

Evaluation of the inhibitory effects of pyridylpyrazole derivatives on LPS-induced nitric oxide and PGE₂ productions in murine RAW 264.7 macrophages

Mahmoud M. Gamal El-Din¹ , Mohammed I. El-Gamal^{2,3,4}, Young-Do Kwon^{5,6}, Su-Yeon Kim^{7,8}, Hee-Soo Han^{7,8} , Sang-Eun Park^{7,8}, Chang-Hyun Oh⁹ , Kyung-Tae Lee^{7,8*} and Hee-Kwon Kim^{5,6,*}.

¹ Pharmaceutical and Drug Industries Research Division, National Research Centre, Dokki-Giza, 12622, Egypt

² Department of Medicinal Chemistry, College of Pharmacy, University of Sharjah, Sharjah 27272, United Arab Emirates

³ Sharjah Institute for Medical Research, University of Sharjah, Sharjah 27272, United Arab Emirates

⁴ Department of Medicinal Chemistry, Faculty of Pharmacy, Mansoura University, Mansoura 35516, Egypt

⁵ Department of Nuclear Medicine, Molecular Imaging & Therapeutic Medicine Research Center, Jeonbuk National University Medical School and Hospital, 20 Geonji-ro, Deokjin-gu, Jeonju 54907, Republic of Korea

⁶ Research Institute of Clinical Medicine of Jeonbuk National University-Biomedical Research Institute of Jeonbuk National University Hospital, 20 Geonji-ro, Deokjin-gu, Jeonju 54907, Republic of Korea

⁷ Department of Pharmaceutical Biochemistry, Kyung Hee University, Seoul 02447, Republic of Korea

⁸ Department of Life and Nanopharmaceutical Sciences, Graduate School, Kyung Hee University, 26, Kyungheedaero, Seoul 02447, Republic of Korea

⁹ Center for Biomaterials, Korea Institute of Science and Technology, PO Box 131, Cheongryang, Seoul 130-650, Republic of Korea

* Corresponding author: Tel.: +82 63 250 2768; fax: +82 63 255 1172; E-mail address: hkkim717@jbnu.ac.kr .
Address: Department of Nuclear Medicine, Molecular Imaging & Therapeutic Medicine Research Center, Jeonbuk National University Medical School and Hospital, 20 Geonji-ro, Deokjin-gu, Jeonju 54907, Republic of Korea.

* Corresponding author: Tel.: +82 2 961 0860; fax: +82 2 961 9580; E-mail address ktlee@khu.ac.kr
. Address: Department of Pharmaceutical Biochemistry, Kyung Hee University, Seoul 02447, Republic of Korea.

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Synthetic procedures

2-Chloro-N-(3-(3-(4-chloro-3-methoxyphenyl)-4-(pyridin-4-yl)-1H-pyrazol-1-yl)phenyl)-acetamide (9a) or *3-chloro-N-(3-(3-(4-chloro-3-methoxyphenyl)-4-(pyridin-4-yl)-1H-pyrazol-1-yl)phenyl)propanamide (9b)*

To a cooled solution of compound **8** (0.5 g, 1.325 mmol) in anhydrous methylene chloride (15 mL) at -10 °C, triethylamine (148 mg, 1.4575 mmol) was added dropwise within 5 minutes then either chloroacetyl chloride or chloropropionyl chloride were added dropwise keeping the reaction mixture temperature at -10 °C for another 5 minutes. To the reaction mixture, water (15 mL) was added, then reaction mixture was swirled then the organic layer was separated. The water layer was further extracted with methylene chloride once again. The combined organic layers were combined, washed with brine and dried using anhydrous Na₂SO₄. Then evaporated under reduced pressure to give the target compounds that were used in the next step without further purification with yield 65%.

N-(3-(3-(4-Chloro-3-methoxyphenyl)-4-(pyridin-4-yl)-1H-pyrazol-1-yl)phenyl)-2-(piperidin-1-yl)acetamide (1a)

To a solution of **9a** (100 mg, 0.175 mmol) in anhydrous methylene chloride (5 mL), triethylamine (20 mg, 0.193 mmol) was added at 0 °C, stirred for 15 min, then morpholine (18.3 mg, 0.21 mmol) was added dropwise. The reaction mixture was stirred for 24 hours at r.t. Upon completion of the reaction, the mixture was dried and then was partitioned between ethyl acetate and aqueous phase. Followed by separation of the organic layer and extraction of the aqueous layer with organic solvent (3x10 mL) was repeated. The collected organic layers were washed with NaCl solution (5%) and the organic solvent was evaporated under vacuum. The residue was purified using column chromatography (silica gel, hexane:ethyl acetate 4:1 v/v) to give the required product as a yellow oil. Yield: 55%; ¹H NMR (400 MHz, CDCl₃) δ 8.48 (d, 2H, *J* = 4.8 Hz, pyridyl protons), 8.14 (s, 1H, pyrazolyl-H), 7.45 (d, 2H, *J* = 4.8 Hz, pyridyl protons), 7.39 (d, 1H, *J* = 8.0 Hz, Ph), 7.38 (t, 1H, *J* = 8.0 Hz, Ph), 7.28 (d, 1H, *J* = 8.0 Hz, Ph), 7.19-7.18 (m, 2H, Ph), 7.07 (brs, 1H, NH), 7.01 (dd, 1H, *J* = 2.0, 8.0 Hz, Ph), 3.74 (s, 3H, OCH₃), 3.22 (s, 2H, COCH₂N), 2.65 (brs, 4H, piperidinyl protons, 2',6'), 1.67 (t, 4H, *J* = 5.2 Hz, piperidinyl protons,

3',5'), 1.47 (brs, 2H, piperidiny l protons, 4'); ¹³C NMR (100 MHz, CDCl₃) δ 170.6 (C=O), 154.9, 150.0, 139.6, 139.3, 138.9, 132.1, 130.3, 130.1, 127.6, 122.9, 122.8, 121.5, 120.3, 117.9, 114.9, 112.3, 110.2 [Ar-C], 62.2 (COCH₂N), 56.3 (OCH₃), 55.2 (piperidiny l carbons, 2',6'), 25.7 (piperidiny l carbons, 3',5'), 23.2 (piperidiny l carbon, 4'); MS m/z: 502.43 [M+H]⁺.

Compounds **1b-g** were synthesized from **9a** and appropriate amine derivatives as reported in the synthesis of **1a**.

N-(3-(3-(4-Chloro-3-methoxyphenyl)-4-(pyridin-4-yl)-1H-pyrazol-1-yl)phenyl)-2-morpholino-acetamide (**1b**)

Yellow oil; yield: 46%; ¹H NMR (400 MHz, CDCl₃) δ 9.33 (brs, 1H, NH), 8.56 (d, 2H, *J* = 4.8 Hz, pyridyl protons), 8.03 (s, 1H, pyrazolyl-H), 7.57 (d, 1H, *J* = 7.6 Hz, Ph), 7.51-7.45 (m, 2H, pyridyl protons), 7.36 (d, 1H, *J* = 8.4 Hz, Ph), 7.29-7.27 (m, 2H, Ph), 7.14 (s, 1H, Ph), 7.09 (d, 1H, *J* = 8.0 Hz, Ph), 3.80 (m, 7H, OCH₃ and morpholino-4H), 3.23 (s, 2H, COCH₂N), 2.69-2.67 (m, 4H, morpholino-4H); ¹³C NMR (100 MHz, CDCl₃) δ 168.1 (C=O), 154.6, 150.1, 149.7, 140.8, 139.9, 138.7, 132.2, 130.5, 130.2, 127.6, 122.9, 122.8, 121.2, 117.9, 114.9, 112.3, 110.2 [Ar-C], 66.9 (morpholino CH₂OCH₂), 62.4 (COCH₂N), 56.1 (OCH₃), 50.8 (morpholino CH₂NCH₂); MS m/z: 504.1 [M+H]⁺.

N-(3-(3-(4-Chloro-3-methoxyphenyl)-4-(pyridin-4-yl)-1H-pyrazol-1-yl)phenyl)-2-(4-methyl-piperazin-1-yl)acetamide (**1c**)

Yellow oil; yield: 48%; ¹H NMR (400 MHz, CDCl₃) δ 9.28 (brs, 1H, NH), 8.58 (s, 2H, pyridyl protons), 8.13-8.10 (m, 2H, pyrazolyl-H and Ph), 7.59-7.56 (m, 2H, pyridyl protons), 7.46 (t, 1H, *J* = 8.0 Hz, Ph), 7.38 (d, 1H, *J* = 8.0 Hz, Ph), 7.29-7.27 (m, 2H, Ph), 7.15-7.08 (m, 2H, Ph), 3.83 (s, 3H, OCH₃), 3.31 (s, 2H, COCH₂N), 2.94-2.60 (m, 8H, piperazinyl protons), 1.28 (s, 3H, N-CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 170.0 (C=O), 154.9, 149.9, 149.7, 140.6, 139.9, 139.8, 132.3, 130.2, 130.0, 127.6, 122.8, 122.6, 121.4, 120.0, 117.5, 114.2, 112.3, 110.2 [Ar-C], 62.7 (COCH₂N), 56.0 (OCH₃), 55.1 (piperazinyl carbons), 45.8 (N-CH₃); MS m/z: 517.42 [M+H]⁺.

N-(3-(3-(4-Chloro-3-methoxyphenyl)-4-(pyridin-4-yl)-1*H*-pyrazol-1-yl)phenyl)-2-(4-ethylpiperazin-1-yl)acetamide (**1d**)

Yellow oil; yield: 49%; ¹H NMR (400 MHz, CDCl₃) δ 9.29 (brs, 1H, NH), 8.58 (brs, 2H, pyridyl protons), 8.22-8.15 (m, 2H, pyrazolyl-H and Ph), 7.59-7.55 (m, 2H, pyridyl protons), 7.48 (t, 1H, *J* = 8.0 Hz, Ph), 7.38 (d, 1H, *J* = 8.0 Hz, Ph), 7.16-7.08 (m, 4H, Ph), 3.83 (m, 3H, OCH₃), 3.27 (s, 2H, COCH₂N), 2.83-2.50 (m, 10H, piperazinyl protons and CH₂CH₃), 1.25 (t, 3H, *J* = 7.6 Hz, CH₂CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 169.0 (C=O), 155.0, 150.1, 149.9, 139.9, 139.3, 138.9, 132.1, 130.3, 130.0, 127.6, 127.5, 122.5, 122.3, 122.1, 121.5, 121.4, 120.3, 117.9, 114.8, 114.7, 112.3, 110.2 [Ar-C], 61.7 (COCH₂N), 56.1 (OCH₃), 52.4 (piperazinyl carbons), 52.2 (piperazinyl carbons and CH₂CH₃), 29.7 (CH₂CH₃); MS *m/z*: 531.0 [M+H]⁺.

N-(3-(3-(4-Chloro-3-methoxyphenyl)-4-(pyridin-4-yl)-1*H*-pyrazol-1-yl)phenyl)-2-(4-phenylpiperazin-1-yl)acetamide (**1e**)

Yellow oil; yield: 60%; ¹H NMR (400 MHz, CDCl₃) δ 8.48 (d, 1H, *J* = 4.8 Hz, pyridyl protons), 8.13 (s, 1H, pyrazolyl-H), 7.63 (brs, 1H, NH), 7.51-7.32 (m, 3H, pyridyl protons and Ph), 7.32-7.18 (m, 6H, Ph), 7.06 (s, 1H, Ph), 6.98 (d, 1H, *J* = 8.0 Hz, Ph), 6.88-6.83 (m, 3H, Ph), 3.71 (s, 3H, OCH₃), 3.25-3.24 (m, 4H, piperazinyl protons), 2.81 (s, 2H, COCH₂N), 2.45-2.30 (m, 4H, piperazinyl protons); MS *m/z*: 578.9 [M+H]⁺.

2-(4-Benzylpiperazin-1-yl)-*N*-(3-(3-(4-chloro-3-methoxyphenyl)-4-(pyridin-4-yl)-1*H*-pyrazol-1-yl)phenyl)acetamide (**1f**)

Yellow oil; yield: 65%; ¹H NMR (400 MHz, CDCl₃) δ 8.57 (d, 2H, *J* = 5.6 Hz, pyridyl protons), 8.38 (brs, 1H, NH), 8.18 (s, 1H, pyrazolyl-H), 7.78-7.75 (m, 3H, Ph), 7.59-7.53 (m, 3H, Ph), 7.45-7.32 (m, 6H, Ph), 7.14-7.07 (m, 2H, Ph), 3.84 (s, 3H, OCH₃), 3.31 (s, 2H, benzyl-CH₂), 3.10 (brs, 4H, piperazinyl protons and COCH₂N), 2.36 (brs, 4H, piperazinyl protons), 2.32 (brs, 2H, piperazinyl protons); MS *m/z*: 592.9 [M+H]⁺.

Compounds **1g-m** were prepared from **9b** and appropriate acid chloride as reported in the synthesis of **1a**

N-(3-(3-(4-Chloro-3-methoxyphenyl)-4-(pyridin-4-yl)-1*H*-pyrazol-1-yl)phenyl)-3-(piperidin-1-yl)propanamide (**1g**)

Yellow oil; yield: 62%; ¹H NMR (400 MHz, CDCl₃) δ 8.59 (brs, 1H, NH), 8.36 (s, 1H, Ph), 8.19 (s, 1H, pyrazolyl-H), 7.57 (d, 1H, *J* = 8.0 Hz, pyridyl protons), 7.44 (t, 1H, *J* = 8.0 Hz, Ph), 7.36 (d, 2H, *J* = 8.0 Hz, pyridyl protons), 7.32-7.29 (m, 3H, Ph), 7.17 (s, 1H, Ph), 7.10 (d, 1H, *J* = 7.6 Hz, Ph), 3.83 (s, 3H, OCH₃), 2.84-2.67 (m, 6H, N-CH₂ and piperidinyl protons), 1.79-1.28 (m, 8H, COCH₂ and piperidinyl protons); ¹³C NMR (100 MHz, CDCl₃) δ 170.7 (C=O), 154.9, 150.1, 149.9, 149.8, 140.1, 139.9, 132.6, 130.5, 130.2, 129.6, 127.6, 122.7, 120.5, 120.2, 117.7, 114.9, 112.2, 110.2 [Ar-C], 56.1 (OCH₃), 54.1 (piperidinyl CH₂NCH₂), 53.6 (CH₂CH₂CO), 32.6 (CH₂CH₂CO), 25.7 (piperidinyl 3', 4', 5'-carbons); MS *m/z*: 516.21 [M+H]⁺.

N-(3-(3-(4-Chloro-3-methoxyphenyl)-4-(pyridin-4-yl)-1*H*-pyrazol-1-yl)phenyl)-3-morpholino-propanamide (**1h**)

Yellow oil; yield: 58%; ¹H NMR (400 MHz, CDCl₃) δ 9.33 (brs, 1H, NH), 8.56 (d, 2H, *J* = 4.8 Hz, pyridyl protons), 8.03 (s, 1H, pyrazolyl-H), 7.57 (d, 1H, *J* = 7.6 Hz, pyridyl protons), 7.51-7.45 (m, 2H, Ph), 7.46 (d, 1H, *J* = 8.4 Hz, Ph), 7.29-7.27 (m, 2H, Ph), 7.16 (s, 1H, Ph), 7.07 (d, 1H, *J* = 8.0 Hz, Ph), 3.83-3.75 (m, 9H, OCH₃, morpholino protons, and CH₂CH₂CO), 3.23 (s, 2H, CH₂CH₂CO), 2.69-2.67 (m, 4H, morpholino protons); ¹³C NMR (100 MHz, CDCl₃) δ 168.1 (C=O), 154.6, 150.1, 149.7, 140.8, 139.9, 138.7, 132.2, 130.5, 130.2, 127.6, 122.9, 122.8, 122.2, 117.9, 114.9, 112.3, 110.2 [Ar-C], 66.9 (morpholino CH₂OCH₂), 62.4 (morpholino CH₂NCH₂), 56.1 (OCH₃), 50.8 (CH₂CH₂CO), 25.2 (CH₂CH₂CO); MS *m/z*: 518.43 [M+H]⁺.

N-(3-(3-(4-Chloro-3-methoxyphenyl)-4-(pyridin-4-yl)-1*H*-pyrazol-1-yl)phenyl)-3-(4-methyl-piperazin-1-yl)propanamide (**1i**)

Yellow oil; yield: 56%; ¹H NMR (400 MHz, CDCl₃) δ 8.49 (d, 2H, *J* = 6.4 Hz, pyridyl protons), 8.29 (s, 1H, Ph), 8.15 (s, 1H, pyrazolyl-H), 7.49 (dd, 1H, *J* = 1.2, 8.0 Hz, pyridyl protons), 7.36 (t, 1H, *J* = 8.0 Hz, Ph), 7.28-7.20 (m, 4H, Ph), 7.08 (s, 1H, Ph), 7.03 (dd, 1H, *J* = 1.6, 8.0 Hz, Ph), 3.73 (s, 3H, OCH₃), 2.73-2.51 (m, 12H, piperazinyl protons and CH₂CH₂CO), 2.31 (s, 3H,

N-CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 170.7 (**C=O**), 154.6, 149.9, 149.6, 140.6, 139.9, 139.8, 132.3, 130.1, 129.6, 127.6, 122.9, 122.6, 121.4, 120.1, 117.6, 114.1, 112.3, 110.2 [**Ar-C**], 56.0 (**OCH₃**), 55.1 (**piperazinyl carbons**), 53.4 (**piperazinyl carbons**), 53.1 (**piperazinyl carbons and CH₂CH₂CO**), 45.8 (**N-CH₃**), 32.5 (**CH₂CH₂CO**); MS m/z: 529.9 [**M+H**]⁺.

N-(3-(3-(4-Chloro-3-methoxyphenyl)-4-(pyridin-4-yl)-1*H*-pyrazol-1-yl)phenyl)-3-(4-ethyl-piperazin-1-yl)propanamide (**1j**)

Yellow oil; yield: 61%; ¹H NMR (400 MHz, CDCl₃) δ 8.56 (d, 2H, *J* = 6.4 Hz, **pyridyl protons**), 8.32 (s, 1H, **NH**), 8.19 (s, 1H, **pyrazolyl-H**), 7.56 (dd, 1H, *J* = 1.2, 8.0 Hz, **Ph**), 7.42 (t, 1H, *J* = 8.0 Hz, **Ph**), 7.39-7.35 (m, 2H, **Ph**), 7.28 (d, 2H, *J* = 7.2 Hz, **pyridyl protons**), 7.14-7.09 (m, 2H, **Ph**), 3.73 (s, 3H, **OCH₃**), 2.73-2.51 (m, 15H, **piperazinyl proton, CH₂CH₂CO, and ethyl protons**), 2.31 (brs, 2H, **COCH₂**); ¹³C NMR (100 MHz, CDCl₃) δ 170.7 (**C=O**), 154.6, 149.9, 149.6, 140.6, 139.9, 139.8, 132.3, 130.1, 129.6, 127.6, 122.9, 122.6, 121.4, 120.1, 117.6, 114.1, 112.3, 110.2 [**Ar-C**], 56.1 (**OCH₃**), 55.5 (**piperazinyl carbons**), 52.5 (**piperazinyl carbons**), 52.3 (**CH₂CH₂CO**), 52.1 (**CH₂CH₃**), 32.3 (**CH₂CH₂CO**), 11.9 (**CH₂CH₃**); MS m/z: 544.9 [**M+H**]⁺.

N-(3-(3-(4-Chloro-3-methoxyphenyl)-4-(pyridin-4-yl)-1*H*-pyrazol-1-yl)phenyl)-3-(4-phenyl-piperazin-1-yl)propanamide (**1k**)

Yellow oil; yield: 67%; ¹H NMR (400 MHz, CDCl₃) δ 8.58 (d, 2H, *J* = 6.0 Hz, **pyridyl protons**), 8.34 (s, 1H, **NH**), 8.21 (s, 1H, **pyrazolyl-H**), 7.58 (d, 1H, *J* = 7.2 Hz, **Ph**), 7.43 (t, 1H, *J* = 8.0 Hz, **Ph**), 7.35-7.28 (m, 5H, **pyridyl protons and Ph**), 7.15-7.08 (m, 2H, **Ph**), 6.96-6.93 (m, 3H, **Ph**), 3.79 (s, 3H, **OCH₃**), 2.96-2.65 (m, 12H, **piperazinyl protons and CH₂CH₂CO**); ¹³C NMR (100 MHz, CDCl₃) δ 169.7 (**C=O**), 155.1, 151.9, 150.9, 150.8, 146.9, 142.9, 140.0, 132.0, 130.3, 129.3, 127.5, 123.1, 122.4, 121.5, 120.5, 120.3, 117.6, 117.2, 116.4, 114.5, 112.2, 110.2 [**Ar-C**], 56.1 (**OCH₃**), 53.1 (**piperazinyl carbons**), 52.4 (**piperazinyl carbons and CH₂CH₂CO**), 32.5 (**CH₂CH₂CO**); MS m/z: 593.43 [**M+H**]⁺.

3-(4-Benzylpiperazin-1-yl)-N-(3-(3-(4-chloro-3-methoxyphenyl)-4-(pyridin-4-yl)-1H-pyrazol-1-yl)phenyl)propanamide (II)

Yellow oil; yield: 71%; ^1H NMR (400 MHz, CDCl_3) δ 8.57 (d, 2H, $J = 6.0$ Hz, pyridyl protons), 8.36 (s, 1H, NH), 8.21 (s, 1H, pyrazolyl-H), 7.58 (dd, 1H, $J = 1.2, 9.2$ Hz, Ph), 7.43 (t, 1H, $J = 8.0$ Hz, Ph), 7.38-7.29 (m, 9H, pyridyl protons and Ph), 7.16-7.11 (m, 2H, Ph), 3.79 (s, 3H, OCH_3), 3.58 (s, 2H, benzyl- CH_2), 2.81-2.58 (m, 12H, piperazinyl protons and $\text{CH}_2\text{CH}_2\text{CO}$); ^{13}C NMR (100 MHz, CDCl_3) δ 170.9 (C=O), 156.9, 150.9, 150.8, 146.9, 142.9, 140.0, 137.6, 132.5, 130.3, 129.1, 127.6, 123.0, 121.5, 120.2, 117.6, 114.3, 112.3, 110.2 [Ar-C], 62.9 (benzyl- CH_2), 56.1 (OCH_3), 53.1 (piperazinyl carbons), 52.3 (piperazinyl carbons and $\text{CH}_2\text{CH}_2\text{CO}$), 32.6 ($\text{CH}_2\text{CH}_2\text{CO}$); MS m/z : 608.1 $[\text{M}+\text{H}]^+$.

3-(4-(4-Fluorobenzyl)piperazin-1-yl)-N-(3-(3-(4-chloro-3-methoxyphenyl)-4-(pyridin-4-yl)-1H-pyrazol-1-yl)phenyl)propanamide (Im)

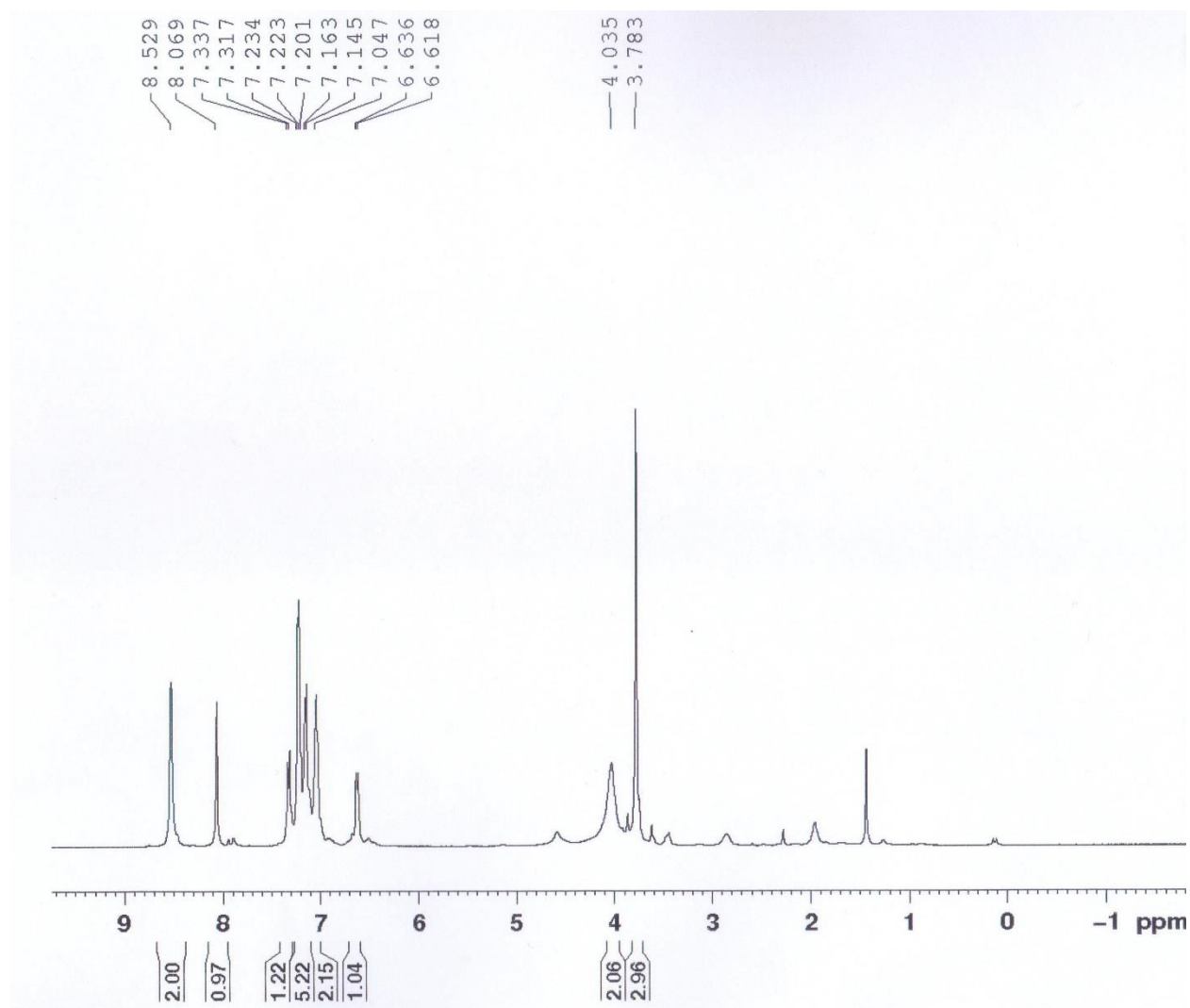
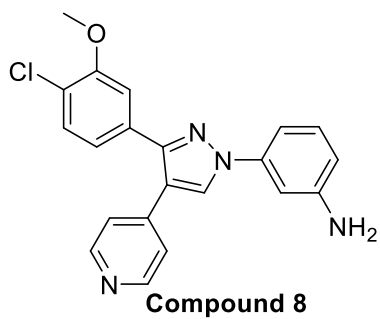
Yellow oil; yield: 68%; ^1H NMR (400 MHz, CDCl_3) δ 8.49 (d, 2H, $J = 6.0$ Hz, pyridyl protons), 8.26 (s, 1H, NH), 8.09 (s, 1H, pyrazolyl-H), 7.48 (d, 1H, $J = 8.0$ Hz, Ph), 7.36 (t, 1H, $J = 8.0$ Hz, Ph), 7.26 (d, 1H, $J = 8.0$ Hz, Ph), 7.19-7.17 (m, 4H, , pyridyl protons and Ph), 7.08-7.01 (m, 2H, Ph), 6.92 (t, 3H, $J = 8.8$ Hz, Ph), 3.71 (s, 3H, OCH_3), 3.44 (s, 2H, benzyl- CH_2), 2.74-2.51 (m, 12H, piperazinyl protons and $\text{CH}_2\text{CH}_2\text{CO}$); ^{13}C NMR (100 MHz, CDCl_3) δ 170.7 (C=O), 154.9, 149.9 (d, $J = 17.0$ Hz, C-F coupling), 140.6, 140.0, 133.2, 132.2, 130.6, 130.3, 127.1, 122.9 (d, $J = 30.0$ Hz, C-F coupling), 121.5, 120.3, 117.5, 115.2 (d, $J = 21.0$ Hz, C-F coupling), 114.3, 112.3, 110.2 [Ar-C], 61.9 (benzyl- CH_2), 56.1 (OCH_3), 53.4 (piperazinyl carbons), 53.2 (piperazinyl carbons and $\text{CH}_2\text{CH}_2\text{CO}$), 32.5 ($\text{CH}_2\text{CH}_2\text{CO}$); MS m/z : 625.0 $[\text{M}+\text{H}]^+$.

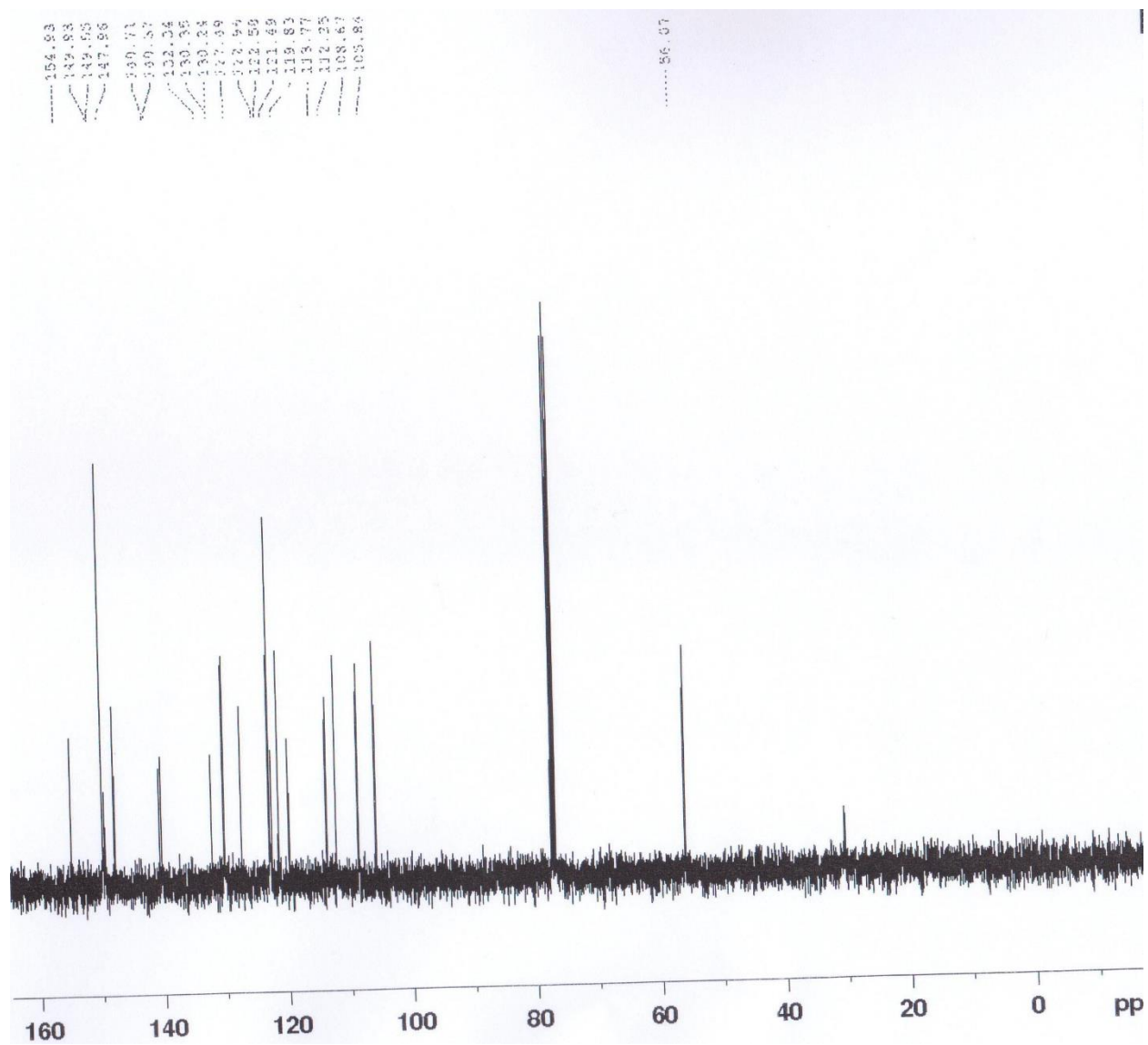
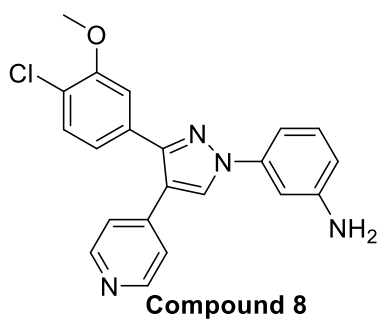
Biological evaluation

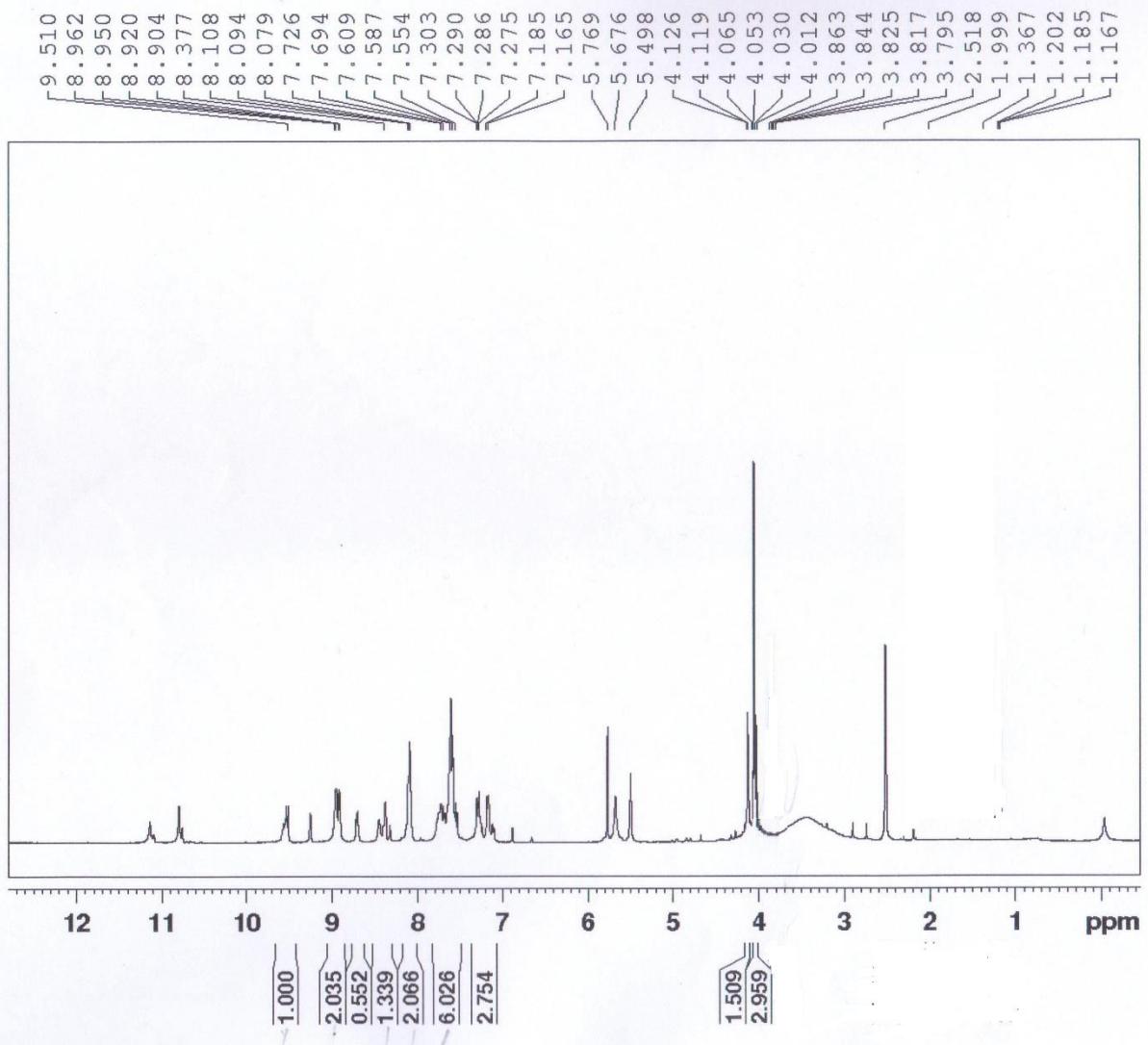
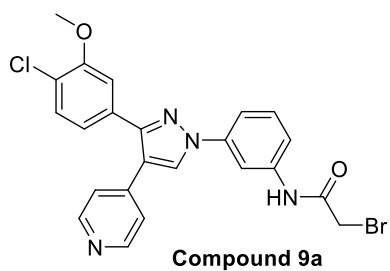
Cell culture and sample treatment, nitrite determination, PGE₂ assay, and MTT assay for cell viability have been carried out following the reported procedures [*Bioorg. Med. Chem. Lett.* **2014**, 24, 571 & *Eur. J. Pharmacol.* **2008**, 584, 175].

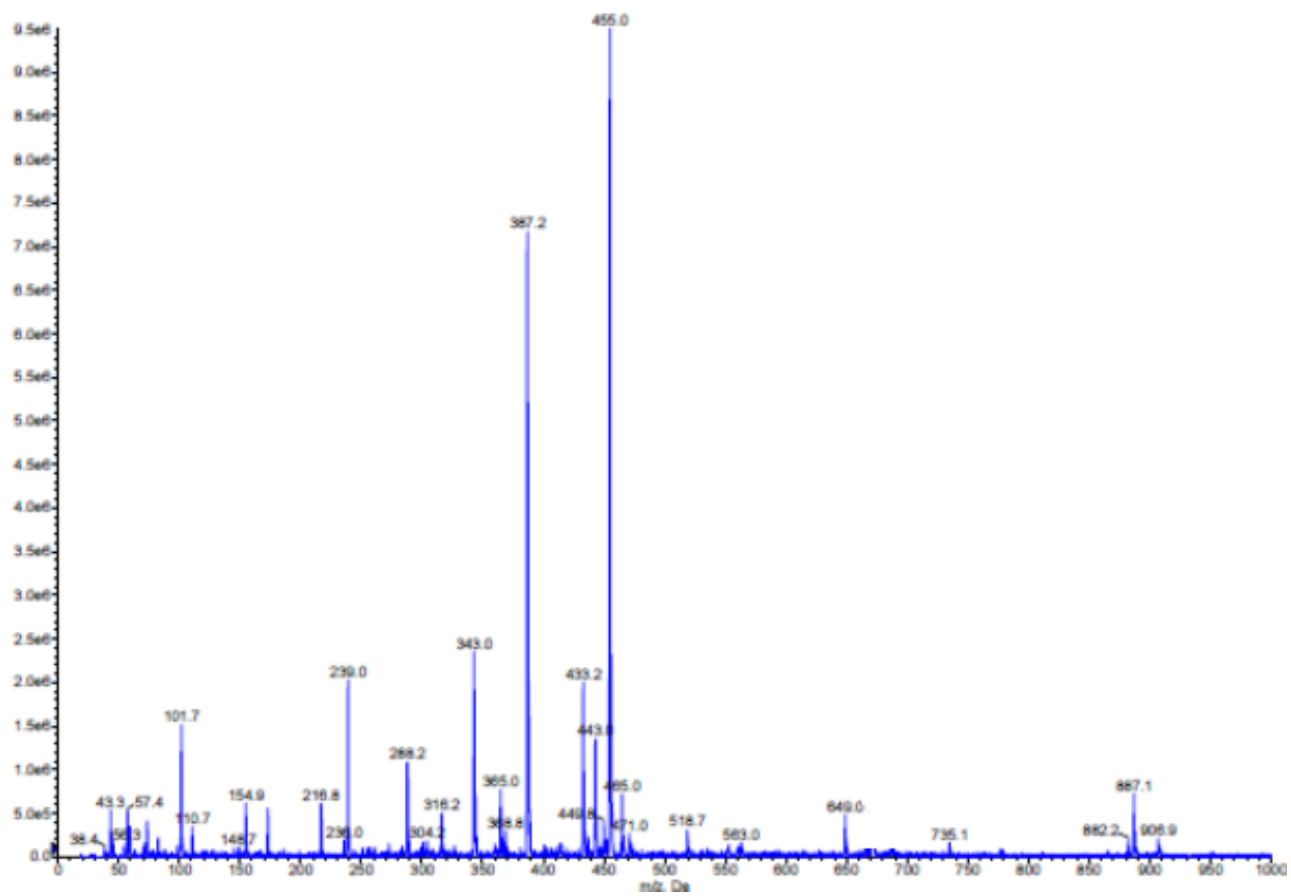
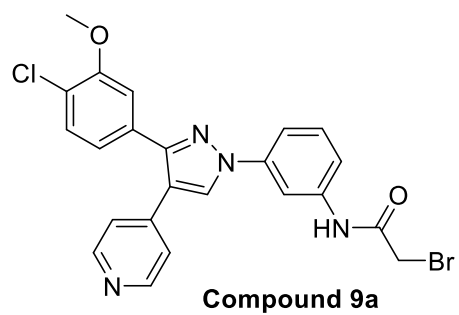
Western blot

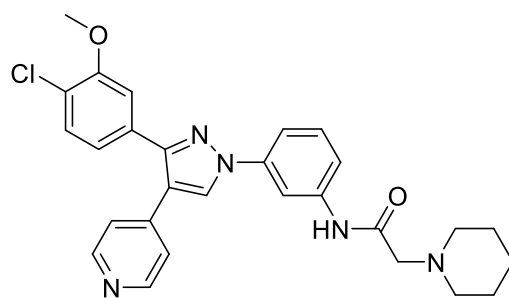
RAW 264.7 macrophage cells were re-suspended in PRO-PREPTM protein extraction solution (Intron Biotechnology, Seoul, Korea) and incubated with 20 min at 4 °C. The cell debris was removed by microcentrifugation, and the supernatants were quickly frozen. The protein concentration was determined using the Bio-Rad protein assay reagent according to the manufacture's instruction. Cellular proteins were electroblotted onto a PVDF membrane following separation on 8-12% SDS-polyacrylamide gel electrophoresis. The immunoblot was incubated with blocking solution (5% skimmed milk) at room temperature for 1 h, followed by incubation overnight with a primary antibody at 4 °C. The blots were washed four times with a Tween 20/Tris-buffered saline (T/TBS) and incubated with a 1:2000 dilution of horseradish peroxidase-conjugated secondary antibody for 2 h at room temperature. The blots were again washed three times with T/TBS, and then developed by enhanced chemiluminescence (GE healthcare, WI, USA).



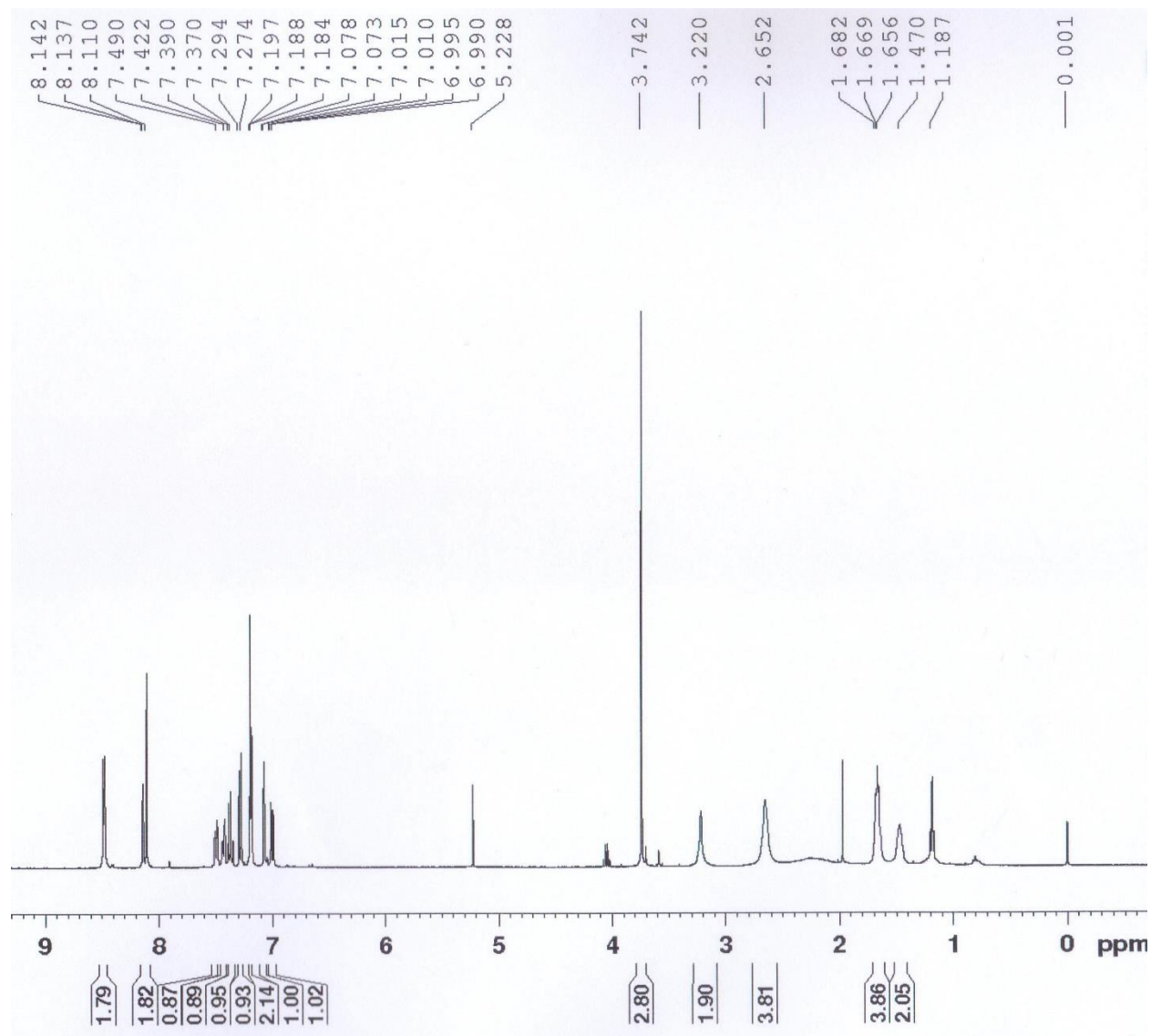


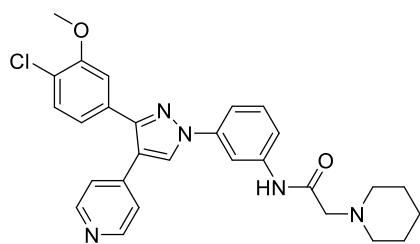




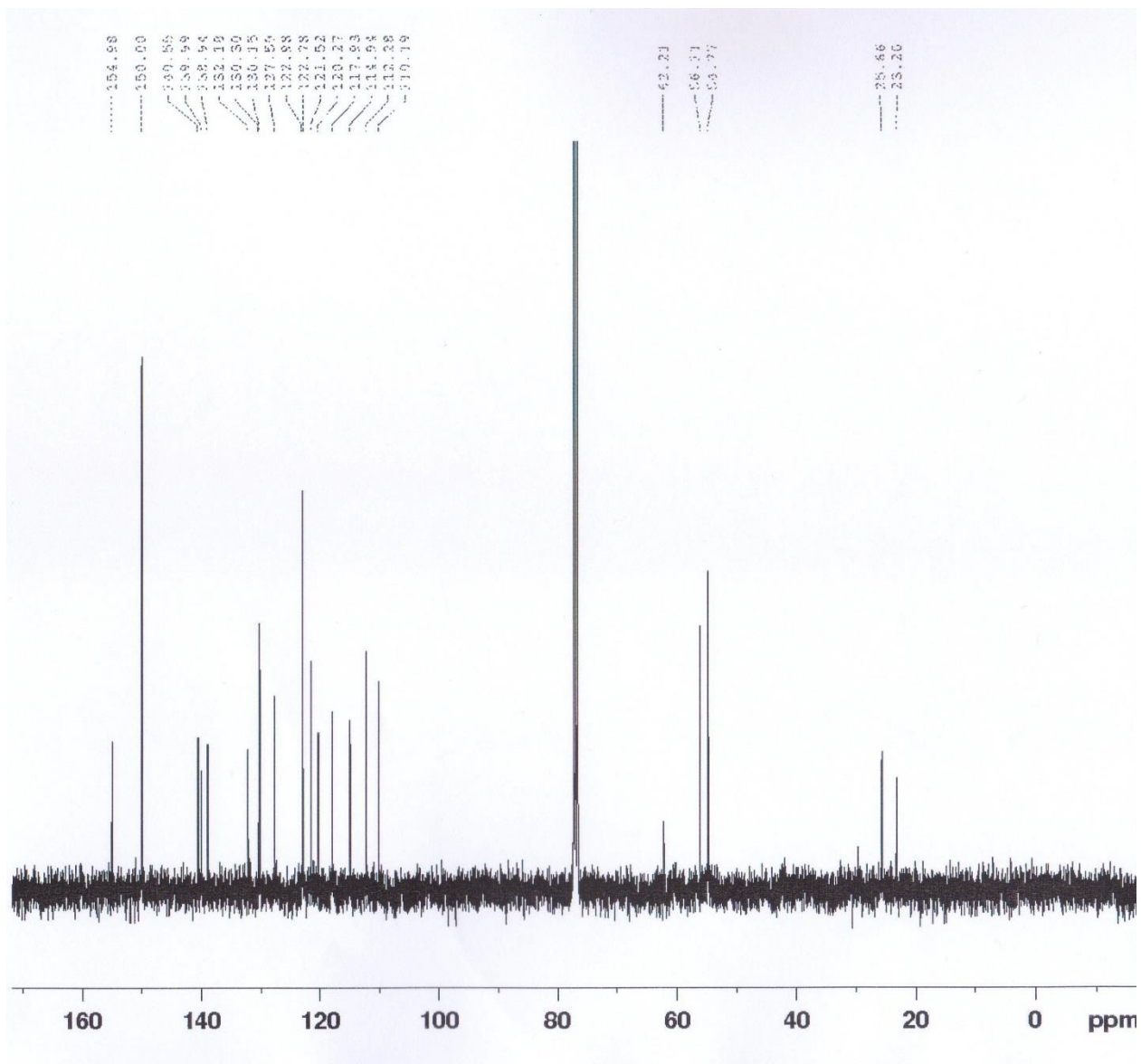


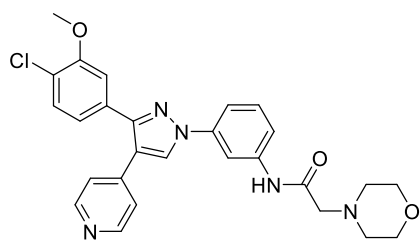
Compound 1a



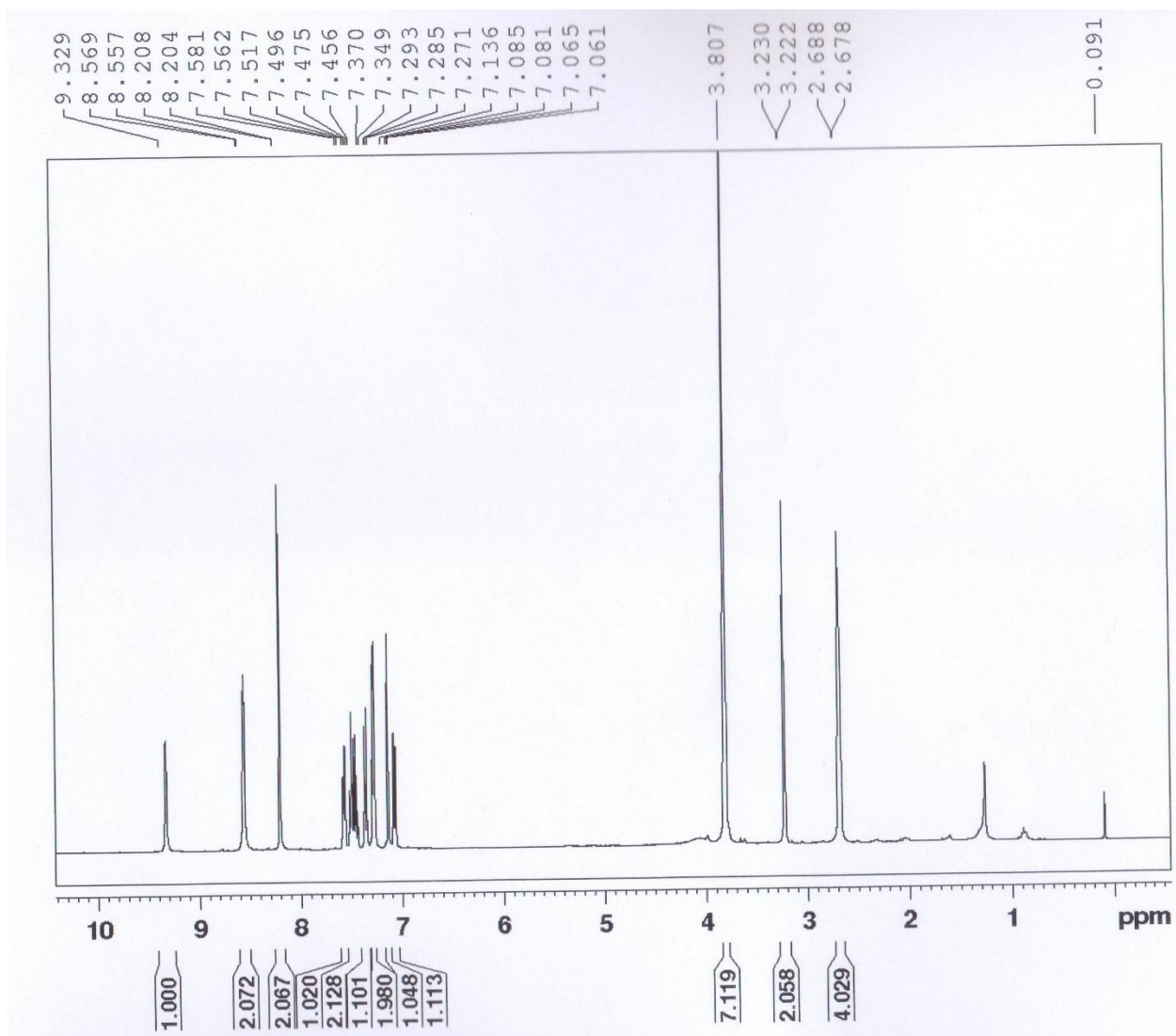


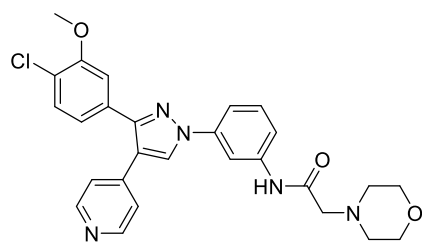
Compound 1a



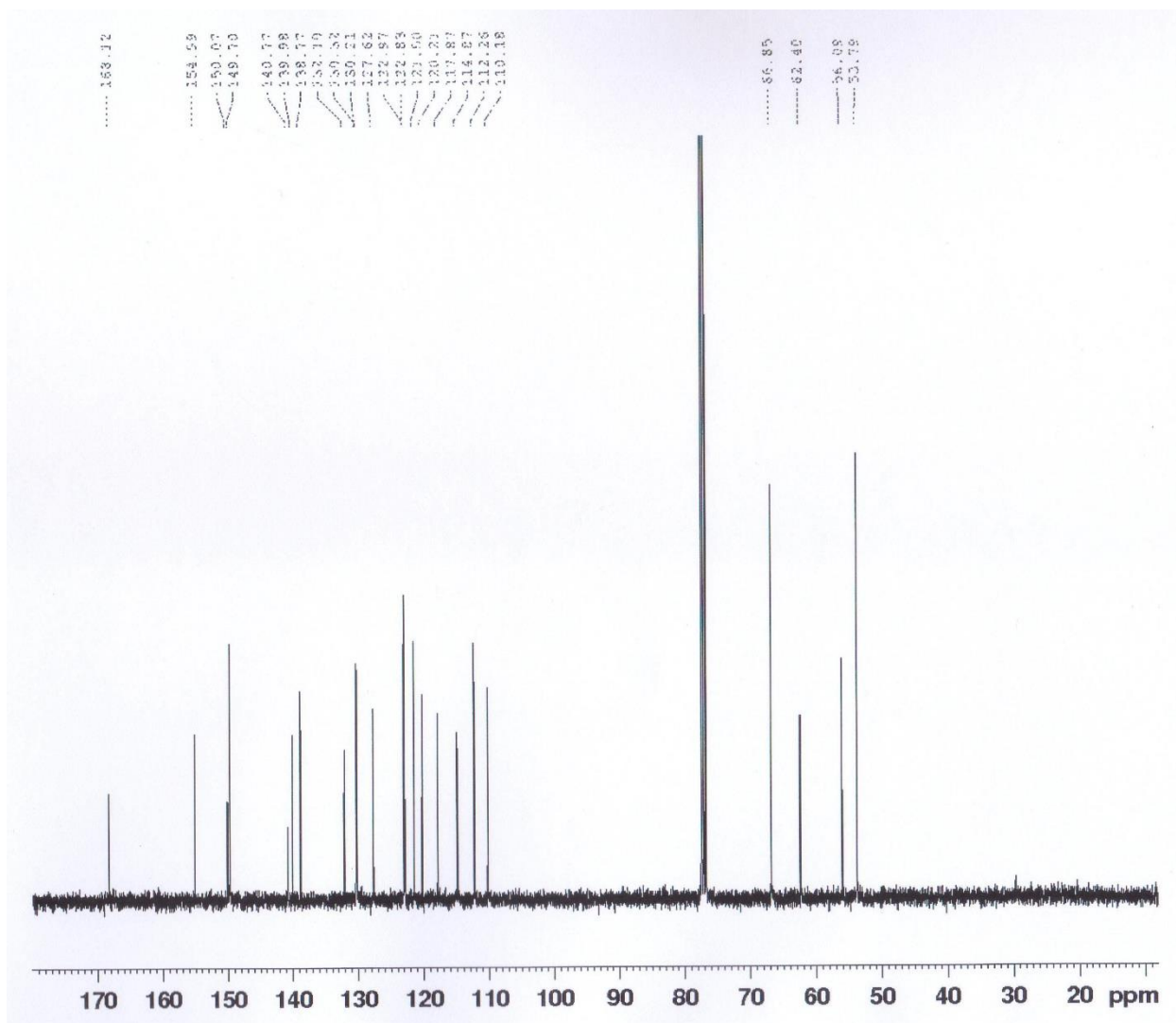


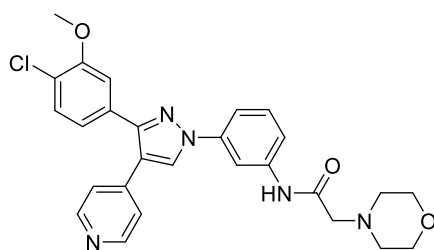
Compound 1b



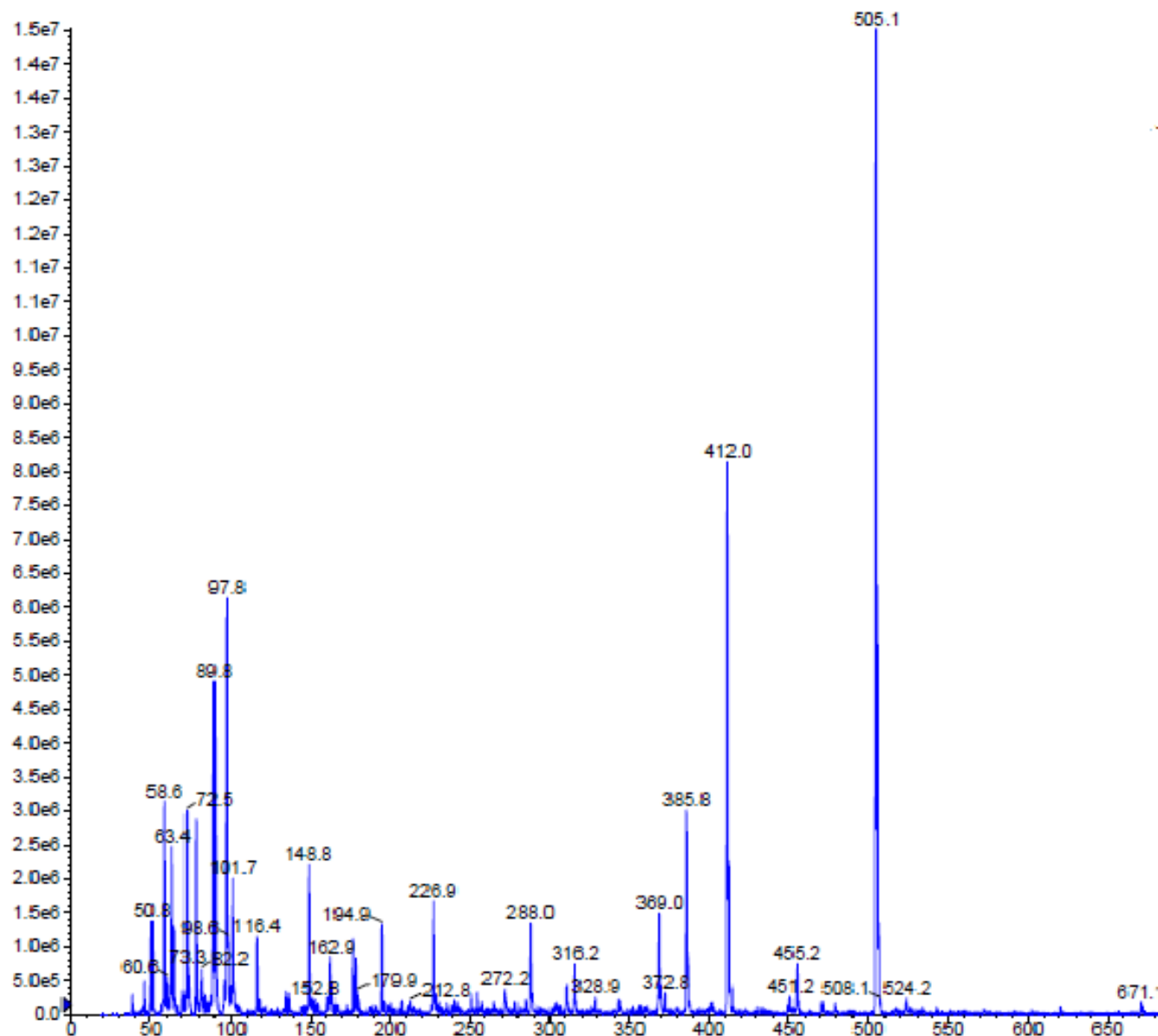


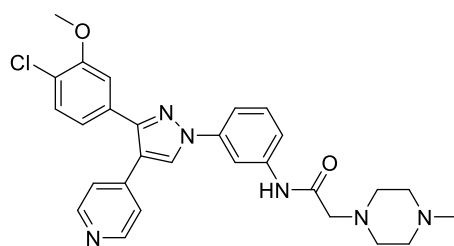
Compound 1b



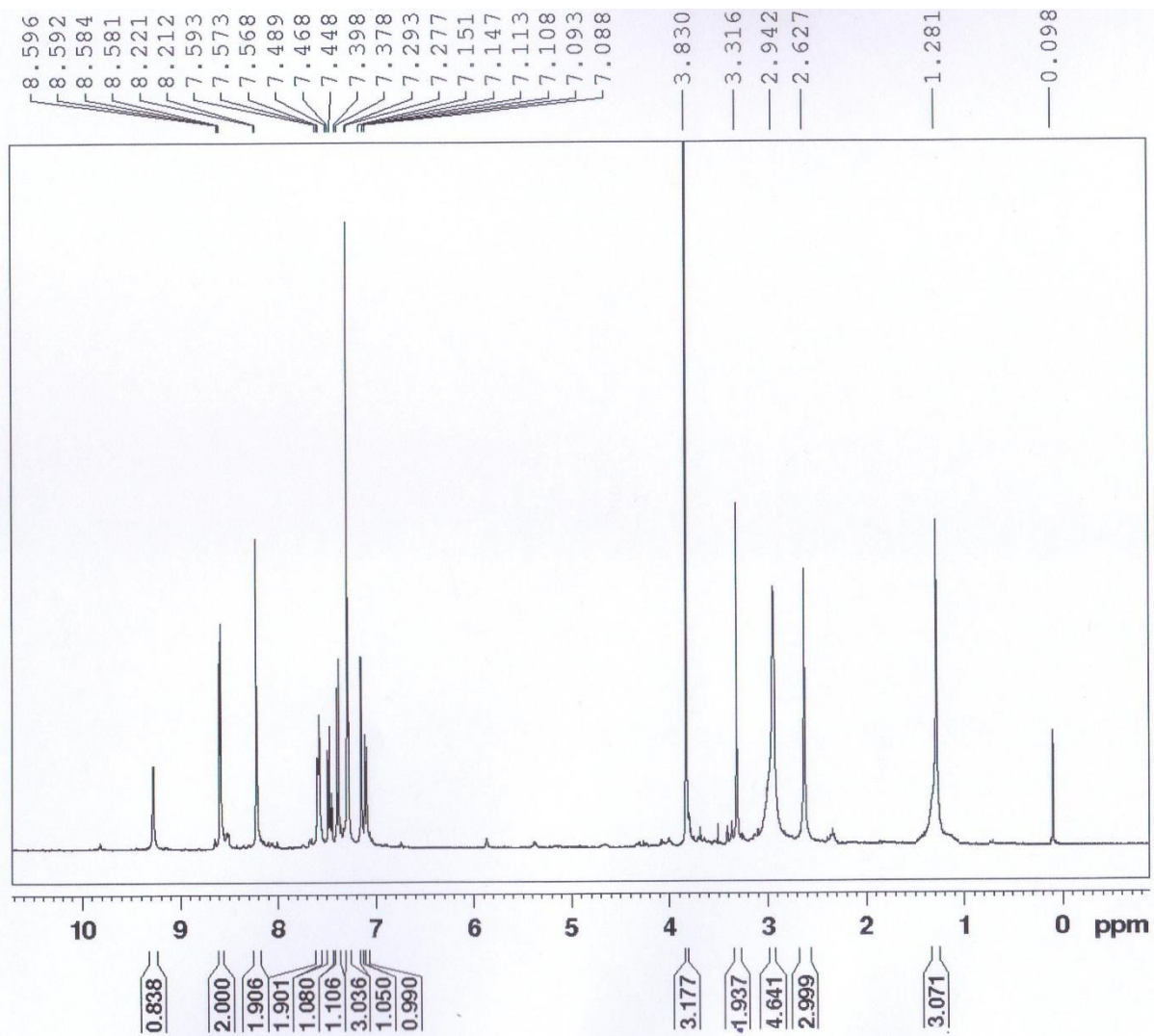


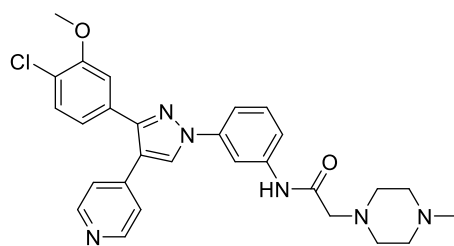
Compound 1b
 Chemical Formula: $C_{27}H_{26}ClN_5O_3$
 $m/z + H^+$: 505.1



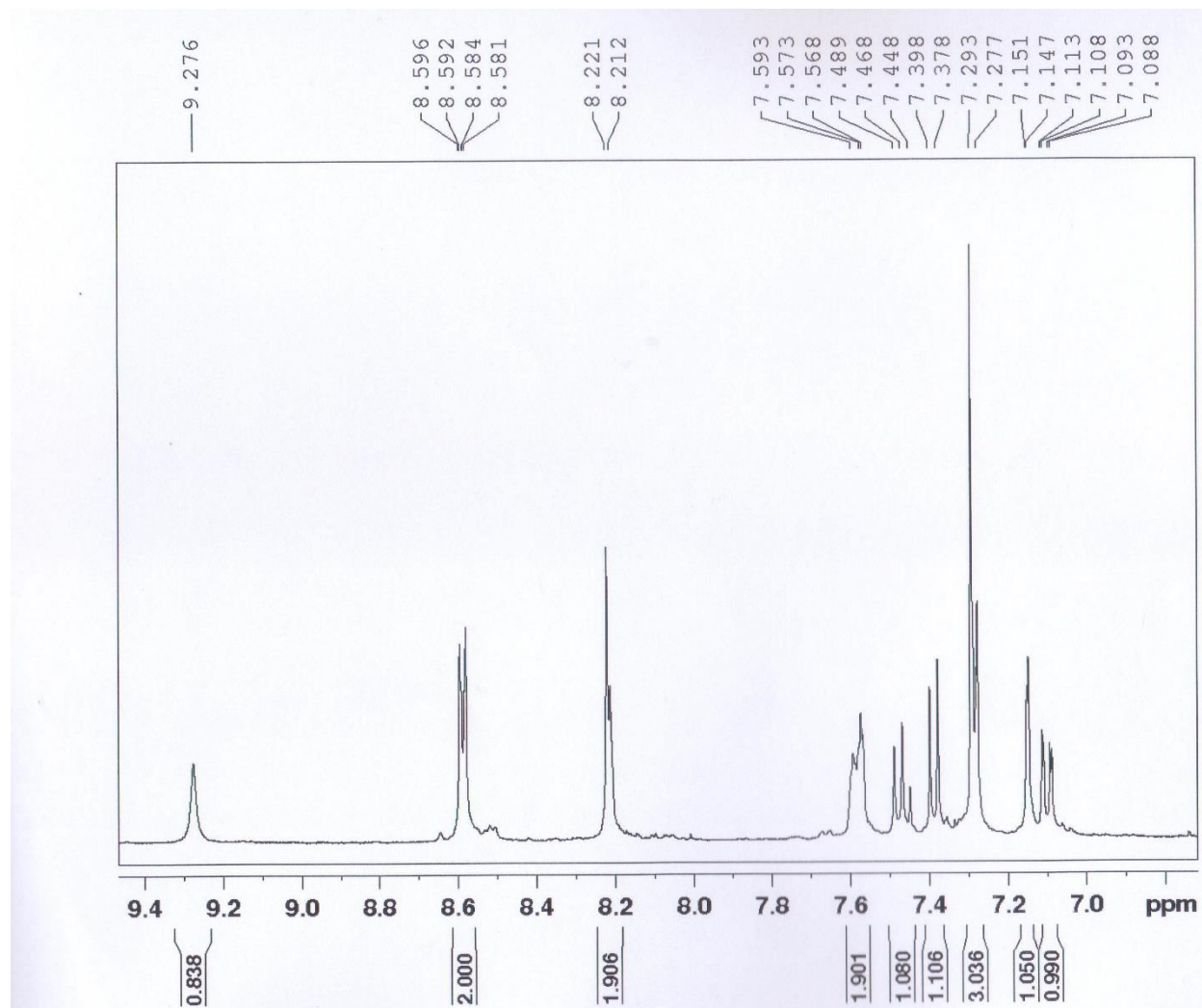


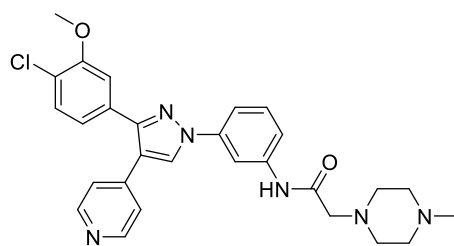
Compound 1c



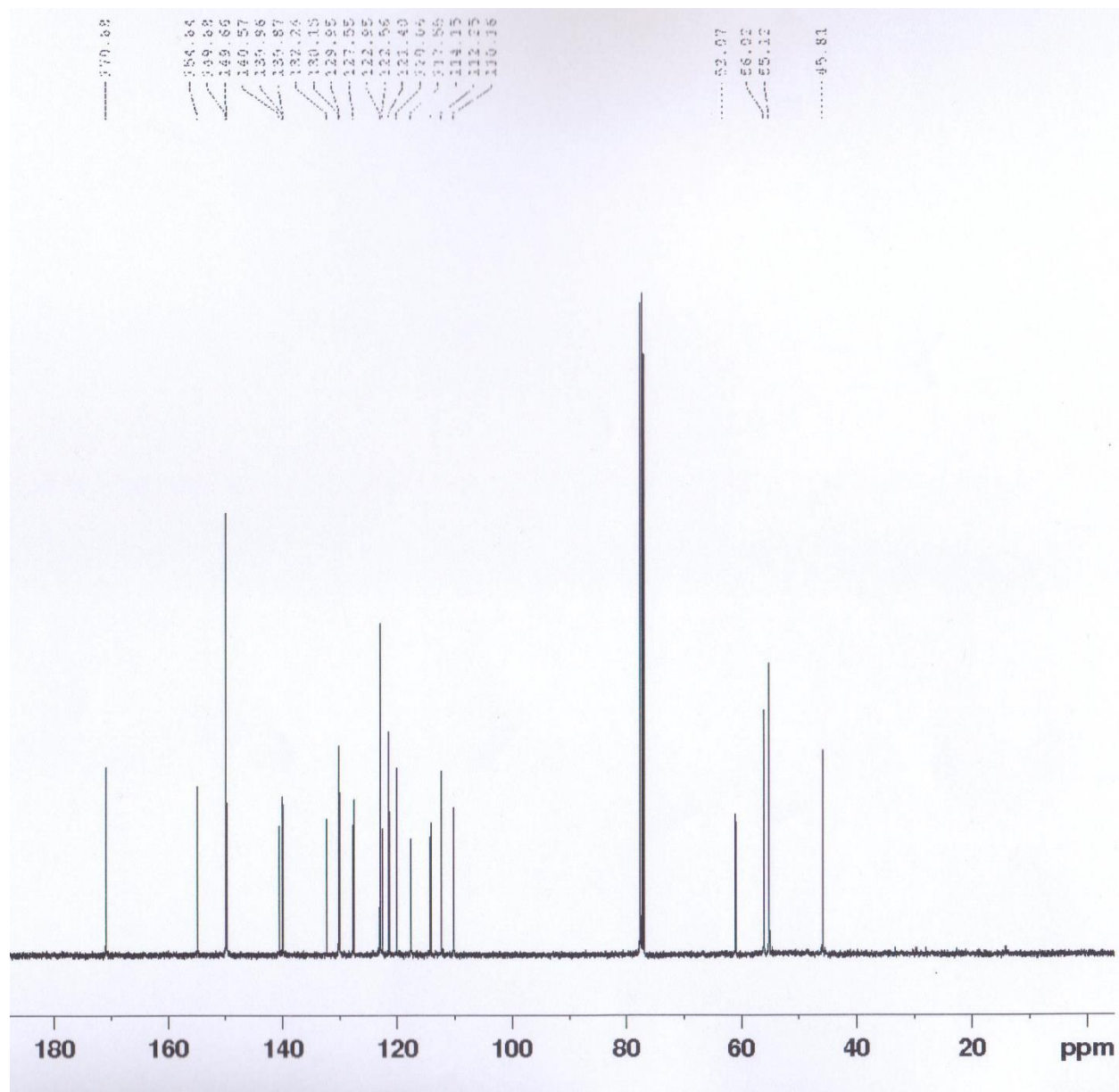


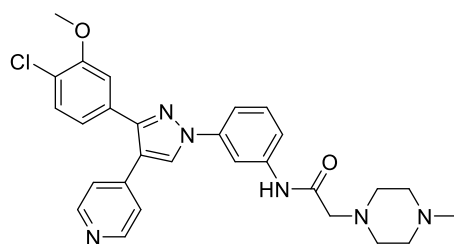
Compound 1c



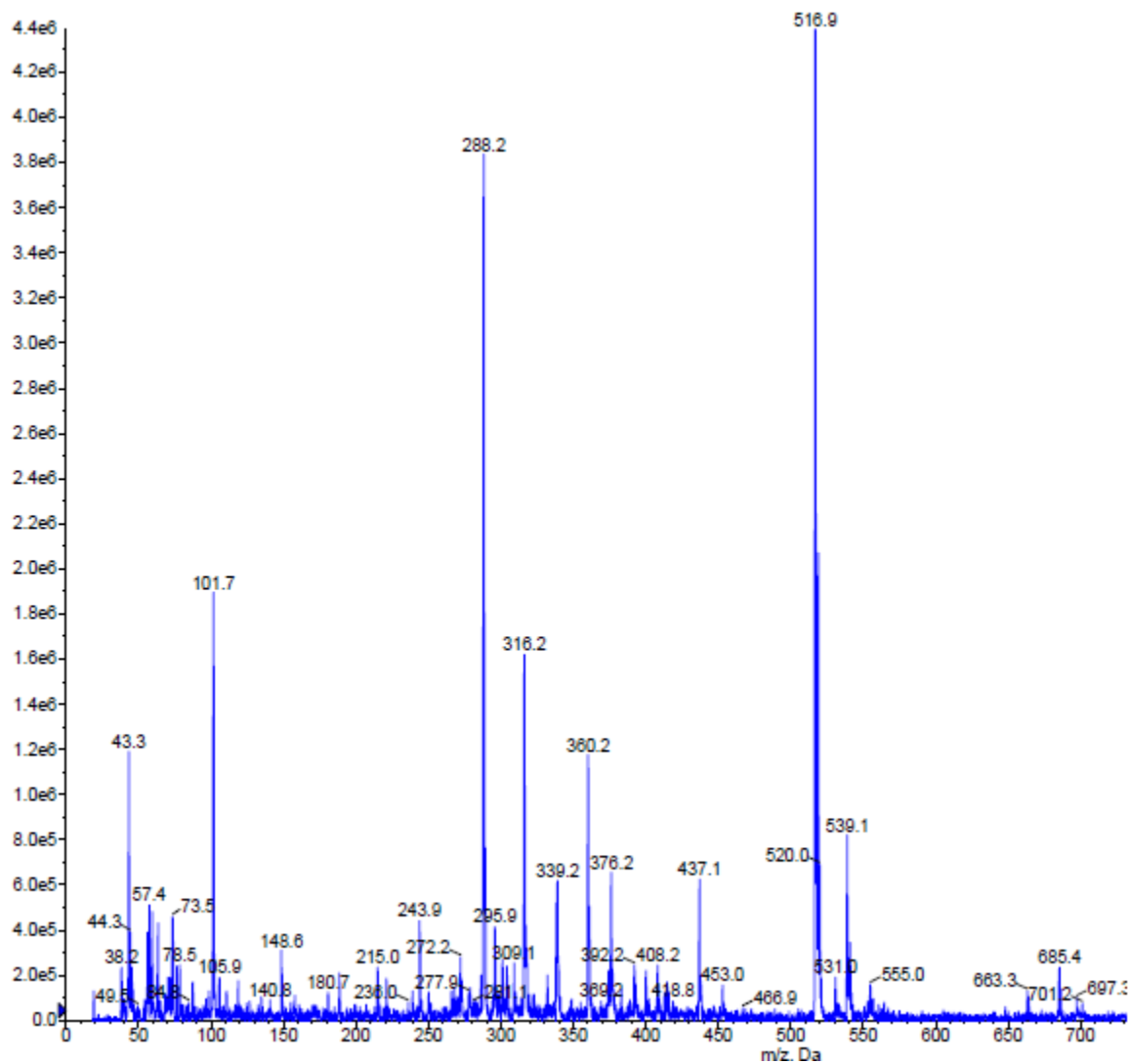


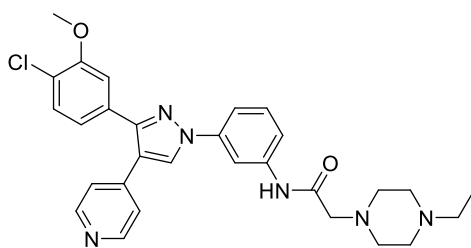
Compound 1c



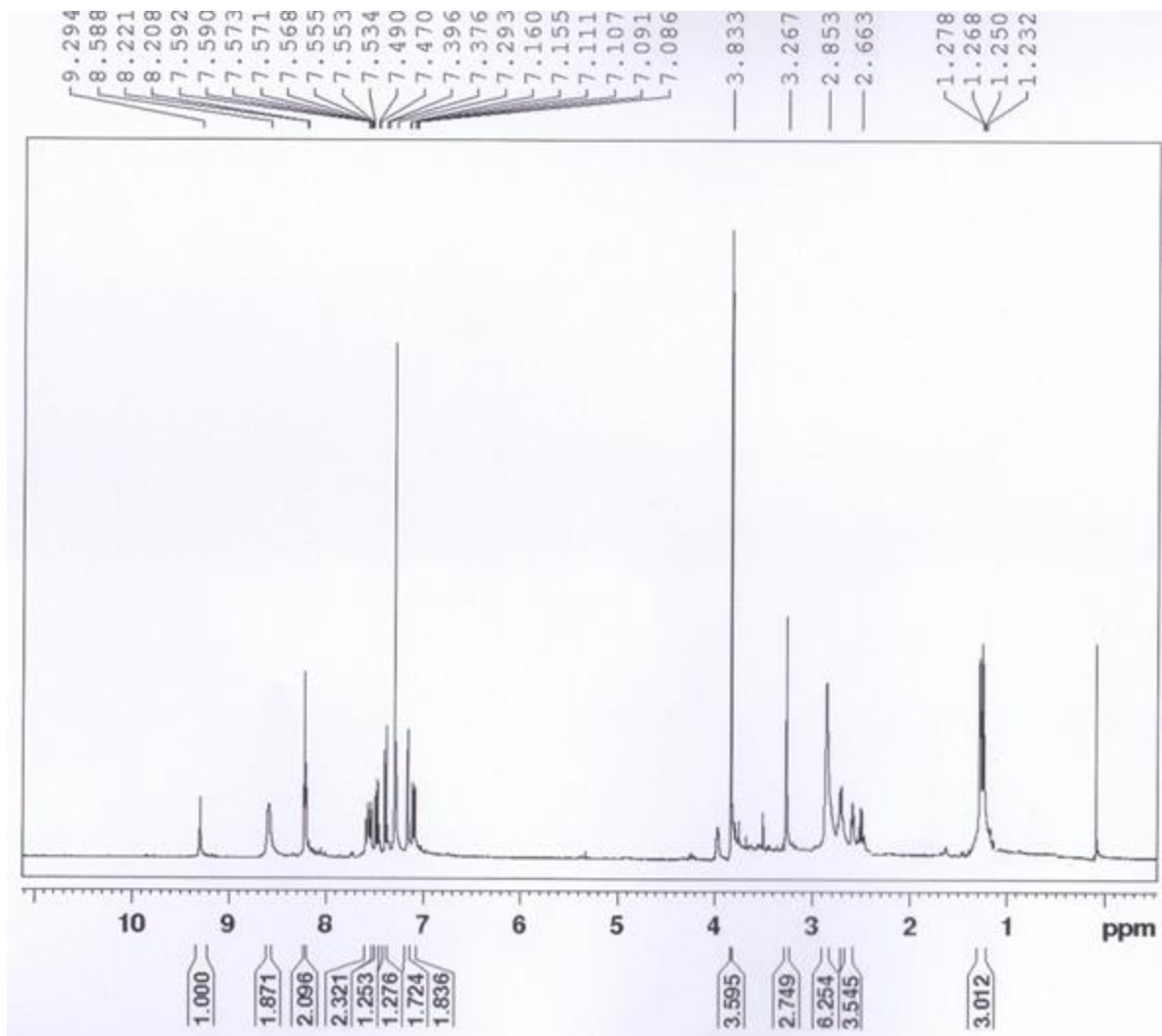


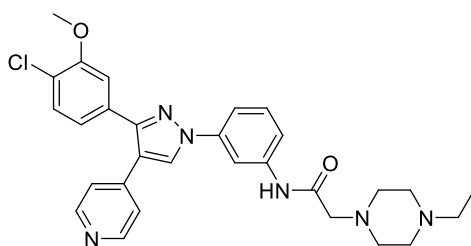
Compound 1c



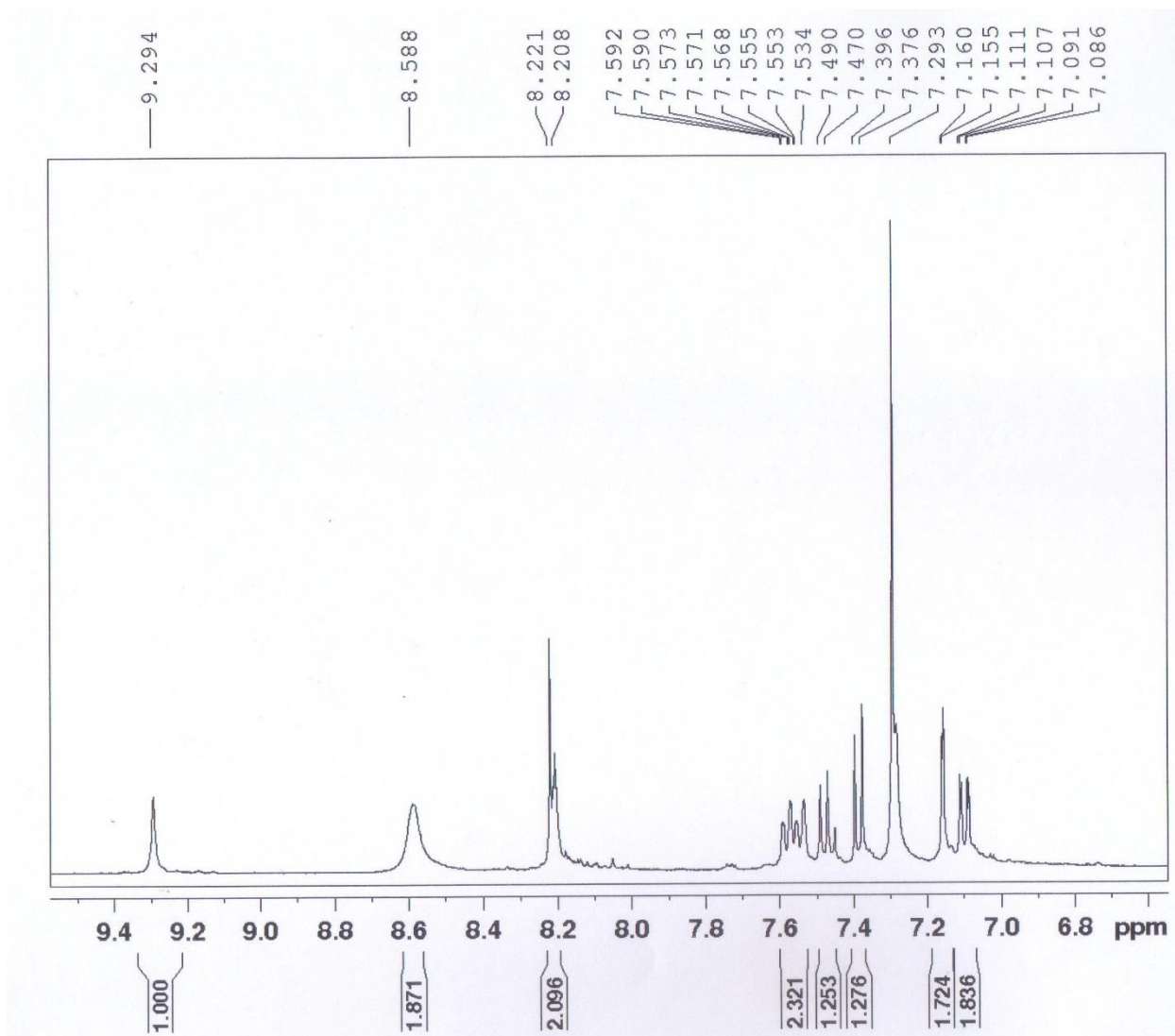


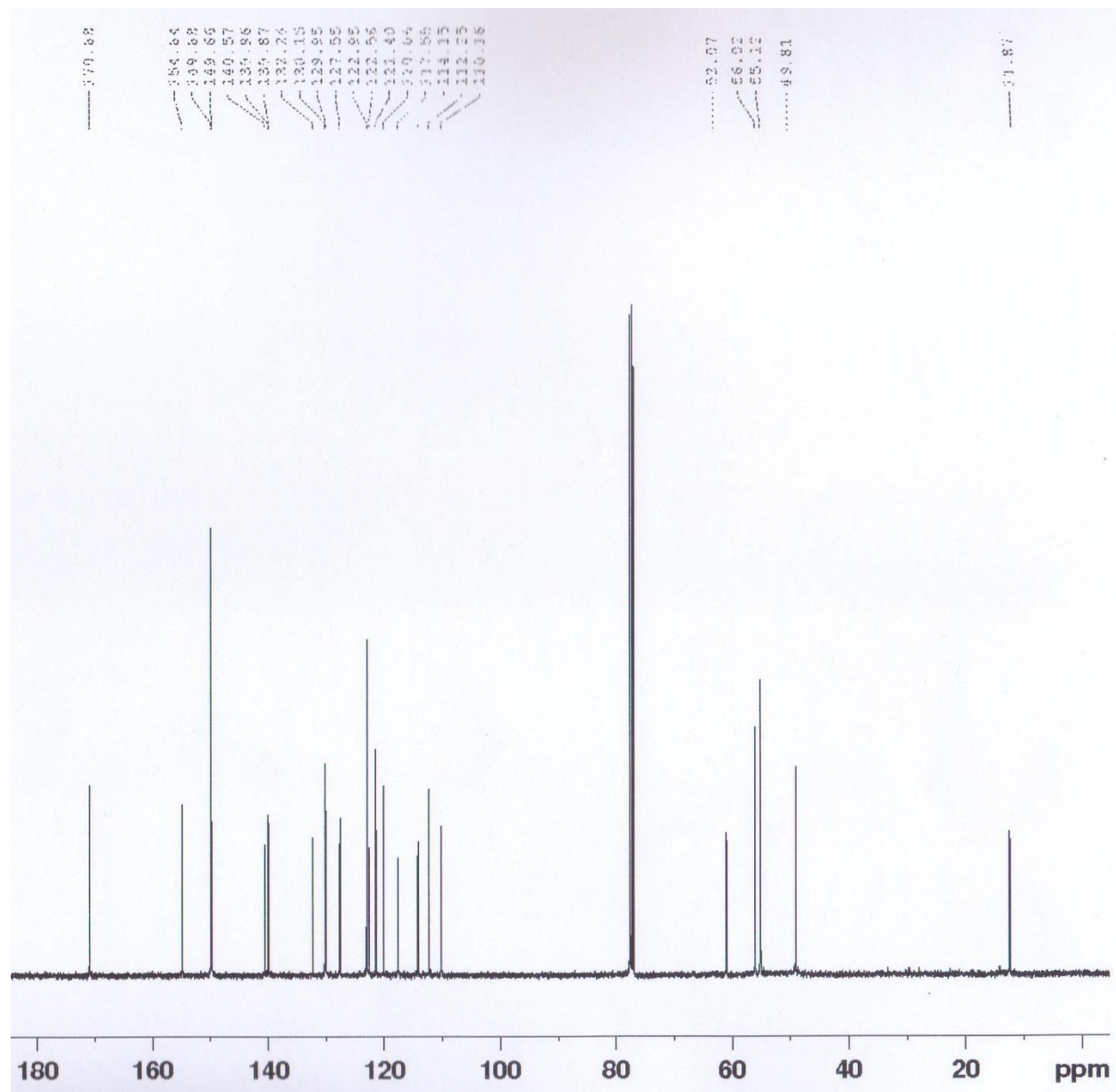
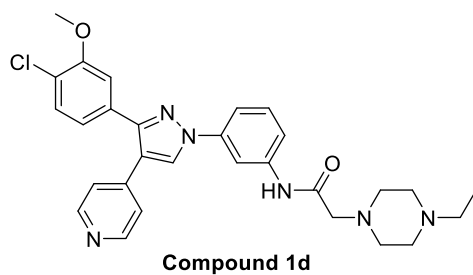
Compound 1d

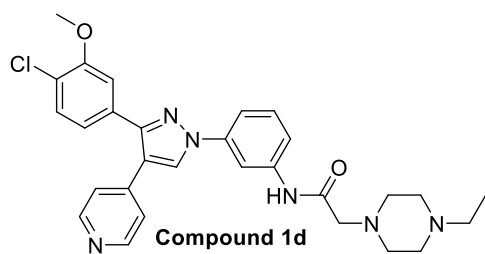




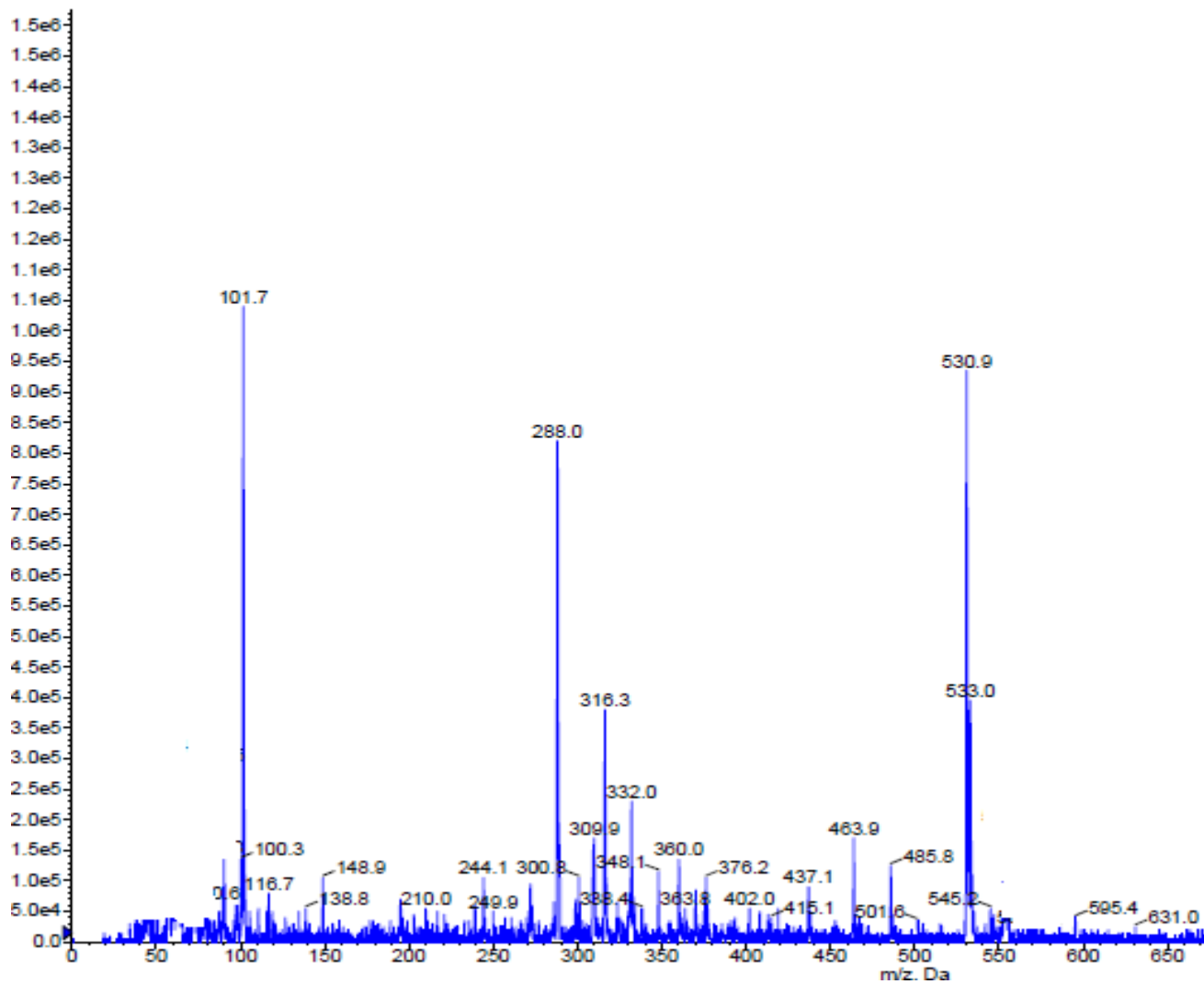
Compound 1d

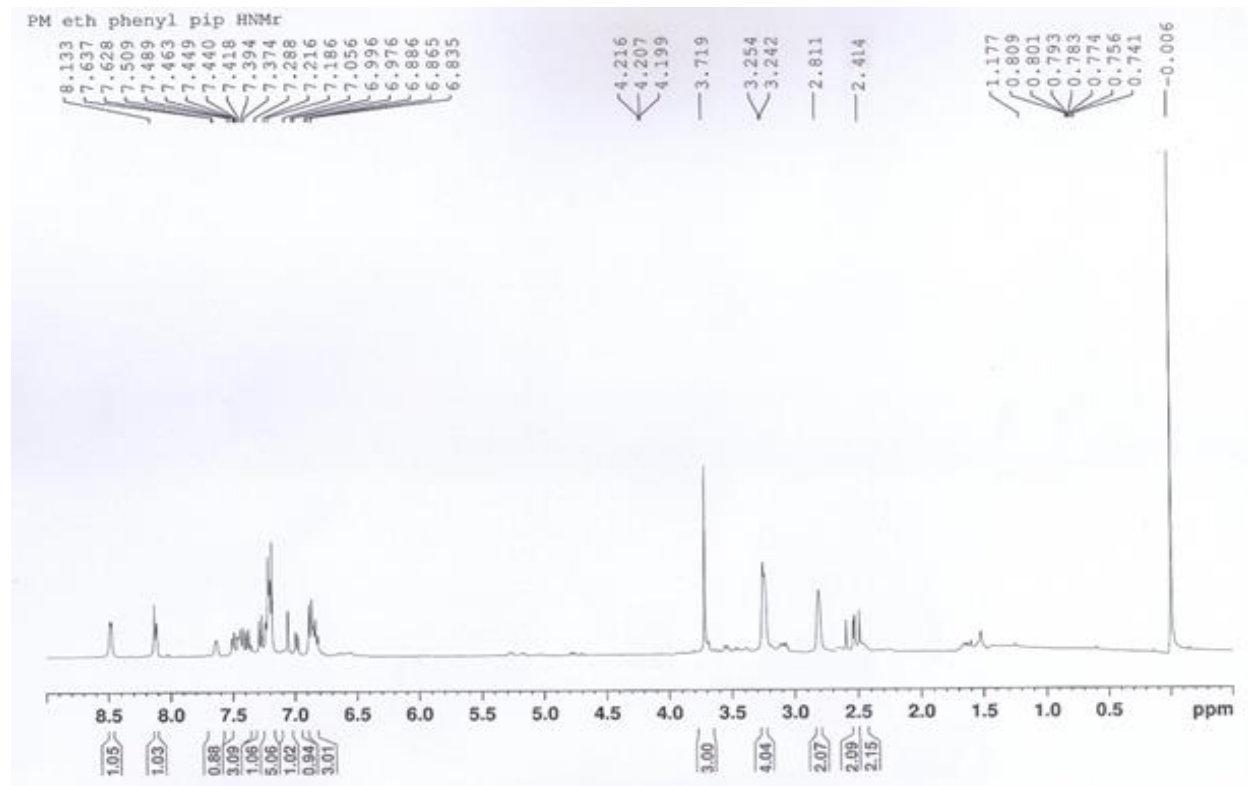
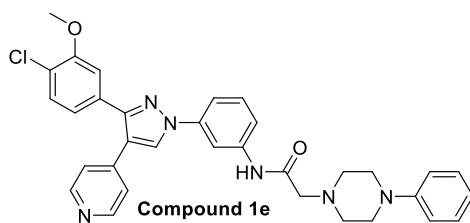


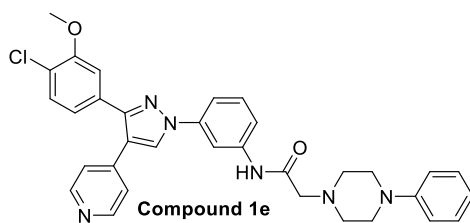




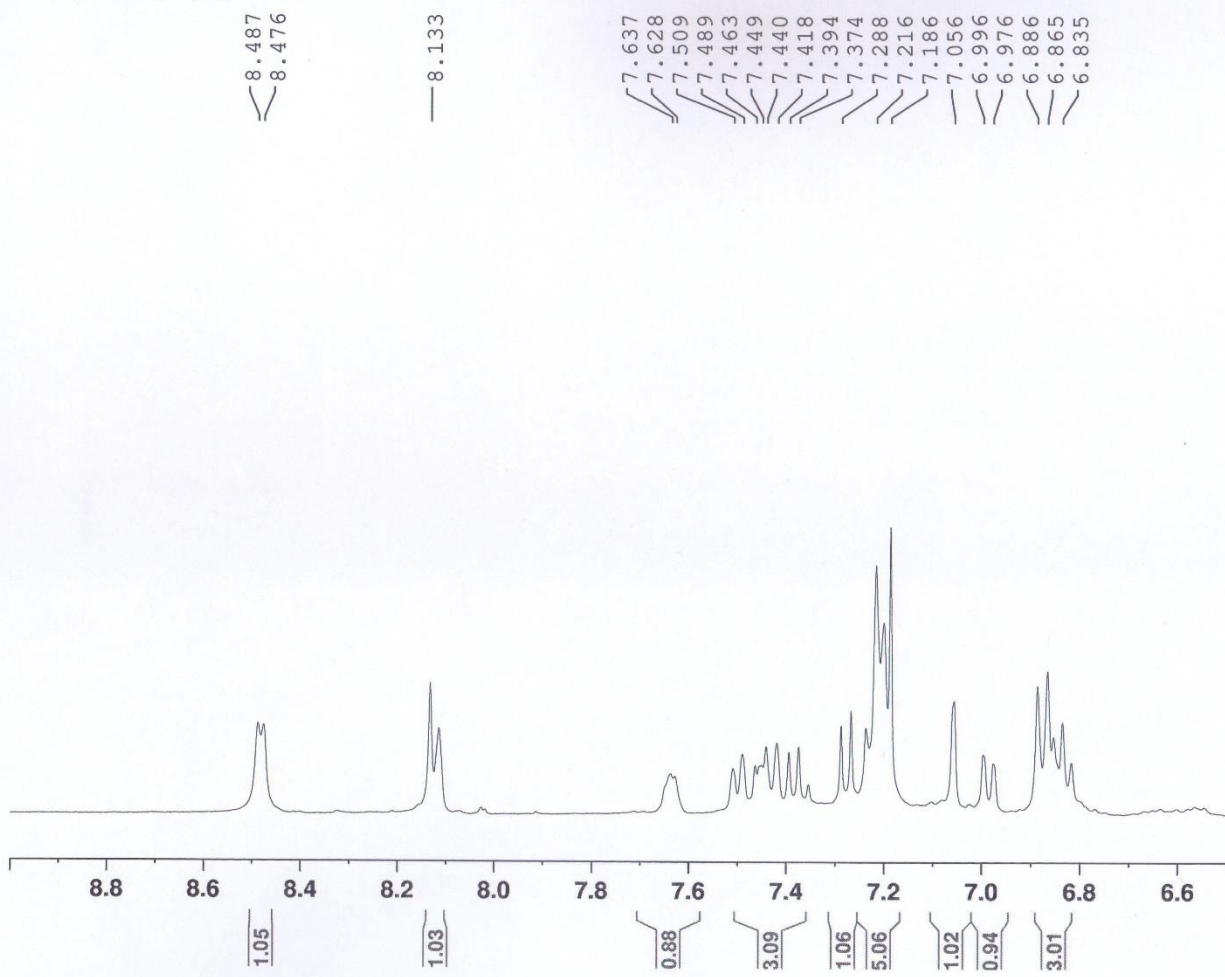
Chemical Formula: $C_{29}H_{31}ClN_6O_2$
 m/z : 531.0

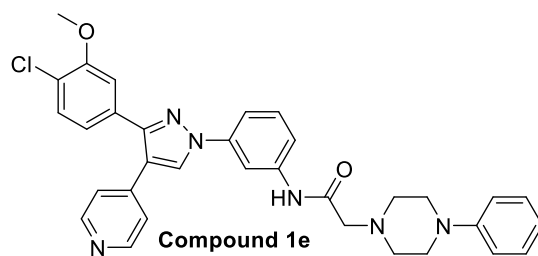




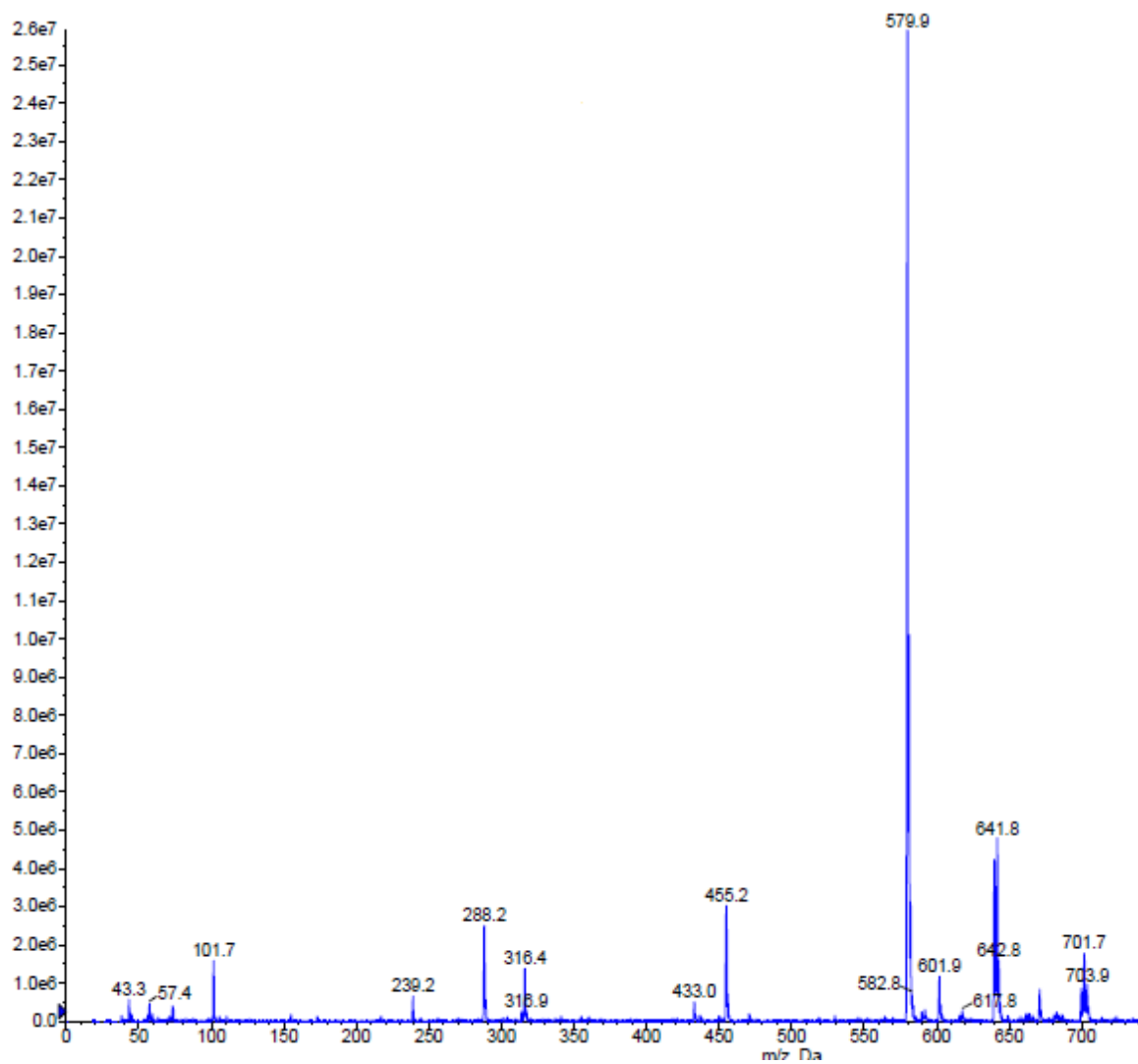


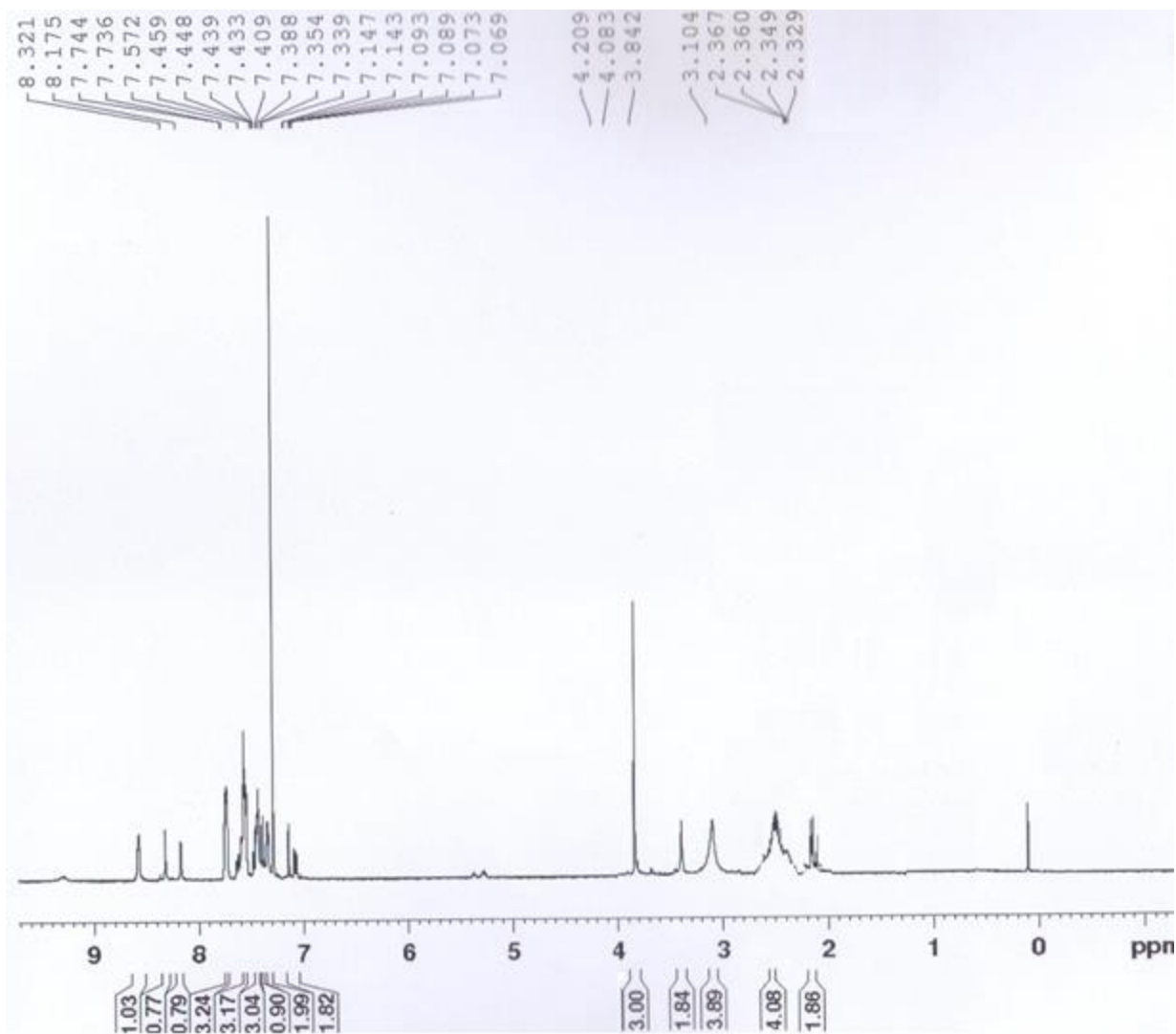
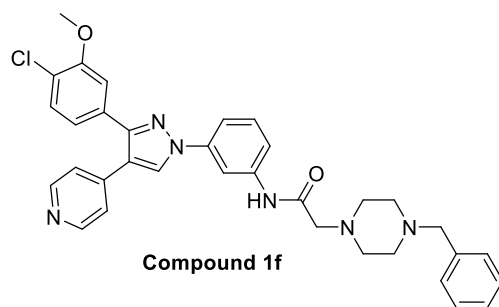
PM eth phenyl pip HNMR

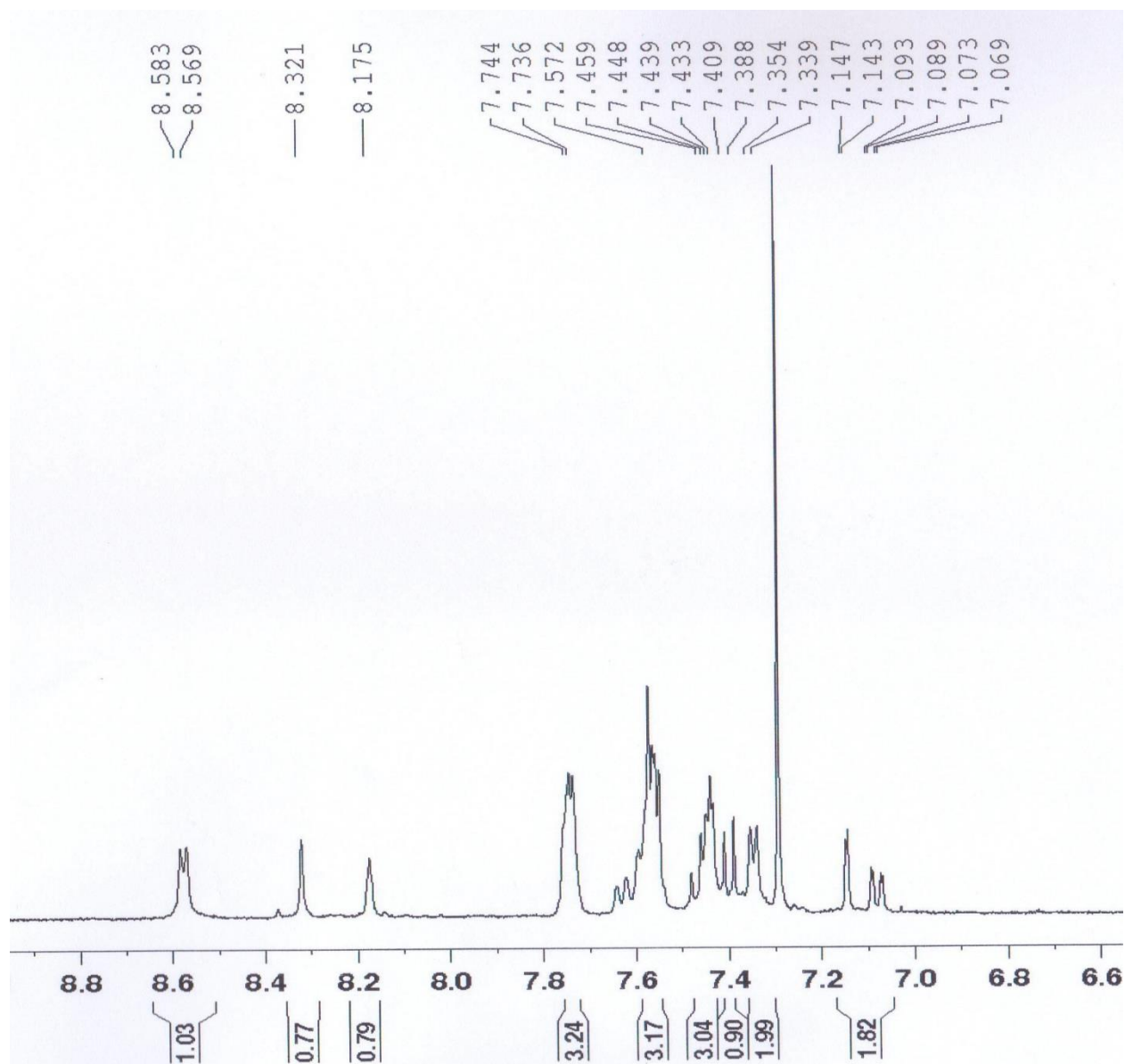
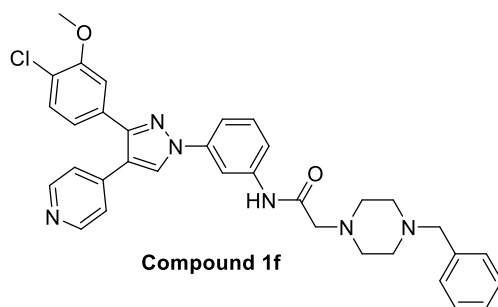


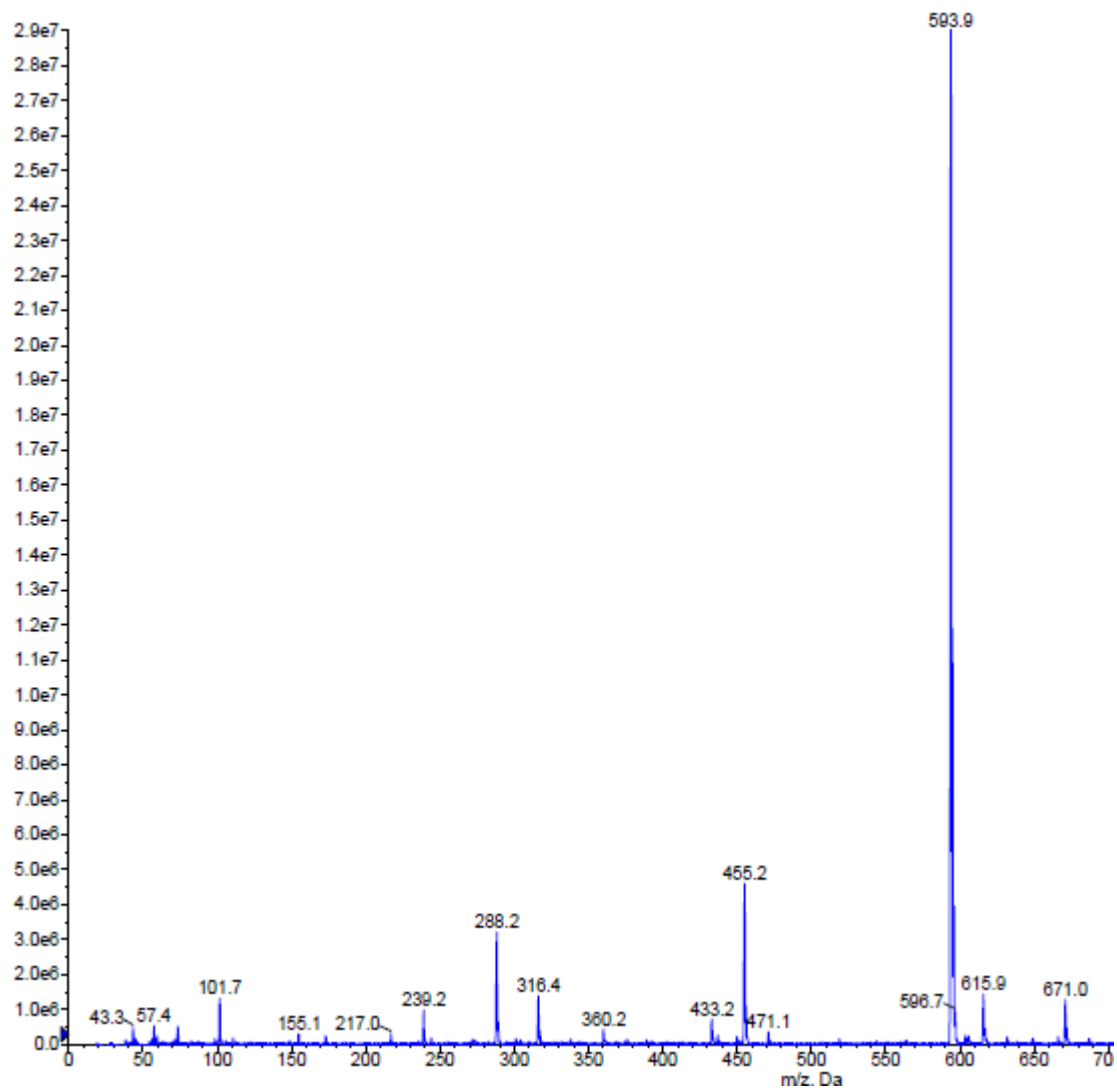
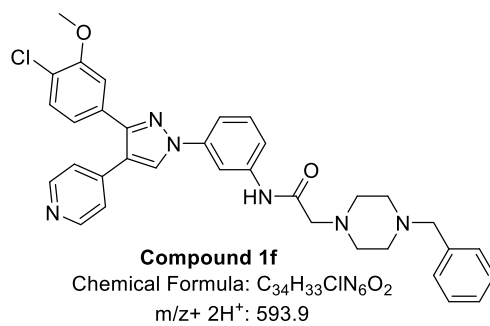


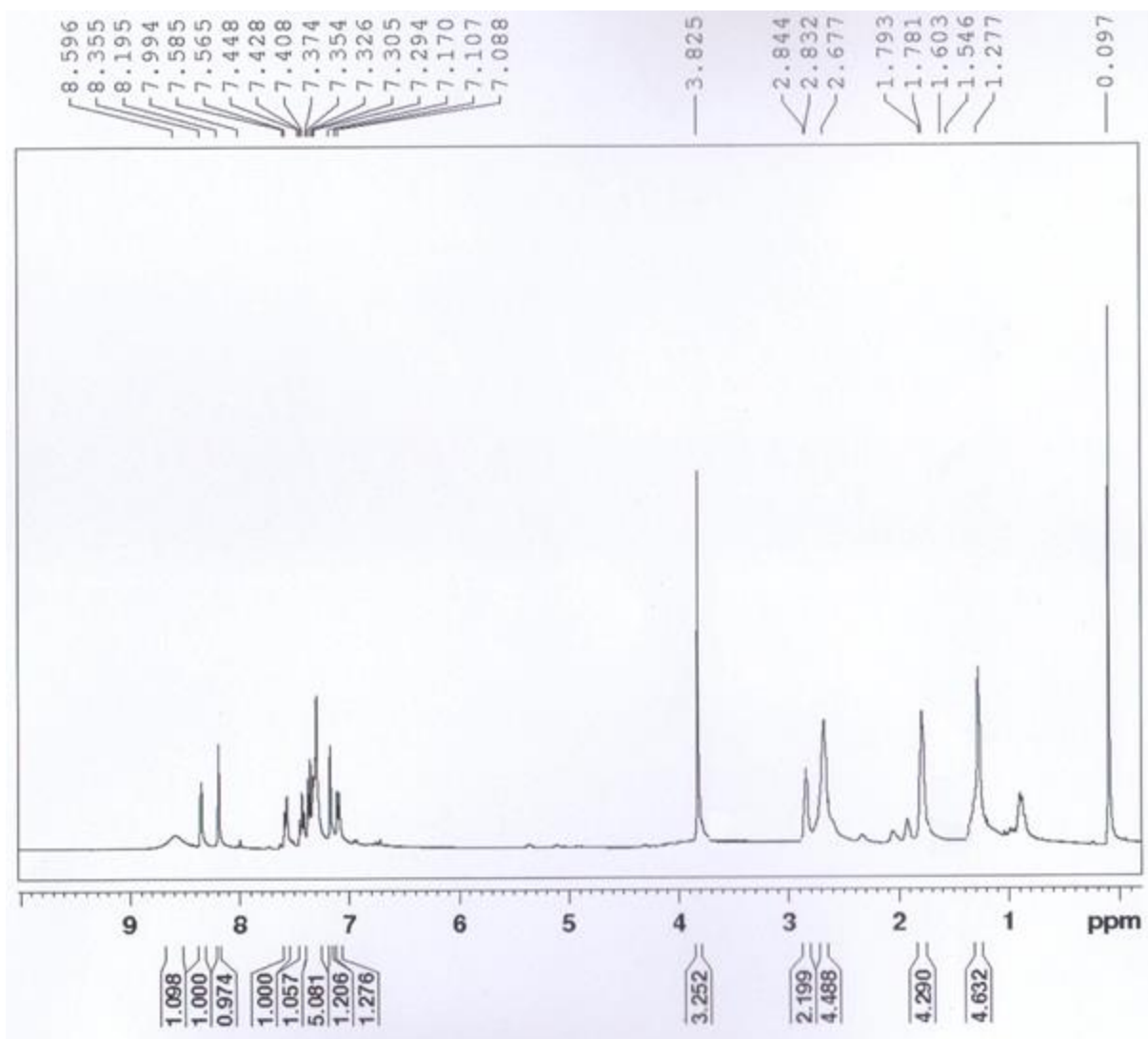
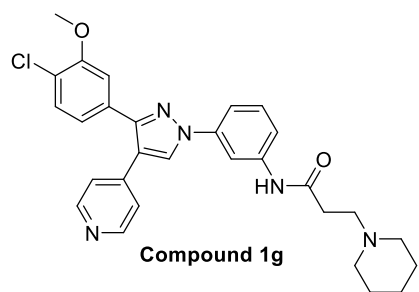
Chemical Formula: $C_{33}H_{31}ClN_6O_2$
 $m/z: + 2H^+ 579.9$

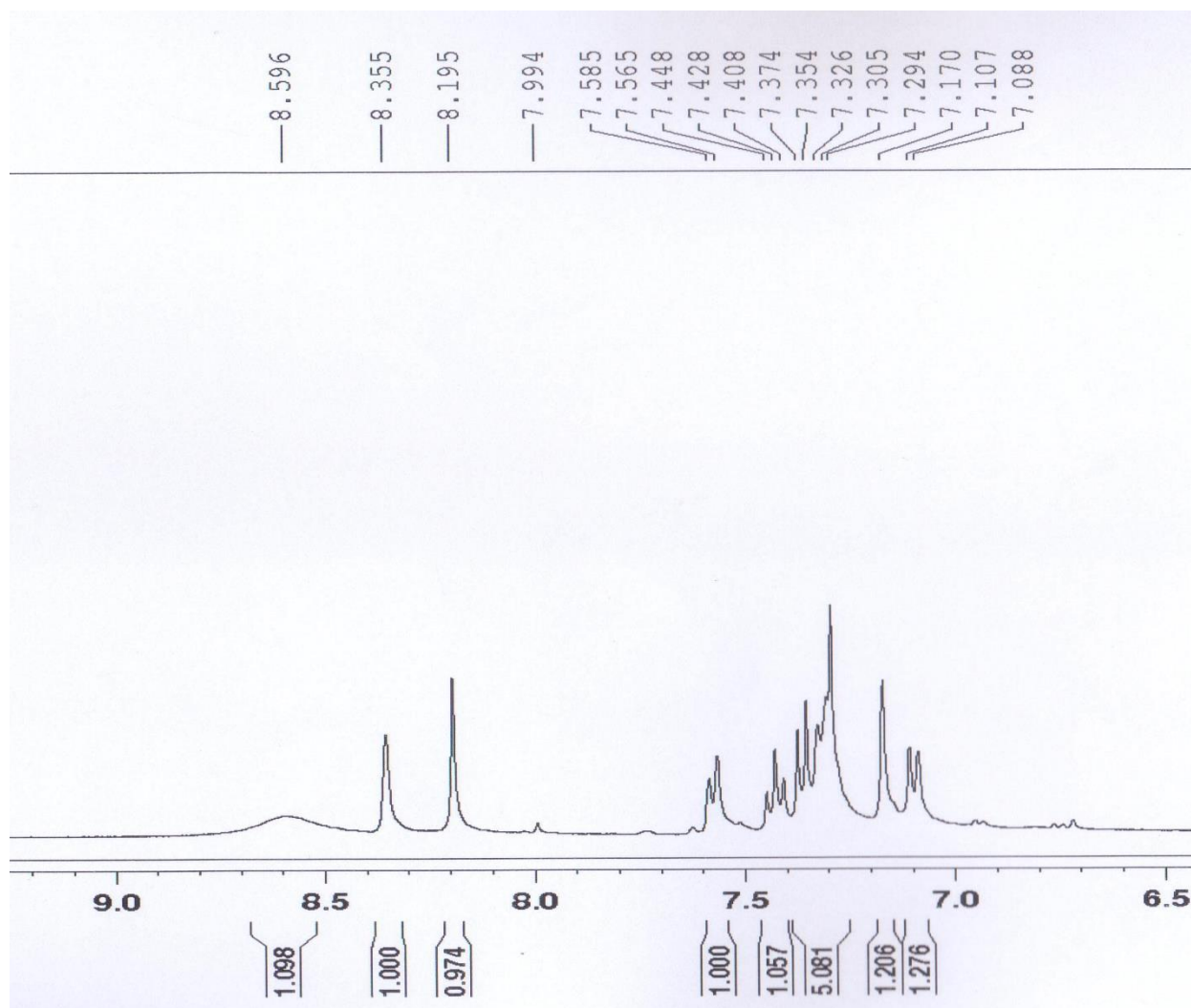
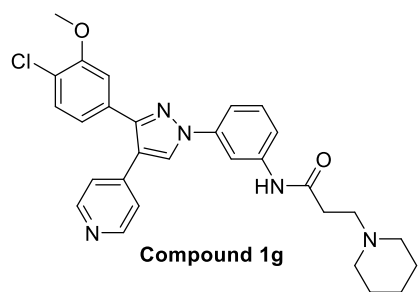


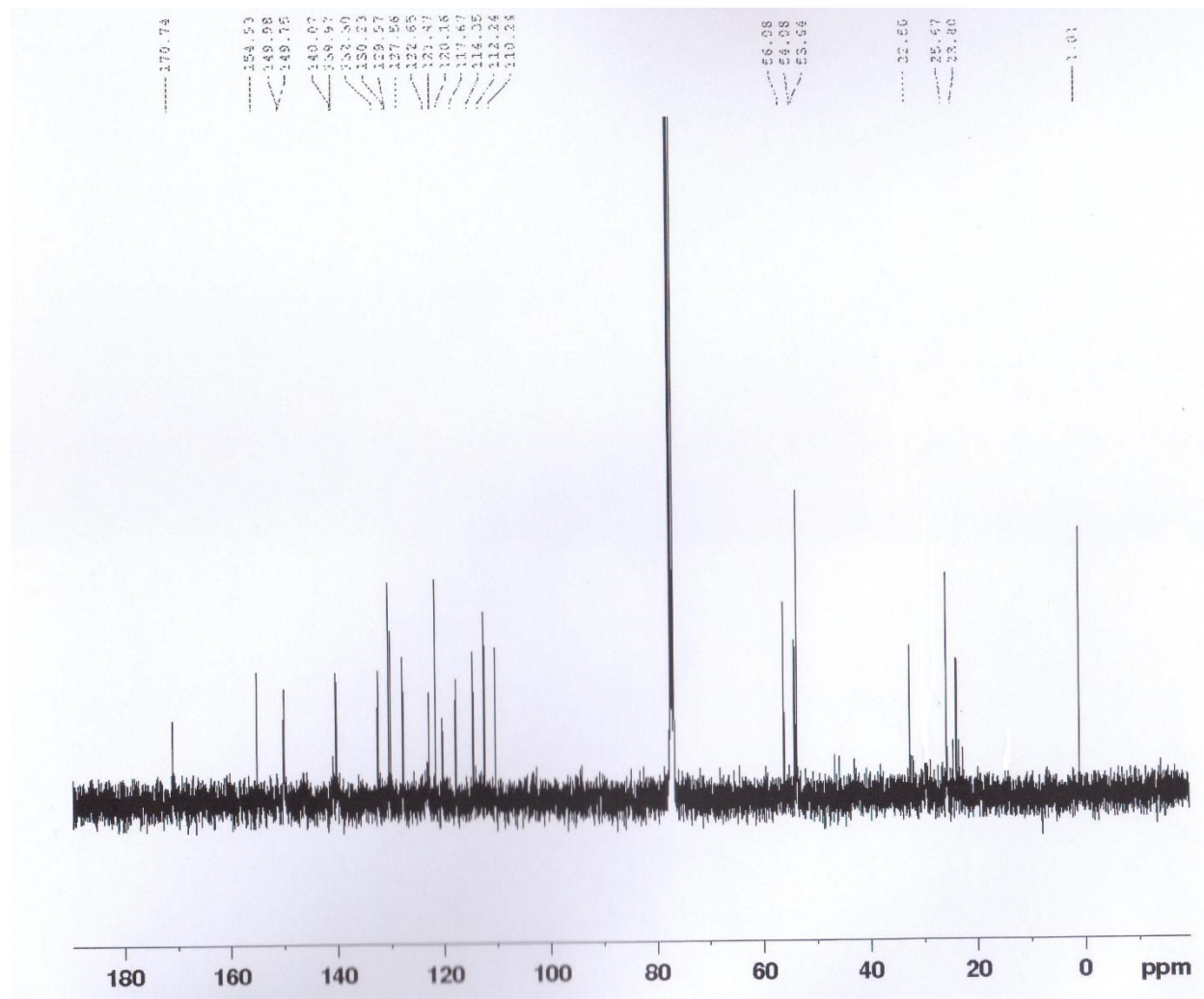
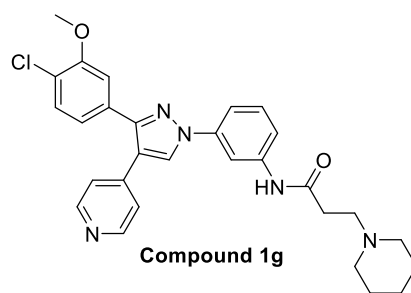


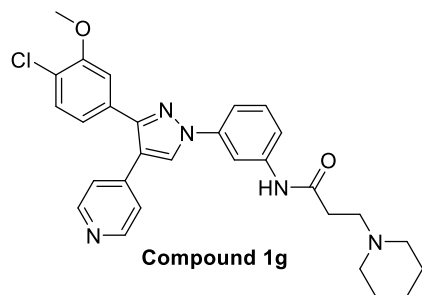




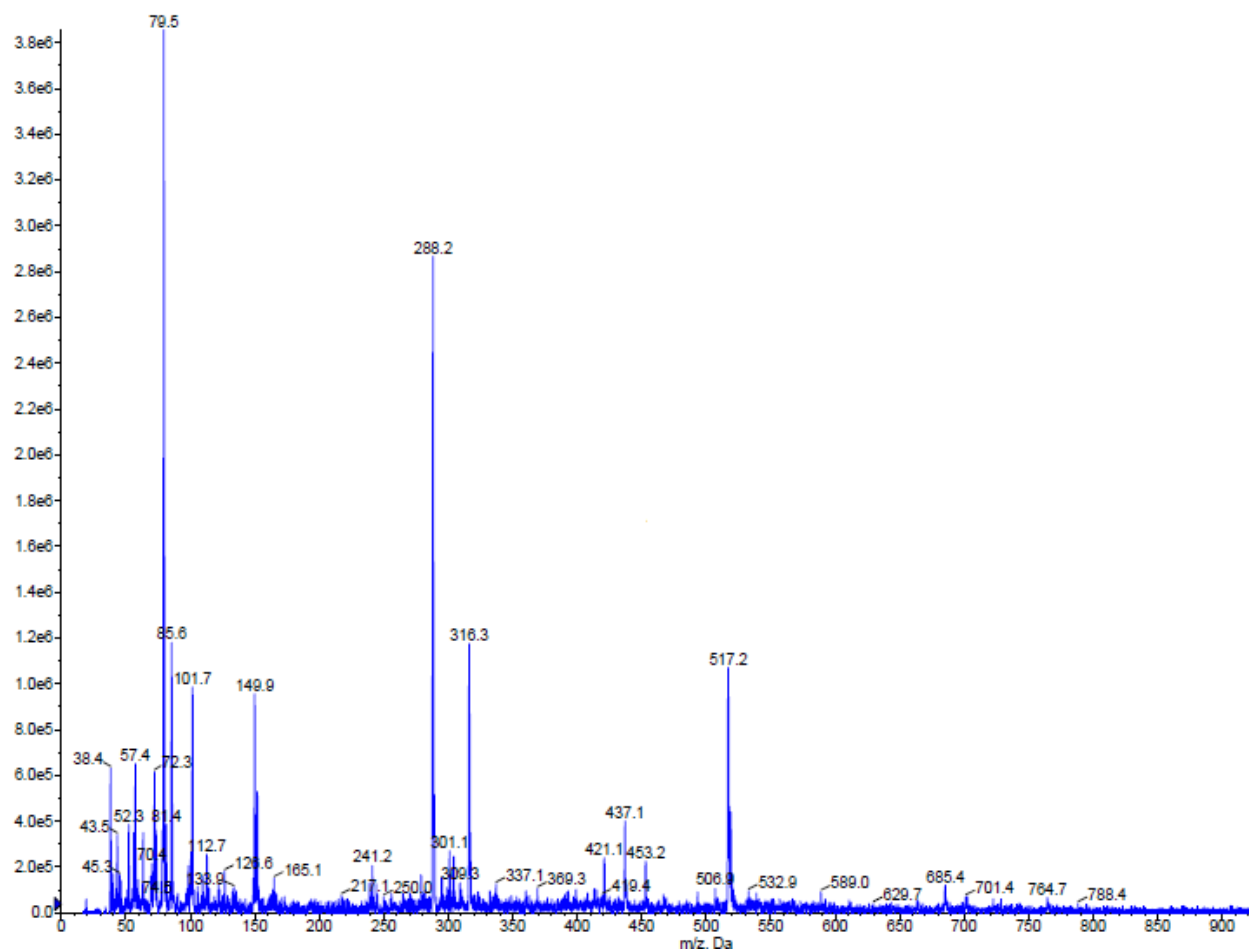


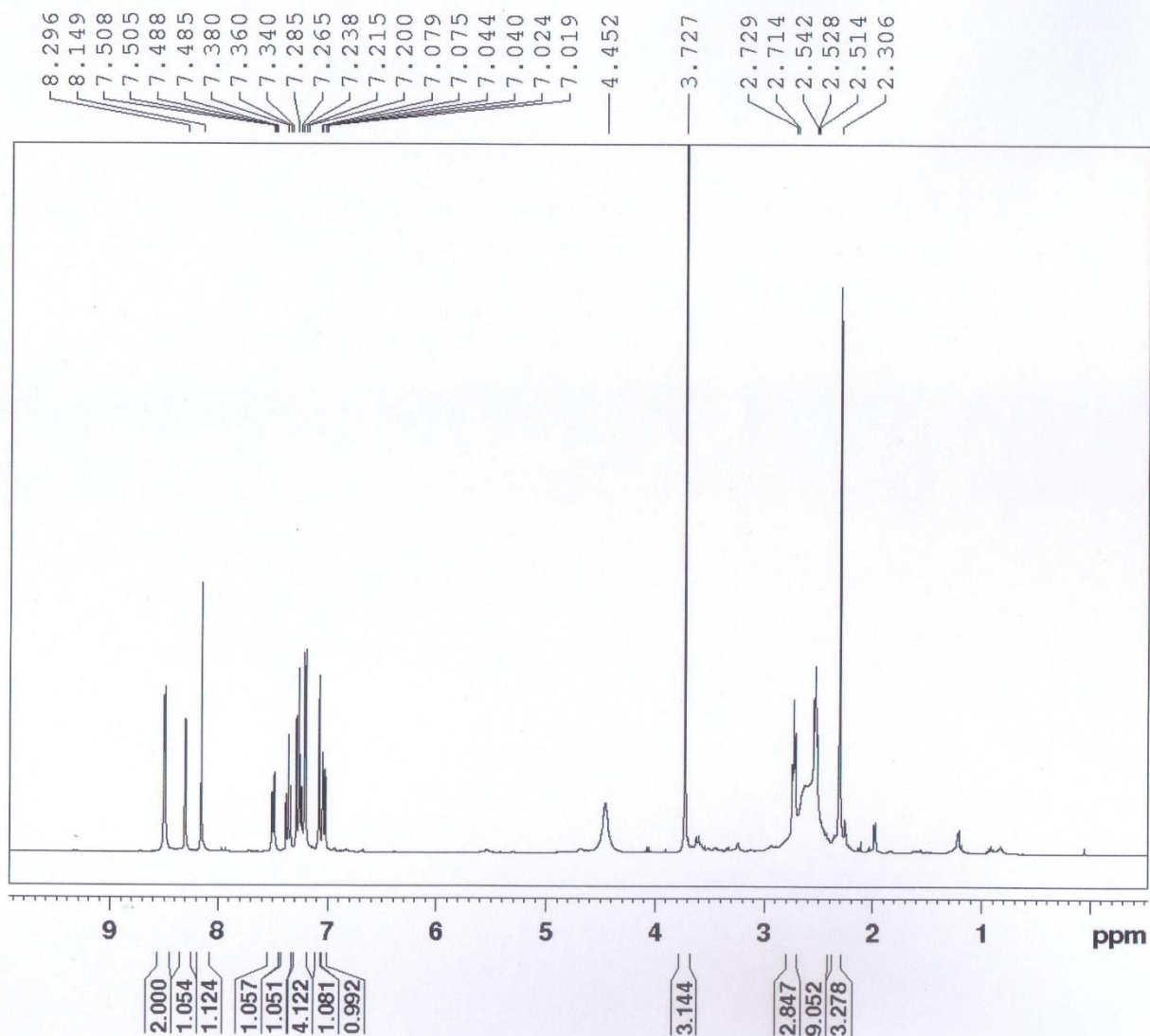
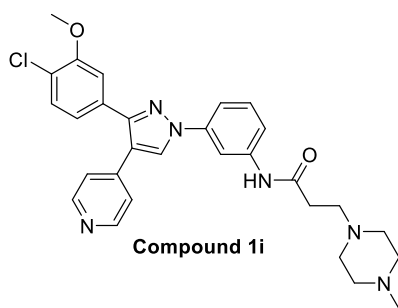


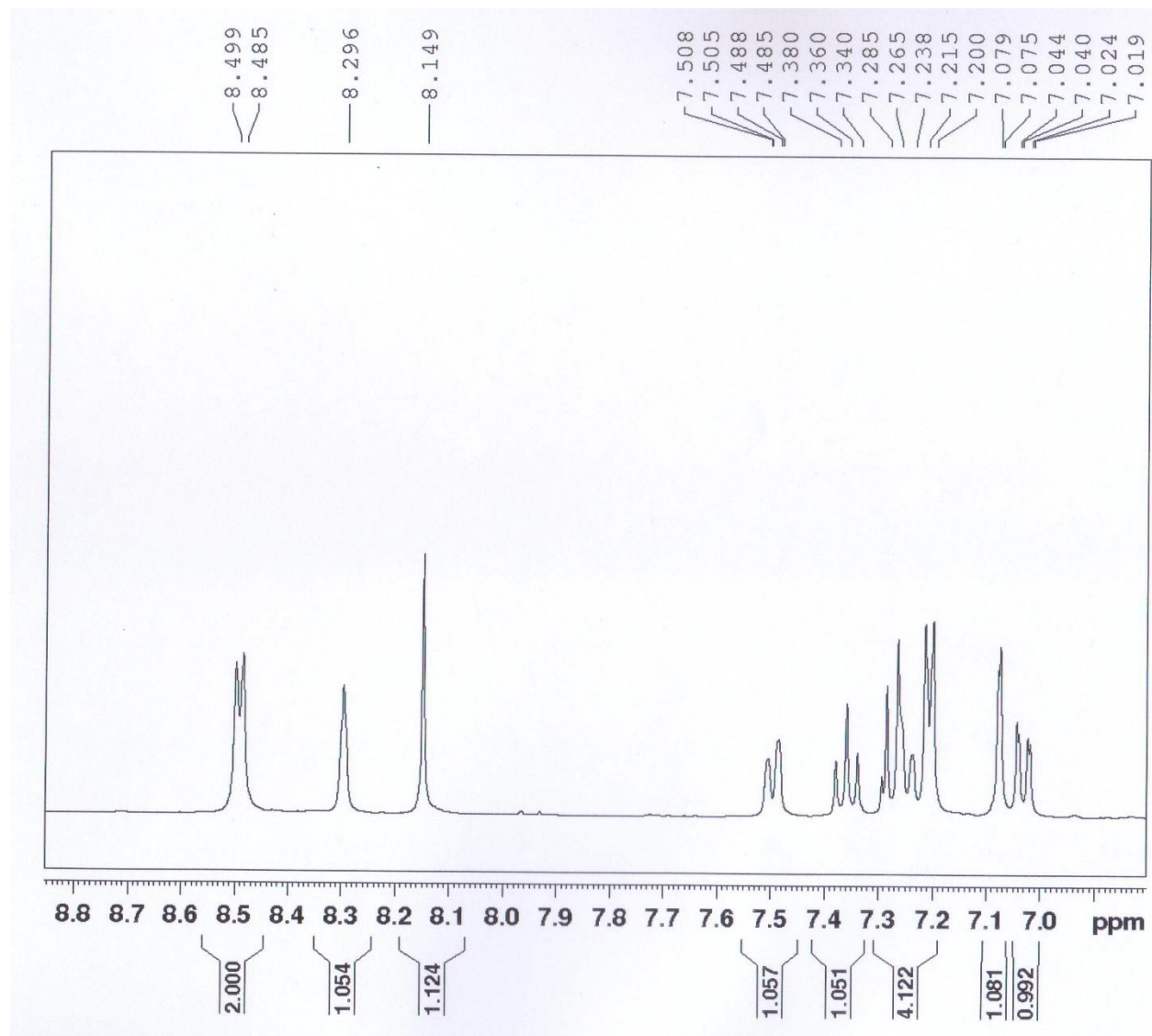
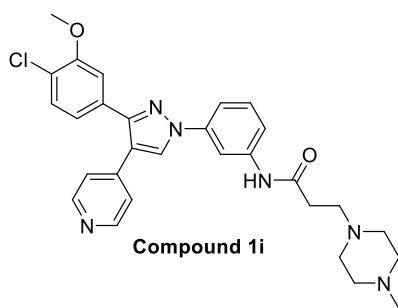


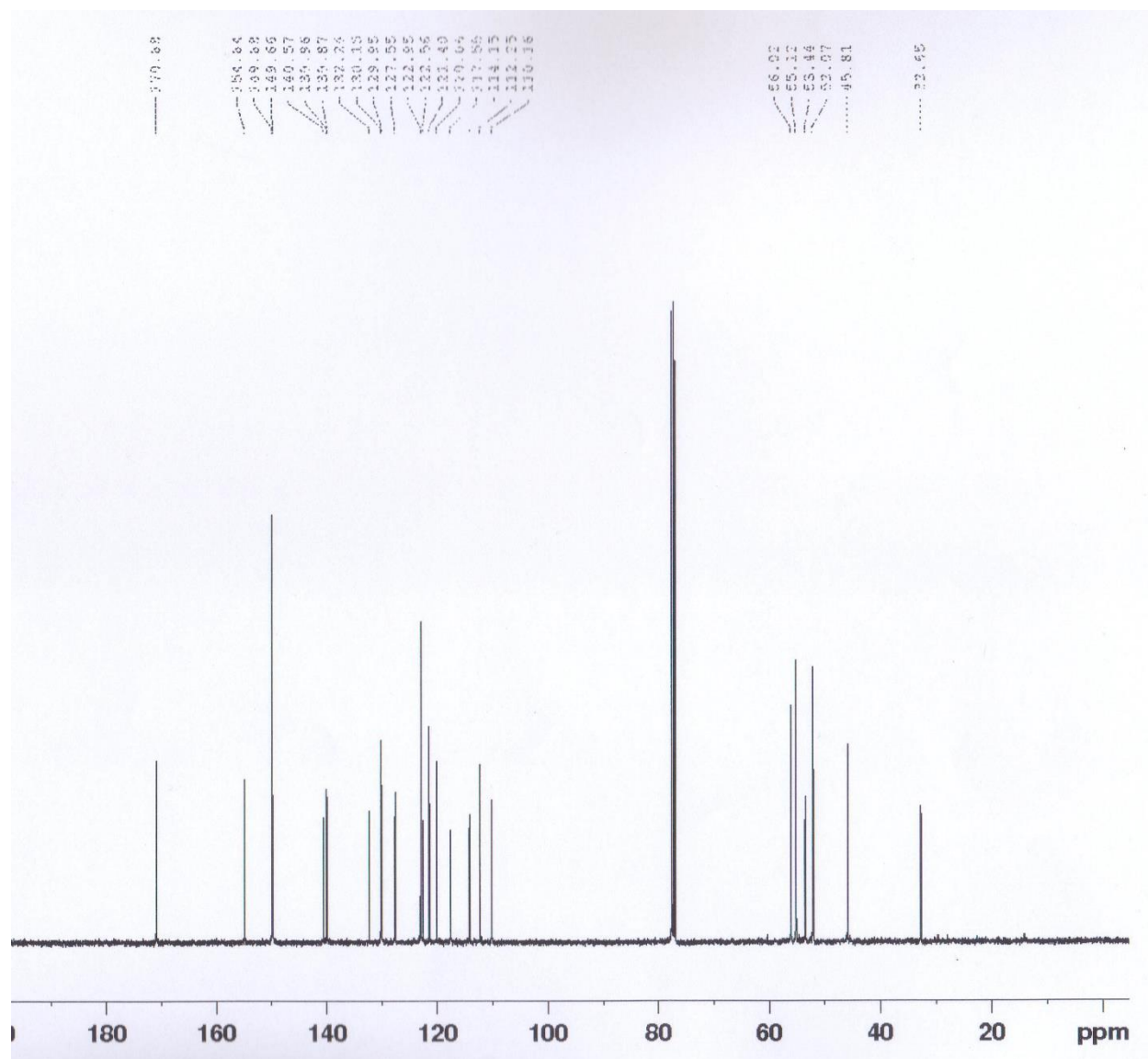
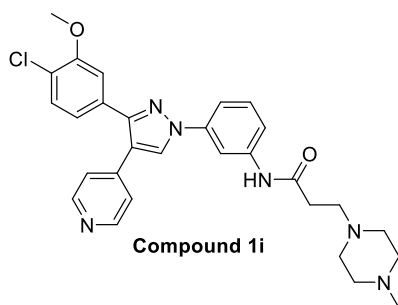


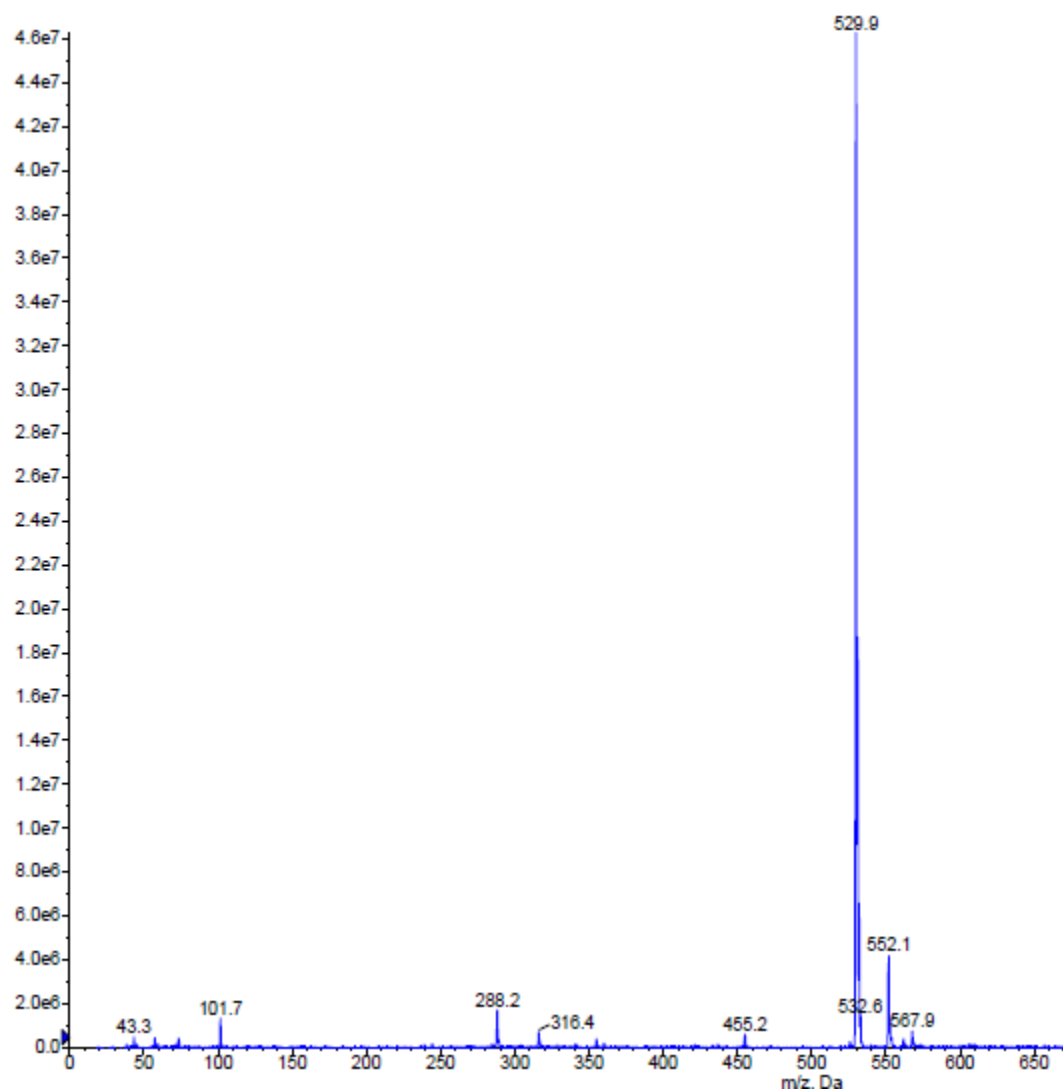
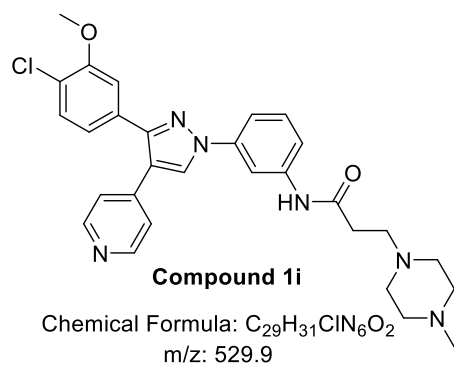
Chemical Formula: $C_{29}H_{30}ClN_5O_2$
 $m/z + 2$: 517.21

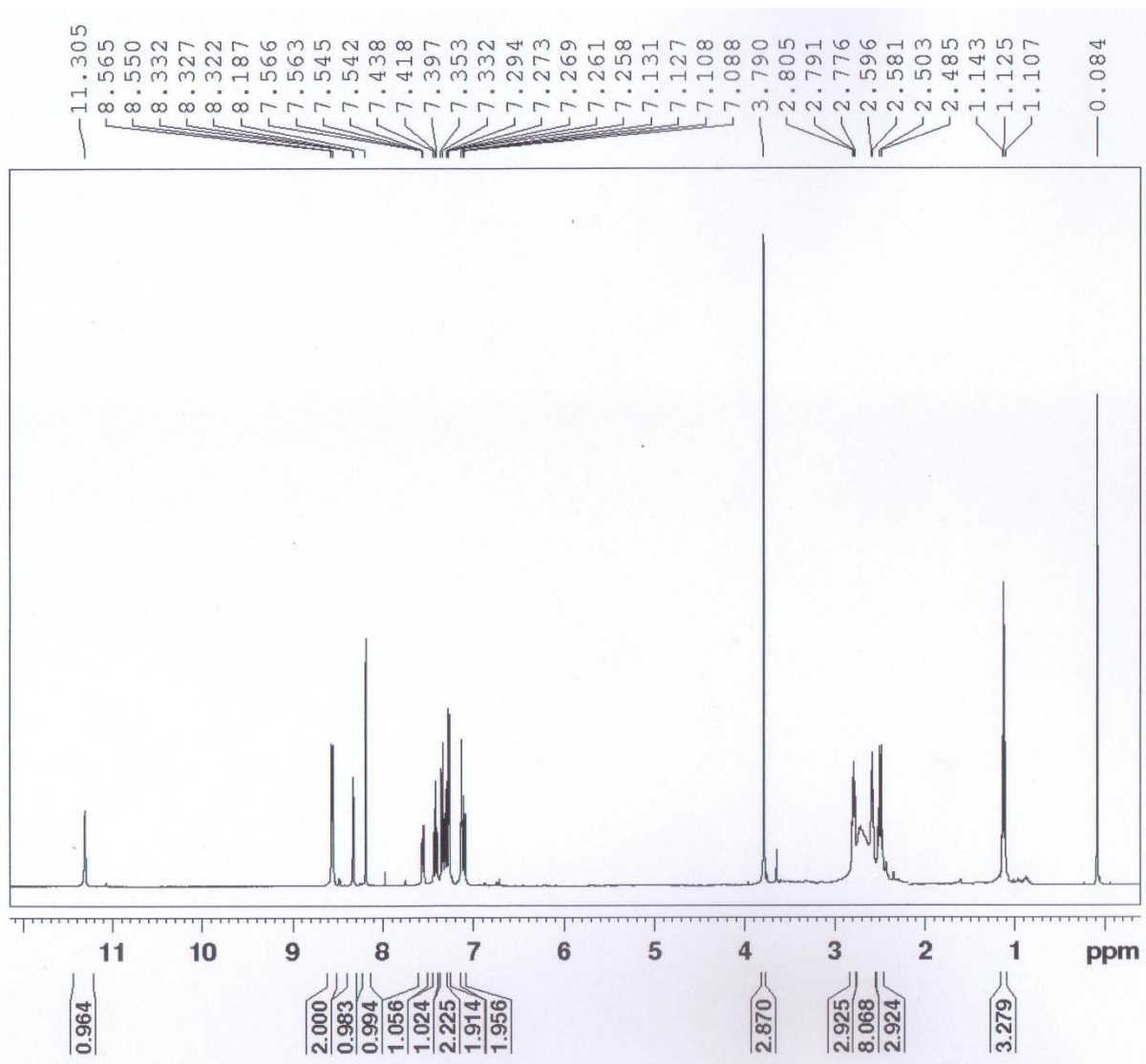
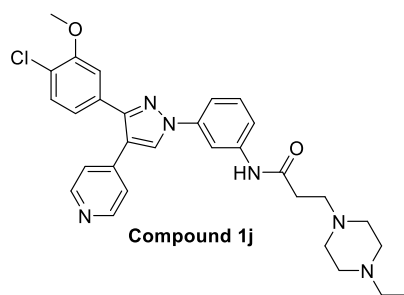


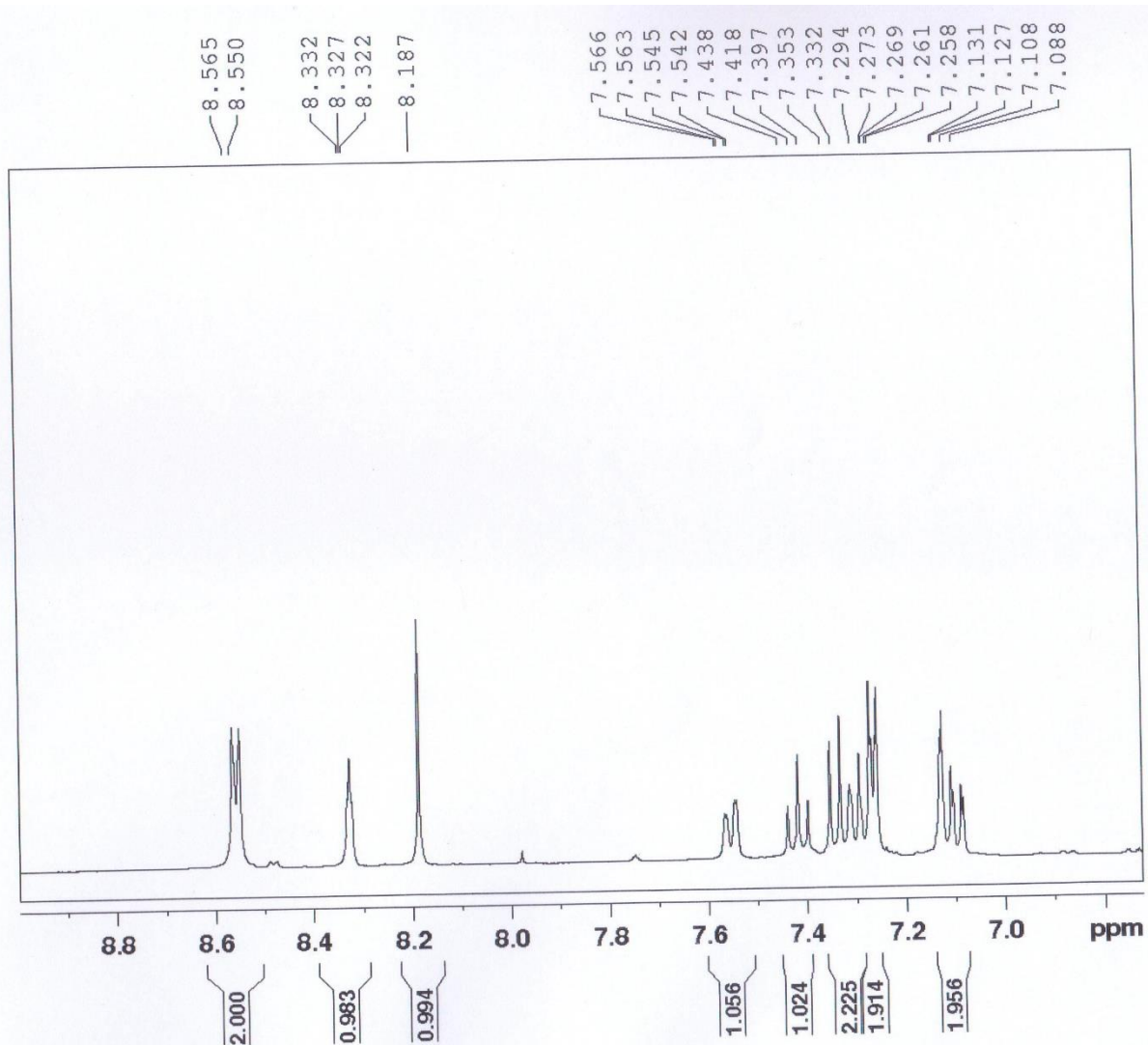
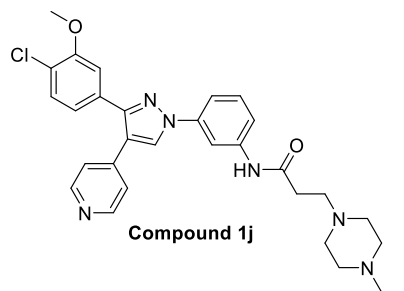


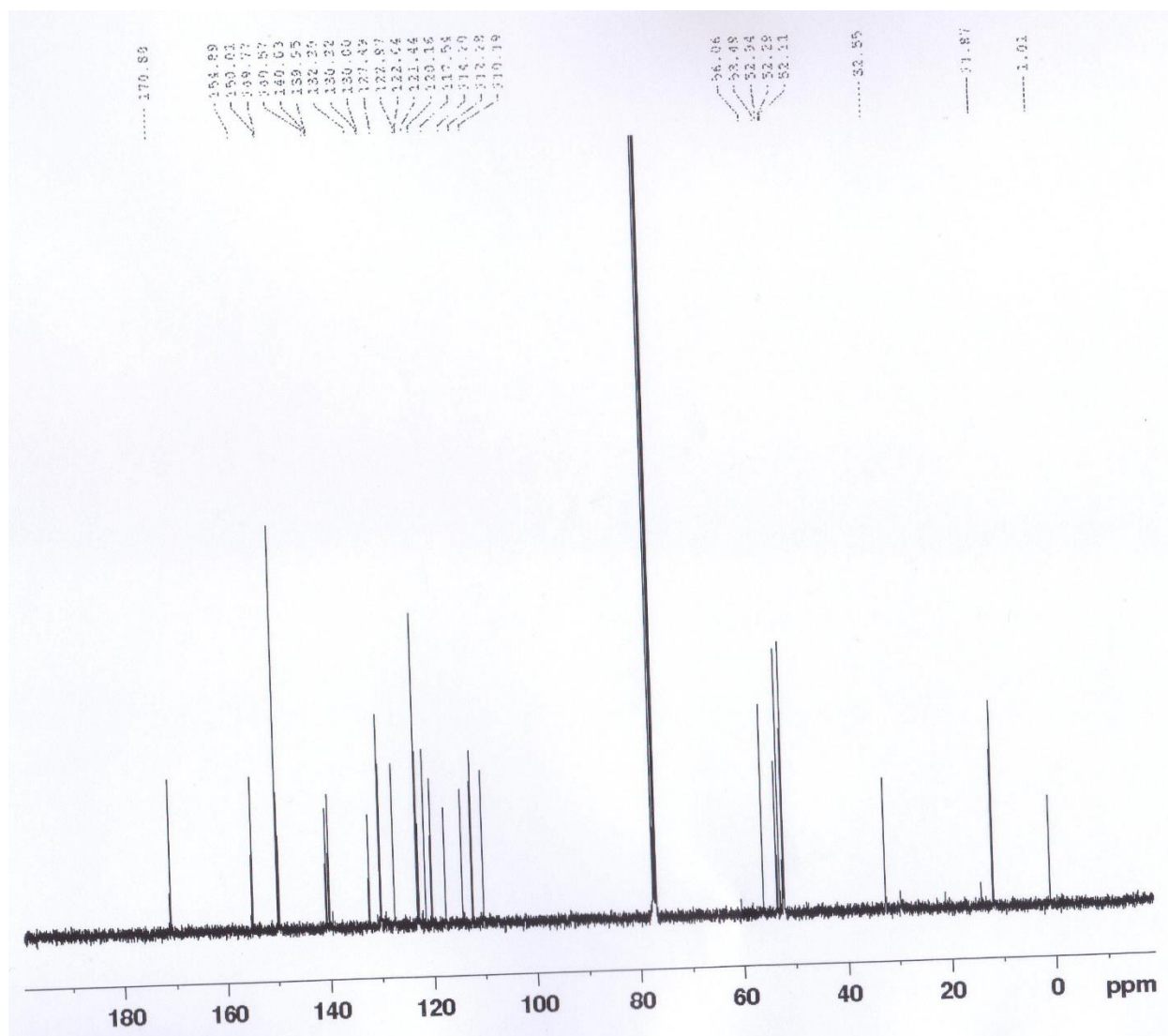
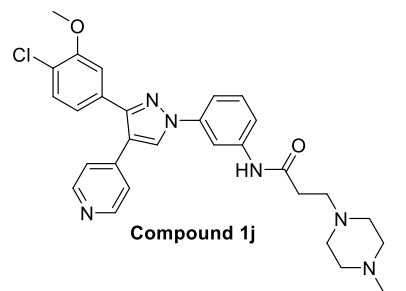


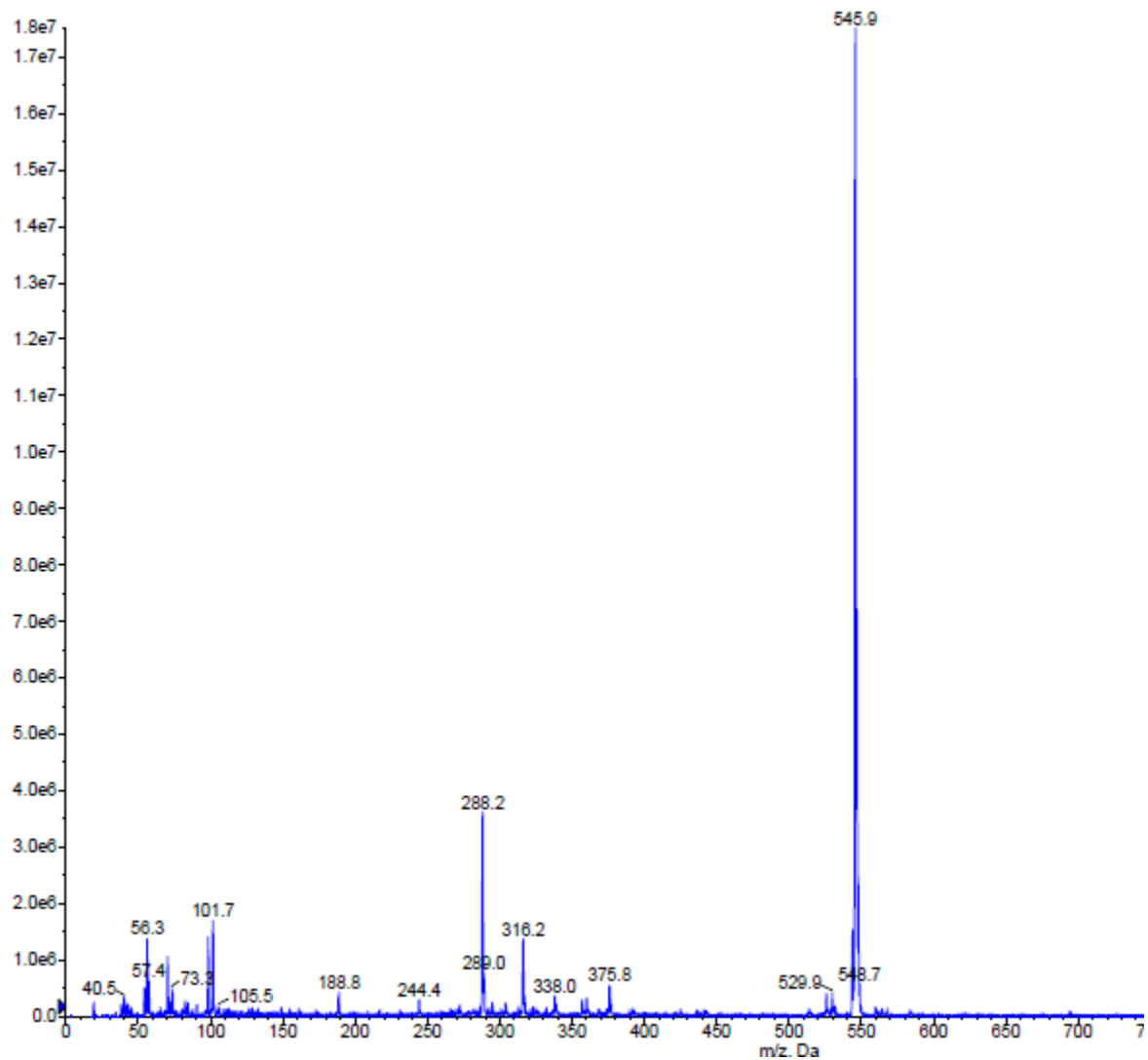
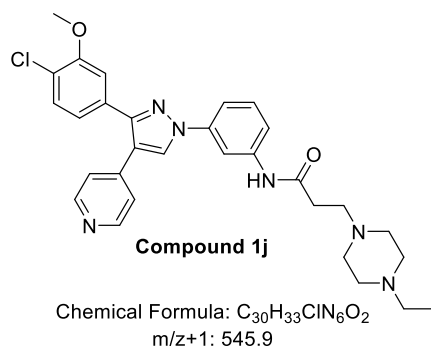


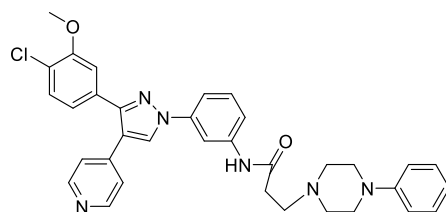






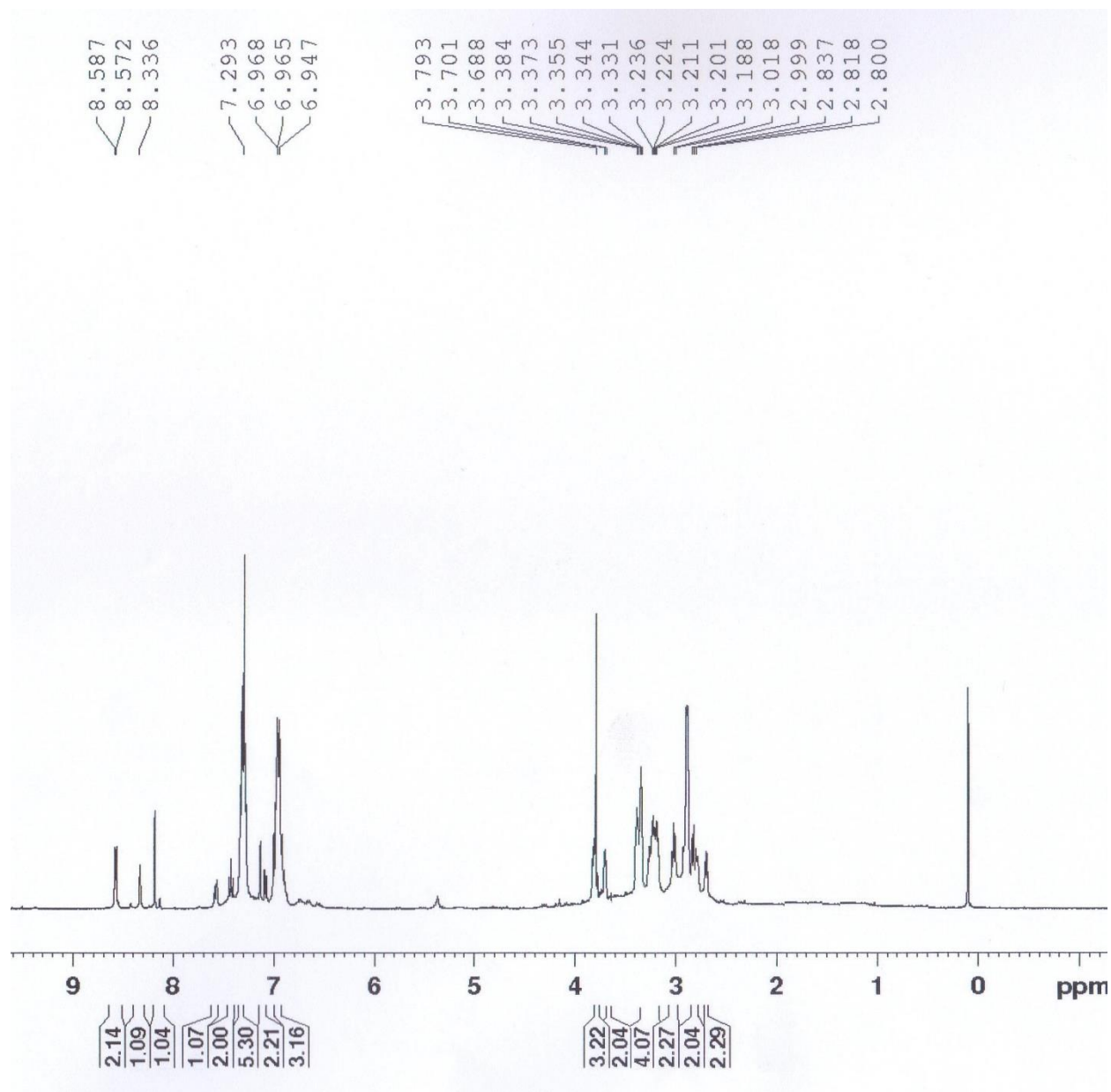


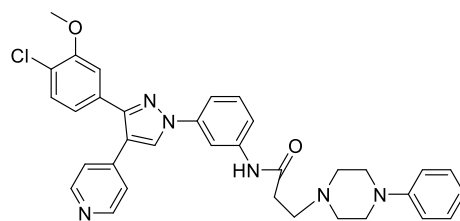




Compound 1K

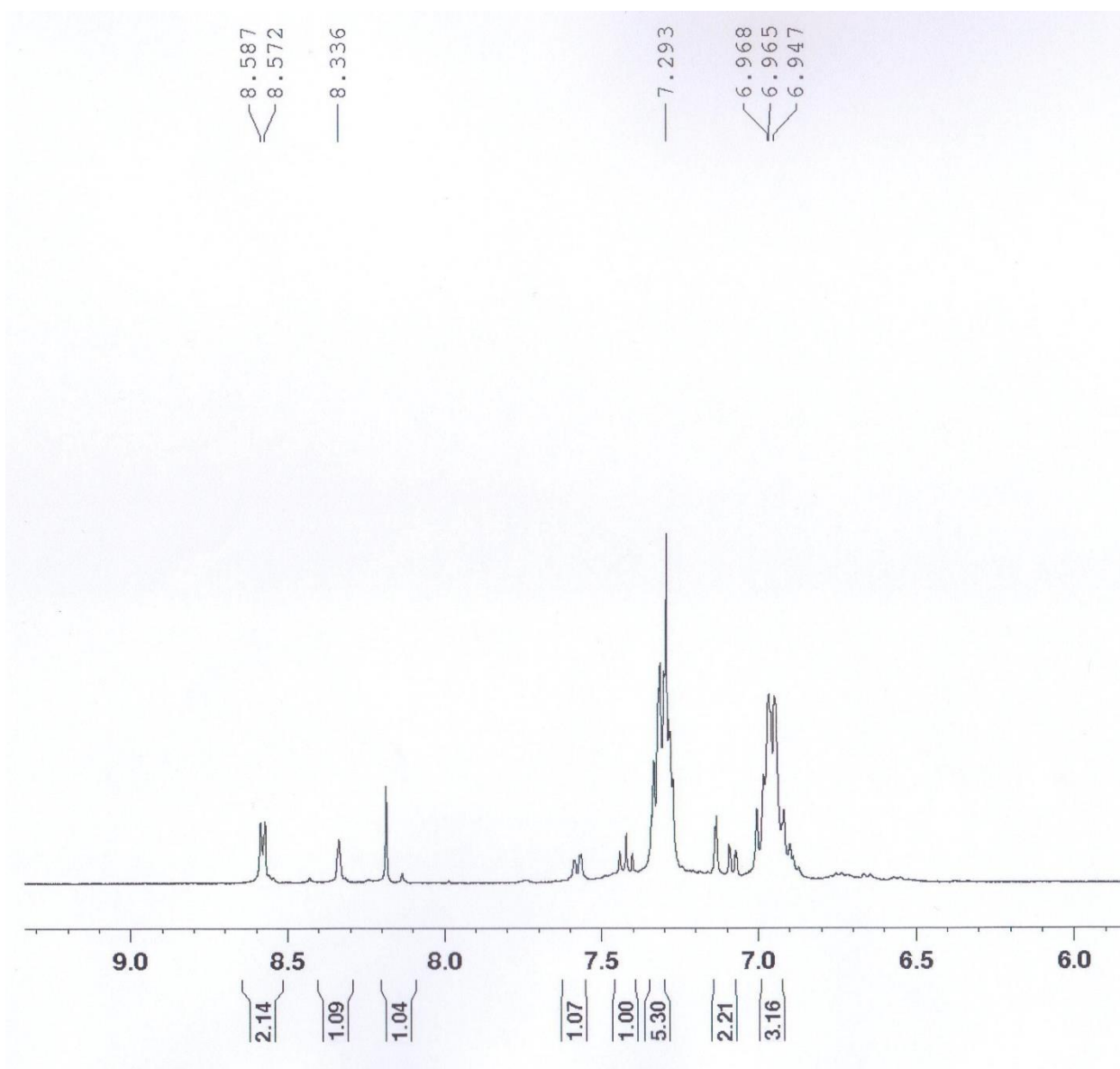
Exact Mass: 592.24

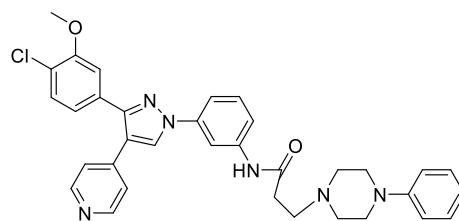




Compound 1K

Exact Mass: 592.24





Compound 1K

Exact Mass: 592.24

