

Unexpected stable dimerisation of an anionic imido pyrrolicarboxylate in polar solution

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Supporting Information

General experimental remarks: Solvents were dried and distilled before use. All other reagents were used as received from Aldrich or Acros. The monobenzyl ester **4** was synthesized according to literature.^[1] All experiments were conducted in oven-dried glassware. Analytical TLC was carried out with SiO₂ aluminium foil-backed plates (60 F254 from Merck). ¹H and ¹³C NMR spectra were recorded with Bruker Avance 300, 400 and 500 spectrometers at room temperature. The chemical shifts are reported relative to the deuterated solvents. Peak assignments were based on either DEPT experiments and/or comparison with literature data. HRMS (ESI) were obtained with a Bruker MicroTOF focus apparatus. Melting points were obtained in open glass capillary tubes with an apparatus from Büchi. IR spectra were recorded by measuring the Attenuated Total Reflectance (ATR) on a FTIR 1600 spectrometer from Perkin–Elmer. NMR titrations were carried out with a Bruker Avance 400 spectrometer.

- [1] Schmuck, C.; Bickert, V.; Merschky, M.; Geiger, L.; Rupprecht, D.; Dudaczek, J.; Wich, P.; Rehm, T.; Machon, U. *Eur. J. Org. Chem.* **2008**, 324-329.

Benzyl 5-(acetylcarbomyl)1H-pyrrole-2-carboxylic acid (7): The monobenzyl ester **4** (200 mg, 0.82 mmol, 1 eq) was dissolved in dry dichloromethane (50 mL) and a few drops of DMF were added. Afterwards oxalyl chloride (70 µL, 2.46 mmol, 3 eq) was added and the resulting mixture was stirred for 1 h at 35 °C. The solvent was removed under reduced pressure and the excess oxalyl chloride was removed in vacuo. The resulting yellow solid was dissolved in dry dichloromethane (10 mL) and added dropwise to a solution of acetamidine hydrochloride (**5**; 154 mg, 1.64 mmol, 2 eq) and DMAP (450 mg, 3.69 mmol, 4.5 eq) in a solvent mixture of dry dichloromethane (40 mL) and DMF (2 mL). During the addition the mixture was cooled with an icebath. The mixture was stirred 40 min at 0 °C and afterwards 1.5 h at ambient temperature. After the addition of hydrochloric acid (5 %, 10 mL), the organic layer was separated, dried with MgSO₄. And evaporated to dryness. The yellow solid was purified by flash column chromatography on silica gel (ethylacetate : hexane = 4 : 1) to give benzyl 5-(acetylcarbomyl)1H-pyrrole-2-carboxylate (**7**) as a colourless solid (85 mg, 0.29 mmol, 36 %): m.p. 204 °C; ¹H-NMR (300 MHz, [D₆]DMSO, 25 °C): δ = 2.35 (s, 3 H, CH₃), 5.33 (s, 2 H, benzyl-CH₂), 6.88 (d, ³J (H,H) = 4.0 Hz, 1 H, pyrrole-CH), 7.10 (d, ³J (H,H) = 4.0 Hz, 1 H, pyrrole-CH), 7.33-7.47 (m, 5 H, aryl-CH), 10.84 (bs, 1 H, NH), 12.61 (bs, 1 H, NH) ppm; ¹³C-NMR (100 MHz, [D₆]DMSO,

25 °C): δ = 25.7 (CH₃), 65.7 (CH₂), 115.6 (pyrrole-CH), 115.7 (pyrrole-CH), 126.3 (aryl-C_q), 127.9 (2 aryl-CH), 128.1 (aryl-CH), 128.5 (2 aryl-CH), 129.3 (aryl-C_q), 136.1 (aryl-C_q), 158.1 (C=O), 159.7 (C=O), 172.1 (C=O) ppm; IR (KBr): ν = 3523, 3283, 2971, 2712, 1707, 1684, 1596, 1558, 1443, 1312, 945, 752 cm⁻¹; HRMS (ESI) calcd. for C₁₅H₁₃N₂O₄⁻ [M-H]⁻: 285.0881; found: 285.0881.

5-(Acetylcarbamoyl)-1H-pyrrole-2-carboxylic acid (3): A mixture of **7** (60 mg, 0.21 mmol) and Pd/C (10 mg) in methanol (50 mL) was stirred under hydrogen atmosphere at 40 °C for 1.5 h. The mixture was filtered over Celite to remove Pd/C, and the solvent was evaporated. The residue was purified by flash column chromatography on RP18 (water) to give the desired product **3** (38 mg, 0.19 mmol, 91 %) as a colourless solid: m.p. 235 °C; ¹H-NMR (300 MHz, [D₆]DMSO, 25 °C): δ = 2.35 (s, 3 H, CH₃), 6.77 (d, ³*J* (H, H) = 4.0 Hz, 1H, pyrrole-CH), 7.05 (d, ³*J* (H, H) = 4.0 Hz, 1 H, pyrrole-CH), 10.80 (bs, 1 H, NH), 12.36 (bs, 1 H, NH), 12.93 (bs, 1 H, COOH) ppm; ¹³C-NMR (100 MHz, [D₆]DMSO, 25 °C): δ = 25.5 (CH₃), 111.3 (pyrrole-CH), 116.3 (pyrrole-CH), 124.9 (pyrrole-C_q), 136.7 (pyrrole-C_q), 158.5 (C=O), 164.2 (C=O), 171.7 (C=O) ppm; IR (KBr): ν = 3420, 3246, 2968, 1728, 1585, 1508, 1365, 1317, 1191, 795 cm⁻¹; HRMS (ESI) calcd. for C₈H₇N₂O₄⁻ [M-H]⁻: 195.0411; found: 195.0419.

Preparation of the alkali metal salts of 3: A suspension of the carboxylic acid **3** was stirred in water at 0 °C and an equimolar amount of either NaOH or CsOH was added. After the suspension has cleared up, the mixture was lyophilized to obtain the corresponding alkali metal salts **3⁻** as white solids.

NMR dilution study of the Cs-salt

