

## Supporting Information

### Enantioselective Synthesis of a Dual Orexin Receptor Antagonist

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### Table of Contents

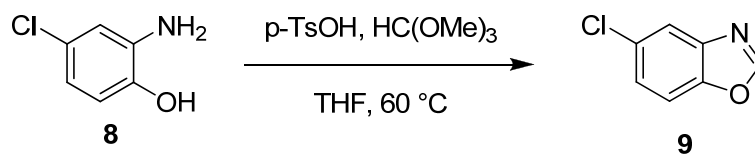
Preparation of Compound <b>9</b> .....	S2
Preparation of Compound <b>11</b> .....	S3
Preparation of Compound <b>12</b> .....	S4
Preparation of Compound <b>14</b> .....	S4
Preparation of Compound <b>21</b> .....	S5
Preparation of Compound <b>19</b> .....	S7
Preparation of Compound <b>1</b> .....	S8
<sup>1</sup> H and <sup>13</sup> C NMR Spectra .....	S10

**General Information.** Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego.<sup>1</sup> Non-aqueous reagents were transferred under nitrogen via syringe or cannula. All reactions were carried out under nitrogen in oven-dried glassware unless otherwise noted. Organic solutions were concentrated under reduced pressure on a Buchi rotary evaporator using a water bath. Chromatographic purification of products was accomplished using forced-flow chromatography on ICN 60 32-64 mesh silica gel 63 according to the method of Still.<sup>2</sup> Thin-layer chromatography (TLC) was performed on EM Reagents 0.25 mm silica gel 60-F plates. Visualization of the developed chromatogram was performed by fluorescence quenching or by anisaldehyde stain.

<sup>1</sup> Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals*; 3<sup>rd</sup> ed., Pergamon Press, Oxford, 1988.

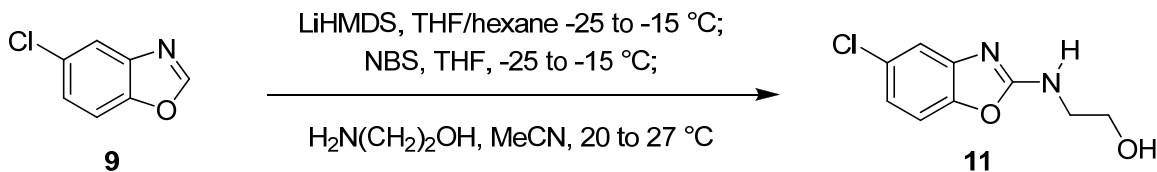
<sup>2</sup> Still, W. C.; Kahn, M.; Mitra, A. J. *J. Org. Chem.* **1978**, *43*, 2923.

$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a Bruker 400 (400 MHz and 100 MHz) as noted, and are internally referenced to residual protio solvent signals. Data for  $^1\text{H}$  NMR are reported as follows: chemical shift ( $\delta$  ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration and coupling constant (Hz). Data for  $^{13}\text{C}$  NMR are reported in terms of chemical shift. Mass spectra were obtained from an Agilent LC/MSD TOF model G1969A.



### Preparation of 5-Chlorobenzoxazole (9)

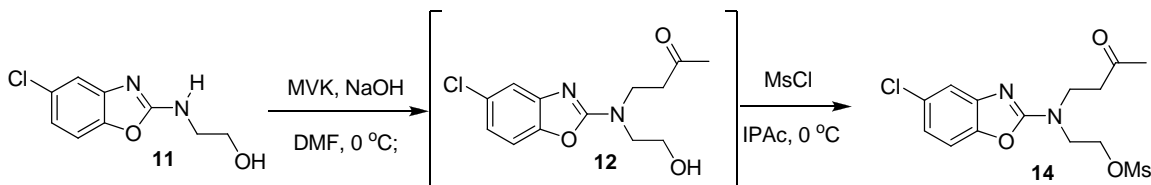
To a 250 mL 3-neck round bottom flask equipped with a distillation head, glass stopper, septum, thermocouple and magnetic stir bar was charged 2-amino-4-chlorophenol (**8**, 20.00 g, 0.139 mol). The solid was dissolved in THF (60 mL) and p-TsOH (0.265 g, 1.39 mmol) was added. The brown solution was warmed to 60 °C over 10 min and aged for 90 min. HPLC assay of the reaction mixture showed 1 LCAP unreacted starting material. The temperature was increased from 60 °C to 74 °C, and at 63 °C solvent distillation began. A total of 58 mL was collected during the first distillation. The mixture was diluted with THF (60 mL) and a total of 67 mL of solvent was removed between 71 and 84 °C. The mixture was again diluted with THF (60 mL) and 61 mL of solvent was removed between 74 and 114 °C. The dark brown solution was cooled to room temperature. The final mass of the solution was 27.96 g. Analysis of the crude stream by  $^1\text{H}$  NMR showed 0.1 wt% MeOH present in the sample.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 8.10 (s, 1H), 7.76 (d,  $J$  = 1.5 Hz, 1H), 7.50 (d,  $J$  = 8.7 Hz, 1H), 7.36 ppm (dd,  $J$  = 8.7, 1.7 Hz, 1H). Spectral data were consistent with reported values, see Li, Y.; Xie, Y.; Zhang, R.; Jin, K.; Wang, X.; Duan, C. *J. Org. Chem.* **2011**, 76, 5444.



### 2-[(5-Chloro-1,3-benzoxazol-2-yl)amino]ethanol (11)

A 500 mL 3-neck round bottom flask equipped with a septum, thermocouple, 125 mL addition funnel, inert gas inlet and magnetic stir bar was purged with nitrogen for 10 min. Hexamethyldisilazane (42 mL, 0.20 mol) and THF (78 mL) were charged against positive nitrogen pressure. The addition funnel was charged with a hexane solution of *n*-butyllithium (78.0 mL, 195 mmol). The amine solution was cooled to -52 °C and *n*-butyllithium was added over 84 min, resulting in a temperature increase to 12.5 °C over the course of the addition. The resulting lithium hexamethyldisilazide solution was removed from the cooling bath and aged for 30 minutes. To a 500 mL 3-neck round bottom flask equipped with a septum, thermocouple, inert gas inlet and magnetic stir bar was charged 5-chlorobenzoxazole (20.00 g, 130 mmol) in THF (100 mL) and the resulting colorless solution was cooled to -25 °C. The freshly prepared lithium hexamethyldisilazide solution was added *via* cannula over 80 minutes. The temperature of the anion solution was maintained between -25 and -15 °C during the addition. The resulting dark brown solution was aged for 90 minutes between -25 and -15 °C. To a 1000 mL 3-neck round bottom flask equipped with a Claisen adapter, septum, thermocouple, inert gas inlet, stir rod bearing, and blade was charged THF (100 mL) and *N*-bromosuccinimide (34.8 g, 195 mmol). The resulting slurry was cooled to -20 °C and the anion solution was added *via* cannula over 150 minutes. During the addition the anion solution and reaction mixture were maintained between -25 and -15 °C. The resulting brown slurry was removed from the cooling bath and aged for 50 minutes while warming to room temperature. To the resulting bromide slurry was added a solution of ethanolamine (12.6 mL, 208 mmol) in MeCN (38 mL) *via* syringe pump over 5 hours. During the addition the reaction temperature was maintained between 20 and 27 °C. The resulting brown slurry was aged at room temperature overnight. The reaction mixture was cooled in an ice water bath and the septum replaced with a 50 mL addition funnel charged with concentrated HCl (32 mL, 390 mmol). The acid solution was added over 10

min, during which time the addition the temperature increased from 10 to 20 °C. The reaction mixture was removed from the ice water bath and aged for 5 min. A 20% (w/w) solution of K<sub>2</sub>HPO<sub>4</sub> in water (170 mL) was added and the resulting biphasic mixture was transferred to a separatory funnel. The flask was washed with THF (3x, 10 mL) and the washings were added. The aqueous phase was cut; the organic phase was washed with 20% (w/w) K<sub>2</sub>HPO<sub>4</sub> in water (200 mL), separated and analyzed. The crude reaction stream had a total mass of 396.47 g. By quantitative HPLC assayed 25.81 g of **11** in the organic phase. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>): δ = 8.17 (t, *J* = 5.6 Hz, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.25 (d, *J* = 1.8 Hz, 1H), 6.97 (dd, *J* = 8.4, 1.8 Hz, 1H), 4.81 (t, *J* = 5.4 Hz, 1H), 3.56 (q, *J* = 5.7 Hz, 2H), 3.35 ppm (q, *J* = 5.8 Hz, 2H). <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 163.5, 146.8, 145.0, 127.7, 119.5, 115.0, 109.4, 59.3, 45.0; HRMS calculated for C<sub>9</sub>H<sub>9</sub>ClN<sub>2</sub>O<sub>2</sub> (M+H): 212.0353, found: 212.0355.

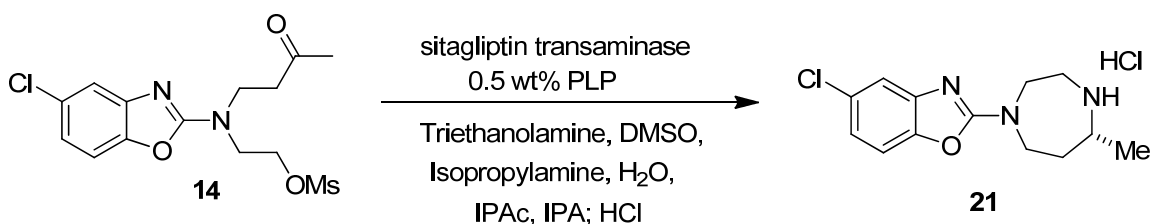


#### Preparation of Methanesulfonic acid 2-[(5-chloro-benzoxazol-2-yl)-(3-oxo-butyl)-amino]-ethyl ester (**14**)

To a 1000 mL 3-neck round bottom flask equipped with a septum, thermocouple, inert gas inlet and magnetic stir bar was charged **11** (25.2 g, 119 mmol). To this flask was added 126 mL DMF, 12.2 mL methyl vinyl ketone (148 mmol) and 0.119 mL 10M NaOH (1.19 mmol). The reaction was then aged for 6 hours, at which time conversion was judged to be complete by HPLC. A small sample of this DMF solution containing **12** was purified via column chromatography (30-60% EtOAc/Hexanes, linear gradient) to obtain an analytical sample of **12** for characterization: <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ = 7.29 (s, 1H), 7.14 (d, *J* = 8.4 Hz, 1H), 6.97 (dd, *J* = 8.4 Hz, 1.6 Hz, 1H), 3.90 (t, *J* = 5.0 Hz, 2H), 3.81 (t, *J* = 6.7 Hz, 2H), 3.73 (t, *J* = 5.0 Hz, 2H), 3.49 (s, 1H), 2.95 (t, *J* = 6.7 Hz, 2H), 2.20 (s, 3H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz) δ 207.2, 163.3, 147.4, 144.0, 129.5,

120.5, 116.2, 109.3, 61.2, 52.9, 45.0, 42.1, 30.3; HRMS calculated for C<sub>13</sub>H<sub>16</sub>ClN<sub>2</sub>O<sub>3</sub> (M+H): 283.0849, found: 283.0844.

The DMF solution was then diluted with 252 mL iPAc and cooled to 0 °C, then 23.1 mL Et<sub>3</sub>N (166 mmol) followed by dropwise addition of 12.0 mL methanesulfonyl chloride (154 mmol) over 45 minutes, maintaining internal temperature less than 10 °C. After a further 30 minutes, conversion was judged to be complete by HPLC. The solution was washed with 3x 63 mL 5 w/w% aqueous NaHCO<sub>3</sub> solution, then 66 mL water. After cutting the aqueous layer, the organics were reduced to approximately two volumes or 50 mL iPAc. The organics were then agitated by an overhead stirrer during slow addition of 151 mL n-Heptane over 4 hours. Over this time a crystalline white precipitate develops, and was allowed to stir overnight. At this time there was a thick slurry, which was filtered and washed with 2x 50 mL 90:10 n-Heptane:iPAc, and after drying with a nitrogen stream over the filter pad, **14** was obtained as a white crystalline solid (34.6 g., 96 mmol). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ = 7.29 (s, 1H), 7.16 (d, *J* = 8.2 Hz, 1H), 6.97 (d, *J* = 7.8 Hz, 1H), 4.46 (s, 2H), 3.92 (s, 2H), 3.81 (t, *J* = 5.9 Hz, 2H), 2.98-2.92 (m, 5H), 2.16 (s, 3H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz) δ 206.8, 162.2, 147.4, 144.0, 129.5, 120.7, 116.4, 109.6, 66.9, 49.3, 46.0, 45.0, 42.1, 37.5, 30.2; HRMS calculated for C<sub>14</sub>H<sub>18</sub>ClN<sub>2</sub>O<sub>5</sub>S (M+H): 361.0625, found: 361.0631.

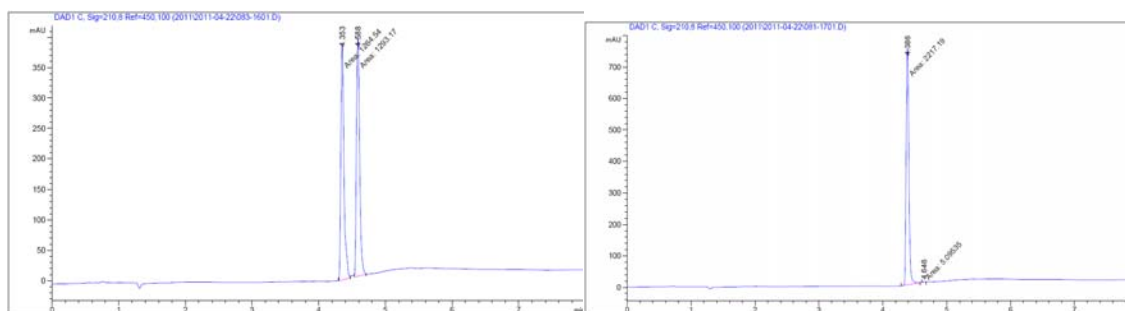


#### Preparation of 5-Chloro-2-((R)-5-methyl-[1,4]diazepan-1-yl)-benzooxazole hydrochloride (**21**)

To a 1000 mL 3-necked flask was charged isopropylamine hydrochloride (25.8 g., 270 mmol) and 525 mL 0.1 M aqueous triethanolamine solution. To this was added 750 mg Pyridoxal 5'-phosphate hydrate and 3.0 g. round 11 transaminase<sup>3</sup> and the suspension stirred until all components dissolved. The solution was heated to 40 °C and the pH of the solution was adjusted to pH 9.5 with an aqueous 4M solution of isopropylamine. Mesylate **14** (15.0 g., 41.6 mmol) was added as a 225 mL DMSO solution via syringe over 6 hours, and the resulting mixture stirred for a further 5 hours. At this time, the solution was poured into a 3L separatory funnel and extracted with 1.5 L of 1:1 iPAc:IPA. The aqueous layer was cut then extracted again with 750 mL 4:1 iPAc:IPA. The organics were combined, then washed with 750 mL brine. Then the organics were concentrated with IPA flushing to establish a 45 mL solution in IPA which was then treated with 4.6M HCl in IPA (9.94 mL, 45.7 mmol) via dropwise addition. The resulting solution was stirred vigorously while 52 mL IPAc was added slowly over 5 hours, creating a slurry of HCl salt **21**. The slurry was then slowly cooled to 0 °C and allowed to stir overnight. At this time the slurry was filtered and dried with a nitrogen stream over the filter pad, providing **21** as a white crystalline solid (7.80 g., 25.8 mmol, 62% yield, >99% ee).

<sup>1</sup>H NMR (500 MHz, CD<sub>3</sub>OD):  $\delta$  = 7.13-7.10 (m, 2H), 6.97 (dd,  $J$  = 8.2, 1.8 Hz, 1H), 3.99-3.79 (m, 3H), 3.67-3.57 (m, 3H), 3.39-3.33 (m, 1H), 2.24 (s, 1H), 2.12-2.07 (m, 1H), 1.42 (d,  $J$  = 6.7 Hz, 3H). <sup>13</sup>C NMR (CD<sub>3</sub>OD, 125 MHz)  $\delta$  164.7, 149.3, 145.2, 131.2, 123.2, 117.4, 112.5, 57.8, 45.9, 34.3, 21.4; HRMS calculated for free amine C<sub>13</sub>H<sub>17</sub>ClN<sub>3</sub>O (M+H): 266.1060, found: 266.1056.  $[\alpha]_D^{25}$  = -4.67 (c = 1.0, MeOH). Enantiomeric ratio was determined by SFC analysis using a Chiralpak AD-H (250 x 4.6 mm, 5  $\mu$ m) column (35 °C, 200 bar, 210 nm, 2 mL/min, 15-50% MeOH with 25 mM *i*-BuNH<sub>2</sub>): (S)-isomer  $t_r$  = 4.6 min, (R)-isomer  $t_r$  = 4.4 min.

<sup>3</sup> This is an evolved variant of ATA-117, see round 11 transaminase in Savile, C. K.; Janey, J. M.; Mundorff, E. C.; Moore, J. C.; Tam, S.; Jarvis, W. R.; Colbeck, J. C.; Krebber, A.; Fleitz, F. J.; Brands, J.; Devine, P. N.; Huisman, G. W.; Hughes, G. J. *Science*, **2010**, 329, 305.



Signal 1: DAD1 C, Sig=210,8 Ref=450,100

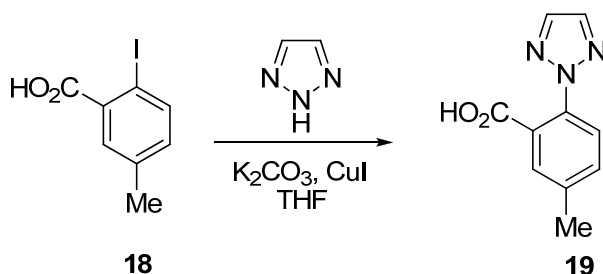
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2	4.588	MM	0.0543	1293.16516	397.12180	50.5596

Totals : 2557.70276 789.28241

Signal 1: DAD1 C, Sig=210,8 Ref=450,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.386	MM	0.0484	2217.18506	763.31787	99.7707
2	4.646	MM	0.0391	5.09535	2.17075	0.2293

Totals : 2222.28041 765.48862



### 5-Methyl-2-[1,2,3]triazol-2-yl-benzoic acid (19)

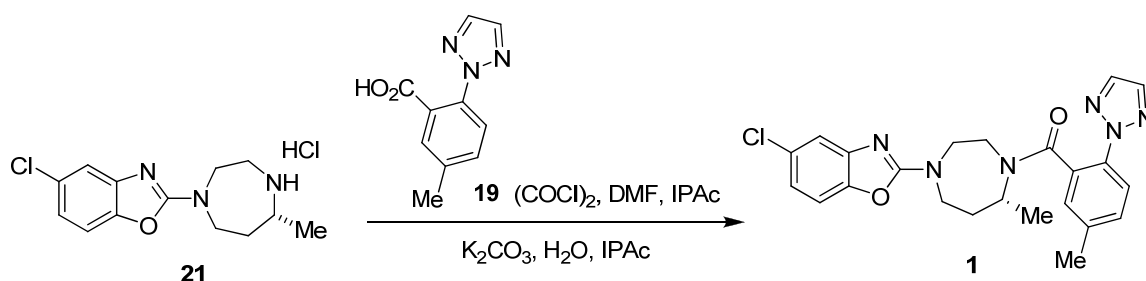
A 50 mL three-neck round bottom flask was equipped with a septum, thermocouple, Claisen adapter, inert gas inlet, stir shaft, bearing and blade. The system was purged with nitrogen and 2-iodo-5-methylbenzoic acid (1.00 g, 3.82 mmol) was added. The solid was dissolved in degassed THF (10.0 mL) to afford a colorless solution. Potassium carbonate (1.32 g, 9.54 mmol) was added affording a mobile white slurry and causing a temperature increase from 22 to 25 °C. Water (0.1 mL, 5.72 mmol) was added. Charged 1H-1,2,3-triazole (0.44 mL, 7.63 mmol) and the slurry was aged at 23 °C for 3 hours, during which time the mixture thickened considerably. A solution of copper(I) iodide (0.036 g, 0.191 mmol) in MeCN (1.5 mL) was added via syringe pump over 90 minutes. During the addition the slurry gradually changed over from white to blue. The resulting blue slurry was aged between 21 and 23 °C for 19 hours. The reaction was quenched with 13 wt% NaCl in 2.5 M HCl (13 mL). The mixture was transferred to a

seperatory funnel, the flask was washed with EtOAc (2x, 3 mL) and the washings were added to the biphasic mixture. The aqueous phase was removed and quantitative HPLC assay of the organic solution showed 0.642 g desired product present, 83% solution yield, 85:15 *N*-2:*N*-1 regiomeric ratio.

A representative triazole acid organic stream (3.88 g, 19.1 mmol by quantitative HPLC assay) was solvent switched to IPA (20 mL/g based on the theoretical amount of triazole acid, KF of the final solution <1000 ppm) and the solution was warmed to 70 °C. A slurry of sodium *tert*-butoxide (2.02 g, 21.000 mmol) in IPA (58 mL) was warmed to 70 °C affording colorless homogeneous solution. The triazole acid solution was added to the base solution via cannula over 1.75 hours. The resulting white slurry was aged at 70 °C overnight. The slurry was cooled from 70 to 30 °C over 60 min and re-warmed to 50 °C. The liquors were assayed by quantitative HPLC at 50 °C and showed a 26:74 *N*-2:*N*-1 regiomeric ratio. The slurry was filtered at 50 °C and the filter cake was washed with IPA (2x, 5 mL). The solids were dried in a vacuum oven at 55 °C under a nitrogen stream. The sodium salt of **19** was isolated as a white crystalline solid (3.07 g, 71% yield).

Sodium salt of **19** was charged to 3.6 M aqueous HCl solution (6 vol) at 25 to 30 °C. The slurry was stirred for 16 hours at 25 to 30 °C. The crude acid was isolated and washed with water (3 vol). After the material was spun dry, the cake was washed with isopropyl acetate:n-heptane (1:2) twice (2 x 1.4 vol) and then spun dry. The wet cake was dried under vacuum at 35 °C for 12 hours. m.p. 167.5 °C. <sup>1</sup>H NMR (400 MHz, d<sub>6</sub>-DMSO): δ 12.09 (br s, 1H), 8.04 (s, 1H), 7.62 (d, 1H, J = 8.4 Hz), 7.58 (d, 1H, J = 1.2 Hz), 7.49 (dd, 1H, J = 8.4, 1.2 Hz), 2.41 (s, 3H). <sup>13</sup>C NMR (100.6 MHz, d<sub>6</sub>-DMSO): δ 168.0, 139.2, 136.4, 135.8, 132.5, 130.3, 128.7, 124.8, 20.9. HRMS (ESI): m/z [M<sup>+</sup> + H] calculated for C<sub>10</sub>H<sub>9</sub>N<sub>3</sub>O<sub>2</sub>: 204.0773; found: 204.0781.





**Preparation of [(R)-4-(5-Chloro-benzooxazol-2-yl)-7-methyl-[1,4]diazepan-1-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone (1).** To a round bottom flask charge 6.86 g of 5-Methyl-2-[1,2,3]triazol-2-yl-benzoic acid along with 7.0 vol or 70 mls of dry iPAc (KF < 200 ppm) forming a slurry. To this charge 0.73 g of DMF then purge system thoroughly with nitrogen and assure temperature is 20- 25°C. Begin charging 5.04 g of oxalyl chloride maintaining 20-25°C and controlling off-gassing since it is extremely vigorous. With the feed of oxalyl chloride the previous slurry dissolves. Age the batch for 1 hr. Sample for acid chloride formation (< 1 LCAP) and proceed to amidation.

In a separate vessel prepare a solution of potassium carbonate in 5.0 vol or 50 mL water (note: exotherm). Cool the solution to to 0 °C. When acid chloride (above) is prepared, add 2.5 vol or 25 mL iPAc to aqueous solution with overhead stirring, then add 10.0 g. amine hydrochloride salt to solution, stir for 15 minutes. Then using a cannula transfer the acid chloride solution over from separate vessel over the course of 1 hour, maintaining less than 5°C internal temperature. Flush the vessel with 2.5 vol or 25 mL iPAc. Sample to determine completion (should already be complete), significant precipitate should be **1**.

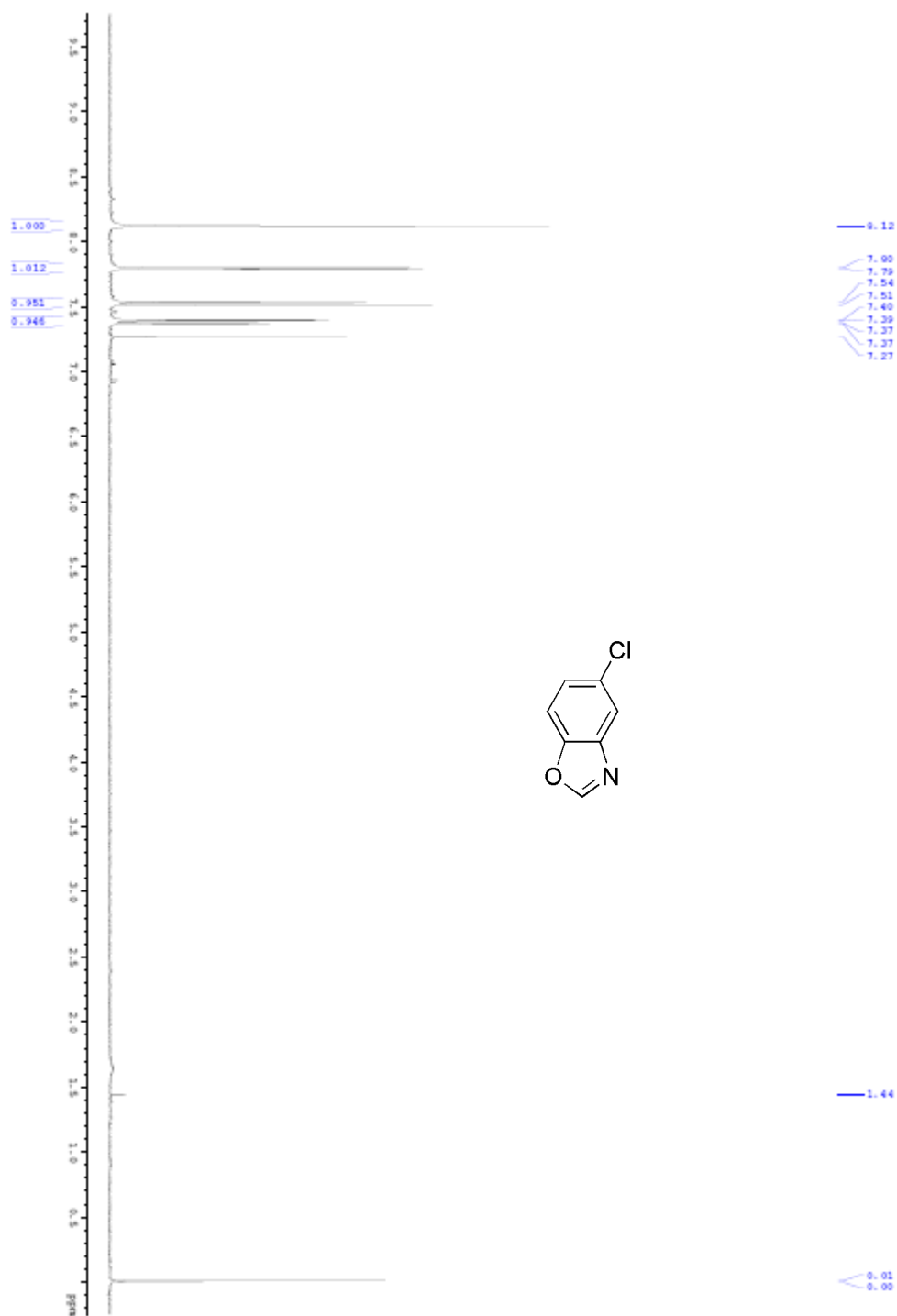
Heat the slurry to 40 °C. Once at 40 °C add 1.5 vol or 15 mL Acetonitrile and agitate for 5 minutes, all material should go into solution (98% AY observed). At this time stop agitation. After phase separation cut the aqueous layer, then stir organics with DARCO (10 wt% **6** basis) at 40°C for 3 hours, then filtered hot and taken through to crystallization. Recover yield from the carbon with an iPAc flush.

Concentrate the batch in iPAc and flush to 7.5 vol (mL/g of **6**) and heat to 80-85°C until complete dissolution. Cool to 65 °C linearly over 2 hrs, adjust agitation speed to high from this point forward. At 65°C, charge 0.3 wt% seed in n-Heptane to the solution

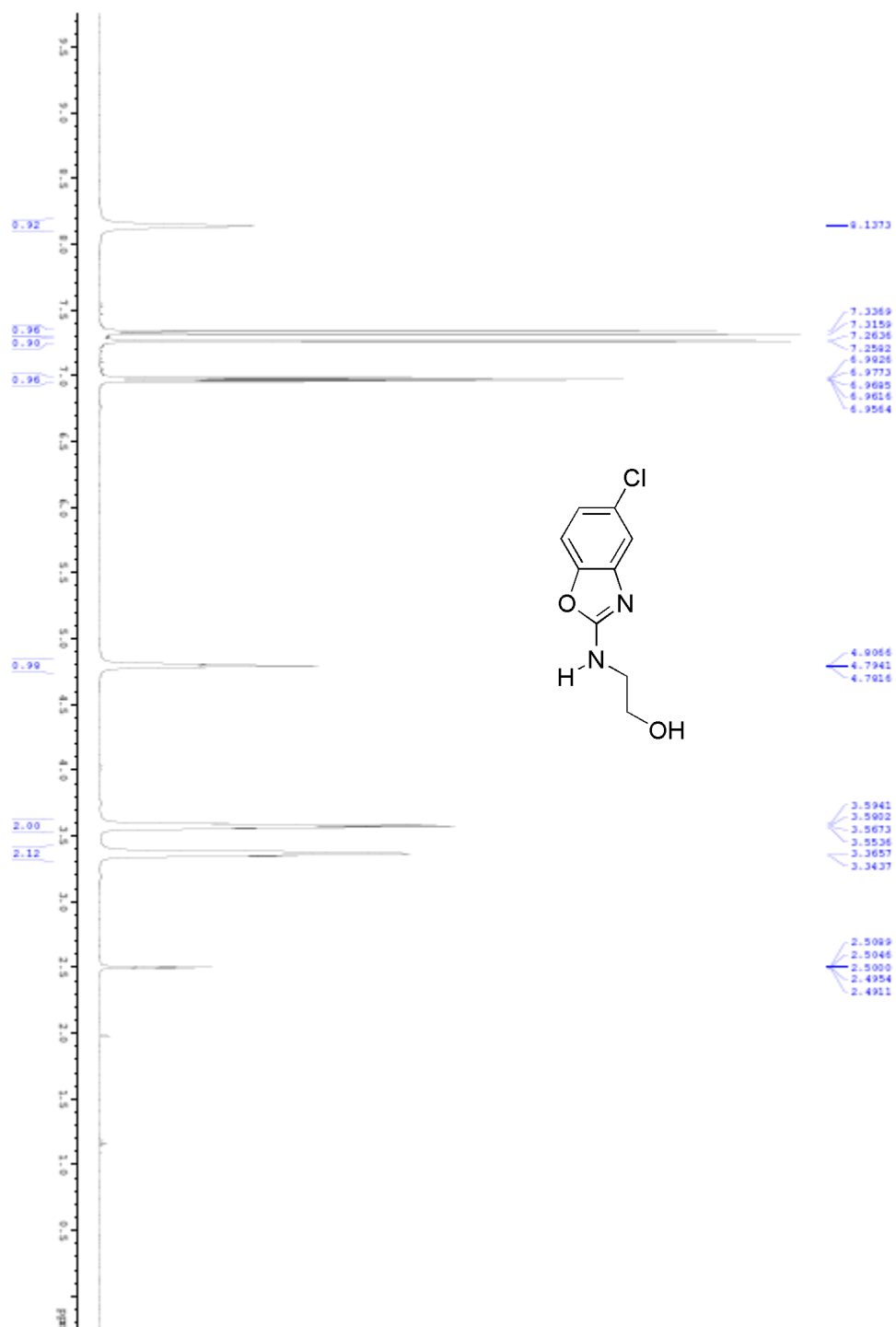
and age for 1 hour. After the age and confirmation of the seed bed cool the batch to 45 °C over 2.5 hrs. At this time solvent switch at constant volume to a ratio of 90:10 n-Heptane:iPAc. Filter hot at 45 °C, wash the cake with 3 vol (mL/g of **1**) of 90:10 n-Heptane:iPAc twice, followed by 3 vol (mL/g of **1**) of n-Heptane twice. Dry the cake at 70 °C under vacuum. Obtained 14.4 g. **1** (31.8 mmol, 96% yield) as a crystalline white powder.

<sup>1</sup>H NMR (500 MHz, CD<sub>3</sub>OD) and <sup>13</sup>C NMR (CD<sub>3</sub>OD, 125 MHz) spectra are provided below; note that the existence of multiple rotamers that did not coalesce during high temperature experiments makes individual assignments complicated. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz) δ 7.91–7.60 (m, 3H), 7.38–6.77 (m, 5H), 4.56 (d, *J* = 12.0 Hz, 1H), 4.38–3.07 (m, 6H), 2.46 (m, 4H), 2.09–1.51 (m, 1H), 1.42–1.25 (m, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz) δ 169.9, 169.4, 163.0, 162.8, 147.5, 144.7, 144.6, 138.6, 138.2, 135.7, 135.6, 135.5, 134.1, 133.6, 130.6, 129.4, 129.0, 128.5, 128.4, 128.3, 128.1, 122.6, 122.2, 122.1, 120.4, 120.3, 116.3, 116.2, 109.4, 109.2, 109.1, 52.2, 51.6, 48.9, 48.4, 48.1, 47.6, 47.3, 47.1, 45.6, 45.1, 44.9, 44.4, 44.0, 43.8, 41.0, 39.8, 36.3, 35.4, 34.2, 33.9, 21.0, 20.9, 19.9, 17.9, 17.8, 16.7; HRMS calculated for C<sub>23</sub>H<sub>24</sub>ClN<sub>6</sub>O<sub>2</sub> (M+H): 451.1649, found: 451.1640.  $[\alpha]_D^{25} = -12.1$  (c = 1.0, MeOH).

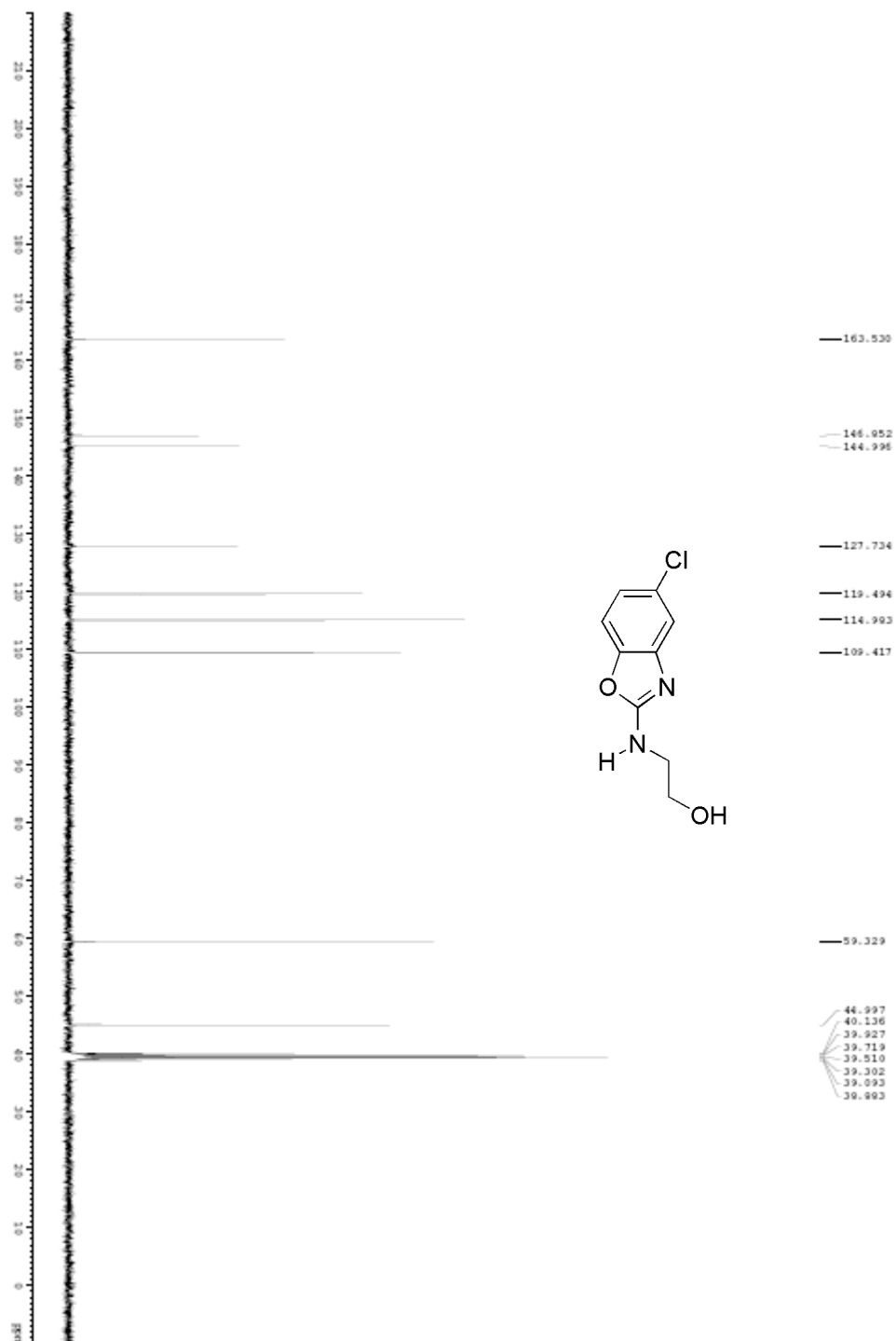
**5-Chlorobenzoxazole (9).**  $^1\text{H}$  NMR (400 MHz).



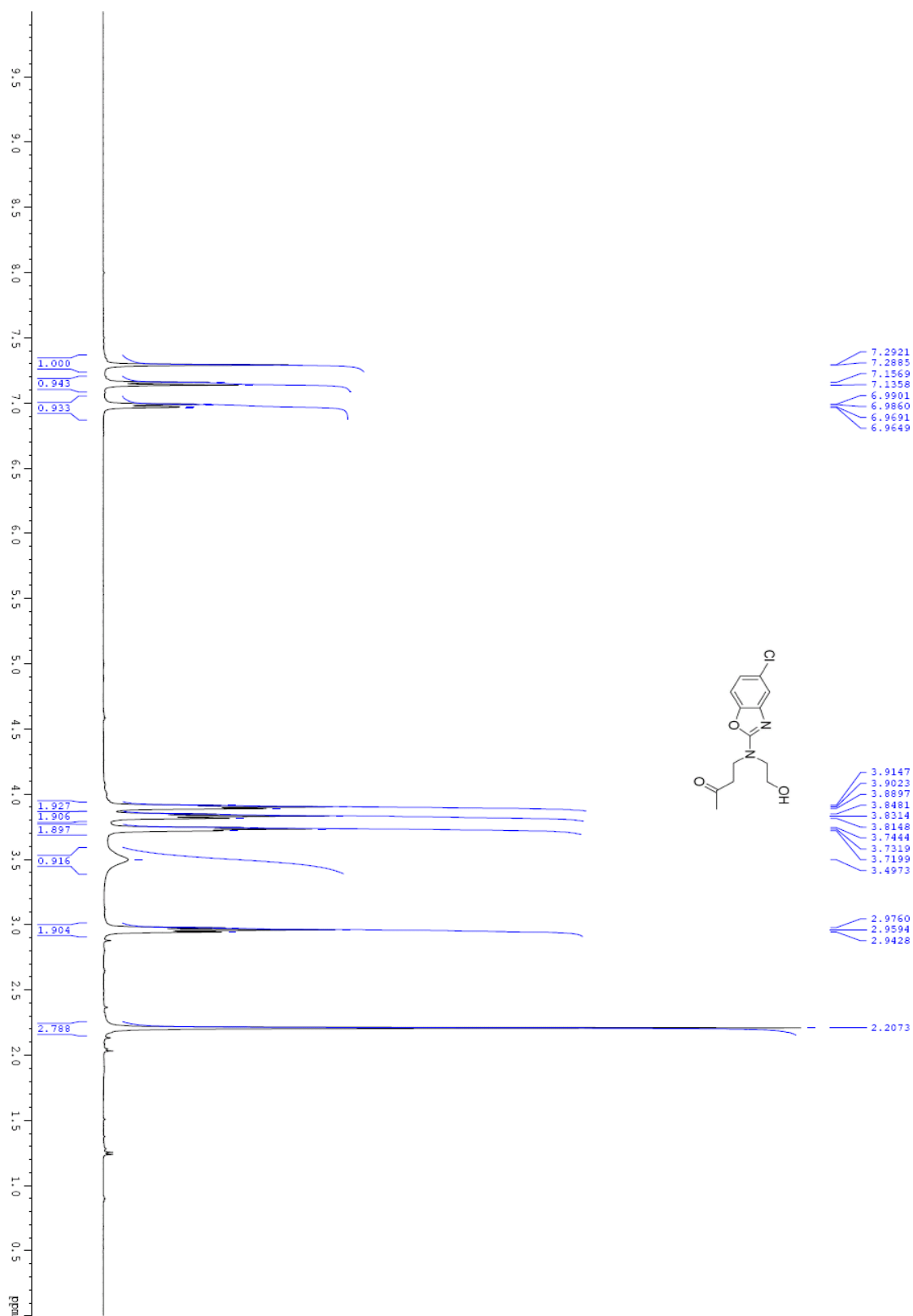
2-[(5-Chloro-1,3-benzoxazol-2-yl)amino]ethanol (11).  $^1\text{H}$  NMR (400 MHz).



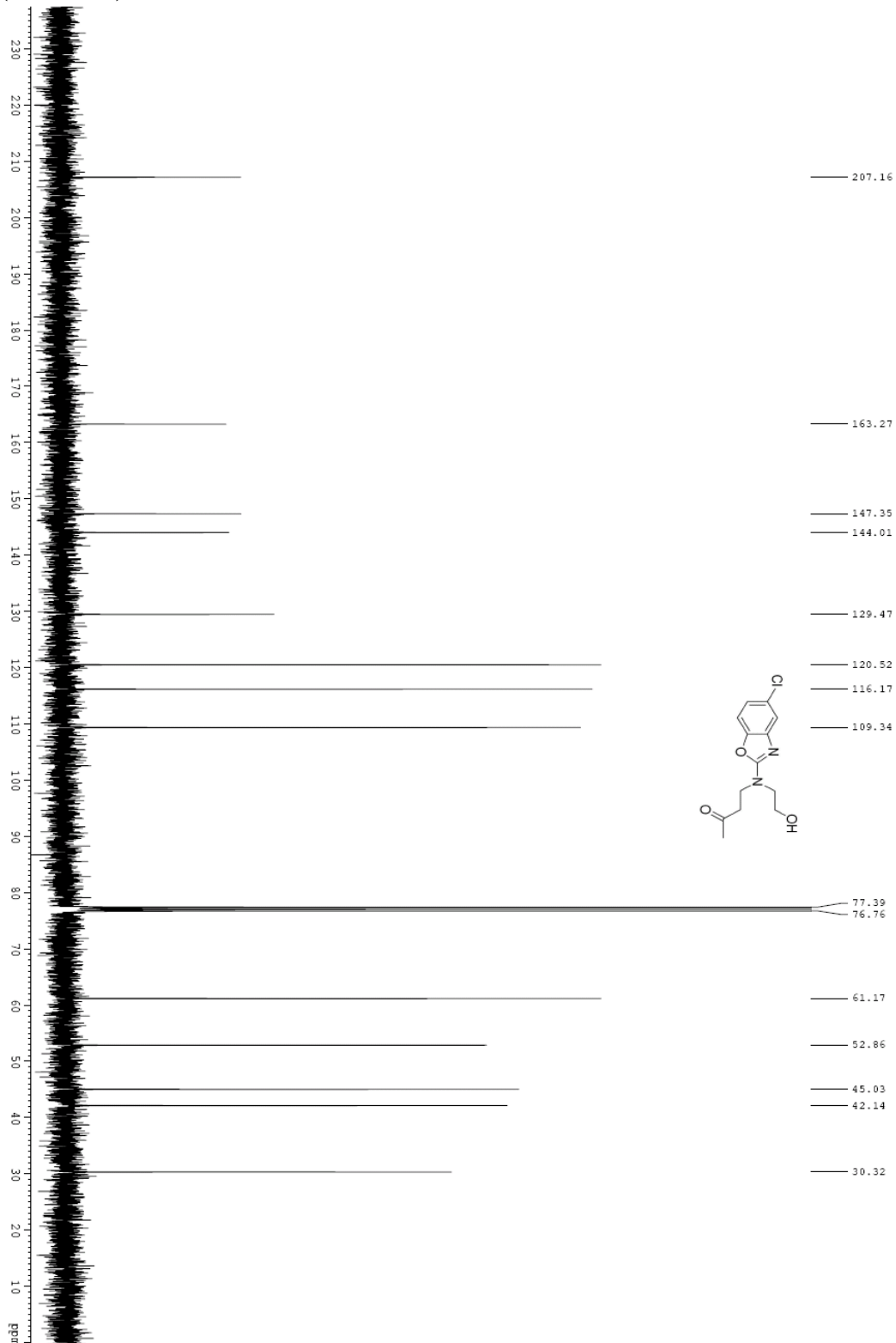
2-[(5-Chloro-1,3-benzoxazol-2-yl)amino]ethanol (11).  $^{13}\text{C}$  NMR (100 MHz).



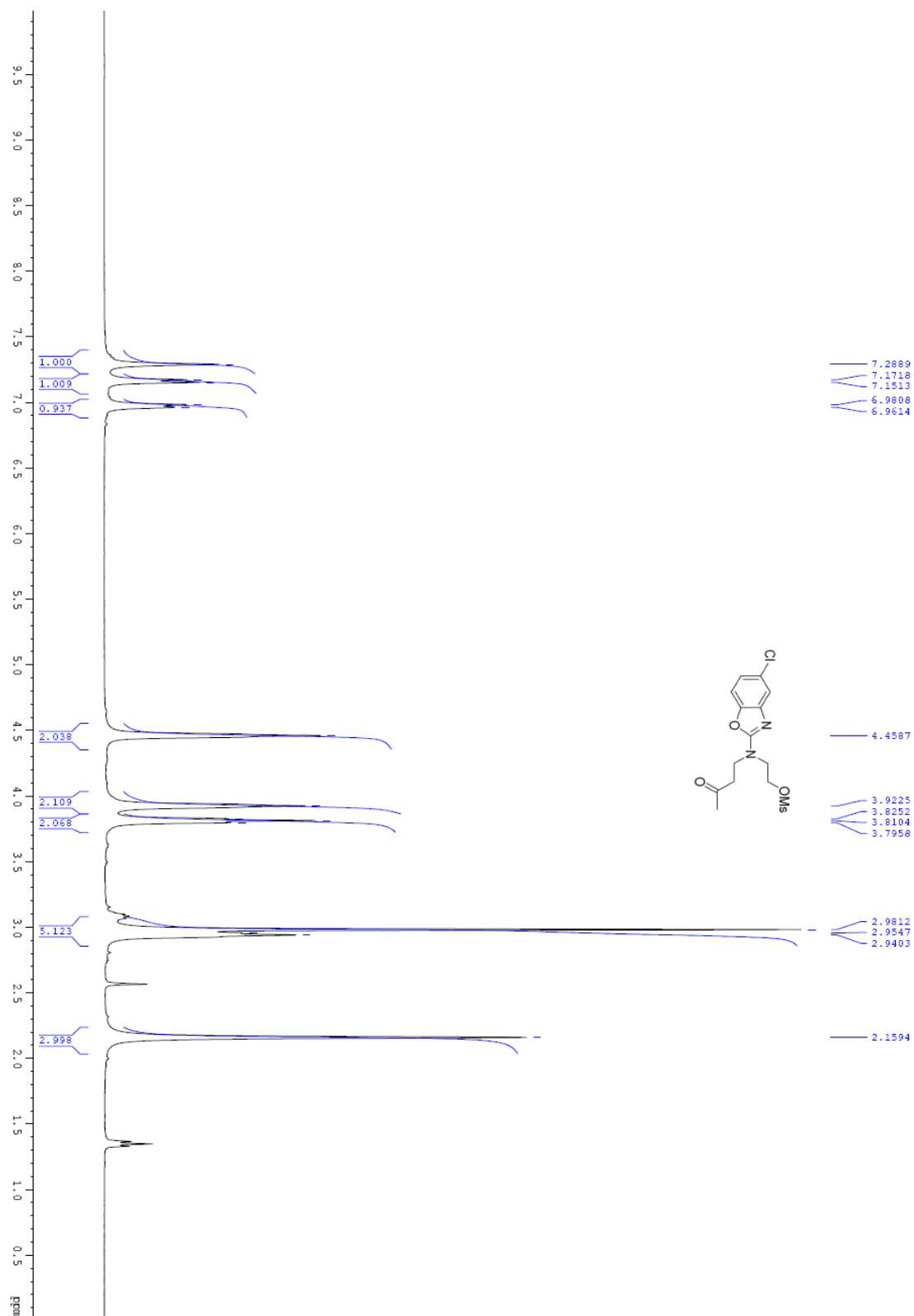
**4-((5-chlorobenzo[d]oxazol-2-yl)(2-hydroxyethyl)amino)butan-2-one (12).  $^1\text{H}$  NMR (400 MHz).**



**4-((5-chlorobenzo[d]oxazol-2-yl)(2-hydroxyethyl)amino)butan-2-one (12).  $^{13}\text{C}$  NMR (100 MHz).**

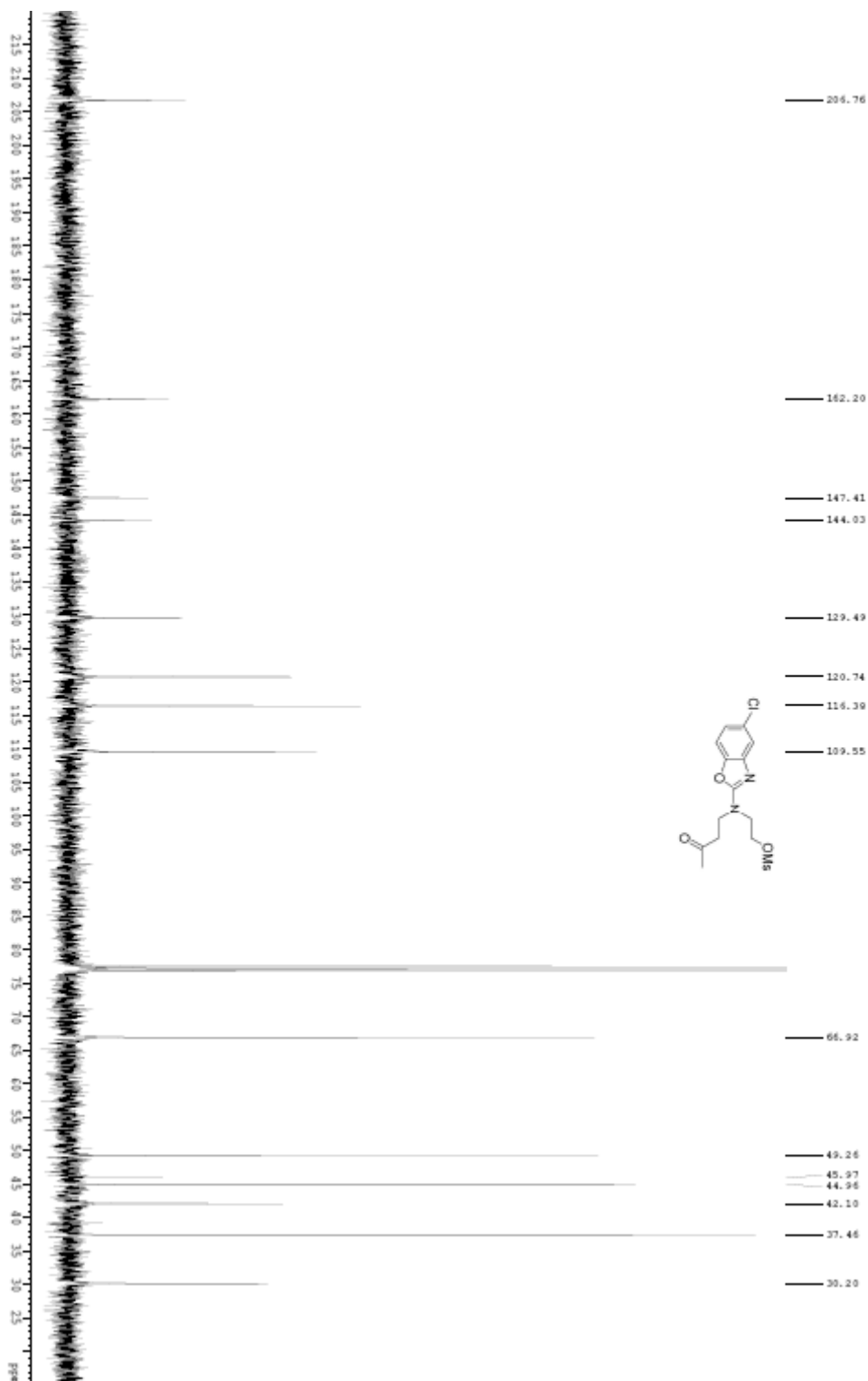


**Methanesulfonic acid 2-[(5-chloro-benzooxazol-2-yl)-(3-oxo-butyl)-amino]-ethyl ester (14).  $^1\text{H}$  NMR (400 MHz).**

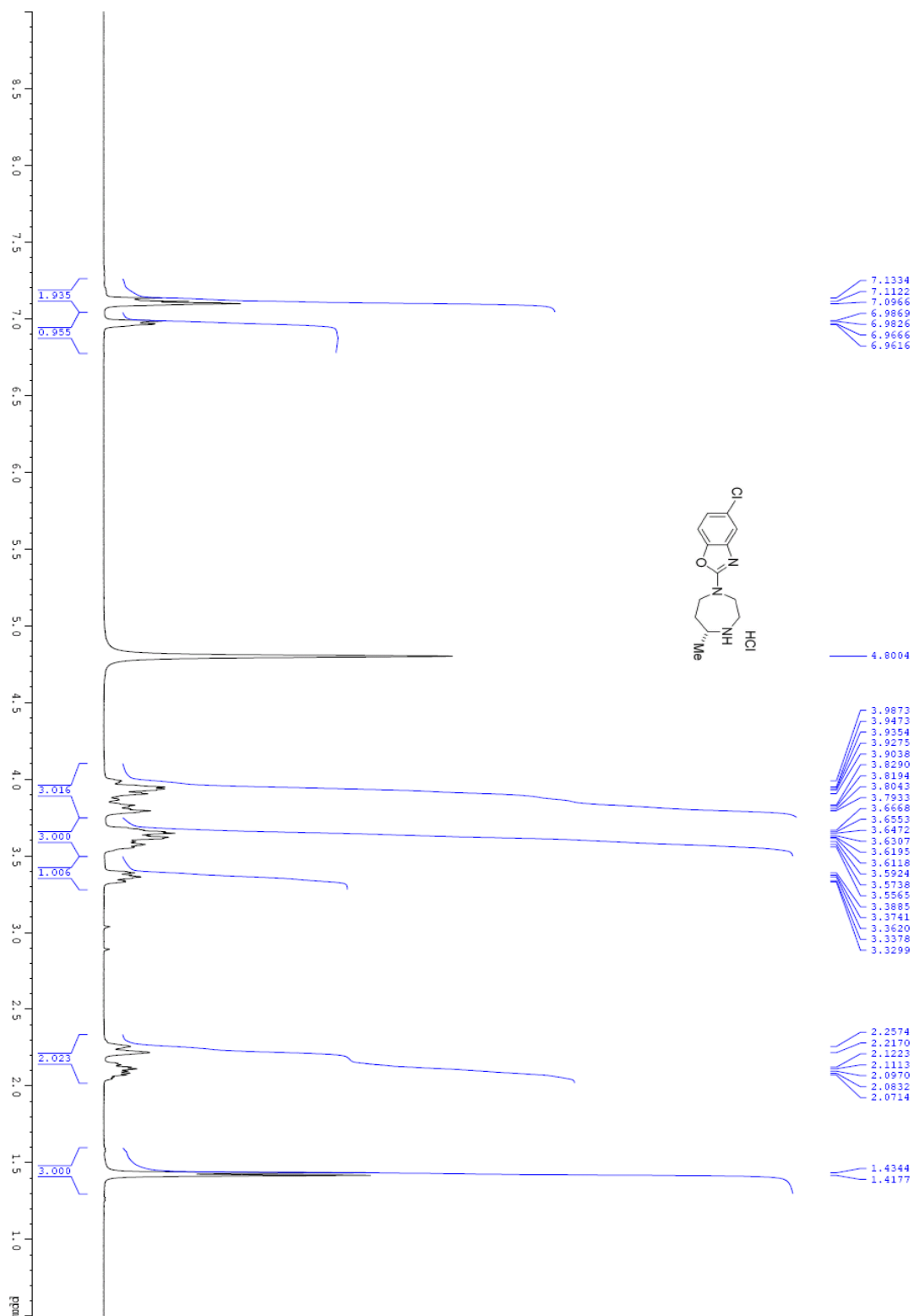




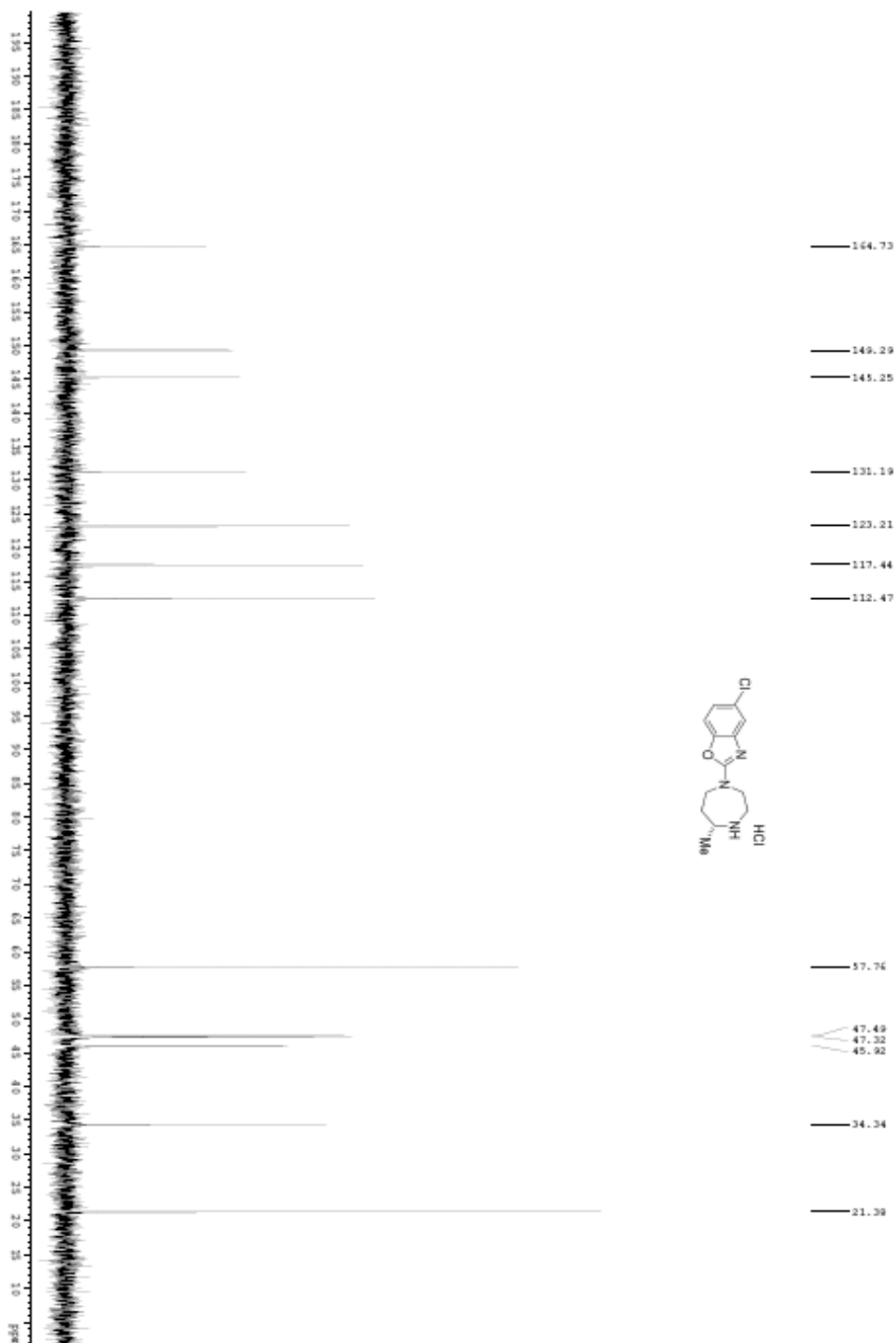
Methanesulfonic acid 2-[(5-chloro-benzooxazol-2-yl)-(3-oxo-butyl)-amino]-ethyl ester (14).  $^{13}\text{C}$  NMR (100 MHz).



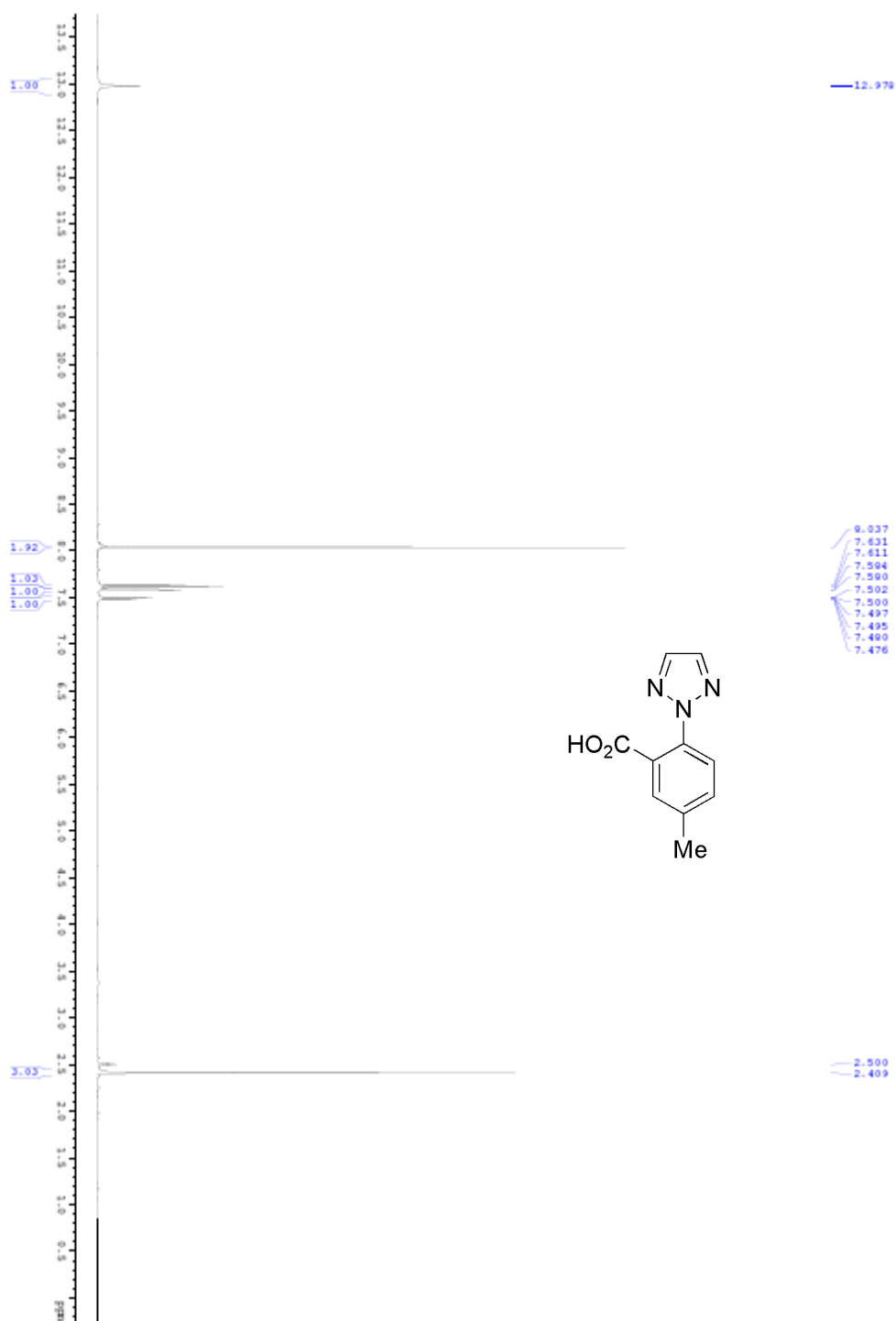
**5-Chloro-2-((R)-5-methyl-[1,4]diazepan-1-yl)-benzoxazole hydrochloride (21).  $^1\text{H}$  NMR (400 MHz).**



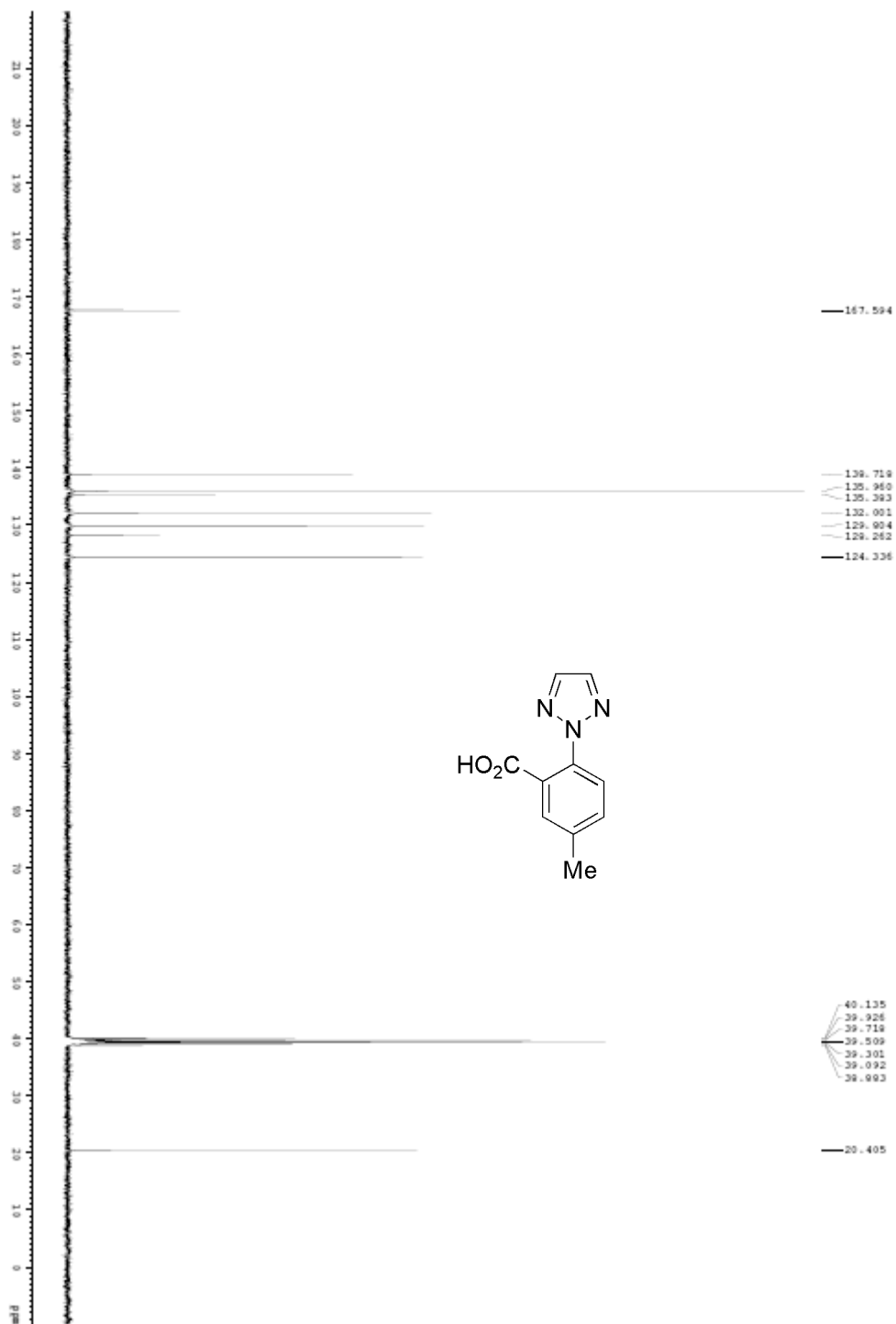
**5-Chloro-2-((R)-5-methyl-[1,4]diazepan-1-yl)-benzoxazole hydrochloride (21).  $^{13}\text{C}$  NMR (100 MHz).**



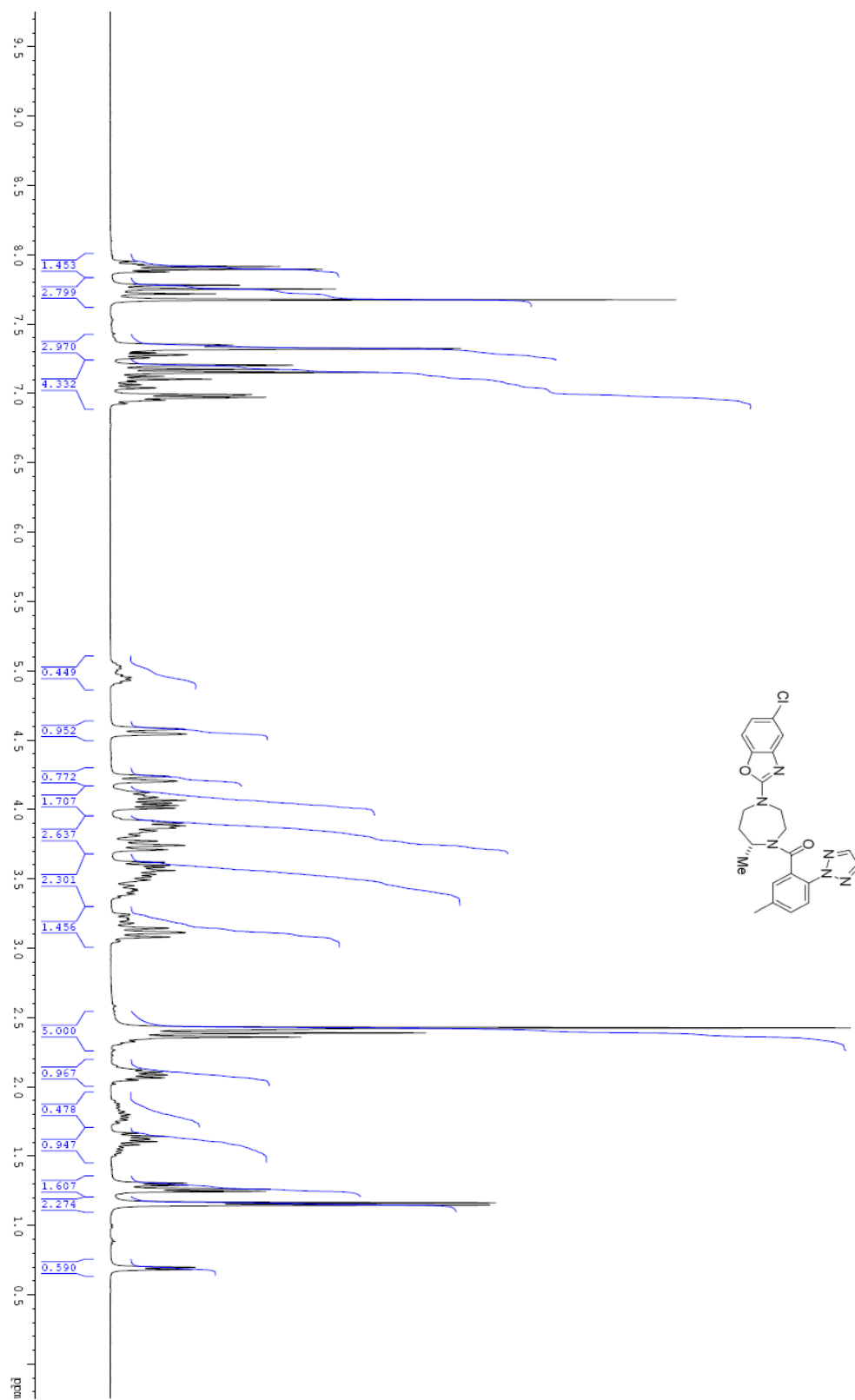
5-Methyl-2-[1,2,3]triazol-2-yl-benzoic acid (19).  $^1\text{H}$  NMR (400 MHz).



5-Methyl-2-[1,2,3]triazol-2-yl-benzoic acid (19).  $^{13}\text{C}$  NMR (100 MHz).



**[(R)-4-(5-Chloro-benzooxazol-2-yl)-7-methyl-[1,4]diazepan-1-yl]-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone (1).  $^1\text{H}$  NMR (400 MHz).**



**[(R)-4-(5-Chloro-benzooxazol-2-yl)-7-methyl-[1,4]diazepan-1-yl)-(5-methyl-2-[1,2,3]triazol-2-yl-phenyl)-methanone (1).  $^{13}\text{C}$  NMR (100 MHz).**

