# Cyanoacetamide MCR (III): Three-Component Gewald Reactions Revisited.

Kan Wang, Dabin Kim, Alexander Dömling*

University of Pittsburgh, Drug Discovery Institute, Pittsburgh 15261, USA.

Corresponding author: Alexander Dömling, *asd30@pitt.edu

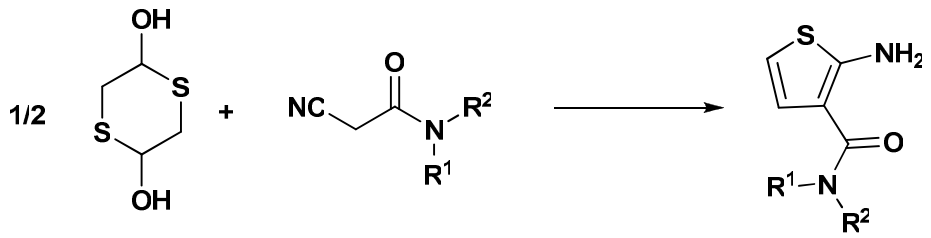
## Supporting Information

**General Information.** All reactions were under air atmosphere. All cyanoacetamides are prepared as the procedure described in the reference. [1]All other reagents and solvents are purchased without further purification. Analytical thin-layer chromatography (TLC) was preformed on $SiO_2$ plates on Alumina available from Whatman. Visualization was accomplished by UV irradiation at 254 nm, or by staining with any one of the following reagents: iodine, ninhydrin (0.3% w/v in glacial acetic acid/*n*-butyl alcohol 3:97), Vaughn's reagent (4.8 g of $(NH_4)_6Mo_7O_{24}\bullet 4H_2O$ and 0.2 g of $Ce(SO_4)_2\bullet 4H_2O$ in 10 mL of conc. $H_2SO_4$ and 90 mL of $H_2O$). Flash column chromatography was performed using $SiO_2$ 60 (particle size 0.040-0.055 mm, 230-400 mesh, EM science distributed by Bioman), Preparative TLC was conducted using Preparative Silica gel TLC plates (1000 μm, 20cm×20cm).

Proton and carbon NMR spectra were obtained on Bruker Avance™ 600 MHz NMR spectrometer. Chemical shifts are reported as δ values in parts per million (ppm) as referenced to residual solvent. 1H NMR spectra are tabulated as follows: chemical shift, multiplicity (s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant(s), and number of protons. High Resolution Mass spectra were obtained at the University of Pittsburgh Mass Spectrometry facility. LC-MS analysis was performed on an SHIMADZU instrument, using an analytical C18 column (Dionex Acclaim 120 Å, 2.1 × 50 mm, 3.0 μm, 0.2 mL/min).

**Gewald Reaction of 1,4-dithiane-2,5-diol**

[1] Wang, K.; Nguyen, K.; Huang, Y. J.; Doemling, A. *J. Comb. Chem.* **2009**, *11*, 920-927.



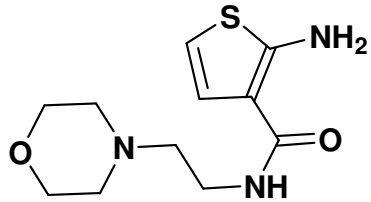
**2-Amino-*N*-cyclopropylthiophene-3-carboxamide (C1,1): General procedure A (Reaction of cyanoacetamides with 1,4-dithiane-2,5-diol):** In a 20 ml glass vial added into 2-cyano-*N*-cyclopropylacetamide (1.24 g, 10 mmol), 1,4-dithiane-2,5-diol (760 mg, 5 mmol), $Et_3N$ (505 mg, 5 mmol) and EtOH (10 ml, 1.0 M solution). Allow the reaction heated in 50 $^oC$ for 12 h. Then add 50 ml ice/water and extracted with dichloromethane (20 X 3 ml). Combine organic phase and dried with anhydrous sodium sulfate. Remove the solvent on vacuum, the crude product was purified with chromatography in silica gel (50 % ethyl acetate in hexanes) to obtain the title compound 637 mg (35 %) as light yellow power. HRMS ESL-TOF for $C_8H_{10}N_2OS$ ($M^+$) found: *m/z*: 182.0508; Calc. Mass 182.0514. $^1H$ NMR ($CDCl_3$, 600 MHz): δ 6.62 (d, J = 6.0 Hz, 1H), 6.19 (d, J = 6.0 Hz, 1H), 6.13 (s, 2H), 5.80 (s, 1H), 2.76-2.78 (m, 1H), 0.79-0.82 (m, 2H), 0.54-0.58 (m, 2H) ppm; $^{13}C$ NMR ($CDCl_3$, 150 MHz): δ 167.3, 160.4, 122.5, 108.6, 107.5, 22.4, 6.8 ppm.

**2-Amino-*N*-benzylthiophene-3-carboxamide (C1,2):** General procedure A was followed employing *N*-benzyl-2-cyanoacetamide (1.74 g, 10 mmol), 1,4-dithiane-2,5-diol (760 mg, 5 mmol). The crude product was purified with chromatography in silica gel (50 % ethyl acetate in hexanes) to obtain the title compound 1.30 g (56 %) as light yellow power. HRMS ESL-TOF for $C_{12}H_{12}N_2OS$ ($M^+$) found: *m/z*: 232.0664; Calc. Mass 232.0670. $^1H$ NMR ($CDCl_3$, 600 MHz): δ 7.25-7.34 (m, 5H), 6.70 (d, J = 6.0 Hz, 1H), 6.22 (d, J = 6.0 Hz, 1H), 6.12 (s, 2H), 6.00 (s, 1H), 4.56 (s, 2H) ppm; $^{13}C$ NMR ($CDCl_3$, 150 MHz): δ 165.6, 161.0, 138.6, 128.7, 127.7, 127.5, 122.6, 108.7, 107.6, 43.2 ppm.

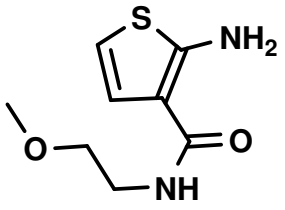
**2-Amino-*N*-butylthiophene-3-carboxamide (C1,3):** General procedure A was followed employing *N*-butyl-2-cyanoacetamide (1.40 g, 10 mmol), 1,4-dithiane-2,5-diol (760 mg, 5 mmol). The crude product was purified with chromatography in silica gel (50 % ethyl acetate in hexanes) to obtain the title compound 1.19 g (60 %) as light yellow power. HRMS ESL-TOF for $C_9H_{14}N_2OS$ ($M^+$) found: *m/z*: 198.0834; Calc. Mass 198.0827. $^1H$ NMR ($CDCl_3$, 600 MHz): δ 6.71 (d, J = 6.0 Hz, 1H), 6.22 (d, J = 6.0 Hz, 1H), 6.09 (s, 2H), 5.69 (s, 1H), 3.69 (dt, J = 7.2, 6.0 Hz, 2H), 1.52-1.58 (m, 2H), 1.35-1.42 (m, 2H), 0.94 (t, J = 7.8 Hz, 3H) ppm; $^{13}C$ NMR ($CDCl_3$, 150 MHz): δ 165.8, 160.6, 122.6, 109.1, 107.5, 38.9, 32.0, 20.2, 13.8 ppm.

**2-Amino-*N*-(2-morpholinoethyl)thiophene-3-carboxamide (C1,4):** General procedure A was followed employing 2-cyano-*N*-(2-morpholinoethyl)acetamide (1.97 g, 10 mmol),

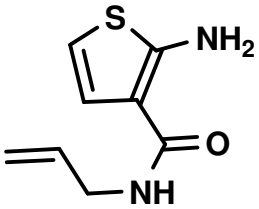
1,4-dithiane-2,5-diol (760 mg, 5 mmol). The crude product was purified with chromatography in silica gel (0-10 % methanol in ethyl acetate) to produce the title compound 1.58 g (62 %) as light yellow power. HRMS ESL-TOF for $C_{11}H_{17}N_3O_2S$ ($M^+$) found: *m/z*: 255.1031; Calc. Mass 255.1041. $^1$H NMR (*d6*-DMSO, 600 MHz): δ 7.63 (s, 1H), 7.17 (s, 2H), 7.03 (d, J = 6.0 Hz, 1H), 6.25 (d, J = 6.0 Hz, 1H), 3.56 (s, 4H), 3.27 (s, 2H), 2.40 (s, 6H) ppm; $^{13}$C NMR (*d6*-DMSO, 150 MHz): δ 165.8, 161.6, 124.5, 107.7, 106.2, 66.6, 58.2, 53.8, 36.1 ppm.



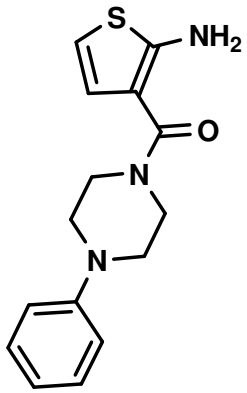

**2-Amino-*N*-(2-methoxyethyl)thiophene-3-carboxamide (C1,5):** General procedure A was followed employing 2-cyano-*N*-(2-methoxyethyl)acetamide (1.42 g, 10 mmol), 1,4-dithiane-2,5-diol (760 mg, 5 mmol). The crude product was purified with chromatography in silica gel (50 % ethyl acetate in hexanes) to obtain the title compound 821 mg (41 %) as light yellow power. HRMS ESL-TOF for $C_8H_{12}N_2O_2S$ ($M^+$) found: *m/z*: XXX; Calc. Mass 200.0619. $^1$H NMR ($CDCl_3$, 600 MHz): δ 6.68 (d, J = 6.0 Hz, 1H), 6.45 (s, 1H), 6.22 (d, J = 6.0 Hz, 1H), 6.11 (s, 2H), 3.51-3.55 (t, J = 5.4 Hz, 2H), 3.48 (t, J = 5.4 Hz, 2H), 3.37 (s, 3H) ppm; $^{13}$C NMR ($CDCl_3$, 150 MHz): δ 165.8, 160.4, 122.8, 109.2, 107.4, 72.3, 58.9, 38.2 ppm.

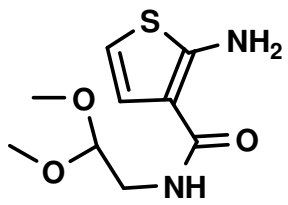



***N*-Allyl-2-aminothiophene-3-carboxamide (C1,6):** General procedure A was followed employing *N*-allyl-2-cyanoacetamide (1.24 g, 10 mmol), 1,4-dithiane-2,5-diol (760 mg, 5 mmol). The crude product was purified with chromatography in silica gel (50 % ethyl acetate in hexanes) to obtain the title compound 694 mg (38 %) as light yellow power. HRMS ESL-TOF for $C_8H_{10}N_2OS$ ($M^+$) found: *m/z*: 182.0511; Calc. Mass 182.0514. $^1$H NMR ($CDCl_3$, 600 MHz): δ 6.73 (d, J = 6.0 Hz, 1H), 6.24 (d, J = 6.0 Hz, 1H), 6.10 (s, 2H), 5.92 (ddt, J = 16.8, 10.2, 5.4 Hz, 1H), 4.01 (t, J = 5.4 Hz, 2H) ppm; $^{13}$C NMR ($CDCl_3$, 150 MHz): δ 165.6, 160.9, 134.7, 122.5, 116.3, 108.6, 107.6, 41.6 ppm.

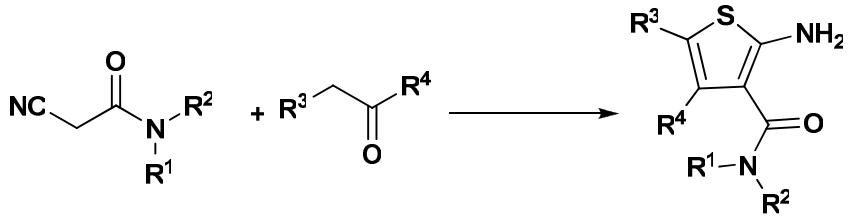



**(2-Aminothiophen-3-yl)(4-phenylpiperazin-1-yl)methanone (C1,7):** General procedure A was followed employing 3-oxo-3-(4-phenylpiperazin-1-yl)propanenitrile (1.15 g, 5 mmol), 1,4-dithiane-2,5-diol (380 mg, 2.5 mmol). The crude product was purified with chromatography in silica gel (75 % ethyl acetate in hexanes) to obtain the title compound 1008 mg (70 %) as light yellow power. HRMS ESL-TOF for $C_{15}H_{17}N_3OS$ ($M^+$) found: *m/z*: 287.1097; Calc. Mass 287.1092. $^1$H NMR ($CDCl_3$, 600 MHz): δ 7.23 (t, J = 7.8 Hz, 2H), 6.95 (d, J = 7.8 Hz, 2H), 6.80 (t, J = 7.2 Hz, 1H), 6.71 (d, J = 6.0 Hz, 1H), 6.47 (s, 2H), 6.35 (d, J = 6.0 Hz, 1H), 3.60-3.70 (m, 4H), 3.10-3.20 (m, 4H) ppm; $^{13}$C NMR ($CDCl_3$, 150 MHz): δ 166.8, 159.4, 151.3, 129.4, 126.3, 119.7, 116.3, 108.9, 107.1, 49.0, 44.9 ppm.

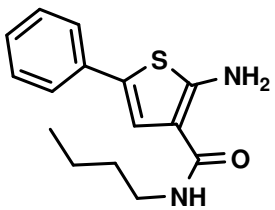




**2-Amino-*N*-(2,2-dimethoxyethyl)thiophene-3-carboxamide (C1,8)**: General procedure A was followed employing 2-cyano-N-(2,2-dimethoxyethyl)acetamide (1.72 g, 10 mmol), 1,4-dithiane-2,5-diol (760 mg, 5 mmol). The crude product was purified with chromatography in silica gel (75 % ethyl acetate in hexanes) to obtain the title compound 1.50 g (65 %) as light yellow power. HRMS ESL-TOF for $C_9H_{14}N_2O_3S$ ($M^+$) found: *m/z*: 230.0722; Calc. Mass 230.0725. $^1$H NMR ($CDCl_3$, 600 MHz): δ 6.72 (d, J = 6.0 Hz, 1H), 6.23 (d, J = 6.0 Hz, 1H), 6.11 (s, 2H), 5.88 (s, 1H), 4.43-4.45 (m, 1H), 3.50-3.53 (m, 2H), 3.42 (s, 6H) ppm; $^{13}$C NMR ($CDCl_3$, 150 MHz): δ 165.8, 161.0, 122.7, 108.7, 107.5, 103.4, 54.6, 40.7 ppm.



***N*-Allyl-2-amino-5-phenylthiophene-3-carboxamide (C2,6): General Procedure B (three-component reactions of aldehyde or ketones, cyanoacetamide and sulfur).** In a 20 ml vial added into *N*-allyl-2-cyanoacetamide (1.24 g, 10 mmol), 2-phenylacetaldehyde (1.20 g, 10 mmol) and sulfur (320 mg, 10 mmol) and triethylamine (1.01 g, 10 mmol) in ethanol (10 ml, 1.0 M solution) with stir bar. The reaction was heated in 50 $^o$C oil bath for 10 h. Cool the reaction down to room temperature, and add 50 ml ice/water. The precipitate was filtered and washed with cold ethanol to obtain the title compound 2.12 g (82 %) as brown power. HRMS ESL-TOF for $C_{14}H_{14}N_2OS$ ($M^+$) found: *m/z*: 258.0825; Calc. Mass 258.0827. $^1$H NMR ($CDCl_3$, 600 MHz): δ 7.38 (d, J = 7.8 Hz, 2H), 7.28 (t, J = 7.8 Hz, 2H), 7.16 (t, J = 7.8 Hz, 1H), 7.07 (s, 1H), 6.37 (s, 2H), 5.89 (ddt, J =16.8, 10.8, 5.4 Hz, 1H), 5.22 (d, J = 16.8 Hz, 1H), 5.12 (d, J = 10.8 Hz, 1H), 3.97 (t, J = 5.4 Hz, 2H) ppm; $^{13}$C NMR ($CDCl_3$, 150 MHz): δ 166.0, 160.8, 134.70 134.1, 128.8, 126.5, 125.0, 124.6, 118.5, 116.1, 109.3, 41.7 ppm.



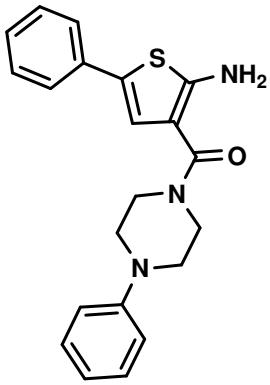
**2-Amino-*N*-butyl-5-phenylthiophene-3-carboxamide (C2,3):** The general procedure B was followed employing 2-phenylacetaldehyde (1.20 g, 10 mmol), *N*-butyl-2-cyanoacetamide (1.40 g, 10 mmol). The precipitate was filtered to produce the title compound 1.92 g (70 %) as the dark yellow solid. HRMS ESL-TOF for $C_{15}H_{18}N_2OS$ ($M^+$) found: *m/z*: 274.1135; Calc. Mass 274.1140. $^1$H NMR ($CDCl_3$, 600 MHz): δ 7.43 (d, J = 7.2 Hz, 2H), 7.33 (t, J = 7.8 Hz, 2H), 7.21 (t, J = 7.8 Hz, 1H), 6.22 (s, 2H), 5.80 (s, 1H), 3.40 (q, J = 6.6 Hz, 2H), 1.56-1.61 (m, 2H), 1.38-1.43 (m, 2H), 0.97 (t, J = 7.2 Hz, 3H) ppm; $^{13}$C NMR ($CDCl_3$, 150 MHz): δ 165.9, 160.2, 134.0, 128.9, 126.6, 125.3, 124.6, 118.1, 109.8, 39.1, 32.0, 20.2, 13.8 ppm.

**2-Amino-*N*-(2-morpholinoethyl)-5-phenylthiophene-3-carboxamide (C2,4):** The general procedure B was followed employing 2-phenylacetaldehyde (1.20 g, 10 mmol), 2-cyano-*N*-(2-morpholinoethyl)acetamide (1.97 g, 10 mmol). The precipitate was filtered to produce the title compound 2.58 g (78 %) as the dark yellow solid. HRMS ESL-TOF for $C_{17}H_{22}N_3O_2S$ ($M+H^+$) found: *m/z*: 332.1455; Calc. Mass 332.1433. $^1$H NMR ($CDCl_3$, 600 MHz): δ 7.43 (d, J = 8.4 Hz, 2H), 7.34 (t, J = 7.8 Hz, 2H), 7.22 (t, J = 7.2 Hz, 1H), 6.99 (s, 1H), 6.43 (s, 1H), 6.23 (s, 2H), 3.75 (t, J = 4.2 Hz, 4H), 3.50 (q, J = 6.0 Hz, 2H), 2.59 (t, J = 6.0 Hz, 2H), 2.51 (brs, 4H) ppm; $^{13}$C NMR ($CDCl_3$, 150 MHz): δ 165.9, 160.3, 134.0, 128.9, 126.7, 125.2, 124.7, 118.2, 109.8, 67.0, 57.2, 53.3, 35.3 ppm.

**2-Amino-*N*-(4-chlorophenethyl)-5-phenylthiophene-3-carboxamide (C2,9):** The general procedure B was followed employing 2-phenylacetaldehyde (1.20 g, 10 mmol), 2-cyano-*N*-4-chlorophenethylacetamide (2.22 g. 10 mmol). The crude product was purified with silica gel column chromatography (50-75 % ethyl acetate in hexanes) to produce the title compound 2.57 g (72 %) as the dark yellow oil. HRMS ESL-TOF for $C_{19}H_{17}ClN_2OS$ ($M^+$) found: *m/z*: 356.0757; Calc. Mass: 356.0750. $^1$H NMR (*d6*-DMSO, 600 MHz): δ 7.86 (t, J = 5.4 Hz, 1H), 7.57 (s, 1H), 7.46 (s, 2H), 7.39 (d, J = 7.8 Hz, 2H), 7.33-7.37 (m, 4H), 7.27 (d, J = 8.4 Hz, 2H), 7.18 (t, J = 7.8 Hz, 1H), 3.41 (q, J = 6.6 Hz, 2H), 2.82 (t, J = 7.2 Hz, 2H) ppm; $^{13}$C NMR (*d6*-DMSO, 150 MHz): δ 165.8, 161.4, 139.2, 134.7, 131.2, 131.0, 129.4, 128.7, 126.3, 124.0, 121.9, 121.1, 108.5, 35.2, 31.2 ppm.

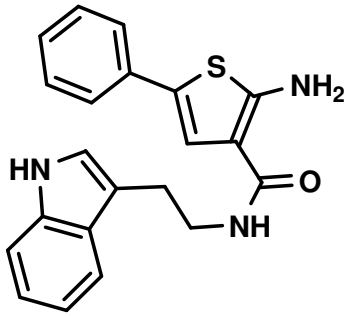
**2-Amino-*N*-(2-methoxyethyl)-5-phenylthiophene-3-carboxamide (C2,5):** The general procedure B was followed employing 2-phenylacetaldehyde (1.20 g, 10 mmol), 2-cyano-*N*-2-methoxyethylacetamide (1.42 g, 10 mmol). The crude product was purified with silica gel column chromatography (50-75 % ethyl acetate in hexanes) to produce the title compound 2.25 g (75 %) as the dark yellow oil. HRMS ESL-TOF for $C_{14}H_{16}N_2O_2SNa$ ($M+Na^+$) found: *m/z*: 299.0801; Calc. Mass: 299.0830. $^1$H NMR ($CDCl_3$, 600 MHz): δ 7.42 (d, J = 7.8 Hz, 2H), 7.33 (t, J = 7.8 Hz, 2H), 7.20 (t, J = 7.8 Hz, 1H), 6.21 (s, 2H), 6.12 (s, 1H), 3.59 (q, J = 6.0 Hz, 2H), 3.55 (t, J = 5.4 Hz, 2H), 3.40 (s, 3H) ppm; $^{13}$C NMR ($CDCl_3$, 150 MHz): δ 165.79, 160.36, 133.95, 128.85, 126.64, 125.28, 124.67, 118.17, 109.64, 71.49, 58.85, 38.87 ppm.

**(2-Amino-5-phenylthiophen-3-yl)(4-phenylpiperazin-1-yl)methanone (C2,7):** The



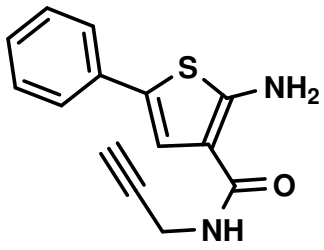
general procedure B was followed employing 2-phenylacetaldehyde (0.60 g, 5 mmol), 3-oxo-3-(4-phenylpiperazin-1-yl)propanenitrile (1.15 g, 5 mmol), sulfur (160 mg, 5 mmol). The precipitate was filtered to produce the title compound 1.74 g (90 %) as the dark yellow solid. HRMS ESL-TOF for $C_{21}H_{21}N_3OSNa$ ($M^+$) found: *m/z*: 386.1291; Calc. Mass: 386.1303. $^1$H NMR ($CDCl_3$, 600 MHz): δ 7.42 (d, J = 8.4 Hz, 2H), 7.34 (t, J = 7.8 Hz, 2H), 7.29 (t, J = 7.2 Hz, 2H), 7.22 (t, J = 7.8 Hz, 1H), 6.96 (s, 1H), 6.96 (s, 2H), 6.92 (t, J = 7.2 Hz, 1H), 5.50 (s, 2H), 3.85 (t, J = 5.4 Hz, 4H), 3.24 (t, J = 5.4 Hz, 4H) ppm; $^{13}$C NMR ($CDCl_3$, 150 MHz): δ 167.08, 159.22, 151.01, 133.97, 129.26, 128.89, 126.70, 125.64, 124.73, 120.79, 120.48, 116.58, 111.07, 49.75 ppm.

***N*-(2-(1H-Indol-3-yl)ethyl)-2-amino-5-phenylthiophene-3-carboxamide (C2,10):**



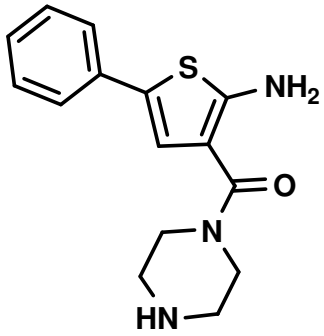
General procedure B was followed employing 2-phenylacetaldehyde (360 mg, 3 mmol), sulfur (96 mg, 3 mmol), *N*-(2-(1H-indol-3-yl)ethyl)-2-cyanoacetamide (682 mg, 3 mmol). The crude product was purified with silica gel column chromatography (50 % ethyl acetate in hexanes) to produce the title compound 1020 mg (85 %) as the light yellow solid. HRMS ESL-TOF for $C_{21}H_{19}N_3OSK$ ($M+K^+$) found: *m/z*: 400.0881; Calc. Mass: 400.0886. $^1$H NMR (*d6*-DMSO, 600 MHz): δ 10.83 (s, 1H), 7.95 (t, J = 5.4 Hz, 1H), 7.63 (s, 1H), 7.61 (d, J = 7.8 Hz, 1H), 7.52 (s, 2H), 7.42 (d, J = 7.8 Hz, 2H), 7.32-7.37 (s, 3H), 7.20 (d, J = 1.8 Hz, 1H), 7.17 (t, J = 7.8 Hz, 1H), 7.09 (t, J = 7.8 Hz, 1H), 7.01 (t, J = 7.2 Hz, 1H), 3.52 (q, J = 6.6 Hz, 2H), 2.96 (t, J = 7.8 Hz, 2H) ppm; $^{13}$C NMR (*d6*-DMSO, 150 MHz): δ 165.8, 161.4, 136.7, 134.7, 129.4, 127.8, 126.3, 124.1, 123.1, 121.9, 121.4, 121.2, 118.8, 118.7, 112.5, 111.9, 108.8, 26.0 ppm.

**2-Amino-5-phenyl-*N*-(prop-2-ynyl)thiophene-3-carboxamide (C2,21):** General



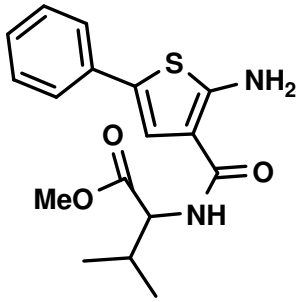
procedure B was followed employing 2-phenylacetaldehyde (1.2 g, 10 mmol), sulfur (320 mg, 10 mmol), 2-cyano-*N*-(prop-2-ynyl)acetamide (1.22 g, 10 mmol). The crude product was purified with silica gel column chromatography (50 % ethyl acetate in hexanes) to produce the title compound 1.98 g (77 %) as the light yellow solid. HRMS ESL-TOF for $C_{14}H_{12}N_2OS$ ($M^+$) found: *m/z*: 256.0668; Calc. Mass: 256.0670. $^1$H NMR ($CDCl_3$, 600 MHz): δ 7.42 (d, J = 7.8 Hz, 2H), 7.33 (t, J = 7.8 Hz, 2H), 7.22 (t, J = 7.8 Hz, 1H), 6.95 (s, 1H), 6.21 (s, 2H), 5.86 (s, 1H), 4.19 (dd, J = 5.4, 2.4 Hz, 2H), 2.27 (d, J = 2.4 Hz, 1H) ppm; 165.3, 160.9, 133.8, 128.9, 126.8, 125.5, 124.7, 117.8, 108.9, 79.9, 71.6, 29.0 ppm.

**(2-Amino-5-phenylthiophen-3-yl)(piperazin-1-yl)methanone (C2,22):** General procedure B was followed employing 2-phenylacetaldehyde (360 mg, 3 mmol), sulfur



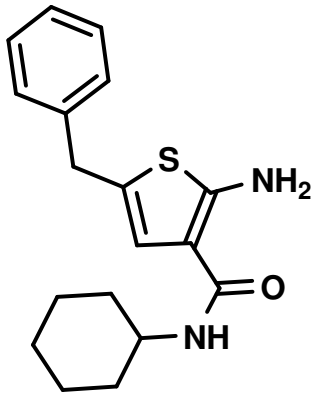
(96 mg, 3 mmol), 3-oxo-3-(piperazin-1-yl)propanenitrile (459 mg, 3 mmol). The crude product was purified with silica gel column chromatography (0-50 % methanol in ethyl acetate) to produce the title compound 207 mg (24 %) as the light yellow solid. HRMS ESL-TOF for $C_{15}H_{18}N_3OS$ ($M+H^+$) found: *m/z*: 288.1188; Calc. Mass: 288.1171. $^1$H NMR ($CDCl_3$, 600 MHz): δ 7.44 (d, J = 7.8 Hz, 2H), 7.31 (t, J = 7.2 Hz, 2H), 7.16 (t, J = 7.2 Hz, 1H), 7.07 (s, 1H), 6.62 (s, 2H), 3.46 (brs, 4H), 3.17 (s, 1H), 2.70 (brs, 4H) ppm; $^{13}$C NMR ($CDCl_3$, 600 MHz): δ 166.2, 158.3, 134.5, 129.4, 126.3, 124.3, 122.9, 122.6, 110.3, 49.1, 46.3 ppm.

**Methyl 2-(2-amino-5-phenylthiophene-3-carboxamido)-3-methylbutanoate (C2,23)**:



The general procedure B was followed employing 2-phenylacetaldehyde (360 mg, 3 mmol), methyl 2-(2-cyanoacetamido)-3-methylbutanoate (594 mg, 3 mmol), sulfur (96 mg, 3 mmol). The crude product was purified with silica gel column chromatography (20 % ethyl acetate in hexanes) to produce the title compound 777 mg (78 %) as the light yellow solid. HRMS ESL-TOF for $C_{17}H_{20}N_2O_3S$ ($M^+$) found: *m/z*: 332.1192; Calc. Mass: 332.1195. $^1$H NMR ($CDCl_3$, 600 MHz): δ 7.84 (s, 1H), 7.74 (d, J = 7.2 Hz, 1H), 7.49 (s, 2H), 7.43 (s, 2H), 7.34 (t, J = 7.2 Hz, 2H), 7.18 (t, J = 7.2 Hz, 1H), 4.25 (t, J = 7.8 Hz, 1H), 3.65 (s, 3H), 2.09-2.15 (m, 1H), 0.98 (d, J = 6.6 Hz, 3H), 0.92 (d, J = 6.6 Hz, 3H) ppm; $^{13}$C NMR ($CDCl_3$, 150 MHz): δ 173.2, 165.9, 162.2, 134.7, 129.4, 126.3, 124.1, 121.8, 121.6, 107.7, 58.2, 52.1, 30.1, 19.7, 19.6 ppm;

**2-Amino-5-benzyl-*N*-cyclohexylthiophene-3-carboxamide (C3,12):** The general procedure B was followed employing 3-phenylpropanal (670 mg, 5 mmol), 2-cyano-*N*-cyclohexylacetamide (830 mg, 5 mmol). The precipitate was filtered to produce the title compound 1.49 g (95 %) as the dark yellow solid. HRMS ESL-TOF for $C_{18}H_{22}N_2OSNa$ ($M+Na^+$) found: *m/z*: 337.1362; Calc. Mass: 337.1351. $^1$H NMR ($CDCl_3$, 600 MHz): δ 7.31 (t, J = 7.8 Hz, 2H), 7.19-7.25 (m, 3H), 6.37 (s, 1H), 5.96 (s, 2H), 5.41 (d, J = 7.2 Hz, 1H), 3.92 (s, 2H), 3.80-3.90 (m, 1H), 1.97 (dd, J = 12.6, 3.0 Hz, 2H), 1.73 (dt, J = 12.6, 3.0 Hz, 2H), 1.38 (qt, J = 13.2, 3.0 Hz, 2H), 1.12-1.18 (m, 3H) ppm; $^{13}$C NMR ($CDCl_3$, 150 MHz): δ 165.0, 159.8, 139.8, 128.6, 128.5, 126.7, 125.8, 119.8, 108.4, 47.9, 36.0, 33.6, 25.6, 25.1 ppm.



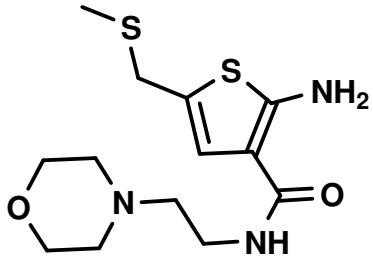
**2-Amino-5-benzyl-*N*-(2-morpholinoethyl)thiophene-3-carboxamide (C3,4):** The general procedure B was followed employing 3-phenylpropanal (670 mg, 5 mmol), 2-cyano-*N*-(2-morpholinoethyl)acetamide (885 mg, 5 mmol), The crude product was purified with silica gel short column chromatography (0-5 % ethyl acetate) to produce the title compound 1.30 g (75 %) as the dark yellow oil. HRMS ESL-TOF for $C_{18}H_{23}N_3O_2S$ ($M^+$) found: *m/z*: 345.1501; Calc. Mass: 345.1511. $^1$H NMR ($CDCl_3$, 600 MHz): δ 7.31 (t, J = 7.2 Hz, 2H), 7.20-7.26 (m, 3H), 6.35 (s, 1H), 6.29 (s, 1H), 6.06 (s, 2H), 3.91 (s, 2H), 3.68 (t, J = 4.8 Hz, 4H), 3.42 (q, J = 6.0 Hz, 2H), 2.53 (t, J = 6.0 Hz, 2H), 2.47 (s, 4H) ppm; $^{13}$C NMR ($CDCl_3$, 150 MHz): δ 165.8, 160.0, 139.7, 128.56, 128.55, 126.6, 125.7, 120.0, 108.0, 66.9, 57.0, 53.2, 35.9, 35.1 ppm.

**2-Amino-5-benzyl-*N*-(3-methoxypropyl)thiophene-3-carboxamide (C3,13):** The general procedure B was followed employing 3-phenylpropanal (670 mg, 5 mmol), 2-cyano-*N*-(3-methoxypropyl)acetamide (780 mg, 5 mmol). The crude product was purified with silica gel column chromatography (50-75 % ethyl acetate in hexanes) to produce the title compound 1.06 g (70 %) as the dark yellow oil. HRMS ESL-TOF for $C_{16}H_{20}N_2O_2SNa$ ($M+Na^+$) found: *m/z*: 327.1144; Calc. Mass: 327.1143. $^1$H NMR ($CDCl_3$, 600 MHz): δ 7.28 (t, J = 7.2 Hz, 2H), 7.18-7.23 (m, 3H), 6.43 (s, 1H), 6.31 (s, 1H), 6.05 (s, 2H), 3.86 (s, 2H), 3.47 (t, J = 6.0 Hz, 2H), 3.41 (q, J = 6.0 Hz, 2H), 3.27 (s, 3H), 1.78 (t, J = 6.0 Hz, 2H) ppm; $^{13}$C NMR ($CDCl_3$, 150 MHz): δ 165.84, 159.81, 139.79, 128.63, 128.57, 126.59, 125.57, 120.15, 108.24, 72.03, 58.73, 37.93, 35.98, 29.07 ppm.

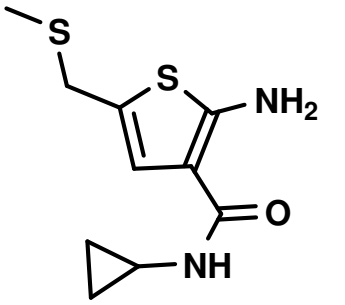
**2-Amino-5-(methylthiomethyl)-*N*-phenethylthiophene-3-carboxamide (C4,11):** The general procedure B was followed employing 3-(methylthio)propanal (412 mg, 3 mmol), 2-cyano-*N*-phenethylacetamide (564 mg, 3 mmol), sulfur (96 mg, 3 mmol). The crude product was purified with silica gel column chromatography (50 % ethyl acetate in hexanes) to produce the title compound 690 mg (75 %) as the light yellow solid. HRMS ESL-TOF for $C_{15}H_{18}N_2OS_2$ ($M^+$) found: *m/z*: XXX; Calc. Mass: 306.0861. $^1$H NMR ($CDCl_3$, 600 MHz): δ 7.32 (t, J = 7.8 Hz, 2H), 7.25 (t, J = 7.8 Hz, 1H), 7.23 (t, J = 7.8 Hz, 2H), 6.39 (s, 1H), 6.09 (s, 2H), 5.67 (s, 1H), 3.64 (s, 2H), 3.61 (q, J = 7.2 Hz, 2H), 2.87 (t, J = 7.2 Hz, 2H), 2.03 (s, 3H) ppm; $^{13}$C NMR ($CDCl_3$, 150 MHz): δ 165.6, 160.5, 139.1, 128.8, 128.7, 126.5, 123.4, 121.0, 107.7, 40.4, 36.1, 33.1, 14.9 ppm;

**2-Amino-5-(methylthiomethyl)-*N*-(2-morpholinoethyl)thiophene-3-carboxamide (C4,4):** The general procedure B was followed employing 3-(methylthio)propanal (412

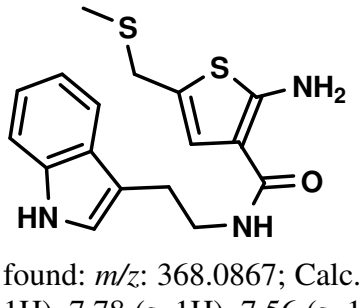
mg, 3 mmol), 2-cyano-*N*-(2-morpholinoethyl)acetamide (591 mg, 3 mmol), sulfur (96 mg, 3 mmol). The crude product was purified with silica gel column chromatography (0-10 % methanol in ethyl acetate) to produce the title compound 493 mg (52 %) as the light yellow solid. HRMS ESL-TOF for $C_{13}H_{21}N_3O_2S_2$ ($M^+$) found: *m/z*: 315.1087; Calc. Mass: 315.1075. $^1$H NMR ($CDCl_3$, 600 MHz): δ 6.54 (s, 1H), 6.22 (s, 1H), 6.10 (s, 2H), 3.74 (t, J = 4.2 Hz, 4H), 3.70 (s, 2H), 3.46 (q, J = 6.0 Hz, 2H), 2.58 (t, J = 6.0 Hz, 2H), 2.51 (s, 4H), 2.08 (s, 3H) ppm; $^{13}$C NMR ($CDCl_3$, 150 MHz): δ 165.7, 160.5, 123.4, 121.1, 107.8, 67.0, 57.1, 53.3, 35.2, 33.1, 14.9 ppm;



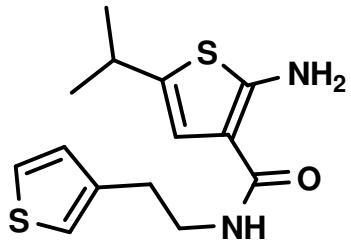

**2-Amino-*N*-cyclopropyl-5-(methylthiomethyl)thiophene-3-carboxamide (C4,1):** The general procedure B was followed employing 3-(methylthio)propanal (412 mg, 3 mmol), 2-cyano-*N*-cyclopropylacetamide (372 mg), sulfur (96 mg, 3 mmol). The precipitate was filtered to produce the title compound 465 mg (64 %) as the dark yellow solid. HRMS ESL-TOF for $C_{10}H_{14}N_2OS_2$ ($M^+$) found: *m/z*: 242.0553; Calc. Mass: 242.0548. $^1$H NMR ($CDCl_3$, 600 MHz): δ 6.43 (s, 1H), 6.10 (s, 2H), 5.67 (s, 1H), 3.63 (s, 2H), 2.72-2.76 (m, 1H), 2.01 (s, 3H), 0.76-0.82 (m, 2H), 0.51-0.56 (m, 2H) ppm; $^{13}$C NMR ($CDCl_3$, 150 MHz): δ 167.2, 160.8, 123.3, 120.9, 107.3, 33.1, 22.4, 14.9, 6.8 ppm.




***N*-(2-(1H-Indol-3-yl)ethyl)-2-amino-5-(methylthiomethyl)thiophene-3-carboxamide (C4,10):** The general procedure B was followed employing 3-(methylthio)propanal (412 mg, 3 mmol), *N*-(2-(1H-indol-3-yl)ethyl)-2-cyanoacetamide (682 mg, 3 mmol), sulfur (96 mg, 3 mmol). The crude product was purified with silica gel column chromatography (50 % ethyl acetate in hexanes) to produce the title compound 664 mg (60 %) as the light yellow solid. HRMS ESL-TOF for $C_{17}H_{19}N_3OS_2Na$ ($M+Na^+$) found: *m/z*: 368.0867; Calc. Mass: 368.0867. $^1$H NMR (*d6*-DMSO, 600 MHz): δ 10.80 (s, 1H), 7.78 (s, 1H), 7.56 (s, 1H), 7.33 (s, 1H), 7.22 (s, 2H), 7.15 (s, 1H), 7.06 (s, 1H), 6.98 (s, 1H), 6.91 (s, 1H), 3,68 (s, 2H), 2.88 (s, 2H), 1.99 (s, 3H) ppm; $^{13}$C NMR (*d6*-DMSO, 150 MHz): δ 165.8, 161.3, 136.7, 127.7, 123.3, 123.0, 121.4, 120.9, 118.8, 118.7, 112.5, 111.8, 106.6, 60.0, 32.9, 26.0, 14.7 ppm.

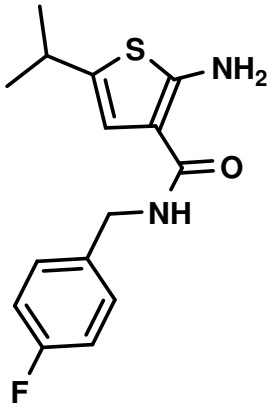



**2-Amino-5-isopropyl-*N*-(2-(thiophen-3-yl)ethyl)thiophene-3-carboxamide (C5,16):** The general procedure B was followed employing 3-methylbutanal (258 mg, 3 mmol), 2-cyano-*N*-(2-(thiophen-3-yl)ethyl)acetamide (582 mg, 3 mmol), sulfur (96 mg, 3 mmol). The crude product was purified with silica gel column chromatography (50 % ethyl acetate in hexanes) to produce the title compound 655 mg (74 %) as the light yellow solid. HRMS ESL-TOF

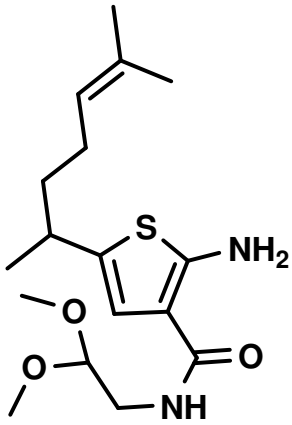


for $C_4H_{18}N_2OS_2$ ($M^+$) found: *m/z*: 294.0847; Calc. Mass: 294.0861. $^1$H NMR (*d6*-DMSO, 600 MHz): δ 7.77 (t, J = 5.4 Hz, 1H), 7.33 (dd, J = 4.8, 0.6 Hz, 1H), 7.04 (s, 2H), 6.95 (dd, J = 4.8, 3.0 Hz, 1H), 6.89 (d, J = 4.8 Hz, 1H), 6.76 (s, 1H), 3.38 (q, J = 7.2 Hz, 2H), 2.99 (t, J = 7.2 Hz, 1H), 2.85 (oct, J = 6.6 Hz, 1H), 1.18 (d, J = 6.6 Hz, 6H) ppm; $^{13}$C NMR (*d6*-DMSO, 150 MHz): δ 166.0, 159.8, 142.2, 131.7, 127.4, 125.5, 124.4, 118.5, 106.5, 40.7, 30.2, 29.3, 24.5 ppm.

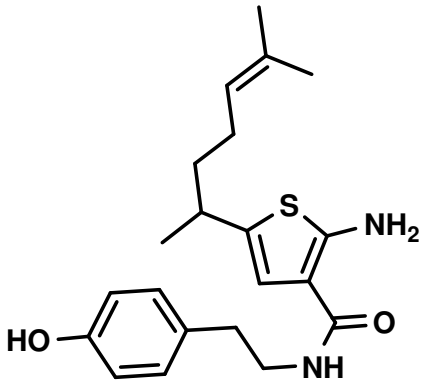
**2-Amino-*N*-(4-fluorobenzyl)-5-isopropylthiophene-3-carboxamide (C5,15):** The general procedure B was followed employing 3-methylbutanal (258 mg, 3 mmol), 2-cyano-*N*-(4-fluorobenzyl)acetamide (576 mg, 3 mmol), sulfur (96 mg, 3 mmol). The crude product was purified with silica gel column chromatography (50 % ethyl acetate in hexanes) to produce the title compound 590 mg (67 %) as the light yellow solid. HRMS ESL-TOF for $C_{15}H_{17}FN_2OS$ ($M^+$) found: *m/z*: 292.1059; Calc. Mass: 292.1046. $^1$H NMR ($CDCl_3$, 600 MHz): δ 7.29 (dd, J = 8.4, 5.4 Hz, 2H), 7.01 (t, J = 8.4 Hz, 2H), 6.32 (s, 1H), 5.96 (s, 2H), 5.86 (s, 1H), 4.51 (d, J = 5,4 Hz, 2H), 2.99 (oct, J = 6.6 Hz, 1H), 1.21 (d, J = 6.6 Hz, 6H) ppm; $^{13}$C NMR ($CDCl_3$, 150 MHz): δ 165.7, 160.2 (d, J = 332 Hz), 134.9 (d, J = 78 Hz), 129.4 (d, J = 9 Hz), 116.1, 115.6, 115.4, 107.5, 42.4, 29.6, 24.2 ppm.




**2-Amino-*N*-(2,2-dimethoxyethyl)-5-(6-methylhept-5-en-2-yl)thiophene-3-carboxamide (C6,8):** The general procedure B was followed employing 3,7-dimethyloct-6-enal (770 mg, 5 mmol), 2-cyano-*N*-(2,2-dimethoxyethyl)acetamide (860 mg, 5 mmol), sulfur (160 mg, 5 mmol). The crude product was purified with silica gel column chromatography (50-75 % ethyl acetate in hexanes) to produce the title compound 850 mg (50 %) as the dark yellow oil. HRMS ESL-TOF for $C_{16}H_{25}N_2O_3S$ ($M\text{-}Me^+$) found: *m/z*: 325.1572; Calc. Mass: 325.1586. $^1$H NMR ($CDCl_3$, 600 MHz): δ 6.36 (s, 1H), 5.98 (s, 2H), 5.81 (t, J = 5.4 Hz, 1h), 5.08 (t, J = 6.0 Hz, 1H), 4.44 (t, J = 5.4 Hz, 1H), 3.44 (t, J = 5.4 Hz, 2H), 3.42 (s, 6H), 2.76-2.80 (m, 1H), 1.95 (q, J = 7.8 Hz, 2H), 1.68 (s, 3H), 1.58 (s, 3H), 1.50-1.56 (m, 2H), 1.22 (d, J = 6.6 Hz, 3H) ppm; $^{13}$C NMR ($CDCl_3$, 150 MHz): δ 165.86, 159.00, 133.68, 131.85, 123.98, 117.29, 107.60, 103.10, 54.58, 40.62, 38.66, 34.82, 25.78, 25.73, 22.66, 17.75 ppm.

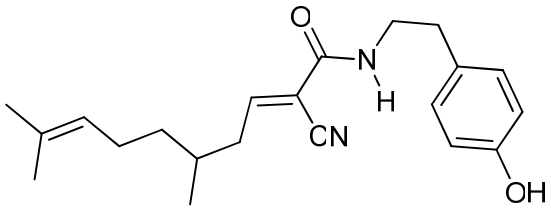



**2-Amino-N-(4-hydroxyphenethyl)-5-(6-methylhept-5-en-2-yl)thiophene-3-carboxamide (C6,17):** Procedure B was followed employing 3,7-dimethyloct-6-enal (308 mg, 2 mmol), 2-cyano-*N*-(4-hydroxyphenethyl)acetamide (408 mg, 2 mmol), sulfur (64 mg, 2 mmol) and triethylamine (606 mg, 6 mmol). The crude product was purified with silica gel column chromatography (50 % ethyl acetate in hexanes) to produce the title compound 670 mg (90 %) as the light yellow solid. HRMS ESL-TOF for $C_{21}H_{28}N_2O_2S$ ($M^+$) found: *m/z*: 372.1875; Calc. Mass: 372.1871. $^1$H NMR ($CDCl_3$, 600 MHz): δ 7.94 (d, 1H), 6.97 (d, J = 8.4 Hz, 2H), 6.79 (d, J = 8.4 Hz, 2H), 6.32 (s, 1H),



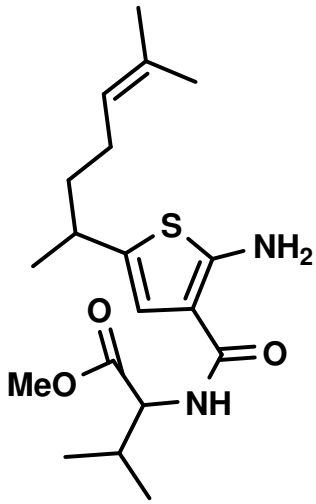

6.07 (t, J = 6.0 Hz, 1H), 5.97 (s, 2H), 5.06 (t, J = 7.2 Hz, 1H), 3.52 (q, J = 7.2 Hz, 2H), 2.73 (t, J = 7.2 Hz, 2H), 2.68-2.74 (m, 1H), 1.93 (q, J = 7.2 Hz, 2H), 1.66 (s, 3H), 1.54 (s, 3H), 1.45-1.53 (m, 2H), 1.18 (d, J = 6.6 Hz, 3H) ppm; $^{13}$C NMR ($CDCl_3$, 150 MHz): δ 171.5, 166.1, 158.8, 155.0, 133.7, 131.6, 129.9, 129.6, 123.8, 117.3, 115.5, 107.6, 60.5, 40.7, 38.5, 35.0, 34.6, 25.6, 25.5, 22.4, 20.9, 17.6, 14.0 ppm.

**(*E*)-2-Cyano-N-(4-hydroxyphenethyl)-5,9-dimethyldeca-2,8-dienamide (D6,17):** The



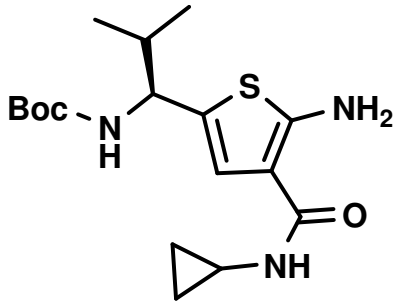

general procedure B was followed employing 3,7-dimethyloct-6-enal (308 mg, 2 mmol), 2-cyano-*N*-(4-hydroxyphenethyl)acetamide (408 mg, 2 mmol), sulfur (64 mg, 2 mmol) and triethylamine (202 mg, 2 mmol). The crude product was purified with silica gel column chromatography (50-75 % ethyl acetate in hexanes) to produce the title compound 510 mg (75 %) as the light yellow solid. HRMS ESL-TOF for $C_{21}H_{28}N_2O_2$ ($M^+$) found: *m/z*: 340.2163; Calc. Mass: 340.2151. $^1$H NMR (*d6*-DMSO, 600 MHz): δ 9.96 (t, J = 4.8 Hz, 1H), 9.20 (s, 1H), 7.02 (d, J = 8.4 Hz, 2H), 6.66 (d, J = 8.4 Hz, 2H), 5.07 (t, J = 7.2 Hz, 1H), 3.60-3.70 (m, 2H), 2.75 (t, J = 7.8 Hz, 2H), 2.48 (dd, J = 12.6, 6.6 Hz, 1H), 2.32 (dd, J = 12.6, 7.8 Hz, 1H), 2.01-2.10 (m, 1H), 1.93-2.00 (m, 1H), 1.86-1.93 (m, 1H), 1.64 (s, 3H), 1.56 (s, 3H), 1.26-1.34 (m, 1H), 1.07-1.13 (m, 1H), 0.80 (d, J = 6.6 Hz, 3H) ppm; $^{13}$C NMR (*d6*-DMSO, 150 MHz): δ 203.3, 156.2, 131.1, 129.9, 129.5, 124.9, 115.6, 53.0, 47.2, 36.5, 33.2, 32.7, 26.0, 25.4, 19.1, 18.1 ppm.

**Methyl 2-(2-amino-5-(6-methylhept-5-en-2-yl)thiophene-3-carboxamido)-3-methylbutanoate (C6,23):** The general procedure B was followed employing 3,7-dimethyloct-6-enal (462 mg, 3 mmol), methyl 2-(2-cyanoacetamido)-3-methylbutanoate (594 mg, 3 mmol), sulfur (96 mg, 3 mmol). The crude product was purified with silica gel column chromatography (50-75 % ethyl acetate in hexanes) to produce the title compound 716 mg (65 %) as the light yellow solid. The NMR indicates the product contains two diastereomers as a ratio of 1:1. HRMS ESL-TOF for $C_{19}H_{30}N_2O_3S$ ($M^+$) found: *m/z*: 366.1962; Calc. Mass: 366.1977. $^1$H NMR ($CDCl_3$, 600 MHz): δ 6.42 (s, 1H), 6.09 (d, J = 8.4 Hz, 1H), 5.96 (s, 2H), 5.09 (t, J = 7.2 Hz, 1H), 4.65 (dd, J = 8.4, 4.8 Hz, 1H), 3.76 (s, 3H), 2.75-2.82 (m, 1H), 2.17-2.22 (m, 1H), 1.97 (q, J = 7.8 Hz, 2H), 1.70 (s, 3H), 1.58 (s, 3H), 1.50-1.56 (s, 2H), 1.23 (d, J = 7.2 Hz, 3H), 0.99 (d, J = 7.2 Hz, 3H), 0.97 (d, J = 7.2 Hz, 3H) ppm; $^{13}$C NMR ($CDCl_3$,



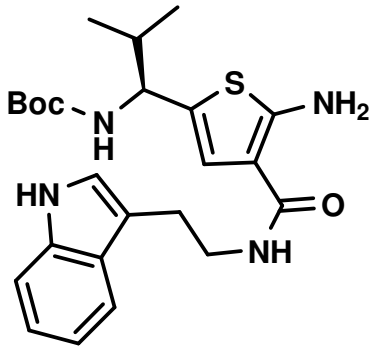
150 MHz): δ 173.13, 173.11, 165.53, 165.50, 159.3, 133.82, 133.80, 131.87, 131.85, 124.03, 123.99, 117.30, 117.26, 107.5, 56.7, 52.2, 38.69, 38.64, 34.90, 34.83, 31.57, 31.55, 25.85, 25.80, 25.75, 22.70, 22.67, 19.00, 18.15, 17.79, 17.77 ppm.

***(R)-tert*-Butyl**



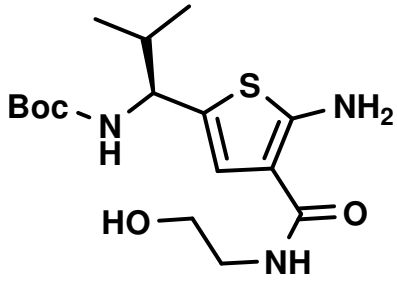

**1-(5-amino-4-(cyclopropylcarbamoyl)thiophen-2-yl)-2-methylpropylcarbamate (C7,1):** The general procedure A was followed employing (*S*)-*tert*-butyl 4-methyl-1-oxopentan-3-ylcarbamate (430 mg, 2 mmol), 2-cyano-N-cyclopropylacetamide (248 mg, 2 mmol), sulfur (64 mg, 2 mmol). The crude product was purified with silica gel column chromatography (50-75 % ethyl acetate in hexanes) to produce the title compound 679 mg (90 %) as the light yellow solid. HRMS ESL-TOF for $C_{17}H_{27}N_3O_3SNa$ ($M+Na^+$) found: *m/z*: 376.1648; Calc. Mass: 376.1671. $^1H$ NMR ($CDCl_3$, 600 MHz): δ 6.51 (s, 1H), 6.22 (s, 2H), 6.11 (s, 1H), 4.83 (s, 1H), 4.41 (s, 1H), 2.75 (s, 1H), 1.87 (s, 1H), 1.42 (s, 9H), 0.94 (s, 3H), 0.89 (s, 3H), 0.77 (s, 2H), 0.56 (s, 2H) ppm; $^{13}C$ NMR ($CDCl_3$, 150 MHz): δ 167.4, 160.0, 155.3, 127.2, 120.0, 107.5, 79.6, 56.6, 33.8, 28.4, 22.4, 19.7, 18.5, 6.63, 6.56 ppm;

***(R)-tert*-Butyl**




**1-(4-(2-(1H-indol-3-yl)ethylcarbamoyl)-5-aminothiophen-2-yl)-2-methylpropylcarbamate (C7,10):** The general procedure B was followed employing (*S*)-*tert*-butyl 4-methyl-1-oxopentan-3-ylcarbamate (646 mg, 3 mmol), *N*-(2-(1H-indol-3-yl)ethyl)-2-cyanoacetamide (682 mg, 3 mmol), sulfur (96 mg, 3 mmol). The crude product was purified with purified with silica gel column chromatography (0-5 % methanol in ethyl acetate) to produce the title compound 1150 mg (84 %) as the light yellow solid. HRMS ESL-TOF for $C_{24}H_{32}N_4O_3S$ Na ($M+Na^+$) found: *m/z*: 479.2093; Calc. Mass: 479.2093. $^1H$ NMR (*d6*-DMSO, 600 MHz): δ 10.79 (s, 1H), 7.78 (t, J = 5.4 Hz, 1H), 7.57 (d, J = 7.8 Hz, 1H), 7.33 (d, J = 7.8 Hz, 1H), 7.16 (s, 1H), 7.12 (s, 2H), 7.06 (t, J = 7.2 Hz, 1H), 6.98 (t, J = 7.2 Hz, 1H), 6.84 (s, 1H), 4.39 (s, 1H), 4.16 (t, J = 9.0 Hz, 1H), 3.71-3.78 (m, 1H), 2.88 (t, J = 7.8 Hz, 2H), 1.81-1.88 (m, 1H), 1.38 (s, 9H), 0.91 (d, J = 6.6 Hz, 3H), 0.79 (d, J = 6.6 Hz, 3H) ppm; $^{13}C$ NMR (*d6*-DMSO, 150 MHz): δ 165.9, 160.6, 155.6, 136.7, 127.7, 126.3, 122.9, 121.4, 121.3, 118.8, 118.7, 112.6 111.8, 106.4, 78.1, 57.2, 55.4, 33.0, 28.7, 26.1, 21.2, 19.7 ppm.

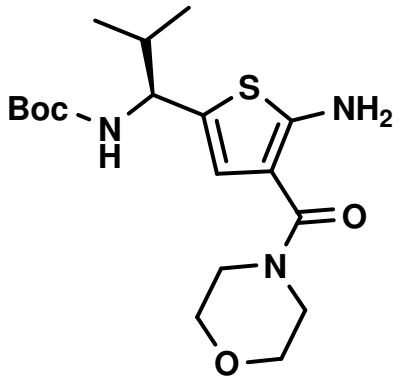
***(R)-tert*-Butyl**




**1-(5-amino-4-(2-hydroxyethylcarbamoyl)thiophen-2-yl)-2-methylpropylcarbamate (C7,14):** The general procedure B was followed employing (*S*)-*tert*-butyl 4-methyl-1-oxopentan-3-ylcarbamate (646 mg, 3 mmol), 2-cyano-*N*-(2-hydroxyethyl)acetamide (384 mg, 3 mmol), sulfur (96 mg, 3 mmol). The crude product was purified with silica gel column chromatography (0-5 % methanol in ethyl acetate) to produce the title compound

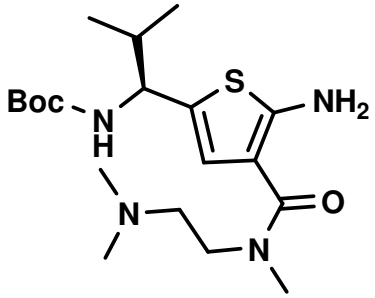
924 mg (86 %) as the light yellow solid. HRMS ESL-TOF for $C_{16}H_{27}N_3O_4S$ ($M^+$) found: *m/z*: 357.1616; Calc. Mass: 357.1722. $^1$H NMR (*d6*-DMSO, 600 MHz): δ 7.57 (s, 1H), 7.17 (d, J = 7.8 Hz, 1H), 7.09 (s, 2H), 6.84 (s, 1H), 4.68 (t, J = 5.4 Hz, 1H), 4.15 (s, 1H), 3.44 (d, J = 5.4 Hz, 2H), 3.21 (s, 2H), 1.81 (s, 1H), 1.37 (s, 9H), 0.90 (d, J = 5.4 Hz, 3H), 0.78 (d, J = 5.4 Hz, 3H) ppm; $^{13}$C NMR (*d6*-DMSO, 150 MHz): δ 165.6, 160.1, 155.1, 125.8, 121.0, 105.8, 77.6, 60.1, 56.7, 42.2, 32.5, 28.2, 20.0, 19.2 ppm.

**(*R*)-*tert*-Butyl**



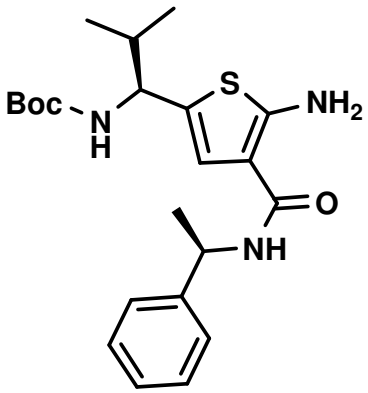

**1-(5-amino-4-(morpholine-4-carbonyl)thiophen-2-yl)-2-methylpropylcarbamate (C7,18) :** The general procedure B was followed employing (*S*)-*tert*-butyl 4-methyl-1-oxopentan-3-ylcarbamate (646 mg, 3 mmol), 3-morpholino-3-oxopropanenitrile (462 mg, 3 mmol), sulfur (96 mg, 3 mmol). The crude product was purified with silica gel column chromatography (0-5 % methanol in ethyl acetate) to produce the title compound 864 mg (75 %) as the light yellow solid. HRMS ESL-TOF for $C_{18}H_{29}N_3O_4S$ ($M^+$) found: *m/z*: 383.1889; Calc. Mass: 383.1879. $^1$H NMR (*d6*-DMSO, 600 MHz): δ 7.20 (d, J = 9.0 Hz, 1H), 6.43 (s, 1H), 6.38 (s, 2H), 4.18 (t, J = 9.0 Hz, 1H), 3.58 (t, J = 4.2 Hz, 4H), 3.46 (t, J = 4.2 Hz, 4H), 1.80-1.90 (m, 1H), 1.37 (s, 9H), 0.87 (d, J = 6.6 Hz, 3H), 0.79 (d, J = 6.6 Hz, 3H) ppm; $^{13}$C NMR (*d6*-DMSO, 150 MHz): δ 166.9, 158.3, 155.6, 126.6, 122.7, 107.3, 78.2, 66.8, 56.5, 45.6, 33.4, 28.7, 21.2, 19.4 ppm.

**(*R*)-*tert*-Butyl**



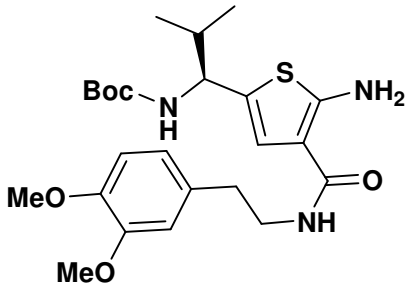

**1-(5-amino-4-((2-(dimethylamino)ethyl)(methyl)carbamoyl)thiophen-2-yl)-2-methylpropylcarbamate (C7,19):** The general procedure B was followed employing (*S*)-*tert*-butyl 4-methyl-1-oxopentan-3-ylcarbamate (646 mg, 3 mmol), 2-cyano-*N*-(2-(dimethylamino)ethyl)-N-methylacetamide (507 mg, 3 mmol), sulfur (96 mg, 3 mmol). The crude product was purified with silica gel column chromatography (0-25 % methanol in ethyl acetate) to produce the title compound 918 mg (71 %) as the light yellow solid. HRMS ESL-TOF for $C_{19}H_{34}N_4O_3S$ ($M^+$) found: *m/z*: 398.2347; Calc. Mass: 398.2352. $^1$H NMR (*d6*-DMSO, 600 MHz): δ 7.20 (d, J = 9.0 Hz, 1H), 6.50 (s, 1H), 6.37 (s, 2H), 4.18 (t, J = 8.4 Hz, 1H), 3.48 (t, J = 6.6 Hz, 2H), 2.96 (s, 3H), 2.54 (s, 2H), 2.25 (s, 6H), 1.80-1.86 (m, 1H), 1.37 (s, 9H), 0.87 (d, J = 6.6 Hz, 3H), 0.79 (d, J = 6.6 Hz, 3H) ppm; $^{13}$C NMR (*d6*-DMSO, 150 MHz): δ 167.7, 157.8, 155.6, 126.4, 122.8, 108.1, 78.1, 56.6, 56.3, 46.0, 45.1, 36.0, 33.4, 28.7, 20.3, 19.5 ppm;

***tert*-Butyl (*R*)-1-(5-amino-4-((*R*)-1-phenylethylcarbamoyl)thiophen-2-yl)-2-methylpropylcarbamate (C7,20):** The general procedure B was followed employing (*S*)-*tert*-butyl 4-methyl-1-oxopentan-3-ylcarbamate (430 mg, 2 mmol), (*R*)-2-cyano-*N*-(1-phenylethyl)acetamide (376 mg, 2 mmol), sulfur (64 mg, 2 mmol). The crude product was purified with silica gel column chromatography (50 % ethyl acetate in hexanes) to



produce the title compound 752 mg (90 %) as the light yellow solid. HRMS ESL-TOF for $C_{22}H_{31}N_3O_3S$ ($M^+$) found: *m/z*: 417.2068; Calc. Mass: 417.2086. $^1$H NMR (*d6*-DMSO, 600 MHz): δ 7.91 (d, J = 7.8 Hz, 1H), 7.35 (d, J = 7.8 Hz, 2H), 7.30 (t, J = 7.2 Hz, 2H), 7.20 (t, J = 7.2 Hz, 1H), 7.16 (d, J = 9.0 Hz, 1H), 7.12 (s, 2H), 7.04 (s, 1H), 5.10 (pent, J = 7.2 Hz, 1H), 4.19 (t, J = 9.0 Hz, 1H), 1.84-1.92 (m, 1H), 1.43 (d, J = 7.2 Hz, 3H), 1.38 (s, 9H), 0.92 (d, J = 6.6 Hz, 3H), 0.81 (d, J = 6.6 Hz, 3H) ppm; $^{13}$C NMR (*d6*-DMSO, 150 MHz): δ 165.1, 161.1, 155.6, 145.9, 128.6, 126.9, 126.6, 126.2, 121.6, 106.1, 78.1, 57.2, 47.8, 33.1, 28.7, 22.7, 21.2, 19.8 ppm.

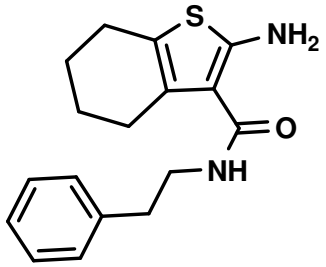
**(*R*)-Methyl 2-(2-amino-5-(1-(*tert*-butoxycarbonylamino)-2-methylpropyl)thiophene-3-carboxamido)-3-methylbutanoate (C7,23):** The general procedure B was followed employing (*S*)-*tert*-butyl 4-methyl-1-oxopentan-3-ylcarbamate (322 mg, 1.5 mmol), methyl 2-(2-cyanoacetamido)-3-methylbutanoate (300 mg, 1.5 mmol), sulfur (48 mg, 1.5 mmol). The crude product was purified with silica gel column chromatography (0-10 % methanol in ethyl acetate) to produce the title compound 540 mg (84 %) as the light yellow solid. The NMR indicates the product contains two diastereomers as a ratio of 2:1. HRMS ESL-TOF for $C_{20}H_{33}N_3O_5SNa$ ($M+Na^+$) found: *m/z*: 450.2058; Calc. Mass: 450.2039.major isomer $^1$H NMR (*d6*-DMSO, 600 MHz): δ 6.58 (s, 1H), 6.05 (d, J = 8.4 Hz, 1H), 6.00 (s, 2H), 5.85 (s, 1H), 4.60-4.65 (m, 1H), 4.49 (s, 1H), 3.76 (s, 3H), 2.15-2.25 (m, 1H), 1.84-1.92 (m, 1H), 1.45 (s, 9H), 0.88-1.00 (m, 12H) ppm; $^{13}$C NMR (*d6*-DMSO, 150 MHz): δ 173.31, 166.05, 165.14, 161.61, 155.68, 126.19, 121.83, 121.68, 105.51, 102.79, 78.12, 58.34, 57.11, 51.94, 50.92, 33.13, 33.08, 29.81, 28.75, 20.56, 20.24, 19.80, 19.70, 19.66, 19.34 ppm.



**(*S*)-*tert*-Butyl 1-(5-amino-4-(3,4-dimethoxyphenethylcarbamoyl)thiophen-2-yl)-2-methylpropylcarbamate (C7,24):** The general procedure B was followed employing (*S*)-*tert*-butyl 4-methyl-1-oxopentan-3-ylcarbamate (430 mg, 2 mmol), 2-cyano-*N*-(3,4-dimethoxyphenethyl)acetamide (496 mg, 2 mmol), sulfur (64 mg, 2 mmol). The crude product was purified with silica gel column chromatography (50 % ethyl acetate in hexanes) to produce the title compound 887 mg (93 %) as the light yellow solid. HRMS ESL-TOF for $C_{24}H_{35}N_3O_5S$ ($M^+$) found: *m/z*: XXX ; Calc. Mass: 477.2297. $^1$H NMR (*d6*-DMSO, 600 MHz): δ 7.67 (t, J = 5.4 Hz, 1H), 7.15 (d, J = 9.0 Hz, 1H), 7.09 (s, 2H), 6.84 (d, J = 7.8 Hz, 1H), 6.81 (s, 1H), 6.78 (s, J = 1.8 Hz, 1H), 6.70 (dd, J = 7.8, 1.2 Hz, 1H), 4.14 (t, J = 9.0 Hz, 1H), 3.70 (s, 3H), 3.69 (s, 3H), 3.25-3.35 (m, 2H), 2.69 (t, J = 7.8 Hz, 2H), 1.78-1.87 (m, 1H), 1.36 (s,

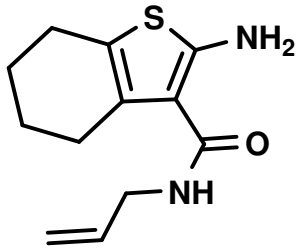
9H), 0.89 (d, J = 6.6 Hz, 3H), 0.77 (d, J = 6.6 Hz, 3H) ppm; $^{13}$C NMR (*d6*-DMSO, 150 MHz): δ 165.9, 160.6, 155.6, 149.0, 147.6, 132.6, 126.3, 121.4, 120.8, 112.9, 112.3, 106.3, 78.1, 57.2, 55.9, 55.8, 35.5, 33.0, 28.7, 20.5, 19.7 ppm.

**2-Amino-N-phenethyl-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxamide (C9,11):**

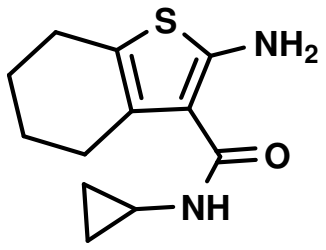



The general procedure C was followed employing cyclohexanone (980 mg, 10 mmol), *N*-benzyl-2-cyanoacetamide (1.74 g, 10 mmol), sulfur (320 mg, 10 mmol). The crude product was purified with silica gel column chromatography (50-75 % ethyl acetate in hexanes) to produce the title compound 750 mg (25 %) as the dark yellow solid. HRMS ESL-TOF for $C_{17}H_{20}N_2OSNa$ ($M+Na^+$) found: *m/z*: 323.1218; Calc. Mass: 323.1194. $^1$H NMR ($CDCl_3$, 600 MHz): δ 7.31 (t, J = 7.8 Hz, 2H), 7.22-7.25 (m, 3H), 5.96 (s, 2H), 5.62 (s, 1H), 3.65 (q, J = 6.0 Hz, 2H), 2.88 (t, J = 7.2 Hz, 2H), 2.49 (t, J = 6.0 Hz, 2H), 2.26 (t, J = 6.0 Hz, 2H), 1.70-1.76 (m, 2H), 1.64-1.69 (m, 2H) ppm; $^{13}$C NMR ($CDCl_3$, 150 MHz): δ 166.49, 158.81, 139.08, 128.93, 128.86, 128.64, 126.53, 118.64, 108.71, 40.24, 35.61, 26.58, 24.48, 22.83 ppm.

***N*-Allyl-2-amino-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxamide (C9,6):** The general procedure B was followed employing cyclohexanone (980 mg, 10 mmol), *N*-allyl-2-cyanoacetamide (1.24 g, 10 mmol), sulfur (320 mg, 10 mmol). The crude product was purified with silica gel column chromatography (50-75 % ethyl acetate in hexanes) to produce the title compound 403 mg (17 %) as the dark yellow oil. HRMS ESL-TOF for $C_{12}H_{16}N_2OSNa$ ($M+Na^+$) found: *m/z*: 259.0894; Calc. Mass: 259.0881. $^1$H NMR ($CDCl_3$, 600 MHz): δ 5.99 (s, 2H), 5.92 (ddt, J = 17.4, 10.8, 6.0 Hz, 1H), 5.73 (s, 1H), 5.23 (dq, J = 17.4, 1.2 Hz, 1H), 5.15 (dq, J = 10.8 Hz, 1H), 4.01 (tt, J = 6.0, 1.2 Hz, 2H), 2.62-2.68 (m, 2H), 2.53-2.57 (m, 2H), 1.78-1.84 (m, 4H) ppm; $^{13}$C NMR ($CDCl_3$, 150 MHz): δ 166.0, 158.1, 136.5, 130.4, 116.5, 115.2, 108.9, 41.3, 26.4, 24.5, 23.2, 23.0 ppm.

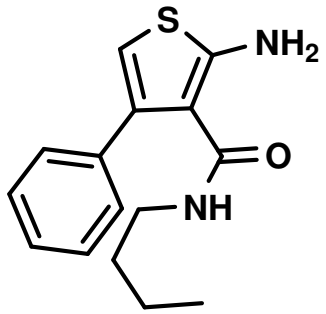



**2-Amino-*N*-cyclopropyl-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxamide (C9,1):**

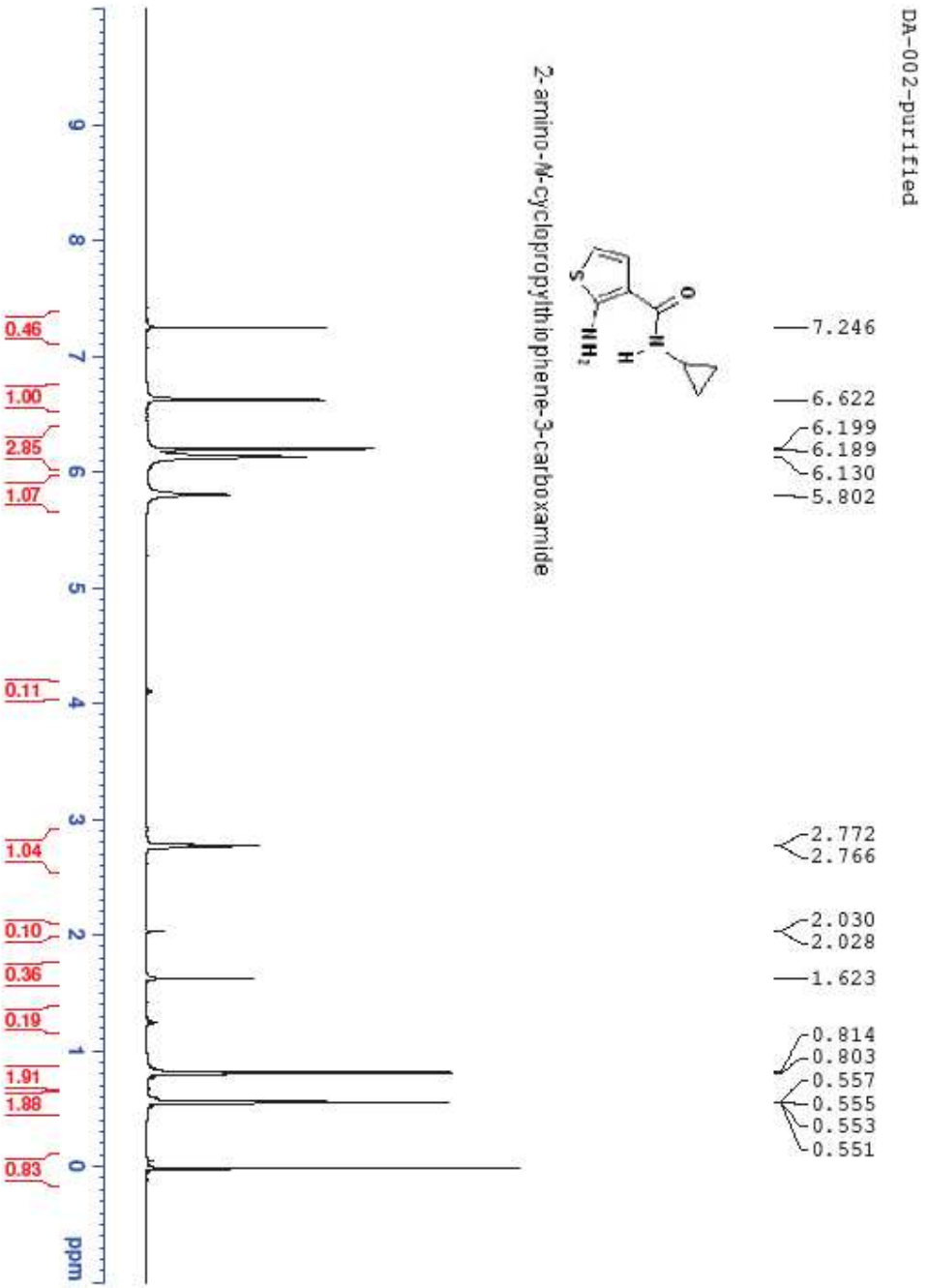


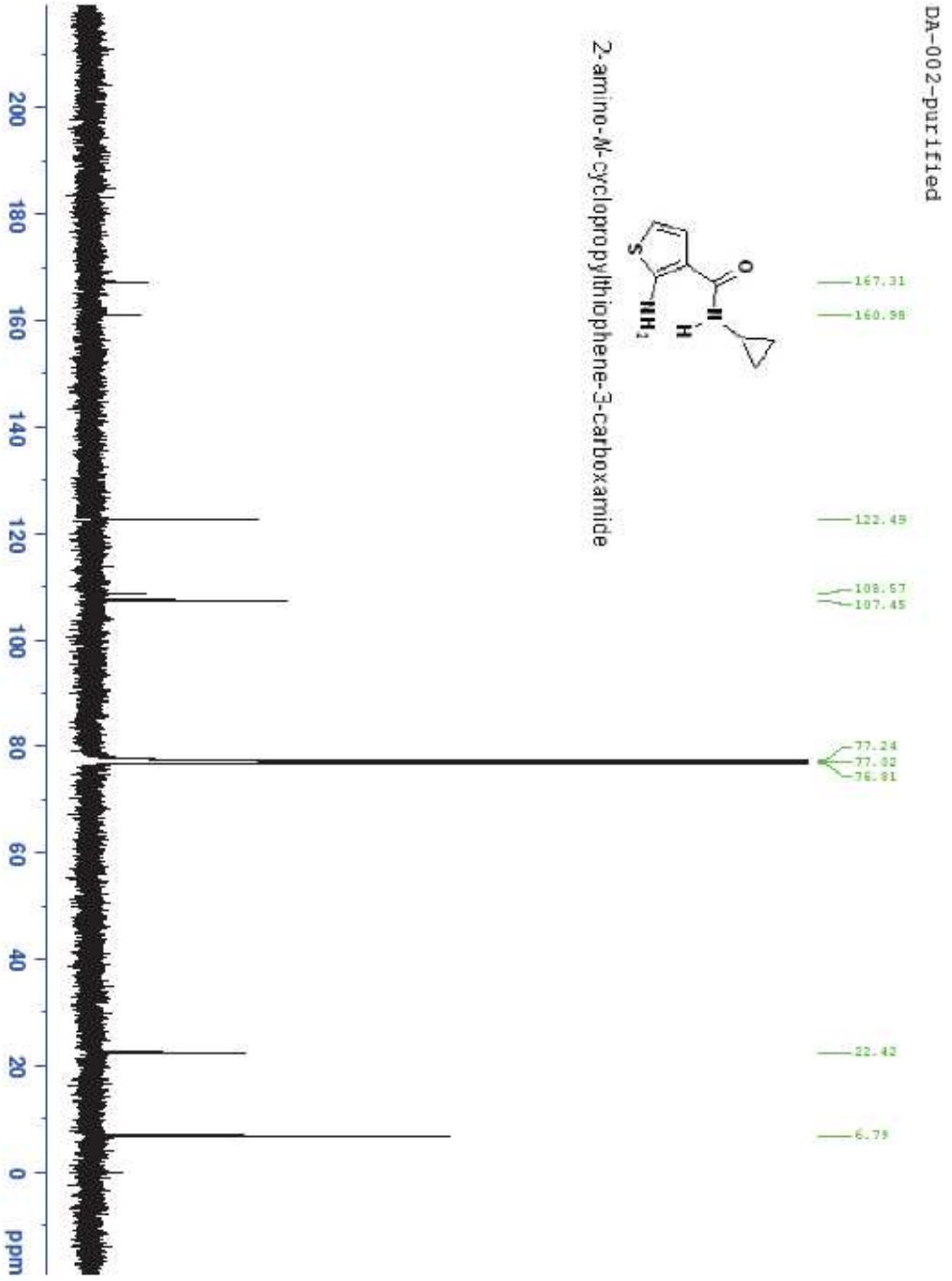

The general procedure B was followed employing cyclohexanone (980 mg, 10 mmol), 2-cyano-*N*-cyclopropylacetamide (1.24 g, 10 mmol), sulfur (320 mg, 10 mmol). The crude product was purified with silica gel column chromatography (50-75 % ethyl acetate in hexanes) to produce the title compound 450 mg (19 %) as the dark yellow solid. HRMS ESL-TOF for $C_{12}H_{16}N_2OSNa$ ($M+Na^+$) found: *m/z*: 259.0872; Calc. Mass: 259.0881. $^1$H NMR ($CDCl_3$, 600 MHz): δ 6.04 (s, 2H), 5.83 (s, 1H), 2.77-2.82 (m, 1H), 2.50-2.56 (m, 4H), 1.78-1.82 (m, 4H), 0.80-0.85 (m, 2H), 0.52-0.58 (m, 2H) ppm; $^{13}$C NMR ($CDCl_3$, 150 MHz): δ 168.1, 159.2, 128.7, 118.9, 108.4, 27.1, 24.5, 22.9, 22.8, 22.4, 6.9 ppm.

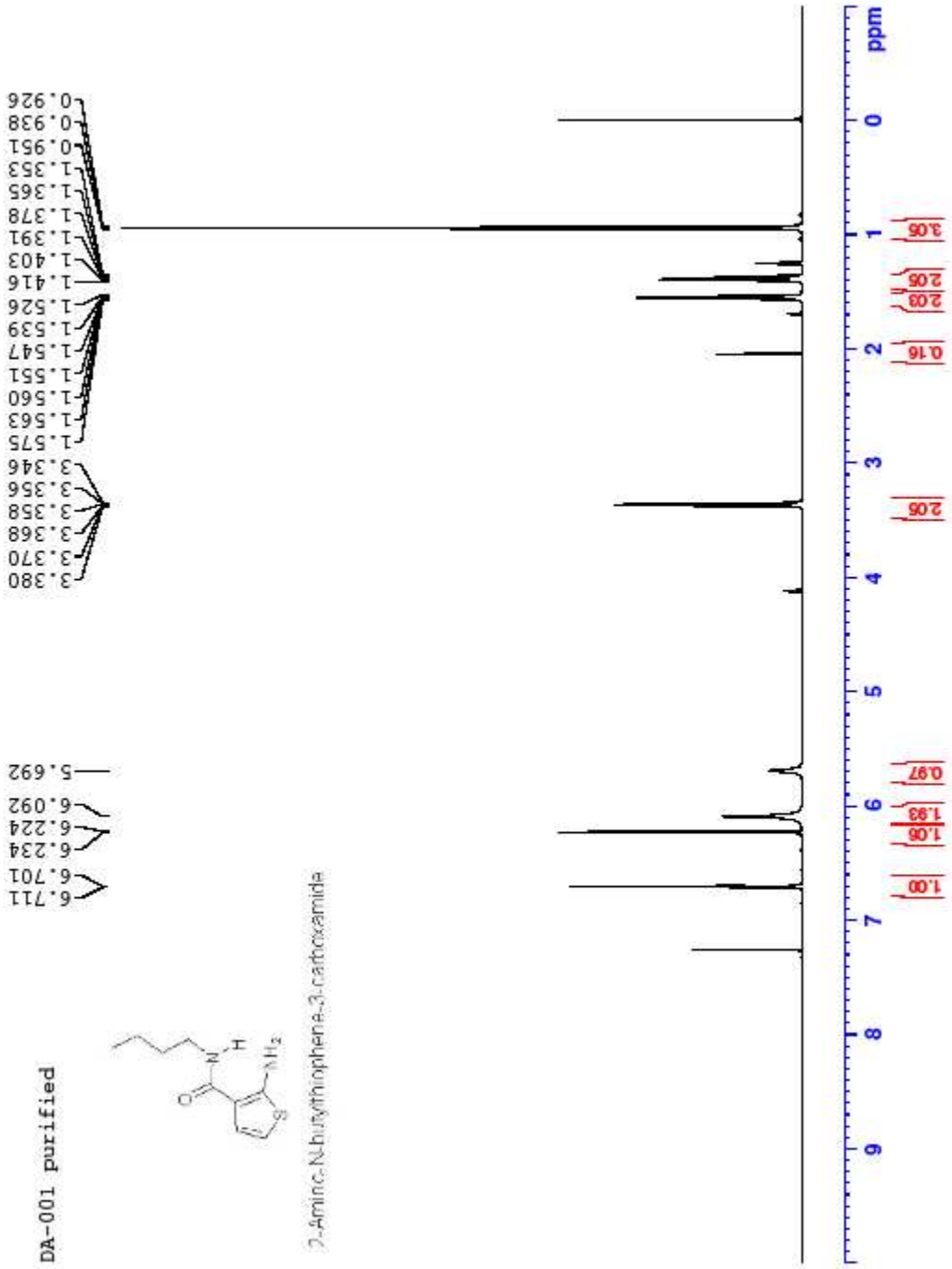
**2-Amino-*N*-butyl-4-phenylthiophene-3-carboxamide (C10,3):** The general procedure B was followed employing acetophenone (600 mg, 5 mmol), *N*-butyl-2-cyanoacetamide (700 mg, 5 mmol), sulfur (160 mg, 5 mmol). The crude product was purified with silica gel column chromatography (50-75 % ethyl acetate in hexanes) to produce the title compound 123 mg (9 %) as the dark yellow oil. HRMS ESL-TOF for $C_{15}H_{18}N_2OS$ ($M^+$) Found: *m/z*: 274.1135; Calc. Mass: 274.1140. $^1$H NMR ($CDCl_3$, 600 MHz): δ 7.34-7.45 (m, 5H), 6.26 (s, 2H), 6.07 (s, 1H), 5.07 (s, 1H), 3.12 (q, J = 6.6 Hz, 2H), 1.13-1.18 (m, 2H), 0.99-1.06 (m, 2H), 0.78 (t, J = 7.2 Hz, 3H) ppm; $^{13}$C NMR ($CDCl_3$, 150 MHz): δ 165.8, 161.6, 138.9, 137.1, 129.2, 128.6, 128.1, 108.4, 105.7, 38.5, 31.0, 19.8, 13.6 ppm.

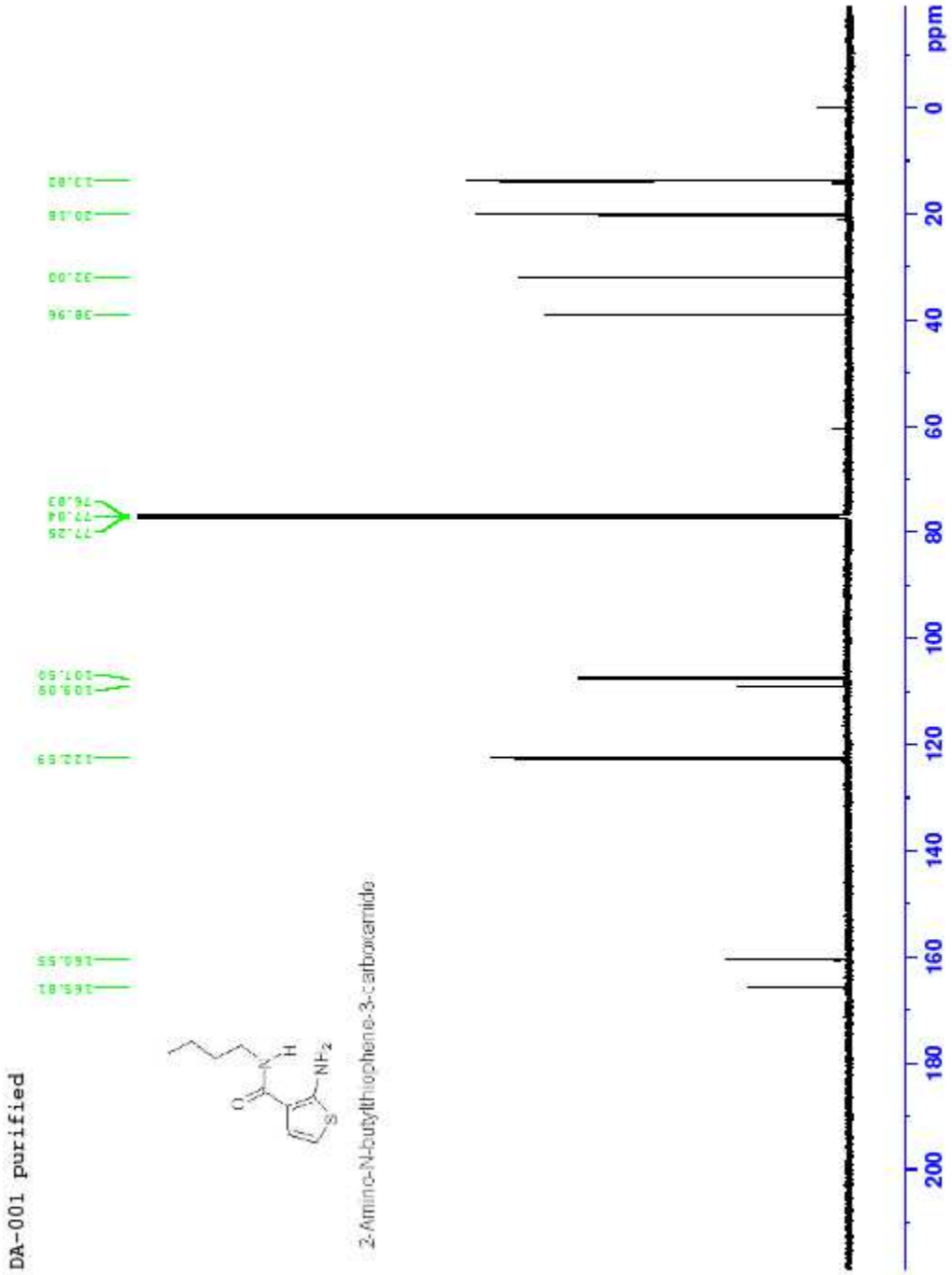


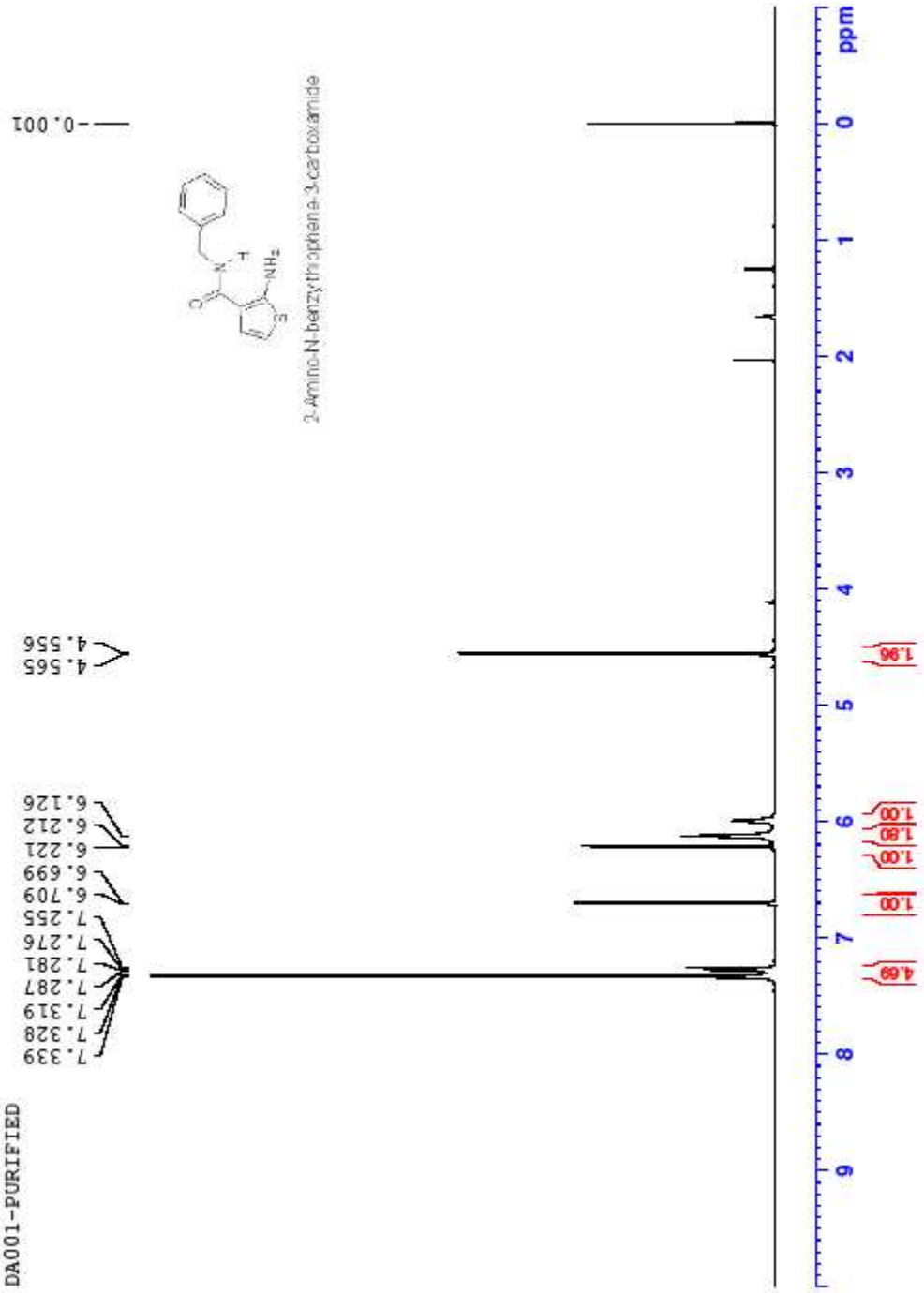
**C1,1**


DA-002-purified
2-amino-N-cyclopropylthiophene-3-carboxamide
7.246
6.622
6.199
6.189
6.130
5.802
2.772
2.766
2.030
2.028
1.623
0.814
0.803
0.557
0.555
0.553
0.551
0.46
1.00
2.85
1.07
0.11
1.04
0.10
0.36
0.19
1.91
1.88
0.83
ppm

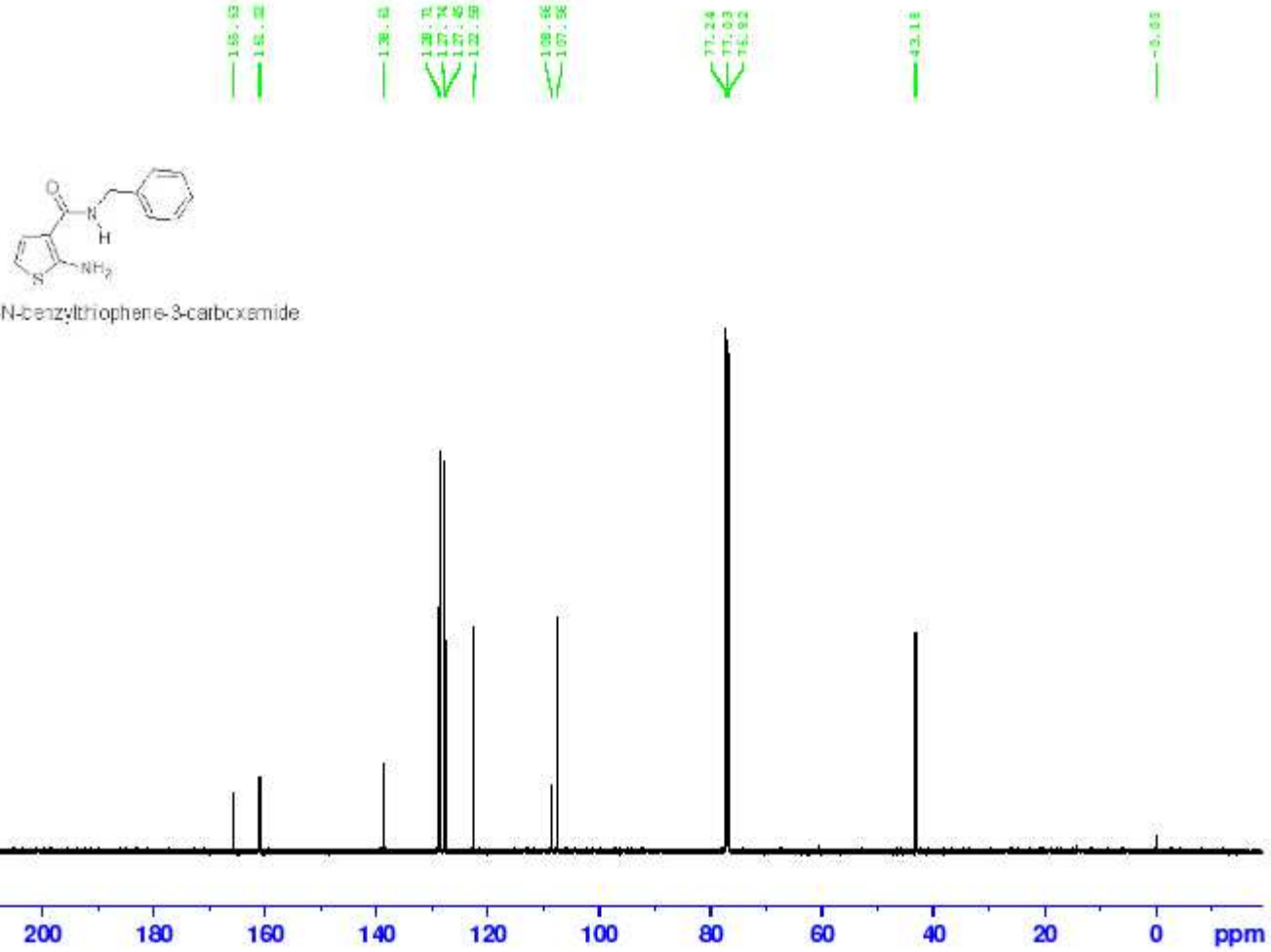

DA-002-purified
2-amino-N-cyclopropylthiophene-3-carboxamide
167.31
160.98
122.49
108.57
107.45
77.24
77.02
76.81
22.42
6.79
200
180
160
140
120
100
80
60
40
20
0
ppm


DA-001 purified
3-Amino-N-butylthiophene-3-carboxamide
6.711
6.701
6.234
6.224
6.092
5.692
3.380
3.370
3.368
3.358
3.356
3.346
1.575
1.563
1.560
1.551
1.547
1.539
1.526
1.416
1.403
1.391
1.378
1.365
1.353
0.951
0.938
0.926
ppm
1.00
1.06
1.93
0.97
2.05
0.16
2.03
2.05
3.05

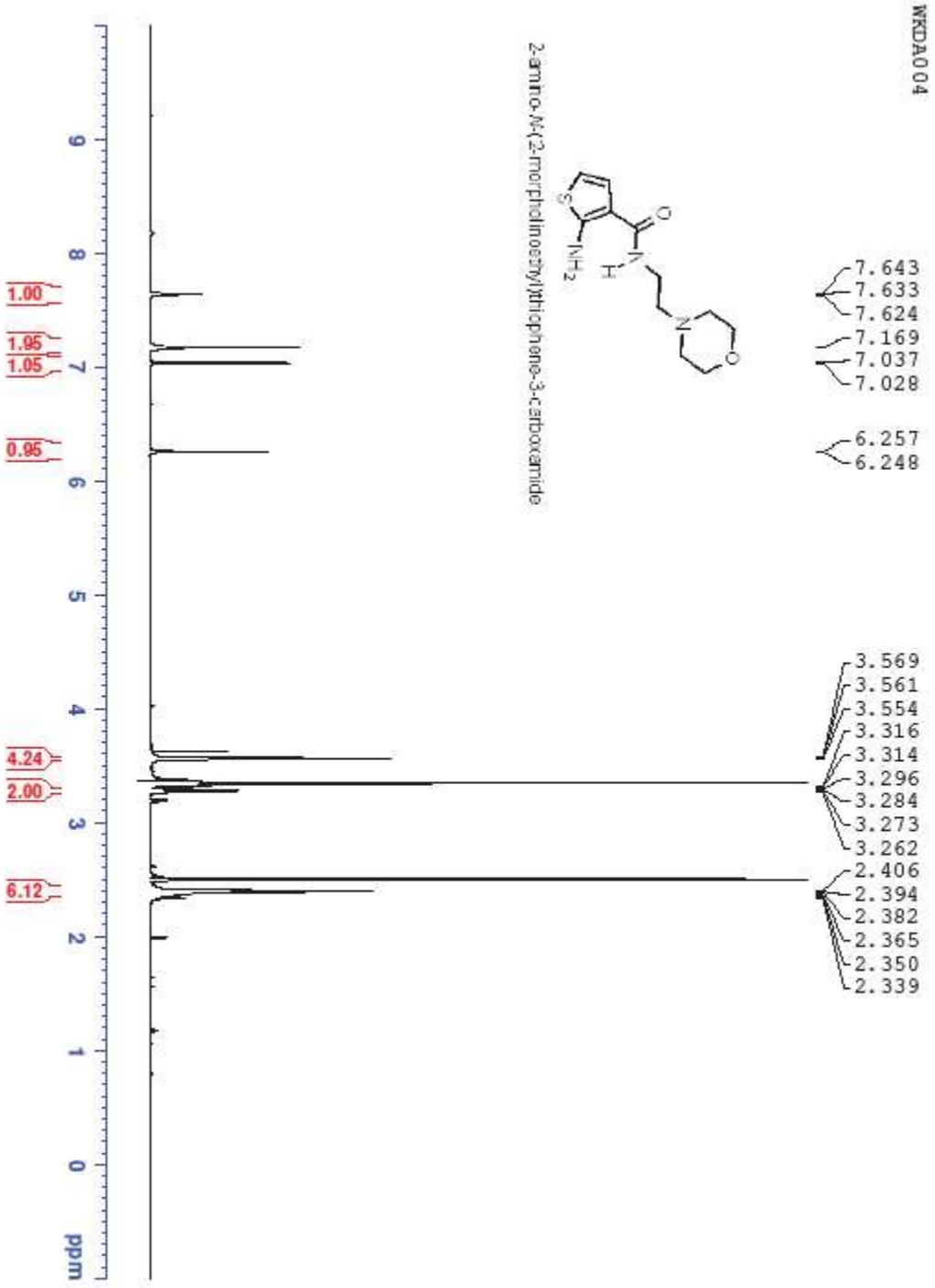

DA-001 purified
2-Amino-N-butylthiophene-3-carboxamide
NH2
O
H
N
S
165.82
160.55
122.89
109.09
107.50
77.25
77.04
76.83
38.96
33.00
20.18
13.82
ppm
0
20
40
60
80
100
120
140
160
180
200

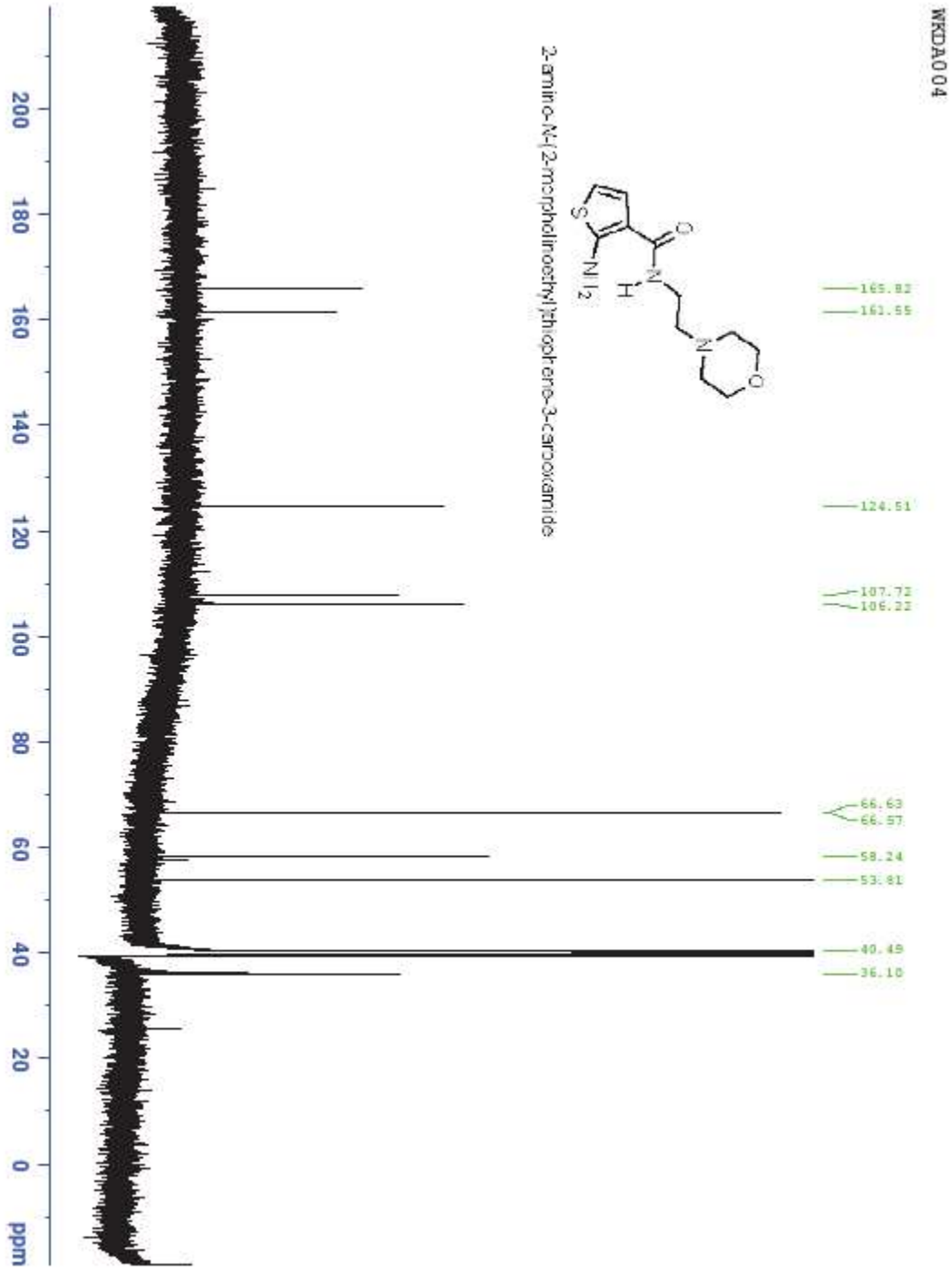

DA001-PURIFIED
7.339
7.328
7.319
7.287
7.281
7.276
7.255
6.709
6.699
6.221
6.212
6.126
4.565
4.556
0.001
2-Amino-N-benzylthiophene-3-carboxamide
ppm
1.96
1.00
1.89
1.00
1.00
4.69

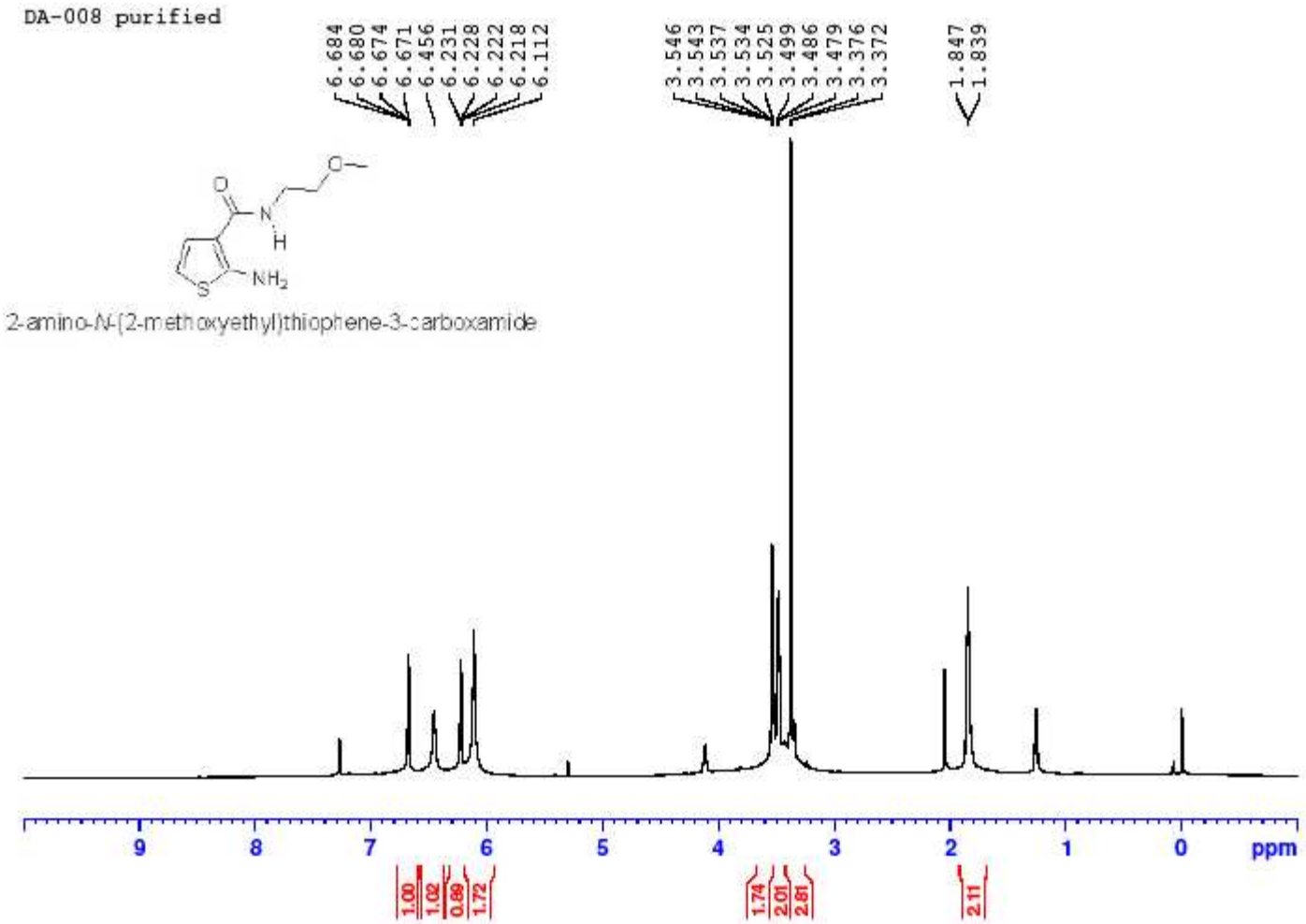
DA001-PURIFIED

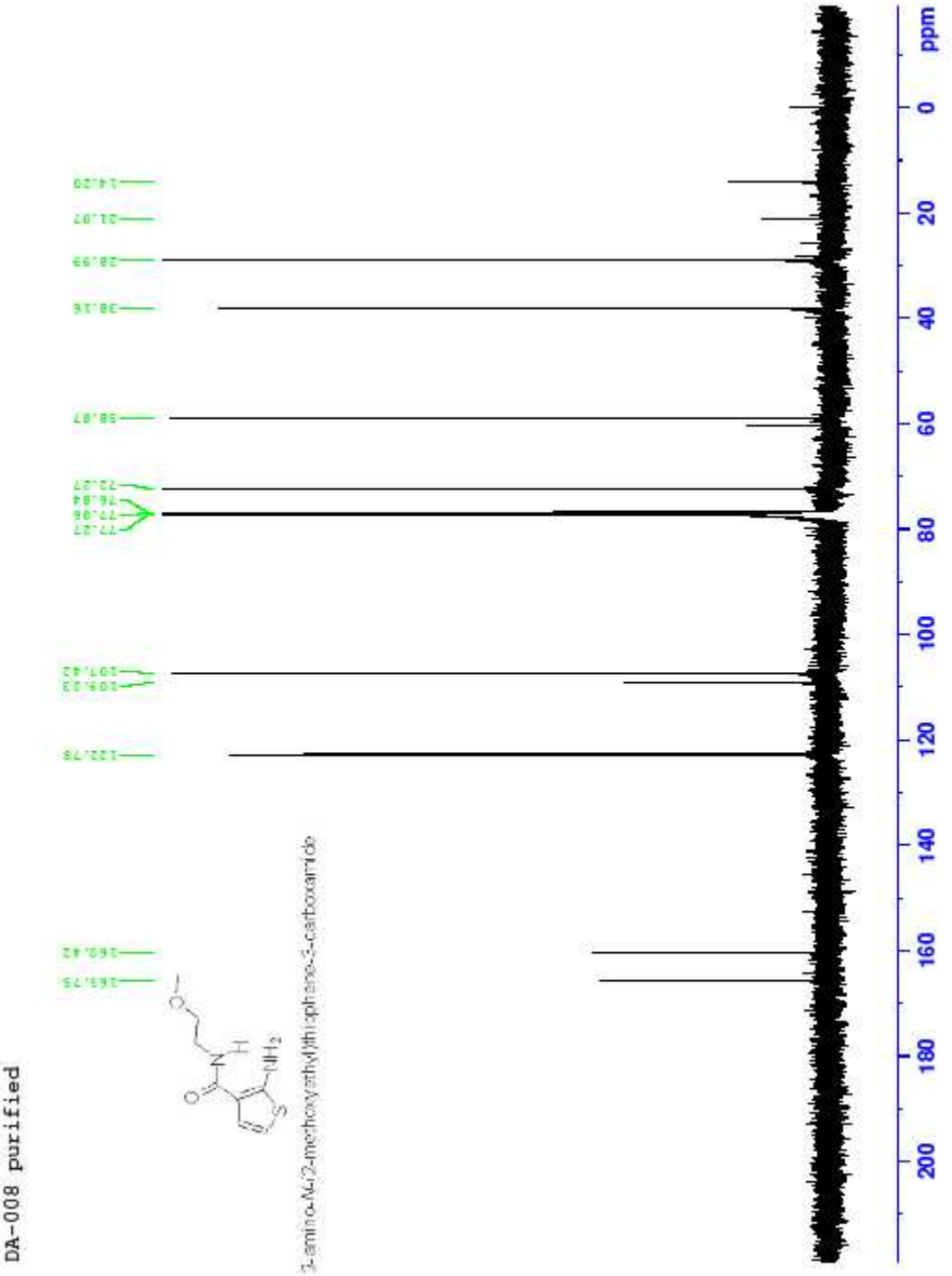


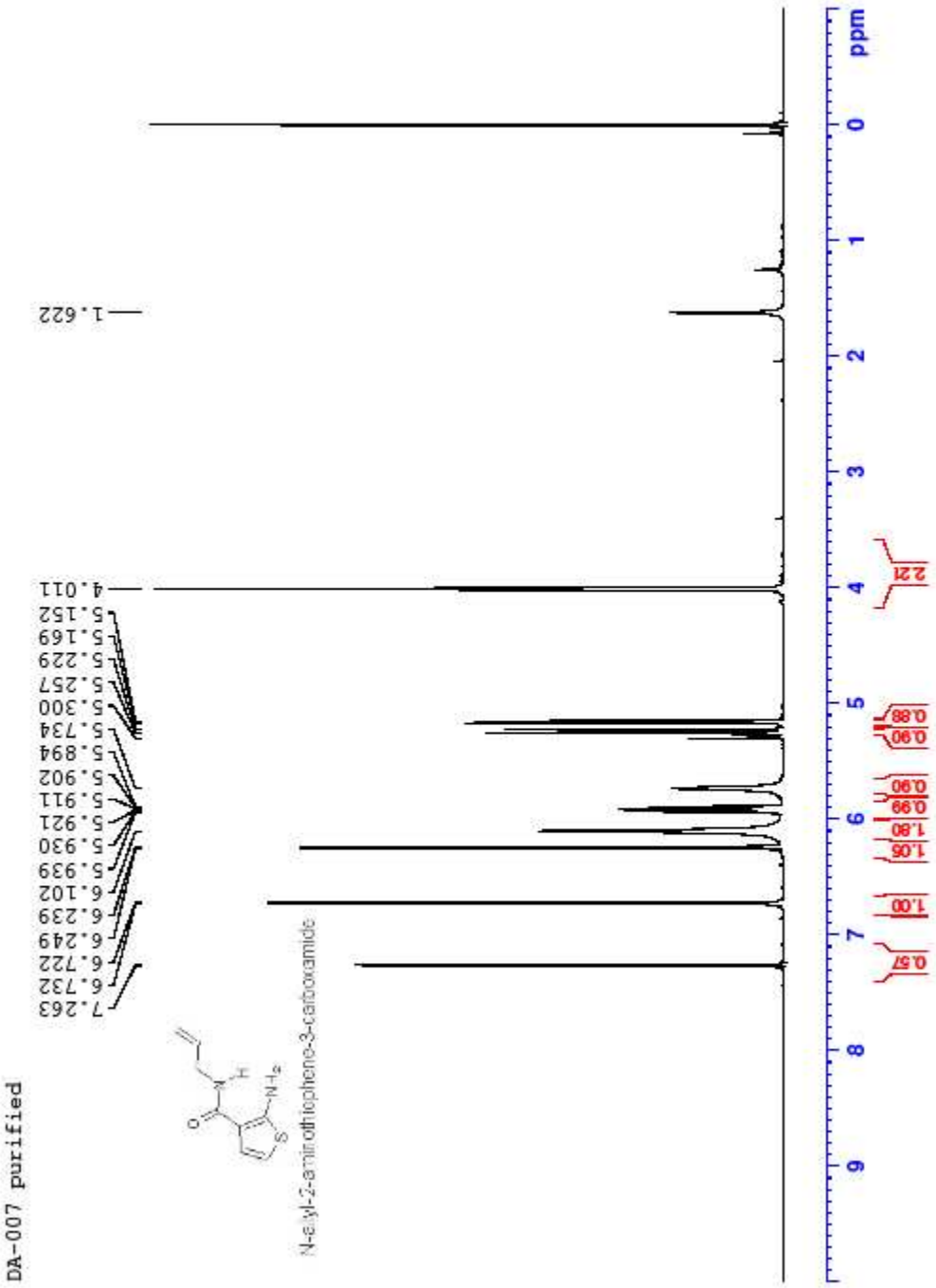

2-Amino-N-benzylthiophene-3-carboxamide


WKDA004
2-amino-N-(2-morpholinoethyl)thiophene-3-carboxamide
7.643
7.633
7.624
7.169
7.037
7.028
6.257
6.248
3.569
3.561
3.554
3.316
3.314
3.296
3.284
3.273
3.262
2.406
2.394
2.382
2.365
2.350
2.339
1.00
1.95
1.05
0.95
4.24
2.00
6.12
ppm

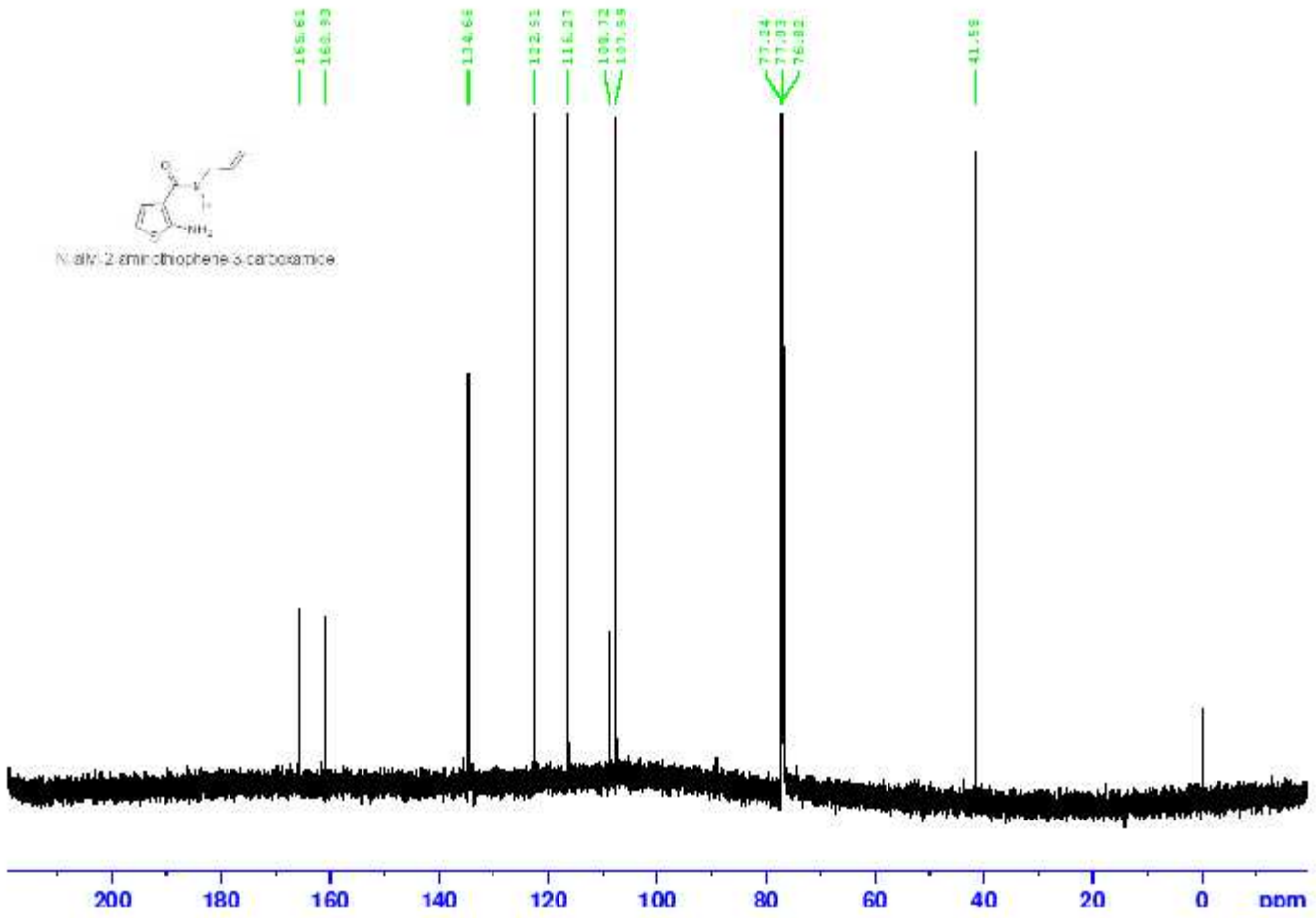

WKDA004
2-amino-N-(2-morpholinoethyl)thiophene-3-carboxamide
165.82
161.55
124.51
107.72
106.22
66.63
66.57
58.24
53.81
40.49
36.10
200
180
160
140
120
100
80
60
40
20
0
ppm

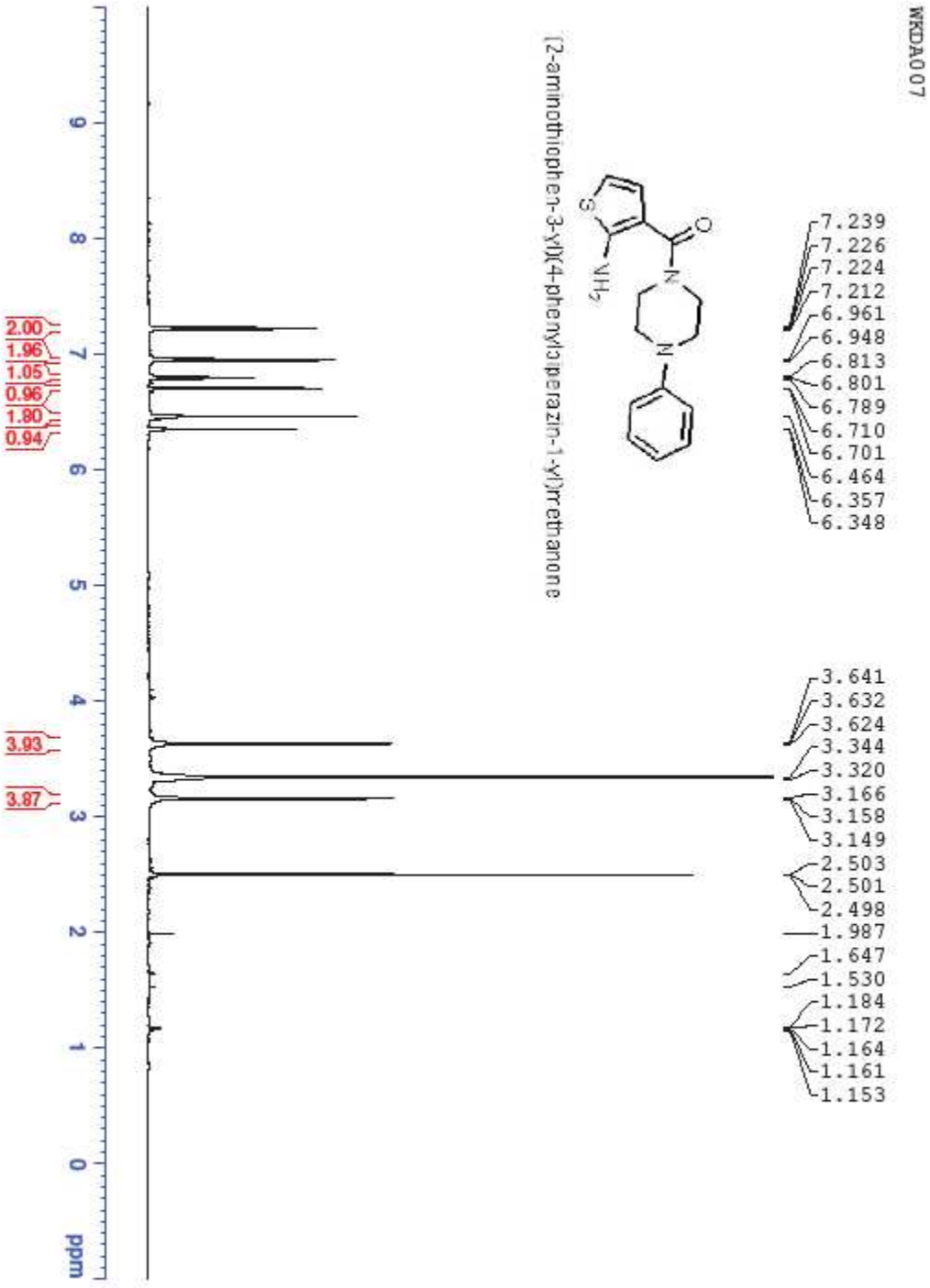

DA-008 purified
6.684
6.680
6.674
6.671
6.456
6.231
6.228
6.222
6.218
6.112
3.546
3.543
3.537
3.534
3.525
3.499
3.486
3.479
3.376
3.372
1.847
1.839
O
N
H
O
NH2
S
2-amino-N-(2-methoxyethyl)thiophene-3-carboxamide
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.02
0.89
1.72
1.74
2.01
2.61
2.11

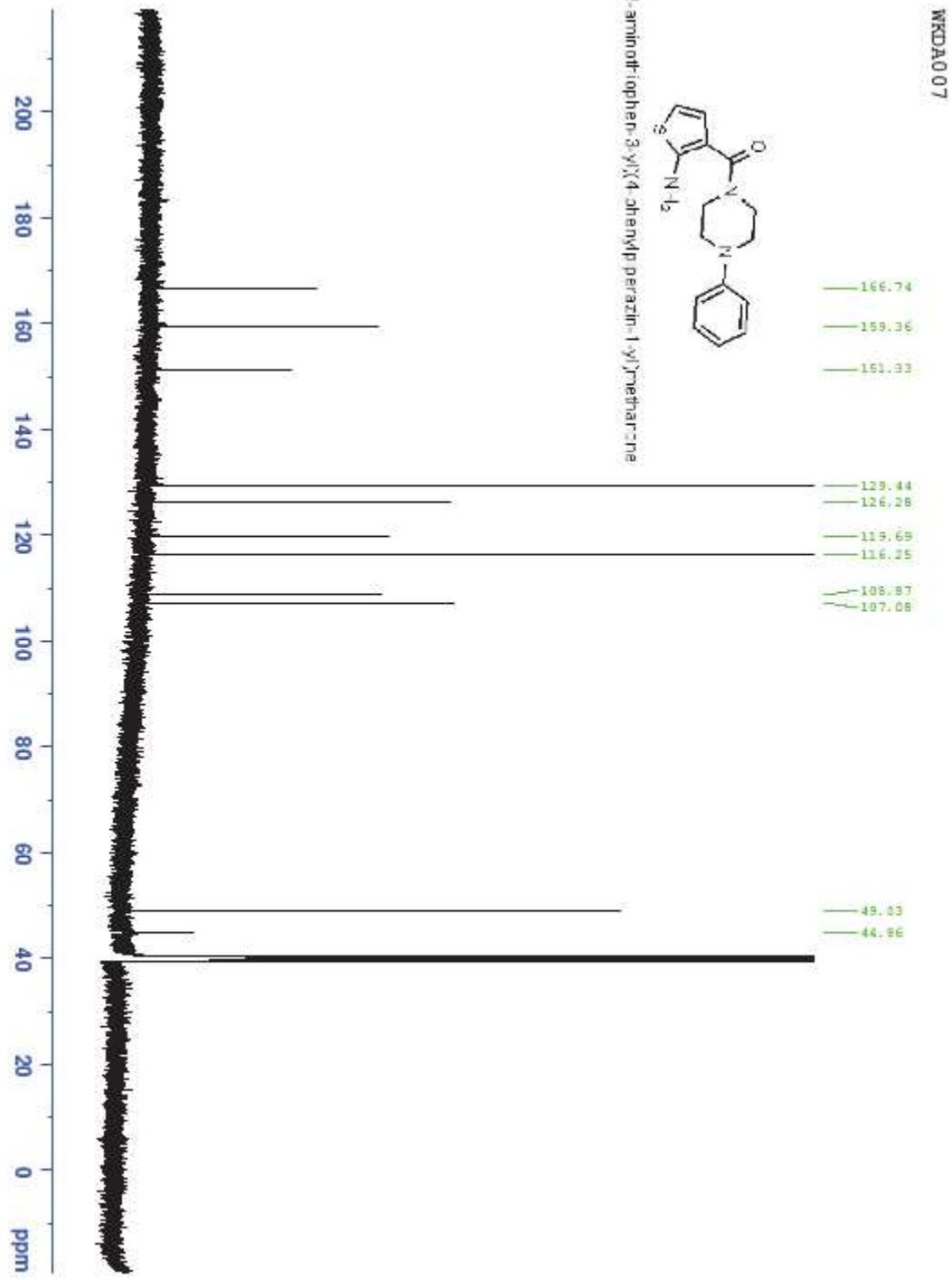

DA-008 purified
3-amino-N-(2-methoxyethyl)thiophene-2-carboxamide
165.75
160.42
132.78
109.23
107.42
77.27
77.06
76.84
73.27
58.87
38.16
28.99
21.07
14.20
ppm
0
20
40
60
80
100
120
140
160
180
200

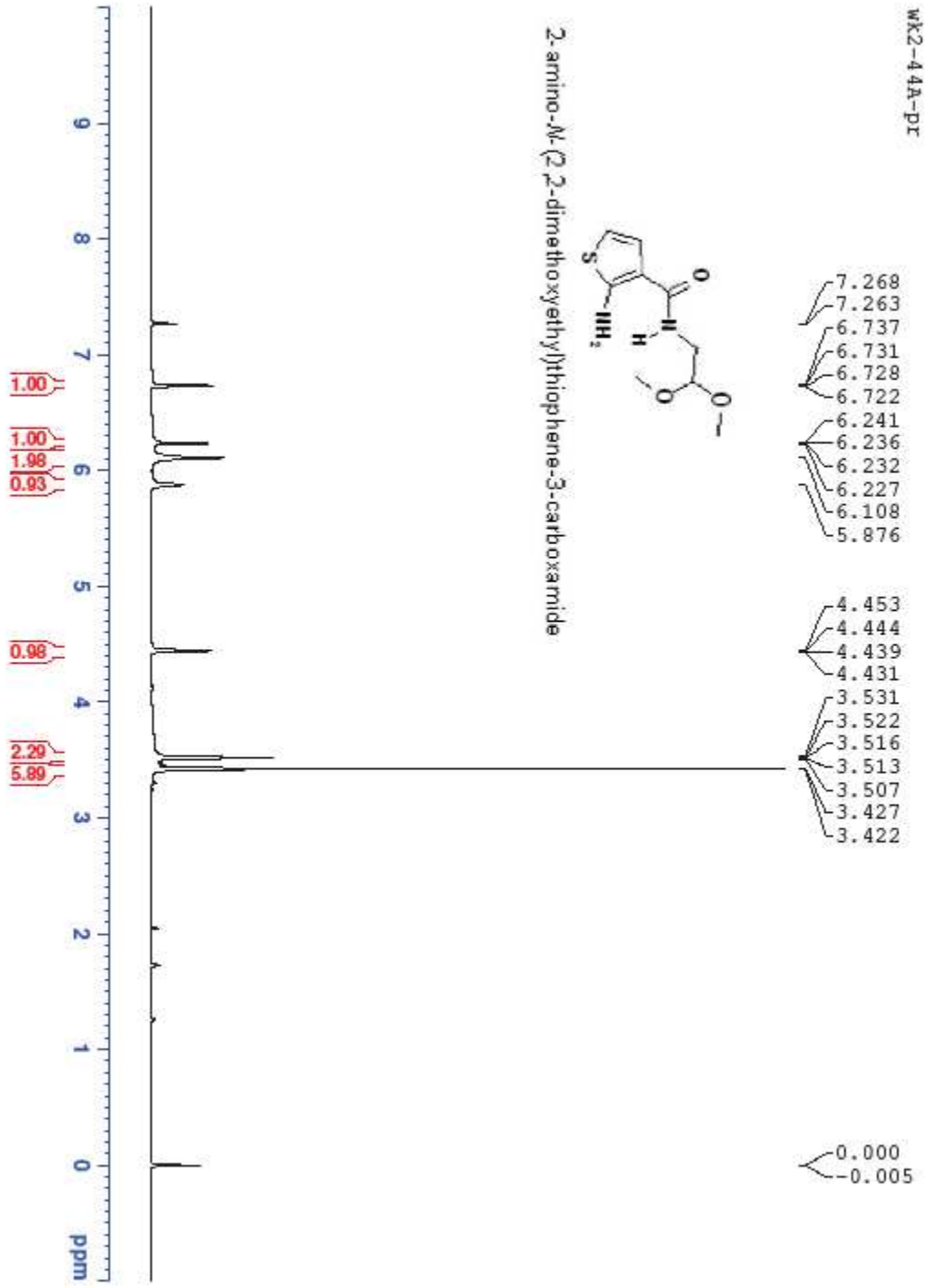

DA-007 purified
7.263
6.732
6.722
6.249
6.239
6.102
5.939
5.930
5.921
5.911
5.902
5.894
5.734
5.300
5.257
5.229
5.169
5.152
4.011
1.622
N-allyl-2-aminothiophene-3-carboxamide
0.57
1.00
1.05
1.80
0.99
0.90
0.90
0.88
2.21
ppm

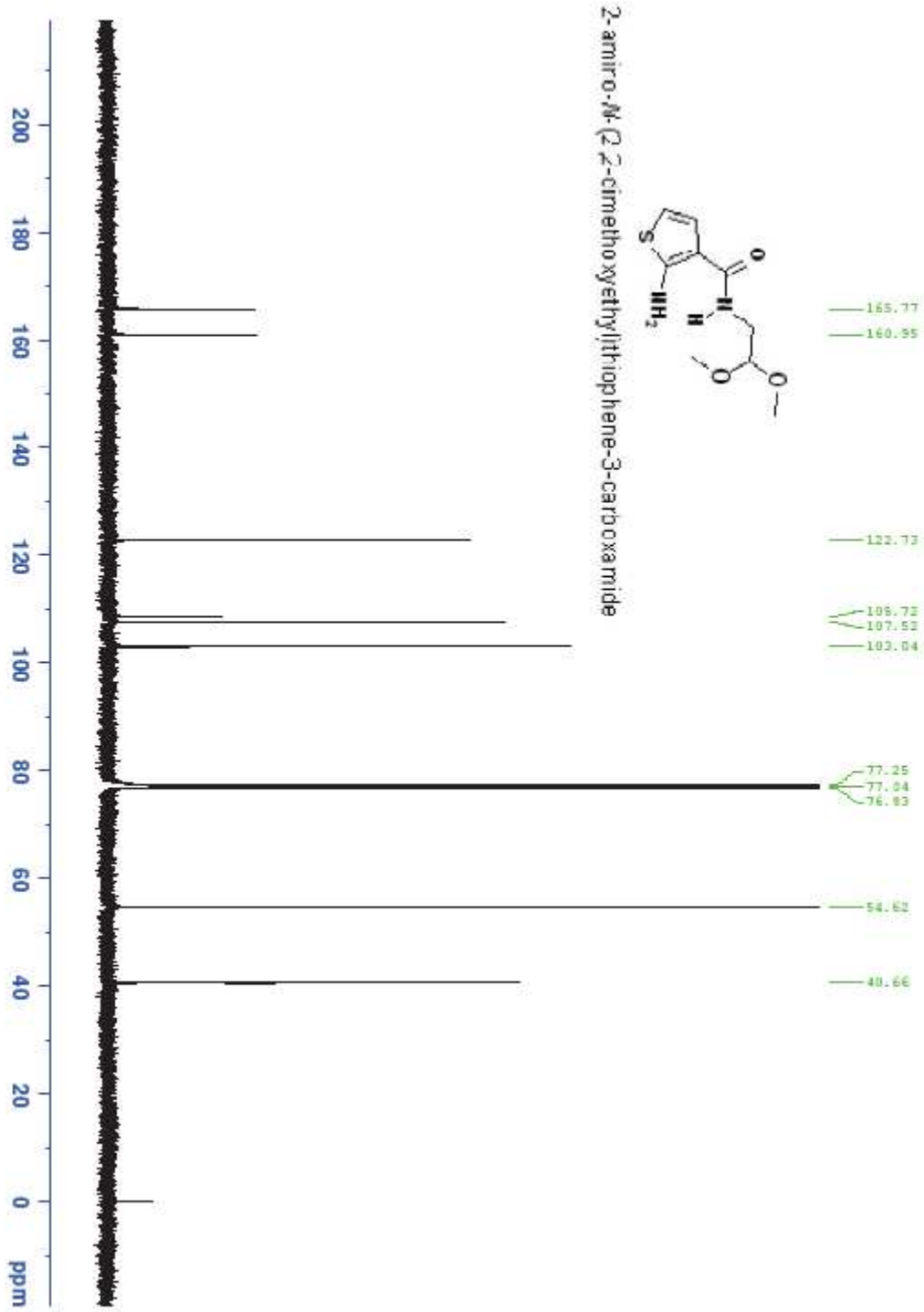
DA-007 purified



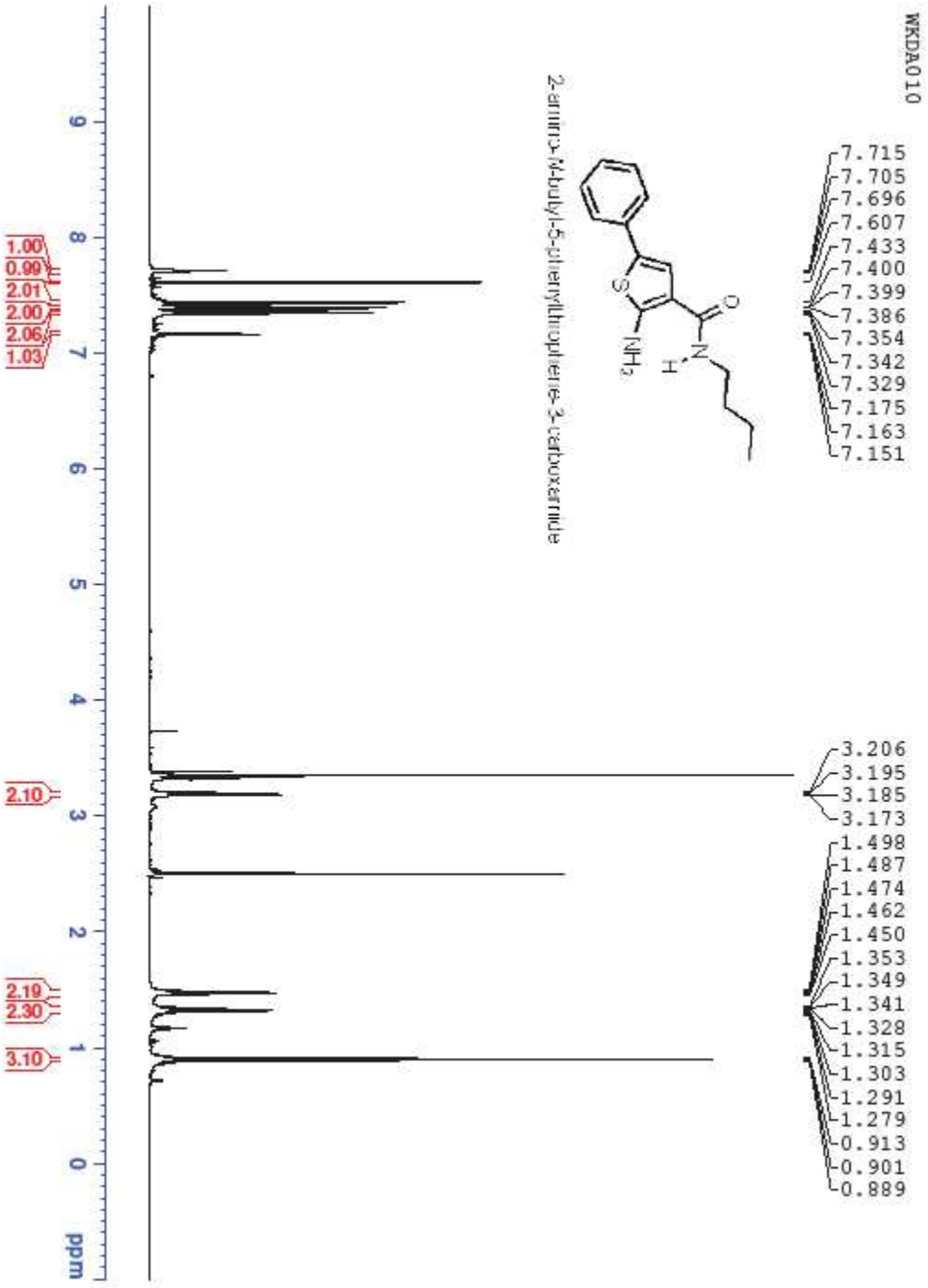

WKDA007
(2-aminothiophen-3-yl)(4-phenylpiperazin-1-yl)methanone
7.239
7.226
7.224
7.212
6.961
6.948
6.813
6.801
6.789
6.710
6.701
6.464
6.357
6.348
3.641
3.632
3.624
3.344
3.320
3.166
3.158
3.149
2.503
2.501
2.498
1.987
1.647
1.530
1.184
1.172
1.164
1.161
1.153
2.00
1.96
1.05
0.96
1.80
0.94
3.93
3.87
ppm

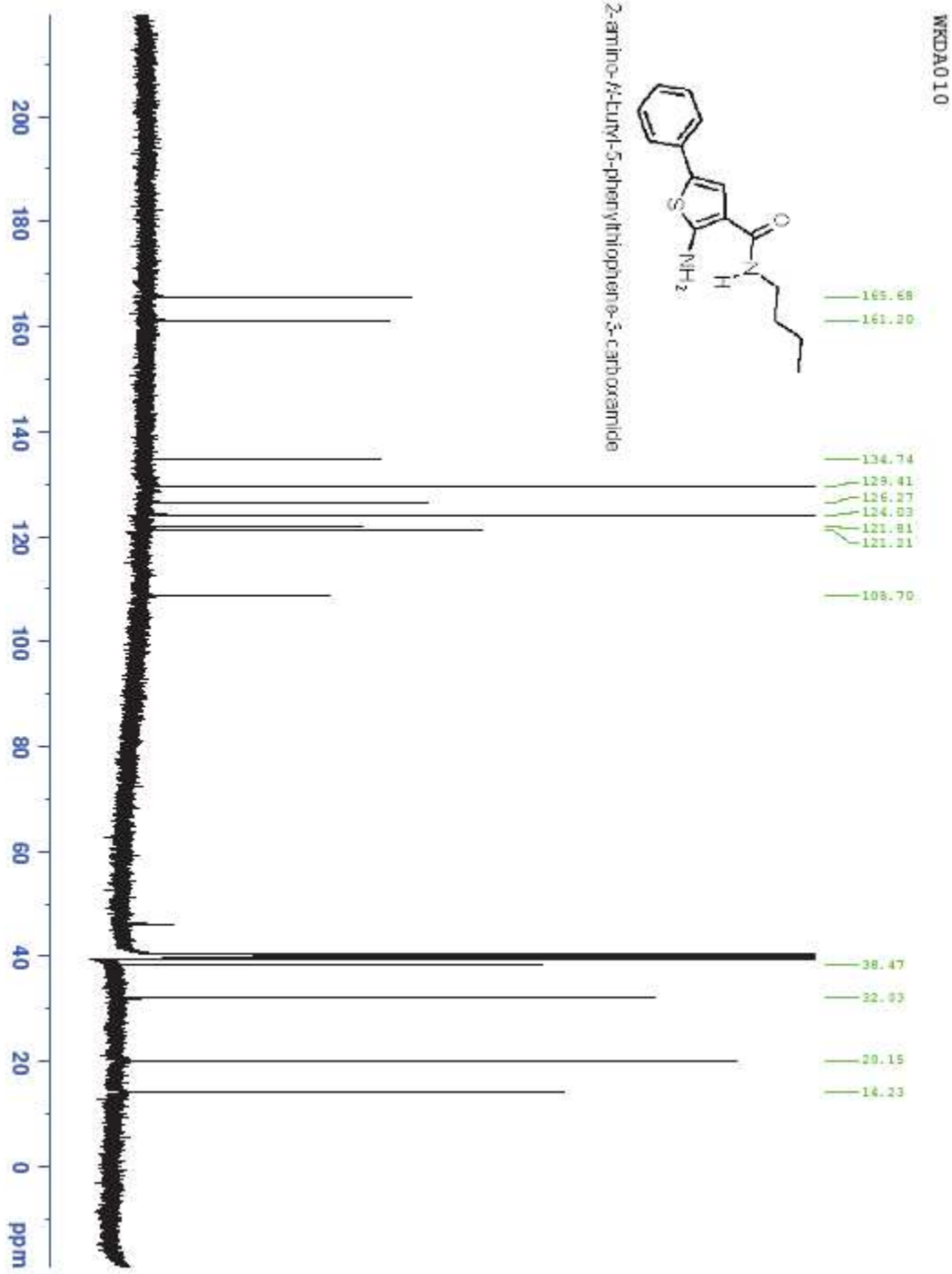

WKDA007
(2-aminothiophen-3-yl)(4-phenylpiperazin-1-yl)methanone
166.74
159.36
151.33
129.44
126.28
119.69
116.25
108.87
107.08
49.03
44.86
200
180
160
140
120
100
80
60
40
20
0
ppm


wk2-44a-pr
2-amino-N-(2,2-dimethoxyethyl)thiophene-3-carboxamide
7.268
7.263
6.737
6.731
6.728
6.722
6.241
6.236
6.232
6.227
6.108
5.876
4.453
4.444
4.439
4.431
3.531
3.522
3.516
3.513
3.507
3.427
3.422
0.000
-0.005
1.00
1.00
1.98
0.93
0.98
2.29
5.89
ppm

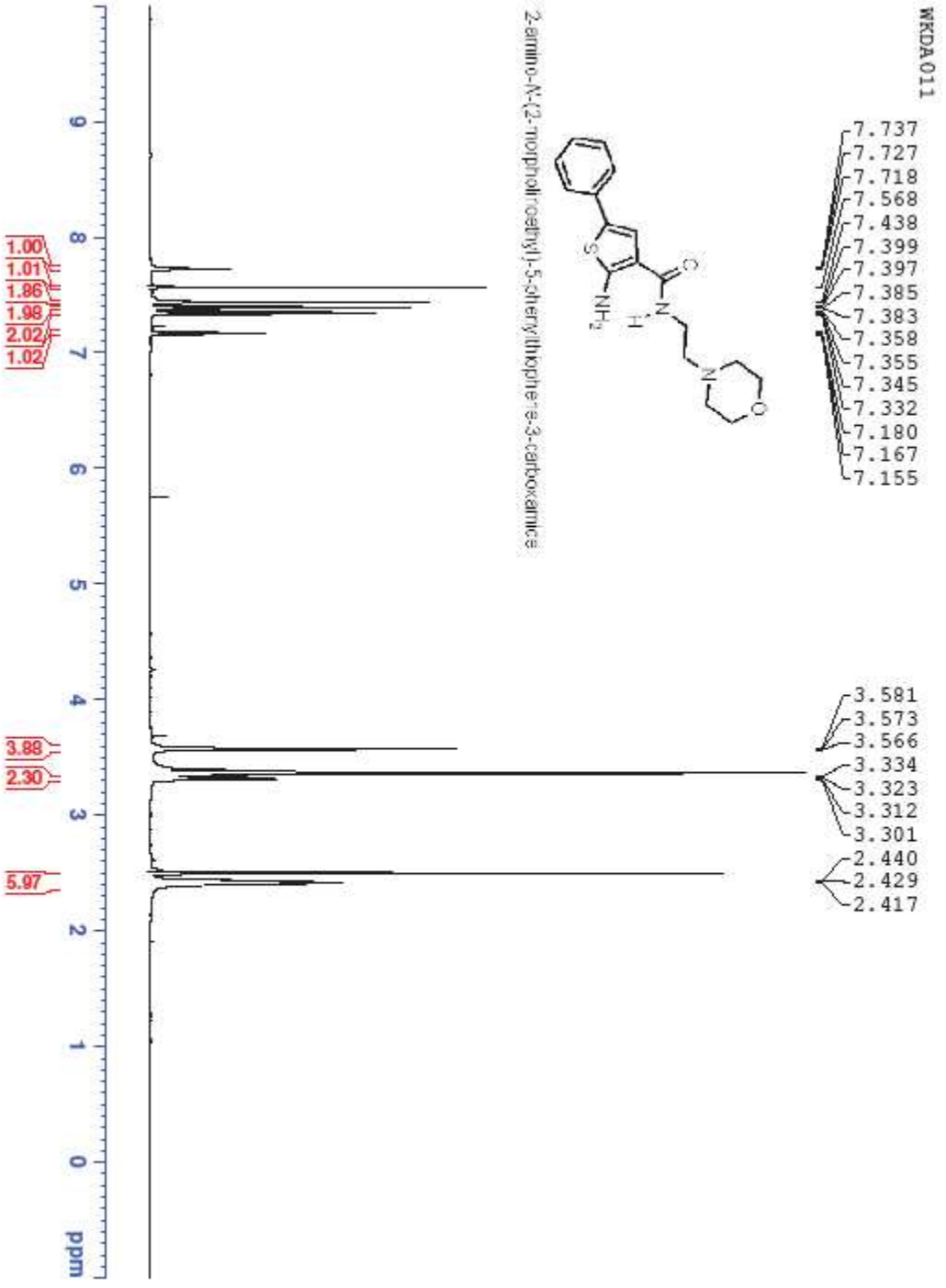

wk2-44a-pr
2-amino-N-(2-methoxyethyl)thiophene-3-carboxamide
165.77
160.95
122.73
108.72
107.52
103.04
77.25
77.04
76.83
54.62
40.66
200
180
160
140
120
100
80
60
40
20
0
ppm

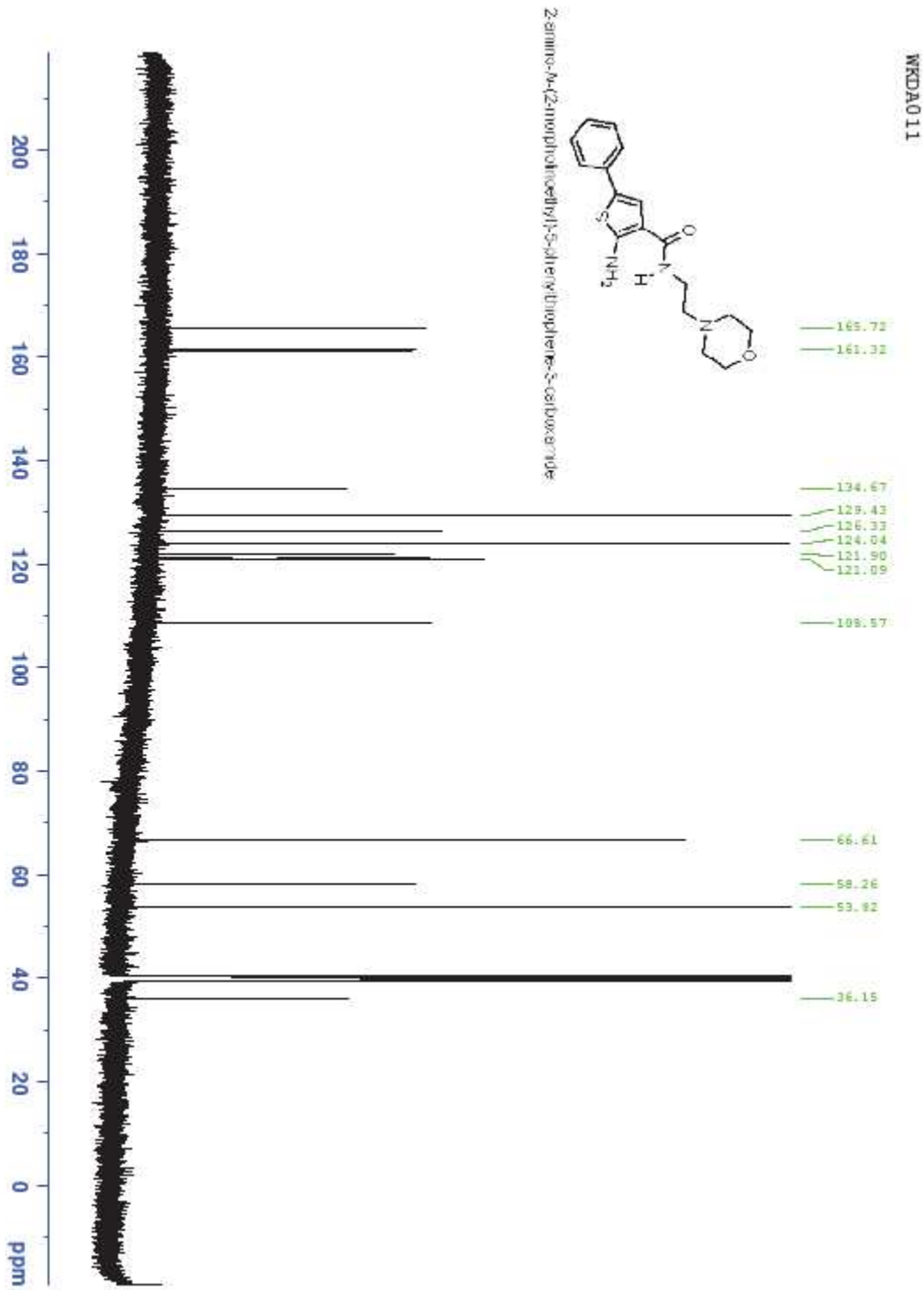
**C2,3**


WKDA010
7.715
7.705
7.696
7.607
7.433
7.400
7.399
7.386
7.354
7.342
7.329
7.175
7.163
7.151
3.206
3.195
3.185
3.173
1.498
1.487
1.474
1.462
1.450
1.353
1.349
1.341
1.328
1.315
1.303
1.291
1.279
0.913
0.901
0.889
1.00
0.99
2.01
2.00
2.06
1.03
2.10
2.19
2.30
3.10
ppm

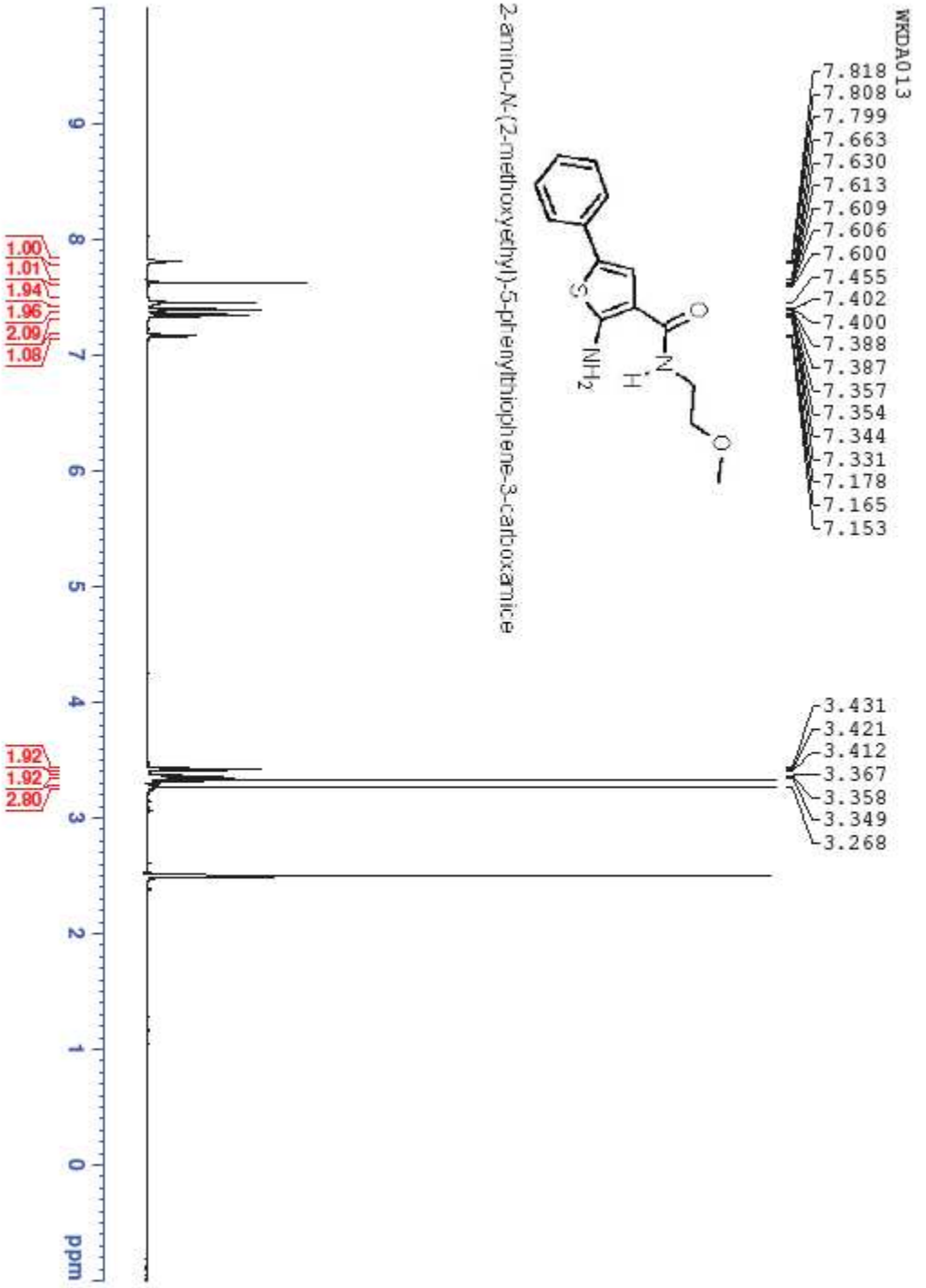

WKDA010
2-amino-N-butyl-5-phenylthiophene-3-carboxamide
NH2
S
O
N
H
165.68
161.20
134.74
129.41
126.27
124.03
121.81
121.31
108.70
38.47
32.03
20.15
14.23
200
180
160
140
120
100
80
60
40
20
0
ppm

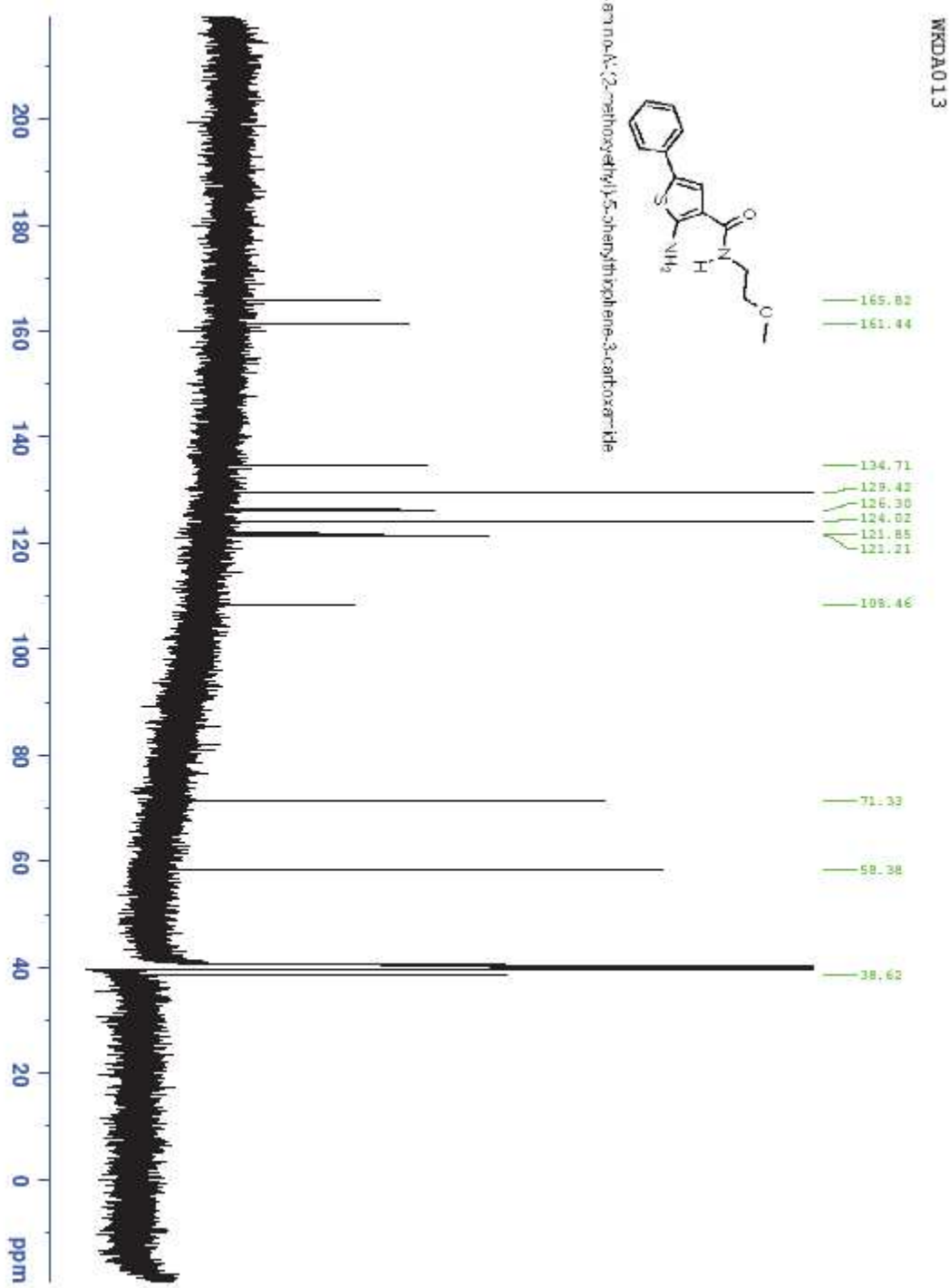
**C2,4**


WKDA011
2-amino-N-(2-morpholinoethyl)-5-phenylthiophene-3-carboxamide
7.737
7.727
7.718
7.568
7.438
7.399
7.397
7.385
7.383
7.358
7.355
7.345
7.332
7.180
7.167
7.155
3.581
3.573
3.566
3.334
3.323
3.312
3.301
2.440
2.429
2.417
1.00
1.01
1.96
1.98
2.02
1.02
3.88
2.30
5.97
ppm

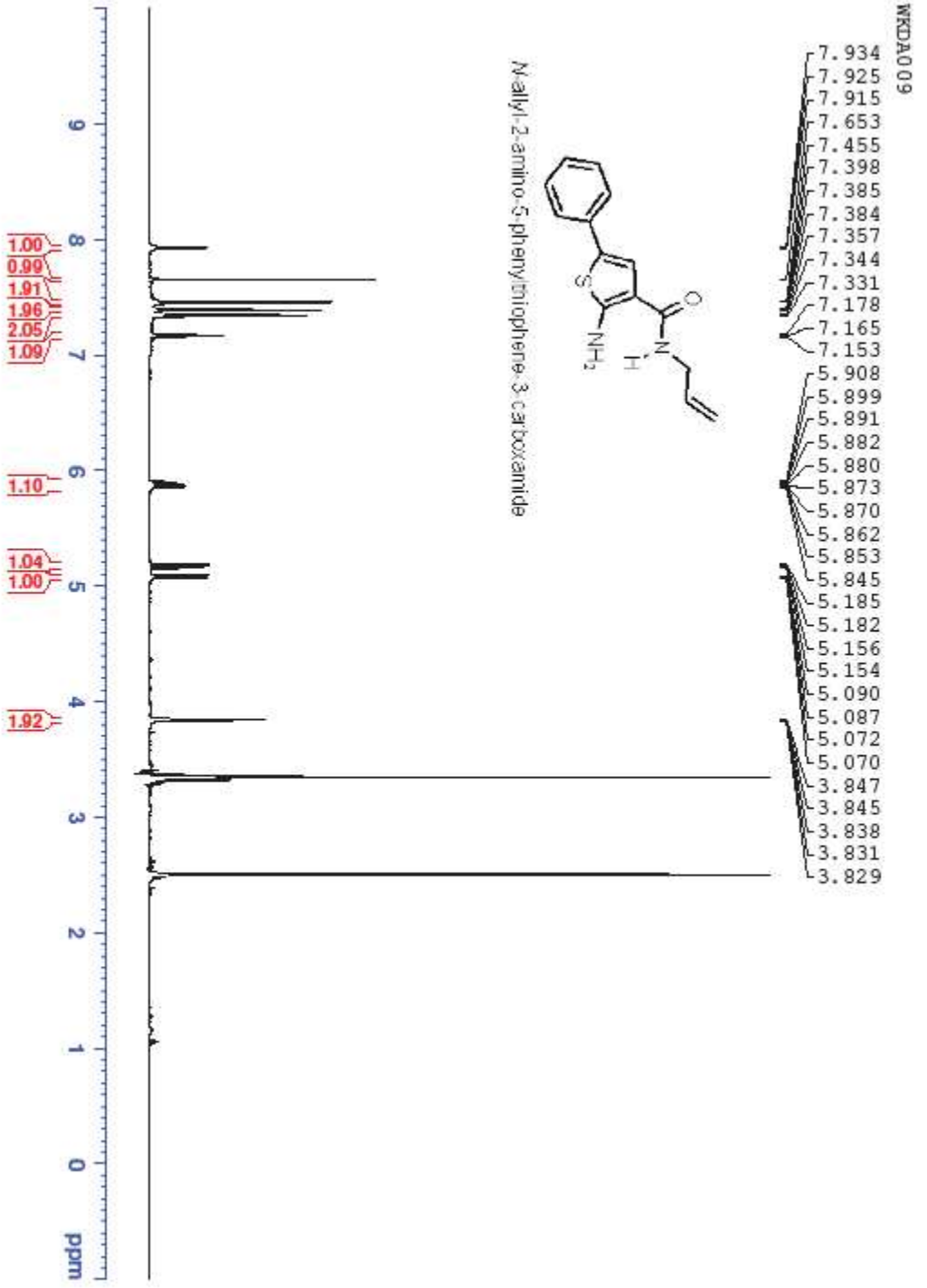

WKDA011
2-amino-N-(2-morpholinoethyl)-5-phenylthiophene-3-carboxamide
165.72
161.32
134.67
129.43
126.33
124.04
121.90
121.09
108.57
66.61
58.26
53.82
36.15
200
180
160
140
120
100
80
60
40
20
0
ppm

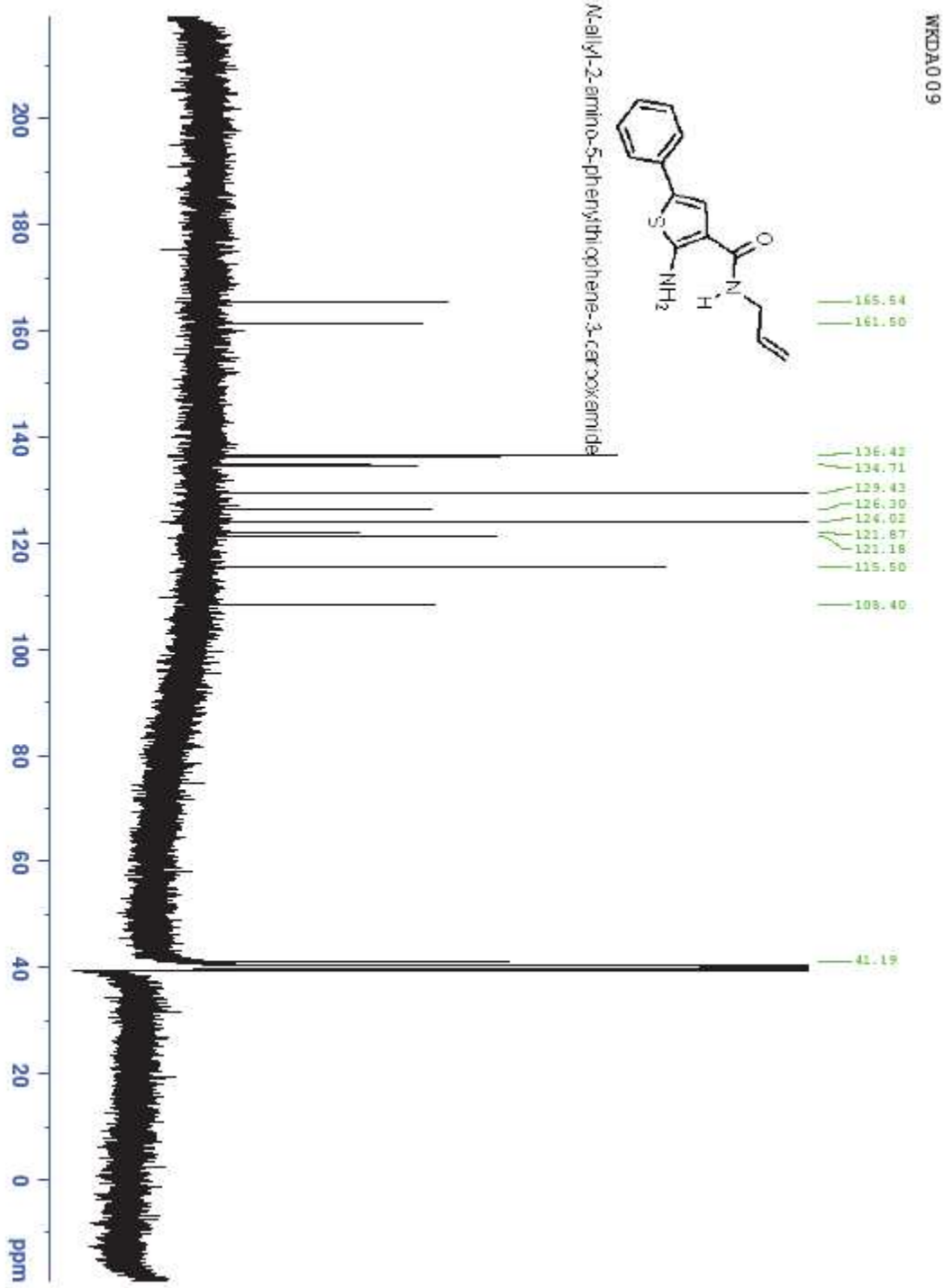
**C2,5**


WKDA013
7.818
7.808
7.799
7.663
7.630
7.613
7.609
7.606
7.600
7.455
7.402
7.400
7.388
7.387
7.357
7.354
7.344
7.331
7.178
7.165
7.153
2-amino-N-(2-methoxyethyl)-5-phenylthiophene-3-carboxamide
3.431
3.421
3.412
3.367
3.358
3.349
3.268
1.00
1.01
1.94
1.96
2.09
1.08
1.92
1.92
2.80
ppm

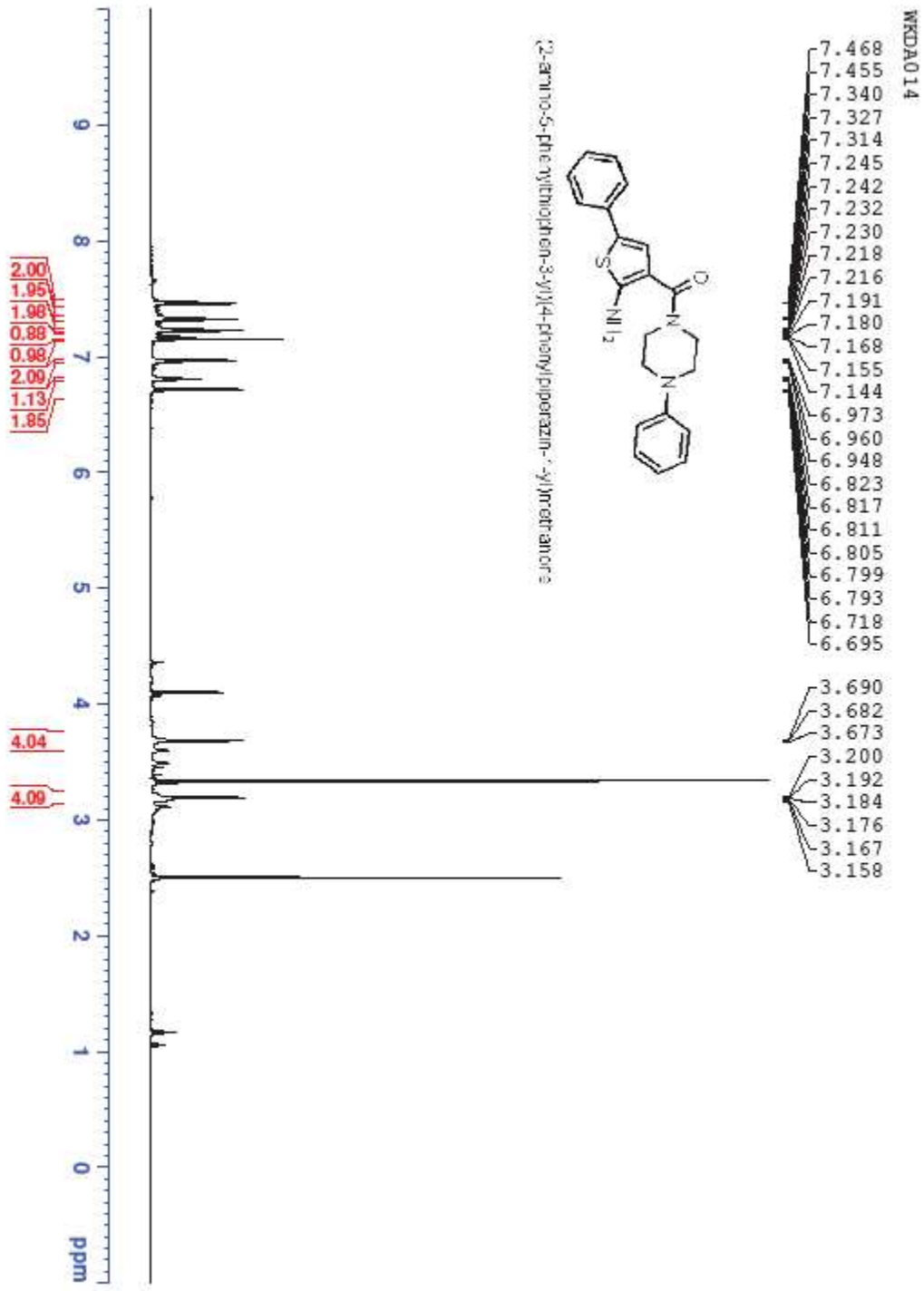

WKDA013
2-amino-N-(2-methoxyethyl)-5-phenylthiophene-3-carboxamide
165.82
161.44
134.71
129.42
126.30
124.02
121.85
121.21
108.46
71.33
59.38
38.62
200
180
160
140
120
100
80
60
40
20
0
ppm

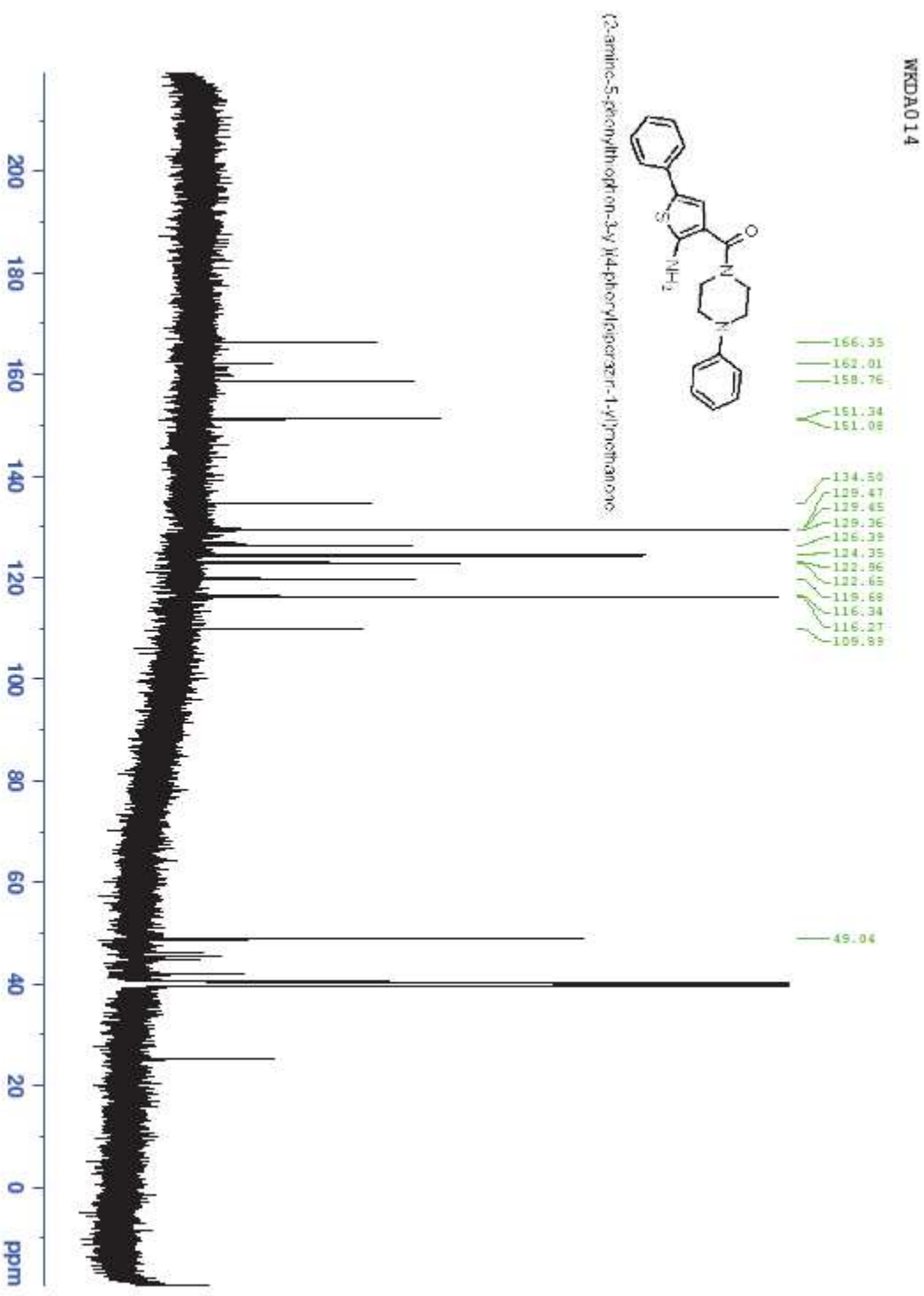
**C2,6**


WKDA009
7.934
7.925
7.915
7.653
7.455
7.398
7.385
7.384
7.357
7.344
7.331
7.178
7.165
7.153
5.908
5.899
5.891
5.882
5.880
5.873
5.870
5.862
5.853
5.845
5.185
5.182
5.156
5.154
5.090
5.087
5.072
5.070
3.847
3.845
3.838
3.831
3.829
N-allyl-2-amino-5-phenylthiophene-3-carboxamide
1.00
0.99
1.91
1.96
2.05
1.09
1.10
1.04
1.00
1.92
ppm

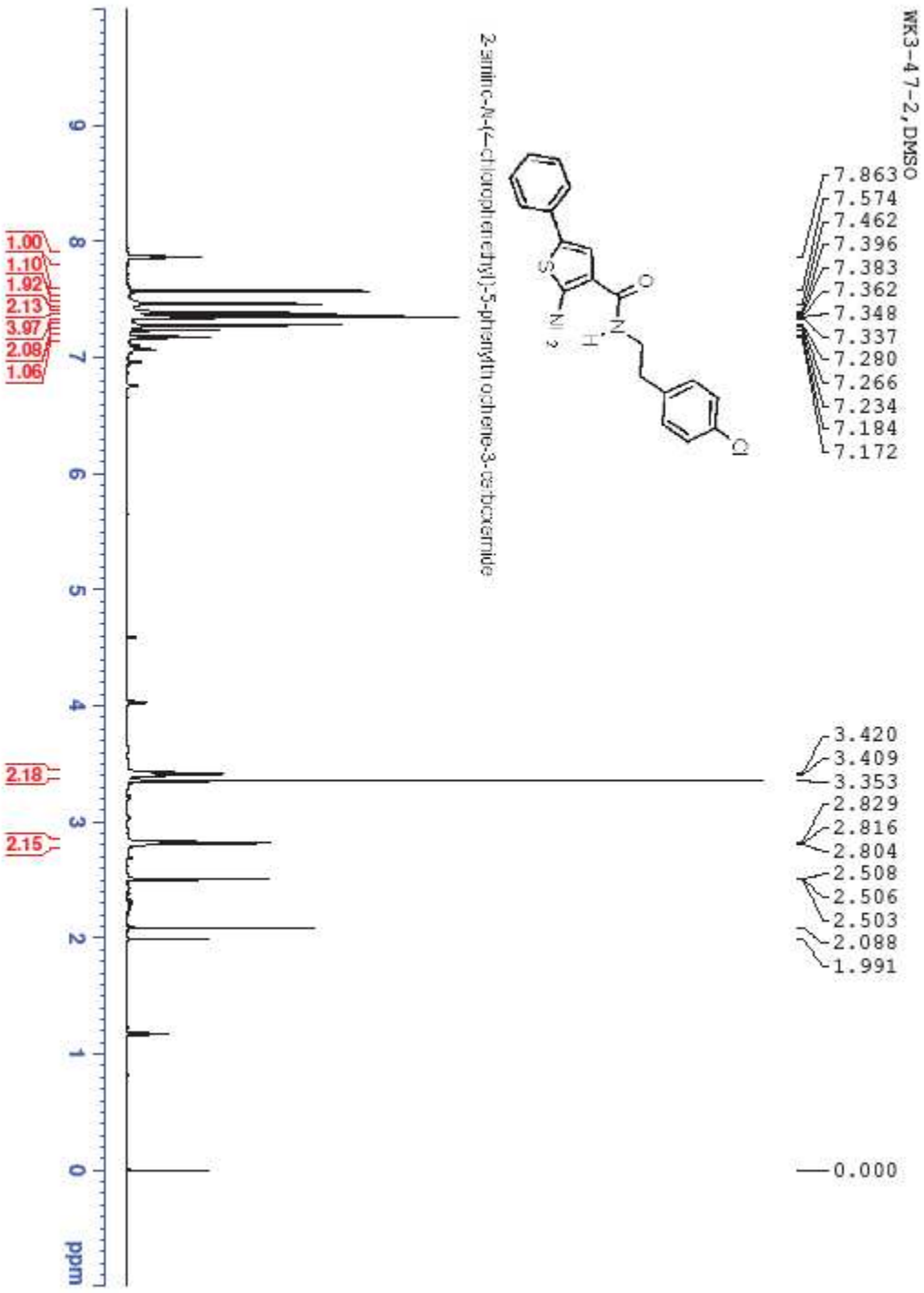

WKDA009
N-allyl-2-amino-5-phenylthiophene-3-carboxamide
165.54
161.50
136.42
134.71
129.43
126.30
124.02
121.87
121.18
115.50
108.40
41.19
200
180
160
140
120
100
80
60
40
20
0
ppm

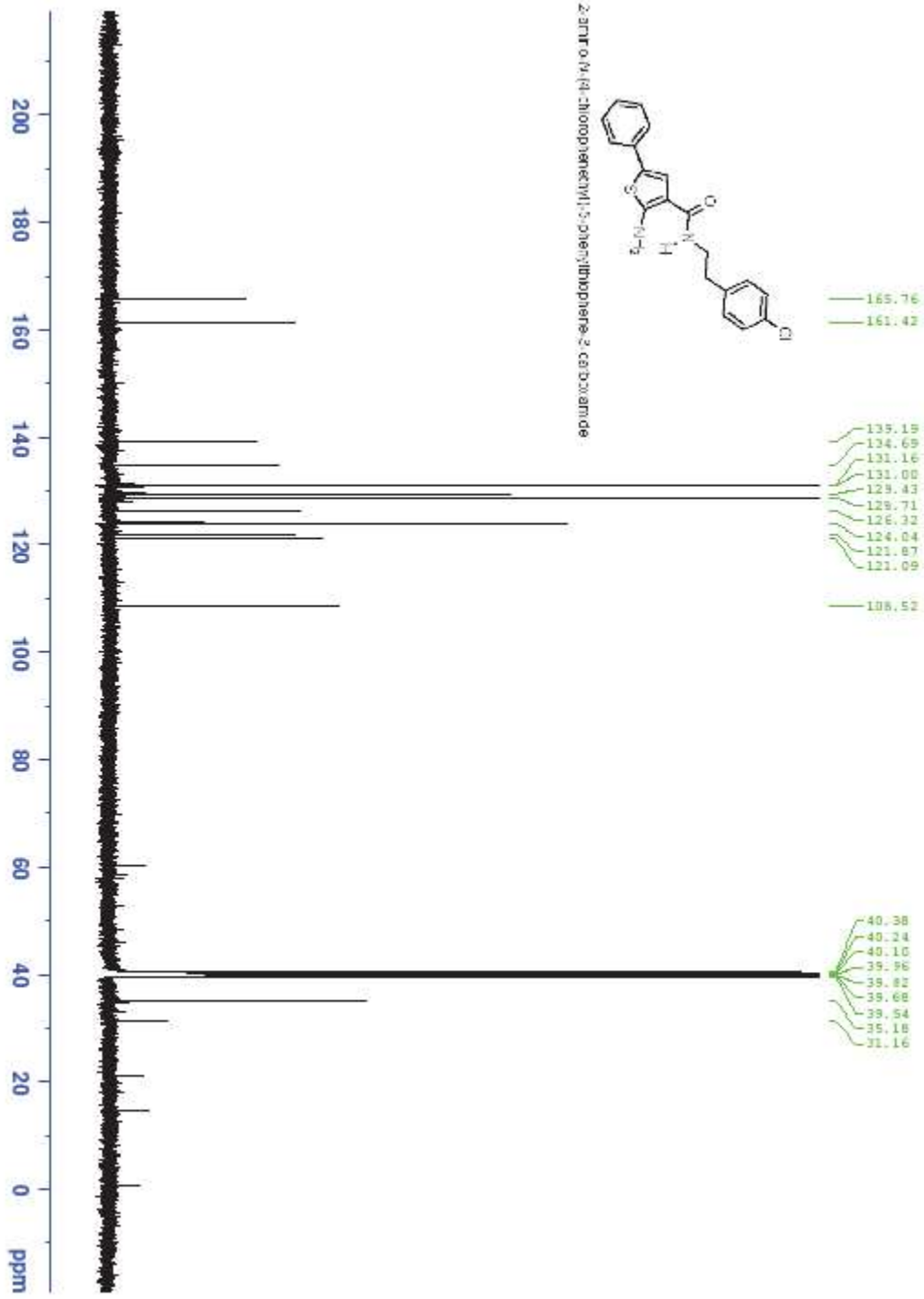
**C2,7**


WKDA014
7.468
7.455
7.340
7.327
7.314
7.245
7.242
7.232
7.230
7.218
7.216
7.191
7.180
7.168
7.155
7.144
6.973
6.960
6.948
6.823
6.817
6.811
6.805
6.799
6.793
6.718
6.695
3.690
3.682
3.673
3.200
3.192
3.184
3.176
3.167
3.158
(2-amino-5-phenylthiophen-3-yl)(4-phenylpiperazin-1-yl)methanone
2.00
1.95
1.98
0.88
0.98
2.09
1.13
1.85
4.04
4.09
ppm

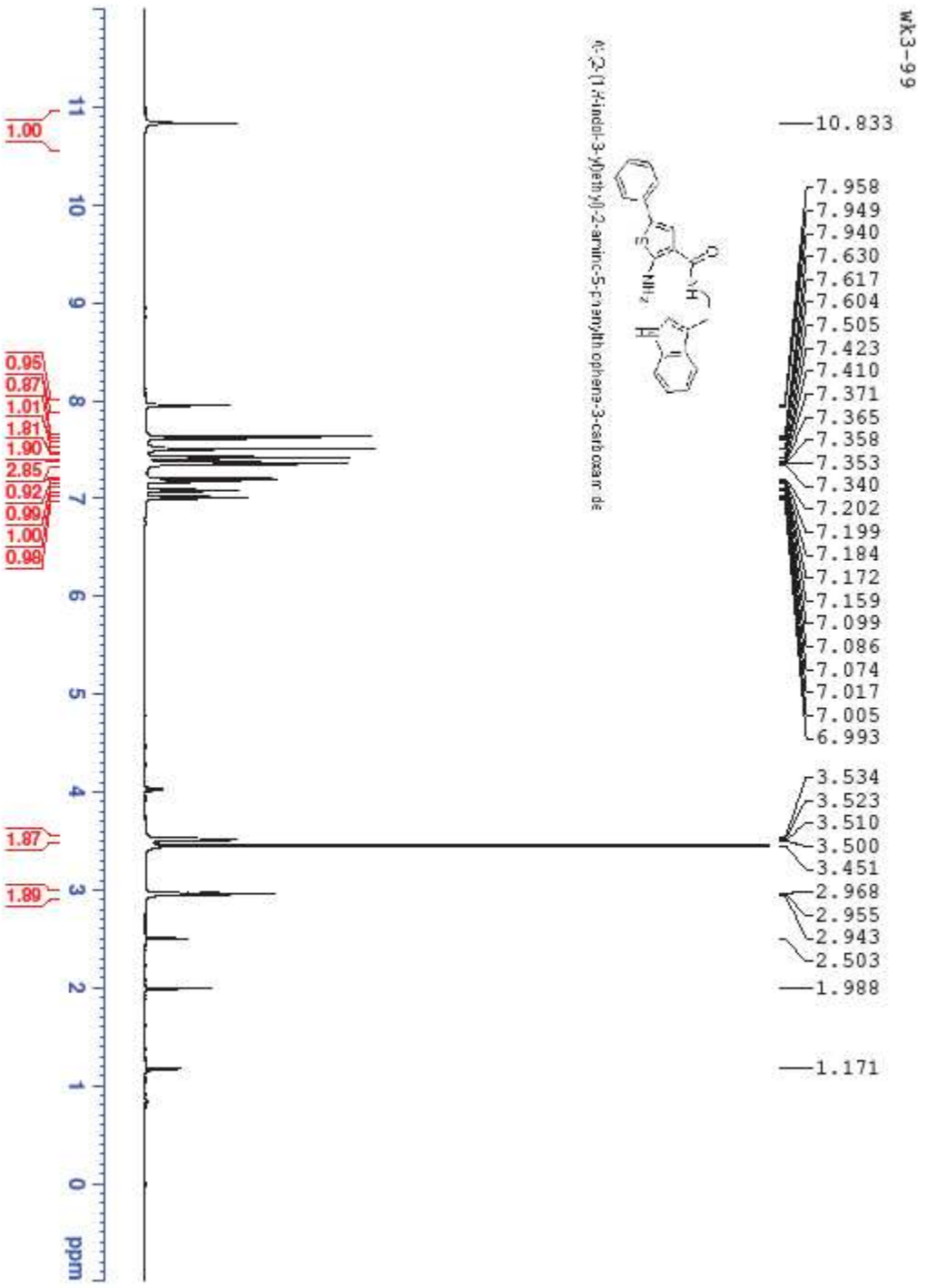

WKDA014
(2-amino-5-phenylthiophen-3-yl)(4-phenylpiperazin-1-yl)methanone
166.35
162.01
158.76
151.34
151.08
134.50
129.47
129.45
129.36
126.39
124.35
122.96
122.65
119.68
116.34
116.27
109.89
49.04
200
180
160
140
120
100
80
60
40
20
0
ppm

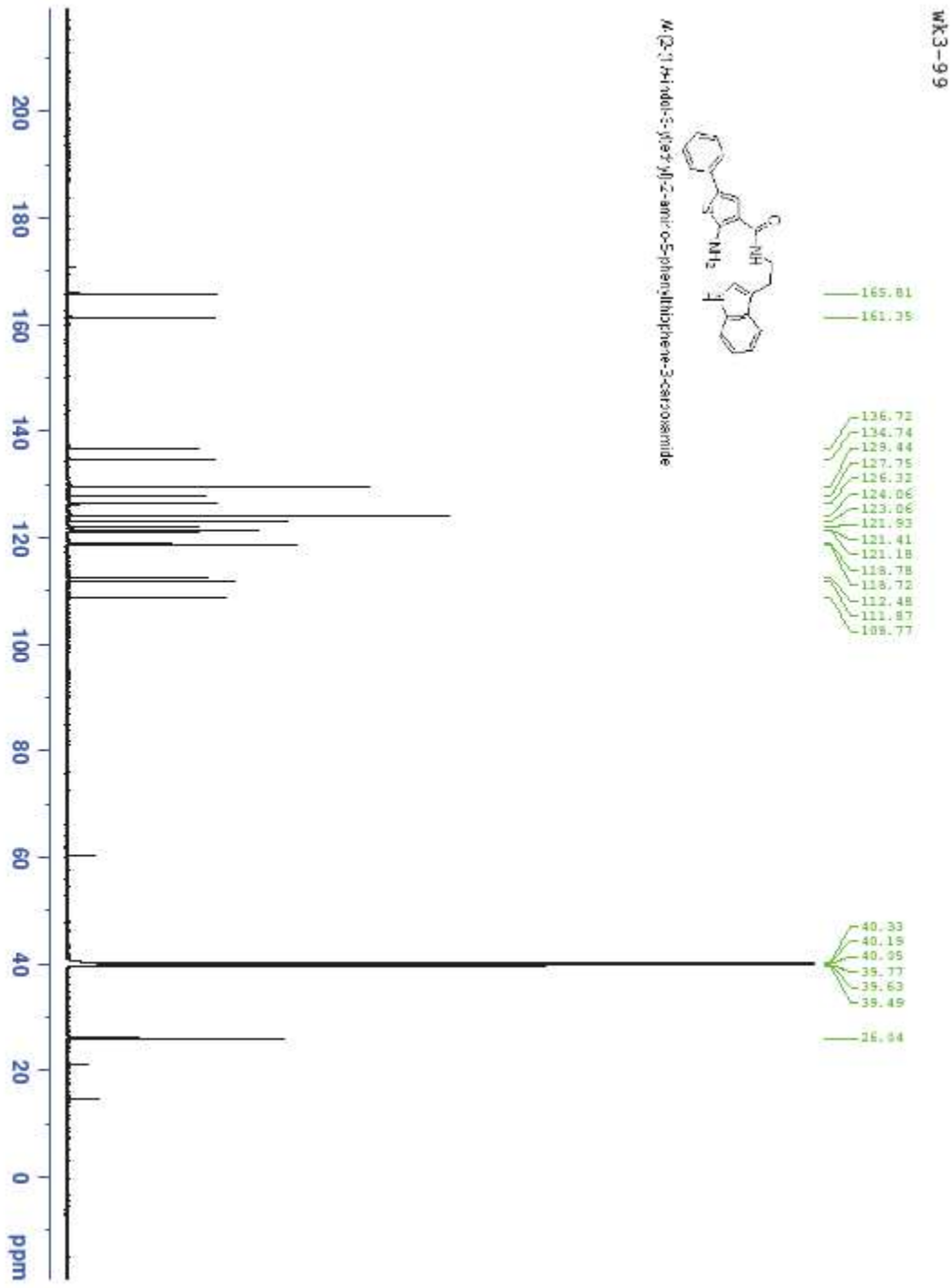
**C2,9**


WK3-47-2, DMSO
7.863
7.574
7.462
7.396
7.383
7.362
7.348
7.337
7.280
7.266
7.234
7.184
7.172
3.420
3.409
3.353
2.829
2.816
2.804
2.508
2.506
2.503
2.088
1.991
0.000
2-amino-N-(4-chlorophenethyl)-5-phenylthiophene-3-carboxamide
1.00
1.10
1.92
2.13
3.97
2.08
1.06
2.18
2.15
ppm

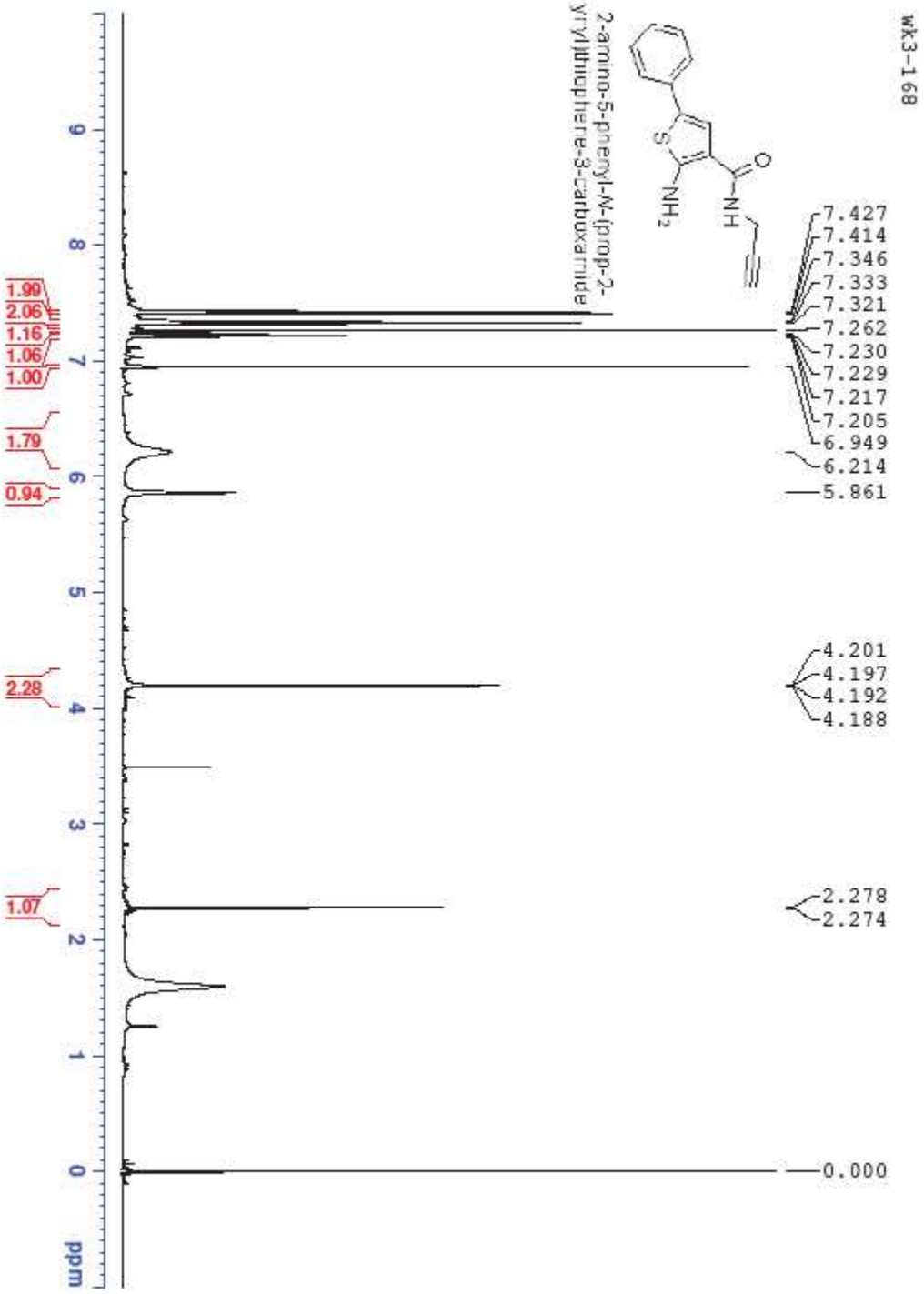

WK3-47-2, DMSO
2-amino-N-(4-chlorophenethyl)-5-phenylthiophene-3-carboxamide
165.76
161.42
135.19
134.69
131.16
131.00
129.43
128.71
126.32
124.04
121.87
121.09
108.52
40.38
40.24
40.10
39.96
39.82
39.68
39.54
35.18
31.16
200
180
160
140
120
100
80
60
40
20
0
ppm

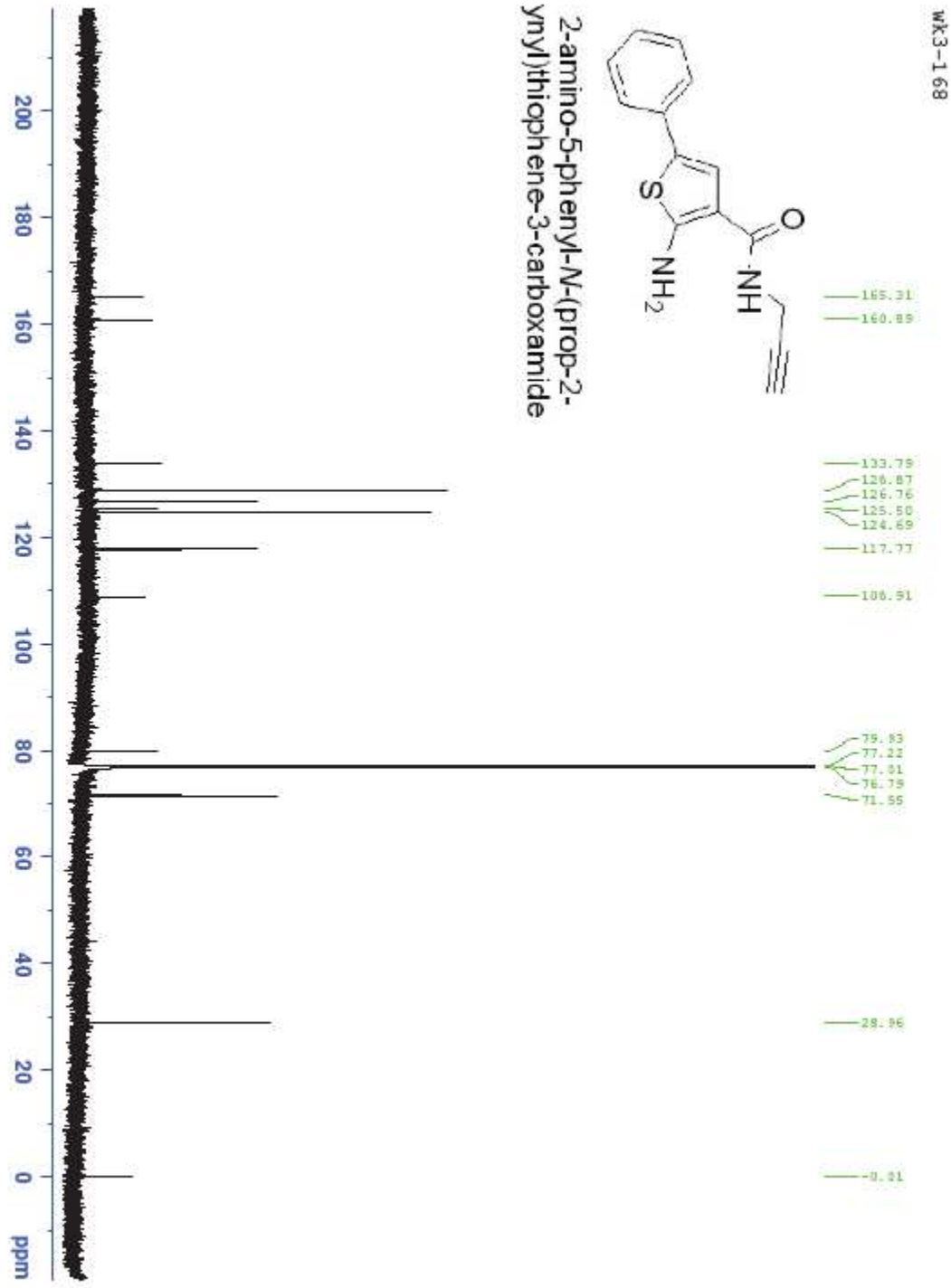
**C2,10**


wk3-99
10.833
7.958
7.949
7.940
7.630
7.617
7.604
7.505
7.423
7.410
7.371
7.365
7.358
7.353
7.340
7.202
7.199
7.184
7.172
7.159
7.099
7.086
7.074
7.017
7.005
6.993
3.534
3.523
3.510
3.500
3.451
2.968
2.955
2.943
2.503
1.988
1.171
1.00
0.95
0.87
1.01
1.81
1.90
2.85
0.92
0.99
1.00
0.98
1.87
1.89
ppm

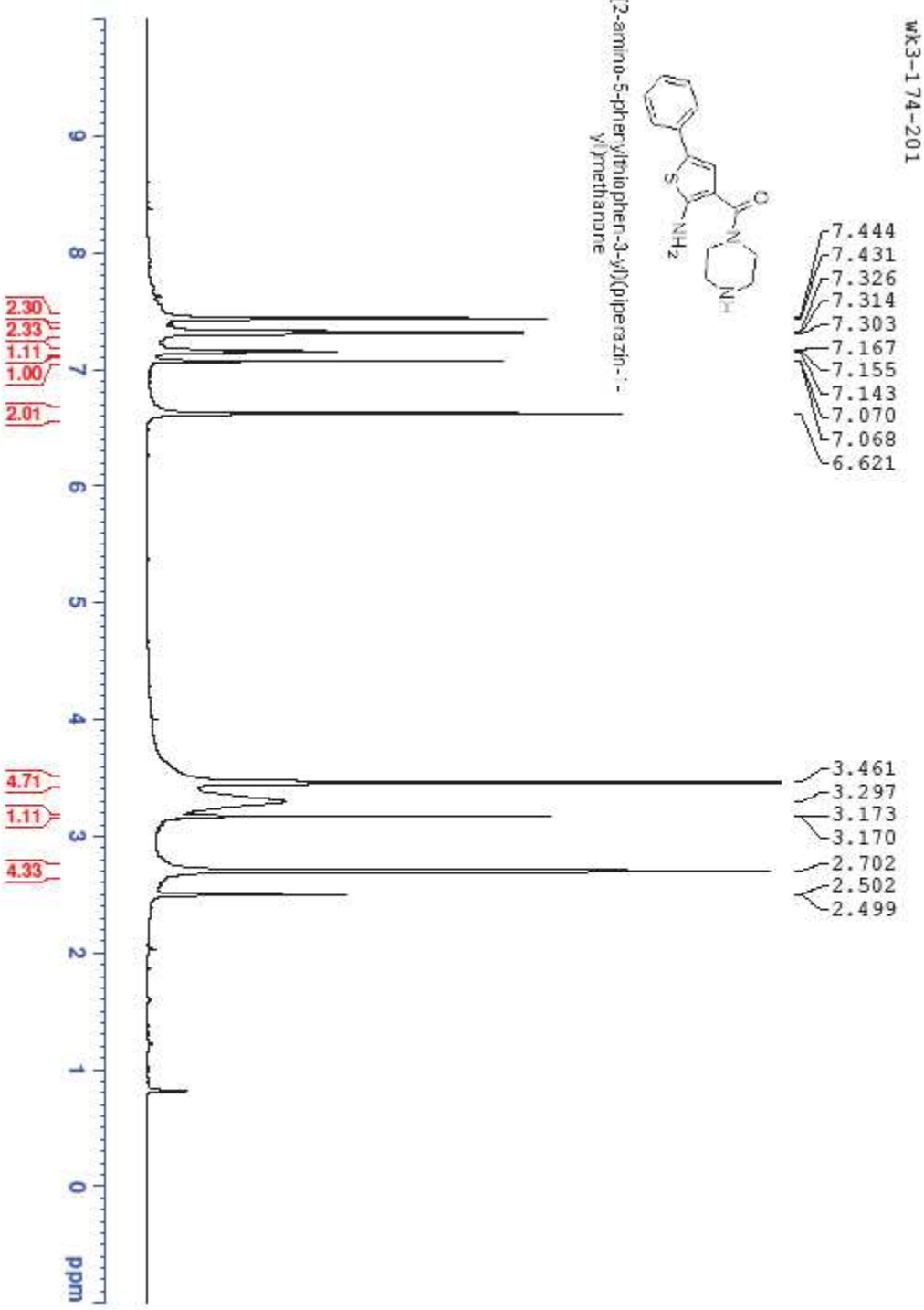

WK3-99
165.81
161.35
136.72
134.74
129.44
127.75
126.32
124.06
123.06
121.93
121.41
121.18
118.78
118.72
112.48
111.87
109.77
40.33
40.19
40.05
39.77
39.63
39.49
26.64
200
180
160
140
120
100
80
60
40
20
0
ppm

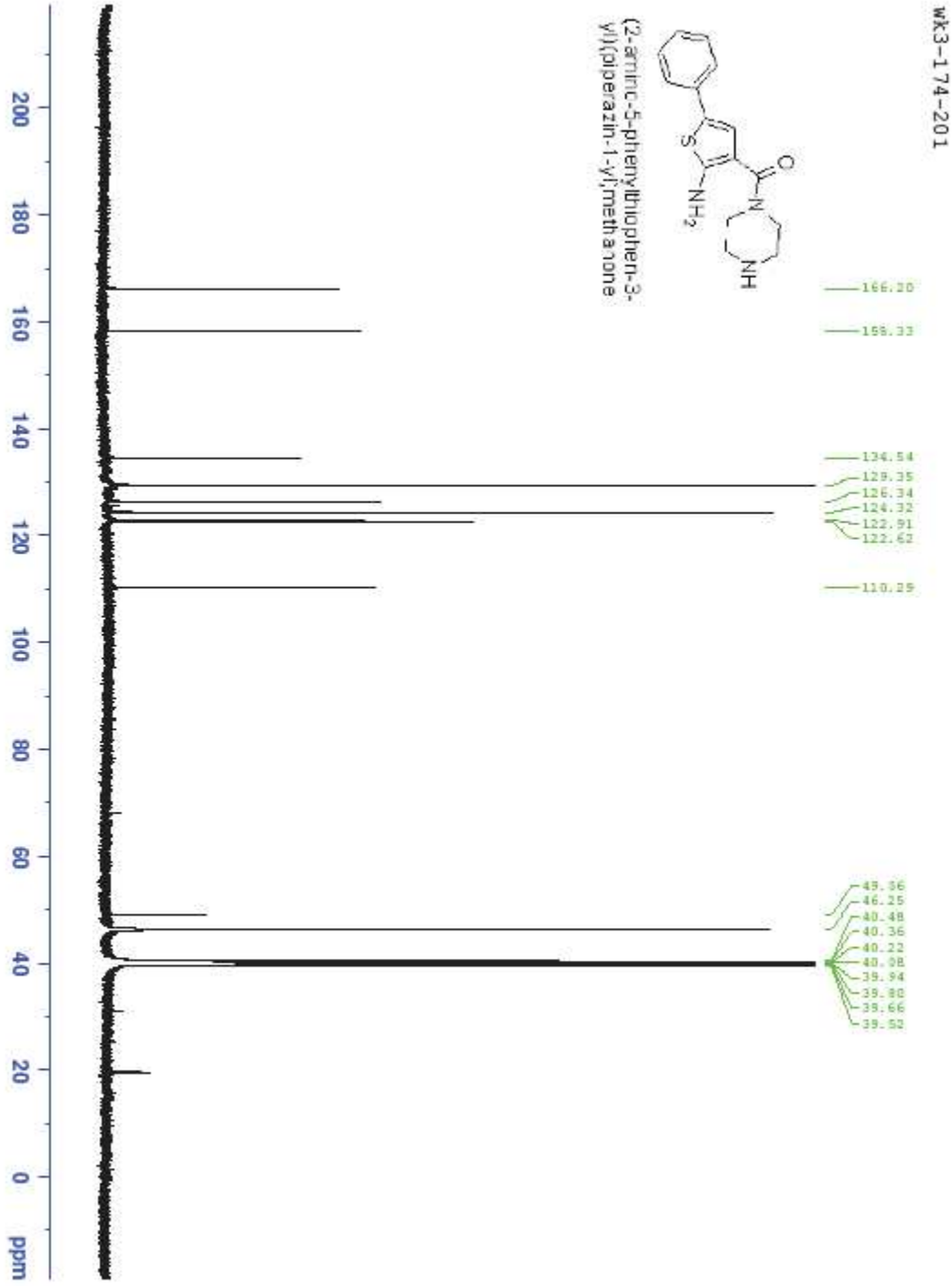
**C2,21**


wk3-168
2-amino-5-phenyl-N-(prop-2-
ynyl)thiophene-3-carboxamide
NH2
S
O
NH
7.427
7.414
7.346
7.333
7.321
7.262
7.230
7.229
7.217
7.205
6.949
6.214
5.861
4.201
4.197
4.192
4.188
2.278
2.274
0.000
1.99
2.06
1.16
1.06
1.00
1.79
0.94
2.28
1.07
ppm

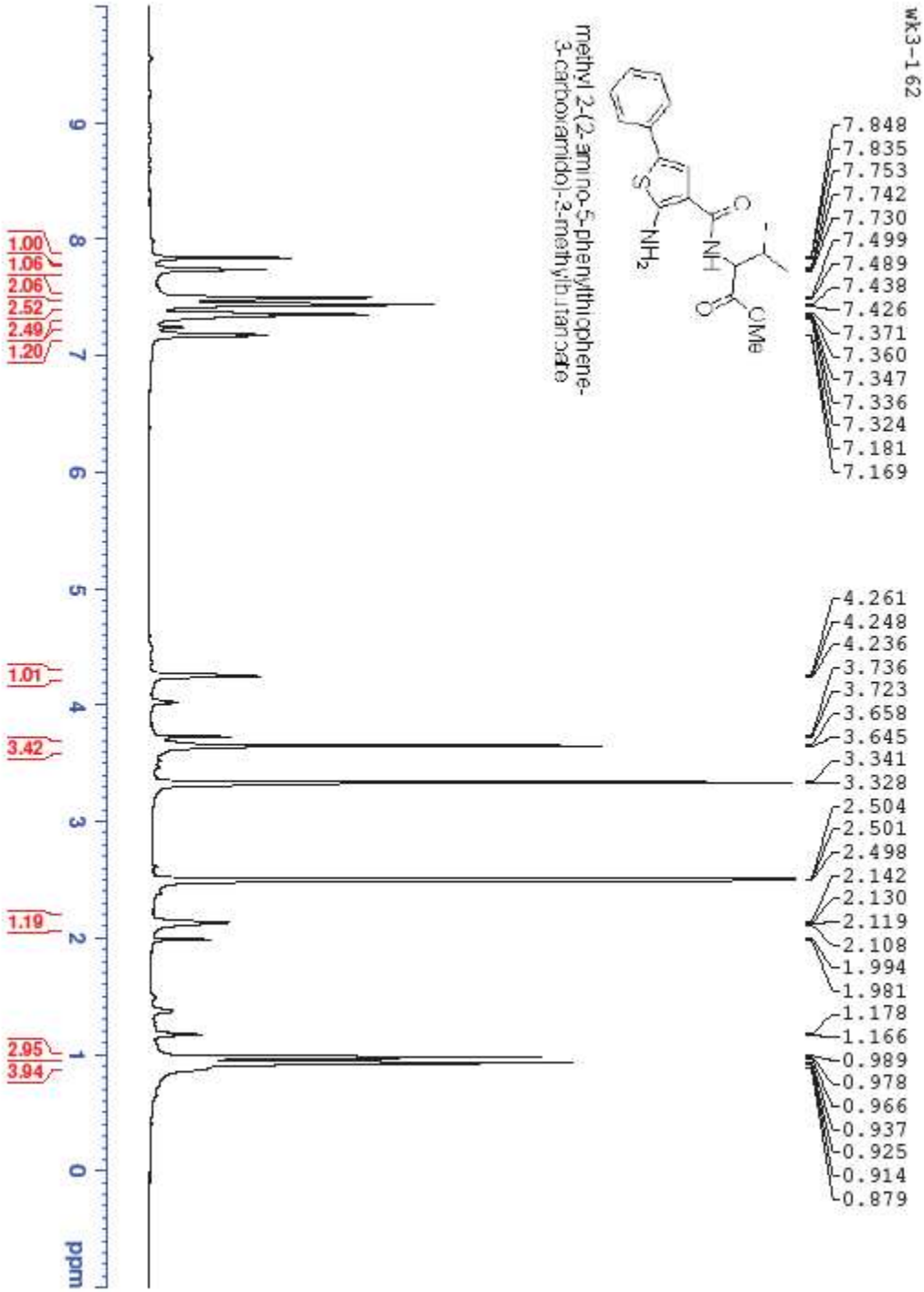

wk3-168
2-amino-5-phenyl-N-(prop-2-ynyl)thiophene-3-carboxamide
S
NH2
O
NH
165.31
160.89
133.79
128.87
126.76
125.50
124.69
117.77
106.91
79.83
77.22
77.01
76.79
71.55
28.96
-0.01
200
180
160
140
120
100
80
60
40
20
0
ppm

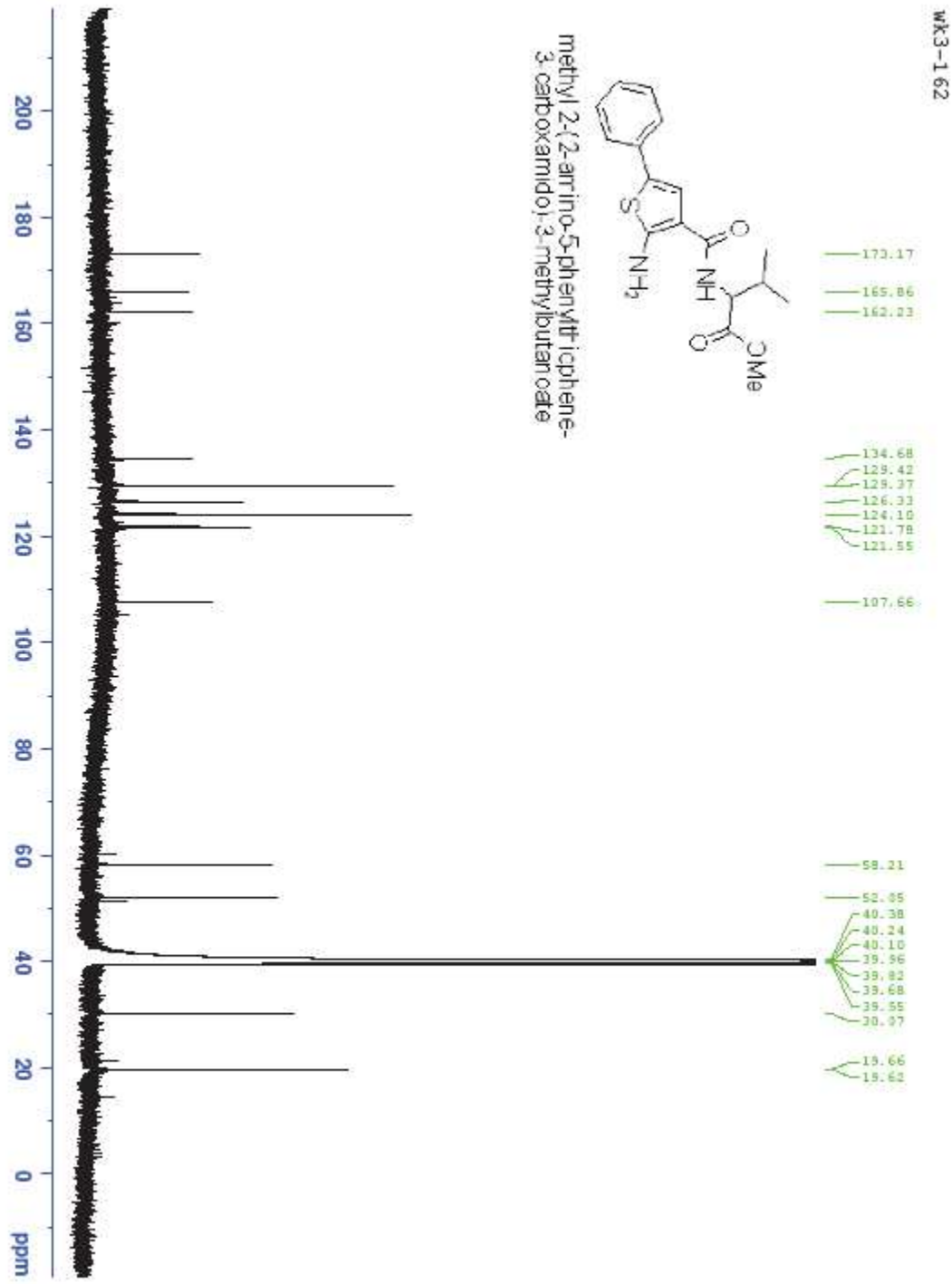
**C2,22**


wk3-174-201
(2-amino-5-phenylthiophen-3-yl)(piperazin-1-yl)methanone
7.444
7.431
7.326
7.314
7.303
7.167
7.155
7.143
7.070
7.068
6.621
3.461
3.297
3.173
3.170
2.702
2.502
2.499
2.30
2.33
1.11
1.00
2.01
4.71
1.11
4.33
ppm

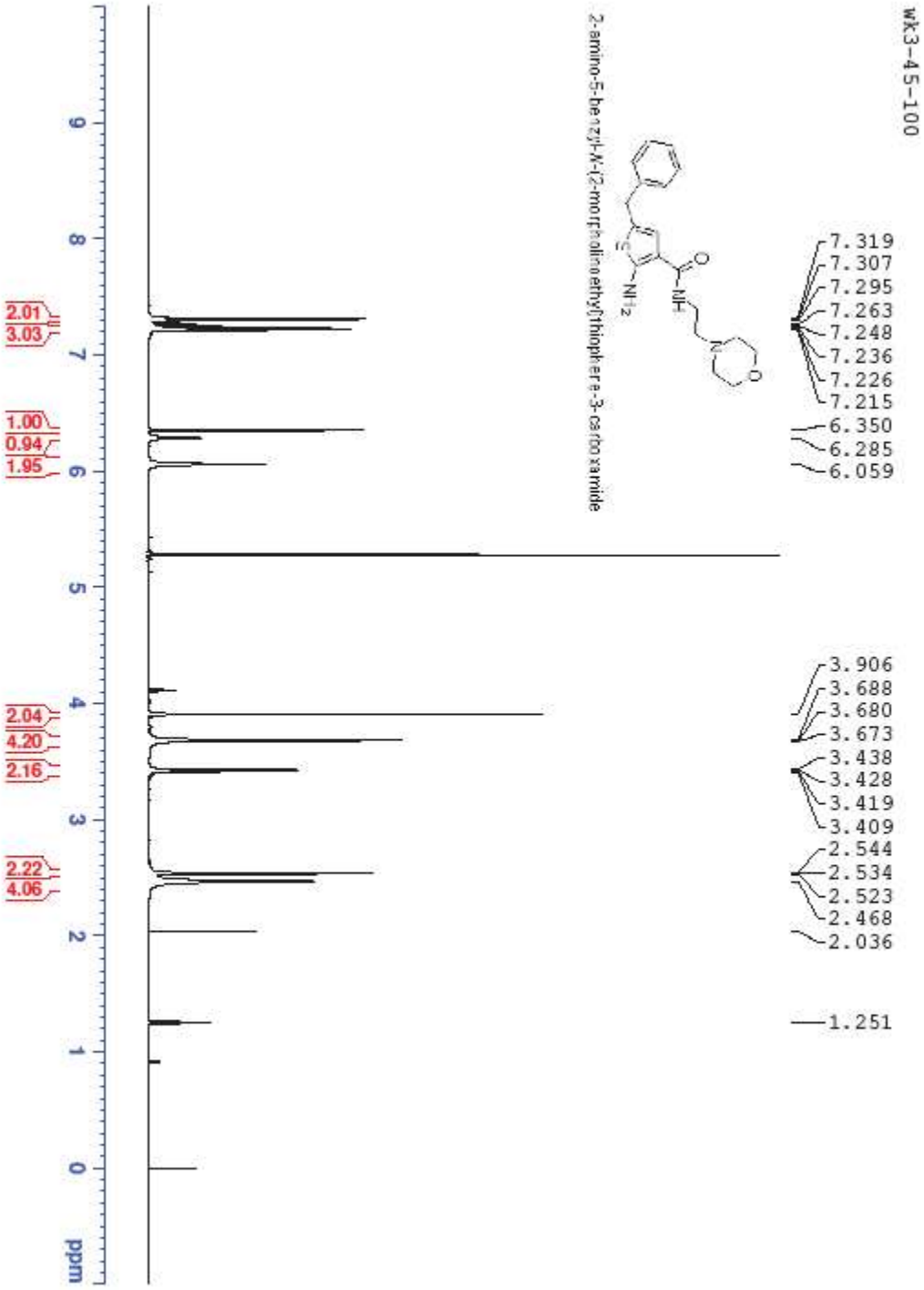

wk3-174-201
(2-amino-5-phenylthiophen-3-yl)(piperazin-1-yl)methanone
NH2
S
O
N
NH
166.20
158.33
134.54
129.35
126.34
124.32
122.91
122.62
110.29
49.56
46.25
40.48
40.36
40.22
40.08
39.94
39.80
39.66
39.52
200
180
160
140
120
100
80
60
40
20
0
ppm

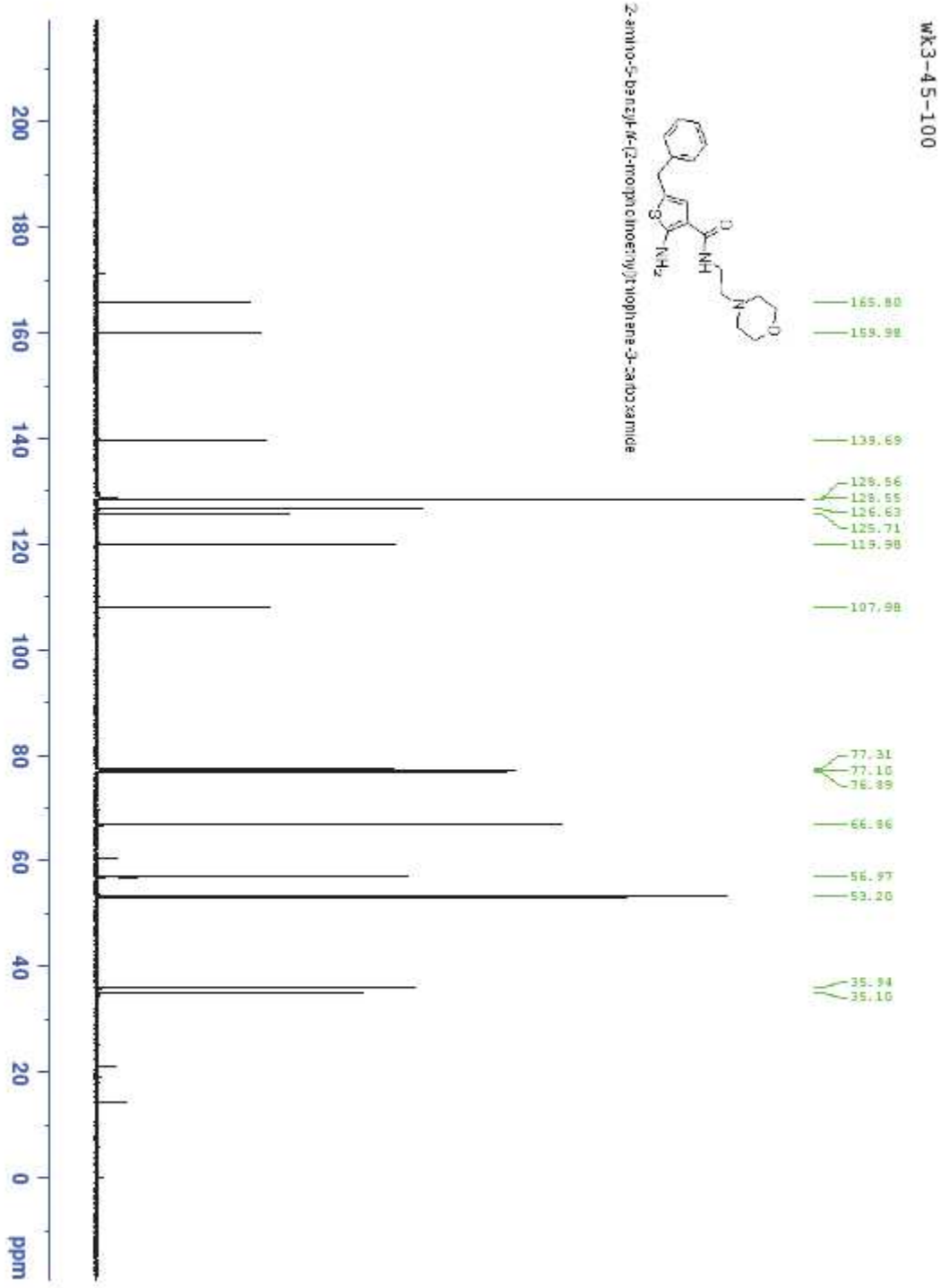
**C2,23**


wk3-162
methyl 2-(2-amino-5-phenylthiophene-3-carboxamido)-3-methylbutanoate
7.848
7.835
7.753
7.742
7.730
7.499
7.489
7.438
7.426
7.371
7.360
7.347
7.336
7.324
7.181
7.169
4.261
4.248
4.236
3.736
3.723
3.658
3.645
3.341
3.328
2.504
2.501
2.498
2.142
2.130
2.119
2.108
1.994
1.981
1.178
1.166
0.989
0.978
0.966
0.937
0.925
0.914
0.879
1.00
1.06
2.06
2.52
2.49
1.20
1.01
3.42
1.19
2.95
3.94
ppm

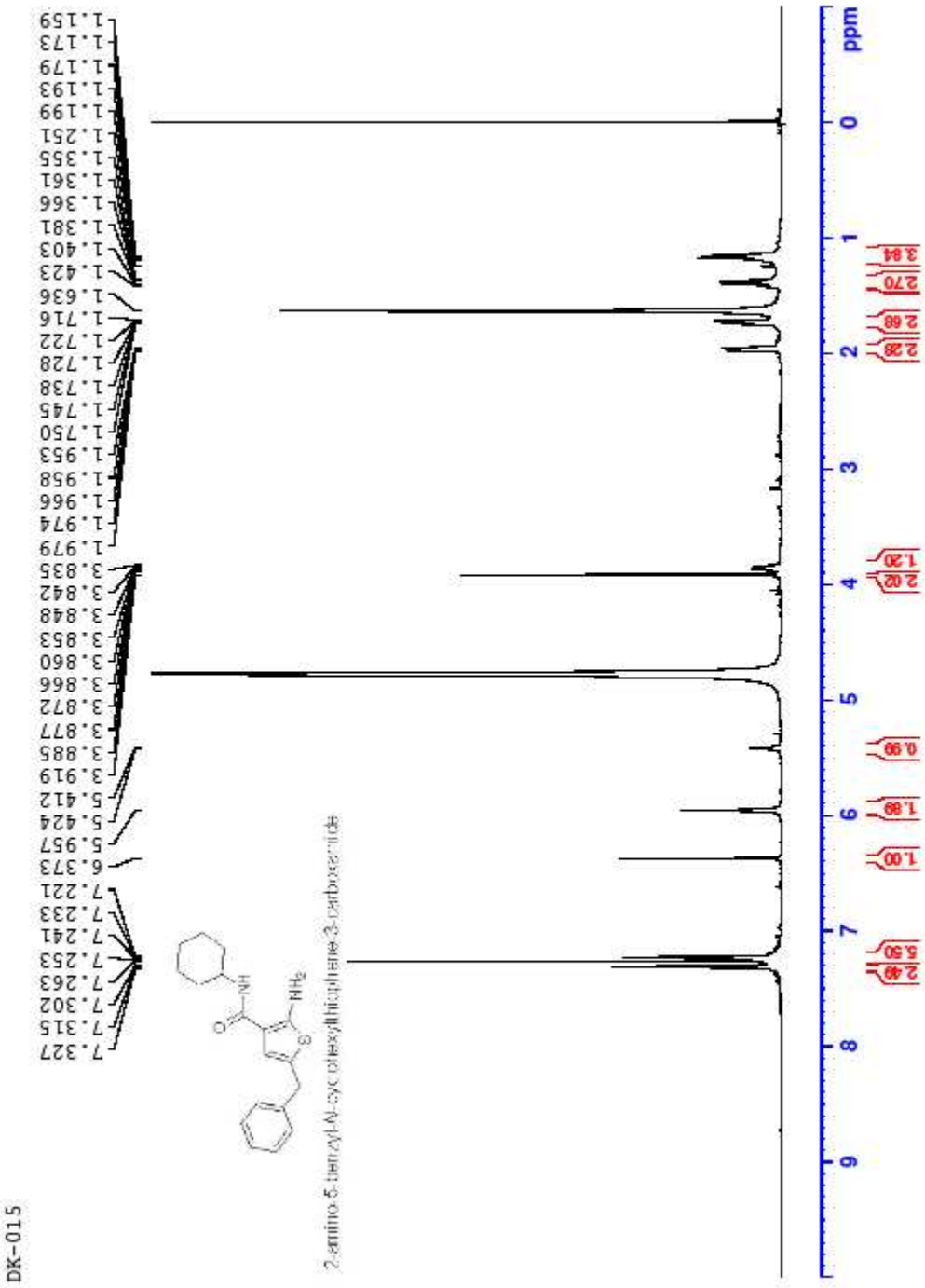

wk3-162
methyl 2-(2-amino-5-phenylthiophene-3-carboxamido)-3-methylbutanoate
NH2
S
NH
O
OMe
O
173.17
165.86
162.23
134.68
129.42
129.37
126.33
124.10
121.78
121.55
107.66
58.21
52.05
40.38
40.24
40.10
39.96
39.82
39.68
39.55
30.07
19.66
19.62
200
180
160
140
120
100
80
60
40
20
0
ppm

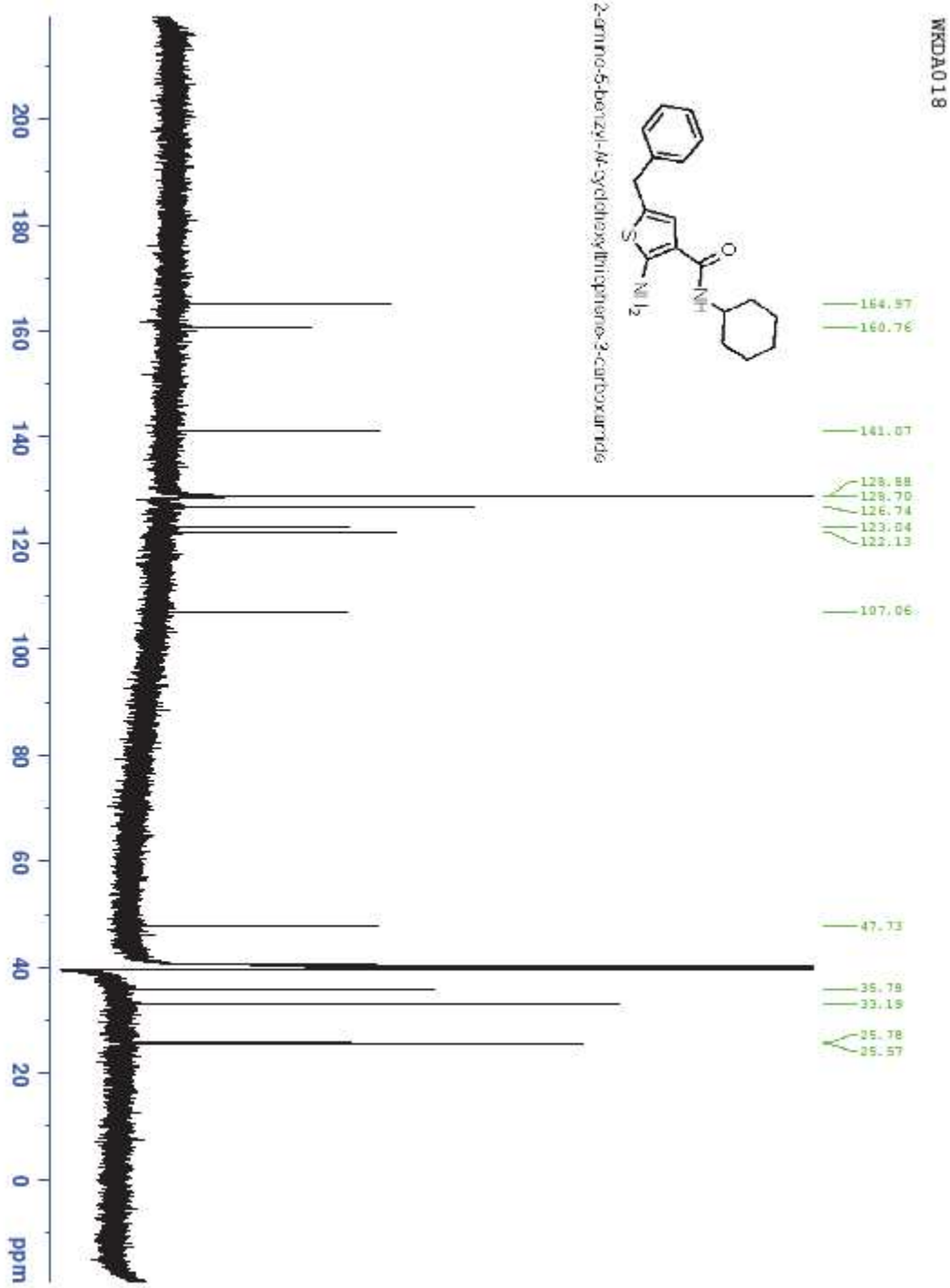
**C3,4**


wk3-45-100
2-amino-5-benzyl-N-(2-morpholinoethyl)thiophene-3-carboxamide
7.319
7.307
7.295
7.263
7.248
7.236
7.226
7.215
6.350
6.285
6.059
3.906
3.688
3.680
3.673
3.438
3.428
3.419
3.409
2.544
2.534
2.523
2.468
2.036
1.251
2.01
3.03
1.00
0.94
1.95
2.04
4.20
2.16
2.22
4.06
ppm

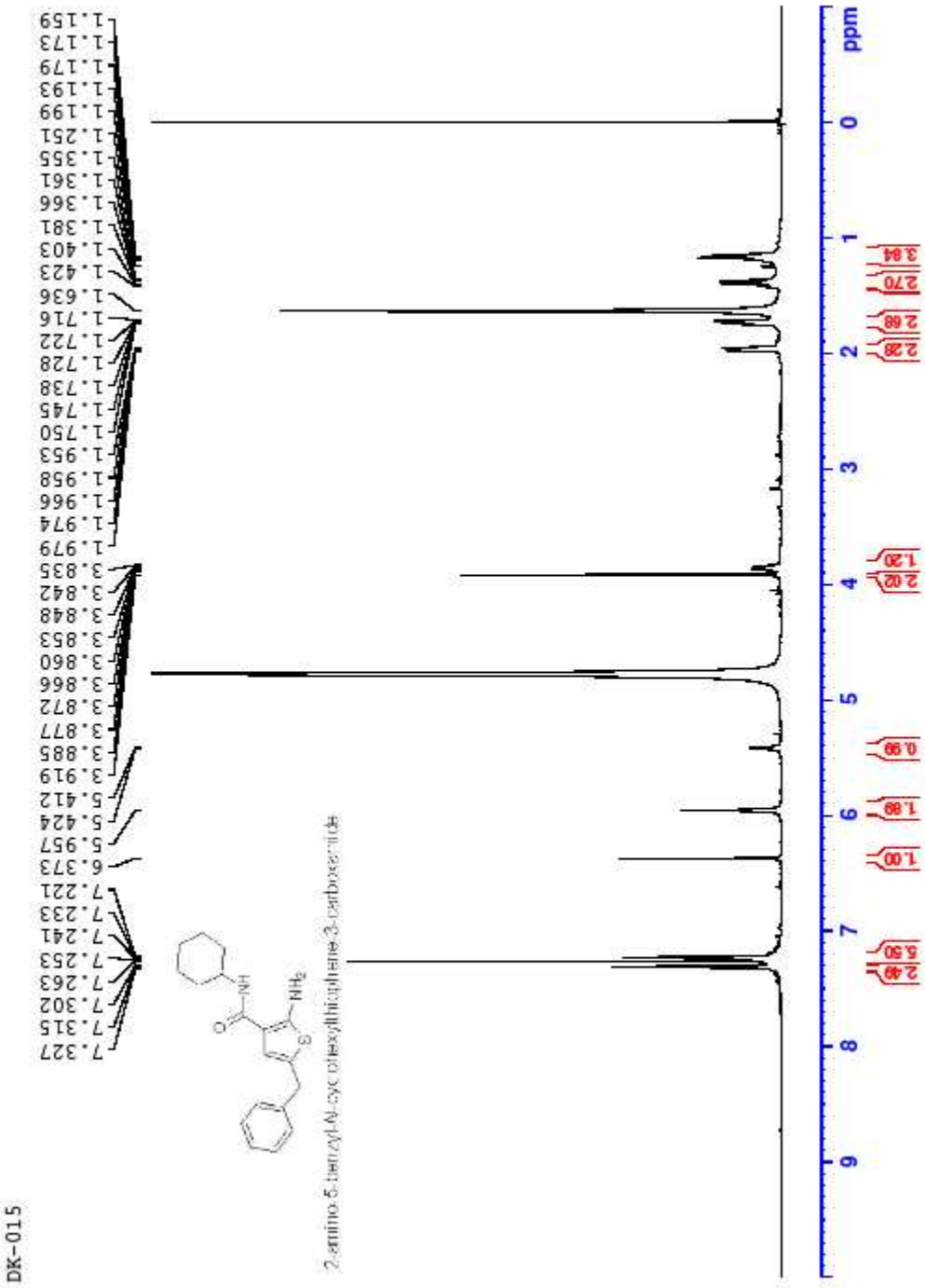

wk3-45-100
2-amino-5-benzyl-N-(2-morpholinoethyl)thiophene-3-carboxamide
165.80
159.98
139.69
128.56
128.55
126.63
125.71
119.98
107.98
77.31
77.10
76.89
66.86
56.97
53.20
35.94
35.10
200
180
160
140
120
100
80
60
40
20
0
ppm

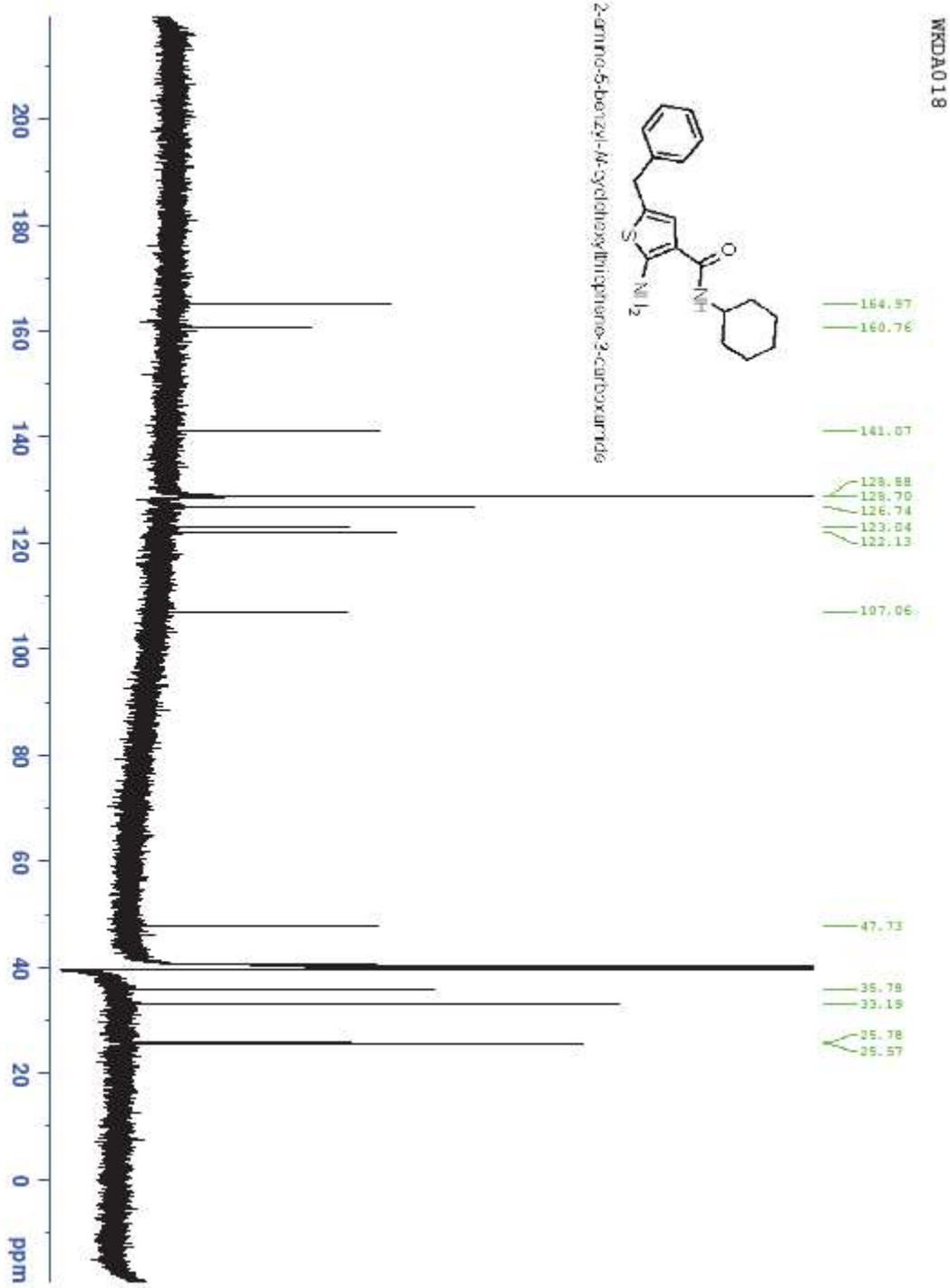
**C3,12**


DK-015
2-amino-5-benzyl-N-cyclohexylthiophene-3-carboxamide
ppm
2.49
5.50
1.00
1.89
0.99
2.02
1.20
2.28
2.68
2.70
3.84

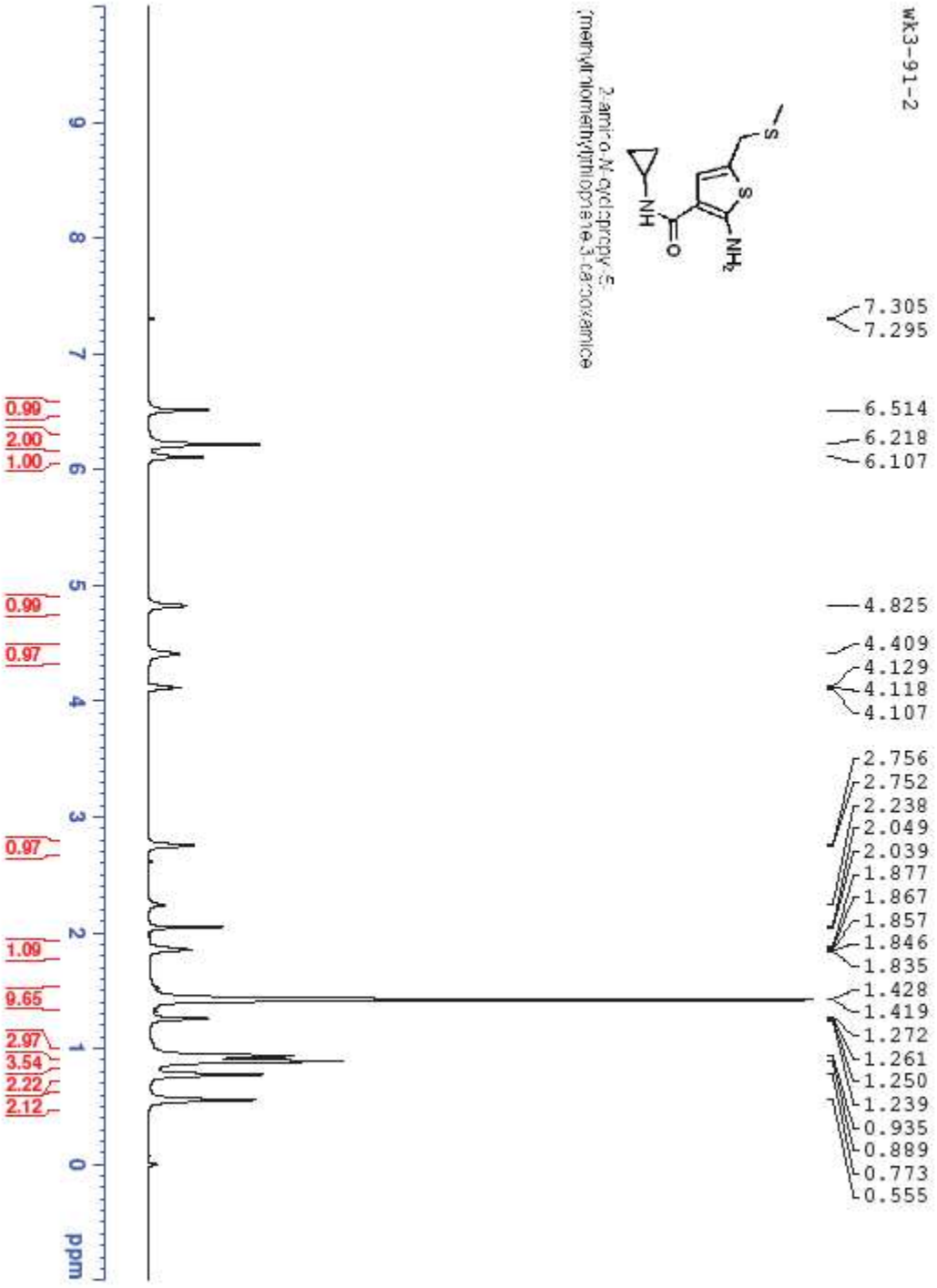

WKDA018
2-amino-5-benzyl-N-cyclohexylthiophene-3-carboxamide
NH2
S
O
NH
164.97
160.76
141.07
128.88
128.70
126.74
123.04
122.13
107.06
47.73
35.78
33.19
25.78
25.57
200
180
160
140
120
100
80
60
40
20
0
ppm

**C3,13**

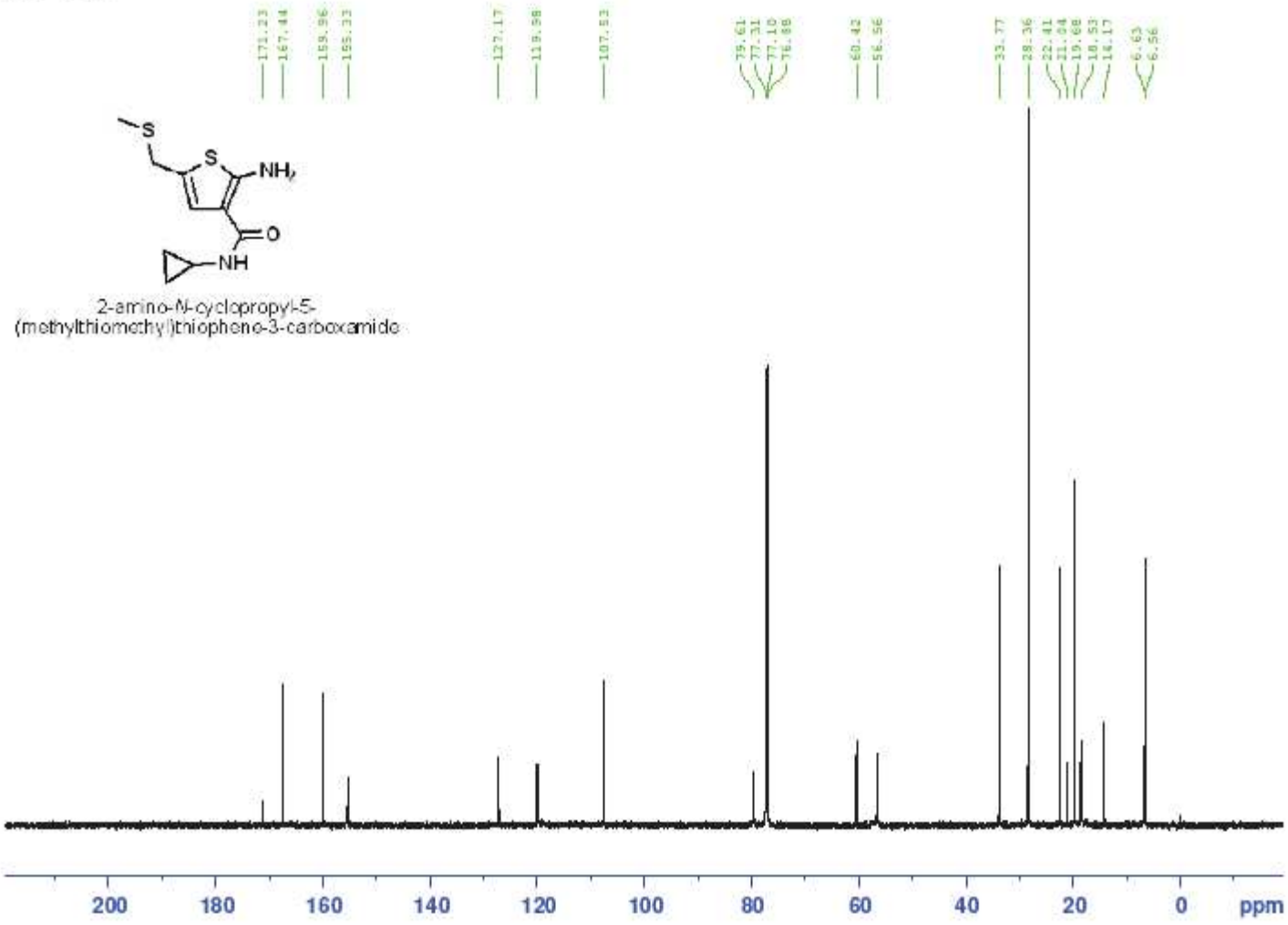

DK-015
2-amino-5-benzyl-N-cyclohexylthiophene-3-carboxamide
ppm
2.49
5.50
1.00
1.89
0.99
2.02
1.20
2.28
2.68
2.70
3.84


WKDA018
2-amino-5-benzyl-N-cyclohexylthiophene-3-carboxamide
NH2
S
O
NH
164.97
160.76
141.07
128.88
128.70
126.74
123.04
122.13
107.06
47.73
35.78
33.19
25.78
25.57
200
180
160
140
120
100
80
60
40
20
0
ppm

**C4,1**

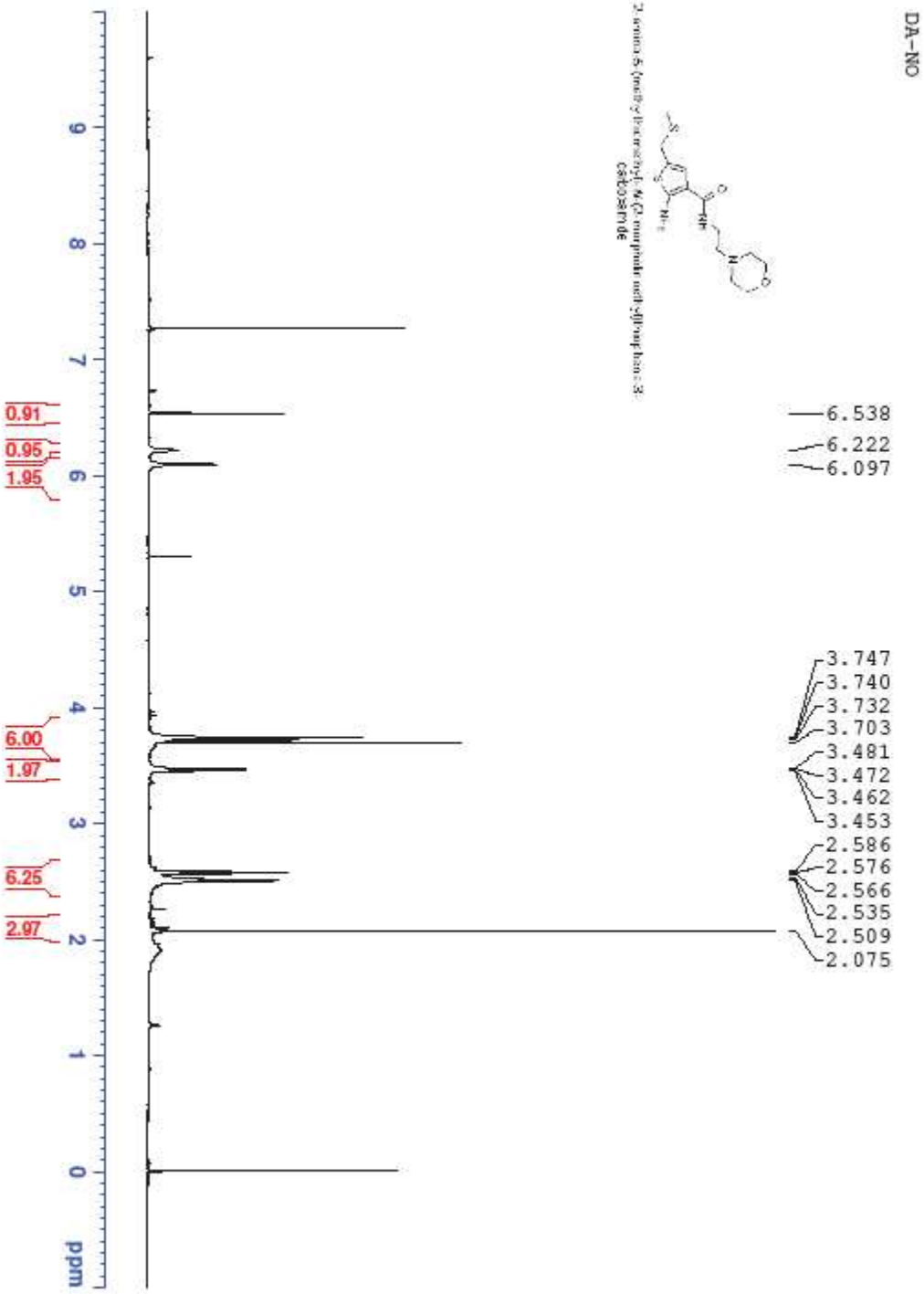

wk3-91-2
2-amino-N-cyclopropyl-5-(methylsulfanylmethyl)thiophene-3-carboxamide
7.305
7.295
6.514
6.218
6.107
4.825
4.409
4.129
4.118
4.107
2.756
2.752
2.238
2.049
2.039
1.877
1.867
1.857
1.846
1.835
1.428
1.419
1.272
1.261
1.250
1.239
0.935
0.889
0.773
0.555
0.99
2.00
1.00
0.99
0.97
0.97
1.09
9.65
2.97
3.54
2.22
2.12
ppm

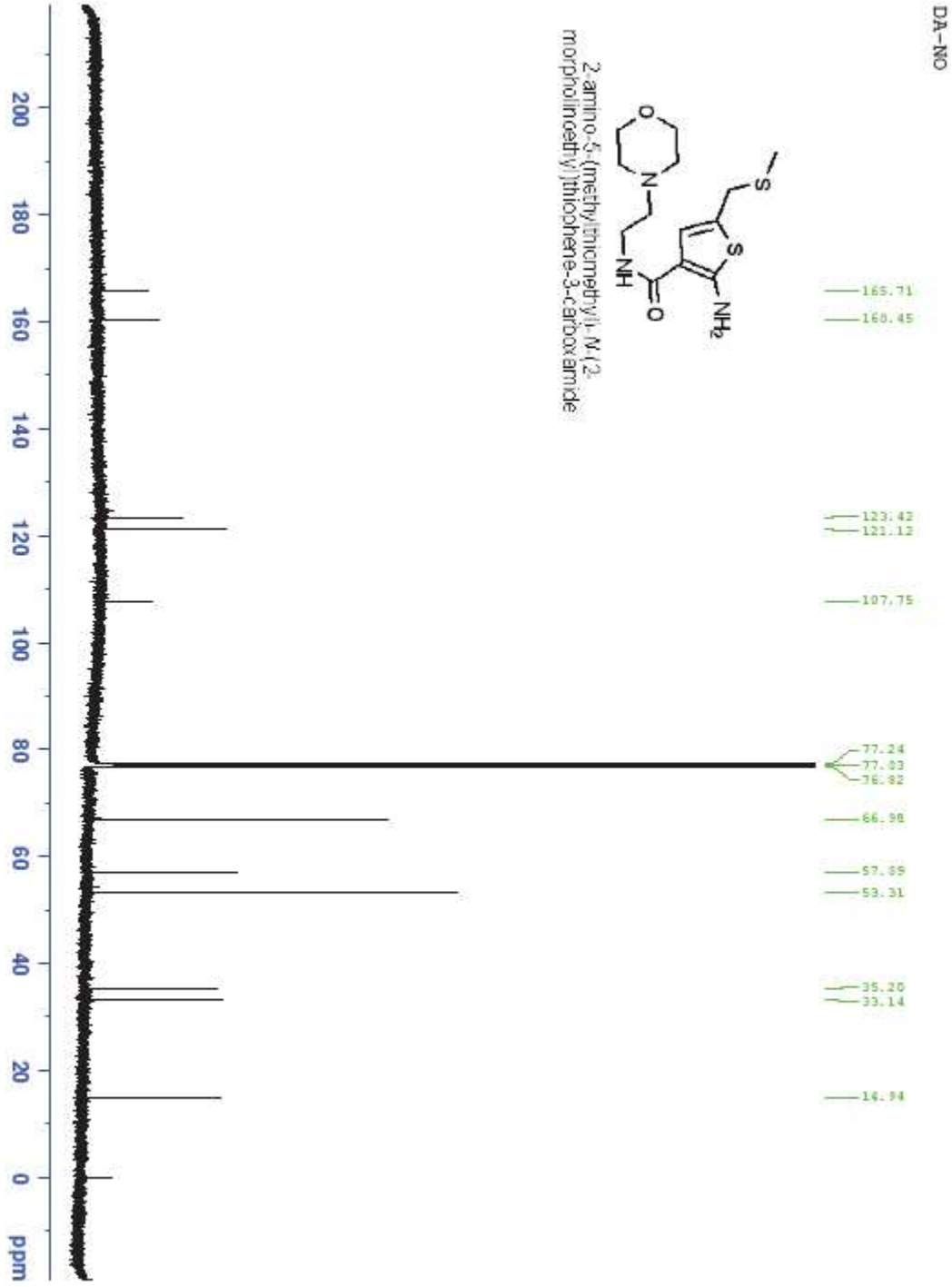
wk3-91-2



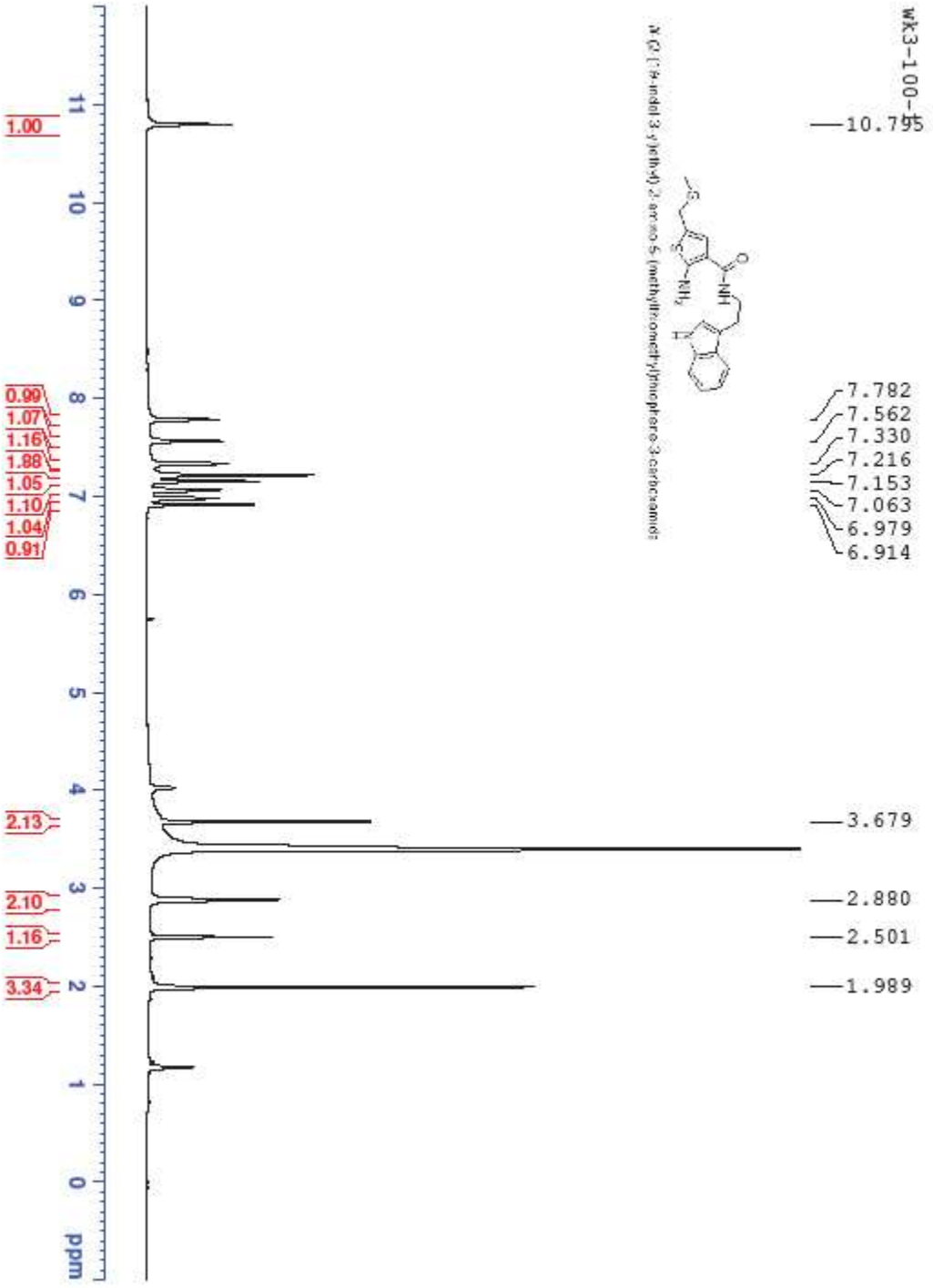

2-amino-N-cyclopropyl-5-(methylthiomethyl)thiophene-3-carboxamide

**C4,4**

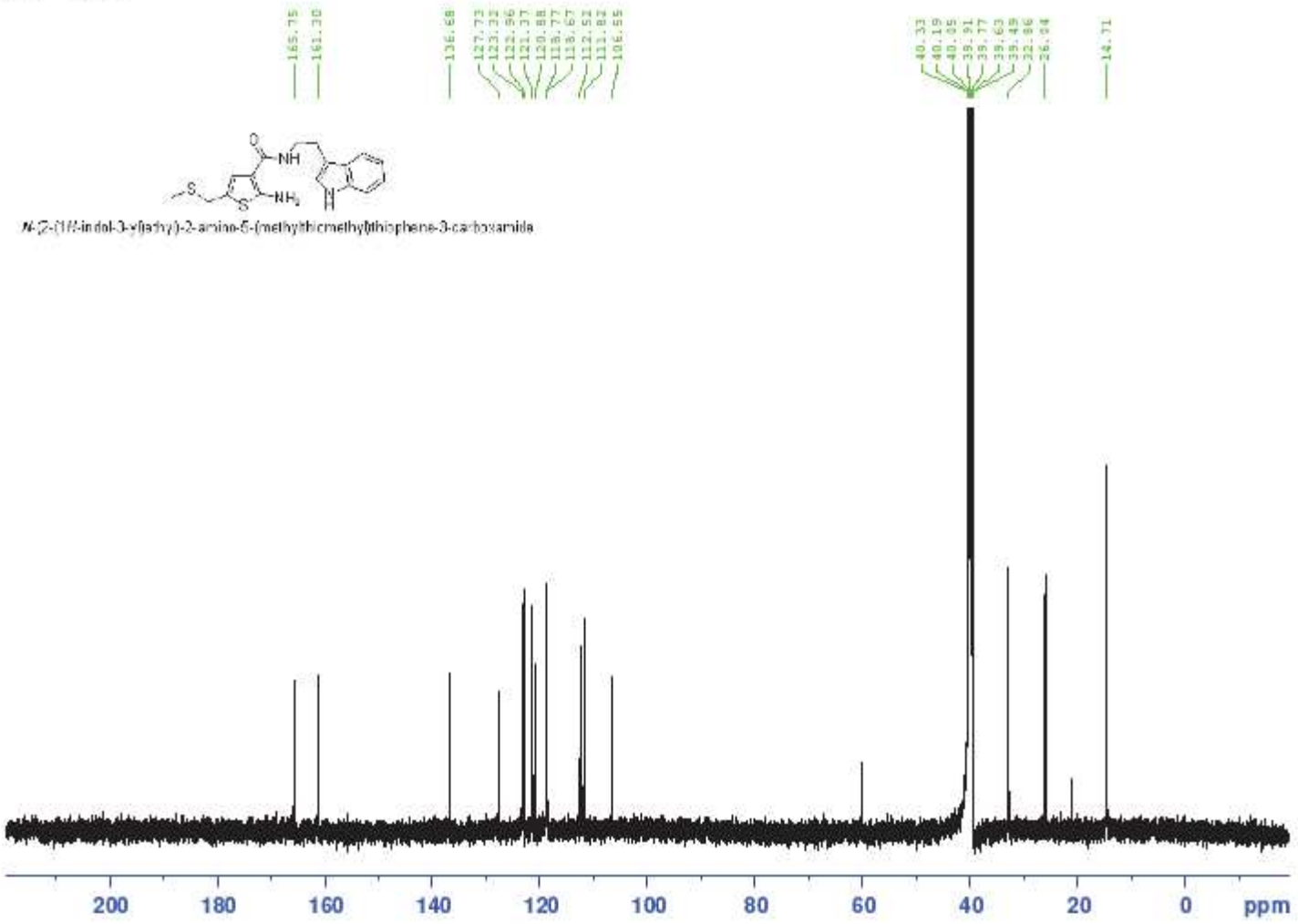

DA-NO
6.538
6.222
6.097
3.747
3.740
3.732
3.703
3.481
3.472
3.462
3.453
2.586
2.576
2.566
2.535
2.509
2.075
0.91
0.95
1.95
6.00
1.97
6.25
2.97
ppm


DA-NO
2-amino-5-(methylthiomethyl)-N-(2-morpholinoethyl)thiophene-3-carboxamide
165.71
160.45
123.42
121.12
107.75
77.24
77.03
76.82
66.98
57.69
53.31
35.20
33.14
16.94
200
180
160
140
120
100
80
60
40
20
0
ppm

**C4,10**

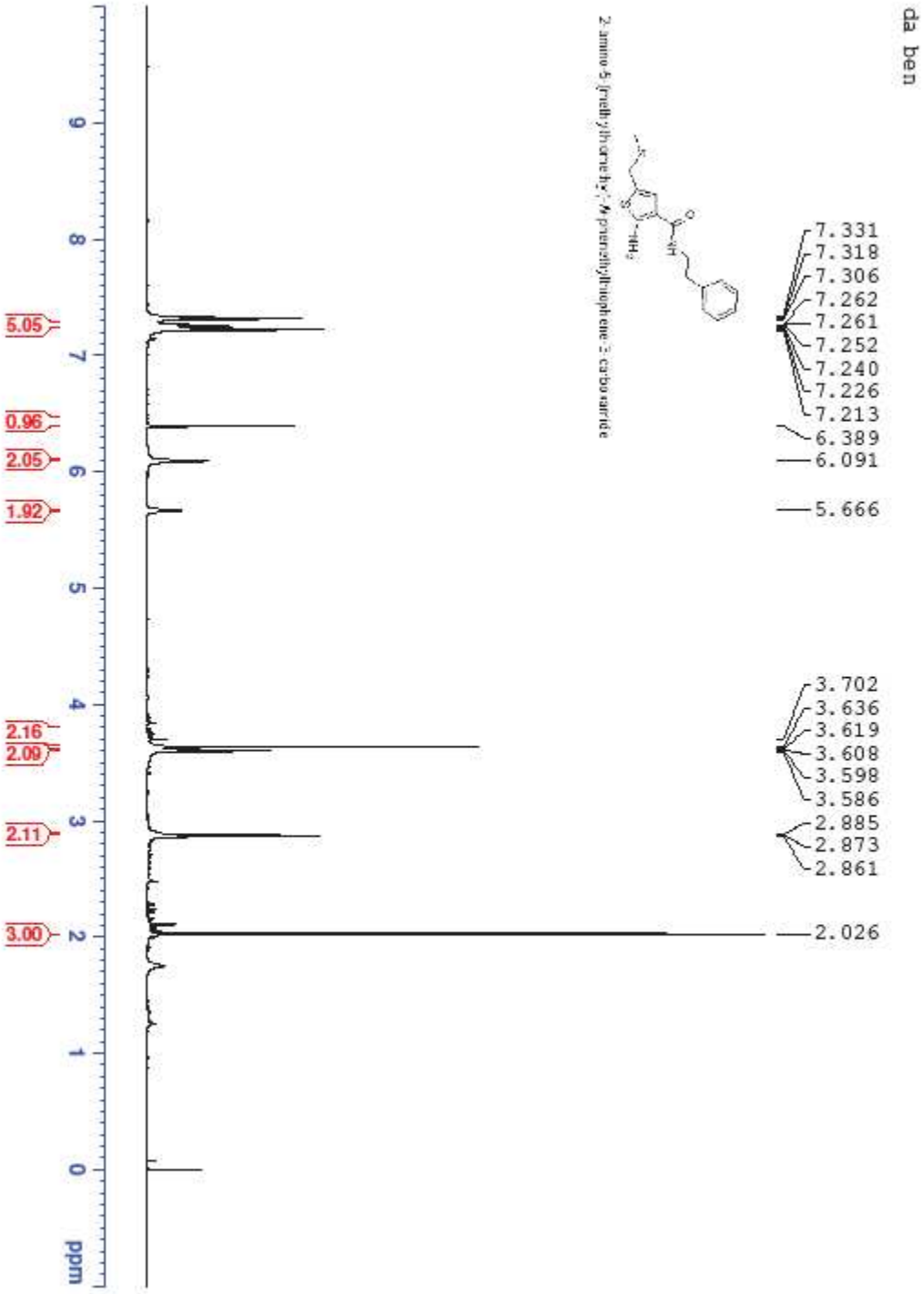

wk3-100-55
10.795
7.782
7.562
7.330
7.216
7.153
7.063
6.979
6.914
3.679
2.880
2.501
1.989
1.00
0.99
1.07
1.16
1.88
1.05
1.10
1.04
0.91
2.13
2.10
1.16
3.34
ppm

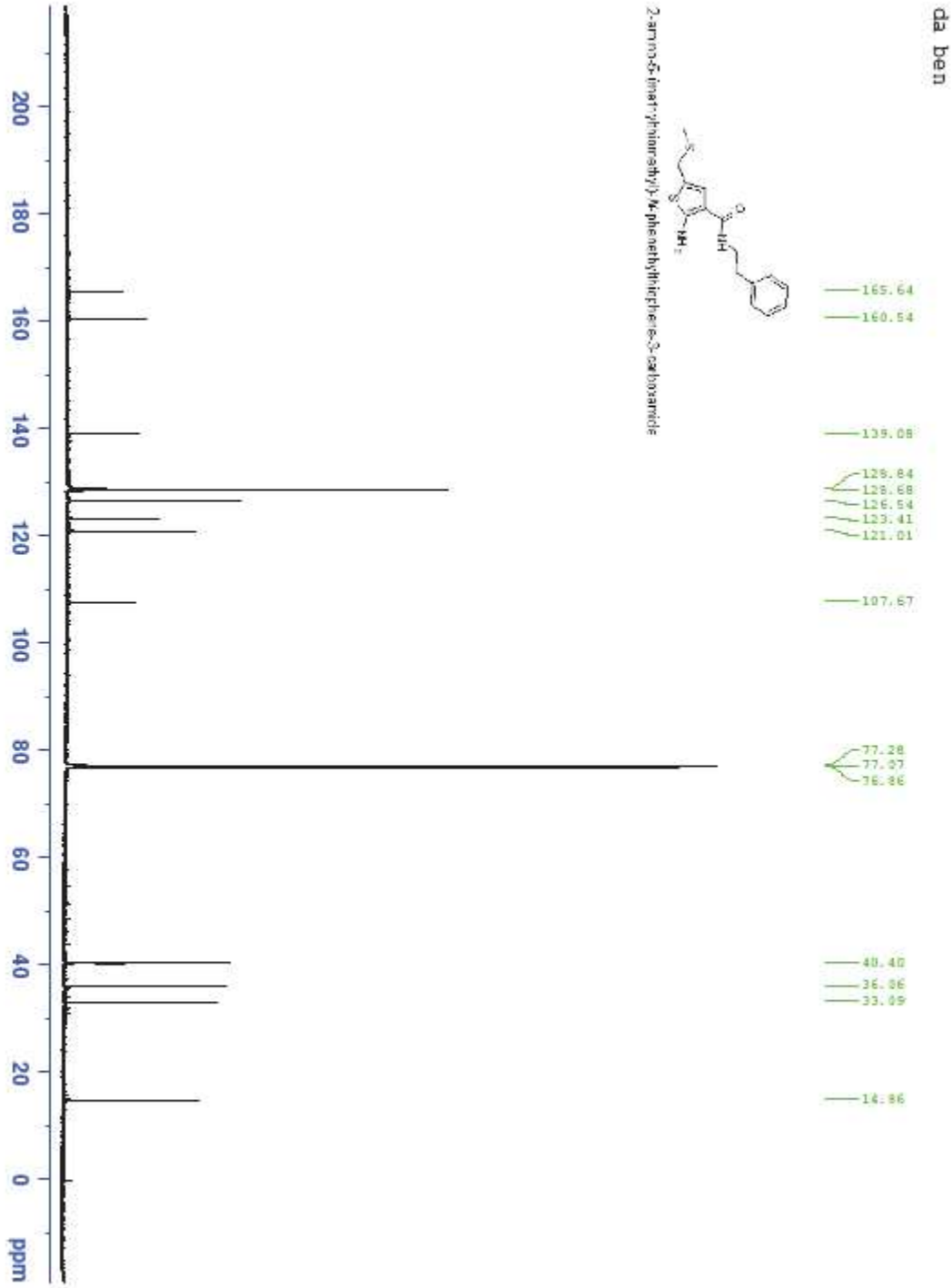
wk3-100-1



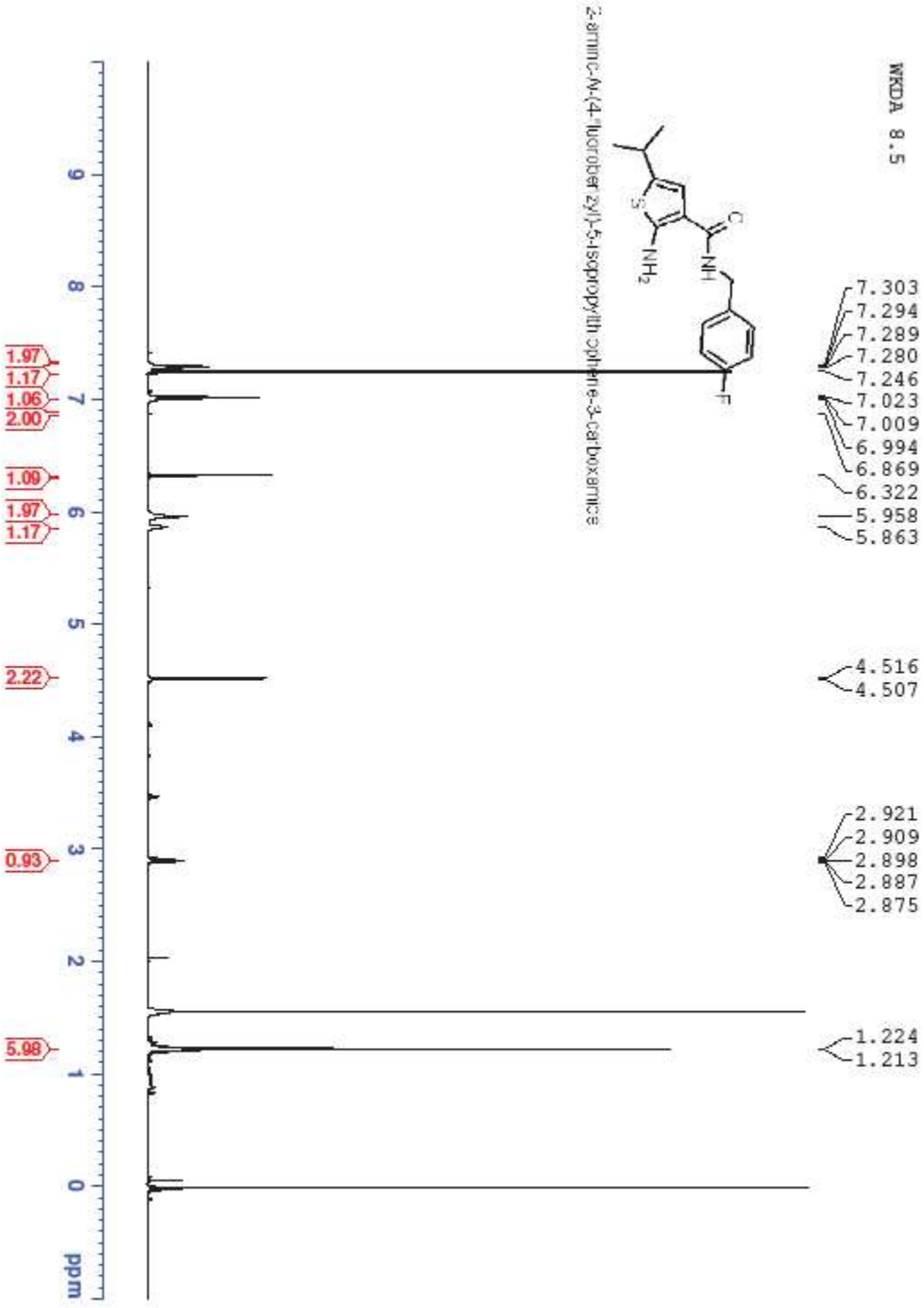

*N*-(2-(1*H*-indol-3-yl)ethyl)-2-amino-5-(methylthiomethyl)thiophene-3-carboxamide

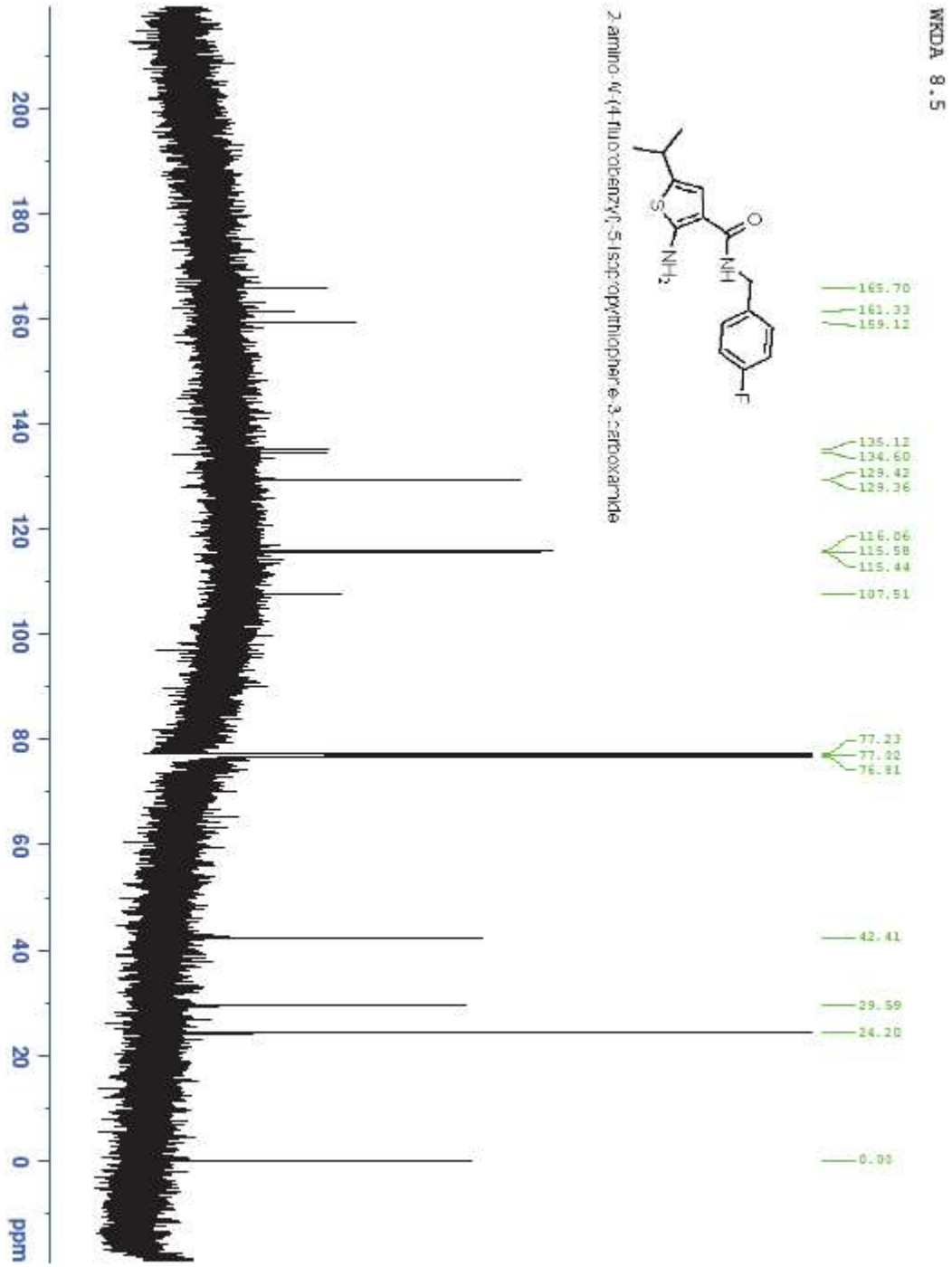
**C4,11**


da ben
7.331
7.318
7.306
7.262
7.261
7.252
7.240
7.226
7.213
6.389
6.091
5.666
3.702
3.636
3.619
3.608
3.598
3.586
2.885
2.873
2.861
2.026
5.05
0.96
2.05
1.92
2.16
2.09
2.11
3.00
ppm

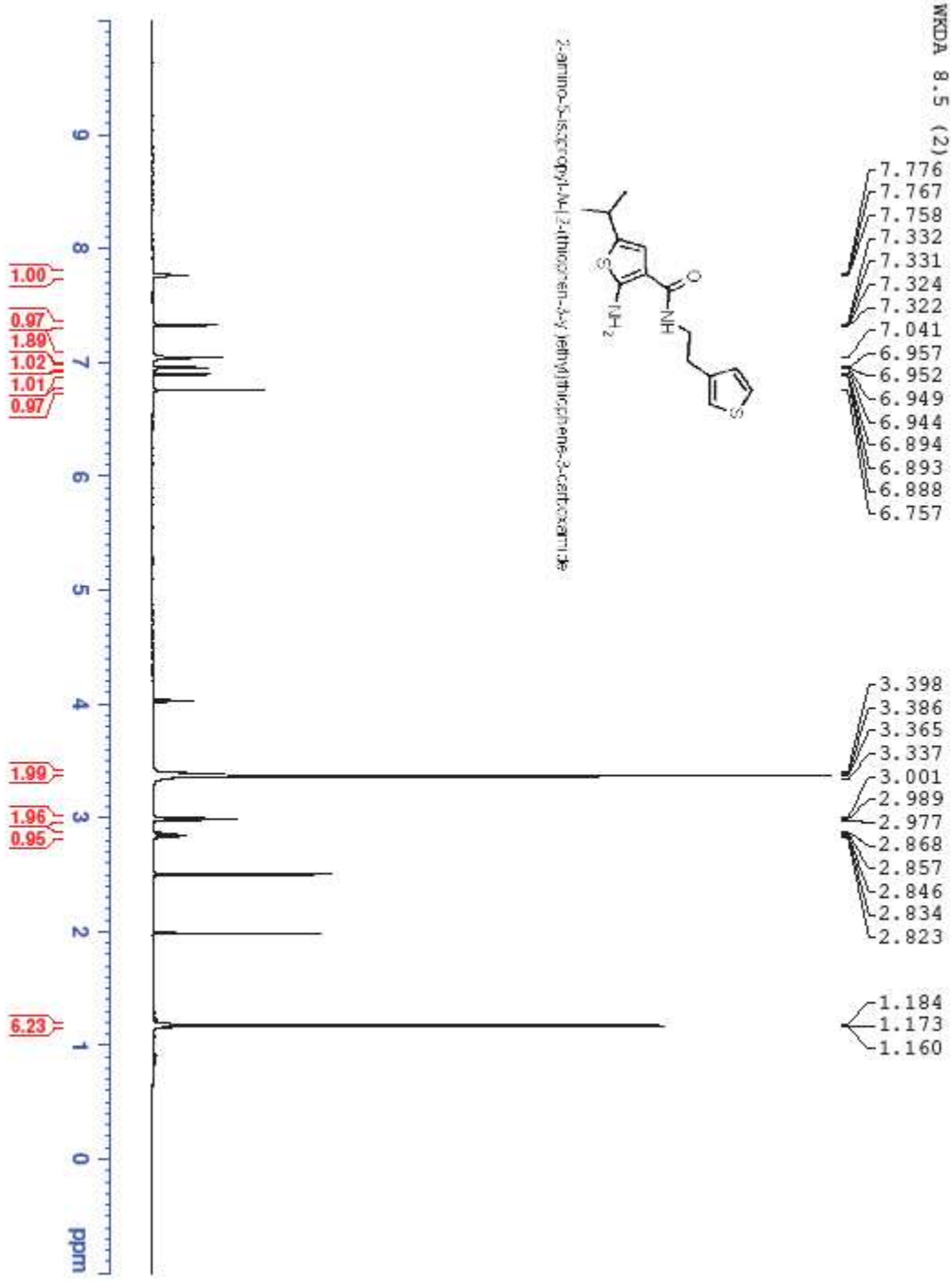

da ben
2-amino-5-(methylthio)-N-phenethylthiophene-3-carboxamide
165.64
160.54
139.08
129.84
128.68
126.54
123.41
121.01
107.67
77.28
77.07
76.86
40.40
36.06
33.09
14.86
200
180
160
140
120
100
80
60
40
20
0
ppm

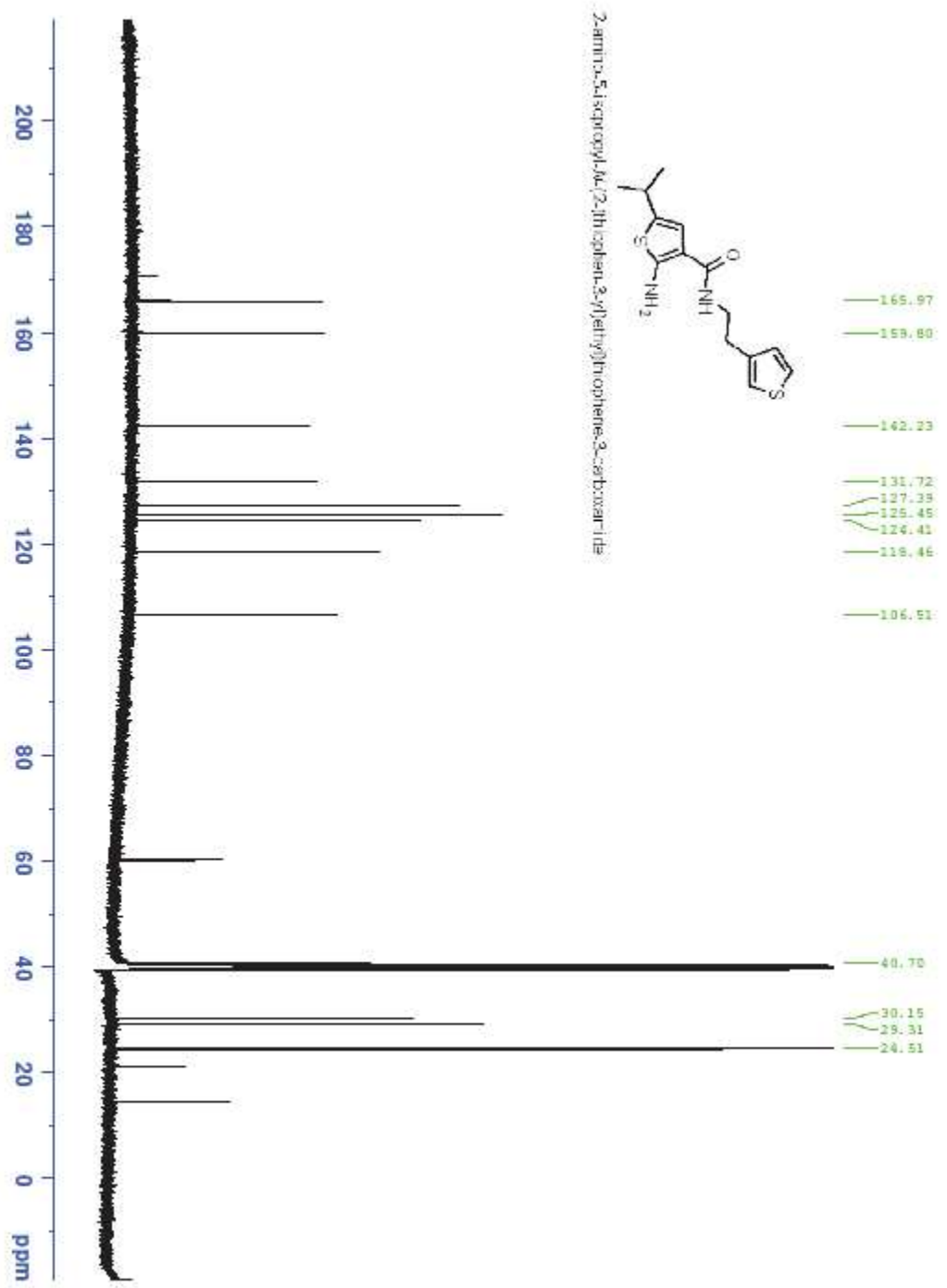
**C5,15**


WKDA 8.5
2-amino-N-(4-fluorobenzyl)-5-isopropylthiophene-3-carboxamide
7.303
7.294
7.289
7.280
7.246
7.023
7.009
6.994
6.869
6.322
5.958
5.863
4.516
4.507
2.921
2.909
2.898
2.887
2.875
1.224
1.213
1.97
1.17
1.06
2.00
1.09
1.97
1.17
2.22
0.93
5.98
ppm

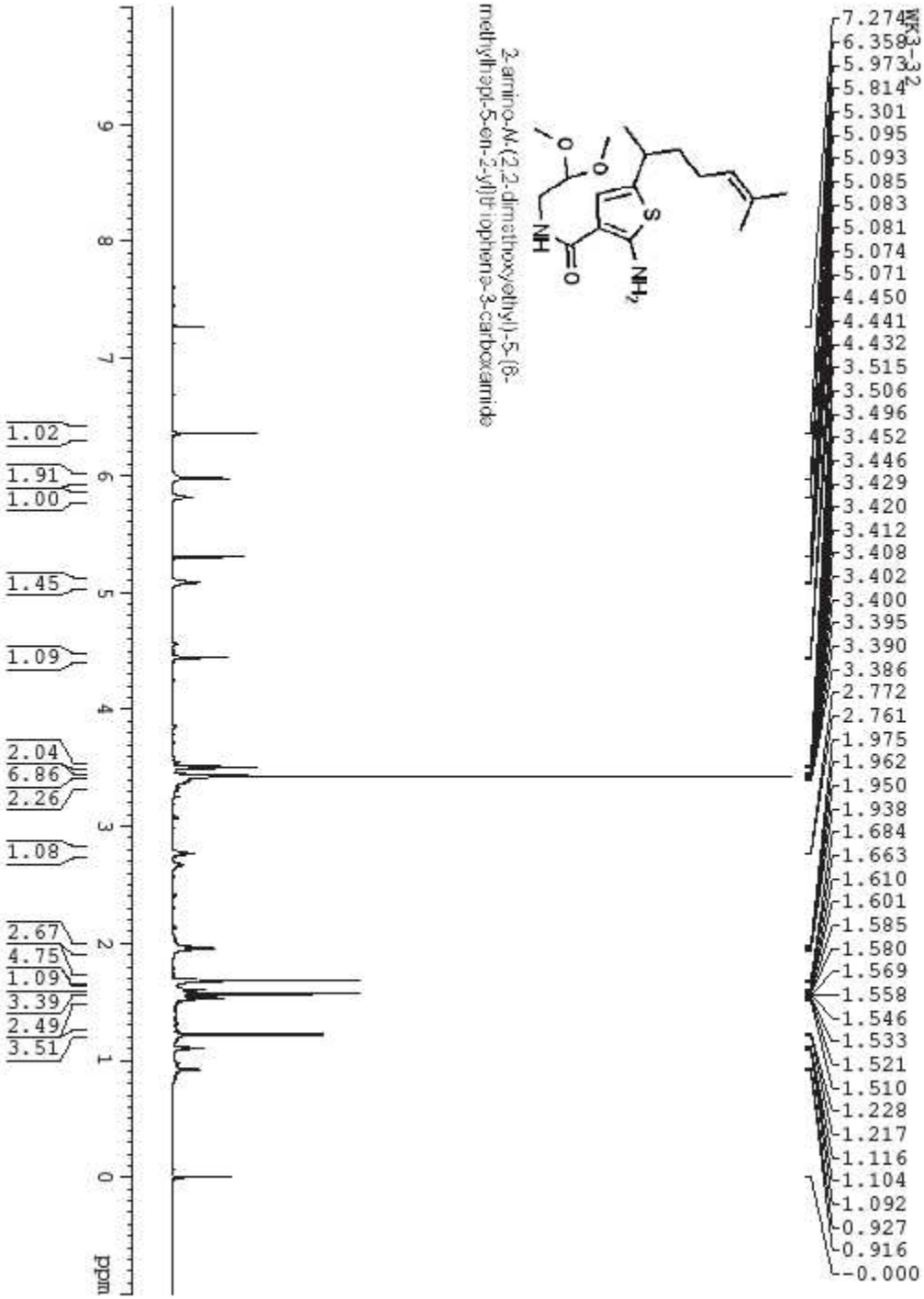

WKDA 8.5
2-amino-4-(4-fluorobenzyl)-5-isopropylthiophene-3-carboxamide
165.70
161.33
159.12
135.12
134.60
129.42
129.36
116.06
115.58
115.44
107.51
77.23
77.02
76.81
42.41
29.59
24.20
0.00
200
180
160
140
120
100
80
60
40
20
0
ppm

**C5,16**

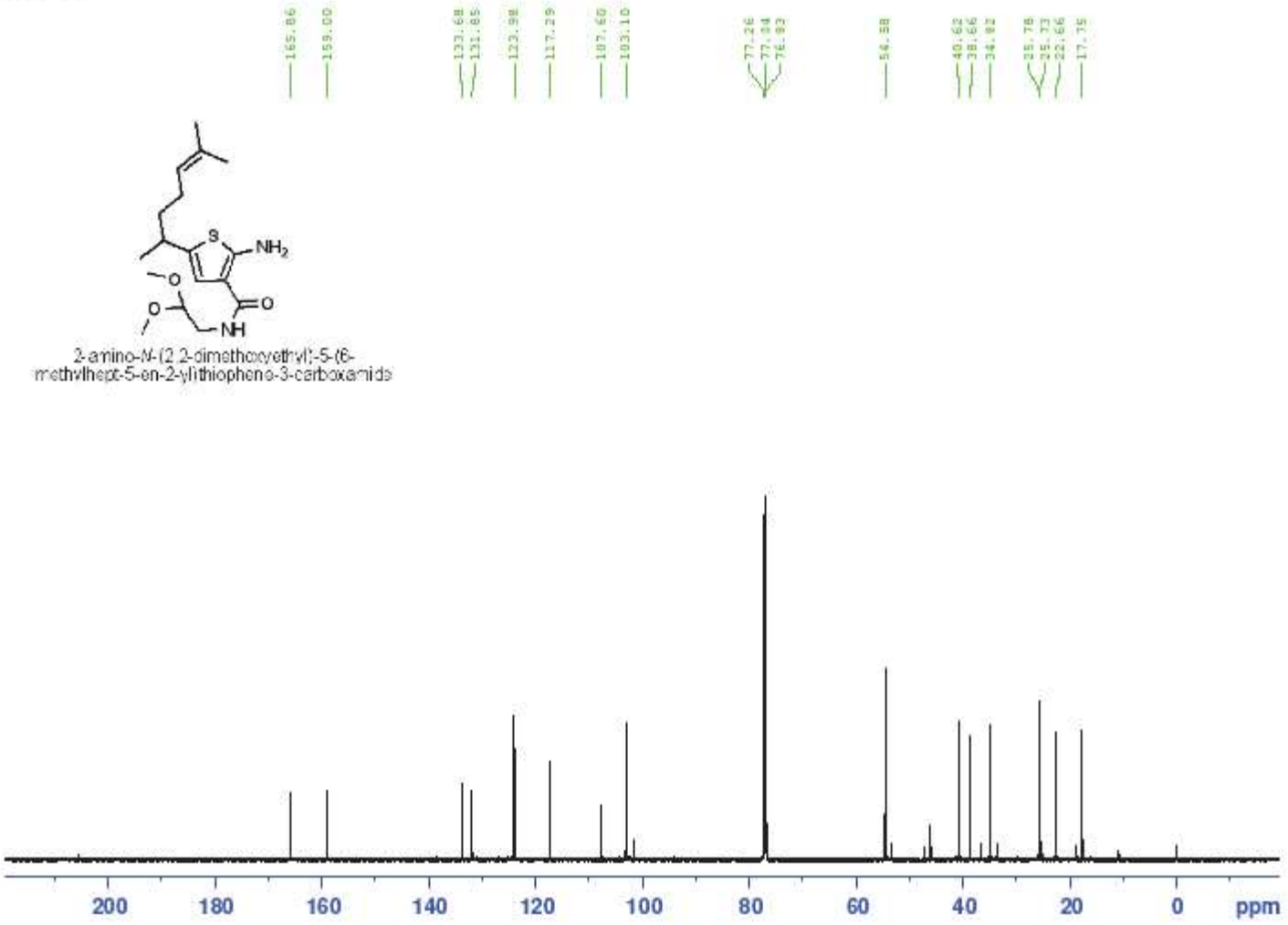

WKDA 8.5 (2)
7.776
7.767
7.758
7.332
7.331
7.324
7.322
7.041
6.957
6.952
6.949
6.944
6.894
6.893
6.888
6.757
3.398
3.386
3.365
3.337
3.001
2.989
2.977
2.868
2.857
2.846
2.834
2.823
1.184
1.173
1.160
1.00
0.97
1.89
1.02
1.01
0.97
1.99
1.96
0.95
6.23
ppm


WKDA 8.5 (2)
2-amino-5-isopropyl-N-(2-(thiophen-2-yl)ethyl)thiophene-3-carboxamide
165.97
159.80
142.23
131.72
127.39
125.45
124.41
118.46
106.51
40.70
30.15
29.31
24.51
200
180
160
140
120
100
80
60
40
20
0
ppm

**C6,8**

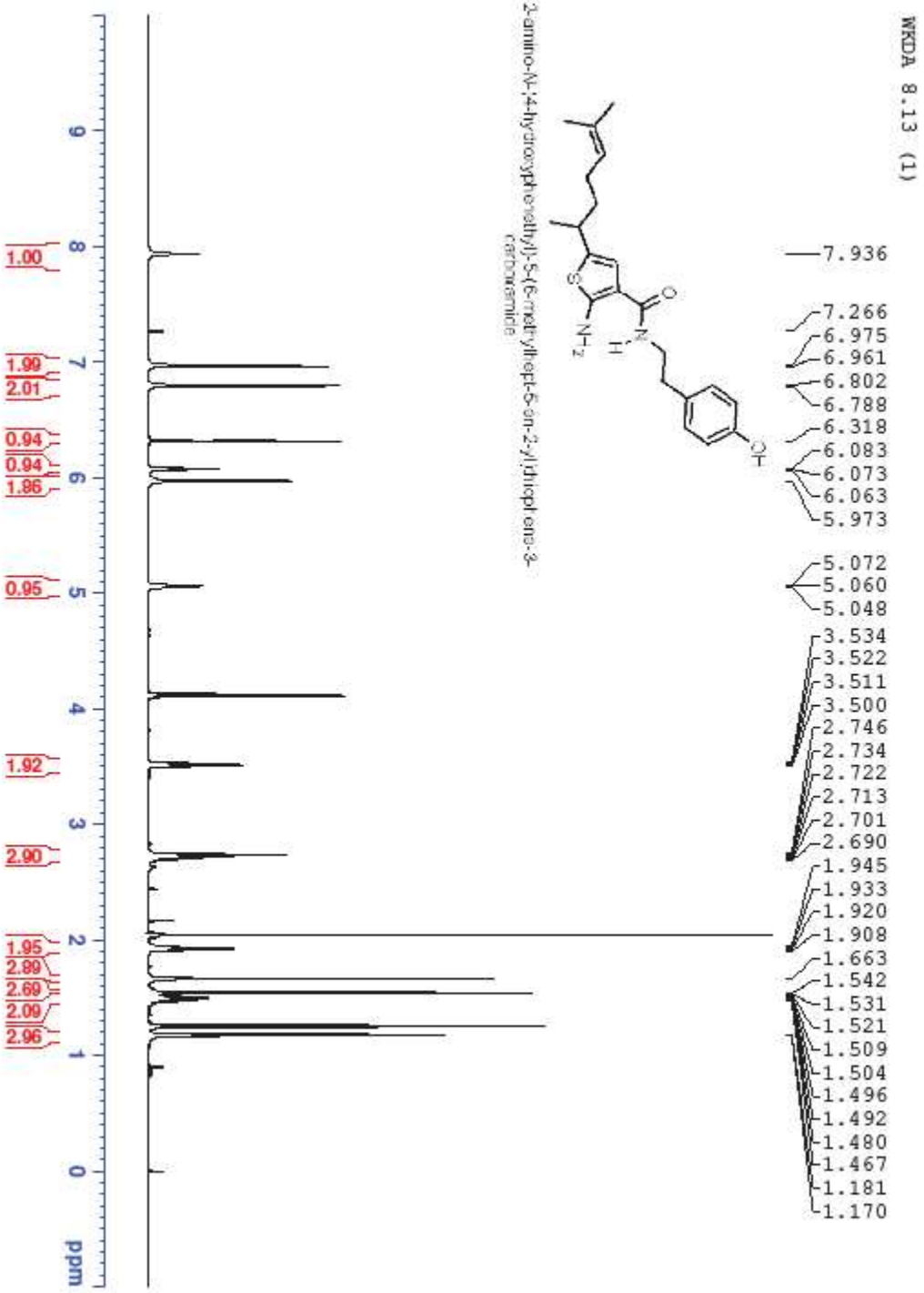

WK3-32
7.274
6.358
5.973
5.814
5.301
5.095
5.093
5.085
5.083
5.081
5.074
5.071
4.450
4.441
4.432
3.515
3.506
3.496
3.452
3.446
3.429
3.420
3.412
3.408
3.402
3.400
3.395
3.390
3.386
2.772
2.761
1.975
1.962
1.950
1.938
1.684
1.663
1.610
1.601
1.585
1.580
1.569
1.558
1.546
1.533
1.521
1.510
1.228
1.217
1.116
1.104
1.092
0.927
0.916
-0.000
2-amino-N-(2,2-dimethoxyethyl)-5-(6-methylhept-5-en-2-yl)thiophene-3-carboxamide
NH
O
O
S
NH2
1.02
1.91
1.00
1.45
1.09
2.04
6.86
2.26
1.08
2.67
4.75
1.09
3.39
2.49
3.51
9
8
7
6
5
4
3
2
1
0
ppm

WK3-32

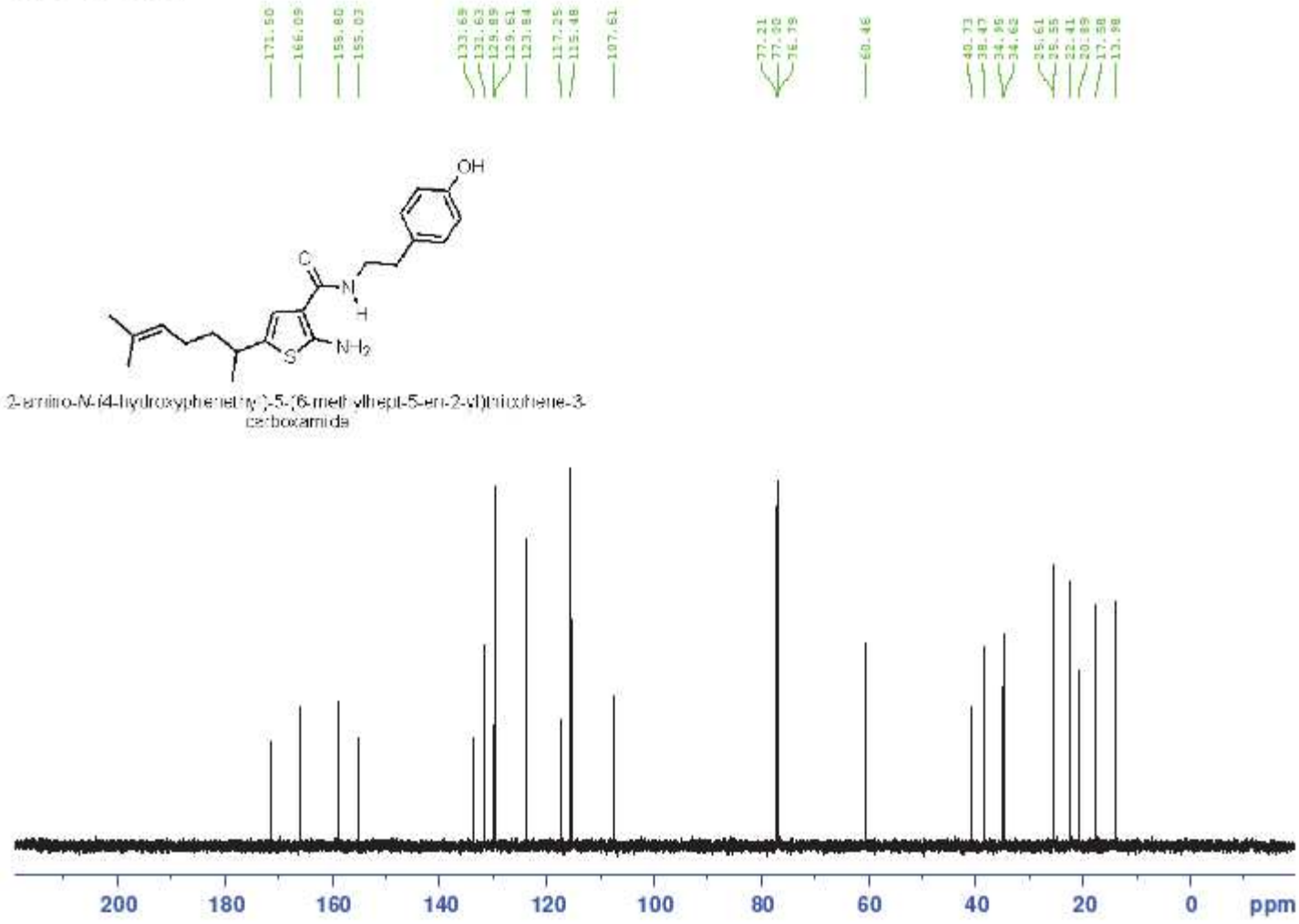



2-amino-*N*-(2,2-dimethoxyethyl)-5-(6-methylhept-5-en-2-yl)thiophene-3-carboxamide

**C6,17**

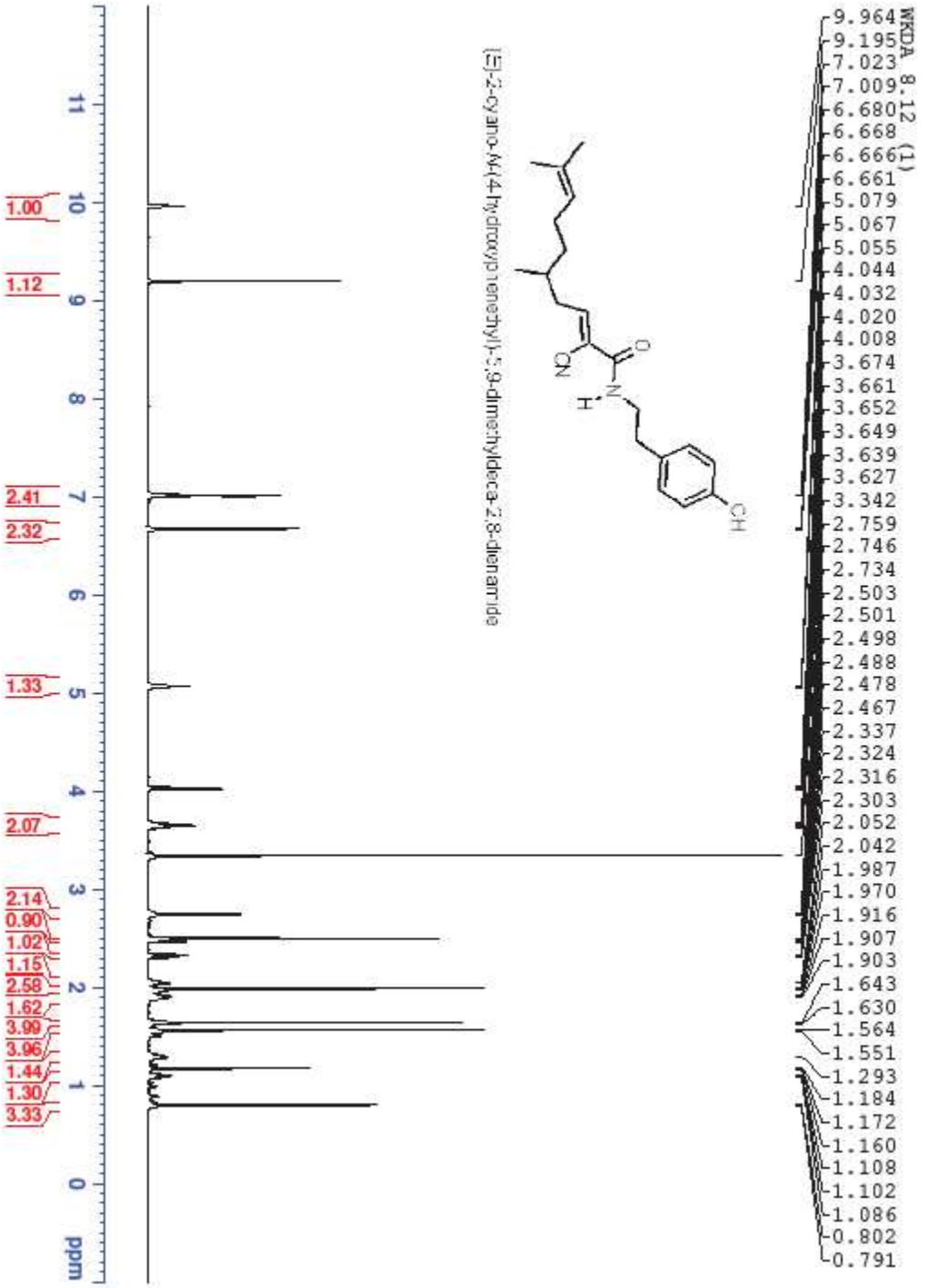

WKDA 8.13 (1)
2-amino-N-[4-hydroxyphenethyl]-5-(6-methylhept-5-en-2-yl)thiophene-3-carboxamide
7.936
7.266
6.975
6.961
6.802
6.788
6.318
6.083
6.073
6.063
5.973
5.072
5.060
5.048
3.534
3.522
3.511
3.500
2.746
2.734
2.722
2.713
2.701
2.690
1.945
1.933
1.920
1.908
1.663
1.542
1.531
1.521
1.509
1.504
1.496
1.492
1.480
1.467
1.181
1.170
1.00
1.99
2.01
0.94
0.94
1.86
0.95
1.92
2.90
1.95
2.89
2.69
2.09
2.96
ppm

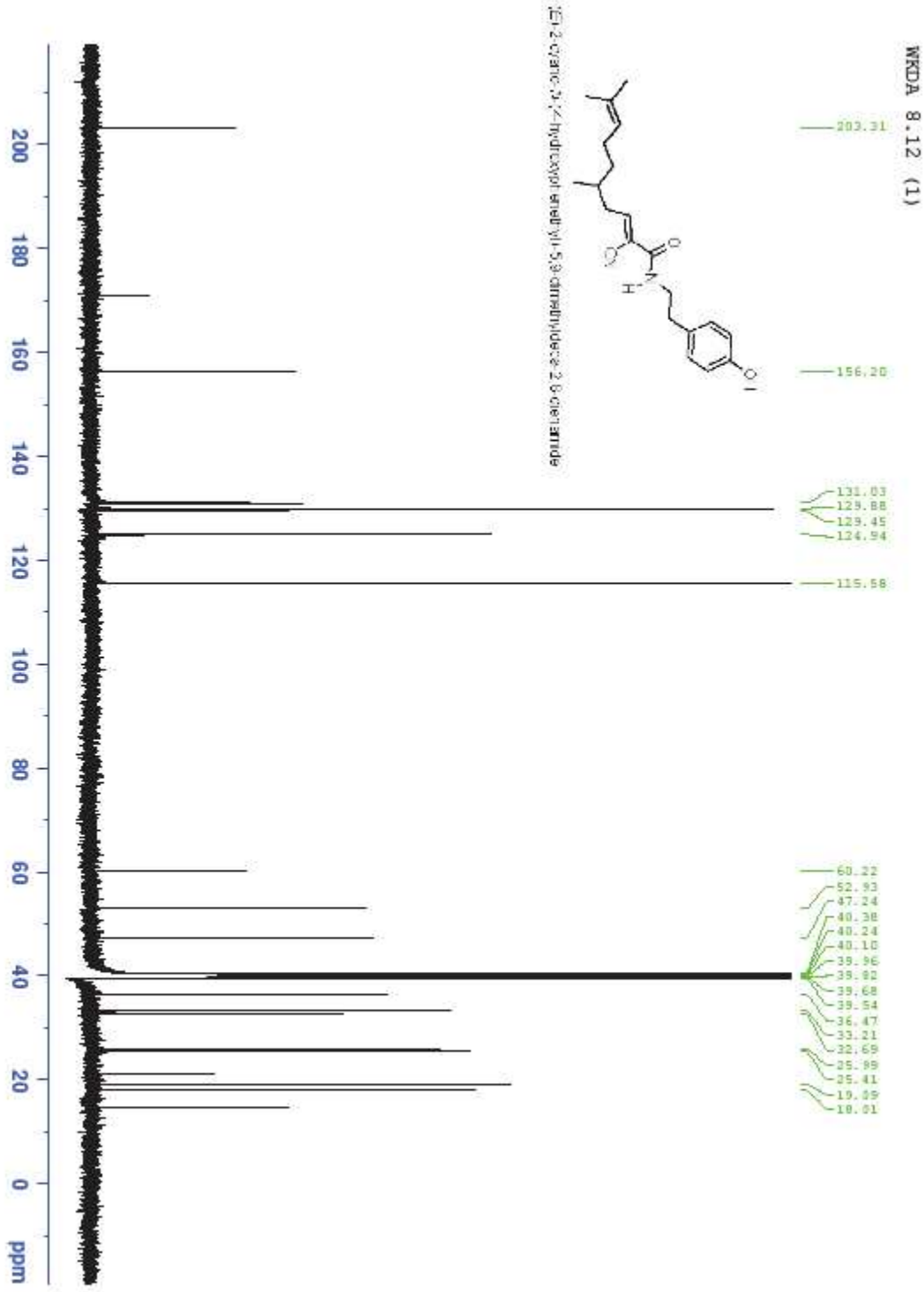
WKDA 8.13 (1)



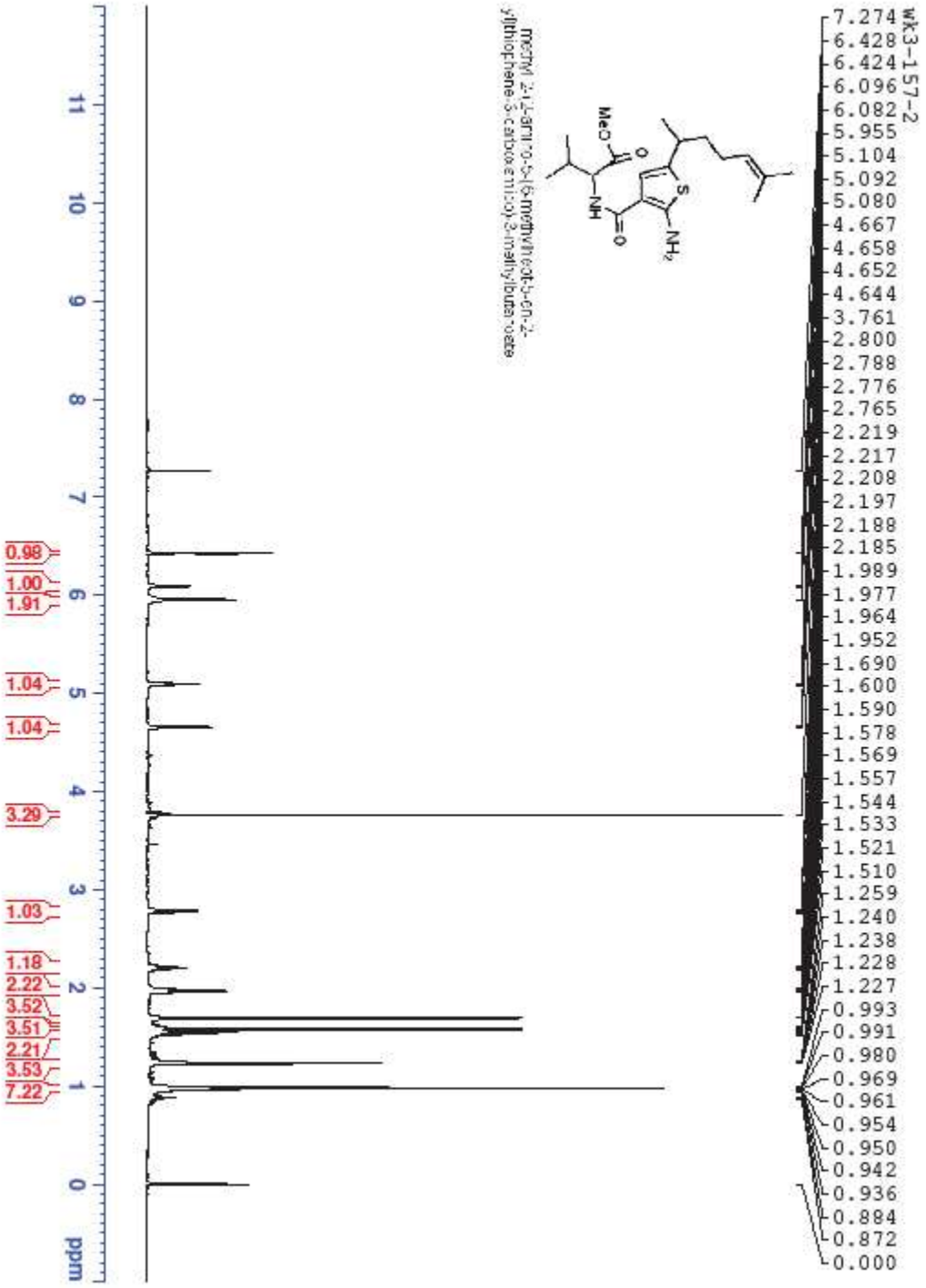

2-amino-N-(4-hydroxyphenethyl)-5-(6-methylhept-5-en-2-yl)thiophene-3-carboxamide

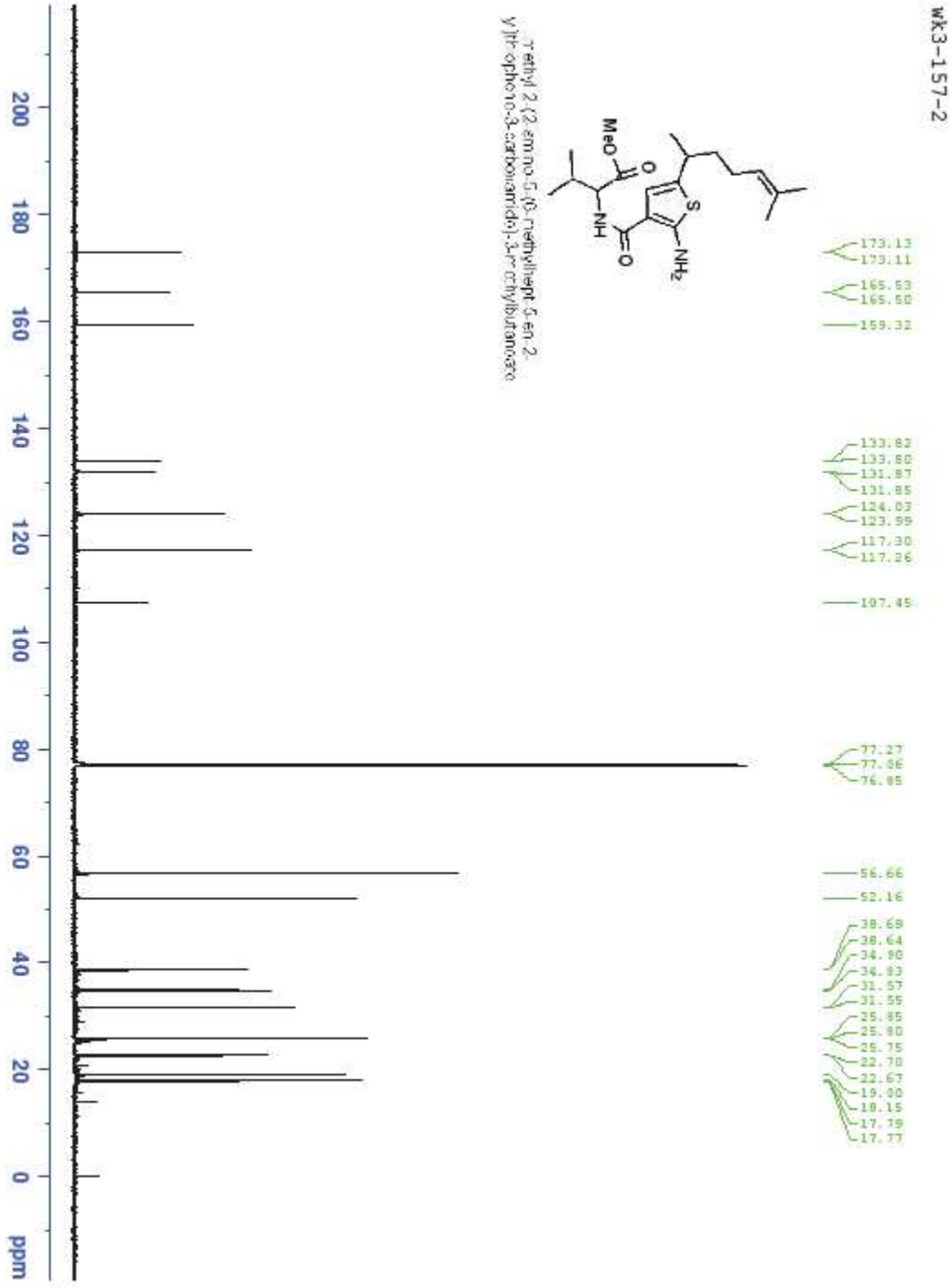
**D6,17**


WKDA 8.12 (1)
9.964
9.195
7.023
7.009
6.680
6.668
6.666
6.661
5.079
5.067
5.055
4.044
4.032
4.020
4.008
3.674
3.661
3.652
3.649
3.639
3.627
3.342
2.759
2.746
2.734
2.503
2.501
2.498
2.488
2.478
2.467
2.337
2.324
2.316
2.303
2.052
2.042
1.987
1.970
1.916
1.907
1.903
1.643
1.630
1.564
1.551
1.293
1.184
1.172
1.160
1.108
1.102
1.086
0.802
0.791
[E]-2-cyano-N-(4-hydroxyphenethyl)-3,9-dimethyldeca-2,8-dienamide
1.00
1.12
2.41
2.32
1.33
2.07
2.14
0.90
1.02
1.15
2.58
1.62
3.99
3.96
1.44
1.30
3.33
ppm

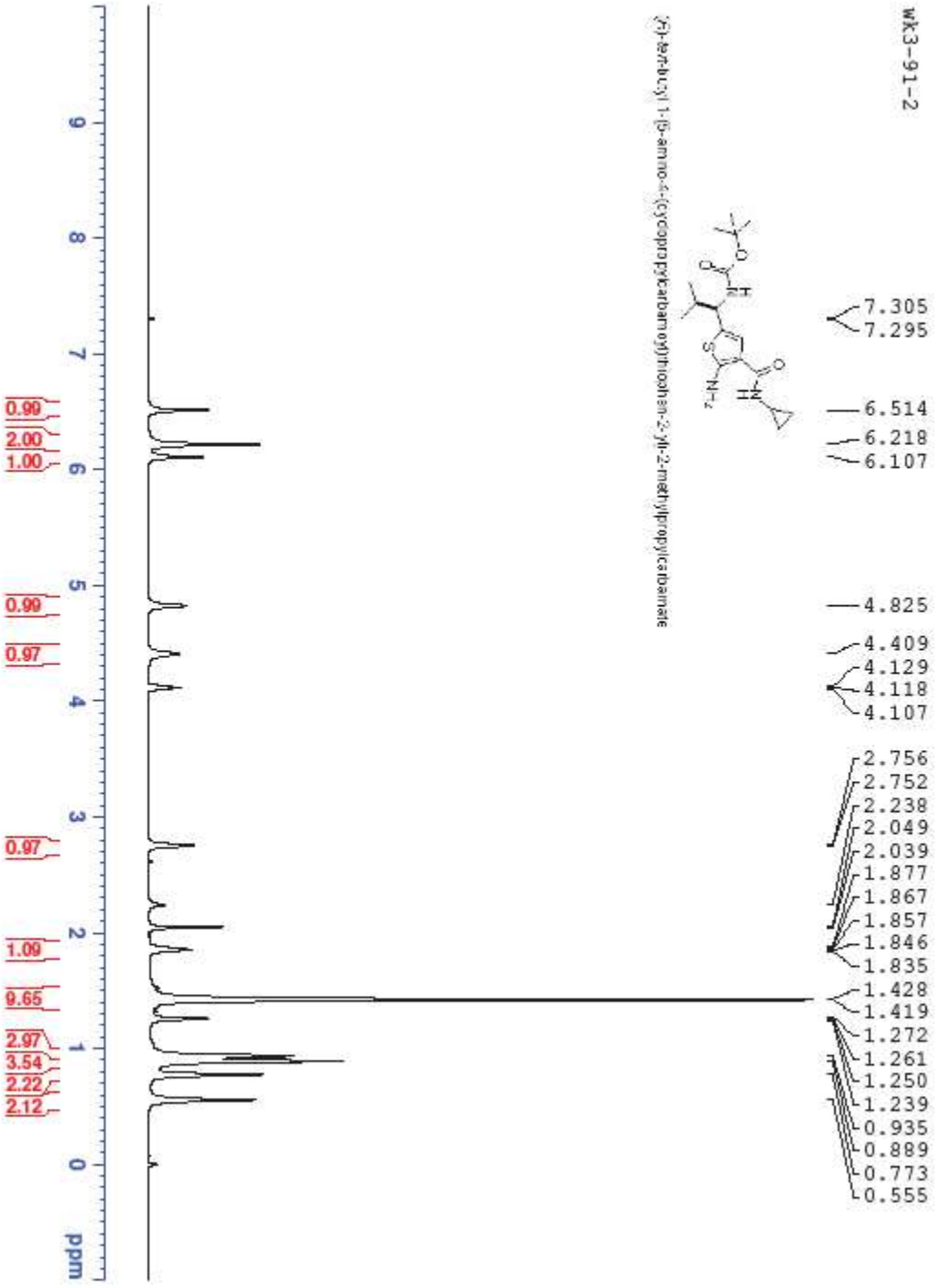

WKDA 8.12 (1)
(E)-2-cyano-3,7-hydroxyphenethyl-5,9-dimethyldeca-2,6-dienamide
203.31
156.20
131.03
129.88
129.45
124.94
115.58
60.22
52.93
47.24
40.38
40.24
40.10
39.96
39.82
39.68
39.54
36.47
33.21
32.69
25.99
25.41
19.09
18.01
200
180
160
140
120
100
80
60
40
20
0
ppm

**C6,23**

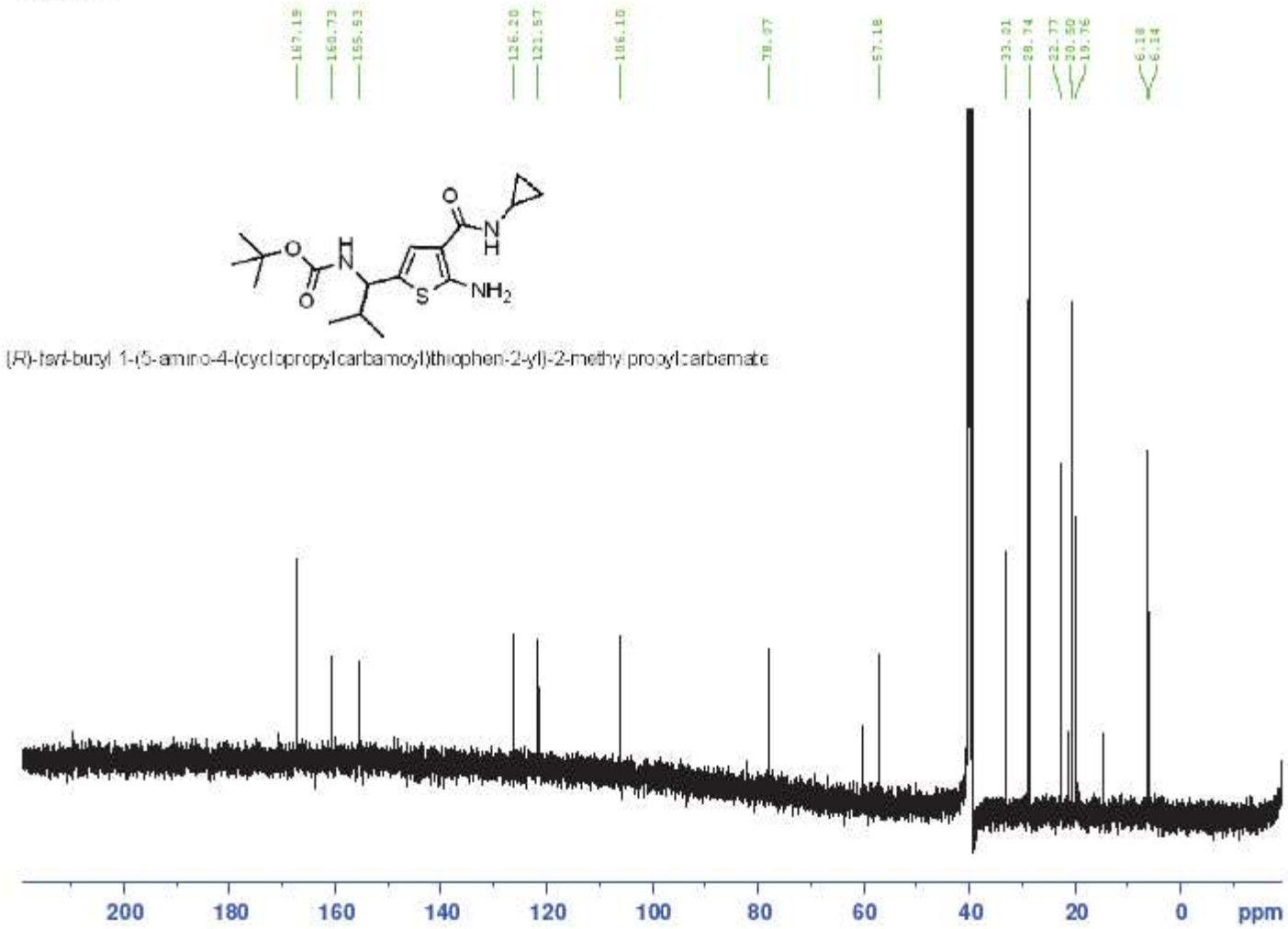

wk3-157-2
7.274
6.428
6.424
6.096
6.082
5.955
5.104
5.092
5.080
4.667
4.658
4.652
4.644
3.761
2.800
2.788
2.776
2.765
2.219
2.217
2.208
2.197
2.188
2.185
1.989
1.977
1.964
1.952
1.690
1.600
1.590
1.578
1.569
1.557
1.544
1.533
1.521
1.510
1.259
1.240
1.238
1.228
1.227
0.993
0.991
0.980
0.969
0.961
0.954
0.950
0.942
0.936
0.884
0.872
0.000
0.98
1.00
1.91
1.04
1.04
3.29
1.03
1.18
2.22
3.52
3.51
2.21
3.53
7.22
ppm


wk3-157-2
methyl 2-(2-amino-5-(6-methylhept-5-en-2-yl)thiophene-3-carboxamido)-3-methylbutanoate
MeO
O
NH
O
S
NH2
173.13
173.11
165.53
165.50
159.32
133.82
133.80
131.87
131.85
124.03
123.99
117.30
117.26
107.45
77.27
77.06
76.85
56.66
52.16
38.69
38.64
34.90
34.83
31.57
31.55
25.85
25.80
25.75
22.70
22.67
19.00
18.15
17.79
17.77
200
180
160
140
120
100
80
60
40
20
0
ppm

**C7,1**

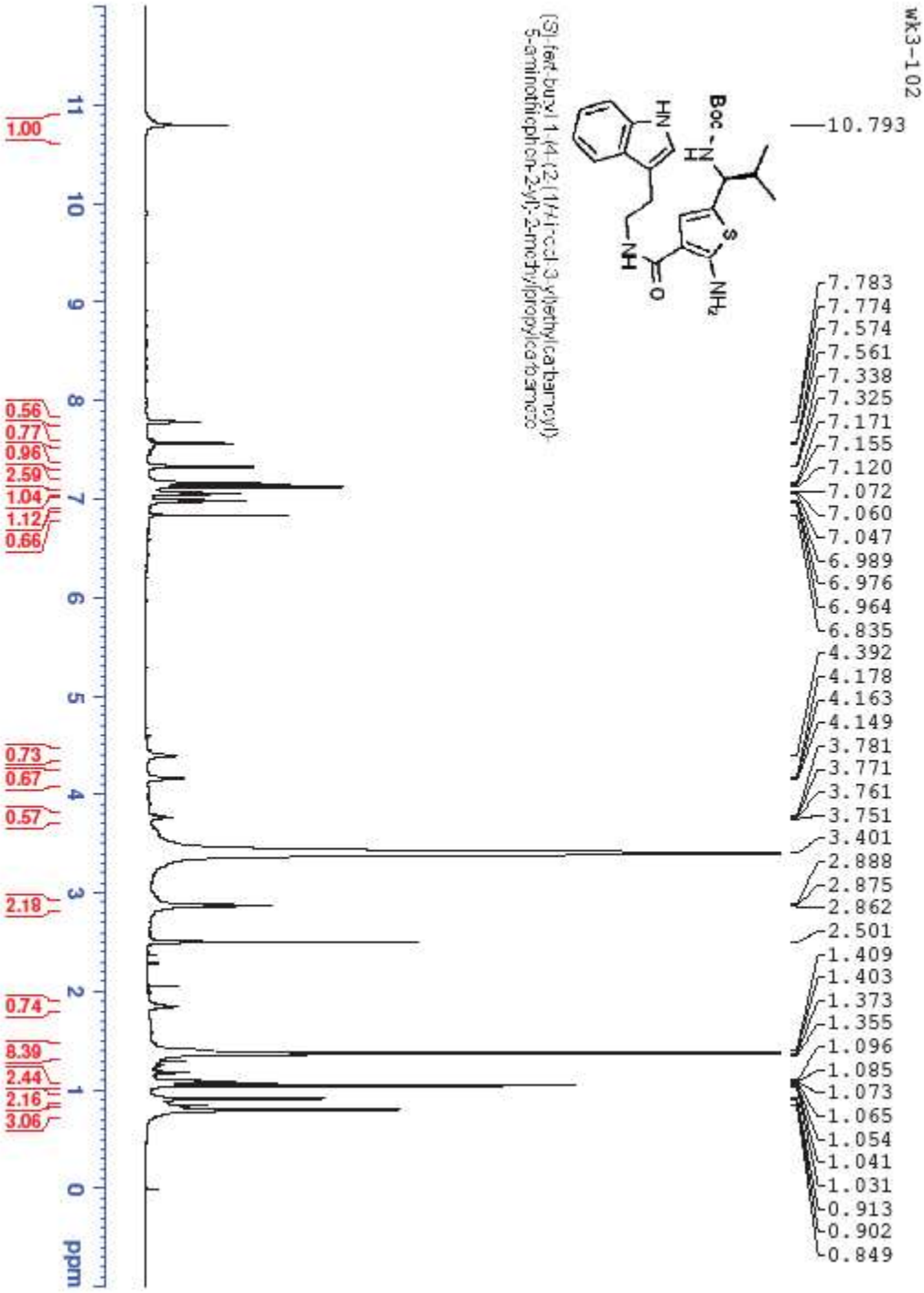

wk3-91-2
tert-butyl (S)-(5-amino-4-(cyclopropylcarbamoyl)thiophen-2-yl)-2-methylpropylcarbamate
7.305
7.295
6.514
6.218
6.107
4.825
4.409
4.129
4.118
4.107
2.756
2.752
2.238
2.049
2.039
1.877
1.867
1.857
1.846
1.835
1.428
1.419
1.272
1.261
1.250
1.239
0.935
0.889
0.773
0.555
0.99
2.00
1.00
0.99
0.97
0.97
1.09
9.65
2.97
3.54
2.22
2.12
ppm

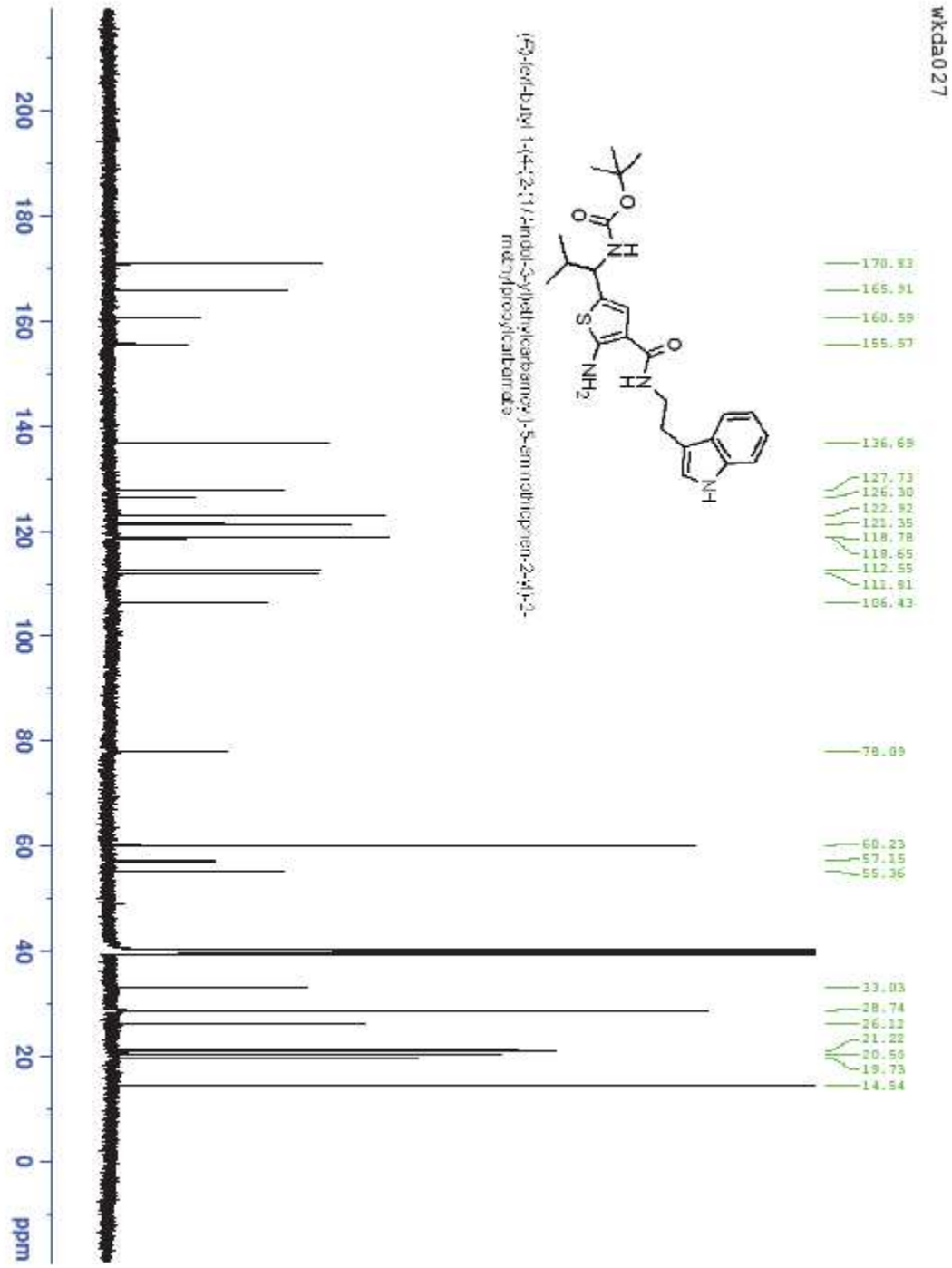
WKDA026



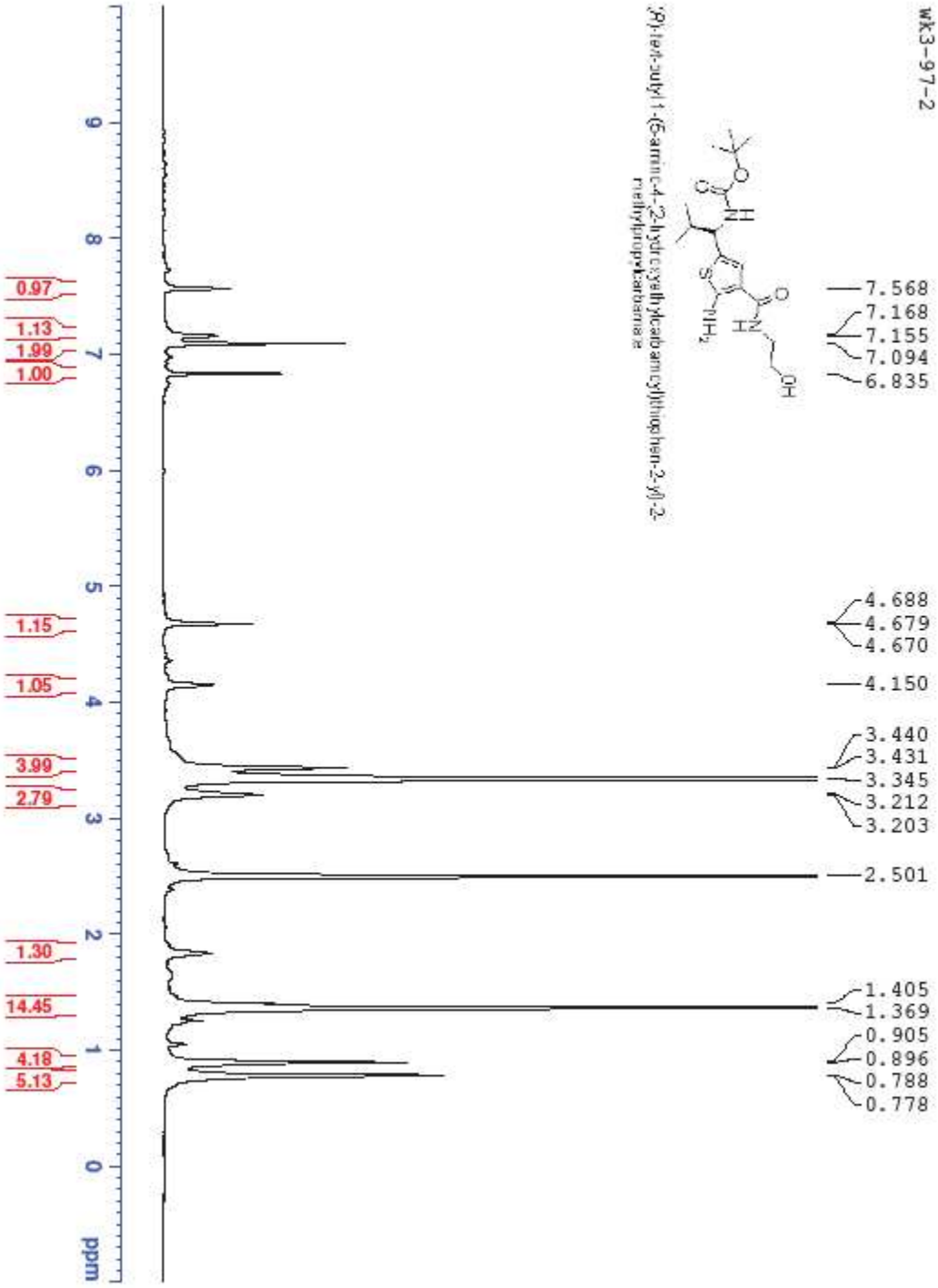

(*R*)-*tert*-butyl 1-(5-amino-4-(cyclopropylcarbamoyl)thiophen-2-yl)-2-methylpropylcarbamate

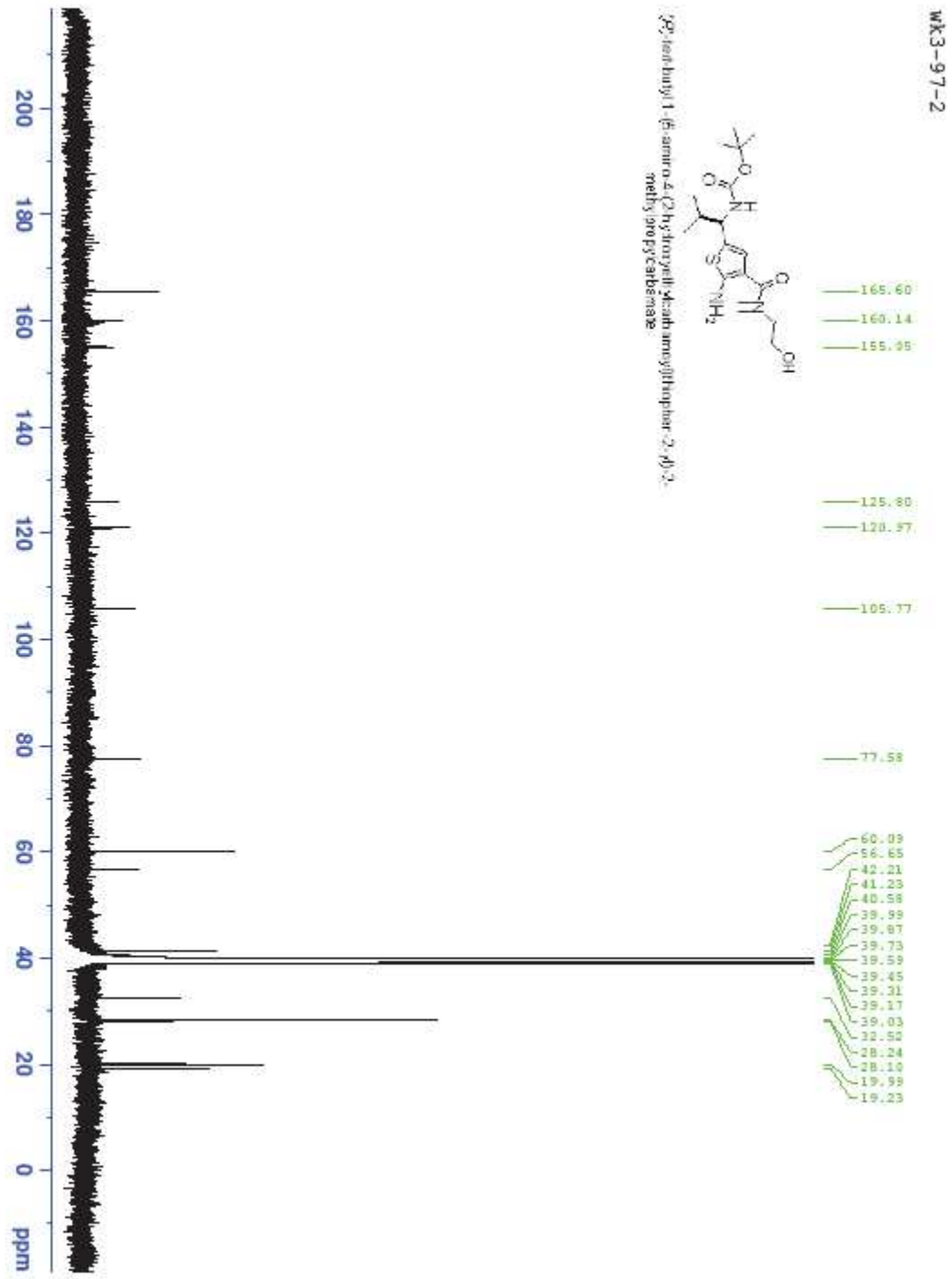
**C7,10**


wk3-102
10.793
7.783
7.774
7.574
7.561
7.338
7.325
7.171
7.155
7.120
7.072
7.060
7.047
6.989
6.976
6.964
6.835
4.392
4.178
4.163
4.149
3.781
3.771
3.761
3.751
3.401
2.888
2.875
2.862
2.501
1.409
1.403
1.373
1.355
1.096
1.085
1.073
1.065
1.054
1.041
1.031
0.913
0.902
0.849
1.00
0.56
0.77
0.96
2.59
1.04
1.12
0.66
0.73
0.67
0.57
2.18
0.74
8.39
2.44
2.16
3.06
ppm

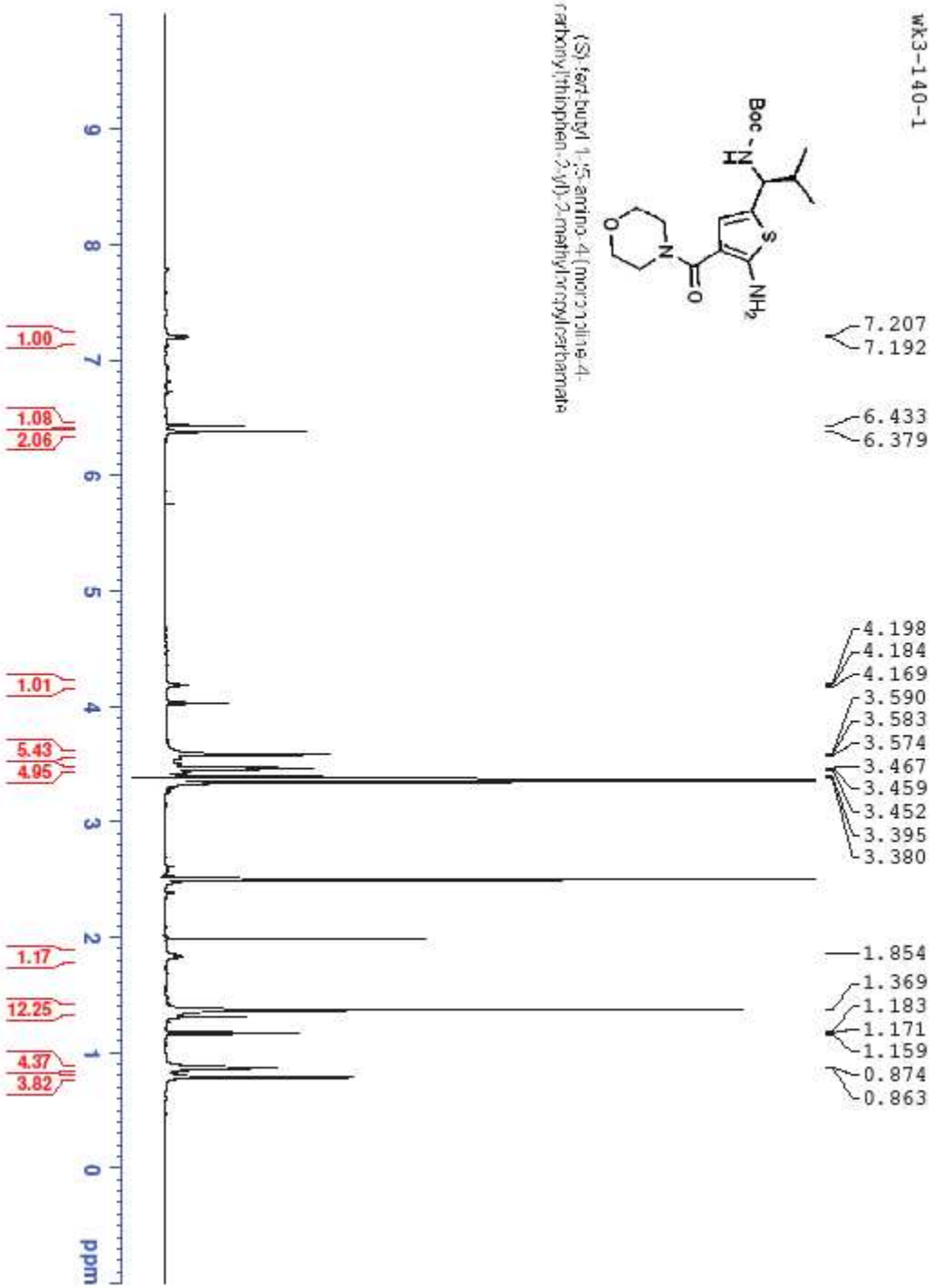

wkda027
(S)-tert-butyl 1-(4-(2-(1H-indol-3-yl)ethylcarbamoyl)-5-ammothiophen-2-yl)-2-methylpropylcarbamate
170.93
165.91
160.59
155.57
136.69
127.73
126.30
122.92
121.35
118.78
118.65
112.55
111.91
106.43
78.09
60.23
57.15
55.36
33.03
28.74
26.12
21.22
20.50
19.73
14.54
200
180
160
140
120
100
80
60
40
20
0
ppm

**C7,14**

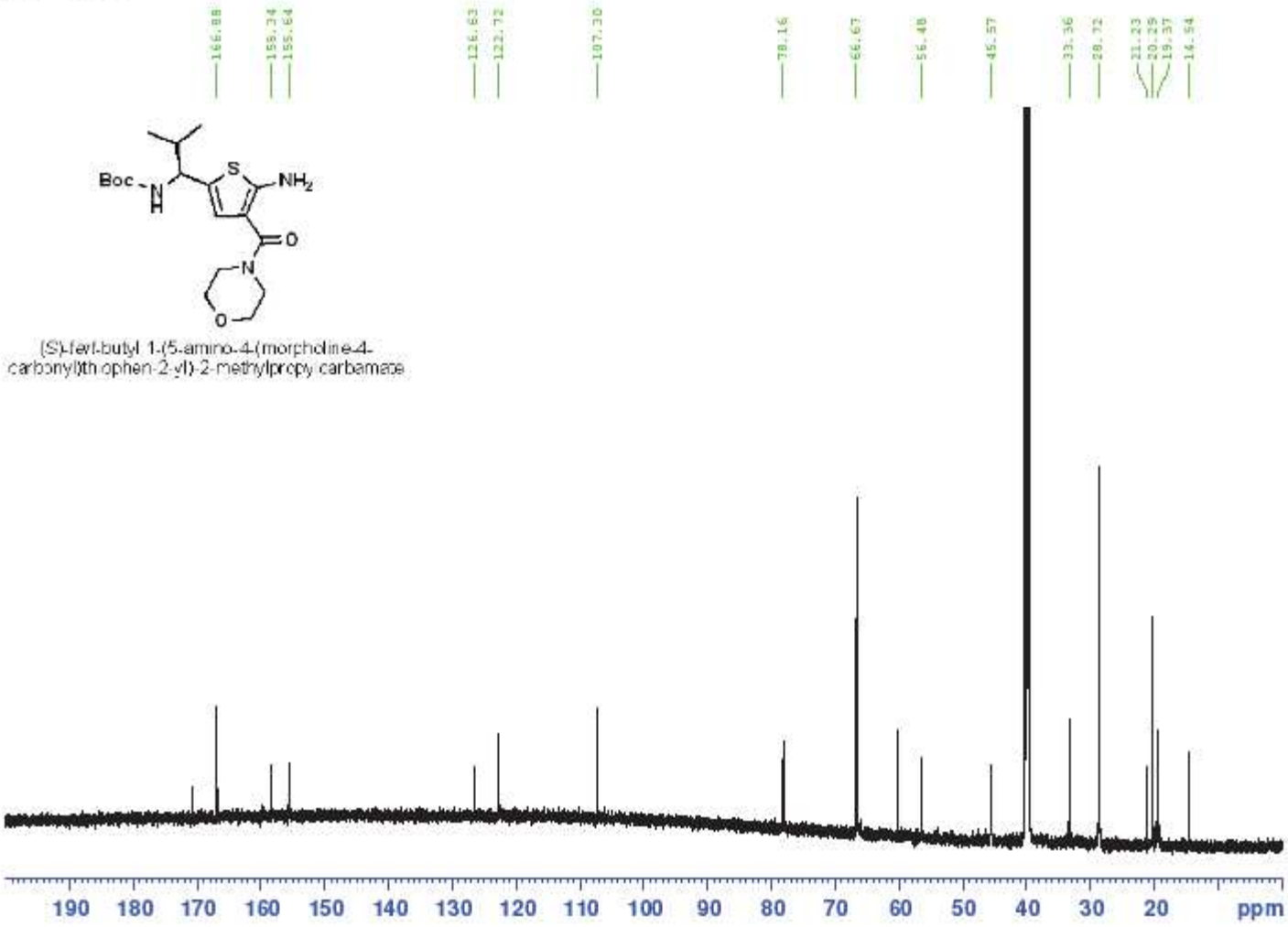

wk3-97-2
(R)-tert-butyl 1-(5-amino-4-(2-hydroxyethylcarbamoyl)thiophen-2-yl)-2-methylpropylcarbamate
7.568
7.168
7.155
7.094
6.835
4.688
4.679
4.670
4.150
3.440
3.431
3.345
3.212
3.203
2.501
1.405
1.369
0.905
0.896
0.788
0.778
0.97
1.13
1.99
1.00
1.15
1.05
3.99
2.79
1.30
14.45
4.18
5.13
ppm


wk3-97-2
(2S)-tert-butyl 1-((5-amino-4-(2-hydroxyethylcarbamoyl)thiophen-2-yl)-2-methyl-1-oxopropan-2-yl)carbamate
165.60
160.14
155.05
125.80
120.97
105.77
77.58
60.09
56.65
42.21
41.23
40.58
39.99
39.87
39.73
39.59
39.45
39.31
39.17
39.03
32.52
28.24
28.10
19.99
19.23
200
180
160
140
120
100
80
60
40
20
0
ppm

**C7,18**

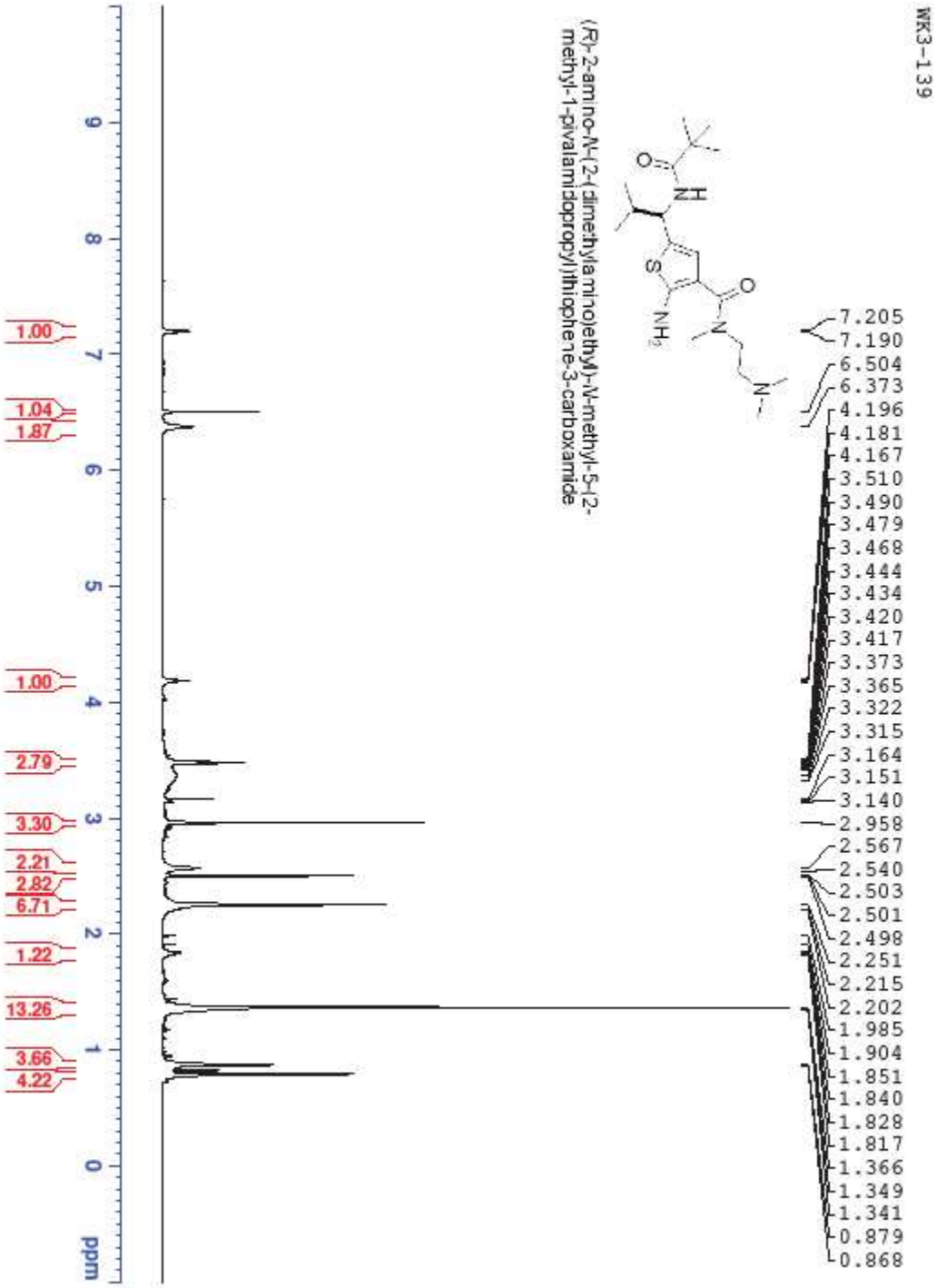

wk3-140-1
(S) tert-butyl 1-(5-amino-4-(morpholine-4-carbonyl)thiophen-2-yl)-2-methylpropylcarbamate
Boc
NH2
7.207
7.192
6.433
6.379
4.198
4.184
4.169
3.590
3.583
3.574
3.467
3.459
3.452
3.395
3.380
1.854
1.369
1.183
1.171
1.159
0.874
0.863
1.00
1.08
2.06
1.01
5.43
4.95
1.17
12.25
4.37
3.82
ppm

wk3-140-1

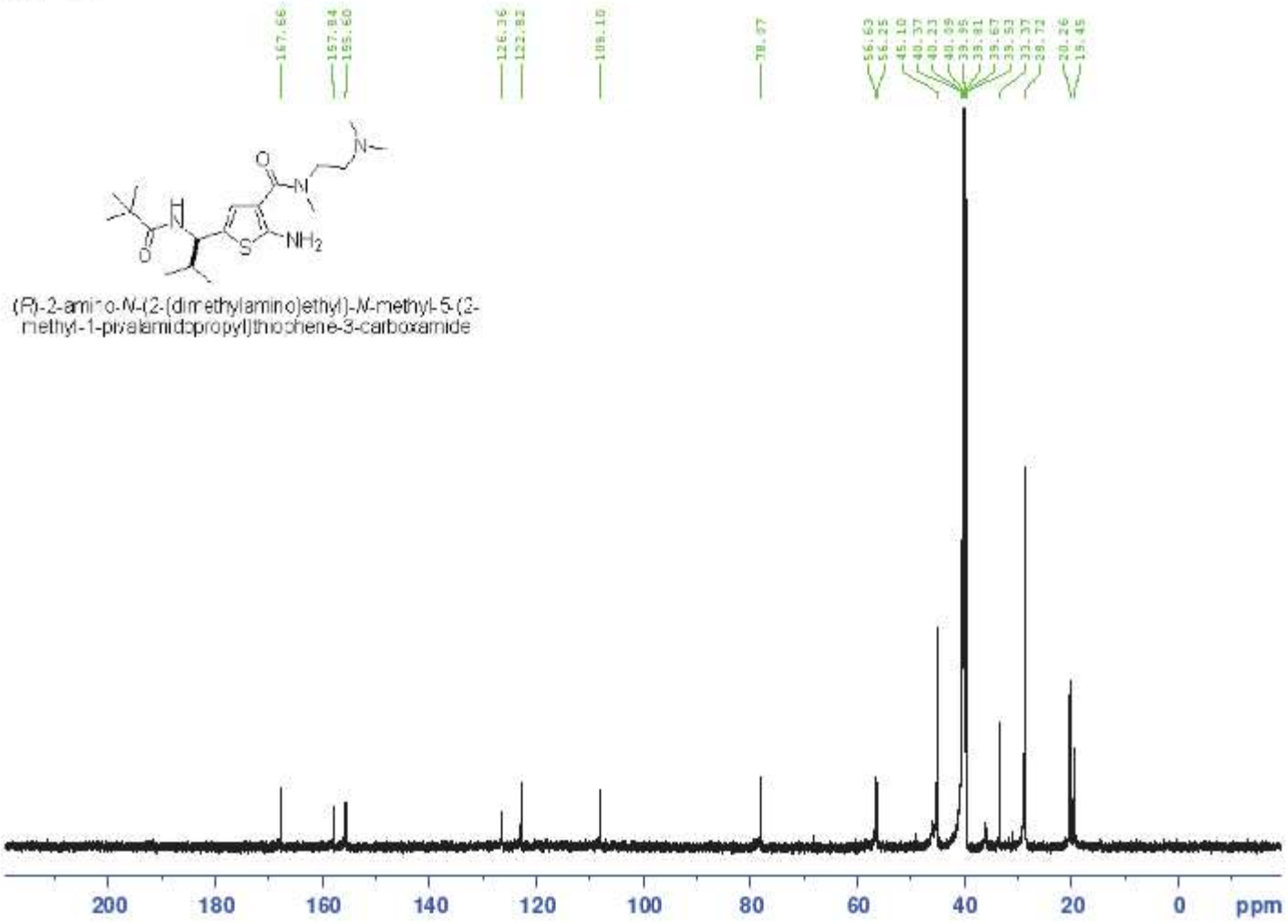



(S)-tert-butyl 1-(5-amino-4-(morpholine-4-carbonyl)thiophen-2-yl)-2-methylpropylcarbamate

**C7,19**

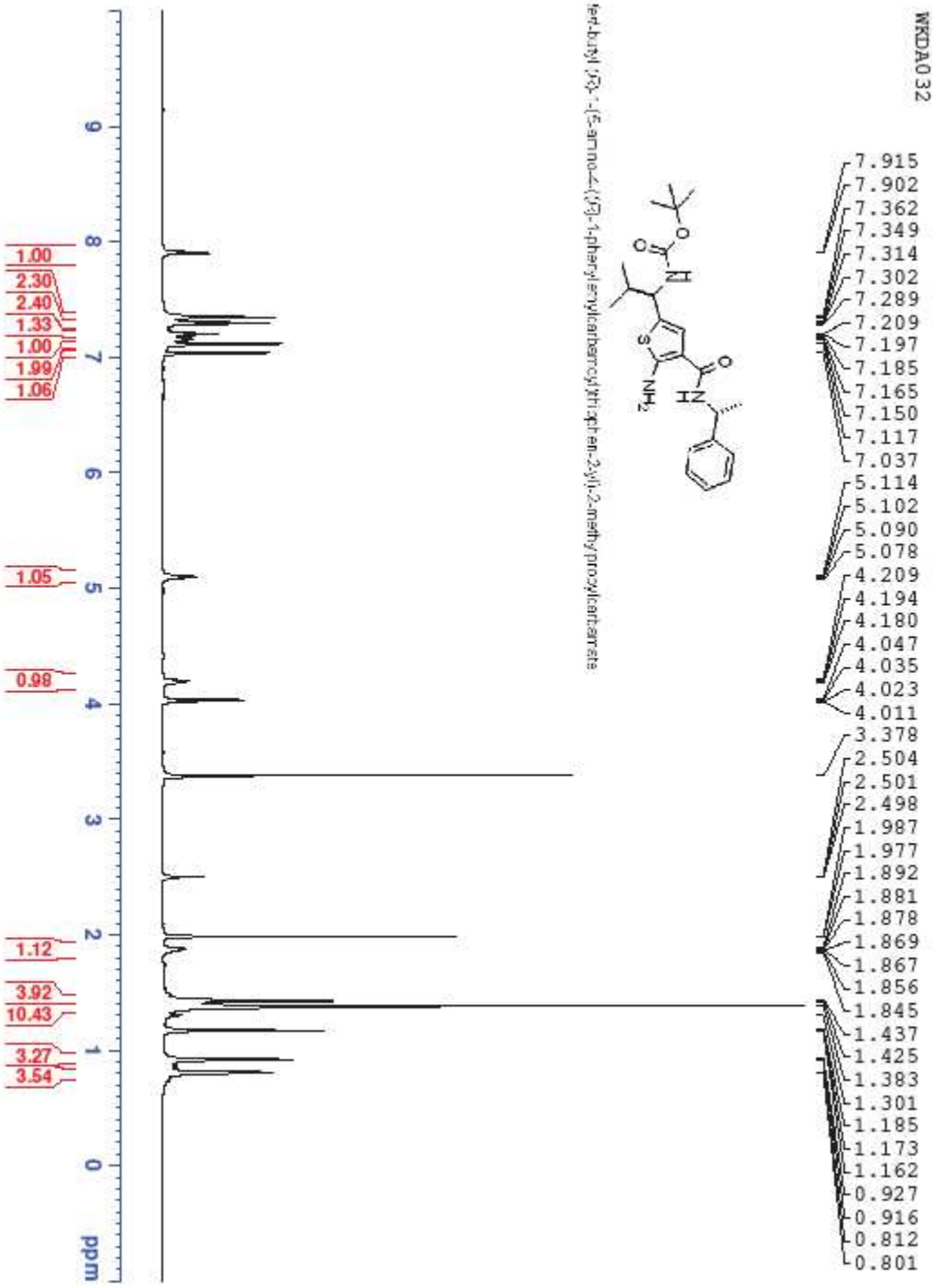

WK3-139
(R)-2-amino-N-(2-(dimethylamino)ethyl)-N-methyl-5-(2-methyl-1-pivalamidopropyl)thiophene-3-carboxamide
7.205
7.190
6.504
6.373
4.196
4.181
4.167
3.510
3.490
3.479
3.468
3.444
3.434
3.420
3.417
3.373
3.365
3.322
3.315
3.164
3.151
3.140
2.958
2.567
2.540
2.503
2.501
2.498
2.251
2.215
2.202
1.985
1.904
1.851
1.840
1.828
1.817
1.366
1.349
1.341
0.879
0.868
1.00
1.04
1.87
1.00
2.79
3.30
2.21
2.82
6.71
1.22
13.26
3.66
4.22
ppm

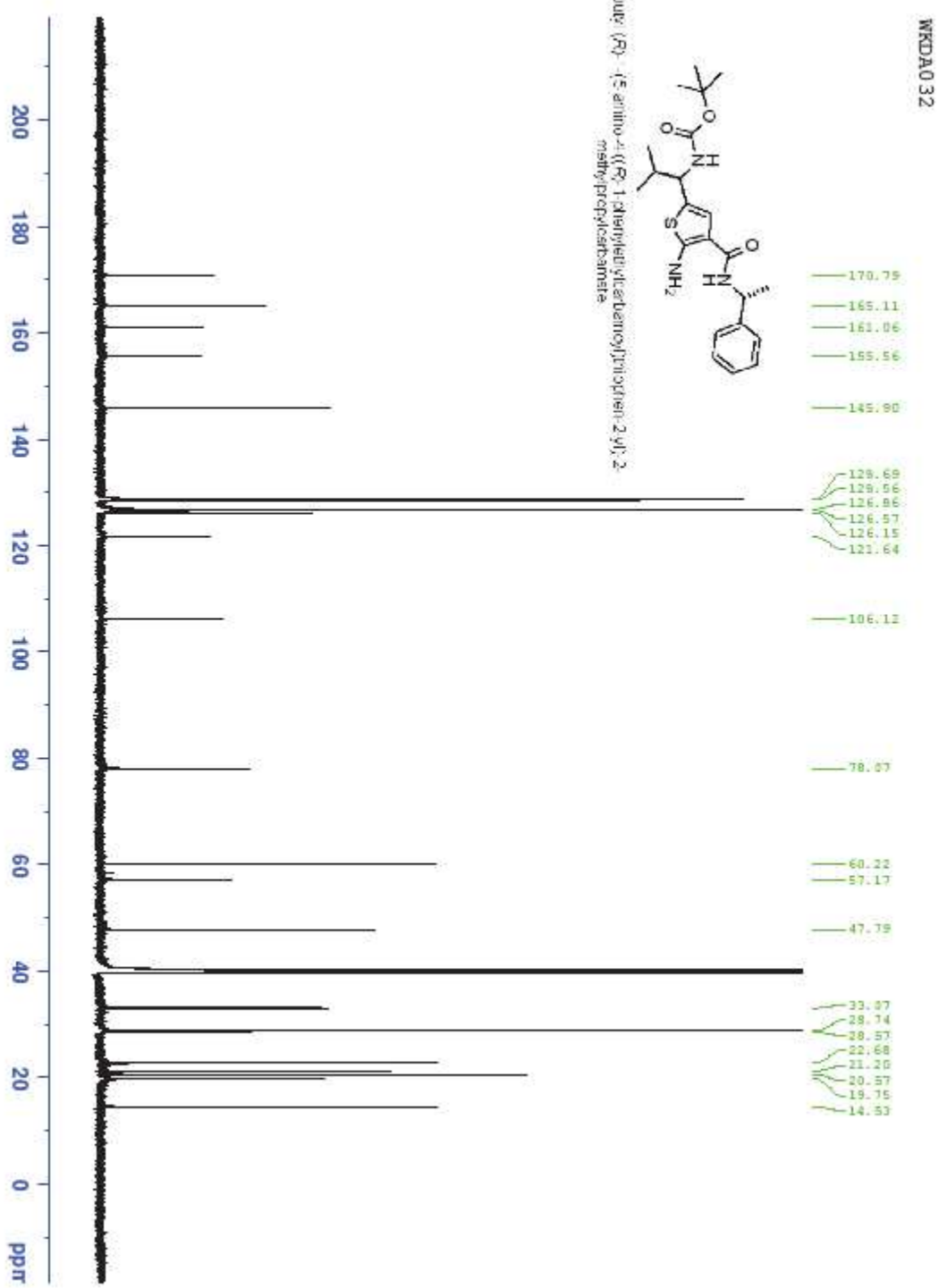
WK3-139



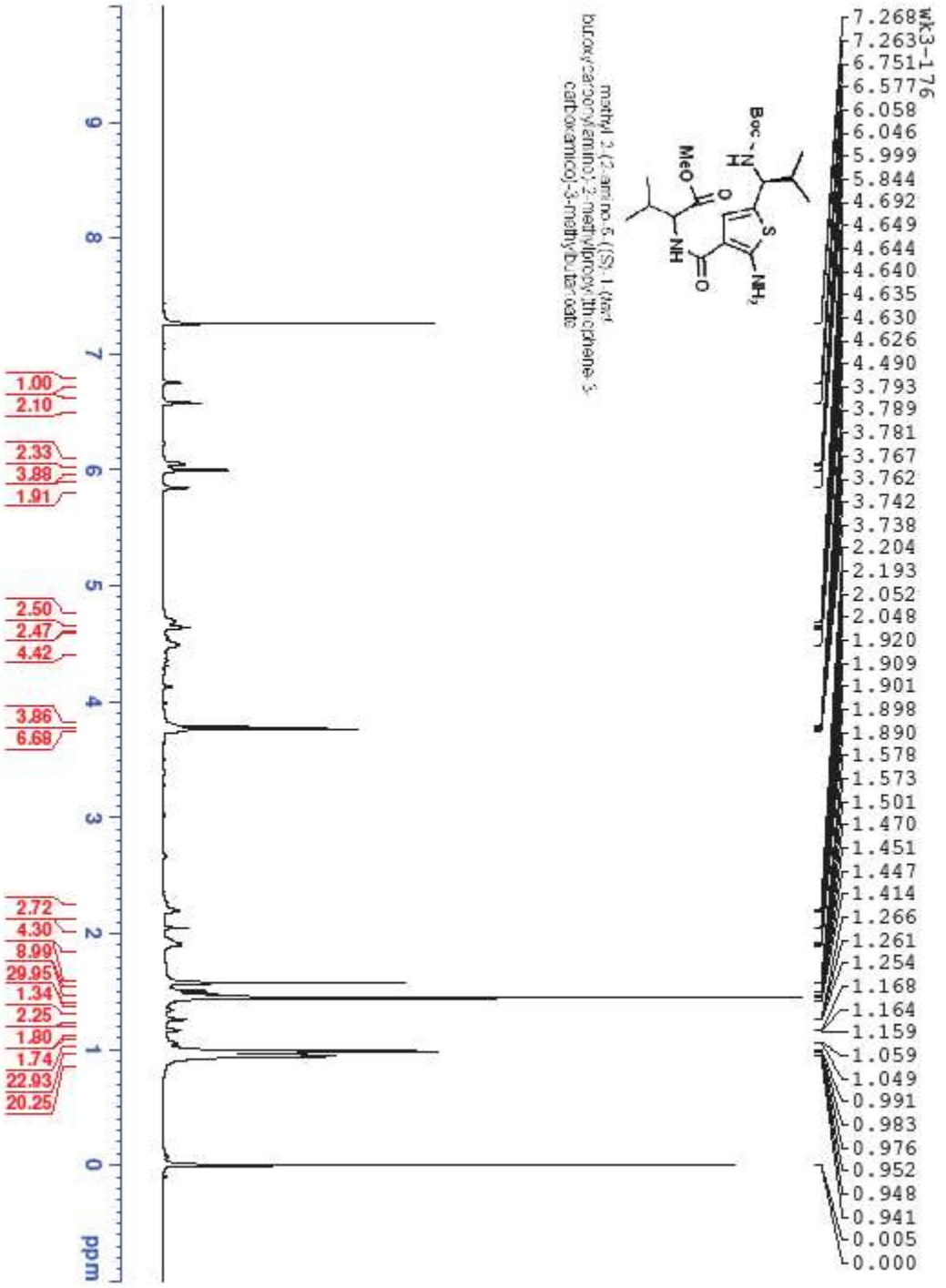

(*R*)-2-amino-*N*-(2-(dimethylamino)ethyl)-*N*-methyl-5-(2-methyl-1-pivalamidopropyl)thiophene-3-carboxamide

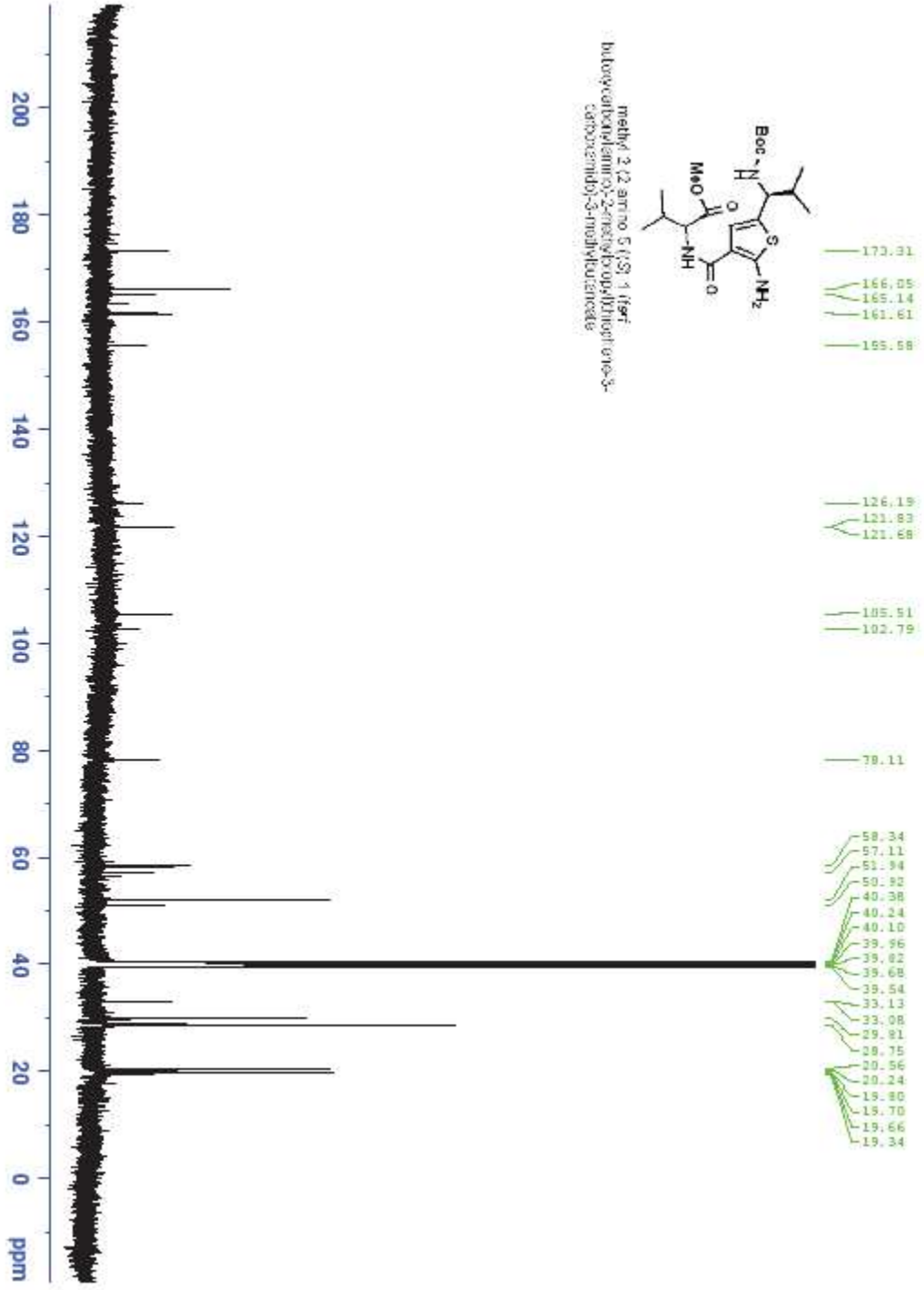
**C7,20**


WKDA032
7.915
7.902
7.362
7.349
7.314
7.302
7.289
7.209
7.197
7.185
7.165
7.150
7.117
7.037
5.114
5.102
5.090
5.078
4.209
4.194
4.180
4.047
4.035
4.023
4.011
3.378
2.504
2.501
2.498
1.987
1.977
1.892
1.881
1.878
1.869
1.867
1.856
1.845
1.437
1.425
1.383
1.301
1.185
1.173
1.162
0.927
0.916
0.812
0.801
1.00
2.30
2.40
1.33
1.00
1.99
1.06
1.05
0.98
1.12
3.92
10.43
3.27
3.54
ppm

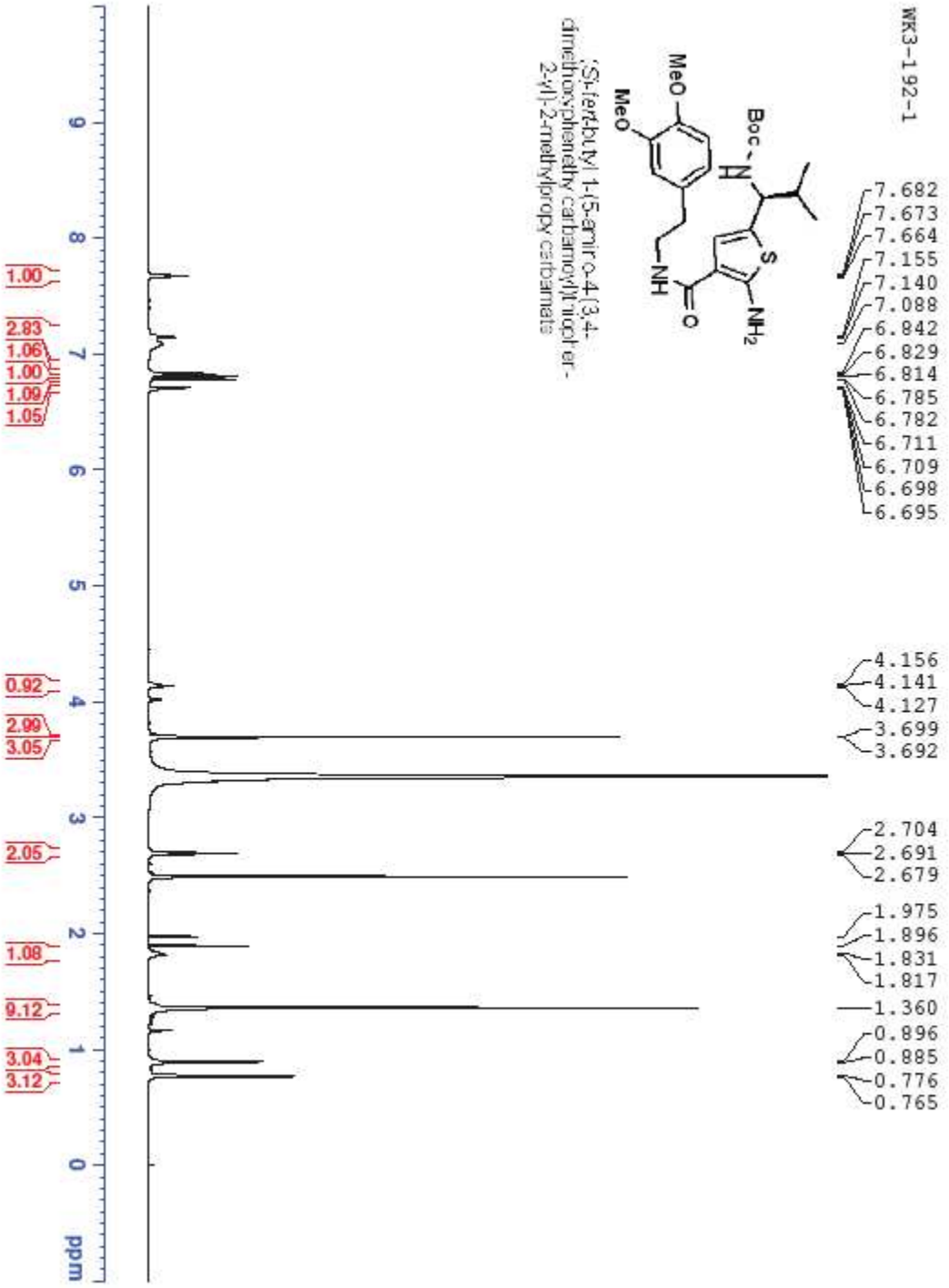

WKDA032
tert-butyl (R)-(5-amino-4-((R)-1-phenylethylcarbamoyl)thiophen-2-yl)-2-methylpropylcarbamate
170.79
165.11
161.06
155.56
145.90
129.69
129.56
126.86
126.57
126.15
121.64
106.12
78.07
60.22
57.17
47.79
33.07
28.74
28.57
22.68
21.20
20.57
19.75
14.53
200
180
160
140
120
100
80
60
40
20
0
ppm

**C7,23**

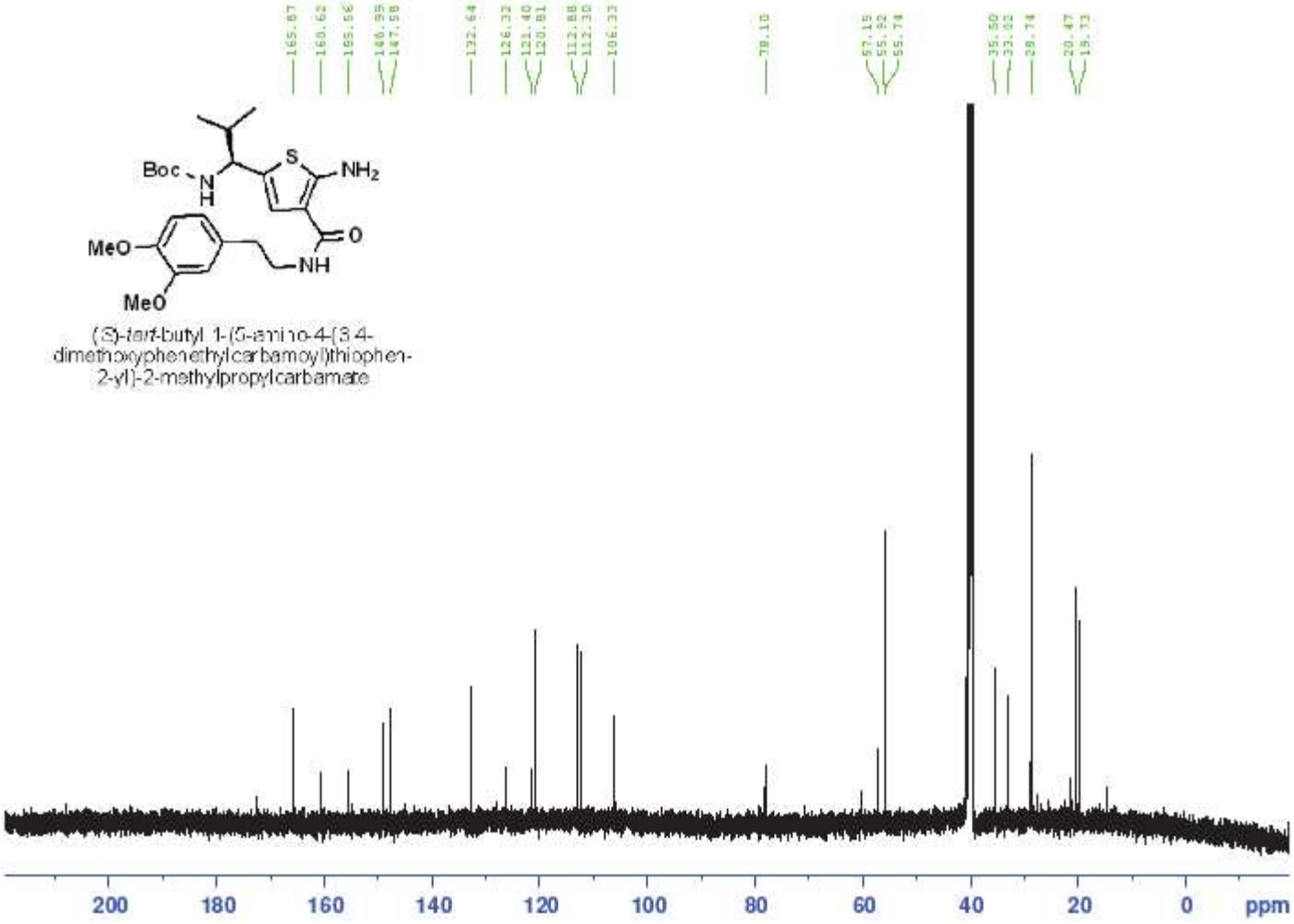

wk3-176
7.268
7.263
6.751
6.577
6.058
6.046
5.999
5.844
4.692
4.649
4.644
4.640
4.635
4.630
4.626
4.490
3.793
3.789
3.781
3.767
3.762
3.742
3.738
2.204
2.193
2.052
2.048
1.920
1.909
1.901
1.898
1.890
1.578
1.573
1.501
1.470
1.451
1.447
1.414
1.266
1.261
1.254
1.168
1.164
1.159
1.059
1.049
0.991
0.983
0.976
0.952
0.948
0.941
0.005
0.000
Boc
N
H
MeO
O
NH
O
S
NH2
methyl 2-[(2-amino-5-{(S)-1-[(tert-butoxycarbonyl)amino]-2-methylpropyl}thiophene-3-carboxamido)-3-methylbutanoate
1.00
2.10
2.33
3.88
1.91
2.50
2.47
4.42
3.86
6.68
2.72
4.30
8.99
29.95
1.34
2.25
1.80
1.74
22.93
20.25
9
8
7
6
5
4
3
2
1
0
ppm


methyl 2-(2-amino-5-((S)-1-((tert-butoxycarbonyl)amino)-2-methylpropyl)thiophene-3-carboxamido)-3-methylbutanoate
Boc
MeO
NH
NH2
S
O
173.31
166.05
165.14
161.61
155.58
126.19
121.83
121.68
105.51
102.79
78.11
58.34
57.11
51.94
50.92
40.38
40.24
40.10
39.96
39.82
39.68
39.54
33.13
33.08
29.81
28.75
20.56
20.24
19.80
19.70
19.66
19.34
200
180
160
140
120
100
80
60
40
20
0
ppm

**C7,24**

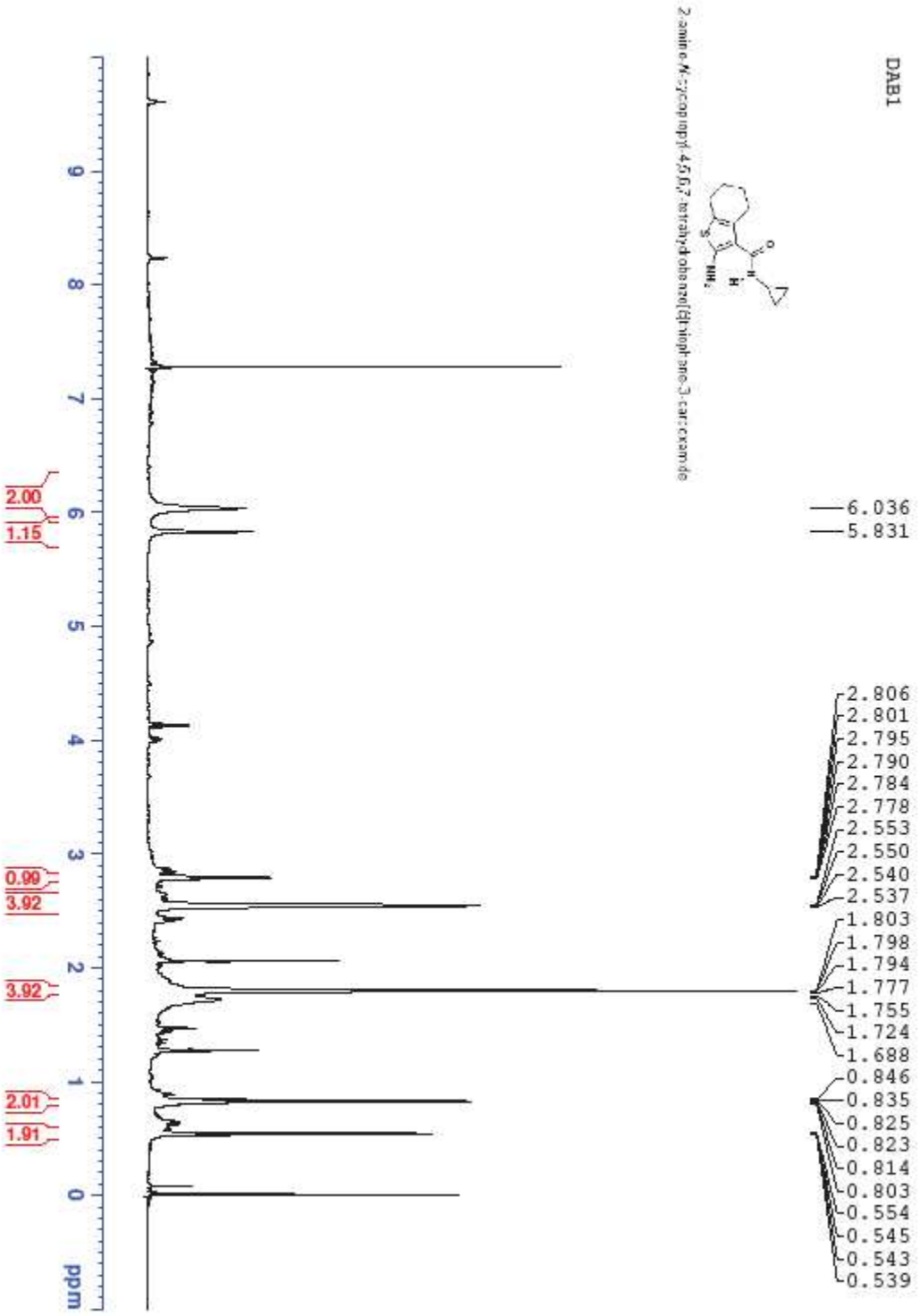

WK3-192-1
7.682
7.673
7.664
7.155
7.140
7.088
6.842
6.829
6.814
6.785
6.782
6.711
6.709
6.698
6.695
4.156
4.141
4.127
3.699
3.692
2.704
2.691
2.679
1.975
1.896
1.831
1.817
1.360
0.896
0.885
0.776
0.765
1.00
2.83
1.06
1.00
1.09
1.05
0.92
2.99
3.05
2.05
1.08
9.12
3.04
3.12
ppm
(S)-tert-butyl 1-(5-amino-4-(3,4-dimethoxyphenethylcarbamoyl)thiophen-2-yl)-2-methylpropylcarbamate
Boc
MeO
MeO
NH
S
NH2
O

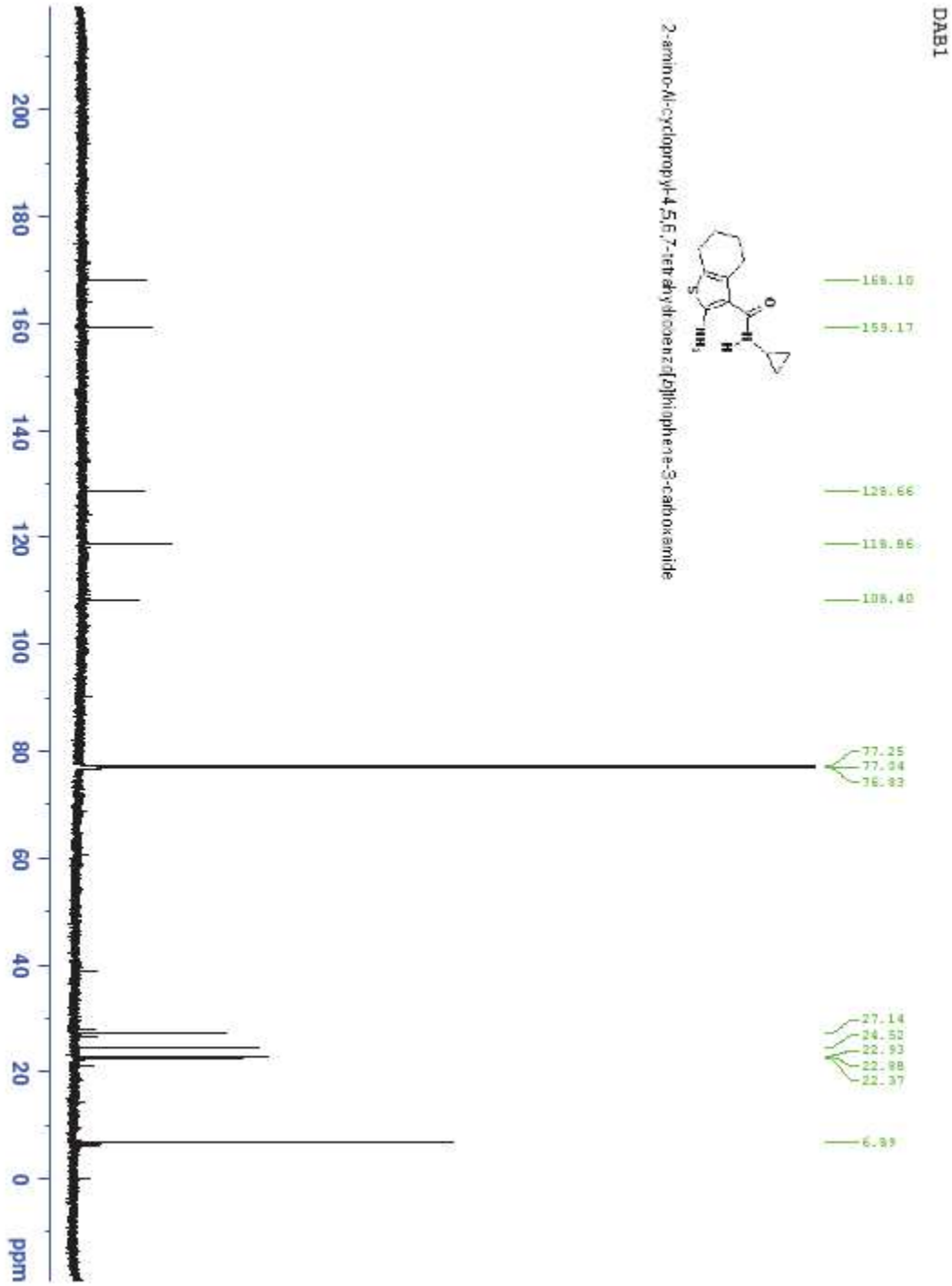
WK3-192-1



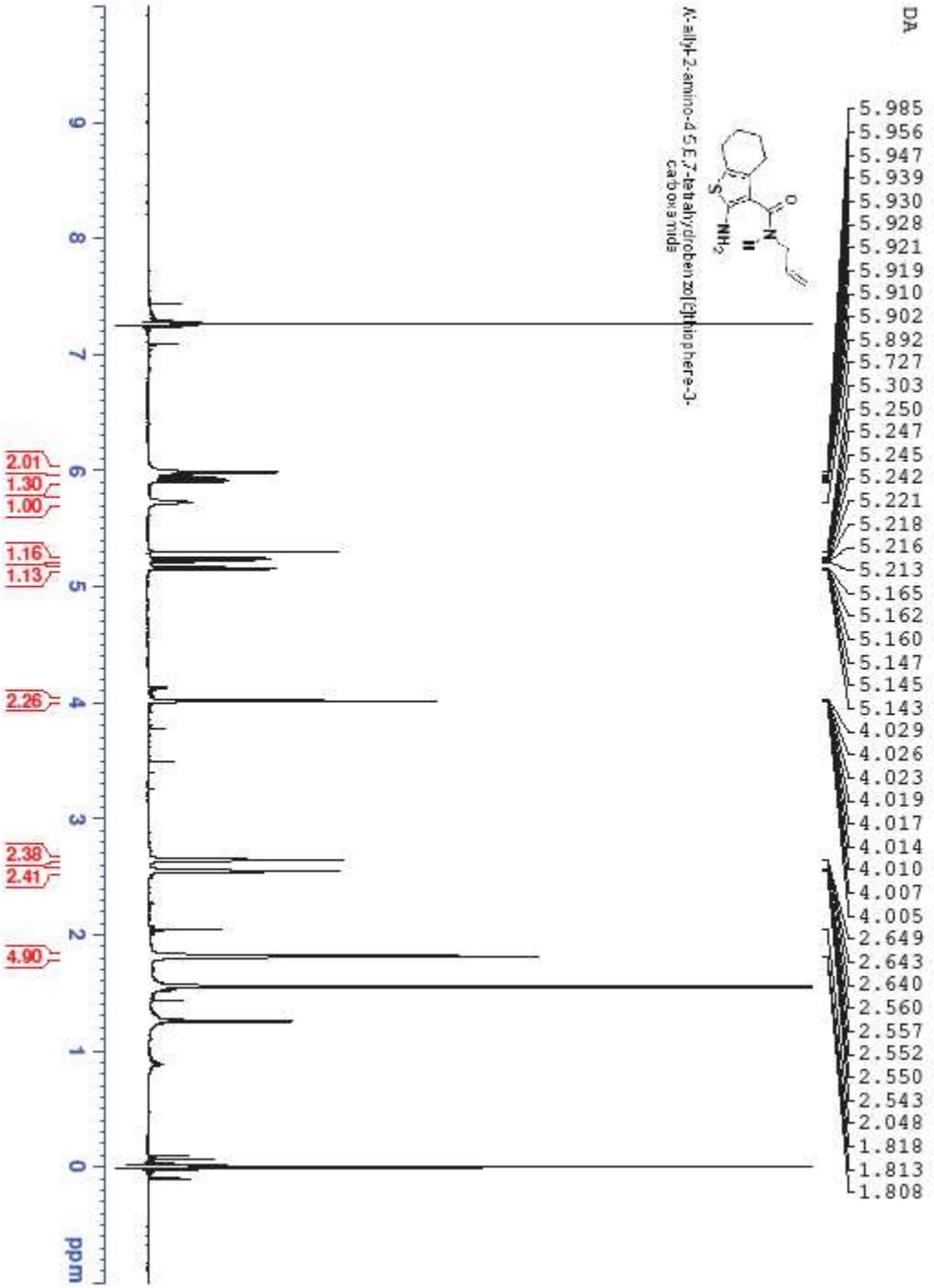

(S)-*tert*-butyl 1-(5-amino-4-(3,4-dimethoxyphenethylcarbamoyl)thiophen-2-yl)-2-methylpropylcarbamate

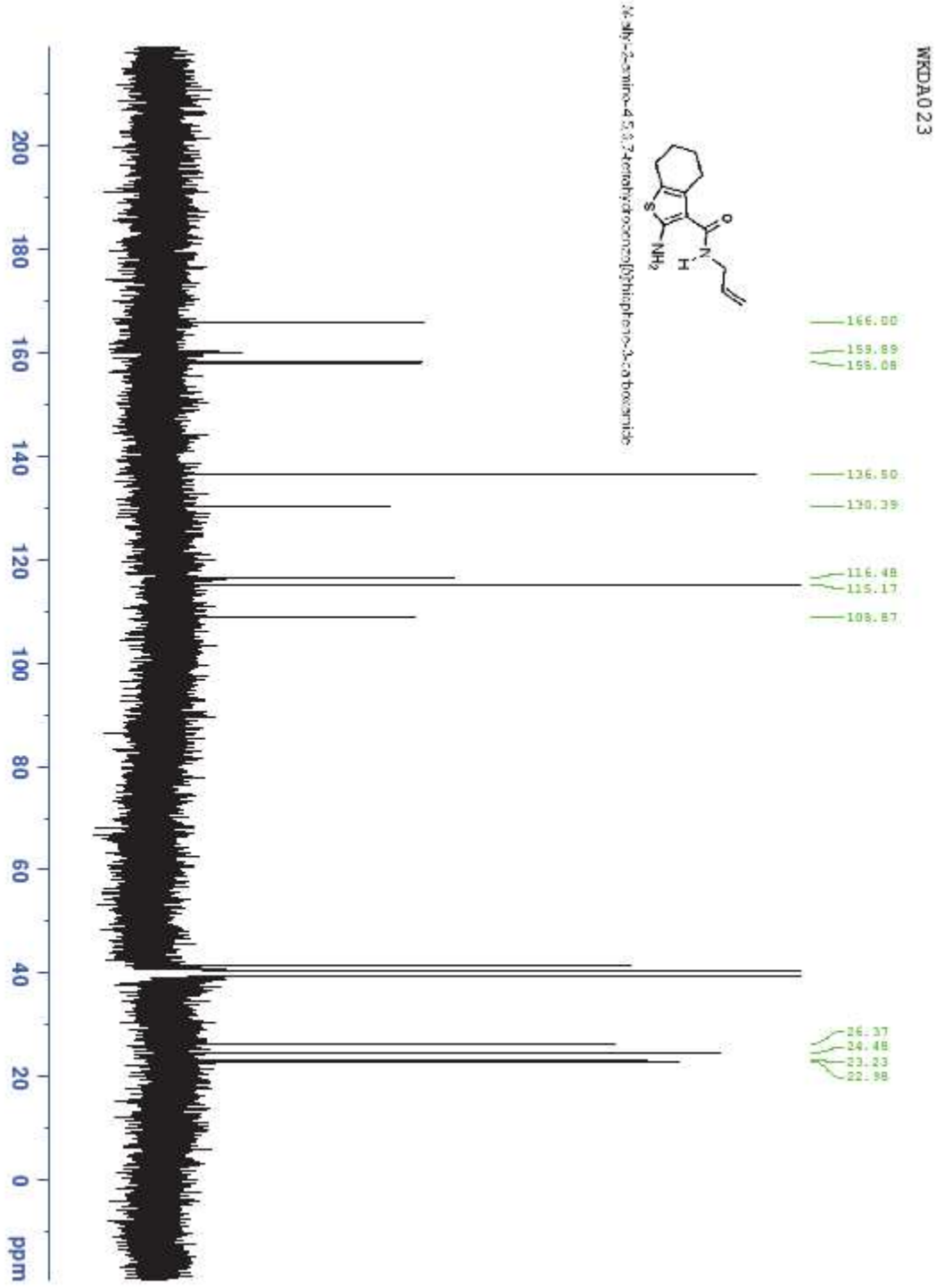
**C9,1**


DAB1
2-amino-N-cyclopropyl-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxamide
6.036
5.831
2.806
2.801
2.795
2.790
2.784
2.778
2.553
2.550
2.540
2.537
1.803
1.798
1.794
1.777
1.755
1.724
1.688
0.846
0.835
0.825
0.823
0.814
0.803
0.554
0.545
0.543
0.539
2.00
1.15
0.99
3.92
3.92
2.01
1.91
ppm

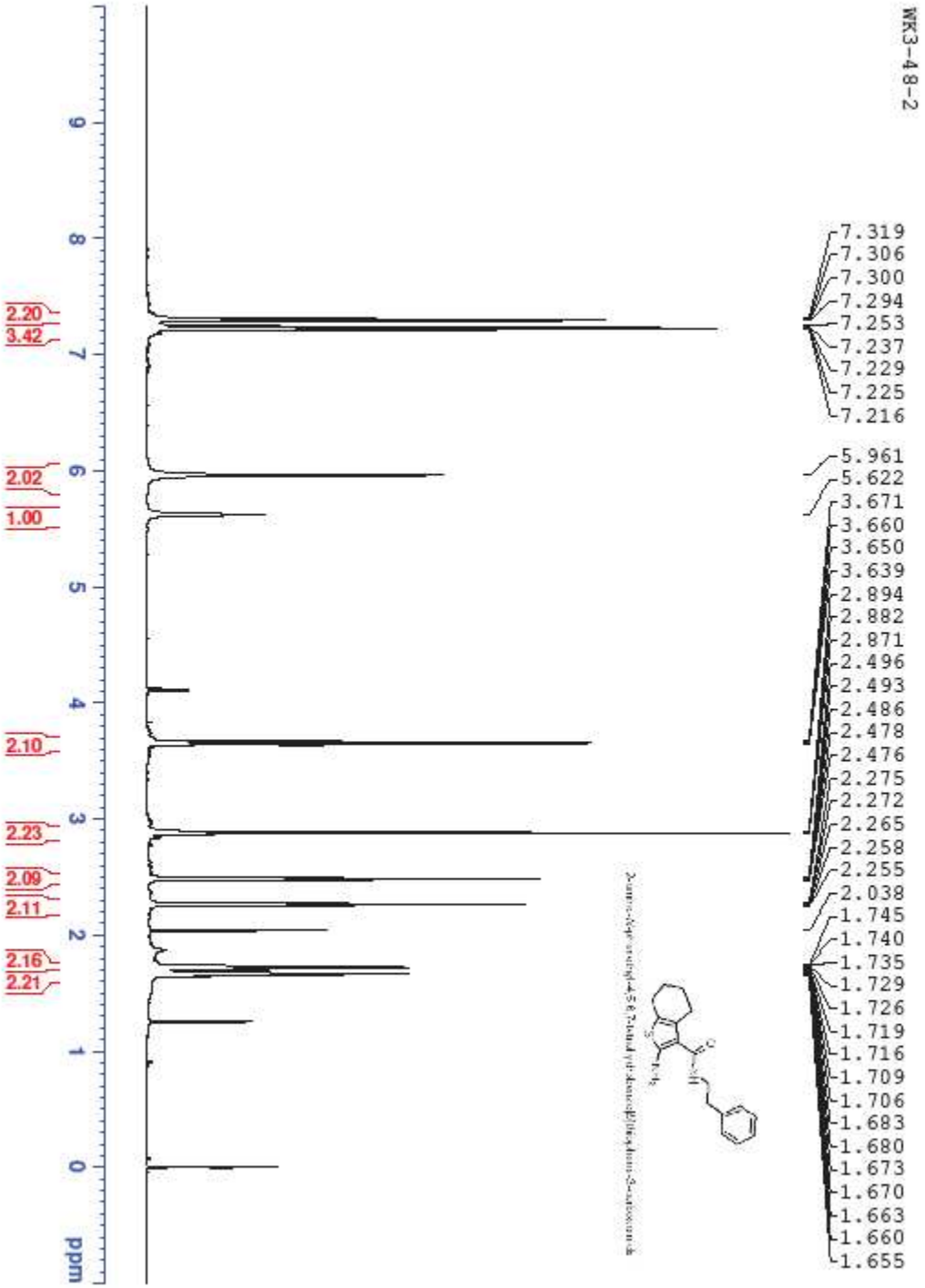

DAB1
2-amino-N-cyclopropyl-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxamide
169.10
159.17
128.66
119.86
108.40
77.25
77.04
76.83
27.14
24.52
22.93
22.88
22.37
6.89
200
180
160
140
120
100
80
60
40
20
0
ppm

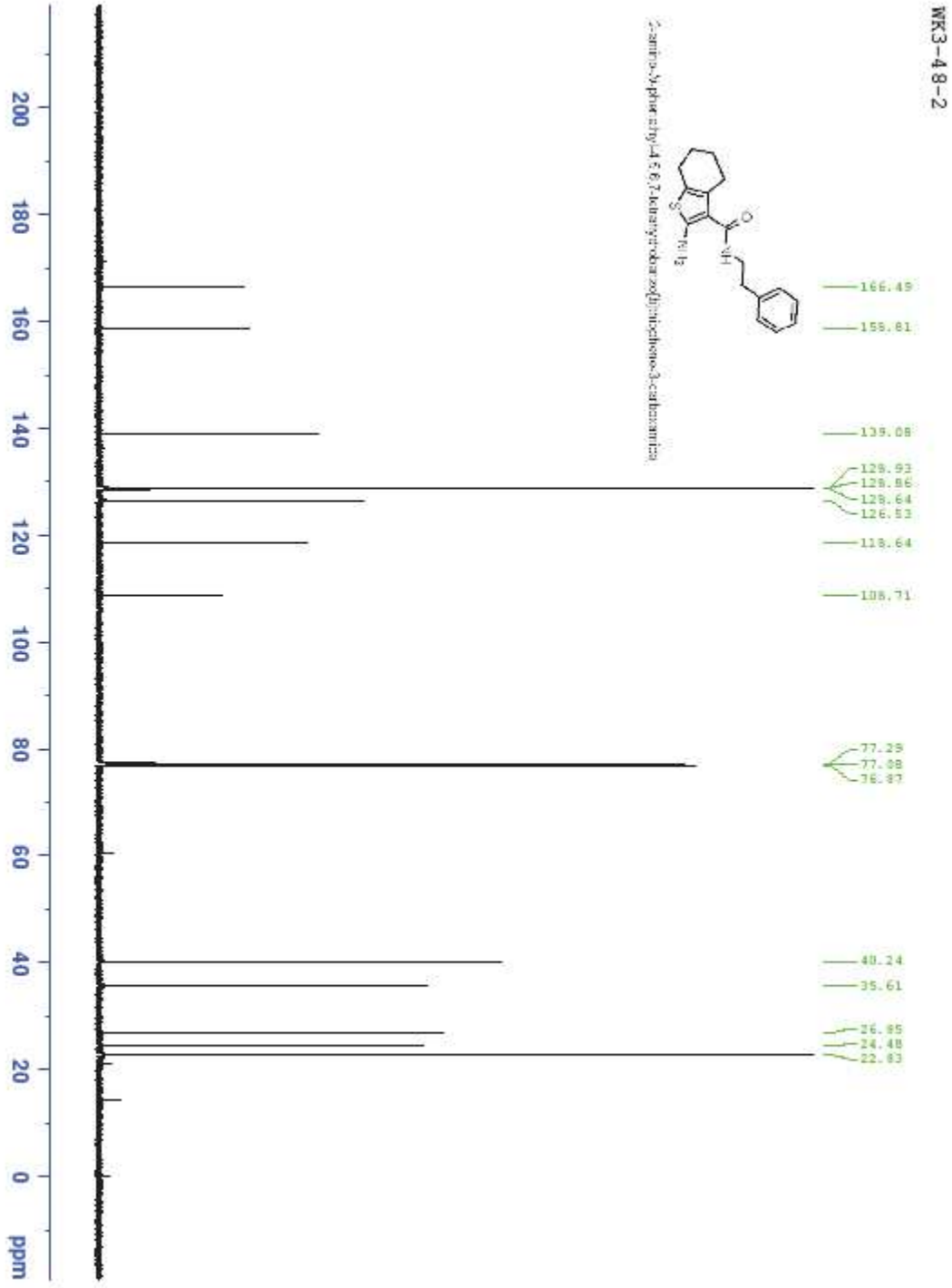
**C9,6**


DA
N-allyl-2-amino-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxamide
5.985
5.956
5.947
5.939
5.930
5.928
5.921
5.919
5.910
5.902
5.892
5.727
5.303
5.250
5.247
5.245
5.242
5.221
5.218
5.216
5.213
5.165
5.162
5.160
5.147
5.145
5.143
4.029
4.026
4.023
4.019
4.017
4.014
4.010
4.007
4.005
2.649
2.643
2.640
2.560
2.557
2.552
2.550
2.543
2.048
1.818
1.813
1.808
2.01
1.30
1.00
1.16
1.13
2.26
2.38
2.41
4.90
ppm

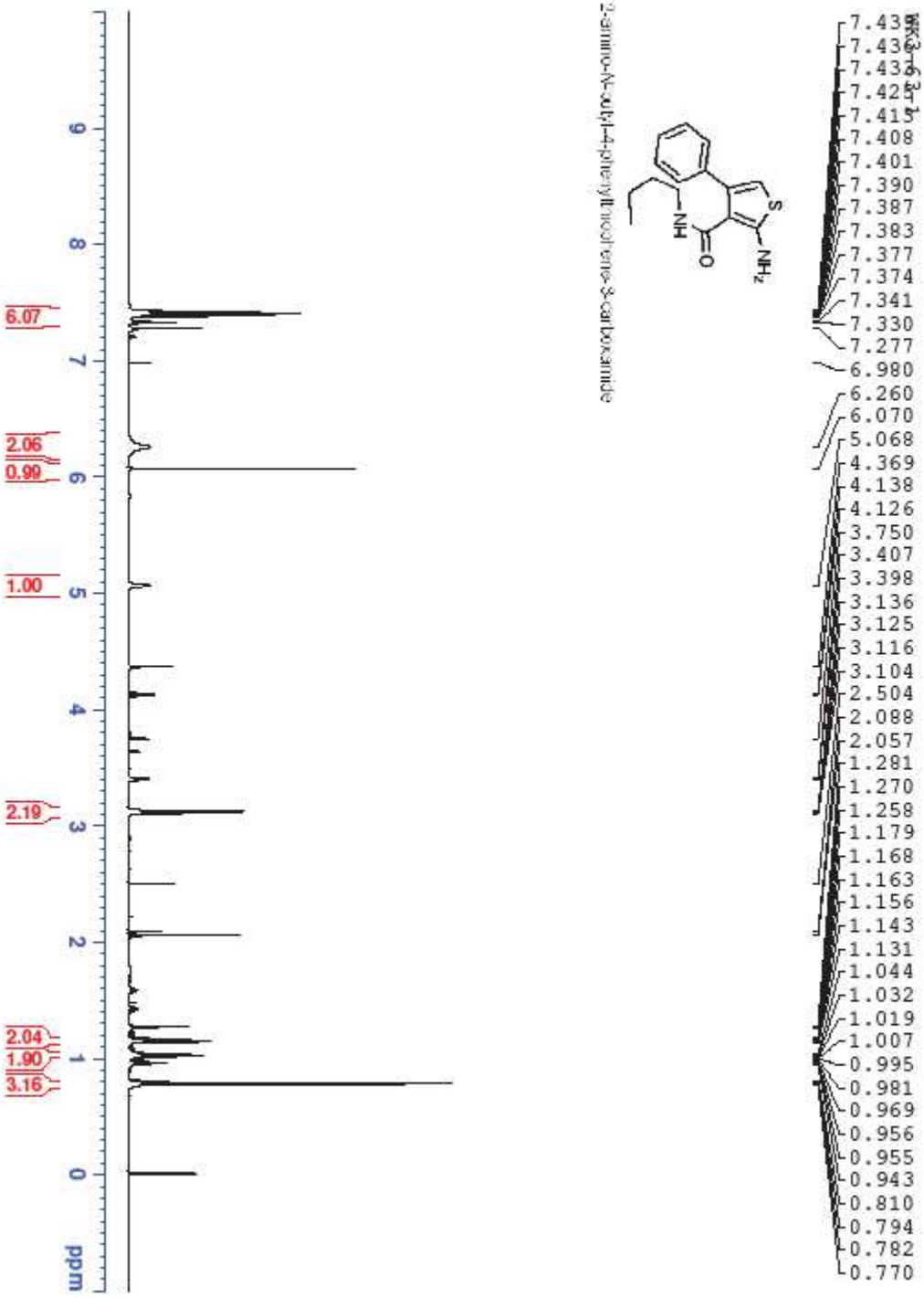

WKDA023
166.00
159.89
158.08
136.50
130.39
116.48
115.17
108.87
26.37
24.48
23.23
22.98
200
180
160
140
120
100
80
60
40
20
0
ppm

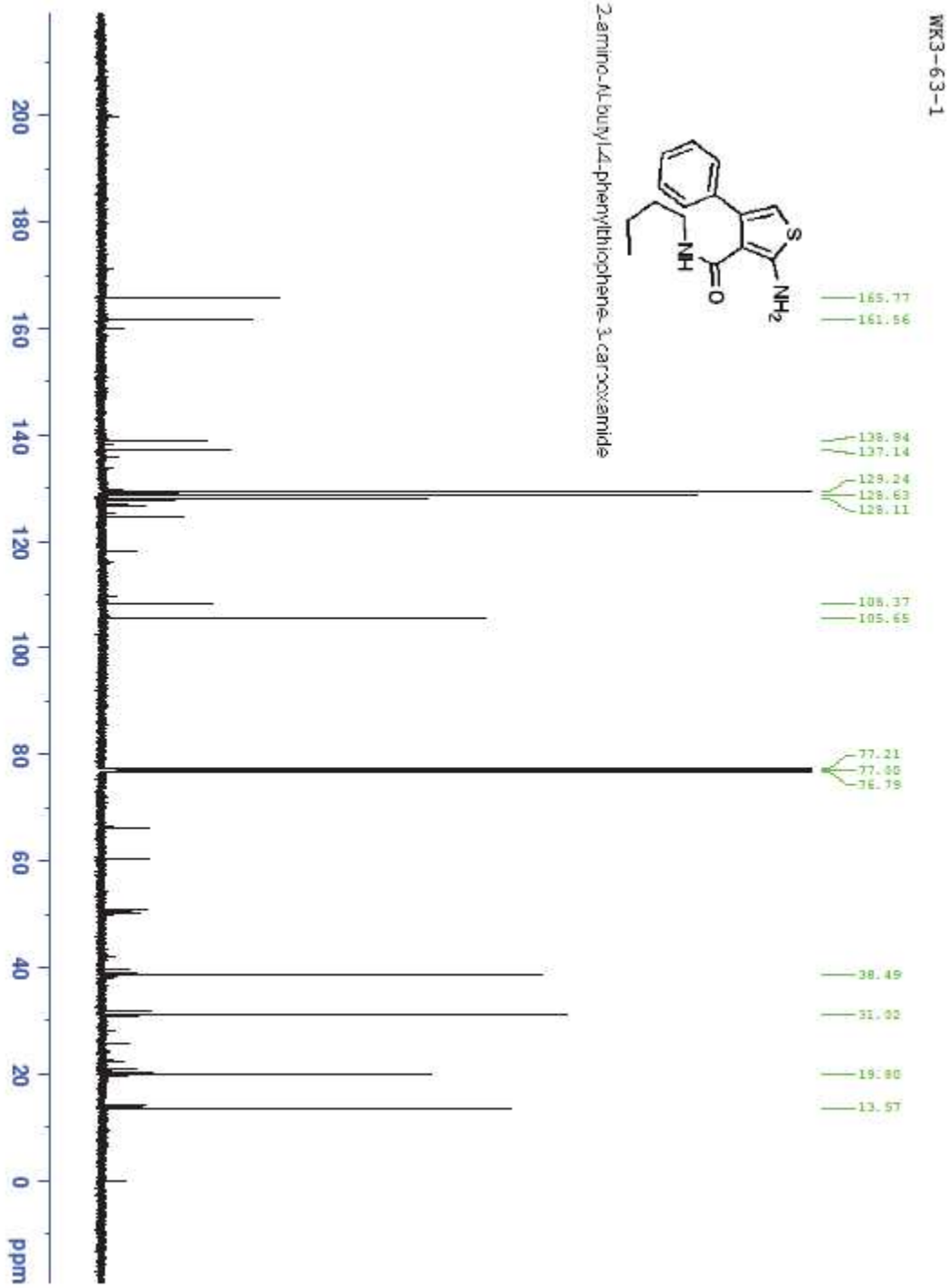
**C9,11**


WK3-48-2
7.319
7.306
7.300
7.294
7.253
7.237
7.229
7.225
7.216
5.961
5.622
3.671
3.660
3.650
3.639
2.894
2.882
2.871
2.496
2.493
2.486
2.478
2.476
2.275
2.272
2.265
2.258
2.255
2.038
1.745
1.740
1.735
1.729
1.726
1.719
1.716
1.709
1.706
1.683
1.680
1.673
1.670
1.663
1.660
1.655
2.20
3.42
2.02
1.00
2.10
2.23
2.09
2.11
2.16
2.21
ppm


WK3-48-2
2-amino-N-phenethyl-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxamide
166.49
159.81
139.08
129.93
129.86
129.64
126.53
118.64
108.71
77.29
77.08
76.87
40.24
35.61
26.85
24.48
22.83
200
180
160
140
120
100
80
60
40
20
0
ppm

**C10,3**


6.07
2.06
0.99
1.00
2.19
2.04
1.90
3.16
ppm
2-amino-N-butyl-4-phenylthiophene-3-carboxamide
NH
O
S
NH2
7.435
7.436
7.432
7.425
7.415
7.408
7.401
7.390
7.387
7.383
7.377
7.374
7.341
7.330
7.277
6.980
6.260
6.070
5.068
4.369
4.138
4.126
3.750
3.407
3.398
3.136
3.125
3.116
3.104
2.504
2.088
2.057
1.281
1.270
1.258
1.179
1.168
1.163
1.156
1.143
1.131
1.044
1.032
1.019
1.007
0.995
0.981
0.969
0.956
0.955
0.943
0.810
0.794
0.782
0.770


WK3-63-1
2-amino-N-butyl-4-phenylthiophene-3-carboxamide
S
NH
O
NH2
165.77
161.56
138.94
137.14
129.24
128.63
128.11
108.37
105.65
77.21
77.00
76.79
38.49
31.02
19.80
13.57
200
180
160
140
120
100
80
60
40
20
0
ppm