Supporting Information:

SmI_2-Mediated Coupling of Nitrones and *tert*-Butanesulfinyl Imines with Allenoates: Synthesis of β-Methylenyl-γ-Lactams and Tetramic Acids

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1- General experimental methods

All reactions were performed under an atmosphere of dry argon in flame dried glassware equipped with a magnetic stir bar. Schlenk tube technique was used for SmI_2-mediated reactions. THF was distilled from sodium/benzophenone, DMF from CaH_2. THF, HFIP, *t*-BuOH and H_2O used in SmI_2-mediated reactions were degassed by freeze and thaw method. Reactions were monitored by thin layer chromatography (TLC) using commercial aluminum-backed silica gel plates (Merck Kiesegel 60 PF_{254}). TLC spots were viewed under UV light at 254 nm and by heating the plate after treatment with a staining agent ($KMnO_4$ or triphenyl tetrazolium chloride). Product purification by gravity column chromatography was performed using Merck Silica Gel 60 (70-230 mesh). Infrared spectra were obtained on a Nicolet Avatar 330 FT-IR spectrometer (spectrometer A) using KBr pellets or on a Nicolet 'Magna 550' spectrometer (spectrometer B) using an ATR (Attenuated Total Reflexion) module. The data are reported in reciprocal centimeters (cm^{-1}). ^1H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$, chemical shifts for ^1H spectra are values from tetramethylsilane in $CDCl_3$ (δ 0.00), chemical shifts for ^{13}C spectra are values from $CDCl_3$ (δ 77.16). ^1H NMR spectra are reported as follows: chemical shift (ppm), multiplicity (br: boad; s: singlet; d: doublet; t: triplet; q: quadruplet; m: multiplet, app t: apparent triplet), integration and coupling constants (Hz). Low resolution mass spectra (LRMS) were recorded on a Bruker Esquire 3000+ spectrometer. High resolution mass spectra (HRMS) were recorded on a Thermoquest Orbitrap spectrometer. Optical rotations were determined with a Perkin-Elmer 341 polarimeter. Melting points were measured using a Yanaco MP-500 micro melting point apparatus and were not corrected.

2- Preparation of 0.1 M solution of SmI_2 in THF

Distilled and degassed THF (50 mL) was added to samarium metal (4 g) under inert atmosphere. The resulting suspension was cooled down to 0 °C then sublimated iodine (5 g) was added. The temperature was allowed to reach room temperature and distilled and degassed THF (150 mL) was added. The suspension was stirred at room temperature until the appearance of typical blue color.

3- Typical experimental procedures

3.1 Screening of conditions for cross coupling of nitrone 1a and allenoate 3a

According to the conditions previously described for the reductive coupling of nitrones with acrylic esters, nitrone **1a** and allenoate **3a** (1.4 equiv) were first treated with 3 equiv SmI_2 in the presence of degased water, at −78 °C.[1] Under these conditions, the expected *N*-hydroxyamine **4aa** was formed (30%), nitrone **1a** was recovered (44%) along with a major side-product (**6a**), resulting from the reduction of allenoate **3a** by SmI_2 (see Table, entry 1). Performing the reaction at −40 °C did not induce any significant change in the distribution of the products (see Table, entry 2).

In light of the work of Ellman,[2] who observed that both lithium bromide and water should be used as additives for achieving high yields and good diastereoselectivities in the SmI_2-mediated reductive coupling of methyl methacrylate with a *N*-*tert*-butanesulfinyl imine, we next introduced 12 equivalents of this salt in the reaction mixture (see Table, entry 3). The yield of **4aa** being increased (to 50%) in the presence of LiBr, further optimizations were performed in its presence.

The effect of different proton sources on the cross coupling of nitrone **1a** with allenoate **3a** was next investigated. When water was replaced by hexafluoro*iso*propanol,[3] a non-coordinating proton source, the yield in **4aa** was significantly improved (see Table, entries 4, 5). *Tert*-butanol, a less expensive, and also non-coordinating additive, proved to have a similar effect (see table, entry 6).

The competitive conjugate reduction of allenoate **3a** by SmI_2, being the major side reaction hampering the isolation of the desired products in high yields, it was thus decided to introduce the starting allenoate **3a** and SmI_2, in several sequential portions (see Table, entries 5-7). When 1.4 equiv of allenoate and the nitrone were reacted first in the presence of 3.5 equiv of *tert*-butanol, 12 equiv of LiBr and 3 equiv of SmI_2, followed by addition of 0.6 equiv of allenoate and 1 equiv of SmI_2, then another 0.5 equiv of allenoate and 0.5 equiv of SmI_2, the desired product **4aa** was obtained in 80% yield (see Table, entry 7). Progressive introduction of the allenoate by using a syringe-pump did not allow to isolate **4aa** in a better yield (see Table, entry 8).

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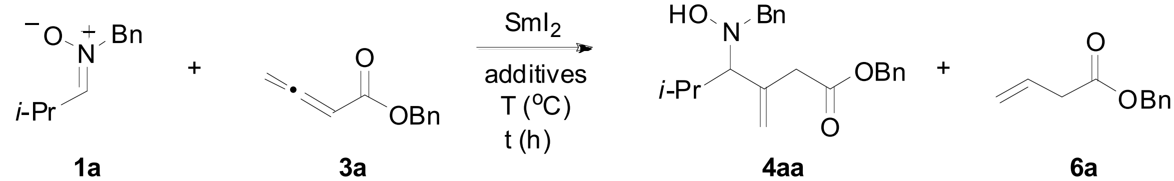
[1] When an equimolar mixture of nitrone **1a** and allenoate **3a** were treated by 2 equiv SmI_2 at −78 °C, with no additive, only trace amount of hydroxylamine **4aa** was detected by NMR, the major isolated products being [3+2] cycloadducts.

[2] Peltier, H. M.; McMahon, J. P.; Patterson, A. W.; Ellman, J. A. *J. Am. Chem. Soc.* **2006**, *128*, 16018-16019.

[3] (a) Nicolaou, K. C.; Li, A.; Edmonds, D. J.; Tria, G. S.; Ellery, S. P. *J. Am. Chem. Soc.* **2009**, *131*, 16905–16918; (b) Nicolaou, K. C.; Li, A.; Edmonds, D. J. *Angew. Chem. Int. Ed.* **2006**, *45*, 7086-7090.

Table. Screening of conditions for the SmI_2-mediated cross-coupling reaction of **1a** and **3a**



entry	**3a** (equiv)	**SmI₂** (equiv)	additives (equiv)	T (°C)	t (h)	**4aa (%)**	**6a**[e] (%)
1[a]	1.4	3	H_2O (8)	−78 to rt	2	**30**	86
2[b]	1.4	3.5	H_2O (8)	−40	16.5	**30**	82
3[b]	1.4	3.5	H_2O (8) LiBr(12)	−40	1	**49**	50
4[b]	1.4	3	HFIP (3) LiBr(12)	−40	0.2	**60**	51
5[c]	2	4	HFIP (3) LiBr(12)	−40	0.5	**65**	123
6[c]	2	3.5	*t*-BuOH (3) LiBr(12)	−40	2.5	**75**	94
7[c]	2.5	4.5	*t*-BuOH (3.5) LiBr(12)	−40	3	**80**	164
8	1+1[d]	4	*t*-BuOH (3.5) LiBr(12)	−40	1.3	**60**	93

[a] SmI_2 was added to a solution of **1a**, **3a** and water in THF at −78 °C, then the temperature was allowed to reach room temperature.
[b] SmI_2 was added to the solution of **1a** (and LiBr) at −40 °C, then the solution of **3a** and water (or HFIP) in THF was added, in one portion.
[c] See general procedure below.
[d] The second portion of allenoate **3a** was added progressively using a syringe pump.
[e] The yields of **6a** were calculated based on the starting nitrone **1a**.

3.2 Typical procedure for the optimized cross coupling of nitrones and allenoates (cf. Table, entry 7): conditions A

(*Z*)-*N*-(2-methylpropylidene)-1-phenylmethanamine-*N*-oxide **1a**[4] (30.7 mg, 0.17 mmol) and LiBr (180 mg, 2.1 mmol) was dissolved in THF (2 mL) under Ar, and the distilled *t*-BuOH (57 µL, 0.60 mmol) was added, then the solution was cooled to −40 °C. Then a solution of allenoate **3a**[5] (42.1 mg, 0.24 mmol) in THF (2.2 mL) was added slowly at −40 °C. Thereafter SmI_2 (3 equiv 5.2 mL) was added slowly (in 1.5 min). 30 min later, TLC showed no more starting allene. Then **3a** (18.1 mg, 0.10 mmol) in THF (1.0 mL) was added slowly at −40 °C. The solution turned yellow, then another 1 equiv SmI_2 (1.8 mL) was added. 30 min later, TLC showed the allene was consumed, and the nitrone was more dilute. Then 0.5 equiv allene in THF (0.8 mL) was added, followed by the addition of 0.5 equiv SmI_2 (0.9 mL). 1.2 h later, the saturated $Na_2S_2O_3$ (10 mL) and saturated $NaHCO_3$ (5 mL) were added. Then the mixture was extracted with EtOAc (3 × 15 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography

[4] Dondoni, A.; Franco, S.; Junquera, F.; Merchan, F.; Merino, P.; Tejero, T. *Synth. Commun.* **1994**, *24*, 2537-2550.
[5] Rout, L.; Harned, A. M. *Chem. Eur. J.* **2009**, *15*, 12926-12928.

on silica gel (EtOAC/Pentane 3/97 → EtOAc/Pentane 1/6 → DCM/MeOH 95/5) gave a colorless oil **4aa** (49 mg, 80%), the recovered **1a** (4.8 mg, 16%) and **6a**[6] (50 mg).

3.3 Typical procedure for the optimized cross coupling of *t*-BS-imines and allenoates: conditions B

(*E*)-2-Methyl-*N*-(2-methylpropylidene)propane-2-sulfinamide **2a**[7] (80 mg, 0.46 mmol) and LiBr (476 mg, 5.48 mmol) were dissolved in THF (2 mL) under Ar, then the solution was cooled to −40 ºC. Then allenoate **3a**[5] (198.8 mg, 1.14 mmol) in THF (2.2 mL) was added at −40 ºC, followed by the addition of *t*-BuOH (152.0 μL, 1.60 mmol). Thereafter SmI_2 (3 equiv 13.7 mL) was added dropwise. 30 min later, allenoate **3a** (47.7 mg, 0.27 mmol) in THF (1.0 mL) was added slowly at −40 ºC. Then another 1 equiv SmI_2 (4.6 mL) was added. 30 min later, 0.5 equiv allenoate **3a** in THF (0.8 mL) was added, followed by the addition of 0.5 equiv SmI_2 (2.3 mL). 3 h later, the saturated $Na_2S_2O_3$ (15 mL) and saturated $NaHCO_3$ (5 mL) were added. Then the mixture was extracted with EtOAc (3 × 15 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. Purification by column chromatography on silica gel (EtOAC/Hexane 1/30 → 1/6 → 2/3) gave a yellow oil **11a** (136.5 mg, 85%, dr = 5:1). The diasterereomers could not be separated at this stage.

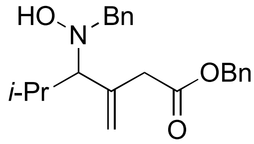
3.4 Typical procedure for cyclisation of *N*-hydroxyamino esters 4 into lactams 5

To a mixture of **4aa** (35 mg, 0.1 mmol) and zinc dust (77 mg, 1.2 mmol) was added glacial acetic acid (2 mL). The solution was heated to 80 ºC and treated with ultrasonic. 1 h later, TLC showed **4aa** was consumed. Then, 15 mL of saturated $NaHCO_3$ was added to the solution carefully, and the $NaHCO_3$ powder was added till the bubble ceased. The mixture was extracted with EtOAc (3 × 15 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography on silica gel (EtOAC/Pentane 1/4 → EtOAc/Pentane 1/1) gave a colorless oil **5a** (22.6 mg, 99%).

[6] Belanger, D.; Tong, X.; Soumare, S.; Dory, Y. L.; Zhao, Y. *Chem. Eur. J.* **2009**, *15*, 4428 – 4436.
[7] Nielsen, L.; Lindsay, K. B.; Faber, J.; Nielsen, N. C.; Skrydstrup, T.. *J. Org. Chem.* **2007**, *72*, 10035-10044.

4. Preparation and characterization of new compounds

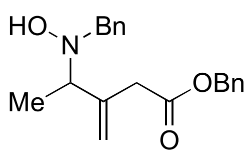
Benzyl 4-(benzyl(hydroxy)amino)-5-methyl-3-methylenehexanoate (4aa)



4aa

Following the typical procedure A (see 3.2), from nitrone **1a**[4] and allenoate **3a**[5] compound **4aa** was obtained in 80% yield, as a colorless oil, accompanied by the recovered **1a** (16%). IR (neat, spectrometer B) ν_{max}: 3478, 3063, 3031, 2958, 2933, 2870, 1733, 1641, 1603, 1496, 1454, 1423, 1375, 1328, 1268, 1214, 1150, 1002 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.45-7.20 (m, 10H), 5.26 (d, *J* = 1.0 Hz, 1H), 5.13 (s, 2H), 5.08 (s, 1H), 4.55 (brs, 1H), 3.92 (d, *J* = 13.5 Hz, 1H), 3.70 (d, *J* = 13.5 Hz, 1H), 3.23 (dd, *J* = 15.0, 1.0 Hz, 1H), 3.15 (d, *J* = 15.0 Hz, 1H), 2.87 (d, *J* = 8.5 Hz, 1H), 2.30-2.05 (m, 1H), 1.05 (d, *J* = 6.5 Hz, 3H), 0.85 (d, *J* = 7.0 Hz, 3H) ppm; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 171.7, 139.1, 138.8, 135.9, 129.0, 128.5, 128.3, 128.2, 128.1, 126.9, 119.4, 78.0, 66.4, 61.1, 39.7, 27.9, 20.6, 19.3 ppm; MS (ESI) *m/z*: 354 [$(M+H)^+$], 376 [$(M+Na)^+$]; HRMS (ESI, *m/z*) calcd for $[C_{22}H_{28}NO_3]^+$: 354.20637; Found: 354.20673.

Benzyl 4-(benzyl(hydroxy)amino)-3-methylenepentanoate (4ba)



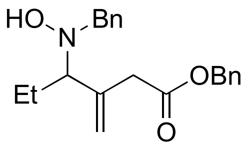
4ba

Following the typical procedure A (see 3.2), from nitrone **1b**[8] and allenoate **3a**[5] compound **4ba** was obtained in 68% yield as a colorless oil, accompanied by the recovered **1b** (31%). IR (neat, spectrometer B) ν_{max}: 3449, 3088, 3063, 3031, 2974, 2939, 2876, 1733, 1647, 1600, 1496, 1454, 1375, 1328, 1261, 1211, 1150 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.39-7.18 (m, 10H), 5.20 (s, 1H), 5.12 (s, 1H), 5.06-5.10 (m, 3H), 3.88 (d, *J* = 13.5 Hz, 1H), 3.73 (d, *J* = 13.5 Hz, 1H), 3.33 (q, *J* = 6.5 Hz, 1H), 3.25 (d, *J* = 15.5 Hz, 1H), 3.11 (d, *J* = 15.5 Hz, 1H), 1.26 (d, *J* = 6.5 Hz, 3H) ppm; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 172.7, 143.4, 138.5, 135.7, 129.0, 128.5, 128.3, 128.2, 128.1, 127.0, 116.9, 66.7,

[8] Aschwanden, P.; Kværnø, L.; Geisser, R. W.; Kleinbeck, F.; Carreira, E. M. *Org. Lett.* **2005**, *7*, 5741-5742.

65.8, 60.0, 39.7, 12.4 ppm; MS (ESI) *m/z*: 326 [$(M+H)^+$], 348 [$(M+Na)^+$]; HRMS (ESI, *m/z*) calcd for [$C_{20}H_{23}NO_3Na$]$^+$: 348.15701; Found: 348.15701.

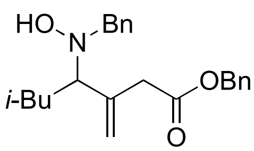
Benzyl 4-(benzyl(hydroxy)amino)-3-methylenehexanoate (4ca)



4ca

Following the typical procedure A (see 3.2), from nitrone **1c**[9] and allenoate **3a**[5] compound **4ca** was obtained in 74% yield as a colorless oil, accompanied by the recovered **1c** (23%). IR (neat, spectrometer B) ν_{max}: 3460 (br), 3087, 3065, 3033, 2966, 2935, 2877, 2838, 1733, 1647, 1605, 1497, 1454, 1378, 1331, 1268, 1213, 1148, 1029, 1001 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.45-7.18 (m, 10H), 5.18 (brs, 1H), 5.17 (s, 1H), 5.16 (s, 1H), 5.09 (s, 2H), 3.80 (s, 1H), 3.79 (s, 1H), 3.22 (dd, *J* = 15.5, 1.0 Hz, 1H), 3.17-3.04 (m, 2H), 1.99-1.78 (m, 1H), 1.41-1.60 (m, 1H), 0.83 (t, *J* = 7.5 Hz, 3H) ppm; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 172.3, 140.4, 138.6, 135.7, 129.1, 128.5, 128.3, 128.2, 128.1, 126.9, 118.5, 74.6, 66.7, 60.4, 38.1, 21.3, 10.9 ppm; MS (ESI) *m/z*: 340 [$(M+H)^+$], 362 [$(M+Na)^+$], 322 [$(M+H-H_2O)^+$]; HRMS (ESI, *m/z*) calcd for [$C_{21}H_{26}NO_3$]$^+$: 340.19072; Found: 340.19090.

Benzyl 4-(benzyl(hydroxy)amino)-6-methyl-3-methyleneheptanoate (4da)



4da

Following the typical procedure A (see 3.2), from nitrone **1d**[4] and allenoate **3a**[5] compound **4da** was obtained in 71% yield as a colorless oil, accompanied by the recovered **1d** (29%). IR (neat, spectrometer B) ν_{max}: 3459, 3088, 3063, 3028, 2952, 2866, 1730, 1496, 1451, 1382, 1366, 1328, 1258, 1214, 1148, 1002 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.44-7.18 (m, 10H), 5.20 (s, 1H), 5.17 (s, 1H), 5.09 (s, 2H), 3.85 (d, *J* = 13.5 Hz, 1H), 3.77 (d, *J* = 13.5 Hz, 1H), 3.36-3.26 (m, 1H), 3.26 (d, *J* = 15.5 Hz, 1H), 3.10 (d, *J* = 15.5 Hz, 1H), 1.67-1.45 (m, 3H), 0.91 (d, *J* = 6.5 Hz, 3H), 0.86 (d, *J* = 6.5 Hz, 3H) ppm; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 172.4, 140.7, 138.4, 135.7, 129.1, 128.5, 128.3, 128.2, 128.1, 127.0, 118.6, 70.7, 66.7, 60.2, 38.4, 37.2, 25.1, 23.8, 21.7 ppm; MS (ESI) *m/z*: 368.2

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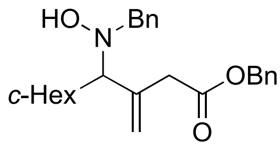
[9] Evans, D. A.; Song, H. –J.; Fandrick, K. R.; *Org. Lett.* **2006**, *8*, 3351-3354.

[(M+H)$^+$], 390.1 [(M+Na)$^+$]; HRMS (ESI, *m/z*) calcd for $[C_{23}H_{29}NO_3Na]^+$: 390.20396; Found: 390.20416.

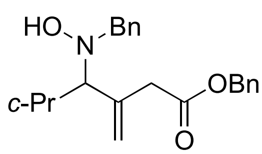
Benzyl 3-((benzyl(hydroxy)amino)(cyclohexyl)methyl)but-3-enoate (4ea)



4ea

Following the typical procedure A (see 3.2), from nitrone **1e**[8] and allenoate **3a**[5] compound **3ea** was obtained in 62% yield as a colorless oil, accompanied by the recovered **1e** (31%). IR (neat, spectrometer B) ν_{max}: 3477, 3085, 3063, 3031, 2920, 2851, 1730, 1635, 1492, 1451, 1375, 1331, 1214 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.42-7.18 (m, 10H), 5.25 (brs, 1H), 5.13 (brs, 2H), 5.05 (s, 1H), 4.57 (s, 1H), 3.90 (d, *J* = 13.5 Hz, 1H), 3.69 (d, *J* = 13.5 Hz, 1H), 3.33 (d, *J* = 15.5 Hz, 1H), 3.15 (d, *J* = 15.5 Hz, 1H), 2.93 (d, *J* = 9.0 Hz, 1H), 2.14-2.01 (m, 1H), 1.92-1.52 (m, 4H), 1.34-0.74 (m, 6H) ppm; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 171.7, 139.0, 138.8, 135.9, 128.9, 128.5, 128.2, 128.1, 128.1, 126.9, 119.4, 76.8, 66.4, 61.0, 39.7, 37.4, 31.0, 29.9, 26.7, 26.3, 26.3 ppm; MS (ESI) *m/z*: 394 [(M+H)$^+$], 416 [(M+Na)$^+$]; HRMS (ESI, *m/z*) calcd for $[C_{25}H_{31}NO_3Na]^+$: 416.21962; Found: 416.21937.

Benzyl 3-((benzyl(hydroxy)amino)(cyclopropyl)methyl)but-3-enoate (4fa)



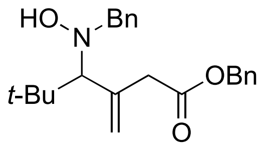
4fa

Following the typical procedure A (see 3.2), from nitrone **1f**[10] and allenoate **3a**[5] compound **4fa** was obtained in 56% yield as a colorless oil, accompanied by the recovered **1f** (43%). IR (neat, spectrometer B) ν_{max}: 3449, 3063, 3028, 3003, 2955, 2885, 2841, 1720, 1647, 1603, 1496, 1454, 1375, 1334, 1280, 1261, 1214, 1150, 1030 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.48-7.17 (m, 10H), 5.42 (brs, 1H), 5.26 (s, 1H), 5.11 (s, 1H), 5.08 (s, 2H), 4.35 (d, *J* = 13.5 Hz, 1H), 3.74 (d, *J* = 13.5 Hz, 1H), 3.35 (d, *J* = 15.5 Hz, 1H), 3.13 (d, *J* = 15.5 Hz, 1H), 2.41 (d, *J* = 9.5 Hz, 1H), 1.18-1.00 (m, 1H), 0.84-0.70 (m, 1H), 0.63-0.51 (m, 1H), 0.51-0.38 (m, 1H), 0.16-0.02 (m, 1H) ppm; ^{13}C-NMR (75

[10] Burchak, O. N.; Masson, G.; Py, S. *Synlett.* **2010**, *11*, 1623-1626.

MHz, $CDCl_3$) δ: 173.1, 142.1, 139.1, 135.6, 128.8, 128.5, 128.3, 128.1, 126.8, 118.2, 77.9, 66.8, 60.1, 39.2, 10.1, 7.8. 2.5 ppm; MS (ESI) *m/z*: 352 [$(M+H)^+$], 374 [$(M+Na)^+$]; HRMS (ESI, *m/z*) calcd for $[C_{22}H_{25}NO_3Na]^+$: 374.17266; Found: 374.17290.

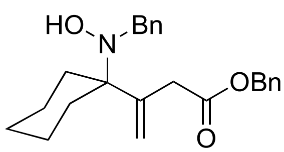
Benzyl 4-(benzyl(hydroxy)amino)-5,5-dimethyl-3-methylenehexanoate (4ga)



4ga

Following the typical procedure A (see 3.2), from nitrone **1g**[8] and allenoate **3a**[5] compound **4ga** was obtained in 44% yield as a colorless oil, accompanied by the recovered **1g** (52%). IR (neat, spectrometer B) ν_{max}: 3493, 3088, 3063, 3031, 2952, 2898, 2866, 1727, 1496, 1454, 1366, 1321, 1306, 1264, 1211, 1179, 1141, 1002 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.43-7.20 (m, 10H), 5.29 (s, 1H), 5.22 (s, 1H), 5.14 (s, 2H), 4.33 (s, 1H), 4.00 (d, J = 13.5 Hz, 1H), 3.66 (d, J = 13.5 Hz, 1H), 3.45 (dd, J = 15.5, 0.9 Hz, 1H), 3.24 (dd apparent d, J = 15.5 Hz, 1H), 2.94 (s, 1H), 1.05 (s, 9H) ppm; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 171.6, 139.1, 138.8, 135.9, 129.1, 128.5, 128.3, 128.2, 127.0, 120.6, 79.3, 66.4, 63.1, 41.7, 35.3, 29.1 ppm; MS (ESI) *m/z*: 368 [$(M+H)^+$], 390 [$(M+Na)^+$]; HRMS (ESI, *m/z*) calcd for $[C_{23}H_{29}NO_3Na]^+$: 390.20396; Found: 390.20413.

Benzyl 3-(1-(benzyl(hydroxy)amino)cyclohexyl)but-3-enoate (4ha)



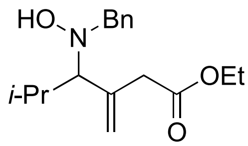
4ha

Following the typical procedure A (see 3.2), from nitrone **1h**[11] and allenoate **3a**[5] compound **4ha** was obtained in 26% yield as a colorless oil, accompanied by the recovered **1h** (30%). IR (neat, spectrometer B) ν_{max}: 3465, 3085, 3063, 3028, 2936, 2854, 1730, 1645, 1603, 1496, 1454, 1372, 1325, 1290, 1261, 1211, 1163, 1141, 1068, 1030, 1002 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.49-7.17 (m, 10H), 5.37 (s, 1H), 5.31 (s, 1H), 5.05 (s, 2H), 4.56 (br s, 1H), 3.77 (s, 2H), 3.28 (s, 2H), 1.20-2.24 (m, 10H) ppm; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 172.6, 141.9, 139.9, 135.9, 129.1, 128.5, 128.3, 128.2,

[11] Franco, S.; Merchán, F. L.; Merino, P.; Tejero, T. *Synth. Commun.* **1995**, *25*, 2275-2284.

128.1, 126.7, 119.6, 67.3, 66.6, 55.3, 38.7, 29.9, 26.5, 22.7 ppm; MS (ESI) *m/z*: 380 [$(M+H)^+$]; HRMS (ESI, *m/z*) calcd for [$C_{24}H_{29}NO_3Na$]$^+$: 402.20396; Found: 402.20433.

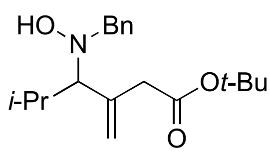
Ethyl 4-(benzyl(hydroxy)amino)-5-methyl-3-methylenehexanoate (4ab)



4ab

Following the typical procedure A (see 3.2), from nitrone **1a**[4] and allenoate **3b**[5], compound **4ab** was obtained in 64% yield as a colorless oil, accompanied by the recovered **1a** (33%). IR (neat, spectrometer B) ν_{max}: 3421, 3088, 3063, 3031, 2984, 2958, 2898, 2873, 2844, 1704, 1499, 1451, 1366, 1302, 1252, 1150, 1125, 1093, 1071, 1027 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.43-7.20 (m, 5H), 5.27 (s, 1H), 5.09 (s, 1H), 4.65 (s, 1H), 4.15 (q, *J* = 7.0 Hz, 2H), 3.93 (d, *J* = 13.5 Hz, 1H), 3.72 (d, *J* = 13.5 Hz, 1H), 3.27 (dd, *J* = 15.5, 1.0 Hz, 1H), 3.09 (d, *J* = 15.5 Hz, 1H), 2.88 (d, *J* = 8.5 Hz, 1H), 2.29-2.10 (m, 1H), 1.26 (t, *J* = 7.0 Hz, 3H), 1.06 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 6.5 Hz, 3H) ppm; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 171.9, 139.3, 138.9, 128.9, 128.2, 126.9, 119.0, 77.9, 61.1, 60.6, 39.8, 27.9, 20.6, 19.3, 14.2 ppm; MS (ESI) *m/z*: 292 [$(M+H)^+$], 314 [$(M+Na)^+$], 274 [$(M+H-H_2O)^+$]; HRMS (ESI, *m/z*) calcd for [$C_{17}H_{26}NO_3$]$^+$: 292.19072; Found: 292.19103.

***tert*-Butyl 4-(benzyl(hydroxy)amino)-5-methyl-3-methylenehexanoate (4ac)**



4ac

Following the typical procedure A (see 3.2), from nitrone **1a**[4] and allenoate **3c**[12] compound **4ac** was obtained in 32% yield as a colorless oil, accompanied by the recovered **1a** (52%). IR (neat, spectrometer B) ν_{max}: 3474, 3066, 3028, 2974, 2930, 2870, 1723, 1638, 1603, 1492, 1454, 1391, 1363, 1331, 1280, 1252, 1144, 1030 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.42-7.18 (m, 5H), 5.27 (brs, 1H), 5.08 (s, 1H), 4.69 (s, 1H), 3.95 (d, *J* = 13.5 Hz, 1H), 3.73 (d, *J* = 13.5 Hz, 1H), 3.18 (d, *J* = 15.0 Hz, 1H), 3.00 (d, *J* = 15.0 Hz, 1H), 2.88 (d, *J* = 8.5 Hz, 1H), 2.26-2.10 (m, 1H), 1.46 (s, 9H), 1.05 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 7.0 Hz, 3H) ppm; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 171.4, 139.8, 139.0, 129.0,

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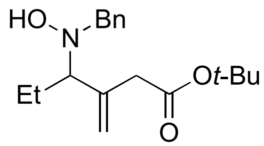
[12] Takagi, K.; Tomita, I.; Endo, T. *Polym. Bull.*, **2003**, *50*, 335-342.

128.2, 126.9, 118.6, 80.6, 78.2, 61.2, 40.8, 28.1, 27.9, 20.6, 19.1 ppm; MS (ESI) *m/z*: 320 [$(M+H)^+$], 342 [$(M+Na)^+$]; HRMS (ESI, *m/z*) calcd for [$C_{19}H_{29}NO_3Na$]$^+$: 342.20396; Found: 342.20390.

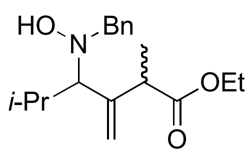
tert-Butyl 4-(benzyl(hydroxy)amino)-3-methylenehexanoate (4cc)



4cc

Following the typical procedure A (see 3.2), from nitrone **1c**[9] and allenoate **3c**[12] compound **4cc** was obtained in 36% yield as a colorless oil. Recovered **1c** was not quantified. IR (neat, spectrometer B) ν_{max}: 3433, 3088, 3063, 3028, 2977, 2930, 2876, 1723, 1644, 1603, 1492, 1454, 1391, 1366, 1334, 1277, 1255, 1144, 1068, 1027 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.50-7.10 (m, 5H), 5.32 (s, 1H), 5.25-5.15 (m, 2H), 3.85 (s, 2H), 3.20-3.05 (m, 2H), 2.95 (d, *J* = 15.5 Hz, 1H), 1.98-1.80 (m, 1H), 1.44 (s, 9H), 0.85 (t, *J* = 7.5 Hz, 3H) ppm; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 172.0, 141.0, 138.7, 129.1, 128.1, 126.9, 117.9, 80.9, 74.9, 60.4, 39.0, 28.0, 21.4, 10.9 ppm; MS (ESI) *m/z*: 306 [$(M+H)^+$], 328 [$(M+Na)^+$]; HRMS (ESI, *m/z*) calcd for [$C_{18}H_{27}NO_3Na$]$^+$: 328.18831; Found: 328.18832.

Ethyl 4-(benzyl(hydroxy)amino)-2,5-dimethyl-3-methylenehexanoate (8)



8

40%, d.r. = 2:1

Following the typical procedure A (see 3.2), from nitrone **1a**[4] and allenoate **7**[13] compound **8** was obtained in 40% yield as a colorless oil (dr = 2:1), accompanied by the recovered **1a** (46%). IR (neat, spectrometer B) ν_{max}: 3478, 3088, 3063, 3031n 2977, 2955, 2936, 2872, 1727, 1635, 1496, 1454, 1366, 1242, 1182, 1093, 1027 cm^{-1}; Major diastereoisomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.20-7.50 (m, 5H), 5.43 (s, 1H), 5.22 (s, 1H), 4.36 (s, 1H), 4.25-4.10 (m, 2H), 3.97 (d, *J*= 12.0 Hz, 1H), 3.65 (d, *J*= 12.0 Hz, 1H), 3.44-3.29 (m, 1H), 3.06-2.93 (m, 1H), 2.35-2.13 (m, 1H), 1.45-1.35 (m, 3H), 1.33-1.22 (m, 3H), 1.15-1.05 (m, 3H), 0.95-0.87 (m, 3H) ppm; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 174.9, 145.5, 139.1, 128.9, 128.2, 127.0, 116.6, 77.8, 61.2, 60.6, 44.3, 28.8, 20.4, 19.2, 17.6, 14.1 ppm; Minor diastereoisomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.20-7.50 (m, 5H), 5.38 (s, 1H), 5.16 (s, 1H), 4.76 (s,

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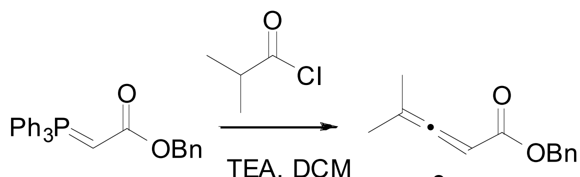
[13] Jung, M. E.; Nishimura, N. *Org. Lett.*, **2001**, *3*, 2113–2115.

1H), 4.25-4.10 (m, 2H), 3.89 (d, *J*= 15.0 Hz, 1H), 3.78 (d, *J*= 15.0 Hz, 1H), 3.44-3.29 (m, 1H), 3.06-2.93 (m, 1H), 2.35-2.13 (m, 1H), 1.45-1.35 (m, 3H), 1.33-1.22 (m, 3H), 1.15-1.05 (m, 3H), 0.95-0.87 (m, 3H) ppm; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 174.8, 145.2, 139.0, 128.9, 128.2, 126.9, 117.0, 77.5, 60.6, 60.5, 43.7, 28.5, 20.7, 19.3, 17.9, 14.2 ppm; MS (ESI) *m*/*z*: 306 [$(M+H)^+$]; HRMS (ESI, *m*/*z*) calcd for $[C_{18}H_{27}NO_3Na]^+$: 328.18831; Found: 328.18807.

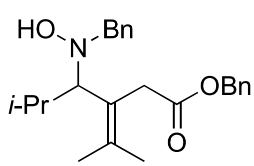
Preparation of benzyl 4-methylpenta-2,3-dienote (9)



9

To a stirring solution of isobutyryl chloride (0.81 mL, 7.67 mmol) and CH_2Cl_2 (18 mL) under Ar, at 0 °C, was added Et_3N (1.22 mL, 8.41 mmol) dropwise via cannula. When the addition was complete, the ice bath was removed and the reaction mixture warmed to rt. To the reaction mixture was slowly added a solution of stabilized ylide benzyl 2-(triphenylphosphoranylidene)acetate (3 g, 7.31 mmol) in CH_2Cl_2 (10 mL) dropwise via cannula and the mixture was stirred at rt overnight, then concentrated under reduced pressure to afford a gummy residue. This was treated with pentane/ether (50/8, 58 mL) and stirred well, then the solid was filtered and washed with pentane (2 × 10 mL). Then the filtrate was concentrated under reduced pressure. Purification by column chromatography on silica gel (eluent: Et_2O/Pentane 1/10) afforded allenoate **9** (500 mg, 33%) as a colorless oil. IR (neat, spectrometer B) ν_{max}: 3063, 3034, 2984, 2942, 2911, 1964, 1717, 1496, 1451, 1404, 1245, 1147, 1021 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.40-7.27 (m, 5H), 5.50 (sept, *J* = 3.0 Hz, 1H), 5.17 (s, 2H), 1.80 (d, *J* = 3.0 Hz, 6H) ppm; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 211.0, 166.4, 136.2, 128.4, 128.0, 128.0, 100.3, 85.9, 66.2, 19.2 ppm; MS (ESI) *m*/*z*: 225 [$(M+Na)^+$]; HRMS (ESI, *m*/*z*) calcd for $[C_{13}H_{14}O_2Na]^+$: 225.08860; Found: 225.08852.

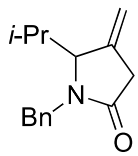
Benzyl 4-(benzyl(hydroxy)amino)-5-methyl-3-(propan-2-ylidene)hexanoate (10)



10

Following the typical procedure A (see 3.2), from nitrone **1a**[4] and allenoate **9**, compound **10** was obtained in 22% yield as a colorless oil, accompanied by the recovered **1a** (70%). IR (neat, spectrometer B) ν_{max}: 3474, 3088, 3063, 3031, 2958, 2933, 2866, 1730, 1499, 1451, 1372, 1331, 1258, 1214, 1147, 1030, 1005 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.44-7.18 (m, 10H), 5.14 (d, *J* = 12.0 Hz, 1H), 5.08 (d, *J* = 12.0 Hz, 1H), 4.98 (brs, 1H), 3.95 (d, *J* = 14.0 Hz, 1H), 3.77 (d, *J* = 14.0 Hz, 1H), 3.52-3.24 (m, 3H), 2.30-2.10 (m, 1H), 1.73 (s, 3H), 1.71 (s, 3H), 1.05 (d, *J* = 6.5 Hz, 3H), 0.89 (d, *J* = 6.5 Hz, 3H) ppm; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 173.0, 139.4, 136.1, 136.0, 128.9, 128.5, 128.3, 128.1, 128.0, 126.7, 72.2, 66.4, 60.7, 35.4, 28.8, 21.6, 21.2, 20.9, 19.2 ppm; MS (ESI) *m/z*: 382 [(M+H)$^{+}$]; HRMS (ESI, *m/z*) calcd for $[C_{24}H_{31}NO_3Na]^+$: 404.21962; Found: 404.21970.

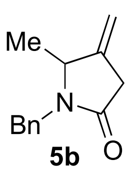
1-Benzyl-5-isopropyl-4-methylenepyrrolidin-2-one (5a)



5a

Following the typical procedure for cyclisation of *N*-hydroxyamino esters into lactams (see 3.4), from compound **4aa** compound **5a** was obtained in 99% yield. IR (neat, spectrometer B) ν_{max}: 3086, 3063, 3031, 2962, 2931, 2874, 1689, 1663, 1495, 1431, 1401, 1386, 1360, 1318, 1284, 1227, 1170, 1081, 1029 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.40-7.18 (m, 5H), 5.15 (d, *J* = 15.5 Hz, 1H), 5.11 (brs, 1H), 4.93 (brs, 1H), 3.93 (d, *J* = 15.0 Hz, 1H), 3.80 (brs, 1H), 3.18 (brd, *J* = 22.0 Hz, 1H), 3.05 (brd, *J* = 21.0 Hz, 1H), 2.20-2.00 (m, 1H), 0.94 (d, *J* = 7.0 Hz, 3H), 0.77 (d, *J* = 7.0 Hz, 3H) ppm; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 172.8, 138.9, 136.2, 128.6, 128.0, 127.5, 110.8, 66.7, 43.7, 38.5, 29.1, 18.2, 15.2 ppm; MS (ESI) *m/z*: 230 [(M+H)$^{+}$], 252 [(M+Na)$^{+}$]; HRMS (ESI, *m/z*) calcd for $[C_{15}H_{19}NONa]^+$: 252.13589; Found: [(M+Na)$^{+}$]: 252.13598.

1-Benzyl-5-methyl-4-methylenepyrrolidin-2-one (5b)

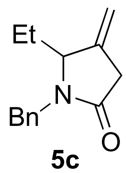


5b

Following the typical procedure for cyclisation of *N*-hydroxyamino esters into lactams (see 3.4), from compound **4ba** compound **5b** was obtained in 75% yield. IR (neat, spectrometer B) ν_{max}: 3088, 3060, 3028, 2974, 2923, 2870, 1689, 1666, 1600, 1492, 1423, 1397, 1359, 1274, 1233, 1176, 1084 cm^{-1}; ^{1}H

NMR (300 MHz, $CDCl_3$) δ: 7.36-7.21 (m, 5H), 5.12-5.02 (m, 2H), 5.02-4.97 (m, 1H), 4.08-3.95 (m, 2H), 3.31-3.10 (m, 2H), 1.26 (d, J = 6.5 Hz, 3H) ppm; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 172.3, 143.3, 136.3, 128.7, 128.0, 127.5, 108.6, 57.3, 43.8, 36.8, 19.4 ppm; MS (ESI) *m/z*: 202 [$(M+H)^+$], 224 [$(M+Na)^+$]; HRMS (ESI, *m/z*) calcd for [$C_{13}H_{15}NONa$]$^+$: 224.10459; Found: 224.10454.

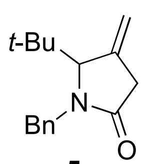
1-Benzyl-5-ethyl-4-methylenepyrrolidin-2-one (5c)



5c

Following the typical procedure for cyclisation of *N*-hydroxyamino esters into lactams (see 3.4), from compound **4ca** compound **5c** was obtained in 91% yield. IR (neat, spectrometer B) ν_{max}: 3088, 3063, 3028, 2965, 2930, 2876, 1689, 1663, 1496, 1439, 1426, 1401, 1359, 1283, 1226, 1173, 1068, 1024 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.37-7.21 (m, 5H), 5.15 (d, *J* = 15.0 Hz, 1H), 5.11 (brs, 1H), 4.97 (brs, 1H), 4.00 (brs, 1H), 3.84 (d, *J* = 15.0 Hz, 1H), 3.17 (s, 2H), 1.87-1.70 (m, 1H), 1.70-1.55 (m, 1H), 0.78 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 172.8, 140.9, 136.2, 128.7, 128.1, 127.6, 109.0, 61.9, 43.7, 37.5, 24.5, 6.7 ppm; MS (ESI) *m/z*: 216 [$(M+H)^+$], 238 [$(M+Na)^+$]; HRMS (ESI, *m/z*) calcd for [$C_{14}H_{17}NONa$]$^+$: 238.12024; Found: [$(M+Na)^+$]: 238.11993.

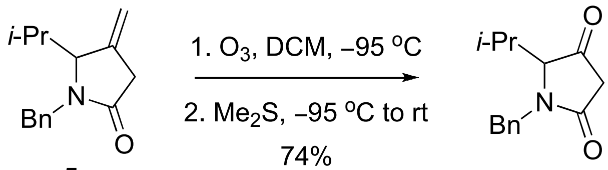
1-Benzyl-5-(tert-butyl)-4-methylenepyrrolidin-2-one (5g)



5g

Following the typical procedure for cyclisation of *N*-hydroxyamino esters into lactams (see 3.4), from compound **4ga** compound **5g** was obtained in 88% yield.. IR (neat, spectrometer B) ν_{max}: 3082, 3060, 3028, 2961, 2904, 2866, 1695, 1663, 1480, 1426, 1397, 1359, 1312, 1268, 1223, 1201, 1160, 1084, 1030 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.42-7.22 (m, 3H), 7.17-7.09 (m, 3H), 5.41 (d, *J* = 15.0 Hz, 1H), 5.09 (brs, 1H), 4.87 (brs, 1H), 4.11 (d, *J* = 15.0 Hz, 1H), 3.55 (s, 1H), 3.26 (dt, *J* = 20.0, 3.0 Hz, 1H), 2.95 (d, *J* = 20.0 Hz, 1H), 0.97 (s, 9H) ppm; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 174.9, 140.9, 136.4, 128.7, 127.7, 127.4, 111.5, 71.3, 47.4, 38.8, 37.0, 27.1 ppm; MS (ESI) *m/z*: 244 [$(M+H)^+$], 266 [$(M+Na)^+$]; HRMS (ESI, *m/z*) calcd for [$C_{16}H_{21}NONa$]$^+$: 266.15154; Found: 266.15203.

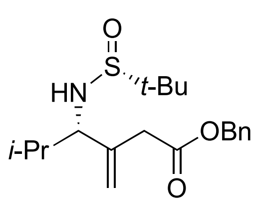
Ozonolysis of 5a



5a

To a solution of **5a** (18 mg, 0.08 mmol) in DCM (4.0 mL) at –95 ºC (melting acetone bath), was bubbled ozone until a persistent blue color appeared (20 min). The mixture was purged with argon to remove the excess of ozone and then dimethyl sulfide (1 mL) was added. Then the solution was warmed natually without removing the bath. 2 h later, 10 mL water was added, then it was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography on silica gel (EtOAC/Pentane 1/4 → EtOAc/Pentane 1/1) gave 1-benzyl-5-isopropylpyrrolidine-2,4-dione[14] as a yellow oil (13.4 mg, 74%). IR (neat, spectrometer B) ν_{max}: 3091, 3063, 3031, 2958, 2933, 2873, 1768, 1689, 1492, 1416, 1388, 1366, 1318, 1264, 1239, 1071, 1027 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.39-7.22 (m, 5H), 5.32 (d, *J* = 14.5 Hz, 1H), 4.00 (d, *J* = 14.5 Hz, 1H), 3.59 (d, *J* = 3.5 Hz, 1H), 3.02 (s, 2H), 2.28-2.10 (m, 1H), 1.06 (d, *J* = 7.0 Hz, 3H), 0.88 (d, *J* = 7.0 Hz, 3H) ppm; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 206.2, 169.2, 135.2, 128.9, 128.3, 128.0, 70.2, 43.7, 42.3, 28.5, 17.9, 16.0 ppm; MS (ESI) *m/z*: 232 [$(M+H)^+$], 254 [$(M+Na)^+$]; HRMS (ESI, *m/z*) calcd for $[C_{14}H_{17}NO_2Na]^+$: 254.11515; Found: [$(M+Na)^+$]: 254.11544.

(*S*)-Benzyl 4-((*R*)-1,1-dimethylethylsulfinamido)-5-methyl-3-methylenehexanoate (11a)



11a

Following the typical procedure A (see 3.2), from *t*-BS-imine **2a**[7] and allenoate **3a**[5] compound **11a** was obtained in 64% yield as a colorless oil (unseparable mixture, d.r = 7:1), accompanied by the recovered **2a** (35%). Following the typical procedure B (see 3.3) compound **11a** was obtained in 85% yield as a yellow oil (unseparable mixture, d.r = 5:1). $[\alpha]^{20}_D$ –20.8 (*c* 0.83, EtOH); IR (neat, spectrometer B) ν_{max}: 3436, 3237, 2955, 2870, 1730, 1644, 1499, 1454, 1363, 1271, 1223, 1150, 1049 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.32-7.23 (m, 5H), 5.14 (brs, 1H), 5.12 (brs, 1H), 5.05 (s, 2H),

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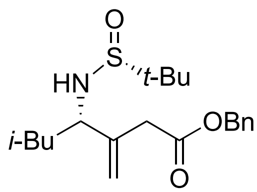
[14] Spatz, J. H.; Welsch, S. J.; Duhaut, D. –E.; Jäger, N.; Boursier, T.; Fredrich, M.; Allmendinger, L.; Ross, G.; Kolb, J.; Burdack, C.; Umkehrer, M. *Tetrahedron Lett.* **2009**, *50*, 1705-1707.

3.46 (dd, J = 8.0, 3.0 Hz, 1H), 3.23 (d, J = 2.5 Hz, 1H), 3.00 (d, J = 15.5 Hz, 1H), 2.93 (d, J = 15.5 Hz, 1H), 1.75-1.60 (m, 1H), 1.11 (s, 9H), 0.91 (d, J = 6.5 Hz, 3H), 0.82 (d, J = 6.5 Hz, 3H) ppm; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 171.1, 140.1, 135.7, 128.5, 128.3, 128.2, 118.2, .66.8, 66.6, 55.3, 36.9, 30.3, 22.5, 19.8, 18.9 ppm; MS (ESI) *m*/*z*: 352 [$(M+H)^+$], 374 [$(M+Na)^+$]; HRMS (ESI, *m*/*z*) calcd for $[C_{19}H_{29}NO_3SNa]^+$: 374.17604; Found: 374.17660.

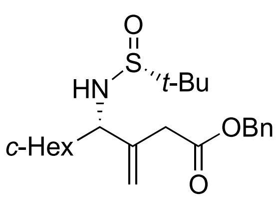
(*S*)-Benzyl 4-((*R*)-1,1-dimethylethylsulfinamido)-6-methyl-3-methyleneheptanoate (11b)



11b

Following the typical procedure A (see 3.2), from *t*-BS-imine **2b**[15] and allenoate **3a**[5] compound **11b** was obtained in 55% yield as a colorless oil (dr = 10:1), accompanied by the recovered **2b** (35%). Following the typical procedure B (see 3.3) compound **11b** was obtained in 87% yield as a colorless oil (dr = 5:1). $[\alpha]^{20}_D$ -41.8 (*c* 1.46, EtOH); IR (neat, spectrometer B) ν_{max}: 3436, 3218, 3091, 3066, 3034, 2958, 2930, 2870, 1733, 1647, 1496, 1454, 1366, 1264, 1211, 1147, 1052, 1005 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: δ7.46-7.30 (m, 5H), 5.25 (s, 1H), 5.16 (s, 1H), 5.13 (s, 2H), 4.08-3.90 (m, 1H), 3.19-3.03 (m, 2H), 1.70-1.32 (m, 3H), 1.18 (s, 9H), 0.90 (d, J = 7.0 Hz, 3H), 0.88 (d, J = 7.0 Hz, 3H) ppm; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 171.3, 141.1, 135.7, 128.5, 128.3, 117.5, 66.6, 58.7, 55.4, 43.5, 36.6, 24.6, 22.7, 22.5, 22.2 ppm; MS (ESI) *m*/*z*: 366 [$(M+H)^+$], 388 [$(M+Na)^+$]; HRMS (ESI, *m*/*z*) calcd for $[C_{20}H_{31}NO_3SNa]^+$: 388.19169; Found: 388.19232.

Benzyl 3-((*S*)-cyclohexyl((*R*)-1,1-dimethylethylsulfinamido)methyl)but-3-enoate (11c)



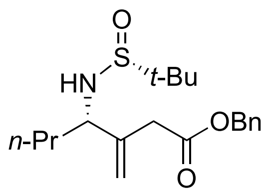
11c

Following the the typical procedure B (see 3.3), from *t*-BS-imine **2c**[16] and allenoate **3a**[5] compound **11c** was obtained in 85% yield as a yellow oil (dr = 4.5:1). $[\alpha]^{20}_D$ –26.4 (*c* 0.68, EtOH); IR (KBr,

[15] Frantz, M. –C.; Pierce, J. G.; Pierce, J. M.; Li, K.; Wan, Q.; Johnson, M.; Wipf, P. *Org. Lett.*, **2011**, *13*, 2318–2321.
[16] Chemla, F.; Ferreira, F. *J. Org. Chem.*, **2004**, *69*, 8244–8250.

spectrometer A) ν_{max}: 3330, 2919, 2849, 1731, 1644, 1600, 1451, 1384, 1262, 1151, 1057 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.42-7.29 (m, 5H), 5.18 (s, 2H), 5.12 (s, 1H), 3.58 (dd, *J* = 8.5, 3.0 Hz, 1H), 3.35 (d, *J* = 3.0 Hz, 1H), 3.06 (d, *J* = 15.0, 1H), 2.99 (d, *J* = 15.0, 1H), 1.90-1.51 (m, 5H), 1.44-1.31 (m, 1H), 1.22-1.08 (m, 2H), 1.17 (s, 9H), 1.04-1.86 (m, 3H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.1, 139.8, 135.6, 128.4, 128.2, 128.2, 118.1, 66.5, 65.9, 55.3, 39.5, 36.2, 30.1, 29.4, 26.1, 25.8, 25.8, 22.4 ppm; MS (ESI) *m*/*z* 414 (M + Na^+, 100%); HRMS calcd for $[C_{22}H_{33}NO_3S+Na]^+$: 414.20734; found: 414.20724.

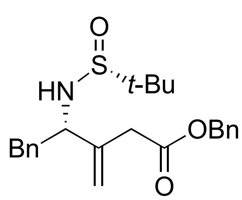
(*S*)-Benzyl 4-((*R*)-1,1-dimethylethylsulfinamido)-3-methyleneheptanoate (11d)



11d

Following the the typical procedure B (see 3.3), from *t*-BS-imine **2d**[17] and allenoate **3a**[5] compound **11d** was obtained in 78% yield as a yellow oil (dr = 5.5:1). $[\alpha]^{20}_{D}$ –43.8 (*c* 0.88, EtOH); IR (KBr, spectrometer A) ν_{max}: 3271, 2954, 2930, 2869, 1735, 1452, 1382, 1363, 1263, 1211, 1150, 1058 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.40-7.28 (m, 5H), 5.22 (s, 1H), 5.14 (s, 1H), 5.11 (s, 2H), 3.91-3.84 (m, 1H), 3.14 (d, *J* = 3.5 Hz, 1H), 3.09 (d, *J* = 15.0 Hz, 1H), 3.03 (d, *J* = 15.0 Hz, 1H), 1.65-1.46 (m, 2H), 1.35-1.23 (m, 2H), 1.17 (s, 9H), 0.88 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.2, 140.9, 135.7, 128.5, 128.3, 117.5, 66.6, 60.4, 55.4, 36.7, 36.5, 22.5, 19.1, 13.7 ppm; MS (ESI) *m*/*z* 374 (M + Na^+, 100%); HRMS calcd for $[C_{19}H_{29}NO_3S+Na]^+$: 374.17604; found: 374.17558.

(*S*)-Benzyl 4-((*R*)-1,1-dimethylethylsulfinamido)-3-methylene-5-phenylpentanoate (11e)



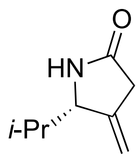
11e

Following the the typical procedure B (see 3.3), from *t*-BS-imine **2e**[18] and allenoate **3a**[5] compound **11e** was obtained in 61% yield as a yellow oil (dr = 8:1). $[\alpha]^{20}_{D}$ –53.1 (*c* 1.20, EtOH); IR (KBr, spectrometer A) ν_{max}: 3284, 3211, 3061, 3028, 2957, 1732, 1497, 1455, 1366, 1260, 1147, 1068 cm^{-1};

[17] Ruan, S. -T.; Luo, J. –M; Du, Y.; Huang, P. -Q. *Org. Lett.* **2011**, *13*, 4938-4941.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.40-7.12 (m, 10H), 5.24 (s, 1H), 5.18 (s, 1H), 5.13 (s, 2H), 4.25-4.16 (m, 1H), 3.40-3.33 (m, 1H), 3.13 (d, J = 4 Hz, 2H), 2.98 (dd, J = 14.0, 6.0 Hz, 1H), 2.84 (dd, J = 14.0, 8.0 Hz, 1H), 1.11 (s, 9H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 171.1, 140.3, 136.6, 135.7, 129.3, 128.7, 128.5, 128,3, 128.3, 126.9, 118.4, 66.7, 60.2, 55.4, 41.1, 37.3, 22.5 ppm; MS (ESI) m/z 400 (M + H^+, 100%); HRMS calcd for $[C_{23}H_{29}NO_3S+Na]^+$: 422.17604; found: 422.17520.

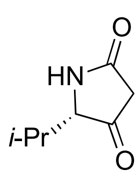
Preparation of 5-isopropyl-4-methylenepyrrolidin-2-one (12a)



12a

To a solution of compound **11a** (95 mg, 0.27 mmol, dr = 5:1) in methanol (5 mL) was added 0.4 mL of 12 N HCl aqueous solution at room temperature. The mixture was then stirred at rt for 25 h. Then the MeOH was removed under reduced pressure, and the $NaHCO_3$ (15 mL) was added carefully to the resultant residue. It was extracted with DCM (3 × 8 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography on silica gel (EtOAC/Hexane 1/4 → 1/1) gave a yellow solid **12a** (29 mg, 77%). M.p. 79-80 ºC (EtOAc/Hexane); $[\alpha]^{20}_{D}$ –61.9 (c 1.00, $CHCl_3$); IR (neat, spectrometer B) ν_{max}: 3189, 3091, 2958, 2927, 2892, 2870, 1695, 1660, 1454, 1375, 1340, 1315, 1287, 1230, 1150, 1027 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.63 (brs, 1H), 5.30-5.10 (m, 1H), 5.10-5.00 (m, 1H), 4.05 (brs, 1H), 3.20-2.93 (m, 2H), 2.05-1.75 (m, 1H), 0.98 (d, J = 7.0 Hz, 3H), 0.88 (d, J = 7.0 Hz, 3H) ppm; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 176.1, 142.7, 109.6, 64.8, 37.2, 33.6, 18.9, 15.9 ppm. MS (ESI) m/z: 162 (M+Na^+, 100); HRMS (ESI, m/z) calcd for $[C_8H_{13}NONa]^+$: 162.08894; Found: 162.08884.

Preparation of 5-isopropylpyrrolidine-2,4-dione (13a)



13a

To a solution of **12a** (48 mg, 0.36 mmol) in DCM (7 mL) at –95 ºC (melting acetone bath), was bubbled ozone until a persistent blue color appeared (20 min). The mixture was purged with argon to remove the excess of ozone and then dimethyl sulfide (0.5 mL) was added. Then the solution was warmed to rt over 1 h. The solution was concentrated under reduced pressure, then the residue was purified by column chromatography on silica gel (EtOAC/Pentane 1/4 → 2/1) to give a white solid **13a** (29.2 mg, 60%), which was recrystallized to give enantionpure **13a**. M.p. 137-138 ºC (EtOAc/Hexane); $[\alpha]^{20}_{D}$ –42.3 (c 0.32, EtOH) {lit.[18] –46.4 (c 1.00, EtOH)}; IR (KBr, spectrometer A) ν_{max}: 3174, 3098, 2967, 2927, 2875, 1769, 1705, 1656, 1385, 1357, 1333, 1311, 1278, 1244, 1125, 1086, 1037 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.24 (brs, 1H), 3.88 (d, *J* = 4.0 Hz, 1H), 3.01-2.94 (m, 2H), 2.24-2.11 (m, 1H), 1.04 (d, *J* = 7.0 Hz, 3H), 0.93 (d, *J* = 7.0 Hz, 3H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 207.3, 171.8, 69.5, 41.4, 30.9, 18.8, 16.6 ppm; MS (ESI) *m*/*z* 164 (M + Na^+, 100%);

5- Copies of ^{1}H and ^{13}C NMR spectra for new compounds

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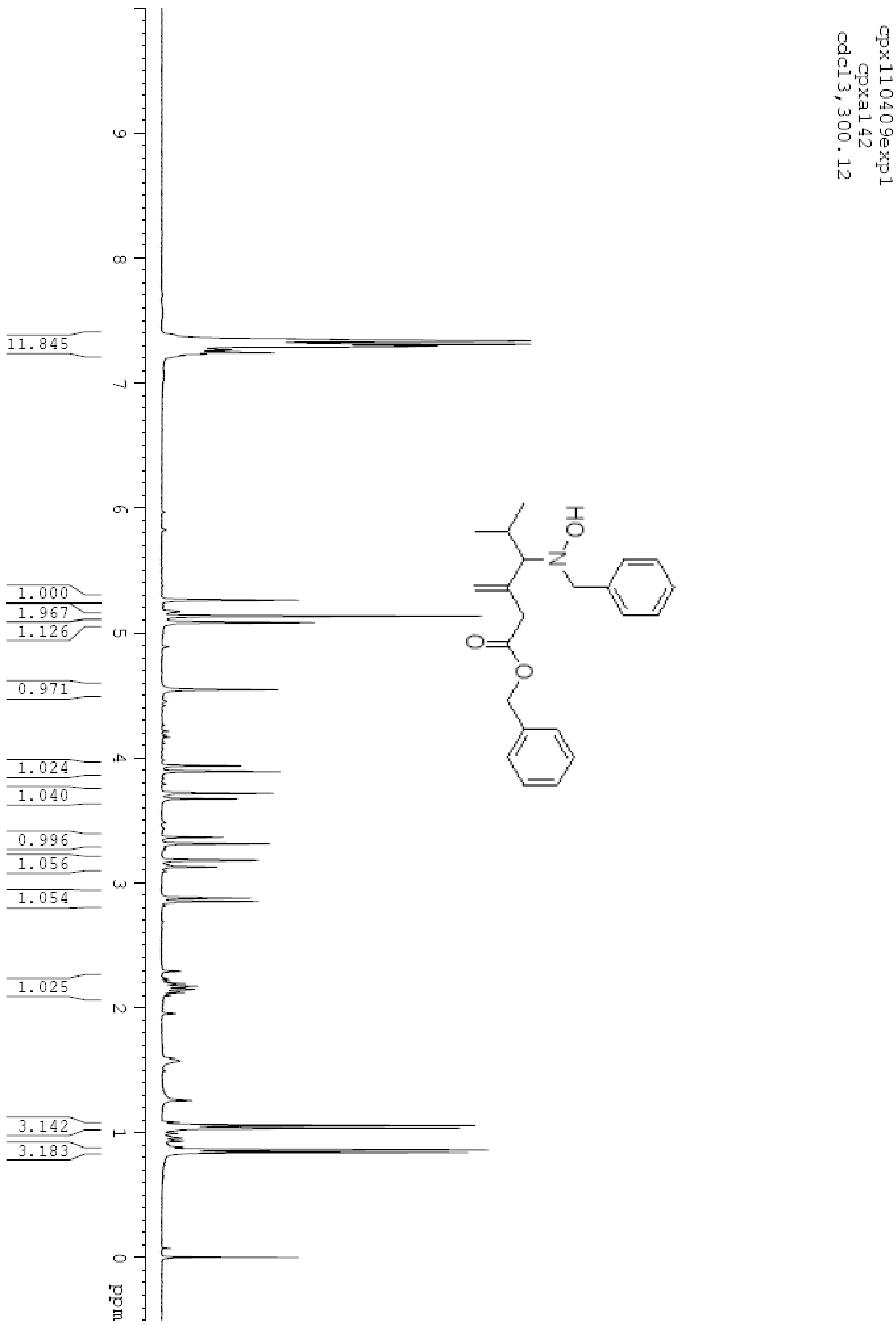
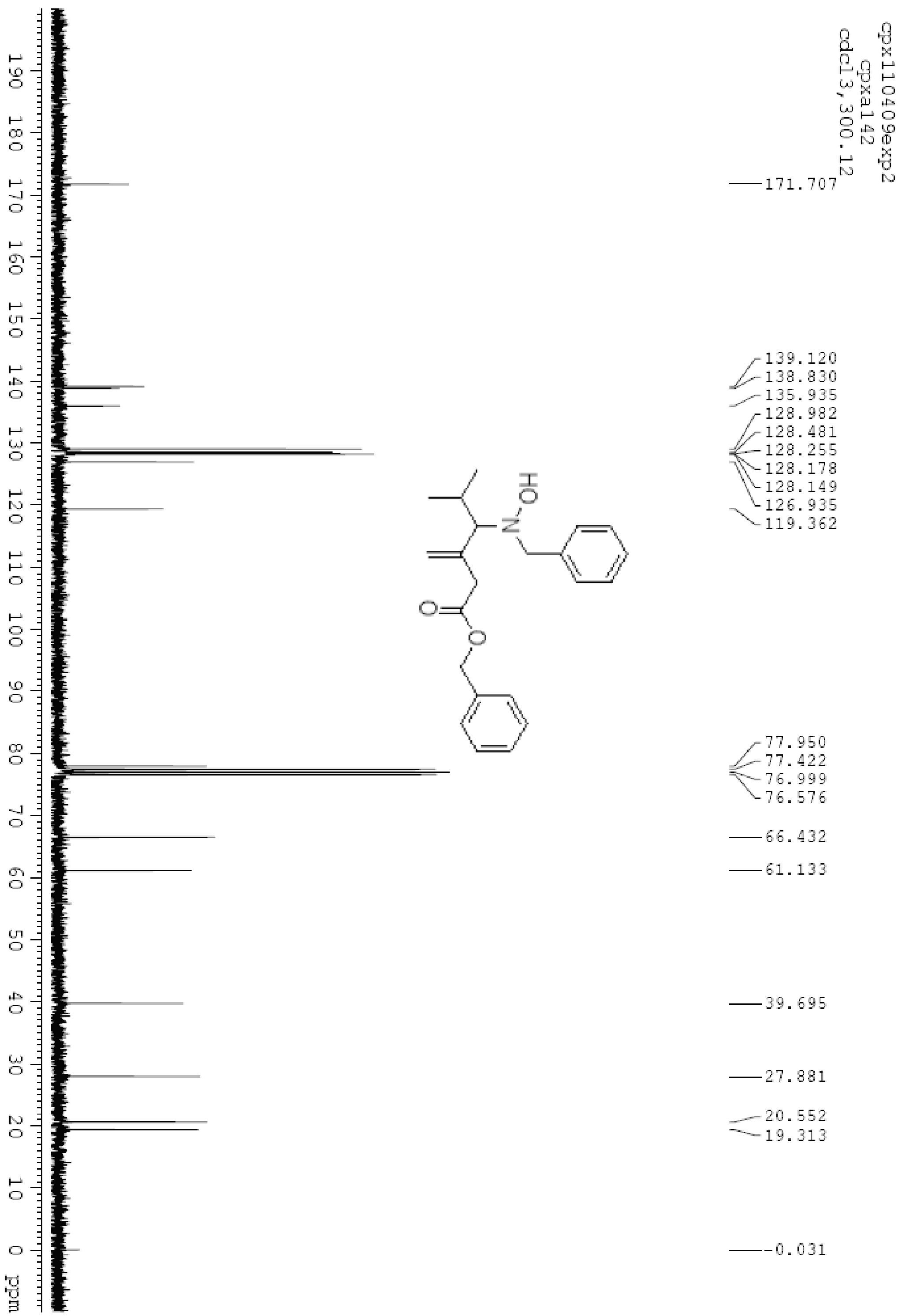
[18] Hosseini, M.; Kringelum, H.; Murray, A.; Tønder, J. E. *Org. Lett.* **2006**, *8*, 2103–2106.

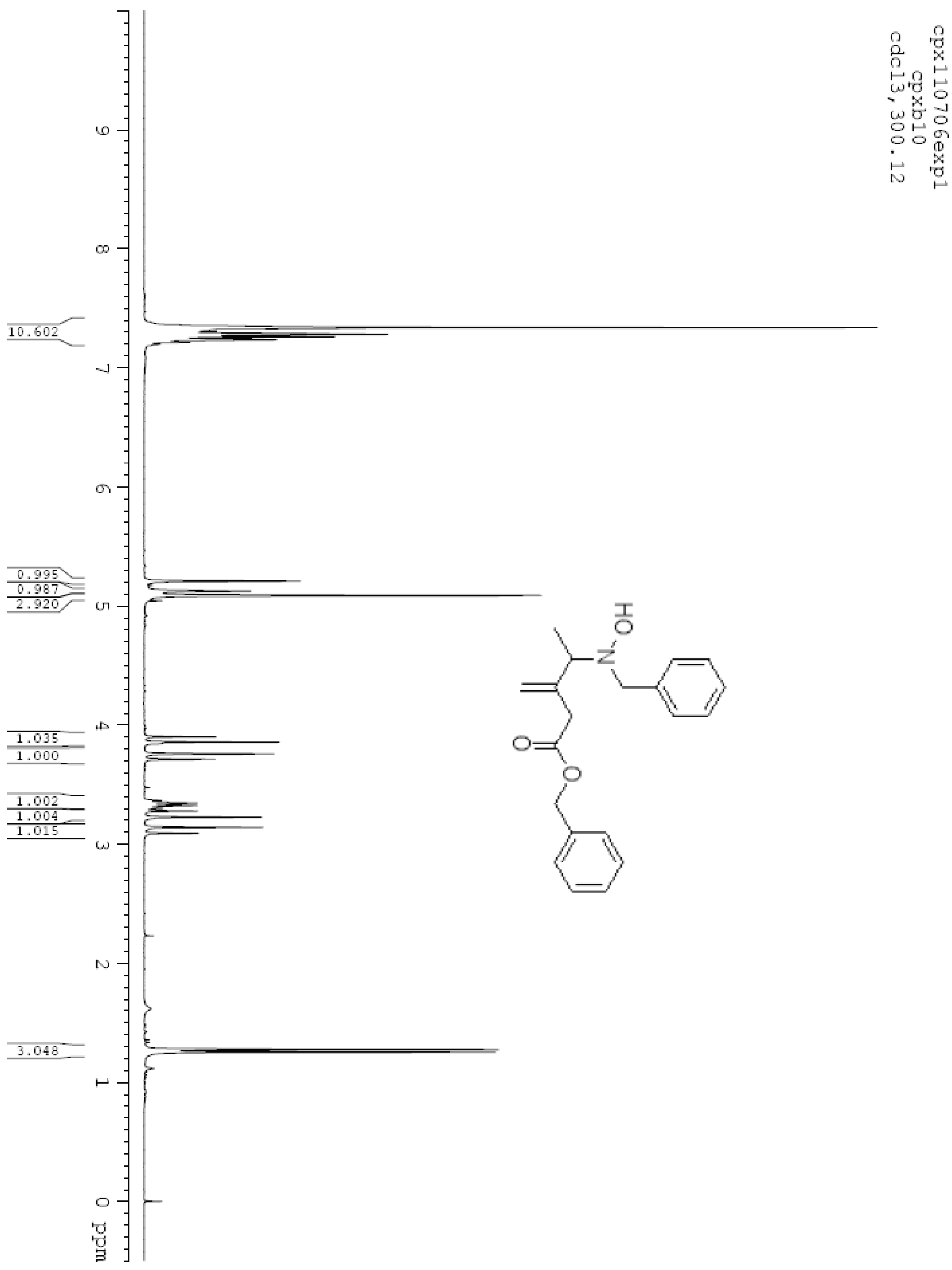
Compound **4aa**:



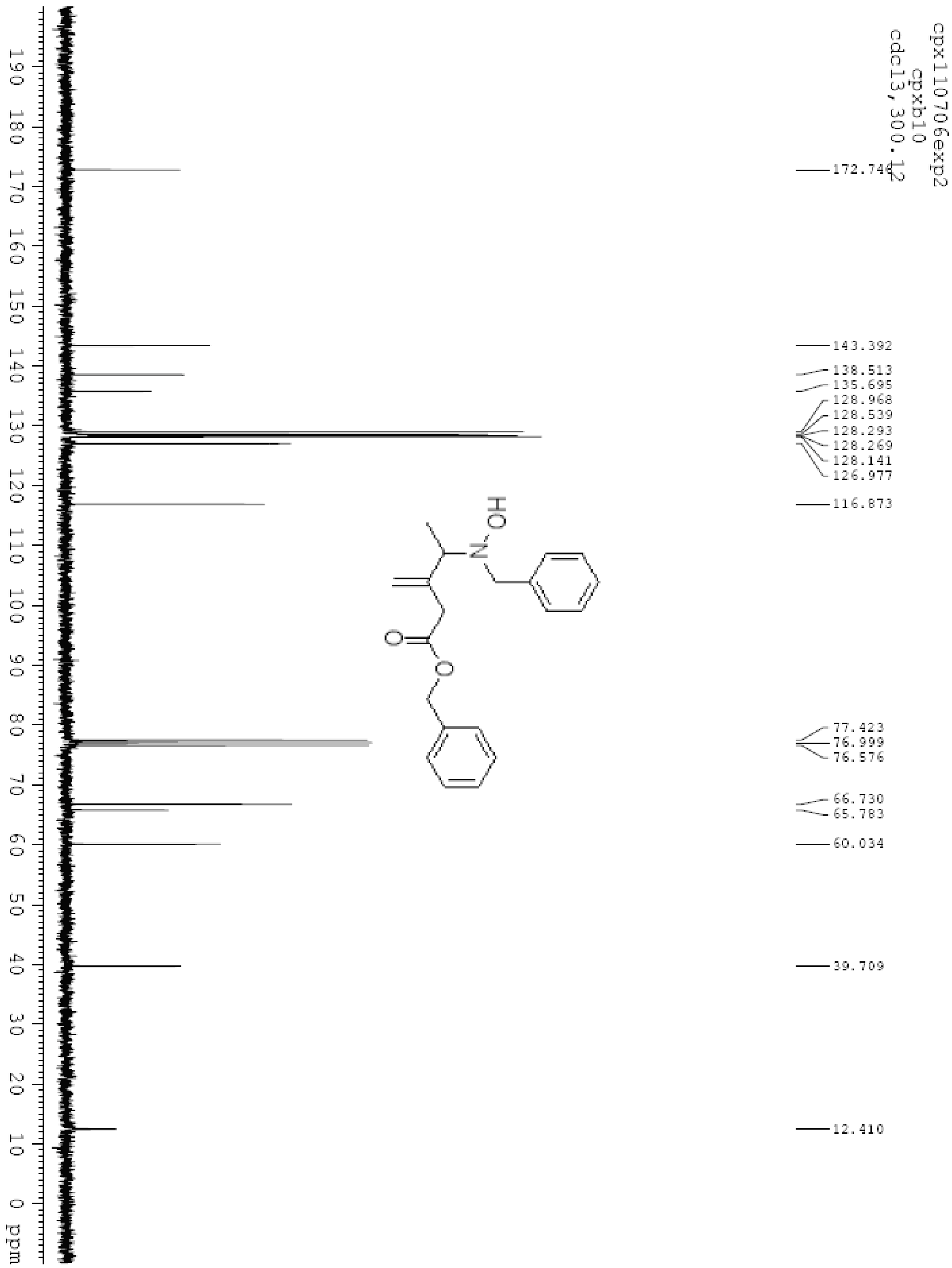
Compound **4aa**:



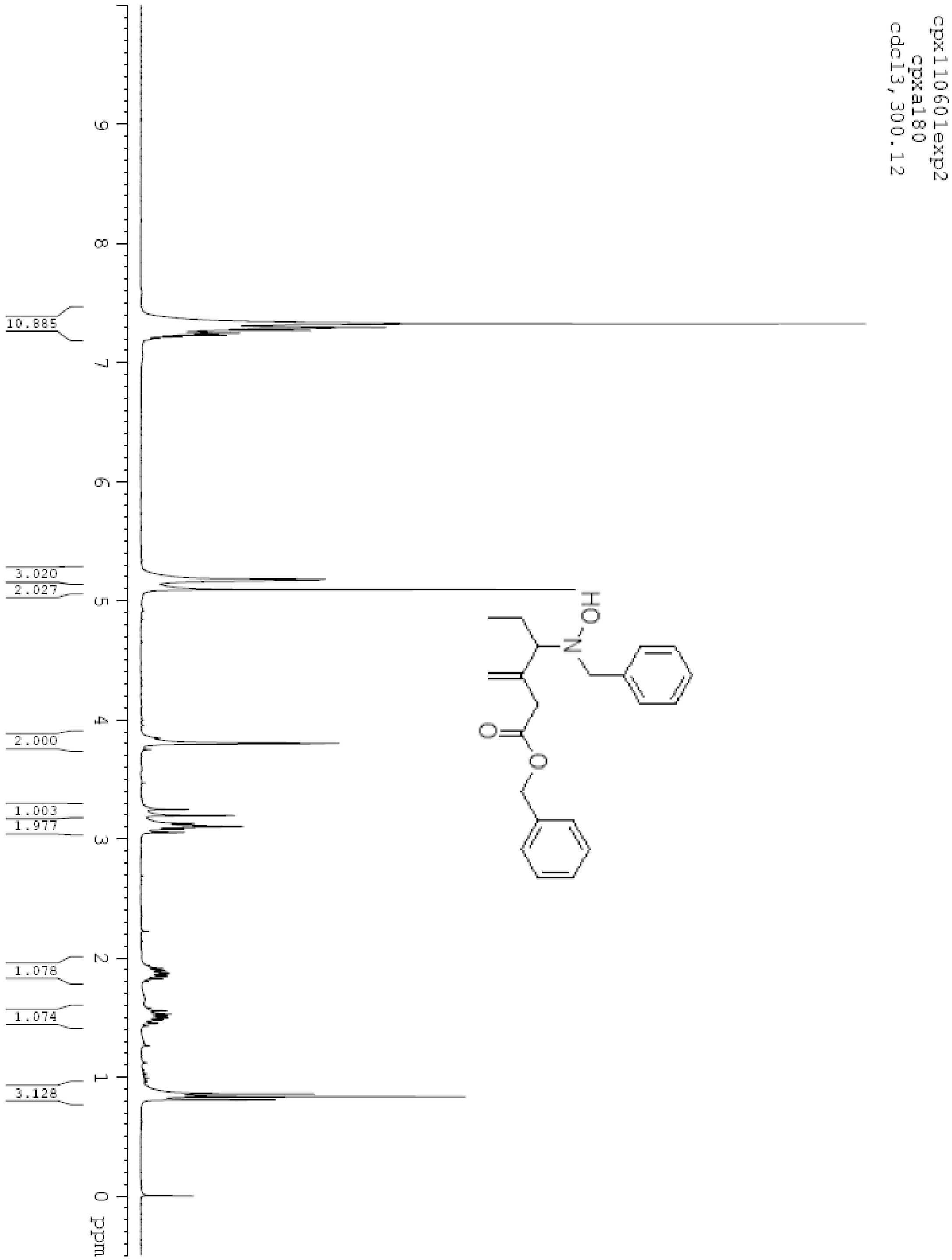
Compound **4ba**:



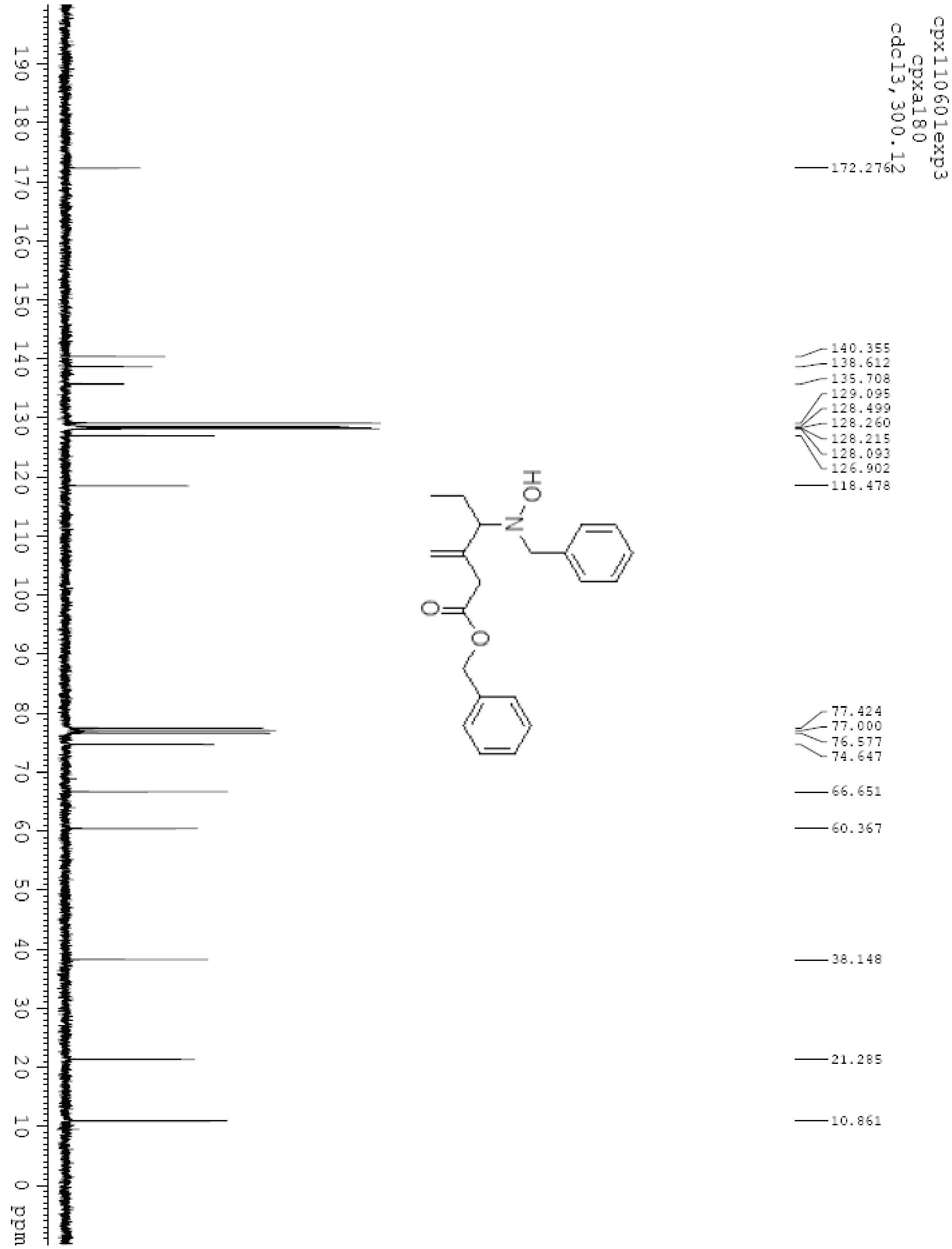
Compound **4ba**:



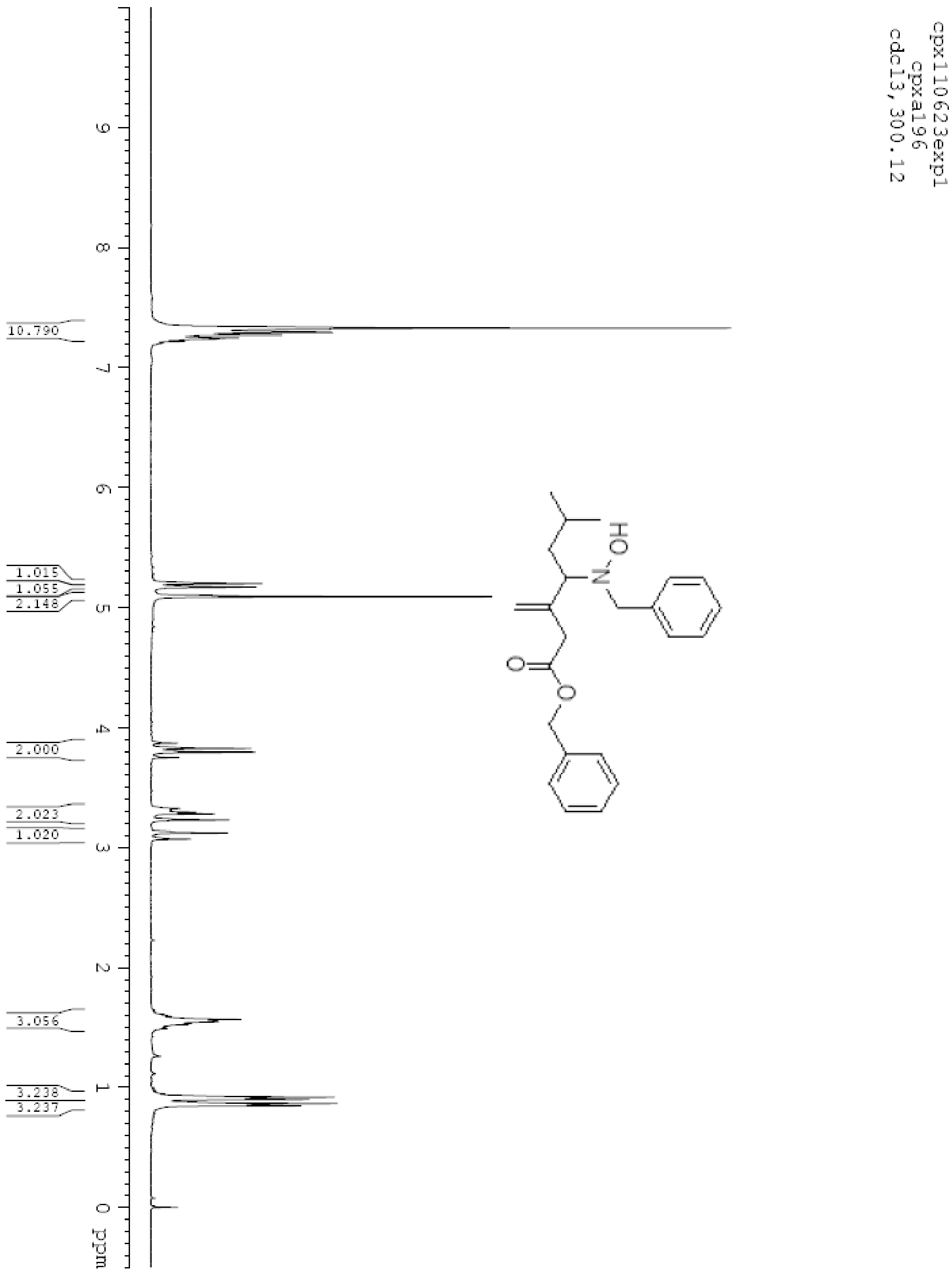
Compound **4ca**:



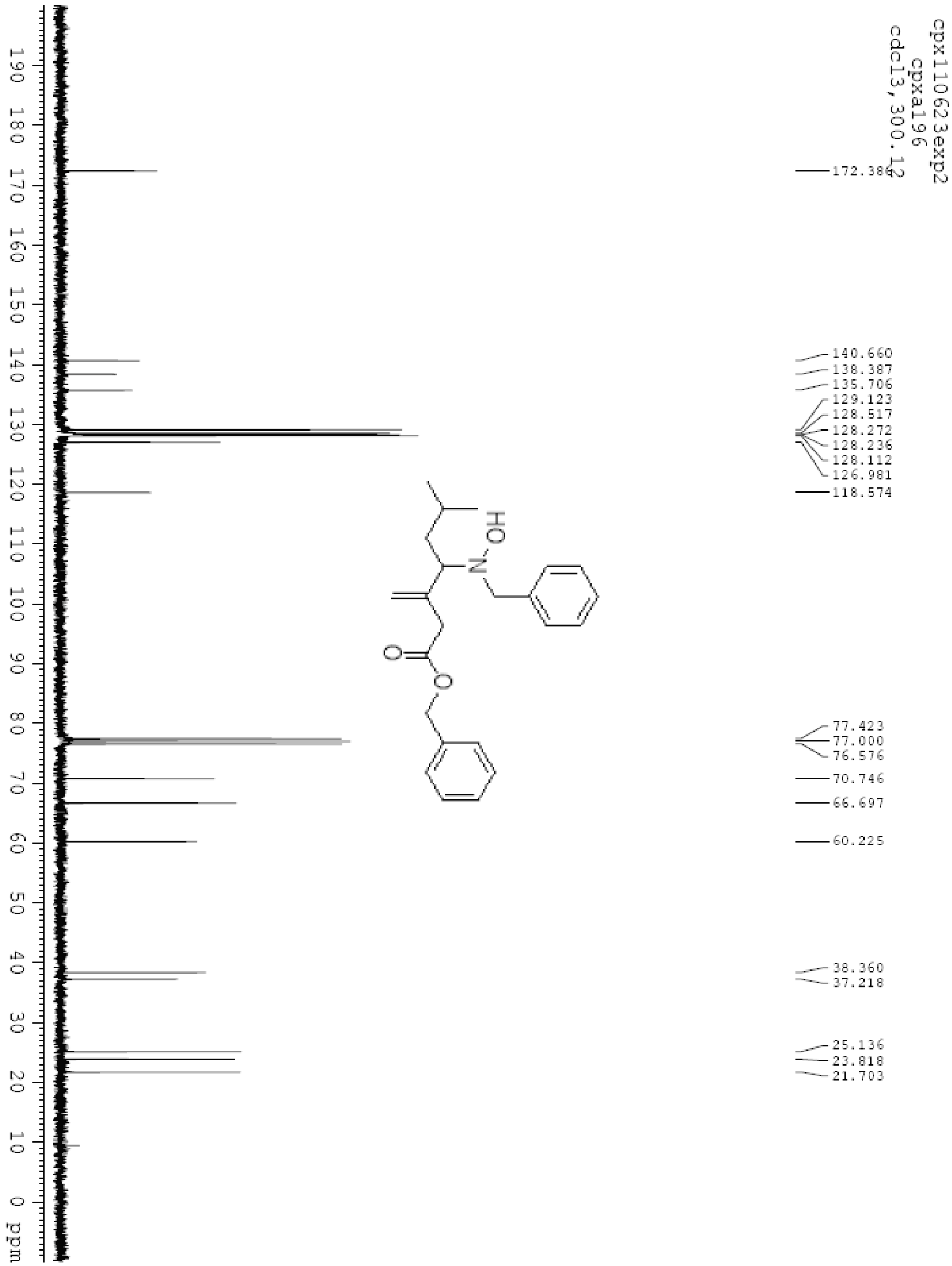
Compound **4ca**:



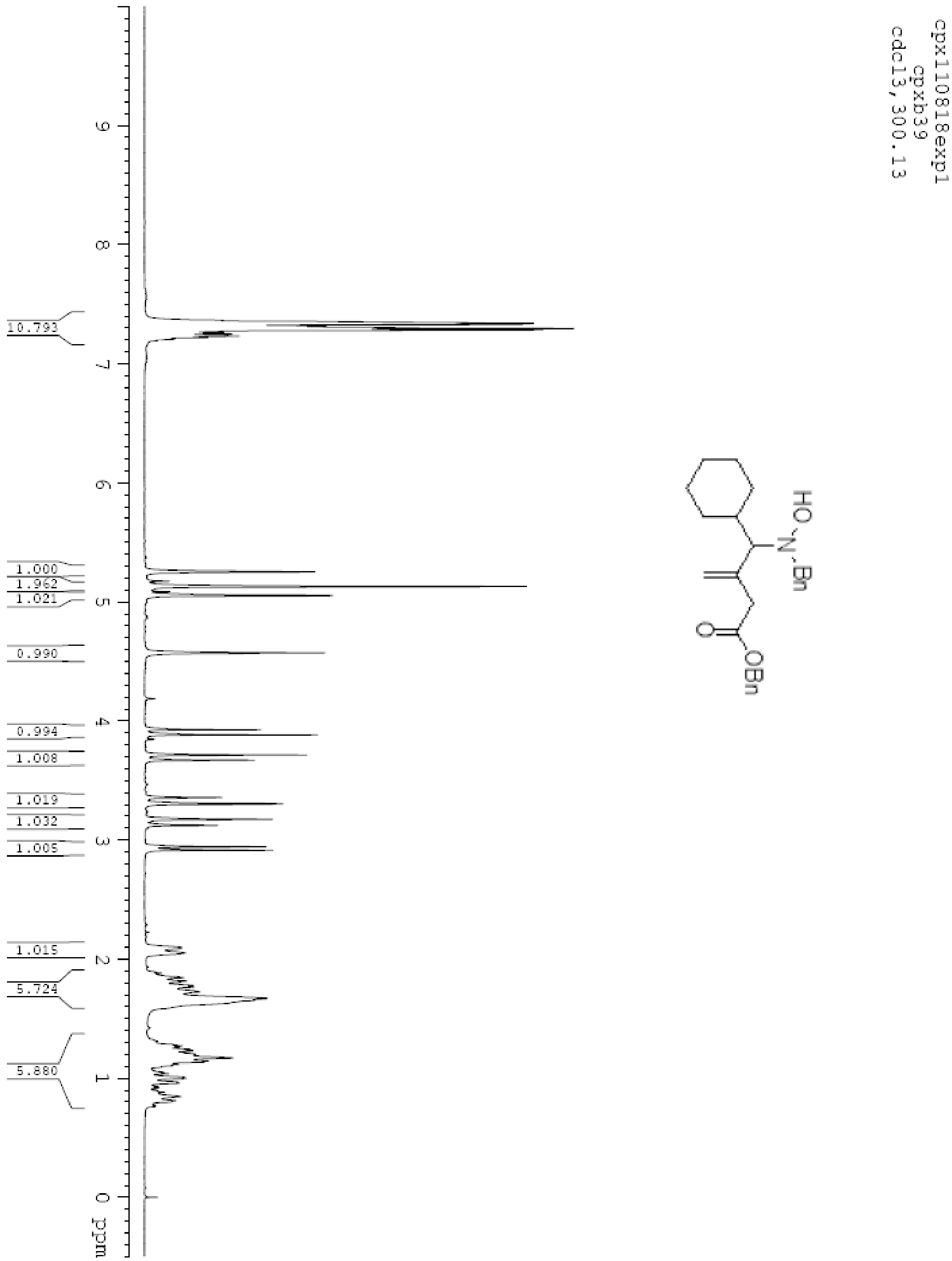
Compound **4da**:



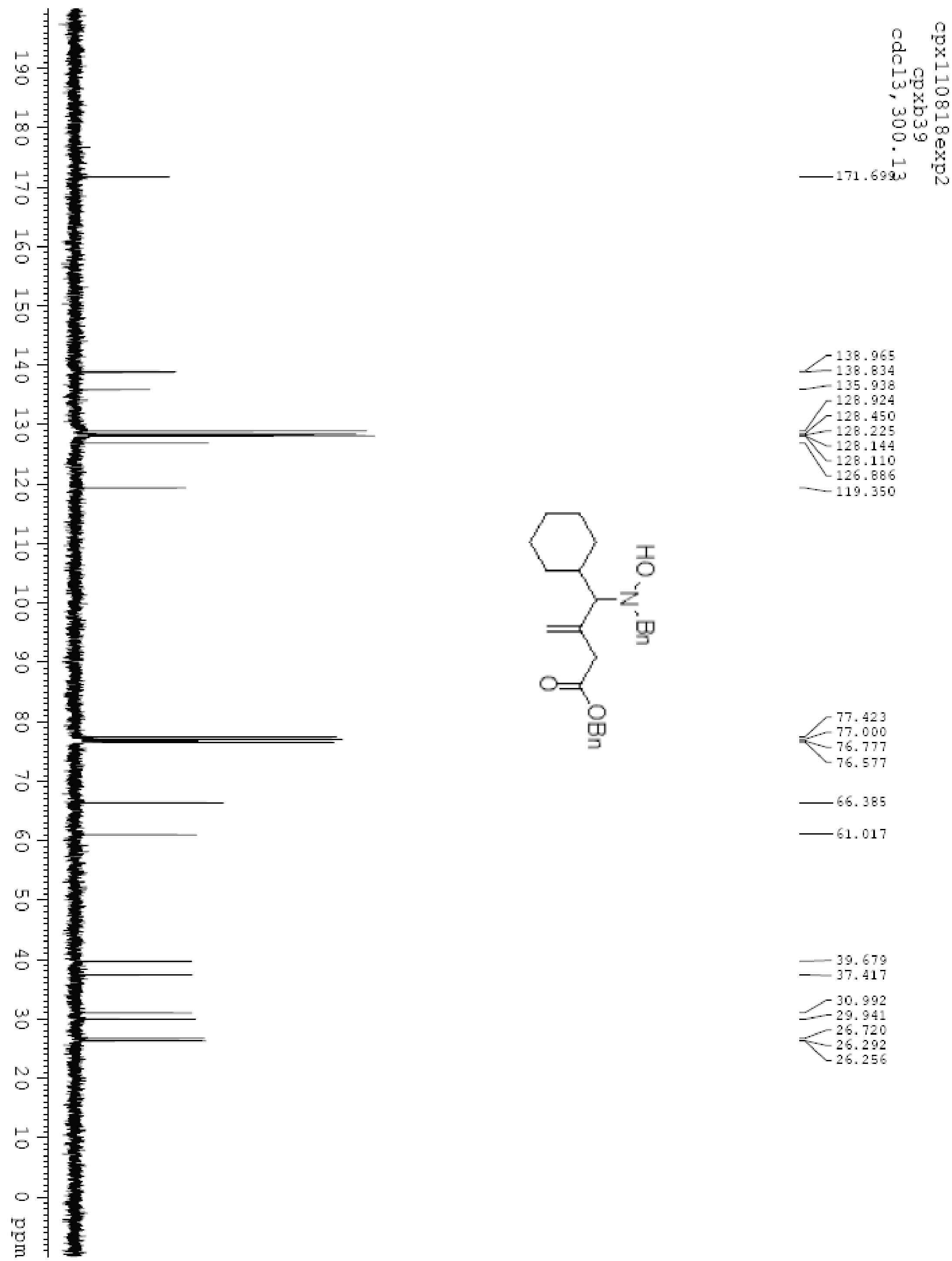
Compound **4da**:



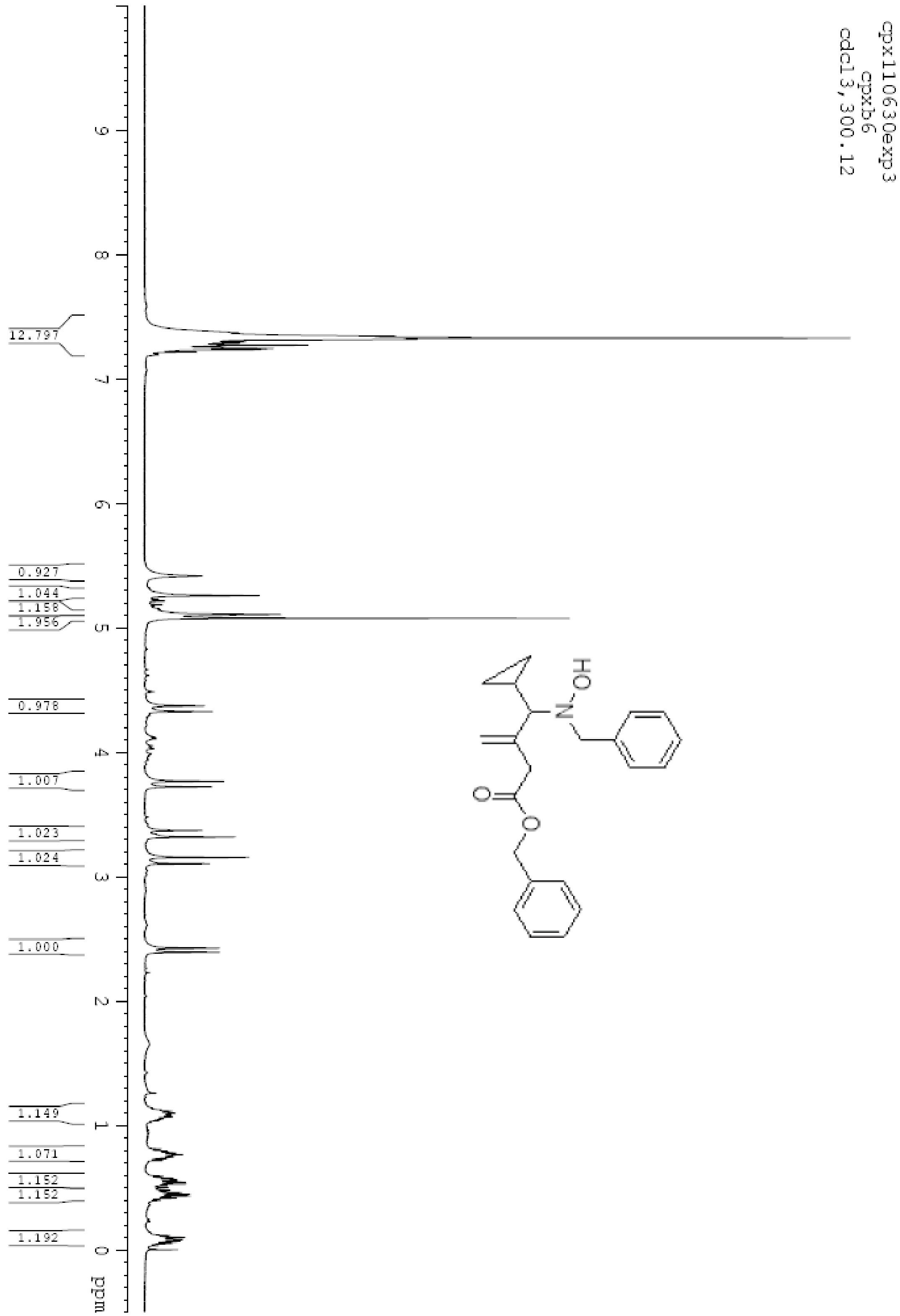
Compound **4ea**:



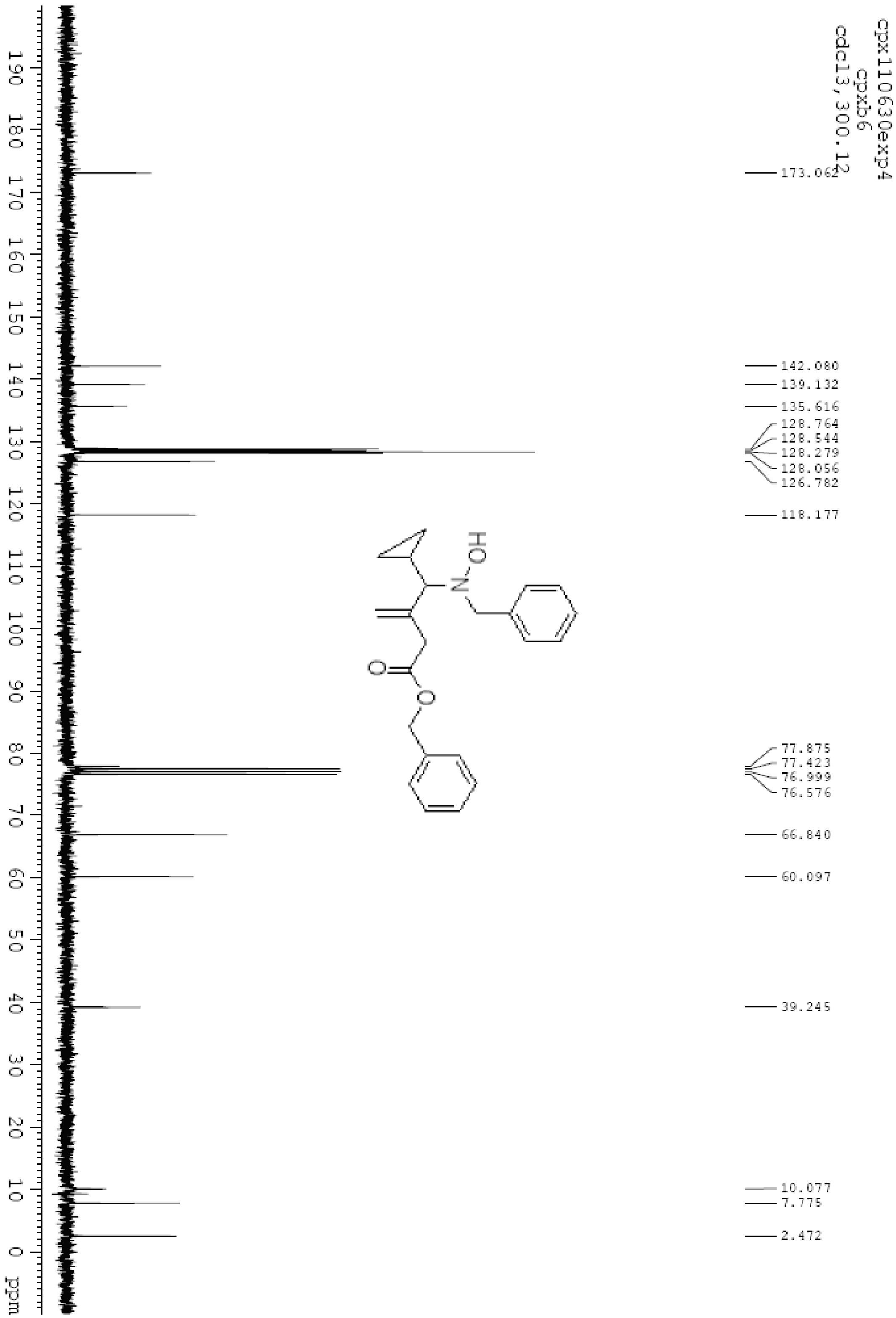
Compound **4ea**:



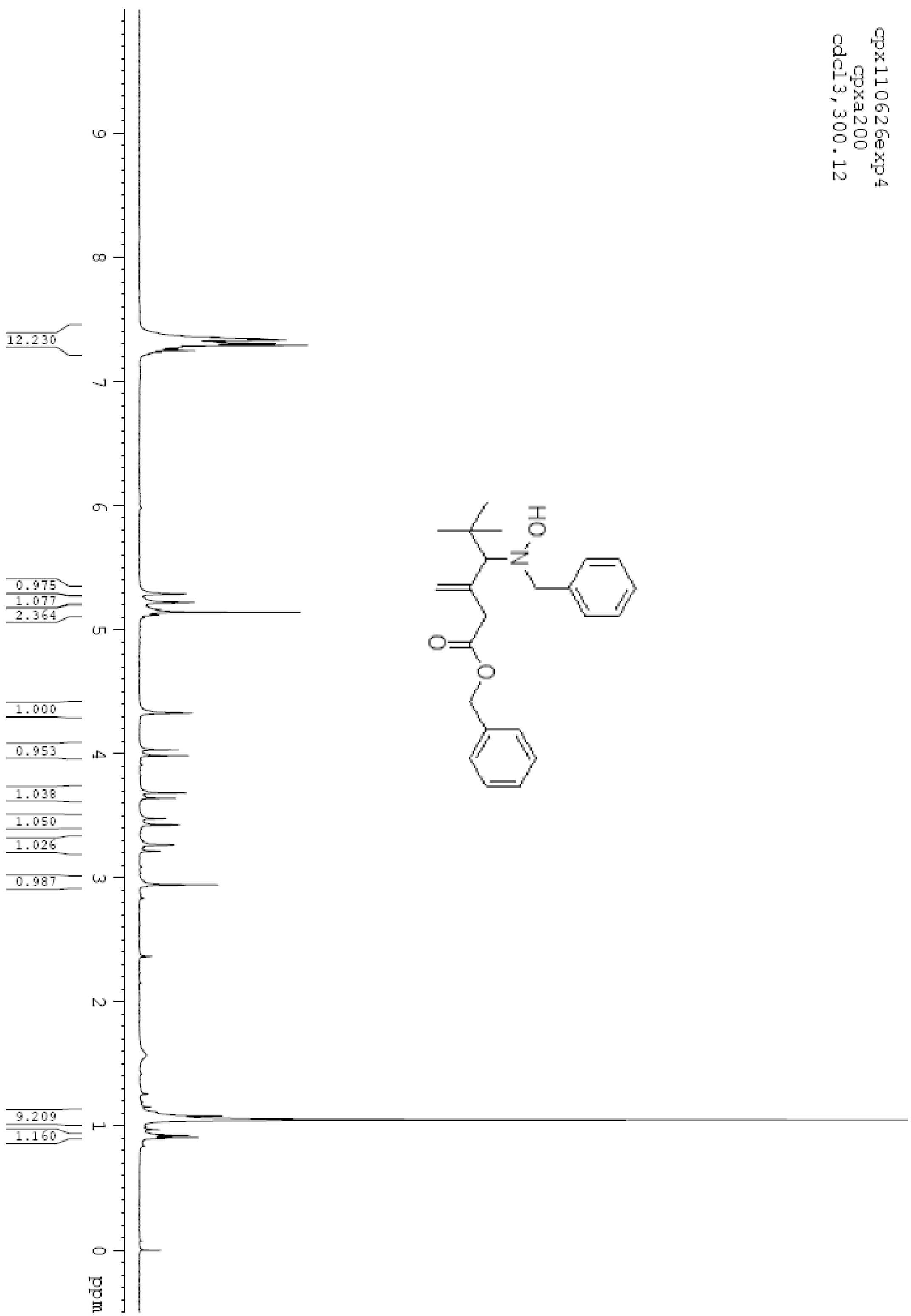
Compound **4fa**:



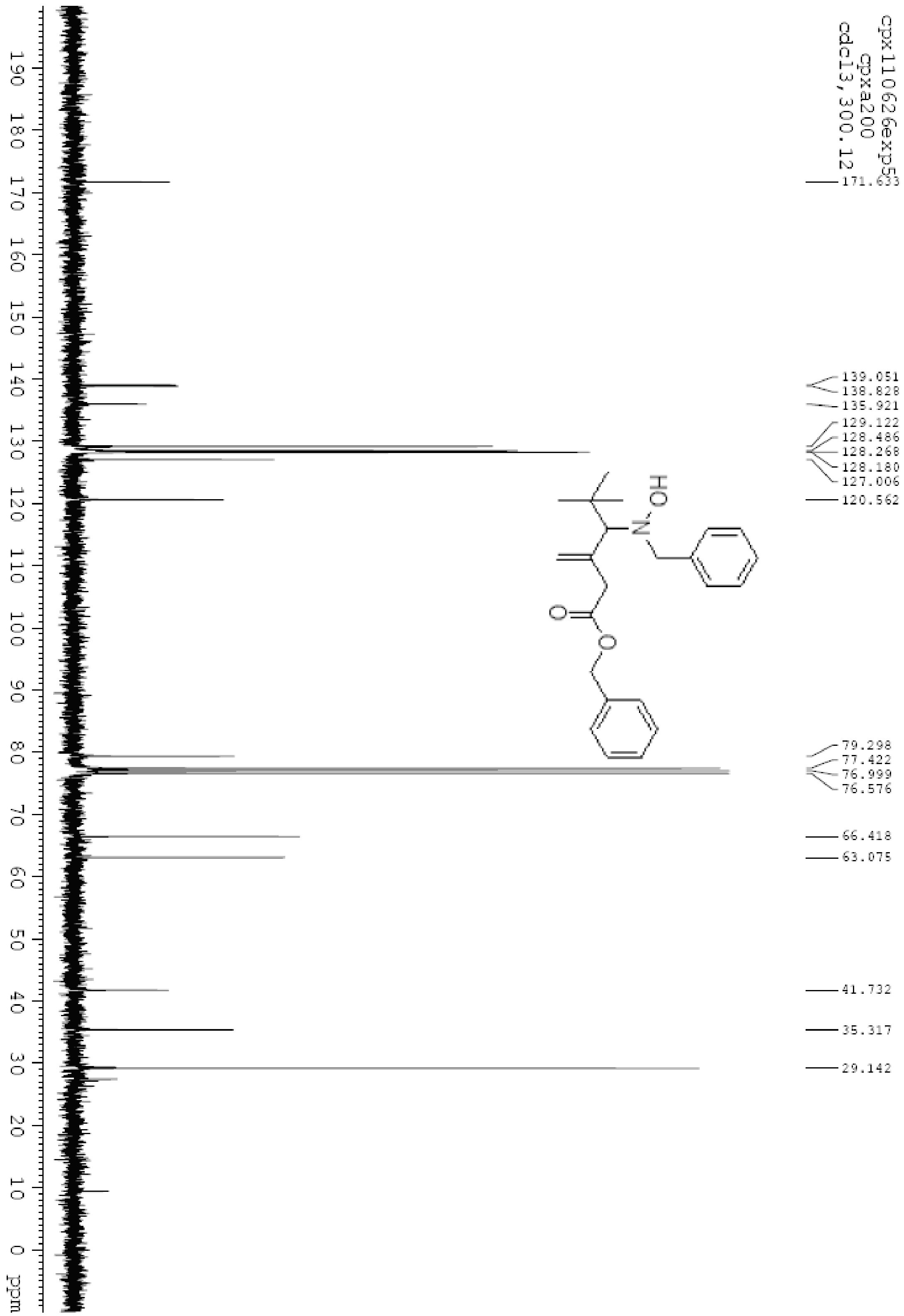
Compound **4fa**:



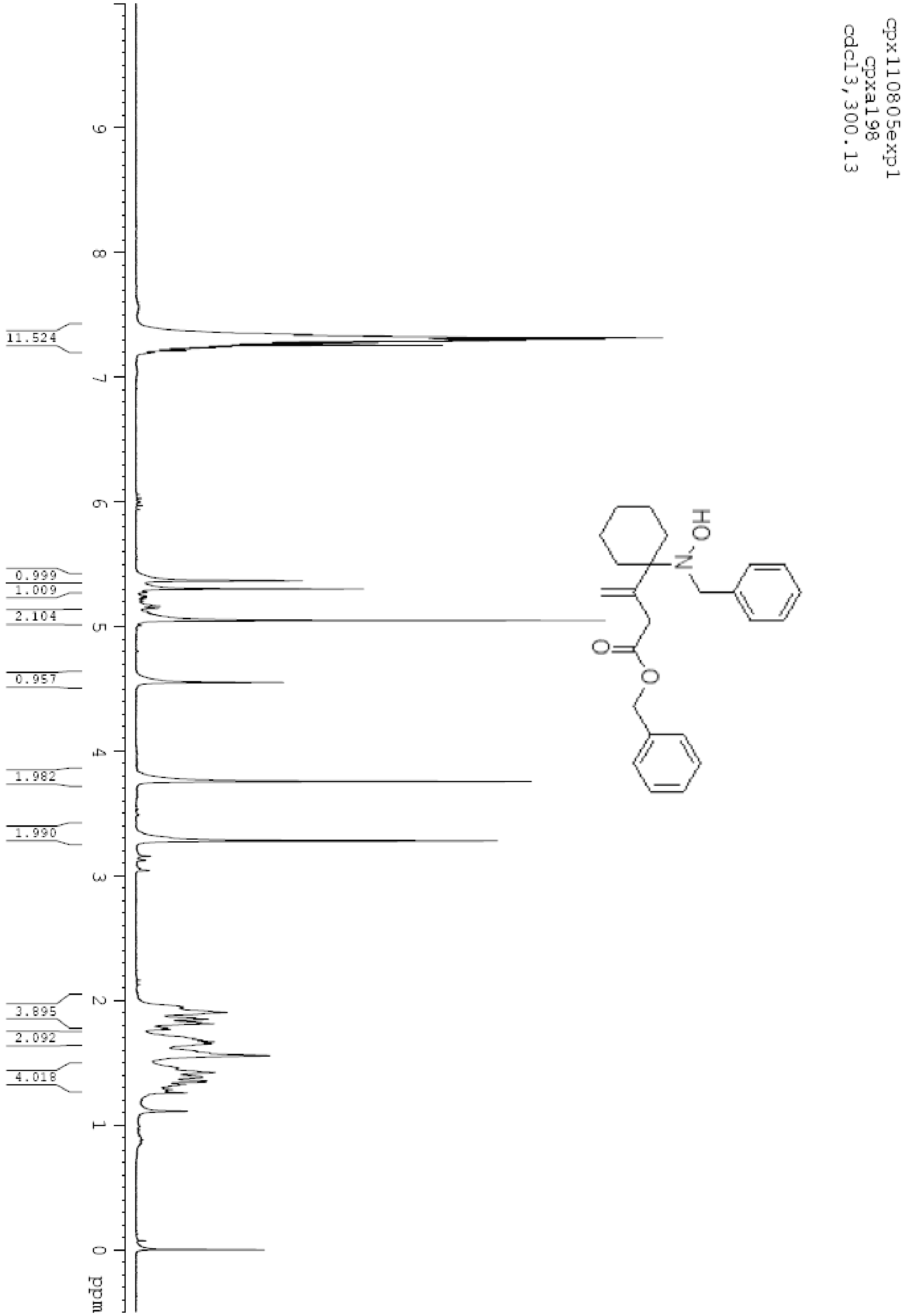
Compound **4ga**:



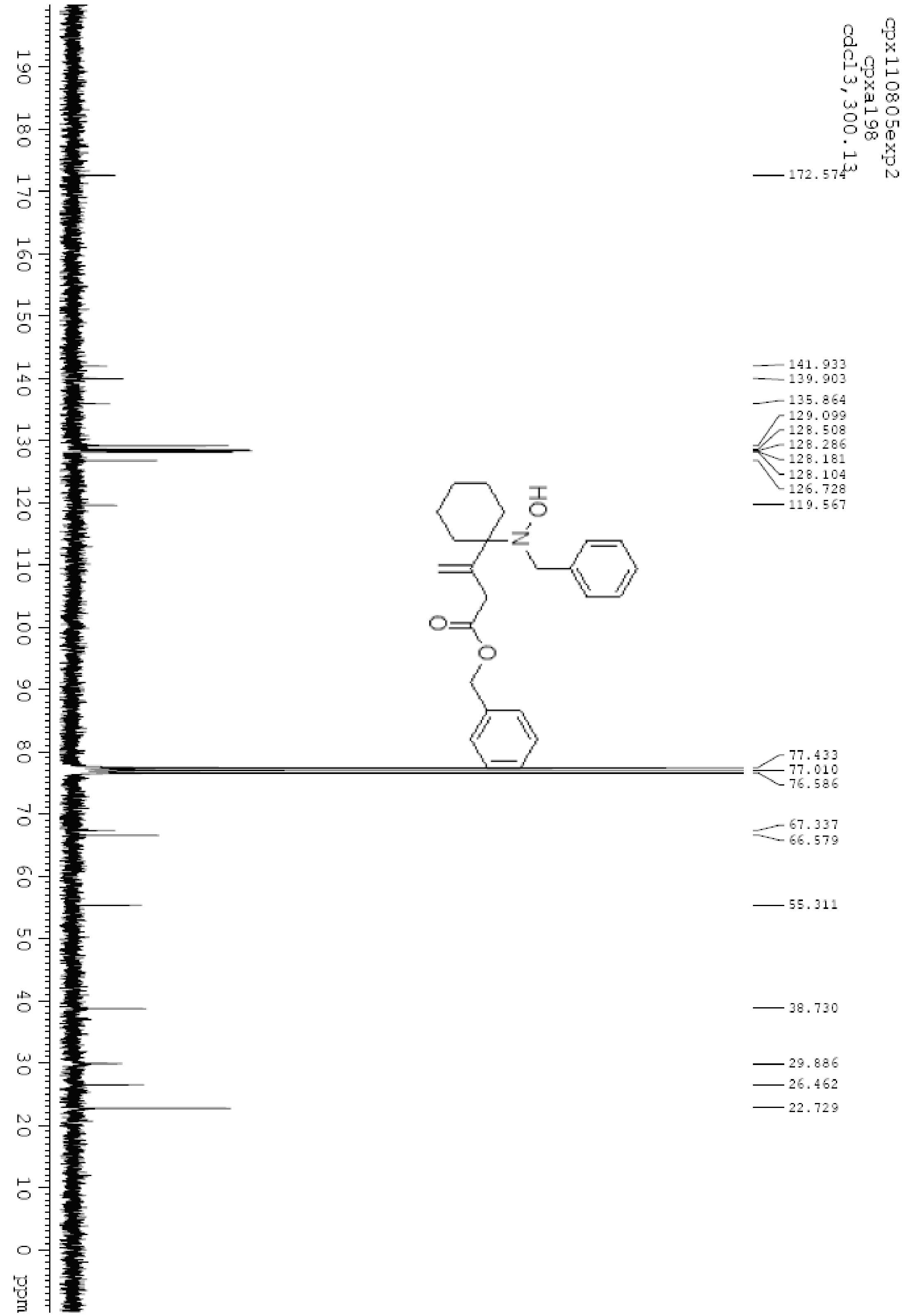
Compound **4ga**:



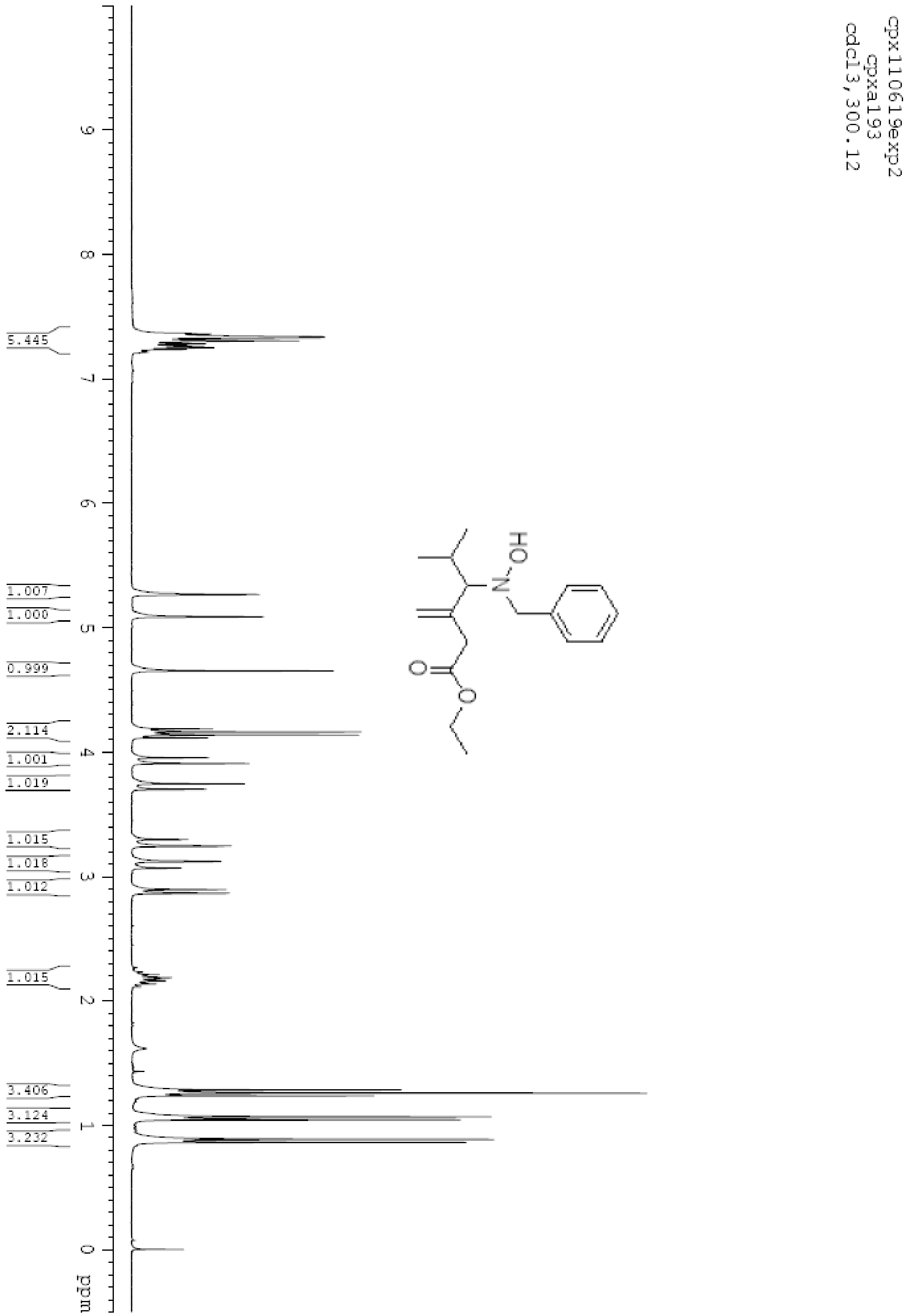
Compound **4ha**:



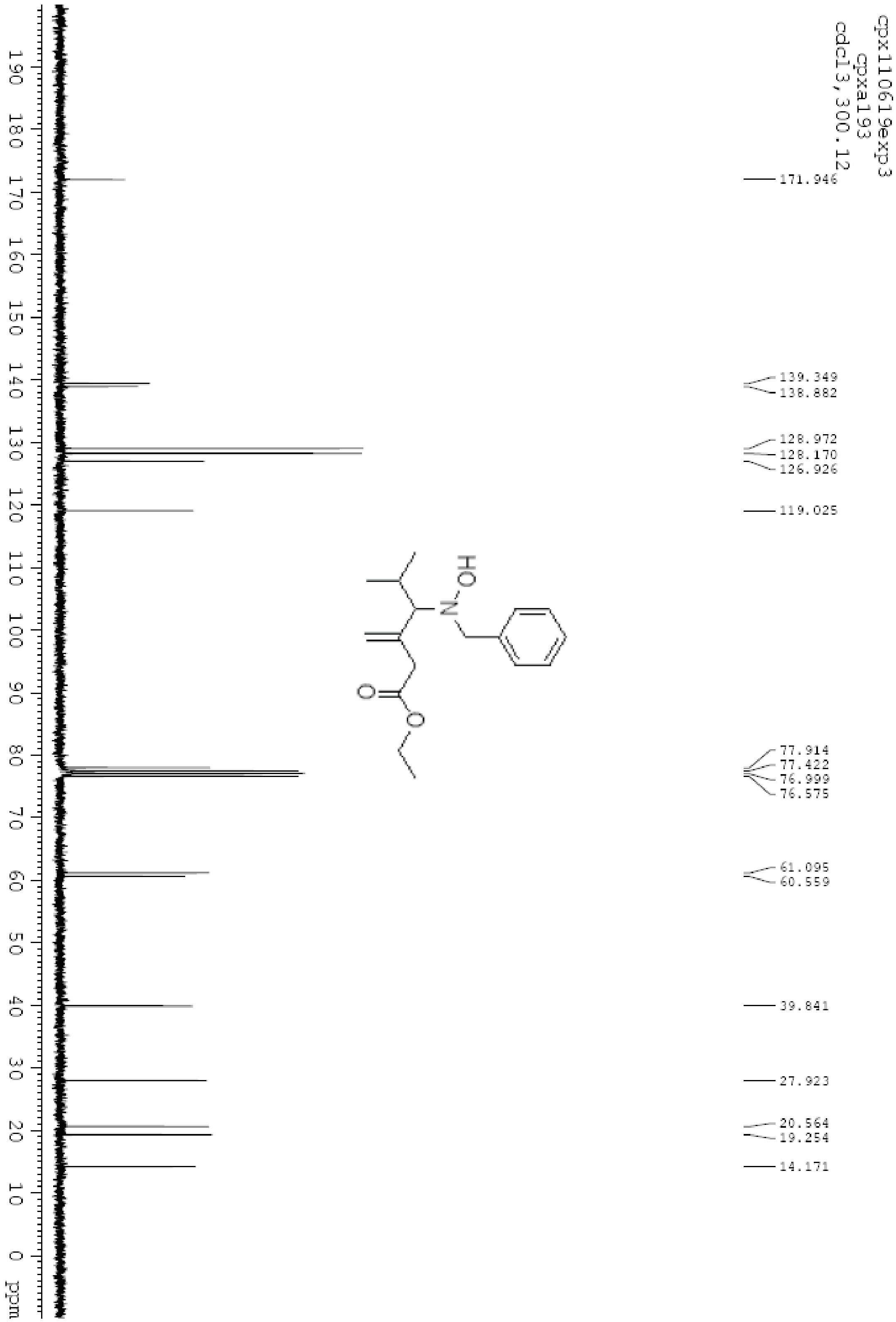
Compound **4ha**:



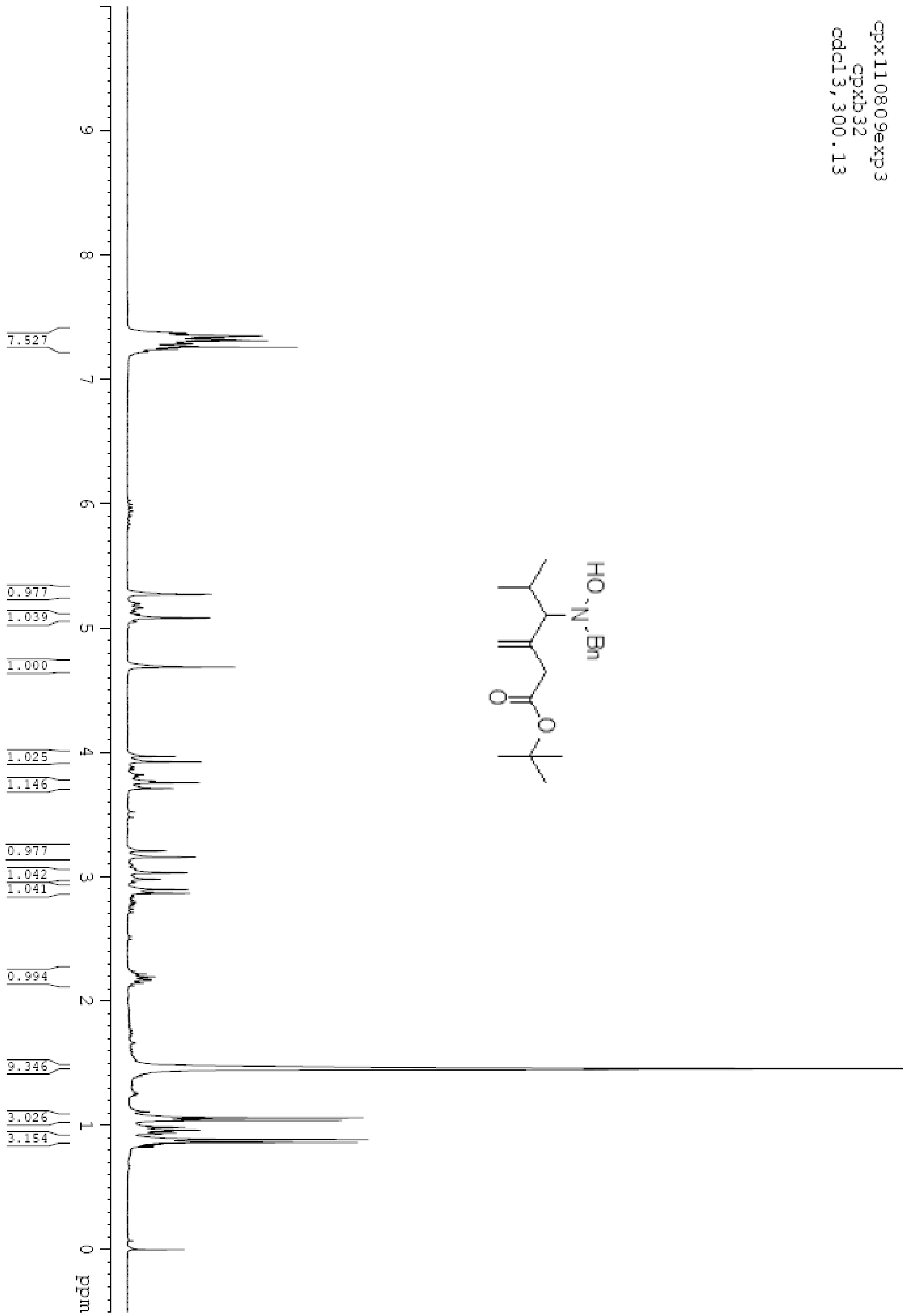
Compound **4ab**:



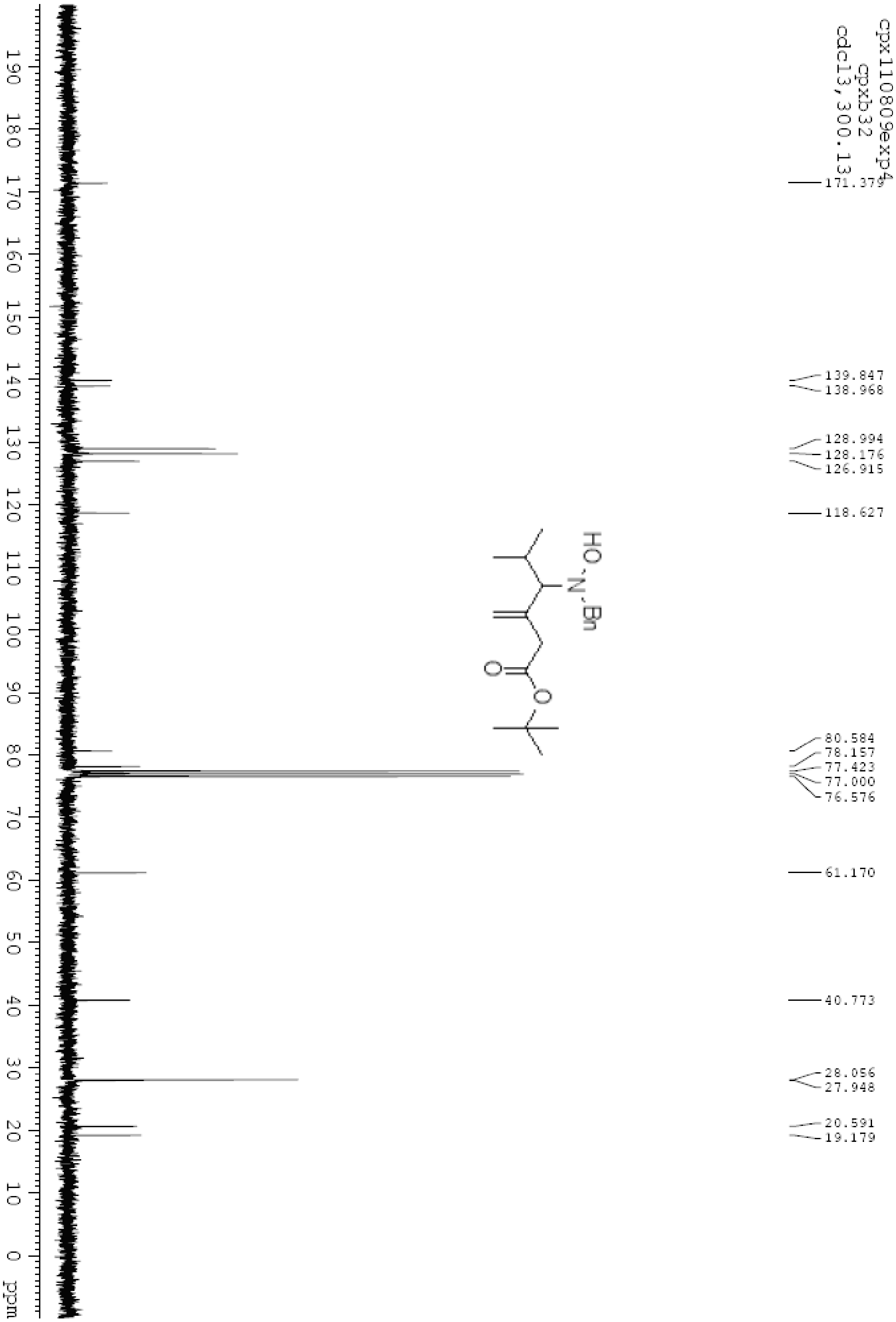
Compound **4ab**:



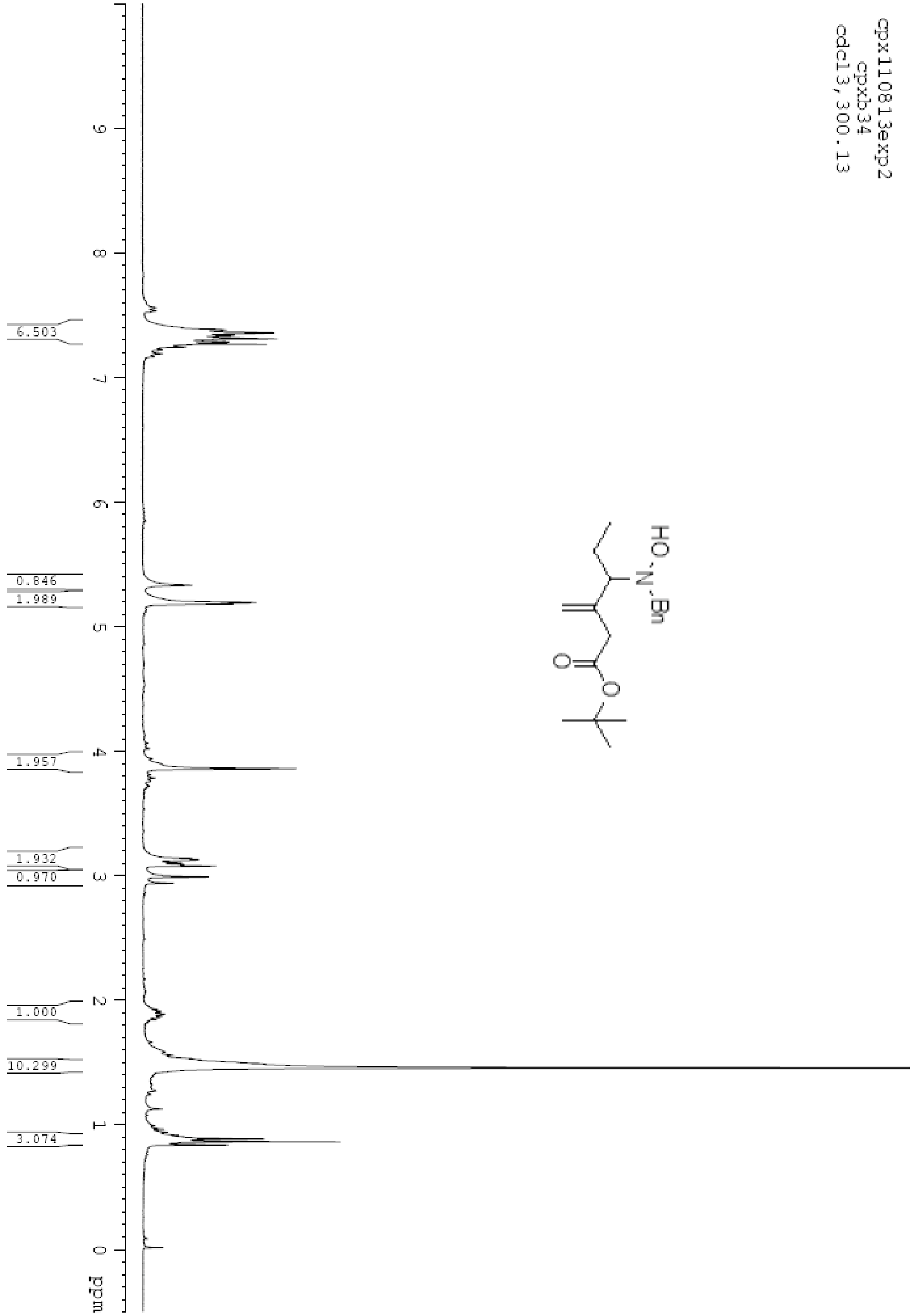
Compound **4ac**:



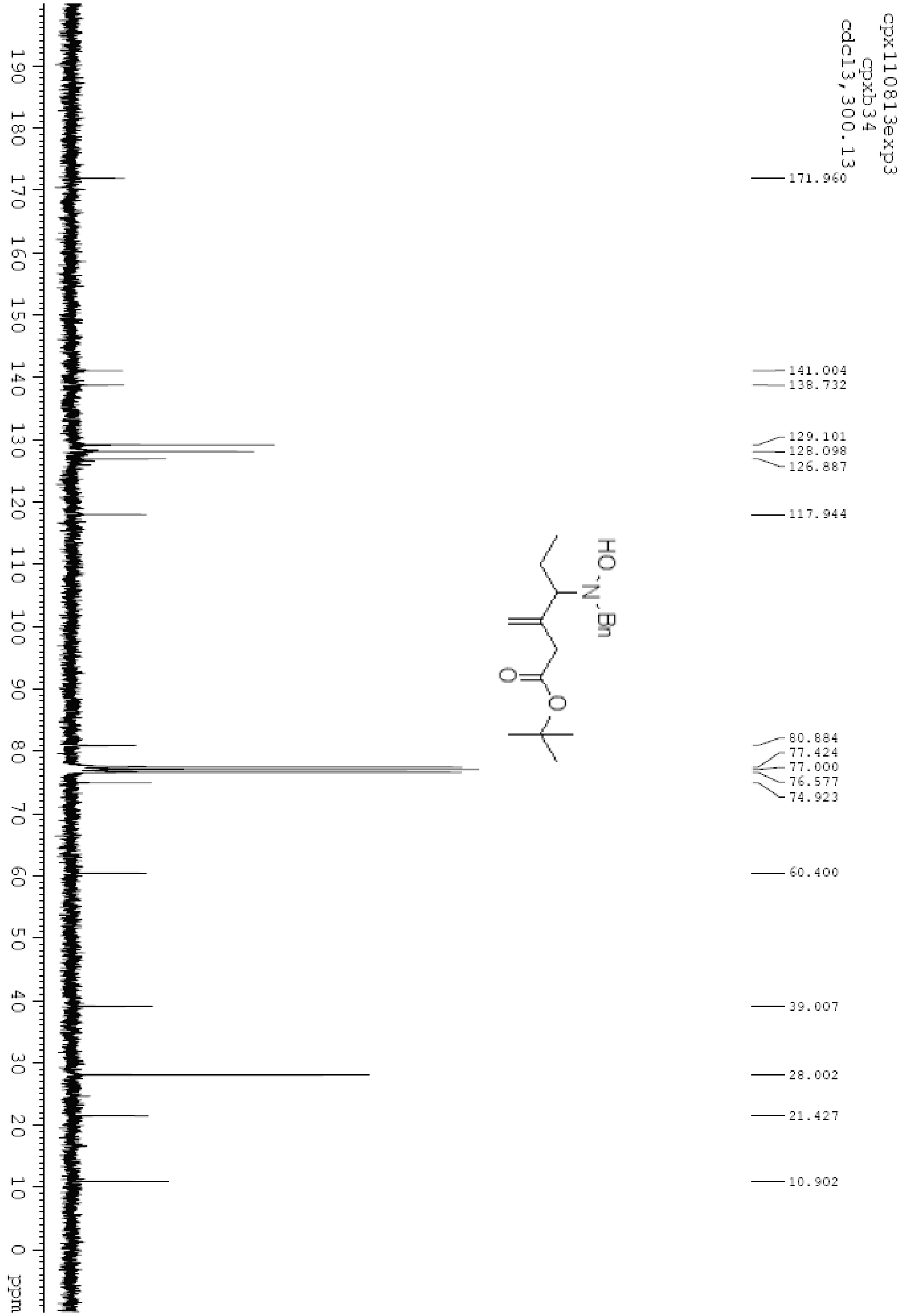
Compound **4ac**:



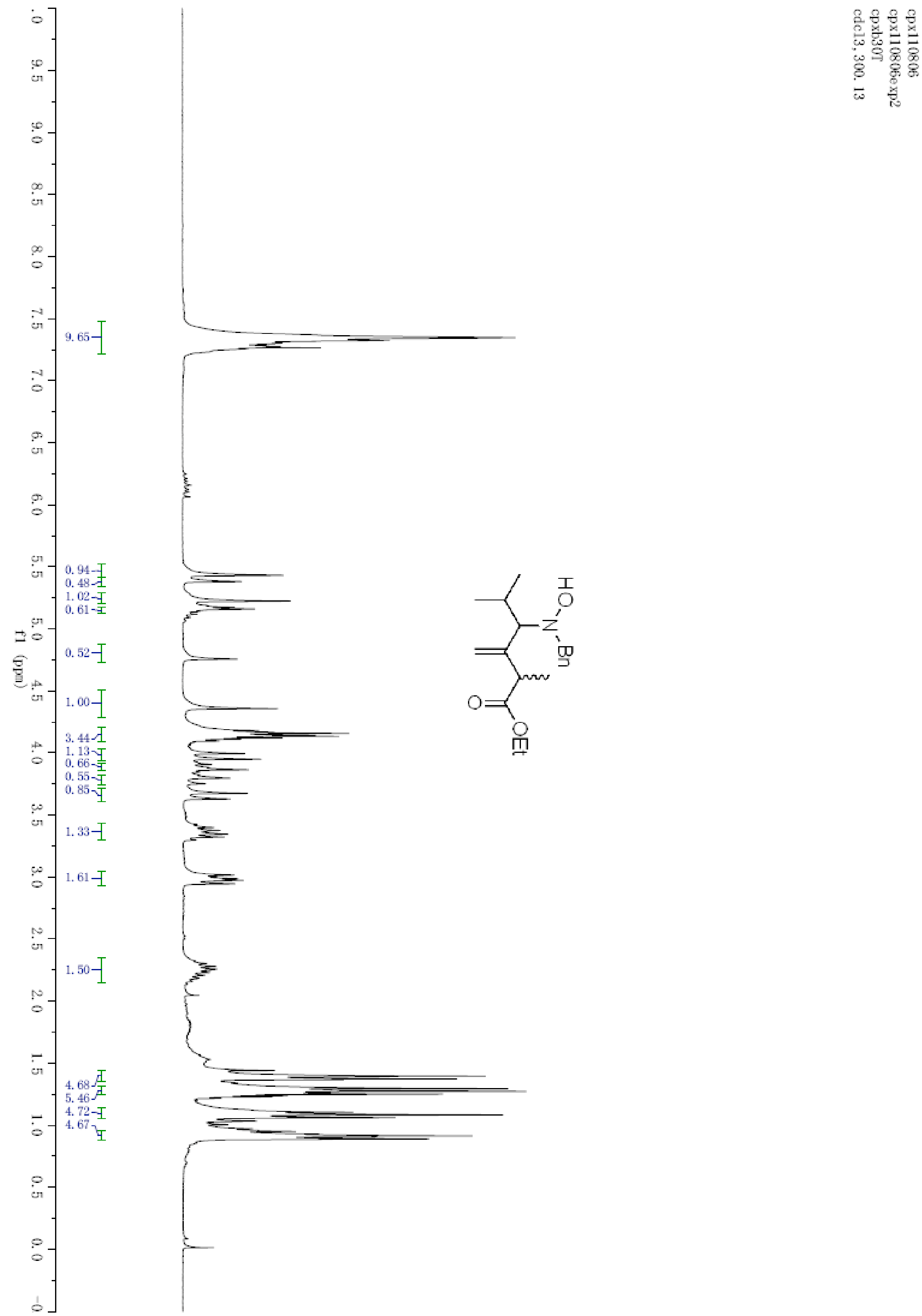
Compound **4cc**:



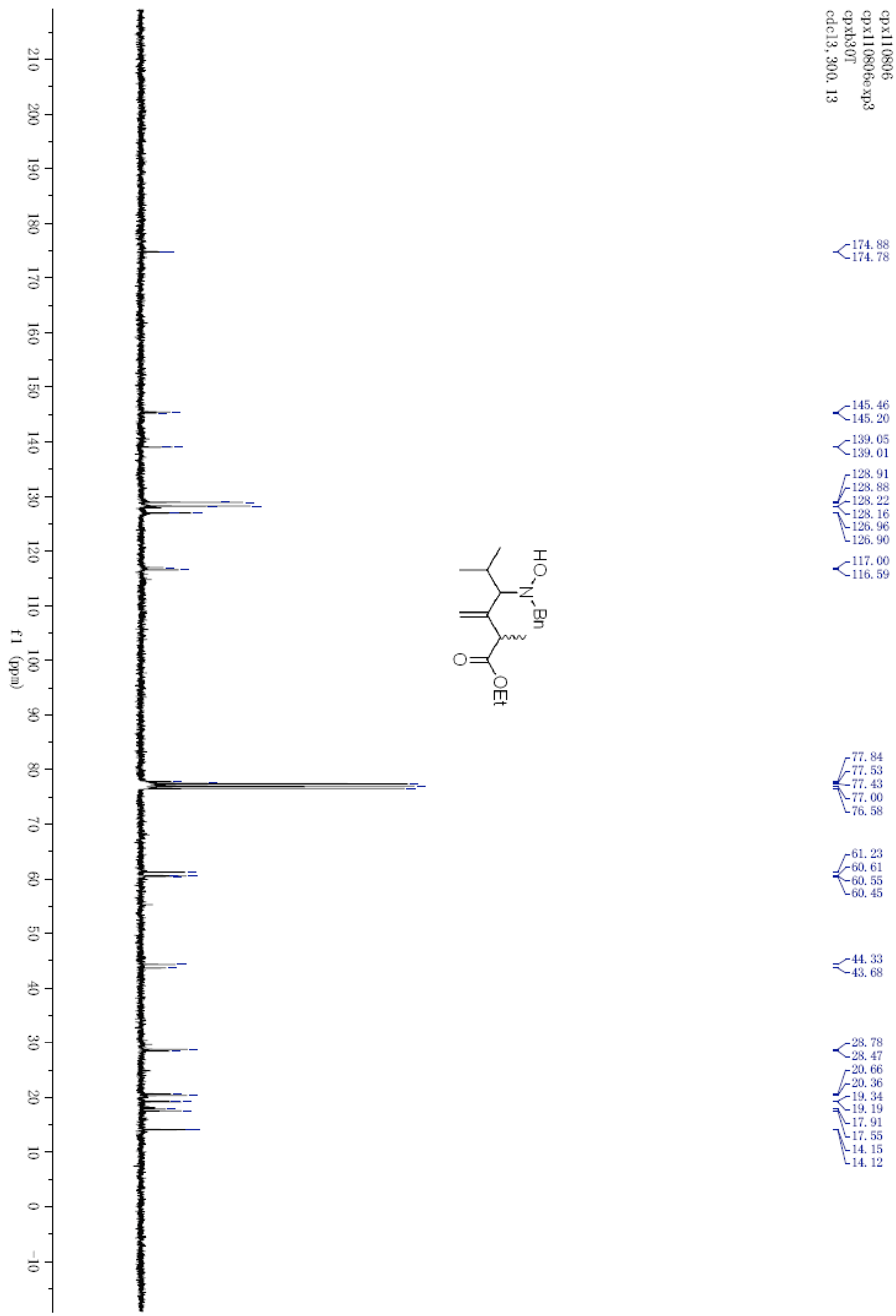
Compound **4cc**:



Compound **8**:

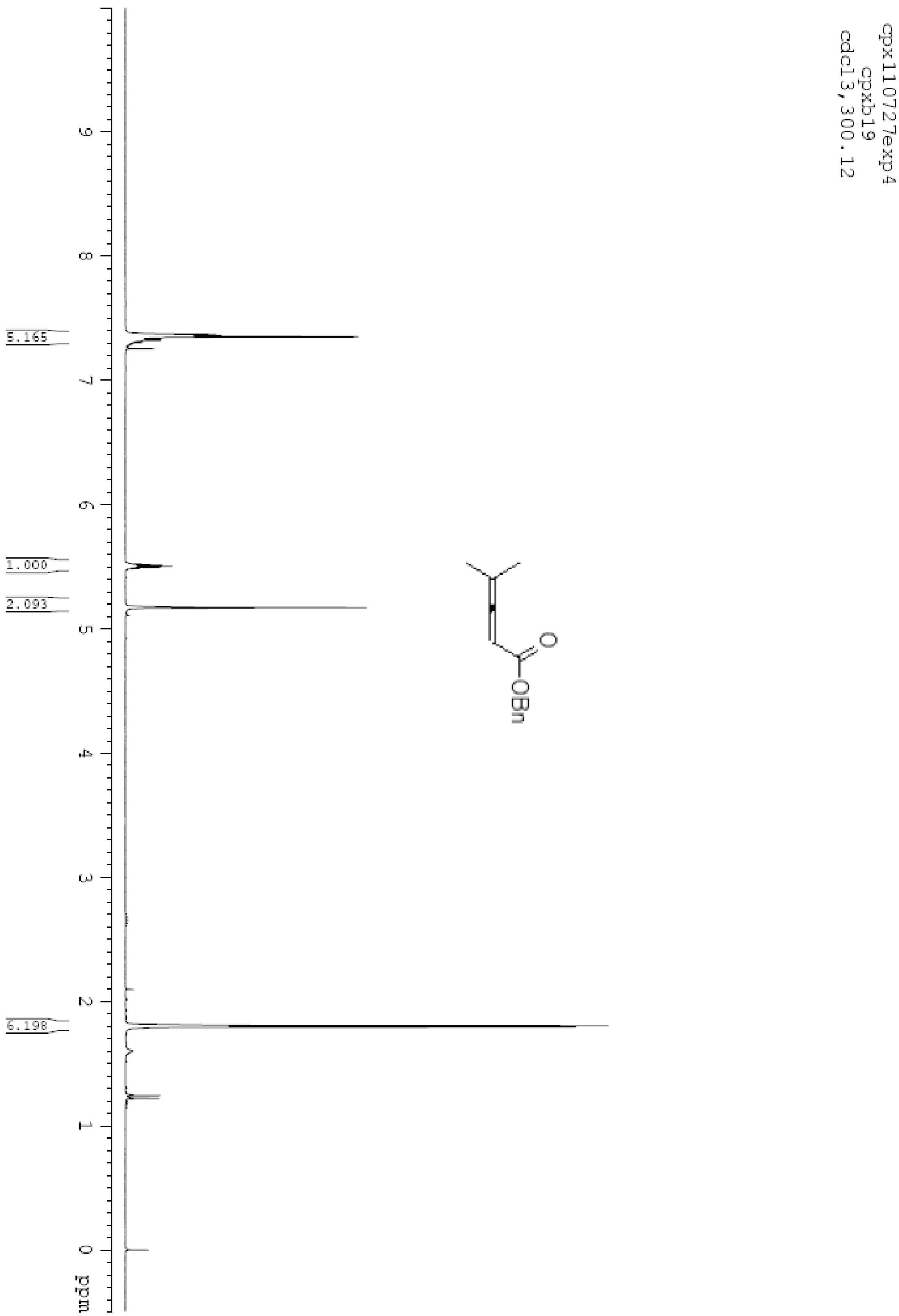

cpx110806
cpx110806exp2
cpxb30T
cdcl3, 300.13
f1 (ppm)
HO
N
Bn
O
OEt

Compound **8**:

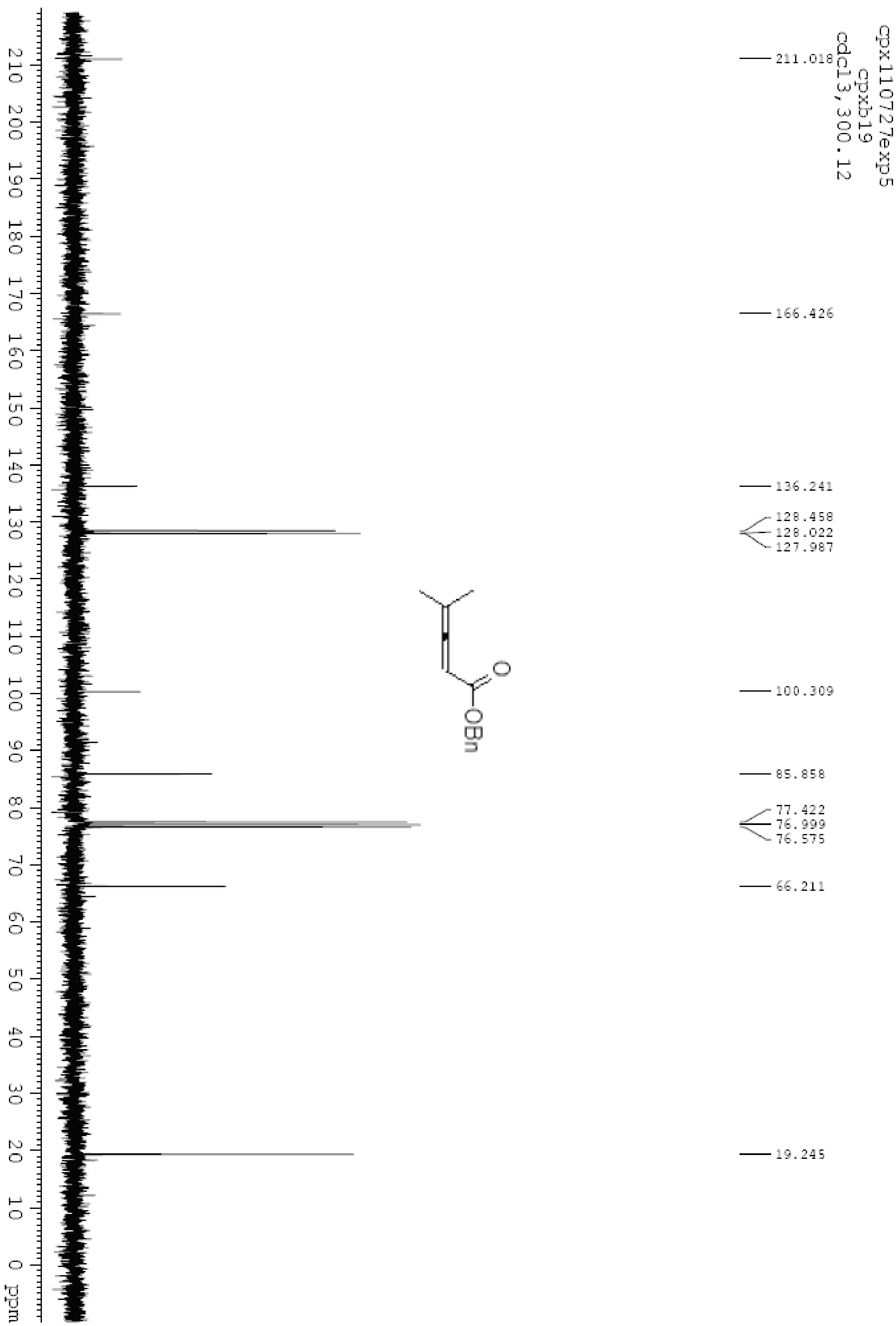


cpx110806
cpx110806exp3
cpxb30T
cdcl3,300.13
174.88
174.78
145.46
145.20
139.05
139.01
128.91
128.88
128.22
128.16
126.96
126.90
117.00
116.59
77.84
77.53
77.43
77.00
76.58
61.23
60.61
60.55
60.45
44.33
43.68
28.78
28.47
20.66
20.36
19.34
19.19
17.91
17.55
14.15
14.12
HO
N
Bn
O
OEt
f1 (ppm)

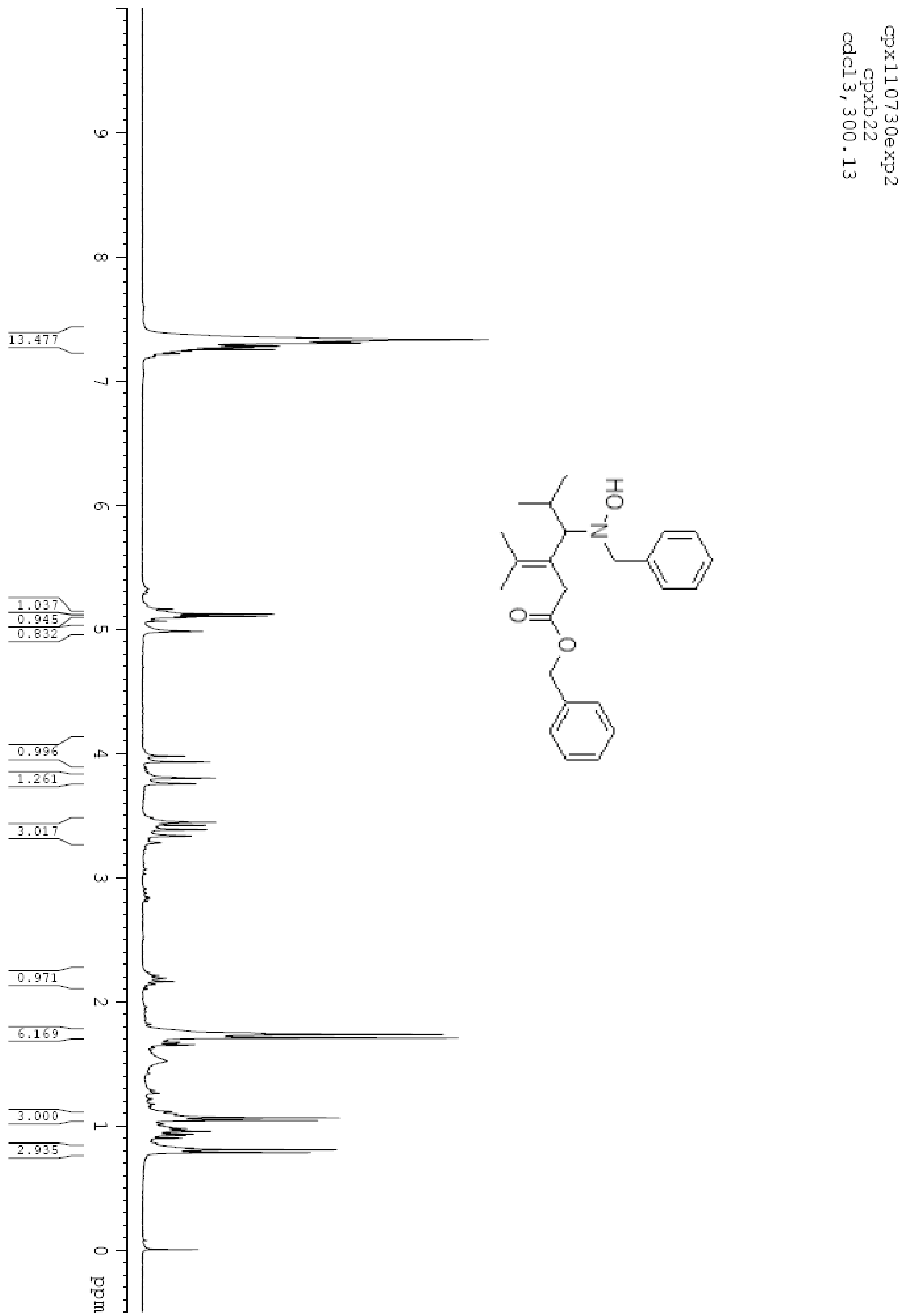
Compound **9**:


cpx110727exp4
cpxb19
cdcl3,300.12
5.165
1.000
2.093
6.198
O
OBn
ppm

Compound **9**:

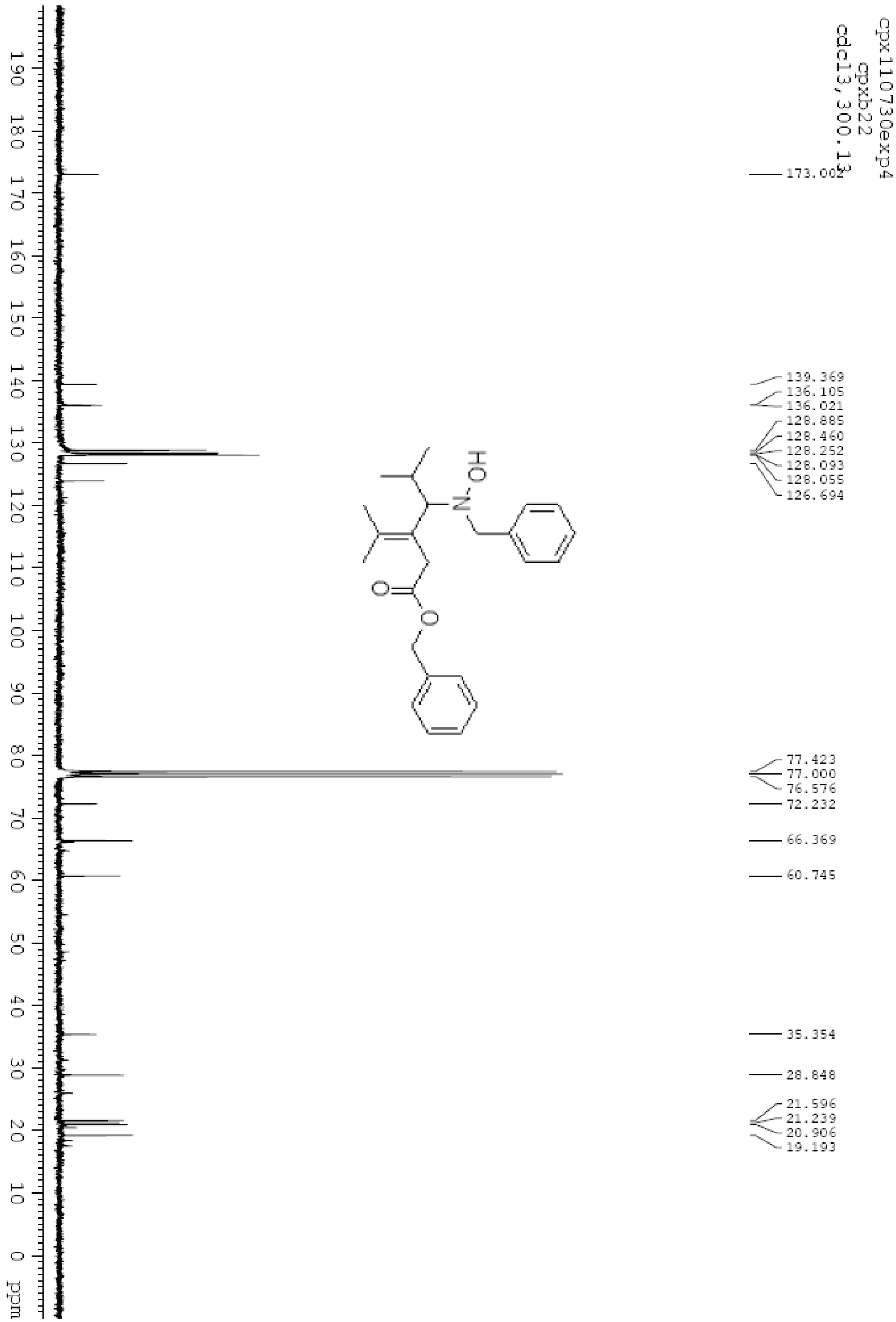

cpx110727exp5
cpxb19
cdcl3,300.12
211.018
166.426
136.241
128.458
128.022
127.987
100.309
85.858
77.422
76.999
76.575
66.211
19.245
O
OBn
ppm

Compound **10**:

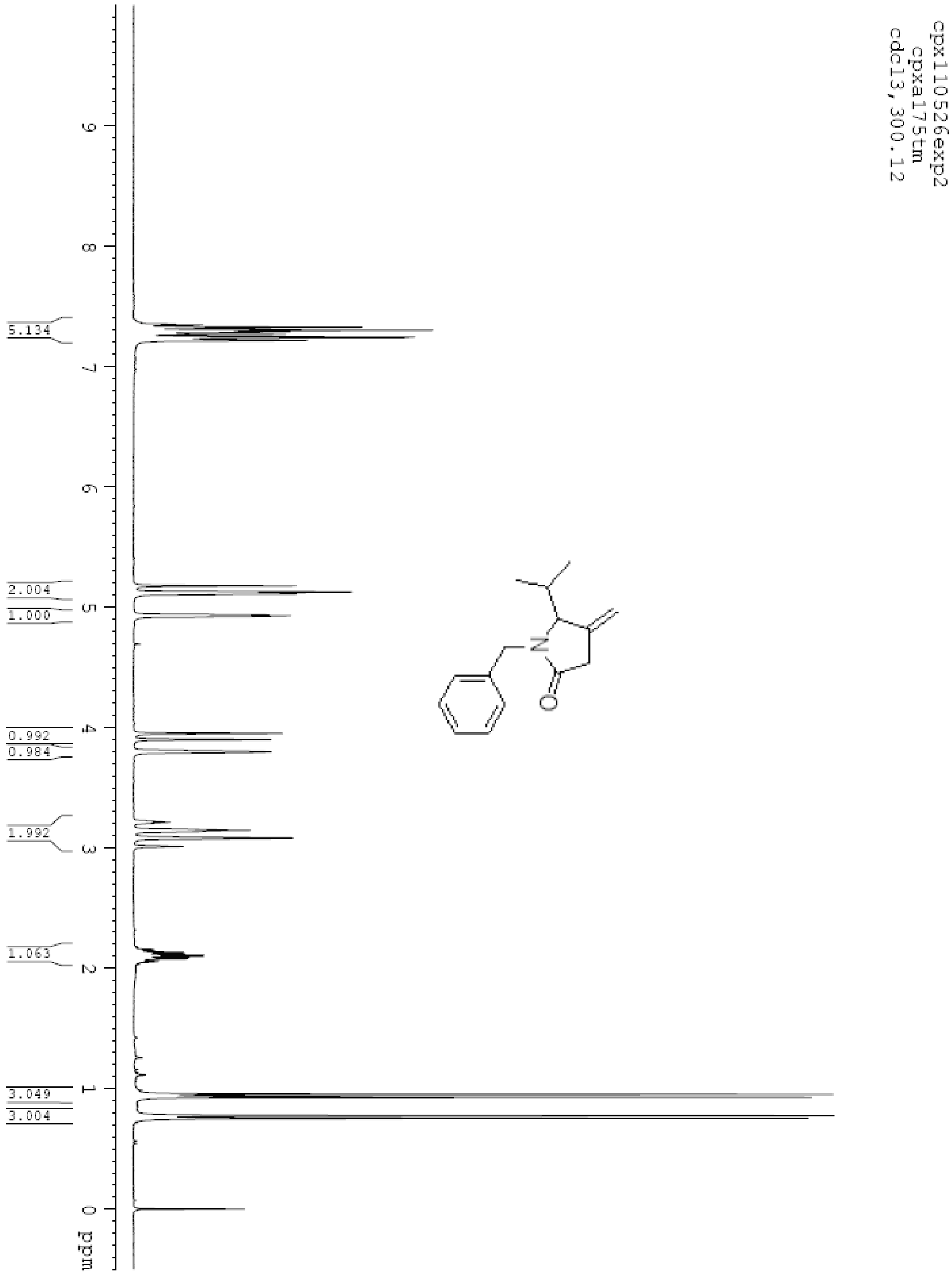


cpx110730exp2
cpxb22
cdcl3,300.13
HO
N
O
O
13.477
1.037
0.945
0.832
0.996
1.261
3.017
0.971
6.169
3.000
2.935
9
8
7
6
5
4
3
2
1
0
ppm

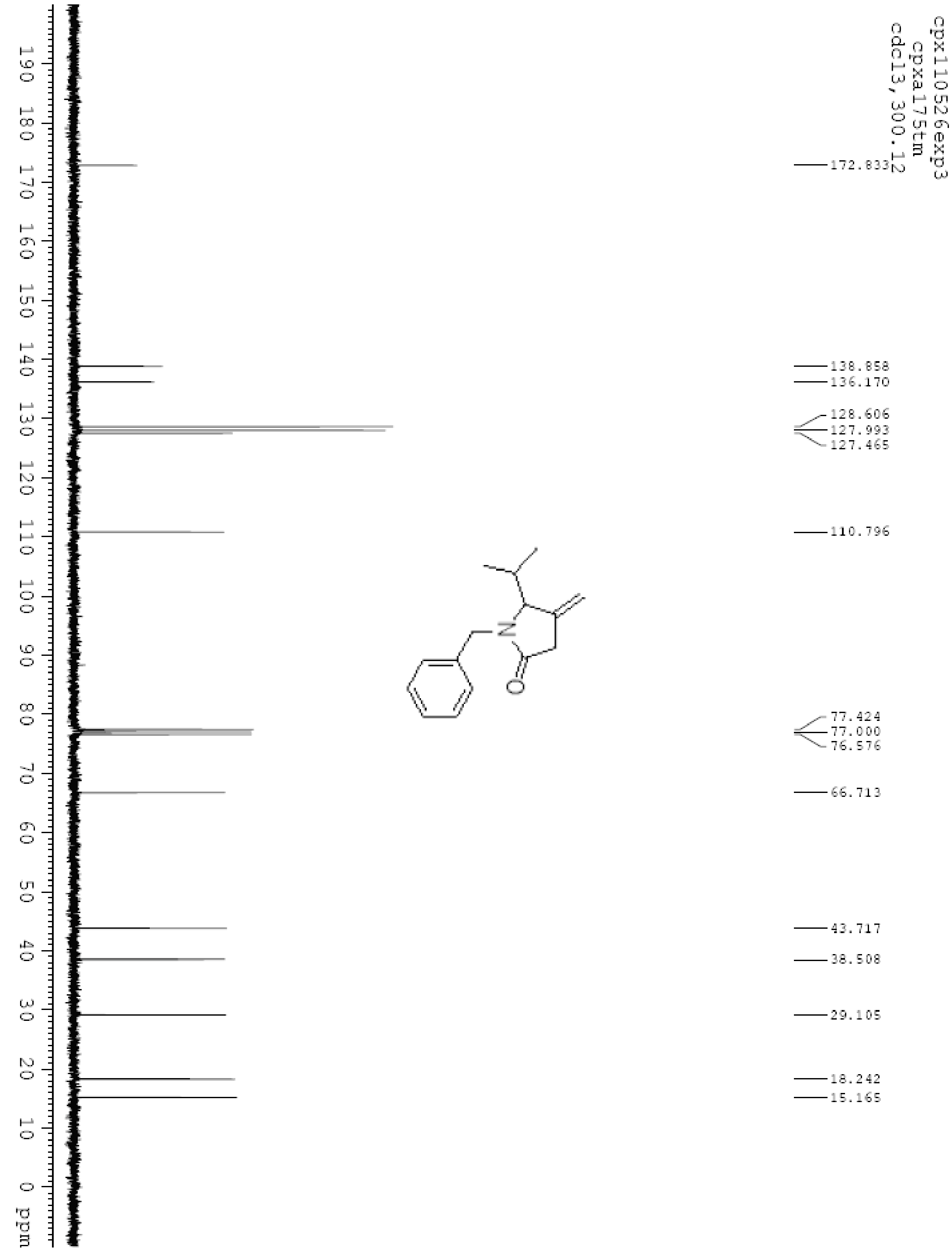
Compound **10**:


cpx110730exp4
cpxb22
cdcl3,300.13
173.002
139.369
136.105
136.021
128.885
128.460
128.252
128.093
128.055
126.694
77.423
77.000
76.576
72.232
66.369
60.745
35.354
28.848
21.596
21.239
20.906
19.193
HO
N
O
O
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

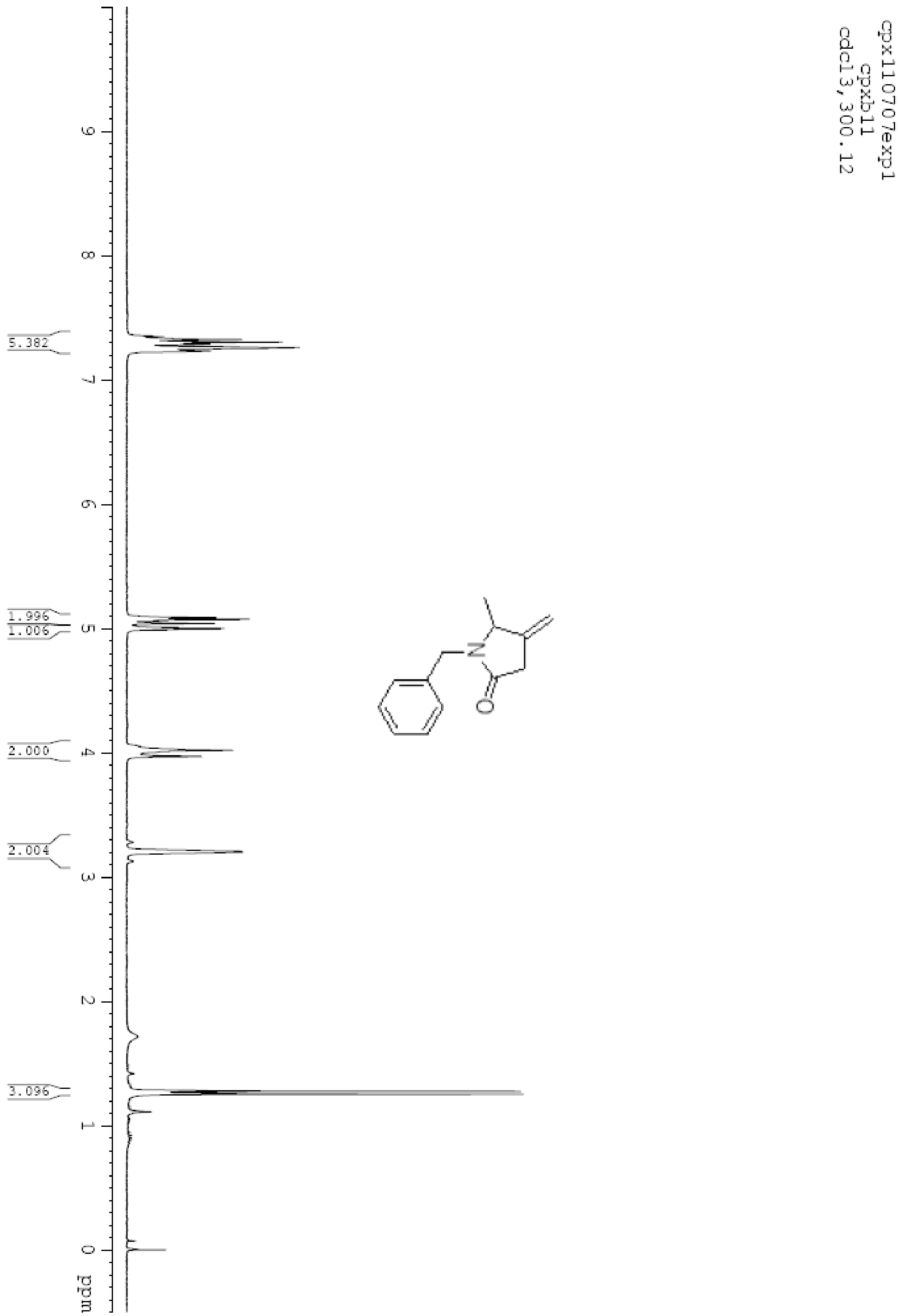
Compound **5a**:


cpx110526exp2
cpxa175tm
cdcl3,300.12
5.134
2.004
1.000
0.992
0.984
1.992
1.063
3.049
3.004
ppm

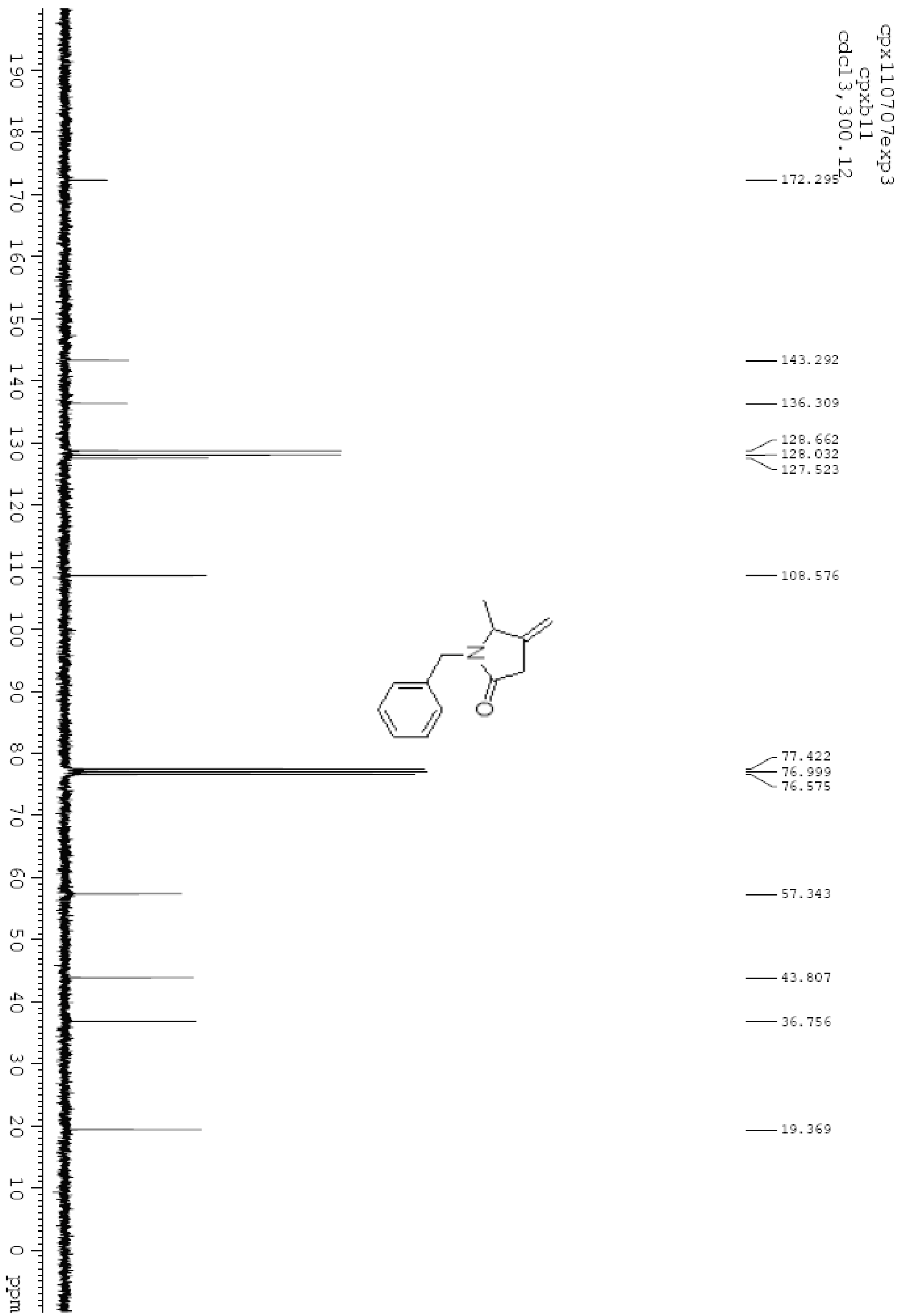
Compound **5a**:


cpx110526exp3
cpxa175tm
cdcl3,300.12
172.833
138.858
136.170
128.606
127.993
127.465
110.796
77.424
77.000
76.576
66.713
43.717
38.508
29.105
18.242
15.165
ppm

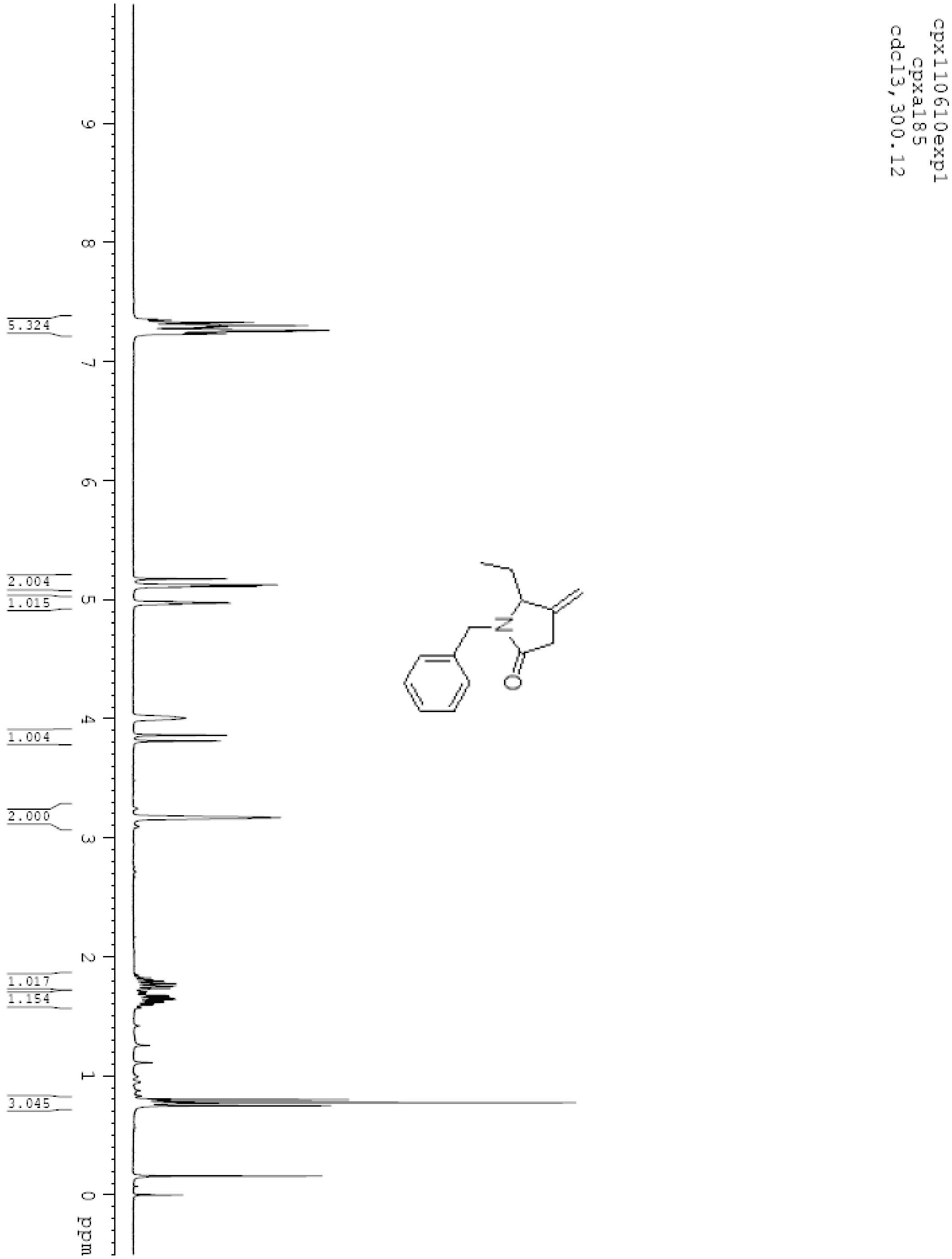
Compound **5b**:


cpx110707exp1
cpxb11
cdcl3,300.12
5.382
1.996
1.006
2.000
2.004
3.096
9
8
7
6
5
4
3
2
1
0
ppm
N
O

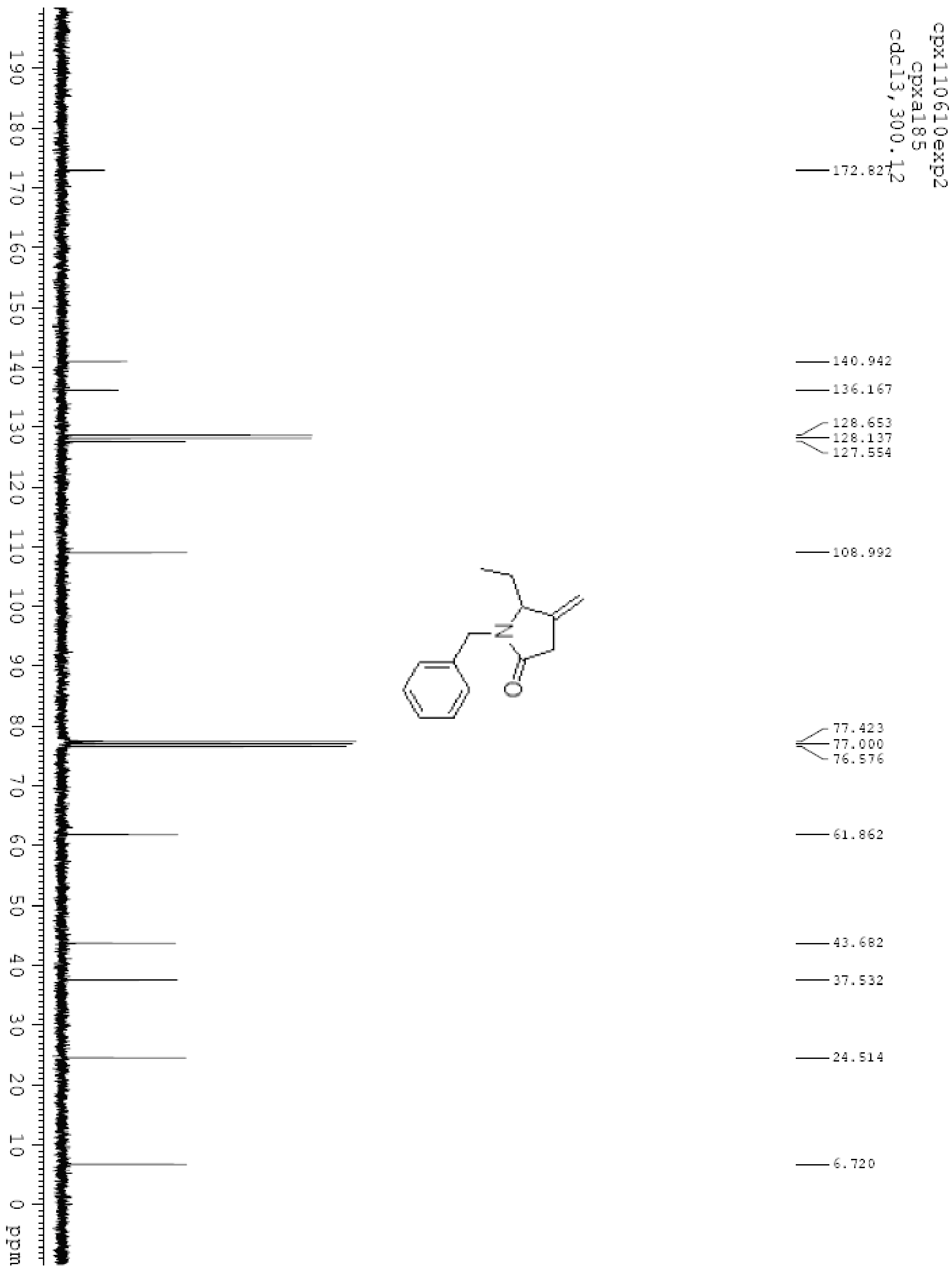
Compound **5b**:


cpx110707exp3
cpxb11
cdcl3,300.12
172.295
143.292
136.309
128.662
128.032
127.523
108.576
77.422
76.999
76.575
57.343
43.807
36.756
19.369
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm
N
O

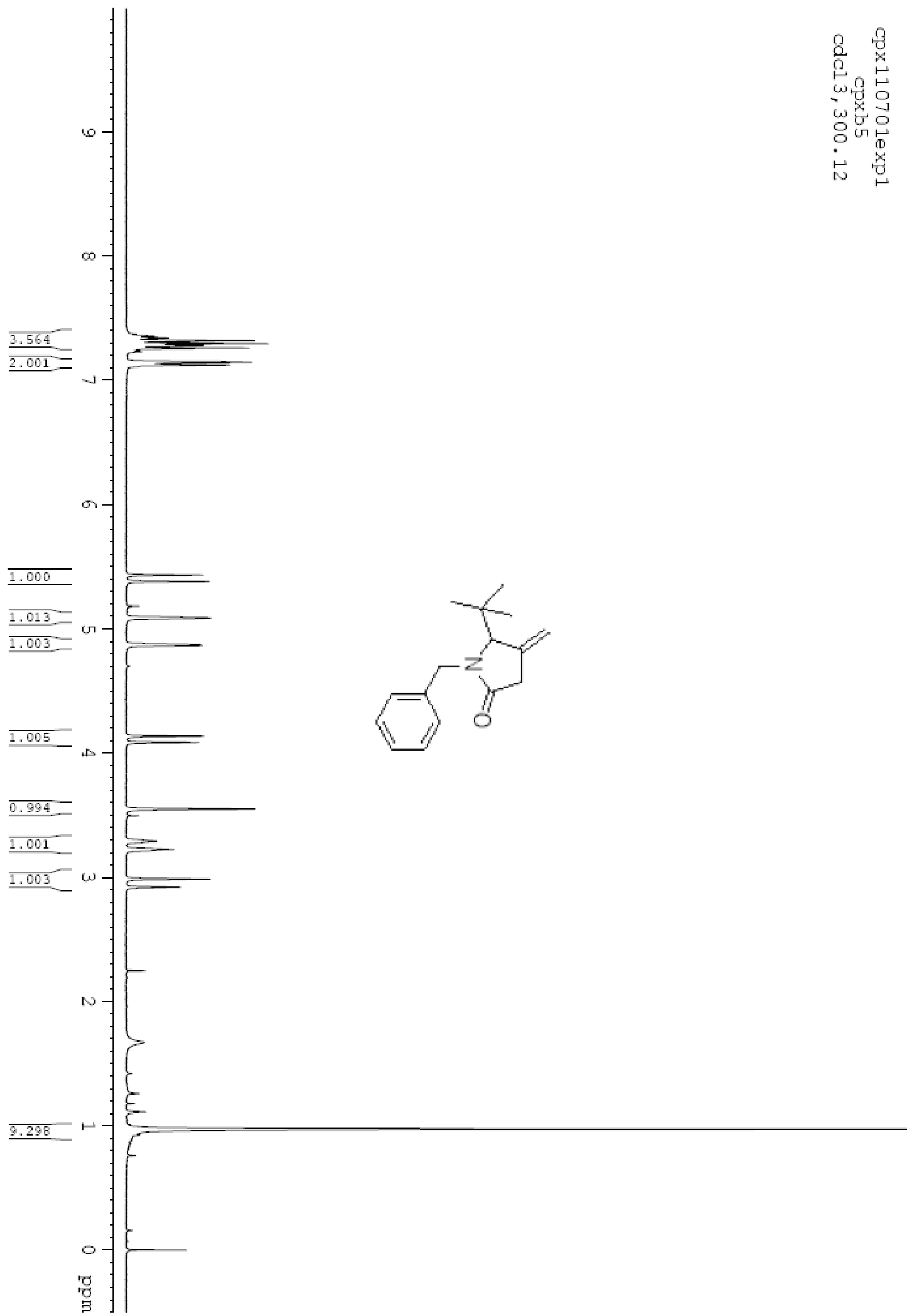
Compound **5c**:


cpx110610exp1
cpxa185
cdcl3,300.12
ppm
5.324
2.004
1.015
1.004
2.000
1.017
1.154
3.045

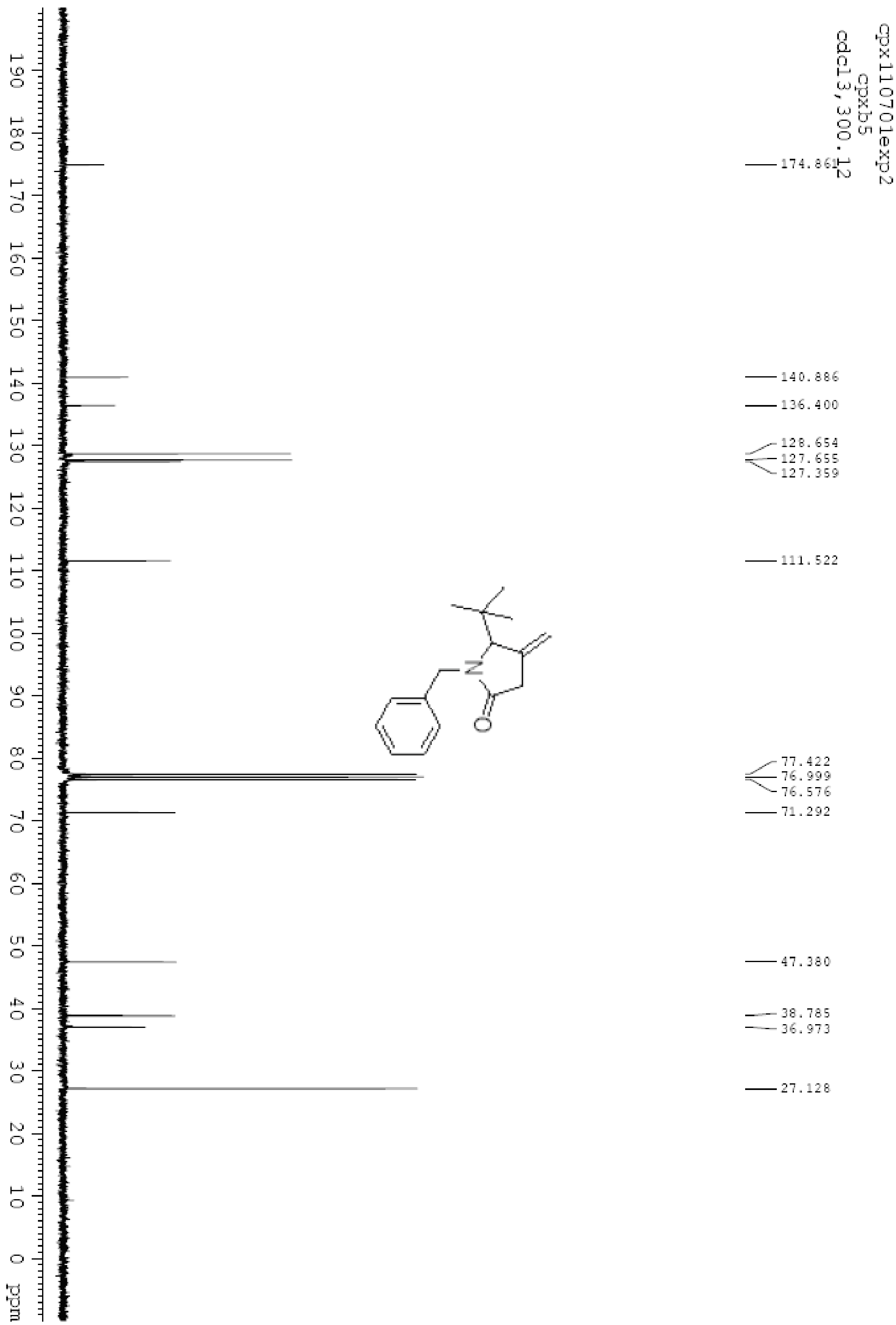
Compound **5c**:


cpx110610exp2
cpxa185
cdcl3,300.12
172.827
140.942
136.167
128.653
128.137
127.554
108.992
77.423
77.000
76.576
61.862
43.682
37.532
24.514
6.720
N
O
ppm

Compound **5g**:

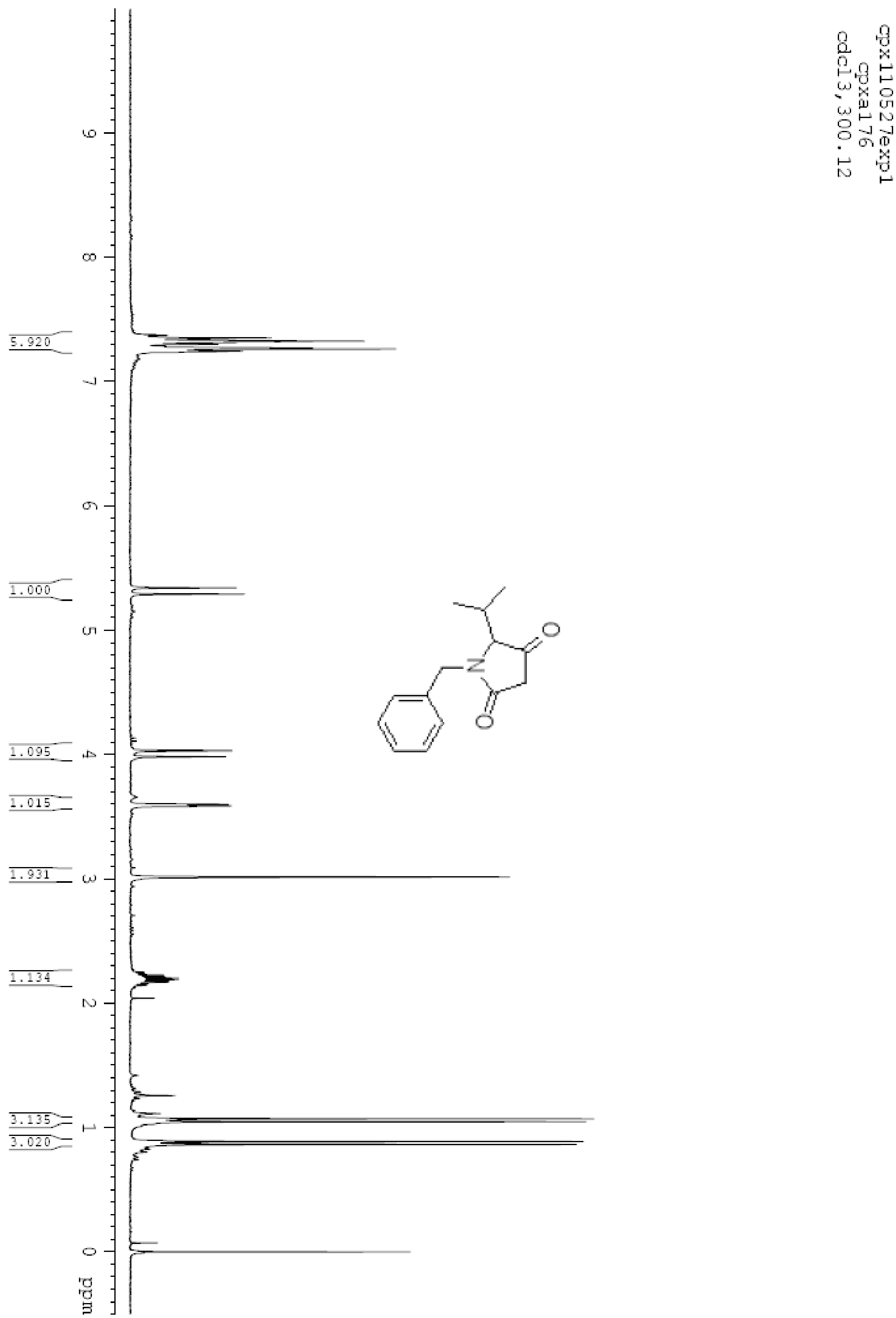

cpx110701exp1
cpxb5
cdcl3,300.12
3.564
2.001
1.000
1.013
1.003
1.005
0.994
1.001
1.003
9.298
9
8
7
6
5
4
3
2
1
0
ppm

Compound **5g**:

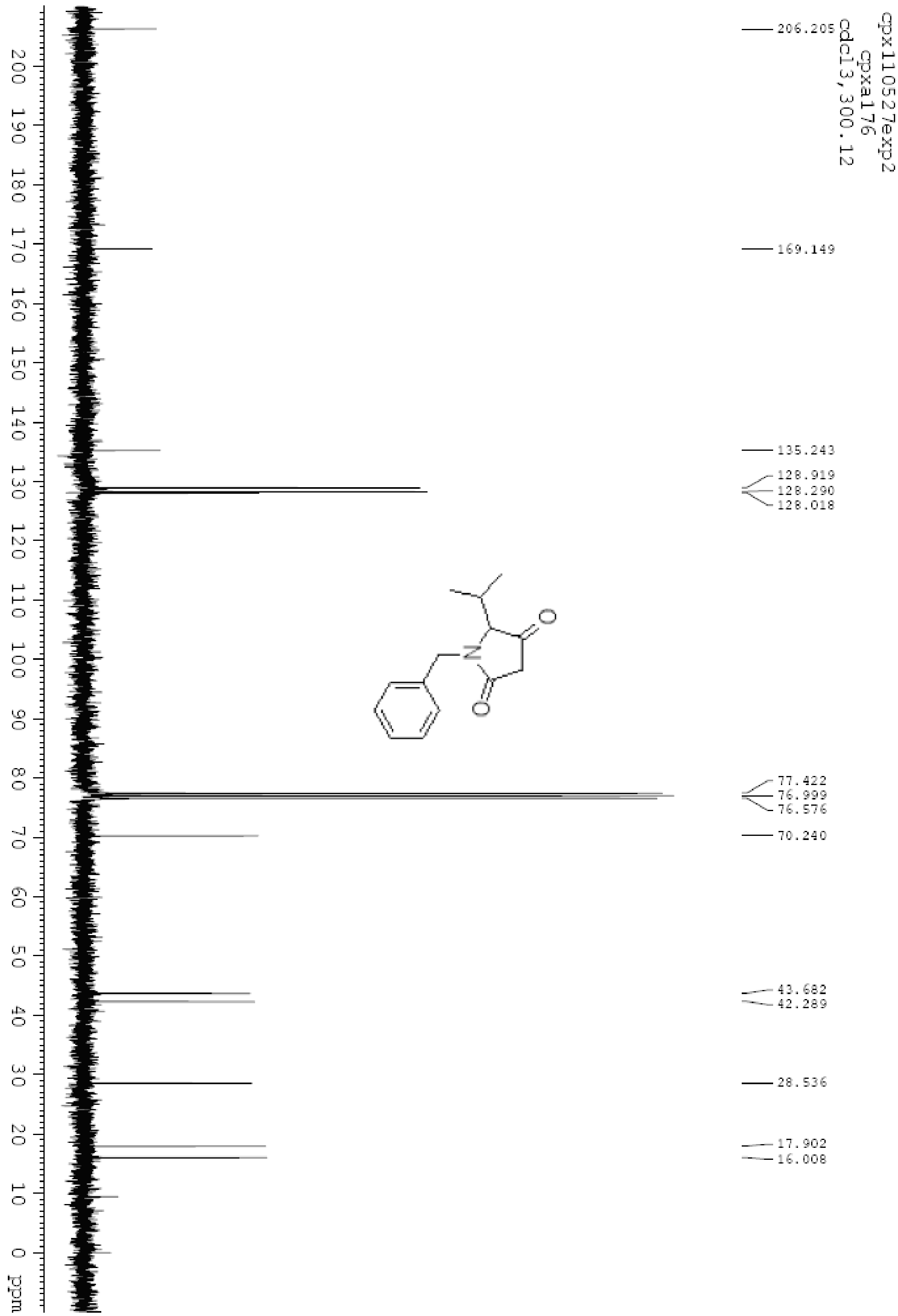


cpx110701exp2
cpxb5
cdcl3,300.12
174.861
140.886
136.400
128.654
127.655
127.359
111.522
77.422
76.999
76.576
71.292
47.380
38.785
36.973
27.128
N
O
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

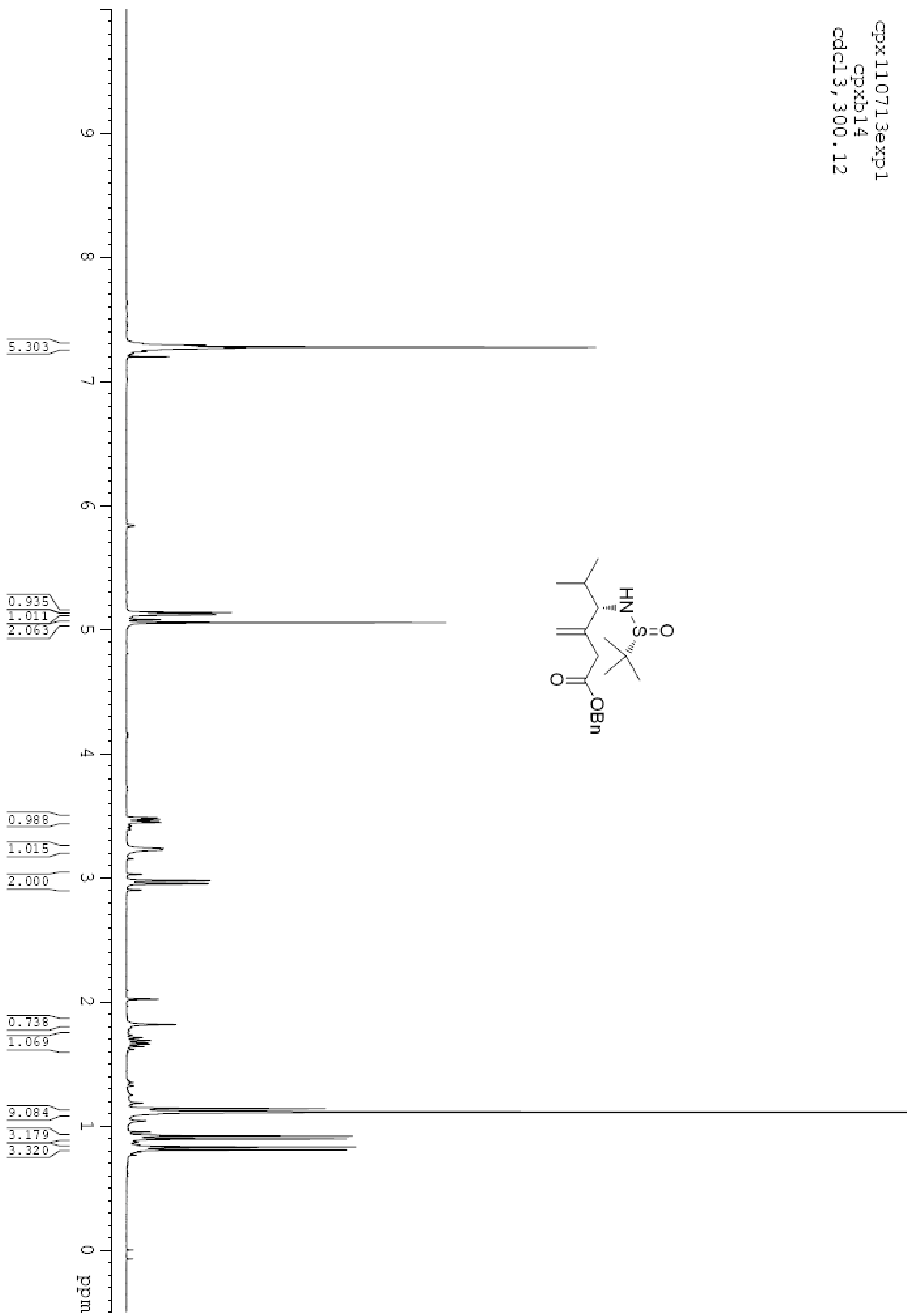
N-benzyl-5-isopropyl tetramic acid:



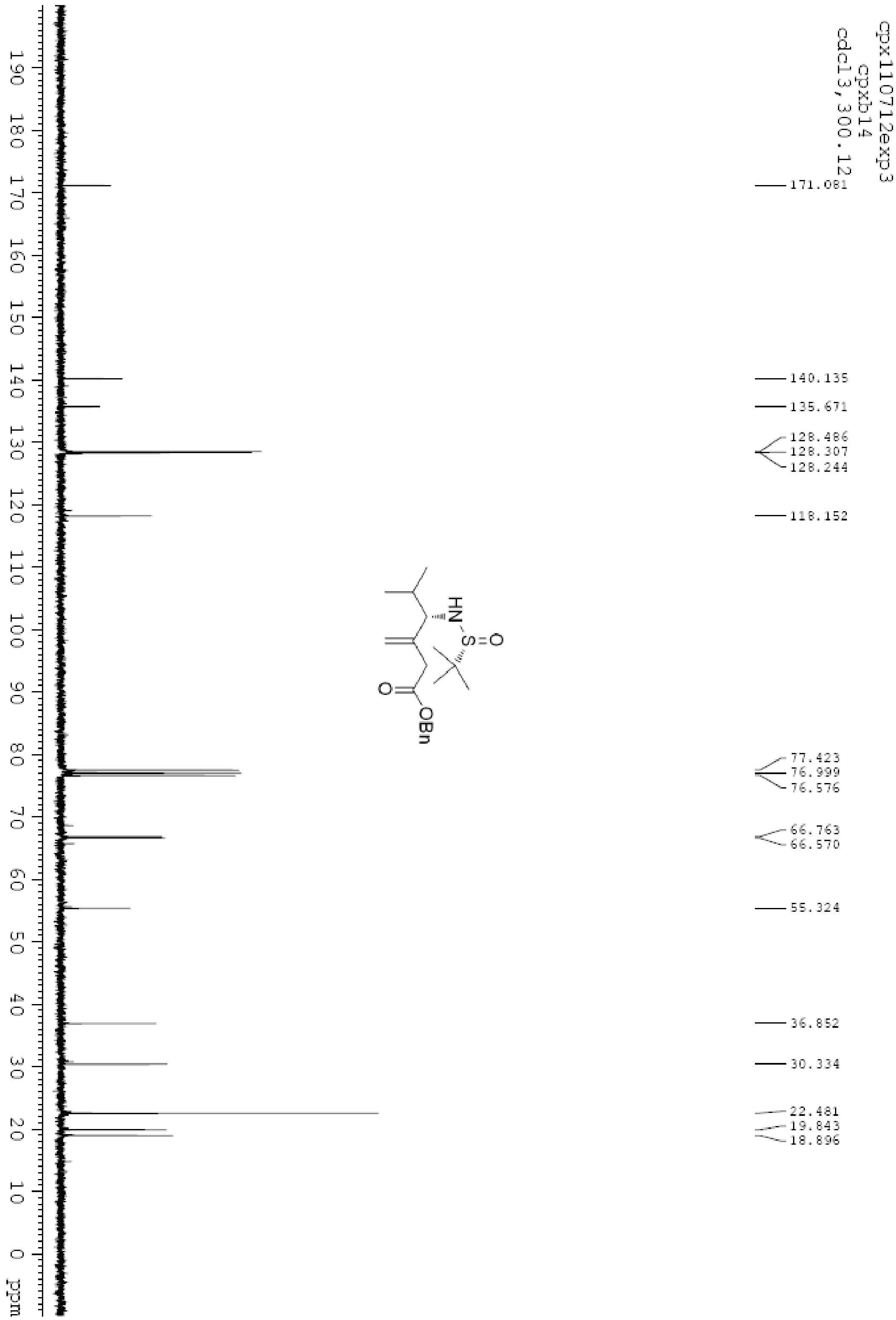
N-benzyl-5-isopropyl tetramic acid:



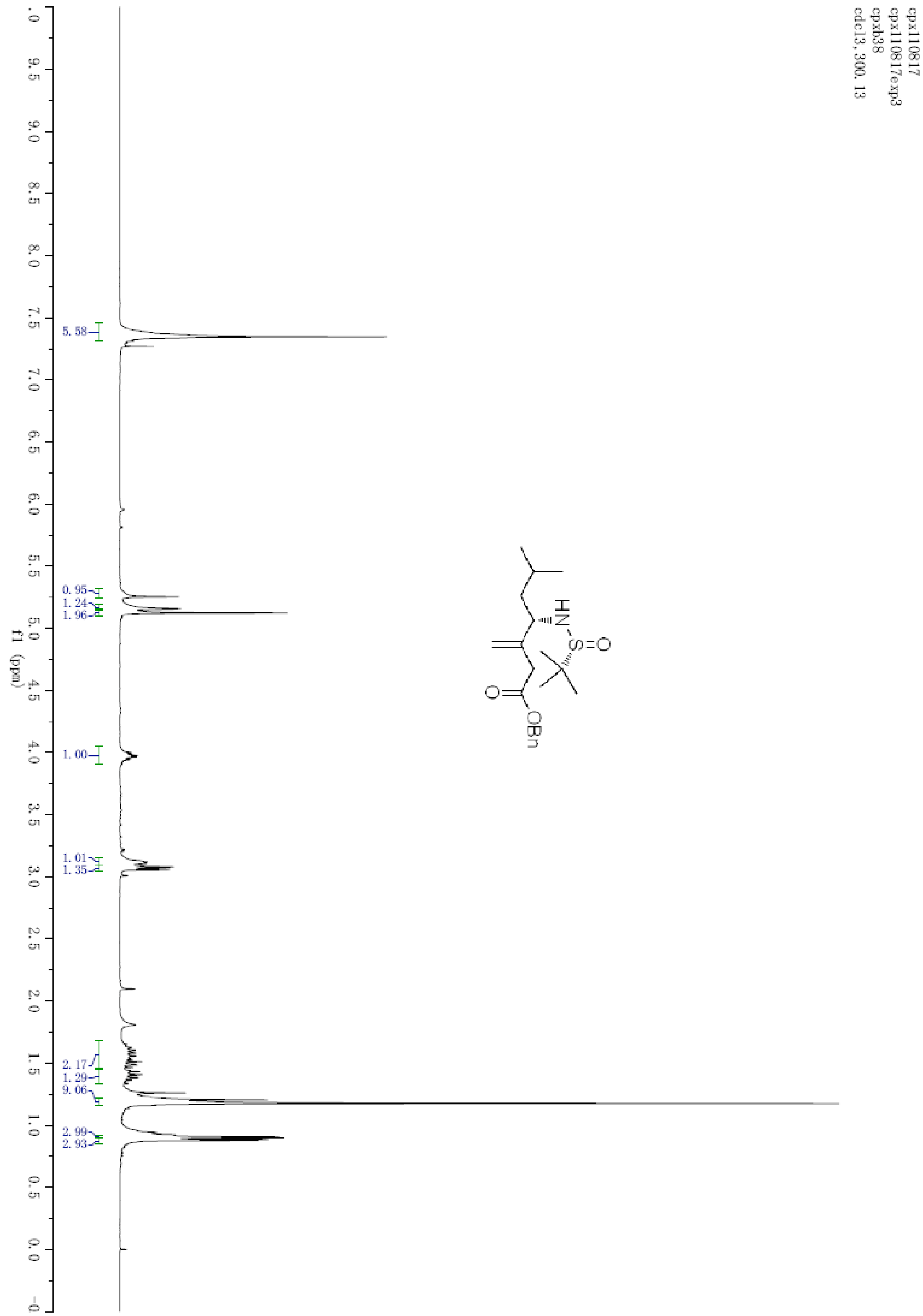
Compound **11a**:



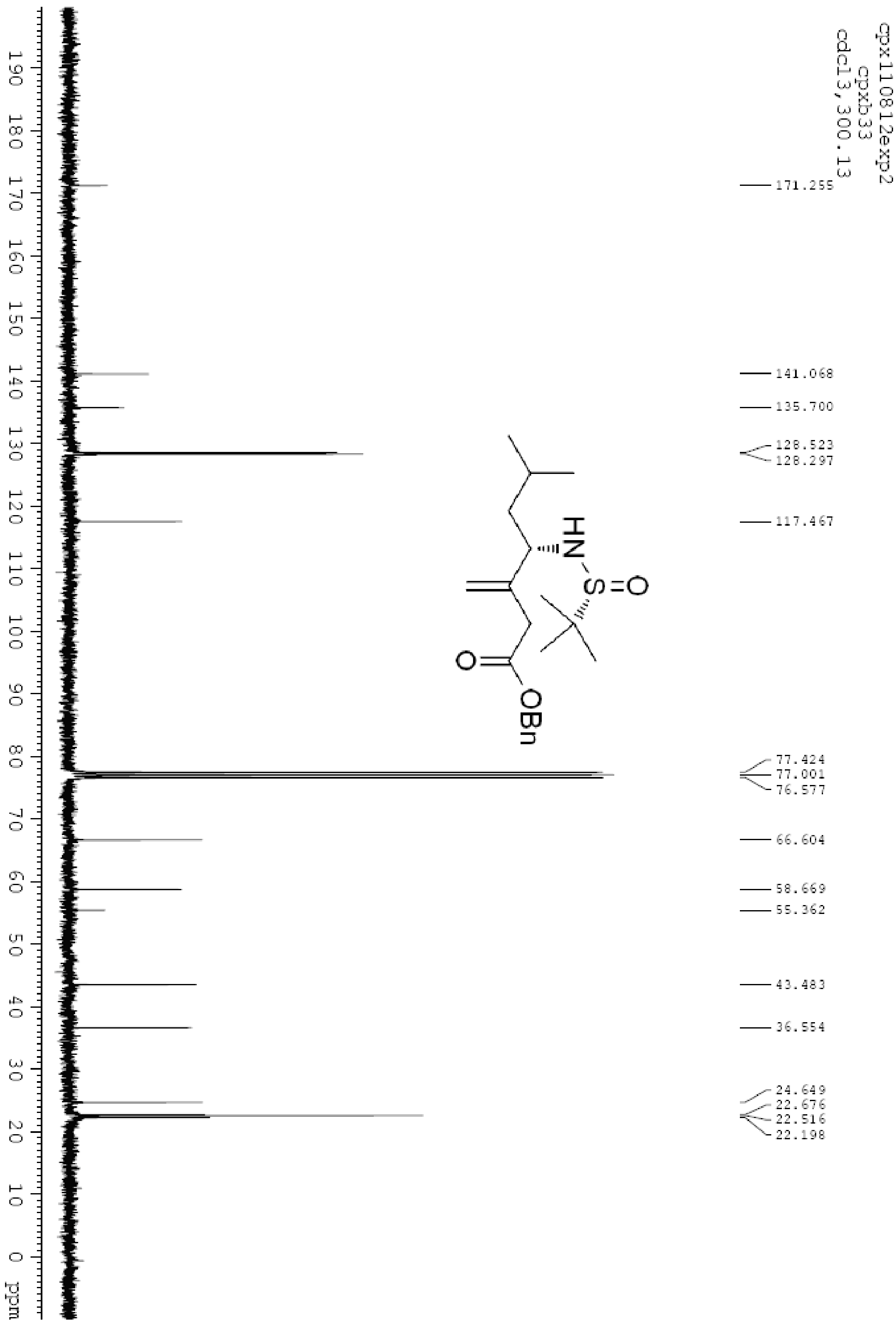
Compound **11a**:



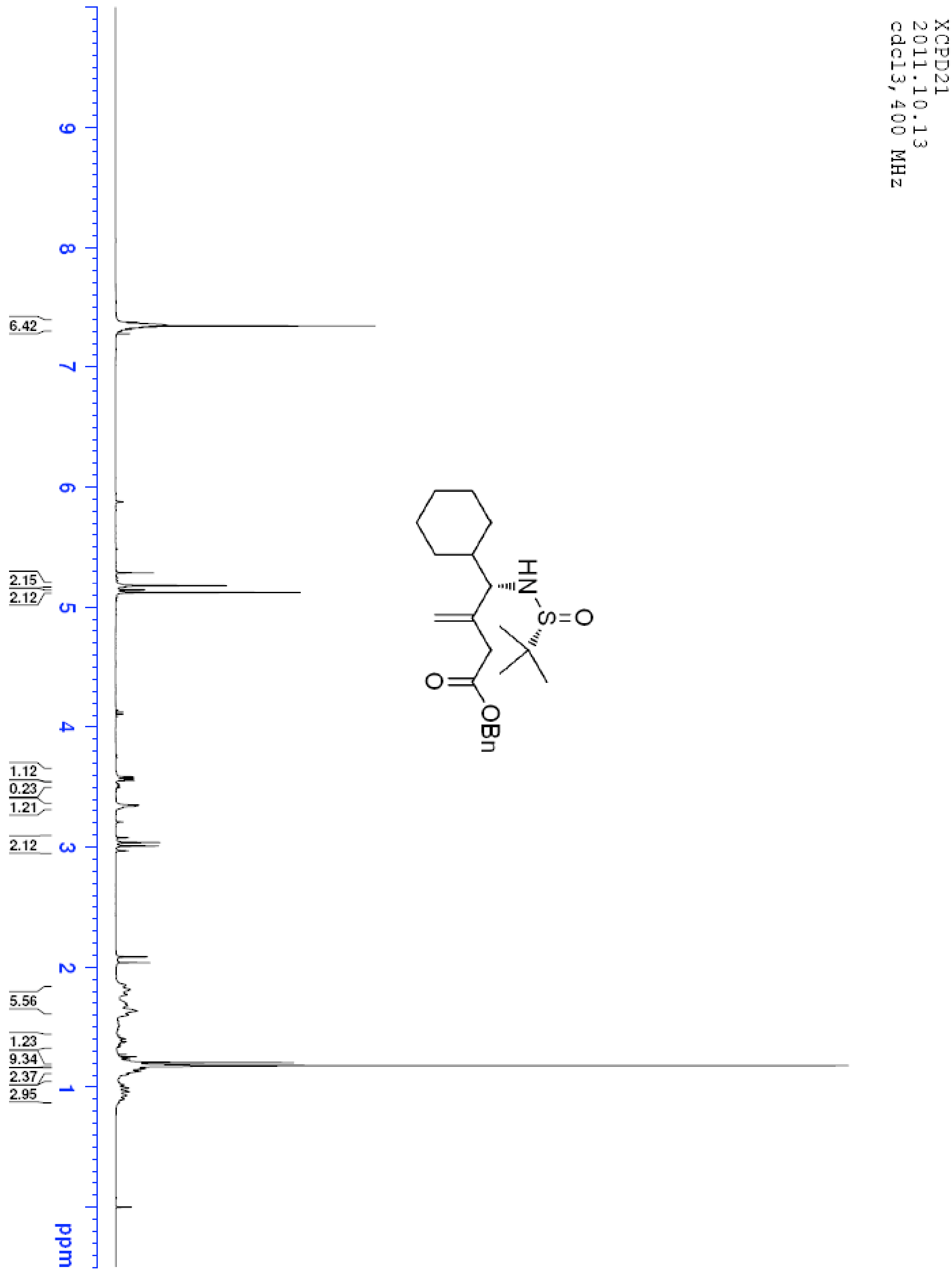
Compound **11b**:



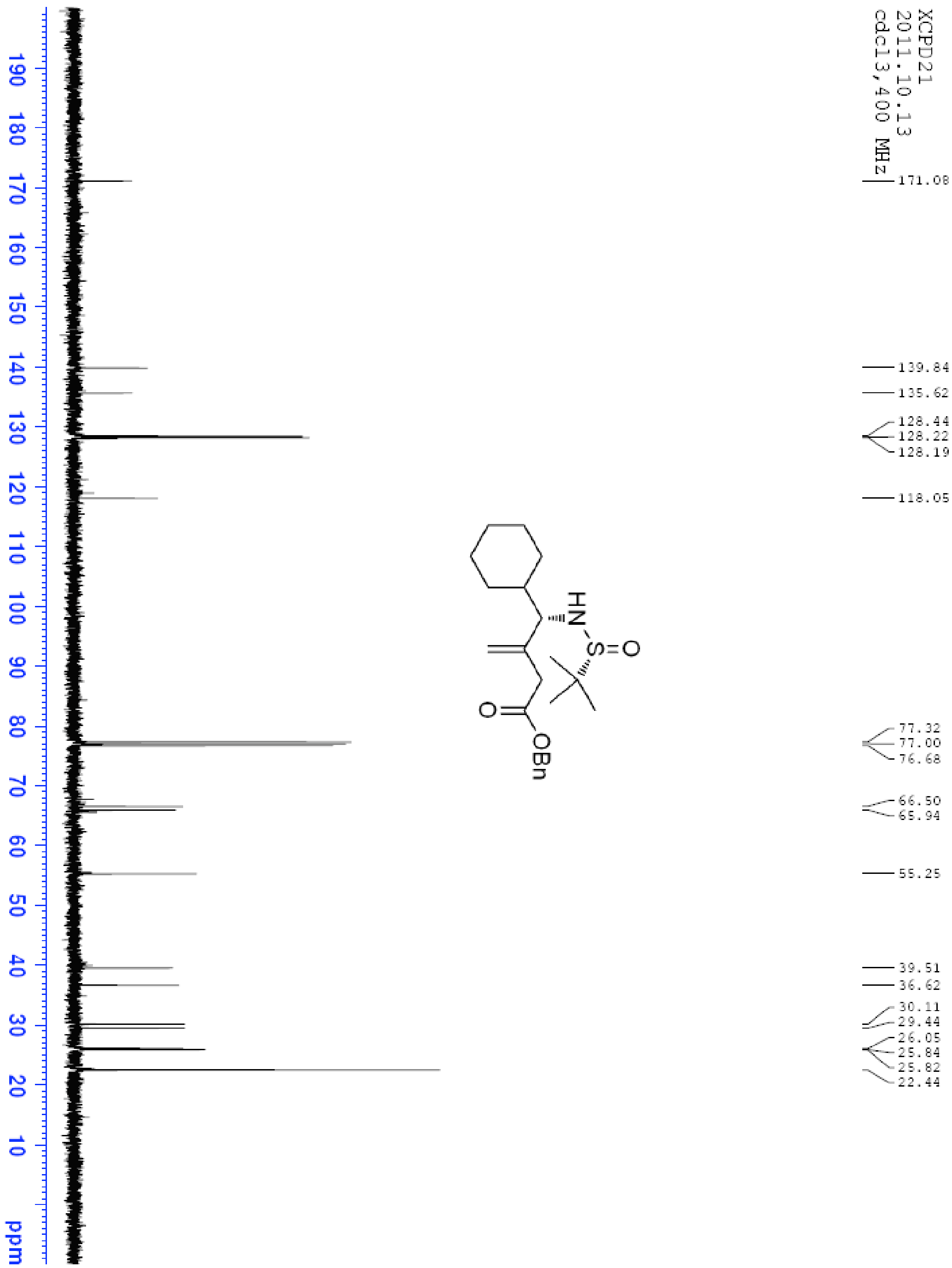
Compound **11b**:



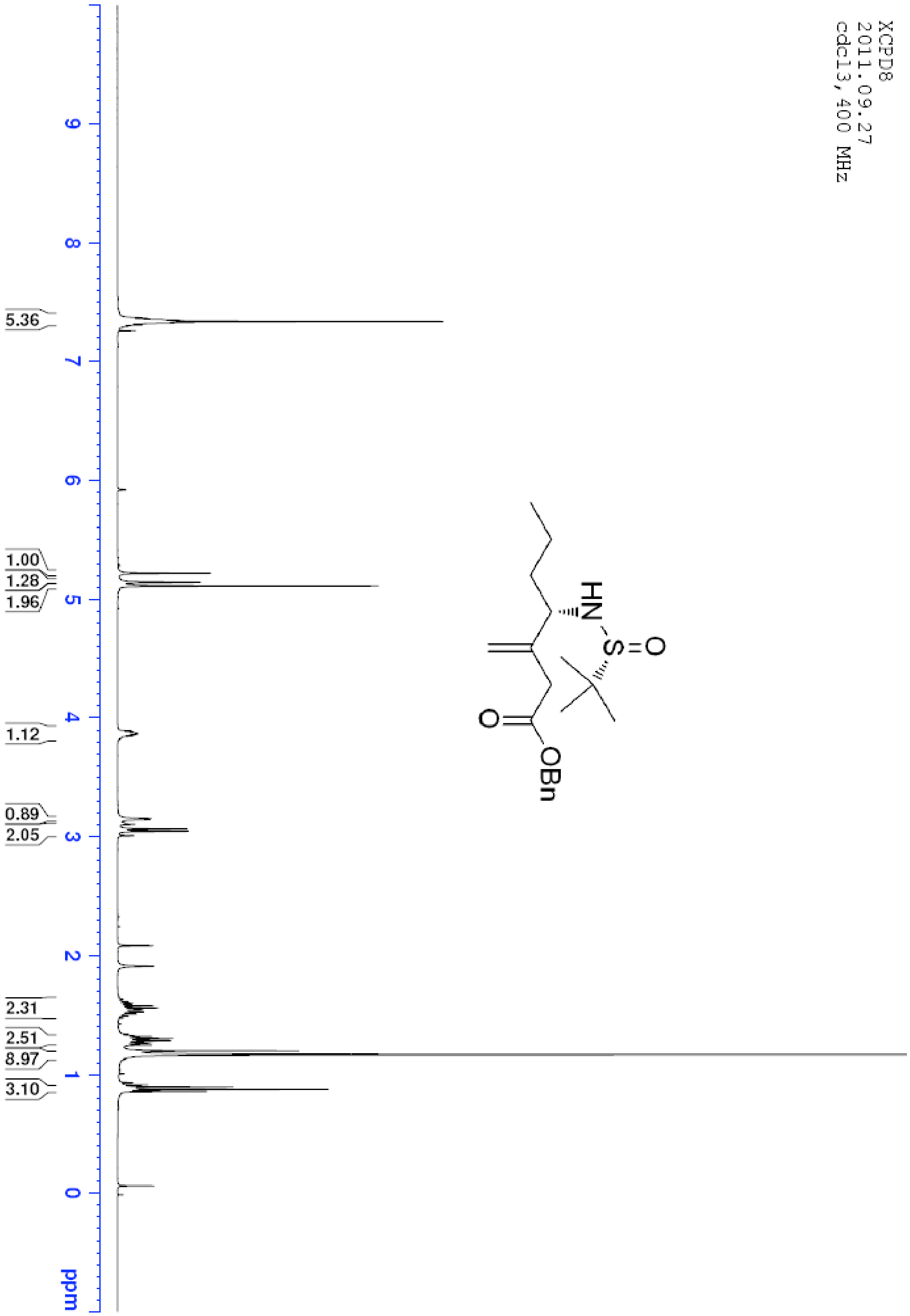
Compound **11c**:



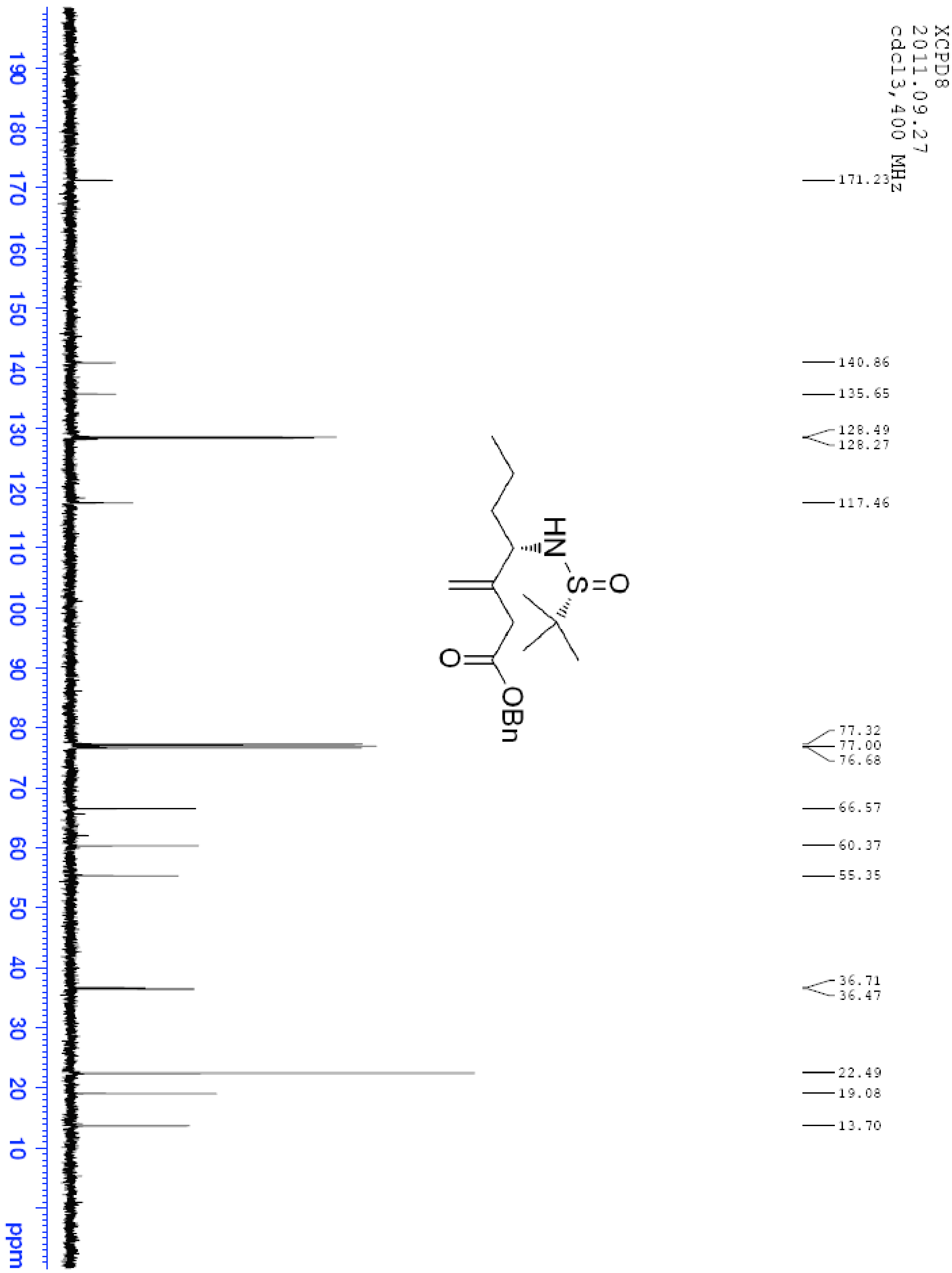
Compound **11c**:



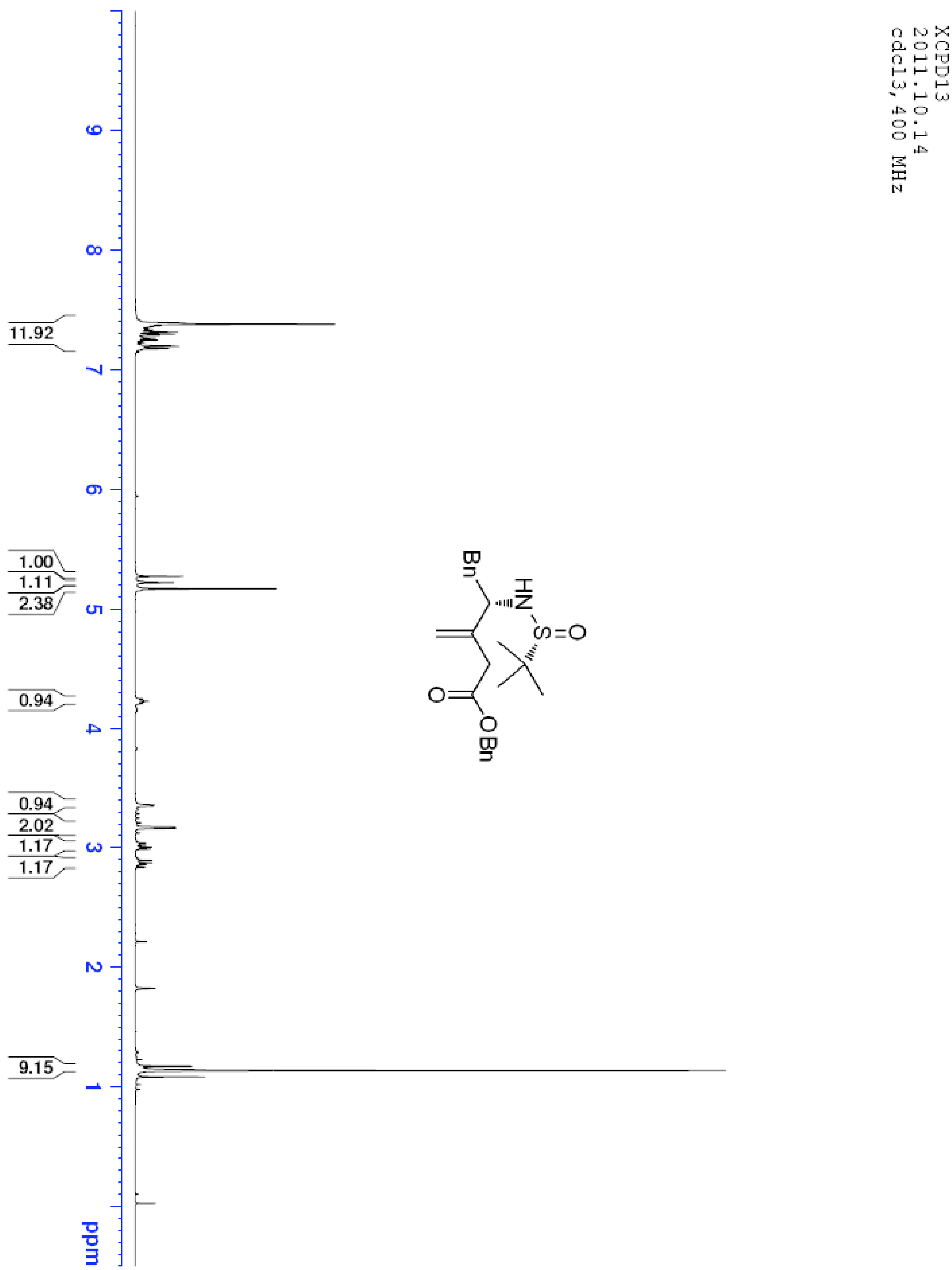
Compound **11d**:



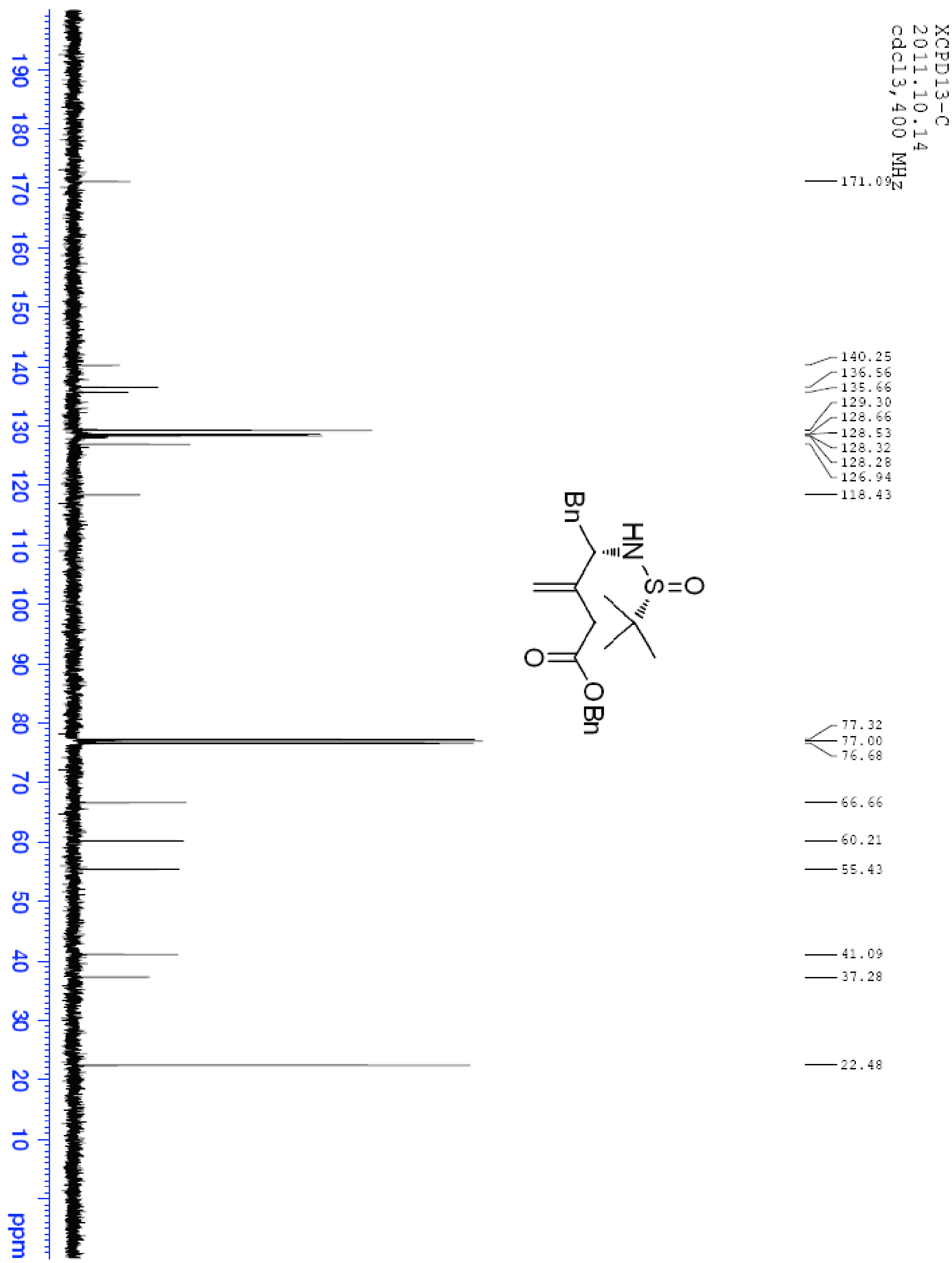
Compound **11d**:



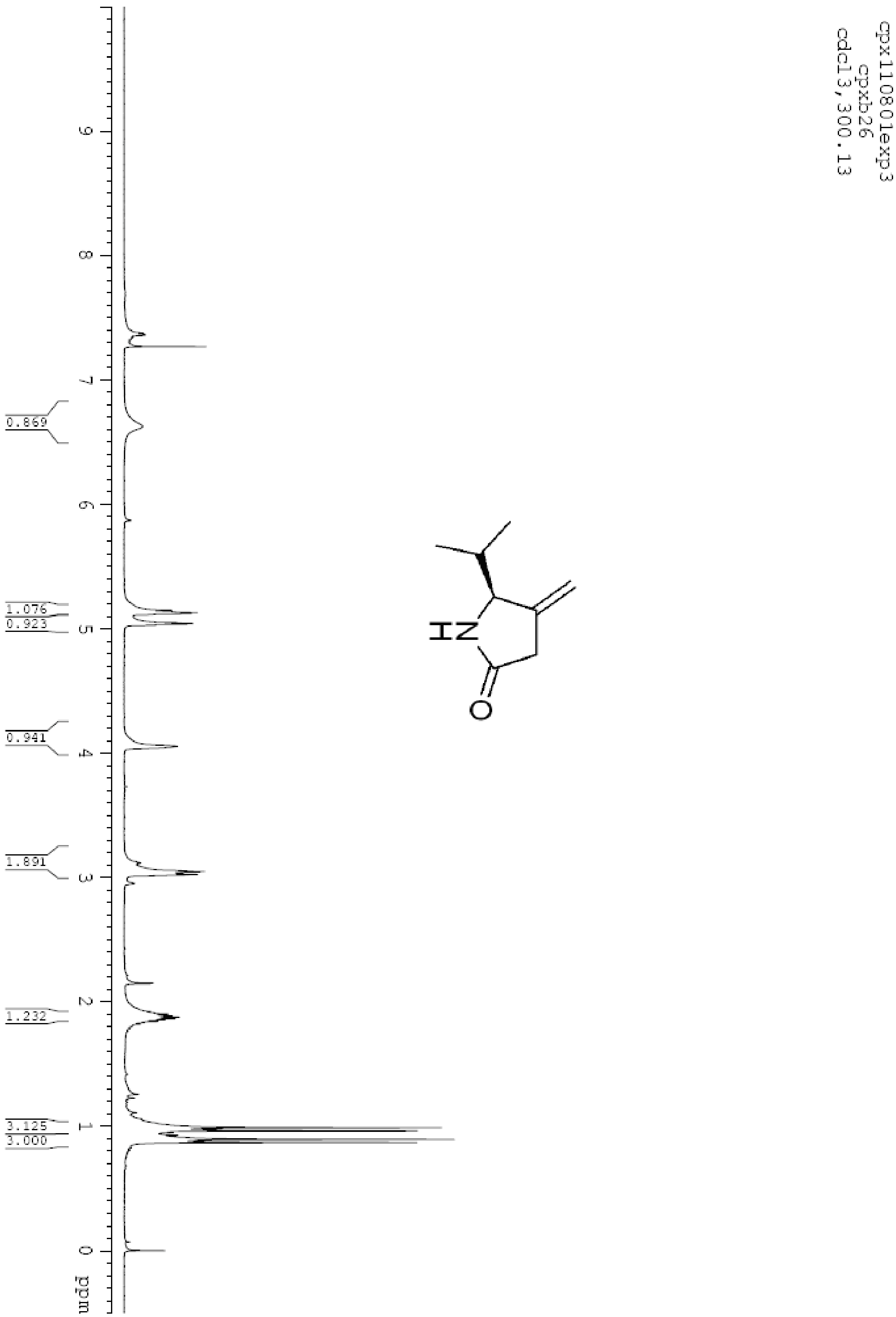
Compound **11e**:



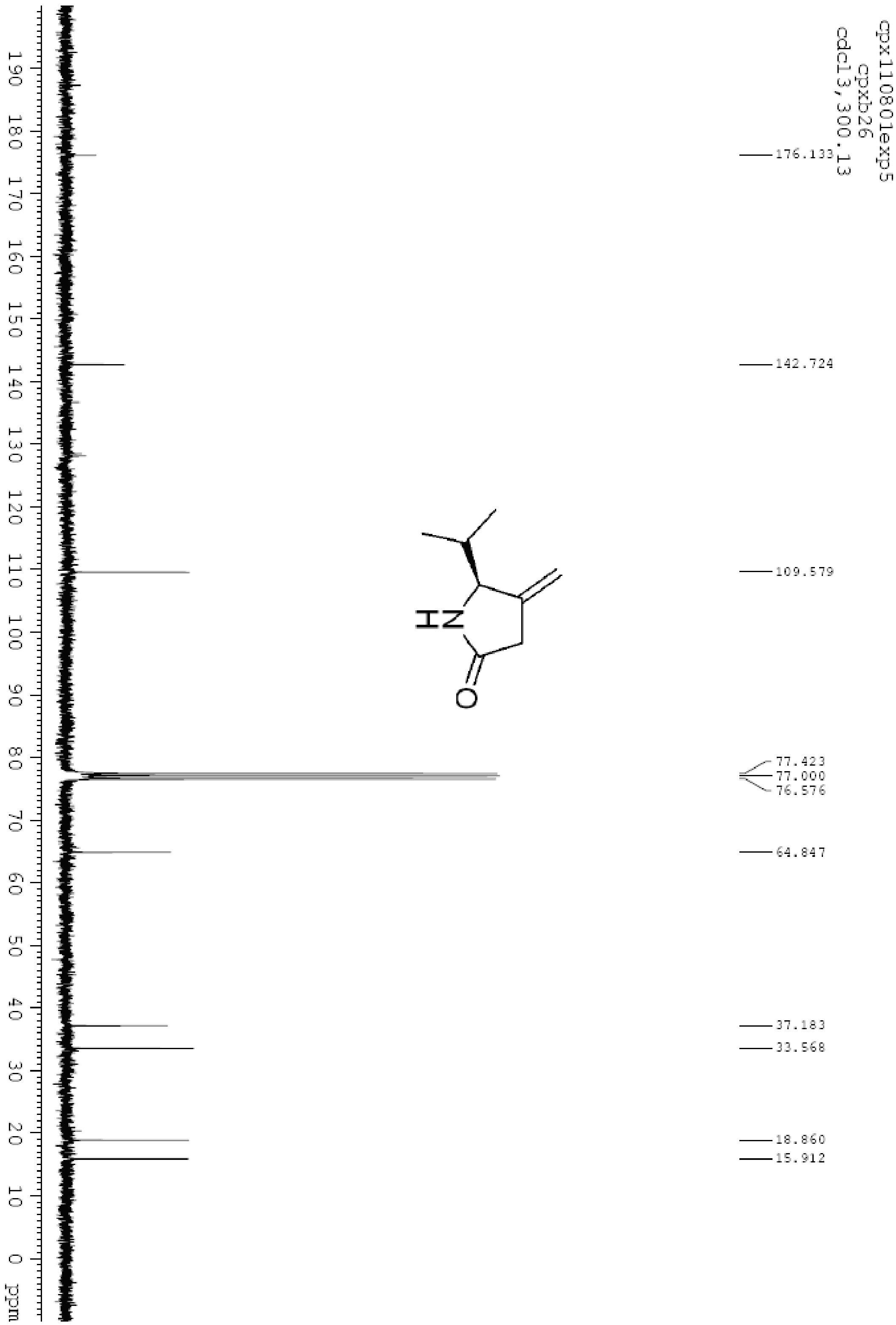
Compound **11e**:



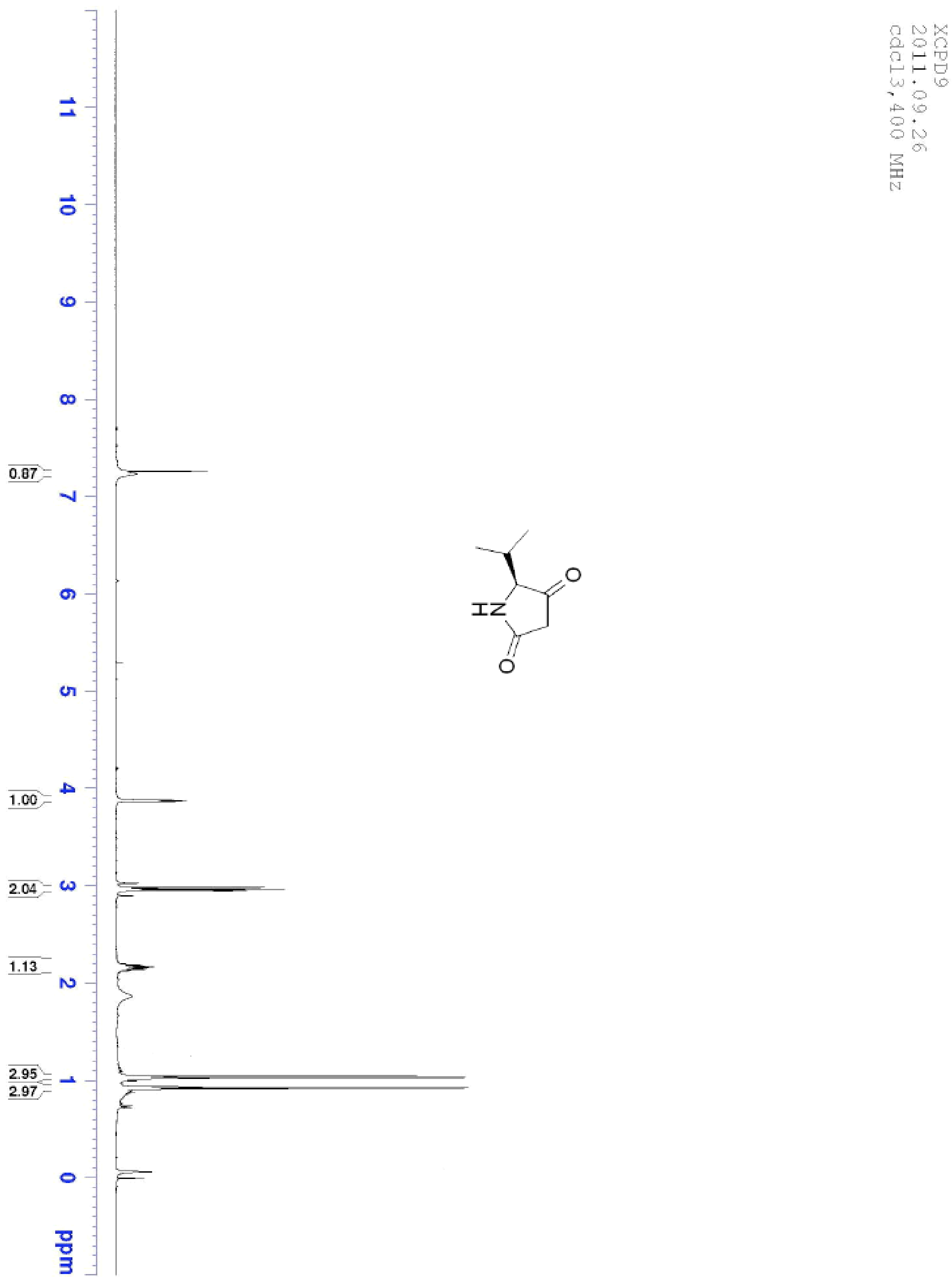
Compound **12a**:



Compound **12a**:



Compound **13a**:



Compound **13a**: