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“CLICKable” azide-functionalized phosphonates for the surface-modification of molecular and solid-state metal oxides

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The covalent functionalization of metal oxide surfaces with organic ligands gives unique organic-inorganic hybrids Here we report a bifunctional organic tether combining a phosphonate for metal oxide anchoring with an organic azide for attachment of organic groups. Stable binding of the tether to molecular and solid-state metal oxides is demonstrated and the subsequent “CLICKability” of the TiO_2-anchored tether is shown. The phosphonate-azide reported could in future allow the general linkage of functional organic groups to metal oxides.

The functionalization of oxide surfaces with organic groups has enabled ground-breaking applications in energy conversion,[1] drug delivery,[2] biological[3] and medical technology[4] as well as opto-electronics[5], catalysis[6] and other fields.[7] These breakthroughs are based on the fact that organo-functionalized oxides form an interface between functional molecular components and technologically important materials such as semiconductors or porous adsorbents. In consequence, the technology has allowed the materials integration of molecular species into macroscopic functional devices.[7]

Ideally, this strategy requires the development of bifunctional tethers featuring one binding site suitable for anchoring to metal oxides and a second linkage site where many functional organic molecules can easily be attached. For metal oxide anchoring, phosphonates have attracted significant attention as they are easily introduced to organic molecules and are capable of anchoring to many metal oxide surfaces,[8,9] leading to applications in metal-oxide/bioconjugates,[10] solar energy conversion[11,12] or targeted drug release.[13] Linkage of the tether to organic molecules ideally uses synthetic routes with a broad chemical scope such as the highly successful CLICK chemistry (i.e. Cu-catalyzed alkyne-azide cycloaddition) which operates at high yields and high selectivity with a large substrate range.[14] In nanoparticle synthesis, these concepts have already been established by Turro *et al.* who developed aliphatic phosphonate - azide groups for the surface modification and linkage of iron oxide nanoparticles.[15]

Notably, in addition to solid-state metal oxide surface modification, phosphonates have also been used for the organo-functionalization of molecular metal oxides, [16–18] so-called polyoxometalates (POMs).[19] POMs are metal oxide cluster anions based on early, high-valent transition metals such as V, Mo or W[20] with a wide range of applications in catalysis, materials science and beyond.[19] The covalent linkage of organic groups to POMs has enormous potential for the design of functional molecular materials; however, covalent linkage of organic groups to POMs is still challenging and typical linkages are specific for a certain cluster type or a specific ligand.[21–25] Thus, the ability to introduce general linkages such as azides for CLICK chemistry[26] can open new avenues for the design of organo-functionalized POMs, e.g. for solar hydrogen generation,[21,27] POM-peptide aggregates[28] or POM-carbon-nanotube composites for Lithium ion batteries.[29] The latest advances in the field have been reviewed recently.[16–18]

Here, we present a new, easily accessible organic tether which combines a phosphonate group for metal oxide linkage with an organo-azide group for general attachment of organic moieties through CLICK-chemistry.[14] Stable attachment of the tether to molecular *and* solid-state metal oxides is shown using a molecular molybdenum oxide and TiO_2 as models. The “CLICKability” of the ligand on TiO_2 is demonstrated, highlighting the accessibility and reactivity of the surface-bound azide. Key parameters for the desired ligand were the presence of an azide and a phosphonate moiety bound at opposite sides of a rigid molecular structure to avoid interference during the respective coupling reaction. To this end, we opted for the simple tether 4-azidobenzyl phosphonate (**2**, Fig. 1). **2** was prepared by de-protection of the commercial precursor diethyl 4-aminobenzyl phosphonate to give the phosphonic acid **1.** Diazotization of **1** with sodium nitride and sodium azide in aqueous HCl (4.3 M) and flash chromatography gave the pure

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target product **2** in quantitative yield. **2** was fully characterized by ^1H-, ^{31}P-NMR-, UV-Vis-, FT-IR-spectroscopy, elemental analysis and TGA (see ESI).

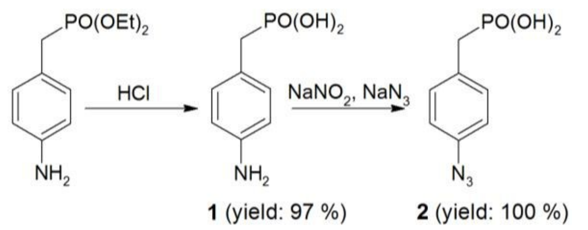

Figure 1: Synthesis of the azide and phosphonate functionalized tether **2**, 4-azidobenzyl phosphonate. For experimental conditions see ESI.

To demonstrate the tethering of **2** to a metal oxide surface and to gain insight into the exact binding mode of the tether, we investigated the linkage of **2** to a molecular molybdenum oxide. Since the interaction of organophosphonate ligands with polyoxomolybdates has already been described in 1975 by Pope *et al.*[30], we targeted the prototype phosphonate functionalized Strandberg anion $[Mo_5O_{15}(PO_3R)_2]^{n-}$ (R = organic group) as a suitable model.[31,32] Tethering of **2** to a Strandberg molybdate was achieved by self-assembly in aqueous solution: **2** was reacted with Na_2MoO_4 x 2 H_2O in aqueous HCl (pH 4.3) under reflux for 30 min. After cooling, $RbNO_3$ was added as source of Rb^+ counter ions. Slow evaporation of the solvent at room temperature gave the single crystalline product **3** (yield: 28 %). **3** was structurally characterized by single-crystal X-ray diffraction[‡] and gave the formula $Rb_4[Mo_5O_{15}(O_3PCH_2PhN_3)_2]$ x *ca* $8H_2O$. The bulk purity and composition of **3** was verified by elemental analysis, FT-IR-, UV-Vis- and ^{31}P-NMR-spectroscopy (see ESI). Crystallographic analysis reveals a Strandberg anion $[Mo_5O_{15}(O_3PCH_2PhN_3)_2]^{4-}$ (**3a**) functionalized with two phosphonate-azide tethers **2** (Fig. 2).

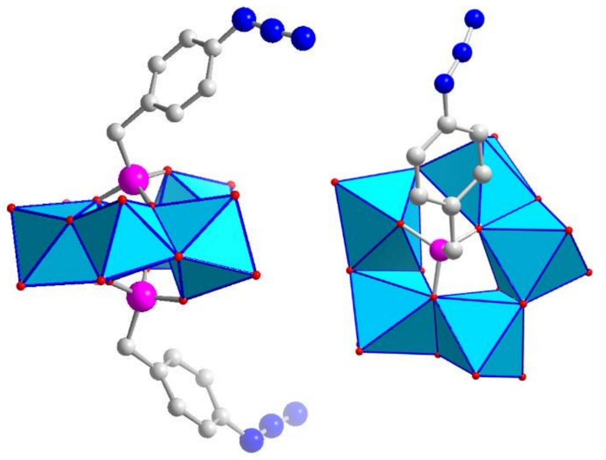

Figure 2: The azide-functionalized Strandberg molybdate anion **3a** in side view (left) and top view (right, only the top organo-phosphonate is shown for clarity). Colour scheme: $[MoO_6]$ octahedra: light blue; O: red; P: pink, N: blue, C: grey; H atoms omitted for clarity.

The molybdenum(VI) oxo framework geometry and bonding situation of **3a** is in line with previous literature reports.[31,32] Briefly, the metal-oxo framework of **3a** is formed by five $[MoO_6]$ octahedra connected through four edge-sharing and one corner-sharing linkages, leading to an asymmetric, chiral metal oxo ring (Fig. 2). On top and bottom of this ring, one organic tether **2** is coordinated *via* its phosphonate functionality. In this way, each $[MoO_6]$ octahedron has four shared and two unshared oxygen atoms ($d_{P\text{-}O}$ *ca.* 1.5 Å; $d_{Mo\text{-}O}$ 2.2-2.4 Å). ^{31}P-NMR of **3a** in DMSO gives one signal at δ = 23.74 ppm and demonstrates that under the given conditions, **3a** is stable in solution over prolonged periods.

The surface modification of solid state metal oxides (model: TiO_2, type Degussa P25) with the phosphonate azide tether **2** was examined by reacting **2** (23.1 mM) with a dispersion of TiO_2 (250 mg) in MeOH for 19 h at room temperature. UV-Vis spectroscopy was used to quantify the adsorption of **2** onto TiO_2 (Fig. 3a). Under non-optimized adsorption conditions, 88 % of **2** present in solution were adsorbed on TiO_2 (corresponding to 4.1 wt.-% or 0.2 mmol/g), giving the functionalized composite **2**@TiO_2. Leaching experiments were performed to assess the stability of the phosphonate-TiO_2 linkage. To this end, **2**@TiO_2 was dispersed in MeOH and stirred for 5 h at room temperature. UV-Vis spectroscopy showed no detectable leaching of the phosphonate into the solvent, indicating the stability of the tethering under the given conditions (Fig. 3a).

The linkage of organic groups to **2**@TiO_2 using CLICK chemistry was investigated by reacting **2**@TiO_2 with the model CLICK reagent phenyl acetylene[33] in MeOH at 40 °C for 19 h in the presence of the copper(I) catalyst Bis[*N,N'*-bis(2,4,6-trimethylphenyl)-1,2-ethanediylidene diamine]copper(I) tetrafluoroborate[34] (see ESI for experimental details).

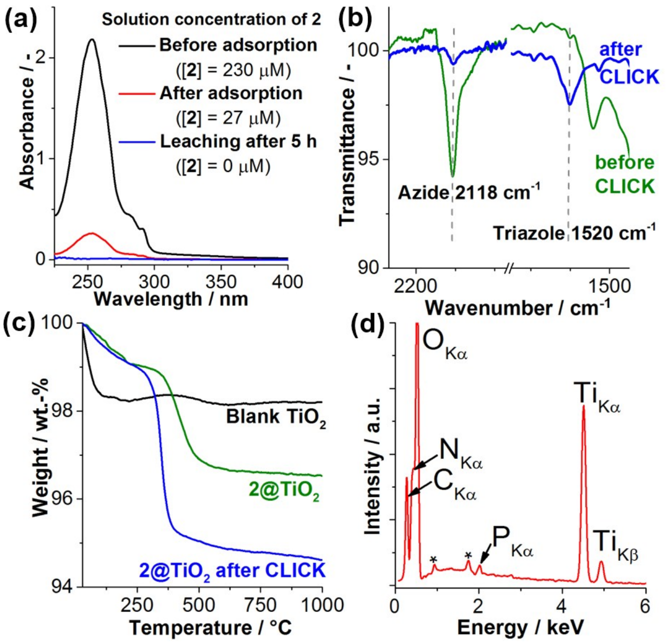

Figure 3: (a) Adsorption of **2** on TiO_2 and leaching experiments of **2**@TiO_2, quantified by UV-Vis spectroscopy. **(b)** Thermogravimetric analysis of pure TiO_2, **2**@TiO_2 (-3.5wt.-%) and **2**@TiO_2 after the CLICK reaction (-5.4wt.-%). **(c)** ATR-FT-IR spectra of **2**@TiO_2 before and after the CLICK reaction. (d) Energy-dispersive X-ray spectroscopy showing the presence of the elements C, N, P on the surface of **2**@TiO_2.

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The success of the CLICK reaction was monitored by ATR-FT-IR spectroscopy where the disappearance of the characteristic azide stretching vibration at 2118 cm^{-1} and the appearance of a characteristic triazole vibrational mode at 1520 cm^{-1} was observed (Fig. 3b). Quantitative information of the CLICK reaction was obtained by thermogravimetric analysis which determines the amount combustible organic materials on the TiO_2 (Fig. 3c). For the azide-functionalized composite **2**@TiO_2, a weight loss of 3.5wt.-% (calcd.: 4.1 wt.-%) was found. After the CLICK reaction, the composite showed a weight loss of 5.4 wt.-% (calcd.: 5.9 wt.-%), suggesting that the CLICK reaction proceeds with ~ 90 % conversion. This is supported by FT-IR data where a small residual azide stretching mode is still observed after the CLICK reaction (Fig. 3b). Finally, scanning electron microscopy/energy-dispersive X-ray spectroscopy (SEM-EDX, Fig. 3d) was performed to obtain qualitative information on the bulk surface modification of **2**@TiO_2. EDX-elemental mapping of a representative TiO_2 sample showed the presence of the elements Ti, O, C, N and P, thus giving further evidence of the bulk surface modification of **2**@TiO_2.

In summary, we present a facile route for the functionalization of metal oxide surfaces with “CLICKable” organic tethers. To this end, a bifunctional, azide and phosphonate-containing linker, 4-azidobenzyl phosphonate was developed. Binding of the linker to molecular and solid-state metal oxides is demonstrated. The binding of the tether to a Strandberg-type molecular molybdenum oxide provides structural insight into the phosphonate binding mode and provides a rare example of an azide-functionalized polyoxometalate. Tethering of the linker to TiO_2 and subsequent CLICK reaction of the azide with phenyl acetylene demonstrates the stability and reactivity of the linker on the metal oxide surface. Future studies will use this linkage strategy to attach functional organic groups or coordination compounds to metal oxide surfaces with a focus on systems for solar energy conversion and photo-electrochemistry.

Notes and references

‡ Crystallographic details: $C_{14}H_{26}Mo_5N_6O_{28}P_2Rb_4$ (M_r =1609.93): monoclinic, space group $P2_1$, a = 10.7278(3) Å, b = 14.7418(3) Å, c = 13.2364(3) Å, β = 107.779(3)°, V = 1993.3(8) $Å^3$, Z = 2, T = 150(2) K, μ(MoKα) = 6.564 mm^{-1}, D_{calc} = 2.682 g/mm^3, R_{int} = 0.0251; R_1 = 0.0465 (I > 2σ(I)); wR_2 = 0.1188 (all data). CSD 1495857 contains the supplementary crystallographic data for **3**.

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