Bifunctional Surface Imprinting of Silica: Thermolytic Synthesis and Characterization of Discrete Thiol−Amine Functional Group Pairs

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In this article we demonstrate the sub-nanometer patterning of mixed chemical functional groups consisting of thiol and primary amine functionality on the surface of silica and characterize the local organization of thiols and amines within these materials. Our approach has required the development of a synthetic method for the thermolytic imprinting of thiols based on a xanthate protection scheme, which enables bifunctional imprints containing carbamate and xanthate functionality to be condensed onto a silica surface and thermolytically deprotected in a single step. This imprinting process is demonstrated for the synthesis of bifunctional imprinted sites containing thiol−amine pairs and groups of two thiols and an amine per imprinted site, and is characterized using solid-state UV/Visible, ^{29}Si CP/MAS NMR, and ^{13}C CP/MAS NMR spectroscopies. Independent titration of thiols with Ellman's reagent and amines with perchloric acid demonstrates that the bulk surface coverage of thiol and amine functionality reflects the expected ratios based on imprint molecule stoichiometry, with yields of accessible bifunctional imprinted sites greater than 80% relative to the amount of imprint used. The high yields in the current methodology overcome previous limitations for the imprinting of mixed functional groups and are facilitated by the low entropic penalty for imprinting multiple groups provided by the unimolecular nature of the thermolysis process. Local chemical functional group organization is investigated by using *o*-phthalaldehyde as a specific binding probe for thiol−amine pairing on the length scale of ∼3 Å. The paired imprinted material shows 2.5-fold higher yield of paired sites relative to a mixed control material consisting of monofunctional thiol and amine sites at the same bulk surface coverage of 0.02 thiol and amine functional groups per nm^2. This result demonstrates that silica surface imprinting can be used to control the local density of mixed chemical functional groups on sub-nanometer length scales in a fashion that is impossible to achieve with most other synthetic methods. Our ability to imprint mixed chemical functionality on the surface of silica and quantitatively characterize the resulting amount of thiol−amine pairing is further used to rigorously investigate imprinted site isolation in mixed control materials. Our results demonstrate that nonrandom surface distributions of immobilized imprint result in these materials, despite low surface coverages, and draw attention to the need for further investigating degree of site isolation when surface-imprinting silica.

Introduction

A longstanding objective in the synthesis of materials is the local organization of disparate chemical functional groups on a sub-nanometer length scale, mimicking the intricate chemical resolution observed within the active sites of biological catalysts. This degree of spatial resolution has enormous potential for controlling the heterogeneous nucleation of matter and synthesis of specific binding domains and photoresponsive materials. Synthetic control over heterogeneous nucleation via organization of mixed chemical functionality has been demonstrated previously on larger length scales using lithography.[1−6] The patterning of binding domains by microcontact printing, for example, enables patterned nucleation and growth of various organic[1−3] and inorganic crystals.[4−6]

Our goal is sub-nanometer patterning of mixed organic functional groups within discrete active sites on the surface of silica. While being too small for synthesis methods based on standard semiconductor etching, such sites could serve as a useful scaffold for affecting nucleation in a variety of applications including bifunctional catalysis,[7−14] chemical

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sensing,[15] photoluminescence,[16,17] as well as the specific adsorption of metal cations,[18] small molecules,[7] and polymers.[19−23] There are few techniques that enable the organization of multiple chemical functional groups on subnanometer length scales. Silica imprinting offers an approach for accomplishing this that is conceptually similar to that of microcontact printing. In imprinting, a molecular "stamp" is used to print organized chemical functional groups on a solid surface. Early work in this field began with the observation that drying silica gels in the presence of benzene, toluene, xylene, and naphthalene atmospheres increased the adsorptive activity of the final material toward the specific vapor in which the gel was dried.[24] A more rigorous analysis was later performed on dye molecules added to sodium silicate solutions prior to gelation.[25] The presence of the dye molecules presumably generates selective micropores via noncovalent interactions with silica during gelation.[26] However, this early research did not address the organization of organic functional groups within an imprinted site. This added complexity was developed later in work involving the covalent imprinting of organic polymers,[12,13,27,28] silica surfaces,[29−33] and bulk silica.[34] The surface of silica has been successfully imprinted with up to three identical functional groups that are organized relative to each other within a site on the length scale of ∼1 nm.[29−33]

The organization of disparate functionalities within an imprinted site on the surface of silica has not been previously demonstrated using a covalent imprinting strategy. Previous attempts in the synthesis of such materials have been made using highly cross-linked organic polymers as the material network for preserving imprinted functional group organization.[8,27,35] These efforts highlight the difficulty of removing the bifunctional imprint fragment using conventional wet-chemical deprotection methods. Indeed, even in cases involving multiple functional groups of one type (i.e., primary amine), covalent imprinting becomes increasingly difficult as the number of groups to be deprotected per site increases.[34,36] This increased difficulty is due to the requirement imposed by microscopic reversibility that multiple chemical deprotection events within a site must occur almost simultaneously in order to accomplish imprint fragment removal. With sites consisting of mixed functionality this difficulty is further exacerbated since the two types of chemical functional groups will, in general, have different efficacy to deprotection conditions. High concentrations of harsh reagents are typically required in such circumstances in order to affect imprint fragment removal. This may lead to an undesired compromise between preserving the integrity of the imprinted material network and achieving even modest yields of bifunctional imprinted sites.[8,27]

The difficulties associated with synthesizing a bifunctional imprinted site consisting of mixed chemical functional groups can be overcome by using a thermolytic imprinting strategy. Thermolysis carries the inherent entropic advantage of being a unimolecular chemical reaction. This eliminates the requirement for the simultaneous delivery and reaction of multiple chemical reagents, such as trimethylsilyliodide.[34] We have successfully demonstrated this principle for the thermolytic synthesis of imprinted amines using immobilized carbamate imprints in bulk silica.[37] These results show that dicarbamate imprints follow the same deprotection reaction progression as do monocarbamate imprints.[37] Thermolytic synthesis has also been used for the surface imprinting of silica particles with isocyanate functionality.[38]

We demonstrate here the first thermolytic imprinting of thiol chemical functionality. Our approach relies on using a grafted xanthate-protected imprint that reacts thermolytically via Chugaev reaction to produce thiol functionality. This proceeds according to a concerted unimolecular cis elimination mechanism and results in an immobilized thiol, with release of carbonyl sulfide and olefin.[7,37,39] Scheme 1 illustrates the reactions involved in the thermolytic imprinting of thiol functionality on the surface of silica.

Combining the dual thermolytic imprinting capabilities for thiols and amines within a single imprint, we synthesize bifunctional sites consisting of mixed chemical functionalities that are locally organized relative to one another. This strategy synthesizes imprinted thiols and amines within a site in unprecedented high yields. We demonstrate this method for the synthesis of imprinted sites on silica surfaces consisting of thiol−amine pairs, as well as groups of two thiols and a single amine per imprinted site. The latter process is schematically represented in Scheme 2. We characterize the bulk stoichiometry and local organization of chemical

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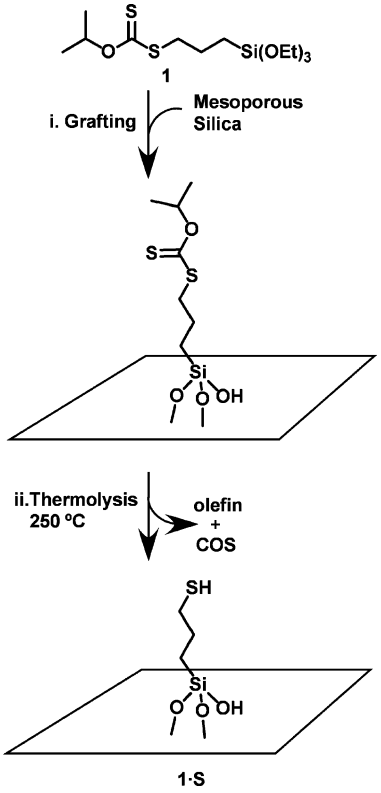
Scheme 1. Imprinting of Silica with Protected Thiol Groups Is Performed by (i) Grafting the Imprint 1 in Refluxing Benzene; Thermolytic Deprotection (ii) of the Protecting Group Yields the Final Material 1·S



functionality in these bifunctional imprinted sites by using molecular probes based on orthogonal coupling strategies for thiols, amines,[40,41] and thiol−amine pairs,[42,43] which have been developed for investigating cysteine and lysine residues in proteins. Our results demonstrate that the bifunctional imprinting developed here defines the thiol and amine stoichiometry in the bulk as well as on a local sub-nanometer length scale corresponding to a single imprint molecule.

We rely on our ability to surface-imprint silica with mixed chemical functionality and quantify thiol−amine pairing in order to investigate the degree of imprinted site isolation in thiol−amine materials. Imprinted site isolation is critical for applications in molecular recognition, photoluminescence, and catalysis.[10,44] Our approach is to compare the amount of thiol−amine pairing across mixed materials that are prepared from homologous surfaces. We expect a random distribution of paired sites in these materials because of the low surface coverages employed (0.02 thiol and primary amine functional groups per nm^2), assuming an absence of specific interactions between surface species. This has been the common assumption in the past, but it has been difficult to prove, due to the inability of synthesizing two materials with different functionality but where the distribution and local surface density of the functionality remains fixed. Thermolytic imprinting allows the synthesis of such

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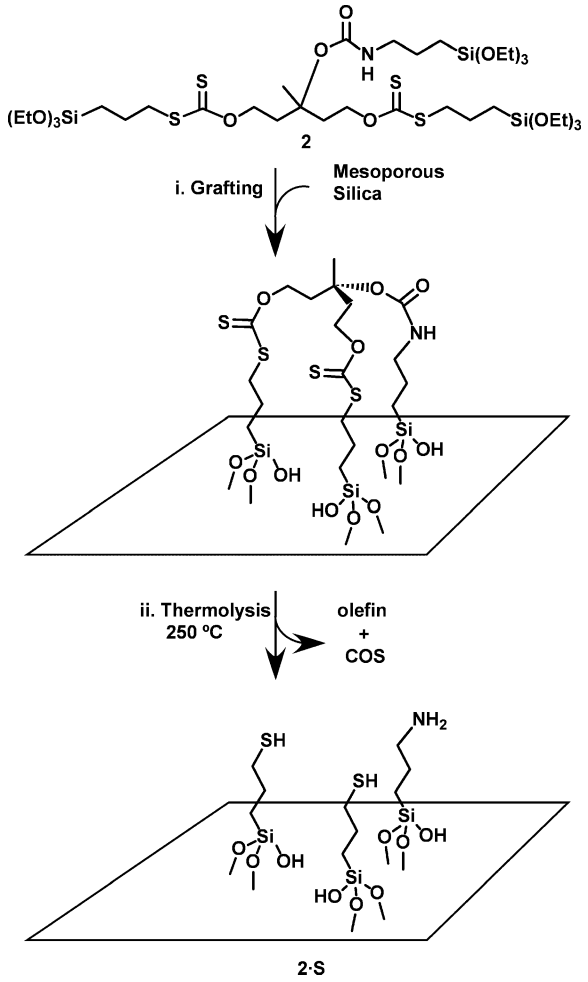
Scheme 2. Imprinting of Silica with Protected Thiol Groups Is Performed by (i) Grafting the Imprint 2 in Benzene To Form the Protected Hybrid Organic−Inorganic Material; Thermolytic Deprotection (ii) of the Protecting Group under an Inert Atmosphere Yields the Final Material 2·S



homologous materials (e.g., the xanthate and mercaptopropyl materials in Scheme 1), and thus enables this investigation.

Results and Discussion

Thermolytic Synthesis of Thiols on Silica. The Chugaev reaction provides a synthetic pathway for enabling the thermolytic imprinting of thiol functionality in high yield and under mild deprotection temperatures.[39] For the thermolytic synthesis of thiols on silica, we synthesized imprint **1** using the procedure depicted in Scheme 3.[45] Starting with the alcohol, treatment with carbon disulfide under alkaline conditions forms the xanthic acid salt, which is subsequently alkylated with 3-iodotriethoxysilane for synthesis of **1**. The final imprint molecule contains a xanthate-protected thiol and an alkoxysilane group that is amenable to grafting onto oxide supports.

Grafting imprint **1** onto the surface of mesoporous silica results in a hybrid organic−inorganic material containing xanthate-protected thiol groups. The xanthate-protecting group is subsequently removed by heating to 250 °C in an

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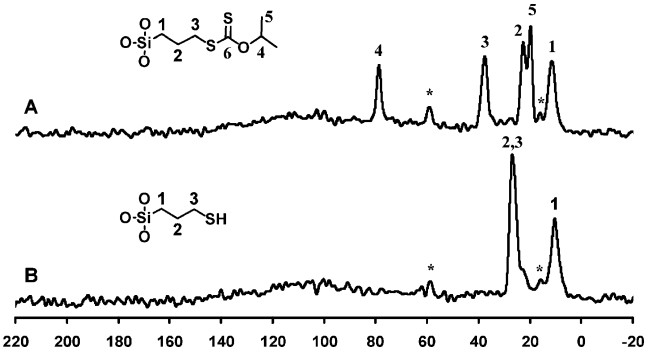


Figure 1. ^{13}C CP/MAS NMR spectra of thiol-imprinted materials (A) before and (B) after thermolytic deprotection to produce **1·S**. The resonances corresponding to the protecting group are lost upon thermolysis, forming the mercaptopropyl functionalized material. Asterisks denote ethoxy resonances. This technique is insensitive to the thiocarbonyl functionality, likely due to its long relaxation time. The surface density is 0.35 molecules **1** nm^{-2}.

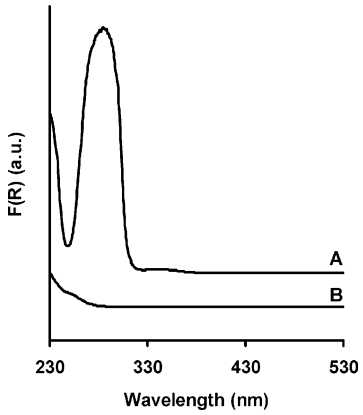
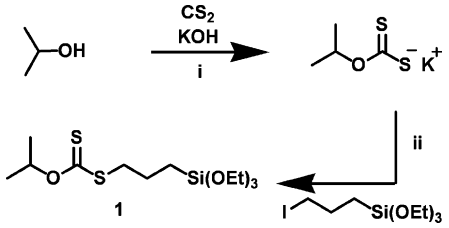


Figure 2. Solid-state diffuse-reflectance UV/Visible spectra of material **1·S** in (A) the protected state showing the characteristic absorption band of the xanthate at 280 nm and (B) after deprotection where this band is no longer apparent. The surface density is 0.12 molecules **1** nm^{-2}.

Scheme 3. Synthesis of Imprint 1 via (i) Treatment of Isopropyl Alcohol with Carbondisulfide and Potassium Hydroxide To Yield the Xanthate Salt and (ii) Alkylation with 3-Iodopropyltriethoxysilane



inert atmosphere, yielding the thiol functionality. These two steps synthesize material **1·S**, as illustrated in Scheme 1. This process is characterized using ^{13}C CP/MAS NMR and solid-state UV/visible spectroscopy as shown in Figures 1 and 2. The top ^{13}C CP/MAS NMR spectrum (Figure 1) demonstrates that the imprint remains intact immediately after condensation with silica. After thermal deprotection, shown in the bottom spectrum, resonances associated with the xanthate-protecting group are supplanted by resonances at 10 and 27 ppm, resulting from 3-mercaptopropylsilane tethered onto silica.[40] UV/visible spectroscopy corroborates this process (Figure 2), showing the complete removal of xanthate functionality by the disappearance of its characteristic absorption near 280 nm.

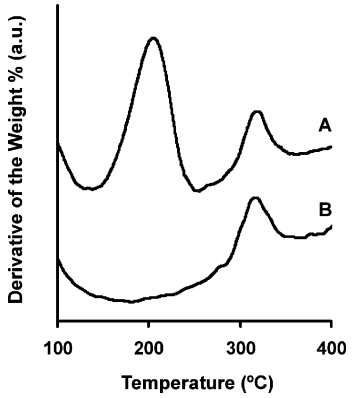


Figure 3. Thermogravametric analysis of **1·S** showing (A) a feature centered around 205 °C due to the loss of the protecting group that results in the formation of the thiol functionality. Further heating under an oxygenated environment results in degradation of the organic functional groups at temperatures above 300 °C. Also shown (B) is a TGA of a material that was thermally deprotected to 250 °C under nitrogen. In this material there is no longer the feature associated with the protecting group. The heating rate is 5 °C min^{-1} on a material containing 0.12 molecules **1** nm^{-2}.

Thermolysis is also followed by thermogravimetric analysis as shown in Figure 3, in which **1·S** is heated at a rate of 5 °C/min under an oxygenated environment. Under these conditions thermolysis rates become significant at ∼150 °C, reach a maximum at 205 °C, and decrease sharply above 250 °C. This range is typical of temperatures required for the thermolysis of homogeneous xanthate protecting groups[46] and corresponds to an activation energy for thermolysis of 26 kcal mol^{-1}.[37,47] Above 300 °C in an oxygenated environment, combustion of the synthesized 3-mercaptopropyl organic groups begins to occur as seen in Figure 3.

Quantification of the number of accessible thiol functional groups synthesized during thermolysis is performed by covalent titration with Ellman's reagent, 5,5′-dithio-bis(2-nitrobenzoic acid).[41] The titration product is the thio anion, 3-carboxyl-4-nitrothiophenolate (NTB), which is measured by solution phase absorption. This method provides excellent sensitivity, quantifying thiol densities below 0.01 SH per nm^2. This sensitivity is crucial for bifunctional imprinting since low submonolayer surface coverages are necessary for the synthesis of discrete organized active sites.

Prior to thermolysis, titration of silica imprinted with **1** using Ellman's reagent showed no detectable levels of thiol groups (<0.5% of imprinted sites are deprotected). This indicates that the xanthate functionality remains intact during grafting as observed via ^{13}C CP/MAS NMR spectroscopy in Figure 1. After thermolysis, titration of **1·S** is quantitative based on the amount of grafted imprint (Table 1). In addition to a titration experiment, Ellman's reagent selectively derivatizes the thiol groups to yield a nitrobenzoic acidic moiety in place of each thiol. This is useful for the synthesis of bifunctional imprinted materials containing organized acid and base functionality (vida infra). The xanthate imprint **1** is also amenable to imprinting in bulk silica using procedures developed for the bulk imprinting of amines.[7,37] Titration of the bulk imprinted thiols with Ellman's reagent reveals that

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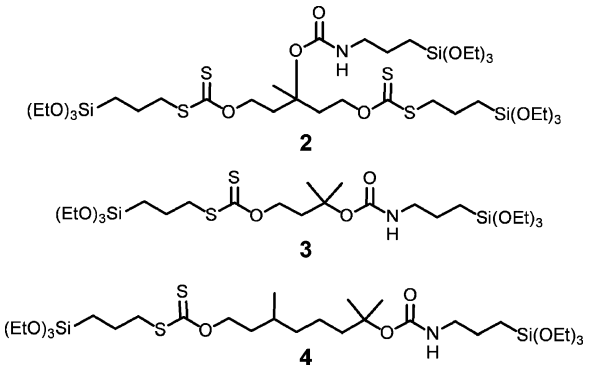
Table 1. Titration of Thiol and Amine Functionalities for Imprinted Materials after Thermolysis[a]

material	thiol count,[c] per nm^2 (%)	amine count,[b] per nm^2 (%)	thiol−amine ratio
1·S	0.125 ± 0.006 (100%)	N/A	N/A
3·S	0.096 ± 0.005 (80%)	0.10 ± 0.008 (85%)	0.94:1 (1:1)[d]
4·S	0.100 ± 0.005 (85%)	0.12 ± 0.01 (100%)	0.83:1 (1:1)[d]
2·S	0.18 ± 0.01 (75%)	0.095 ± 0.004 (80%)	1.9:1 (2:1)[d]

[a] All materials were imprinted with 0.12 imprint nm^{-2}. Error bars represent uncertainty as ascertained by repetitive titration experiments. [b] Titration with perchloric acid in acetic acid. [c] Titration with Ellman's reagent, 5,5′-dithio-bis(2-nitrobenxoic acid). [d] Expected ratio.

70% of sites are accessible after thermolysis and that less than 5% of sites adventitiously deprotect during synthesis.

Imprinting Mixed Functional Groups. Imprinted sites containing mixed functional groups are synthesized using **2**, **3**, and **4**. These imprints contain a combination of thermally labile xanthate and carbamate moieties, which serve to protect the chemical functionalities and covalently link the two disparate protected functional groups until they are immobilized. Such materials can consist of discrete thiol−amine pairs (such as deprotected materials **3·S** and **4·S**), or multiple organized functional groups, such as two thiols and one amine (such as deprotected material **2·S**).



Covalently linking the thiol and amine moieties prior to attachment allows these imprints to be used for defining the local stoichiometry of the final material on the length scale of the imprint molecule. Because of the different condensation rates between various alkoxysilanes, as well as the likely thermodynamic tendency of some alkoxysilanes to phase separate on a sufficiently local level, materials with such locally defined stoichiometry would be difficult to synthesize by co-condensing distinct, monofunctional entities.

The synthesis of imprint **2** starting from 3-methyl-1,3,5-pentanetriol is shown in Scheme 4. Potassium *tert*-butoxide is used in combination with carbon disulfide to synthesize the dipotassium xanthate salt, **5**, which is then alkylated with 3-iodopropyltriethoxysilane forming the intermediate **6**. Coupling the tertiary alcohol using 3-isocyanopropyltriethoxysilane in the presence of di-*n*-butytindilaurate forms carbamate imprint **2** (^{1}H and ^{13}C NMR are shown in the Supporting Information).

The imprinting procedure, as illustrated in Scheme 2 using imprint **2**, begins with the immobilization of imprint onto mesoporous silica to yield the protected hybrid organic−inorganic material. Thermolysis is then conducted under an inert atmosphere at 250 °C to yield the final imprinted

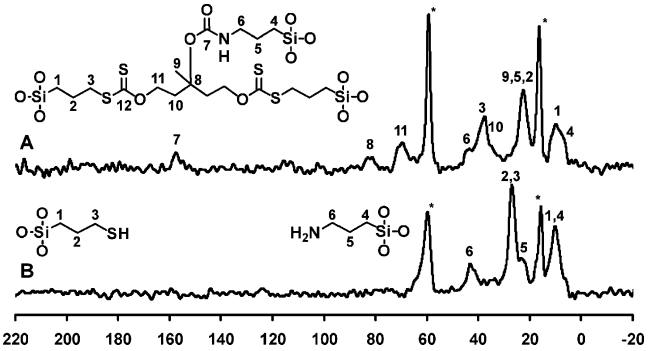
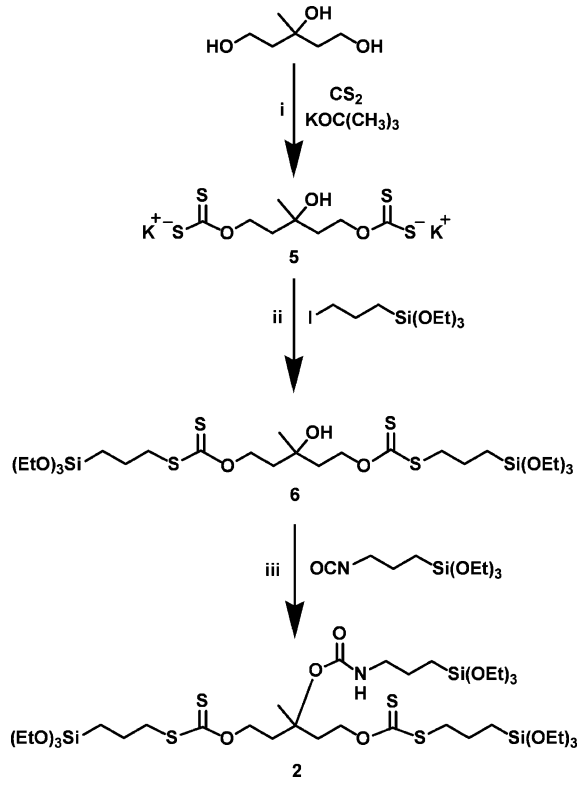


Figure 4. ^{13}C CP/MAS NMR spectra of the mixed thiol−amine material imprinted with **2** (A) before and (B) after thermolytic deprotection to form **2·S**. The resonances corresponding to the protecting group are removed upon thermolysis, forming a material with mercaptopropyl and aminopropyl functional groups. Asterisks denote ethoxy resonances. Surface density was 0.12 imprints nm^{-2}. Materials imprinted with **3** and **4** show similar behavior (see Supporting Information).

Scheme 4. Synthesis of Imprint 2 via (i) Treatment of the Triol with Carbon Disulfide and Potassium *tert*-Butoxide To Yield the Dixanthate Salt, 5, (ii) Alkylation of 5 with 3-iodopropyltriethoxysiliane to Form the Dixanthate 6, and (iii) Treatment of This Tertiary Alcohol with 3-Isocyanopropyltriethoxysilane in the Presence of Di-*n*-butyltindilaurate Catalyst



material **2·S**. Figure 4 shows the ^{13}C CP/MAS NMR spectra of a material imprinted with **2** before and after thermolysis. The protected material has resonances expected of the imprint molecule **2** condensed with silica. Upon thermolytic deprotection, forming **2·S**, resonances for the covalently bound aminopropysilane (9, 21, and 42 ppm)[34,37] and the covalently bound mercaptopropylsilane (at 10 and 27 ppm)[40] are observed. The solid-state UV/visible spectra show complete disappearance of the xanthate absorption near 280 nm (Supporting Information), indicating quantitative cleavage of this group. In contrast, previous attempts at chemically

deprotecting two disparate functionalities within an imprinted site typically achieved imprint removal of less than 30%.[8,27,35]

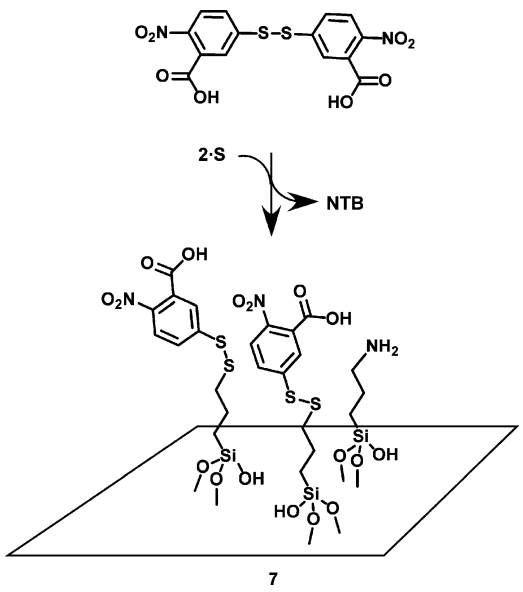
The integrity of imprinted site functional group organization depends critically on its covalent attachment to the silica surface.[48] We estimate the degree of imprint condensation to the silica surface using ^{29}Si CP/MAS NMR spectroscopy,[49] though relative amounts infered from these measurements are approximate due to the nonquantitative nature of the analytical technique. Imprints are observed to be predominately condensed via multiple points of attachment prior to thermolysis, with typical estimated $T^3/T^2/T^1$ ratios of 25/55/20 (see Supporting Information). The T^1 fraction is further reduced by a factor of 2 to 4 after thermolysis due to additional condensation at elevated temperatures. This multiple point connectivity to the surface is expected to retain local imprinted functional group organization when stored dry.[48]

Amine and thiol groups in materials **2·S**, **3·S**, and **4·S** were independently titrated with perchloric acid (amines)[37] and Ellman's reagent (thiols). These results are summarized in Table 1. All of these imprinted materials produce high yields of thiol and amine groups. The stoichiometry of the mixed materials is also very close to that defined by molecular precursors, being near 1:1 for materials **3·S** and **4·S**, and near 2:1 for material **2·S**.

Thiol−amine imprinted materials such as **2·S**, **3·S**, and **4·S** are amenable to further derivatization using selective coupling strategies for the creation of new functional materials. The use of Ellman's reagent provides a relevant example since it creates an acid−base bifunctional material based on the molecular scale architecture of the parent material. The product upon exposure to Ellman's reagent is **7**, where the thiol has been selectively derivatized to a nitrobenzoic acid moiety as seen in Scheme 5. This acidic species is observed in the solid-state diffuse-reflectance UV/Vis spectrum of mixed materials upon titration with Ellman's reagent, shown in Figure 5 for material **7**, which has an absorbance band at 332 nm, while the untreated precursor material shows no absorbance in the same region. The diffuse-reflectance UV/Vis absorption can be used to quantify the amount of chromaphore covalently bound to silica by using the calibration curve in the inset of Figure 5.

Local Organization of Functionality on Imprinted Surfaces. In addition to defining the bulk stoichiometry of the surface, the covalent linkage of xanthate- and carbamate-protecting groups in imprints **2**−**4** is used to define the local stoichiometry of thiols and amines on the surface. This stoichiometry exists on the length scale of the molecular imprint, approximately 1 nm. To measure this local organization of functional groups, we use *o*-phthalaldehyde[42] as a selective probe for thiol−amine pairs. This probe forms the fluorescent isoindole **8** upon covalent reaction with one thiol and one amine (Scheme 6).[50] The identity of **8** was confirmed by its absorbance at 330 nm, its fluorescence emission at 410 nm, and its ability to react with acetylenedicarboxylate[51] to form a characteristic charge-transfer complex (absorbance at 425 nm). These characteristics were not observed for materials containing only grafted amines or grafted thiols upon exposure to *o*-phthaldehyde. The S to N distance in this chromaphore is 2.75 Å, based on single-crystal diffraction of an analogous acetylenedicarboxylate adduct.[51] Therefore, given the inherent flexibility of the propyl tethers connecting the thiol and amine groups to the silica surface, *o*-phthalaldehyde provides a probe for determining the existence of thiol−amine pairing on the length scale of imprint molecules **2**, **3**, and **4**.

Scheme 5. Derivatization of Thiol Groups on 2·S Using Ellman's Reagent Yields the Nitrobenzoic Acid 7 Bound to the Surface[a]



[a] This species is observed by solid-state UV/Visible spectroscopy by its absorbance at 332 nm.

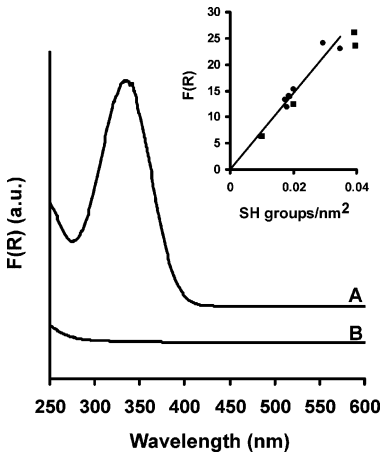
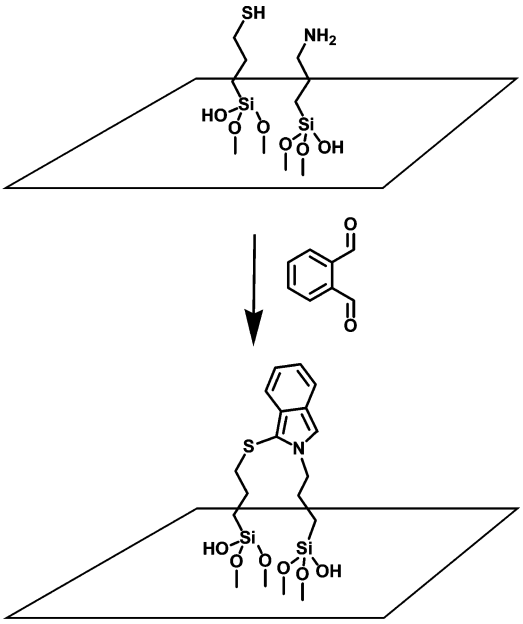


Figure 5. Solid-State UV/Visible spectra of (A) material **2·S** after quantitative reaction (100% as measured by evolved NTB) with Ellman's reagent and (B) material **2·S** after thermolysis but prior to exposure to Ellman's reagent. The material in (A), **7**, shows an absorbance feature at 332 nm that is not present in the material before Ellman's addition. The loading was 0.02 SH groups nm^{-2}. Inset: the peak maximum of bound Ellman's reagent shows the expected linear dependence on coverage for both (●) **1·S** and (■) **4·S** up to detector saturation at 0.04 SH groups nm^{-2}.

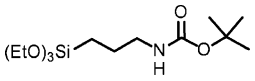
(48) Wang, H. B.; Harris, J. M. *J. Am. Chem. Soc.* **1994**, *116*, 5754−5761.
(49) Sudholter, E. J. R.; Huis, R.; Hays, G. R.; Alma, N. C. M. *J. Colloid Interface Sci.* **1985**, *103*, 554−560.
(50) Simons, S. S.; Johnson, D. F. *J. Am. Chem. Soc.* **1976**, *98*, 7098−7099.
(51) Simons, S. S.; Ammon, H. L.; Doherty, R.; Johnson, D. F. *J. Org. Chem.* **1981**, *46*, 4739−4744.

Scheme 6. Derivatization of a Thiol−Amine Pair by *o*-Phthalaldehyde Yields the Fluorescent Chromaphore 8, Which Has an Absorbance of 330 nm and an Emission Centered at 410 nm



8

To quantify the bifunctional imprinting effect, amine−thiol pairing in material **4·S** was characterized and compared against two control materials: (i) the first prepared by grafting a one-to-one molar mixture of 3-aminopropyltriethoxysilane and 3-mercaptopropyltriethoxysilane and (ii) the second prepared by grafting a one-to-one molar mixture of the thiol precursor, **1**, and the thermally labile carbamate (3-triethoxysilylpropyl)-*tert*-butylcarbamate, **9**, as an amine precursor. This latter material has been used previously for bulk silica imprinting.[37]



9

The results in Figure 6 demonstrate a 2.5-fold greater amount of chromaphore formation for the material imprinted with **4** as compared to the control materials. Since the bulk stoichiometry by Ellman's and perchloric acid titration is the same in all of these three materials, it is the local stoichiometry being closer to unity that is responsible for the larger chromaphore formation for the material imprinted with **4**.

We estimated the absolute amount of thiol−amine pairing in these materials by comparing the solid-state diffuse-reflectance absorption spectra of chromaphore **8** with that of chromaphore **7**. This is possible using the Kubelka−Munk formalism,[52] noting that the absorbance ($F(R)$) of **7** is linearly dependent on coverage up to instrument detector saturation as shown in Figure 5 (inset). Differences in extinction coefficients are accounted for by using values for analogous compounds in solution.[51,53,54] By this approach, at least 4%

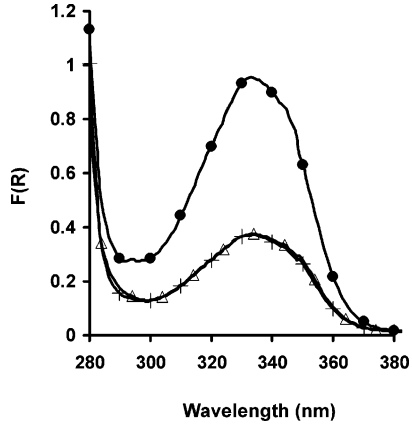


Figure 6. Solid-state diffuse-reflectance UV/Visible spectra upon exposure to *o*-phthalaldehyde of a surface imprinted with (●) the imprinted material **4·S** and two control materials: (△) a one-to-one mixture of 3-mercaptopropyltriethoxysilane and 3-aminopropyltriethoxysilane and (+) a one-to-one mixture **1** and **9**. The observed absorption feature is due to production of chromaphore **8**. The higher yield of this chromaphore in the material imprinted with the thiol−amine bifunctional imprint **4** is evidence of local organization of thiol−amine structure on the material surface. Surface coverages are 0.02 SH and NH_2 groups/nm^2 for all materials.

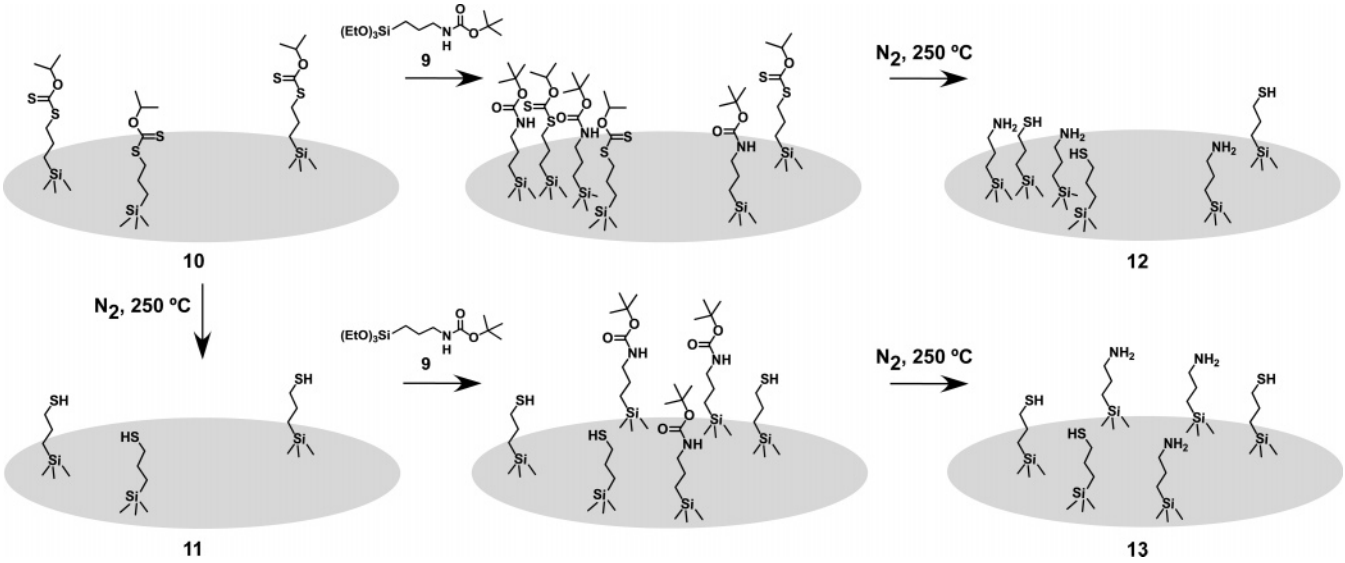
of the thiol groups are paired with an amine in the control materials. A pairing of about 7% for the control materials is expected based on a random surface distribution at the same surface coverage of thiols and amines (Supporting Information). In the imprinted material, at least 11% of the thiol−amine sites are paired.[55]

These pairing values are only a lower bound on the percent pairing since the yield of the reaction is not known. In other systems, the yield of **8** is known to be sensitive to both sequence of addition and thiol/amine stoichiometry,[56] which are fixed in the solid-state materials here. The order of addition is especially critical since the aldehyde must complex the thiol prior to reacting with the amine. Otherwise, irreversible side products may be formed with the amine.[56] This would prevent chromaphore formation regardless of the organization on the surface. We obtained comparable pairing results using 2,3-naphththalenedicarboxyaldehyde, a naphthyl analog of *o*-phthalaldehyde, which has similar reaction sensitivities and identical geometric requirements[43] (see Supporting Information).

Treating the system with excess external thiol groups can provide an estimate as to what the maximum yield of **8** may be for imprinted amines on silica under the most favorable conditions. Mixing an excess amount (20 molar equivalents) of mercaptoethanol with the *o*-phthalaldehyde prior to addition with the imprinted materials causes 35% of amines to react to form chromaphore in both the imprinted and control materials. This suggests that the yield of this reaction is inherently low for amine groups on silica, and this low yield could not be improved by either conducting the

(52) Kubelka, P.; Munk, F. *Z. Tech. Phys.* **1931**, *12*, 593−601.
(53) Kuwata, K.; Uebori, M.; Yamada, K.; Yamazaki, Y. *Anal. Chem.* **1982**, *54*, 1082−1087.
(54) Simons, S. S.; Johnson, D. F. *J. Org. Chem.* **1978**, *43*, 2886−2891.
(55) These pairing percentages were obtained by maximizing chromaphore formation via optimization of the reaction conditions by varying solvent, temperature, number of equivalents, and reactant concentration (the solvent having the largest effect on the reaction yield).
(56) Zuman, P. *Chem. Rev.* **2004**, *104*, 3217−3238.
(57) Boots, B. N.; Getis, A. *Point Pattern Analysis*; Sage Publications: Newbury Park, CA, 1988.

Scheme 7. Interactions during Condensation between Carbamate 9 and the Immobilized Xanthate and Mercaptopropyl Species on Homologous Surfaces 10 and 11 Impact the Distribution of Species on the Final Surfaces 12 and 13[a]



[a] These interactions can be indirectly probed by measuring the pairing of thiol and amine groups in **12** and **13** upon exposure to *o*-phthalaldehyde.

coupling reaction with *o*-phthalaldehyde at a range of different temperatures (−40 to 60 °C) or by changing the solvent for the coupling reaction (pyridine, triethylamine, dimethyl sulfoxide, and various alcohols, among others, were attempted). The yield also remained low when 2,3-naphthalenedicarboxaldehyde was used instead of *o*-phthalaldehyde as the coupling reagent. Assuming that this represents the maximum yield for the coupling reaction in our system, ∼30% of the imprinted thiol amine pairs in **4·S** would be able to access the 2.75 Å distance requirement needed for chromaphore formation. For the control materials, ∼11% of grafted functionalities could access this requirement. These values would be expected to be even larger if the order of addition of thiol and amine could be controlled in our system.

The reaction of *o*-phthalaldehyde with thiol−amine pairs may be used as a sensitive probe of imprinted site isolation. Site isolation is important to characterize, as the aggregation of imprinted sites is highly detrimental for applications in selective molecular recognition,[44] photoresponsive materials, and catalysis.[10] We investigate site isolation by measuring the amount of thiol−amine pairing on silica surfaces containing thiol and amine functionality. The carbamate imprint **9** is grafted (Scheme 7) onto two surfaces containing the same surface distribution and density of active sites: xanthante functionality on surface **10** and mercaptopropyl functionality on **11**. The homology between **10** and **11** is achieved by preparing **11** directly from **10** using thermolysis. After grafting **9**, a final thermolysis step synthesizes surfaces **12** and **13**, each containing 0.02 grafted thiol and amine groups nm^{-2}.

An increase in the amount of thiol−amine pairing in **12** relative to **13** requires a greater tendency to condense **9** next to immobilized **1** on surface **10**, relative to condensing **9** next to immobilized mercaptopropyl groups on surface **11**. Spectra in Figure 7 demonstrate that there is such a tendency, as evidenced by the 2-fold larger amount of chromaphore product upon treatment with *o*-phthalaldehyde of material **12** (Figure 7 (◇)) relative to material **13** (Figure 7 (△)). In

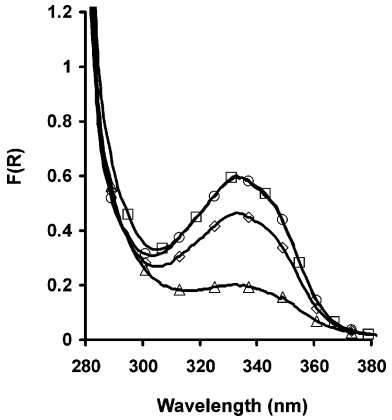


Figure 7. Solid-state UV/Visible spectroscopy of materials imprinted with sequential combinations of the xanthate-protected thiol **1** and the carbamate-protected amine **9** upon exposure to *o*-phthalaldehyde. The order of addition and deprotection are vital in determining the final surface morphology as probed by the amount of pairing of thiol−amine groups forming chromaphore **8** upon exposure to *o*-phthalaldehyde. The largest extent of pairing is achieved by (○) grafting **9**, filtration, grafting **1**, deprotection or by (□) grafting **9**, filtration, deprotection, grafting **1**, deprotection. Slightly less pairing is seen by (◇) grafting **1**, filtration, grafting **9**, deprotection. Relatively minimal pairing is seen by (△) grafting **1**, filtration, deprotection, grafting **9**, deprotection. These data indicate that imprint−imprint interactions are important in determining the surface structure of these materials. Surface coverages are fixed at 0.02 SH and NH_2 groups/nm^2 for all materials.

contrast, almost no difference is observed between grafting **1** to a surface consisting of grafted **9** (Figure 7 (○)), versus grafting **1** onto the homologous surface consisting of grafted aminopropyl functionality (Figure 7 (□)). This control result infers similar tendencies to condense xanthate next to carbamate as to condense xanthate next to primary amine and demonstrates that pairing differences are not an artifact of the synthesis methods. Differences in the relative thiol−amine pairing are also observed in materials containing imprints **9** and **1** depending on whether **1** is grafted first (Figure 7 (◇)), **9** is grafted first (Figure 7 (○)), or whether **1** and **9** are grafted together (Figure 6 (+)). These dependences of extent of thiol−amine pairing on the sequence of imprint addition proves that there is a nonrandom distribution

of imprint on the surface, despite the low surface coverage of 0.02 thiol and amine groups nm^{-2}. This nonrandom distribution may be the result of either specific interactions between surface species or a kinetically driven phenomenon. However, regardless of the procedure used to synthesize the mixed control materials using imprints **1** and **9**, we do not observe pairing that approaches what is achieved after thermolysis of the grafted bifunctional imprint **4** at the same surface coverage. The amount of chromaphore produced upon *o*-phthalaldehyde binding in these mixed control materials is at most 60% of the result obtained by grafting bifunctional imprint **4**. These results have been reproduced on three different synthesis batches, with the *o*-phthalaldehyde adsorption experiments repeated at least twice on each batch.

Conclusions

A thermolytic imprinting strategy based on the Chugaev reaction is developed for the synthesis of thiol groups on silica. The imprinting process is characterized using covalent binding of Ellman's reagent, solid-state UV/Visible, ^{29}Si CP/MAS NMR, and ^{13}C CP/MAS NMR spectroscopies. Together these techniques show that the xanthate protecting group remains intact prior to thermolysis and yields ~100% of thiols after deprotection relative to the amount of immobilized imprint.

Combining the thermolytic synthesis of thiols with our previous work in thermolytically imprinting amines, we demonstrate the first imprinting of mixed functional groups within the same site on a silica surface. Thermolytic deprotection leads to synthesis of thiol−amine pairs, using imprints **3** and **4**, or a group of two thiols and one amine using imprint **2**. Orthogonal coupling strategies may be used to create additional functional materials, such as the acid−base bifunctional material based on the thiol derivative **7**. These imprints serve to fix not only the bulk stoichiometry of the surface but also the local stoichiometry on the molecular length scale. This latter result is determined by treatment with *o*-phthalaldehyde, a probe that we demonstrate is sensitive to thiol−amine pairing on the sub-nanometer length scale. This probe in conjunction with our mixed imprinting methods is further used to demonstrate that nonrandom distributions of condensed organosilane on silica can result even at low surface coverages.

Experimental Section

General. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ (293 K) either on a Bruker AV-300 (300 MHz) instrument or on an AVB-400 (400 MHz) instrument. The ^{1}H NMR data are referenced to residual $CHCl_3$. FAB mass spectra were recorded at the UCB Mass Spectrometry Facility. Solid-state NMR spectroscopy was performed at the Caltech Solid-State NMR Facility using a Bruker DSX 200 or a Bruker DSX 500 operating at a spin rate of 14 kHz. UV/Vis spectroscopy was performed on a Varian Cary 400 Bio UV/Vis spectrophotometer equipped with a Harric Praying Mantis accessory for diffuse-reflectance measurements on solids at room temperature. Nonaqueous potentiometric titrations were performed using a Brinkmann/Metrohm 765 Dosimat with an Accumet AR15 pH meter and a Corning High Performance glass combination electrode with a Silver Scavenger reference. High-resolution thermogravimetric analysis was performed on a TA Instruments TGA 2950 system. Water was distilled, purified with a Barnstead Nanopure Infinity system to at least 18 MΩ purity, and passed through a 0.2 μm filter. 3-Iodopropyltrimethoxysilane was purchased from Gelest. All other reagents, unless otherwise reported, were purchased from Aldrich at analytical grade and used as-received.

3-Iodopropyltriethoxysilane. To a solution of 3-iodopropyltrimethoxysilane (10 mL, 51 mmol) in 50 mL of absolute ethanol was added a catalytic amount of *p*-toluenesulfonic acid. The mixture was refluxed overnight whereupon approximately 20 mL of solution was distilled off and replaced with a fresh 20 mL of absolute ethanol. More solution was then distilled off (20 mL) and the reaction cooled to room temperature. The solution was filtered over a short bed of silica and subsequent evacuation of the solvent yielded a pale yellow oil (14.9 g, 88% yield). ^{1}H NMR ($CDCl_3$): 0.662 (2H, m, C*H*$_2$); 1.246 (9H, t, J = 7.0 Hz, Si(OCH$_2$C*H*$_3$)$_3$); 1.949 (2H, m, C*H*$_2$); 3.238 (2H, t, J = 7.0 Hz, C*H*$_2$); 3.838 (6H, q, J = 7.0 Hz, Si(OC*H*$_2$CH$_3$)$_3$). ^{13}C NMR ($CDCl_3$): 11.05 (*C*H$_2$); 12.51 (*C*H$_2$); 18.57 (*C*H$_3$); 27.82 (*C*H$_2$); 58.74 (*C*H$_2$).

Synthesis of Imprint 1. *S-(3-Triethoxysilylpropyl) O-Isopropyl Dithiocarbonate (Imprint **1**).* To a solution of *O*-isopropylxanthic acid potassium salt (525 mg, 3 mmol) in acetone (15 mL) at room temperature under N_2 was added 3-iodopropyltriethoxysilane (1.0 g, 3 mmol) in 10 mL of acetone dropwise. After 24 h, the mixture was filtered through silica, reduced via rotary evaporation, and purified by silica chromatography (Silica Gel 60, hexanes/ethyl acetate) to yield a pale yellow oil (0.84 g, 2.5 mmol, 82% yield). ^{1}H NMR ($CDCl_3$): 0.752 (2H, t, J = 8.0 Hz, C*H*$_2$); 1.223 (9H, t, J = 6.8 Hz, Si(OCH$_2$C*H*$_3$)$_3$); 1.395 (6H, d, J = 6.0 Hz, C*H*$_3$); 1.814 (2H, q, J = 8.0 Hz, C*H*$_2$); 3.124 (2H, t, J = 7.6 Hz, C*H*$_2$); 3.814 (6H, t, J = 6.8 Hz, Si(OC*H*$_2$CH$_3$)$_3$); 5.776 (1H, q, J = 6.4, C*H*). ^{13}C NMR ($CDCl_3$): 10.08 (*C*H$_2$); 18.24 (*C*H$_3$); 21.3 (*C*H$_3$); 22.28 (*C*H$_2$); 38.42 (*C*H$_2$); 58.42 (*C*H$_2$); 77.55 (*C*H); 214.27 (*C*═S).

Synthesis of Imprint 2. *3-Methyl-1,5-Dithiocarbonatopentan-3-ol Dipotassium Salt (**5**).* Under nitrogen a solution of potassium *tert*-butoxide (35 mL, 1.0 M in *tert*-butyl alcohol) was added to a solution containing 3-methyl-1,3,5-pentanetriol at room temperature. After 20 min carbon disulfide (2.1 mL, 35 mmol) was added and the resulting slurry was left to stir overnight. Filtration and washing with dichloromethane yielded a white powder (6.45 g, 100% yield) that was used without further purification.

*S-(3-Triethoxysilylpropyl) O-[5-(3-Triethoxysilane-propylsulfanylthiocarboxyoxy)-3-hydroxy-3-methyl-pentyl] Dithiocarbonate (**6**).* To a slurry of **5** (2.5 g, 6.8 mmol) in 50 mL of acetone at room temperature was added 3-iodopropyltriethoxysilane (4.5 g, 13.6 mmol). After 7 days dichloromethane was added and the mixture filtered. Rotary evaporation and a silica column (hexanes/ethyl acetate) yielded a pale yellow oil (34% yield). ^{1}H NMR ($CDCl_3$): 0.785 (4H, m, CH_2); 1.263 (18H, t, J = 7 Hz, Si(OCH$_2$CH$_3$)$_3$); 1.354 (3H, s, CH_3); 1.645 (1H, m, OH); 1.853 (4H, m, CH_2); 2.089 (4H, m, CH_2); 3.196 (4H, m, CH_2); 3.865 (12H, q, J = 7 Hz, Si-(OCH$_2$CH$_3$)$_3$); 4.82 (4H, m, CH_2);

*S-(3-Triethoxysilylpropyl) O-[5-(3-Triethoxysilane-propylsulfanylthiocarboxyoxy)-3-triethoxysilylpropylcarbamolyloxy-3-methyl-pentyl] Dithiocarbonate (Imprint **2**).* To a mixture of **6** (1.4 mg, 2.0 mmol) and 3-(triethoxysilyl)propyl isocyanate (0.75 g, 3.0 mmol) was added a catalytic amount of dibutyltin dilaurate (2 drops). The mixture was heated to 50 °C and left overnight. Purification via silica column (hexanes/ethyl acetate) yielded a pale yellow oil (1.35 g, 72% yield). ^{1}H NMR ($CDCl_3$): 0.604 (2H, m, CH_2); 0.7.29 (4H, m, CH_2); 1.204 (18H, t, J = 7 Hz, Si(OCH$_2$-CH$_3$)$_3$); 1.503 (3H, s, CH_3); 1.565 (2H, m, CH_2); 1.787 (4H, m, CH_2); 2.273 (2H, m, CH_2); 2.458 (2H, m, CH_2); 3.118 (6H, m, (2)CH_2); 3.803 (12H, q, J = 7 Hz, Si(OCH$_2$CH$_3$)$_3$); 4.681 (4H, m, CH_2); 4.886 (1H, m, NH). ^{13}C NMR ($CDCl_3$): 7.93 (CH_2); 10.37 (CH_2); 18.57 (CH_3); 22.32 (CH_2); 23.47 (CH_2); 24.89 (CH_3); 37.55 (CH_2); 39.09 (CH_2); 43.41 (CH_2); 57.80 (CH_2); 69.90 (CH_2); 80.22

(C); 155.36 (C═O); 215.37 (C═S). Mass spectrum (FAB ^{7}Li): m/z 948.357810 (^{7}Li $C_{36}H_{75}NO_{13}S_4Si_3$, 948.358919). NMR spectra are available in the Supporting Information.

Synthesis of Imprint 3. *O-(3-Hydroxy-3-methyl-butyl) Dithiocarbonate Potassium Salt.* 3-Methyl-1,3-butanediol (15 mL, 140 mmol) was added to potassium hydroxide (1.64 g, 30 mmol) in 10 mL of dimethyl sulfoxide. The solution was briefly heated to facilitate dissolution and then cooled in an ice bath whereupon carbon disulfide (1.8 mL, 30 mmol) was added dropwise. After 30 min the reaction was brought to room temperature and ether added (150 mL). The pale yellow solid product was removed by filtration and washed with ether (3 × 50 mL). The solid was then dried under vacuum, yielding 2.97 g of product (45% yield) that was used without further purification.

S-(3-Triethoxysilylpropyl) O-(3-Hydroxy-3-methyl-butyl) Dithiocarbonate. Acetone was distilled over calcium sulfate prior to use. To a solution of the above salt (2.18 g, 10 mmol) in 15 mL of acetone was added dropwise 3-iodopropyltriethoxysilane (3.33 g, 10 mmol) in 50 mL of acetone at room temperature. The mixture was stirred overnight. Ether was added (30 mL) and the mixture filtered through a short bed of silica. After removal of the solvent, ether was again added (30 mL) and filtered through a short bed of silica. Removal of the solvent and purification via silica column (hexanes/ethyl acetate) yielded 1.7 g (44% yield) of a pale yellow oil.

*S-(3-Triethoxysilylpropyl) O-(3-Methyl-3-(3-triethoxysilylpropylcarbamolyloxy)-butyl) Dithiocarbonate (Imprint **3**).* In a dry reaction flask under nitrogen was added the above dithiocarbonate (1.47 g, 3.84 mmol) and 3-(triethoxysilyl)propyl isocyanate (1.42 g, 5.75 mmol). To this was added a catalytic amount of dibutyltin dilaurate (2 drops). The mixture was heated to 50 °C and left overnight. Purification via a silica column (hexanes/ethyl acetate) yielded a pale yellow oil (1.5 g, 62% yield). ^{1}H NMR ($CDCl_3$): 0.649 (2H, m, CH_2); 0.768 (2H, m, CH_2); 1.249 (9H, t, Si(OCH$_2$CH_3)$_3$); 1.251 (9H, t, Si(OCH$_2$CH_3)$_3$); 1.515 (6H, s, CH_3); 1.626 (2H, m, CH_2); 1.831 (2H, m, CH_2); 2.314 (2H, m, CH_2); 3.162 (4H, m, (2)CH_2); 3.842 (6H, q, Si(OCH_2CH$_3$)$_3$); 3.844 (6H, q, Si(OCH_2CH$_3$)$_3$); 4.716 (2H, t, CH_2); 4.860 (1H, m, N*H*). ^{13}C NMR ($CDCl_3$): 7.68 (*C*H$_2$); 10.11 (*C*H$_2$); 18.31 (*C*H$_3$); 22.14 (*C*H$_2$); 23.28 (*C*H$_2$); 26.82 (*C*H$_3$); 38.73 (*C*H$_2$); 38.97 (*C*H$_2$); 43.10 (*C*H$_2$); 58.45 (*C*H$_2$); 70.20 (*C*H$_2$); 79.27 (*C*); 155.53 (*C*═O); 215.11 (*C*═S). Mass spectrum (FAB ^{7}Li): *m/z* 638.285820 (^{7}Li$C_{27}H_{58}N_2O_{10}Si_2$, 638.286038).

Synthesis of Imprint 4. *O-(7-Hydroxy-3,7-dimethyl-octyl) Dithiocarbonate Potassium Salt.* Hydroxycitronellol (15 mL, 80 mmol) was added to potassium hydroxide (1.64 g, 30 mmol) in 15 mL of dimethyl sulfoxide. The solution was briefly heated to facilitate dissolution and then cooled in an ice bath whereupon carbon disulfide (1.8 mL, 30 mmol) was added dropwise. After 30 min the reaction was brought to room temperature and left to stir overnight. The solution was then added to 1500 mL of dichloromethane, filtered, and washed with dichloromethane (4 × 50 mL). The white solid was then dried under vacuum, yielding 4.33 g of product (50% yield) that was used without further purification.

S-(3-Triethoxysilylpropyl) O-(7-Hydroxy-3,7-dimethyl-octyl) Dithiocarbonate. To a solution of the above salt (2.78 g, 9.6 mmol) in 50 mL of acetone was added dropwise 3-iodopropyltriethoxysilane (3.27 g, 9.6 mmol) in 10 mL of acetone at room temperature. The mixture was stirred for 5 h whereupon ether was added (30 mL) and the mixture filtered through a short bed of silica. Removal of the solvent and purification via a silica column (hexanes/ethyl acetate) yielded 3.16 g (72% yield) of a pale yellow oil. ^{1}H NMR ($CDCl_3$): 0.750 (2H, m, CH_2); 0.945 (3H, m, CH_3); 1.244 (9H, m, Si(OCH$_2$CH_3)$_3$); 1.246 (3H, s, CH_3); 1.34−1.82 (10H, m, (4)CH_2,CH,OH,); 1.831 (2H, m, CH_2); 1.820 (3H, m, CH_3CH$_2$); 3.144 (2H, t, CH_2); 3.818 (12H, q, Si(OCH_2CH$_3$)$_3$); 4.631 (2H, m, CH_2); 4.796 (1H, m, N*H*).

*S-(3-Triethoxysilylpropyl) O-(3,7-Dimethyl-7-(3-triethoxysilylpropylcarbamolyloxy)-octyl) Dithiocarbonate (Imprint **4**).* In a dry reaction flask under nitrogen was added the above dithiocarbonate (2.7 g, 5.94 mmol) and 3-(triethoxysilyl)propyl isocyanate (2.2 g, 8.9 mmol). To this was added a catalytic amount of dibutyltin dilaurate (2 drops). The mixture was heated to 50 °C and left overnight. Purification via a silica column (hexanes/ethyl acetate) yielded a pale yellow oil (2.5 g, 60% yield). ^{1}H NMR ($CDCl_3$): 0.670 (2H, m, CH_2); 0.773 (2H, m, CH_2); 0.985 (3H, t, J = 6 Hz, CH_3); 1.23 (2H, m, CH_2); 1.250 (18H, t, J = 7 Hz, Si(OCH$_2$CH_3)$_3$); 1.35 (2H, m, CH_2); 1.424 (6H, s, CH_3); 1.626 (4H, m, (2)CH_2); 1.72 (2H, m, CH_2); 1.831 (2H, m, CH_2); 2.314 (3H, m, CH_3CH$_2$); 3.151 (4H, m, (2)CH_2); 3.843 (12H, q, J = 7 Hz, Si(OCH_2CH$_3$)$_3$); 4.644 (2H, m, CH_2); 4.796 (1H, m, N*H*). ^{13}C NMR ($CDCl_3$): 7.61 (*C*H$_2$); 10.11 (*C*H$_2$); 18.31 (*C*H$_3$); 19.48 (*C*H$_3$); 21.41 (*C*H$_2$); 22.20 (*C*H$_2$); 23.37 (*C*H$_2$); 26.40 (*C*H$_3$); 29.89 (*C*H); 35.08 (*C*H$_2$); 37.17 (*C*H$_2$); 38.69 (*C*H$_2$); 41.35 (*C*H$_2$); 43.09 (*C*H$_2$); 58.44 (*C*H$_2$); 72.48 (*C*H$_2$); 80.97 (*C*); 155.91 (*C*═O); 215.21 (*C*═S). Mass spectrum (FAB ^{7}Li): *m/z* 708.362190 (^{7}Li$C_{27}H_{58}N_2O_{10}Si_2$, 708.364288).

Imprinting Silica. Imprint (in a quantity determined by the desired surface coverage given 100% grafting yield) was dissolved in 10 mL of benzene and added to a mixture of mesoporous silica (4.5 g of untreated Selecto Silica (Fisher Scientific), 60 Å pores, 250−500 μm, 500 m^2/g) and benzene (40 mL) in a 100 mL round-bottom flask. Materials based on imprints **2** and **3** were capped and shaken at room temperature overnight. All other materials were fitted with a condenser and heated to reflux on a shaker plate overnight. Materials were subsequently filtered, washed with 150 mL of acetonitrile, 150 mL of benzene, and 50 mL of pentane. Materials were collected and stored in sealed vials (those with free thiol groups were stored under nitrogen to prevent oxidation). No differences were seen in pairing for identical materials prepared at room temperature vs refluxing temperatures via *o*-phthalaldehyde.

Quantification of Thiol Functionality Using Ellman's Reagent. Ellman's solution (1.5 mM 5,5′-dithio-bis(2-nitrobenxoic acid) acid in phosphate buffer solution (0.1 M), 13% methanol, 0.9 mM EDTA, pH 7.3) was added to 20 mg of silica sample to give a 20:1 ratio of disulfide:thiol. After 1 h the solution was separated from the solids using a 0.7 μm syringe filter, and the concentration of the evolved 3-carboxyl-4-nitrothiophenolate was measured via UV/Vis spectroscopy using experimentally derived extinction coefficient (11850 M^{-1}). The solids were then washed with water (2 × 1 mL), methanol (3 × 1 mL), and pentane (2 × 1 mL) and dried for solid-state diffuse-reflectance UV/Vis analysis. Experiments to ascertain uncertainty in thiol counts, as reported in Table 1, were conducted on several material batches.

Formation of Chromaphore 8 by Exposure to *o*-Phthalaldehyde. To a 25 mg silica sample was added 2 equiv of *o*-phthalaldehyde (0.25 mL, 3.3 mM in acetonitrile degassed with N_2 for 10 min). After 1 h, 0.5 mL of acetonitrile was added and the solution was filtered. The silica was then washed with acetonitrile (2 × 0.5 mL) and pentane (3 × 0.5 mL) and immediately analyzed. Experiments were reproduced on different synthesis batches with *o*-phthalaldehyde adsorption measurements repeated at least twice on each batch.

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Supporting Information Available: Supplementary figures referenced in the text and the calculation for pairing on a randomly distributed surface. This information is available free of charge via the Internet at http://pubs.acs.org.

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