

Novel building blocks for crystal engineering: the first synthesis of oligo(imidazole)s†

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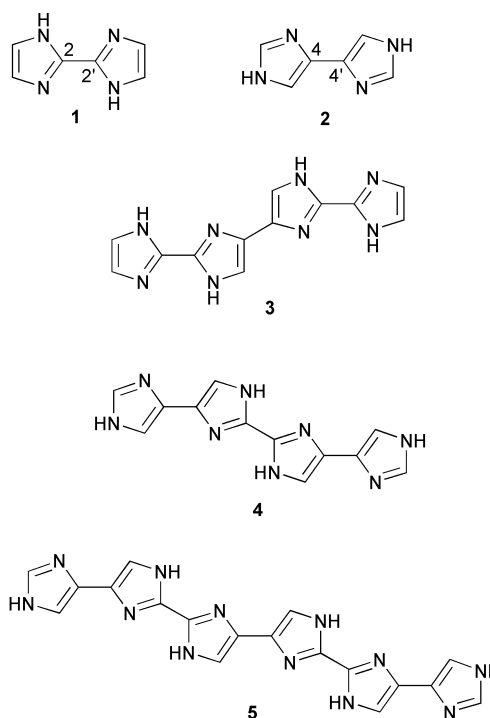
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A 4,4'-biimidazole, two kinds of quaterimidazoles, and a sexiimidazole were designed and synthesized for the first time as novel building blocks for supramolecules. The one-dimensional zigzag ribbonlike hydrogen-bonded structure of 4,4'-biimidazole containing protonated 4,4'-biimidazole was confirmed by single crystal structure analysis.

Noncovalent interactions such as hydrogen-bonding (H-bonding), coordination bonding and π - π interactions play a central role in the creation of a variety of molecular architectures for supramolecules and molecular recognition in chemical, physical and biological sciences.¹ 2,2'-Biimidazole (**1**) is a bidentate chelating ligand and possesses one-dimensional intermolecular parallel H-bonded chain structures in the solid state.² Recently, we have demonstrated that a monoanion of **1** served as an interesting building block for assembled metal complexes through the N-H...N type complementary H-bonding interactions.³ Furthermore, **1** can act as a redox-active molecule and form a variety of charge-transfer (CT) complexes with electron-deficient molecules.⁴ Despite the rich chemistry of **1**, the studies of 4,4'-biimidazole (**2**), which is an isoelectronic isomer of **1** with a centrosymmetric nature, and its derivatives are not sufficiently explored.⁵ Thus, the studies on **2** and its derivatives, designed in view of the introduction of a 4,4'-biimidazole moiety and amplification of the coordination sites with proton donor and acceptor functionalities, may provide a unique opportunity for the construction of novel molecular assemblies. In addition to compound **2**, we describe herein the novel oligo(imidazole)s **3**, **4** and **5**, which are composed only of imidazole moieties by linear ring assemblies in 4,4'- and 2,2'-fashions. We report on their first synthesis, rapid tautomerization in solution and intermolecular H-bonding nature in the solid state.

The syntheses of the novel oligo(imidazole)s were achieved by metal-induced homo-coupling reactions as key steps (Scheme 1). The amino groups of 2,2'-biimidazole (**1**) were protected by SEM-Cl (SEM = [2-(trimethylsilyl)ethoxy]methyl), and the resulting SEM-amine **6** was brominated by NBS, to give a mixture of 4-bromo- and 5-bromo-2,2'-biimidazole derivatives (**7** and **8**). The regiochemistries of **7** and **8** were unambiguously determined in terms of the measurement of a NOESY spectrum. The homo-coupling reaction of the 4-bromo-derivative **7** with an *in situ* generated stoichiometric amount of a Ni(0) reagent in a DMF solution in a sealed ampule gave a quaterimidazole **9** in moderate yield, while the reaction of 5-bromo-derivative **8** under the same conditions gave **6** (yield 80%) and no homo-coupling product.⁶ In the case of 4,4'-biimidazole-based compounds, **2**, **4** and **5**, the synthesis commenced with the SEM-protection reaction of 4-iodoimid-

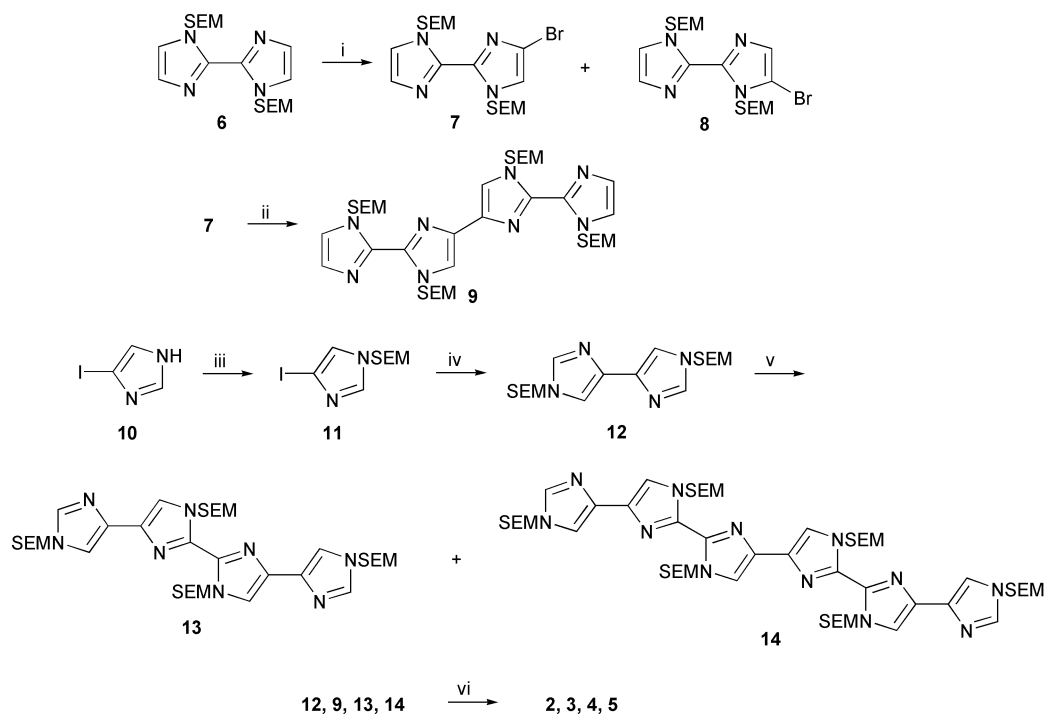


azole (**10**).^{7,8} Treatment of the resulting SEM-amine **11** with a catalytic amount of palladium(0) in the presence of Et₃N in a DMF solution in a sealed ampule⁵ gave the 4,4'-biimidazole derivative **12** in high yield. The dimerization and trimerization reactions of **12** were conducted by the lithiation reaction using one equivalent of *n*-BuLi in a THF solution followed by the addition of one equivalent of CuBr·SMe₂ with continuous bubbling of O₂, to furnish quaterimidazole **13** and sexiimidazole **14**.⁹ Alternative oxidising agents for the lithiated derivative of **12**, CuCl₂ or [Fe(C₅H₅)₂]⁺PF₆⁻, gave no coupling product or only 19% yield of **13**, respectively. The final deprotection reactions of the resulting SEM-amines **12**, **9**, **13** and **14** were carried out by the treatment of a 5 M HCl solution, to give oligoimidazoles **2**, **3**, **4** and **5**, respectively, as white-yellowish gray powders.¹⁰

¹H NMR spectra of these oligo(imidazole)s measured at 80 °C in DMSO-*d*₆ show broad singlet signals in the aromatic region with a ratio of 1 : 1 (for **2**), 1 : 2 (for **3**), 1 : 1 : 1 (for **4**) and 1 : 1 : 1 : 1 (for **5**), indicating the reversible exchange of all N-H protons by rapid tautomerization.

For the investigation of the intermolecular H-bonding nature in the solid state, we have measured IR spectra in KBr. The observed widely spread absorption bands around 3700–2500 cm⁻¹ indicate the strong N-H...N intermolecular H-bonding interactions in the solid state. Fortunately, the monocation dimer containing a neutral component of 4,4'-biimidazole,

† Electronic supplementary information (ESI) available: synthetic procedures and characterisation details for **2**, **3**, **4** and **5**, and X-ray crystallographic data and packing views. See <http://www.rsc.org/suppdata/p1/b2/b208777d/>



Scheme 1 Reagents and conditions: (i) 1.1 equiv. NBS, CCl_4 , reflux, 2.5 h, 21% (for **7**), 28% (for **8**); (ii) $\text{NiCl}_2(\text{PPh}_3)_2\text{-PPh}_3$ (2 equiv.)–Zn, DMF, 100 °C, 46 h, in a sealed ampule, 40%; (iii) NaH, DMF, rt; SEM–Cl, 40 °C, 51%; (iv) 4 mol% $\text{Pd}(\text{PPh}_3)_4$, 8 equiv. Et_3N , DMF, 100 °C, 72 h, in a sealed ampule, 93%; (v) *n*-BuLi, THF, –78 °C, 1 h; $\text{CuBr}\cdot\text{SMe}_2$, O_2 bubbling, –78 °C, 2 h, 41% (for **13**), 3% (for **14**); (vi) 5 M HCl aq, EtOH, reflux, 3 h; neutralization with 25% NH_3 aq or sat. K_2CO_3 aq, 54% (for **2**), 98% (for **3**), 79% (for **4**), 80% (for **5**).

$2\cdot(2\cdot\text{HCl})_2(\text{H}_2\text{O})_2$ crystallises in the monoclinic space group $C2/c$, which provides the first structural study based on 4,4'-biimidazole (Fig. 1).[‡] The monoprotonated monocation of

3.40 Å face-to-face distance (Fig. S2). Water molecules interact with the N–H protons of the neutral 4,4'-biimidazole, while Cl^- interacts with those of the monocation dimer. Furthermore, the interactions between the water molecules and Cl^- form anionic networks along the *b*-axis and may actually play an important role in the generation and stabilization of the three-dimensional lattice structure.

In conclusion, we have prepared a series of oligo(imidazole)s for the first time. A single crystal of $2\cdot(2\cdot\text{HCl})_2(\text{H}_2\text{O})_2$ has demonstrated that the zigzag ribbonlike H-bonding network of 4,4'-biimidazole compared to that of 2,2'-biimidazole.² Investigations are currently being conducted for obtaining the assembled metal complexes as well as the CT complexes.

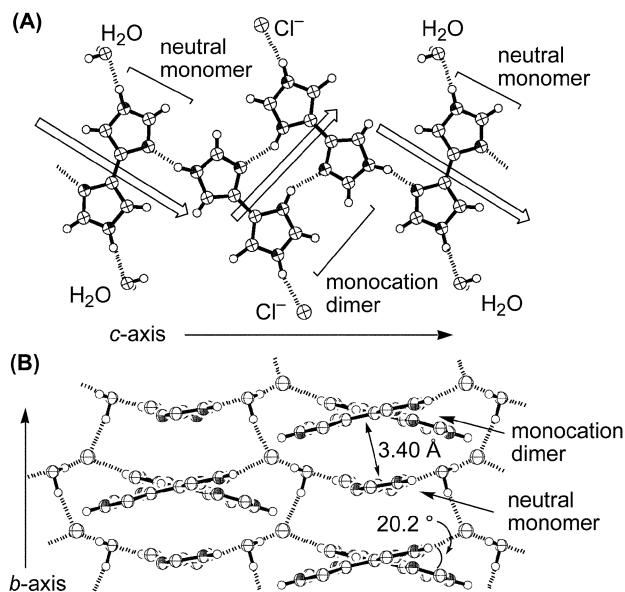


Fig. 1 Crystal structure of $2\cdot(2\cdot\text{HCl})_2(\text{H}_2\text{O})_2$. One-dimensional zigzag ribbonlike H-bonded structure elongated along the *c*-axis (A), the arrows show the zigzag ribbonlike H-bonding network; stacking of the neutral monomer with the monocation dimer elongated along the *b*-axis (B). This view direction is approximately the [101].

4,4'-biimidazole formed a dimer structure through the complementary double N–H \cdots N H-bondings, and this dimer interacted with two neutral 4,4'-biimidazoles by single N–H \cdots N H-bonding, resulting in the formation of a one-dimensional H-bonded structure elongated along the *c*-axis in a zigzag fashion (Fig. S2). Each component of the monocation dimer was found to be twisted by 20.2°, and the imidazole ring of 4,4'-biimidazole was also twisted by 20.2° with respect to the central C–C bond (Fig. S2). The monocation dimer and neutral 4,4'-biimidazole form an alternated stacking column with

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Notes and references

[‡] The single crystal of $2\cdot(2\cdot\text{HCl})_2(\text{H}_2\text{O})_2$ was obtained from $2\cdot(\text{HCl})_2$ by partial neutralization with an aqueous NH_3 solution in MeOH. $\text{C}_{18}\text{H}_{24}\text{Cl}_2\text{N}_{12}\text{O}_2$, $M = 511.37$, crystal dimensions $0.10 \times 0.40 \times 0.40$ mm³, yellow color, Rigaku AFC7R (rotating anode), CuK α radiation, $T = 23.0$ °C, monoclinic, space group $C2/c$ (no. 15), $a = 23.445(3)$ Å, $b = 6.949(3)$ Å, $c = 15.974(2)$ Å, $\beta = 111.514(7)^\circ$, $V = 2421.2(9)$ Å³, $Z = 4$, $D_{\text{calcd}} = 1.403$ g cm⁻³, 2325 reflections collected, 1960 unique intensities reflections observed [$I > 3.0 \sigma(I)$], $2 \theta_{\text{max}} = 130.1^\circ$, structure solution with direct methods (SIR92) and refinement on F with 167 parameters, R (R_w) = 0.056 (0.105), S (GOF) = 1.25. CCDC reference number 188286. See <http://www.rsc.org/suppdata/p1/b2/b208777d/> for crystallographic data in .cif or other electronic format.

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- 5 The derivatives of 2,4'- and 4,4'-biimidazoles are known (see: P. J. Steel, in *Advances in Heterocyclic Chemistry*, ed. A. R. Katritzky, Academic Press, New York, 1997, vol. 67, pp. 1–117), but 4,4'-biimidazole itself is an unknown molecule, see also; (a) M. D. Cliff and S. G. Pyne, *Synthesis*, 1994, 681–682.
- 6 **Procedure for 9.** The Ni(0) reagent generated from NiCl₂(PPh₃)₂ (251 mg, 0.38 mmol), PPh₃ (201 mg, 0.77 mmol) and activated Zn (25 mg, 0.38 mmol) in DMF (2 mL) was mixed with the 4-bromobiimidazole **7** (181 mg, 0.38 mmol). After being degassed by a repeated freeze–pump–thaw method the tube was sealed and the mixture was stirred at 100 °C for 46 h. The reaction mixture was poured into a sat. NaCl aqueous solution and the resulting mixture was extracted with ethyl acetate. For details, see the ESI†.
- 7 (a) K. L. Kirk, *J. Heterocycl. Chem.*, 1985, **22**, 57–59; (b) H. B. Bensusan and M. S. R. Naidu, *Biochemistry*, 1967, **6**, 12–15; (c) K. J. Brunings, *J. Am. Chem. Soc.*, 1947, **69**, 205–208; (d) B. Iddon and B. L. Lim, *J. Chem. Soc., Perkin. Trans. 1*, 1983, 735–739.
- 8 We have also prepared the *tert*-butyloxycarbonyl- and triphenylmethyl derivatives of 4-iodoimidazole. But the next dimerization and further oligomerization reaction did not proceed at all.
- 9 **Procedure for 13 and 14.** The biimidazole **12** (2.00 g, 5.06 mmol) was dissolved with THF (20 mL). *n*-BuLi (1.6 M hexane solution, 3.30 mL, 5.28 mmol) was added at –78 °C, and the reaction mixture was stirred at this temperature for 1 h. CuBr·SMe₂ (1.04 g, 5.06 mmol) was added to this mixture at –78 °C, and the reaction mixture was stirred with O₂-bubbling at this temperature for 2 h. After addition of a sat. Na₂S₂O₃ aqueous solution, the resulting mixture was extracted with ethyl acetate. For details see ESI†.
- 10 Selected physical data: **2**, mp 280–282 °C; TLC *R_f* 0.24 (MeOH); ¹H NMR (270 MHz, DMSO-*d*₆) δ 7.19 (br s, 2H), 7.58 (s, 2H); IR (KBr)/cm⁻¹ 3600–2200, 1531, 754 cm⁻¹; EI-MS, *m/z* 134 (M⁺, 100%); anal. calcd for C₆H₆N₄: C, 53.72; H, 4.51; N, 41.77. Found: C, 53.68; H, 4.40; N, 41.51. **3**, mp 298–300 °C; ¹H NMR (270 MHz, DMSO-*d*₆, 80 °C) δ 7.08 (s, 2H), 7.37 (s, 1H); IR (KBr) 3600–2400, 1530 cm⁻¹; EI-MS, *m/z* 266 (M⁺, 100%); anal. calcd for C₁₂H₁₀N₈: C, 54.13; H, 3.79; N, 42.08. Found: C, 46.16; H, 4.47; N, 34.96. **4**, mp 280–282 °C; ¹H NMR (270 MHz, DMSO-*d*₆, 80 °C) δ 7.24 (s, 2H), 7.32 (s, 2H), 7.59 (s, 2H); IR (KBr) 3600–2400, 1534, 758 cm⁻¹; EI-MS, *m/z* 266 (M⁺, 64%); anal. calcd for (C₁₂H₁₀N₈)(H₂O)₄: C, 42.60; H, 5.36; N, 33.12. Found: C, 42.72; H, 5.24; N, 32.76. **5**, mp >300 °C; TLC *R_f* 0.31 (1 : 1 : 1 BuOH–H₂O–formic acid); ¹H NMR (270 MHz, DMSO-*d*₆, 80 °C) δ 7.27 (s, 2H), 7.35 (br s, 2H), 7.41 (br s, 2H), 7.61 (s, 2H); FAB-MS *m/z* 399 (M⁺ + H); IR (KBr) 3500–2200, 1526 cm⁻¹; anal. calcd for C₁₈H₁₄N₁₂: C, 54.27; H, 3.54; N, 42.19. Found: C, 44.11; H, 3.94; N, 33.12. Due to the highly hygroscopic nature and difficulties in removing the salts, especially KCl, the elemental analyses do not always give the appropriate values. The elemental analyses of the corresponding SEM-amines and the HCl salts of **2–5**, however, can provide alternative characterization of **2–5**; see ESI†.