Amine-linked Covalent Organic Frameworks as a Powerful Platform for Post-Synthetic Modification: Structure Interconversion and Combined Linkage- and Pore-Wall-Modification

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Abstract

Covalent organic frameworks have emerged as a powerful synthetic platform for installing and interconverting dedicated molecular functions on a crystalline polymeric backbone with atomic precision. Here, we present a novel strategy to directly access amine-linked covalent organic frameworks, which serve as a scaffold enabling pore-wall modification and linkage-interconversion by new synthetic methods based on Leuckart-Wallach reduction with formic acid and ammonium formate. Frameworks connected entirely by secondary amine linkages, mixed amine/imine bonds, and partially formylated amine linkages are obtained in a single step from imine-linked frameworks, or directly from corresponding linkers in a one-pot crystallisation-reduction approach. The new, 2D amine-linked covalent organic frameworks, rPI-3-COF, rTTI-COF, and rPy1P-COF, are obtained with high crystallinity and large surface areas. Secondary amines, installed as reactive-sites on the pore wall, enable further post-synthetic functionalisation to access tailored covalent organic frameworks, with increased hydrolytic stability, as potential heterogeneous catalysts.

Introduction

In recent years, covalent organic frameworks (COFs) have emerged as a versatile class of crystalline porous polymers, which have been pushing the frontiers of single-site heterogeneous catalysis ever since. The unique combination of ordered and tuneable pore structures, with high surface areas and versatile (opto-)electronic properties, offers great opportunities beyond gas storage and separation, including sensing,
electrochemical energy storage, optoelectronics, and heterogeneous (photo-)catalysis.\textsuperscript{1, 2, 3, 4}

Imine-linked COFs constitute the most widely studied subclass of COFs owing to their wide synthetic scope and facile building block synthesis. The dichotomy of dynamic covalent chemistry in COF synthesis implies that while reversible bond formation is critical for crystallisation, the reversibility of imine bond formation also causes its limited stability against hydrolysis. To address this issue, several post-synthetic locking strategies have been developed in the past, e.g. converting labile imine-linked COFs into stable benzothiazole-,\textsuperscript{5, 6} amide-,\textsuperscript{7} or quinoline-linked frameworks.\textsuperscript{4, 8, 9, 10, 11, 12, 13} Although these methods significantly increase the material’s hydrolytic stability, most do not activate, but rather deactivate potential reactivity of the linkages for further pore-wall modification. To achieve the latter, reactive centres have to be installed into the linker moieties, which are often incompatible with synthesis conditions. This incompatibility requires an additional pore-wall activation step, e.g. reduction of nitro groups to amines,\textsuperscript{14} or deprotection of ethers to alcohols.\textsuperscript{15} In essence, a typical synthetic route would consist of at least four sequential steps, including a) framework crystallisation, b) linkage transformation, c) pore-wall activation and d) pore-wall functionalisation to obtain both stable and decorated frameworks. Being faced with varying conversion yields and loss of material between each step, innovative synthetic methods condensing these transformations into fewer steps, or even a single synthetic step, are highly desirable.

As a solution to the challenges discussed, we here demonstrate amine-linked covalent organic frameworks as a powerful platform for facile pore-wall modification and linkage-interconversion enabled by new synthetic methods based on Leuckart-
Wallach\textsuperscript{16,17} reduction with formic acid and ammonium formate. By fine-tuning the reaction conditions, frameworks connected entirely by secondary amine linkages, mixed amine/imine bonds, and partially formylated amine-linkages are accessible in a single step from imine-linked frameworks, or directly from the corresponding linkers in an one-pot crystallisation-reduction approach. We thus present a novel strategy enabling direct access to amine-linked covalent organic frameworks. In addition, we reveal correlations between topologically equivalent disordered and crystalline frameworks which are not accessible by typical X-ray powder diffraction (XRPD) analysis, using pair distribution function (PDF) analysis, solid-state nuclear magnetic resonance spectroscopy (ssNMR) and quantum-chemical calculations. These findings enable us to identify unique pH-dependent amorphisation pathways and hence expand our fundamental understanding of amine-linked covalent organic frameworks as an important, yet underexplored class of heterogeneous catalysts.

**Results**

**Previous Strategies and Drawbacks**

During our studies, we found that a reduction of imine-linkages would both increase the hydrolytic stability of the framework and introduce secondary amine-linkages as reactive centres for further functionalisation of the pore-wall. This transformation, familiar from small organic molecules as well as molecular cages, is usually achieved using borohydride-based reducing agents, such as sodium borohydride or sodium cyanoborohydride.\textsuperscript{18,19,20} Borohydride-based reduction has successfully been used for robust and rigid 3D systems, while 2D frameworks have only been obtained with
diminished crystallinity and low surface areas at best.\textsuperscript{11, 15, 21} While highly reactive, reactions with sodium borohydride, in particular, suffer from limited selectivity and low functional group tolerance.\textsuperscript{5, 22} With these shortcomings in mind, we sought an alternative, mild reduction procedure affording crystalline and porous amine-linked covalent organic frameworks. To this end, we identified the Leuckart-Wallach reduction with formic acid, reported for small organic molecules by R. Leuckart in 1885 and further developed by O. Wallach, as a suitable reduction strategy.\textsuperscript{16, 17}
Synthesis of Amine-linked COFs

Figure 1: (a) Synthesis of amine-linked covalent organic frameworks. (b) FT-IR spectra, (c) $^{13}$C CP-MAS ssNMR spectra and (d) XRPD pattern comparison of PI-3-COF (green) and rPI-3-COF (blue). (e-1) Chemical structure of a single pore of rPI-3 (e), rTTI (f) and rPy1P-COF (g). (h-j) Rietveld refinements for rPI-3 (h), rTTI-COF (i) and rPy1P-COF (j).
As a model system, we first synthesised the imine-linked PI-3-COF from 1,3,5-triformyl benzene (TFB) and 4,4',4''-(1,3,5-triazine-2,4,6-triyl)trianiline (TTA) under solvothermal conditions in a 2:1 mesitylene:1,4-dioxane mixture with aqueous 6M AcOH at 120°C for 72h, according to a modified literature procedure.\textsuperscript{23} Upon reacting the imine-linked PI-3 framework in a sequential step with 19 equivalents (equiv.) of formic acid in the same solvent, a new vibration appeared at 3405 cm\(^{-1}\) as probed by Fourier transform infra-red spectroscopy (FT-IR), attributed to a secondary amine (\(v_{\text{N-H}}\)) stretching mode. The intensity of the imine vibration (\(v_{\text{C=N}}\)) at 1630 cm\(^{-1}\) gradually decreased over prolonged reaction time at 120°C (Supplementary Fig. S1). Extensive screening for highest relative intensities of the secondary amine vibrations in the IR spectrum yielded optimal synthetic conditions at 21 equiv. of formic acid in a 2:1 mesitylene:1,4-dioxane mixture and a reaction time of 24 h at 120°C. Under these conditions, the samples did not show any residual imine stretch vibration (\(v_{\text{C=N}}\)), hinting at the complete transformation of the parent PI-3-COF structure (Fig. 1b).\textsuperscript{13}C cross polarisation magic angle spinning (CP-MAS) solid-state NMR (ssNMR) spectroscopy similarly shows the disappearance of the characteristic imine carbon signal at 155.3 ppm, while a new aliphatic carbon signal at 45.4 ppm is visible for the reduced PI-3-COF (rPI-3-COF). Besides that, new signals at 119 ppm and 114 ppm become visible for rPI-3-COF, assigned to the aromatic carbons next to the amine bond (Fig. 1c). \textsuperscript{15}N ssNMR of rPI-3-COF shows distinct signals at -313.3 ppm for the secondary amine nitrogen, and at -141.4 ppm for the triazine (Supplementary Fig. S29). The absence of the imine nitrogen at -59.0 ppm further suggests a quantitative reduction of imine into amine linkages in rPI-3-COF. The measured ssNMR chemical
shifts are in good agreement with values obtained by quantum-chemical calculations of representative molecular and single pore models (Supplementary Table S5).

Structural analysis of rPI-3-COF via XRPD reveals high crystallinity (Supplementary Table S3), represented by four narrow reflections at $2\theta = 5.6$, 9.7, 11.2, 14.9°, indexed as 100, 110, 200 and 210 reflections (space group P-6), and a broad stacking reflection at $2\theta = 25.3°$. Compared to its parent imine structure (PI-3-COF), the apparent hexagonal symmetry and crystallinity are retained, while a significant shift of the broad stacking reflection at $2\theta = 25.6°$ (PI-3-COF) towards smaller angles appears. Rietveld refinement gives a larger in-plane unit cell parameter of $a = 18.090(7)$ Å and an increased stacking distance of $c = 3.5425(12)$ Å in rPI-3-COF ($a = 18.034(7)$ Å and $c = 3.5058(12)$ Å for PI-3-COF) (Supplementary Table S1). While the cell parameter $a$ is affected by increased C-N (149 pm) vs. C=N (127 pm) bond lengths, the stacking distance ($c$ parameter) is also influenced by both enhanced steric repulsion of the benzylic (CH$_2$) protons of adjacent layers and higher flexibility of the secondary amine bond in rPI-3-COF. Notably, sorption isotherms reveal complete retention of porosity and pore-size distributions (Supplementary Fig. S59, S62) of the materials with Brunauer-Emmett-Teller (BET) surface areas of 1395 m$^2$g$^{-1}$ for rPI-3-COF (Supplementary Fig. S73) and 1404 m$^2$g$^{-1}$ for PI-3-COF (Supplementary Fig. S68), even exceeding those previously published for PI-3-COF ($\sim$1000 m$^2$g$^{-1}$). It must be noted, however, that the porosity of rPI-3-COF is strongly influenced by the drying procedure: simple vacuum-drying from dichloromethane resulted in a reduced BET surface area of 966 m$^2$g$^{-1}$ (Supplementary Fig. S74), while solvent exchange to methanol (Soxhlet extractor) and subsequent activation with supercritical CO$_2$ (scCO$_2$) gave the best results for rPI-3-COF with
1395 m^2g^{-1} (Supplementary Fig. S67, S73). While this effect was not observed for the rigid imine PI-3 framework, increased flexibility in rPI-3-COF and modulated pore wall polarity upon reduction are expected to enhance solvent interactions and capillary effects, potentially intensifying drying-induced disorder and pore collapse.\textsuperscript{26,27} Scanning electron microscopy (SEM) and transmission electron microscopy (TEM) images reveal intergrown, coral-shaped particle morphologies with sizes between 600 to 1000 nm, decorated with 200 nm long and 60 nm wide stings, for both imine-linked and reduced PI-3-COF (Supplementary Fig. S77, S80). The similarity of the morphology before and after reduction renders intermediate recrystallisation processes unlikely to be at play. TEM images show uniformly distributed crystallinity and extended porous channels of hexagonal symmetry in the materials, which are consistent with the structural model derived from XRPD data and Rietveld refinement (Supplementary Fig. S85, S90).

To demonstrate the general applicability of this protocol, we applied it to two additional imine COFs with larger pores, different linker composition and pore geometry. Both TTI-COF and Py1P-COF were successfully reduced to their new amine-linked derivatives rTTI-COF, and rPy1P-COF with high crystallinity as evident from sharp reflections at $2\theta = 4.0^\circ$ (100), $6.9^\circ$ (110), $8.1^\circ$ (200), $25.6^\circ$ (stacking) for rTTI and $2\theta = 3.7^\circ$ (110), $5.4^\circ$ (020), $7.5^\circ$ (220), $8.5^\circ$ (130), $11.3^\circ$ (330), $23.2^\circ$ (stacking), rPy1P-COF, respectively. During our screenings to find the optimum reduction conditions for rPy1P-COF, we noticed palladium contamination in both the building blocks and the framework, introduced by palladium-based cross-coupling reactions during linker synthesis. TEM images of an initial sample of Py1P-COF (Pd contaminated) show unevenly distributed palladium nanoparticles in the material (Supplementary Fig. S88,
While this contaminant did not affect the crystallisation step of Py1P-COF, the metal particles "overcatalysed" the reduction with formic acid, causing a partial digestion of the framework. To avoid this contamination, the 4,4',4'',4'''-(pyrene-1,3,6,8-tetrayl)tetraaniline linker was further purified on a metal scavenger (Biotage® Isolute Si-TMT). A purified imine-linked Py1P-COF was then crystallised and reduced with formic acid to form rPy1P-COF without any noticeable decomposition. SEM and TEM images of rTTI and rPy1P-COF thus show full retention of the porous, crystalline features of their parent frameworks (Supplementary Fig. S86, S87, S93, S94).

Similar to the rPI-3-COF model system, new N-H vibrations at 3407 cm\(^{-1}\) (rTTI) or 3398 cm\(^{-1}\) (rPy1P) in the FT-IR spectra, and secondary amine nitrogen signals at -314.9 ppm (rTTI) and -317.6 ppm in the \(^{15}\)N-ssNMR spectra prove the conversion into amine-linked frameworks (Supplementary Fig. S3, S4, S34, S37). Although both samples show good porosity (1419 m\(^2\)g\(^{-1}\) rTTI, 1042 m\(^2\)g\(^{-1}\) rPy1P), the BET surface area of rPy1P is reduced, compared to 1883 m\(^2\)g\(^{-1}\) in Py1P-COF (Supplementary Fig. S69, S70, S72, S73). Comparing linker geometries in small pore hexagonal rPI-3, large pore hexagonal rTTI, and square-net rPy1P-COF frameworks, those consisting of more rigid tritopic+tritopic [3+3] linker combinations (rPI-3 and rTTI-COF) show full retention of the BET surface area, while the tetratopic+bitopic [4+2] linker combination in rPy1P-COF was obtained with slightly reduced surface area. This is in line with the expected additional flexibility around the molecular axis of the bitopic terephthalaldehyde linker, which facilitates local distortions in the network, causing reduced accessibility of the pores and thus smaller surface area in rPy1P-COF.
Upon reduction, the in-plane cell parameters of larger pore square-net rPy1P-COF were barely influenced, with C-N bond lengths contributing only a small percentage to the overall pore-to-pore distance. On the other hand, the increased stacking distance caused an expansion of the unit cell from $c = 3.818(4)$ Å to $c = 4.069(9)$ Å, similar to the small pore rPI-3-COF. At first sight, these trends cannot be found for the rTTI framework in direct comparison to TTI-COF. Apparent symmetry\textsuperscript{29} changes (peak splitting) in the XRPD pattern, however, shows that upon reduction the stacking behaviour of TTI-COF changes from antiparallel slip-stacked TTI (P1) to more eclipsed-like stacking in rTTI with an average crystallographic symmetry of $P6_3/m$ (Supplementary Fig. S9, S13, Supporting Table S1, S2). Similar symmetry correlations have been described for the TTI-COF system by Haase et. al. in comparison to its randomly stacked TTI (rsTTI) framework, resulting in both in-plane and interlayer contractions.\textsuperscript{29, 30} This trend is also observed with rTTI-COF: The increase in symmetry is accompanied by a pore contraction ($a = 25.786(12)$ Å (TTI) vs. $a = 25.147(9)$ Å (rTTI)), caused by changed bond angles of antiparallel amine bonds, resulting in overall reduced intralayer cell parameters for rTTI. Furthermore, enhanced interlayer interactions in the eclipsed-stacked rTTI-COF compensate repulsive steric effects of benzylic protons, and thus stacking distances decrease from $3.578(9)$ Å in TTI to $3.504(2)$ Å in the reduced framework (Supplementary Table S1, S2).

\textbf{One-pot procedure: Reductive crystallisation}

When comparing the conditions needed for the synthesis of the imine framework and the following reduction, acids and the same solvent mixture are used in both cases, and only the amount and type of acid changes. Thus, we expected formic acid could act as a
catalyst for both the formation and reduction of the framework, condensing the individual steps into a single one-pot crystallisation-reduction approach.

Indeed, with 21 equiv. of formic acid in a 2:1 mixture of mesitylene:1,4-dioxane at 120°C for 72 h, a crystalline sample of rPI3-COF was obtained directly from its corresponding aldehyde and amine building blocks (Supplementary Fig. S15). Compared to its two-step analogue, it was obtained in a different, spherical morphology (Supplementary Fig. S82). As visible from broadened signals in the $^{13}$C ssNMR and FT-IR spectra (Supplementary Fig. S7, S48), this sample is structurally less well-defined with a major impact on the resulting porosity (BET area of 174 m$^2$g$^{-1}$, Supplementary Fig. S76). During our studies, we noticed a significant impact of the reaction temperature on the obtained product. While formic acid catalyses the imine condensation both at high (120°C) and already at low (60°C) temperature, the subsequent reduction is fast only at elevated temperature (Supplementary Fig. S16). As such, the one-pot protocol can be used to thermally switch between the reversible synthesis of an imine-linked COF at low temperature or the irreversible “locking” of the framework structure by simultaneous reduction to the amine-linked COF using otherwise identical reaction conditions. We expect this unique property to be key for the adaptation to other covalent organic frameworks. Besides this “thermo-switchability” it highlights formic acid as a versatile, yet underexplored catalyst for the synthesis of imine-linked COFs at reduced temperature.

Reductive formylation: Combined reduction and protection

Solid ammonium formate as a green, less toxic, and less corrosive alternative to formic acid was also effective for the reduction of imine bonds under solvent-free conditions. Reacting a salt-melt of ammonium formate and PI-3-COF for 3 h at 170°C in a closed
vessel afforded a product with broadened secondary amine vibrations at $v_{\text{N-H}} = 3370 \text{ cm}^{-1}$ and carbonyl stretching modes at $v_{\text{C=O}} = 1669 \text{ cm}^{-1}$ in the FT-IR spectrum (Supplementary Fig. S6). An additional signal at 162.8 ppm in the $^{13}$C ssNMR spectrum, referring to an N-formyl-carbon (Supplementary Fig. S42, S45), shows that besides the reduction, a subsequent N-formylation resulted in a partially formylated, reduced PI-3 framework (pfrPI-3-COF). Comparison of FT-IR and ssNMR spectra excludes a degradation of the chemical connectivity. The XRPD pattern shows substantial reduction in the long-range order reminiscent of an amorphous solid, although a small feature corresponding to the 100 peak further suggests that the intralayer connectivity is maintained (Supplementary Fig. S17). When reacting pfrPI-3-COF with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in dichloromethane, the secondary amine linkages are oxidised back to the imine linkages, affording re-oxidized, partially formylated reduced PI-3-COF (opfrPI-3-COF). Remarkably, after this treatment sharp signals in the XRPD pattern similar to the parent PI-3 framework become visible (Supplementary Fig. S11, S17. The feasibility of this amorphous-to-crystalline conversion suggests a significant topological and structural similarity of the reduced, amorphous COF to the crystalline compound, and led us to further investigate the correlations between crystalline and non-crystalline amine-linked frameworks.

**Crystalline vs. Disordered**

During our screenings to find optimal reduction conditions for the imine-linked frameworks, we noticed that a large excess of formic acid can decrease the crystallinity of the product, suggesting a profound role of protonation on the layer structure. Using 59.5 equiv. of formic acid with PI-3-COF under the same conditions as above leads to a
practically X-ray amorphous structure with slightly broadened but otherwise essentially identical signals as rPI-3-COF in the FT-IR and ssNMR spectra (Supplementary Fig. S5, S47). SEM and TEM did not show any morphological changes of the particles (Supplementary Fig. S81, S91). Stability tests of rPI-3-COF, e.g. under acidic conditions, show similar effects on the reflections in the XRPD patterns. In contrast to the imine-linked PI-3-COF, the amine-linked rPI-3-COF does not show any hydrolytic decomposition, though sharp reflections in the XRPD pattern broaden or disappear completely upon treatment with excess acid – illustrating local structural changes and distortion of the stacked 2D layers (Supplementary Fig. S95, S96).
To elucidate conformational changes in the structure of PI-3-COF upon reduction, quantum-chemical calculations on PBE0-D3/def2-TZVP level of theory were performed to obtain optimised structures for model compounds.\textsuperscript{31, 32, 33, 34} The surface plot for combined rotations around dihedral angles U and Z in molecular models PI-3 M and rPI-3 M (Supplementary Fig. S97-S99) shows increased flexibility for the amine-linked molecular model, apparent from a broad range of low energy conformations (Fig. 2a-c). Optimised single-pore models PI-3 SP and rPI-3 SP (Supplementary Fig. S100, S101)
depict discrete points on the surface close to the lowest energy conformations of their molecular models with dihedral angles (U) of 27.4° (PI-3 SP) and 6.46° (rPI-3 SP). Although interlayer steric repulsion in the amine framework is increased due to additional benzylic protons (C-10, Fig. 1c) that align perpendicular to the 2D surface, reduced 1,4-repulsion between protons at C-9 and C-10 causes a flattening of the dihedral angle U, albeit combined with increased flexibility of the structure. These results corroborate the cell parameter changes upon reduction as observed by Rietveld analysis of the crystalline rPI-3-COF. To elucidate possible amorphisation pathways, resulting in a disordered structure of rPI-3 if synthesized with an excess of formic acid, additional protonation must be considered. When protonated at the amine nitrogen, the dihedral angle U undergoes a significant widening to 86.6° in the molecular model H+rPI-3 M (Supplementary Fig. S99) – a rotation associated with an energy barrier of approximately 50 kJ/mol in the molecular model rPI-3 M (without protonation). Considering conformational restrictions in the layer geometry of the rPI-3-COF, less pronounced, but still substantial conformational changes, combined with interlayer charge repulsion, are expected, leading to significant disruption of the periodicity of the stacked layers as a function of the pH. This effect is further supported by a vast signal broadening at 119 ppm (C-7) in the $^{13}$C ssNMR spectrum with increasing disorder in rPI-3-COF (Supplementary Fig. S47), whereas in the actual, well-ordered rPI-3-COF structure, a narrow statistical distribution of dihedral angles indicates a preferred conformation and thus a fairly sharp signal for this carbon (C-7). A protonation-dependent broad distribution in the disordered rPI-3-COF causes this signal to broaden and, ultimately, to vanish, however without disrupting the overall connectivity of the layer.
To determine the local and intermediate length-scale structure modifications due to conformation induced disordering, we performed pair distribution function (PDF) analysis on X-ray total scattering synchrotron data. Notably, high similarity in the reduced total scattering patterns (Fig. 2d) from ~5-20 Å⁻¹ and peak positions up to approximately 7 Å in the PDFs of all samples evidence intact, imine or amine bonded layer connectivity in the disordered state. The PDFs of PI-3-COF and rPI-3-COF (Fig. 2e) show distinct medium- and long-range ordered structuring, consisting of two primary oscillations due to the ordering of the stacked layers (higher frequency), and porous channels (lower frequency). The structural correlations are more strongly damped for disordered rPI-3-COF and pf rPI-3-COF, becoming relatively flat around 12 Å. This indicates that the spatial relationships of atoms in stacked layers and across porous channels are largely reduced, although as seen in the diffraction patterns, there are still weakly correlated motifs over at least a few layers or pore distances (Fig. 2e). Distinct differences could be visualised between crystalline and disordered structures by refinement of a 16-layer structure model to the PDFs for rPI-3-COF and disordered rPI-3-COF PDFs, with random translations allowed in a single direction (Fig. 2f, g). For the disordered sample, much larger translations were required to damp out the interlayer and ordered pore channel structure signals. It must be noted that these models may overpredict layer translations due to undersampling the number of layers. Furthermore, the interlayer correlations could also be damped by larger, and random torsions of the amine or phenyl bonds, as shown in quantum-chemical single-pore models. Average stacking offsets were estimated by refining models to the PDFs in the range of neighbouring layers, i.e., r < 6 Å, using PDFgui. The values obtained are 1.0 Å (PI-3-COF), 1.2 Å (rPI-3-COF), 3.3 Å.
(disordered rPI-3-COF), and 3.3 Å (pfrPI-3-COF). As visible from the disordered model, random layer translations drastically reduce pore accessibility and thus help to explain reduced BET surface areas for the disordered models.

Hybrid Materials and Functionalisation

Figure 3: (a) Reaction sequence for post-synthetic functionalisation of amine-linked covalent organic frameworks. Depending on the synthetic conditions, frameworks entirely connected by secondary amine linkages (rCOF), or hybrid materials with mixed amine/imine bonds (prCOF), and partially formylated amine-linkages (pfrCOF) are accessible in a single step from imine COFs. As experimentally shown with pfrPI-3-COF (middle), N-formyl groups in pfrCOFs can be deprotected under acidic conditions. Released secondary amine linkages may allow two-step functionalisation to afford bi-functionalised frameworks. Amine/N-formyl amine ratio is arbitrary. (b-c) FT-IR spectra of rTTI-COF samples functionalised with benzoyl chloride (BzCl) (b) and toluenedisocyanate (TDI) (c) are shown and compared to rTTI-COF. Grey areas in (b) highlight reduced N-H, emerging C=O and characteristic C=C vibrations in BzCl-rTTI-COF. For TDI-rTTI-COF vibrations of dangling -NCO and emerging C=O vibrations are highlighted (grey).
Besides frameworks containing only amine or imine-linkages, hybrid materials with varying imine/amine linkage content can also be obtained with our method by adjusting reaction time, and the amount of formic acid (Fig. 3a, Supplementary Fig. S1). As an example, partially reduced Py1P-COF (prPy1P-COF) was synthesized, showing distinct signals at 149.0 ppm (imine) and 146.4 ppm (amine) in the $^{13}$C ssNMR spectrum for the aromatic carbon next to the nitrogen (approx. 42% amine sites, Supplementary Fig. S39). Another example, already introduced, is partially formylated reduced PI-3-COF (pfrPI-3-COF) obtained from PI-3-COF via salt-melt reduction with ammonium formate. The presence of N-formyl groups opens up further avenues for additional framework functionalisation. For instance, partially functionalised frameworks may be generated by reacting the partially formylated framework with an electrophile, since formyl groups act as protecting group for secondary amine sites. Partial functionalisation can avoid reduced pore accessibility and diffusion limitations, which is critical for example in catalysis. In a more complex case, bi-functionalised frameworks may be synthesized in a subsequent step, after exposing previously protected amine sites. Deprotection of N-formyl groups in pfrPI-3-COF was achieved under acidic conditions (aqueous 1 M HCl, 120°C, 20 min), affording rPI-3-COF as evident from a vanishing formyl signal at 162.8 ppm in the $^{13}$C ssNMR spectrum (Supplementary Fig. S45), while acid chlorides or isocyanates have proven as strong and effective electrophiles to derivatise secondary amines in rTTI-COF (Fig. 3b-c).
In summary, amine-linked frameworks were introduced as a hydrolytically stable and tailorable system for further post-synthetic modification, which can be accessed from imine-linked frameworks or directly from their corresponding amine and aldehyde building blocks (Fig. 4). In contrast to many earlier locking strategies, generating amide, benzoxazole or benzothiazole linked frameworks, our approach locks and simultaneously activates the connectivity of the framework for further functionalisation.\textsuperscript{5, 7, 11, 37} The introduced reduction methods using either formic acid or ammonium formate give access to a range of fully amine-linked, or intermediate amine/imine-linked crystalline frameworks with large surface areas, or topologically identical, disordered analogues with reduced pore-accessibility. Importantly, the degree of amine functionalisation can be rationally controlled by adjusting the amount of acid and reaction time. For the first time, we
demonstrate amine-linked frameworks as a modular platform enabling the facile
interconversion of chemically and structurally distinct frameworks, including reduction-
re-oxidation cycles, crystalline-to-disordered, and disordered-to-crystalline conversions.
Finally, we show that the obtained amine linkages readily react with electrophiles such as
acid chlorides and isocyanates, opening new avenues to the facile post-synthetic
functionalisation of COFs at the linkage site with a built-in protection-deprotection strategy
and without the need for additional building block engineering. In essence, the
demonstrated methods enable hitherto undiscovered functionalisation strategies that are
widely applicable to all imine-linked covalent organic frameworks, the largest family of
COFs to date.

Methods:

Synthesis of rPI-3-COF:
To a suspension of PI-3-COF (30.0 mg) in mesitylene (2 mL) and 1,4-dioxane (1 mL),
formic acid (97%, 53.0 µL) was added. The suspension was heated at 120°C for 48 h.
The precipitate was collected via suction filtration and extracted with MeOH in a Soxhlet
extractor for 12 h. Extraction with supercritical CO₂ afforded rPI-3-COF (28.0 mg, 92%)
as a yellow powder.

Synthesis of rTTI-COF:
To a suspension of TTI-COF (30.0 mg) in mesitylene (2 mL) and 1,4-dioxane (1 mL),
formic acid (97%, 19.3 µL) was added. The suspension was heated at 120°C for 48 h.
The precipitate was collected via suction filtration and extracted with MeOH in a Soxhlet
extractor for 12 h. Extraction with supercritical CO$_2$ afforded rTTI-COF (27.1 mg, 90%) as a yellow powder.

**Synthesis of rPy1P-COF:**

To a suspension of Py1P-COF (15.0 mg) in mesitylene (2 mL) and 1,4-dioxane (1 mL), formic acid (97%, 13.4 µL) was added. The suspension was heated at 120°C for 24 h. The precipitate was collected via suction filtration and extracted with MeOH in a Soxhlet extractor for 12 h. Extraction with supercritical CO$_2$ afforded rPy1P-COF (14.2 mg, 94%) as an orange solid.

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L.G. led the project and wrote the manuscript. G.S. performed quantum-chemical calculations. M.W.T. performed synchrotron x-ray measurements and PDF analysis. M.E. helped with synchrotron measurements. R.E.D. helped with measurements and
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Competing Interests statement:

The authors declare no competing interests.