

Green implementation of aza-Michael reactions for the synthesis of bi-functional linkers forming microporous coordination polymers

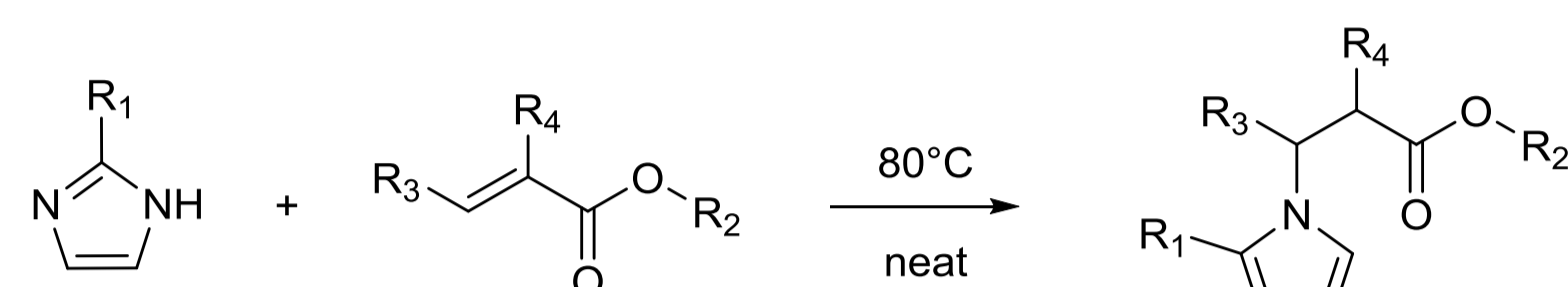
Katharina Kodolitsch,[†] Florian Gobec,[†] Ana Torvisco,[‡] Paolo Falcaro[§] and Christian Slugovc^{†,*}

Introduction

The direct addition of amines to α,β -unsaturated olefins called aza-Michael reaction (or conjugate addition) is one of the simplest and most effective strategies to prepare β -amino carbonyls with high atom economy from readily available starting materials under strongly acidic or basic conditions. However, high temperatures and long reaction times are required so that such reactions exhibit poor compatibility with various functional groups. Furthermore, the substrate scope is limited to aliphatic amines. In order to overcome these limitations, a variety of Lewis acid metal catalysts have been proposed to perform the conjugate addition of aromatic amines to electron-deficient olefins under mild conditions.^{1,2} Despite the great advance in metal-catalyzed aza-Michael additions, their shortcomings still exist. Examples are the use of expensive often air and moisture-sensitive (precious) metal complexes or the need to remove the catalyst at the end of the reaction. Over the past decades, reaction conditions using ionic liquids or water as solvents have been successfully developed and partially addressed the above-described drawbacks.^{1,3}

Here we disclose truly green reaction conditions for the synthesis of 3-(1H-imidazol-1-yl)propanoic acid derivatives via 3-(1H-imidazol-1-yl)propanoates derived from aza-Michael reactions performed under solvent less conditions without using a catalyst minimizing the effort necessary during the work-up. Furthermore, the products were used as linkers in the preparation of porous coordination polymers with Zn^{2+} as the central atom.⁴

Aza-Michael reaction

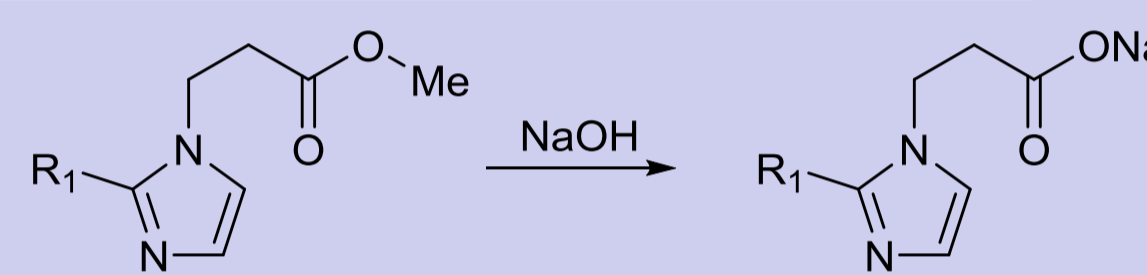
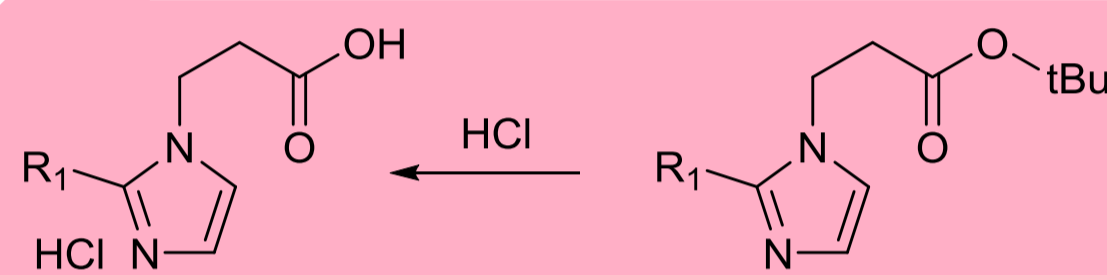


- 1: $R_1 = H$
2: $R_1 = Me$
3: $R_1 = Ph$
- A: $R_2 = Me, R_3 = H, R_4 = H$
B: $R_2 = tBu, R_3 = H, R_4 = H$
C: $R_2 = Me, R_3 = Me, R_4 = H$
D: $R_2 = Me, R_3 = H, R_4 = Me$

- 1A: $R_1 = H, R_2 = Me, R_3 = H, R_4 = H$
2A: $R_1 = Me, R_2 = Me, R_3 = H, R_4 = H$
3A: $R_1 = Ph, R_2 = Me, R_3 = H, R_4 = H$
1B: $R_1 = H, R_2 = tBu, R_3 = H, R_4 = H$
2B: $R_1 = Me, R_2 = tBu, R_3 = H, R_4 = H$
1C: $R_1 = H, R_2 = Me, R_3 = Me, R_4 = H$
2C: $R_1 = Me, R_2 = Me, R_3 = Me, R_4 = H$
1D: $R_1 = H, R_2 = Me, R_3 = H, R_4 = Me$
2D: $R_1 = Me, R_2 = Me, R_3 = H, R_4 = Me$

The corresponding imidazole (1-3, 1 eq.) was placed in a lockable reaction vessel and the respective Michael acceptor (A-D, 1.2 eq.) was added. The vessel was closed and placed without stirring in an oven operating at 80°C. After 24 h full conversion was achieved and the excess of the Michael acceptor was removed under vacuum yielding analytically pure products (1A-2D) in virtually quantitative yield.

acidic ester cleavage for alkaline salts like ZnO



Ester-cleavage

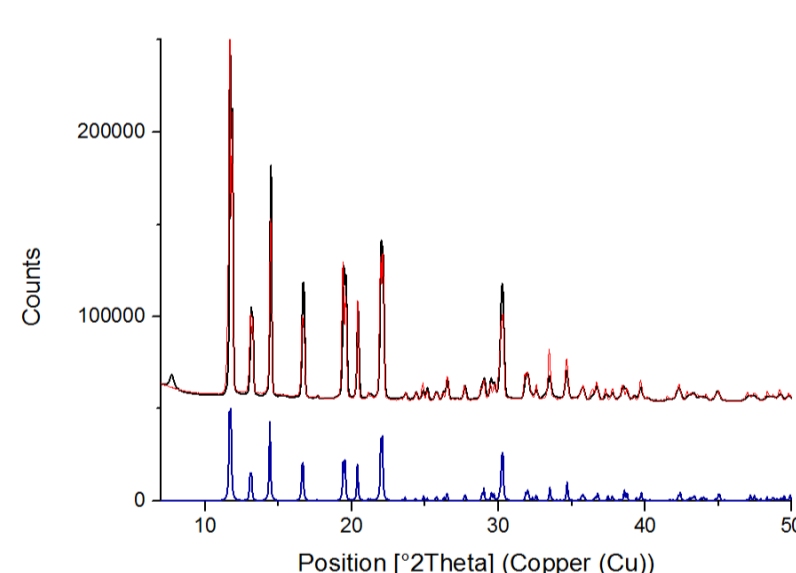
alkaline saponification for 'neutral' salts like $Zn(NO_3)_2$

Ester cleavage was either accomplished upon addition of 1.03 eq. aqueous NaOH to the corresponding methyl ester compound and placing the open reaction vessel in an oven at 80°C or

upon adding 2.05 eq. of aqueous HCl to the respective *tert.*-butyl ester derivative, yielding the corresponding analytically pure ester cleaved products upon drying in virtually quantitative yield.

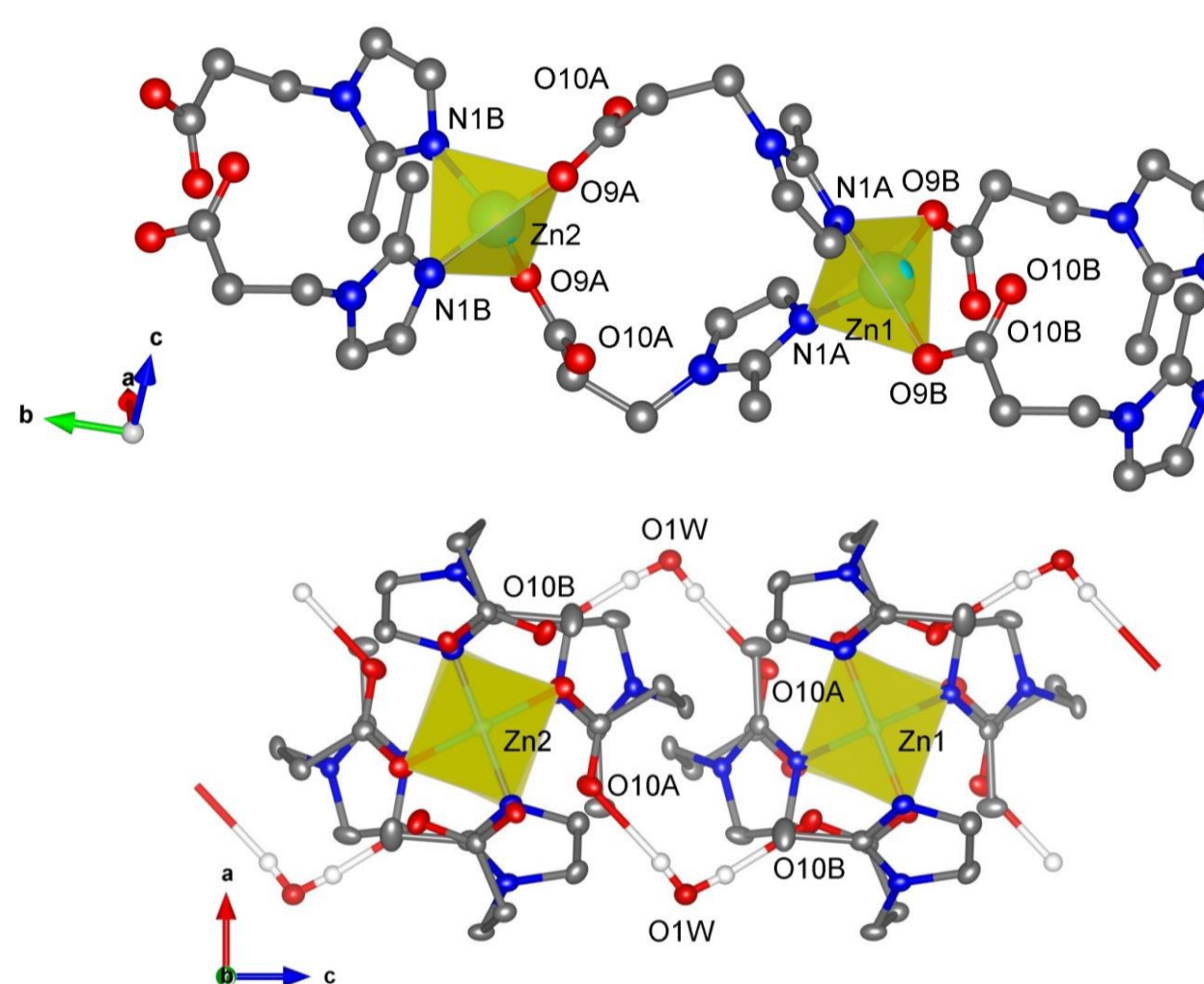
Microporous coordination polymers

The reaction of sodium 3-(2-methyl-1H-imidazol-1-yl)propanoate (2 eq.) with $Zn(NO_3)_2$ in water yielded immediately a microcrystalline precipitate, which, under gentle hydrothermal conditions, converted into single crystals suitable for scX-ray determination. The compound crystallizes as 1D coordination polymer chains with additional water molecules (O1W) affording hydrogen bonding to the nonbonding oxygen atom of the carboxylate group creating a 3D scaffold.

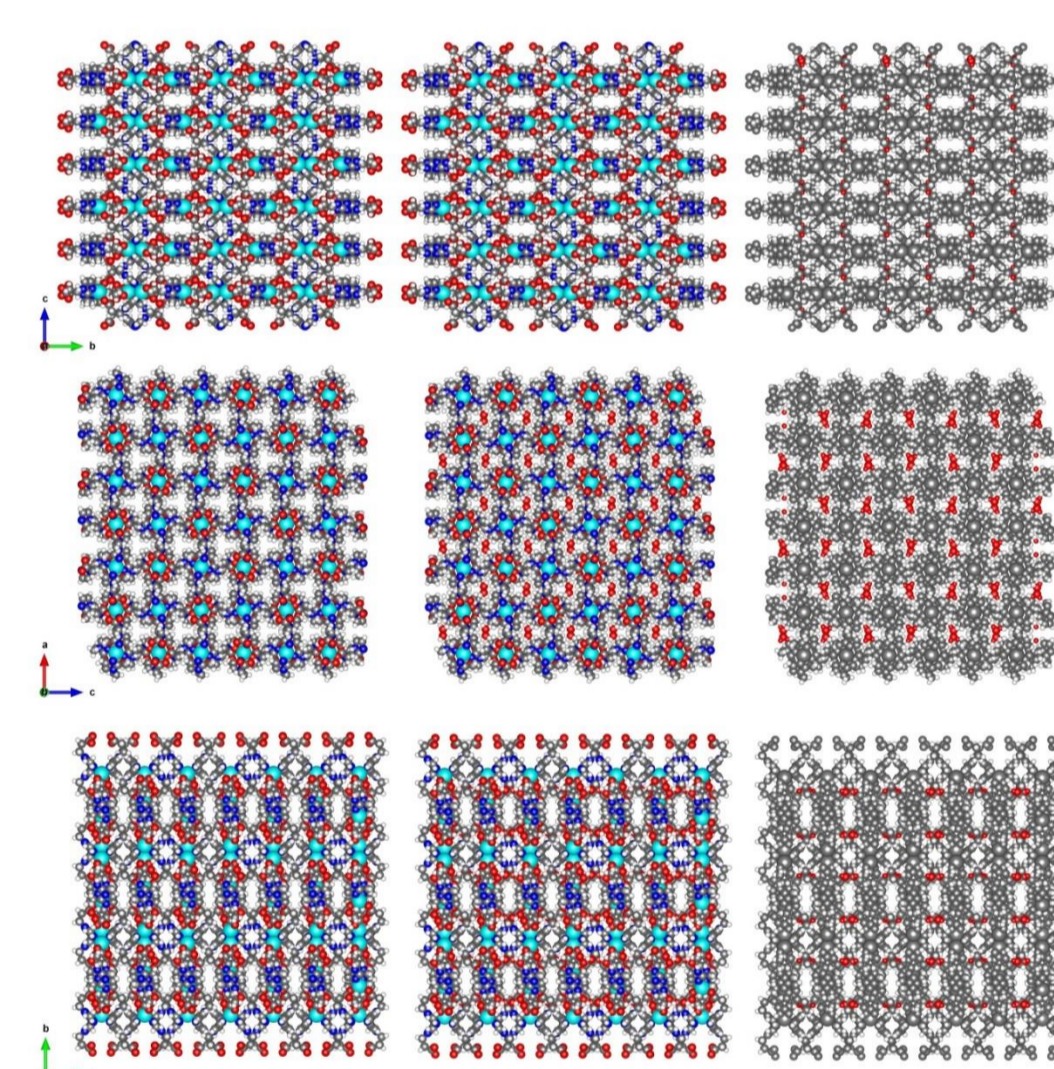


properties	
BET Surface	110 m ² /g
Pore size	56 Å
Thermal stability (N ₂)	295°C

pXRD red: precipitate;
black: crystals after BET measurement;
blue: calculated from scXRD

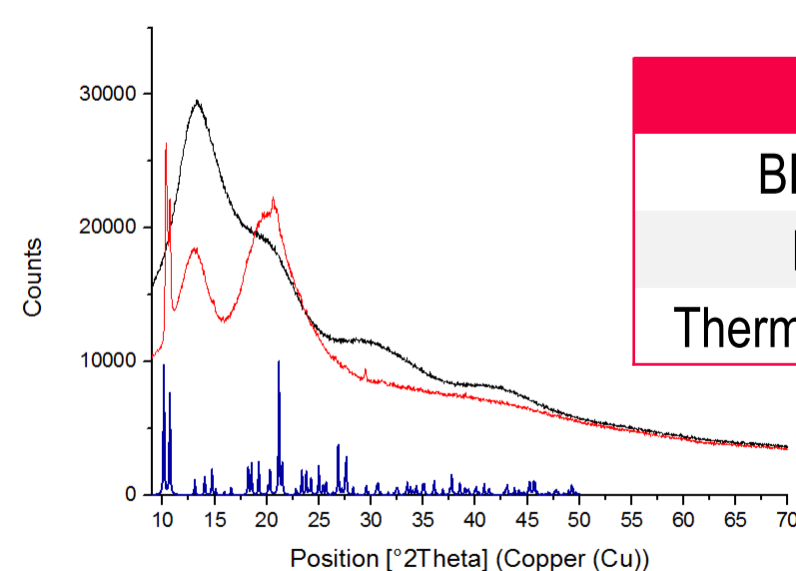


scXRD above: views of molecular structure (hydrogens, except for water omitted); below: views of the coordination around Zn²⁺; view of the 2D sheet (hydrogen and water omitted); cartoon showing the formation of the 3D structure via hydrogen bonding



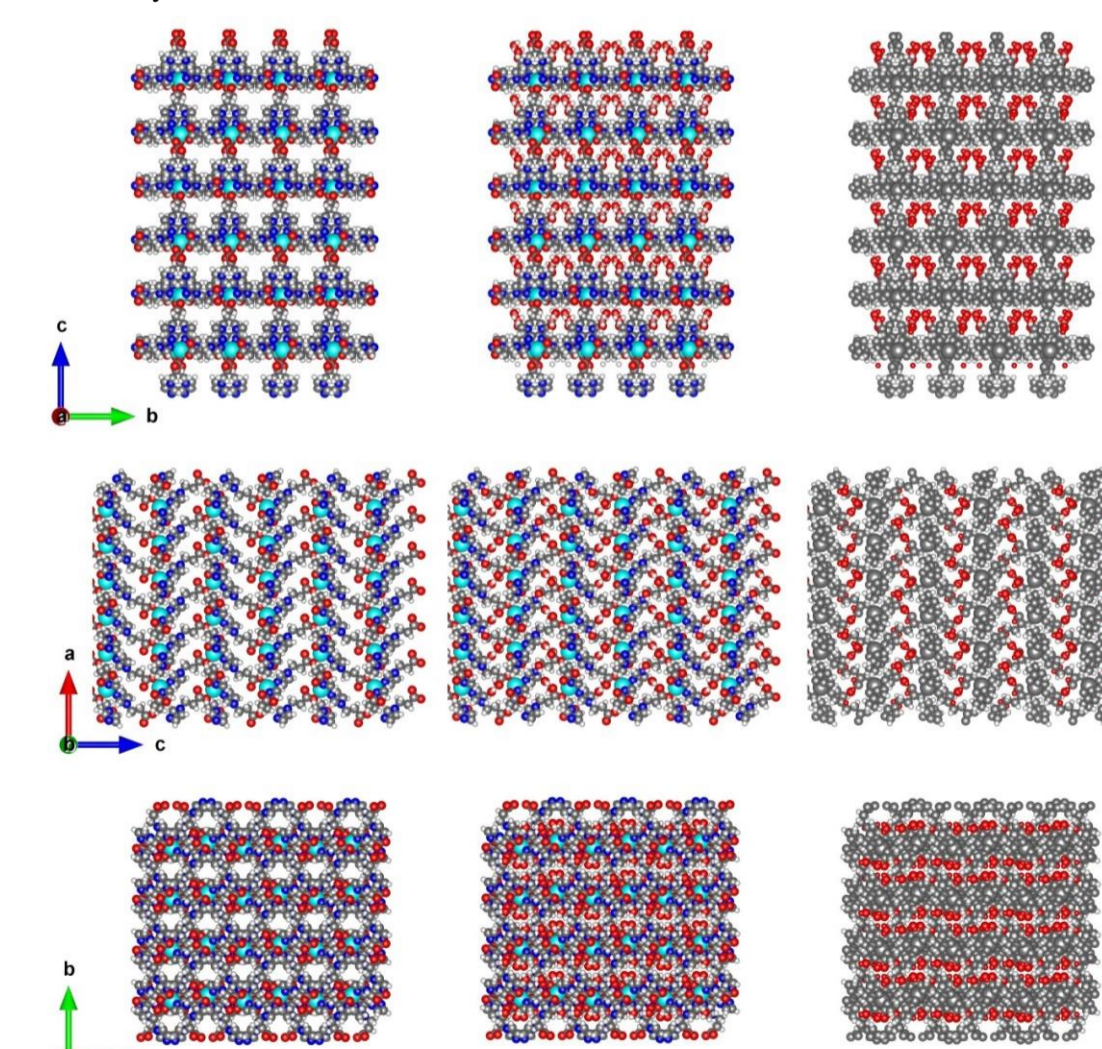
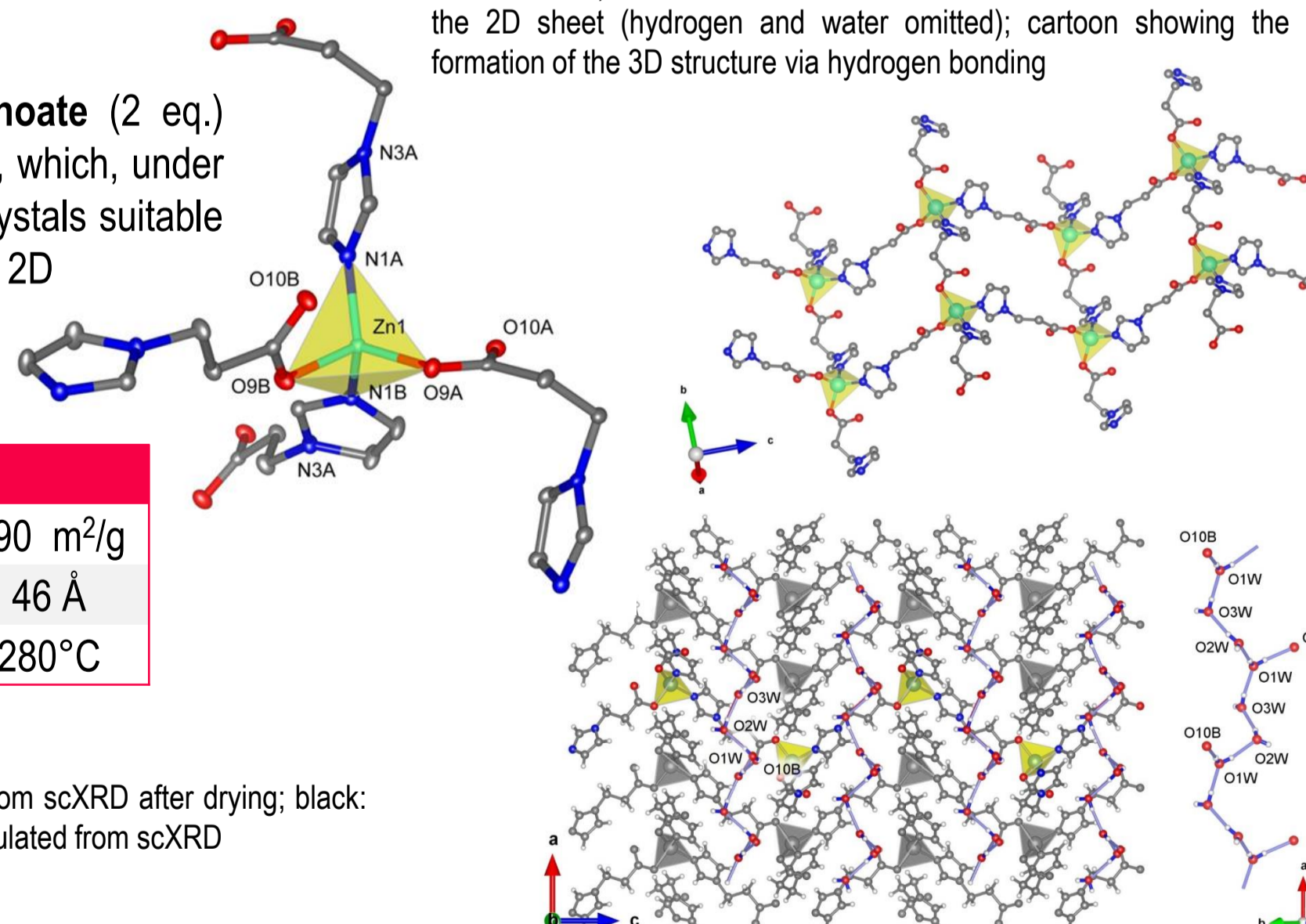
scXRD based models: views along a, b and c axes (left column: water omitted, middle column: water NOT omitted; right column: only water colored in red)

The reaction of sodium 3-(1H-imidazol-1-yl)propanoate (2 eq.) with $Zn(NO_3)_2$ in water yielded an amorphous precipitate, which, under gentle hydrothermal conditions, converted into single crystals suitable for scX-ray determination. The compound crystallizes as 2D coordination polymer sheets linked to a 3D network by water molecules.



properties	
BET Surface	190 m ² /g
Pore size	46 Å
Thermal stability (N ₂)	280°C

pXRD red: crystals from scXRD after drying; black: precipitate; blue: calculated from scXRD



Conclusion

A green route including the aza-Michael reaction of imidazole and enoates and a subsequent ester cleavage allowed for the preparation of a library of different N-heterocyclic carboxylates suited as ligands for the preparation of coordination polymers. Two examples of such, in these cases, microporous coordination polymers have been disclosed and their solid state structures have been described. The 2-methylimidazole based linker is of particular interest, because it forms 1D coordination polymers which are organized in a 3D scaffold hold together by hydrogen bonding with crystal water. This 3D structure features porous channels which are presumably accessible for guests.

References

- 1 Gmach, J.; Joachimiak, Ł.; Błażewska, K. M. *Synthesis* **2016**, *48*, 2681-2704. 2 a) Stevanovic, D.; Pejović, A.; Damjanović, I.; Vukićević, M.; Bogdanović, G. A.; Vukićević, R. D. *Tetrahedron Lett.* **2012**, *53*, 6257-6260; b) Solè, D.; Pérez-Janer, F.; Mancuso, R. *Chem. Eur. J.* **2015**, *21*, 4580-4584. 3 Roy, S. R.; Chakraborti, A. K. *Org. Lett.* **2010**, *12*, 3866-3869 and references therein. 4 Zhai, Q.-G.; Zeng, R.-R.; Li, S.-N.; Jiang, Y.-C.; Hu, M.-C. *Cryst. Eng. Comm.* **2013**, *15*, 965-976 and references therein.

Acknowledgment

Financial support by the leadproject LP-03 is gratefully acknowledged. We thank F. Mautner (pXRD), J. Hobisch (TGA) and R. Ricco (BET).