Supplementary Materials

ORTHOGONALLY POSITIONED DIAMINO PYRROLE- AND IMIDAZOLE- CONTAINING POLYAMIDES: SYNTHESIS OF 1-(3-SUBSTITUTED-PROPYL)-4- NITROPYRROLE-2-CARBOXYLIC ACID AND 1-(3-CHLOROPROPYL)-4- NITROIMIDAZOLE-2-CARBOXYLIC ACID

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The general experimental information along with the syntheses and characterization of esters **14b**, **14c**, and **18**, as well as acids **11b**, **11c**, and **12** are given in this section.

General

Solvents and organic reagents were used without further purification. Melting points (mp) were uncorrected. The major bands of the Infrared spectra are reported in wave numbers (cm⁻¹). ¹H NMR spectra were obtained at 20 °C using a 400 MHz instrument. Chemical shifts (δ) are reported in parts per million (ppm) downfield from tetramethylsilane. High-resolution (HRMS) and low-resolution mass spectra (MS) were recorded using EI, CI or electrospray ionization methods. The mass analyzer used in the EI and CI experiments was a magnetic sector mass

selector, and for the ESI studies a micromass QTOF analyzer was used. Reaction progress was assessed by thin layer chromatography (TLC) using Merck silica gel (60 F₂₅₄). Visualization was achieved with UV light at 254 nm and/or 366 nm, I₂ vapor staining or ninhydrin spray.

Ethyl 4-nitro-1-(3-cyanopropyl)pyrrole-2-carboxylate **14b**

A suspension of ester **13** (1.00 g, 5.47 mmol), anhydrous K₂CO₃ (2.51 g, 18.2 mmol), KI (1.03 g, 6.20 mmol), and 4-bromobutyronitrile (0.54 mL, 43 mmol) in dry acetone (100 mL) was heated to reflux for 30 min. An additional quantity of 4-bromobutyronitrile (0.54 mL, 43 mmol) was added and the reaction mixture was heated to reflux overnight. Concentration of reaction mixture under reduced pressure gave a residue, which was partitioned between water (30 mL) and CHCl₃ (30 mL). The organic layer was collected and the aqueous solution was extracted with CHCl₃ (30 mL x 2). The combined organic layers were dried over anhydrous Na₂SO₄. Silica gel column purification of the crude material gave the desired ester **14b** as a white solid (1.35 g, 99%). Mp 77–78°. *R*_f 0.25 (2% MeOH/CHCl₃). IR (Nujol): 3134, 2981, 2248, 1713, 1540, 1506, 1423, 1364, 1316, 1251, 1191, 1109, 1017. ¹H NMR (CDCl₃): 7.67 (d, *J* = 2.0, 1H); 7.47 (d, *J* = 2.0, 1H); 4.51 (t, *J* = 8.0, 2H); 4.32 (quart, *J* = 7.2, 2H); 2.40 (t, *J* = 8.0, 2H); 2.22 (quint, *J* = 6.8, 2H); 1.38 (t, *J* = 7.2, 3H). ¹³C NMR (CDCl₃): 159.99; 135.87; 126.71; 122.48; 118.14; 113.46; 61.25; 48.70; 26.78; 14.49; 14.23. MS (EI): 251 (M⁺, 100%). HR-MS (EI): 251.0901 (M⁺, C₁₁H₁₃N₃O₄⁺; calc. 251.0906).

4-Nitro-1-(3-cyanopropyl)pyrrole-2-carboxylic acid **11b**

Ester **14b** (1.30 g, 5.17 mmol) was dissolved in MeOH (26 mL) and water (7.8 mL). Aq. NaOH (4.0 M, 6.5 mL) was added and the solution was heated to reflux for 30 min, at which

time TLC analysis indicated no ester was left. The MeOH was removed under reduced pressure and the remaining aqueous solution was diluted with water to a volume of 10 mL, and it was chilled in an ice-water bath. The pH was adjusted to 1 using 6.0 M HCl. The precipitated solid was filtered, washed with water, and dried. The filtrate was also extracted with EtOAc, dried, and concentrated to afford additional product. The total amount of acid **11b** was obtained as a pale pinkish solid (904 mg, 78%). Mp 177–178°. R_f 0.19 (20% MeOH/CHCl₃). IR (Nujol): 3500-2550 br, 3122, 2957, 2923, 2872, 2854, 2248, 1682, 1543, 1504, 1467, 1377, 1313, 1261, 1108; ¹H NMR (DMSO-d₆): 13.24 (s, 1H); 8.28 (d, J = 2.0, 1H); 7.30 (d, J = 2.0, 1H); 4.43 (t, J = 7.2, 2H); 2.52 (t, J = 7.2, 2H); 2.08 (quint, J = 7.2, 2H). ¹³C NMR (DMSO-d₆): 160.80; 134.43; 128.74; 123.11; 119.71; 112.07; 48.21; 26.13; 13.56. MS (EI): 223 (M⁺, 100%). HR-MS (EI): 223.0591 (M⁺, C₉H₉N₃O₄⁺; calc. 223.0593).

Ethyl 4-nitro-1-(4-pentynyl)pyrrole-2-carboxylate 14c

A suspension of ester **13** (1.42 g, 7.73 mmol) and anhydrous K₂CO₃ (3.2 g, 23.2 mmol) in dry acetone (30 mL) was heated to reflux for 30 min. To the reaction mixture was added dropwise a solution of 5-iodo-1-pentyne (1.50 g, 7.73 mmol) in dry acetone (10 mL). After refluxing the reaction mixture overnight the solvent was removed under reduced pressure. Water (30 mL) was added to the residue and the mixture was extracted with CHCl₃ (25 mL x 3). After drying the organic extracts over anhydrous Na₂SO₄, the solvent was removed and the residue was purified by silica gel column chromatography using CHCl₃ as eluent. The product **14c** was obtained as a colorless oil (1.78 g, 92%). R_f 0.65 (50% ethyl acetate/hexane). IR (Nujol): 3290, 3136, 2963, 2926, 2857, 2120, 1713, 1539, 1508, 1425, 1369, 1316, 1249, 1191, 1104, 1019. ¹H NMR (CDCl₃): 7.71 (d, J = 2.0, 1H); 7.44 (d, J = 2.0, 1H); 4.51 (t, J = 6.8, 2H); 4.32 (quart, J =

7.2, 2H); 2.22 (dt, $J = 4.0, 6.8$, 2H); 2.07 (t, $J = 4.0$, 1H); 2.04 (quint, $J = 6.8$, 2H); 1.38 (t, $J = 7.2$, 3H). ^{13}C NMR (CDCl_3): 159.94; 135.43; 127.18; 122.43; 113.27; 82.12; 70.28; 61.00; 48.95; 29.17; 15.40; 14.25. MS (CI, CH_4): 251 ($\text{M}+\text{H}^+$, 85%). HR-MS (CI, CH_4): 251.1026 ($\text{M}+\text{H}^+$, $\text{C}_{12}\text{H}_{14}\text{N}_2\text{O}_4^+$; calc. 251.1032).

4-Nitro-1-(4-pentynyl)pyrrole-2-carboxylic acid 11c

A solution of ethyl 4-nitro-1-(4-pentynyl)pyrrole-2-carboxylate **14c** (1.78 g, 7.11 mmol) and NaOH (0.30 g, 7.50 mmol) in EtOH (20 mL) and water (20 mL) was heated to reflux for 30 min, at which time TLC analysis indicated no ester was left. The EtOH was removed under reduced pressure and the remaining aqueous solution was chilled in an ice-water bath and the pH was adjusted to about 2 using 6.0 M HCl. The precipitated solid was filtered, washed with water, and dried. The filtrate was also extracted with EtOAc, dried, and concentrated to afford additional product. The total amount of acid **11c** isolated as a white solid was 1.10 g (70%). Mp 128–130°. R_f 0.20 (50% Ethyl acetate/Hexane). IR (Nujol): 3500-2550 br, 3299, 3119, 2921, 2854, 2109, 1678, 1543, 1501, 1412, 1368, 1310, 1257, 1193, 1163, 1099. ^1H NMR (CDCl_3): 7.77 (d, $J = 2.0$, 1H); 7.60 (d, $J = 2.0$, 1H); 4.52 (t, $J = 7.2$, 2H); 2.23 (t, $J = 7.2$, 2H); 2.09 (t, $J = 4.0$, 1H); 2.05 (quint, $J = 7.2$, 2H). ^{13}C NMR (CDCl_3): 164.60; 135.75; 128.36; 121.05; 115.45; 81.90; 70.47; 49.17; 29.13; 15.38. MS (CI, CH_4): 223 ($\text{M}+\text{H}^+$, 25%). HR-MS (CI, CH_4): 223.0719 ($\text{M}+\text{H}^+$, $\text{C}_{10}\text{H}_{11}\text{N}_2\text{O}_4^+$; calc. 223.0719).

Ethyl 1-(3-chloropropyl)-4-nitroimidazole-2-carboxylate 18

To a solution of ethyl 4-nitro-1*H*-imidazole-2-carboxylate **17** [20] (1.17 g, 6.32 mmol) in dry DMF (7 mL) was added anhydrous K_2CO_3 (1.7 g, 12.6 mmol) followed by 1-bromo-3-

chloropropane (0.75 mL, 7.58 mmol). The reaction mixture was heated at 60-65°C for 2.5 h. DMF was distilled off on a Kugelröhr apparatus. The residue obtained was purified by column chromatography using silica gel and gradient CH₃OH/CHCl₃ as the eluent to yield ester **18** as a yellow solid (1.22 g, 74%). Mp 80–82° (dec). *R*_f 0.69 (10% MeOH/CHCl₃). IR (Nujol): 3052, 2985, 1724, 1546, 1420, 1357, 1320, 1112, 896, 745. ¹H NMR (CDCl₃): 7.93 (s, 1H); 4.68 (t, *J* = 6.5, 2H); 4.46 (t, *J* = 7.2, 2H); 3.56 (t, *J* = 6.5, 2H); 2.36 (quint, *J* = 6.5, 2H); 1.44 (t, *J* = 7.2, 3H). ¹³C NMR (CDCl₃): 158.14; 146.35; 134.59; 123.80; 62.75; 47.10; 40.87; 32.74; 14.18. MS (EI): 261 (³⁵M⁺, 20%), 263 (³⁷M⁺, 7%). HR-MS (EI): 261.0516 (³⁵M⁺, C₉H₁₂³⁵ClN₃O₄⁺: calc. 261.0516). Compound **18** was recrystallized from ethanol. All diffraction data were collected at 100 K using monochromatic Mo Kα radiation with the omega scan technique. Data were collected, their unit cells determined, and the data integrated and corrected for absorption and other systematic errors using the Apex2 suite of programs. The structures were solved by direct methods and refined by full matrix least squares against *F*² with all reflections using SHELXTL. Structure refinement revealed minor disorder of **18** with its 3-bromopropyl derivative due to nucleophilic reaction at the chloro rather bromo atom of 1-bromo-3-chloropropane. In the crystal analyzed the chloro to bromo rates refined to 90.17(15)% and 9.83(15)%, respectively. This is consistent with a small amount of bromo isomer of **18** present in the NMR spectrum. X-ray structural information for **18** are given in cif format, CCDC 922340. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

1-(3-Chloropropyl)-4-nitroimidazole-2-carboxylic acid **12**

To a solution of ethyl 1-(3-chloropropyl)-4-nitroimidazole-2-carboxylate **18** (1.03 g, 3.94 mmol) in THF (8 mL) and water (8 mL) was added LiOH monohydrate (0.25 g, 5.90 mmol). The reaction mixture was stirred overnight at room temperature and concentrated under reduced pressure to remove the THF. The remaining solution was chilled in an ice-water bath and acidified using dilute hydrochloric acid (6.0 M HCl) to pH 1. The precipitated white solid was filtered, washed with water and dried to afford the desired acid **12** (0.81 g, 88%). Mp 86–87° (dec). R_f 0.10 (20% MeOH/CHCl₃). IR (KBr); 3509-2500 br, 3050, 2978, 2848, 1777, 1735, 1654, 1460, 1365, 1289, 1239, 1165, 1069, 1039, 993, 909, 657. ¹H NMR (DMSO-*d*₆): 8.62 (s, 1H); 4.55 (t, J = 6.5, 2H); 3.66 (t, J = 6.5, 2H); 2.27 (quint, J = 6.5, 2H). ¹³C NMR (DMSO-*d*₆): 159.09; 145.16; 135.40; 125.85; 46.86; 42.04; 32.57. MS (EI): 189 (³⁵M⁺-CO₂, 67%), 191 (³⁷M⁺-CO₂, 22%). MS (CI, CH₄): 190 (³⁵M⁺+H-CO₂, 100%), 192 (³⁷M⁺+H-CO₂, 30%). MS (ESI TOF, neg. ion): 232 (³⁵M-H⁺, 62%), 234 (³⁷M+H⁺, 22%). HR-MS (ESI TOF, neg. ion): 232.0123 (³⁵M-H⁺, C₇H₇ClN₃O₄⁻; calc. 232.0125).

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The ¹H and ¹³C-NMR spectra for esters **14a-c** and **18** as well as those for acids **11a-c** and **12** are provided.

¹ H-NMR spectra	Page	¹³ C-NMR spectra	Page
Pyrrole chloro ester 14a	2	Pyrrole chloro ester 14a	10
Pyrrole chloro acid 11a	3	Pyrrole chloro acid 11a	11
Pyrrole cyano ester 14b	4	Pyrrole cyano ester 14b	12
Pyrrole cyano acid 11b	5	Pyrrole cyano acid 11b	13
Pyrrole alkyne ester 14c	6	Pyrrole alkyne ester 14c	14
Pyrrole alkyne acid 11c	7	Pyrrole alkyne acid 11c	15
Imidazole chloro ester 18	8	Imidazole chloro ester 18	16
Imidazole chloro acid 12	9	Imidazole chloro acid 12	17