Bis(1-methylimidazol-2-yl)propionates and Bis(1-methylbenzimidazol-2-yl)-propionates: A New Family of Biomimetic *N,N,O* Ligands – Synthesis, Structures and Cu^{II} Coordination Complexes

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A general synthetic route towards new tridentate, tripodal *N,N,O* ligands, bearing one carboxylate group and two of the biologically relevant imidazole moieties, is presented. The parent compounds of this new family of ligands, A[MIm_2Pr] (**1**) and A[$BenzMIm_2Pr$] (**2**) (A = H, K, Bu_4N) were synthesized in two steps and high overall yield. The structures of $HMIm_2Pr$ (**1a**) and $HBenzMIm_2Pr$ (**2a**) were confirmed by X-ray crystal structure determination, both molecules forming infinite one-dimensional hydrogen bonded chains. The synthetic route allows for the fine-tuning of the physical properties of both ligand systems, e.g., solubility and ease of crystallization. The capability of the two ligands to coordinate facially through all donor atoms was investigated and two isostructural mononuclear copper(II) complexes of the type [CuL_2] were obtained. Both [$Cu(MIm_2Pr)_2$]·$2H_2O$ (**3**) and [$Cu(BenzMIm_2Pr)_2$]·$3.12(H_2O)$·$1.74(C_2H_5OH)$ (**4**) have been characterized by X-ray crystallography, ESI-MS, elemental analysis, UV/Vis, IR, and EPR spectroscopy. In both structures the copper atoms are on an inversion center, which results in a tetragonally distorted octahedral coordination geometry. The CuN_4O_2 chromophores consist of four equatorially coordinated imidazole nitrogen atoms and two axially coordinated carboxylate groups. The non-coordinated water molecules of both crystal structures are involved in a one-dimensional hydrogen-bonded network. Two neighboring octahedrons are connected by two water molecules, each water molecule forming two hydrogen bonds with the non-coordinated oxygen atoms of the carboxylate group. This results in the formation of infinite one-dimensional chains. EPR spectroscopy and ESI-MS measurements provide evidence for the integrity of the complexes in solution.

Introduction

The study of synthetic active site analogues has made a vast contribution to the understanding of the structure-function relationship of many metalloenzymes, as has been recently highlighted in a thematic review issue.[1] In particular, the use of tripodal ligand systems has received much attention, the most well-known example probably being the tris(pyrazolyl)borates.[2] Despite their remarkable versatility and the impressive results that have been obtained, these "scorpionates" also illustrate two of the drawbacks associated with many of the reported tripodal ligands. First, most ligand systems are fully symmetrical and provide, for instance, an all-*N* donor set. Second, the *N* donor groups are often found to be non-biologically relevant heterocycles (such as pyrazole or pyridine), which differ both in size, and chemical and electronic properties from the histidyl imidazole-side chain found in biological systems. Since the coordination environment of many metalloenzyme active sites is made up of different donor groups, the interest of synthetic chemists has shifted towards the design of *mixed* ligand systems incorporating different functionalities, i.e. "heteroscorpionates".[3]

We are particularly interested in a group of enzymes exhibiting the so-called 2-His-1-carboxylate motif at their active site.[4,5] This structural motif is found in several crystallographically characterized mononuclear non-heme iron enzymes,[5] like deacetoxycephalosporin C synthase (DAOCS)[6] and naphthalene 1,2-dioxygenase (NDO),[7] in which two histidines and one carboxylate occupy one face of the iron(II) coordination environment. The same facial

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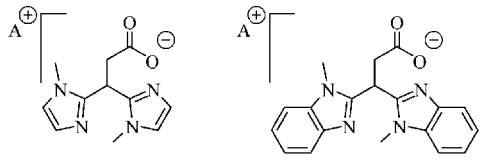
capping by two histidines and one carboxylate is found in several zinc containing enzymes, e.g. carboxypeptidase and thermolysin.[8] This triad is therefore an interesting target for structural modeling.

Most modeling efforts at mimicking this facial triad used either the tridentate tris(pyrazolyl)borato-*N*,*N*,*N* or the tetradentate tris(2-pyridylmethyl)amine-*N*,*N*,*N*,*N*′ ligands.[5,8] However, suitable structural mimics of this triad should preferably be tridentate, tripodal, monoanionic ligands systems with a potentially facially coordinating *N*,*N*,*O* donor set. *N*,*N*,*O* ligands are relatively rare and, to the best of our knowledge, only three tridentate examples have been reported of these mixed ligands bearing a carboxylate group. The bis(pyrazol-1-yl)acetates were introduced by Otero et al.[9] and have been studied by Burzlaff et al. as mimics of the 2-His-1-carboxylate motif.[10] A drawback of this system is the use of the non-biologically relevant pyrazole groups as the two *N* donor groups. The second example is the bis(imidazolyl)propionato ligand (HBIP) already reported in the late 1970s by Joseph et al.[11] This ligand system, however, suffers from a difficult synthetic route, complicating acid-base chemistry, and limited solubility in non-aqueous media. Parkin indirectly constructed an *N*,*N*,*O* donor set by the insertion of carbon dioxide or formaldehyde into the B–H bond of a [bis(pyrazolyl)hydroborato]zinc complex.[12]

Recently, we became interested in biomimetic ligand systems which in principle could accommodate the desired facial coordination geometry and would incorporate the biologically relevant *N*,*N*,*O* donor atom set. A further requirement would be access to a straightforward synthetic route, which would allow for facile modification of the *N*,*N*,*O* ligands and therefore tuneability of their physical properties.

With this in mind, we have developed a new *N*,*N*,*O* ligand family, i.e. the 3,3-bis(1-methylimidazol-2-yl)- and 3,3-bis(1-methylbenzimidazol-2-yl)propionates **1** and **2**, incorporating the biomimetic 1-methylimidazole and carboxylate groups in a tripodal, monoanionic, tridentate ligand framework (Figure 1).



A[MIm$_2$Pr] (1) **A[BenzMIm$_2$Pr] (2)**

Figure 1. *N*,*N*,*O* ligands A[MIm$_2$Pr] (**1**) and A[BenzMIm$_2$Pr] (**2**)

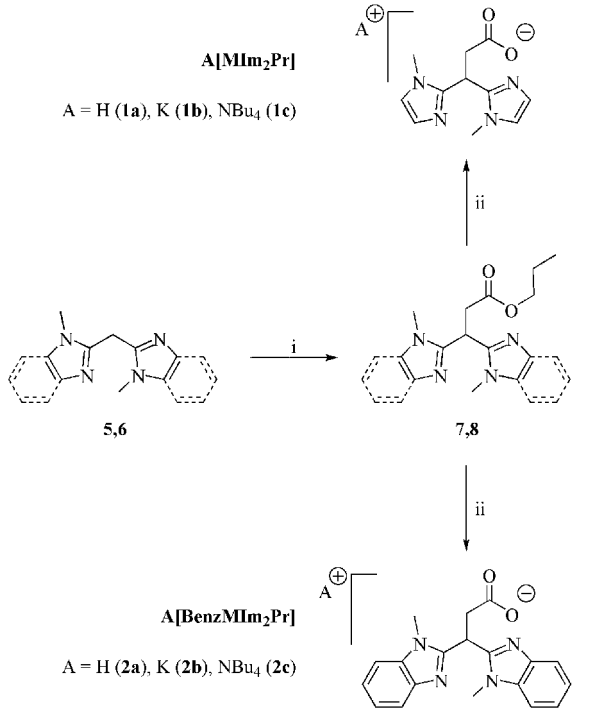
These *N*,*N*,*O* ligands are also of interest in connection with the biomimetic study of copper proteins. Various (polynuclear) copper enzymes are known in which the metal centers are found in an imidazole-rich coordination environment.[13] Furthermore, copper(II) can be used as a probe metal to test the ability of the ligands to facially cap a metal center.[14]

Herein we report the synthesis and structural characterization of two new *N*,*N*,*O* ligands, A[MIm$_2$Pr] (**1**) and A[BenzMIm$_2$Pr] (**2**) (A represents different possible cations), and their copper(II) coordination complexes.

Results

Synthesis and Structural Characterization of the *N*,*N*,*O* Ligands

A general synthetic route for the 3,3-bis(1-methylimidazol-2-yl)- and 3,3-bis(1-methylbenzimidazol-2-yl)propionates was developed (Scheme 1). This route is based on the readily available bis(1-methylimidazol-2-yl)methane framework. Both bis(1-methylimidazol-2-yl)methane (**5**)[15] and bis(1-methylbenzimidazol-2-yl)methane (**6**)[16] can be easily synthesized on a multigram scale.



Scheme 1. i) a. *n*-butyllithium, –78 °C, 1 h, b. propyl bromoacetate, –78 °C → room temp., overnight; ii) a. 1 equiv. KOH, room temp., 3 h, b. 1 equiv. HCl (**1a/2a**); 1 equiv. KOH, room temp., 3 h (**1b/2b**); 1 equiv. [Bu$_4$N]OH, room temp., 3 h (**1c/2c**)

Lithiation of **5** and **6** at the bridging methylene group with *n*-butyllithium at –78 °C in THF and subsequent dropwise addition of propyl bromoacetate resulted in the clean formation of the propyl esters MIm$_2$PrPr (**7**) and BenzMIm$_2$PrPr (**8**). Basic hydrolysis of these ligand precursors in THF with 1 equiv. of a potassium hydroxide solution in water gave the potassium salts of 3,3-bis(1-methylimidazol-2-yl)propionic acid, K[MIm$_2$Pr] (**1b**), and 3,3-bis(1-methylbenzimidazol-2-yl)propionic acid, K[BenzMIm$_2$Pr] (**2b**), in quantitative yields. Likewise, treatment of the esters with [Bu$_4$N]OH resulted in the quantita-

tive formation of the tetrabutylammonium salts [Bu_4N][MIm_2Pr] (**1c**) and [Bu_4N][$BenzMIm_2Pr$] (**2c**). Subsequent addition of 1 equiv. of hydrochloric acid to a solution of the hydrolyzed esters and purification by recrystallization gave 3,3-bis(1-methylimidazol-2-yl)propionic acid, $HMIm_2Pr$ (**1a**), and 3,3-bis(1-methylbenzimidazol-2-yl)propionic acid, $HBenzMIm_2Pr$ (**2a**), in good yields. The propionate salts **1b/1c** and **2b/2c** are very hygroscopic and can only be obtained as fine powders if they are completely solvent-free. This is also reflected in the IR spectra of the compounds. The exact position of the bands depends on the amount of water present in the sample or accumulated during measurement. The carboxylate group asymmetric stretching vibrations $\nu_{as}(COO^-)$ can be found at 1702 (**1a**) and 1716 cm^{-1} (**2a**) for the acids and at 1581 (**1b/1c**) and 1597 (**2c**) for the K and Bu_4N salts. The $\nu_{as}(COO^-)$ of **2b** is split into two bands of equal intensity at 1582 and 1598 cm^{-1}. The symmetric stretch vibration $\nu_s(COO^-)$ is less intense and could only be unambiguously identified for the potassium salts **1b** and **2b** (1393 and 1386 cm^{-1}, respectively).

The molecular structures of acids **1a** and **2a** were studied by single-crystal X-ray diffraction (Figure 2). Suitable single crystals of $HMIm_2Pr$ (**1a**) were obtained by slow vapor diffusion of diethyl ether into a methanolic solution. Recrystallization of the crude product from ethanol/water (95:5) resulted in the formation of a different crystalline phase.[17] Single crystals of $HBenzMIm_2Pr$ (**2a**) were obtained by slow cooling of a hot, saturated solution of **2a** in methanol.

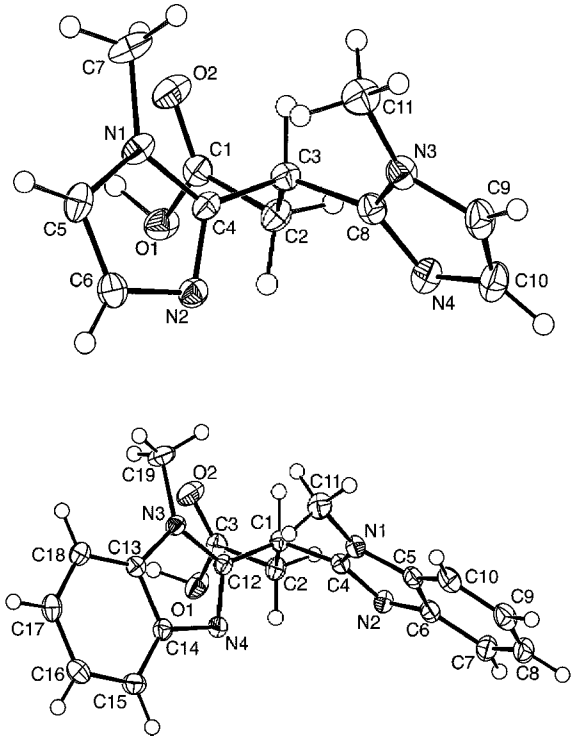


Figure 2. Molecular structure of $HMIm_2Pr{\cdot}MeOH$ (**1a**, top) and $HBenzMIm_2Pr$ (**2a**, bottom) in the crystals; the co-crystallized molecule of methanol (**1a**) has been omitted for clarity; displacement ellipsoids are drawn at the 50 % probability level

The molecular structures of the acids **1a** and **2a** are very similar and their solid-state structures clearly show the general predisposition of tripodal ligands towards facial capping of a metal center.[8b] Rotation around a single C–C bond, i.e. C2–C3 in **1a**, will orient the *N,N,O* lone pairs to a virtual metal center in a facial manner. Interestingly, **1a** and **2a** do not crystallize as zwitterions; the carboxylate oxygen atom O1 is protonated, the imidazole nitrogen atoms are non-protonated. Thus, atom O1 can act as hydrogen-bond donor and the imidazole nitrogen atoms as hydrogen-bond acceptors. In the solid state, molecules of $HMIm_2Pr$ (**1a**) thus form an infinite hydrogen-bonded chain along the crystallographic *c*-axis (Figure 3, Table 1). The co-crystallized methanol solvent molecule is also participating as a hydrogen-bond donor with imidazole nitrogen atom N4 as acceptor. Consequently, both imidazole nitrogen atoms are used for hydrogen bonding. In the crystal structure of **2a**, there are no co-crystallized solvent molecules and therefore only imidazole nitrogen atom N4 accepts hydrogen bonds to form a one-dimensional hydrogen bonded chain along the crystallographic *c*-axis (see Table 1 and Supporting Information). In both crystal structures the non-protonated oxygen atom O2 is not involved in strong hydrogen bonds. Weak C–H···O and C–H···N interactions involve O2 in both structures and nitrogen atom N2 of compound **2a**; π-π stacking interactions between the aromatic systems of the (N1,N2,C4–C10)-benzimidazole rings with average interplanar distances of 3.40 and 3.49 Å are also observed for **2a** (see Supporting Information).

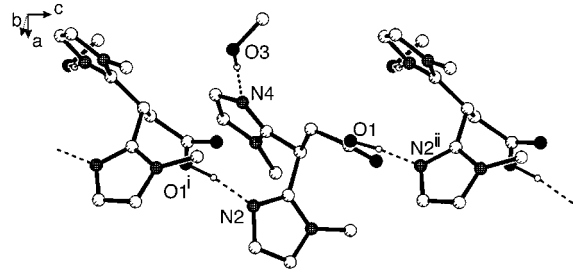


Figure 3. Hydrogen bonding pattern in $HMIm_2Pr$ (**1a**); C–H hydrogen atoms have been omitted for clarity; symmetry operations: i: *x*, 0.5 – *y*, *z* – 0.5; ii: *x*, 0.5 – *y*, *z* + 0.5

Table 1. Selected hydrogen bond lengths [Å] and angles [°] for $HMIm_2Pr{\cdot}CH_3OH$ (**1a**) and $HBenzMIm_2Pr$ (**2a**); symmetry operations: i: *x*, 0.5 – *y*, *z* + 0.5; ii: *x*, 1.5 – *y*, *z* + 0.5

	Donor–H···Acceptor	D–H	H···A	D···A	D–H···A
1a	O1–H1O···N2^{i}	1.02(2)	1.65(2)	2.6649(13)	171(2)
	O3–H3O···N4	0.86(2)	2.01(2)	2.8589(16)	171.8(17)
2a	O1–H1O···N4^{ii}	1.02(2)	1.65(2)	2.6659(13)	171(2)

Synthesis of Cu^{II} Complexes

To investigate the facial capping potential of the new *N,N,O* ligands, their coordination chemistry towards copper(II) cations was investigated. Two new, neutral copper complexes of the type [CuL_2] were synthesized and charac-

terized by X-ray crystallography, IR, UV/Vis and EPR spectroscopy, and ESI-MS. The mononuclear copper complex $[Cu(MIm_2Pr)_2]\cdot 2H_2O$ (**3**) was obtained by reaction of 1 equiv. of $CuCl_2\cdot 2H_2O$ with 2 equiv. of $K[MIm_2Pr]$ (**1b**) in hot ethanol. Complex **4**, identified as $[Cu(BenzMIm_2Pr)_2]\cdot 3.12(H_2O)\cdot 1.74(C_2H_5OH)$, with a comparable coordination environment was isolated when $CuCl_2\cdot 2H_2O$ was treated with 2 equiv. of $K[BenzMIm_2Pr]$ (**2b**) in hot ethanol. In both cases, blue single crystals suitable for X-ray diffraction analysis crystallized after several weeks. The complexes can also be obtained directly as powders, nicely illustrating how the judicious choice of solvent and ligand cation can simplify isolation and purification (see Discussion section). In this way, reaction of $CuCl_2$ with 2 equiv. of $[Bu_4N][BenzMIm_2Pr]$ (**2c**) in dry methanol resulted in the formation of the pale blue precipitate $[Cu(BenzMIm_2Pr)_2]$. Separation by centrifugation and purification by simple washings with dichloromethane allowed for the facile isolation of the copper complex.

Description of the Crystal Structures

[Cu(MIm$_2$Pr)$_2$]·2H$_2$O (3)

Two monoanionic MIm_2Pr ligands were found to be arranged centrosymmetrically around the copper ion, coordinating through all three donor groups, i.e. two 1-methylimidazole nitrogen atoms and one carboxylate oxygen atom each, resulting in an elongated octahedral geometry (Figure 4). The four 1-methylimidazole imine nitrogen atoms occupy the equatorial plane [Cu–N 2.0109(18) and 1.9929(18) Å] and the two carboxylate oxygen atoms are located in the axial positions [Cu–O 2.4004(17) Å]. Crystallographic data and selected bond lengths and angles are given in Tables 2 and 3. The Cu–N bond lengths are similar to those found in other CuN_4O_2 chromophores with imidazole nitrogen donors.[18,19] The Cu–O bonds are shorter than those found in, for instance, bis(acetato)tetrakis(imidazole)copper(II),[20] due to ligand constraints.

The non-coordinated water molecules are involved in a one-dimensional hydrogen-bonded network. Two neighboring octahedrons are connected by two water molecules, each water molecule forming two hydrogen bonds to the non-coordinated oxygen atoms of the carboxylate group. This results in the formation of infinite linear chains in the direction of the crystallographic *a*,*b*,*c*-diagonal as shown in Figure 5. The OH stretching vibrations characteristic for hydrogen-bonded water molecules are present in the IR spectrum of **3** at 3347 cm^{-1}. A related $[CuL_2]$ structure was recently reported for $[Cu(bdmpza)_2]\cdot 2H_2O$ [bdmpza = bis(3,5-dimethylpyrazol-1-yl)acetate] by Reedijk et al. in which the two co-crystallized water molecules play an identical role.[20] Copper(II) complexes of the related HBIP ligand have also been reported, but no facial capping of the ligand through all donor atoms was observed.[21]

[Cu(BenzMIm$_2$Pr)$_2$]·3.12(H$_2$O)·1.74(C$_2$H$_5$OH) (4)

Complex **4** was found to have a comparable copper geometry as in complex **3** (Figure 6). Crystallographic data

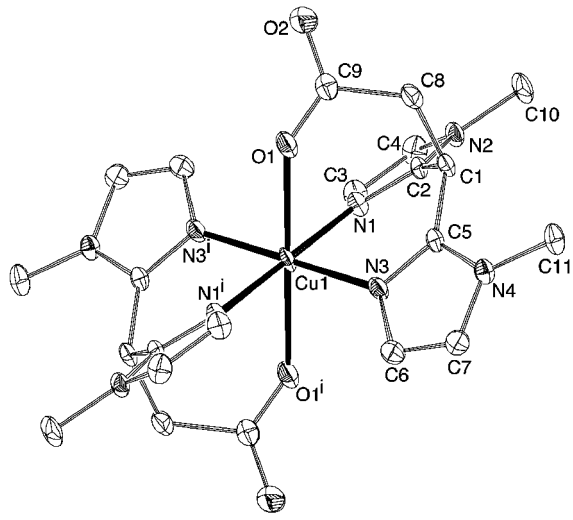


Figure 4. Molecular structure of $[Cu(MIm_2Pr)_2]\cdot 2H_2O$ (**3**) in the crystal; hydrogen atoms and non-coordinated water molecules have been omitted for clarity; displacement ellipsoids are drawn at the 50 % probability level

Table 2. Selected bond lengths [Å] and angles [°] for $[Cu(MIm_2Pr)_2]\cdot 2H_2O$ (**3**) and $[Cu(BenzMIm_2Pr)_2]\cdot 3.12(H_2O)\cdot 1.74(C_2H_5OH)$ (**4**)

$[Cu(MIm_2Pr)_2]\cdot 2H_2O$ (**3**)		$[Cu(BenzMIm_2Pr)_2]\cdot 3.12(H_2O)\cdot 1.74(C_2H_5OH)$ (**4**)	
Cu1–N1	2.0109(18)	Cu1–N1	2.0086(15)
Cu1–N3	1.9929(18)	Cu1–N11	2.0151(15)
Cu1–O1	2.4004(17)	Cu1–O24	2.3475(14)
N1–Cu1–N3	86.45(8)	N1–Cu1–N11	85.58(6)
N3–Cu1–N1^i	93.55(8)	N11–Cu1–N1^i	94.42(6)
N1–Cu1–O1	85.68(7)	N1–Cu1–O24	89.23(6)
N3–Cu1–O1	86.23(7)	N11–Cu1–O24	87.80(6)
N1^i–Cu1–O1	94.32(7)	N1^i–Cu1–O24	90.77(6)
N3^i–Cu1–O1	93.77(7)	N11^i–Cu1–O24	92.20(6)

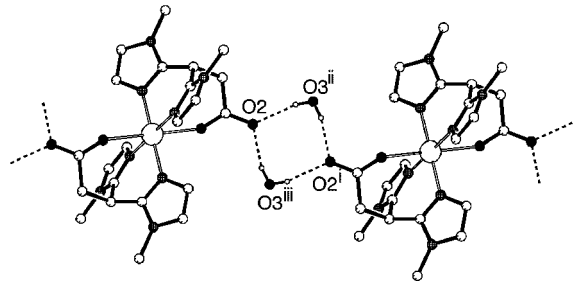


Figure 5. Hydrogen bonding network of **3** resulting in infinite linear chains; C–H hydrogen atoms have been omitted for clarity; symmetry operations: i: –*x*, –*y*, –*z*; ii: –*x*, 1 – *y*, –*z*; iii: *x*, *y* – 1, *z*

and selected bond lengths and angles are given in Tables 2 and 3. The replacement of imidazole for benzimidazole hardly affects the *N*,*N*,*O* tridentate coordination to the copper center. However, the Cu–O bond in **4** [2.3476(14) Å] is significantly shorter than the one found in **3** [2.4005(18) Å]. The Cu–N bond lengths compare well to the only other crystallographically characterized CuN_4O_2 chromophore with four benzimidazole donor groups.[22]

Table 3. Crystallographic data for compounds **1a**, **2a**, **3**, and **4**

	1a	**2a**	**3**	**4**
Empirical formula	$C_{11}H_{14}N_4O_2 \cdot CH_3OH$	$C_{19}H_{18}N_4O_2$	$C_{22}H_{26}CuN_8O_4 \cdot 2H_2O$	$C_{38}H_{34}CuN_8O_4 \cdot 1.74(C_2H_5OH) \cdot 3.12(H_2O)$
Formula mass	266.30	334.37	566.08	866.64
Crystal size [mm]	0.06 × 0.30 × 0.43	0.18 × 0.42 × 0.42	0.12 × 0.12 × 0.18	0.09 × 0.15 × 0.33
Cryst system	monoclinic	monoclinic	triclinic	monoclinic
Space group	$P2_1/c$ (no. 14)	$P2_1/c$ (no. 14)	$P\bar{1}$ (no. 2)	$P2_1/c$ (no. 14)
a [Å]	14.8340(10)	8.5910(1)	8.3128(9)	8.5293(1)
b [Å]	8.2221(6)	22.8189(2)	8.3514(9)	18.8885(2)
c [Å]	10.6605(7)	8.2417(1)	9.9368(17)	12.6452(2)
α [°]	90	90	96.457(13)	90
β [°]	91.652(6)	102.7895(6)	94.540(10)	100.3961(4)
γ [°]	90	90	118.353(8)	90
V [Å^3]	1299.69(15)	1575.59(3)	596.27(14)	2003.77(4)
Z	4	4	1	2
$D_{calcd.}$ [g/cm^3]	1.361	1.410	1.576	1.436
μ [mm^{-1}]	0.100	0.095	0.973	0.612
Absorption correction range	0.90–1.00	-	0.69–0.89	0.88–0.94
Collected reflections	26945	29513	8358	31917
Unique reflections	2975	3623	2708	4591
Parameter/restraints	183/0	232/0	179/0	280/0
$R1/wR2$ [$I > 2\sigma(I)$]	0.0358/0.0869	0.0370/0.0957	0.0410/0.1018	0.0379/0.1033
$R1/wR2$ (all reflections)	0.0485/0.0928	0.0429/0.1000	0.0500/0.1072	0.0494/0.1106
S	1.046	1.032	1.085	1.065
Min/max residual density [e/Å^3]	–0.21/0.23	–0.28/0.29	–0.90/0.73	–0.49/0.51

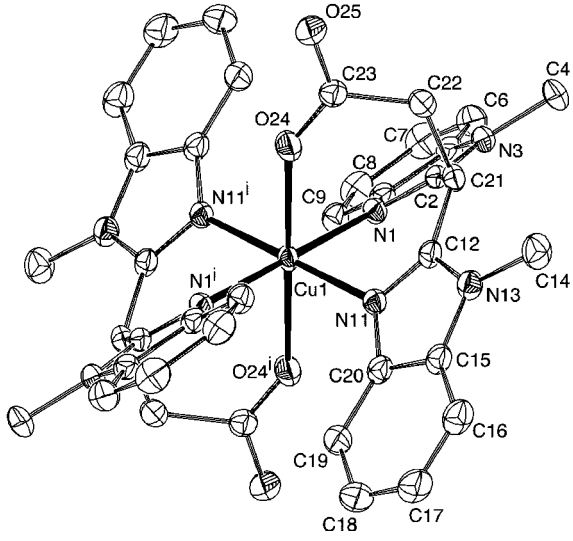


Figure 6. Molecular structure of $[Cu(BenzMIm_2Pr)_2] \cdot 3.12(H_2O) \cdot 1.74(C_2H_5OH)$ (**4**) in the crystal; hydrogen atoms and solvent molecules have been omitted for clarity; displacement ellipsoids are drawn at the 50 % probability level

Also, the hydrogen bonding pattern is similar to the one found in complex **3**. Again two water molecules connect the octahedrons through four hydrogen bonds to form an infinite chain in the direction of the crystallographic *c*-axis. Yet, the water molecules here act also as hydrogen-bond acceptors for co-crystallized ethanol molecules (Figure 7). Additionally, there are water molecules present in the crystal structure which do not participate in the hydrogen bonding. The latter water and ethanol molecule positions in the crystal lattice are not fully occupied (probably due to evaporation), hence the non-integer coefficients in the structural formulation of compound **4**.

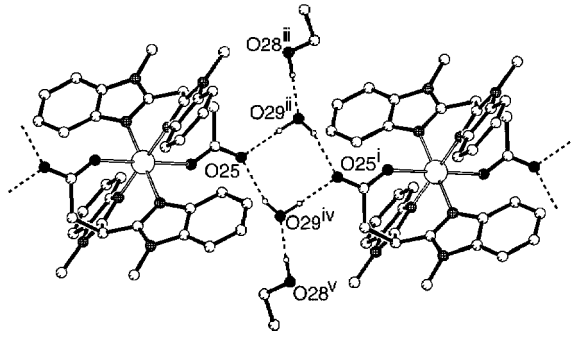


Figure 7. Hydrogen bonding network of **4** resulting in infinite linear chains; C–H hydrogen atoms and water molecules, which do not participate in the hydrogen bonding, have been omitted for clarity; symmetry operations: i: 1 – *x*, 1 – *y*, –*z*; ii: *x*, 0.5 – *y*, *z* – 0.5; iii: *x* – 1, 0.5 – *y*, *z* – 0.5; iv: 1 – *x*, *y* + 0.5, 0.5 – *z*; v: 2 – *x*, *y* + 0.5, 0.5 – *z*

ESI-MS

The ESI mass spectra of **3** and **4** dissolved in a methanol/acetonitrile mixture were recorded and very clean spectra were obtained for both complexes. Also, reference spectra of $K[MIm_2Pr]$ (**1b**) and $K[BenzMIm_2Pr]$ (**2b**) were recorded for comparison. For complex $[Cu(MIm_2Pr)_2] \cdot 2H_2O$ (**3**) only two, equally intense peaks were detected. The peak at *m*/*z* 551.78 corresponds to the $\{[Cu(MIm_2Pr)_2] + Na\}^+$ adduct ion, while the peak at *m*/*z* 529.96 is assigned to $\{[Cu(MIm_2Pr)_2] + H\}^+$. The same adduct ions were found for compound **4**, giving an *m*/*z* of 752.14 for

{[Cu(BenzMIm$_2$Pr)$_2$] + Na}$^+$ and 730.25 for {[Cu(BenzMIm$_2$Pr)$_2$] + H}$^+$. The observed copper isotope patterns were in good agreement with the calculated ones and furthermore, no free ligand was found in the spectra of both complexes. These data strongly suggest the prevalence of the [CuL$_2$] motif and shows the complexes [Cu(MIm$_2$Pr)$_2$] and [Cu(BenzMIm$_2$Pr)$_2$] as predominant species in solution.

UV/Vis, EPR

The UV/Vis spectrum of **3** in methanol shows three absorption bands at 215, 293 (sh), and 587 nm. The first two bands are also present in reference spectra of the ligand and are therefore assigned to intraligand transitions. The broad absorption centered at 587 nm is assigned to d–d transitions of the copper(II) center. The d–d band for **4** in methanol was found around 666 nm and four intraligand transitions could be detected (228, 252, 271, and 284 nm). Changing the nitrogen donor groups from imidazole to benzimidazole affects the ligand field splitting parameter and results in a red-shift of about 80 nm for complex **4** with respect to complex **3**. This red shift reflects the smaller axial Jahn–Teller distortion and corresponds to the shorter Cu–O bond as found in the crystal structure of complex **4**. The spectral parameters are in the range expected for d–d transitions of tetragonally distorted monomeric CuN_4O_2 chromophores.[18]

The complexes **3** and **4** were studied by EPR as powders at room temperature and as frozen solutions at 77 K (Figure 8). The solid-state EPR spectra of both complexes at room temperature display broad features due to dipolar coupling of the Cu^{II} centers, but are typically axial with $g_\perp$ = 2.06 and $g_\parallel$ = 2.22 for complex **3** and $g_\perp$ = 2.06 and $g_\parallel$ = 2.25 for complex **4**. The hyperfine splitting of the spectrum with the Cu^{II} ion was observed in the parallel region in both cases with $A_\parallel$ = 200 G (**3**) and $A_\parallel$ = 177 G (**4**), the latter being better resolved. This smaller hyperfine coupling $A_\parallel$ of complex **4** is in line with the red shift observed in the UV/Vis spectra. An EPR spectrum of a frozen solution of **3** in methanol/water (1:5, v/v) was also recorded and again an EPR envelope typical for an axially elongated mononuclear Cu^{II} species was observed ($g_\perp$ = 2.04, $g_\parallel$ = 2.24, $A_\parallel$ = 193 G). Additional superhyperfine splitting due to interaction with the ^{14}N nuclei of the ligands is resolved, consistent with four equivalent nitrogens in the equatorial plane ($A_\perp$ = 15.5 G). A frozen methanolic solution of **4** gave a similar EPR spectrum. Again, both the hyperfine and superhyperfine couplings were resolved and the relevant parameters in this case are $g_\perp$ = 2.05, $g_\parallel$ = 2.25, $A_\parallel$ = 187 G, and $A_\perp$ = 14.5 G. The EPR data of the powders and the frozen solutions are consistent with the structure description derived from the X-ray analyses and the ESI-MS measurements, respectively. The spectral parameters for **3** and **4** are characteristic of tetragonally elongated monomeric copper(II) complexes[23] and are comparable to the EPR parameters obtained for other CuN_4O_2 chromophores with four imidazole nitrogen donors.[18,19]

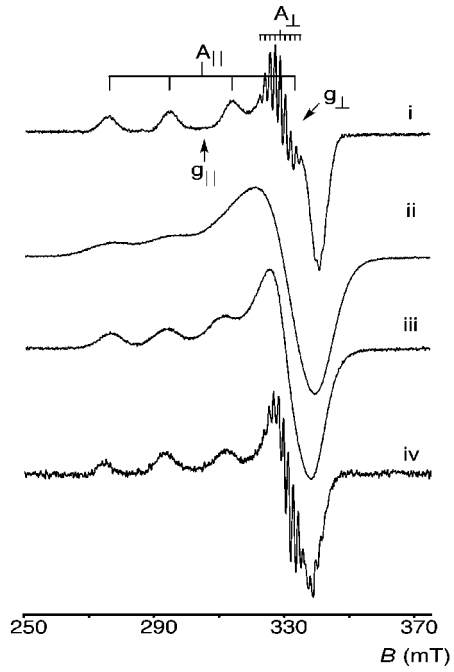


Figure 8. EPR spectra of compounds **3** and **4**; i) frozen methanol/water solution of **3** at 77K, ii) solid **3** at room temp., iii) solid **4** at room temp., iv) frozen methanol solution of **4** at 77K

Discussion and Conclusion

A relatively straightforward, high yielding, two-step route for the synthesis of two new *N*,*N*,*O* ligands on a multigram scale has been developed. Compounds **1** (A[MIm$_2$Pr]) and **2** (A[BenzMIm$_2$Pr]) can be regarded as parent compounds, as the synthetic route offers the possibility of further expansion of this series of ligands. For instance, the bis(heteroaryl)methane synthesis (**5** and **6**) [15,16] allows for the incorporation of (poly)substituted (benz)imidazoles; thus, introduction of other functionalities and further modification of this *N*,*N* backbone is feasible. Both physical properties like solubility, ease of crystallization, and steric requirements as well as the electronic properties of the ligand can therefore be controlled by design. Alterations in the fourth substituent of the central carbon atom [C3 (**1a**) and C1 (**2a**) in Figure 2] and the type of introduced electrophile offer further possibilities for structural variation.

The two cation series of ligands, A[MIm$_2$Pr] and A[BenzMIm$_2$Pr] (A = H, K, and Bu$_4$N), were developed to vary the solubility of one single member of a ligand family and simplify the syntheses and purification of different metal complexes. The reaction of a monoanionic ligand with a metal salt generally results in the formation of two new salts, i.e. the desired complex and an (inorganic) byproduct. The solubility properties of both the desired complex and the byproduct are often comparable and this then hampers purification. Choosing the right cation allows control over the solubility properties of the formed byproduct and therefore purification of the desired metal complexes can in principle be achieved by a simple washing procedure. An example of this approach is described here for the synthesis of

[Cu(BenzMIm$_2$Pr)$_2$] (**4**). The solubility properties of the Bu$_4$N ligands (**1c**, **2c**) also allow the use of relatively apolar solvents, solvents in which the potassium salts (**1b**, **2b**) and acids (**1a**, **2a**) are insoluble.

The ligands **1** and **2** were designed to provide a transition metal with a facial donor array of one carboxylate and two imidazole groups, as found in the enzymes exhibiting the 2-His-1-carboxylate motif.[4,5,8] Using copper(II) as a probe, the neutral [CuL$_2$] complexes **3** and **4** nicely illustrate the facial *N,N,O* capping potential of both new ligands.

This facial capping of the *N,N,O* ligands A[MIm$_2$Pr] (**1**) and A[BenzMIm$_2$Pr] (**2**) renders this new family of ligands suitable candidates for mimicking the 2-His-1-carboxylate motif and we are therefore currently studying the iron and zinc coordination chemistries of these ligands.

Experimental Section

General Remarks: Air-sensitive reactions were carried out under dry, oxygen-free N$_2$ using standard Schlenk techniques. THF was dried with sodium/benzophenone ketyl and distilled under N$_2$ prior to use. Methanol was dried with magnesium methoxide and distilled under N$_2$ prior to use. ^{1}H and ^{13}C{^{1}H} NMR spectra were recorded with a Varian Inova 300 spectrometer at 300 and 75 MHz, respectively, operating at 25 °C. Elemental microanalyses were carried out by the Microanalytisches Laboratorium Dornis and Kolbe, Mülheim a. d. Ruhr, Germany. Infrared spectra were recorded with a Perkin–Elmer Spectrum One FT-IR instrument. ESI-MS spectra were recorded with a Micromass LC-TOF mass spectrometer by the department of Biomolecular Mass Spectrometry, Utrecht University. UV/Vis spectra were recorded with a Cary 50 Varian spectrometer. EPR spectra were measured with a modified Bruker ESP300 spectrometer equipped with an ER4103TM cavity (TM$_{110}$ mode with unloaded Q = 12000). The microwave frequency was near 9.52 GHz and the spectrometer settings involved 4 Gauss field modulation. Bis(1-methylimidazol-2-yl)methane and bis(1-methylbenzimidazol-2-yl)methane were prepared according to literature procedures.[15,16] All other chemicals were commercially obtained and used as received.

Propyl 3,3-Bis(1-methylimidazol-2-yl)propionate, MIm$_2$PrPr (7): A solution of *n*-butyllithium in hexanes (18 mL, 28.8 mmol, 1.6 M in hexanes) was added dropwise to a stirred solution of bis(1-methylimidazol-2-yl)methane (**5**) (5.02 g, 28.5 mmol) in THF (150 mL) at –78 °C. The solution was stirred at –78 °C for 1 h, followed by the dropwise addition of propyl bromoacetate (3.8 mL, 29 mmol). The temperature was allowed to rise to room temperature overnight, resulting in a yellow-white suspension. The reaction mixture was quenched with H$_2$O (25 mL) and all volatiles were evaporated in vacuo. The water layer was extracted with ethyl acetate (4 × 30 mL) and the combined organic layers were dried with magnesium sulfate, filtered, and the solvents evaporated to dryness. The product was obtained as a yellow oil, which solidified upon standing (6.51 g, 83 %). This product can be purified using column chromatography (silica; eluent ethyl acetate/methanol, 9:1), but the crude product is pure enough for further use. ^{1}H NMR (300 MHz, CDCl$_3$, 25 °C): δ = 0.82 (t, $^3J_{H,H}$ = 7.8 Hz, 3 H, OCH$_2$CH$_2$C*H*$_3$), 1.54 (sext, $^3J_{H,H}$ = 7.5 Hz, 2 H, OCH$_2$C*H*$_2$CH$_3$), 3.28 (d, $^3J_{H,H}$ = 7.8 Hz, 2 H, CHC*H*$_2$), 3.46 (s, 6 H, NC*H*$_3$), 3.96 (t, $^3J_{H,H}$ = 6.9 Hz, 2 H, OC*H*$_2$CH$_2$CH$_3$), 4.94 (t, $^3J_{H,H}$ = 7.8 Hz, 1 H, C*H*CH$_2$), 6.72 (s, 2 H, H_{imid}), 6.88 (s, 2 H, H_{imid}) ppm. ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$, 25 °C): δ = 10.19, 21.82, 32.81, 34.42, 36.34, 66.32, 121.95, 127.15, 145.29, 171.21 ppm. IR (solid): $\tilde{\nu}$ = 3099.1, 2967.2, 1727.1, 1492.3, 1282.9, 1189.7, 1174.9, 1129.8, 744.0 cm^{-1}. C$_{14}$H$_{20}$N$_4$O$_2$ (276.33) calcd. C 60.85, H 7.30, N 20.28; found C 60.74, H 7.22, N 20.18.

Propyl 3,3-Bis(1-methylbenzimidazol-2-yl)propionate, BenzMIm$_2$PrPr (8): Compound **8** was synthesized using the procedure described above for compound **7**. The product was obtained as an off-white solid (2.89 g, 92 %). This product can be purified using column chromatography (silica; eluent ethyl acetate/methanol, 7:1), but the crude product is pure enough for further use. ^{1}H NMR (300 MHz, CDCl$_3$, 25 °C): δ = 0.86 (t, $^3J_{H,H}$ = 7.5 Hz, 3 H, OCH$_2$CH$_2$C*H*$_3$), 1.58 (sext, $^3J_{H,H}$ = 7.2 Hz, 2 H, OCH$_2$C*H*$_2$CH$_3$), 3.61 (d, $^3J_{H,H}$ = 7.5 Hz, 2 H, CHC*H*$_2$), 3.76 (s, 6 H, NC*H*$_3$), 4.02 (t, $^3J_{H,H}$ = 6.3 Hz, 2 H, OC*H*$_2$CH$_2$CH$_3$), 5.45 (t, $^3J_{H,H}$ = 7.5 Hz, 1 H, C*H*CH$_2$), 7.26 (m, 6 H, $H_{benzimid}$), 7.76 (m, 2 H, $H_{benzimid}$) ppm. ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$, 25 °C): δ = 10.20, 21.84, 30.25, 35.94, 36.19, 66.64, 109.23, 119.74, 122.18, 122.84, 136.44, 142.07, 151.19, 170.89 ppm. IR (solid): $\tilde{\nu}$ = 2973.2, 1733.9, 1467.1, 1439.7, 1389.1, 1179.2, 733.7 cm^{-1}. C$_{22}$H$_{24}$N$_4$O$_2$ (376.45) calcd. C 70.19, H 6.43, N 14.88; found C 69.98, H 6.41, N 14.69.

3,3-Bis(1-methylimidazol-2-yl)propionic Acid, HMIm$_2$Pr (1a): To a solution of ester **7** (2.24 g, 8.1 mmol) in THF (20 mL) was added 1 equiv. of potassium hydroxide in water (8.20 mL, 0.989 M, 8.1 mmol) and the solution was stirred at room temperature for 3 h. Subsequently, 1 equiv. of a hydrochloric acid solution in water (8.11 mL, 1 M, 8.1 mmol) was added to the hydrolysed reaction mixture. Evaporation of the solvents resulted in a white mixture of product and potassium chloride. Most of the KCl was removed after extraction of the powder with dry methanol (3 × 15 mL). Evaporation of the solvent and recrystallization from EtOH/H$_2$O (95:5) gave the product as colorless crystals of composition HMIm$_2$Pr·4H$_2$O (1.6 g, 65 %). Single crystals of the composition HMIm$_2$Pr·CH$_3$OH were obtained by slow diffusion of diethyl ether in a concentrated solution of **1a** in methanol. ^{1}H NMR (300 MHz, CD$_3$OD, 25 °C): δ = 3.16 (d, $^3J_{H,H}$ = 7.8 Hz, 2 H, CHC*H*$_2$), 3.62 (s, 6 H, NC*H*$_3$), 5.00 (t, $^3J_{H,H}$ = 7.2 Hz, 1 H, C*H*CH$_2$), 6.99 (s, 2 H, H_{imid}), 7.11 (s, 2 H, H_{imid}) ppm. ^{13}C{^{1}H} NMR (75 MHz, CD$_3$OD, 25 °C): δ = 33.63, 33.86, 38.87, 123.88, 125.92, 146.76, 175.17 ppm. IR (solid): $\tilde{\nu}$ = 3130.0, 1701.5, 1491.2, 1348.4, 1285.6, 1266.7, 1220.9, 1135.5, 772.3 cm^{-1}. C$_{11}$H$_{14}$N$_4$O$_2$·4H$_2$O (306.32) calcd. C 43.13, H 7.24, N 18.29; found C 43.31, H 7.16, N 18.34.

3,3-Bis(1-methylbenzimidazol-2-yl)propionic Acid, HBenzMIm$_2$Pr (2a): The acid **2a** was synthesized using the procedure as described above for the acid **1a**. KCl could in this case be removed by washing the product with water (3 × 20 mL). Recrystallization from methanol gave the product as colorless crystals (0.59 g, 64 %). Slow cooling of a hot saturated solution of **2a** in methanol resulted in crystals suitable for X-ray analysis. ^{1}H NMR (300 MHz, CD$_3$OD, 25 °C): δ = 3.53 (d, $^3J_{H,H}$ = 7.2 Hz, 2 H, CHC*H*$_2$), 3.78 (s, 6 H, NC*H*$_3$), 5.40 (t, $^3J_{H,H}$ = 7.2 Hz, 1 H, C*H*CH$_2$), 7.28 (m, 4 H, $H_{benzimid}$), 7.48 (d, $^3J_{H,H}$ = 7.2 Hz, 2 H, $H_{benzimid}$) 7.63 (d, $^3J_{H,H}$ = 7.2 Hz, 2 H, $H_{benzimid}$) ppm. ^{13}C{^{1}H} NMR (75 MHz, CD$_3$OD, 25 °C): δ = 30.52 35.27, 37.60 111.01, 119.60, 123.59, 124.25, 137.32, 142.69, 153.46, 174.41 ppm. IR (solid): $\tilde{\nu}$ = 2934.4, 1716.3, 1467.8, 1392.8, 1332.3, 1282.8, 762.1, 739.6 cm^{-1}. C$_{19}$H$_{18}$N$_4$O$_2$ (334.37) calcd. C 68.25, H 5.43, N 16.76; found C 68.15, H 5.49, N 16.83.

General Procedure for the Synthesis of the Potassium and Tetrabutylammonium Salts 1b/c and 2b/c: To a solution of the appropriate ester **7** or **8** in THF (20 mL) was added 1 mol-equiv. of a KOH or [Bu$_4$N]OH solution in water (volumetric standard) and the reaction mixture was stirred at room temperature for 3 h. Evaporation of

the solvents resulted in an oil. Repeated azeotropic drying of the oil with toluene, gave the desired product as a powder in quantitative yield.

Potassium 3,3-Bis(1-methylimidazol-2-yl)propionate, K[MIm$_2$Pr] (1b): Yellowish powder (1.97 g). ^{1}H NMR (300 MHz, CD_3OD, 25 °C): δ = 3.08 (d, $^3J_{H,H}$ = 7.2 Hz, 2 H, CHCH_2), 3.52 (s, 6 H, NCH_3), 4.92 (t, $^3J_{H,H}$ = 7.2 Hz, 1 H, CHCH$_2$), 6.83 (s, 2 H, H_{imid}), 6.95 (s, 2 H, H_{imid}) ppm. ^{13}C{^{1}H} NMR (75 MHz, CD_3OD, 25 °C): δ = 35.22, 35.59, 41.09, 123.16, 127.11, 148.34, 178.60 ppm. IR (solid): $\tilde{\nu}$ = 1580.2, 1393.0, 665.2 cm^{-1}. $C_{11}H_{13}KN_4O_2$ (272.34) calcd. C 48.51, H 4.81, N 20.57; found C 48.36, H 4.92, N 20.47. ESI-MS: *m*/*z* = 311.08 {(K[MIm$_2$Pr] +K)$^+$, calcd. 311.03}, 583.04 {(2K[MIm$_2$Pr] + K)$^+$, calcd. 583.10}.

Tetrabutylammonium 3,3-Bis(1-methylimidazol-2-yl)propionate, [Bu$_4$N][MIm$_2$Pr] (1c): White powder (1.97 g). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.92 (m, 12 H, $CH_2CH_2CH_2CH_3$), 1.35 (m, 8 H, $CH_2CH_2CH_2CH_3$), 1.57 (m, 8 H, $CH_2CH_2CH_2CH_3$), 3.06 (d, $^3J_{H,H}$ = 6.5 Hz, 2 H, CHCH_2), 3.26 (m, 8 H, $CH_2CH_2CH_2CH_3$), 3.58 (s, 6 H, NCH_3), 5.08 (t, $^3J_{H,H}$ = 6.5 Hz, 1 H, CHCH$_2$), 6.65 (s, 2 H, H_{imid}), 6.77 (s, 2 H, H_{imid}) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, 25 °C): δ = 13.69, 19.68, 24.04, 33.00, 35.16, 40.80, 58.56, 120.79, 126.53, 148.87, 174.66 ppm. IR (solid) $\tilde{\nu}$ = 2962.5, 2936.7, 1581.6, 1489.7, 1363.2, 1280.6, 1128.0, 770.5 cm^{-1}. $C_{27}H_{49}N_5O_2$ (475.71) calcd. C 68.17, H 10.38, N 14.72; found C 67.89, H 10.31, N 14.63.

Potassium 3,3-Bis(1-methylbenzimidazol-2-yl)propionate, K[BenzMIm$_2$Pr] (2b): Yellowish powder (2.27 g). ^{1}H NMR (300 MHz, CD_3OD, 25 °C): δ = 3.35 (d, $^3J_{H,H}$ = 7.2 Hz, 2 H, CHCH_2), 3.78 (s, 6 H, NCH_3), 5.40 (t, $^3J_{H,H}$ = 7.2 Hz, 1 H, CHCH$_2$), 7.23 (m, 4 H, $H_{benzimid}$), 7.44 (d, $^3J_{H,H}$ = 7.8 Hz, 2 H, $H_{benzimid}$), 7.61 (d, $^3J_{H,H}$ = 7.8 Hz, 2 H, $H_{benzimid}$) ppm. ^{13}C{^{1}H} NMR (75 MHz, CD_3OD, 25 °C): δ = 29.31, 35.47, 39.84, 09.61, 118.42, 122.01, 122.66, 136.21, 141.80, 153.61, 176.78 ppm. IR (solid) $\tilde{\nu}$ = 1598.0, 1581.9, 1385.7, 1282.7, 737.8 cm^{-1}. $C_{19}H_{17}KN_4O_2$ (372.46) calcd. C 61.27, H 4.60, N 15.04; found C 61.05, H 4.68, N 14.86. ESI-MS: *m*/*z* = 327.18 {([BenzMIm$_2$C$_2$H$_2$] + K)$^+$, calcd. 327.10}, 411.12 {(K[BenzMIm$_2$Pr] + K)$^+$, calcd. 411.06}, 783.19 {(2K[BenzMim$_2$Pr] + K)$^+$, calcd. 783.16}.

Tetrabutylammonium 3,3-Bis(1-methylbenzimidazol-2-yl)propionate, [Bu$_4$N][BenzMIm$_2$Pr] (2c): Yellow powder (1.52 g). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.92 (t, $^3J_{H,H}$ = 7.2 Hz, 12 H, $CH_2CH_2CH_2CH_3$), 1.33 (m, 8 H, $CH_2CH_2CH_2CH_3$), 1.53 (m, 8 H, $CH_2CH_2CH_2CH_3$), 3.19 (m, 8 H, $CH_2CH_2CH_2CH_3$), 3.37 (d, $^3J_{H,H}$ = 6.6 Hz, 2 H, CHCH_2), 3.82 (s, 6 H, NCH_3), 5.58 (t, $^3J_{H,H}$ = 6.3 Hz, 1 H, CHCH$_2$), 7.20 (m, 6 H, $H_{benzimid}$), 7.65 (m, 2 H, $H_{benzimid}$) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, 25 °C): δ = 13.56, 19.58, 23.91, 30.21, 36.17, 39.52, 58.65, 109.06, 119.29, 121.29, 121.89, 136.38, 142.41, 154.25, 174.12 ppm. IR (solid) $\tilde{\nu}$ = 2960.0, 2874.0, 1596.5, 1465.8, 1380.2, 1275.5, 736.1 cm^{-1}. $C_{35}H_{53}N_5O_2$ (575.83) calcd. C 73.00, H 9.28, N 12.16; found C 72.89, H 9.38, N 12.22.

[Cu(MIm$_2$Pr)$_2$]·2H$_2$O (3): To a colorless solution of K[MIm$_2$Pr] (**1b**) (414 mg, 1.52 mmol) in hot ethanol (20 mL) was added a solution of $CuCl_2$·$2H_2O$ (129 mg, 0.76 mmol) in hot ethanol (10 mL). The solution immediately turned dark blue and the reaction mixture was heated to reflux for 1 h. Upon cooling of the solution to room temperature, a white precipitate formed (KCl). The solution was filtered and concentrated in vacuo. The resulting dark blue powder was recrystallized from a minimal amount of refluxing ethanol and cooled to 4 °C to give the title compound as blue crystals (201 mg, 47 %). Single crystals formed after three weeks from a concentrated solution of **3** in ethanol upon standing. $C_{22}H_{26}CuN_8O_4$·$2H_2O$ (566.06) calcd. C 46.86, H 5.34, N 19.80; found C 46.60, H 5.44, N 19.72. IR (solid) $\tilde{\nu}$ = 3347.5, 3275.9, 3126.5, 1582.1, 1506.9, 1383.9, 1289.8, 1153.1, 745.9 cm^{-1}. UV/Vis (methanol): λ_{max} = 215, 219, 587 nm. ESI-MS: *m*/*z* = 529.96 {[{Cu(MIm$_2$Pr)$_2$} + H]$^+$, calcd. 530.14}, 551.78 {[{Cu(MIm$_2$Pr)$_2$} + Na]$^+$, calcd. 552.13}.

[Cu(BenzMIm$_2$Pr)$_2$] (4): To a colorless solution of [Bu$_4$N][BenzMIm$_2$Pr] (**2c**) (470 mg, 0.82 mmol) in hot, dry methanol (20mL) was added a solution of $CuCl_2$ (55 mg, 0.41 mmol) in hot, dry methanol (10 mL). Immediately the solution turned green-blue and the reaction mixture was refluxed for 1 h, during which a pale blue precipitate formed. The reaction mixture was allowed to cool to room temperature and the precipitate was collected by centrifugation. The crude product was washed with methanol (1 × 10 mL) and dichloromethane (3 × 10 mL) and dried in vacuo. The title compound was isolated as a light blue powder (162 mg, 54 %). Slow evaporation of the solvent of a concentrated solution of **4** in ethanol resulted in the formation of single crystals of the composition [Cu(BenzMIm$_2$Pr)$_2$]·3.12(H_2O)·1.74(C_2H_5OH) formed after six weeks. $C_{38}H_{34}CuN_8O_4$ (730.27) calcd. C 62.50, H 4.69, N 15.34; found C 62.36, H 4.62, N 15.23. IR (solid) $\tilde{\nu}$ = 3349.8, 1583.1, 1458.0, 1385.5, 1304.1, 1284.8, 742.8 cm^{-1}. UV/Vis (methanol): λ_{max} = 228, 252, 271, 666 nm. ESI-MS: *m*/*z* = 730.25 {[{Cu(BenzMIm$_2$Pr)$_2$} + H]$^+$, calcd. 730.21}, 752.14 {[{Cu(BenzMIm$_2$Pr)$_2$} + Na]$^+$, calcd. 752.19}.

X-ray Crystallographic Study: X-ray intensities were measured with a Nonius KappaCCD diffractometer with rotating anode (graphite monochromator, λ = 0.71073 Å) at a temperature of 150 K. The structures were solved with Direct Methods (compounds **1a**,[24] **2a**,[25] and **4**[24]) or automated Patterson methods (compound **3**[26]). The structures were refined with SHELXL-97[27] against F^2 of all reflections up to $(\sin\theta/\lambda)_{max}$ = 0.65 Å^{-1}. Structure calculations, drawings, and checking for higher symmetry was performed with the PLATON[28] package. Further details are given in Table 3. In crystal structures **1a**, **2a**, and **3** all hydrogen atoms were located in the difference Fourier map. C–H hydrogen atoms were refined as rigid groups. O–H hydrogen atoms were refined freely with isotropic displacement parameters. In crystal structure **4**, the position of water molecule O29 is fully occupied. Water molecule O30 was refined with an occupancy of 56 % and the ethanol molecule with an occupancy of 87 %. All hydrogen atoms were located in the difference Fourier map. C–H hydrogen atoms were refined as rigid groups. O–H hydrogen atoms were kept fixed in the located position. CCDC-249589 (**1a**), -249590 (**2a**), -249591 (**3**) and -249592 (**4**) contain the supplementary crystallographic data for this paper. These data can be obtained free from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

Supporting Information (see also footnote on the first page of this article): Two figures are included depicting the hydrogen bonding pattern and π-π stacking the crystal structure of HBenzMIm$_2$Pr (**2a**).

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