

An Introduction to SAMs: Self-Assembled Monolayers in Organic Chemistry

Self-assembled monolayers, SAMs, are formed when surfactant molecules spontaneously adsorb in a monomolecular layer on surfaces. Two of the most widely studied systems of SAMs are gold-alkylthiolate monolayers and alkylsilane monolayers.

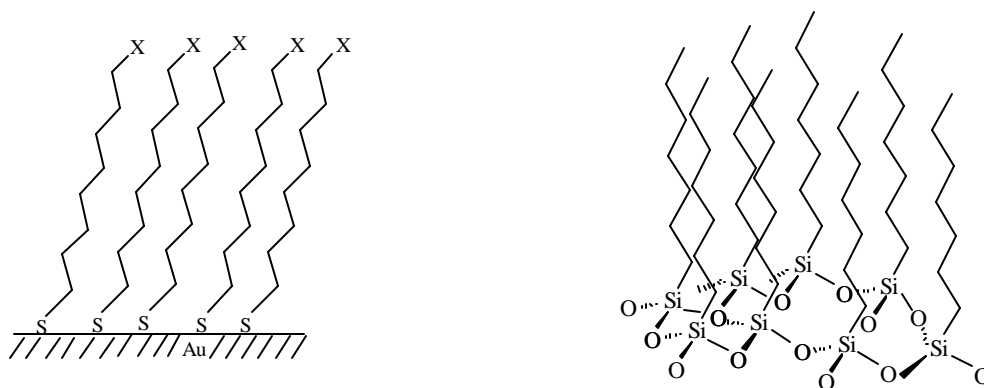


Figure 1. Gold thiolate monolayer and alkylsilane monolayer

The first gold-alkylthiolate monolayer was produced by Allara and Nuzzo at Bell laboratories in 1983[1]. They realized the utility of combining a relatively inert gold surface with a bifunctional organic molecule in well-ordered, regularly-oriented array.

SAMs offer a unique combination of physical properties that allow fundamental studies of interfacial chemistry, solvent-molecule interactions and self-organization. Their well-ordered arrays and ease of functionalization make them ideal model systems in many fields[2]. SAMs are invaluable substrates in bioanalytical, organometallic, physical organic, bioorganic and electrochemistry.

Preparation

Gold-thiol monolayers are stable when exposed to air, and aqueous or ethanolic solutions for several months[3]. They are also quite facile to produce. A 1-5 nm film of titanium is evaporated onto a glass coverslip or silicon wafer to promote adhesion of gold to the surface. A 10-200 nm film of gold is then evaporated onto the surface. The resulting gold surface is then immersed into a 2mM solution of ethanolic alkylthiol, (disulfide solutions may also be used). Mixed monolayers may be formed if the ethanolic solution of T-functionalized alkylthiols contains two or more different thiols.

Several procedures exist for producing patterned mixed monolayers. Lithography lies at the heart of all of these techniques[4]. One popular method is microcontact printing, : CP. “Stamps” with patterned reliefs are formed from elastomers, such as poly(dimethylsiloxane), PDMS, that have been poured over a master, cured and then peeled. The masters are manufactured from photolithography, e-beam writing, micromachining or relief structures etched into metals. Each master may be used to produce up to 50 “stamps”, and each stamp may be used multiple times. The “stamp” is “inked” with an ethanolic solution of T-functionalized thiol and brought into contact with the gold surface for 10-20 seconds resulting in a gold thiolate monolayer at the areas of contact.

Characterization

Methods for studying monolayers can differ greatly from characterization techniques of solution chemistry. Ellipsometry[5] measures the change in amplitude and phase of light upon reflection. Using these values, the thickness and refractive index of a film can be calculated. This procedure can be used to determine the thickness of a monolayer before and after reactions to detect

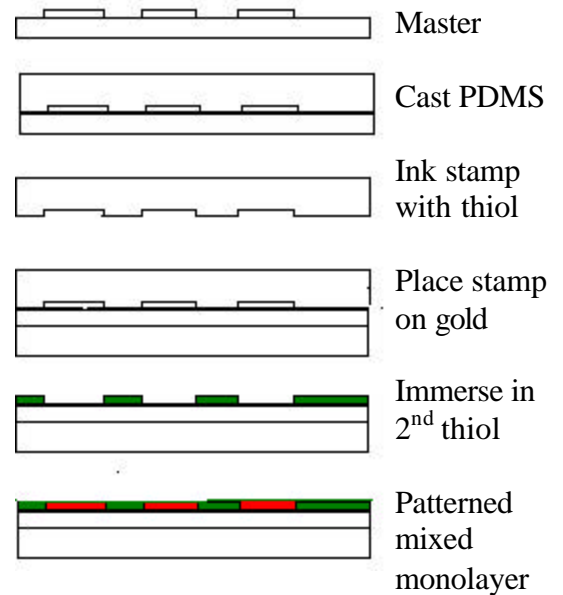


Figure 2. Microcontact

Printing

adsorption of molecules onto the SAM. Since the commercialization of surface plasmon resonance spectrometers, surface plasmon resonance spectroscopy has become a vital tool in for imaging reactions on SAMs. Surface plasmon resonance is an *in situ* technique that measures changes in the refractive index of a monolayer attached to a metal surface[6]. This allows for collection of both kinetic and thermodynamic information about a system in real time. X-Ray photoelectron spectroscopy (XPS) [7] is a technique which quantifies the elemental composition of monolayers.

Reactivity

Reactivity of monolayers varies substantially from analogous solution reactions[8]. Due to the close proximity of the alkyl chains, interchain reactions, also known as intrafilm reactions, can occur. Interchain reactions can lead to stabilizing hydrogen bonding [9], dimerizations [10] or chain polymerizations[11].

Reaction kinetics can vary widely from those observed in bulk solution. Often, heterogeneous kinetics are observed for interfacial chemistry. This arises from the rate of the reaction changing as the surface is modified.

Using cyclic voltammetry, Mrksich and co-workers investigated the kinetics of the Diels-Alder reaction of cyclopentadiene with monolayer-bound benzoquinone[12]. In this system, kinetic rates stayed constant over the course of the reaction. The kinetics were dependent on the environment of the immobilized dienophile. With alkyl hydroxy chains co-adsorbed onto the monolayer, the reaction had a second-order rate constant consistent with the bimolecular solution reaction. With methyl terminated mixed monolayer, the reaction did not follow second-order kinetics, but was consistent with the cyclopentadiene adsorbing on the monolayer and then following a first order Diels-Alder reaction. This demonstrates the importance of solution-monolayer dynamics and how the environment of the monolayer can effect the kinetics of a reaction.

Acidity and basicity can be effected by the presence of a monolayer [13]. Ionization of the monolayer leads to an accumulation of charge across the surface. The formation of a double-layer changes the pH in the vicinity of the monolayer from that of the bulk solution. In general, acids become less acidic and bases become less basic by 2-5 pK_a units.

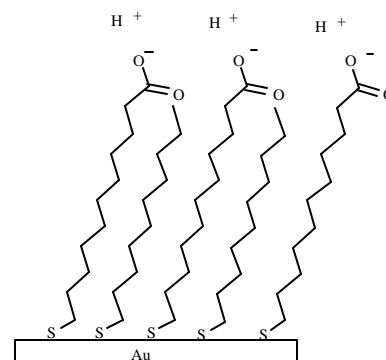


Figure 3. Doublelayer

Sterics play a large role in the reactivity of monolayers. Tightly packed monolayers can inhibit cis-trans photoisomerism of azobenzene molecules. When spacer molecules are integrated into the monolayer surface, photoisomerism is observed. [14]. S_N2 reactions on planar SAMs were investigated by Fryxell and coworkers with T-bromoalkylsilane monolayers[15]. They noted that only NaN_3 completely displaced bromide after 48 hours of reaction. Other nucleophiles, such as thiocyanate and cysteine thiolate, only reached 75% completion, even after 48 hours. These reactions are significantly slower than the analogous solution reactions. The bromide reactivity was probed with hexamethylditin, and the radical reaction was quite facile. Since the bromide was shown to be reactive, the authors postulated that steric crowding around the monolayer causes the lack of reactivity in S_N2 reactions. The incoming nucleophile has to approach the electron-deficient carbon-bromine antibonding (F^*) orbital, which is located under the rigid surface of the monolayer. This demand gives rise to a substantial kinetic barrier.

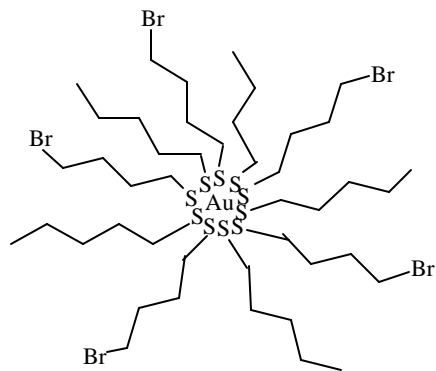


Figure 4. MPC

One way to lower this barrier is to create a more flexible monolayer. Alkyl thiolates can adsorb onto gold nanoparticles and form monolayer-protected gold clusters, MPCs [16]. The reactivity of these 3D molecules is quite different than that of planar SAMs. Due to the curvature of the gold core, the chain density of the monolayer decreases as the chain radiates from the core. T-Bromoalkylthiolates

adsorbed onto gold can undergo S_N2 reactions with primary amines with rates that are similar to the solution state[17]. Submerging the bromide under the monolayer, by forming mixed monolayers with longer alkyl chains than bromoalkyl chains, caused a reduction in the rate of reaction, but the reaction still went to completion.

Mrksich and Houseman noticed an interesting steric effect in the glycosylation reaction of N-acetylglucosamine [18]. They observed that the enzymatic activity of bovine β -1,4-galactosyltransferase (GalTase) is dependent on the density of adsorbed ligand. As the density of immobilized N-acetylglucosamine increased, the amount of ^{14}C -labelled galactose increased linearly. When the monolayer had a ligand density of 70%, incorporation of ^{14}C -labelled galactose reached a maximum, then decreased with increasing ligand density. This is explained by the steric crowding of the ligands inhibiting substrate-enzyme interactions or the steric crowding of the disaccharide.

Common functionalizations of monolayers are similar to solid phase peptide synthesis. Carbonyl group activation, with coupling reagents such as DDC, EDC or $SOCl_2$, followed by reaction with alcohols or amines yield esters or amides, respectively. Microcontact printing can also be used to selectively functionalize patterned monolayers. Once a monolayer has activated carbonyl groups, the PDMS stamp can be inked with an amine or alcohol. Then amide or ester formation occurs only in the areas of contact with the stamp. Whitesides and coworkers used this method to create an amide bond between an immobilized activated ester group and an amine linked to a biotin molecule [19]

Applications

SAMs have many applications in organic chemistry. Catalysis reactions are a common area where a defined presentation of a specific face of a molecule could be beneficial. Immobilizing catalysts on SAMs has been successfully performed for a number of systems [20]. Asymmetric dihydroxylation can be carried out on MPCs. Unoptimized conditions afford similar yields to monomeric solutions (~80%) and similar ee's to polymer bound catalysts (80-90%) [21]. If the monolayer immobilizes the catalyst in a beneficial orientation, desired

reaction rates can increase dramatically. Tremel and coworkers attached a ruthenium ROMP catalyst to MPCs and found that the catalyst not only catalyzed ring-opening metathesis of norbornene, its turnover frequency increased from 3000 h^{-1} to $16,000 \text{ h}^{-1}$. When the catalyst was immobilized to a planar monolayer, the turnover frequency increased to $80,000 \text{ h}^{-1}$ [22].

Molecular recognition is another important application for SAMs [23]. Macromolecules, including DNA [24], proteins [25], and even cells [26] can be immobilized onto monolayers. A major breakthrough came when Whitesides and Prime realized that oligo(ethylene glycol) chains prevent non-specific binding of proteins [27]. This allows for adherence of specific biomolecules without unspecific binding events. Utilizing techniques, such as SPR and ellipsometry, binding and recognition of biomolecules can be measured in real time to allow for calculation of association and dissociation constants. Competitive binding experiments and many other physical properties of biological systems can be assayed using SAMs.

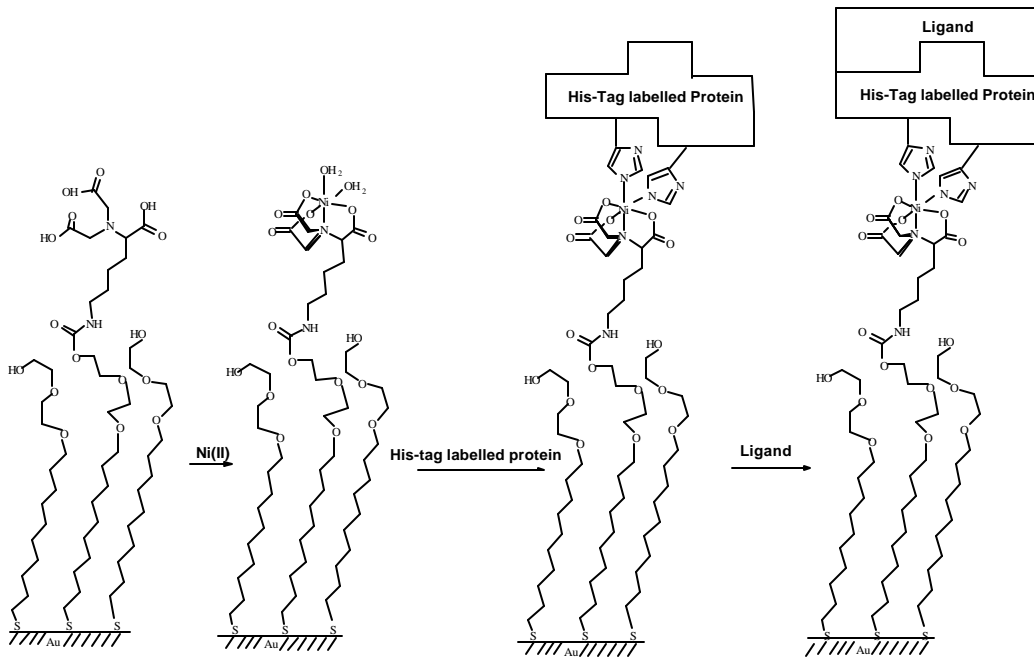


Figure 5. Protein immobilization of His-tag labeled proteins

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