Synthesis of a series of pyridine-functionalised benzoimidazole-based N-heterocyclic carbene ligands

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A series of pyridine-functionalised bis(benzoimidazolium) dichlorides, dibromides and dihexafluorophosphate with different alkyl bridged length (n = 2–4) were synthesised in high yield. All the compounds are new and fully characterised by ^{1}H and ^{13}C NMR, IR and elemental analyses.

Keywords: N-heterocyclic carbene ligand, pyridine-functionalised, tetradentate, benzoimidazole

The chemistry of N-heterocyclic carbenes (NHCs) and their complexes has been investigated with great intensity in recent years, and many publications and reviews relating to NHC complexes have been published.[1–5] Easy preparation and modification on NHCs may have helped their great development. Various donor functions, such as containing N, O, S or P donor atom can be introduced at the nitrogen atom of the imidazole in a simple manner, and a donor-functionalised NHC can act as a polydentate ligand upon coordination to a metal centre. Various complexes with donor-functionalised NHC and their use in catalysis have been explored.[6,7] We have developed an interest in exploring the utility of N-heterocyclic carbenes in chemical catalysis,[8–10] and reported the synthesis of non-functionalised N-heterocyclic carbene precursors based on imidazole and triazole.[11–13] As an extension to our work on O-functionalised NHC precursors based on imidazole and benzoimidazole,[14] we now report the preparation of a series of pyridine-functionalised tetradentate N-heterocyclic carbene precursors based on benzoimidazole.

1-(Pyridin-2-ylmethyl)-1H-benzoimidazole was synthesised by the nucleophilic substitution reaction of 2-(chloromethyl) pyridine with benzoimidazole in 30% NaOH aqueous solution with TBAB (tetra-*n*-butylammonium bromide) as a phase transition catalyst in 92% yield (Scheme 1). The alkane bridged pyridine-functionalised bisbenzoimidazolium dichlorides or dibromides were synthesised by direct reaction of dialkyl halides with the pyridine-functionalised benzoimidazole in toluene at an elevated temperature in good yields, ranging from 80 to 89%. As the alkyl bromides are more reactive than alkyl chlorides, the reaction temperature for bromides is 10 degree lower (120 °C) than that for chlorides (130 ºC). All the reactions can be completed within 5 h.

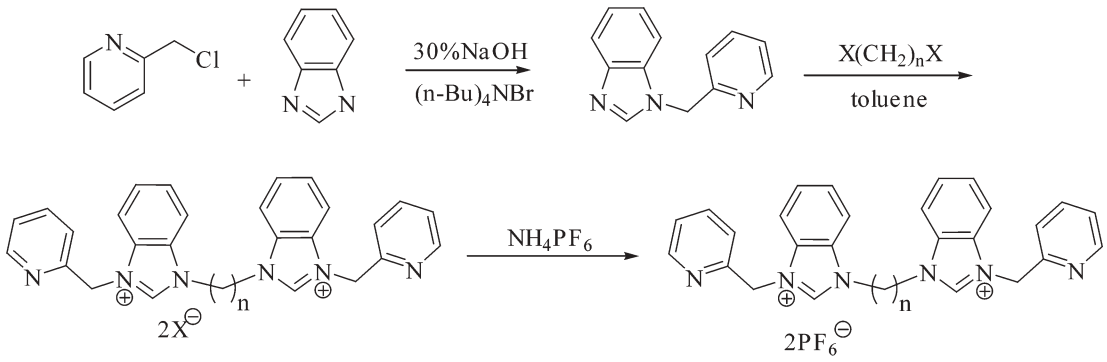
When the saturated aqueous solution of NH_4PF_6 was added into the aqueous solution of the bis(benzoimidazolium) dichlorides or dibromides, their corresponding dihexafluorophosphate salts precipitated out quantitatively (Scheme 1). This showed that both bisimidazolium dichloride and dibromide salts can be easily converted to dihexafluorophosphate salts in near quantitative yield. All the compounds are new, so they are fully characterised by NMR spectroscopy and give satisfactory elemental analyses.

In conclusion, we have demonstrated an easy process to prepare a series of pyridine-functionalised bis(benzoimidazolium) dichlorides, dibromides and dihexafluorophosphate with different alkyl bridged length (n = 2–4) in high yield.

Experimental

All reagents were commercially available and were used without further purification. ^{1}H NMR spectra were recorded on a Bruker DPX 400 MHz spectrometer at room temperature and referenced to the residual ^{1}H signals of the solvent. Coupling constants J are given in Hz. IR spectra were recorded on KBr pellets on a FTIR-Tensor 27 spectrometer. Melting points were detected by microscope melting point apparatus. Elemental analyses were performed on a EuroVektor Euro EA-300 elemental analyser.

1-(Pyridin-2-ylmethyl)-1H-benzoimidazole:[15] To the mixture of 1H-benzoimidazole (10 mmol, 1.181 g), tetra-*n*-butylammonium bromide (TBAB) (0.05 g) and 30% NaOH aqueous solution (10 mL) in a 50 mL of round-bottom flask was added 2-(chloromethyl)pyridine (12 mmol, 1.531 g). The reaction mixture was stirred at room temperature for 2 h, while a large amount of light yellow solid appeared. Water (20 mL) was added to the slurry, and the solid was filtered and washed with plenty of water to give the product as a white solid in 92% yield (1.92 g). M.p. 119–120 ºC. ^{1}H NMR (400 MHz, $CDC1_3$) δ = 8.61 (d, J = 4.0 Hz, 1H, *o*-C_5H_5N), 8.06 (s, 1H, NC*H*N), 7.83 (dd,



n = 2, X = Cl (**1**); n = 2, X = Br (**4**);
n = 3, X = Cl (**2**); n = 3, X = Br (**5**);
n = 4, X = Cl (**3**); n = 4, X = Br (**6**)

n = 2 (**7**); n = 3 (**8**); n = 4 (**9**)

Scheme 1 Synthesis of alkyl-bridged bisimidazolium dichlorides.

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J = 1.6 Hz, *J* = 6.8 Hz, 1H, *m*-C_6H_4), 7.59 (dt, *J* = 1.6 Hz, *J* = 7.6 Hz, 1H, *p*-C_5H_5N), 7.31–7.33 (m, 1H, *m*-C_6H_4), 7.26–7.30 (m, 2H, *o*-C_6H_4), 7.21–7.24 (m, 1H, *m*-C_5H_5N), 6.90 (d, *J* = 7.6 Hz, 1H, *m*-C_5H_5N), 5.49 (s, 2H, NCH_2C).

1,1′-Di-(pyridin-2-ylmethyl)-4,4′-(1,2-ethanediyl)bisbenzoimidazolium dichloride (**1**): To a 10 mL heavy wall pressure tube was added 1-(pyridin-2-ylmethyl)-1H-benzoimidazole (5 mmol, 1.046 g), 1,2-dichloroethane (2.5 mmol, 0.247 g) and toluene (1 mL). The reaction mixture was heated at 130 ºC for 3.5 h, while a large amount of white solid appeared. The solid was filtered and washed with DCM to give the product as white solids in 84% yield (1.09 g). M.p. > 300 ºC. IR (KBr): 3457, 2955, 1628, 1573, 1560, 1435, 1183, 1090, 997, 761, 569 cm^{-1}. ^{1}H NMR (400 MHz, D_2O) δ = 8.32 (d, *J* = 4.0 Hz, 2H, C_5H_5N), 7.77 (t, *J* = 7.6 Hz, 2H, C_6H_4), 7.67 (d, *J* = 8.4 Hz, 2H, C_6H_4), 7.50 (t, *J* = 7.6 Hz, 2H, C_5H_5N), 7.37–7.25 (m, 8H, C_6H_4, C_5H_5N), 5.70 (s, 4H, NCH_2C), 5.26 (s, 4H, NCH_2). ^{13}C NMR (100 MHz, D_2O) δ = 151.2, 149.6, 139.0, 131.0, 128.0, 127.8, 124.7, 123.5, 113.9, 113.2, 111.8, 51.6, 46.6. Anal. Calcd for $C_{28}H_{26}Cl_2N_6$ (517.45 g mol^{-1}): C, 64.99; H, 5.06; N, 16.24. Found: C, 64.71; H, 5.15; N, 16.45%.

1,1′-Di-(pyridin-2-ylmethyl)-4,4′-(1,3-propanediyl)bisbenzoimidazolium dichloride (**2**): To a 10 mL heavy wall pressure tube was added 1-(pyridin-2-ylmethyl)-1H-benzoimidazole (10 mmol, 2.092 g), 1,3-dichloropropane (5 mmol, 0.565 g) and toluene (2 mL). The reaction mixture was heated at 130 ºC for 3.5 h, while a large amount of white solid appeared. The solid was filtered and washed with DCM to give the product as white solids in 86% yield (2.30 g). M.p. > 300 ºC. IR (KBr): 3395, 2967, 2361, 2342, 1560, 1438, 762, 669, 649 cm^{-1}. ^{1}H NMR (400 MHz, D_2O) δ = 8.38 (d, *J* = 4.8 Hz, 2H, C_5H_5N), 7.88 (t, *J* = 7.6 Hz, 2H, C_6H_4), 7.79 (d, *J* = 8.4 Hz, 2H, C_6H_4), 7.62–7.53 (m, 8H, C_6H_4, C_5H_5N), 7.39 (t, *J* = 5.6 Hz, 2H, *m*-C_5H_5N), 5.72 (s, 4H, NCH_2C), 4.76 (t, *J* = 7.2 Hz, 4H, NCH_2), 2.90-2.83 (m, 2H, CH_2). ^{13}C NMR (100 MHz, D_2O) δ = 151.5, 149.4, 138.9, 131.2, 131.1, 127.6, 127.5, 124.6, 123.5, 113.7, 113.1, 51.4, 44.5, 28.0. Anal. Calcd for $C_{29}H_{28}Cl_2N_6$ (531.48 g mol^{-1}): C, 65.54; H, 5.31; N, 15.81. Found: C, 65.31; H, 5.22; N, 15.93%.

1,1′-Di-(pyridin-2-ylmethyl)-4,4′-(1,4-butanediyl)bisbenzoimidazolium dichloride (**3**): To a 10 mL heavy wall pressure tube was added 1-(pyridin-2-ylmethyl)-1H-benzoimidazole (2 mmol, 0.419 g), 1,4-dichlorobutane (1 mmol, 0.113 g) and toluene (1 mL). The reaction mixture was heated at 130 ºC for 5 h, while a large amount of white solid appeared. The solid was filtered and washed with dichloromethane to give the product as white solids in 80% yield (0.41 g). M.p. 275–277 ºC. IR (KBr): 3415, 3130, 3039, 2361, 2341, 1616, 1591, 1561, 1481, 1428, 1178, 997, 770, 649 cm^{-1}. ^{1}H NMR (400 MHz, D_2O) δ = 8.35 (d, *J* = 4.4 Hz, 2H, C_5H_5N), 7.87 (t, *J* = 7.2 Hz, 2H, C_6H_4), 7.56 (t, *J* = 7.6 Hz, 6H, C_6H_4, C_5H_5N), 7.47 (t, *J* = 7.6 Hz, 2H, C_5H_5N), 7.39–7.32 (m, 4H, C_6H_4), 5.75 (s, 4H, NCH_2C), 4.58 (s, 4H, NCH_2), 2.03 (s, 4H, CCH_2C). ^{13}C NMR (100 MHz, D_2O) δ = 151.6, 149.3, 138.8, 131.2, 130.7, 127.3, 127.0, 124.5, 123.5, 113.5, 112.9, 51.3, 46.7, 24.6. Anal. Calcd for $C_{30}H_{30}Cl_2N_6$ (545.51 g mol^{-1}): C, 66.05; H, 5.54; N, 15.41. Found: C, 65.78; H, 5.63; N, 15.62%.

1,1′-Di-(pyridin-2-ylmethyl)-4,4′-(1,2-ethanediyl)bisbenzoimidazolium dibromide (**4**): To a 10 mL heavy wall pressure tube was added 1-(pyridin-2-ylmethyl)-1H-benzoimidazole (10 mmol, 2.093 g), 1,2-dibromoethane (5 mmol, 0.939 g) and toluene (2 mL). The reaction mixture was heated at 120 ºC for 3 h, while a large amount of white solid appeared. The solid was filtered and washed with DCM to give the product as white solids in 87% yield (2.65 g). M.p. >300 ºC. IR (KBr): 3441, 2170, 1661, 1453, 1402, 1184, 1077, 986, 848, 759, 558 cm^{-1}. ^{1}H NMR (400 MHz, D_2O) δ = 8.37 (d, *J* = 4.4 Hz, 2H, C_5H_5N), 7.82 (t, *J* = 7.6 Hz, 2H, C_6H_4), 7.72 (d, *J* = 8.4 Hz, 2H, C_6H_4), 7.55 (t, *J* = 6.8 Hz, 2H, C_5H_5N), 7.42–7.29 (m, 8H, C_5H_5N, C_6H_4), 5.74 (s, 4H, NCH_2C), 5.31 (s, 4H, NCH_2). ^{13}C NMR (100 MHz, D_2O) δ = 151.2, 149.6, 139.0, 131.0, 128.0, 127.8, 124.7, 123.6, 113.9, 111.8, 51.6, 46.6. Anal. Calcd for $C_{28}H_{26}Br_2N_6$ (606.35 g mol^{-1}): C, 55.46; H, 4.32; N, 13.86. Found: C, 55.31; H,4.39; N, 13.93%.

1,1′-Di-(pyridin-2-ylmethyl)-4,4′-(1,3-propanediyl)bisbenzoimidazolium dibromide (**5**): To a 10 mL heavy wall pressure tube was added 1-(pyridin-2-ylmethyl)-1H-benzoimidazole (5.0 mmol, 1.046 g), 1,3-dibromopropane (2.5 mmol, 0.505 g) and toluene (1 mL). The reaction mixture was heated at 120 ºC for 3 h, while a large amount of white solid appeared. The solid was filtered and washed with DCM to give the product as a white solid in 89% yield (1.38 g). M.p. 147–148 °C. IR (KBr): 3433, 2170, 1660, 1454, 1401, 1190, 1077, 987, 847, 763, 558 cm^{-1}. ^{1}H NMR (400 MHz, D_2O) δ = 8.39 (d, *J* = 4.8 Hz, 2H, C_5H_5N), 7.89 (t, *J* = 7.6 Hz, 2H, C_6H_4), 7.81–7.79 (m, 2H, C_6H_4), 7.63–7.58 (m, 6H, C_6H_4, C_5H_5N), 7.54 (d, *J* = 8.0 Hz, 2H, C_5H_5N),7.40 (t, *J* = 5.6 Hz, 2H, C_5H_5N), 5.72 (s, 4H, NCH_2C), 4.77 (t, *J* = 7.2 Hz, 4H), 2.91-2.84 (m, 2H, CH_2). ^{13}C NMR (100 MHz, D_2O): δ = 151.5, 149.5, 138.9, 131.3, 131.2, 127.6, 127.5, 124.6, 123.6, 113.7, 113.1, 51.5, 44.6, 28.0. Anal. Calcd for $C_{29}H_{28}Br_2N_6$ (620.38 g mol^{-1}): C, 56.14; H, 4.55; N, 13.55. Found: C, 55.88; H, 4.45; N, 13.66%.

1,1′-Di-(pyridin-2-ylmethyl)-4,4′-(1,4-butanediyl)bisbenzoimidazolium dibromide (**6**): To a 10 mL heavy wall pressure tube was added 1-(pyridin-2-ylmethyl)-1H-benzoimidazole (5.0 mmol, 1.046 g), 1,4-dibromobutane (2.5 mmol, 0.540 g) and toluene (1 mL). The reaction mixture was heated at 120 ºC for 3 h, while a large amount of white solid appeared. The solid was filtered and washed with dichloromethane to give the product as white solids in 82% yield (1.29 g). M.p. 276–277 °C. IR (KBr): 3433, 2170, 1638, 1454, 1401, 1076, 986, 848, 747, 558 cm^{-1}. ^{1}H NMR (400 MHz, D_2O) δ = 8.34 (d, *J* = 4.8 Hz, 2H, C_5H_5N), 7.86 (t, *J* = 7.6 Hz, 2H, C_6H_4), 7.59–7.53 (m, 6H, C_6H_4, C_5H_5N), 7.46 (t, *J* = 8.4 Hz, 2H, C_6H_4), 7.38–7.31 (m, 4H, C_5H_5N), 5.74 (s, 4H, NCH_2C), 4.56 (s, 4H, NCH_2), 2.02 (s, *4*H, CH_2). ^{13}C NMR (100 MHz, D_2O) δ = 151.6, 149.4, 138.8, 131.2, 130.9, 127.3, 127.0, 124.5, 123.5, 113.6, 112.9, 51.3, 46.7, 24.8. Anal. Calcd for $C_{30}H_{30}Br_2N_6$ (634.41 g mol^{-1}): C, 56.80; H, 4.77; N, 13.25. Found: C, 56.53; H, 4.69; N, 13.37%.

1,1′-Di-(pyridin-2-ylmethyl)-4,4′-(1,2-ethanediyl)bisbenzoimidazolium dihexafluorophosphate (**7**): To compound **1** (2.0 mmol, 1.033 g) or **4** (2.0 mmol, 1.213 g) dissolved into water (6 mL) in a 50 mL beaker was added dropwise saturated NH_4PF_6 aqueous solution (30 mL). A large amount of white solid appeared. The solid was filtered and washed with water to give the product as a white solid in 99% yield (1.46 g). M.p. 228–230 °C. IR (KBr): 3346, 1675, 1635, 1402, 1190, 1077, 986, 848, 765, 558 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) δ = 9.87 (s, 2H, NC*H*N), 8.47 (d, *J* = 4.4 Hz, 2H, C_5H_5N), 7.93–7.88 (m, 4H, C_6H_4), 7.81 (t, *J* = 8.4 Hz, 2H, C_5H_5N), 7.62–7.56 (m, 4H, C_6H_4), 7.46 (t, *J* = 7.6 Hz, 2H, C_5H_5N), 7.39 (t, *J* = 6.4 Hz, 2H, C_5H_5N), 5.88 (s, 4H, NCH_2C), 5.20 (s, 4H, NCH_2). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 152.5, 149.5, 143.5, 137.5, 131.0, 130.9, 126.9, 126.6, 123.7, 122.7, 113.8, 113.0, 50.9, 45.8. Anal. Calcd for $C_{28}H_{26}F_{12}N_6P_2$ (736.47 g mol^{-1}): C, 45.66; H, 3.56; N, 11.41. Found: C, 45.46; H, 3.48; N, 11.60%.

1,1′-Di-(pyridin-2-ylmethyl)-4,4′-(1,3-propanediyl)bisbenzoimidazolium dihexafluorophosphate (**8**): To compound **2** (2.0 mmol, 1.063 g) or **5** (2.0 mmol, 1.241 g) dissolved into water (6 mL) in a 50 mL beaker was added dropwise saturated NH_4PF_6 aqueous (30 mL) solution. A large amount of white solid appeared. The solid was filtered and washed with water to give the product as a white solid in 99% yield (1.49 g). M.p. 235–237 °C. IR (KBr): 3431, 3334, 3465, 1662, 1638, 1615, 1572, 1455, 1401, 1190, 892, 841, 757, 558 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) δ = 9.96 (s, 2H, NC*H*N), 8.48 (d, *J* = 4.0 Hz, 2H, C_5H_5N), 8.11 (d, *J* = 8.0 Hz, 2H, C_6H_4), 7.98 (d, *J* = 7.6 Hz, 2H, C_6H_4), 7.91 (t, *J* = 7.2 Hz, 2H, C_5H_5N), 7.72-7.65 (m, 6H, C_5H_5N, C_6H_4), 7.40–7.37 (m, 2H, C_5H_5N), 5.93 (s, 4H, NCH_2C), 4.73 (t, *J* = 6.8 Hz, 4H, NCH_2), 2.67–2.63 (m, *2*H, CH_2). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 152.8, 149.5, 143.1, 137.5, 131.3, 131.0, 126.8, 126.6, 123.7, 122.7, 113.8, 113.6, 50.8, 43.9, 28.0. Anal. Calcd for $C_{29}H_{28}F_{12}N_6P_2$ (750.50 g mol^{-1}): C, 46.41; H, 3.76; N, 11.20. Found: C, 46.29; H, 3.80; N, 11.37%.

1,1′-Di-(pyridin-2-ylmethyl)-4,4′-(1,3-butanediyl)bisbenzoimidazolium dihexafluorophosphate (**9**): To compound **3** (2.0 mmol, 1.091 g) or **6** (2.0 mmol, 1.269 g) dissolved into water (6 mL) in a 50 mL beaker was added dropwise saturated NH_4PF_6 aqueous solution (30 mL). A large amount of white solid appeared. The solid was filtered and washed with water to give the product as a white solid in 99% yield (1.51 g). M.p. 208–209 °C. IR (KBr): 3433, 2170, 1638, 1454, 1401, 1076, 987, 846, 764, 558 cm^{-1}. ^{1}H NMR (DMSO-d_6, 400 MHz) δ = 9.94 (s, 2H, NC*H*N), 8.41 (d, *J* = 4.4 Hz, 2H, C_5H_5N), 8.10–8.08 (m, 2H, C_6H_4), 7.97–7.88 (m, 4H, C_5H_5N, C_6H_4), 7.68–7.65 (m, 6H, C_5H_5N, C_6H_4), 7.37–7.34 (m, 2H, C_5H_5N), 5.92 (s, 4H, NCH_2C), 4.65 (s, 4H, NCH_2), 2.03 (s, 4H, CH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 152.8, 149.5, 143.1, 137.5, 131.3, 130.9, 126.8, 126.5, 123.6, 122.7, 113.8, 113.7, 50.7, 46.1, 25.4. Anal. Calcd for $C_{30}H_{30}P_2F_{12}N_6$ (764.53 g mol^{-1}): C, 47.13; H, 3.96; N, 10.99. Found: C, 46.88; H, 3.90; N, 11.15%.

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