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Detoxification of Nerve Agents

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Breaking Down Chemical Weapons by Metal–Organic Frameworks

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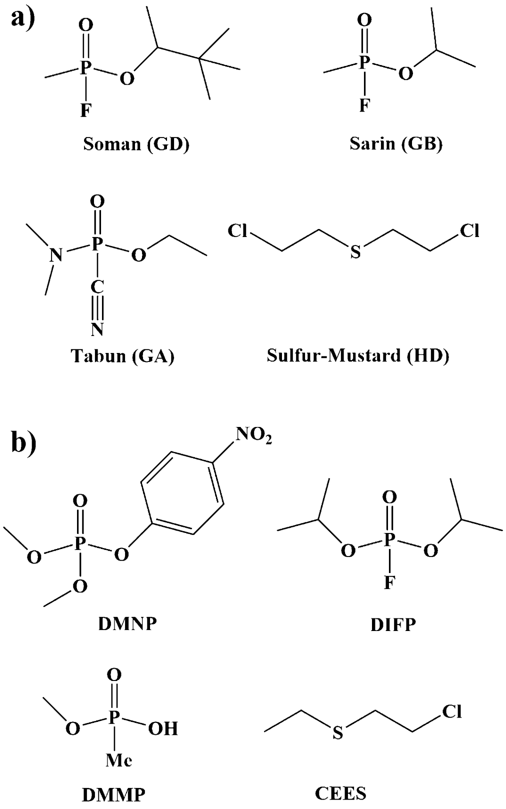
heterogeneous catalysis · hydrolysis · metal–organic frameworks · nerve agents · silk fibroin

In the 1930s, highly lethal organophosphonates were discovered while searching for new pesticides. These chemicals, later known as G-type nerve agents, include soman (GD), sarin (GB), and tabun (GA; Scheme 1 a). As a consequence of their ability to rapidly substitute halogen or pseudohalogen substituents by forming irreversible phosphonate ester bonds with acetylcholinesterase, nerve agents are highly pernicious.[1] The most common method by which phosphonate-based nerve agents can be detoxified is the hydrolysis of the labile P−X bond (X = F, CN in the case of G-series nerve agents). Even though nerve agents autohydrolyze over time in water and at high pH values, decontaminating materials that can be attached to a surface while maintaining their reactive nature for the selective and active catalytic degradation of phosphonate ester bonds are of interest. This is particularly important for the development of filtration media or fabrics that can protect individuals from chemical warfare agents (CWAs).[2]



Scheme 1.
a) CWAs and b) CWA simulants.

The current state-of-the-art filters use activated carbons modified with impregnates (metals, metal salts, acids, and amines) which exhibit many desirable characteristics for the detoxification or filtration of toxic chemicals, including CWAs. Nevertheless, low sorptive capacities, deactivation of the active sites, slow degradation kinetics, and/or a lack of tailorability suggest that there is significant room for the development of new materials. The modern systems aim to provide more protection than previous systems, but in a smaller volume to reduce the burden on the users. Sorbents must possess the ability to withstand prolonged periods of high levels of moisture as well as high temperatures with limited degradation prior to use. It should be noted that humidity (either external or from the body) will always be present under real conditions, and water molecules will constitute an important competitor in the adsorption of these toxic molecules.[1]

In this context, water-stable thermally robust metal–organic frameworks (MOFs) are promising candidates for the selective capture and effective catalytic degradation of CWAs under humid conditions. Although thermally stable MOFs have been known for some time, concepts to stabilize MOFs against hydrolysis have only been explored over the last few years. They include the enhancement of the strength of metal–ligand bonds, which increase in line with the oxidation state of the metal and the Brønsted basicity as well as the denticity of the linker.[3,4] Moreover, introducing hydrophobic linker molecules into the frameworks[5] and postsynthetic modifications lead to enhanced water stability.[6] A high hydrothermal stability has been demonstrated for several MOFs, such as MIL-101(Cr), MIL-53(Al), ZIF-8, and UiO-66.[7] They can be used as solid catalysts in both humid atmospheres and aqueous media.[8] However, in these media the adsorption of water in the MOFs[7] could have a critical effect on the catalysis, particularly in Lewis acid catalysis, because of the

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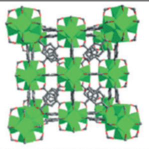
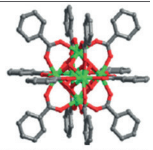
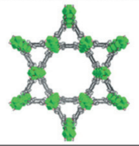
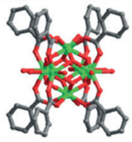
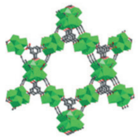
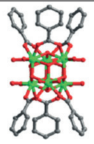
strong coordination of the active sites with water, which makes the interaction of these sites with substrates and reagents unfavorable. For example, under dry-air conditions, a functionalized variation of UiO-66, UiO-66-OH, interacts favorably with ammonia ($0.1\,g\,g^{-1}$ MOF), which is a toxic industrial chemical,[9] but under humid-air conditions a decrease in the ammonia capacity was observed ($0.05\,g\,g^{-1}$ MOF), which was caused by the competition between water and ammonia molecules for adsorption on the active sites. In contrast, UiO MOFs were used as selective adsorbents to remove phosphate from water as well as urine.[10]

Along this line, Farha, Hupp, and co-workers[11–13] as well as Barea, Navarro, and co-workers[14] have recently identified and applied Zr^{IV}-containing MOFs, which are able to rapidly capture simulants of organophosphonate nerve agents and of mustard gas as well as the CWA soman (Scheme 1), and to degrade them by effective catalytic hydrolysis. The Zr^{IV}-based MOF catalysts (MOF-808 and Li*Ot*Bu-doped UiO-66) are promising materials for protective equipment as well as the elimination of large stores of nerve agents.

Table 1: The node connectivity, formula, and structure of UiO-66, NU-1000, and MOF-808; Zr green, O red, C gray; hydrogen atoms are omitted for clarity (reprinted from Ref. [13]; Copyright 2015, Wiley-VCH).

MOF and formula (connectivity of the nodes)	Structure	Node
UiO-66 $Zr_6(\mu_3\text{-}O)_4(\mu_3\text{-}OH)_4(BDC)_6$ (12-coordinated)		
NU-1000 $Zr_6(\mu_3\text{-}O)_4(\mu_3\text{-}OH)_4(OH)_4(H_2O)_4(TBAPy)_2$ (8-coordinated)		
MOF-808-activated $Zr_6(\mu_3\text{-}O)_4(\mu_3\text{-}OH)_4(OH)_6(H_2O)_6(BTC)_2$ (6-coordinated)		

UiO-66 consists of 12-coordinated $\{Zr_6(\mu_3\text{-}O)_4(\mu_3\text{-}OH)_4\}$ cluster nodes and ditopic benzene-1,4-dicarboxylate linkers (BDC^{2-}) (Table 1).[15] The combination of strongly Lewis acidic Zr^{IV} centers with bridging basic hydroxide anions at the cluster nodes of UiO-66 gives rise to biomimetic phosphotriesterase activity. Farha, Hupp, and co-workers showed that the hydrolysis of the nerve agent simulant dimethyl 4-nitrophenylphosphate (DMNP, Scheme 1b) is catalyzed in the presence of UiO-66 in an aqueous *N*-ethylmorpholine-buffered solution, but only with decomposition half-lives ($t_{1/2}$) of 35–50 min. The sorptive capacity and the resultant hydrolysis activity of DMNP are mainly restricted to sites on the exterior of the UiO-66 particles (presumably at missing-linker defect sites).[16] This is because with a size of about 11 × 4.5 Å, DMNP is too large to access the interior of UiO-66, whose apertures are about 6 Å across. To overcome this problem, the authors assayed the suitability of their recently reported zirconium MOF NU-1000.[12] NU-1000 is constructed from 8-coordinated $\{Zr_6(\mu_3\text{-}O)_4(\mu_3\text{-}OH)_4(OH)_4(H_2O)_4\}$ cluster nodes and tetratopic 1,3,6,8-tetrakis(*p*-benzoate)pyrene linkers ($TBAPy^{4-}$; Table 1). The large apertures of NU-1000 (10–31 Å) facilitate the delivery of DMNP into the interior space of the MOF, where the majority of potential catalytic active sites are situated. Moreover, the four substitutionally labile aqua ligands at each Zr_6 node could be easily displaced by DMNP. Both aspects together lead to a decrease in the $t_{1/2}$ value for the hydrolysis of DMNP to 15 min. Consistent with a Lewis-acidic activation pathway for the substitution of water molecules by DMNP at the hydrated Zr^{IV} sites and involving P=O binding, intentional dehydration of the nodes of NU-1000 was found to further accelerate the hydrolysis reaction, with the $t_{1/2}$ value dropping to 1.5 min. The observed $t_{1/2}$ value for the hydrolytic destruction of the CWA soman (GD) was found to be just 3 min under conditions similar to those used for the decomposition of DMNP.

The above-mentioned results for 12-coordinated UiO-66 as well as 8-coordinated NU-1000 indicated that Zr_6-node-based MOFs with even lower connectivity might be more effective for fast hydrolysis of nerve agent or simulant molecules (Table 1). This would mainly be caused by the availability of a much larger number of reactant-accessible labile water ligands. In fact, in the presence of catalytic amounts of activated 6-coordinated MOF-808, in which each node is connected to six benzene-1,3,5-tricarboxylate (BTC^{3-}) linkers to form pores with diameters of 4.8 to 18 Å, DMNP is nearly instantaneously hydrolyzed ($t_{1/2} = 0.5$ min).[13] So far, MOF-808 exhibits the highest rate for the hydrolysis of nerve-agent simulant DMNP by a MOF. Moreover, MOF-808 was used effectively as the catalytic element of a plug-flow reactor. Used in a simple filtration scheme, the reactor displayed high conversion of DMNP under continuous flow conditions and was readily reusable.

In a systematic study, Barea, Navarro, and co-workers showed different postsynthetic approaches for the introduction of acidic and basic sites and/or missing-linker defects to improve the phosphotriesterase activity of UiO-66 for the capture and hydrolytic degradation of the CWA simulants diisopropyl fluorophosphate (DIFP), dimethyl methylphosphonate (DMMP), and (2-chloroethyl)ethyl sulfide (CEES; Scheme 1b).[14] The authors had success with the catalytic hydrolysis of DIFP, DMMP, and CEES by using UiO-66 doped with lithium *tert*-butoxide (Li*Ot*Bu; $[Zr_6O_6(BDC)_6(LiOtBu)_{0.3}]$, short: [UiO-66@Li*Ot*Bu]) in aqueous solutions. [UiO-66@Li*Ot*Bu] exhibits a $t_{1/2}$ value of only 5 min ($TOF = 0.13\,min^{-1}$) for the hydrolysis of the P−F bond of DIFP, which means it is three times faster than UiO-66. The results also show that while the catalytic activity of UiO-66 is poisoned by the acidic degradation products, the insertion of Li*Ot*Bu leads to complete degradation of the toxic compounds, regardless of the presence of degradation products. Under the experimental conditions used for the hydrolytic degradation reactions, [UiO-66@Li*Ot*Bu] clearly outperforms porous ZrO_2. These results demonstrate the synergistic combination of *t*BuO basicity and Lewis acidity of Zr^{IV}

centers for improving the phosphotriesterase activity of UiO-66. It was finally shown by ^{31}P MAS NMR experiments that the diffusion of DIFP and DMMP molecules into the porous network of [UiO-66@LiO*t*Bu] is fast. The CWA simulants are captured by [UiO-66@LiO*t*Bu] and degraded at the catalytic sites, not only at the exterior but also in the interior of the particles.

[UiO-66@LiO*t*Bu] was deposited onto a textile (silk fibroin fabrics). Remarkably, the [UiO-66@LiO*t*Bu] maintains its crystallinity as well as its porosity in the hybrid silk@[UiO-66@LiO*t*Bu] composites, while the air permeability of the textile fabric is also preserved. The silk@MOF composite fabrics combine the self-detoxifying properties of the catalytic phosphotriesterase activity of [UiO-66@LiO*t*Bu] for the hydrolysis of P−F, P−O, and C−Cl bonds with the air-permeation properties of textiles. These results could lead to a breakthrough in the development of future protective fabrics which are capable of self-detoxifying CWAs.

In summary, the capture and hydrolysis of CWAs are extraordinarily efficient in Zr-type MOFs. The catalytic activity of MOF-808 for simulant DMNP and CWA soman as well as of [UiO-66@LiOtBu] for DIFP, DMMP, and CEES demonstrated the advantages of presenting Zr_6-based clusters containing accessible Lewis-acidic Zr^{IV} sites for substrate binding within a highly porous network for the heterogeneous catalytic hydrolysis of P−F, P−O, and C−Cl bonds. The Zr^{IV} centers act as substrate-recognition sites for substrate capturing as well as catalytic conversion, although the mode of operation of the basic groups (hydroxide, alkoxide) to mimic phosphotriesterase activity effectively is not fully understood, particularly in the case of [UiO-66@LiOtBu]. The creation of silk@[UiO-66@LiOtBu] composites as self-detoxifying filters for CWAs and the identification of the highly effective catalytic properties of MOF-808 for the destruction of organophosphonate nerve agents are not only important for new effective protective fabrics, but also for the development of other catalytic multicomponent MOF composites that function in humid gas mixtures and aqueous solutions.

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