Chemical modification of self-assembled silane based monolayers by surface reactions

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Received 1st October 2009
First published as an Advance Article on the web 27th April 2010
DOI: 10.1039/b920491a

In this *critical review*, we look at how the functionalization of solid substrates by self-assembly processes provides the possibility to tailor their surface properties in a controllable fashion. One class of molecules, which attracted significant attention during the past decades, are silanes self-assembled on hydroxyl terminated substrates, *e.g.* silicon and glass. These systems are physically and chemically robust and can be applied in various fields of technology, *e.g.*, electronics, sensors, and others. The introduction of chemical functionalities in such monolayers can be generally obtained *via* two methods. This involves either the use of pre-functionalized molecules, which can be synthesized by different synthetic routes and subsequent self-assembly of these moieties on the surface. The second method utilizes chemical surface reactions for the modification of the monolayer. The latter method offers the possibility to apply a large variety of different organic reaction pathways on surfaces, which allows the introduction of a wide range of terminal end groups on well-defined base monolayers. In contrast to the first approach an important advantage is that the optimization of the reaction conditions for suitable precursor molecules is circumvented. The following review highlights a selection of chemical surface reactions, *i.e.*, nucleophilic substitution, click chemistry and supramolecular modification, which have been used for the functionalization of solid substrates (80 references).

1. Introduction

Self-assembled monolayers (SAMs) have attracted significant attention since their introduction in 1980 by Sagiv.[1] Since then a large variety of self-assembly systems have been studied, including mainly thiols on gold,[2] and alkylsilanes on silicon,[3] which represent the most popular combinations of self-assembling molecules and substrates. The following review focuses on the chemical modification of silane terminated monolayers on silicon and glass substrates. This limitation was introduced due to the advantages that result from the use of silane based monolayer systems. One important advantage is that silane terminated monolayers show a higher physical and chemical stability in contrast to thiol terminated monolayers. Therefore, it is possible to apply a broader range of chemical reactions to the monolayer. However, the formation

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of silane SAMs is more complex than the assembly of thiol molecules onto gold substrates. Moreover, in contrast to thiol compounds a disadvantage of the silane molecules is the high reactivity, in particular in the case of trichlorosilanes to water, which needs a careful handling of the chemicals during the assembly steps. Nevertheless, highly ordered and well-packed monolayers can be obtained. The self-assembly of silane molecules represents additionally an interesting research area as they form covalently attached monolayers on technologically relevant surfaces, in particular, silicon and glass.[3] The functionalization of surfaces provides the possibility to tailor the properties of surfaces, *e.g.* the wettability, friction, adhesion, and conductivity in a controlled fashion as the modification of the terminal end groups offers the effective tuning of these properties.[4] These surfaces find many applications in a wide range of research areas, such as microelectronics, optoelectronics, thin-film technology, protective coatings, chemical sensors, biosensors, nanotechnology, bioactive surfaces, cell adhesion, protein adsorption and others.[5–8]

Alkylsiloxane monolayers are usually prepared by a covalent adsorption process of self-assembling molecules, such as trichloro-, trimethoxy- or triethoxysilanes, onto the solid substrate.[2] After the first report on self-assembled monolayers by Sagiv, several studies were performed to investigate the mechanism of the formation of the SAM.[9] Whereas Sagiv proposed, for example, the hydrolysis of the chlorosilane molecules and subsequent reaction with the –OH groups on the surface and other OTS molecules to obtain a polymerized network, other groups proposed a mechanism which included the reaction of the self-assembling molecules with the adsorbed water layer on the substrate. This resulted in the formation of a two-dimensional, cross-linked network of Si–O–Si bonds with only a few bonds to the surface. Additionally, controversy exists in literature concerning the formation by an island-type growth or by a homogenous growth (*e.g.* ref. 10). However, it has to be mentioned here that the self-assembly process is depending on several parameters, such as the water content, the utilized solvent, the age of the solution, the deposition time and the applied temperature, which play an important role in the formation of the monolayer and might have a significant influence also on the monolayer formation process itself, which makes the results rather difficult to compare.

The self-assembling molecules consist generally of three parts: the head group, the alkyl chain and the terminal end group.[6] The head group, *i.e.*, trichloro-, trimethoxy- or triethoxysilane, is responsible for the anchoring of the molecules onto the substrate. The alkyl chain provides the stability of the monolayer, due to van der Waals interactions, and has a significant influence on the ordering of the SAM;[8] the terminal end group introduces chemical functionality into the monolayer system and is important for the overall properties of surfaces. Suitable molecules are to a certain extent commercially available or can be prepared by different chemical reactions. The synthesis of trichlorosilanes can be performed by, *e.g.*, the reaction of bromine functionalized compounds with Mg, followed by the addition of $SiCl_4$.[11] Furthermore, alkali metal organic compounds can be transformed to $RSiCl_3$ by the reaction with $SiCl_4$.[12] A third preparation method utilizes a three step synthesis, which starts from the chlorination of an alcohol with tri-*n*-butyl or triphenyl phosphine and CCl_4, a Grignard reaction with the chlorinated product as well as Mg and subsequent addition of $SiCl_4$.[13] An alternative possibility that is reported in literature is the platinum catalyzed addition of $HSiCl_3$ to carbon–carbon double bonds.[3] The challenge of the preparation of trichlorosilanes is the high reactivity of the head group and the water sensitivity of these molecules. This limits the possibility for the incorporation of functional terminal end groups due to incompatibility and/or interaction of the chlorosilane with these groups, which can potentially prevent the self-assembly process and, therefore, the formation of a well-ordered monolayer. An elegant approach to circumvent this problem is the use of chemical surface reactions performed on a precursor SAM with defined organization that is assembled on a substrate. The successful modification of the surface properties relies on the reliable functionalization of densely packed monolayers to obtain a homogenous and well reproducible self-assembled monolayer system. In contrast to reactions performed in solution, the yield of a functionalization routine might be affected by the steric hindrance due to the close packing of the molecules on the surface. Moreover, the stability of the monolayers is an issue that has to be taken into account. This includes the use of the possible solvents in which the functionalization is performed and, moreover, also the potential byproducts that are formed during the process. Cleaning issues are important points that have to be taken into consideration, as classical chromatographic tools are not applicable and alternative rinsing and sonication steps have to be used. As a consequence, it is obvious that only reactions with a high yield are regarded as good candidates to obtain well-defined functional monolayer systems. Reaction times might suffer from the dense packing but might also accelerate and support binding properties. The following paragraphs will provide an overview over the functionalization of substrates by such chemical surface reaction approaches.

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2. Surface modification of solid substrates

Surface chemistry represents an important tool for the preparation of a large variety of differently functionalized SAMs bearing a diversity of functional groups. Several criteria, such as the high yields obtained under mild reaction conditions, the compatibility of different functional groups, no required catalytic activation and the absence of byproducts, are advantageous for such chemical surface modification reactions.[14] Several recent reviews highlight the use of different modification sequences to introduce chemical functionalities into monolayer systems.[9,15,16]

In this contribution we will summarize the progress that has been made during the last years with respect to the utilization of the highly important and powerful nucleophilic substitution reactions, the click chemistry approach and metallo-supramolecular modification on, mainly, silicon and glass surfaces. These represent important modification schemes that have attracted significant attention in terms of their versatile possibilities to modify self-assembled monolayer systems. Some of the used reaction schemes are summarized in Table 1.

2.1 Nucleophilic substitution

Nucleophilic substitution reactions are an important class of chemical reactions in organic and inorganic chemistry.[17] Thereby, a nucleophile attacks an atom with a positive or partially positive charge, which is connected to a leaving group. Common nucleophiles are hydroxide, cyanide and azide ions, water, ammonia and others. The nucleophilic substitution follows two main mechanisms, the S_N1 and the S_N2 reactions, respectively.[17] Typically reported nucleophilic substitution reactions in solution are the exchange of halogen atoms in alkyl halides by various nucleophiles, such as NH_3, $-OH$, $-N_3$, $-CN$, *etc.*, the Williamson ether synthesis, the Finkelstein reaction and others.[17–19] Already in 1988 Balachander and Sukenik recognized the potential to use nucleophilic displacement reactions for the modification of solid substrates.[20] The authors described the preparation of amine terminated surfaces by the nucleophilic displacement of bromine terminated substrates with sodium azide and subsequent reduction of the $-N_3$ groups to $-NH_2$ functionalities. The complete exchange of bromine by azide was confirmed by the disappearance of the Br signal in the X-ray photoelectron spectroscopy (XPS) spectrum and the appearance of an absorption peak at 2098 cm^{-1} in the infrared (IR) spectrum. Two years later the authors published a series of nucleophilic transformations on alkyl bromine terminated substrates to introduce a large variety of functional groups into the monolayer.[21] Bromine terminated surfaces were reacted with various nucleophiles, such as $-SCN$, $-S^{2-}$, $-S_2{}^{2-}$ and $-N_3$, to generate different surface functionalities (Fig. 1). IR spectroscopy and XPS as well as contact angle analysis were performed to investigate the conversion of the reactions and indicated a quantitative conversion of the bromine functionalities. Subsequent treatment with $LiAlH_4$ and H_2O_2 yielded $-SH$, $-NH_2$ and $-SO_2$ moieties, respectively. As a result, a large variety of different functional groups could be generated starting from a commercially available bromine terminated precursor SAM, as summarized in Fig. 1.

Fryxell *et al.* described the nucleophilic displacement reactions on mixed monolayers, terminated with bromine and methyl groups.[22] The authors showed the substitution of $-Br$ by sodium azide, thiocyanate, and cysteine. In contrast to the results of Balachander and Sukenik the required reaction times were significantly longer. The authors explained the prolonged reaction times by the difference in the quality of the prepared

Table 1 Overview of used modification concepts to obtain functional self-assembled monolayers

Reaction	Functional groups	Ref.
Nucleophilic substitution		
Radical bromination	$-CH_3 \rightarrow -Br$	23
Reactions on –Br terminated SAMs	$-SCN$, $-S^{2-}$, $-S_2{}^{2-}$, $-N_3$	21–23, 27, 30
Reduction of functionalized SAMs	$-SH$, $-NH_2$, $-SO_2$	22, 24, 27, 32
Functionalization of halide terminated SAMs	$-SO_3Na$	30, 31, 33
Deprotection	$-Br \rightarrow -NH_2$	28
Attachment of	Proteins/Peptides	30, 33
	Polyimides	26
	Fullerenes	28
	Polyaniline	30
	DNA	27
	Supramolecular ligands	32
Click chemistry		
Copper free clicking	Proteins	34
Cycloaddition of	Proteins	42, 47–49, 58
	Polymers	43, 51
	Dyes	44
	Dendrimers	46, 56
	Ferrocene	45, 50
	Biotin	40, 58
	Lactose	58
	Cells	57
	DNA	59, 60
Supramolecular modification		
Functionalization with	Bipyridines and complexation	61, 62, 66, 77
	Terpyridines and complexation	58, 73, 74
	Cyclodextrines	63

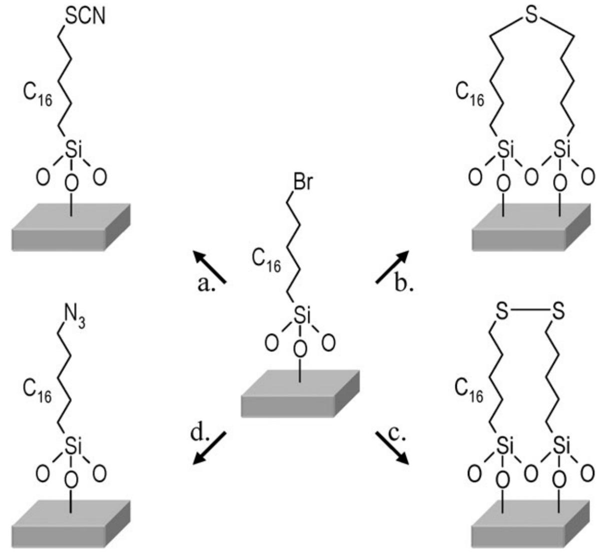

Fig. 1 Schematic representation of nucleophilic substitution reactions on bromine terminated monolayers on glass substrates and Si ATR crystals. (a) KSCN, (b) Na_2S, (c) Na_2S_2 and (d) NaN_3.

monolayers, as dense, highly rigid monolayers were used for the chemical transformations. Additionally, the poor reactivity of bromine terminated alkyl SAMs was assigned to the fact that the nucleophile needs to penetrate below the surface to attack the carbon atom from the back, resulting in a substantial kinetic barrier of the nucleophilic substitution. Baker and Watling demonstrated the functionalization of alkyl terminated monolayers *via* free radical bromination and subsequently modified the surface further.[23] In their approach the authors treated a monolayer of hexadecylsiloxane with bromine in CCl_4 to obtain bromine terminated SAMs. In this experiment, bromination occurred at the methyl and the methylene groups in the monolayer. The bromine terminated monolayers were treated afterwards with different nucleophiles, such as azide, sulfide and thiocyanate. A quantitative exchange of bromine by $-N_3$ and $-S^{2-}$ was observed, whereas thiocyanates could be incorporated into the SAM only with yields of 80 to 90%.

The nucleophilic substitution of –Br by $-N_3$ represents a potentially important chemical surface reaction as the introduced azide moieties can be used for further post-modification reactions. Heise and co-workers described the *in situ* modification of mixed silane monolayers by nucleophilic transformation of –Br by $-N_3$ and subsequent reduction to $-NH_2$,[24] which could be used for the grafting of polypeptides onto the substrates.[25] The use of amine terminated trimethoxysilanes was not favorable, as the self-assembly of these compounds resulted in the formation of disordered monolayers. Therefore, the previously mentioned two step procedure was chosen to obtain amine terminated monolayers of good quality. A reaction yield of 80% was achieved for the nucleophilic substitution of –Br by $-N_3$ and 100% for the reduction step to obtain the amine moieties. The fabrication of well-defined polyimide functionalized surfaces was reported by Lee and Ferguson.[26] In this way bromine terminated monolayers served as pre-functionalized SAMs, which were reacted with sodium azide, followed by treatment with $LiAlH_4$ to yield $-NH_2$ functionalities. Those amine moieties were reacted with phthalic anhydride to obtain the imide terminated surfaces. The nucleophilic transformation was characterized by contact angle measurements, IR spectroscopy as well as XPS and revealed the full exchange of –Br by $-N_3$. The contact angle decreased from 81 to 85° for the –Br terminated surface to 75 to 79° for the $-N_3$ moieties. The IR spectrum revealed the appearance of the characteristic absorption peak at 2097 cm^{-1} for the azide groups and indicated the preservation of the $-CH_2$ vibrations, indicating that no significant damage of the monolayer occurred. XPS revealed the disappearance of the Br(3d) signal at 71 eV and the appearance of two peaks at 402 and 405 eV in the N(1s) region, which could be assigned to the $-N_3$ moieties present on the surface. Wang *et al.* reported a study on the preparation of maleimido terminated SAMs *via* different synthetic routes.[27] One method included the use of nucleophilic substitution reactions to obtain azide moieties, which were reduced to $-NH_2$ groups and subsequently reacted with sulfosuccinimidyl 4-(*N*-maleimidomethyl) cyclohexane-1-carboxylate to yield the desired surface maleimido functionalities.

An interesting surface modification route *via* nucleophilic substitution was demonstrated by Chupa *et al.*[28] A bromine terminated silicon oxide substrate was treated with anions, which were formed by the reaction of 4-methylpyridine with lithium diisopropylamide. The resulting pyridyl moieties were coupled with OsO_4 and C_{60} to introduce buckminster fullerenes for the modification of the electronic and optical responses of the solid substrates. The introduction of amine functionalities onto silicon oxide surfaces was realized *via* the 'hidden amine route' reported by Ofir and co-workers (Fig. 2a).[29] It involves the nucleophilic displacement of bromine moieties by potassium phthalimide after three hours of reaction time, followed by the cleavage of the protecting group to yield $-NH_2$ groups. The authors emphasized as a main advantage of this reaction pathway, that the functionalization of surfaces with amine moieties is faster compared to the exchange by NaN_3 and the subsequent reduction step with, *e.g.*, $LiAlH_4$.

The formation of polyaniline films *via* a four step modification sequence was demonstrated by Sfez *et al.*[30] Monolayers of iodopropyltrimethoxysilane were treated with mercapto ethanesulfonic acid sodium salt and resulted in the substitution of –I by $-SO_3Na$ (Fig. 2b). Chemical proof for the successful substitution was obtained by XPS analysis, which revealed the complete disappearance of the iodine signal after substitution and the appearance of a sodium signal at $\sim$1070 eV. These surfaces were furthermore modified by the attachment of aniline monomers *via* electrostatic interactions, which were polymerized by either chemical or electrochemical oxidation. Koloski and co-workers performed nucleophilic displacement reactions on benzyl halide (–Cl and –I) terminated substrates.[31] For this purpose, monolayers of benzyl chloride were treated with sodium iodide, which resulted in an exchange of –Cl by –I with yields between 45 and 60%. This reaction is also known as Finkelstein reaction. The incomplete exchange of –Cl by –I was explained by the larger size of the iodine atom and the differences in the C–I and C–Cl bond lengths. The benzyl chloride and iodide terminal groups were

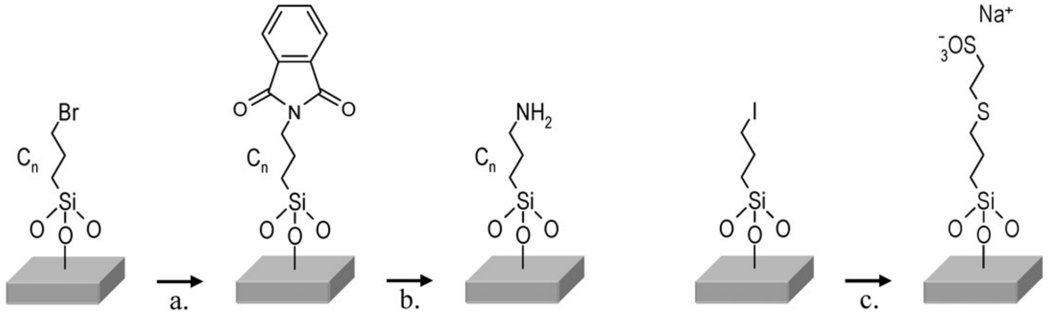

Fig. 2 Schematic representation of nucleophilic substitution reactions of bromine and iodine terminated monolayers on glass, quartz, indium-tin oxide and silicon oxide substrates. (a) Nucleophilic substitution with potassium phthalimide, (b) cleavage of the phthalimide groups by CH_3NH_2 and (c) nucleophilic substitution with mercapto ethanesulfonic acid sodium salt.

used afterwards for substitution reactions with *N*-lithiodiaminoethane and 3-lithiopyridine. UV/vis spectroscopy and XPS were performed to investigate the conversion as well as the rate of the reaction and revealed a higher reactivity for the –I terminated species.

As already mentioned earlier, not only negatively charged ions can act as nucleophiles, but also neutral molecules, *e.g.*, water, amines and thiols, can be used for the nucleophilic displacement. The reaction of 16-bromohexadecyl and brominated hexadecylsiloxane monolayers with mercury(II) perchlorate in a water-dimethoxyethane mixture for 3 and 24 h resulted in a quantitative exchange of –Br by –OH, respectively.[23] Attempts to exchange the bromine moieties by hexylamine and butanethiol were not successful. XPS analysis of the surfaces revealed no signals for N or S in the XPS spectra and thus there was no indication for an exchange of –Br by the amine and thiol compounds. Haensch *et al.* reported the exchange of bromine by propargylamine and 5-(2,2′:6′,2″-terpyridin-4′-yloxy)-pentylamine and subsequent post-modification routes.[32] Optimization of the reaction parameters showed a complete displacement of the halide by propargylamine after 3 days at 80 °C or 4 days at 60 °C, respectively. The more bulky character of the terpyridine functionalized amine resulted in a non-quantitative substitution of the bromine. This could be caused by the steric hindrance of the large molecule. The introduced amine moieties could be used for interesting post-modification reactions, *e.g.*, click chemistry and supramolecular complexation reactions. Lee and co-workers investigated the selective attachment of peptides onto halide terminated surfaces.[33] This approach involved the nucleophilic substitution of halide terminated substrates by tri- and nonapeptides *via* the thiol group of cysteine moieties. The surfaces, consisting of alkyl and benzyl halides and α-haloacetyl monolayers, showed differences in the electrophilicity depending on the halide atoms. The reactivity towards the exchange by thiols was found to decrease from iodine to bromine and chlorine and from α-haloacetyl over benzyl to alkyl. This methodology represents a powerful tool for the controlled attachment of peptides, proteins and sugar moieties to various substrates and was suggested furthermore to be used for the fabrication of biocompatible inorganic materials and biosensors.

Besides the previously described nucleophilic displacement reactions on halide terminated monolayers also the use of other functional end groups for this reaction mechanism has been reported. Fryxell and co-workers demonstrated the nucleophilic substitution on mixed monolayers of trifluoroethyl ester and methyl moieties by primary amines, *e.g.*, *N*,*N*-dimethylethylenediamine, hydrazine, and hydroxylamine.[22] A low amount of trifluoroethyl ester groups on the surface resulted in the exchange of the trifluoroethyl functionalities and the formation of amide groups. With increasing percentage of the trifluoroethyl moieties a competitive cross-linking reaction occurred, which resulted in the formation of imide functionalities. Maleimido terminated silicon substrates were exposed to a large variety of different nucleophilic compounds, *e.g.*, decylthiol, octadecylthiol, aliphatic amines, isoindole, thioacetamide and thiol-tagged DNA oligonucleotides (Fig. 3).[27] The investigation of the substitution reactions with decylthiol and octadecylthiol was performed by attenuated total reflection infrared (ATR-IR) spectroscopy and revealed an increase in the absorption intensities of the methylene vibrations. The attachment of aliphatic amines, isoindole and thioacetamide was confirmed by the appearance of a characteristic absorption peak between 2100 and 2300 cm^{-1} in the IR spectrum for the –CN groups, which were introduced in the nucleophiles as IR spectroscopic marker. Biomolecules, such as oligonucleotides, could also be successfully attached to the monolayer system. XPS revealed the appearance of a signal at 133.9 eV, which was assigned to the phosphates in the DNA backbone.

Sawoo and co-workers described the modification of silicon and glass surfaces for protein immobilization *via* subsequently performed nucleophilic displacement reactions.[34] These included the nucleophilic exchange of bromine by azide and subsequent copper-free clicking with an alkoxy Fischer-type metallocarbene complex. In a second nucleophilic substitution step the SAM was reacted either with 1-pyrenemethylamine, which acted as a fluorescent marker, or with bovine serum albumin (BSA). The introduced 1-pyrenemethylamine revealed a broad emission at 480 nm in the fluorescence spectrum indicating the successful attachment of the Fischer carbene complex to the substrate. The attachment of the protein was investigated by atomic force microscopy (AFM), which showed a dense coverage of the surface. This research demonstrated the covalent linkage of biomolecules onto solid substrates under mild reaction conditions.

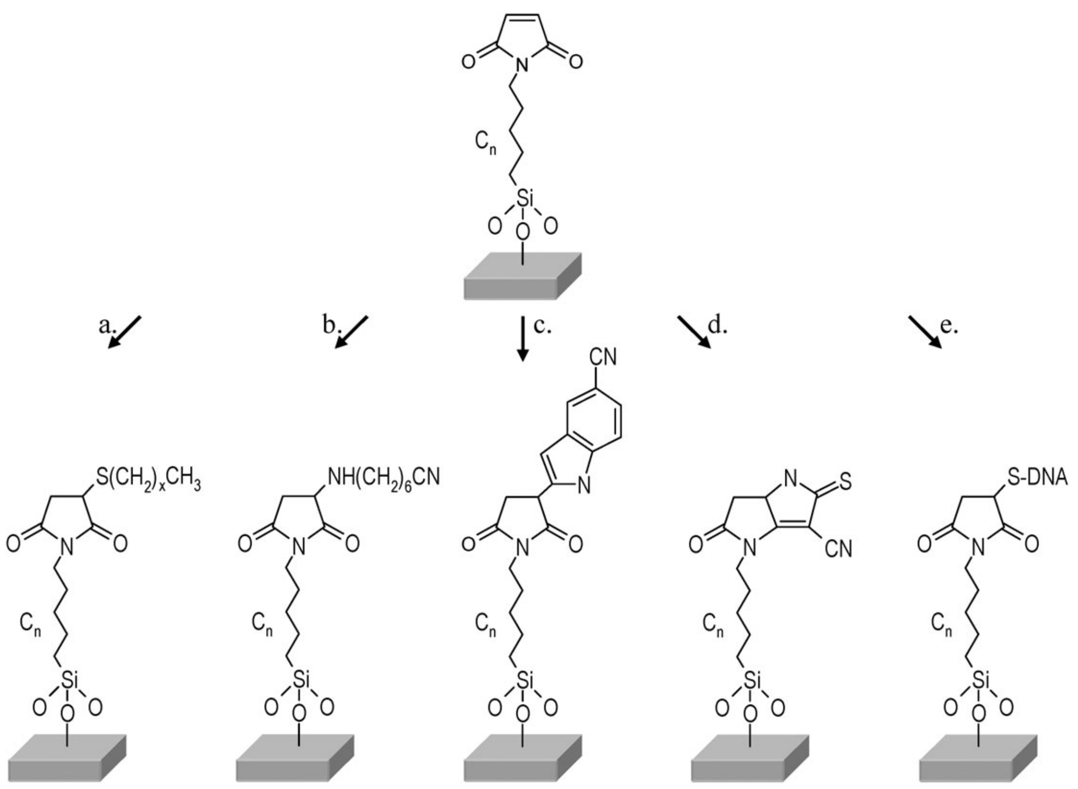

Fig. 3 Schematic representation of nucleophilic addition reactions on maleimido terminated monolayers on silicon oxide substrates. (a) Decylthiol, (b) aliphatic amine, (c) isoindole, (d) thioacetamide and (e) DNA-SH.

2.2 Click chemistry

A different reaction mechanism also matches the criteria for efficient surface reactions. The click chemistry approach has attracted significant attention in various fields of chemistry, such as in materials science and polymer chemistry during the past years, since it was introduced by Sharpless in 2001.[35–37] The definition of click-chemistry fulfils several criteria that are also advantageous for reactions performed on surfaces. The reactions are modular and wide in scope. They provide furthermore very high yields, byproducts, that do not affect the monolayer quality or their functional integrity, are stereospecific, can be performed under mild reaction conditions and rely on easily available starting materials.[35] The purification can be preferably achieved by nonchromatographic methods. A large variety of chemical transformations are part of this approach, *e.g.* the 1,3-dipolar cycloaddition reactions and Diels–Alder transformations, nucleophilic substitution chemistry, formation of ureas, thioureas, aromatic heterocycles, oxime ethers, hydrazones, amides, and additions to carbon–carbon multiple bonds, *e.g.* epoxidation, dihydroxylation, aziridination, sulfenyl halide addition and Michael additions. The most perfectly working click reaction up to date is the Huisgen 1,3-dipolar cycloaddition of organic azides and acetylenes.[38] Hereby, a mixture of 1,4- and 1,5-disubstituted 1,2,3-triazole systems is formed. A variant of this reaction is the copper catalyzed coupling of azides and terminal acetylenes, which selectively results in the formation of the 1,4-disubstituted triazole.[39–41] The general characteristics of the click chemistry approach fit very well with the requirements of chemical reactions performed on surfaces. This is documented by a number of literature examples, which demonstrate the use of click chemistry for the introduction of functional groups into the monolayer system on different substrates.[42] Thereby, two synthetic preparation methods are used to introduce 1,2,3-triazole moieties into the monolayer. Whereas the first method uses azide terminated substrates for the coupling with functional acetylenes, the second modification sequence involves the generation of surfaces with terminal acetylene moieties. Both modification sequences will be discussed in more detail in the following sections.

Click chemistry on azide terminated substrates. The first preparation method to obtain 1,2,3-triazoles utilizes azide terminated substrates, which can be obtained by the nucleophilic displacement of –Br by $-N_3$, and a subsequent cycloaddition reaction. The first report on the Huisgen 1,3-dipolar cycloaddition performed on silicon substrates, covered with a layer of native oxide, was published by Lummerstorfer and Hoffmann.[14] 11-Bromoundecylsiloxane monolayers were substituted by sodium azide and $-N_3$ functionalities were obtained, which were subsequently reacted with different acetylenes (Fig. 4). Methoxycarbonyl and *bis*-(ethoxycarbonyl) acetylene could be quantitatively coupled to the $-N_3$ terminated surfaces after reaction times of 24 h at 70 °C. Surface-enhanced IR reflection spectroscopy was performed to characterize the substrates and revealed the complete disappearance of the azide absorption peak, which was found at 2102 cm^{-1}. The authors used no catalyst, which resulted most likely in the formation of a mixture of the 1,4- and

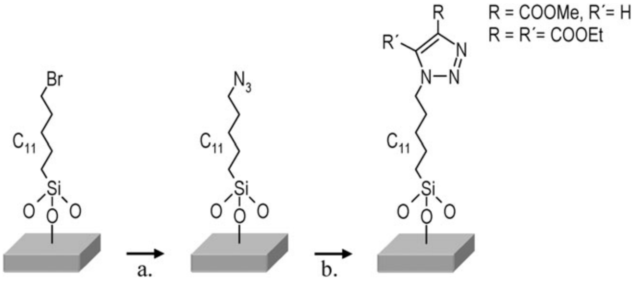

Fig. 4 Schematic representation of the 1,3-dipolar cycloaddition on bromine terminated monolayers on silicon oxide substrates. (a) Nucleophilic substitution with sodium azide and (b) cycloaddition with methoxycarbonyl or *bis*(ethoxycarbonyl) acetylene.

1,5-disubstituted products; however, the authors assumed that the 1,4-disubstituted triazole ring is most likely due to steric reasons.

Prakash *et al.* demonstrated the cycloaddition of linear and branched polymers, *e.g.* poly(amido amine) dendrimers, poly(2-ethyloxazoline), poly(ethylene glycol) and poly(ethylene imine), to –N_3 terminated silica and microfluidic glass channels.[43] The substrates were characterized by Fourier transform infrared (FT-IR) spectroscopy and XPS as well as by contact angle and electro-osmotic flow (EOF) measurements. Investigations by XPS revealed the disappearance of the –Br peak after the nucleophilic substitution and the appearance of a characteristic split peak in the N(1s) region for the –N_3 moieties. After cycloaddition the double peak disappeared and a single peak was observed in the N(1s) region. FT-IR ATR spectroscopy furthermore indicated the successful cycloaddition of the alkyne functionalized polymers to –N_3 surfaces by the disappearence of the absorption peak at 2100 cm^{-1}, which is characteristic for the azide moiety. EOF measurements were performed to classify the electroosmotic velocity in the modified microchannels. The modification with triazoles resulted in a change of the zeta potential and therefore the EOF in the channels could be changed in a systematic fashion. The fabrication of bio-active surfaces *via* a copper-free click reaction was demonstrated by Sawoo and co-workers.[34] Azide terminated glass and silicon surfaces were reacted with a Fischer carbene complex for the immobilization of proteins, which could find potential applications in the fabrication of biosensors. Ellipsometry revealed an increase in height of the monolayer of about 0.66 nm after the cycloaddition. Immobilization tests on these surfaces were performed with bovine serum albumin. AFM and high resolution scanning electron microscopy were performed to analyze the immobilized proteins on the surface. The amount of molecules was calculated to be $\sim$330 molecules per μm^2. Reaction with dansyl chloride allowed furthermore investigation of the substrate by fluorescence microscopy. Haensch *et al.* demonstrated the functionalization of silicon and glass substrates with a fluorescent dye molecule.[44] In this experiment, an acetylene modified coumarin dye was synthesized in an one step procedure, which could be coupled under Cu(I) catalysis onto the solid substrate. UV/vis measurements on the functionalized glass surface revealed an absorption peak at 442 nm, which is in good agreement with the absorption characteristic of the coumarin molecule.

The chemical derivatization of hydrogenated silicon substrates was demonstrated by Marrani and co-workers.[45] The silicon surfaces were treated with 11-bromo-1-undecene, followed by substitution with NaN_3 and subsequent cycloaddition of ethynylferrocene under Cu(I) catalysis. Next to the characterization by XPS, which revealed the successful attachment, also cyclic voltammetry was performed to investigate the functionalized substrates. The electrochemical properties of the ferrocene terminated substrates revealed the formation of a well-defined SAM as well as an efficient charge transfer reaction to the ferrocene redox head group.

Vestberg *et al.* presented the formation of multilayer films *via* click chemistry.[46] Thereby, –NH_2 terminated silicon substrates were reacted with 4-azidobutanoic anhydride to obtain azide functionalities on the surface. These moieties were further modified by alternating cycloaddition reactions with acetylene and azide terminated dendrimers to obtain multilayers. Ellipsometry was used to measure the thickness of each layer and XPS revealed structural information about the multilayer. Another example of regio- and chemoselective immobilization of proteins onto glass surfaces was presented by Gauchet *et al.* (Fig. 5).[47] In this way, azide functionalized substrates were prepared *via* a multi step procedure, utilizing the transformation of –NH_2 surfaces to carbamates followed by the attachment of azide terminated PEG-containing amine linkers and subsequent deactivation of the residual carbamates. Afterwards a green fluorescent protein was attached *via* click chemistry and was analyzed by phosphor imaging, which revealed the successful attachment of the protein.

Govindaraju and co-workers introduced the functionalization of glass substrates *via* the click sulfonamide reaction.[48] Sulfonylazide terminated surfaces were reacted with alkyne modified biomolecules, followed by the immobilization of

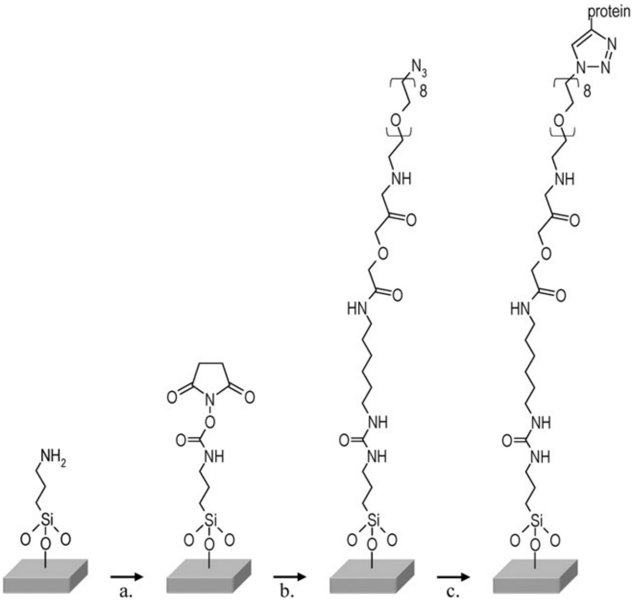

Fig. 5 Schematic representation of the 1,3-dipolar cycloaddition on amine terminated monolayers on glass substrates. (a) Reaction with *N*,*N*-disuccinimidyl carbonate, (b) attachment of an azide terminated PEG-containing amine linker and (c) cycloaddition with a green fluorescent protein.

fluorescently labelled proteins. The presented results demonstrated the site- and chemoselective immobilization of alkyne terminated molecules under mild reaction conditions. The fabrication of a protein microarray was demonstrated by Lin and co-workers.[49] Azide terminated glass surfaces were prepared by a two step synthesis starting from amine modified slides, which were reacted with glutaric acid *bis-N*-hydroxysuccinimide ester and were subsequently treated with 3-azidopropanylamine. Further reaction with enhanced green fluorescent proteins under Cu(I) catalysis resulted in protein functionalized substrates, which were analyzed by fluorescence microscopy and revealed the preservation of the tertiary structure of the protein.

Click chemistry on acetylene terminated substrates. The second possibility to implement click chemistry into surface modification processes is the functionalization of silicon surfaces with terminal acetylene moieties, which can be accessed by different approaches. Acetylenylation can be obtained by chlorination of hydrogenated silicon and subsequent reaction with Na–C$\equiv$CH.[50] An electroactive benzoquinone was coupled to the –C$\equiv$CH functionalities and resulted in a coverage of 7% of the molecules on the surface (Fig. 6). The low yield was explained by the assumption that effective click reactions could only take place at the step edges of the Si(111) substrate. Subsequently applied surface chemistry resulted in the immobilization of ferrocene and biotin onto these surfaces. The presented results are supposed to find applications in the selective biopassivation of arrays of various types of sensor devices.

Ostaci *et al.* reported the use of ethynyldimethylchlorosilane to obtain acetylene terminated surfaces on silicon substrates covered with a 525 µm thick layer of SiO_2.[51] Thereby, the acetylene group is directly attached to the silicon atom, which prevents the formation of a well-ordered monolayer. These surfaces were used to perform click reactions with different azide terminated polymers, *e.g.* polystyrene, poly(ethylene oxide) and poly(methyl methacrylate). Polymer brushes with heights of ~6 nm could be obtained by this approach, which offers therefore the possibility to graft a large variety of different polymer systems onto the surface. Yam and co-workers demonstrated the functionalization of silicon substrates with acetylene moieties by the reaction of terminal $–NEt_2$ groups with organic molecules containing acidic protons.[52,53] The $–NEt_2$ terminated surfaces were obtained by the treatment of –OH functionalized substrates with $SiCl_4$ or $SnCl_4$ followed by the reaction with $HNEt_2$.[52] Subsequent reaction with different modified dialkynes, containing acidic protons, led to the fabrication of various terminal –C$\equiv$CH moieties. An improvement of the procedure concerning the amount of reaction steps was published a few years later.[53] Herein, –OH functionalized surfaces were reacted with $Sn(NEt_2)_4$ to obtain the $–NEt_2$ groups in one steps. The formation of well-ordered acetylene terminated monolayers was reported by different groups *via* the reaction of hydrogenated Si with 1,8-nonadiyne[54] or 1,6-heptadiyne.[55] Ciampi and co-workers presented the use of 1,8-nonadiyne for the fabrication of –C$\equiv$CH terminated silicon and used them for subsequent click chemistry reactions (Fig. 7).[54] The acetylene monolayers were characterized by contact angle measurements, XPS as well as X-ray reflectrometry and revealed well-defined and densely packed monolayers. These –C$\equiv$CH moieties were afterwards used for the 1,3-dipolar cycloaddition with various azides, including 1-azidobutane, 4-azidophenacyl bromide and 11-azido-3,6,9-trioxaundecan-1-ol. XPS was utilized to calculate the chemical conversion of the reaction and revealed yields between 35 and 80% under different reaction conditions. These functionalized surfaces represent interesting candidates for the use as biosensors and in molecular electronics.

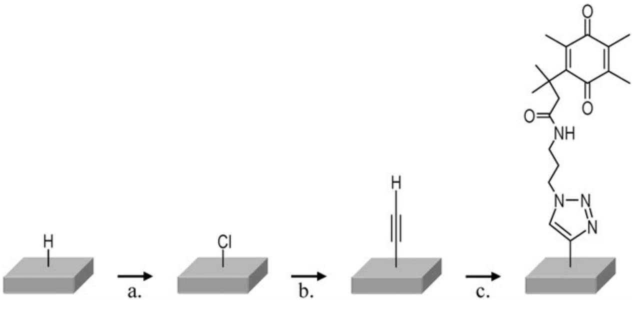

Fig. 6 Schematic representation of the 1,3-dipolar cycloaddition on hydrogenated silicon substrates. (a) PCl_5, (b) Na–C$\equiv$CH and (c) cycloaddition with benzoquinone.

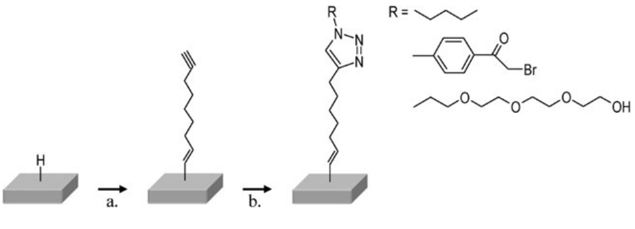

Fig. 7 Schematic representation of the 1,3-dipolar cycloaddition on hydrogenated silicon substrates. (a) Reaction with 1,8-nonadiyne and (b) cycloaddition with azide functionalized molecules.

Britcher *et al.* also demonstrated the functionalization of porous silicon wafers by click chemistry.[55] 1,6-Heptadiyne was reacted with hydrogenated Si, followed by the coupling of an azide terminated PEG. The successful attachment of the polymer was proven by XPS. Treatment of the surface with human serum albumin revealed their resistance towards protein adsorption and the substrates were suggested to be useful for targeted protein delivery applications. Another possibility to obtain acetylene terminated surfaces is the use of chemical surface reactions. Vestberg *et al.* presented the formation of acetylene moieties by reaction of $–NH_2$ surface groups with 4-pentynoic anhydride.[46] Alternating cycloaddition with azide and acetylene terminated dendrimers resulted in the formation of dendritic multilayers. This modification sequence allowed the growth of extremely regular and defect-free dendritic thin films, which thicknesses could be controlled by the generations of the dendrimer. A similar approach to obtain acetylene moieties was presented by Long and co-workers who reacted $–NH_2$ functionalized silicon supports with 4-pentynoic acid, which resulted in the formation of acetylenes moieties.[56] These groups were furthermore used for cycloaddition reactions with azide functionalized dendrons. This surface modification was not only shown on an entire substrate, but was also performed with an AFM tip to obtain localized triazoles. Several literature examples demonstrated the use of click chemistry for the preparation of active biosurfaces. The introduction of $-C{\equiv}CH$ moieties *via* reaction of carboxylic acid terminated silicon or glass substrates with a bifunctional propargyl-derivatized linker was described by Gallant and co-workers.[57] This was followed by cycloaddition of the acetylene moieties with an azide functionalized peptide by using $CuSO_4$ and sodium ascorbate as catalytic species. Cell adhesion tests were performed with smooth muscle cells and were analyzed by fluorescence microscopy. The presented approach could find potential applications in biomaterials research. Sun *et al.* demonstrated the surface modification *via* the reaction of maleimido terminated glass with an alkyne-PEG_4-cyclodiene linker, which resulted in the formation of $-C{\equiv}CH$ groups.[58] Subsequent clicking of different biomolecules, *e.g.* biotin, lactose and a recombinant protein, was successful, which was demonstrated by subsequent labeling with fluorescent dyes and confocal fluorescence imaging. Seo and co-workers introduced the reaction of amine terminated glass chips with succinimidyl *N*-propargyl glutariamidate to yield terminal $-C{\equiv}CH$ moieties.[59,60] The acetylene terminated substrates were afterwards treated with azido functionalized DNA under CuI catalysis and were analyzed by AFM and contact angle measurements. Subsequently DNA polymerase reactions using photocleavable fluorescent nucleotides were carried out to investigate the functionality, accessibility and stability of the attached DNA.

2.3 Supramolecular modification

The fabrication of smart functional surfaces with tailor-made functional groups is an important research area in various fields of technology. Thereby, it is of great importance to control and switch the surface properties in a reliable fashion. Such systems may find many potential applications in, *e.g.* sensors, memory elements, optical/electronic switches, nanodevices, displays, data storage and others.[61,62] The fabrication of such systems can be achieved by, *e.g.*, the functionalization of surfaces with supramolecular binding motifs. Representative literature examples include the modification of silicon and glass supports with cyclodextrins, which can be used for supramolecular host–guest complexations with organic molecules, such as adamantyl functionalized dyes.[63] The preparation of β-cyclodextrins on glass and silicon oxide substrates was shown by Onclin and co-workers (Fig. 8).[63] This involved a three step synthesis starting from cyano terminated monolayers. The –CN functionalities were treated with sodium *bis*(2-methoxyethoxy)aluminium dihydride solution to yield $-NH_2$ moieties, which were subsequently reacted with 1,4-phenylene diisothiocyanate. The last step of the functionalization sequence involved the reaction of the obtained isothiocyanate groups with per-6-amino-β-cyclodextrin. Characterization of the functionalized surfaces was performed by different methods, including contact angle measurements, ellipsometry, FT-IR spectroscopy, XPS and TOF-SIMS. The disappearance of the –CN absorption using FT-IR spectroscopy at 2246 cm^{-1} after the reduction indicated a full conversion to the corresponding amine groups. The successful reaction of the $-NH_2$ functionalities to –NCS moieties was demonstrated by ellipsometry, which revealed an increase of height of about 0.4 nm, which correlates well with the height of the introduced molecule. Changes in the polarity of the surface after the modification with β-cyclodextrins could be observed by a decrease of the contact angle to 49° compared to 68° for the –NCS terminated surface. Such surfaces were afterwards used for a desorption experiment to investigate the interaction of the cyclodextrin terminated monolayer with a guest molecule containing two adamantyl units and a fluorescein dye. Comparison of the obtained results on glass with the ones on gold revealed the same guest binding properties.

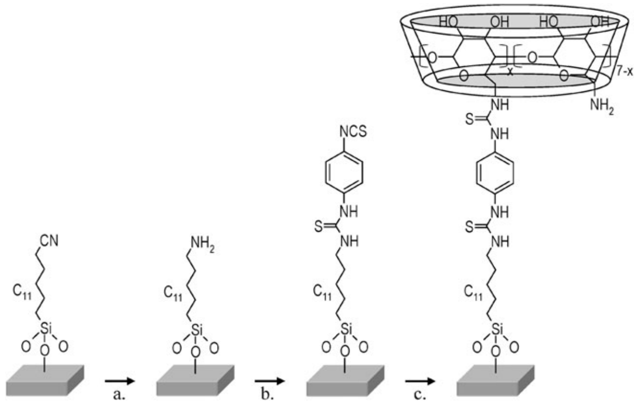

Fig. 8 Schematic representation of β-cyclodextrins on glass and silicon oxide substrates. (a) Reduction with sodium *bis*(2-methoxyethoxy)aluminium dihydride, (b) reaction with 1,4-phenylene diisothiocyanate and (c) reaction with per-6-amino-β-cyclodextrin.

Another class of suitable candidates for the fabrication of such molecular switches and/or responsive surfaces are metal complexes as they allow the introduction of interesting optical and electrical properties *via* the metal–ligand interaction within the monolayer system[64] (for general examples on metallo-supramolecular systems, see *e.g.* ref. 65 and 66). These surface assemblies can change their properties by triggers in their environment, such as electrical, mechanical, and chemical influences, or changes in pH value or temperature.[67–71] The preparation of such metal-based surfaces can be achieved *via* different chemical routes. One possibility is the synthesis of self-assembling molecules containing the metal complex. Literature examples demonstrated the fabrication of osmium[61,62,68] and ruthenium[68] based metal complexes, coordinated with bipyridine ligands. Gupta and co-workers demonstrated the synthesis of an osmium bipyridyl complex functionalized with a trimethoxy group, which could be used for the attachment onto silicon and glass substrates.[61] The schematic representation of the synthesis of this metal complex is depicted in Fig. 9. This involved a two step procedure starting from 4′-methyl-4-(2-pyridin-4-yl-vinyl)-[2,2′]bipyridinyl, which was reacted with $Os(2,2'\text{-bipyridine})_2Cl_2 \times 2\ H_2O$ and subsequent treatment with 3-iodo-*n*-propyl-1-trimethoxysilane to obtain the desired complex with the $-Si(OMe)_3$ functionality. Characterization by NMR and UV/vis spectroscopy as well as mass spectroscopy and elemental

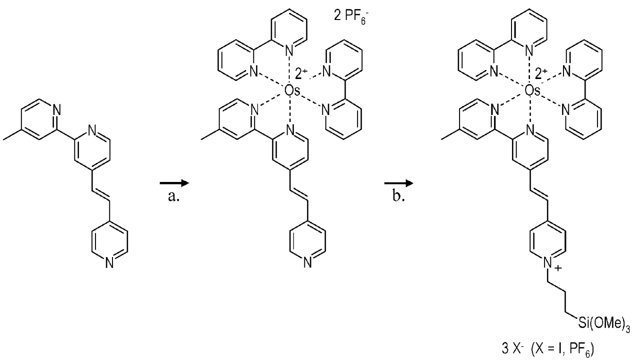

Fig. 9 Schematic representation of the synthesis of a bipyridine containing osmium complex, which was used for the attachment onto silicon surfaces. (a) $Os(bpy)_2Cl_2 \times 2\ H_2O$, NH_4PF_6, EtOH–H_2O, 110 °C, 24 h and (b) $I(CH_2)_3Si(OMe)_3$, THF–MeCN, 90 °C, 72 h, N_2.

analysis revealed the formation of the proposed metal complex.

This complex was afterwards used as self-assembling molecule for the attachment onto glass and silicon substrates. Successful formation of a monolayer of these molecules was proven by UV/vis spectroscopy, which revealed the appearance of two characteristics peaks at 516 and 692 nm of the metal complex.[61] The reversible switching between Os^{2+}/Os^{3+} was performed in solutions of ammonium hexanitratocerate(IV) and *bis*(cyclopentadienyl)cobalt as oxidizing and reducing agents in acetonitrile and revealed the stability of the system for at least 25 redox cycles, which could be followed by UV/vis transmission spectroscopy. Furthermore, it could be demonstrated that these monolayers were suitable candidates for the fabrication of sensor systems concerning the detection of $FeCl_3$ in organic and aqueous solutions.[62] In this experiment, solutions containing 0.5 to 162 ppm and 100 to 1000 ppm of Fe^{3+} in CH_3CN and water, respectively, were found to result in an one-electron transfer process, changing the oxidation state from Os^{2+} to Os^{3+}, which could be followed by UV/vis spectroscopy. The formed iron(II) ions could be optically detected by the addition of 2,2′-bipyridyl, which resulted in the formation of a $[Fe(bipy)_3]^{2+}$ complex. Additionally, studies concerning the reversibility, response time, reproducibility, selectivity, stability, on/off ratio, and the ppm level detection limit of the sensor systems were performed. Furthermore, the authors reported the fabrication of a redox-active monolayer system.[68] Thereby, an information transfer between two interfaces, functionalized with osmium and ruthenium bipyridyl complexes, was triggered by Fe(II)/(III) metal ions as electron carriers. Such systems could effectively be used for the fabrication of advanced interfacial communication systems.

A second method for the construction of supramolecular metal assemblies onto solid substrates relies on the attachment of the metal complex to a functional substrate *via* surface chemistry. Shukla and co-workers demonstrated the formation of a ruthenium based monolayer onto glass, indium tin oxide modified glass and silicon supports.[72] The functional monolayer was obtained by the coupling of surface bounded benzyl halides with a phenol terminated *tris*(bipyridyl)-ruthenium complex. Surface sensitive characterization tools, *e.g.* AFM, XPS, UV/vis spectroscopy and cyclic voltammetry, were performed to characterize the resulting monolayers and revealed the reversible switching of the oxidation state of the metal center. Another convenient coupling procedure uses the 1,3-dipolar cycloaddition of azides and acetylenes.[35,38]

Haensch *et al.* demonstrated the reaction of $-N_3$ terminated silicon and glass substrates with acetylene functionalized iron *bis*(terpyridine) complexes for the construction of switchable supramolecular binding motifs (Fig. 10).[73] UV/vis spectroscopy proved the successful attachment of the complex by the appearance of an absorption band at 580 nm, which was in good agreement with the UV/vis spectrum of the Fe(II) complex in solution. Next to the previously described methods another possibility to functionalize solid substrates with metal complexes relies on the covalent binding of functional ligand systems onto the surface. Iron *bis*-terpyridine complexes, covalently linked *via* click chemistry to silicon or glass, offered the possibility to be "opened" by simply treating the substrates in acidic acid resulting in monolayers terminated with the free terpyridine moieties.[73] These surface bounded ligands could be complexed with different metal ions or precursors, *e.g.* zinc(II) ions or an iridium precursor, to introduce switchable optical properties.

Next to the previously described methods another possibility to functionalize solid substrates with metal complexes relies on the covalent binding of functional ligand systems onto the surface and subsequent complexation reactions. The construction of a two-dimensional network consisting of gold nanoparticles

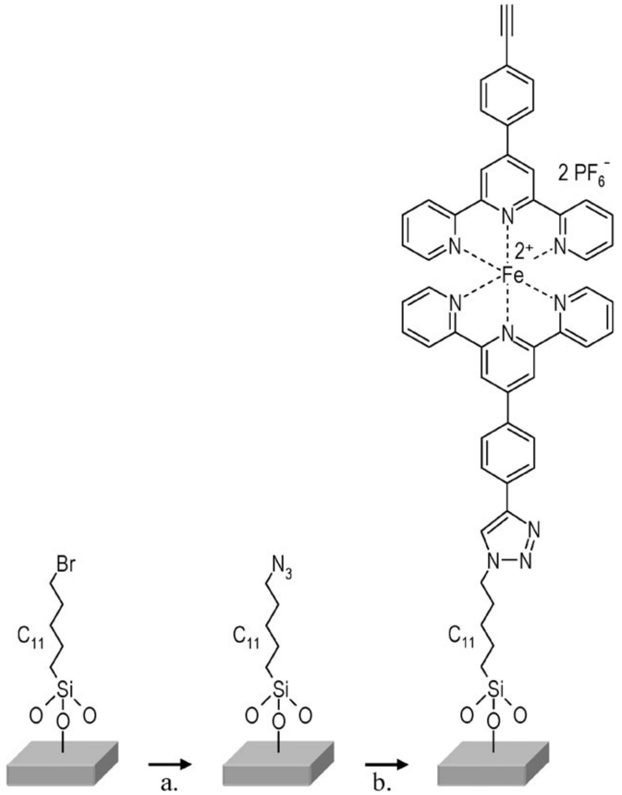

Fig. 10 Schematic representation of the 1,3-dipolar cycloaddition on bromine terminated monolayers on silicon oxide substrates. (a) Nucleophilic substitution with sodium azide and (b) cycloaddition with iron *bis*(terpyridine) complex.

attached to each other *via* supramolecular interactions was demonstrated by Hobara and co-workers.[74] Four differently modified thiol terpyridine systems were used for the attachment onto Au particles, followed by the transfer onto a silicon substrate covered with a layer of SiO_2. The complexation with iron(II) ions led to the formation of a conductive network with a conductivity which was 4 to 5 times higher than the non-conjugated derivative. Such devices represent potential candidates for the development of high-performance molecular devices.

3. Conclusions

The highlighted examples demonstrate the capabilities that evolve from the chemical modification of self-assembled monolayers by chemical reaction processes. The broad range of functionalization schemes and the large diversity of functional surfaces that can be obtained by this method offer countless possibilities to tailor the properties of surfaces and to add function to the monolayer systems. However, performing chemical reactions on surfaces implies more demanding reaction conditions which have to be carefully adapted to the requirements in order to obtain a high degree of functionalization. Besides the fact that well-defined base monolayers improve the degree of functionalization and should therefore carefully be selected, the applied surface functionalization routes have to fulfill several criteria. The presented selection of chemical reactions, *i.e.*, nucleophilic substitution, click chemistry and supramolecular functionalization demonstrate the potential to introduce various functional end groups on solid substrates, *e.g.* silicon and glass; however, other functionalization procedures are also possible. In particular the click chemistry approach offers a large variety of possible functionalization routes, as *e.g.* acetylene derivatized reaction moieties are either rather easy to prepare or are readily available. Therefore, a strong interest in this functionalization approach is observed. Nucleophilic displacement reactions are mainly performed on halide terminated surfaces due to a high reactivity of the halides towards the exchange by nucleophilic molecules and offer in this respect also a wide spectrum of possible functionalization schemes. Relatively few examples are reported in literature where complexation reactions and supramolecular approaches are employed for the functionalization of surfaces. This might be associated also with the large dimensions of the complexes itself, that make a control of the surface coverage as well as the performance of chemical complexation reactions with a high yield more demanding. However, in particular the reversible modification and switching of surface properties represents an attractive advantage evolving from this functionalization approach. Moreover, using, among other techniques, *e.g.* electro-oxidative modification approaches based on conductive AFM methods the SAMs can be modified with nanometer precision,[75–78] also with different attached systems[79] and in an automated fashion.[80] Taking into account the importance of functional surfaces and surfaces with tailor-made properties a strongly growing interest in the development of new functionalization schemes is expected in the future.

Acknowledgements

The authors thank the Nederlandse Wetenschappelijke Organisatie for funding (NWO, VICI grant awarded to U. S. Schubert).

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