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Metal–Organic Frameworks

Electronic Effects of Linker Substitution on Lewis Acid Catalysis with Metal–Organic Frameworks**

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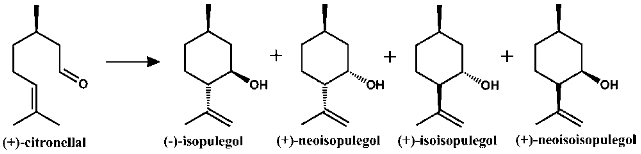
Metal–organic frameworks (MOFs) are hybrid porous materials which hold great promise in adsorptive separation,[1] where selectivity is controlled by channel size and shape,[2] hardness or softness of exposed framework ions,[3a–b] framework hydrophobicity, and so on.[3c] They are attracting increasing interest in catalysis.[4] Some catalytic MOFs, like HKUST-1 and the Fe-trimesate MIL-100,[5] have open metal sites at structural nodes. In other cases, homogeneous catalysts, such as Mn Schiff bases, are integrated in the struts between the nodes,[6] so that molecular catalysts are isolated in an inert porous matrix.

In homogeneous catalysis, steric and electronic ligand effects are decisive for activity and stereoselectivity, and in some cases quantitative linear free-energy relationships (LFER) have been found between characteristics like the enantiomeric ratio and the stereo-electronic substituent parameters.[7] For heterogeneous catalysts, it is less obvious to establish quantitative structure–activity relationships. For some zeolites, the number and nature of the isomorphously substituting cations affect the number and strength of the Brønsted or Lewis acid sites; however, the effects are not always easily rationalized due to site heterogeneity.[8] Although the effect of cation variation on catalytic activity has been shown for MOFs,[4d] there are no systematic studies on the effects of framework substitution on the catalytic activity of the structural ions. Here we demonstrate that the concept of electronic modulation of the active site can be transferred from the familiar paradigm of homogeneous catalysis to catalytic frameworks of the MOF type. For a series of functionalized Zr terephthalate materials with UiO-66 structure,[9] the activity in Lewis acid catalyzed reactions can be much more effectively tuned than in inorganic porous solids, and a Hammett-type structure–activity LFER is readily identified. To support this concept, molecular modeling calculations were performed to calculate rates for individual reactions at various modified sites.

In the cubic Zr terephthalate UiO-66, each $Zr_6O_4(OH)_4$ octahedron is surrounded by maximally 12 terephthalate linkers, resulting in large octahedral and small tetrahedral cages. UiO-66 materials were synthesized with eight benzene-1,4-dicarboxylates (BDC-X; X = H, NH_2, CH_3, OCH_3, F, Cl, Br, NO_2). To test the effect of the substituents, the cyclization of citronellal was selected (Scheme 1). The isopulegol product of this carbonyl-ene reaction is a precursor of synthetic menthol. The selectivity for the isopulegol isomers depends strongly on the Lewis acidity of the active site.[10] Before reaction, each catalyst was activated at 493 K. For UiO-66 materials, this results in dehydration of the $Zr_6O_4(OH)_4$ cluster, with formation of Zr_6O_6.[9a] Conversion profiles for reactions in toluene are given in Figure 1.



Scheme 1. Cyclization of (+)-citronellal to isopulegol and its isomers.

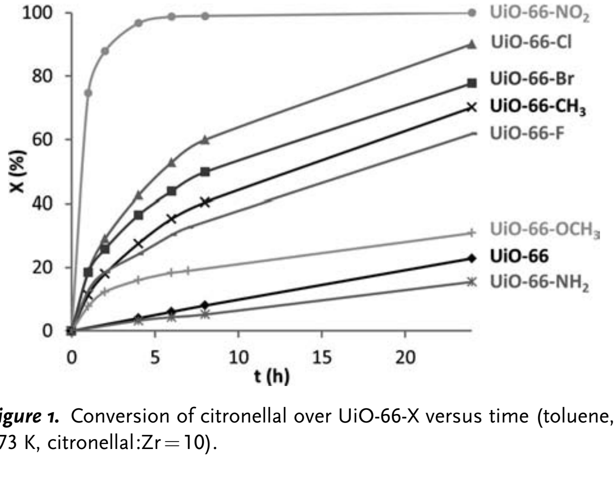


Figure 1. Conversion of citronellal over UiO-66-X versus time (toluene, 373 K, citronellal:Zr = 10).

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While all materials are active, the rate is dramatically enhanced by electron-withdrawing groups on the linker (F, Cl, Br, NO_2). UiO-66-NO_2 is by far the most active material, reaching full conversion after only 6 h. The reaction is first-order in citronellal (for more details see Supporting Information), and calculated rate constants are listed in Table 1.

Table 1: Reaction rate constants k_X, relative initial rates with respect to the unfunctionalized material, and isopulegol selectivities at maximum conversion for the different UiO-66-X.

Catalyst	k_X [h^{-1}]	Relative reaction rate	Selectivity to isopulegol [%]
UiO-66-NH_2	0.005	0.43	75
UiO-66-H	0.012	1	75
UiO-66-OCH_3	0.030	2.5	70
UiO-66-F	0.043	3.6	82
UiO-66-CH_3	0.067	5.6	74
UiO-66-Br	0.083	6.9	77
UiO-66-Cl	0.108	9.0	78
UiO-66-NO_2	0.673	56	81

Remarkably, introduction of a nitro group results in a 56-fold increase in rate, which clearly points to electronic active site modulation. The substituent effect is also apparent in the selectivities (Table 1); the highest values are observed for catalysts bearing electron-withdrawing groups.[10,11]

Reference experiments with the corresponding linkers proved that the activity is due to the MOFs, and not to residual linkers (Supporting Information Table S1). In all materials, activity is independent of crystal size, which implies that all catalytic sites equally contribute to the activity (Supporting Information Figures S3 and S4). While a perfectly crystalline UiO-66 material should have all Zr ions fully coordinated, detailed study of the thermogravimetric analysis profiles revealed that of the 12 linkers surrounding each cluster, approximately three are systematically missing for the real materials (Supporting Information Table S2).[9b] Such linker deficiency allows coordinatively unsaturated sites on Zr to be identified as the active sites. We attempted to correlate the activity to electronic effects of the linkers using Hammett's σ values. The choice of a suitable type of σ value is not obvious, since each substituent is either *ortho* or *meta* to a Zr-coordinating carboxylate group. An excellent correlation was found by plotting $\log k_X$ values from Table 1 versus the σ_m values, including inductive and resonance contributions.[12] The strong positive correlation of the $\log k$ values with σ_m results in a LFER ($\log(k_X/k_H) = \rho\sigma_m$) with $\rho = 2.35$ (Figure 2). Thus, Lewis acid sites are stronger in materials with an electron-withdrawing group close to the Zr site.

To check whether these trends are general, the Oppenauer oxidation of geraniol by furfural was studied (Figure 3). This hydride-transfer reaction requires simultaneous coordination of an alcohol and a carbonyl compound to a Lewis acid site.[13] While the kinetics are substantially more complex, it is immediately obvious that a similarly large rate increase is realized when a MOF with electron-withdrawing substituents is used.

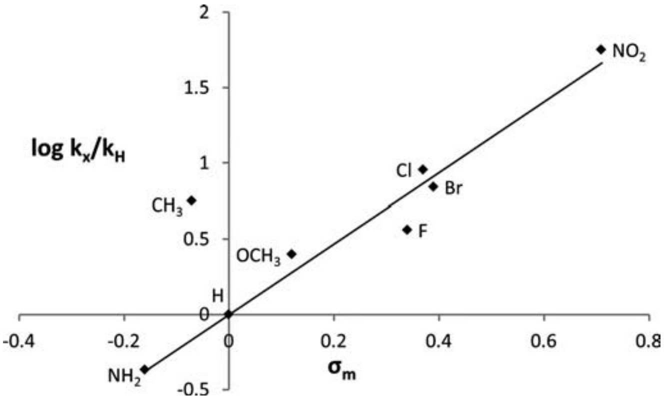

Figure 2. Hammett plot for cyclization of citronellal with different UiO-66-X catalysts.

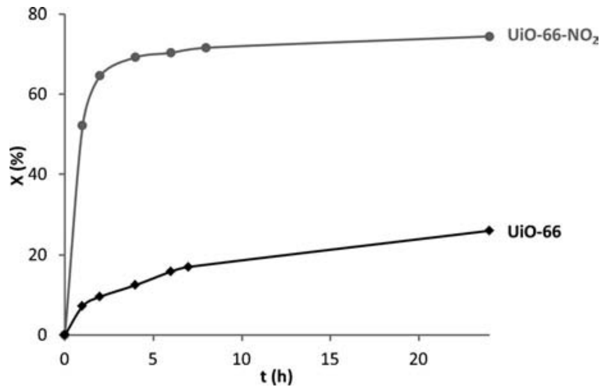

Figure 3. Conversion of geraniol in the Oppenauer oxidation with furfural over UiO-66 and UiO-66-NO_2 (toluene, 368 K, geraniol:Zr = 10).

To rationalize the electronic modulation of the active sites, molecular modeling calculations were performed to predict rates for citronellal cyclization on UiO-66 and UiO-66-NO_2. First-principles kinetic calculations were performed on an extended cluster which is representative for the active site environment. As possible active sites, four different clusters were built (Supporting Information Figure S5). Reasonable transition states were only found for Zr clusters in which at least one terephthalate was missing (Supporting Information Figure S6 and Table S3). Clusters with one missing linker were therefore used as models for both UiO-66 and UiO-66-NO_2 (Supporting Information Figure S7). As isopulegol is the most abundant product, the mechanism of its formation was studied in detail. A variety of different transition states were found which differ in the adsorption mode of citronellal; only the two most stable transition states are discussed. Critical points and the corresponding free-energy profile along the reaction pathway are shown in Figures 4 and 5. As a reference level the extended cluster state of the catalyst and citronellal in the gas phase was chosen.

Citronellal is slightly more strongly adsorbed on the nitro-modified cluster, with free energies of adsorption of -15.7 and -23.7 kJ mol^{-1} for UiO-66 and UiO-66-NO_2, respectively

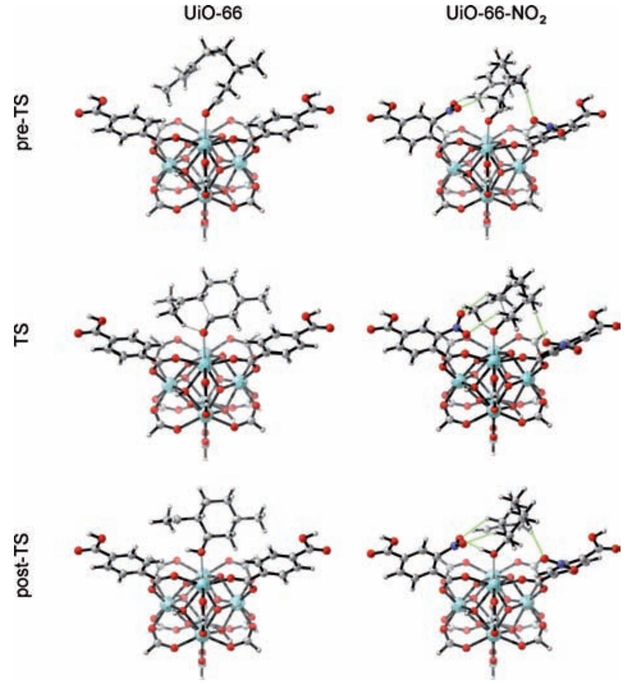

Figure 4. Critical points along the reaction profile of citronellal towards isopulegol for UiO-66 (left) and UiO-66-NO$_2$ (right). One carboxylate linker has been omitted from the cluster. From top to bottom, the figures correspond to the adsorbed state of citronellal, the transition state for cyclization, and the adsorbed isopulegol product state. Interactions between the hydrogen atoms of citronellal and the nitro groups at distances shorter than 3 Å are indicated by green lines.

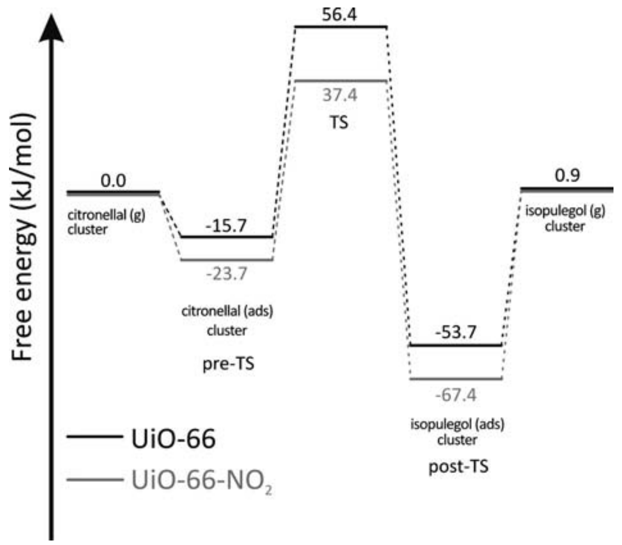

Figure 5. Gibbs free-energy profiles, calculated at 373 K, for citronellal cyclization to isopulegol.

(Table 2). The Zr site with nitro-substituted linkers is clearly a stronger Lewis acid, as reflected in shorter distances between the carbonyl oxygen atom of citronellal and Zr (Supporting Information Table S4). In addition, the NO$_2$ groups strongly interact with some hydrogen atoms of the adsorbate in the pre-reactive complex, the transition state, and adsorbed-product state (Figure 5). The theoretically obtained transition states point towards a concerted mechanism in which carbon–carbon bond formation and proton transfer occur in the same reaction step, albeit not completely synchronously, as evidenced by inspecting the distances of these crucial bonds in the transition state (Supporting Information Table S4). For the nitro-modified cluster, the same features as in the adsorbed state are observed, and lead overall to a more stabilized transition state. Indeed the difference between the Gibbs free-energy barriers amounts to about 19 kJ mol^{-1}.

Table 2: Kinetic data for citronellal cyclization to isopulegol at 373 K.[a]

		ΔG^{ads}_{373}	ΔH^{ads}_{373}	$-T\Delta S^{ads}_{373}$	
pre-TS	UiO-66	−15.7	−88.6	72.9	
	UiO-66-NO$_2$	−23.7	−104	80.4	
		$\Delta G^{\ddagger}_{373}$	$\Delta H^{\ddagger}_{373}$	$-T\Delta S^{\ddagger}_{373}$	k^{fwd}_{373}
apparent kinetics	UiO-66	56.4	−44.2	100.6	3.03×10^{3}
	UiO-66-NO$_2$	37.4	−67.8	105.2	1.40×10^{6}
	relative ratio				460
intrinsic kinetics	UiO-66	72.1	44.4	27.8	6.15×10^{2}
	UiO-66-NO$_2$	61.1	36.4	24.7	2.17×10^{4}
	relative ratio				35

[a] Free energy and enthalpic and entropic contributions in the adsorbed state (ads) and in the transition state (‡) [kJ mol^{-1}]. The rate constants (k^{fwd}_{373}) are given in units of m^3 mol^{-1} s^{-1} for the apparent kinetics and in s^{-1} for the intrinsic kinetics. The relative rates of UiO-66-NO$_2$ versus UiO-66 are also given.

To quantify the relative rates on UiO-66 and UiO-66-NO$_2$, both intrinsic and apparent kinetics were evaluated, which merely differ in the reference level chosen for the reactants. The intrinsic analysis starts from the pre-transition state reactants, which is the local reactant minimum closest to the transition state, while the apparent analysis starts from the UiO-66 cluster and citronellal in the gas phase.[14] The calculated kinetic data are collected in Table 2, together with the enthalpic and entropic contributions to the Gibbs free energies. Both apparent and intrinsic kinetic coefficients are higher in the case of UiO-66-NO$_2$. Intrinsically, the calculations predict citronellal cyclization which is a factor of 35 faster. Using apparent kinetics, which additionally take into account the extra stabilization of the adsorbed citronellal on the nitro cluster, an acceleration factor of 460 is obtained. The partition of the free energies into enthalpic and entropic contributions along the reaction path shows that the nitro-substituted cluster yields both a higher adsorption enthalpy (−104 vs. −89 kJ mol^{-1}) and a lower intrinsic enthalpy barrier (36 vs. 44 kJ mol^{-1}). In UiO-66-NO$_2$, adsorption is stronger due to the stronger Lewis acidity, and, additionally, the transition state is stabilized due to preferred electrostatic interactions between the adsorbate and the nitro groups. The overall acceleration seems to be governed by the enthalpic preference both in adsorbed and transition state for the nitro-substituted cluster, rather than by entropic effects.

In conclusion, the activity of MOF catalysts with coordinatively unsaturated sites can be strongly increased by using functionalized linkers. A clear LFER was found between the electronic nature of the linker substituents and the reaction rate in a carbonyl-ene reaction, and the concept was extended to other Lewis acid reactions. This is the first LFER ever observed for MOF catalysts. Molecular modeling indicated that nitro substitution lowers the adsorption and activation free energy of the reaction. The predicted rate acceleration nicely corresponds to the experimentally observed ratio of about 60 at 373 K. The substituents not only alter the Lewis acidic properties but also induce additional stabilizing or destabilizing effects on the reactants depending on their electronic properties.

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Keywords: heterogeneous catalysis · Lewis acidity · metal–organic framework · structure–activity relationships · substituent effects

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