Post-synthetic modification of zirconium metal–organic frameworks by catalyst-free aza-Michael additions†

Harina Amer Hamzah, Tom S. Crickmore, Daniel Rixson and Andrew D. Burrows*

The reactions of the zirconium MOF [Zr6O4(OH)4(bdc-NH2)3] (UiO-66-NH2, bdc-NH2 = 2-amino-1,4-benzenedicarboxylate) with the Michael acceptors acrylonitrile (CH2=CHCN), acrylic acid (CH2=CHCO2H), methyl acrylate (CH2=CHCH2CO2H) and methyl vinyl ketone (CH2=CHC(O)Me) led to post-synthetic modification of the MOF through C=N bond formation without loss of crystallinity. The reactions with acrylonitrile and acrylic acid go to completion, yielding [Zr6O4(OH)4(bdc-NHCH2CH2CN)6] (UiO-66-AN, 1) and [Zr6O4(OH)4(bdc-NHCH2CH2CO2H)6] (UiO-66-AA, 2) respectively, whereas those with methyl acrylate and methyl vinyl ketone are incomplete, yielding [Zr6O4(OH)4(bdc-NH2)0.66(bdc-NHCH2CH2CN)4] (UiO-66-AN, 1) and [Zr6O4(OH)4(bdc-NH2)2.76(bdc-NHCH2CH2CO2H)3.24] (UiO-66-MVK, 4), respectively. The acrylonitrile-modified MOF UiO-66-AN undergoes further reaction with sodium azide in the presence of zinc(ii) chloride in n-butanol to form the tetrazolate-modified MOF [Zr6O4(OH)4(bdc-NHCH2CH2CN)4]74(bdc-NHCH2CH2CNH4)26] (UiO-66-TZ, 5).

A wide range of covalent post-synthetic modification reactions have been developed over recent years, including conversion of primary amines into amides,8 isocyanates,9 ureas,10 azides,11 β-amidoketones12 and secondary amines,13 aldehydes into hydrazones,14 azides into triazoles15 and bromides into nitriles,16 in addition to oxidation,17 reduction18 and Mannich reactions.19 Many of these post-synthetic modification reactions were developed on zinc MOFs, whose limited moisture stability places constraints on the reactions that can be utilised and the applications of the modified MOFs. The more recent extension of post-synthetic modification protocols to moisture- and acid-stable MOFs allows the use of reactions that would destroy more sensitive frameworks. Thus, for example, we previously reported that the amino groups in [Cr3O3(OH)(H2O)3(bdc-NH2)3] (MIL-101(Cr)-NH2, bdc-NH2 = 2-amino-1,4-benzenedicarboxylate) could be transformed into diazonium ions, which could subsequently be converted into halides or azo dyes.20 Post-synthetic modifications of derivatives of the water-stable zirconium MOF [Zr6O4(OH)4(bdc)3] (UiO-66, bdc = 1,4-benzenedicarboxylate) have recently been reviewed by Marshall and Forgan.21 We are interested in developing new post-synthetic methods that allow different functional groups to be incorporated into stable MOFs. In this context, aza-Michael reactions provide a potential method of introducing a range of functionalities into MOF structures. The aza-Michael reaction is a conjugate addition in which a nitrogen nucleophile adds to the...
β-carbon of an electron-deficient alkene. The reaction is a versatile method for constructing new C-N bonds, and it generally requires a Lewis acid catalyst such as Bi(OTf)₃ or SmI₂ to proceed. More recent studies have shown that theaza-Michael reaction can take place without the aid of a catalyst. For example, Li and co-workers demonstrated that azoles react readily with a range of α,β-unsaturated α-keto esters to afford new C-N bond adducts, whereas Legros, Crouse and co-workers reported that aza-Michael additions could progress in polar protic solvents without any promoting agent. In this report, they demonstrated that the choice of the solvent is crucial in determining the products obtained, with both the mono-adduct and the di-adduct accessible.

Encouraged by the precedence for catalyst-free Michael additions, we sought to assess whether such reactions could be employed in the post-synthetic modification of MOFs. To this end we have investigated the aza-Michael addition reactions between [Zr₆O₄(OH)₄(hdc-NH₂)₆] (UiO-66-NH₂) and acrylonitrile (CH₂=CHCN), acrylic acid (CH₂=CHCO₂H), methyl acrylate (CH₂=CHCO₂Me) and methyl vinyl ketone (CH₂=CHC(O)Me). The reaction in an autoclave at 120 °C for 24 hours was collected for 24 hours. Subsequently, the yellow microcrystalline material was collected via centrifugation and dried under reduced pressure. The reaction between UiO-66-NH₂ and acrylonitrile was initially carried out under reflux for 24 h using a range of solvents. While a small degree of conversion (4–5%) was observed using the polar protic solvents hexafluoroorisopropanol and 2,2,2-trifluoroethanol, the best conversion (38%) was found using water as the solvent. In all cases, the degree of conversion was obtained from the ¹H NMR spectrum of the digested MOF. Most previous work has used hydrofluoric acid to digest UiO-66 and its derivatives. We found that UiO-66-NH₂ and its derivatives were readily digested in ammonium fluoride solution, and have used NH₄F/D₂O as a digestion method throughout this work in order to avoid the hazards associated with HF, with DMSO-d₆ added for ³¹H NMR analyses.

Lengthening the reaction time from 24 h to 5 days increased the extent of modification to 50%, though further increase of the reaction time did not lead to higher percentage conversions. However, complete conversion was achieved on leaving the reaction in an autoclave at 120 °C for 2 days to yield a product with the formula [Zr₆O₄(OH)₄(hdc-NHCH₂CH₂CN)₆] (UiO-66-AN, 1) (Scheme 1). It is likely that the closed environment created by the autoclave prevents acrylonitrile vapour from being lost from the reaction vessel, and this combined with the higher temperature leads to full conversion.

The ¹H NMR spectrum for UiO-66-AN following digestion (Fig. S1†) shows triplets at δ 2.71 ppm and δ 3.42 ppm which correspond to the β- and α-protons to the secondary nitrogen of D₂hdc-NHCH₂CH₂CN. The resonances at δ 6.95 (dd), 7.05 (d) and 7.65 (d) ppm correspond to the protons from the aromatic ring of D₂hdc-NHCH₂CH₂CN. The addition of a second acrylonitrile molecule into UiO-66-AN to form the di-adduct with bdc-N(CH₂CH₂CN)₂ substituents was ruled out through comparison of the integrals for the aromatic and aliphatic protons. Furthermore, the negative ion ESI mass spectrum of UiO-66-AN digested in NH₄F/H₂O confirms the presence of the singly deprotonated anion of H₂bdc-NHCH₂CH₂CN at m/z = 233.0561 (predicted [M − H]⁻ = 233.0562). The FTIR spectrum for UiO-66-AN (Fig. S2†) shows a broad peak at 3364 cm⁻¹

Results and discussion

UiO-66-NH₂ was synthesised using a previously reported procedure. The as-synthesised MOF was rinsed and soaked in 14492 | Dalton Trans., 2018, 47, 14491–14496

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which corresponds to $\nu$(N–H) of the modified framework. The presence of $\nu$(C==N) at 2161 cm$^{-1}$ confirms the presence of the cyanoethoxy groups. The high similarity between the powder X-ray diffraction (PXRD) pattern of UiO-66-AN and that of UiO-66-NH$_2$ indicates that the structural integrity of the MOF was retained upon post-synthetic modification (Fig. S3†). This illustrates the robustness of the UiO-66 framework, as neither the post-synthetic modification reaction nor the high-temperature employed has any effect on the crystallinity of the MOF. The greater intensity of the peak at 20 12° in the PXRD pattern compared with that in the simulated pattern is consistent with previous observations with UiO-66 type MOFs and is related to desolvation, with the calculated pattern based on the activated framework.

Following this optimisation of the reaction conditions, the aza-Michael reaction was repeated using acrylic acid, methyl acrylate, methyl vinyl ketone and vinyl phosphonic acid as Michael acceptors. Successful conversions were observed in the cases of acrylic acid, methyl acrylate and methyl vinyl ketone, as summarised in Scheme 2. Reactions with vinyl phosphonic acid yielded amorphous powders as evidenced by PXRD and were not explored further.

For the reaction with acrylic acid, the $^1$H NMR spectrum of the NH$_4$F/D$_2$O-digested product UiO-66-AA (Fig. S4†) showed peaks at $\delta$ 6.94 (dd), 7.09 (d) and 7.54 (d) ppm, corresponding to the aromatic protons of D$_2$bdc-NHCH$_2$CH$_2$CO$_2$D. Two sets of triplets at $\delta$ 2.34 and 3.23 ppm were also observed and the absence of peaks corresponding to D$_2$bdc-NH$_2$ confirmed full conversion to [Zr$_6$O$_4$(OH)$_4$(bdc-NHCH$_2$CH$_2$CO$_2$H)$_4$]$_2$. PXRD (Fig. S5†) revealed that this product has retained crystallinity and is structurally similar to UiO-66-NH$_2$. Despite the success of these small scale reactions, efforts to scale up the synthesis of 2 proved difficult. $^1$H NMR spectra carried out on the digested products of larger scale reactions were more complicated than those of the small scale reactions, efforts to scale up the synthesis of 2 proved difficult. $^1$H NMR spectra carried out on the digested products of larger scale reactions were more complicated than those of the small scale reactions, efforts to scale up the synthesis of 2 proved difficult. $^1$H NMR spectra carried out on the digested products of larger scale reactions were more complicated than those of the small scale reactions, efforts to scale up the synthesis of 2 proved difficult. $^1$H NMR spectra carried out on the digested products of larger scale reactions were more complicated than those of the small scale reactions, efforts to scale up the synthesis of 2 proved difficult. $^1$H NMR spectra carried out on the digested products of larger scale reactions were more complicated than those of the small scale reactions, efforts to scale up the synthesis of 2 proved difficult.

For the reaction with methyl vinyl ketone, the $^1$H NMR spectrum of the NH$_4$F/D$_2$O-digested product (Fig. S6†) showed peaks at $\delta$ 6.88 (d), 7.03 (s) and 7.61 (d) ppm, corresponding to the aromatic protons of D$_2$bdc-NHCH$_2$CH$_2$CO$_2$Me, indicating that the post-synthetic modification was successful. Furthermore, two sets of triplets at $\delta$ 2.27 and 3.21 ppm can be seen in the aliphatic region, which correspond to the $\beta$- and $\alpha$-protons to the secondary nitrogen, respectively. By comparing the integrals of the aromatic protons for D$_2$bdc-NHCH$_2$CH$_2$CO$_2$Me with those for D$_2$bdc-NH$_2$, present, the degree of conversion can be calculated as 89%. This gives an average formula for UiO-66-MA of [Zr$_6$O$_4$(OH)$_4$(bdc-NH$_2$)$_{0.8}$bdc-NHCH$_2$CH$_2$CO$_2$Me]$_{3.14}$ 3. The negative ion ESI mass spectrum of NH$_4$F/H$_2$O-digested UiO-66-MA confirmed the presence of singly deprotonated anion of H$_2$bdc-NHCH$_2$CH$_2$CO$_2$Me at $m/z$ 266.0661 (predicted $M − H^− = 266.0665$). The FTIR spectrum showed a weak peak at 3364 cm$^{-1}$ (Fig. S7†), which corresponds to $\nu$(N–H). The presence of ester groups on the modified framework was confirmed by observation of $\nu$(C==O) at 1712 cm$^{-1}$. PXRD (Fig. S8†) revealed that UiO-66-MA was crystalline, and the similarities between its powder pattern and that for UiO-66-NH$_2$ confirmed that the framework remained intact and retained its crystallinity upon the aza-Michael reaction.

The reaction with methyl vinyl ketone was undertaken using the same conditions as those with acrylonitrile and methyl acrylate. The $^1$H NMR spectrum of the digested product (Fig. S9†) confirmed that reaction had occurred, with new signals in both the aromatic and aliphatic regions. Specifically, signals at $\delta$ 6.90 (d), 7.05 (s) and 7.63 (d) ppm correspond to the aromatic protons in D$_2$bdc-NHCH$_2$CH$_2$C(O)Me, whereas triplets at $\delta$ 2.72 and 3.27 ppm correspond to the $\beta$- and $\alpha$-protons relative to the secondary nitrogen atom. Based on the aromatic signals for D$_2$bdc-NH$_2$ and D$_2$bdc-NHCH$_2$CH$_2$C(O)Me, it can be deduced that the reaction proceeded with 54% conversion. The formula for UiO-66-MVK can therefore be expressed as [Zr$_6$O$_4$(OH)$_4$(bdc-NH$_2$)$_{2.76}$bdc-NHCH$_2$CH$_2$C(O)Me]$_{3.24}$ 4. The FTIR spectrum of the solid sample shows a broad peak at 3367 cm$^{-1}$ (Fig. S10†) which corresponds to $\nu$(N–H). The presence of ketone functional groups on the modified framework was confirmed by observation of $\nu$(C==O) at 1710 cm$^{-1}$. PXRD (Fig. S11†) revealed that UiO-66-MVK has the same gross structure as UiO-66-NH$_2$, showing that, as with the aza-Michael additions using acrylonitrile, acrylic acid and methyl acrylate, post-synthetic modification does not affect the crystallinity of the MOF.

The results from the post-synthetic aza-Michael reactions are summarised in Table 1. The degree of conversion from primary amine to the aza-Michael product is related to the electron withdrawing power of the acceptor used, with the nitrile group in acrylonitrile being more electron withdrawing than the ester and ketone groups in methyl acrylate and methyl vinyl ketone, respectively.

In order to access whether the nitrile groups in UiO-66-AN can be transformed into other functional groups, further post-synthetic modification reactions were assessed. Initial results suggested that the most promising of these was the reaction of UiO-66-AN with sodium azide in the presence of zinc(II) chlor-
Table 1  Outcomes of aza-Michael post-synthetic modification reactions carried out on UiO-66-NH$_2$ at 120 °C for 48 h

<table>
<thead>
<tr>
<th>Michael acceptor</th>
<th>% Conversion</th>
<th>Product</th>
</tr>
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<tbody>
<tr>
<td>CH$_3$=CHCN</td>
<td>100</td>
<td>[Zr$_6$O$_4$(OH)$_4$(bdc-NHCH$_2$CH$_2$CN)$_2$.76$(bdc-NHCH$_2$CH$_2$O(Me)$<em>3$)$</em>{2.76}$] 4 (UiO-66-MVK)</td>
</tr>
<tr>
<td>CH$_3$=CHCO$_2$H</td>
<td>100</td>
<td>[Zr$_6$O$_4$(OH)$_4$(bdc-NHCH$_2$CO$_2$H)$_2$.6$(bdc-NHCH$_2$CH$_2$O(Me)$<em>3$)$</em>{3.36}$] 3 (UiO-66-MA)</td>
</tr>
<tr>
<td>CH$_3$=CHCO$_2$Me</td>
<td>89</td>
<td>[Zr$_6$O$_4$(OH)$_4$(bdc-NH$_2$)$_2$.76$(bdc-NHCH$_2$CH$_2$O(Me)$<em>3$)$</em>{2.76}$] 4 (UiO-66-MVK)</td>
</tr>
<tr>
<td>CH$_3$=CH(CO)Me</td>
<td>54</td>
<td>[Zr$_6$O$_4$(OH)$_4$(bdc-NH$_2$)$_2$.76$(bdc-NHCH$_2$CH$_2$O(Me)$<em>3$)$</em>{2.76}$] 4 (UiO-66-MVK)</td>
</tr>
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</table>

* Small scale reaction.

Scheme 3  Post-synthetic modification of UiO-66-AN on reaction with sodium azide in the presence of zinc(ii) chloride and n-butanol.

ide, which was anticipated to convert the nitrile groups into tetrazoles. This reaction was found to be very dependent on the solvent used, with no conversion observed using water, ethanol, $n$-propanol, DMF or acetonitrile. In contrast, a reaction was observed when $n$-butanol was used as the solvent (Scheme 3).

The successful conversion of nitrile groups to tetrazoles was confirmed by $^1$H NMR spectroscopy of the digested product (Fig. S12†). New sets of peaks ($6.92$ d, $7.08$s and $7.61$d ppm) were observed in the aromatic region, in addition to the peaks which correspond to the aromatic protons of D$_2$bdc-NH$_2$CH$_2$CN. The new peaks correspond to the protons from the benzene ring of D$_2$bdc-NH$_2$CH$_2$CN$_2$H. A triplet due to the $\alpha$-protons to the secondary nitrogen of D$_2$bdc-NHCH$_2$CN$_2$H is clearly visible at $\delta$ 3.0 ppm, though the triplet of the neighbouring $\beta$-protons is only partly visible due to overlapping with the more dominant triplet resulting from D$_2$bdc-NH$_2$CH$_2$CN$_2$H. The percentage conversion from nitrile to tetrazole was estimated on the basis of the integrals to be approximately 21%, which gives an formula for UiO-66-TZ as [Zr$_6$O$_4$(OH)$_4$(bdc-NHCH$_2$CH$_2$CN)$_2$.76$(bdc-NHCH$_2$CH$_2$O(Me)$_3$)$_{2.76}$] 5.

The negative ion ESI mass spectrum of the digested product confirmed the singly deprotonated anion of H$_2$bdc-NH$_2$CH$_2$CN$_2$H at $m/z = 276.0727$ (predicted [M − H]$^-$ = 276.0733).

In order to investigate the structural integrity of the PSM product, PXRD was carried out on the solid sample UiO-66-TZ. The sample was extensively rinsed with $n$-BuOH prior to the PXRD measurement and the pattern of the $n$-BuOH-rinsed sample shows additional peaks at $2\theta$ 31.5°, 34.5°, 36.0° and 47.5° in addition to those corresponding to the UiO-66 framework (Fig. S13†). These additional peaks do not derive from unreacted reagents, and they were removed by washing the sample with water. Reactions were undertaken using different times and catalyst loadings, but conversion could not be raised above 21%. This is likely to be a consequence of pore blocking by the relatively large ethyltetrazole groups, which is consistent with the nitrogen adsorption data (vide infra).

The thermal stability of the post-synthetically modified products 1 and 3–5 was assessed by thermogravimetric analysis (TGA) (Fig. S14†). The samples were rinsed with water prior to the TGA measurements. An initial mass loss of 2–17% was seen in all cases between 50 and 120 °C. This can be attributed to the loss of included water molecules, and the different amounts reflect the remaining pore space following the modification reactions. A second small (~3%) and gradual mass loss (120 °C–440 °C) may be attributed to residual DMF solvent in the pores and/or the dehydroxylation of the Zr$_6$O$_4$(OH)$_4$ nodes. The UiO-66 series of MOFs are known to undergo complete dehydroxylation reactions below 300 °C.34 Normally, a plateau region in a TGA profile represents the range of temperature that can be used to produce the activated form of a MOF. Due to the gradual mass loss in the 120 °C–440 °C region, 120 °C was chosen as the activation temperature, which is consistent with that used in previous studies on UiO-66 derivatives.36–38 The mass loss above 440 °C corresponds to decomposition of the framework, and is similar to previous reports for UiO-66-NH$_3$ and related MOFs.32,39 These results implies that post-synthetic modification does not alter the thermal stability of UiO-66-NH$_3$.

In order to investigate the porosity of the products, N$_2$ adsorption measurements were carried out on 1 and 3–5 at 77 K. Prior to the measurements, the samples were activated at 120 °C for 12 h. $^1$H NMR analysis of the digested activated samples confirmed that no solvent molecules were present upon activation. Furthermore, the PXRD patterns of the activated samples were similar to those prior to activation, indicating that the activation conditions did not alter the crystallinity of the MOFs. The N$_2$ adsorption isotherms for UiO-66-NH$_3$ and 1 and 3–5 are shown in Fig. 2, and the calculated BET surface areas for these MOFs are given in Table 2.

The BET surface area for UiO-66-NH$_3$ obtained in this work is similar to values reported in the literature for this material, which range from 778 to 1293 m$^2$ g$^{-1}$32,39–42 The derivatives 1, 3 and 4 exhibited Type I isotherms with each product showing a lower degree of porosity than UiO-66-NH$_3$, which is consistent with the mass increase caused by the tag groups in the pores which also reduce the space available for guest inclusion. The percentage conversion of the post-synthetic
Modification reaction also has an impact on the BET surface area and, in general, the higher the percentage conversion, the lower the surface area observed. This accounts for the higher value of $S_{BET}$ for 4 in comparison to 1 and 3. The effect of pore blocking with large introduced substituents is especially apparent in the essentially non-porous nature of 5, which shows a Type II isotherm.

The CO$_2$ isotherms of 1 and 3–5 at 273 K were also recorded, and are shown in Fig. 3. The CO$_2$ uptakes are lower than that for UiO-66-NH$_2$, which is likely to be related to the pore blocking effect of the tag groups as this limits diffusion of CO$_2$ molecules into the pores. Furthermore, the absence of the primary amine group in the pores may contribute to the lower CO$_2$ uptake. It is notable than the CO$_2$ uptake for 1 is higher than that for 3. This is likely to be due to the relative sizes of the tag groups. Unexpectedly, the CO$_2$ loading of 5 is somewhat higher than that for 4 despite the former being non-porous to nitrogen. One possible reasoning for this observation is the strong interaction of CO$_2$ molecules with the tetrazole moieties. MOFs with nitrogen-rich environments such as those with tetrazole- and triazole-functionalties have been previously reported to have high affinity towards CO$_2$, and in the case of 5 much of this may occur on external surfaces.

Conclusions

A new versatile, single-step post-synthetic modification reaction for MOFs has been developed. In this process, the primary amino group in UiO-66-NH$_2$ is converted into a range of secondary amines bearing different functional groups via a catalyst-free aza-Michael addition. The reaction was achieved by reacting UiO-66-NH$_2$ with four different alkenes containing electron withdrawing groups, CH$_2$=CHR (R = CN, CO$_2$H, CO$_2$CH$_3$, C(O)CH$_3$). The degrees of conversion were governed by the strength of the electron withdrawing groups attached to the alkenes with the stronger electron withdrawing groups leading to higher conversion. Following optimisation, the highest conversion (100%) was achieved whilst using either acrylonitrile or acrylic acid, with incomplete reactions for methyl acrylate (89%) and methyl vinyl ketone (54%). A second post-synthetic modification was successfully performed on UiO-66-AN in which the MOF was treated with NaN$_3$ and ZnCl$_2$ catalyst in n-BuOH. This reaction resulted in the partial conversion of the nitrile groups into tetrazoles.

We anticipate that the aza-Michael process described is likely to be readily extended to other MOF systems that possess high stability towards H$_2$O and alcohols. Current work is seeking to investigate this in addition to expanding the range of alkenes that can be used as Michael acceptors in this process. Furthermore, we are studying additional post-synthetic modification reactions on UiO-66-AN and investigating the acid behaviour of UiO-66-AN.

Conflicts of interest

There are no conflicts to declare.

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Notes and references