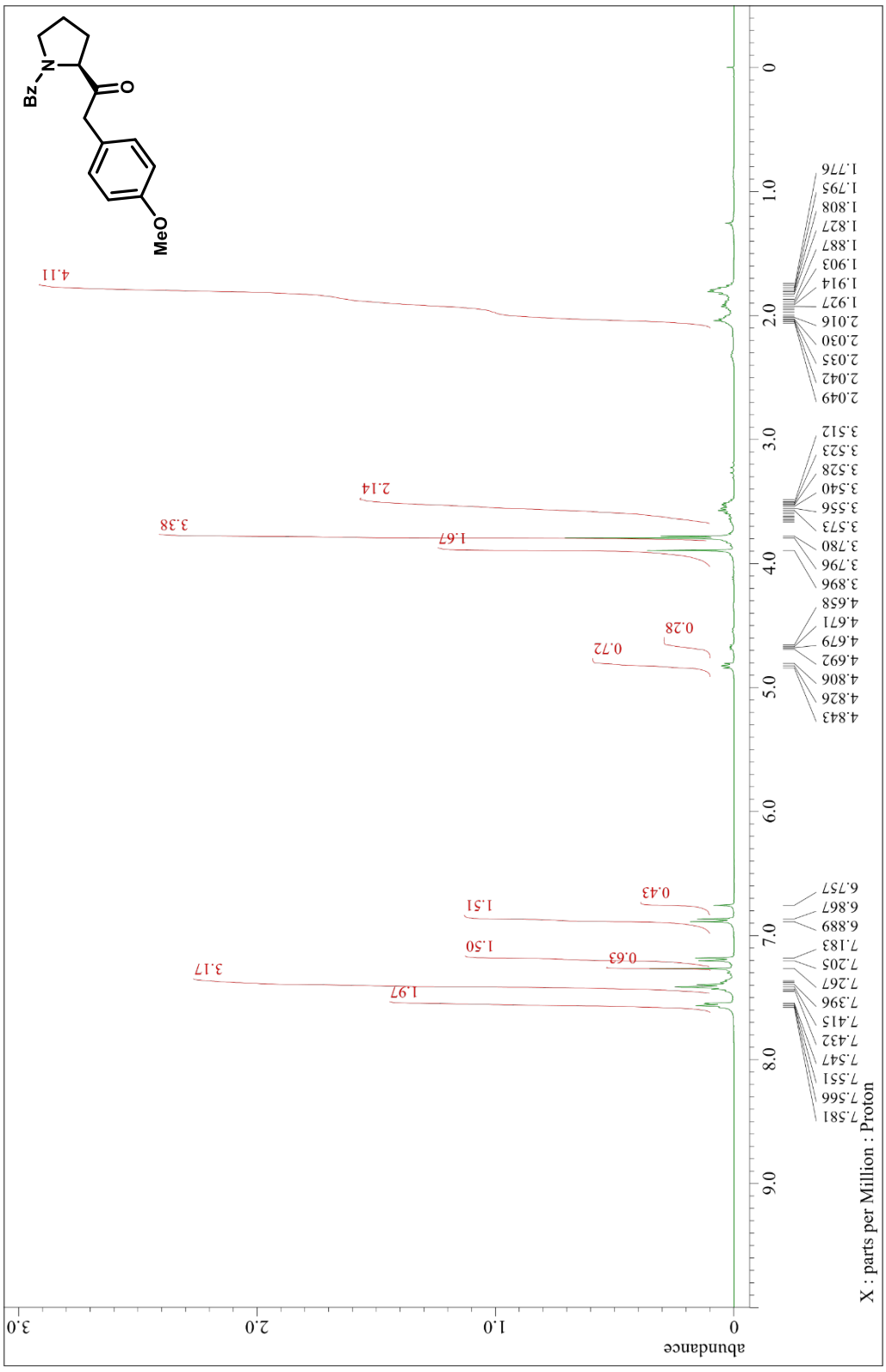

Bz
N
O
18.063
18.907
22.605
25.519
29.840
31.470
46.850
50.165
60.678
63.160
76.844
77.160
77.476
124.968
125.361
126.617
127.402
128.313
128.677
129.549
130.133
136.506
143.003
169.269
199.244
(thousandths)
0
10.0
20.0
X : parts per Million : Carbon13

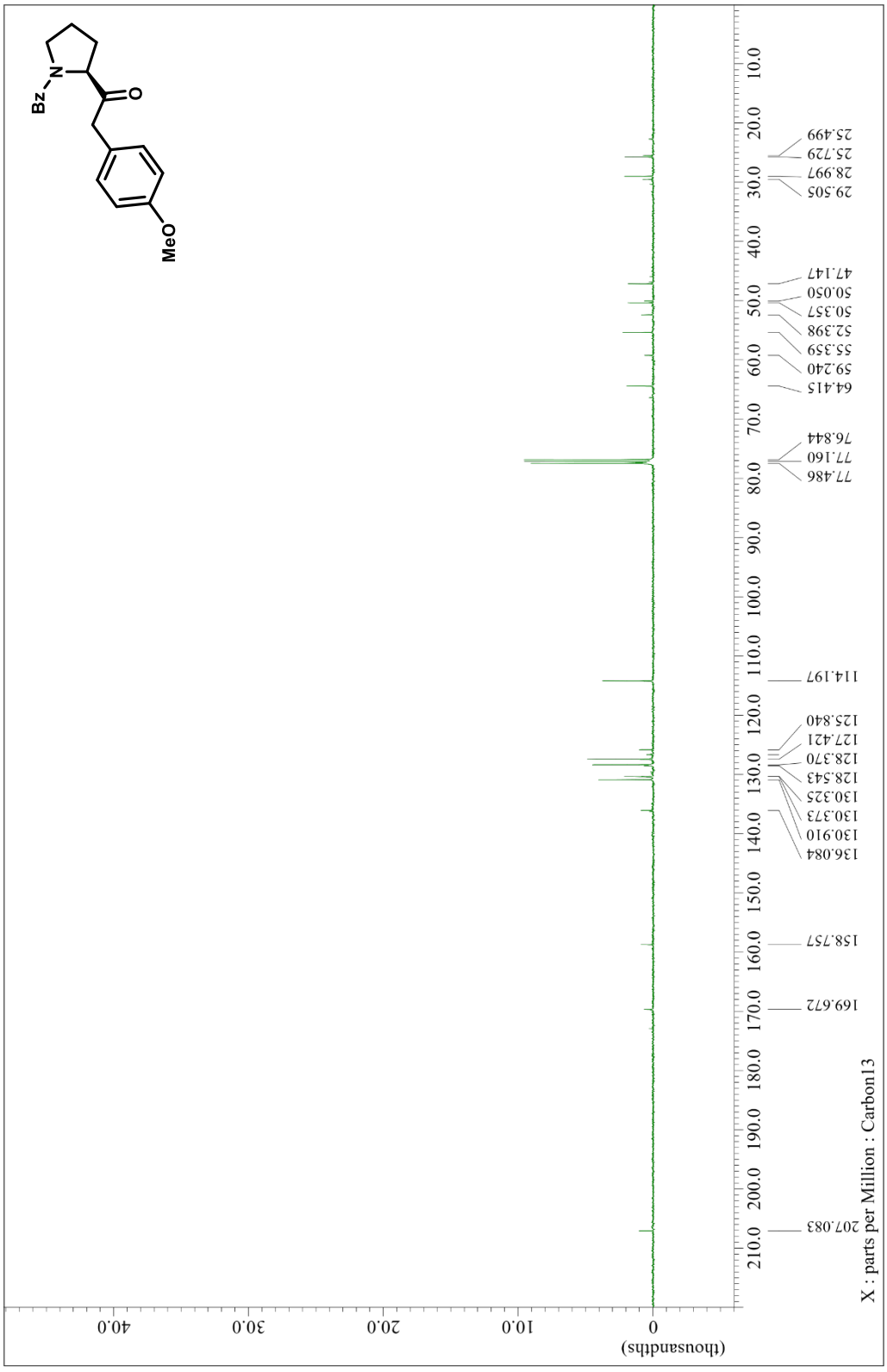
1-((*S*)-1-benzoylpyrrolidin-2-yl)-2-methylpropyl carbamate (1k)



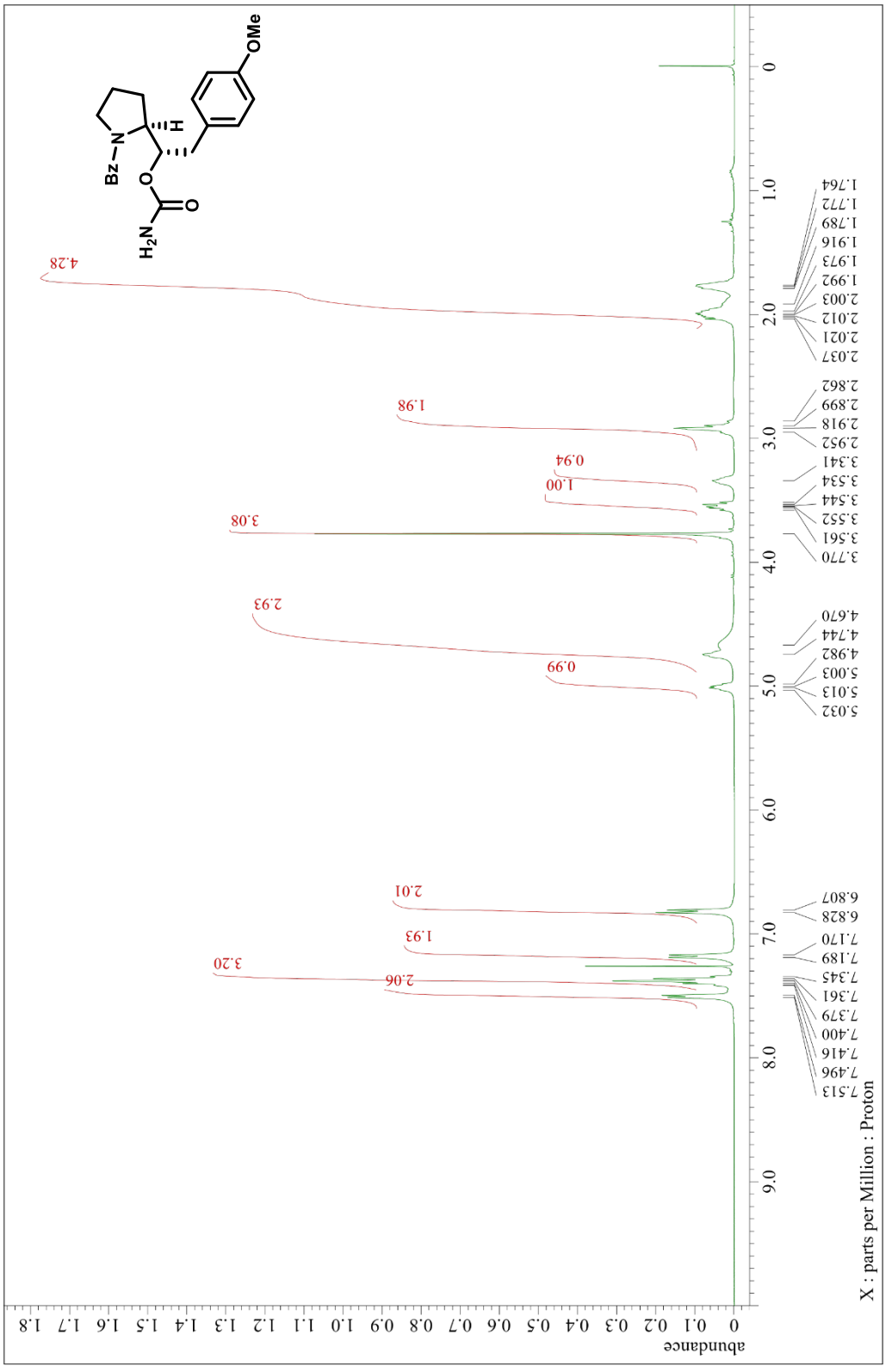

Bz
N
H
O
O
H2N
15.547
16.773
20.328
20.510
22.590
25.321
28.340
29.739
30.544
30.745
48.578
48.789
49.000
49.211
49.431
58.190
61.400
78.084
80.498
128.288
128.431
129.418
130.568
131.364
138.167
160.141
173.240
X : parts per Million : Carbon13
(thousandths)

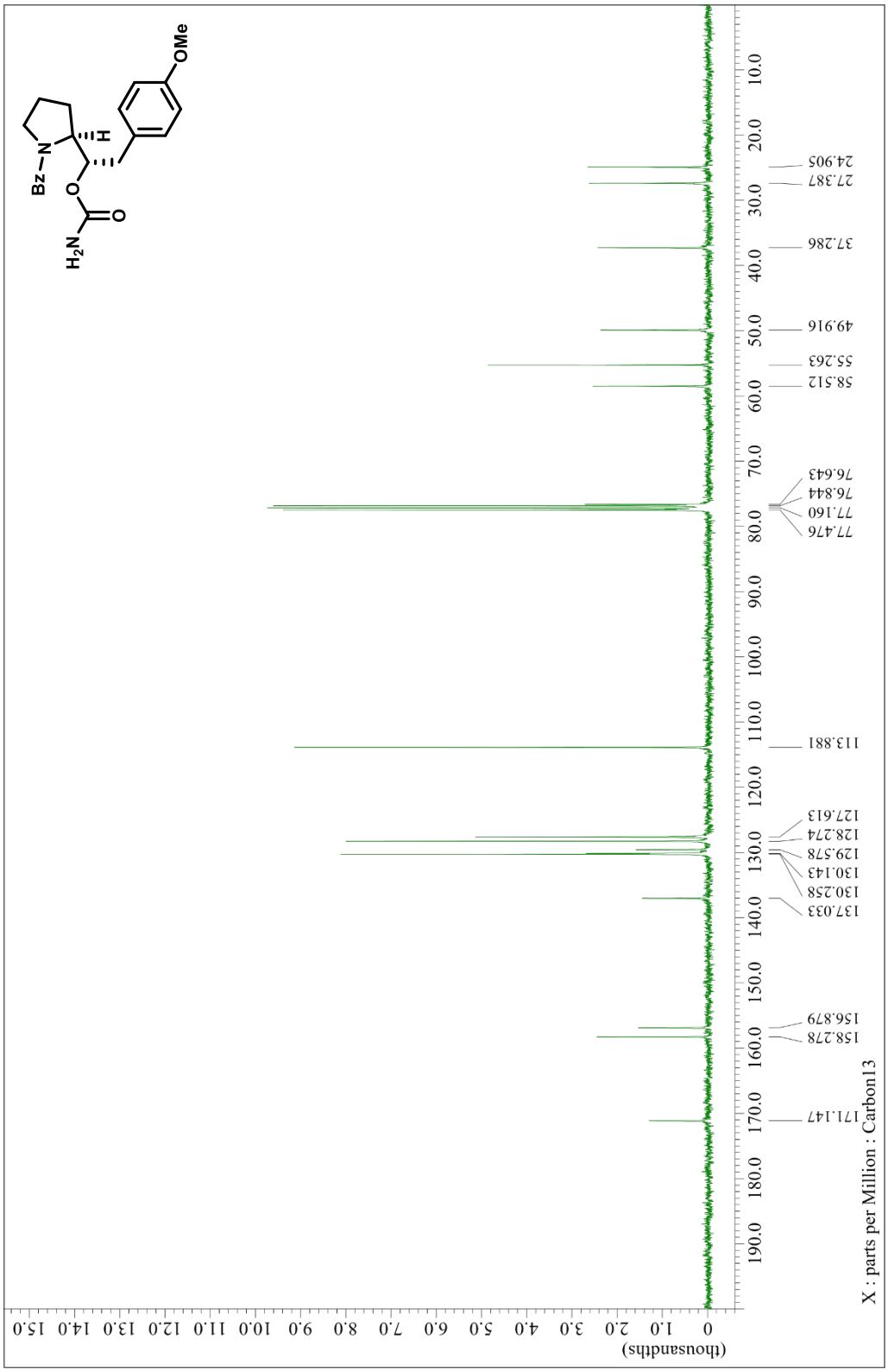
(*S*)-1-(1-benzoylpyrrolidin-2-yl)-2-(4-methoxyphenyl)ethan-1-one (s2l)



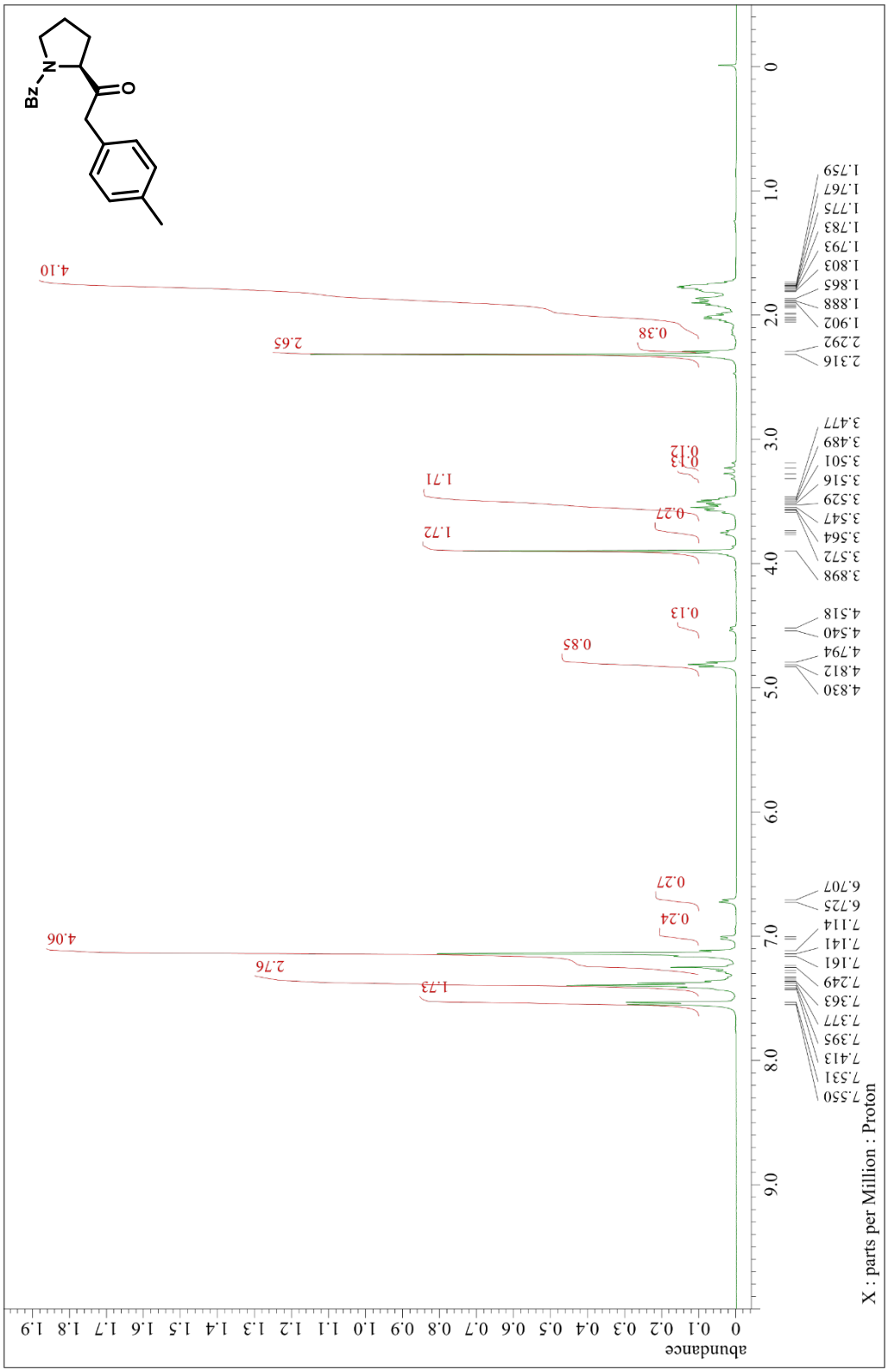

Bz
N
O
MeO
(thousandths)
0
10.0
20.0
30.0
40.0
X : parts per Million : Carbon13
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0
200.0
210.0
25.499
25.729
28.997
29.505
47.147
50.050
50.357
52.398
55.359
59.240
64.415
76.844
77.160
77.486
114.197
125.840
127.421
128.370
128.543
130.325
130.373
130.910
136.084
158.757
169.672
207.083

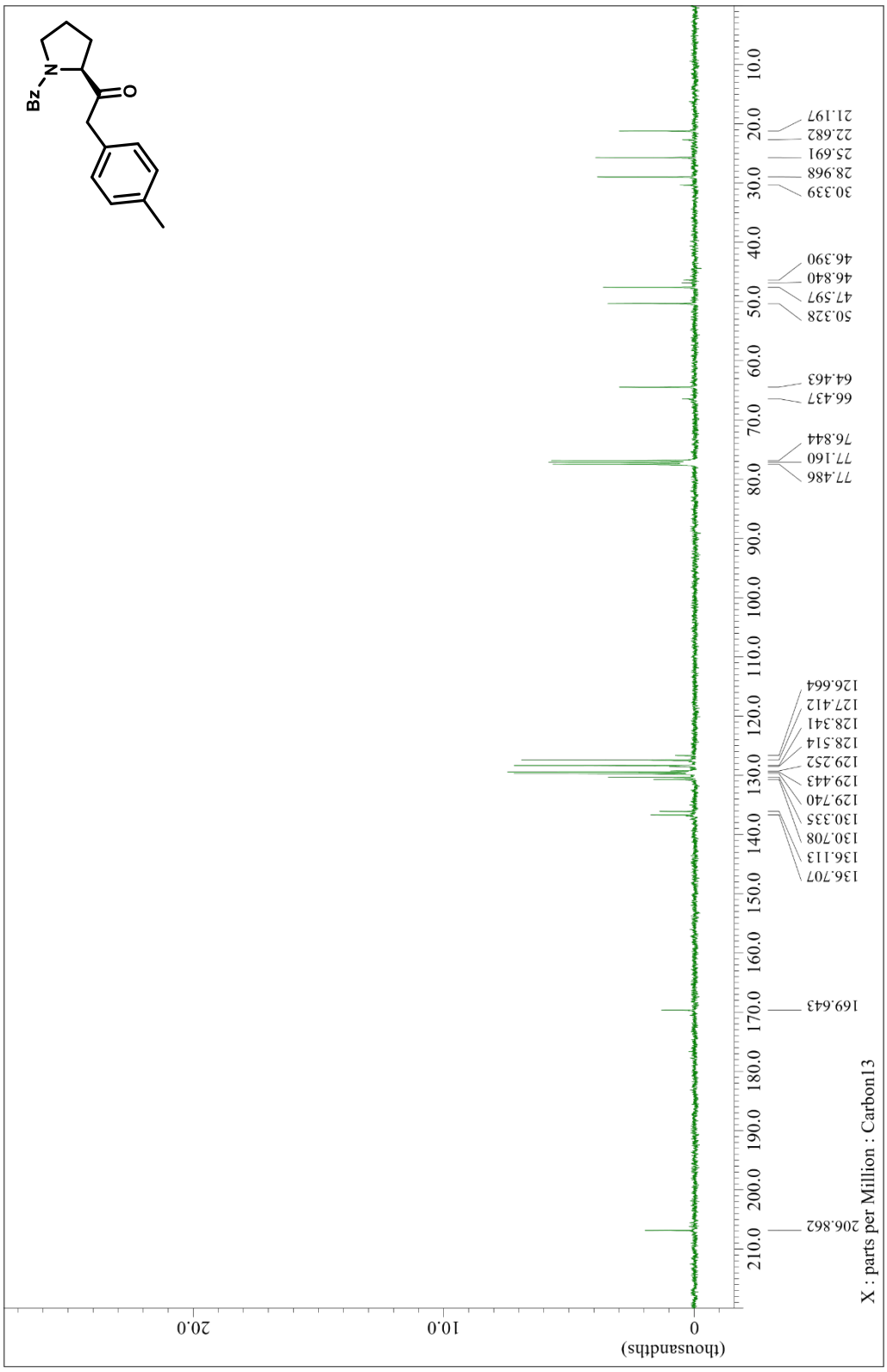
(*S*)-1-((*S*)-1-benzoylpyrrolidin-2-yl)-2-(4-methoxyphenyl)ethyl carbamate (1l)



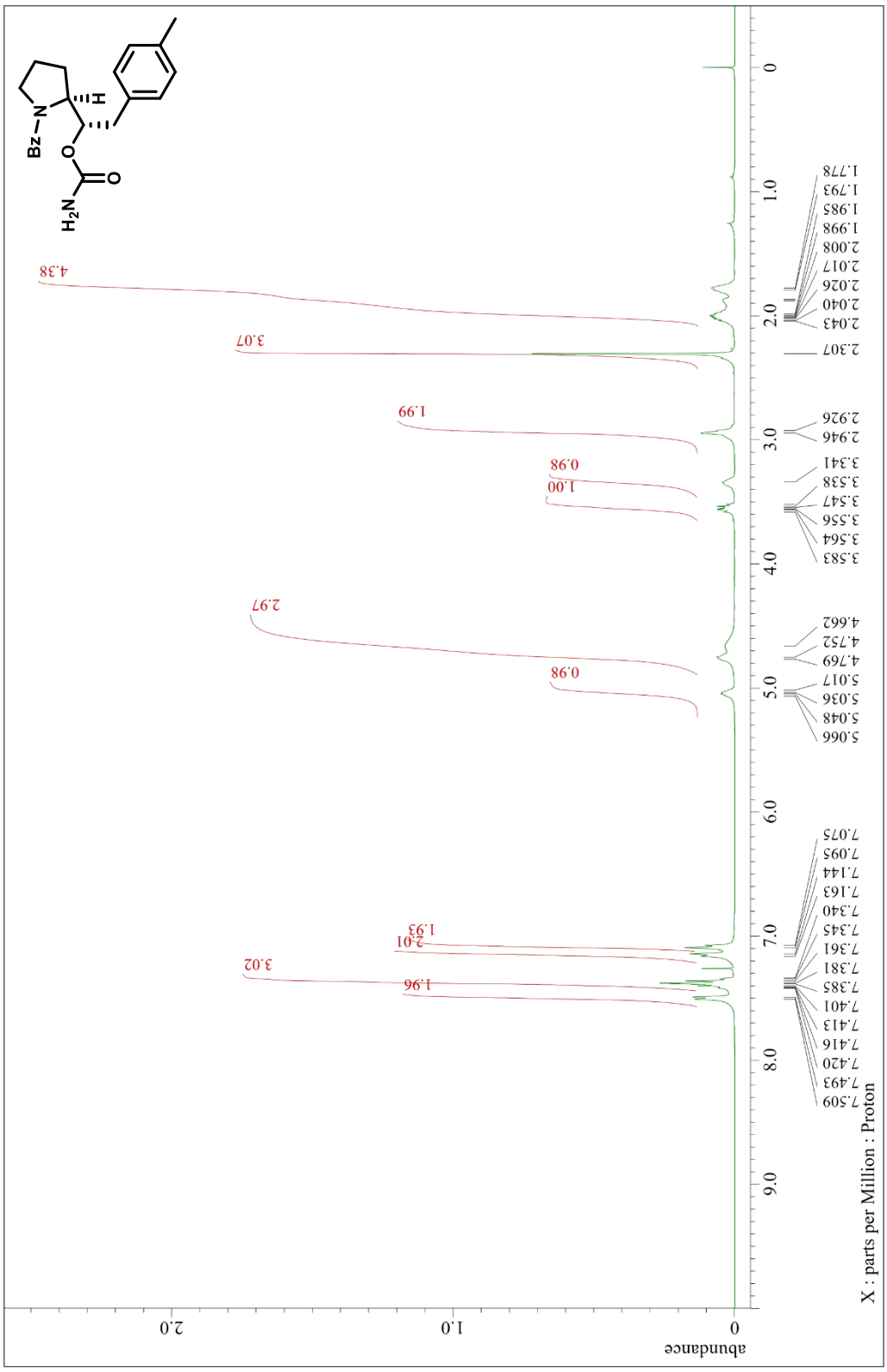

OMe
H
Bz
N
O
O
H2N
(thousandths)
X : parts per Million : Carbon13
171.147
158.278
156.879
137.033
130.258
130.143
129.578
128.274
127.613
113.881
77.476
77.160
76.844
76.643
58.512
55.263
49.916
37.286
27.387
24.905

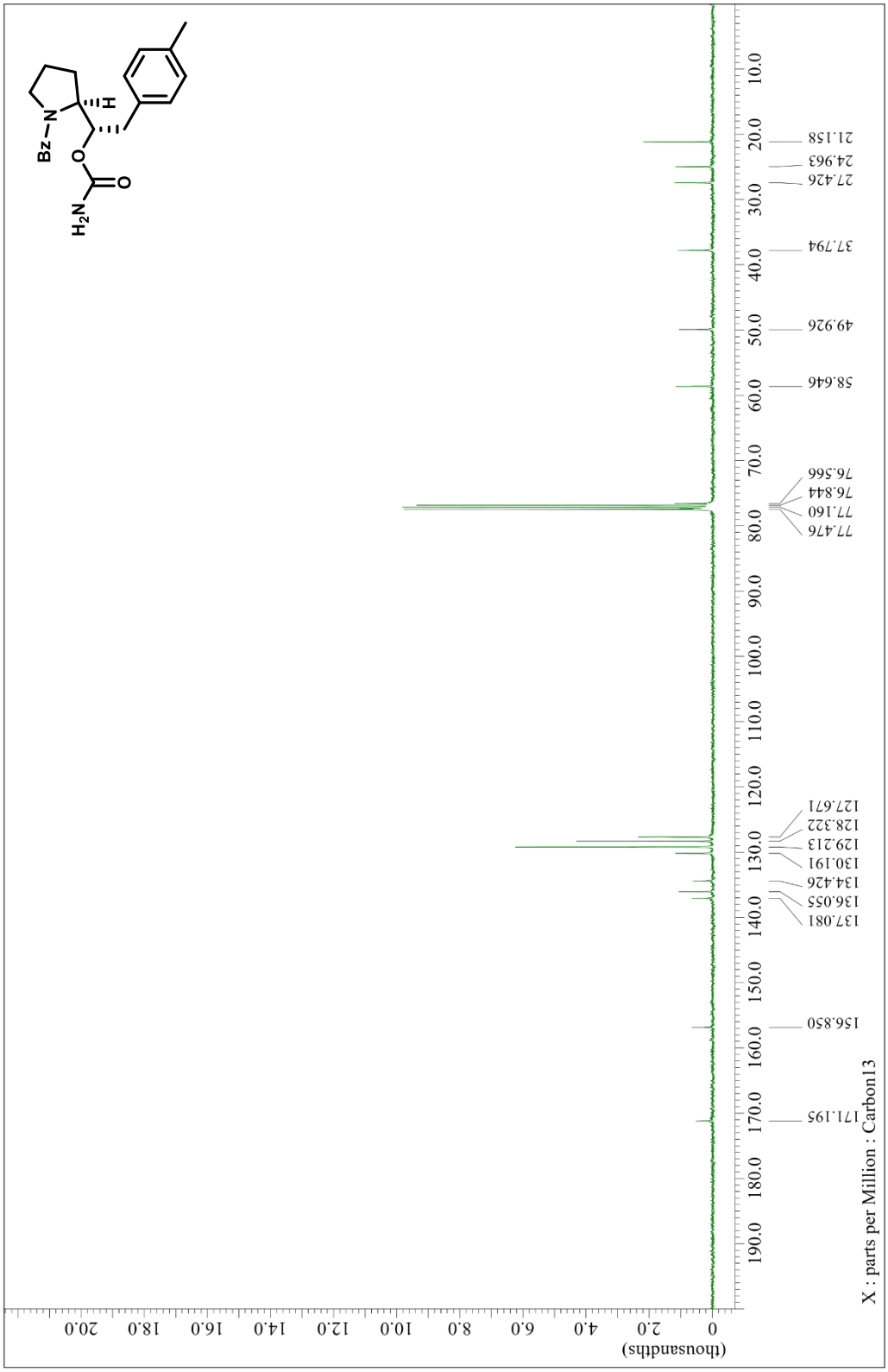
(*S*)-1-(1-benzoylpyrrolidin-2-yl)-2-(*p*-tolyl)ethan-1-one (s2m)



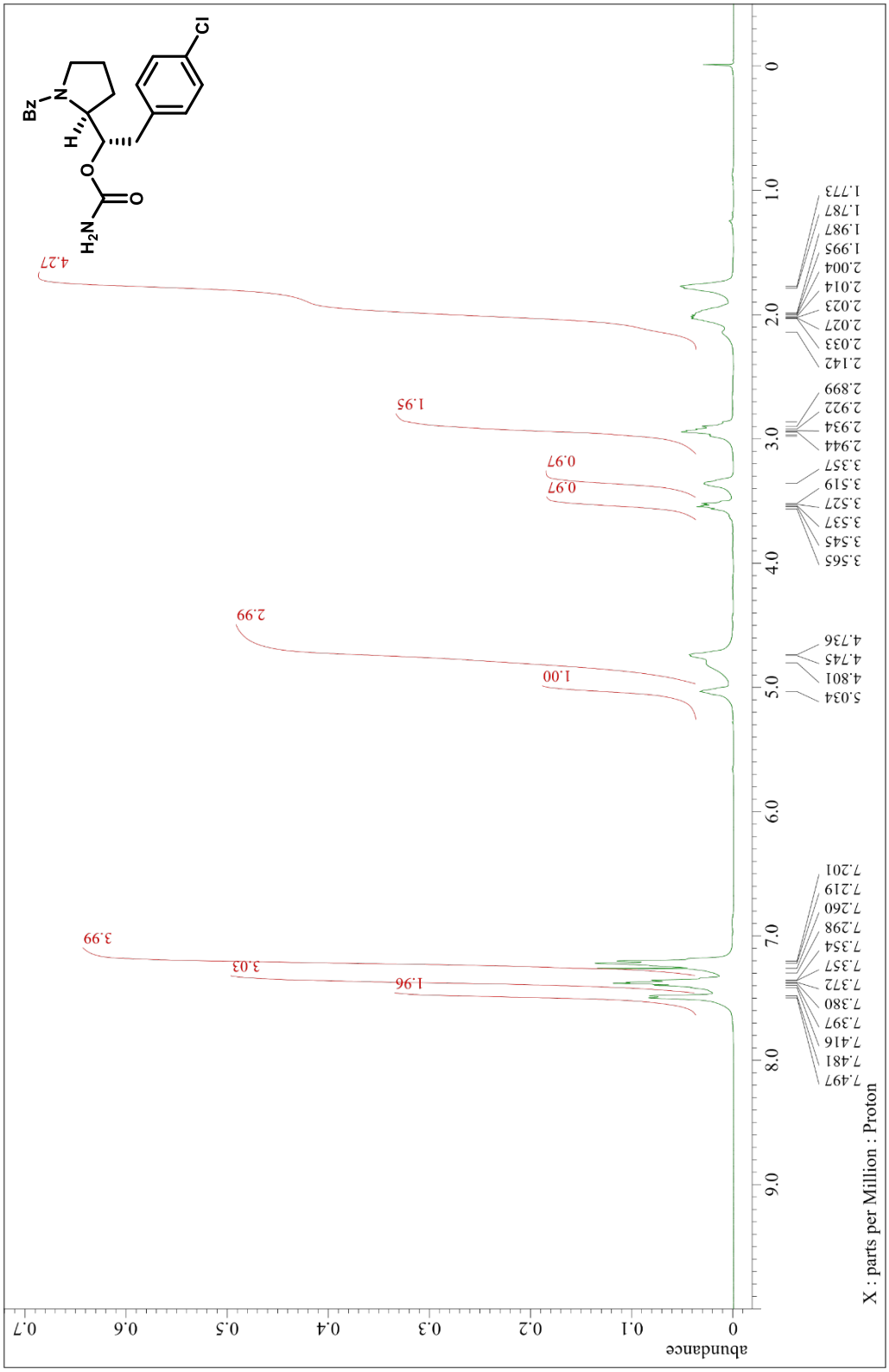

Bz
N
O
(thousandths)
0
10.0
20.0
X : parts per Million : Carbon13
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0
200.0
210.0
21.197
22.682
25.691
28.968
30.339
46.390
46.840
47.597
50.328
64.463
66.437
76.844
77.160
77.486
126.664
127.412
128.341
128.514
129.252
129.443
129.740
130.335
130.708
136.113
136.707
169.643
206.862

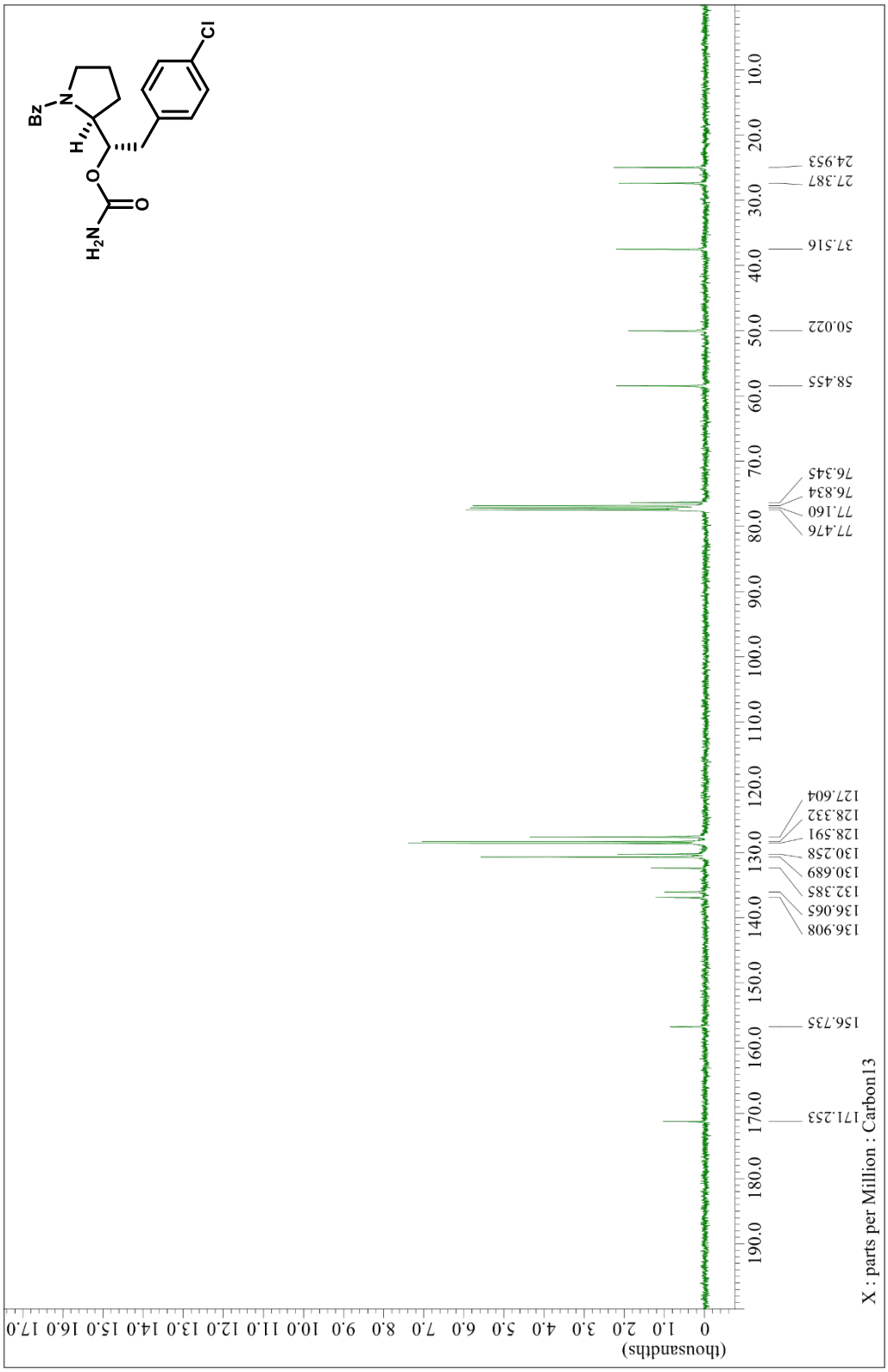
(*S*)-1-((*S*)-1-benzoylpyrrolidin-2-yl)-2-(*p*-tolyl)ethyl carbamate (1m)



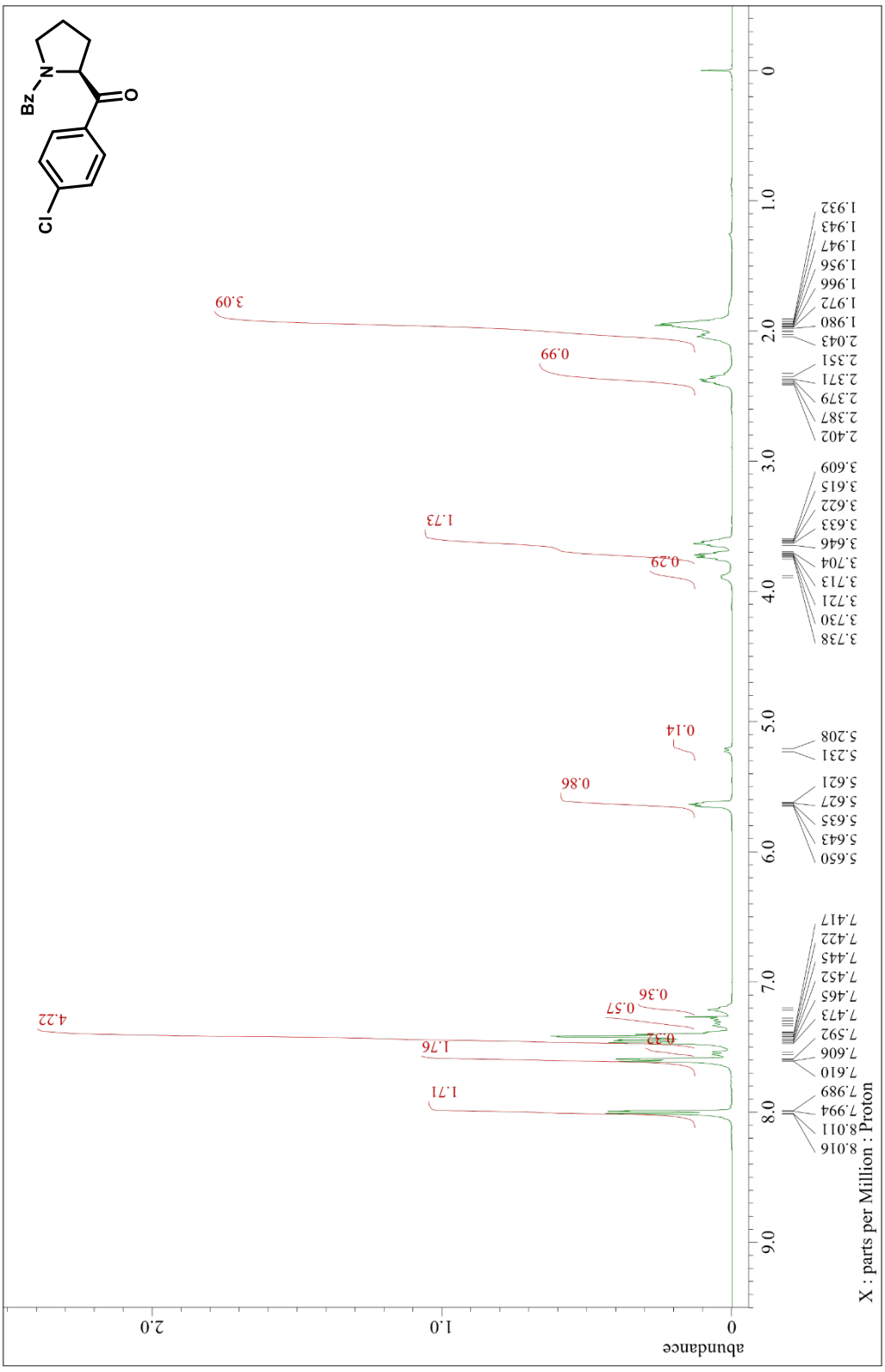

Bz
N
H
O
O
H_2N
21.158
24.963
27.426
37.794
49.926
58.646
76.566
76.844
77.160
77.476
127.671
128.322
129.213
130.191
134.426
136.055
137.081
156.850
171.195
X : parts per Million : Carbon13
(thousandths)

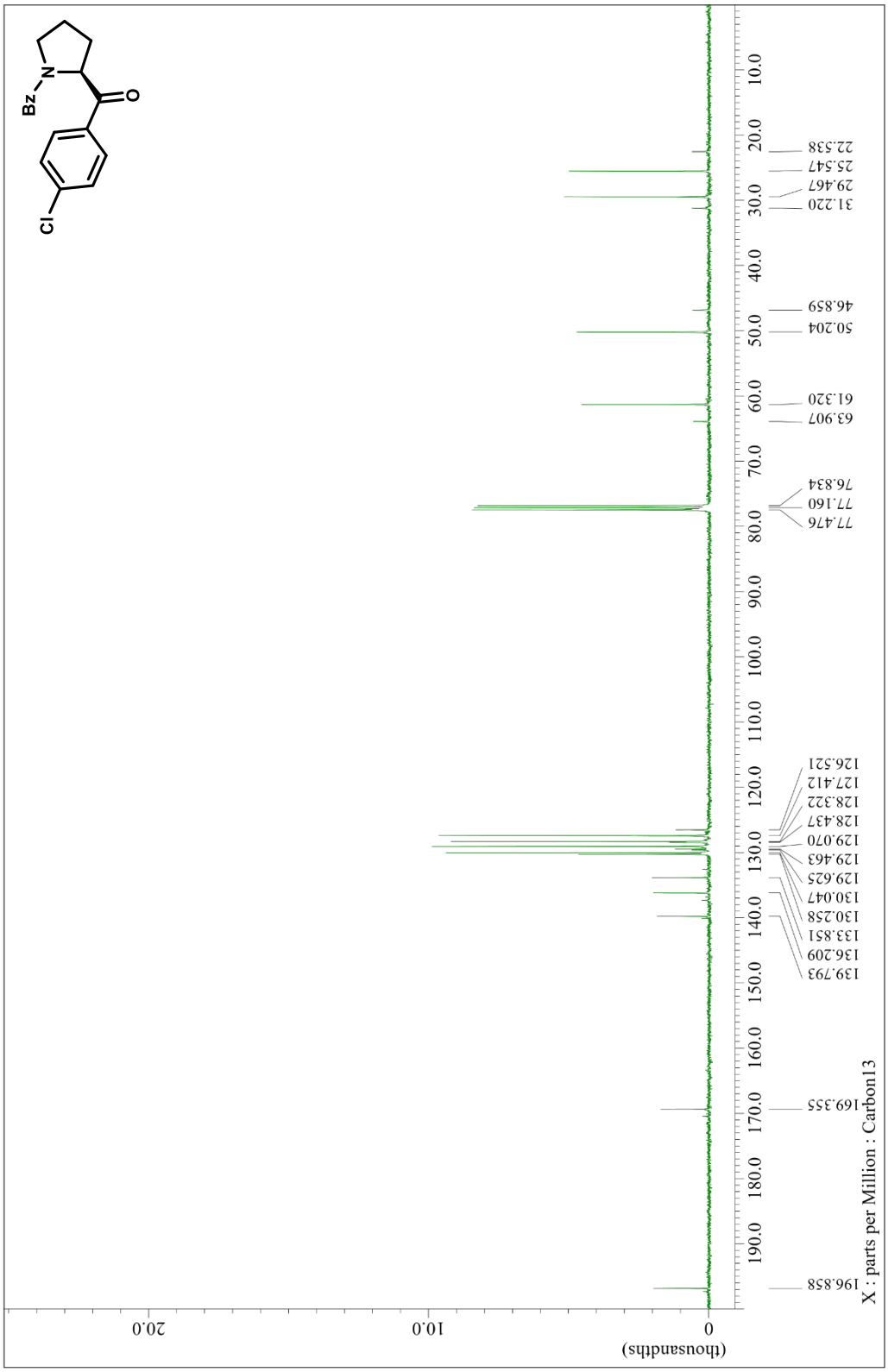
(*S*)-1-((*S*)-1-benzoylpyrrolidin-2-yl)-2-(4-chlorophenyl)ethyl carbamate (1n)



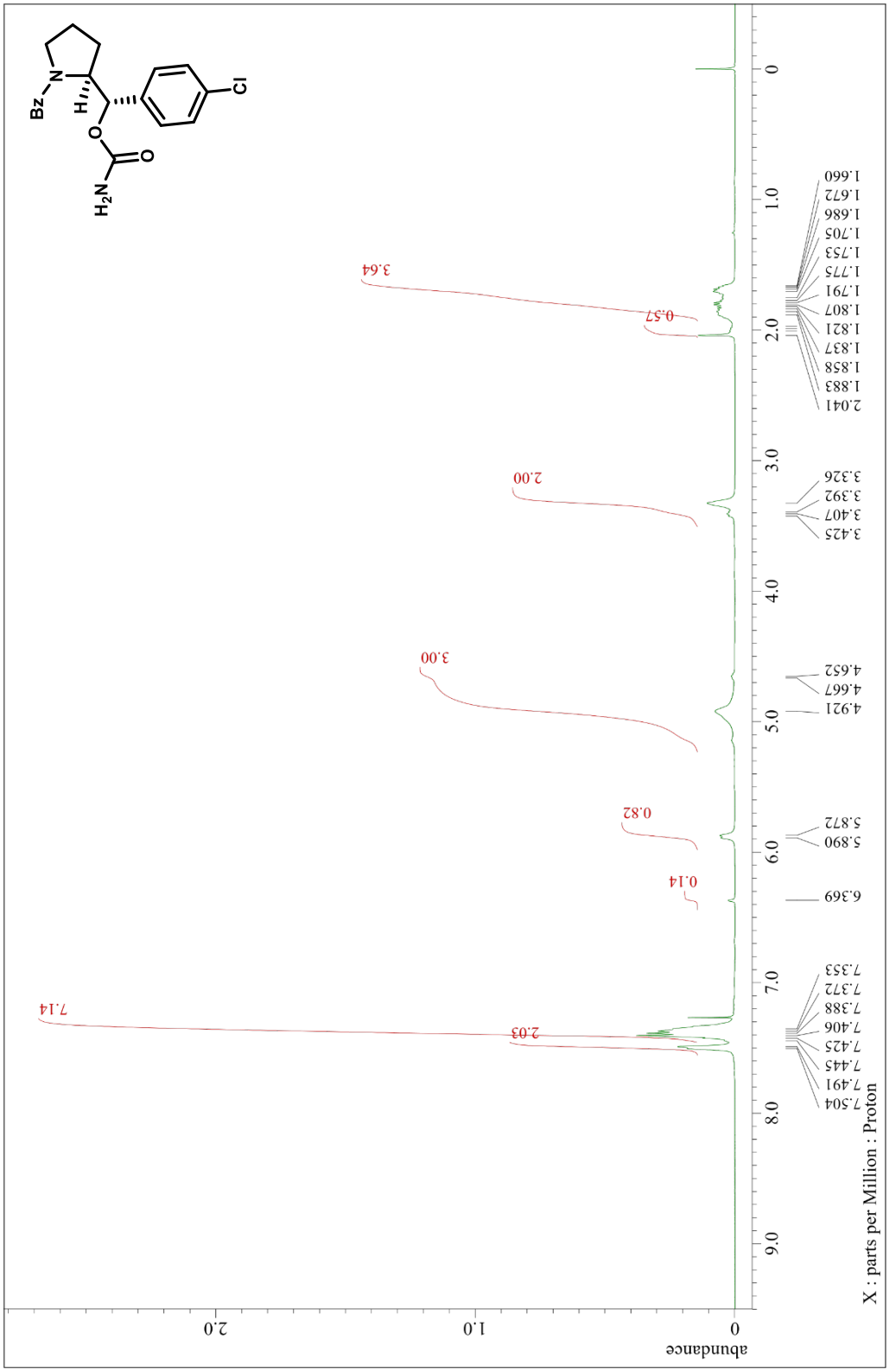

Cl
Bz
N
H
O
O
H_2N
(thousandths)
X : parts per Million : Carbon13
24.953
27.387
37.516
50.022
58.455
76.345
76.834
77.160
77.476
127.604
128.332
128.591
130.258
130.689
132.385
136.065
136.908
156.735
171.253

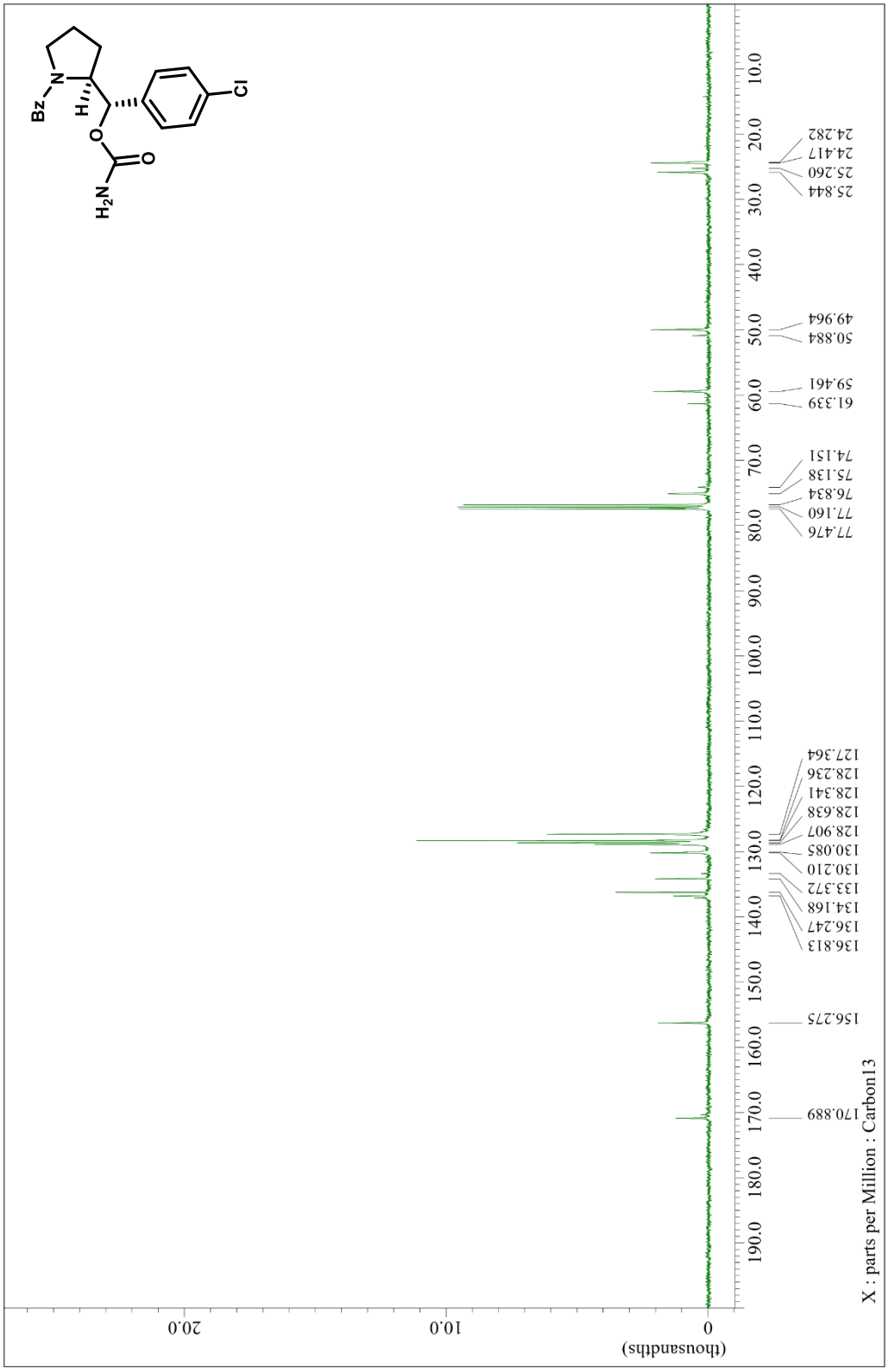
(*S*)-(1-benzoylpyrrolidin-2-yl)(4-chlorophenyl)methanone (s3o)



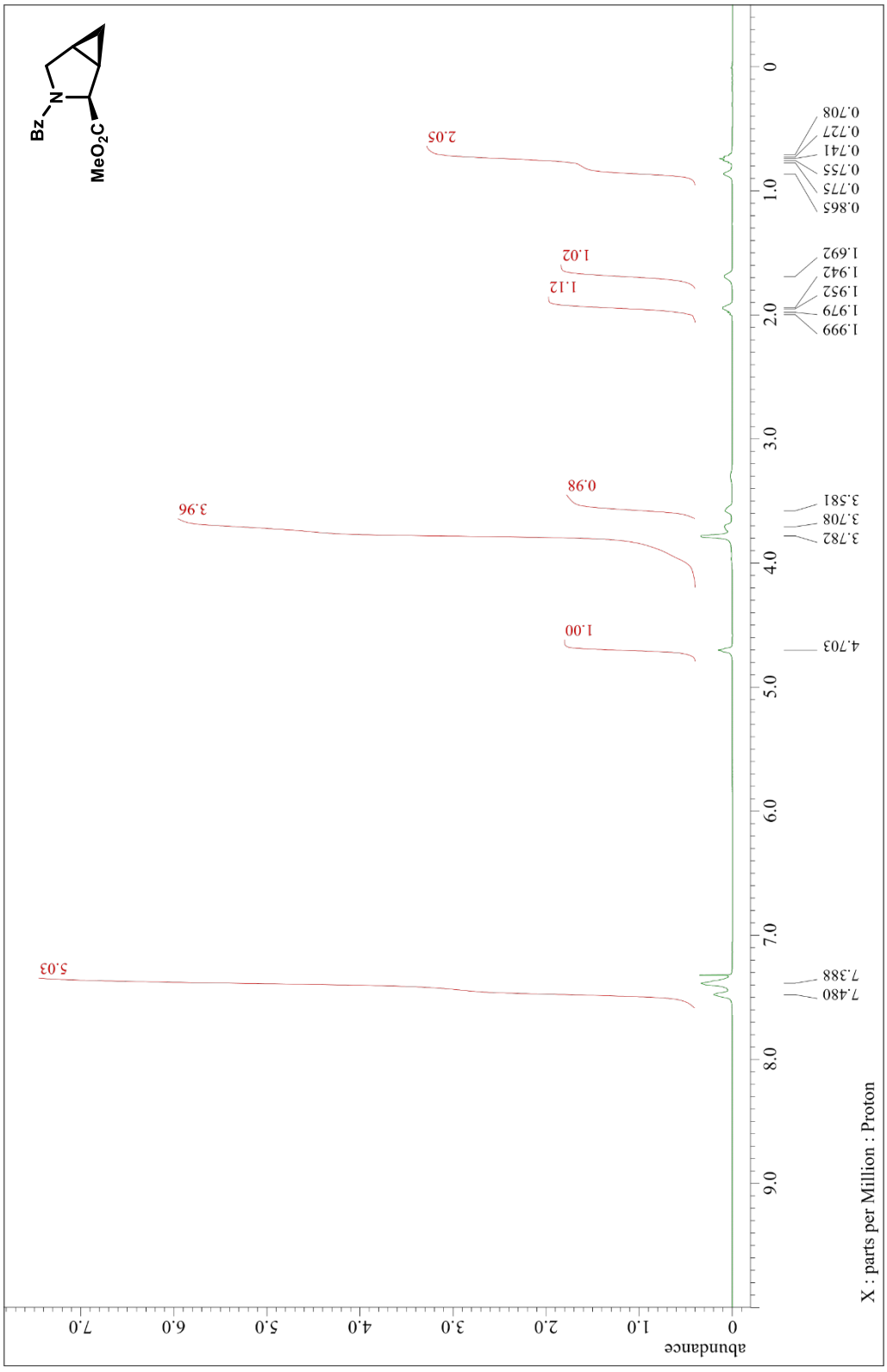

Bz
N
O
Cl
196.858
169.355
139.793
136.209
133.851
130.258
130.047
129.625
129.463
129.070
128.437
128.322
127.412
126.521
77.476
77.160
76.834
63.907
61.320
50.204
46.859
31.220
29.467
25.547
22.538
X : parts per Million : Carbon13
(thousandths)

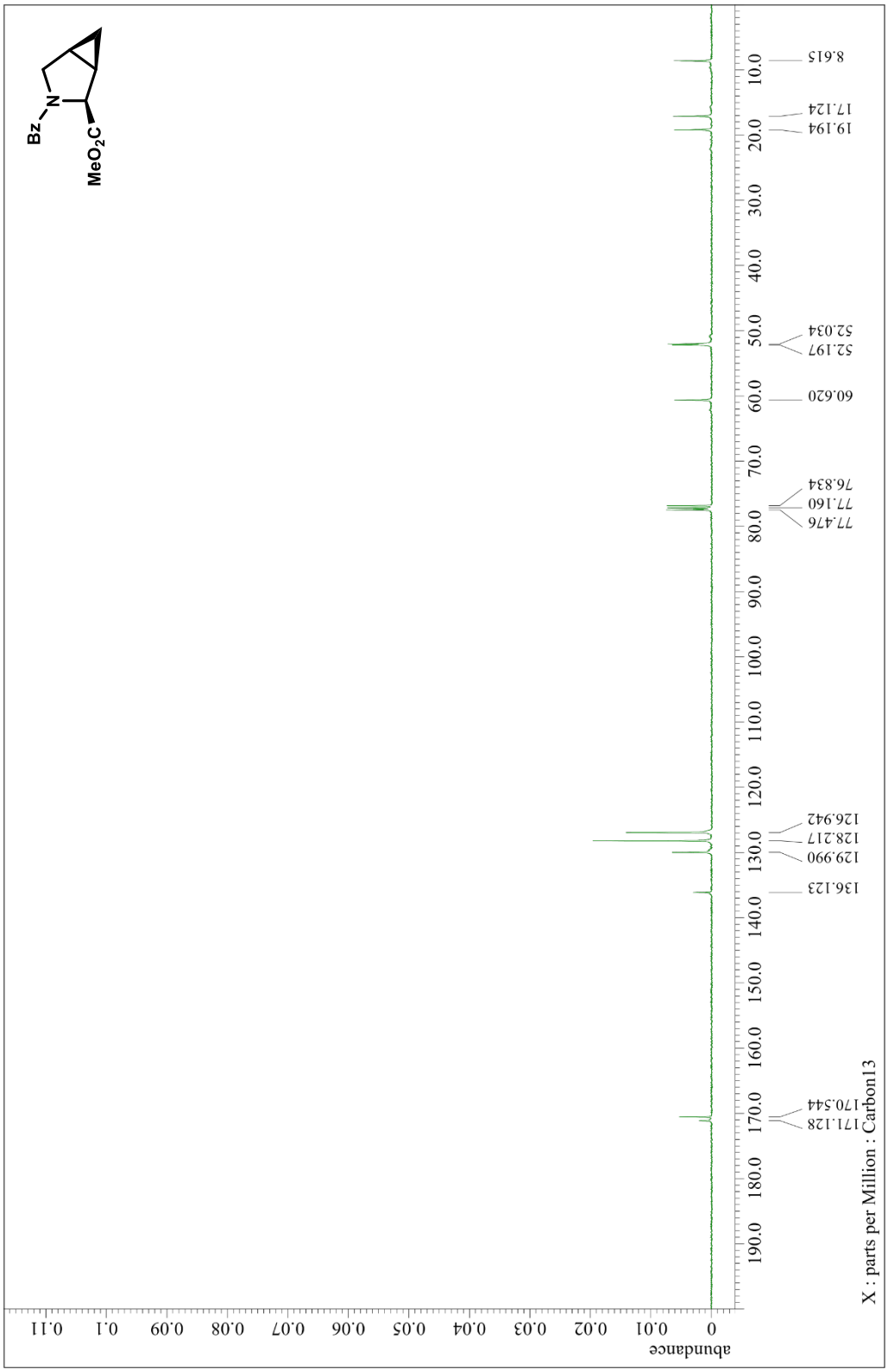
(*S*)-((*S*)-1-benzoylpyrrolidin-2-yl)(4-chlorophenyl)methyl carbamate (1o)



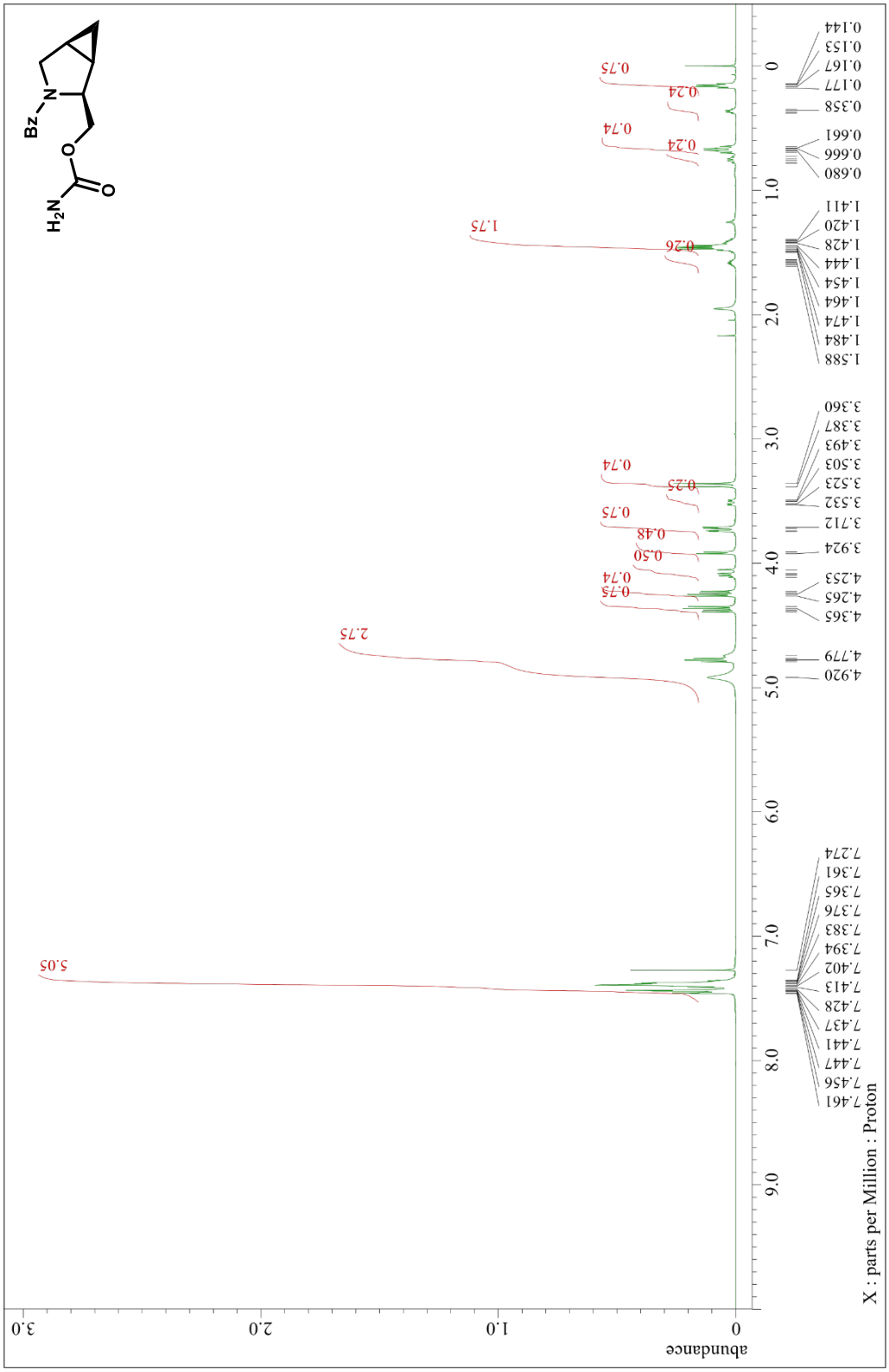

Bz
N
H
O
O
H_2N
Cl
(thousandths)
0
10.0
20.0
X : parts per Million : Carbon13
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0
25.844
25.260
24.417
24.282
50.884
49.964
61.339
59.461
77.476
77.160
76.834
75.138
74.151
136.813
136.247
134.168
133.372
130.210
130.085
128.907
128.638
128.341
128.236
127.364
156.275
170.889

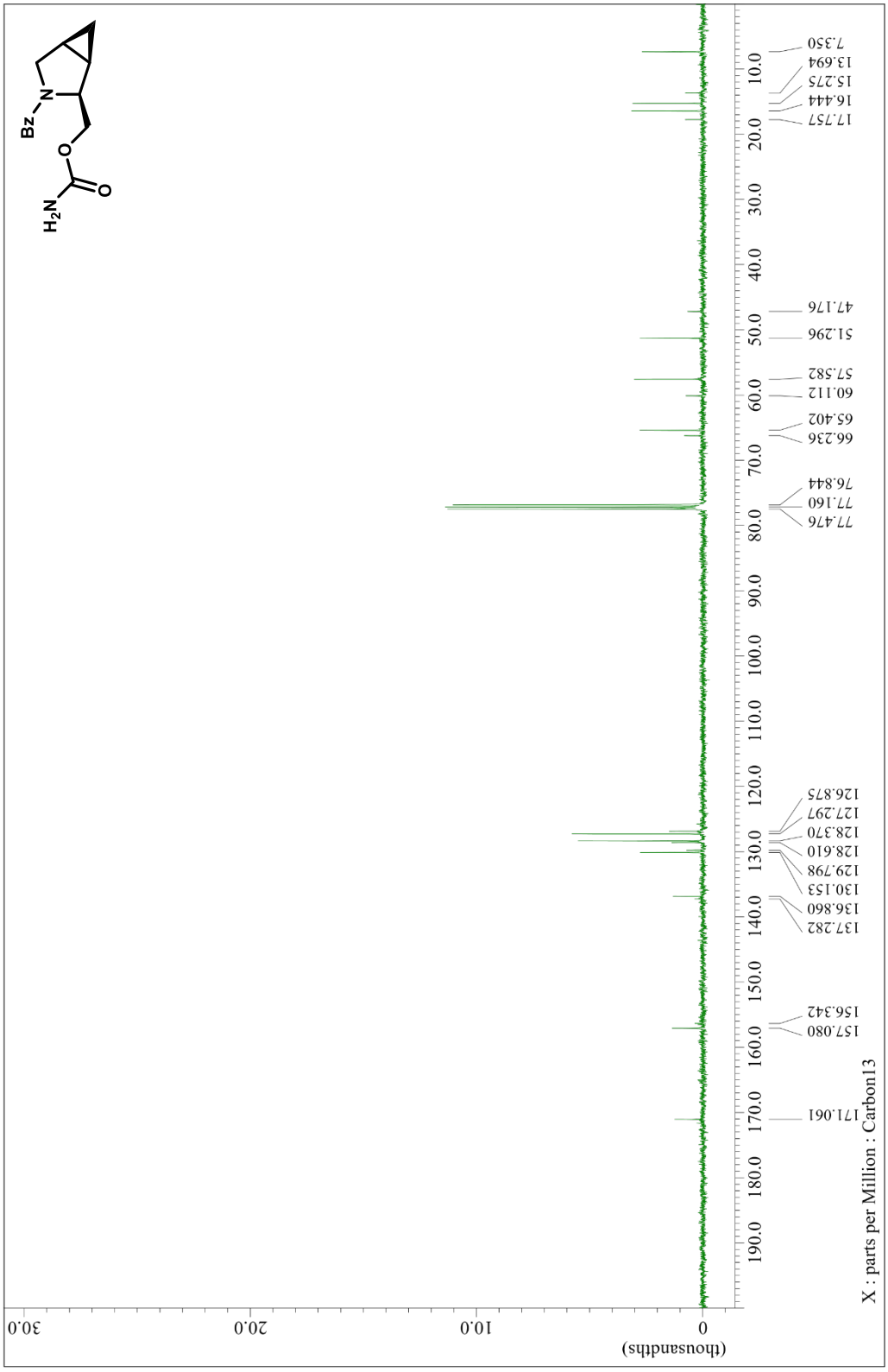
Methyl (1*R*, 2*S*, 5*S*)-3-benzoyl-3-azabicyclo[3.1.0]hexane-2-carboxylate (s1p)




Bz
N
MeO2C
8.615
17.124
19.194
52.034
52.197
60.620
76.834
77.160
77.476
126.942
128.217
129.990
136.123
170.544
171.128
X : parts per Million : Carbon13
abundance

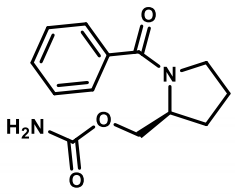
((1R,2S,5S)-3-benzoyl-3-azabicyclo[3.1.0]hexan-2-yl)methyl carbamate (1p)



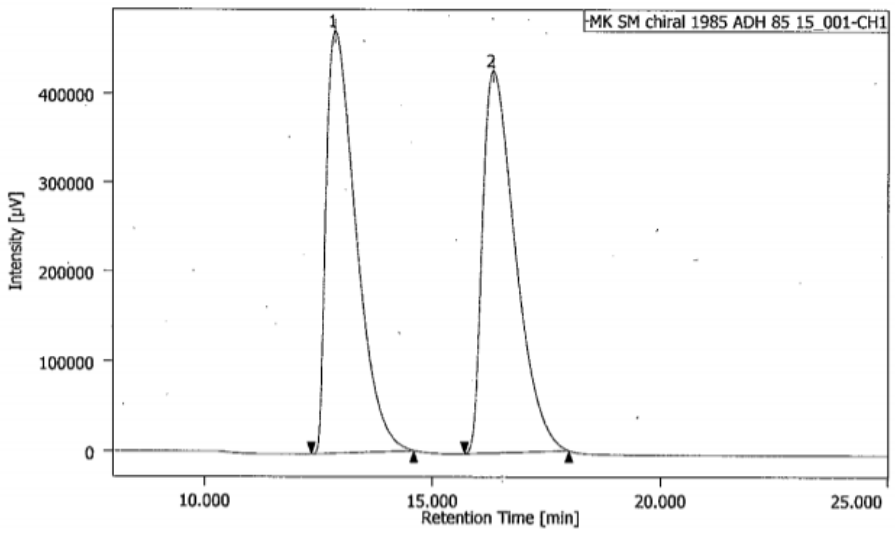

Bz
N
O
O
H2N
7.350
13.694
15.275
16.444
17.757
47.176
51.296
57.582
60.112
65.402
66.236
76.844
77.160
77.476
126.875
127.297
128.370
128.610
129.798
130.153
136.860
137.282
156.342
157.080
171.061
X : parts per Million : Carbon13
(thousandths)
0
10.0
20.0
30.0
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
190.0

9. Chiral and racemic HPLC traces

(*S*)-(1-Benzoylpyrrolidin-2-yl)methyl carbamate (1b)

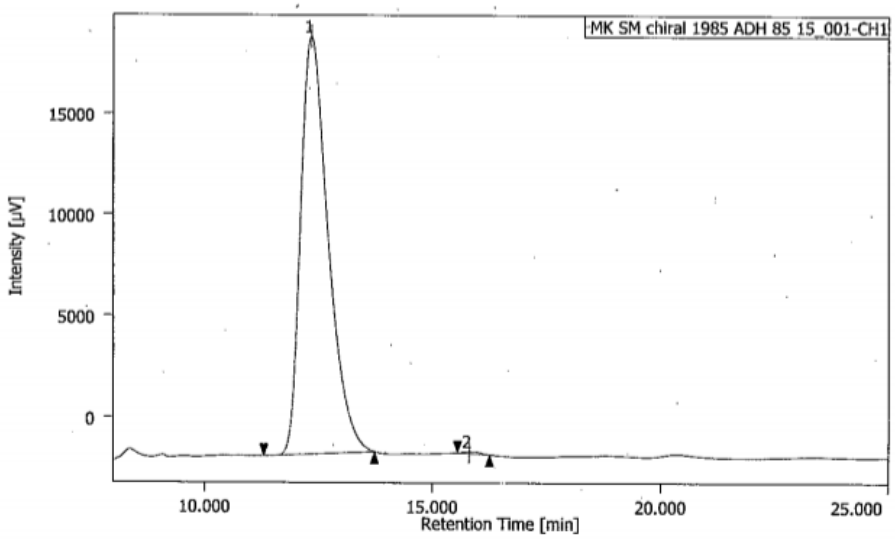


mk 473_1024 MK SM chiral 1985 ADH 85 15_001 2020/07/30 15:53:29



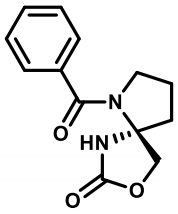
#	tR [min]	Area [µV·sec]	Area%	Height [µV]	Height%
1	12.875	21411888	50.096	471860	52.495
2	16.342	21329798	49.904	427001	47.505

MK 1985 SM chiral MK SM chiral 1985 ADH 85 15_001 2020/07/30 16:50:16

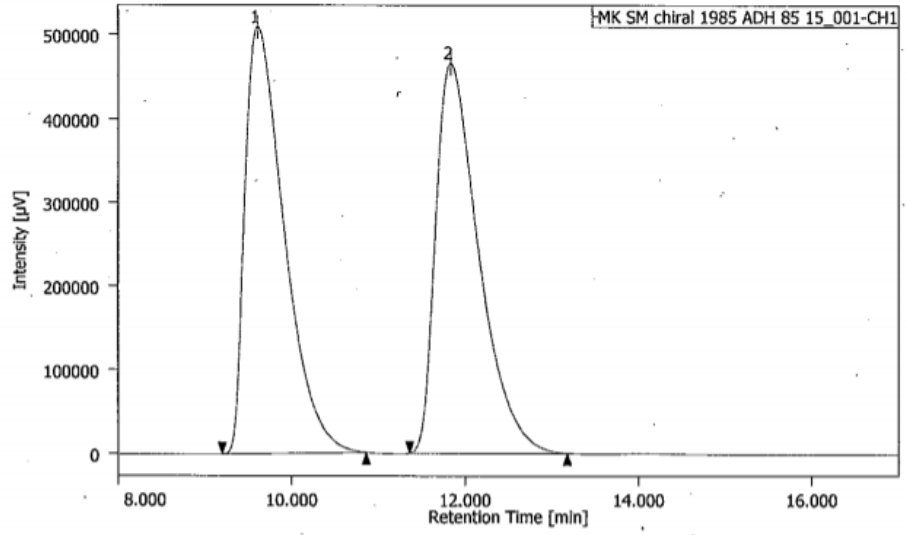


#	tR [min]	Area [µV·sec]	Area%	Height [µV]	Height%
1	12.342	865952	99.710	20854	99.520
2	15.808	2523	0.290	100	0.480

(*S*)-6-benzoyl-3-oxa-1,6-diazaspiro[4.4]nonan-2-one (3b)

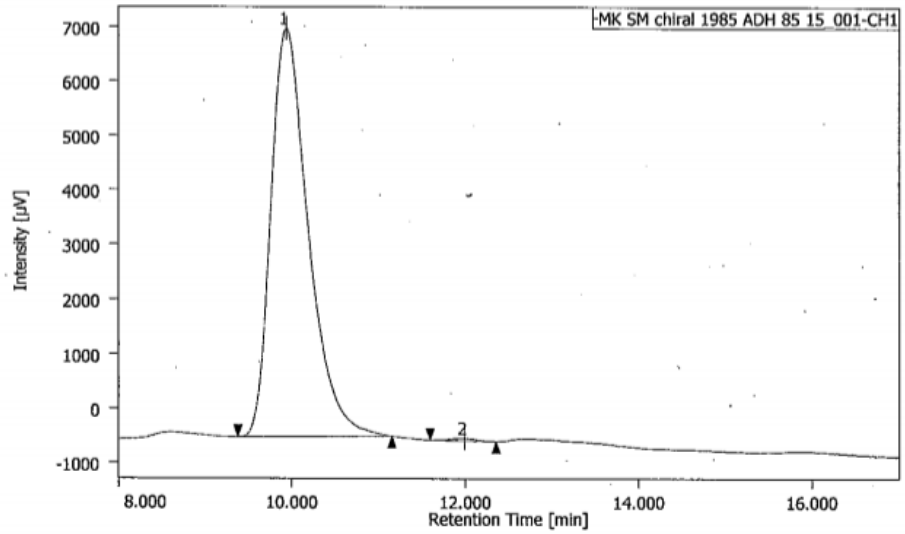


mk 474_1024 MK SM chiral 1985 ADH 85 15_001 2020/07/30 16:02:23



#	tR [min]	Area [µV·sec]	Area%	Height [µV]	Height%
1	9.608	16065723	49.984	508710	52.213
2	11.833	16076299	50.016	465588	47.787

MK 481 TM chiral MK SM chiral 1985 ADH 85 15_001 2020/07/30 16:45:32



#	tR [min]	Area [µV·sec]	Area%	Height [µV]	Height%
1	9.933	223944	99.553	7497	99.356
2	11.992	1006	0.447	49	0.644

10. References

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