COOPERATIVE CATALYSIS BY BIFUNCTIONALIZED MESOPOROUS SILICA

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Dedicated in loving memory to

Fay Feller

and

Dinah Margelefsky

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ABSTRACT

The objective of my work was to prepare heterogeneous catalysts that can perform cooperative catalysis. Cooperative catalysis occurs when the presence of two or more functional groups provide an acceleration of a chemical reaction beyond what is possible when either of the two species is used independently. New catalytic materials were synthesized by functionalizing mesoporous silica (SBA-15) with two different functional groups. The spatial arrangement of these two functional groups was controlled either by two-site imprinting (the two groups are covalently attached to one another by a linker, then each is tethered to the silica surface followed by spacer cleavage) or by single-site bifunctionalization (both organic functionalities are attached to the surface by a single carbon tether). The dependence of catalytic activity and selectivity on the surface arrangement (random vs. paired, distance between paired species) was investigated for several different condensation reactions.

Catalysts featuring both sulfonic acid and thiol groups were investigated for the synthesis of various bisphenols from a ketone and phenol. Alkylsulfonic acid and thiol groups were organized into pairs by ring-opening surface-bound propanesultone groups with various thiolate nucleophiles. Paired acid/thiol catalysts outperformed randomly-distributed catalysts in the synthesis of bisphenol A and bisphenol Z, whereas the synthesis of bisphenol AF was insensitive to spatial arrangement. The distance between the two groups in the acid/thiol pair was varied and the activity and selectivity were found to diminish rapidly as the acid/thiol distance grows. Catalysts containing stronger arylsulfonic acid and thiol groups were synthesized using a two-point imprinting approach

in which disulfide and sulfonate ester bonds were cleaved to generate the paired thiol and acid groups. This paired acid/thiol catalyst outperformed randomly-distributed catalysts in the synthesis of bisphenol Z, whereas the synthesis of bisphenol A was insensitive to spatial arrangement.

The second reaction investigated was the aldol reaction in order to investigate the possibility of acid/base cooperativity. A catalyst containing alkylsulfonic acid and primary amines grouped into pairs were generated by opening surface sultone rings with ammonia. This material was catalytically inactive in the aldol reaction due to acid/base neutralization, whereas randomly-distributed acid-base materials exhibit good catalytic activity. Primary amine/carboxylic acid cooperativity was also investigated, both with homogeneous amino acids and bifunctional heterogeneous silicas. While amine/acid cooperativity was conclusively demonstrated with the homogeneous catalysts, in the heterogeneous case the cooperativity due to surface silanol groups actually overshadowed the effect of the carboxylic acids.

The results obtained provide evidence that the spatial arrangement of disparate functional groups on the surface of a heterogeneous catalyst can have profound effects on the activity and selectivity of the catalyst. Spatial positioning is a catalyst parameter that should be taken into consideration in the design of inorganic/organic hybrid catalysts, and may allow (for some reactions) catalytic performance unachievable with randomly-distributed materials.

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INTRODUCTION—HYBRID INORGANIC/ORGANIC MATERIALS AND COOPERATIVE CATALYSIS

The immobilization of organic catalysts is a common way to make catalysts easier to separate from a reaction mixture. There are many ways of immobilizing a homogeneous catalyst on an insoluble support; these include polymer encapsulation, covalent tethering to a polymer backbone, and covalently tethering to an inorganic framework such as silica to form an organic/inorganic hybrid material. The latter case is advantageous because of the low cost and thermal stability of silicate materials and the wide variety of low-cost organosilanes available for covalent surface modification.

There are innumerable reports in the literature of functionalizing silica materials with a single organic functionality for use in catalysis. The most common groups used for this purpose are acids and bases (for a review see Ref. 1), although more complex molecules such as cinchona alkaloids[2, 3] or enzymes[4] have also been immobilized on silica for use in heterogeneous catalysis. Immobilization on an inorganic support not only aids in the separation and recovery of the catalyst, but in some instances the heterogeneous catalyst outperforms its homogeneous analog, either due to solid/liquid partitioning which concentrates reactants near the catalytic sites, interactions with the support, or other concentration-dependent effects due to the concentration of the active catalytic sites on a 2-dimensional surface.

Cooperative Catalysis

While catalysts functionalized with a single functional group are sufficient for many purposes, bifunctionalized materials allow for cooperative catalysis between the two different functionalities. Cooperative catalysis is defined here as the synergistic catalytic effect of at least two different entities which act together to increase the rate of a reaction beyond the sum of the rates achievable from the individual entities alone.* By functionalizing a surface with two (or more) types of organic groups, catalytic activity and selectivity can be improved or tuned, and in some instances novel reactivity can be achieved which is impossible in solution, as in the case of acid/base cooperativity.

Cooperativity between multiple functional groups within a single catalytic site is typified by the active sites of enzymes. In these catalysts (many of which are so efficient that the reactions they catalyze are diffusion-limited due to millions of years of evolution) adjacent residues within a single active site interact with each other and with various reacting species and cofactors through covalent, electrostatic, and hydrogen-bonding interactions to increase the rate of reaction many orders of magnitude beyond the uncatalyzed rate. In these catalysts, the spatial positioning of the cooperating moieties is fixed by the enzyme's backbone, with sufficient flexibility endowed by the conformational flexibility of the backbone and the short (usually two- to four-carbon) linkers between the peptide backbone and the functional group.

The *de novo* design of bifunctional heterogeneous catalysts to take advantage of the same kind of cooperative catalytic interactions utilized by enzymes is a key challenge

* The term *cooperative catalysis* as used herein is not to be confused with the same term as used in enzyme catalysis, in which it is describes the change in the binding constant of a reactant to an allosteric enzyme by the binding of another reactant molecule, leading to sigmoidal kinetic behavior.

for the future of synthetic catalysis. There are a number of important design parameters which must be investigated. Of primary importance is the identity of the different functional groups. Once a set of two or more cooperating functional groups is chosen for a given reaction, the second design parameter is the arrangement of these groups on the surface of the catalyst. The first of these challenges has its foundation in homogeneous catalysis, in which combinatorial approaches are well suited to finding combinations of catalysts which are effective at catalyzing a given reaction. Most of the reported examples of cooperative heterogeneous catalysis utilize a set of functional groups determined by solution-phase experiments and later immobilized onto a surface.

The second of these challenges, the effect of the spatial positioning of cooperative functional groups, is unique to heterogeneous catalysis. In solution there is no well-defined spatial arrangement; the reacting molecules are constantly diffusing and rearranging, and at any given time there is a broad distribution of distances. On the surface of a solid catalyst particle, on the other hand, the catalytic species are fixed locally with respect to the surface and to one another.

In order to determine the ideal distance between cooperating groups, one must first devise a synthetic methodology by which to arrange the relevant surface species; and second, one must be able to vary this distance methodically. This dissertation is primarily focused on the former challenge, describing new methods of generating paired bifunctional surfaces and the effect of this arrangement on catalytic behavior. In the specific case of alkylsulfonic acid/thiol pairs, the latter challenge (tuning of the acid/thiol distance) is also addressed.

Heterogeneous Cooperative Catalysis in the Literature

Cooperativity in homogeneous catalysis has been reported using multiple monofunctional molecules (*e.g.*, two different Brønsted acids[5], a Lewis acid and amine,[6] urea and amine,[7] or a Ruthenium complex, amine base, and sodium salt[8]) or polyfunctional molecular catalysts (*e.g.*, heterobinuclear organometallic complexes,[9, 10] amine and urea/thiourea groups[11-13], or proline-type catalysts[14-16]). In each of these cases, separation and reuse of the catalyst is much more difficult than with heterogeneous catalysts. Thus heterogeneous bifunctional cooperative catalysts are highly desirable.

There have been several reports of bifunctional polymeric catalysts in which a flexible polymeric backbone is decorated with two different types of functionalities which provide cooperative catalysis.[17-20] These polymers are used as homogeneous catalysts but have the advantage of easy separation from the reaction mixture by precipitation. The flexibility of the polymer backbone makes it difficult to spatially isolate or position the different groups. Cross-linked polymers have also been used as supports for bifunctionalization;[21-23] the cross-linking eliminates catalyst solubility but still allows for the flexible catalyst particles to swell and change shape in different solvent environments.

Most heterogeneous cooperative organocatalysts reported in the literature use some form of silica as a rigid insoluble support (for a review, see Ref. 24). These include acid/thiol bifunctionalized mesoporous silica for bisphenol A synthesis[25, 26] and aldol catalysts containing amine and urea groups[27, 28] or acid and base groups.[29-31] Few reports exist in the literature of heterogeneous catalysts containing organic functional groups with a non-random spatial positioning. Homodimeric pairs of sulfonic acids[32, 33] and

amines[34, 35] have been created on silica surfaces, but while these types of materials have shown promise in molecular recognition and sensing, the reported effects of dimeric pairing on catalytic activity have been minor.

Some bifunctional materials containing a non-random spatial arrangement have been reported. Amine and sulfonic acid groups have been incorporated into mesoporous silica with some degree of spatial isolation (acidic framework and basic pores) but no catalytic properties were reported.[36] Non-covalent imprinting has been used to direct the self-assembly of multiple functional groups. In this technique, monomers are polymerized in the presence of an imprint molecule with which they interact weakly, and the imprint molecules are removed by extraction after polymerization. This method has been used to generate protease-like trifunctional catalysts but the catalytic improvement due to the imprinting process is modest.[37] In some cases the effects attributed to the imprinting process are due only to the presence of residual imprint which survives the extraction process, rather than to the organizing effect of the imprint.[38] Surface lithography has been used to pattern a monolayer with alternating stripes of imidazole and alcohol groups, which led to improved hydrolytic activity at the interface between the two groups[39] but this technique has a very limited degree of spatial resolution.

The only known report in which two different functional groups were arranged into pairs on a silica surface was published by Bass and Katz in 2006.[40] A mesoporous silica was functionalized with primary amine/thiol pairs derived from the thermolysis of a grafted xanthate/carbamate precursor, but the catalytic properties of this material were never investigated.

In this dissertation the synthesis and catalytic activity of hybrid inorganic/organic mesoporous silica catalysts functionalized with pairs of either acid and base groups or acid and thiol groups are reported. The activity of the paired catalysts is compared to that of catalysts in which the two groups are arranged randomly on the surface. In some instances, the distance between the two groups in the paired catalysts can be varied, which allows insight into the dependence of the catalytic reaction on the distance between the cooperating catalytic moieties.

The Functionalization of SBA-15

Mesoporous silica materials have pore diameters of 2–50 nm. These materials, such as MCM-41[41] and SBA-15,[42] are commonly used as supports for immobilizing organic catalysts. Compared to amorphous silica, mesoporous silica has a more regular structure, which leads to more uniform catalytic sites. The high surface area allows for a greater density of functional groups. Compared to microporous silicates, such as zeolites, the larger pore size of mesoporous materials allows for better reactant and product diffusion, reducing mass transfer limitations and allowing even large molecules to access the catalytic sites.

The synthesis of SBA-15 employs a triblock copolymer surfactant as structure directing agent (SDA), leading to pores 6–10 nm in diameter and with a regular hexagonal 1-D structure (see Figure 1.1). Because of its high surface area (~ 800 m^2/g) and high silanol density, SBA-15 is easy to functionalize with a high loading of organic functional groups, and its large pore diameter allows large molecules to enter the pores with less mass transfer limitation than materials with a smaller pore size. For these

reasons, SBA-15 was chosen as the support for all of the heterogeneous catalysts described herein.

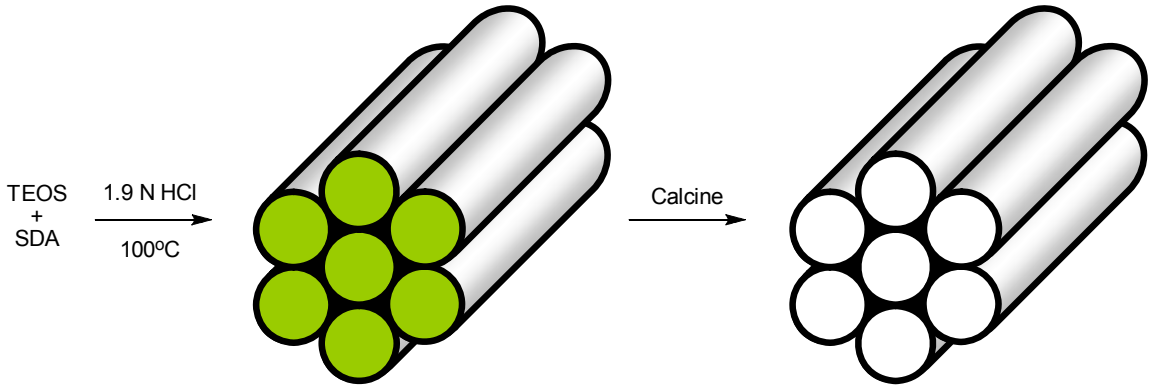

Figure 1.1. Synthesis of SBA-15. The structure-directing agent (SDA) is a triblock copolymer of ethylene oxide (EO) and propylene oxide (PO) with formula $(EO)_{20}(PO)_{70}(EO)_{20}$. The calcination process (at 550°C) burns out the SDA, leaving the pores empty. The silica source is tetraethyl orthosilicate (TEOS).

Silica can be functionalized with organic groups in two ways. In a direct synthesis (also known as a one-pot synthesis), a silica precursor is polymerized in the presence of functional organosilanes in a single step. Using this route to functionalized silica materials, higher loadings of functional groups can be achieved and those groups can be well distributed within the silica matrix. The disadvantages of the method include the necessity to extract the structure-directing agent (since calcination would destroy the organic functionality) and, in the case of ordered materials, the possibility of the functional silanes disrupting the long-range order. Mesoporous silicas typically become less well ordered as the organic loading increases, and microporous materials often will not crystallize in the presence of large amounts of organosilanes.

Postsynthetic modification, or grafting, involves covalently attaching organosilanes to the surface silanols of a pre-made silica material. In general, a more-reactive silane will lead to higher organic loadings but do so to give less well-distributed surfaces (*e.g.*, clustering due to silane-silane interactions and preferential grafting at pore mouths). Trichlorosilanes (highly reactive) or trialkoxysilanes (less reactive) are often used. Since the silica is synthesized before grafting, highly ordered silica geometries can be maintained even at moderately high organic loadings.

For the application of investigating the spatial organization of bifunctionalized surfaces, the grafting of trialkoxysilanes was chosen as the method of functionalization. This method leads to functional groups which are all on the pore surfaces, unlike one-pot syntheses which can lead to organic groups buried within the pore walls. Furthermore, the grafting process does not involve the harsh conditions found in one-pot syntheses (1.9N HCl, 100°C) which is important when the organosilanes feature hydrolytically sensitive functional groups, as is the case for many of the silanes described in this work. In comparing randomly-organized vs. positioned functional groups, low organic loadings are needed, so highly reactive molecules such as trichlorosilanes can be avoided. Instead, triethoxysilanes can be used, which can be equilibrated within the silica pores at room temperature before the high-temperature grafting reaction begins, minimizing pore-mouth clustering.

Additionally, a whole family of catalysts can be generated by grafting different organosilanes onto identical silicate frameworks, such that there is no difference in pore size or uniformity among the members of the family. In the case of one-pot syntheses, different batches prepared with different organosilanes (or different amounts of

organosilanes) often have slightly different pore size, surface area, or pore regularity, all of which can affect catalytic performance. Finally, calcining the SBA-15 before grafting ensures that no SDA remains in the pores; with co-condensation, the SDA must be extracted with an appropriate solvent (since post-synthetic calcination would destroy the organic functionality) and there is almost always some residual SDA in the pores after extraction.

Summary of Bifunctional Site-Paired Catalysts Described in This Work

As test reactions for bifunctional cooperative catalysis, two condensation reactions were chosen, each with literature precedents for bifunctional cooperativity: the reaction between a ketone and phenol to form bisphenols (such as the industrially relevant bisphenol A) catalyzed by acids and thiols; and the aldol reaction of acetone and nitrobenzaldehyde, the catalysis of which is enhanced by the presence of both acid and base groups. A summary of the four types of catalyst discussed is shown in Figure 1.2.

In the following chapters, the catalytic performance of each of these site-paired bifunctional materials is evaluated and compared with that of randomly-distributed organic groups. In some cases, the paired materials outperform the random; in others, there is no difference or (in the case of strong acid/base materials) the paired material is inactive. The key conclusion is that spatial positioning of surface organic groups is an important design criterion in heterogeneous catalysis—one that has heretofore been largely ignored. While spatial positioning is not important in every reaction, it is worthy of consideration any time cooperative catalysis is operating.

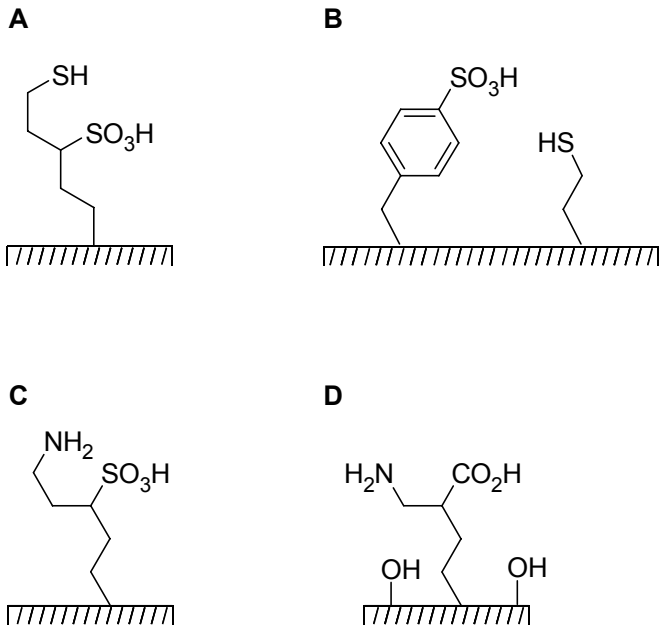

Figure 1.2. Summary of the four polyfunctional SBA-15 catalysts described in this work.

(**A**) Alkylsulfonic acid/thiol catalysts for the synthesis of bisphenol A

(**B**) Arylsulfonic acid/thiol catalysts for the synthesis of bisphenol A and bisphenol Z

(**C**) Alkylsulfonic acid/amine catalysts for the aldol reaction

(**D**) Carboxylic acid/amine/silanol catalysts for the aldol reaction

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