Supplementary Material for Organic & Biomolecular Chemistry

Facile one-pot synthesis of 5-substituted hydantoins

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Electronic Supplementary Information

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General experimental methods

^{1}H NMR spectra were recorded at 300.1 MHz, 499.9 MHz or 400.0 MHz, using deuteriochloroform (or other indicated solvent) as reference and internal deuterium lock. The chemical shift data for each signal are given as δ in units of parts per million (ppm) relative to tetramethylsilane (TMS) where δ_{TMS} = 0.00 ppm. *^{13}C NMR spectra* were recorded at 125 MHz, 100 MHz or 75.5 MHz using the PENDANT sequence and internal deuterium lock with broadband proton decoupling and internal deuterium lock. The chemical shift data for each signal are given as δ in units of ppm relative to TMS where δ_{TMS} = 0.00 ppm. *IR spectra* were recorded potassium bromide disks as. Absorption maxima are reported in wavenumbers (cm^{-1}). *Melting points* are uncorrected. *Analytical thin layer chromatography* (TLC) was carried out on pre-coated 0.25 mm F_{254} silica gel plates. Visualization was by absorption of UV light, or thermal development after dipping in either an an aqueous solution of potassium permanganate, potassium carbonate and sodium hydroxide or a solution of ninhydrin in butan-2-ol. *Flash Column chromatography* was carried out on silica gel or on activated aluminium oxide as indicated, under a positive pressure of compressed air. Dichloromethane was distilled from calcium hydride in a recycling still, or by passage through two columns of alumina using an MBRAUN (SPS-800) solvent purification system. Diethyl ether was distilled from sodium in a recycling still using benzophenone ketyl as an indicator. Anhydrous *N,N*-dimethyl formamide was dried by distillation from 4 Å molecular sieves onto 4 Å molecular sieves under an atmosphere of nitrogen. Reagents and solvents were purchased from commercial sources and were purified and dried, where necessary, by standard techniques.[1] Where appropriate and if not stated otherwise, all non aqueous reactions were performed under an inert atmosphere of nitrogen or argon, using a vacuum manifold with nitrogen passed through 4 Å molecular sieves and self-indicating silica gel. *In vacuo* refers to the use of a rotary evaporator attached to a diaphragm pump. Hexane refers to a mixture of hexanes and petroleum ether to the fraction boiling between 40-60 ºC. Room temperature (rt) refers to the temperature of 25 °C.

General conditions for amino nitrile synthesis

Conditions A

To a solution of ammonium chloride in water, was added potassium cyanide and ketone. The reaction solution was stirred for the time stated at rt, after which time TLC analysis indicated that a new product had been formed. The solution was extracted with diethyl ether (3 × 50 mL), dried (magnesium sulfate) and filtered, prior to the solvent being removed carefully *in vacuo*.[2]

Conditions B

A solution of ammonium chloride, ketone and ammonium hydroxide (30 % v/v sol. in H_2O) in water and methanol, was cooled to 4 °C and potassium cyanide was added, portion-wise over a period of 10 min. The reaction solution was stirred for the time stated at rt, after which time TLC analysis indicated that a new product had been formed. The organic components were extracted with ether (3 × 30 mL), combined, washed with water (30 mL), brine (30 mL), dried (magnesium sulfate), filtered and the solution concentrated to a volume of ~10 mL. A solution of hydrogen chloride (2.0 M in ether) was added and the salt was allowed to precipitate at 0 °C overnight. The precipitate was isolated by filtration, and recrystallised from water to give the amino nitrile hydrochloride salt.[3]

Conditions C

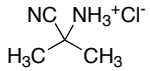
A solution of ammonium chloride, ketone and ammonium hydroxide (30 % v/v sol. in H_2O) in water was cooled to 4 °C and potassium cyanide was added, portion-wise over a period of 10 min. The reaction solution was stirred for the time stated at rt, after which time TLC analysis indicated that a new product had been formed. The organic components were extracted with diethyl ether (3 × 30 mL), combined, washed with water (30 mL), brine (30 mL), dried (magnesium sulfate), filtered and the solution concentrated to a volume of ~10 mL. A solution of hydrogen chloride (2.0 M in ether) was added and the salt allowed to precipitate at 0 °C overnight. The precipitate was isolated by filtration, and recrystallised from water to give an amino nitrile hydrochloride salt.[3]

Condition D

A slurry of potassium cyanide and ammonium chloride in dimethylsulfoxide and water was stirred and a solution of ketone in dimethylsulfoxide (2 mL) was added and allowed to stir for the time stated at rt. The mixture was suspended in water (20 mL) and the organic components were extracted with diethyl ether (3

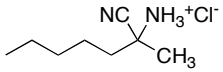
× 30 ml), combined, washed with water (30 mL), dried (magnesium sulfate), filtered and the solution concentrated to a volume of ~10 mL. A solution of hydrogen chloride (2.0 M in ether) was added and the salt allowed to precipitate at 0 °C. The precipitate was isolated by filtration, and recrystallised from water to give an amino nitrile hydrochloride salt.[4]

2-Amino-2-methylpropionitrile (1)



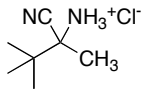
Synthesised using conditions C and the following reagents: Ammonium chloride (2.44 g, 45.6 mmol); water (20 mL); potassium cyanide (2.97 g, 45.6 mmol) and acetone (2.50 g, 3.16 mL, 43.0 mmol). 40 h at rt. 1.60 g, 30% as an off-white solid. mp 148-149 °C (from water, Lit.[5] 144-146 °C); ^{1}H NMR (400 MHz, D_2O) δ 1.69 (s, 6H); ^{13}C NMR (100 MHz, D_2O) δ 118.5, 47.1, 24.5; HRMS *m/z* (ES^+) [found $(M - Cl)^+$ 85.0759, $C_4H_9N_2$ requires M^+ 85.0760]; *m/z* (ES^+) 85 ([M - Cl]$^+$, 100).

2-Amino-2-methylheptanonitrile hydrochloride (5)



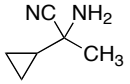
Synthesised using conditions B and the following reagents: Ammonium chloride (1.24 g, 23.2 mmol); 2-heptanone (2.50 g, 3.08 mL, 21.9 mmol); ammonium hydroxide (30 % v/v sol. in H_2O) (3.10 mL, 23.2 mmol); water / methanol (3:2) (25 mL); potassium cyanide (1.47 g, 23.2 mmol); hydrogen chloride (2.0 M in diethyl ether) (11 mL). 20 h at rt. 3.16 g, 82% as a colourless solid. mp 116-118 °C (from water); ^{1}H NMR (400 MHz, D_2O) δ 1.97-1.82 (m, 1H), 1.67 (s, 3H), 1.51-1.38 (m, 2H), 1.33-1.19 (m, 4H), 0.78 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, D_2O) δ 118.3, 51.5, 37.7, 30.7, 23.5, 23.1, 21.9, 13.4; HRMS *m/z* (ES^+) [found $(M - Cl)^+$ 141.1385, $C_8H_{17}N_2$ requires M^+ 141.1386]; *m/z* (ES^+) 141 ([M - Cl]$^+$, 100).

2-Amino-2,3,3-trimethylbutyronitrile hydrochloride (6)



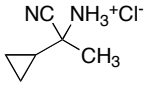
Synthesised using conditions C and the following reagents: Ammonium chloride (1.42 g, 26.5 mmol); 2,2-dimethyl-3-butanone (2.50 g, 3.11 mL, 21.9 mmol); ammonium hydroxide (30 % v/v sol. in H_2O) (3.52 mL, 26.5 mmol); water (20 mL), potassium cyanide (1.73 g, 26.5 mmol). 20 h at rt. To purify, the product was suspended in 2-butanol (5 mL) and a solution of hydrogen chloride (2.0 M in diethyl ether) (12 mL) added. 0.93 g, 23% as a colourless solid. mp 158-159 °C (from water, Lit.[6] 165-166 °C); ^{1}H NMR (300 MHz, D_2O) δ 1.67 (s, 3H), 1.08 (s, 9H); ^{13}C NMR (75 MHz, D_2O) δ 118.1, 59.5, 36.9, 24.3, 19.7; *m/z* (ES^+) 451 ([(2 × M) + (1 × M - Cl)]$^+$, 10), 253 ([M - HCl_2]$^+$, 10), 127 ([M - Cl]$^+$, 100), 100 ([M - HCNCl]$^+$, 15).

2-Amino-2-cyclopropylpropionitrile (2a)



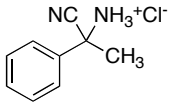
Synthesised using conditions C and the following reagents: Ammonium chloride (1.70 g, 31.8 mmol); cyclopropylmethyl ketone (2.55 g, 3.00 mL, 30.0 mmol); ammonium hydroxide (30 % v/v sol. in H_2O) (3.78 mL, 31.8 mmol); water (15 mL), potassium cyanide (2.07 g, 31.8 mmol). 20 h at rt. The crude solution was distilled (0.5 mbar, rt). 2.89 g, 88% as a colourless liquid. R_f 0.6 (ethyl acetate/petroleum ether, 50:50); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.85 (br s, 1H), 1.59 (s, 3H), 1.14-1.07 (m, 1H), 0.67-0.52 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 120.7, 50.7, 26.1, 18.7, 0.11, 0.02. The ^{1}H NMR spectrum is in agreement with the literature.[3]

2-Amino-2-cyclopropylpropionitrile hydrochloride (2b)



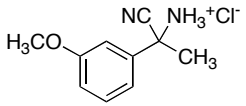
Synthesised using conditions C and the following reagents: Ammonium chloride (2.05 g, 38.4 mmol); cyclopropylmethyl ketone (3,06 g, 3.60 mL, 36.2 mmol); ammonium hydroxide (30 % v/v sol. in H_2O) (5.20 mL, 38.4 mmol); water (20 mL), potassium cyanide (2.50 g, 38.4 mmol), hydrogen chloride (2.0 M in diethyl ether) (18 mL). 20 h at rt. 3.31 g, 63% as a colourless solid. mp 110 - 111°C (from water); ^{1}H NMR (300 MHz, D_2O) δ 1.70 (s, 3H), 1.35-1.28 (m, 1H), 0.79-0.57 (m, 4H); ^{13}C NMR (75 MHz, D_2O) δ 113.7, 52.0, 20.5, 14.3, 0.30, 0.00; HRMS *m/z* (ES^+) [found $(M\text{-}Cl)^+$ 111.0917, $C_6H_{11}N_2$ requires M^+ 111.0917]; *m/z* (ES^+) 111 ($[M\text{-}Cl]^+$, 70), 94 ($[M - NH_3Cl]^+$, 100), 84 ($[M - HCNCl]^+$, 30).

2-Amino-2-phenylpropionitrile hydrochloride (7)



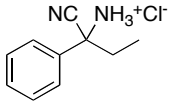
Synthesised using conditions D and the following reagents: Potassium cyanide (1.63 g, 25.0 mmol); ammonium chloride (1.34 g, 25.0 mmol); dimethylsulfoxide / water (6:1) (20 mL); acetophenone (1.50 g, 1.46 mL, 12.5 mmol) in dimethylsulfoxide (2 mL); hydrogen chloride (2.0 M in diethyl ether) (6 mL). 20 h at rt. 1.03 g, 46% as colourless crystals. mp 116-118 °C (from water); ^{1}H NMR (300 MHz, D_2O) δ 7.63-7.56 (m, 2H), 7.54-7.47 (m, 3H), 2.09 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.3, 131.2, 130.1, 125.6, 118.1, 53.8, 25.4; HRMS *m/z* (ES^+) [found $(M - Cl)^+$ 147.0917, $C_9H_{11}N_2$ requires M^+ 147.0917]; *m/z* (ES^+) 147 ($[M - Cl]^+$, 20), 130 (100).

2-Amino-2-(3'-methoxyphenyl)propionitrile hydrochloride (8)



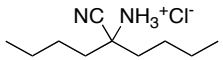
Synthesised using conditions D and the following reagents: Potassium cyanide (1.73 g, 26.6 mmol); ammonium chloride (1.42 g, 26.6 mmol); dimethylsulfoxide / water (6:1) (20 mL); 3'-methoxyacetophenone (2.00 g, 13.3 mmol) in dimethylsulfoxide (2 mL); hydrogen chloride (2.0 M in diethyl ether) (7 mL). 40 h at rt. 1.15 g, 41% as a colourless solid. mp 120 °C dec. (from water); ^{1}H NMR (300 MHz, D_2O) δ 7.40 (apparent t, *J* = 8.1 Hz, 1H); 7.15 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.10 (apparent t, *J* = 2.1 Hz, 1H), 7.03 (dd, *J* = 8.1, 2.1 Hz, 1H), 3.77 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (75 MHz, D_2O) δ 159.7, 134.8, 131.1, 117.8, 117.6, 116.0, 111.3, 55.6, 53.2, 25.2; HRMS *m/z* (ES^+) [found $(M\text{-}Cl)^+$ 177.1023, $C_{10}H_{13}N_2O$ requires M^+ 177.1022]; *m/z* (ES^+) 177 ($[M\text{-}Cl]^+$, 20), 160 ($[M - NH_3Cl]^+$, 100), 134 ($[M - CN_2H_3Cl]^+$, 35).

2-Amino-2-phenylbutyronitrile hydrochloride (9)



Synthesised using conditions D and the following reagents: Potassium cyanide (1.46 g, 22.4 mmol); ammonium chloride (1.20 g, 22.4 mmol); dimethylsulfoxide / water (4:1) (20 mL); propiophenone (1.50 g, 1.49 mL, 11.2 mmol) in dimethylsulfoxide (2 mL); hydrogen chloride (2.0 M in diethyl ether) (6 mL). 24 h at rt. 0.52 g, 24% as colourless crystals. mp 124-126 °C (from water, Lit.[7] 119 °C); ^{1}H NMR (400 MHz, D_2O) δ 7.58-7.46 (m, 5H), 2.34 (q, *J* = 7.4 Hz, 2H), 0.92 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, D_2O) δ 134.1, 133.3, 132.3, 128.2, 119.2, 61.7, 34.7, 10.6; HRMS *m/z* (ES^+) [found $(M - Cl)^+$ 161.1072, $C_{10}H_{13}N_2$ requires M^+ 161.1073]; *m/z* (ES^+) 553 ($[(2 \times M) + (1 \times M - Cl)]^+$, 5), 481 ($[(2 \times M - HCl) + (1 \times M - Cl)]^+$, 10), 321 ($[(M - HCl) + (M - Cl)]^+$, 40), 161 ($[M - Cl)]^+$, 90), 134 ($[M - CNH_2Cl)]^+$, 100).

2-Amino-2-^{n}butylhexanenitrile hydrochloride (10)



Synthesised using conditions D and the following reagents: Potassium cyanide (1.34 g, 21.2 mmol); ammonium chloride (1.13 g, 21.2 mmol); dimethylsulfoxide / water (4:1) (20 mL); 5-nonanone (2.84 g, 3.5 mL, 20.0 mmol) in dimethylsulfoxide (2 mL); hydrogen chloride (2.0 M in diethyl ether) (10 mL). 20 h at rt. 0.29 g, 7% as colourless crystals. mp 116-118 °C (from water); ^{1}H NMR (400 MHz, D_2O) δ 1.99-1.85 (m, 4H), 1.43-1.25 (m, 8H), 0.81 (t, *J* = 7.3 Hz, 6H); ^{13}C NMR (75 MHz, D_2O) δ 117.5, 55.0, 35.3, 25.2, 21.5, 12.8; HRMS *m/z* (ES^+) [found $(M - Cl)^+$ 169.1699, $C_{10}H_{21}N_2$ requires M^+ 169.1699]; *m/z* (ES^+) 169 ($[M - Cl)]^+$, 100).

General method for hydantoin synthesis from amino nitriles

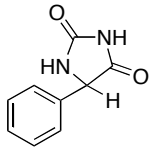
A solution of aminonitrile (1 equiv.) and Hünig's base (3 equiv.) in dry dichloromethane (5 mL), was stirred at rt with $CO_{2(g)}$ (from dry ice sublimation) bubbled, initially through 4 Å molecular sieves, then through the reaction solution continuously, with the excess $CO_{2(g)}$ dissipated through a bubbler. After 30 h, TLC analysis indicated that the starting material had been consumed. The solvents were removed *in vacuo*, and the resulting paste was suspended in water (10 mL), and extracted with ethyl acetate (3 × 30 mL). The organic portions were combined, washed with dilute HCl (0.1 M, 10 mL), and water (10 mL). The organic

phase was dried ($MgSO_4$), filtered and the solvent was removed *in vacuo*. The resulting solid was purified by concentration under reduced pressure, or by silica gel column chromatography. Further purification by crystallisation from ethanol was also performed, where necessary.

General method for the one-pot hydantoin synthesis from aldehydes or ketones

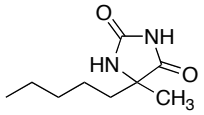
A mixture of ketone or aldehyde (1 equiv.) and gallium (III) triflate (0.1 equiv.) in dichloromethane (5 mL) was prepared in a dry 2-neck reaction vessel (under a positive pressure of N_2), fitted with a dry-ice condenser (containing an ethanol/dry ice cooling mixture). Approximately 10 mL of liquid ammonia was condensed into the reaction solution at -78 °C. This temperature was maintained for 3 h, after which, a solution of hydrogen cyanide was added. [Dichloromethane (2 mL) and trimethylsilyl cyanide (2 equiv.) were combined, cooled to 5 ºC, methanol added (2 equiv.), and the solution was stirred for 2 h]. After 30 min, the reaction vessel was warmed to rt, and the solution was stirred for the time stated, after which, TLC analysis indicated the presence of an aminonitrile. Hünig's base (3 equiv.) was added to the reaction solution and $CO_{2(g)}$, sublimed from dry ice (and passed through 4 Å molecular sieves), was bubbled through the reaction solution for the time stated, after which time TLC analysis of the reaction mixture indicated the starting material had been consumed. The solvent was removed *in vacuo*, and the resulting paste was suspended in water (5 mL), and the organic components were extracted with ethyl acetate (3 × 10 mL), and combined. The organic components were washed with 0.1 M HCl (10 mL), water (10 mL), brine (10 mL), dried ($MgSO_4$), filtered and the solvent was removed *in vacuo*. The resulting solid was purified by concentration under reduced pressure, or by silica gel column chromatography. Further purification by crystallisation from ethanol was also performed, where necessary.

5-Phenyl-imidazolidine-2,4-dione (11)



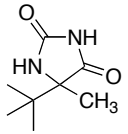
One pot: Amino nitrile formation time: 20 h; Hydantoin formation time: 17 h; R_f 0.6 (ethyl acetate); mp 176-178 °C (from ethanol, Lit.[5] 174-176 °C); ^{1}H NMR (300 MHz, DMSO-D_6) δ 10.78 (br s, 1H), 8.39 (s, 1H), 7.43-7.30 (m, 5H), 5.15 (s, 1H); ^{13}C NMR (125 MHz, D_6-DMSO) δ 174.8, 158.1, 136.6, 129.1, 128.7, 127.2, 61.6; *m/z* (ES^-) 175 ([M - H]$^-$, 100).

5-Methyl-5-pentylimidazolidine-2,4-dione (12)



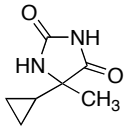
One pot: Amino nitrile formation time: 17 h; Hydantoin formation time: 7 h; R_f 0.6 (ethyl acetate); mp 97-98 °C (from ethanol, Lit.[8] 101 °C); ν_{max} ($CHCl_3$)/cm^{-1} 3241 (s), 2923 (s), 2859 (s), 1785 (s), 1707 (s), 1468 (s), 1433 (s), 1290 (m), 1241 (m), 1193 (m), 814 (m), 776 (s), 649 (m); ^{1}H NMR (400 MHz, DMSO-D_6) δ 10.53 (br s, 1H), 7.87 (br s, 1H), 1.60-1.41 (m, 2H), 1.32-1.15 (m, 8H), 1.10-0.99 (m, 1H), 0.83 (t, J = 7Hz, 3H); ^{13}C NMR (75 MHz, D_6-DMSO) δ 181.7, 159.4, 65.1, 40.2, 34.1, 26.8, 25.7, 25.0, 16.9; HRMS *m/z* (ES^+) [found $(M + NH_4)^+$ 202.1551, $C_9H_{20}N_3O_2$ requires M^+ 202.1550]; *m/z* (ES^+) 207 ([M + Na]$^+$, 100).

5-^{t}Butyl-5-methylimidazolidine-2,4-dione (13)



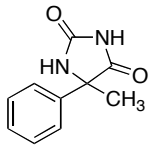
Ethanol used as solvent. One pot: Amino nitrile formation time: 20 h; Hydantoin formation time: 17 h; R_f 0.5 (ethyl acetate); mp 219-220 °C (from ethyl acetate, Lit.[9] 218-219 °C); ^{1}H NMR (300 MHz, DMSO-D_6) δ 10.58 (br s, 1H), 8.04 (br s, 1H), 1.30 (s, 3H), 0.99 (s, 9H); ^{13}C NMR (75 MHz, D_6-DMSO) δ 178.1, 156.7, 66.7, 36.1, 24.5, 18.8; *m/z* (ES^+) 193 ([M + Na]$^+$, 100). These data are in agreement with the literature values.[9]

5-Cyclopropyl-5-methylimidazolidine-2,4-dione (4)



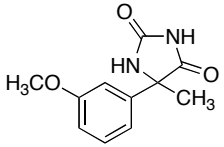
One pot: Amino nitrile formation time: 24 h; Hydantoin formation time: 3 h; . R_f 0.5 (ethyl acetate); mp 145-146 °C (from ethyl acetate, Lit.[10] 147-148 °C); ν_{max} ($CHCl_3$)/cm^{-1} 3420 (s), 3240 (s), 3010 (m), 1775 (s), 1720 (s), 1429 (m), 1265 (w), 1113 (w), 792 (w), 771 (w), 760 (w); ^{1}H NMR (300 MHz, D_6-DMSO) δ 10.4 (br s, 1H), 7.60 (s, 1H), 1,18 (s, 3H), 0.99-0.88 (m, 1H), 0.34-0.14 (3H, m), 0.05-0.06 (m, 1H); ^{13}C NMR (75 MHz, D_6-DMSO) δ 178.8, 156.9, 61.3, 23.4, 17.4, 0.61, 0.00; HRMS *m/z* (ES^+) [found (M + Na)$^+$ 177.0642, $C_7H_{10}N_2O_2Na$ requires M$^+$ 177.0640]; *m/z* (ES^+) 177 ([M+Na]$^+$, 100). Anal. Calcd for $C_7H_{10}N_2O_2$: C, 54.5; H, 6.5; N, 18.2. Found: C, 54.1; H, 6.7; N, 18.1. Kleinpeter *et al.*[11] did not observe the highfield resonance for the cyclopropyl ring in their ^{1}H NMR spectrum, which was recorded at the same frequency and in the same solvent as our spectrum. In numerous re-syntheses of this compound this resonance was a re-occurring feature in our spectra. Our ^{13}C NMR data match more closely with those of Kleinpeter.

5-Methyl-5-phenylimidazolidine-2,4-dione (14)



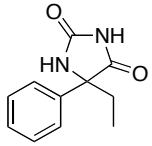
One pot: Amino nitrile formation time: 20 h; Hydantoin formation time: 5 h; R_f 0.5 (methanol/ethyl acetate, 10:90); mp 196-198 °C (from ethanol, Lit.[8] 194-195 °C); ^{1}H NMR (400 MHz, DMSO-D_6) δ 10.82 (br s, 1H), 8.67 (s, 1H), 7.55-7.51 (m, 2H), 7.48.7.43 (m, 2H), 7.41-7.36 (m, 1H), 1.71 (s, 3H); ^{13}C NMR (75 MHz, D_6-DMSO) δ 176.9, 156.2, 139.9, 128.4, 127.8, 125.3, 63.9, 24.9; *m/z* (ES^+) 213 ([M + Na]$^+$, 100). These data are in agreement with the literature values.[11]

5-(3'Methoxyphenyl)-5-methylimidazolidine-2,4-dione (15)



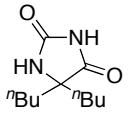
One pot: Amino nitrile formation time: 20 h; Hydantoin formation time: 7 h; R_f 0.5 (ethyl acetate); mp 100-102 °C (from methanol and ethyl acetate); ν_{max} ($CHCl_3$)/cm^{-1} 3256 (m), 3020 (w), 1773 (s), 1720 (s), 1599 (m), 1492 (w), 1426 (m), 1263 (m), 795 (w), 773 (w), 715 (w); ^{1}H NMR (400 MHz, DMSO-D_6) δ 10.74 (br s, 1H), 8.60 (s, 1H), 7.30 (apparent t, J = 8.0 Hz, 1H), 7.04 (ddd, J = 8.0, 2.2, 0.8 Hz, 1H), 6.99 (apparent t, J = 2.2 Hz, 1H), 6.89 (ddd, J = 8.0, 2.2, 0.8 Hz, 1H), 3.75 (s, 3H), 1.62 (s, 3H); ^{13}C NMR (75 MHz, D_6-DMSO) δ 177.1, 159.6, 156.5, 141.9, 130.0, 117.9, 113.2, 111.8, 64.2, 55.5, 25.5; HRMS *m/z* (CI^+) [found $(M + H)^+$ 221.0919, $C_{11}H_{13}N_2O_3$ requires M^+ 221.0926]; *m/z* (CI^+) 221 ($[M + H]^+$, 100). Anal. Calcd for $C_{11}H_{12}N_2O_3$: C, 60.0; H, 5.5; N, 12.7 Found: C, 60.1; H, 5.3; N, 12.6.

5-Ethyl-5-phenylimidazolidine-2,4-dione (16)



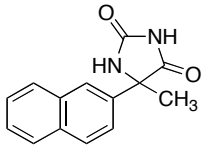
One pot: Amino nitrile formation time: 20 h; Hydantoin formation time: 6 h; R_f 0.5 (ethyl acetate); mp 194-196 °C (from ethanol, Lit.[12] 201-202 °C); ^{1}H NMR (400 MHz, DMSO-D_6) δ 10.82 (br s, 1H), 8.71 (s, 1H), 7.59-7.54 (m, 2H), 7.49-7.43 (m, 2H), 7.41-7.36 (m, 1H), 2.18-2.08 (m, 1H), 2.01-1.90 (m, 1H), 0.87 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, D_6-DMSO) δ 176.2, 156.6, 139.0, 128.3, 127.7, 125.4, 68.0, 31.1, 8.0; HRMS *m/z* (ES^+) [found $(M + Na)^+$ 227.0797, $C_{11}H_{12}N_2O_2Na$ requires M^+ 227.0796]; *m/z* (ES^-) 203 ($[M - H]^-$, 100).

5,5-Di-(^{n}butyl)imidazolidine-2,4-dione (17)



One pot: Amino nitrile formation time: 20 h; Hydantoin formation time: 14 h; R_f 0.6 (ethyl acetate); mp 156-158 °C (from ethanol, Lit.[13] 159-161 °C); ^{1}H NMR (400 MHz, DMSO-D_6) δ 10.54 (br s, 1H), 7.78 (s, 1H), 1.60-1.42 (m, 4H), 1.28-1.16 (m, 6H), 1.08-096 (m, 2H), 0.83 (t, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, D_6-DMSO) δ 178.0, 156.8, 65.5, 36.2, 25.0, 22.1, 13.8; HRMS *m/z* (CI^+) [found $(M + H)^+$ 213.1597, $C_{11}H_{21}N_2O_2$ requires M^+ 213.1603]; *m/z* (ES^+) 235 ($[M + Na]^+$, 100).

5-Methyl-5-naphthylimidazolidine-2,4-dione (19)



One pot: Amino nitrile formation time: 24 h; Hydantoin formation time: 6 h; R_f 0.2 (ethyl acetate/petroleum ether, 50:50); mp 246-248 °C (from ethanol, Lit.[14] 247-248 °C); ν_{max} ($CHCl_3$)/cm^{-1} 3450 (s), 1773 (m), 1719 (m), 1638 (m), 1400 (w), 638 (w); ^{1}H NMR (300 MHz, DMSO-D_6) δ 10.76 (br s, 1H), 8.71 (s, 1H), 8.00-7.88 (m, 4H), 7.59 (dd, J = 8.6, 2.0 Hz, 1H), 7.56-7.49 (m, 2H), 1.75 (s, 3H); ^{13}C NMR (75 MHz, D_6-DMSO) δ 177.3, 156.7, 137.7, 132.9, 132.6, 128.6, 128.5, 127.8, 126.9, 126.8, 124.5, 124.0, 64.5, 25.1; HRMS *m/z* (CI^+) [found $(M + H)^+$ 241.0975, $C_{14}H_{13}N_2O_2$ requires M^+ 241.0977]; *m/z* (CI^+) 241 ($[M + H]^+$, 100), 113 (70). Anal. Calcd for $C_{14}H_{12}N_2O_2$: C, 70.0; H, 5.0; N, 11.7 Found: C, 69.8; H, 4.8; N, 11.6.

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