SUPPORTING INFORMATION

Efficient Synthesis of Pentasubstituted Pyrroles *via* Intramolecular C-arylation

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General information

Solvents and chemicals were purchased from Sigma-Aldrich (Milwaukee, USA, www.sigmaaldrich.com), Acros Organic (Geel, Belgium, www.acros.com) and Fluorochem (Derbyshire, UK, www.fluorochem.co.uk). Rink Amide resin (100-200 mesh, 1% DVB, 0.6 mmol/g) and Wang resin (100-200 mesh, 1% DVB, 1.4 mmol/g) were obtained from AAPPTec (Louisville, USA, www.aapptec.com). Solid-phase synthesis was carried out in plastic reaction vessels (syringes, each equipped with a porous disk) using a manually operated synthesizer (Torviq, Niles, USA, www.torviq.com). Dry solvents were dried over 4Å molecular sieves or stored as received from commercial suppliers.

All reactions were carried out at ambient temperature (23 °C) unless stated otherwise. For the LC/MS analyses, a sample of resin (~5 mg) was treated with 50% TFA in DCM, the cleavage cocktail was evaporated under a stream of nitrogen, the cleaved compounds dissolved in CH_3CN /H_2O (20% or 50%; 1 mL) and the resin was removed by filtration.

LC/MS analyses were carried out using UPLC-MS system consisting of UPLC chromatograph Acquity with photodiode array detector and single quadrupole mass spectrometer (Waters), using C18 X-Select HSS T3 column (2.5 µm, 3.0 mm x 50 mm) at 30 °C and flow rate of 0.6 mL/min. Mobile phase was (A) 0.01M ammonium acetate (AmAc) in H_2O, and (B) CH_3CN, linearly programmed gradient elution. The ESI source operated at capillary voltage of 3 kV, desolvation temperature of 350 °C and source temperature of 120 °C.

Purification was carried out using semipreparative HPLC chromatograph with MS detector (YMC-Actus Pro C18 column, 20 x 100 mm, 5 µm, MP 0.01M aqueous AmAc/ CH_3CN, flow rate 15 mL/min, gradient elution) or by normal phase (silica gel chromatography). Residual solvents (H_2O and AmAc buffer) were lyophilized by the ScanVac Coolsafe 110-4 operating at -110 °C.

HRMS analysis was performed using LC-MS (Dionex Ultimate 3000, Thermo Fischer Scientific, USA) with Exactive Plus Orbitrap high-resolution mass spectrometer (Thermo Exactive plus, Thermo Fischer Scientific, USA) operating at positive or negative full scan mode (120 000 FWMH) in the range of 100-1000 *m/z* with electrospray ionization operating at 150 °C and the source voltage of 3.6 kV. Chromatographic separation was performed on Phenomenex Gemini column (C18, 50 x 2 mm, 3 μm particle size) with isocratic elution and mobile phase (MP) containing MeOH/H_2O/formic acid 95:5:0.1. The samples were dissolved in CH_3CN or MeOH/H_2O (95:5 v/v).

NMR experiments were performed with the use of ECX500 spectrometer (JEOL RESONANCE, Tokyo, Japan) at magnetic field strength of 11.75 T corresponding to ^{1}H, ^{13}C and ^{15}N resonance

frequencies of 500.16 MHz, 125.77 MHz and 50.7 MHz at 25 °C. The assignment of ^{1}H, ^{13}C and ^{15}N signals was done by the combination of ^{1}H, $^{13}C\{^{1}H\}$, ^{1}H-^{1}H COSY, ^{1}H-^{1}H NOESY, ^{1}H-^{13}C HMQC, ^{1}H-^{13}C HMBC, ^{1}H-^{15}N HMQC and ^{1}H-^{15}N HMBC experiments. In case of **14** and **15**, the proton measurements were performed at 25°C, 35°C, 45°C, 55°C, 85°C and 115°C. Chemical shifts (δ) are reported in parts per million (ppm) and coupling constants (*J*) are reported in Hertz (Hz). The signals of DMSO-d_6 were set at 2.52 ppm in ^{1}H NMR spectra and at 39.52 ppm in ^{13}C NMR spectra. ^{15}N chemical shifts were referenced to external 90% formamide in DMSO-d_6 (112.00 ppm).[1] Abbreviations in NMR spectra: br. s – broad singlet, s – singlet, d – doublet, dd – doublet of doublets, ddd – doublet of doublets of doublets, dt – doublet of triplets, t - triplet, m – multiplet.

General Method for Calculation of Yields Using ^{1}H NMR: ^{1}H NMR spectra of external standard in DMSO-d_6 at three different concentrations were measured. In each spectrum solvent signal was integrated followed by the integration of selected H_{Ar} signals of external standard. Ratios of solvent/standard signal areas along with a known quantity of the standard were used to construct a calibration curve. Then ^{1}H NMR spectra of the studied sample were measured, and the ratio of solvent/sample (selected H_{Ar} signal) areas was determined. Using the calibration curve, the quantity of compound in the sample was calculated.

Quantification of the resin loading: Quantification of loading of Rink or Wang resin with immobilized Fmoc-Asp(OMe)-OH, Fmoc-Ala-OH, Fmoc-Pro-OH, Fmoc-Sar-OH or 2-(Fmoc-amino)ethanol: After the immobilization, the sample of resin **2**, **2e**, **1b**, **1c**, **1d**, **1f** (~30 mg) was washed with DCM (3x), with MeOH (5x), dried and divided into two samples (2 × 10 mg). Both samples were cleaved from the resin using TFA in DCM (0.5 mL, 50%) for 2 h at ambient temperature. The cleavage cocktail was evaporated by a stream of nitrogen and oily residue was extracted into 1 mL of MeOH and analyzed by UPLC-UV-MS. Loading of resin was calculated with the use of an external standard (Fmoc-Ala-OH, 0.5 mg/mL).

Quantification of resin with immobilized 1,3-diaminopropane: After the immobilization, the resin **1g** (~30 mg) was reacted with Fmoc-OSu (65 mg, 0.2 mmol) in DCM (0.5 mL) for 30 min at room temperature and subsequently washed with DCM (3x), with MeOH (5x), dried and divided into two samples (2 × 10 mg). The quantification was carried out according to the procedure described in the previous paragraph.

Experimental procedures

Immobilization of Fmoc-Asp(OMe)-OH on Wang resin and Rink amide resin (2a, 2e)

Rink amide resin (1 g, 0.6 mmol/g) was washed with DCM (3x) and with DMF (3x) and then subjected to Fmoc-deprotection using 50% solution of piperidine in DMF (10 mL) at room temperature. After shaking for 20 min, the resin was washed with DMF (5x). Wang resin (1 g, 1.4 mmol/g) was washed with DCM (3x) and DMF (3x). A solution of Fmoc-Asp(OMe)-OH (739 mg; 2 mmol), HOBt (306 mg, 2.0 mmol), DMAP (61 mg, 0.5 mmol, used only for Wang resin), and DIC (312 μL, 2.0 mmol) in DMF/DCM (10 mL, 50%) was added to the swollen Wang resin and deprotected Rink amide resin, and the reaction mixtures were shaken for 24 h at ambient temperature. Both resins were washed with DMF (3x) and with DCM (3x). The quantification was carried out as described in the paragraph "Quantification of the resin loading". Calculated loadings of immobilized amino acids: 0.6 mmol/g for Wang resin and 0.3 mmol/g for Rink amide resin.

Immobilization of Fmoc-Sar-OH, Fmoc-Ala-OH and Fmo-Pro-OH on Rink amide resin (1b, 1c, 1d)

Rink amide resin (1 g, 0.6 mmol/g) was washed with DCM (3x) and with DMF (3x) and then subjected to Fmoc-deprotection using 50% solution of piperidine in DMF (10 mL) at room temperature. After shaking for 20 min, the resin was washed with DMF (5x). A solution of Fmoc-AA-OH (2 mmol), HOBt (306 mg, 2.0 mmol) and DIC (312 μL, 2.0 mmol) in DMF/DCM (10 mL, 50%) was added and the resin slurry was shaken for 24 h at ambient temperature. After the reaction, the resin was washed with DMF (3x) and with DCM (3x) and quantified as described above. Calculated loadings of immobilized amino acids were 0.3 mmol/g.

Immobilization of 2-(Fmoc-amino)ethanol to Wang resin (1f)

Wang resin (1g; 1.4 mmol/g) was washed with anhydrous DCM (3x) and a solution of trichloroacetonitrile (15 mmol; 1.5 mL) in 10 mL anhydrous DCM was added. The resin was kept in a freezer for 30 min. Then solution of DBU (0.67 mmol; 100 µL) in 2 mL anhydrous DCM was added, the resin slurry was shaken for 1 h and subsequently washed with anhydrous DCM (3x) and with anhydrous THF (3x). Solution of 2-(Fmoc-amino)ethanol (3 mmol; 849 mg) in 10 mL anhydrous THF was added to the resin followed by dropwise addition of $BF_3{\cdot}Et_2O$ (0.3 mmol; 63 µL) and the resin slurry was shaken for 30 min. Resin was washed with THF (3x), MeOH (3x) and with DCM (3x). The quantification was carried out as described in the paragraph "Quantification of the resin loading". Calculated loading was 0.33 mmol/g.

Immobilization of 1,3-diaminopropane (1g)

Wang resin (1 g, 1.4 mmol/g) was washed with DCM (3x). A solution of CDI (810 mg, 5.0 mmol) and pyridine (400 μL, 5.0 mmol) in 10 mL DCM was added and the resin slurry was shaken for 2 h at ambient temperature. The resin was then washed with DCM (3x) and a solution of 1,3-diaminopropane (421 μL, 5.0 mmol) in 10 mL DCM was added. The resin was shaken for 16 h and washed with DCM (5x). Sample of resulting resin was derivatized with FmocOSu according to procedure described in the paragraph "Quantification of the resin loading". Calculated loading was 0.6 mmol/g.

Acylation with Fmoc-Asp(OMe)-OH (2b-d, 2f-g)

Resin **1b**, **1c**, **1d** and **1f** were washed with DCM (3x) and with DMF (3x) and then subjected to Fmoc-deprotection using 20% solution of piperidine in DMF (10 mL) at room temperature. After shaking for 20 min, the resins were washed with DMF (5x). Subsequently, resins **1b**, **1c**, **1d** and **1f**, **1g** were shaken with solution of Fmoc-Asp(OMe)-OH (739 mg; 2 mmol), HOBt (306 mg, 2.0 mmol), and DIC (312 μL, 2.0 mmol) in DMF/DCM (10 mL, 50%) for 16 h at ambient temperature. All resins were washed with DMF (3x) and with DCM (3x) and analyzed by the standard procedure.

Nosylation with 4-nitrobenzenesulfonyl chloride (3)

Resins **2** (1 g) were treated with 20% piperidine in DMF (10 ml) for 20 min and subsequently washed with DMF (3x) and DCM (5x). A solution of 4-NsCl (640 mg; 3 mmol) and 2,6-lutidine (380 µL, 3 mmol) in DCM (10 mL) was added to the resin and the resin slurry was shaken for 16 h. Resins were then washed with DCM (5x) and analyzed by the standard procedure.

Alkylation with α-bromoketones (4)

Resins **3** (300 mg) were washed with DMF (3x) and a solution of α-bromoketone (0.6 mmol) and DIPEA (209 μL, 1.2 mmol) in DMF (3 mL) was added. The reaction mixtures were shaken for 16 h at ambient temperature. The resin was washed with DMF (3x) and with DCM (3x) and analyzed by the standard procedure.

TMSOK-based cyclization and cleavage from the resin (6-9; 14-16)

Resins **4** (300 mg) were washed with DCM (3x), DMF (3x) and a 0.3 M solution of TMSOK (116 mg; 0.9 mmol) in 3 mL DMF was added. The reaction mixtures were shaken at room temperature for 30 min. After the reaction, the resins were washed with DMF (3x) and DCM (3x). Subsequently, the resins were treated with 50% TFA in DCM for 1 h. The cleavage cocktails were separated and each resin was washed with 50% TFA in DCM (2x). The washes were collected and evaporated by a stream of nitrogen. The crude compounds **6**, **7** and **9** were purified using column chromatography in EtOAc as

mobile phase. In cases of **8**, **14**- **16,** the crude compounds were dissolved in CH_3CN and purified by semipreparative HPLC.

Alkylation with 1-chloropropan-2-one with thermal pyrrole cyclization (10-13)

Resins **3a**, **3c**, **3f** and **3g** (500 mg) were washed with DCM (3x) and DMSO (3x). Then, the swollen resins were shaken with solution of 1-chloropropan-2-one (207 μL; 2.5 mmol), DIPEA (875 μL; 5 mmol) in 5 mL DMSO for 16 h at 80°C. The resins were washed with DMSO (3x) and DCM (3x) and treated with 50% TFA in DCM for 1 h. The cleavage cocktails were separated and each resin was washed with 50% TFA in DCM (2x). The washes were collected and evaporated by a stream of nitrogen. The crude compounds were dissolved in CH_3CN and purified by semipreparative HPLC.

Pyrrole on-resin alkylation (19, 20)

Resin **5** (500 mg) was washed with DCM (3x) and DMF (3x). For methyl derivative: 5 mL of 10% solution of methyl iodide in DMF and TMSOK (320 mg; 2.5 mmol) was added to the resin and the resin slurry was shaken at room temperature for 16 h. For benzyl derivative: 5 mL of 10% solution of benzyl bromide in *N*-methyl pyrrolidone (NMP) and TMSOK (320 mg; 2.5 mmol) was added and the resin slurry was shaken at 110°C for 16 h. After the reaction, the resin was washed with DMF (3x), DCM (3x). In both cases, the alkylated products were cleaved from resin and purified by semipreparative HPLC.

Amide post-cleavage formation (23, 24)

Resin **5** (300 mg) was washed with DCM (3x) and shaken with cleavage cocktail (3 mL) at room temperature for 1 h. The cleavage cocktail was then collected, and the combined washes were evaporated using a stream of nitrogen. The oil residue was dissolved in 2 mL of DCM and evaporated again using a stream of nitrogen. Resulting crude compound **6** was dissolved in 1 mL of propan-1-amine or 3-aminopropan-1-ol and heated at 80°C for 24 h (for 3-aminopropan-1-ol) or 48 h (for propan-1-amine). In the latter, additional 0.5 mL of propan-1-amine was added after 24 h. The reaction mixture was diluted with 3 ml DCM and 3 mL water. Conc. HCl was added until the acidic *p*H of the aqueous layer was obtained. The DCM layer was separated, the water layer was extracted 2x with 2 mL of DCM, combined DCM layers were extracted with 2 mL of 10% solution of HCl, then with brine and dried with magnesium sulfate. Resulting solution was adsorbed to silica gel and purified by column chromatography using mobile phase DCM/MeOH (9/1).

Reduction with sodium dithionite (22)

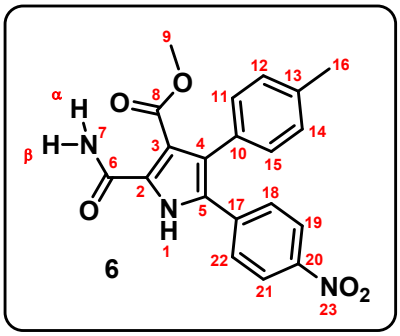
Resin **5** (300 mg) was washed with DCM (3x) and 4 mL of DCM was added. Then a solution of sodium dithionite (840 mg; 4 mmol), potassium carbonate (760 mg; 5.6 mmol) and tetrabutylammonium hydrogen sulfate (TBAHS) (136 mg; 0.4 mmol) in 8 mL of water was prepared and immediately added to the reaction mixture. The resin slurry was shaken for 16 h, then washed with mixture water/DCM (1/1) (3x), DMF (3x) and with DCM (3x). The final compound was cleaved from resin and purified by semipreparative HPLC. The NMR measurement revealed the presence of TBAHS and for this reason, the final compound **22** was re-purified by using column chromatography in EtOAc as mobile phase.

Preparation of indazole-oxide (27)

Resin **2** (0.5 g) was treated with 20% piperidine in DMF (5 ml) for 20 min and subsequently washed with DMF (3x) and DCM (5x). A solution of 2,4-NsCl (400 mg; 1.5 mmol) and 2,6-lutidine (190 µL, 1,5 mmol) in DCM (10 mL) was added and the reaction slurry was shaken for 16 h. Resin was washed with DCM (5x). DMF (3x) and a solution of 2-bromoacetophenone (210 µL; 1 mmol) and DIPEA (348 μL, 2 mmol) in DMF (5 mL) was added. The resin was shaken for 16 h, washed with DMF (3x) and with DCM (3x). The product was cleaved from the resin and purified by using semipreparative HPLC as described above.

1. G. E. Martin and C. E. Hadden, *J. Nat. Prod.,* 2000, **63**, 543−585.

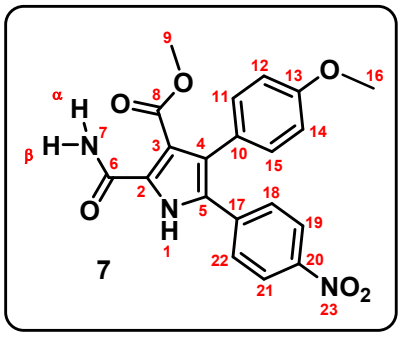
Methyl 2-carbamoyl-5-(4-nitrophenyl)-4-(*p*-tolyl)-1*H*-pyrrole-3-carboxylate (6)



Yellow solid 22 mg (77% yield). ^{1}H-NMR (500 MHz, DMSO-d$_6$) δ 12.52 (s, 1H; N^{1}-H), 8.45 (bs, 1H; N^{7}-H$^{\alpha}$), 8.09 – 8.11 (m, 2H; C^{19}-H, C^{21}-H), 7.74 (bs, 1H; N^{7}-H$^{\beta}$), 7.48-7.45 (m, 2H; C^{18}-H), 7.16 (d, *J* = 8.0 Hz, 2H; C^{12}-H, C^{14}-H), 7.04 (d, *J* = 8.0 Hz, 2H; C^{11}-H, C^{15}-H), 3.53 (s, 3H; C^{9}-H$_3$), 2.34 (s, 3H; C^{16}-H). ^{13}C-NMR (126 MHz, DMSO-*d*$_6$) δ 166.2 (C^{8}), 160.7 (C^{6}), 145.9 (C^{20}), 137.5 (C^{17}), 136.1 (C^{13}), 131.2 (C^{10}), 129.9 (C^{11}, C^{15}), 128.9 (C^{18}, C^{22}), 128.8 (C^{12}, C^{14}), 128.6 (C^{5}), 125.7 (C^{4}), 123.2 (C^{19}, C^{21}), 115.8 (C^{3}), 51.6 (C^{9}), 20.8 (C^{16}) ppm. ^{15}N NMR (51 MHz, DMSO-*d*$_6$) δ 369.6 (N^{23}), 162.8 ('*J* = 96.4 Hz; N^{1}), 105.0 ('*J* = 90.0 Hz; N^{7}) ppm. HRMS (ESI): m/z calcd $C_{20}H_{17}N_3O_5$ for $[M+H]^+$ = 380.1241, found $[M+H]^+$ = 380.1240.

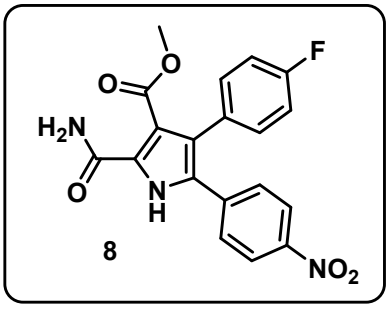
Methyl 2-carbamoyl-4-(4-methoxyphenyl)-5-(4-nitrophenyl)-1*H*-pyrrole-3-carboxylate (7)

Yellow solid 16 mg (54% yield). ^{1}H-NMR (500 MHz, DMSO-*d*$_6$) δ 12.48 (s, 1H;N^{1}-H), 8.45 (s, 1H; N^{7}-H$^{\alpha}$),



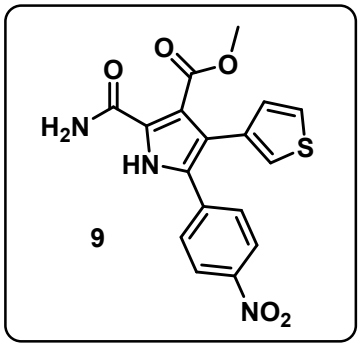
8.11-8.08 (m, 2H; C^{19}-H, C^{21}-H), 7.72 (s, 1H; N^{7}-H$^{\beta}$), 7.47-7.44 (m, 2H; C^{18}-H, C^{22}-H), 7.07-7.04 (m, 2H; C^{11}-H, C^{15}-H), 6.91-6.88 (m, 2H; C^{12}-H, C^{14}-H), 3.76 (s, 3H; C^{16}-H$_3$), 3.52 (s, 3H; C^{9}-H$_3$) ppm. ^{13}C-NMR (126 MHz, DMSO-*d*$_6$) δ 166.2 (C^{8}), 160.7 (C^{6}), 158.3 (C^{13}), 145.8 (C^{20}), 137.6 (C^{17}), 131.2 (C^{11}, C^{15}), 129.9 (C^{2}), 128.9 (C^{18}, C^{22}), 128.6 (C^{5}), 126.3 (C^{10}), 125.5 (C^{4}), 123.2 (C^{19}, C^{21}), 115.8 (C^{3}), 113.6 (C^{12}, C^{14}), 55.0 (C^{16}), 51.6 (C^{9}) ppm. ^{15}N NMR (51 MHz, DMSO-*d*$_6$) δ 369.6 (N^{23}), 162.7 ('*J* = 96.3 Hz; N^{1}), 105.1 ('*J* = 90.0 Hz; N^{7}) ppm. HRMS (ESI): m/z calcd $C_{20}H_{17}N_3O_6$ for $[M+H]^+$ = 396.1190, found $[M+H]^+$ = 396.1191.

Methyl 2-carbamoyl-4-(4-fluorophenyl)-5-(4-nitrophenyl)-1*H*-pyrrole-3-carboxylate (8)



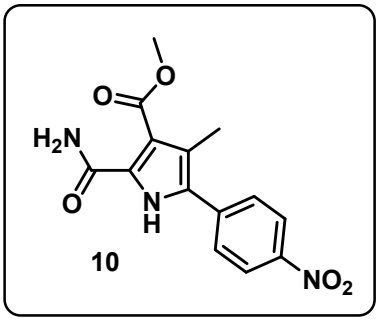
Yellow solid 14.3 mg (50% yield). ^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ 12.62 (s, 1H), 8.58 (s, 1H), 8.13-8.10 (m, 2H), 7.79 (s, 1H), 7.47-7.44 (m, 2H), 7.22-7.16 (m, 4H), 3.53 (s, 3H) ppm. ^{13}C NMR (126 MHz, DMSO-*d*$_6$) δ 166.0, 161.3 (d, $^{1}J_{C-F}$ = 243.8 Hz), 160.7, 146.0, 137.2, 132,1 (d, $^{3}J_{C-F}$ = 8.2 Hz), 130.8 (d, $^{4}J_{C-F}$ = 3.3 Hz), 130.3, 129.1, 128.9, 124.8, 123.3, 115.3, 115.0 (d, $^{2}J_{C-F}$ = 21.4 Hz), 51.6 ppm. HRMS (ESI): m/z calcd $C_{19}H_{14}FN_3O_5$ for $[M+H]^+$ = 384.0990, found [M+H]+ = 384.0989.

Methyl 2-carbamoyl-5-(4-nitrophenyl)-4-(thiophen-3-yl)-1*H*-pyrrole-3-carboxylate (9)



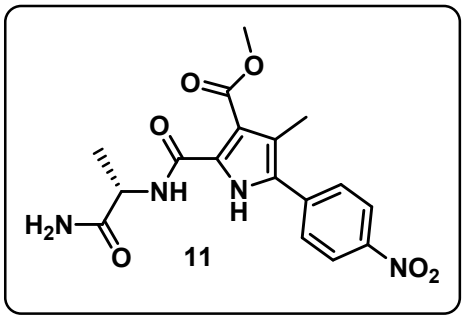
Yellow solid 10.4 mg (55% yield). ^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ 12.54 (s, 1H), 8.49 (s, 1H), 8.13 – 8.10 (m, 2H), 7.74 (s, 1H), 7.54 (dd, *J* = 4.9, 2.9 Hz, 1H), 7.50 – 7.47 (m, 2H), 7.21 (dd, *J* = 2.9, 1.2 Hz, 1H), 6.94 (dd, *J* = 5.0, 1.3 Hz, 1H), 3.56 (s, 3H) ppm. ^{13}C-NMR (126 MHz, DMSO-*d*$_6$) δ 166.1, 160.6, 146.0, 137.4, 133.8, 130.1, 129.6, 129.1, 128.8, 125.5, 124.1, 123.2, 120.5, 115.8, 51.6 ppm. HRMS (ESI): m/z calcd $C_{17}H_{13}N_3O_5S$ for $[M+H]^+$ = 372.0649, found $[M+H]^+$ = 372.0648.

Methyl 2-carbamoyl-4-methyl-5-(4-nitrophenyl)-1*H*-pyrrole-3-carboxylate (10)



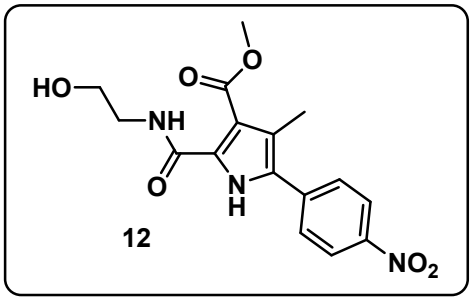
Yellow solid 6.7 mg (23% yield). ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.37 (s, 1H), 8.85 (s, 1H), 8.29 – 8.26 (m, 2H), 7.78 – 7.75 (m, 2H), 7.71 (s, 1H), 3.84 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 166.7, 160.7, 146.0, 137.6, 130.8, 129.4, 129.2, 123.4, 121.0, 114.4, 51.8, 12.3. HRMS (ESI): m/z calcd $C_{14}H_{13}N_3O_5$ for $[M+H]^+$ = 304.0928, found [M+H]+ = 304.0934.

Methyl (*S*)-2-((1-amino-1-oxopropan-2-yl)carbamoyl)-4-methyl-5-(4-nitrophenyl)-1*H*-pyrrole-3-carboxylate (11)



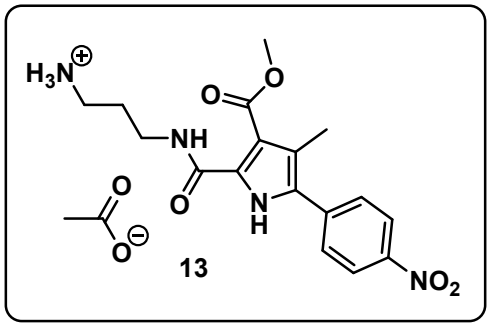
Yellow solid 5 mg (9% yield). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 12.41 (s, 1H), 9.65 (d, J = 7.2 Hz, 1H), 8.29-8.26 (m, 2H), 7.78-7.76 (m, 2H), 7.47 (s, 1H), 7.18-7.00 (m, 2H), 4.48-4.42 (m, 1H), 3.86 (s, 3H), 2.31 (s, 3H), 1.34 (d, J = 7.0 Hz, 3H) ppm. ^{13}C-NMR (126 MHz, DMSO-d_6) δ 173.8, 166.4, 158.7, 146.0, 137.6, 130.6, 129.4, 129.2, 123.4, 120.9, 114.3, 51.9, 48.6, 18.6, 12.2 ppm. HRMS (ESI): m/z calcd $C_{17}H_{18}N_4O_6$ for $[M+H]^+$ = 375.1299, found [M+H]+ = 375.1302.

Methyl 2-((2-hydroxyethyl)carbamoyl)-4-methyl-5-(4-nitrophenyl)-1*H*-pyrrole-3-carboxylate (12)



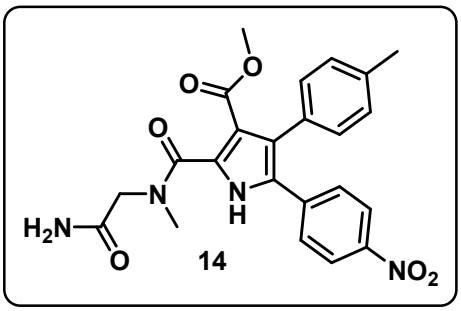
Yellow solid 10.6 mg (20% yield). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 12.40 (s, 1H), 9.53 (t, *J* = 5.4 Hz, 1H), 8.31-8.28 (m, 2H), 7.80-7.77 (m, 2H), 4.79 (t, *J* = 5.0 Hz, 1H), 3.86 (s, 3H), 3.56 (dd, *J* = 10.5, 5.5 Hz, 2H), 3.41 (q, *J* = 5.8 Hz, 2H), 2.33 (s, 3H) ppm. ^{13}C-NMR (126 MHz, DMSO-d_6) δ 166.5, 159.4, 145.9, 137.7, 131.1, 129.3, 129.0, 123.4, 120.9, 114.0, 59.7, 51.8, 41.8, 12.3 ppm. HRMS (ESI): m/z calcd $C_{16}H_{17}N_3O_6$ for $[M+H]^+$ = 348.1190, found [M+H]+ = 348.1194.

2-(3-(Methoxycarbonyl)-4-methyl-5-(4-nitrophenyl)-1*H*-pyrrole-2-carboxamido)ethan-1-aminium acetate (13)



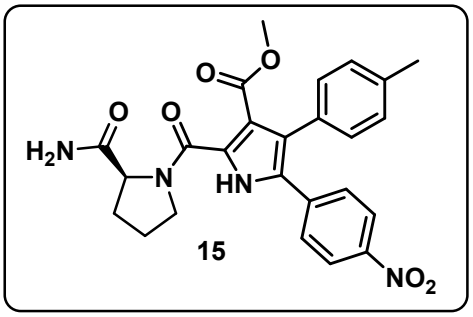
Brown solid 11.8 mg (19% yield). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 9.38 (t, *J* = 5.6 Hz, 1H), 8.28-8.25 (m, 2H), 7.77 (m, 2H), 4.43 (s, 3H), 3.81 (s, 3H), 3.36 (dd, *J* = 12.5, 6.6 Hz, 2H), 2.73 (t, *J* = 7.0 Hz, 2H), 2.31 (s, 3H), 1.81 (s, 3H), 1.70 (q, *J* = 6.9 Hz, 2H) ppm. 13C-NMR (126 MHz, DMSO-d_6) δ 173.1, 166.4, 159.8, 145.8, 137.9, 131.3, 129.0, 128.8, 123.5, 120.6, 114.5, 51.7, 37.8, 36.3, 30.2, 22.5, 12.1 ppm. HRMS (ESI): m/z calcd $C_{17}H_{20}N_4O_5$ for $[M+H]^+$ = 361.1506, found [M+H]+ = 361.1508.

Methyl 2-((2-amino-2-oxoethyl)(methyl)carbamoyl)-5-(4-nitrophenyl)-4-(*p*-tolyl)-1*H*-pyrrole-3-carboxylate (14)



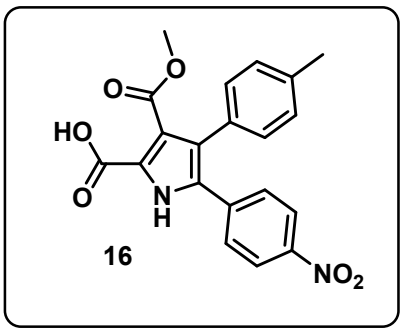
Yellow solid 20 mg (30%). Measured at 25°C: ^{1}H-NMR (500 MHz, DMSO-d_6) δ 12.66 (s, 1H), 8.10 (d, J = 8.4 Hz, 2H), 7.40 (d, J = 8.3 Hz, 2H), 7.38-7.23 (multiplet for NH_2 rotamers, 2H), 7.18 (d, *J* = 7.9 Hz, 2H), 7.13-7.11 (m, 2H), 4.1 and 3.9 (two singlets of CH_2 rotamers, 2H), 3.55 (s, 3H), 3.05 and 2.99 (two singlets of CH_3 rotamers, 3H), 2.36 (s, 3H) ppm. Measured at 115°C: ^{1}H-NMR (500 MHz, DMSO-d_6) δ 12.04 (s, 1H), 8.07-8.05 (m, 2H), 7.47-7.44 (m, 2H), 7.18 (d, *J* = 7.7 Hz, 2H), 7.14 (d, *J* = 8.2 Hz, 2H), 6.97 (s, 2H), 4.05 (s, 2H), 3.57 (s, 3H), 3.04 (s, 3H), 2.38 (s, 3H) ppm. ^{13}C-NMR (126 MHz, DMSO-d_6) δ 169.7, 163.8, 163.3, 145.5, 138.0, 136.2, 132.5, 131.1, 130.3, 128.7, 127.7, 127.4, 124.6, 123.6, 113.1, 51.1, 49.8, 37.1, 20.9 ppm. HRMS (ESI): m/z calcd $C_{23}H_{22}N_4O_6$ for $[M+H]^+$ = 451.1612, found [M+H]+ = 451.1609.

Methyl 2-(2-carbamoylpyrrolidine-1-carbonyl)-5-(4-nitrophenyl)-4-(*p*-tolyl)-1*H*-pyrrole-3-carboxylate (15)



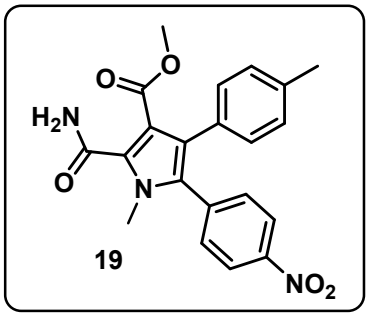
Yellow solid 7.2 mg (17% yield). Measured at 25°C: ^{1}H-NMR (500 MHz, DMSO-d_6) δ 12.43 (s, 1H), 8.10-8.04 (two doublets of C_{Ar}-H_{Ar}, 2H), 7.40-7.34 (two doublets of C_{Ar}-H_{Ar}, 2H), 7.24 (s, 2H), 7.16 (d, *J* = 7.9 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 4.41 (dd, *J* = 8.5, 4.5 Hz, 1H), 3.52 (s, 3H), 3.46-3.37 (m, 2H), 2.31-2.38 (3H), 2.21-2.13 (m, 1H), 2.00-1.94 (m, 1H), 1.92-1.80 (m, 2H) ppm. Measured at 115°C. ^{1}H-NMR (500 MHz, DMSO-d_6) δ 11.85 (s, 1H), 8.07-8.04 (m, 2H), 7.47-7.45 (m, 2H), 7.18 (d, J = 7.9 Hz, 2H), 7.13 (dd, J = 6.2, 2.0 Hz, 2H), 6.87 (s, 2H), 4.48 (q, J = 4.2 Hz, 1H), 3.56 (s, 3H), 3.55-3.48 (m, 2H), 2.38 (s, 3H), 2.23-2.15 (m, 1H), 2.11-2.05 (m, 1H), 2.00-1.85 (m, 2H) ppm. ^{13}C-NMR (126 MHz, DMSO-d_6) δ 173.1, 164.0, 161.7, 145.5, 138.0, 136.2, 133.4, 131.0, 130.3, 128.7, 127.7, 127.3, 124.5, 123.6, 113.0, 59.7, 51.1, 48.3, 29.6, 24.2, 20.9 ppm. HRMS (ESI): m/z calcd $C_{25}H_{24}N_4O_6$ for $[M+H]^+$ = 477.1769, found [M+H]+ = 477.1771.

3-(methoxycarbonyl)-5-(4-nitrophenyl)-4-(*p*-tolyl)-1*H*-pyrrole-2-carboxylic acid (16)



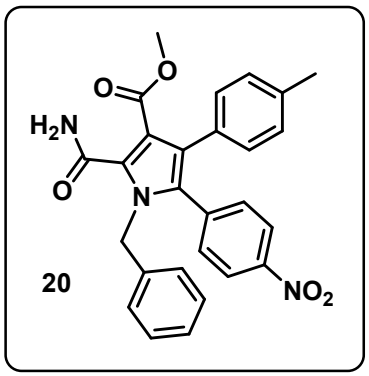
Yellow solid 14.4 mg (22% yield). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 8.11 (d, *J* = 8.9 Hz, 2H), 7.52 (d, *J* = 9.0 Hz, 2H), 7.13 (d, *J* = 7.9 Hz, 2H), 7.03 (d, *J* = 8.0 Hz, 2H), 3.61 (s, 3H), 2.30 (s, 3H) ppm. ^{13}C-NMR (126 MHz, DMSO- d_6) δ 166.2, 161.2, 146.0, 137.5, 136.4, 130.3, 129.3, 129.2, 129.1, 124.3, 123.4, 123.3, 122.0, 51.8, 20.7 ppm. HRMS (ESI): m/z calcd $C_{20}H_{16}N_2O_6$ for $[M+H]^+$ = 381.1081, found [M+H]+ = 381.1082.

Methyl 2-carbamoyl-1-methyl-5-(4-nitrophenyl)-4-(*p*-tolyl)-1*H*-pyrrole-3-carboxylate (19)



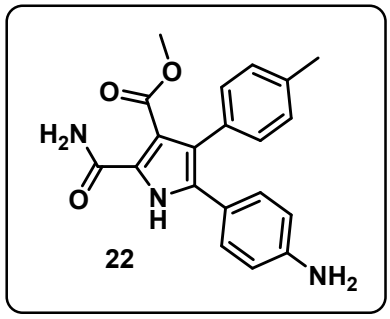
Yellow solid 9.6 mg (16% yield). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 8.20-8.17 (m, 2H), 8.06 (s, 1H), 7.79 (s, 1H), 7.48-7.46 (m, 2H), 7.03 (d, *J* = 7.9 Hz, 2H), 6.95 (d, *J* = 8.0 Hz, 2H), 3.56 (s, 3H), 3.54 (s, 3H), 2.26 (s, 3H) ppm. ^{13}C-NMR (126 MHz, DMSO-d_6) δ 164.0, 163.2, 146.7, 137.4, 135.5, 134.1, 132.2, 130.7, 130.4, 130.3, 128.2, 123.9, 123.3, 112.3, 50.9, 33.5, 20.7 ppm. HRMS (ESI): m/z calcd $C_{21}H_{19}N_3O_5$ for $[M+H]^+$ = 394.1397, found [M+H]+ = 394.1398.

Methyl 1-benzyl-2-carbamoyl-5-(4-nitrophenyl)-4-(*p*-tolyl)-1*H*-pyrrole-3-carboxylate (20)



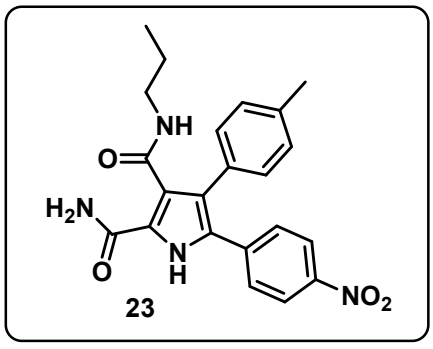
Light yellow solid 19.7 mg (30% yield). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 8.09-8.06 (m, 3H), 7.72 (s, 1H), 7.30-7.28 (m, 2H), 7.23-7.17 (m, 3H), 7.00 (d, J = 8.0 Hz, 2H), 6.97-9.95 (m, 2H), 6.85-6.83 (m, 2H), 5.29 (s, 2H), 3.58 (s, 3H), 2.24 (s, 3H) ppm. ^{13}C-NMR (126 MHz, DMSO-d_6) δ 164.1, 163.2, 146.8, 137.6, 137.1, 135.5, 133.5, 132.3, 130.8, 130.4, 130.2, 128.3, 128.2, 127.2, 126.3, 124.3, 123.2, 113.2, 51.1, 48.5, 20.7 ppm. HRMS (ESI): m/z calcd $C_{27}H_{23}N_3O_5$ for $[M+H]^+$ = 470.1710, found [M+H]+ = 470.1712.

Methyl 5-(4-aminophenyl)-2-carbamoyl-4-(*p*-tolyl)-1*H*-pyrrole-3-carboxylate (22)



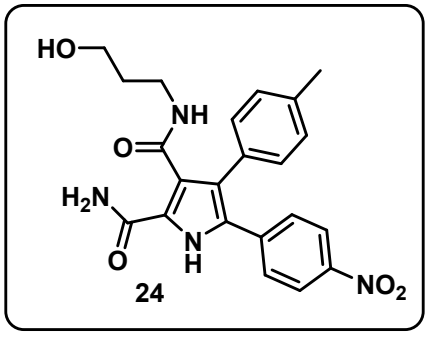
White solid 7 mg (22%). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 11.69 (s, 1H), 8.25 (s, 1H), 7.44 (s, 1H), 7.08-7.06 (m, 2H), 6.98-6.96 (m, 2H), 6.89-6.86 (m, 2H), 6.42-6.39 (m, 2H), 5.15 (s, 2H), 3.49 (s, 3H), 2.29 (s, 3H) ppm. ^{13}C-NMR (126 MHz, DMSO-d_6) δ 167.1, 160.8, 148.1, 135.1, 132.4, 132.3, 129.9, 129.1, 128.4, 126.3, 121.4, 118.2, 116.1, 113.3, 51.4, 40.1, 40.0, 39.9, 39.9, 39.8, 39.7, 39.6, 39.5, 39.4, 39.4, 39.2, 39.0, 20.8 ppm. HRMS (ESI): m/z calcd $C_{20}H_{19}N_3O_3$ for $[M+H]^+$ = 350.1499, found [M+H]+ = 350.1500.

5-(4-nitrophenyl)-N^3-propyl-4-(*p*-tolyl)-1*H*-pyrrole-2,3-dicarboxamide (23)



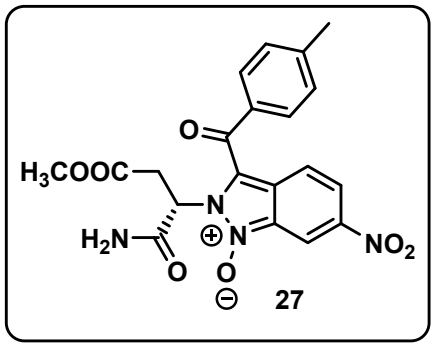
Yellow solid 10.7 mg (29% Yield). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 12.32 (s, 1H), 8.27 (s, 1H), 8.12-8.10 (m, 2H), 7.51-7.48 (m, 3H), 7.45 (t, *J* = 5.7 Hz, 1H), 7.17 (d, *J* = 7.9 Hz, 2H), 7.09 (dd, *J* = 6.3, 1.7 Hz, 2H), 2.99 (dd, *J* = 12.7, 6.8 Hz, 2H), 2.33 (s, 3H), 1.19 (td, *J* = 14.3, 7.3 Hz, 2H), 0.59 (t, *J* = 7.4 Hz, 3H) ppm. ^{13}C-NMR (126 MHz, DMSO-D6) δ 165.8, 161.3, 145.8, 137.8, 136.4, 130.6, 130.1, 129.0, 128.8, 128.2, 126.6, 123.9, 123.3, 122.0, 40.7, 21.8, 20.8, 11.1 ppm. HRMS (ESI): m/z calcd $C_{22}H_{22}N_4O_4$ for $[M+H]^+$ = 407.1714, found [M+H]+ = 407.1713.

***N*^{3}-(3-hydroxypropyl)-5-(4-nitrophenyl)-4-(*p*-tolyl)-1*H*-pyrrole-2,3-dicarboxamide (24)**



Yellow solid 25 mg (66% Yield). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 12.32 (s, 1H), 8.29 (s, 1H), 8.11 (dt, *J* = 9.4, 2.3 Hz, 2H), 7.51-7.48 (m, 3H), 7.45 (t, *J* = 5.7 Hz, 1H), 7.17 (dd, *J* = 8.3, 0.6 Hz, 2H), 7.09-7.07 (m, 2H), 4.29 (t, *J* = 5.2 Hz, 1H), 3.18 (dd, *J* = 11.4, 6.1 Hz, 2H), 3.09 (dd, *J* = 12.8, 6.8 Hz, 2H), 2.34 (s, 3H), 1.36-1.30 (m, 2H) ppm. ^{13}C-NMR (126 MHz, DMSO-d_6) δ 165.8, 161.3, 145.8, 137.9, 136.4, 130.6, 130.0, 129.1, 128.8, 128.2, 126.7, 123.9, 123.3, 122.0, 58.2, 36.3, 31.8, 20.8 ppm. HRMS (ESI): m/z calcd $C_{22}H_{22}N_4O_5$ for $[M+H]^+$ = 423.1663, found [M+H]+ = 423.1659.

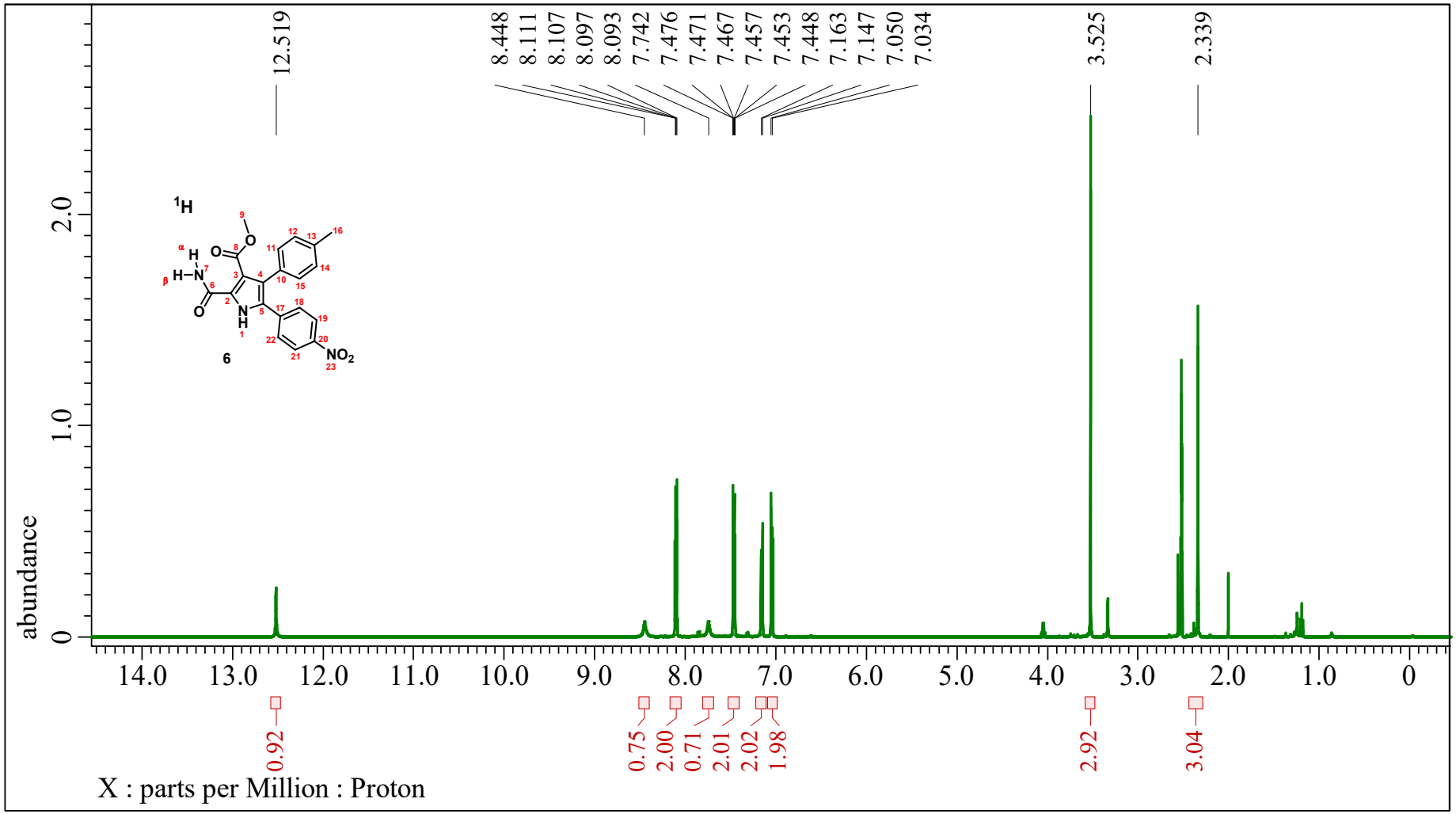
(*S*)-2-(1-amino-4-methoxy-1,4-dioxobutan-2-yl)-3-(4-methylbenzoyl)-6-nitro-2*H*-indazole 1-oxide (27)

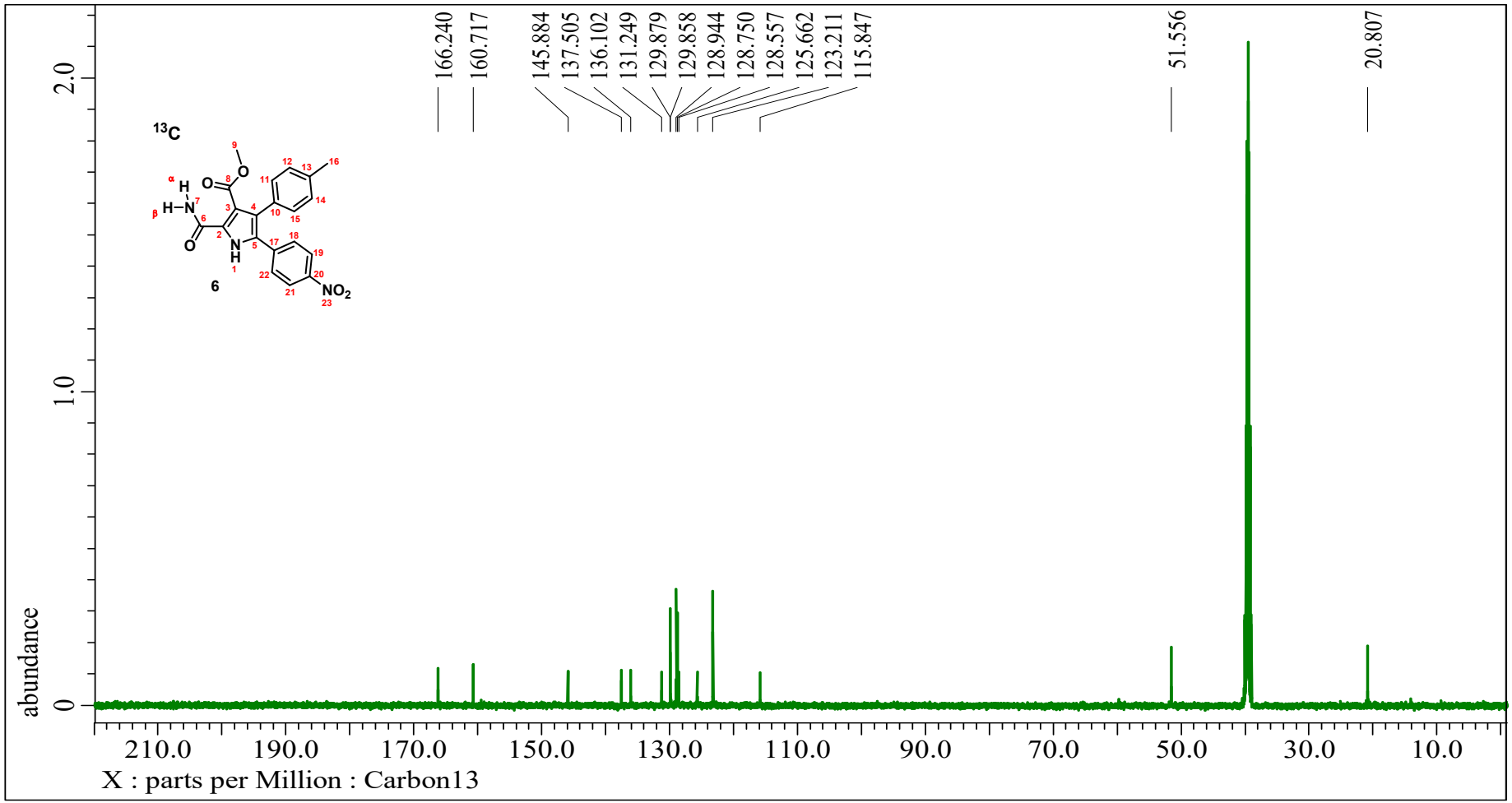


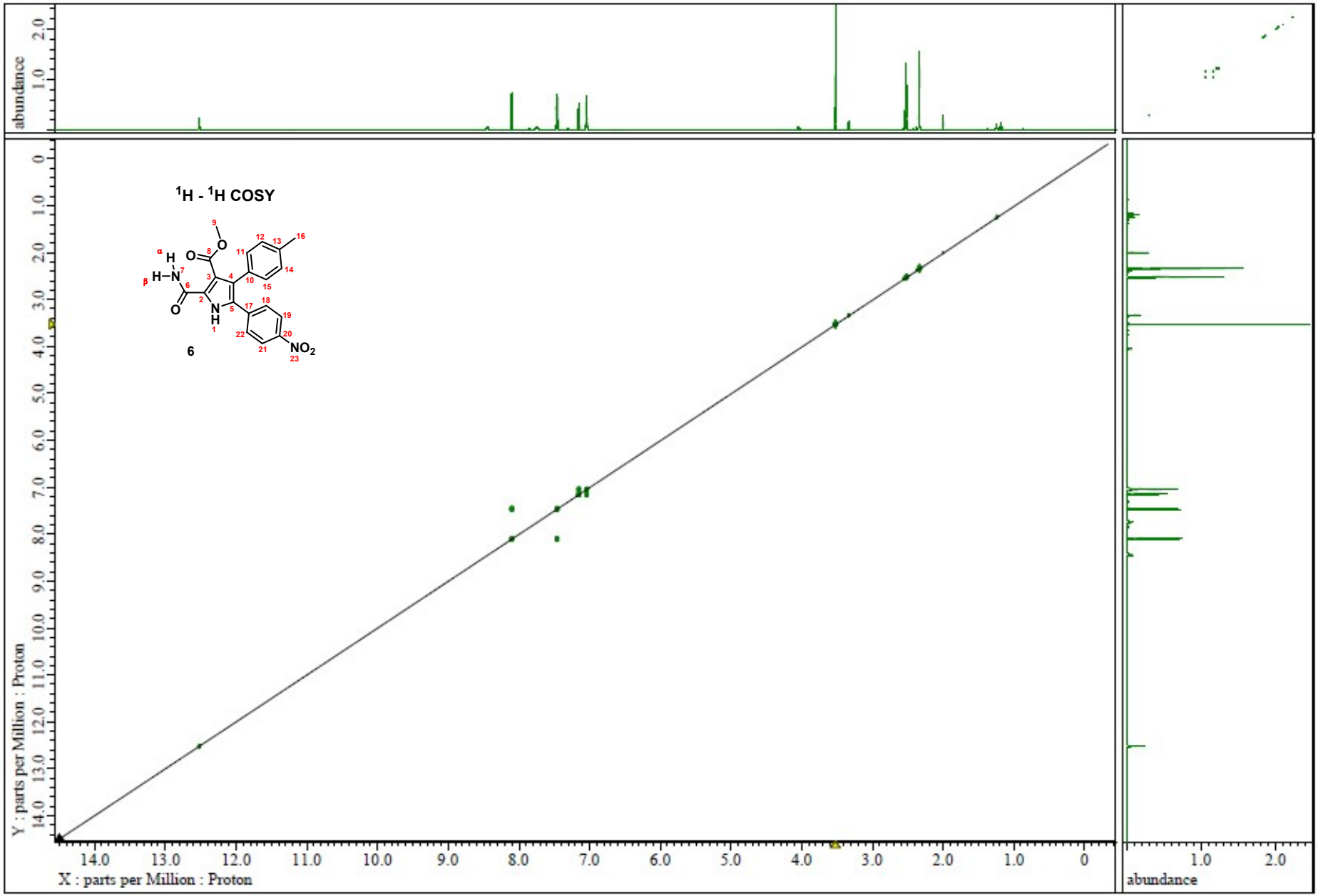
Yellow solid 25mg (65% yield). ^{1}H-NMR (500 MHz, DMSO-d_6) δ 8.64 (dd, *J* = 2.1, 0.6 Hz, 1H), 7.98 (dd, *J* = 9.5, 2.0 Hz, 1H), 7.77 (d, *J* = 8.2 Hz, 2H), 7.48-7.46 (m, 3H), 7.44 (br.s, 1H), 7.10 (dd, *J* = 9.5, 0.7 Hz, 1H), 6.48 (dd, *J* = 7.0 Hz, *J* = 6.4 Hz, 1H), 3.59 (dd, *J* = 17.0, 6.4 Hz, 1H), 3.55 (s, 3H), 3.22 (dd, *J* = 17.0, 7.0 Hz, 1H), 2.49 (s, 3H) ppm. ^{13}C-NMR (126 MHz, DMSO-d_6) δ 181.6, 170.4, 166.2, 145.3, 144.1, 135.7, 129.5, 129.5, 127.2, 122.3, 120.9, 120.9, 118.7, 111.5, 56.2, 51.8, 32.6, 21.3 ppm. NMR data were compared with analogical 2*H*-Indazole 1-oxides reported in Bouillon, I. et al. J. Org. Chem 2008, 73, 9027-9032. HRMS (ESI): m/z calcd $C_{20}H_{18}N_4O_7$ for $[M+H]^+$ = 427.1248, found [M+H]+ = 427.1247.

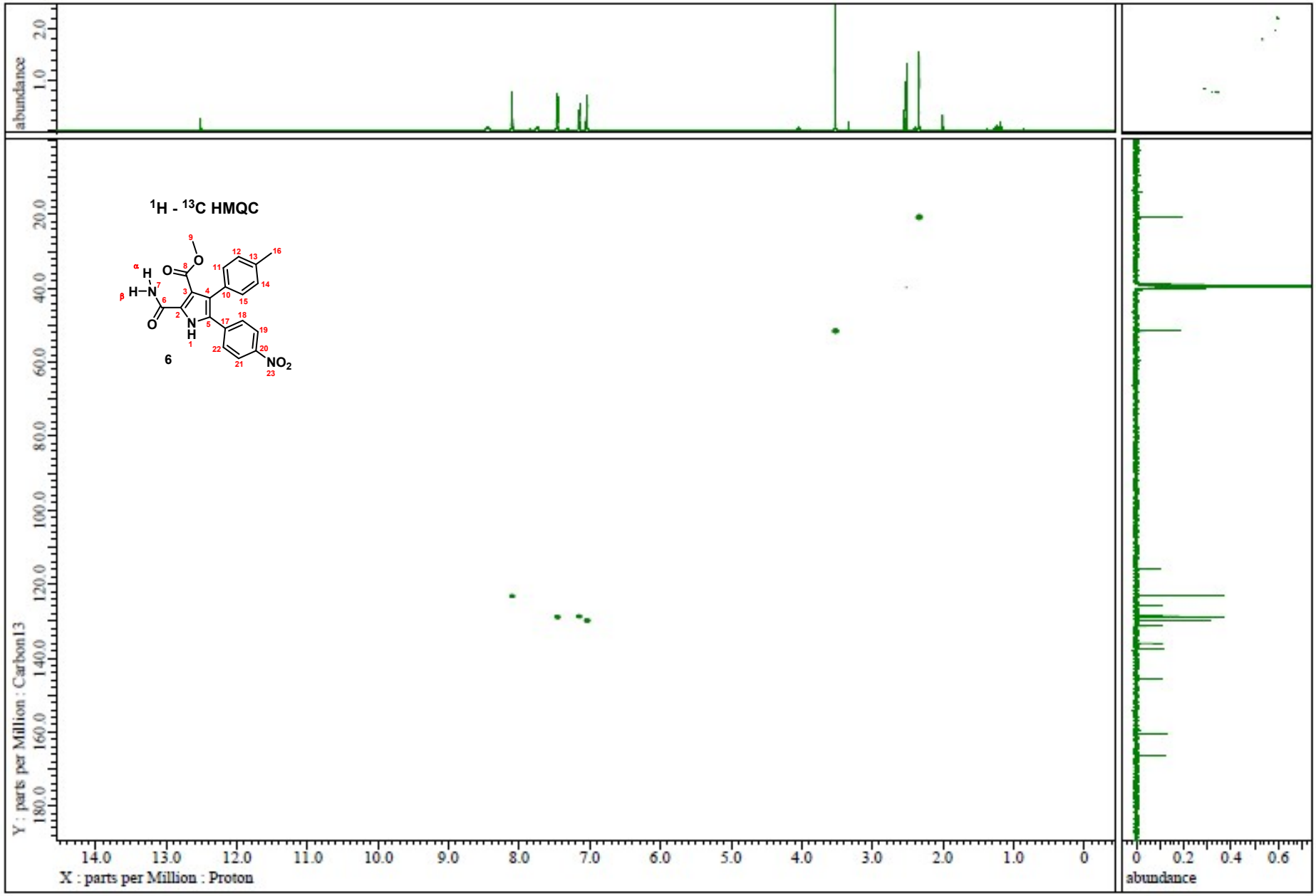
NMR spectra of the final compounds

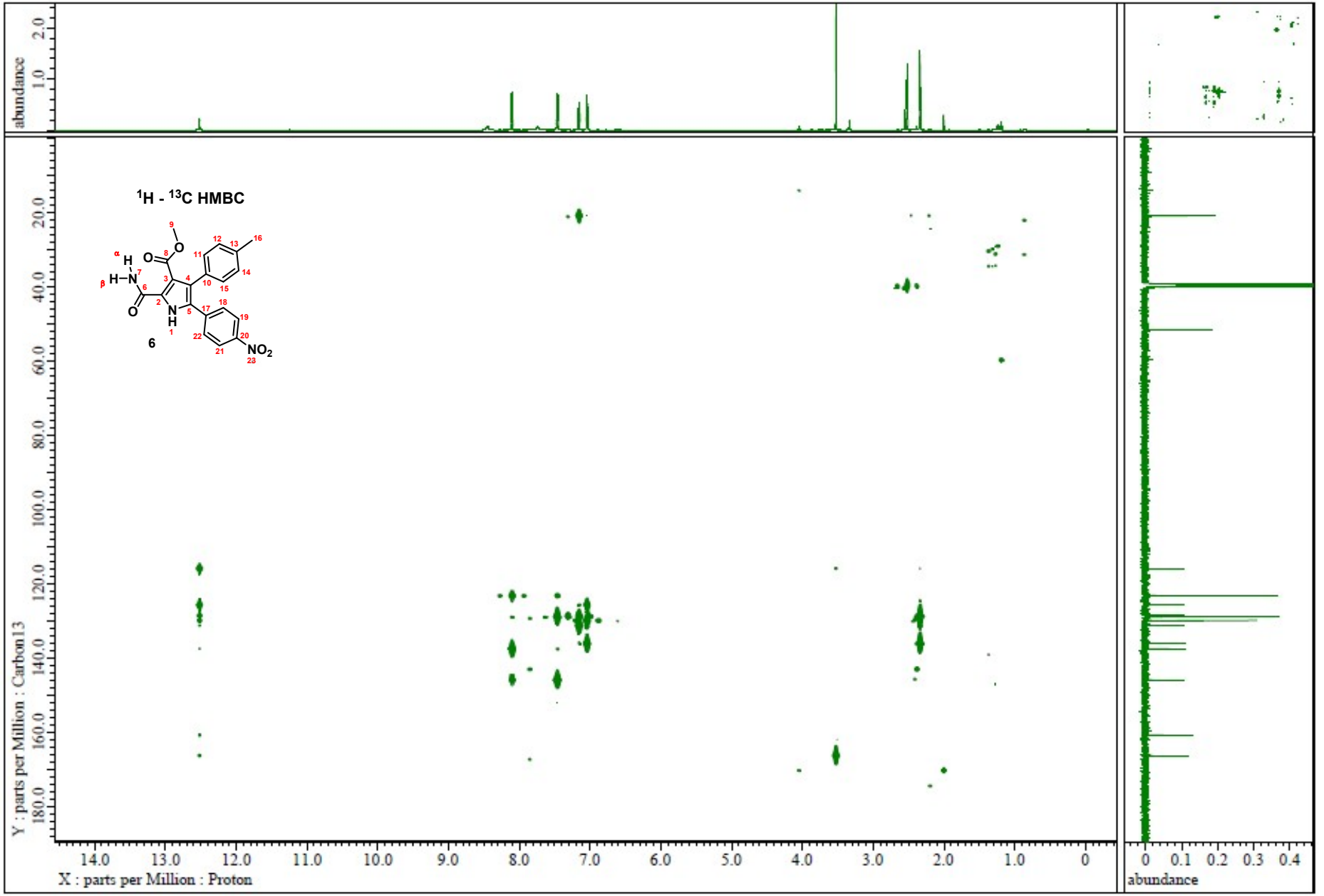
Methyl 2-carbamoyl-5-(4-nitrophenyl)-4-(p-tolyl)-1*H*-pyrrole-3-carboxylate (6)

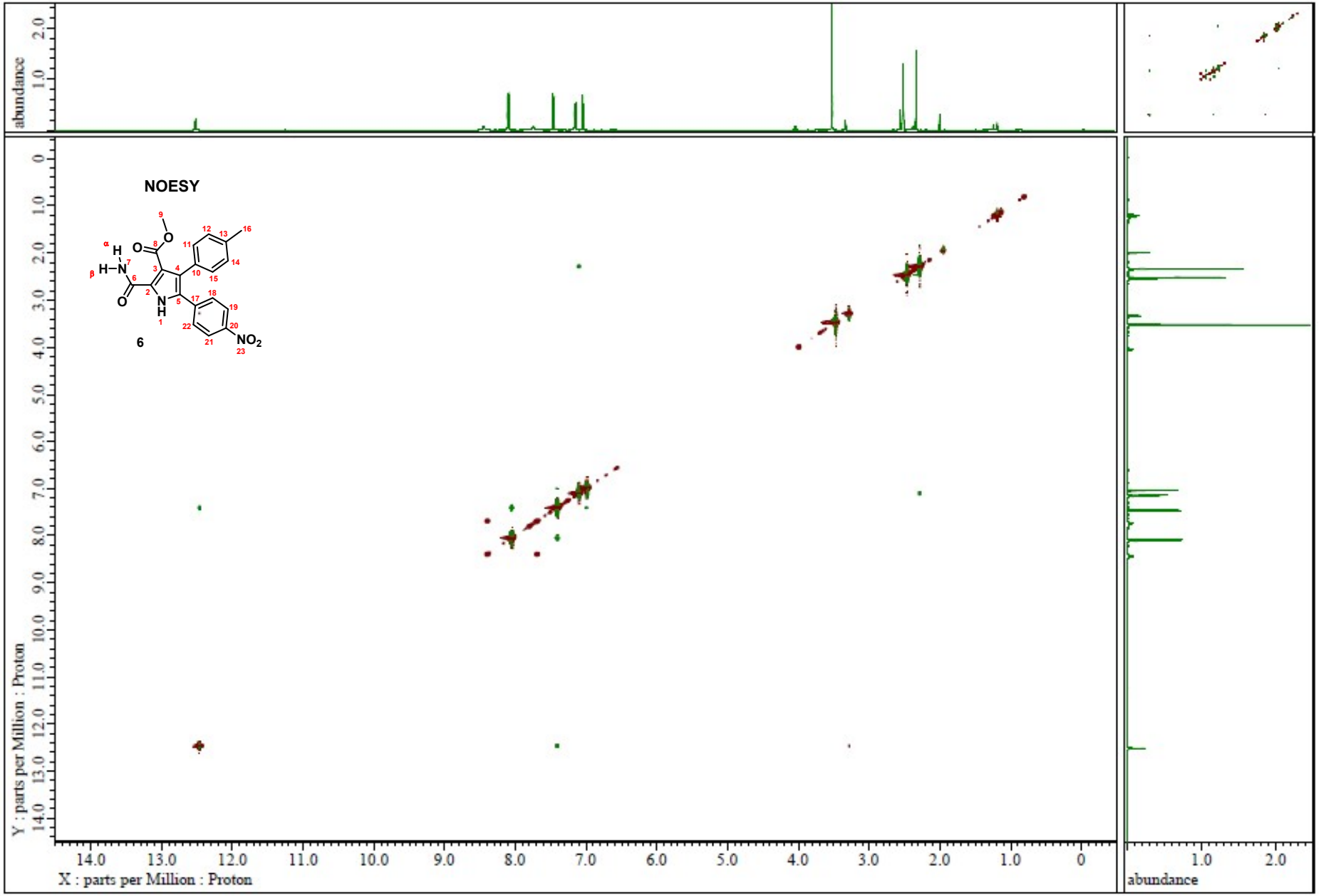


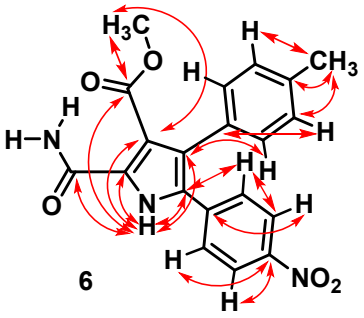

166.240
160.717
145.884
137.505
136.102
131.249
129.879
129.858
128.944
128.750
128.557
125.662
123.211
115.847
51.556
20.807
13C
6
abundance
2.0
1.0
0
210.0
190.0
170.0
150.0
130.0
110.0
90.0
70.0
50.0
30.0
10.0
X : parts per Million : Carbon13


abundance
2.0
1.0
^{1}H - ^{1}H COSY
6
Y : parts per Million : Proton
X : parts per Million : Proton
14.0 13.0 12.0 11.0 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
abundance
1.0 2.0

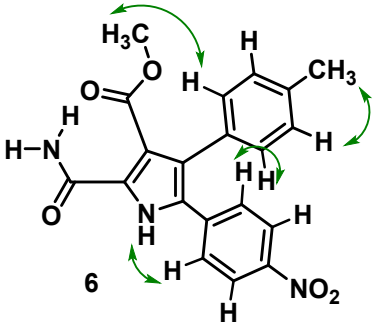

abundance
2.0
1.0
^{1}H - ^{13}C HMQC
6
Y : parts per Million : Carbon13
20.0
40.0
60.0
80.0
100.0
120.0
140.0
160.0
180.0
14.0
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton
0
0.2
0.4
0.6
abundance


abundance
2.0
1.0
^{1}H - ^{13}C HMBC
6
Y : parts per Million : Carbon13
20.0
40.0
60.0
80.0
100.0
120.0
140.0
160.0
180.0
14.0
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton
0
0.1
0.2
0.3
0.4
abundance

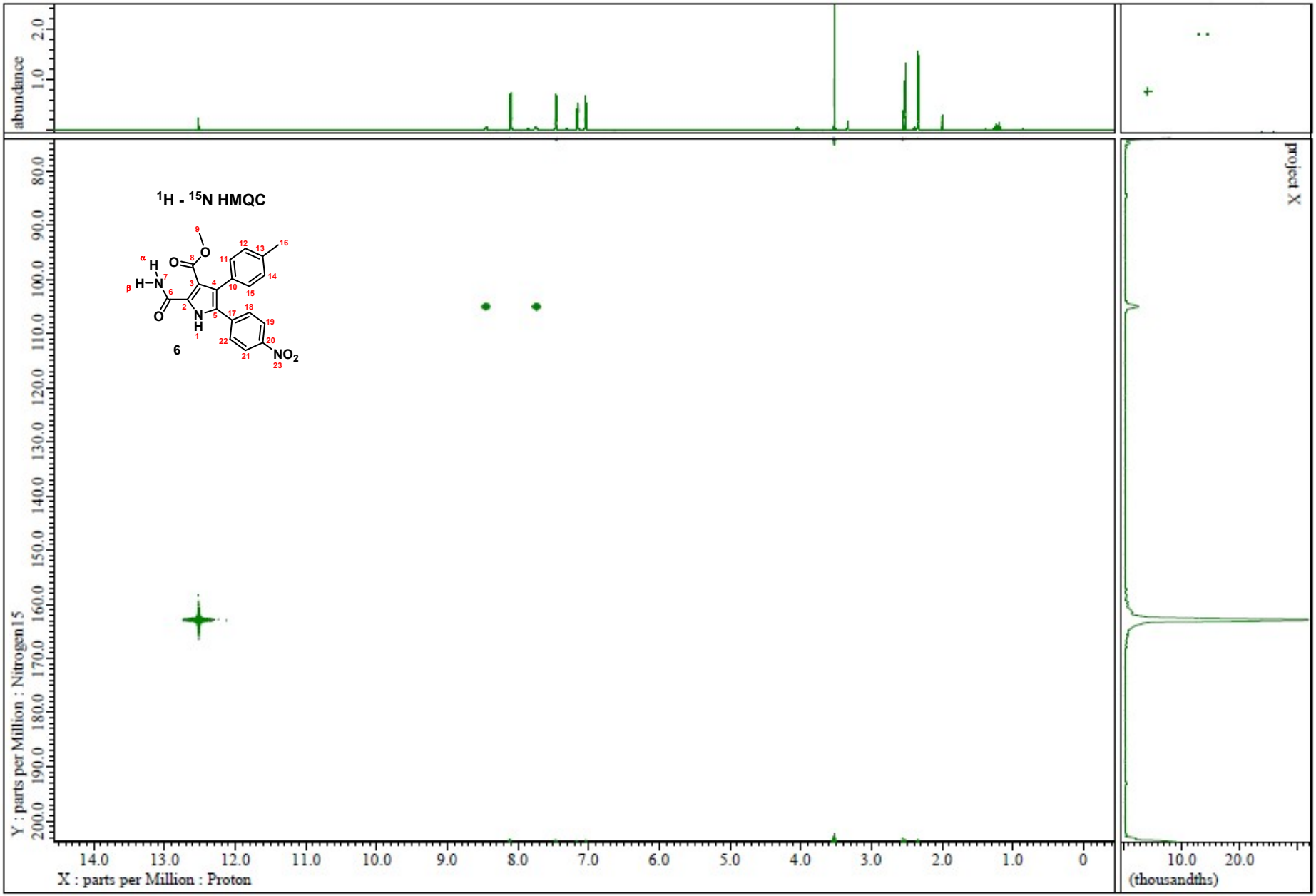

NOESY
6
abundance
Y : parts per Million : Proton
X : parts per Million : Proton
abundance

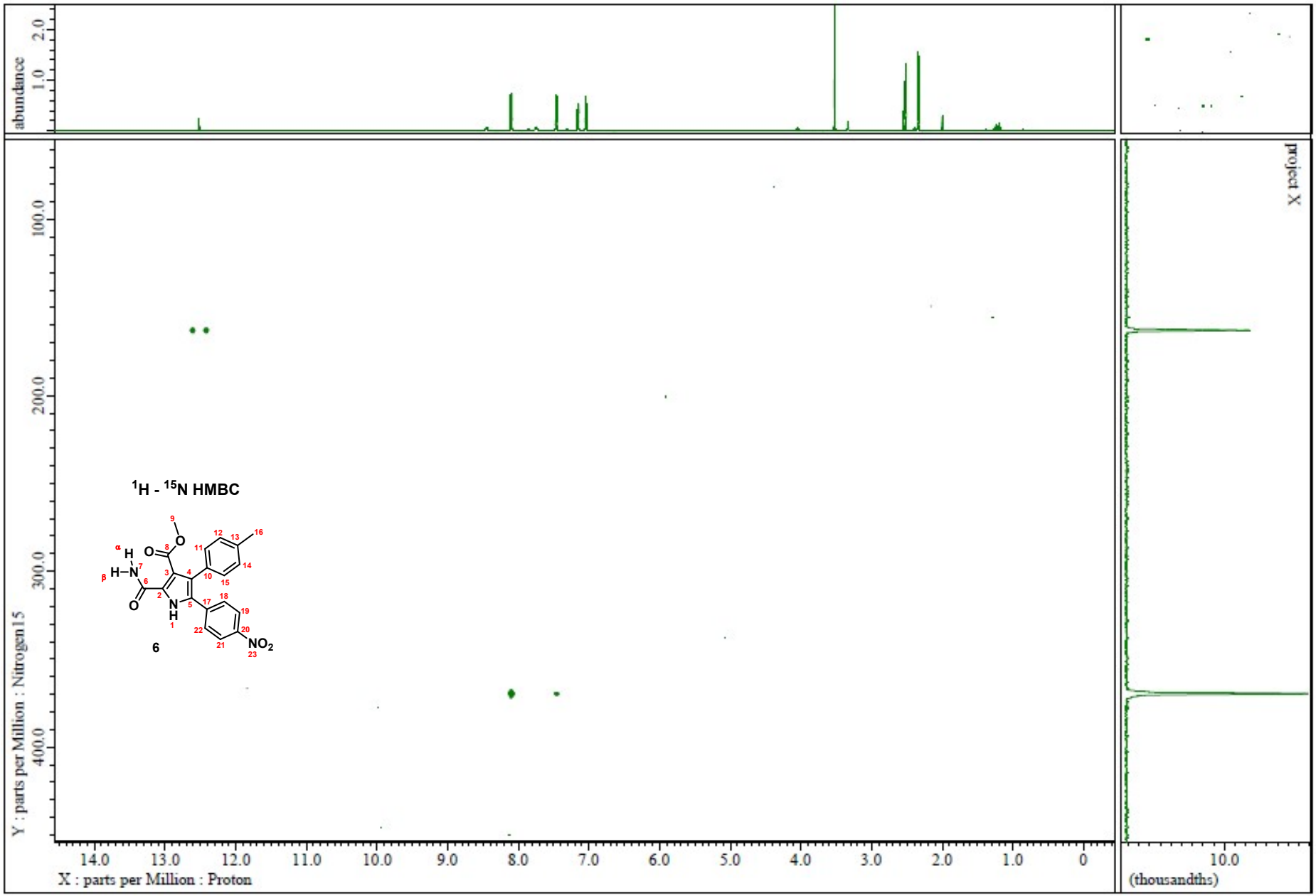


^{1}H -^{13}C HMBC Correlations

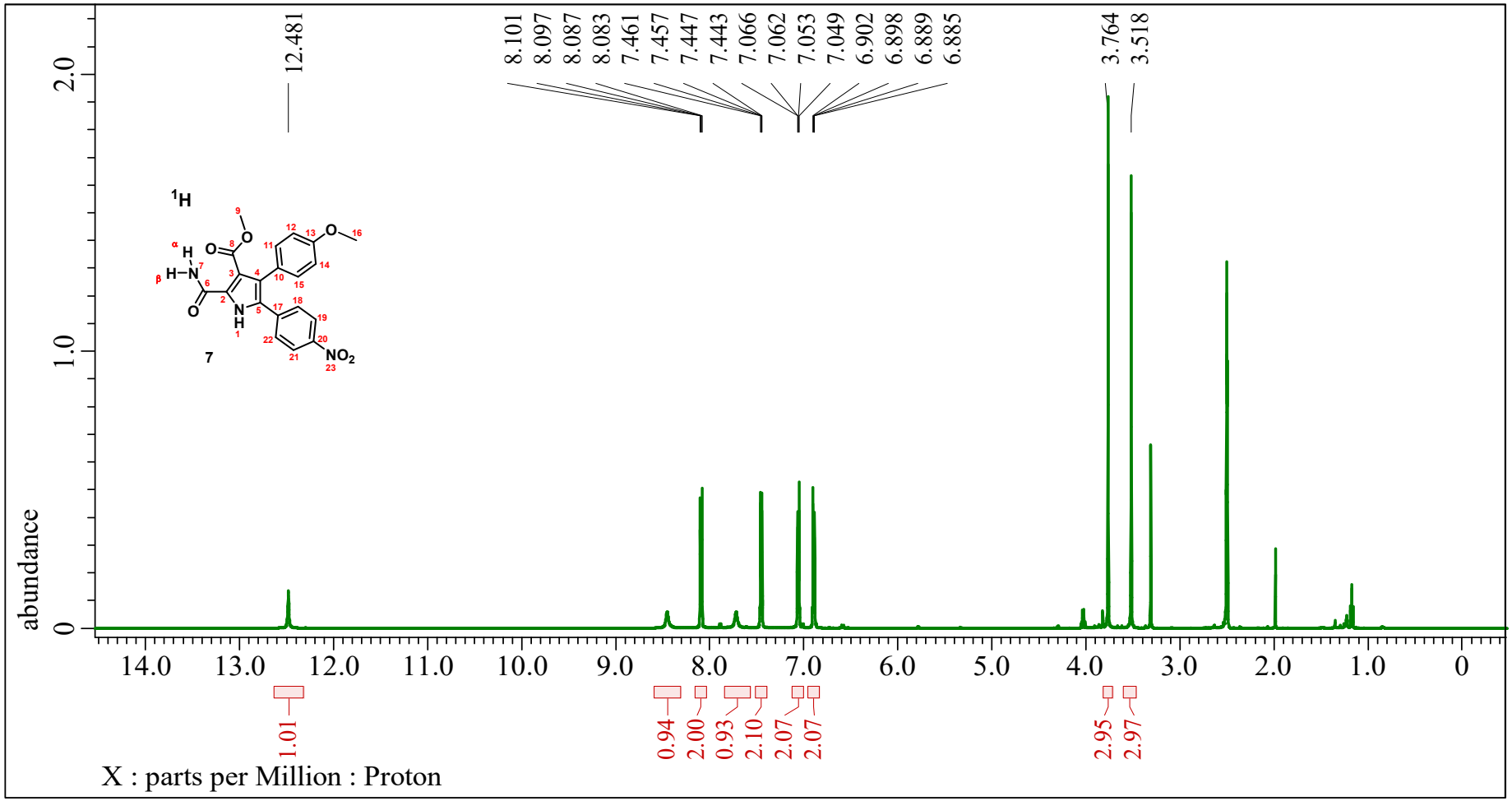


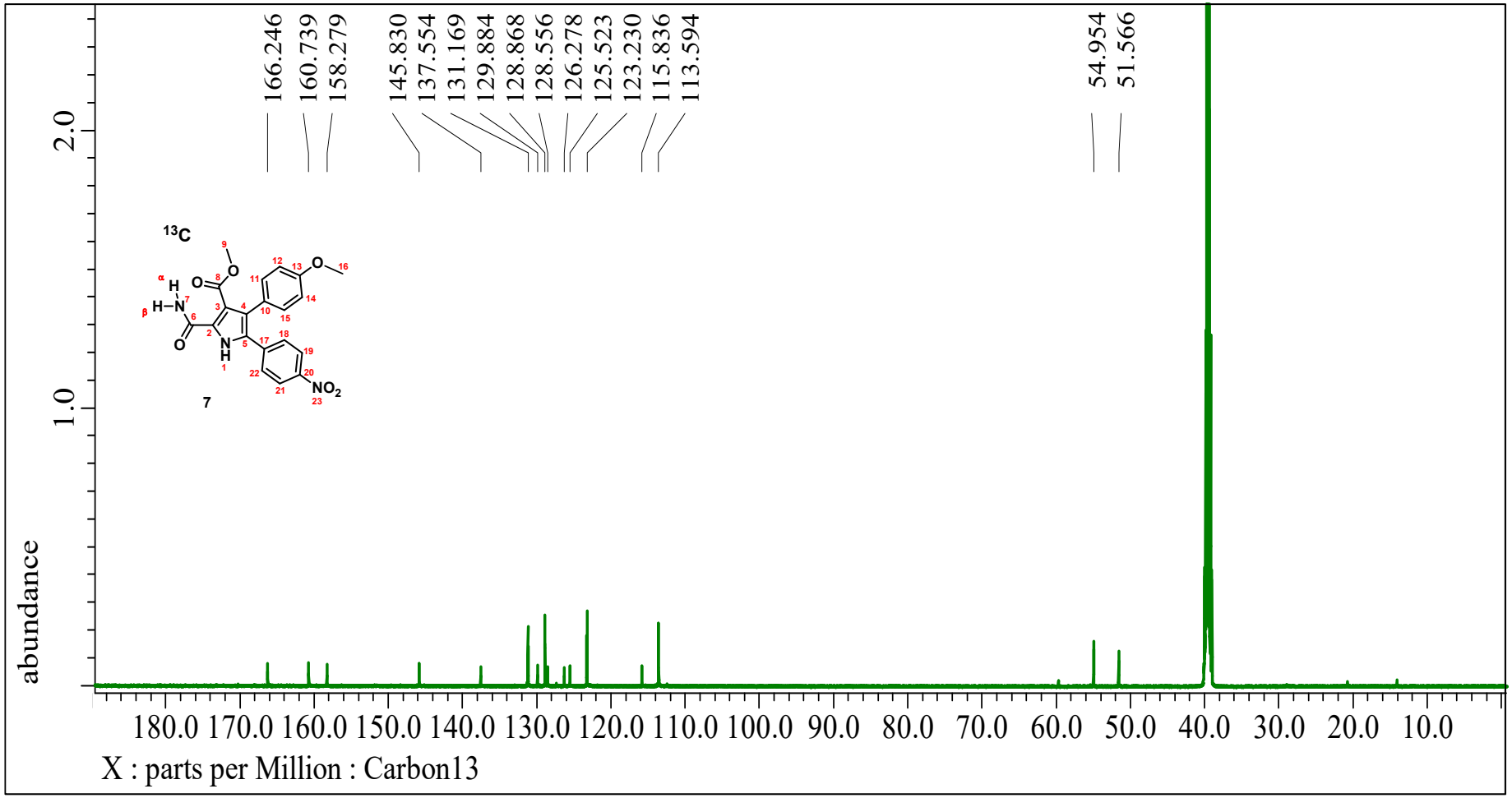
^{1}H -^{1}H NOESY Correlations

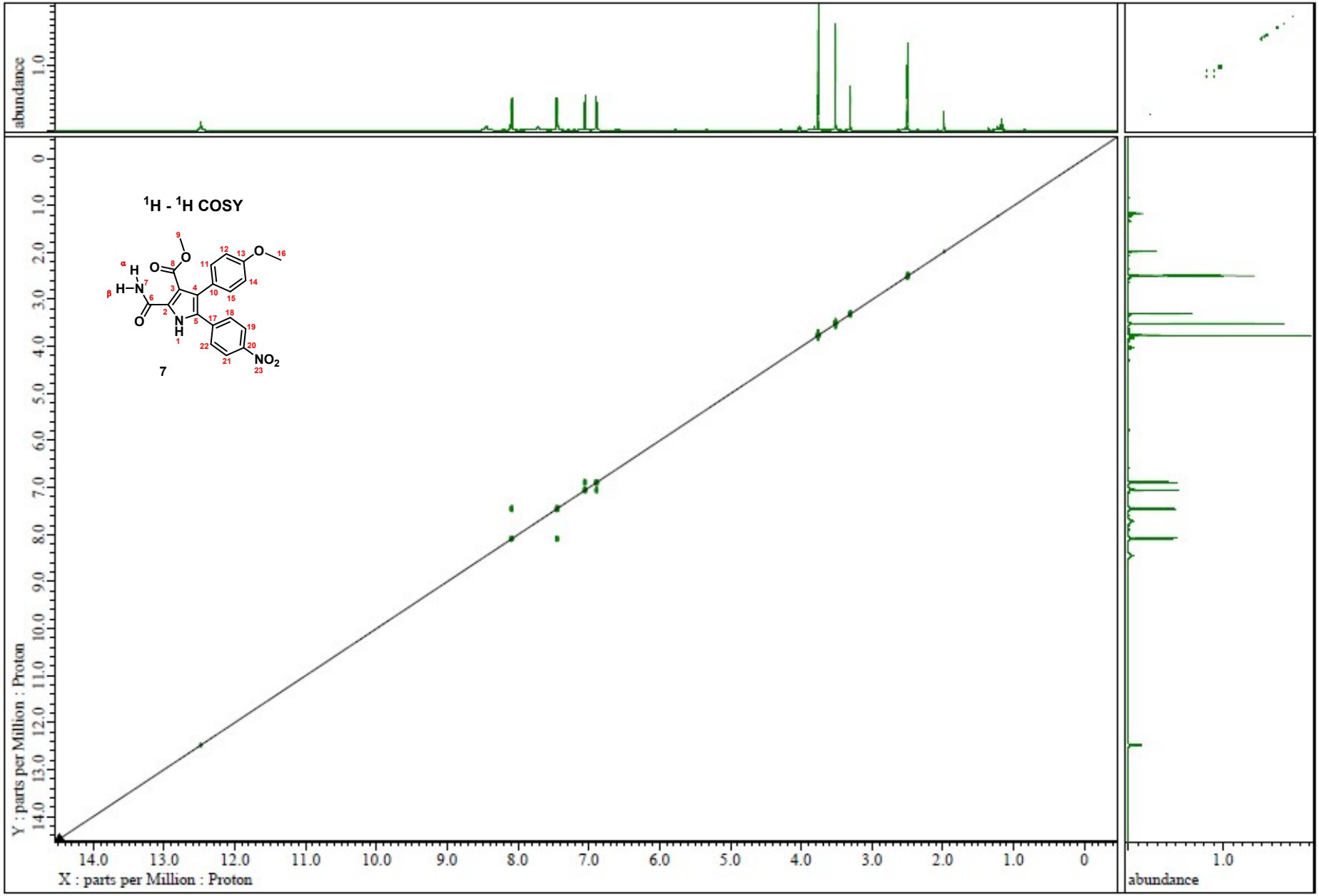

abundance
2.0
1.0
Projection X
^{1}H - ^{15}N HMQC
6
Y : parts per Million : Nitrogen15
X : parts per Million : Proton
14.0 13.0 12.0 11.0 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
10.0 20.0
(thousandths)

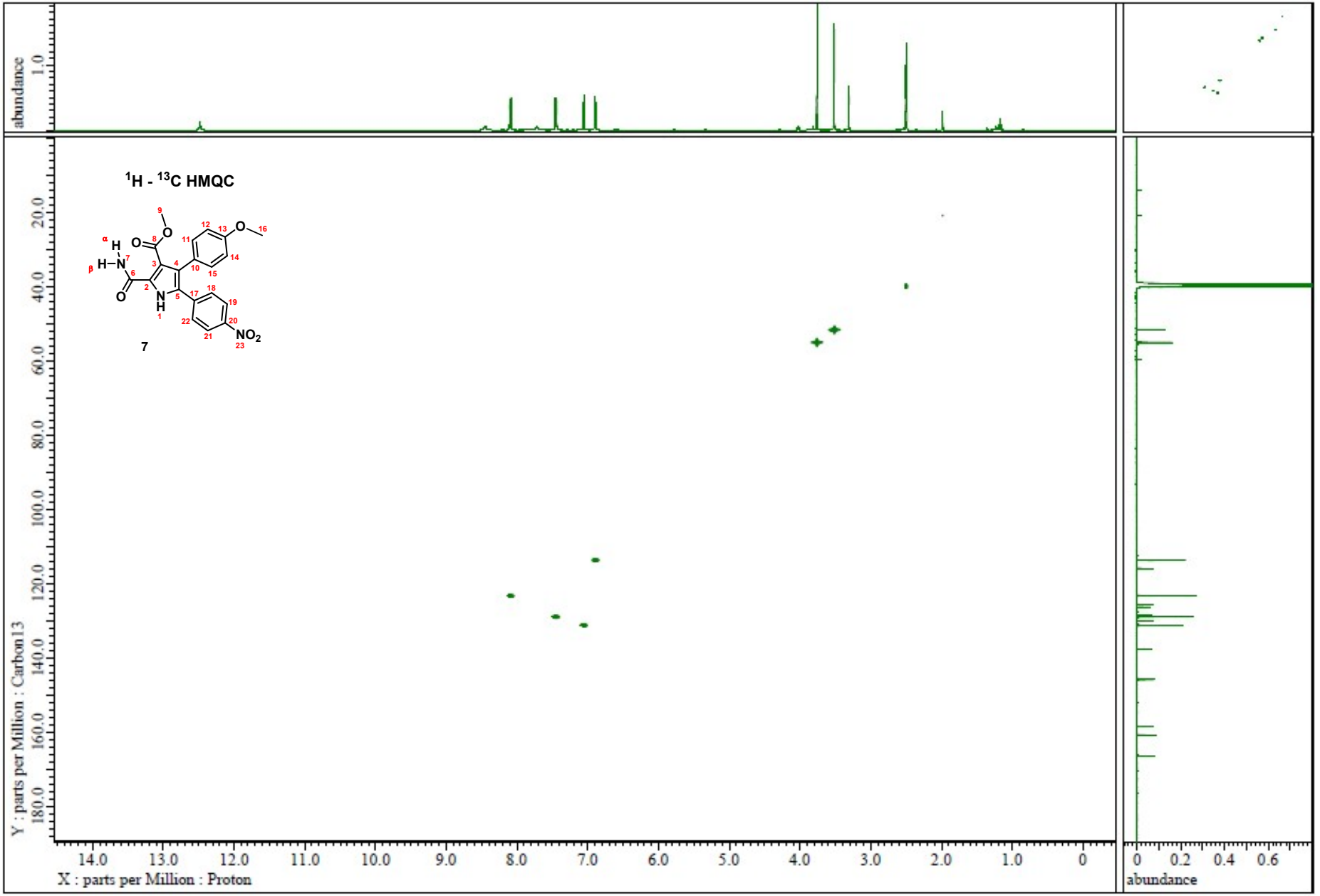

abundance
2.0
1.0
Projection X
100.0
200.0
300.0
400.0
Y : parts per Million : Nitrogen15
14.0
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton
10.0
(thousandths)
^{1}H - ^{15}N HMBC
6

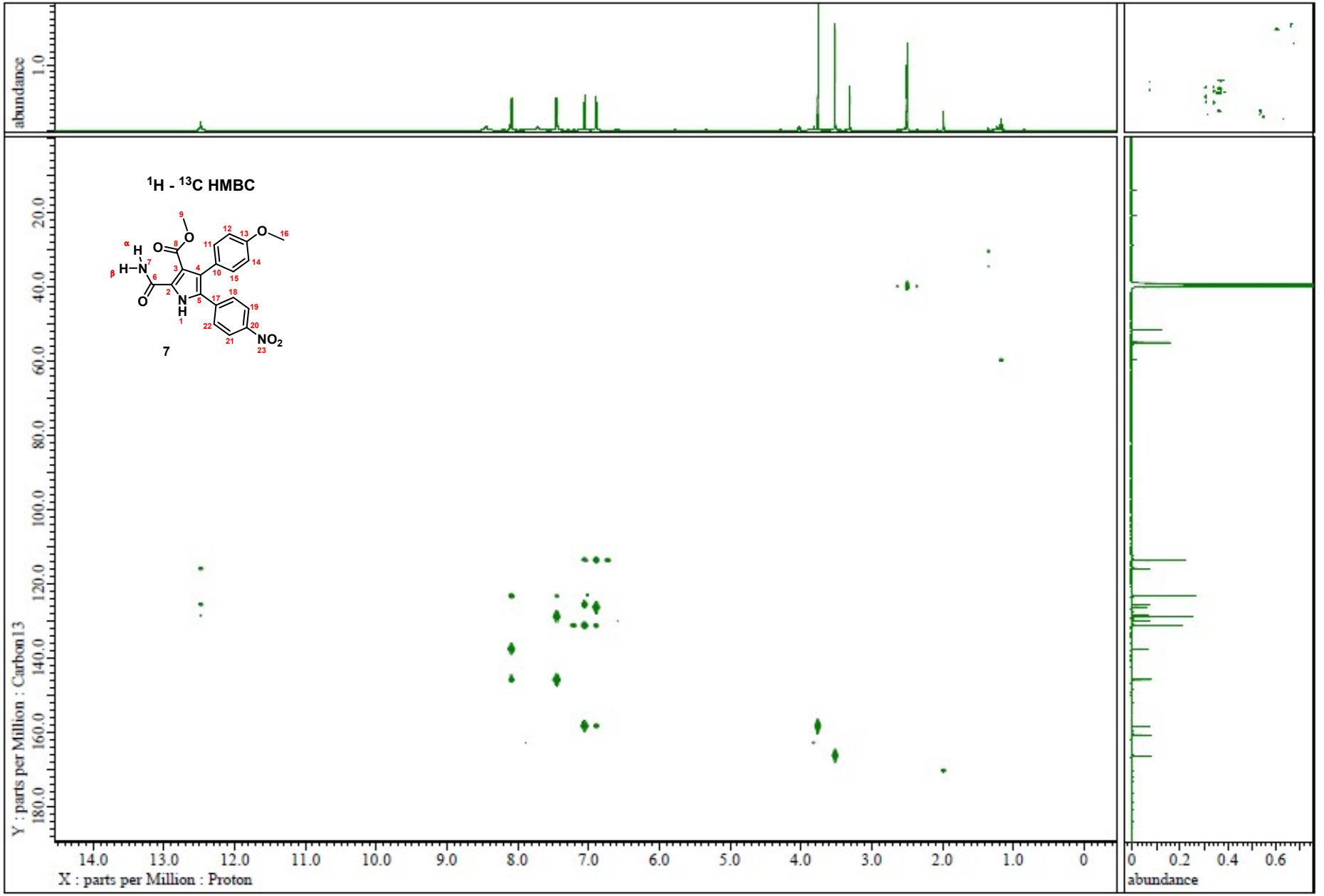
Methyl 2-carbamoyl-4-(4-methoxyphenyl)-5-(4-nitrophenyl)-1*H*-pyrrole-3-carboxylate (7)

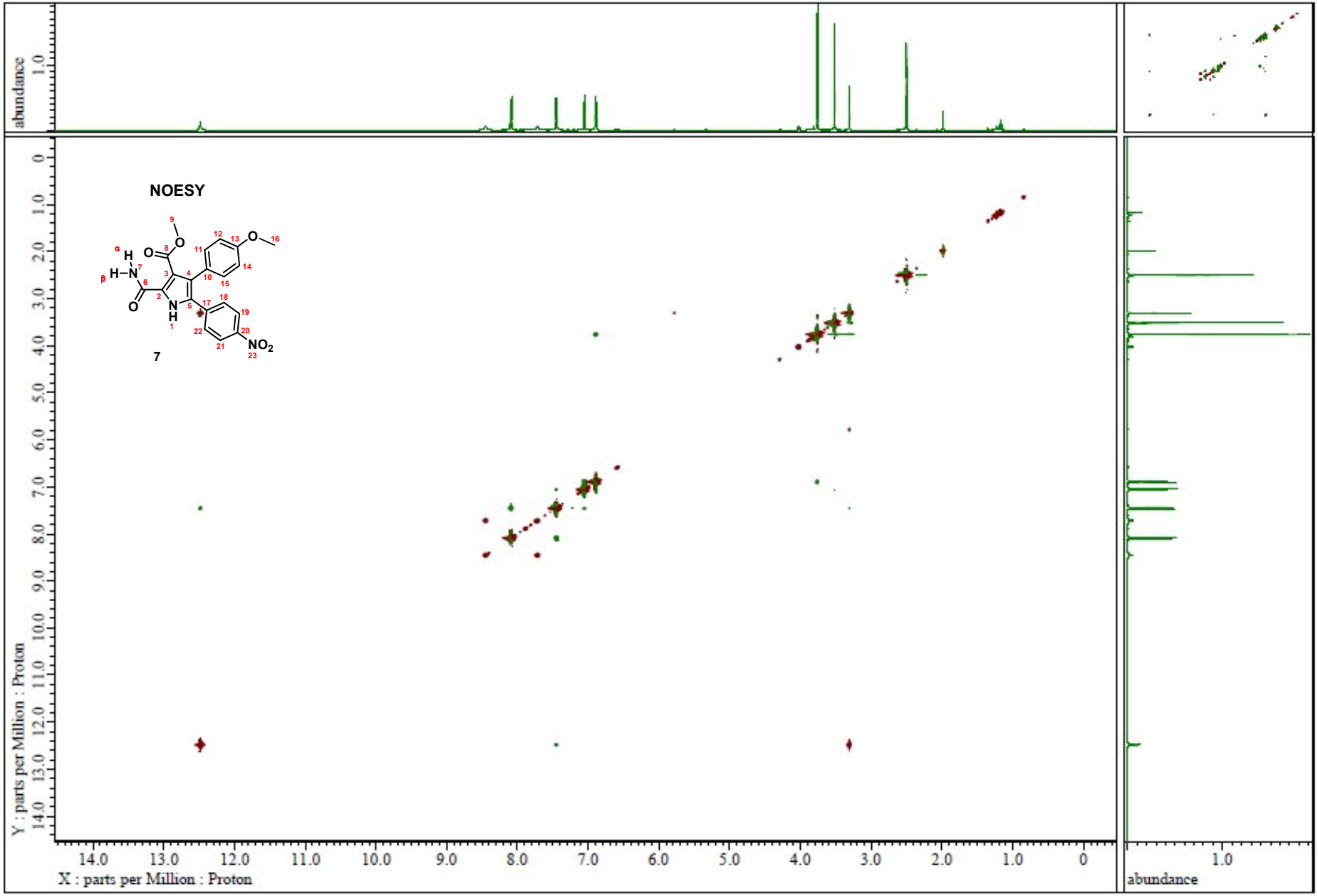


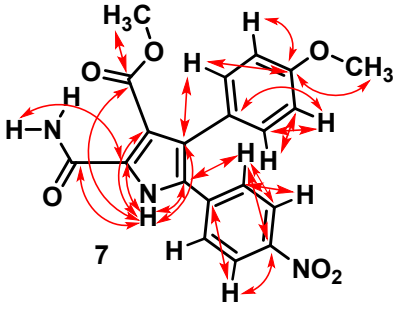

166.246
160.739
158.279
145.830
137.554
131.169
129.884
128.868
128.556
126.278
125.523
123.230
115.836
113.594
54.954
51.566
2.0
1.0
abundance
180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0
X : parts per Million : Carbon13
13C
7


abundance
1.0
^{1}H - ^{1}H COSY
7
Y : parts per Million : Proton
X : parts per Million : Proton
14.0 13.0 12.0 11.0 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
abundance
1.0

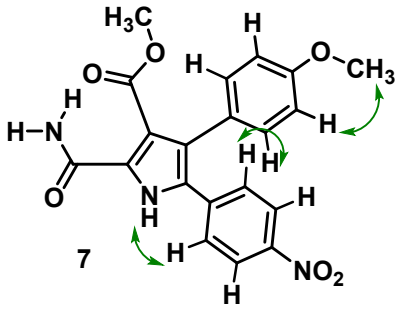

abundance
1.0
^{1}H - ^{13}C HMQC
7
Y : parts per Million : Carbon13
20.0
40.0
60.0
80.0
100.0
120.0
140.0
160.0
180.0
14.0
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton
0
0.2
0.4
0.6
abundance


abundance
1.0
^{1}H - ^{13}C HMBC
7
Y : parts per Million : Carbon13
20.0
40.0
60.0
80.0
100.0
120.0
140.0
160.0
180.0
14.0
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton
0
0.2
0.4
0.6
abundance

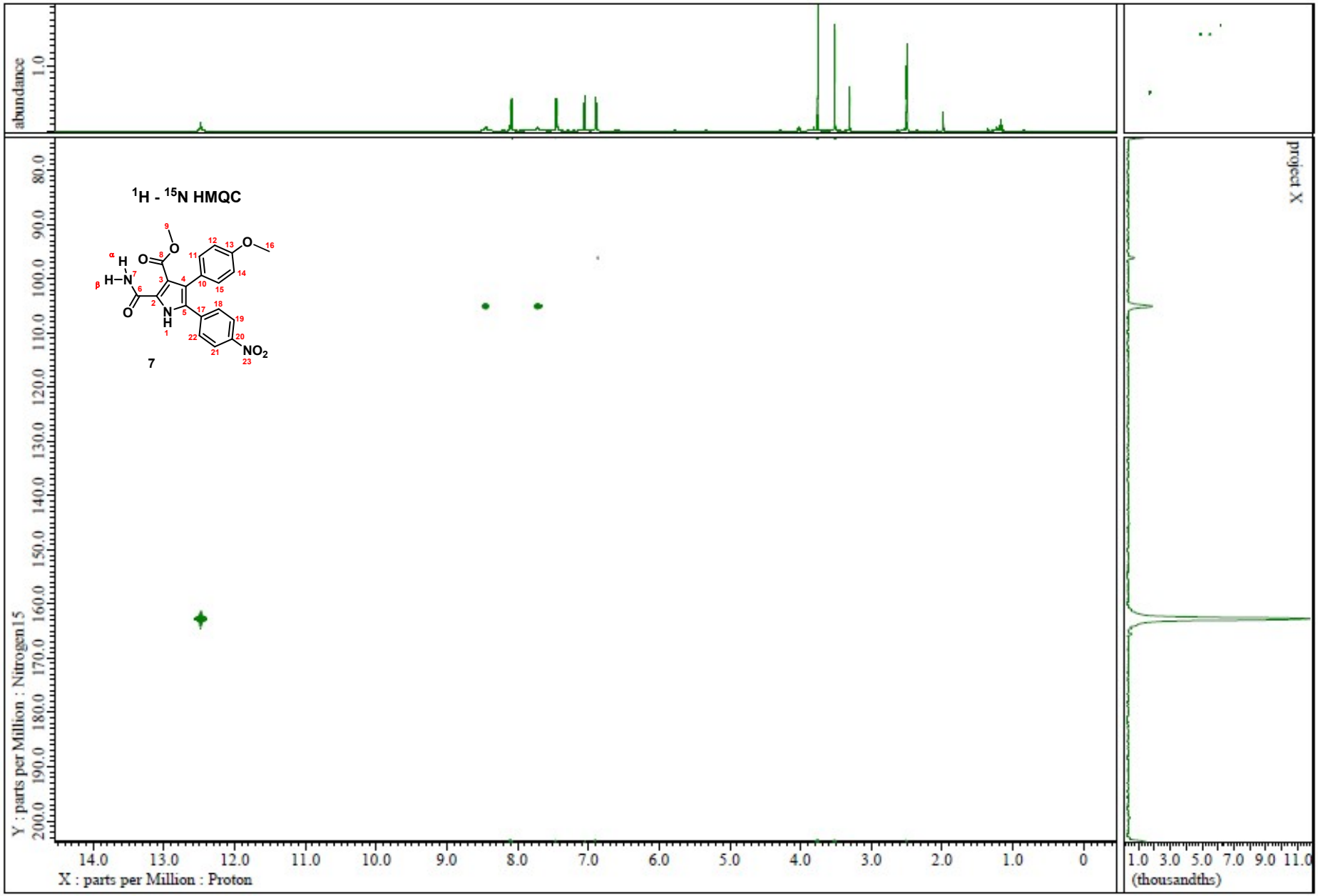

NOESY
7
abundance
Y : parts per Million : Proton
X : parts per Million : Proton
abundance

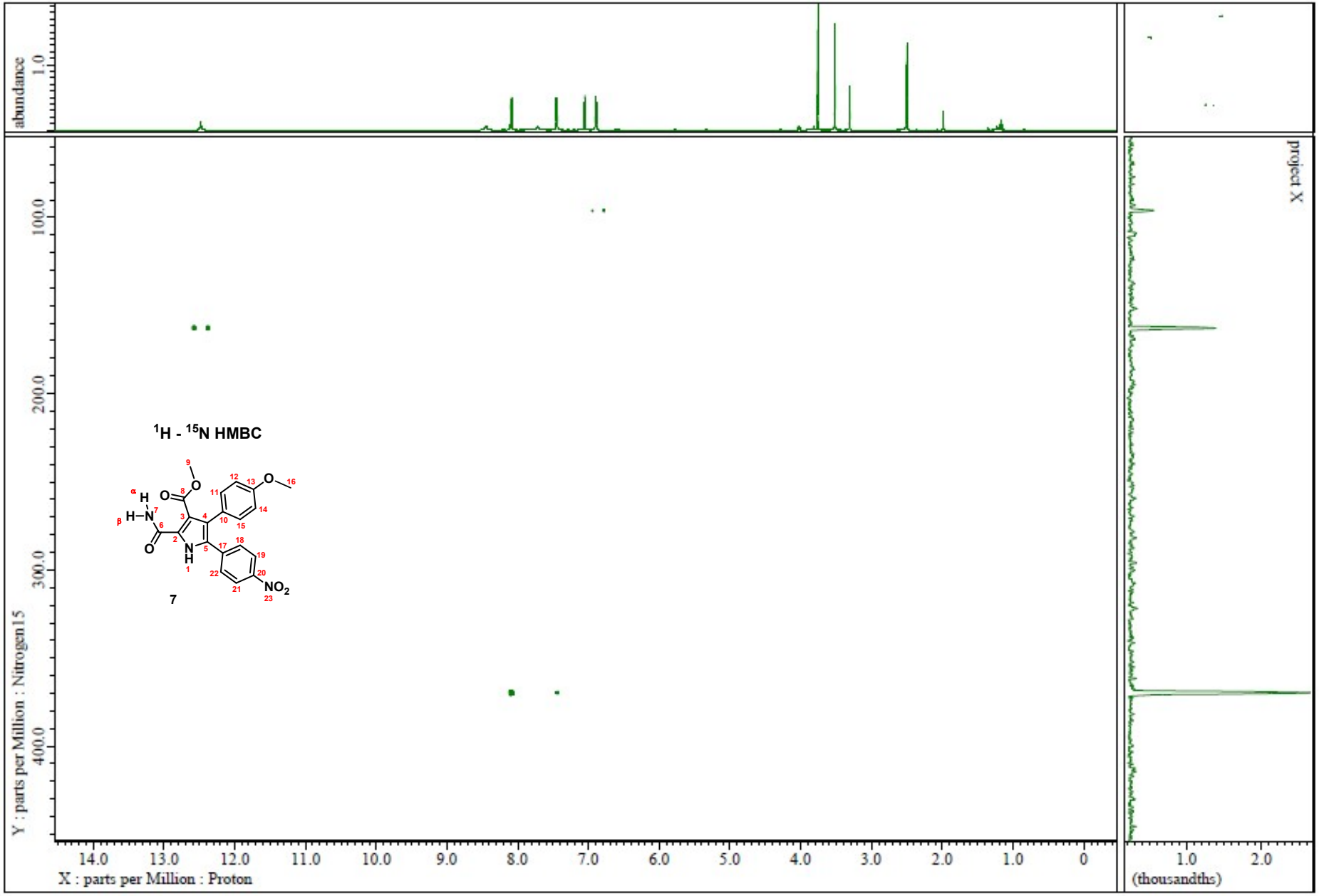


^{1}H-^{13}C HMBC Correlations

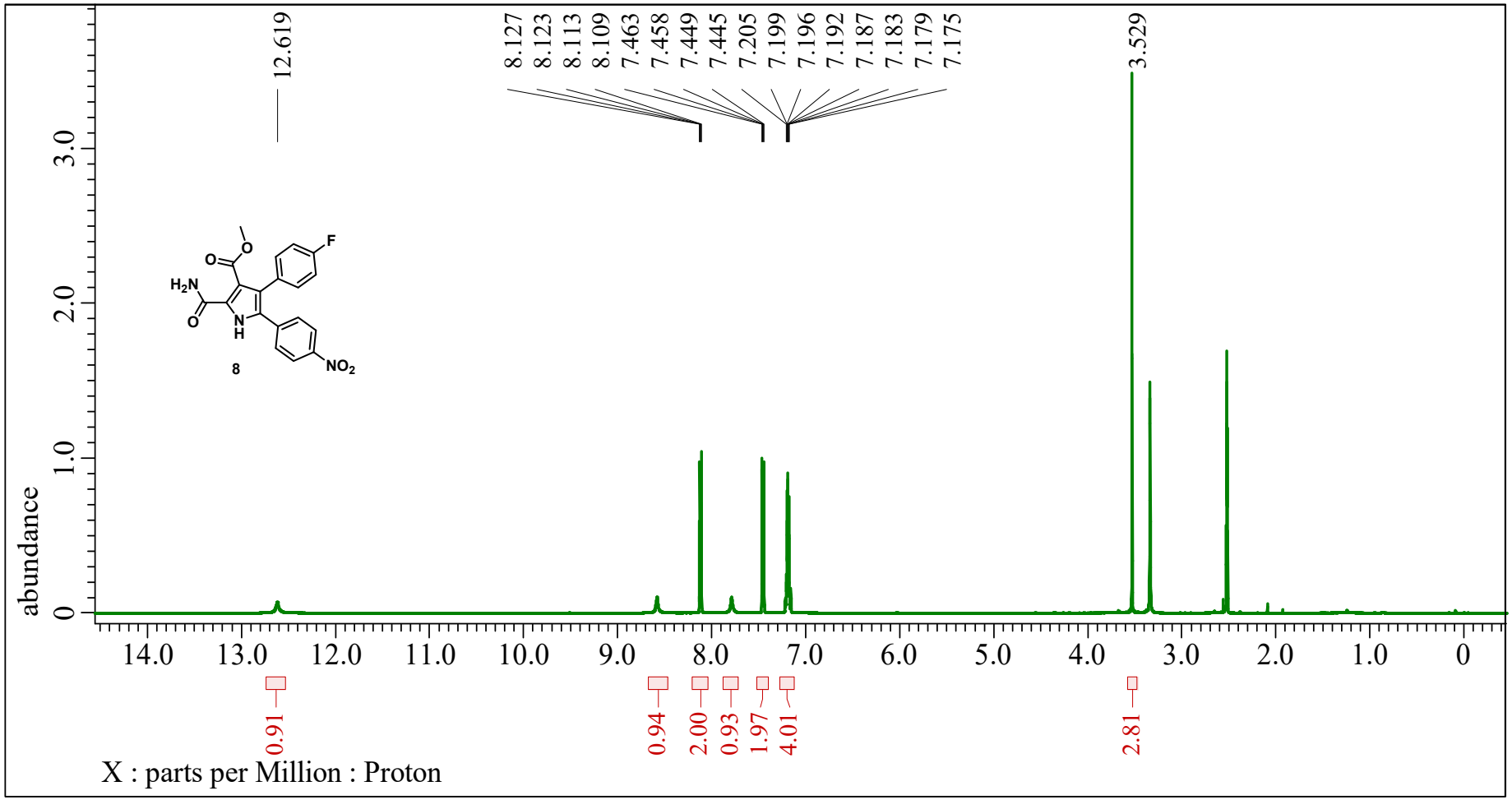


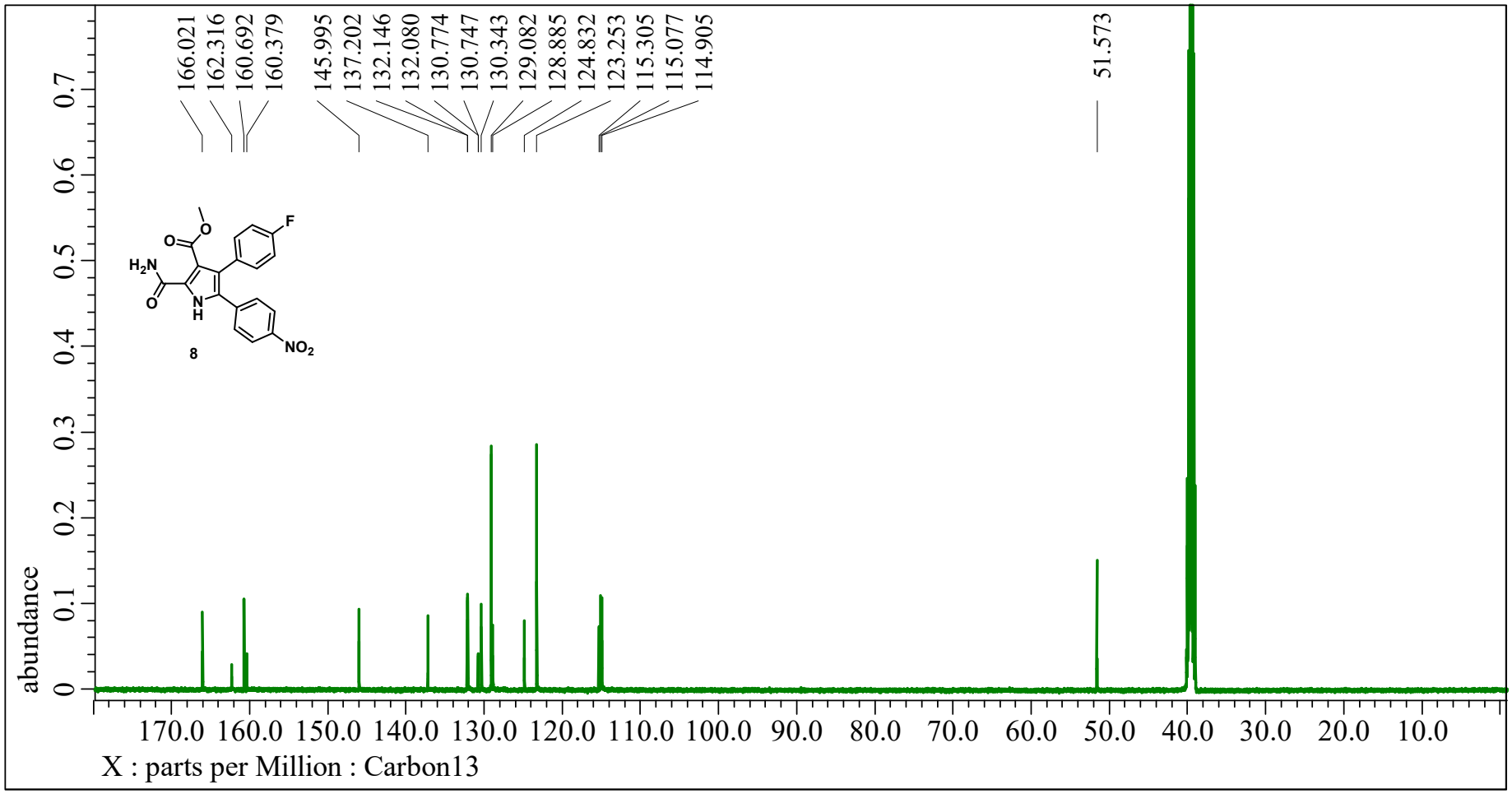
^{1}H -^{1}H NOESY Correlations


abundance
1.0
^{1}H - ^{15}N HMQC
7
project X
Y : parts per Million : Nitrogen15
X : parts per Million : Proton
14.0 13.0 12.0 11.0 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
80.0 90.0 100.0 110.0 120.0 130.0 140.0 150.0 160.0 170.0 180.0 190.0 200.0
1.0 3.0 5.0 7.0 9.0 11.0
(thousandths)

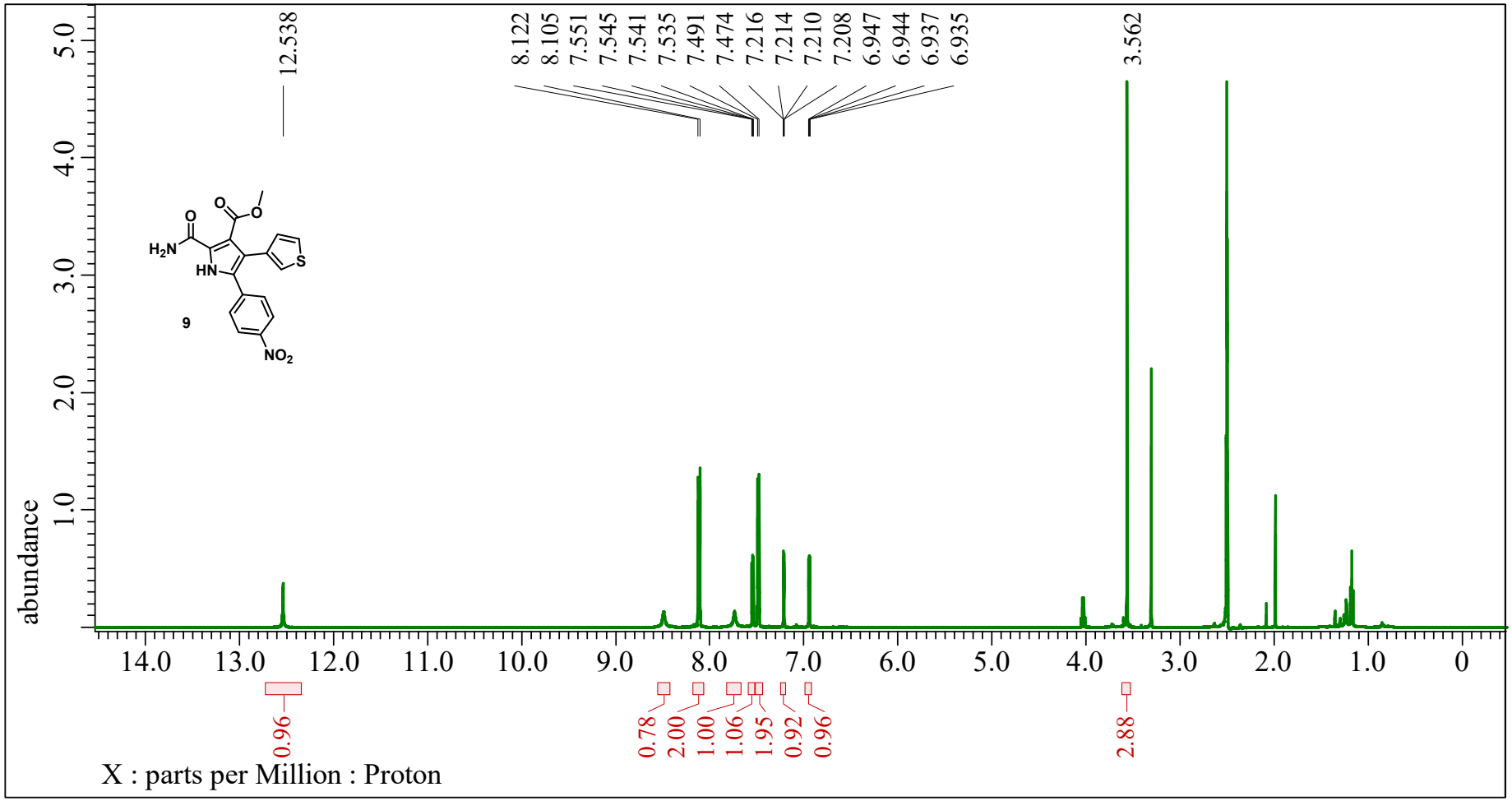

abundance
1.0
project X
100.0
200.0
300.0
400.0
Y : parts per Million : Nitrogen15
14.0
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton
1.0
2.0
(thousandths)
1H - 15N HMBC
7

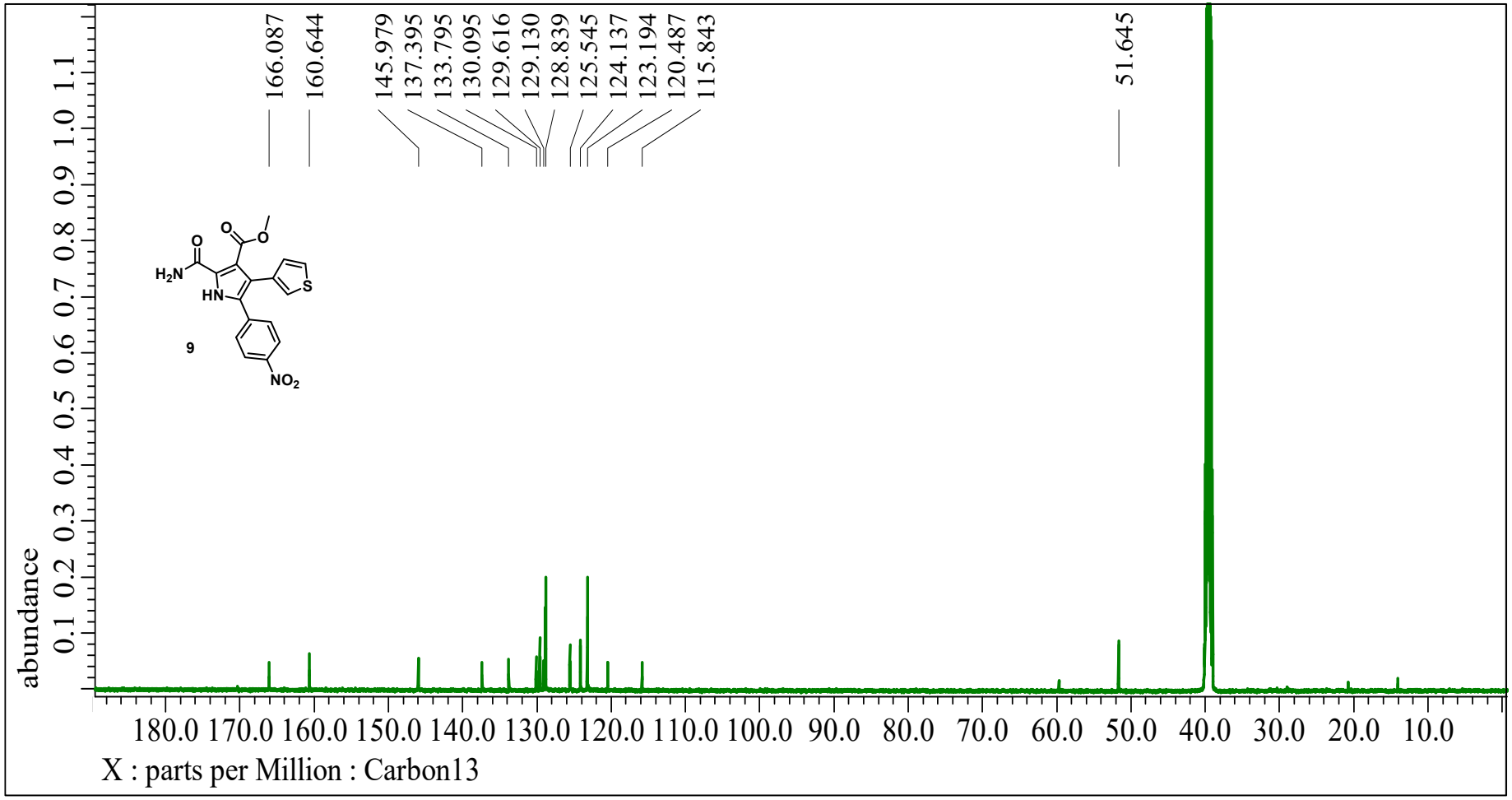
Methyl 2-carbamoyl-4-(4-fluorophenyl)-5-(4-nitrophenyl)-1*H*-pyrrole-3-carboxylate (8)



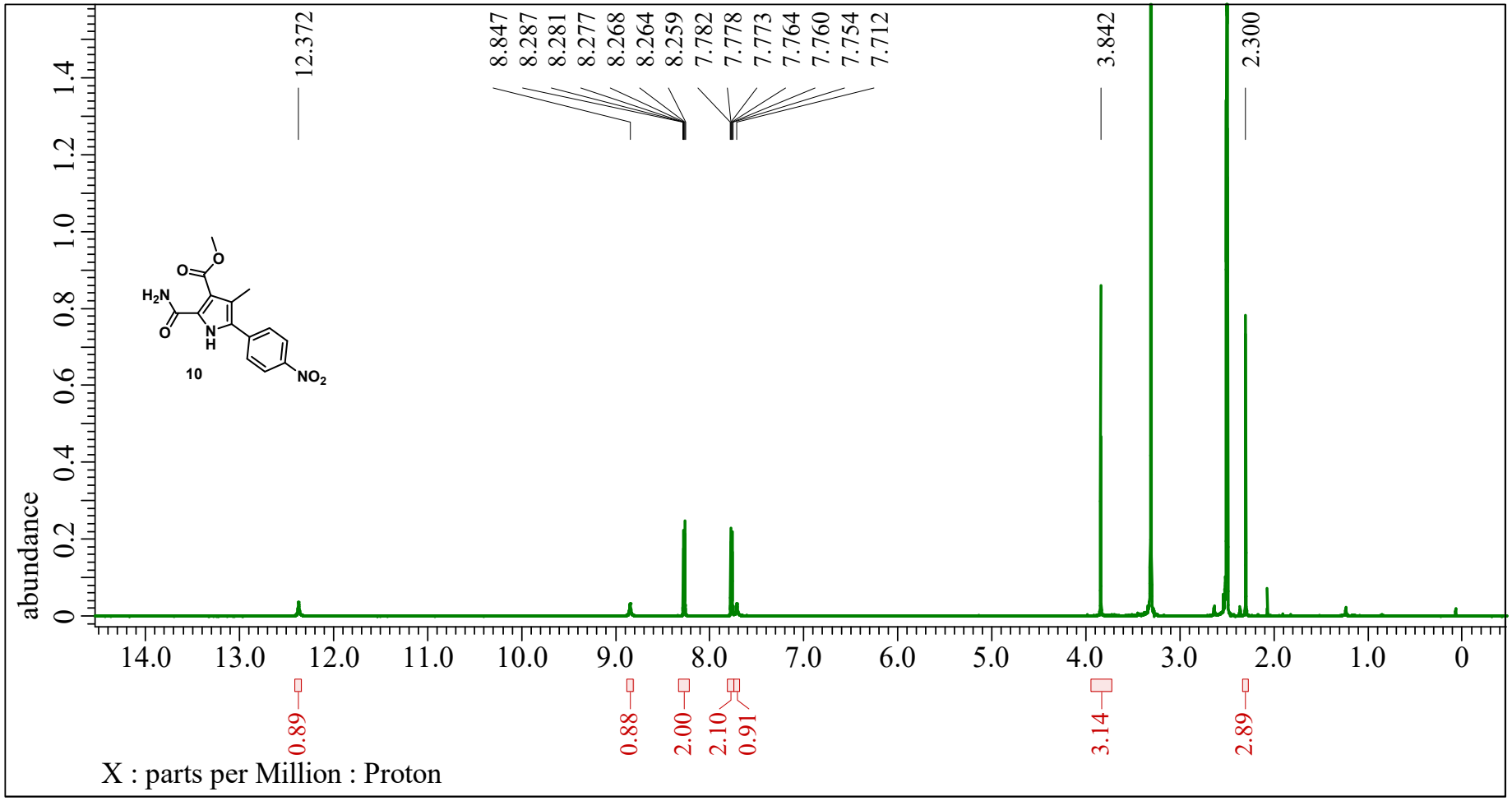

166.021
162.316
160.692
160.379
145.995
137.202
132.146
132.080
130.774
130.747
130.343
129.082
128.885
124.832
123.253
115.305
115.077
114.905
51.573
F
O
O
H2N
O
N
H
NO2
8
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0
X : parts per Million : Carbon13

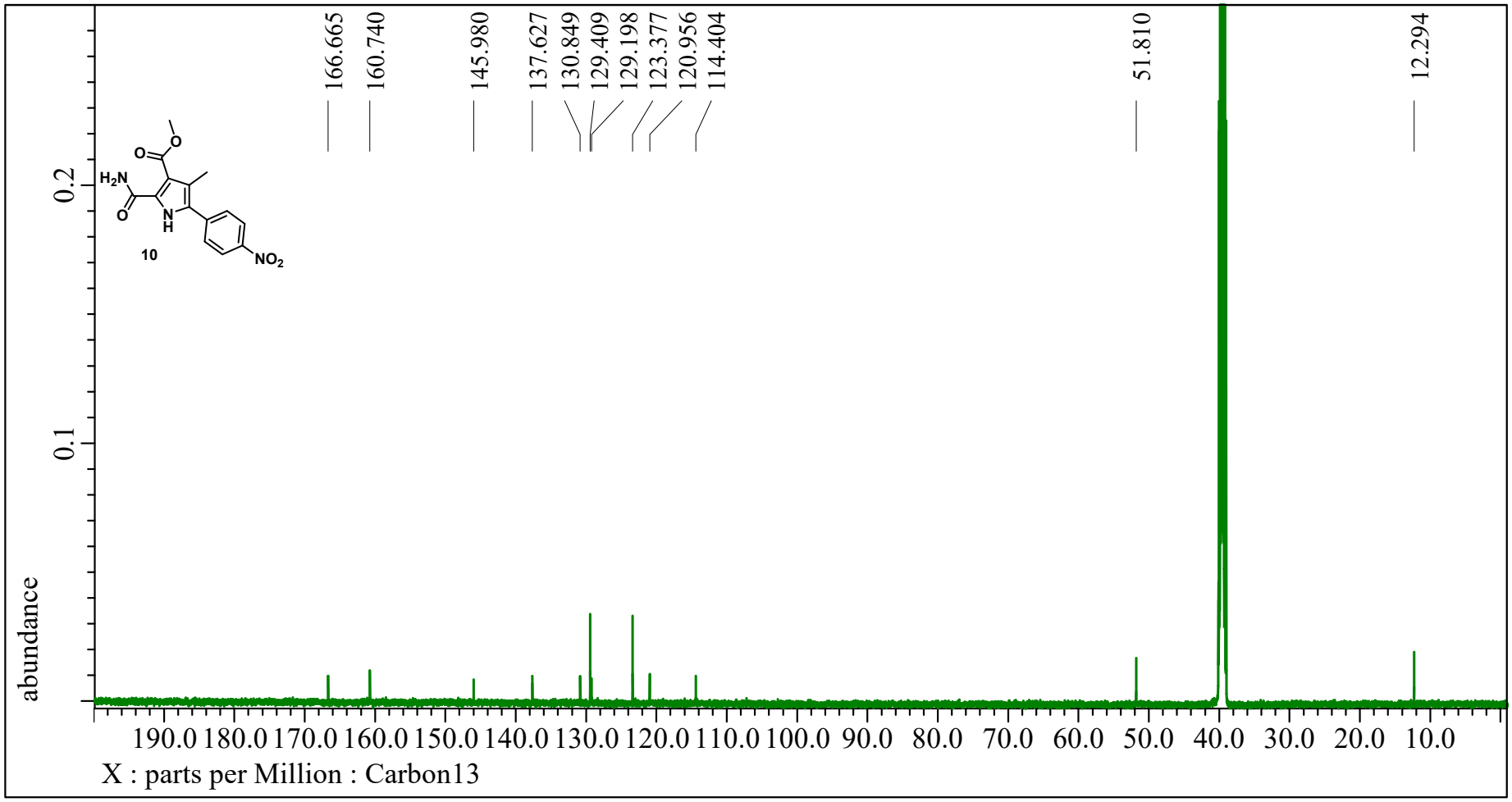
Methyl 2-carbamoyl-5-(4-nitrophenyl)-4-(thiophen-3-yl)-1*H*-pyrrole-3-carboxylate (9)



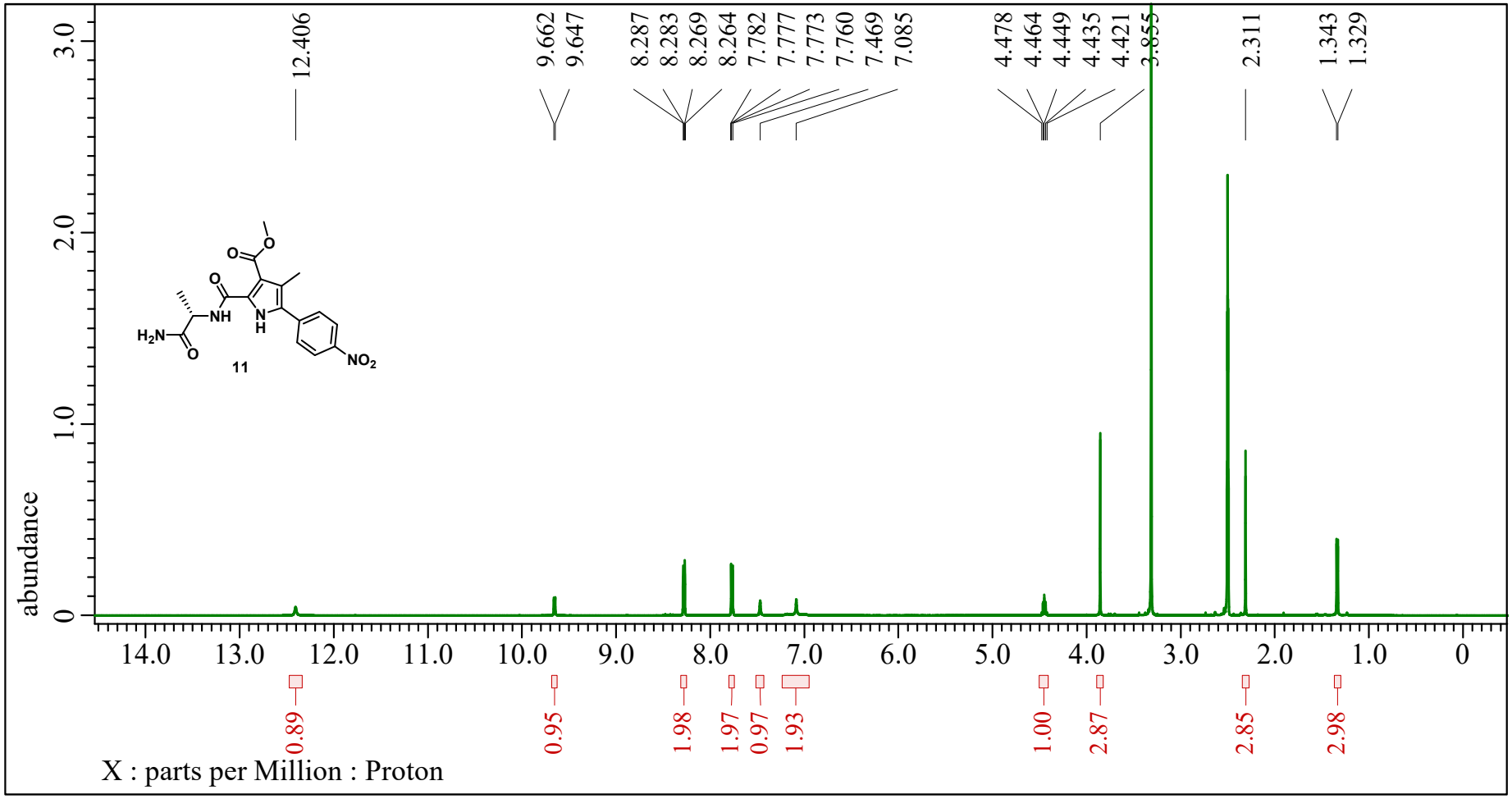

166.087
160.644
145.979
137.395
133.795
130.095
129.616
129.130
128.839
125.545
124.137
123.194
120.487
115.843
51.645
abundance
0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0 1.1
9
180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0
X : parts per Million : Carbon13

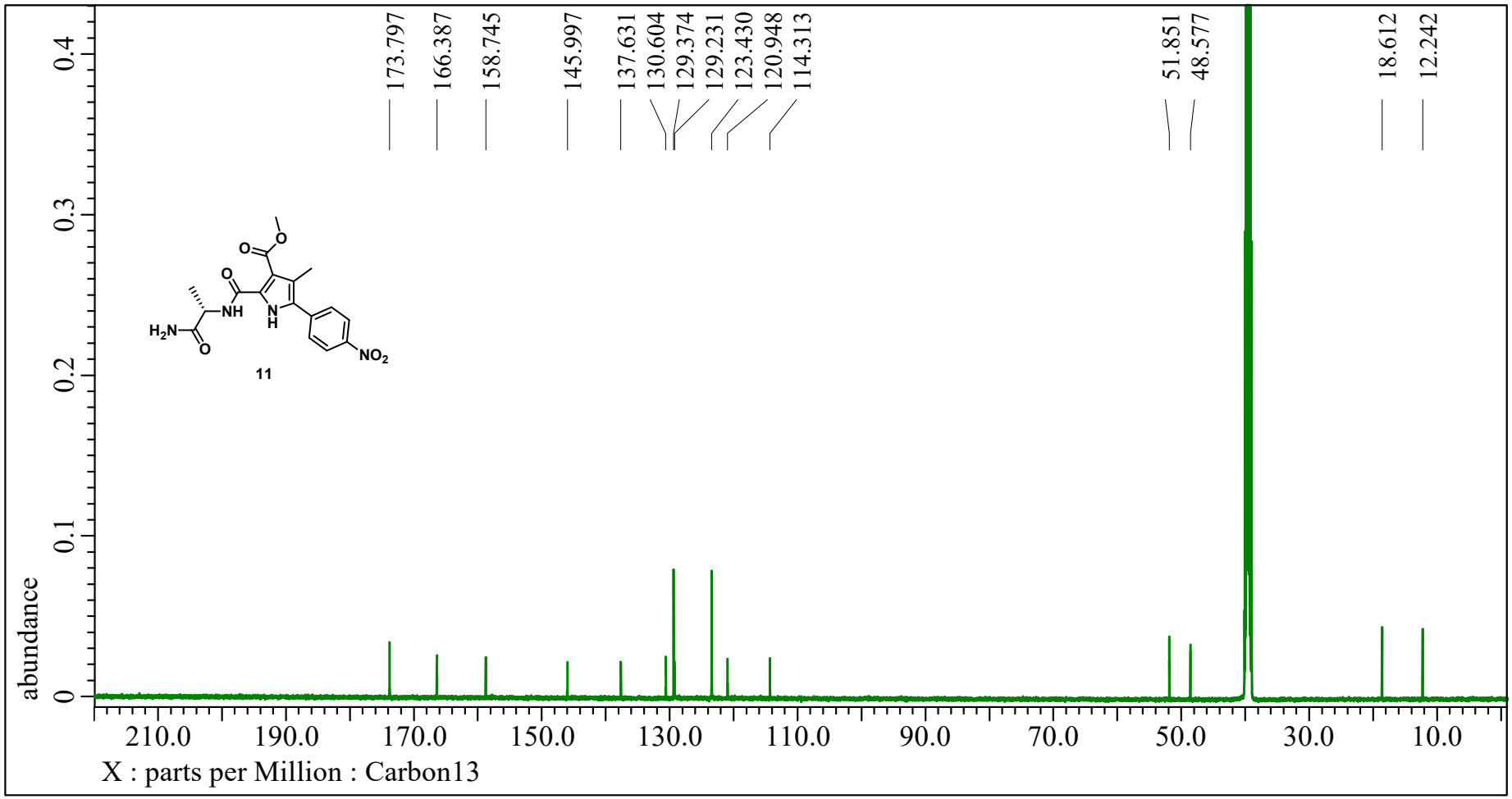
Methyl 2-carbamoyl-4-methyl-5-(4-nitrophenyl)-1*H*-pyrrole-3-carboxylate (10)



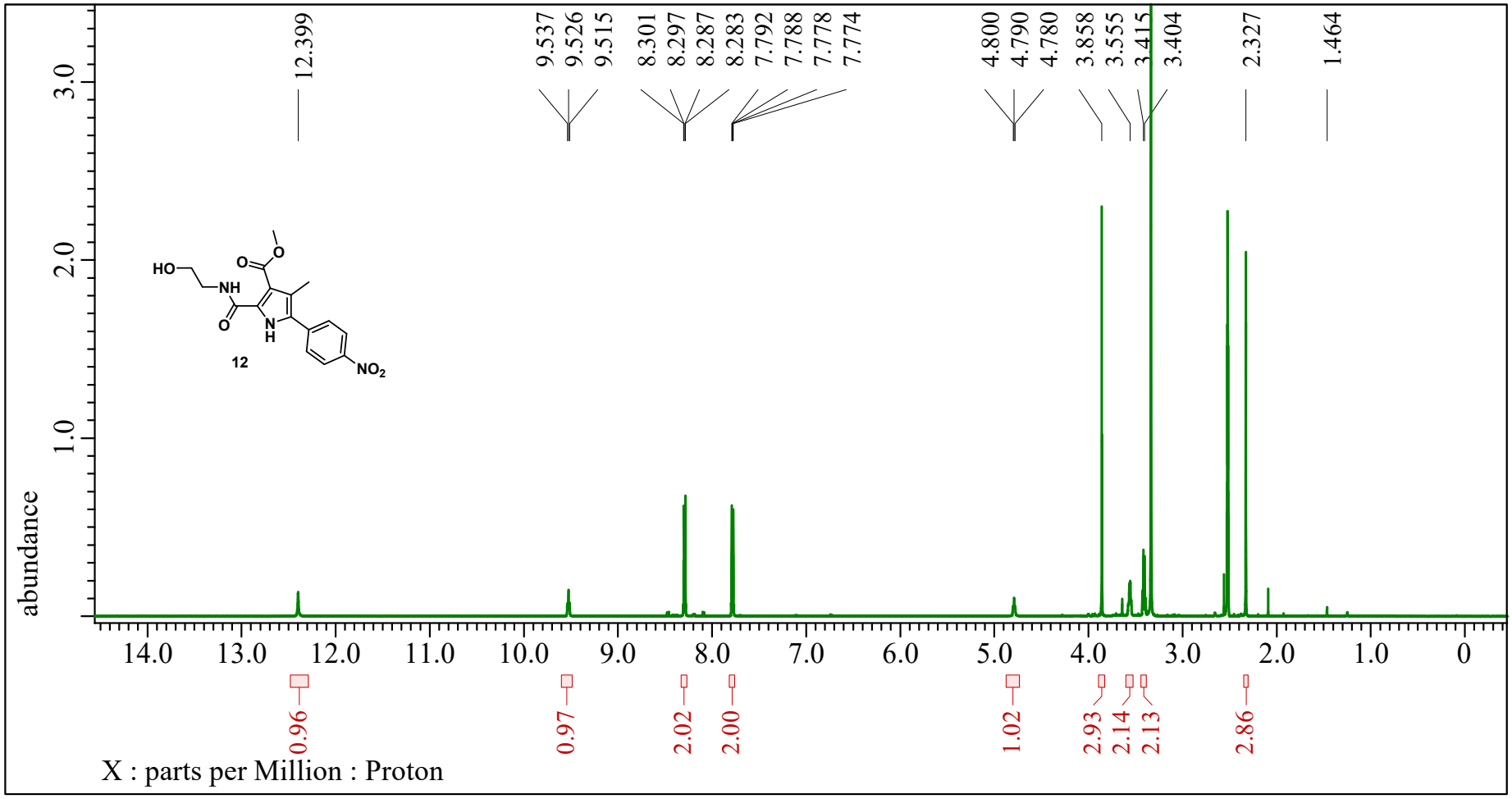

166.665
160.740
145.980
137.627
130.849
129.409
129.198
123.377
120.956
114.404
51.810
12.294
0.2
0.1
abundance
10
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0
X : parts per Million : Carbon13

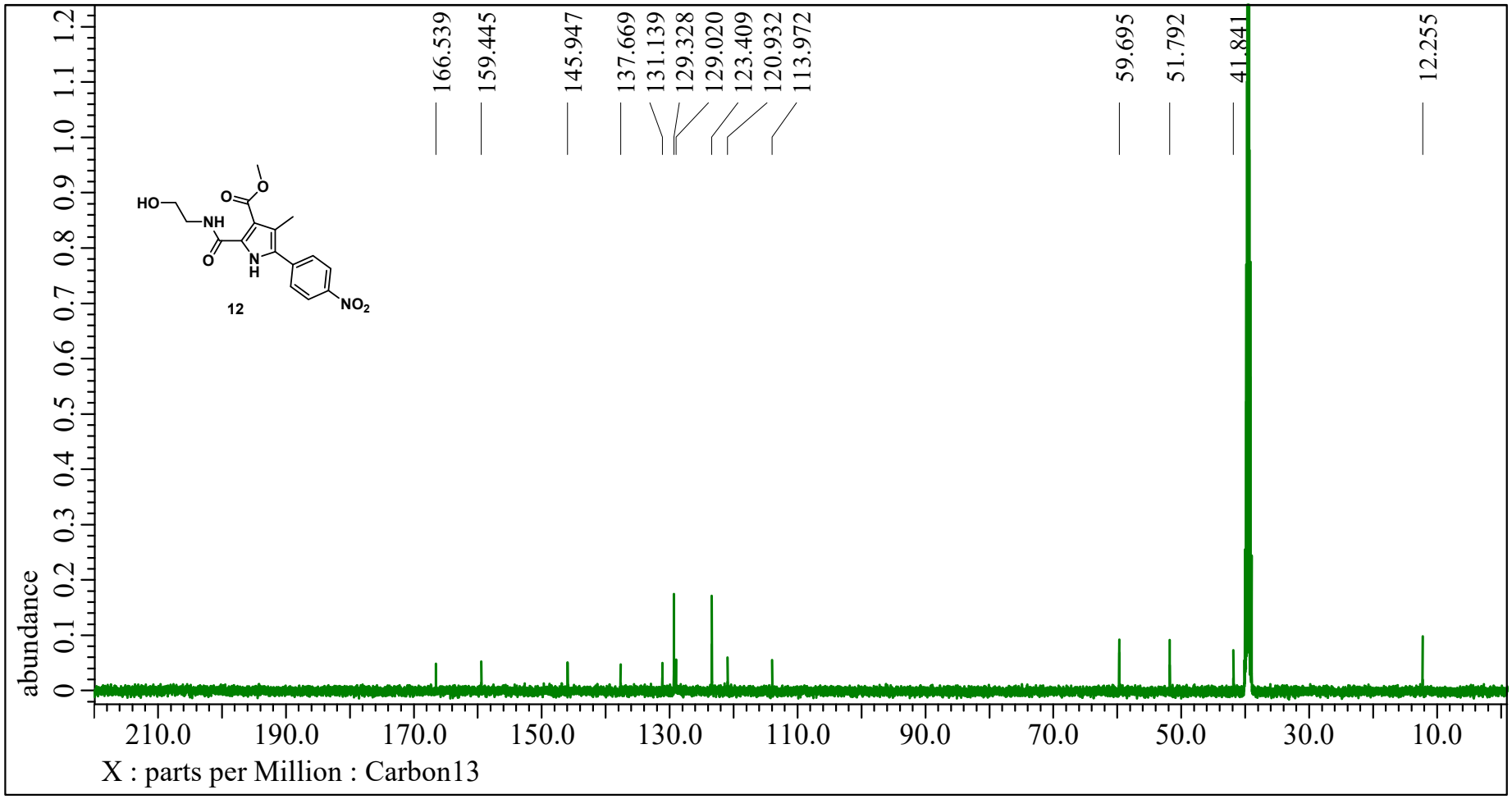
Methyl (*S*)-2-((1-amino-1-oxopropan-2-yl)carbamoyl)-4-methyl-5-(4-nitrophenyl)-1*H*-pyrrole-3-carboxylate (11)



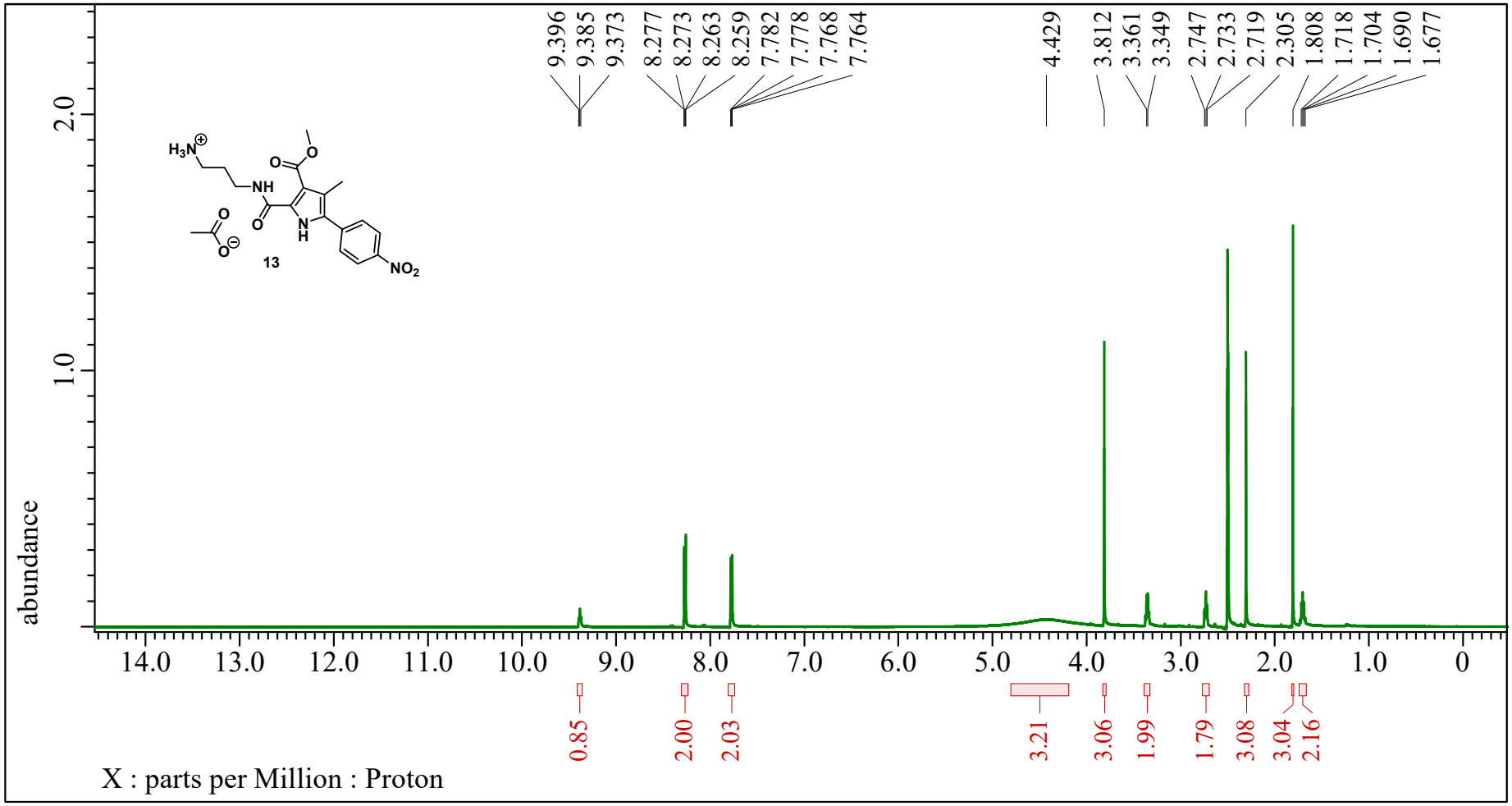

173.797
166.387
158.745
145.997
137.631
130.604
129.374
129.231
123.430
120.948
114.313
51.851
48.577
18.612
12.242
11
abundance
0
0.1
0.2
0.3
0.4
210.0
190.0
170.0
150.0
130.0
110.0
90.0
70.0
50.0
30.0
10.0
X : parts per Million : Carbon13

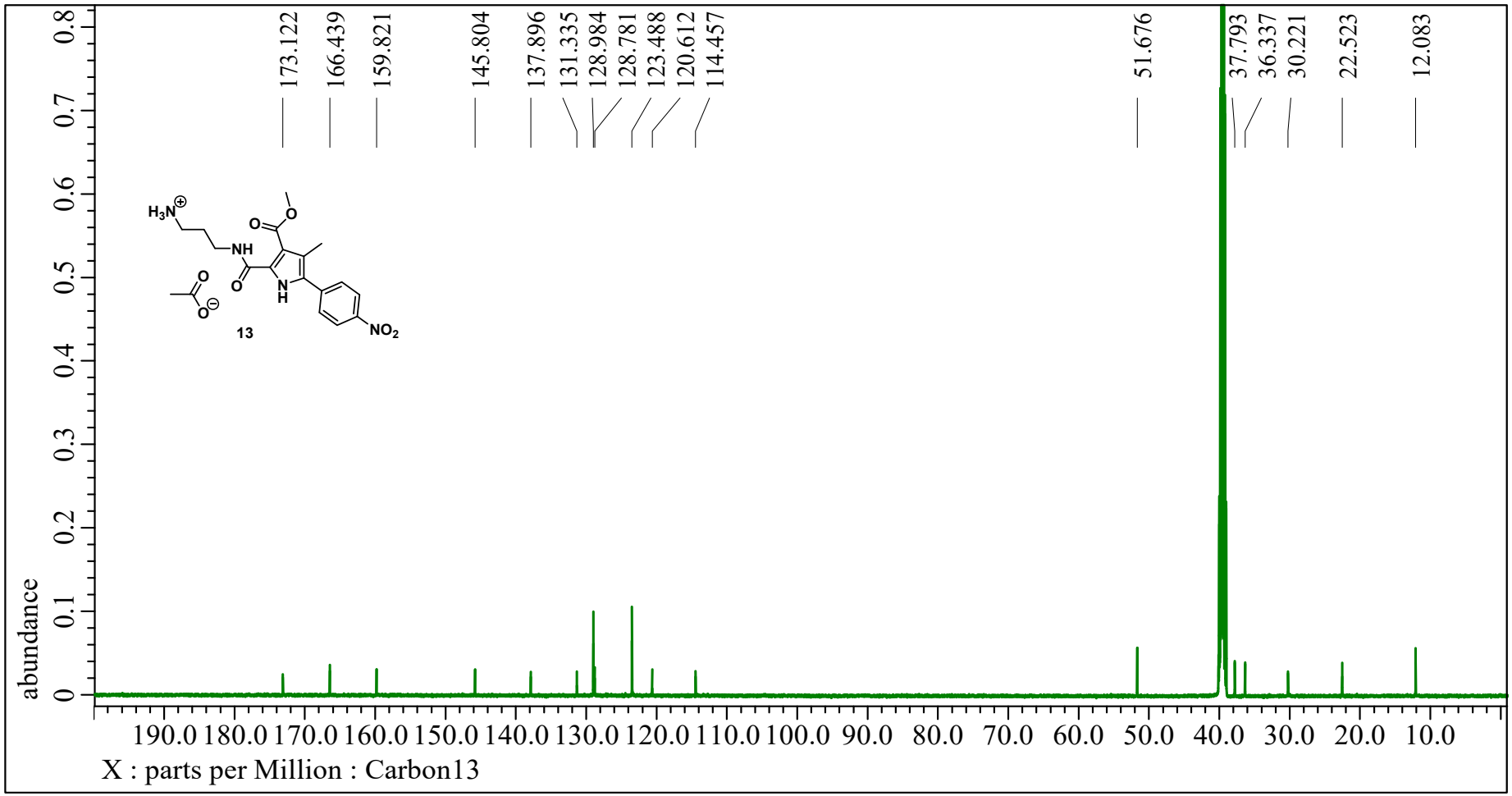
Methyl 2-((2-hydroxyethyl)carbamoyl)-4-methyl-5-(4-nitrophenyl)-1*H*-pyrrole-3-carboxylate (12)




166.539
159.445
145.947
137.669
131.139
129.328
129.020
123.409
120.932
113.972
59.695
51.792
41.841
12.255
HO
NH
O
O
O
N
H
NO2
12
abundance
0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0 1.1 1.2
210.0 190.0 170.0 150.0 130.0 110.0 90.0 70.0 50.0 30.0 10.0
X : parts per Million : Carbon13

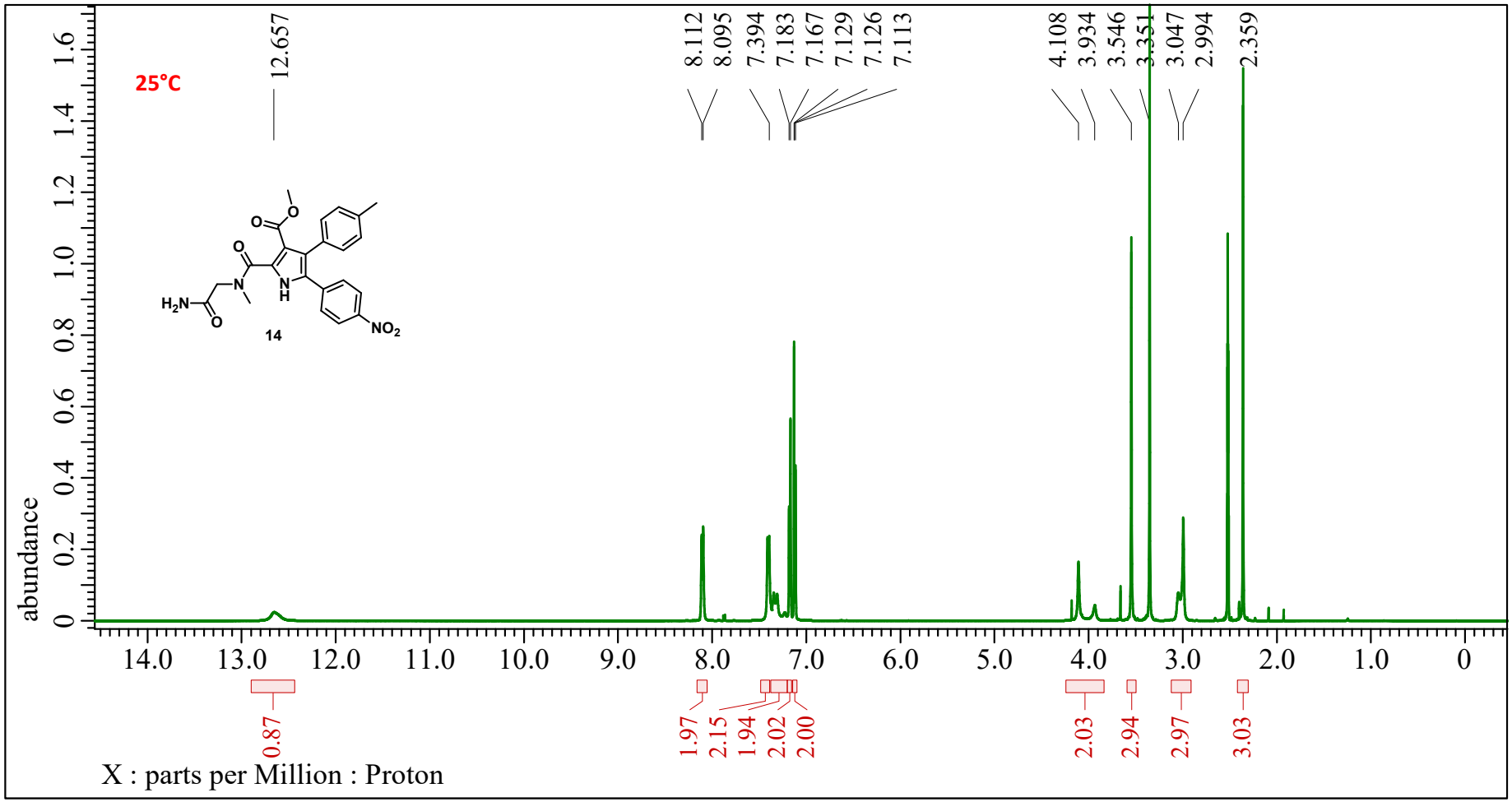
2-(3-(Methoxycarbonyl)-4-methyl-5-(4-nitrophenyl)-1*H*-pyrrole-2-carboxamido)ethan-1-aminium acetate (13)

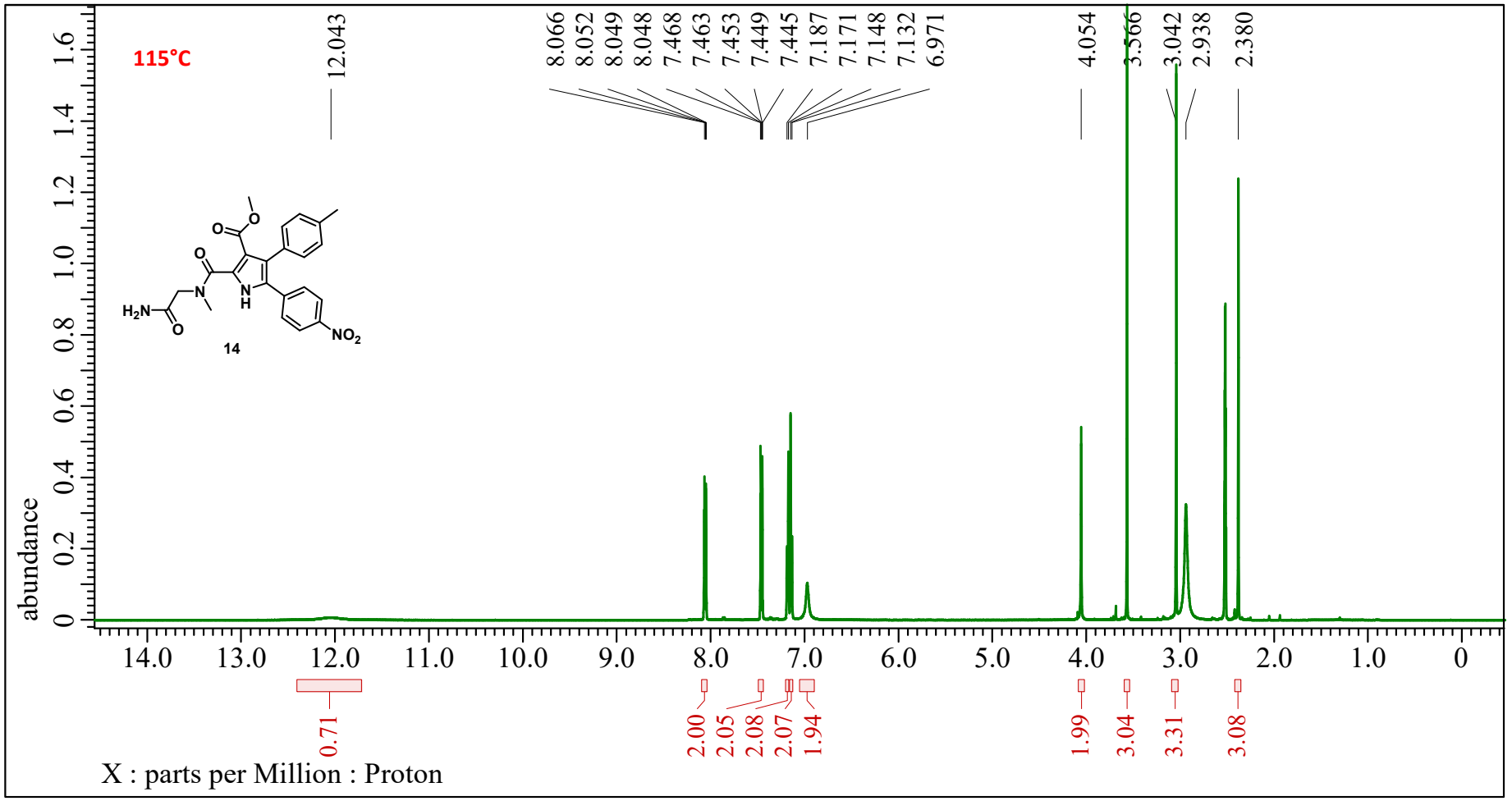



173.122
166.439
159.821
145.804
137.896
131.335
128.984
128.781
123.488
120.612
114.457
51.676
37.793
36.337
30.221
22.523
12.083
13
abundance
X : parts per Million : Carbon13

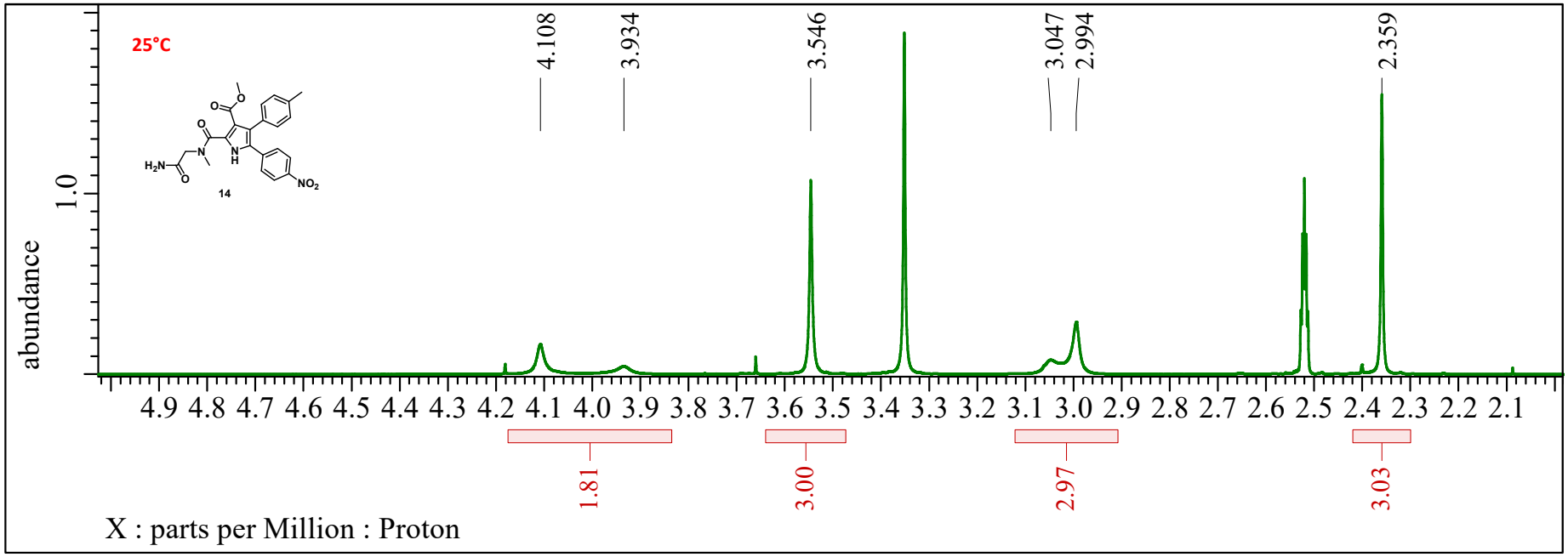
Methyl 2-((2-amino-2-oxoethyl)(methyl)carbamoyl)-5-(4-nitrophenyl)-4-(*p*-tolyl)-1*H*-pyrrole-3-carboxylate (14)

The presence of rotamers was confirmed by temperature-dependent proton measurements at 25°C, 35°C, 45°C, 55°C, 85°C and 115°C. We present only proton spectra at standard 25°C and the highest temperature 115°C.

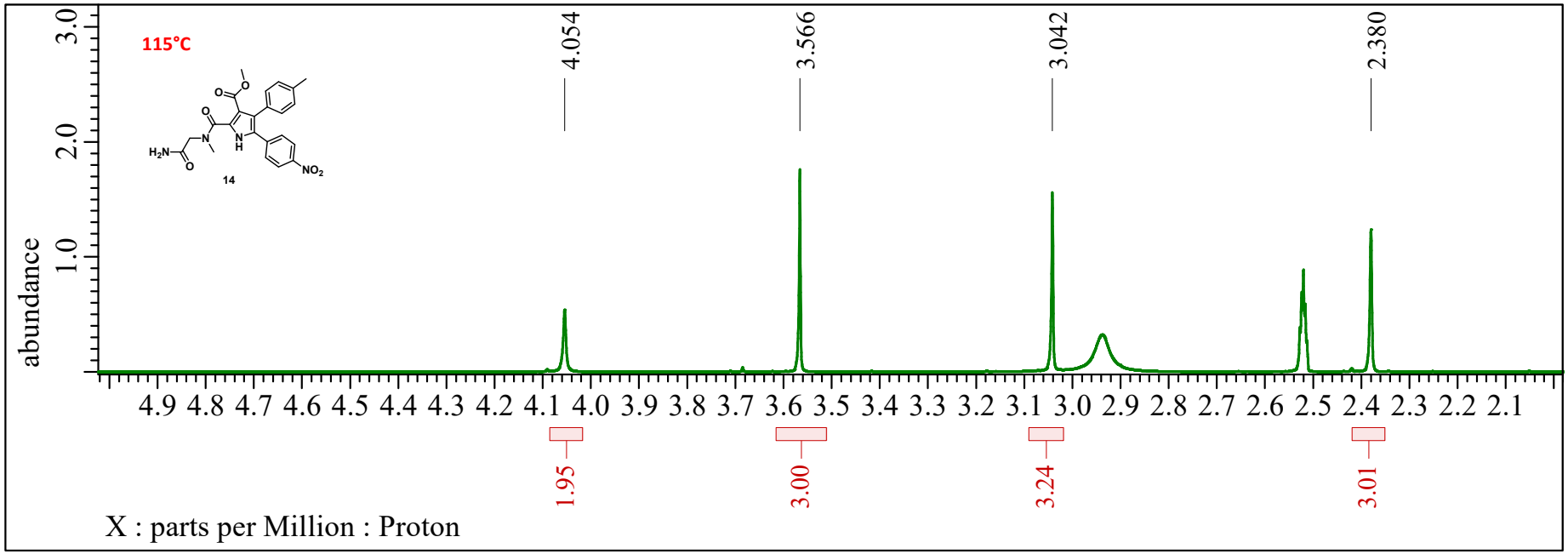



115°C
12.043
8.066
8.052
8.049
8.048
7.468
7.463
7.453
7.449
7.445
7.187
7.171
7.148
7.132
6.971
4.054
3.566
3.042
2.938
2.380
14
abundance
X : parts per Million : Proton
0.71
2.00
2.05
2.08
2.07
1.94
1.99
3.04
3.31
3.08

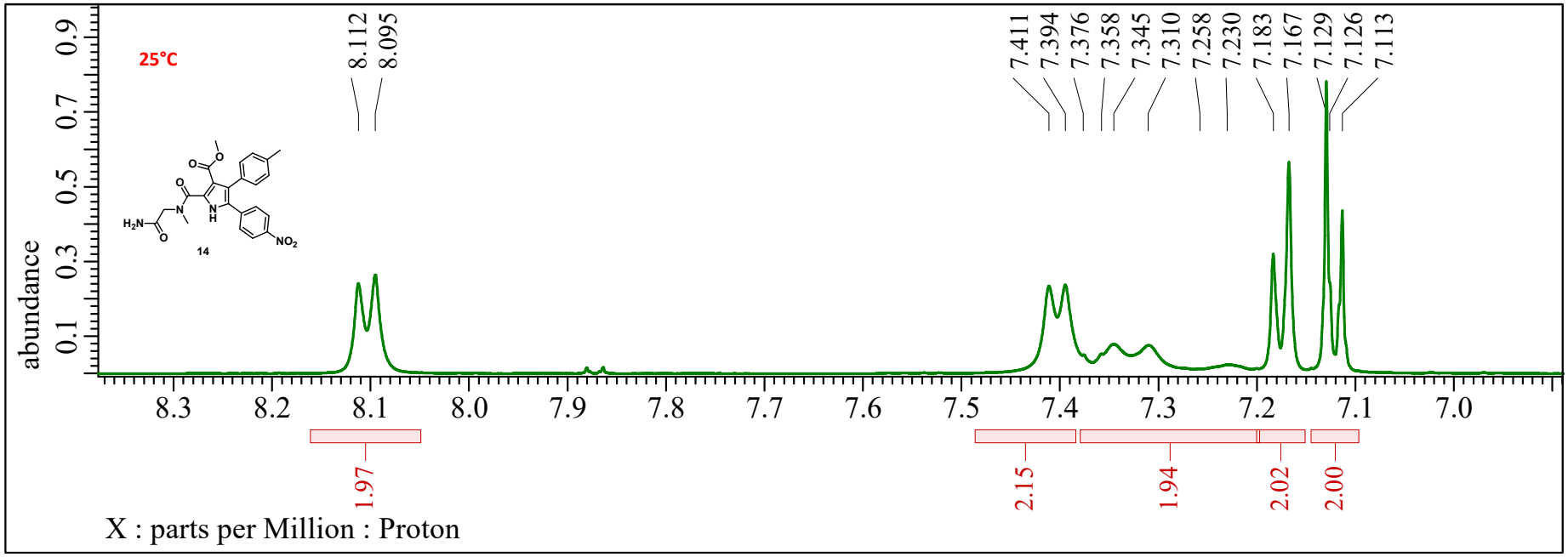
^{1}H Proton spectra of compound **14** at 25°C - Selected area



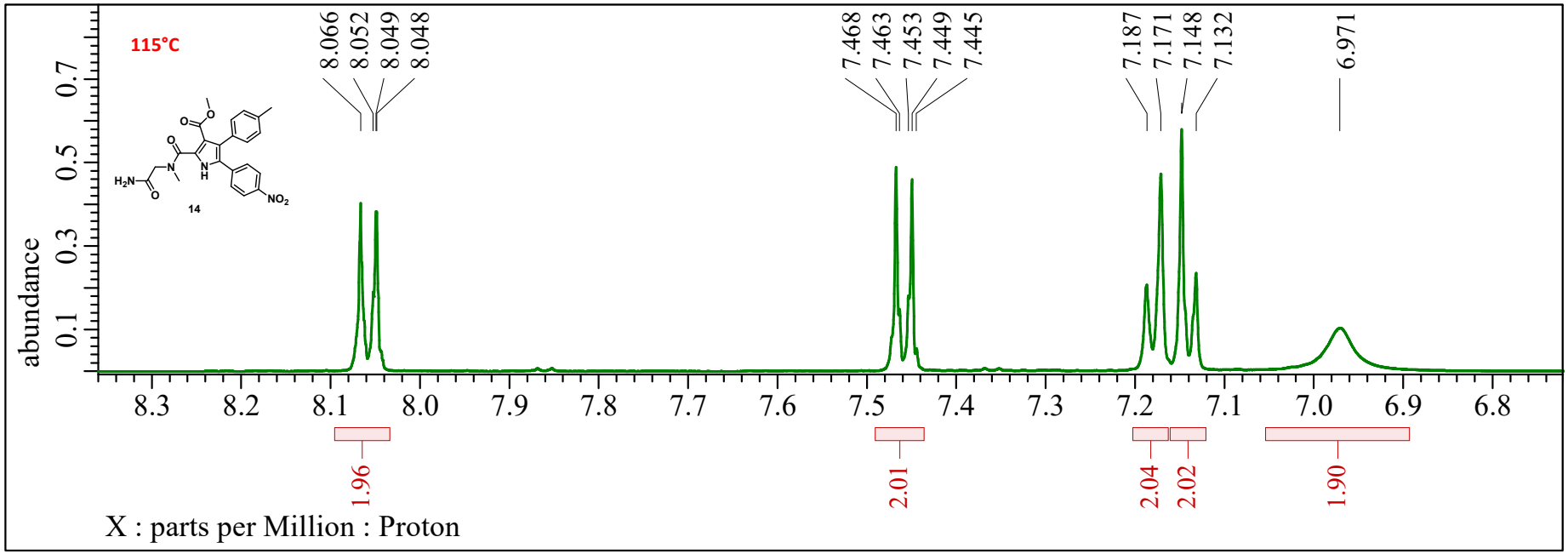
[1]H Proton spectra of compound **14** at 115°C - Selected area

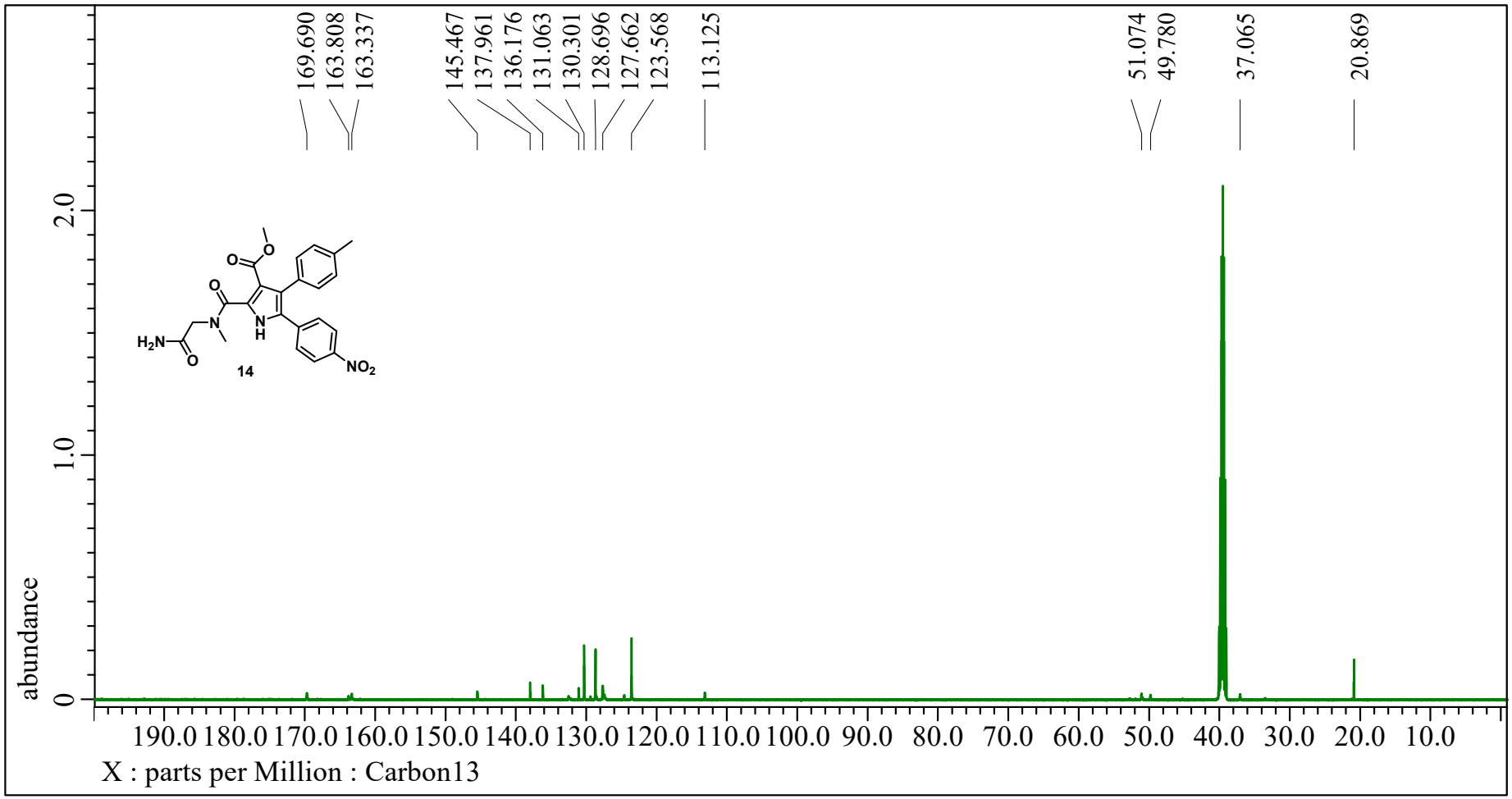


^{1}H Proton spectra of compound **14** at 25°C - Selected area



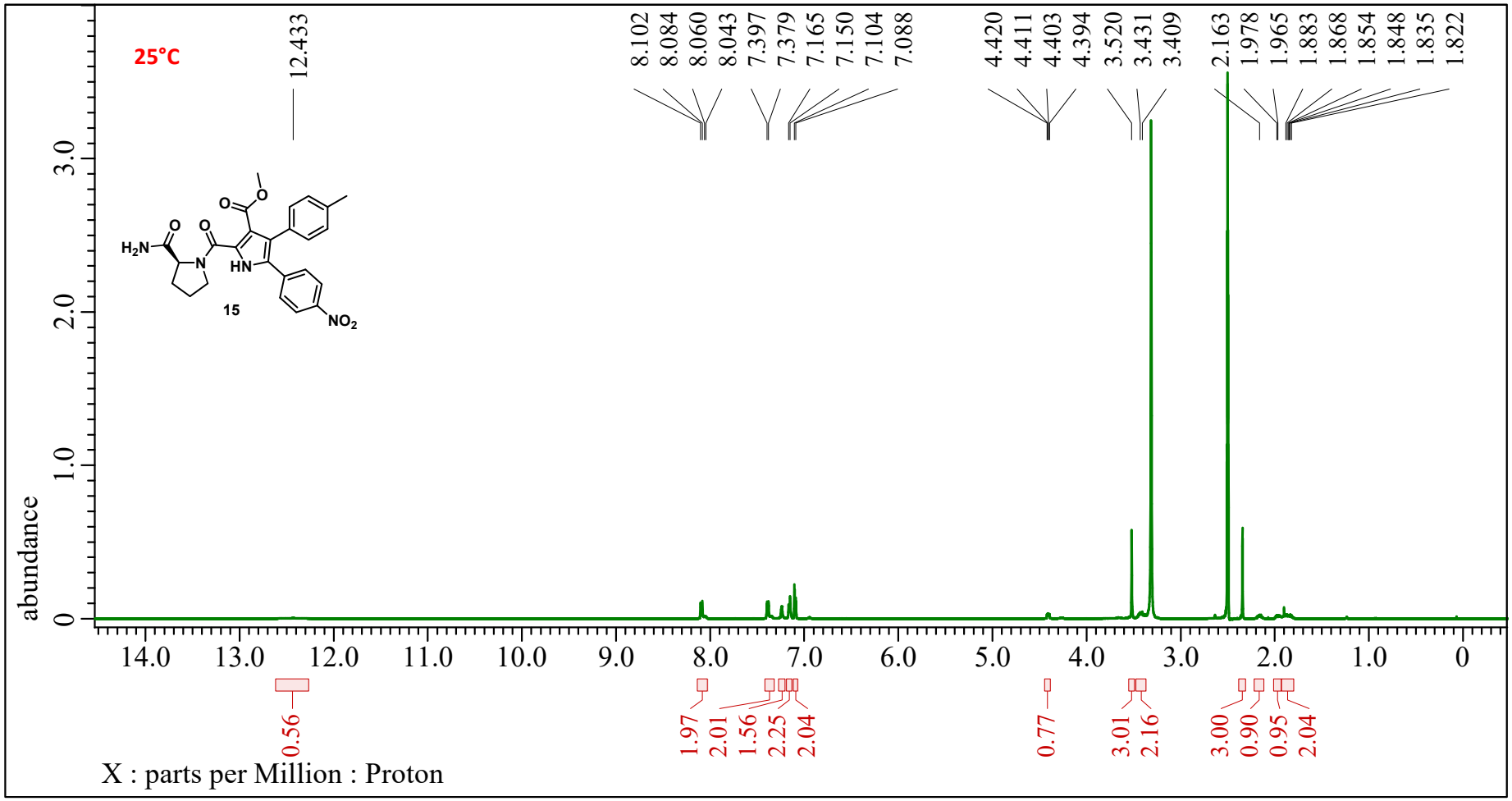
^{1}H Proton spectra of compound **14** at 115°C - Selected area

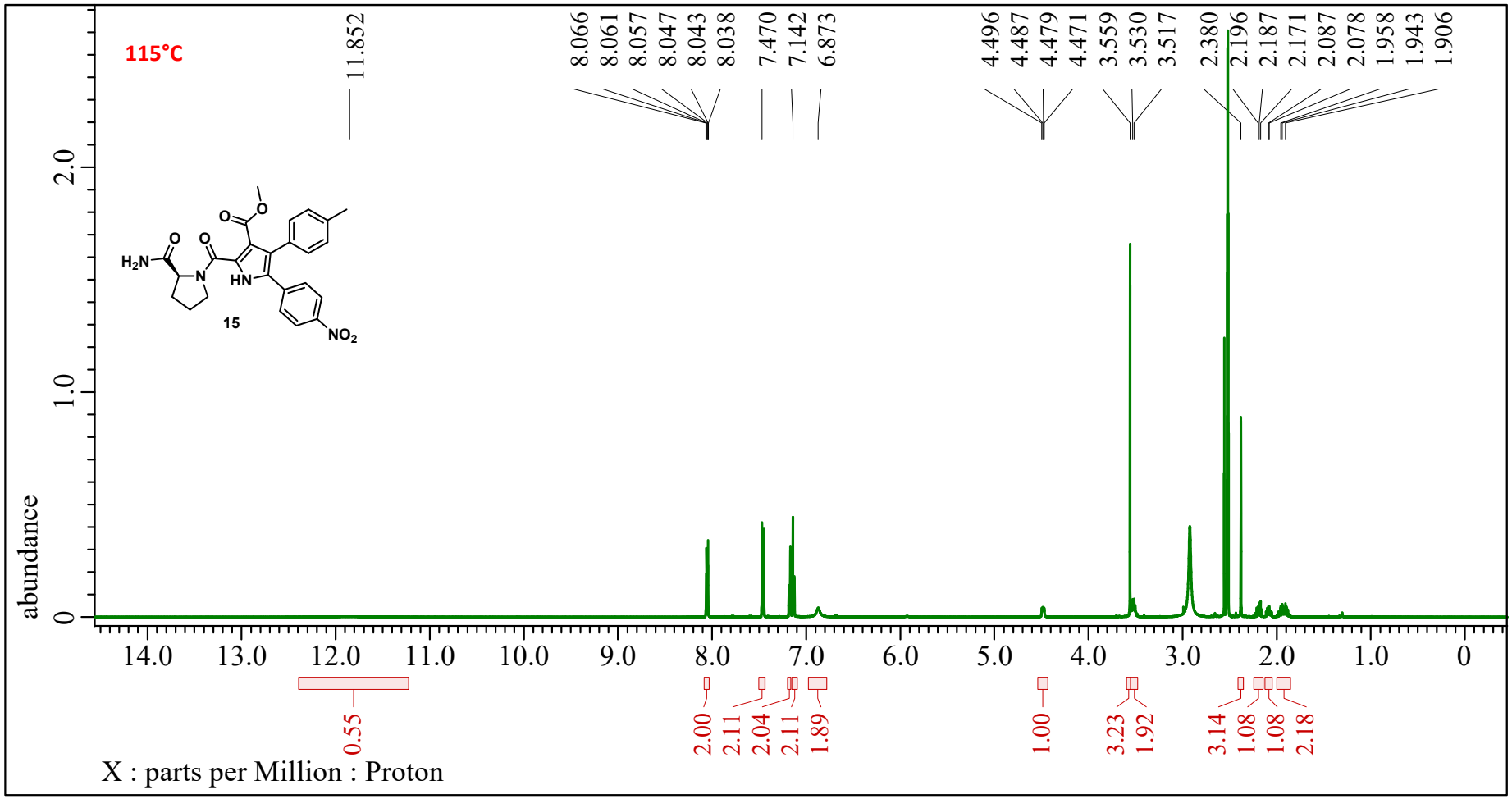



169.690
163.808
163.337
145.467
137.961
136.176
131.063
130.301
128.696
127.662
123.568
113.125
51.074
49.780
37.065
20.869
14
abundance
2.0
1.0
0
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0
X : parts per Million : Carbon13

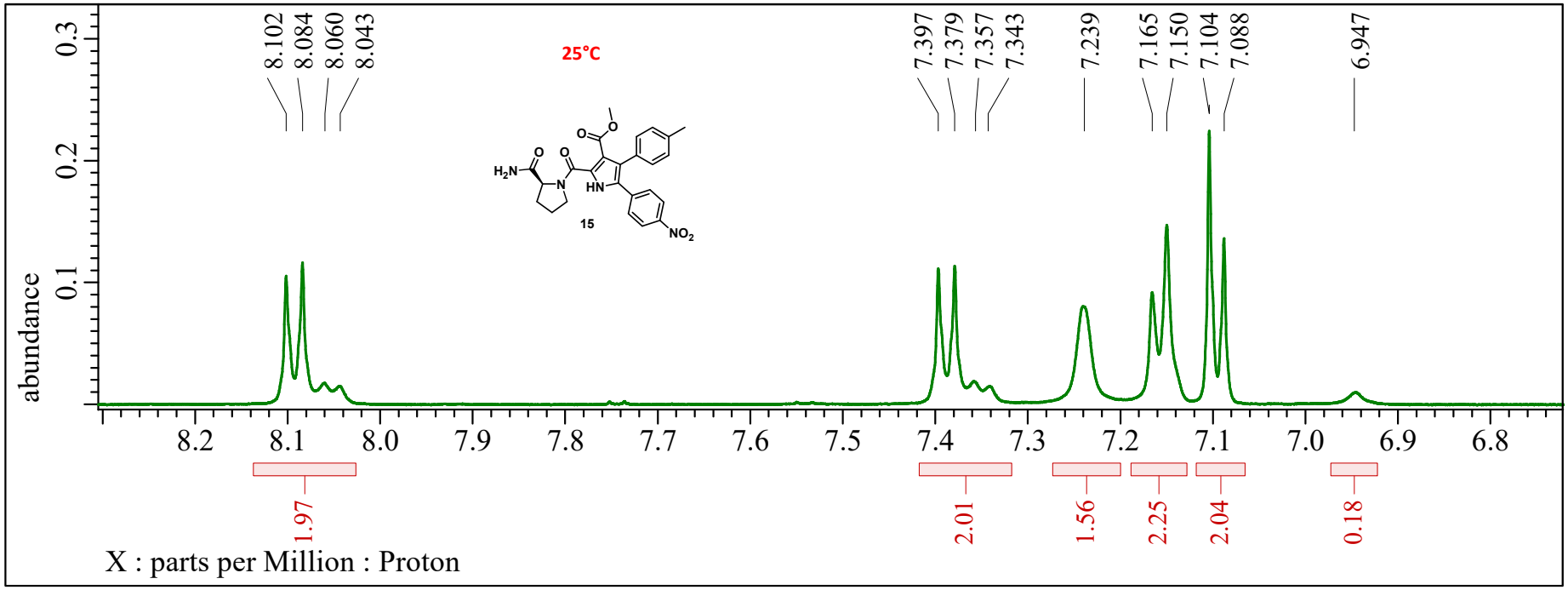
Methyl 2-(2-carbamoylpyrrolidine-1-carbonyl)-5-(4-nitrophenyl)-4-(*p*-tolyl)-1*H*-pyrrole-3-carboxylate (15)

The presence of rotamers was confirmed by temperature-dependent proton measurements at 25°C, 35°C, 45°C, 55°C, 85°C and 115°C. We present only proton spectra at standard 25°C and the highest temperature 115°C.

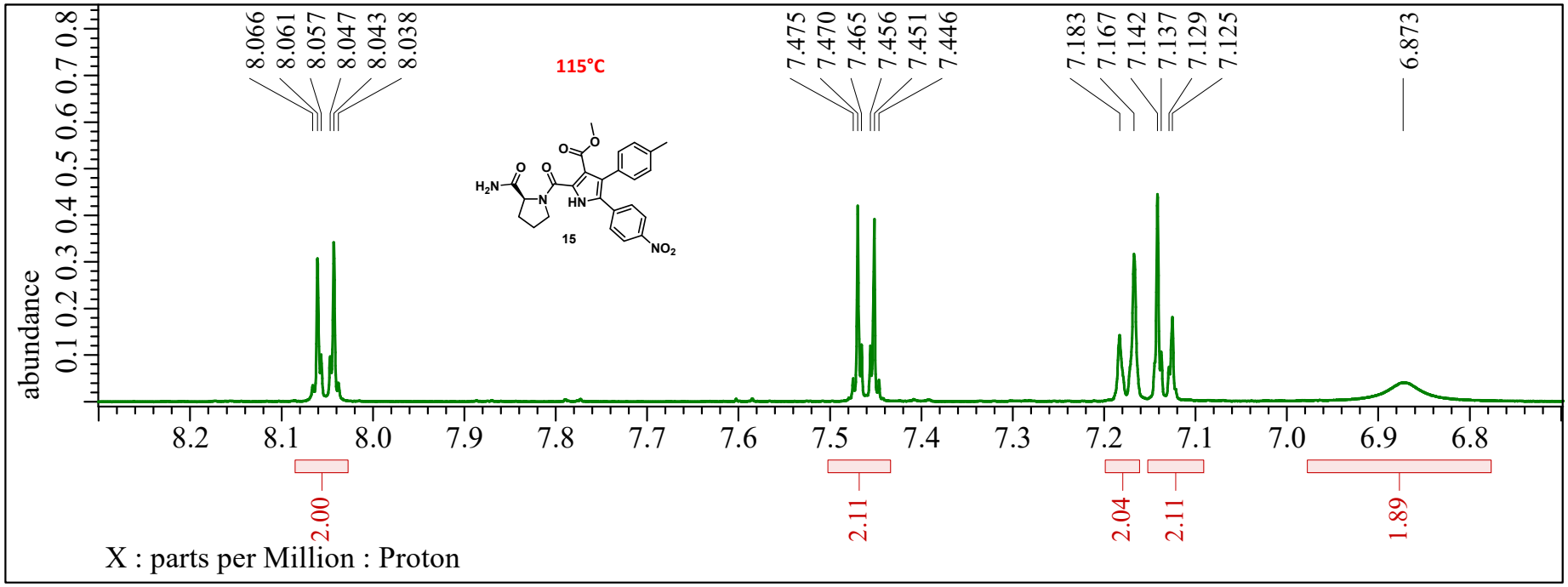


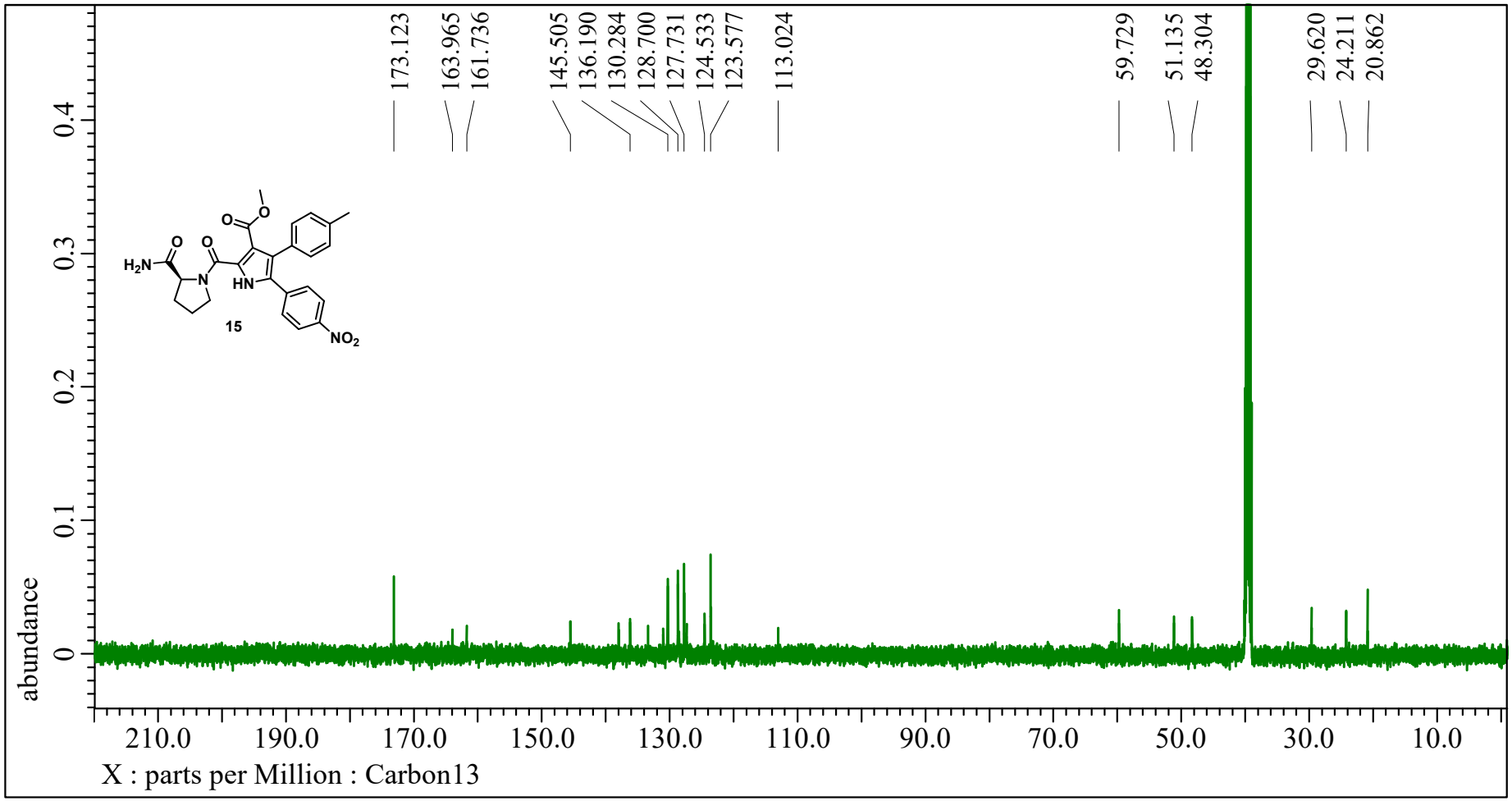

115°C
11.852
8.066
8.061
8.057
8.047
8.043
8.038
7.470
7.142
6.873
4.496
4.487
4.479
4.471
3.559
3.530
3.517
2.380
2.196
2.187
2.171
2.087
2.078
1.958
1.943
1.906
15
abundance
2.0
1.0
0
14.0
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
0.55
2.00
2.11
2.04
2.11
1.89
1.00
3.23
1.92
3.14
1.08
1.08
2.18
X : parts per Million : Proton

[1]H Proton spectra of compound **15** at 25°C - Selected area

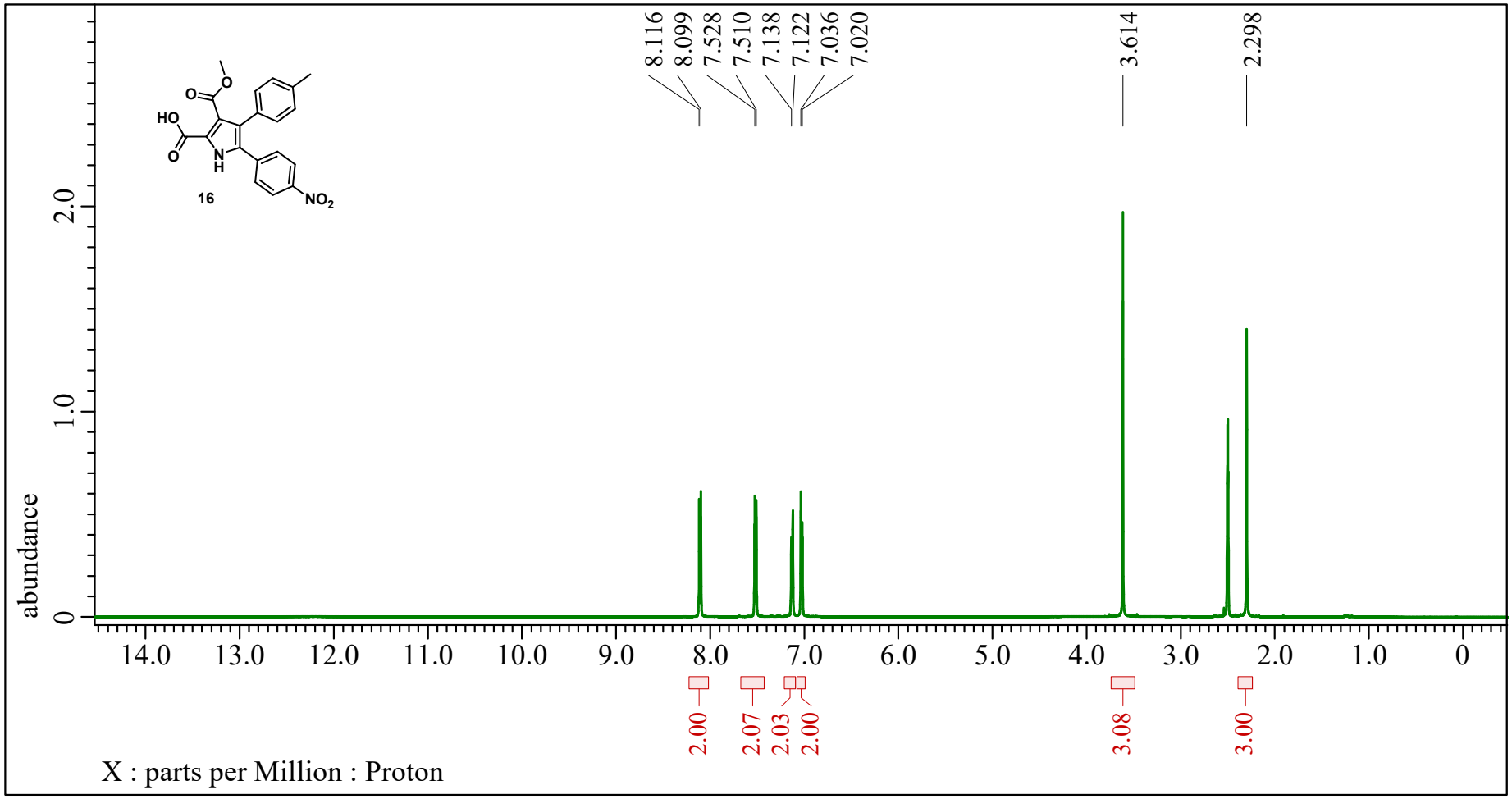


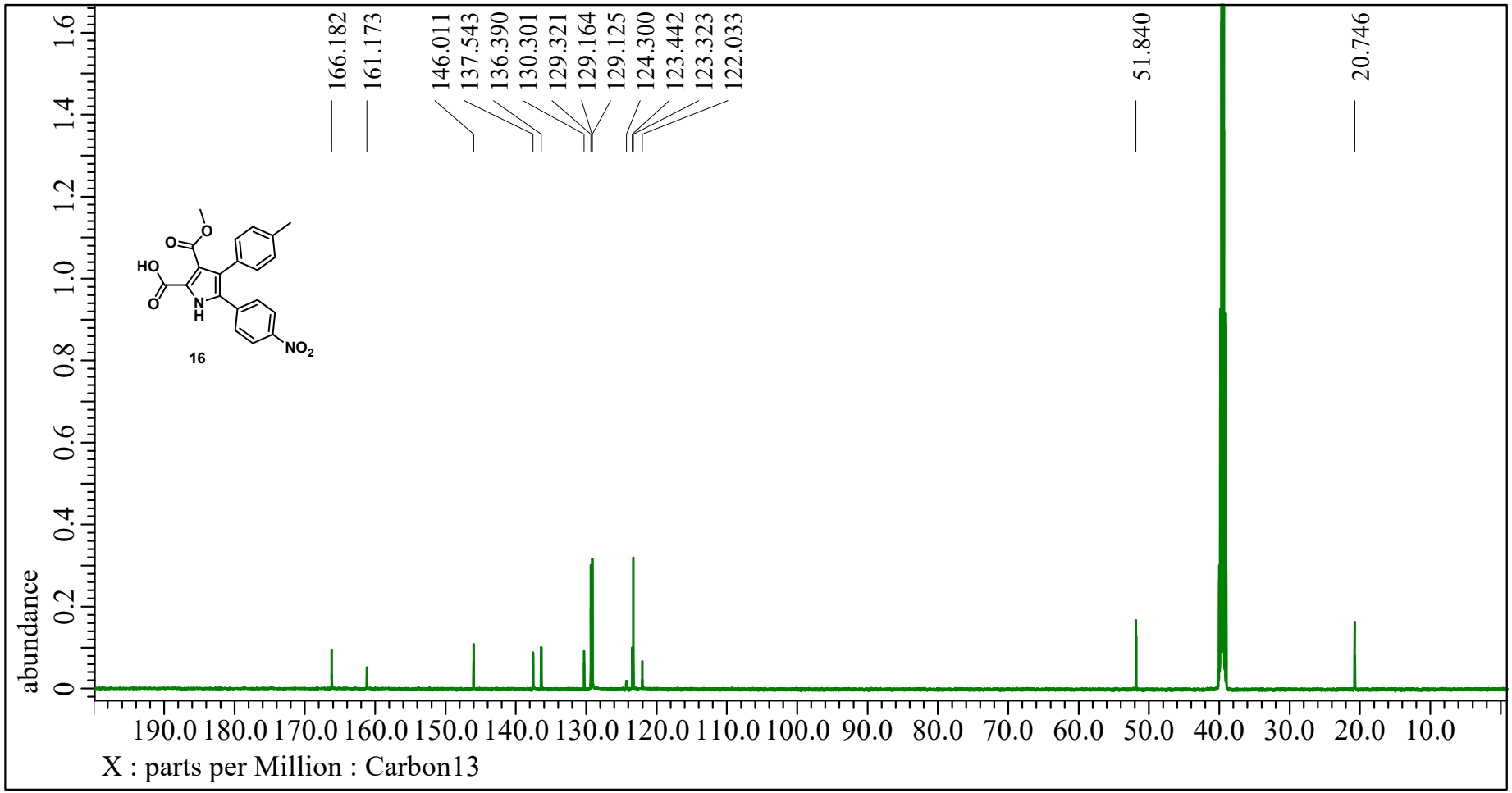
[1]H Proton spectra of compound **15** at 115°C - Selected area



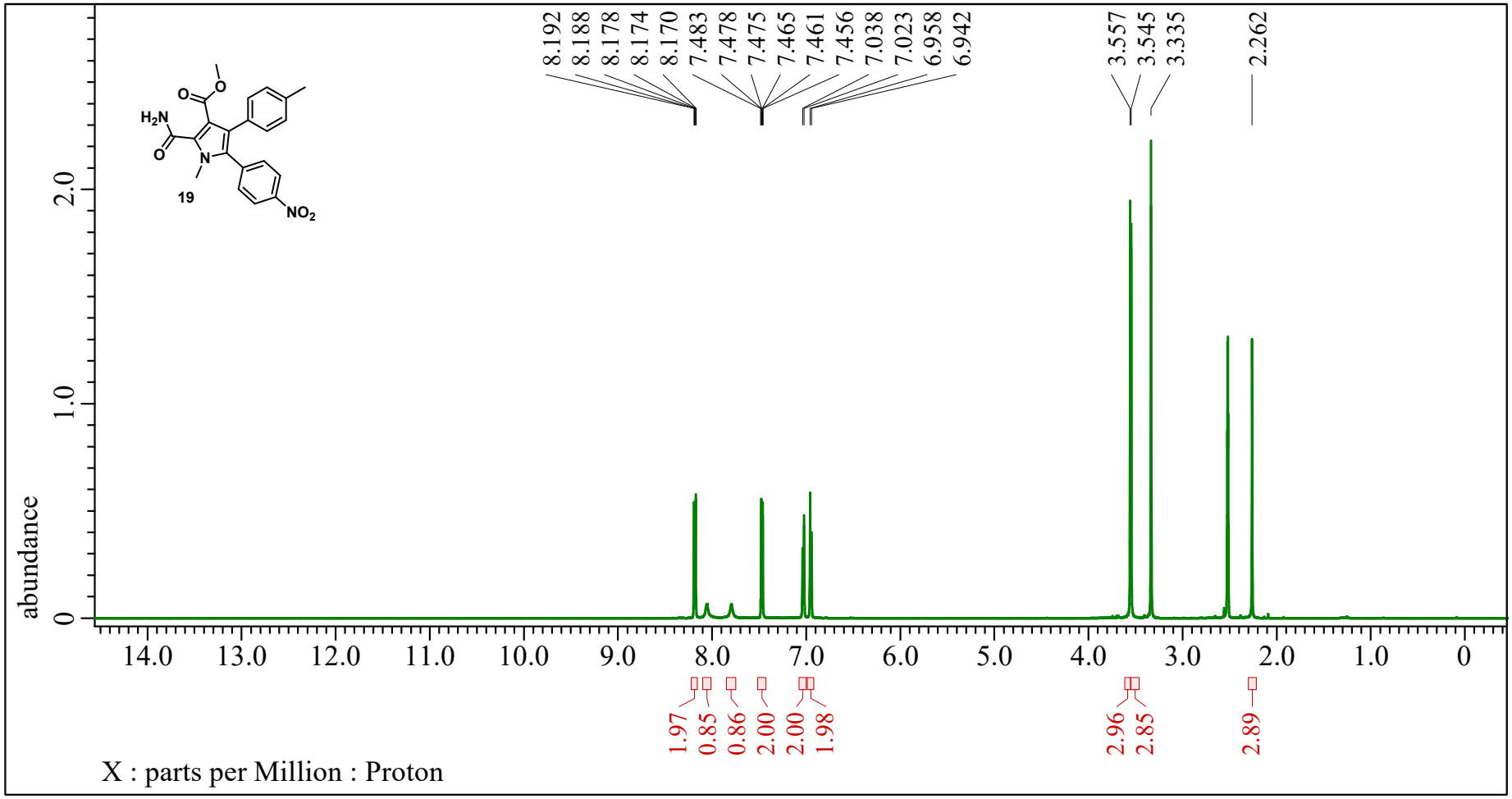

173.123
163.965
161.736
145.505
136.190
130.284
128.700
127.731
124.533
123.577
113.024
59.729
51.135
48.304
29.620
24.211
20.862
15
abundance
0
0.1
0.2
0.3
0.4
210.0
190.0
170.0
150.0
130.0
110.0
90.0
70.0
50.0
30.0
10.0
X : parts per Million : Carbon13

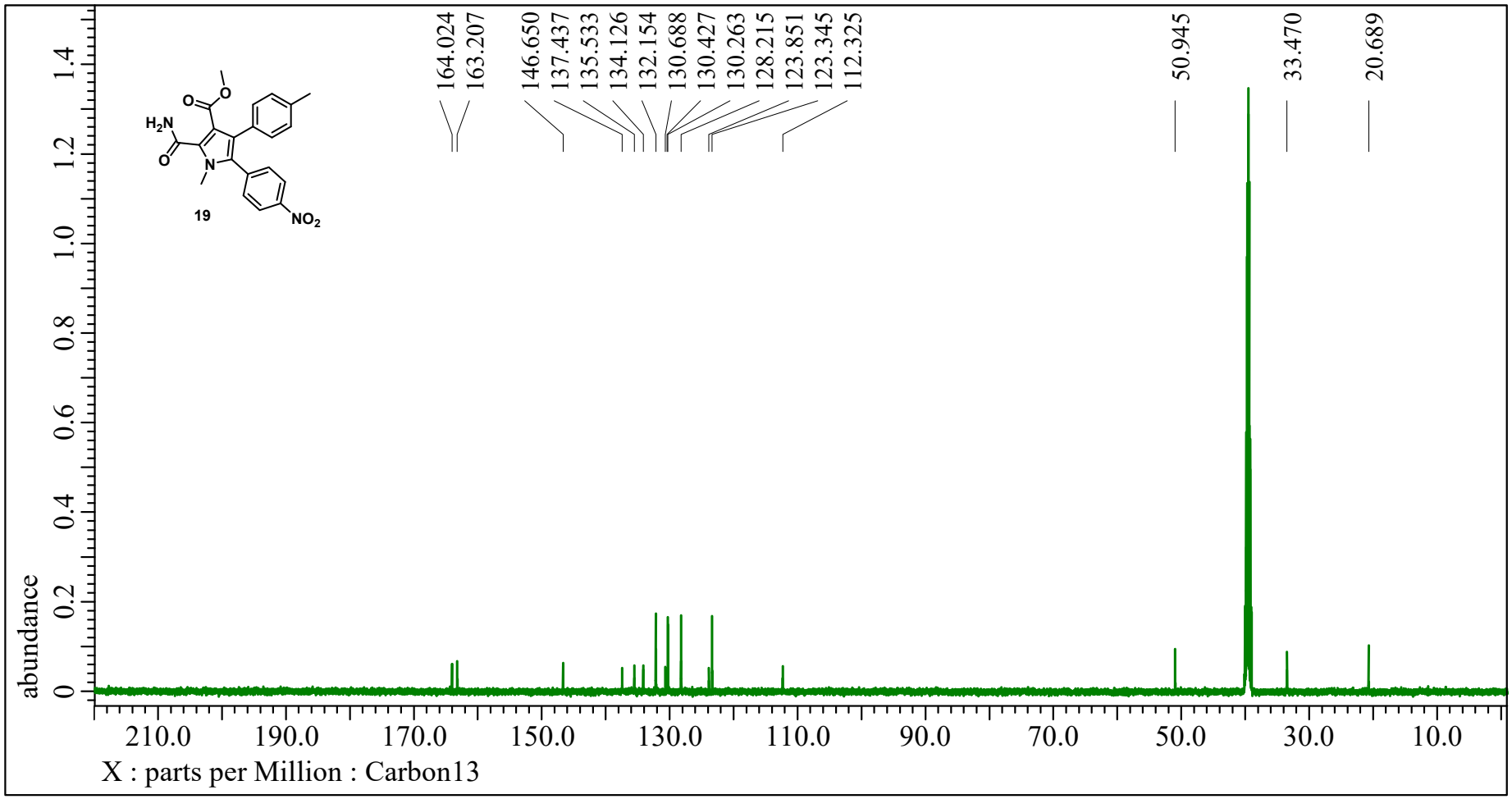
3-(methoxycarbonyl)-5-(4-nitrophenyl)-4-(p-tolyl)-1*H*-pyrrole-2-carboxylic acid (16)



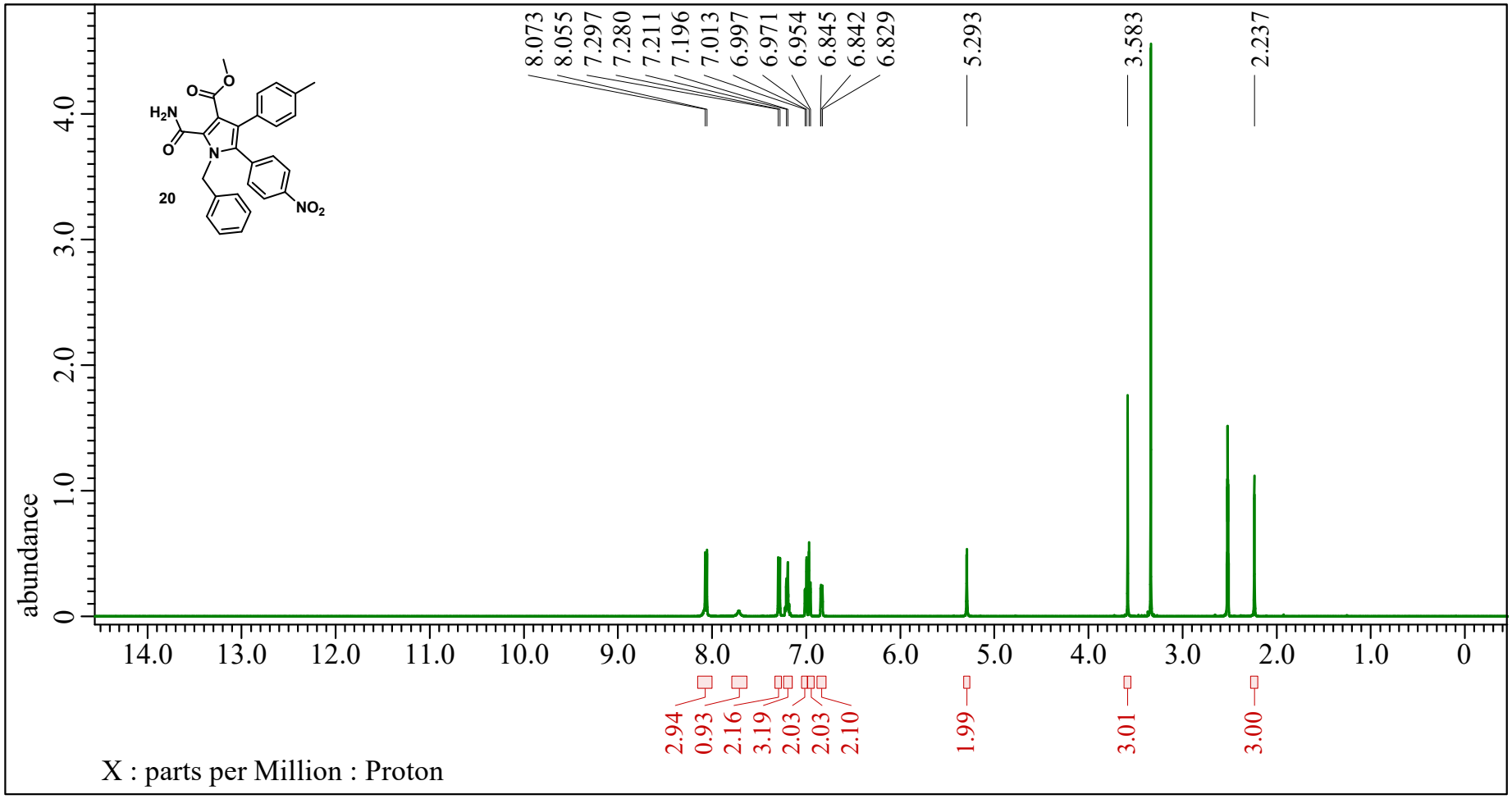

166.182
161.173
146.011
137.543
136.390
130.301
129.321
129.164
129.125
124.300
123.442
123.323
122.033
51.840
20.746
HO
O
O
O
N
H
NO2
16
abundance
0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
1.6
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0
X : parts per Million : Carbon13

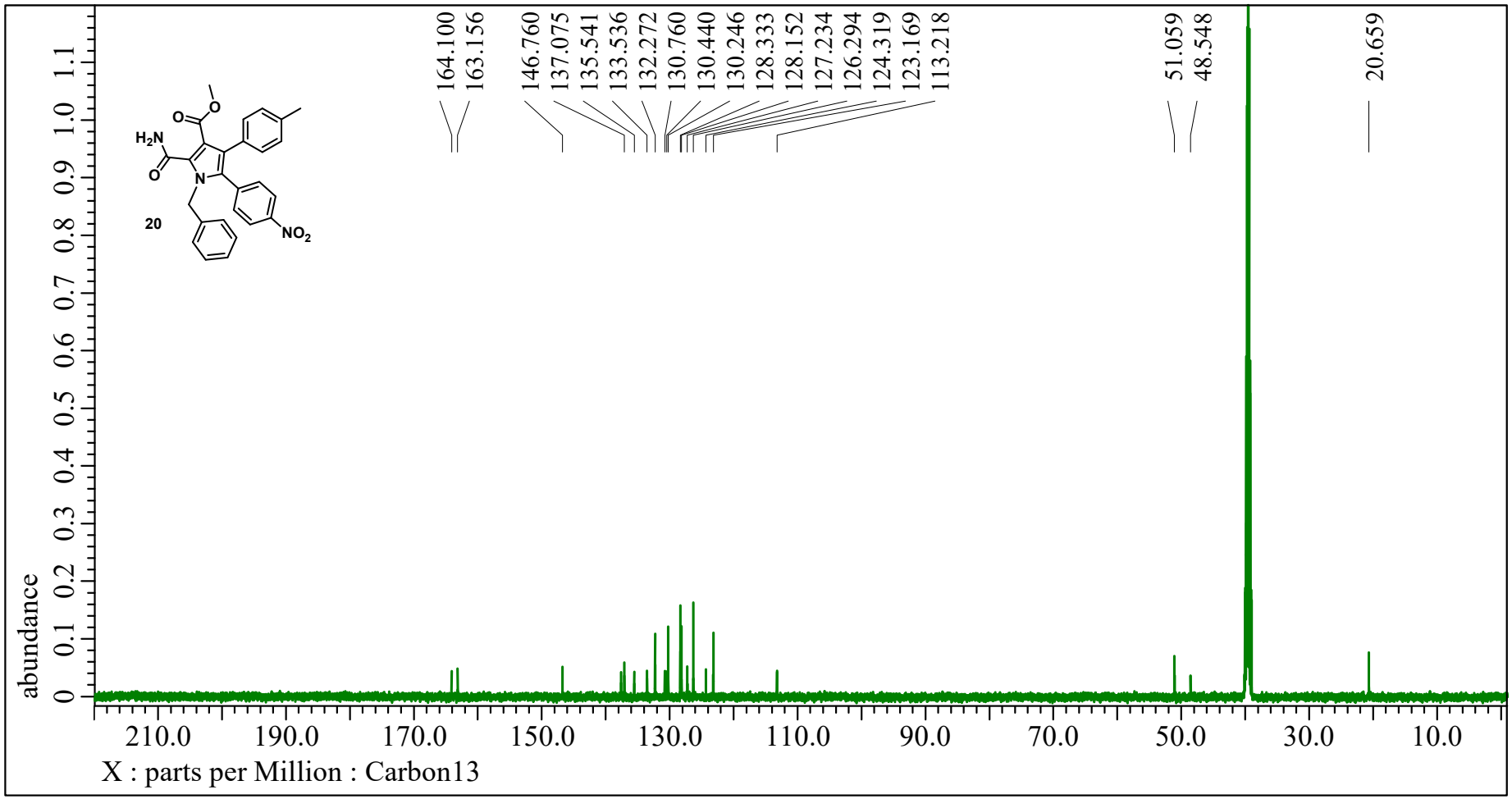
Methyl 2-carbamoyl-1-methyl-5-(4-nitrophenyl)-4-(*p*-tolyl)-1*H*-pyrrole-3-carboxylate (19)



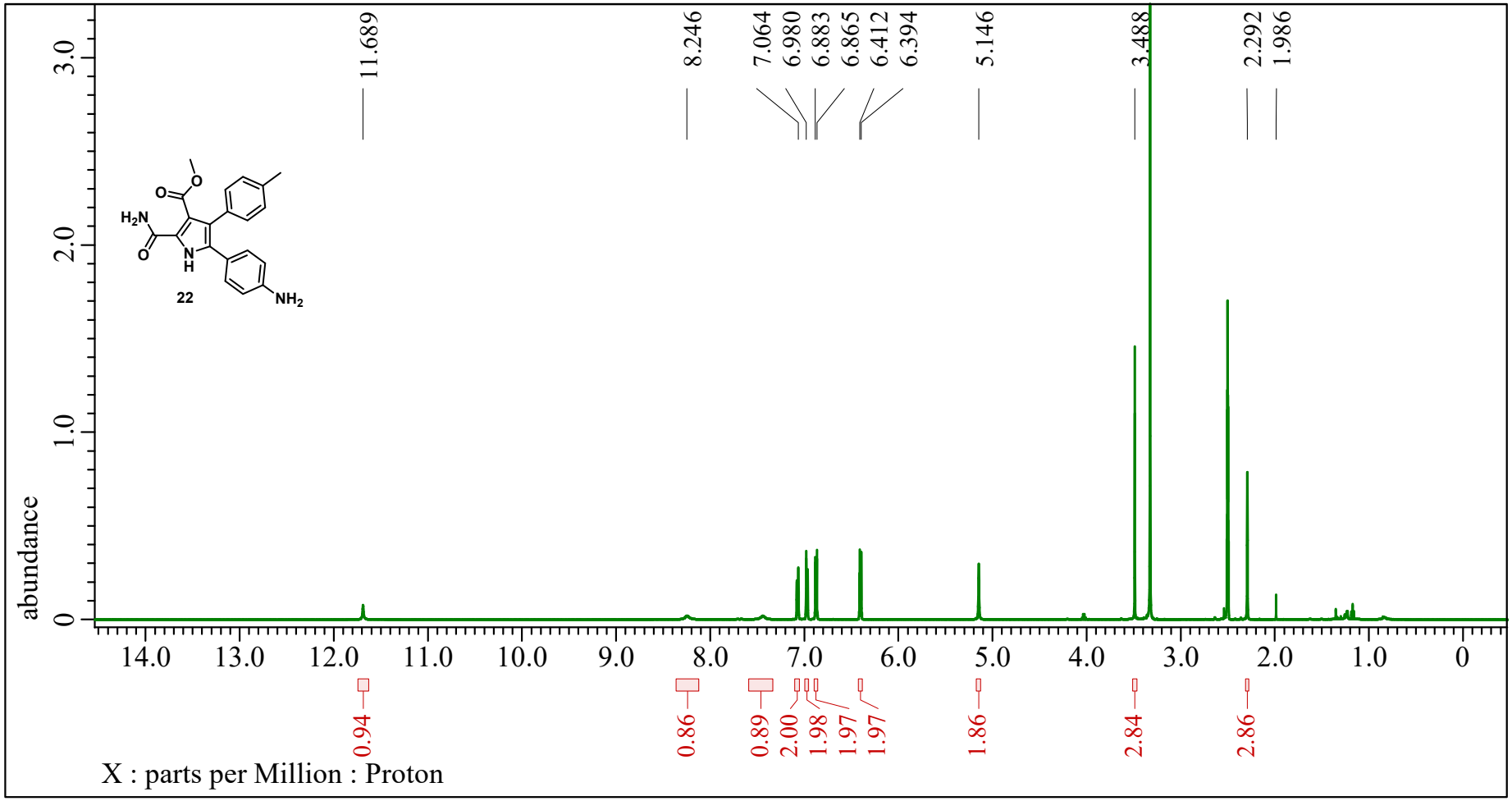

164.024
163.207
146.650
137.437
135.533
134.126
132.154
130.688
130.427
130.263
128.215
123.851
123.345
112.325
50.945
33.470
20.689
19
abundance
0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
210.0
190.0
170.0
150.0
130.0
110.0
90.0
70.0
50.0
30.0
10.0
X : parts per Million : Carbon13

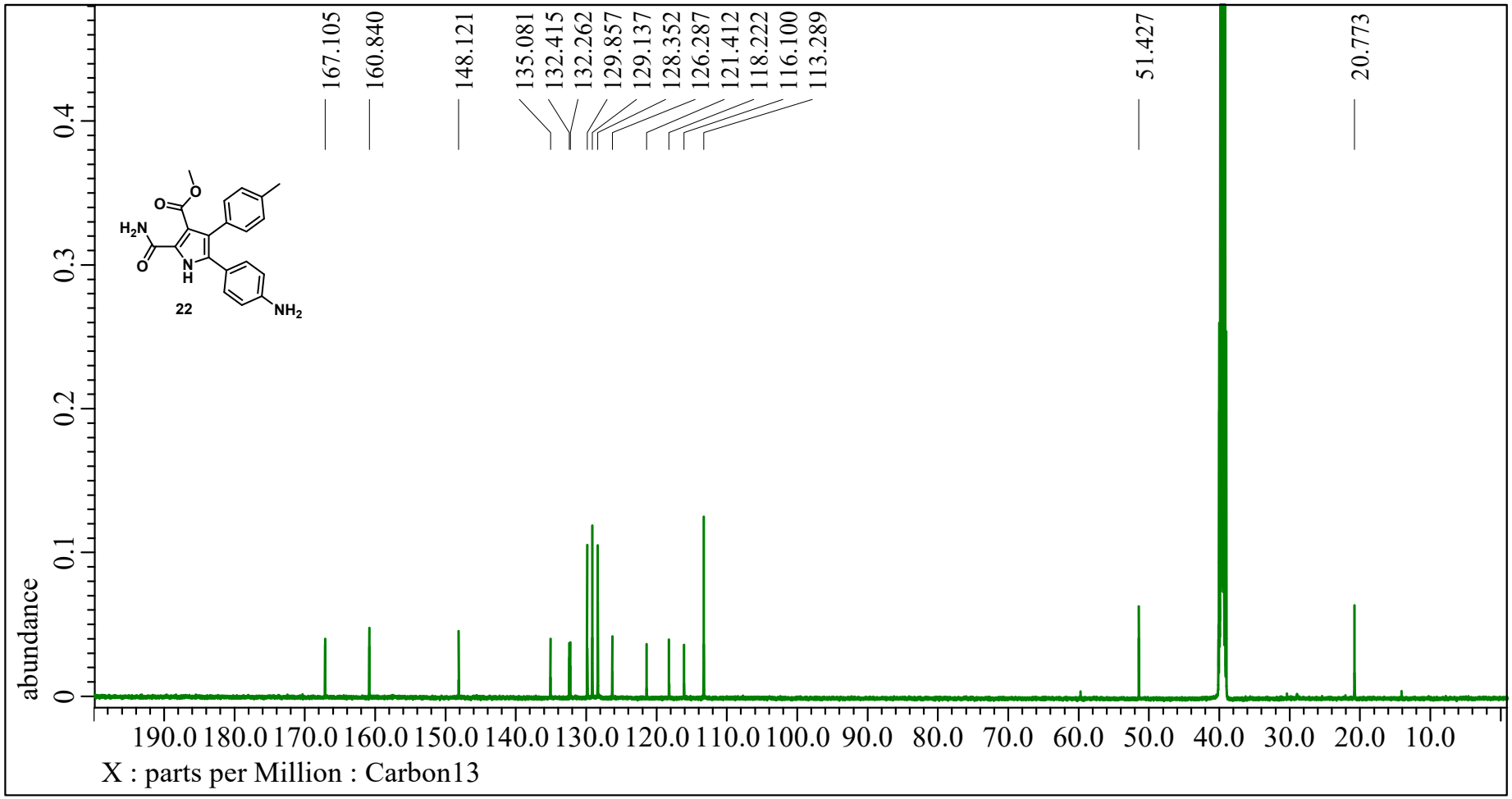
Methyl 1-benzyl-2-carbamoyl-5-(4-nitrophenyl)-4-(*p*-tolyl)-1*H*-pyrrole-3-carboxylate (20)



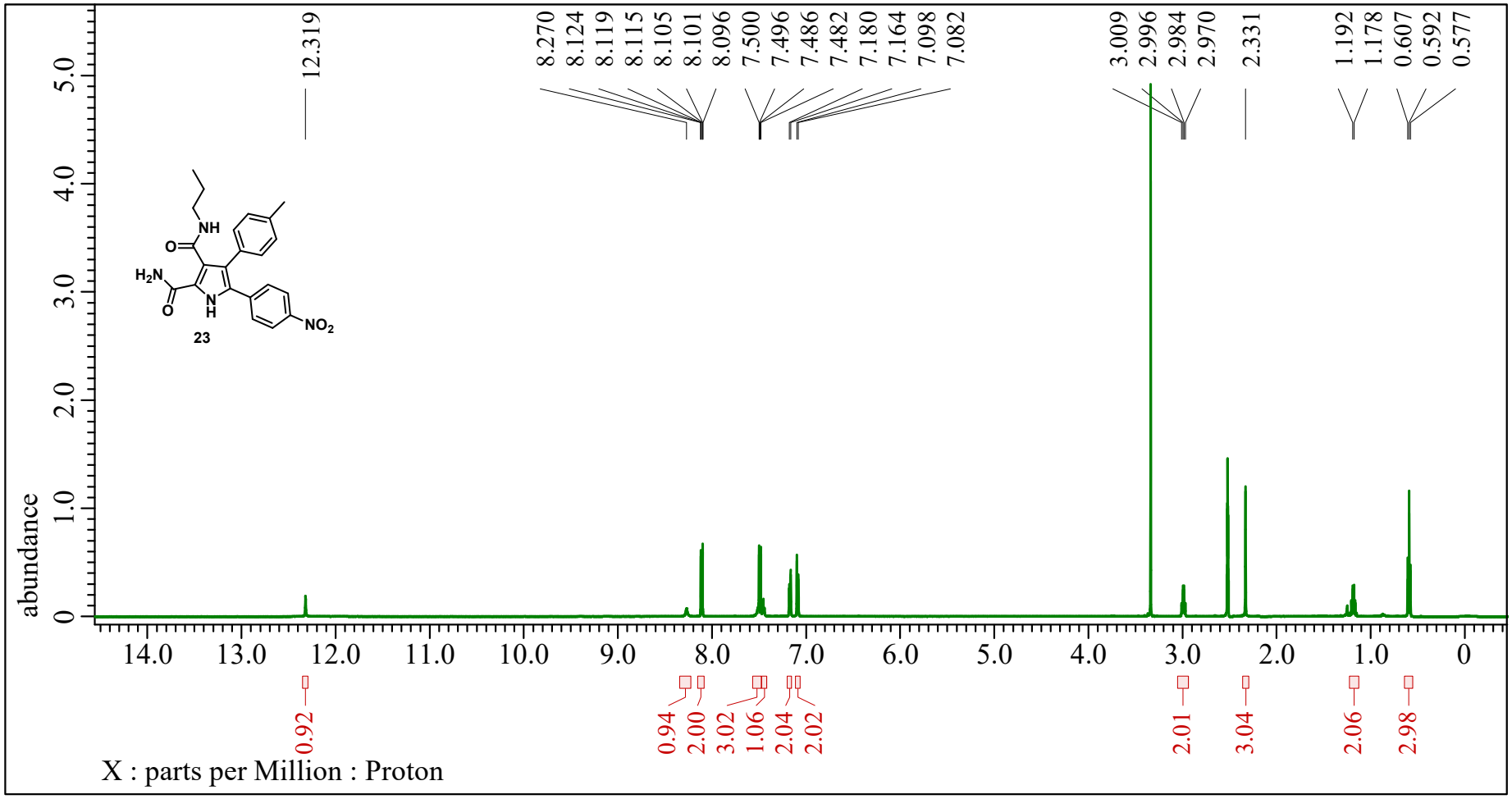

164.100
163.156
146.760
137.075
135.541
133.536
132.272
130.760
130.440
130.246
128.333
128.152
127.234
126.294
124.319
123.169
113.218
51.059
48.548
20.659
20
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
1.1
210.0
190.0
170.0
150.0
130.0
110.0
90.0
70.0
50.0
30.0
10.0
X : parts per Million : Carbon13

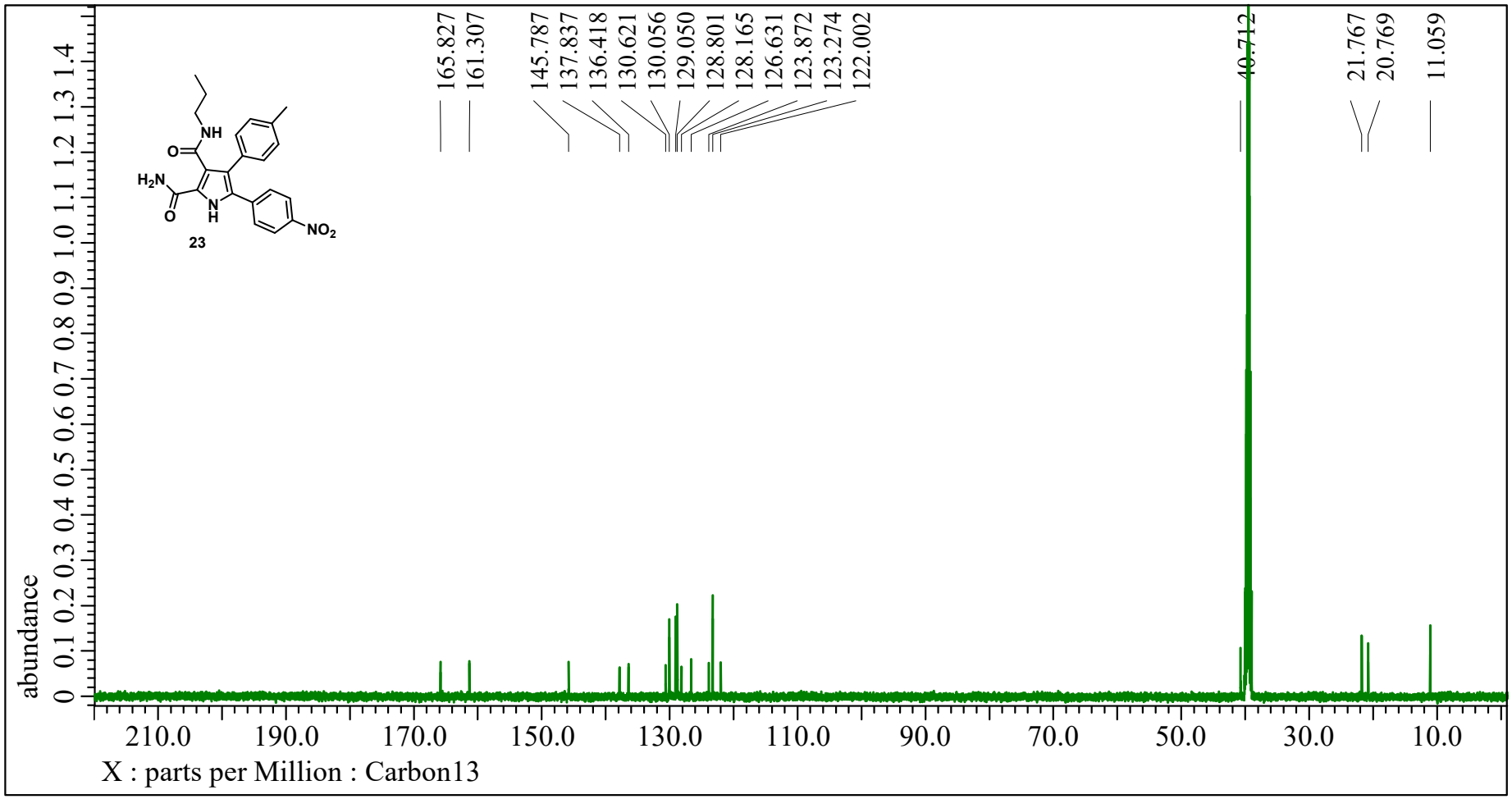
Methyl 5-(4-aminophenyl)-2-carbamoyl-4-(*p*-tolyl)-1*H*-pyrrole-3-carboxylate (22)



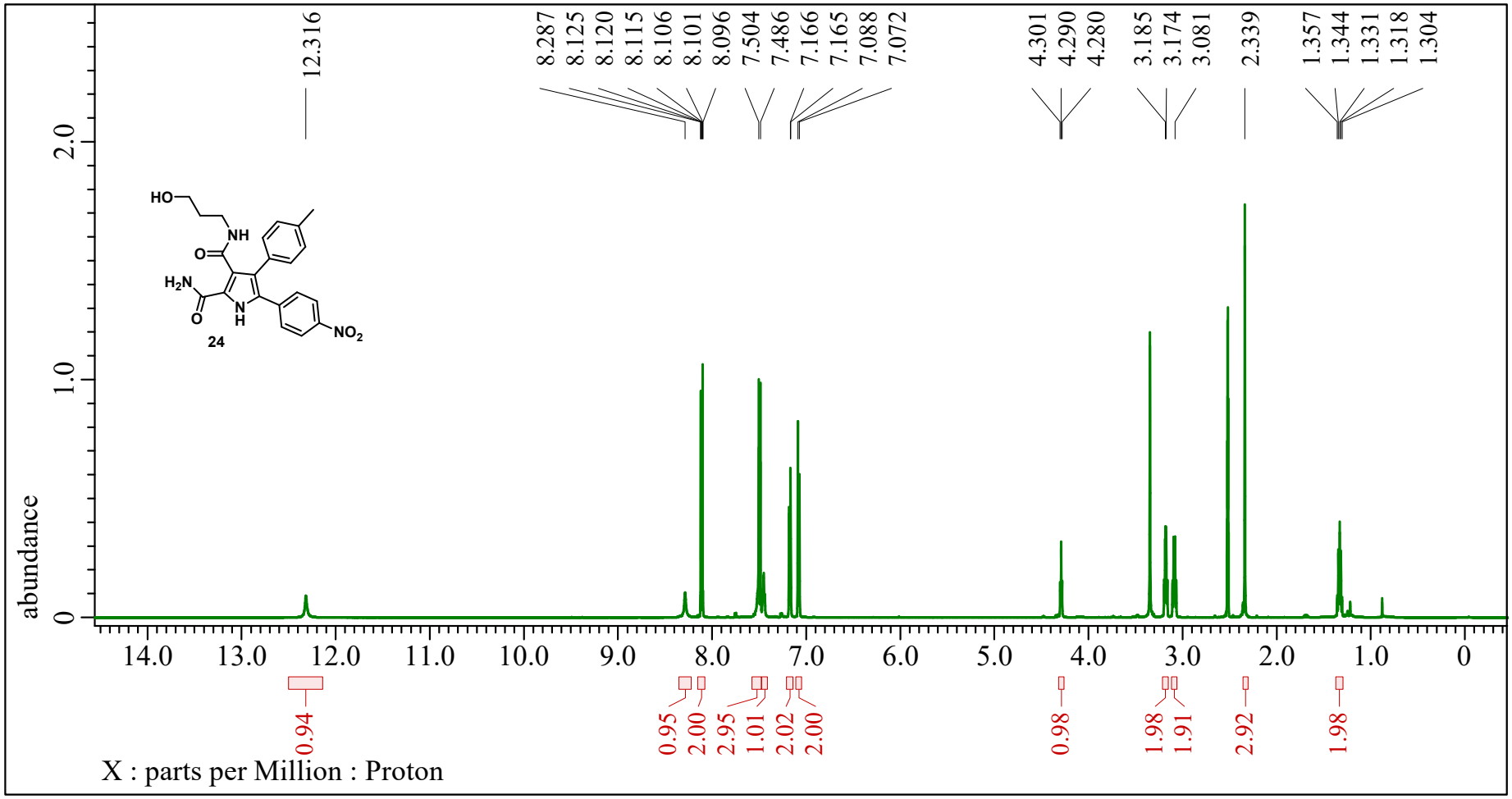

167.105
160.840
148.121
135.081
132.415
132.262
129.857
129.137
128.352
126.287
121.412
118.222
116.100
113.289
51.427
20.773
22
abundance
0
0.1
0.2
0.3
0.4
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0
X : parts per Million : Carbon13

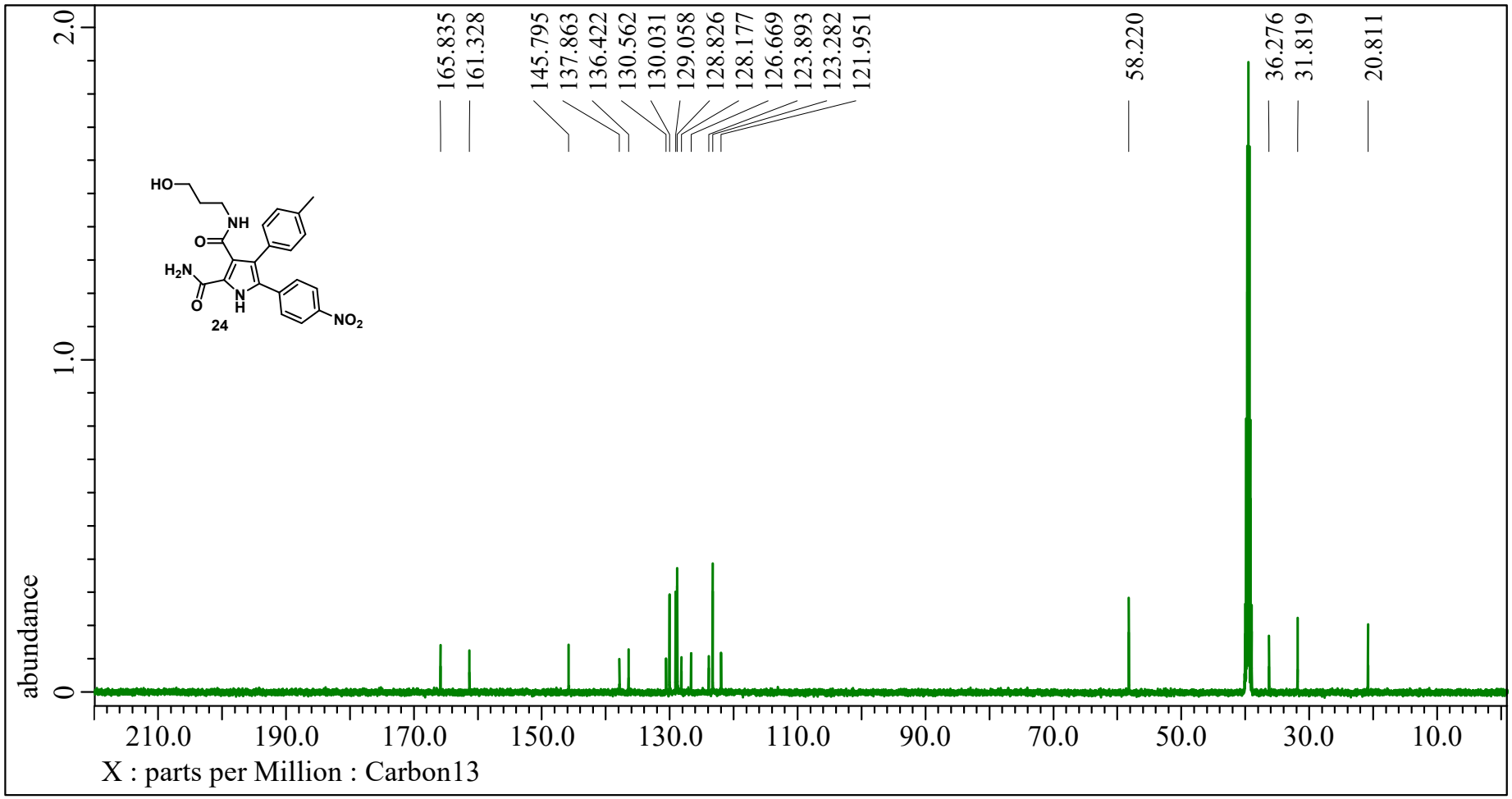
5-(4-nitrophenyl)-*N*^{3}-propyl-4-(*p*-tolyl)-1*H*-pyrrole-2,3-dicarboxamide (23)



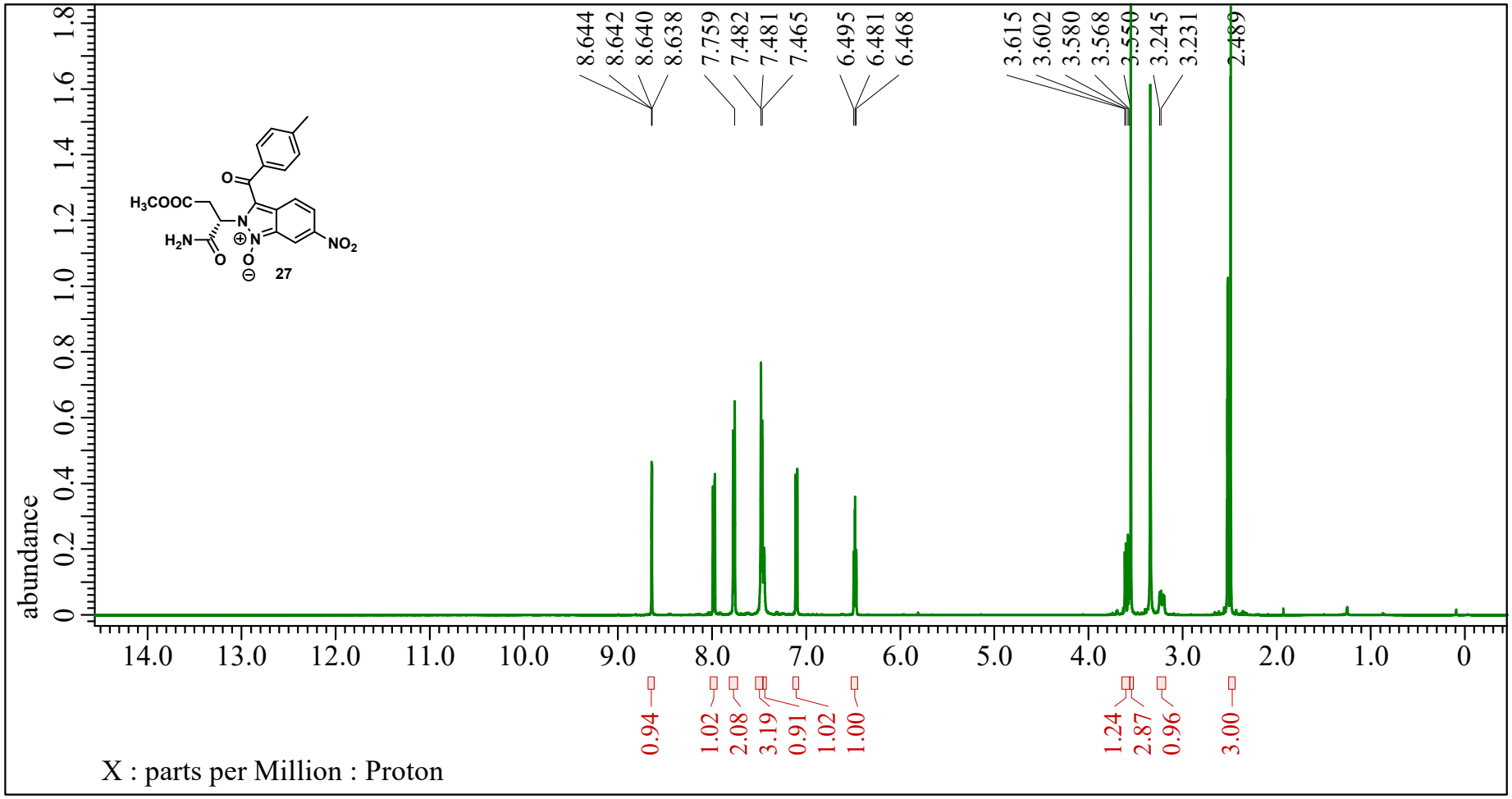

165.827
161.307
145.787
137.837
136.418
130.621
130.056
129.050
128.801
128.165
126.631
123.872
123.274
122.002
40.712
21.767
20.769
11.059
NH
O
H2N
O
N
H
NO2
23
abundance
0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0 1.1 1.2 1.3 1.4
210.0
190.0
170.0
150.0
130.0
110.0
90.0
70.0
50.0
30.0
10.0
X : parts per Million : Carbon13

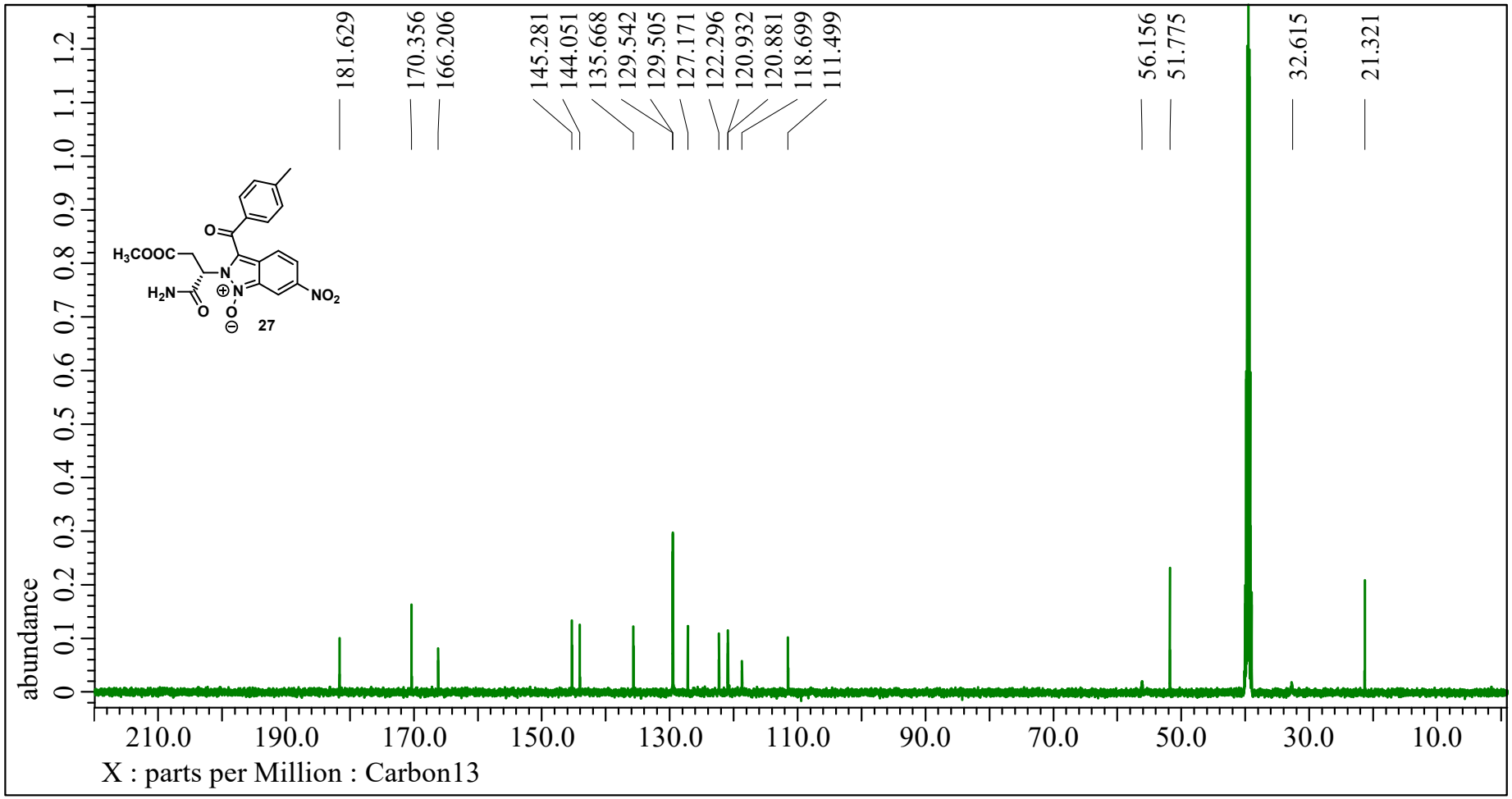
***N*³-(3-hydroxypropyl)-5-(4-nitrophenyl)-4-(*p*-tolyl)-1*H*-pyrrole-2,3-dicarboxamide (24)**




165.835
161.328
145.795
137.863
136.422
130.562
130.031
129.058
128.826
128.177
126.669
123.893
123.282
121.951
58.220
36.276
31.819
20.811
HO
NH
O
H2N
O
N
H
NO2
24
2.0
1.0
0
abundance
210.0
190.0
170.0
150.0
130.0
110.0
90.0
70.0
50.0
30.0
10.0
X : parts per Million : Carbon13

***S*)-2-(1-amino-4-methoxy-1,4-dioxobutan-2-yl)-3-(4-methylbenzoyl)-6-nitro-2*H*-indazole 1-oxide (27)**




181.629
170.356
166.206
145.281
144.051
135.668
129.542
129.505
127.171
122.296
120.932
120.881
118.699
111.499
56.156
51.775
32.615
21.321
27
abundance
0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0 1.1 1.2
210.0 190.0 170.0 150.0 130.0 110.0 90.0 70.0 50.0 30.0 10.0
X : parts per Million : Carbon13