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Immobilization of a Photoswitchable Piperidine Base

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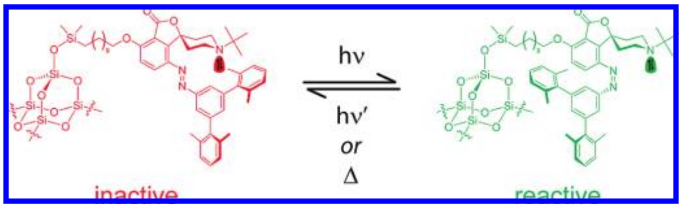
ABSTRACT



The synthesis of a photoswitchable piperidine base, carrying a monochlorosilane anchoring group, and its immobilization on silica gel, mimicking an oxide surface, is reported. Efficient photoswitching between the *E* and *Z* isomers of the azobenzene photochrome was demonstrated for the immobilization precursor in solution and the immobilized piperidine base in suspension of the functionalized silica gel.

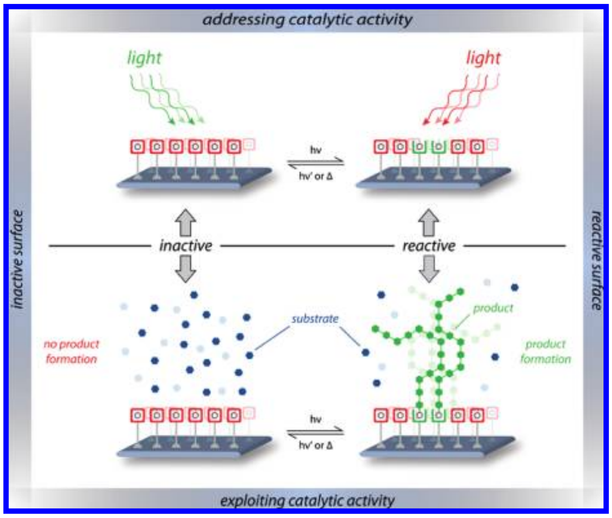


Figure 1. Concept of addressing catalytic activity on a surface by light and exploiting the induced reactivity differences for local functionalization, for example by a polymerization process.

The ability to selectively address catalytic activity in space and time is an attractive target since numerous sophisticated applications can be envisioned based on the precise control of chemical reactivity. Furthermore, gated catalytic systems offer the unique possibility to translate an incoming stimulus into a chemical signal, which can be greatly amplified in the subsequent catalytic cycle(s). Among a variety of possible stimuli, light can be considered superior due to the attainable spatial and temporal resolution as well as its noninvasive character, helping to suppress unwanted side effects such as the build up of interfering byproducts. Therefore, we recently engaged in developing photoswitchable piperidine bases. The basicity differences associated with the two switching states of the incorporated azobenzene photochrome were successfully translated into activity differences of general base catalysts, as exemplified by successful photoregulation of the conversion in a nitroaldol (Henry) model reaction.[1] These experiments were performed in homogeneous solution, consequently leading to general reactivity differences throughout the entire system. However, to exploit the advantages of light as an external stimulus offering superb spatial and temporal control over the energy input required for photoswitching, it is mandatory to prevent dissipation of the incident

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[1] (a) Peters, M. V.; Stoll, R. S.; Kühn, A.; Hecht, S. *Angew. Chem., Int. Ed*. **2008**, *47*, 5968–5972. (b) Stoll, R. S.; Peters, M. V.; Kühn, A.; Heiles, S.; Goddard, R.; Bühl, M.; Thiele, C. M.; Hecht, S. *J. Am. Chem. Soc*. **2009**, *131*, 357–367.

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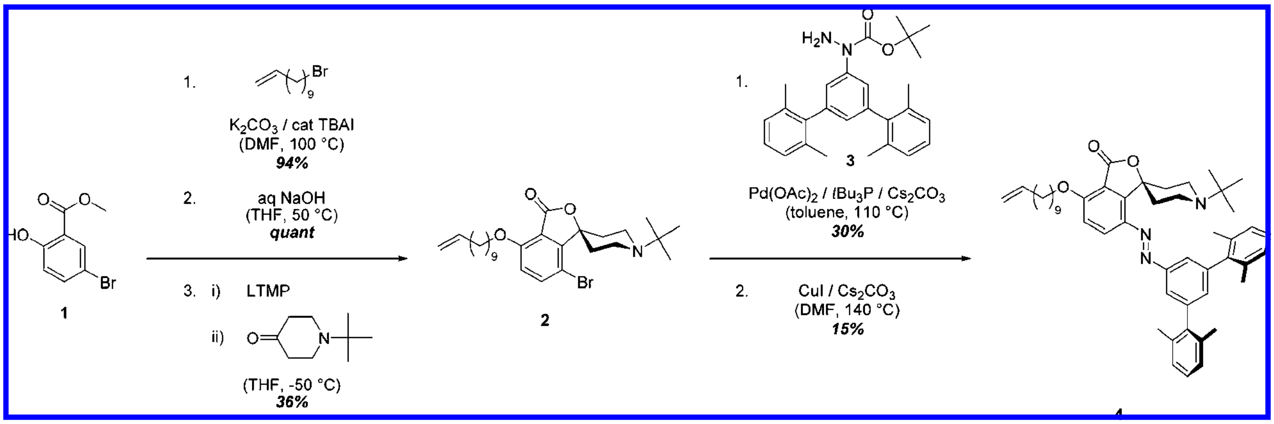
Scheme 1. Synthesis of Immobilization Precursor **4** (TBAI, tetrabutylammonium iodide; LTMP, lithium 2,2,6,6-tetramethylpiperidide)



information by means of diffusion to other loci or compartments of the reaction system. Efficient suppression of diffusion should be achieved by covalently linking the base to a solid substrate and hence locally confining its reactivity (Figure 1).

In addition to providing a locally fixed component, immobilization of photoswitchable catalysts should lead to significantly improved switching performance as problems encountered in solution, employing catalytically effective concentrations associated with high optical densities, are overcome in single- or multilayer arrangements. The low loading on surfaces as compared to loadings encountered in bulk or solution phase catalysis does not pose a drawback because effective catalyst concentrations in the vicinity of the surface are high and reactions should necessarily be confined to the substrate. Furthermore, the linkage chemistry employed should be applicable to a variety of different substrates. Here, we report on the synthesis and characterization of modified photoswitchable piperidine bases, carrying a suitable anchor group, and its immobilization on a silica surface.

Introduction of the anchoring group was realized by adapting synthetic procedures reported for the preparation of the parent photoswitchable piperidine bases.[1] Established design principles (e.g., the conformationally restricted six-membered piperidine ring and the orthogonal position of the azobenzene blocking group) were preserved, and essential structural features, such as a bulky *tert*-butyl substituent on the piperidine's *N*-atom to prevent *N*-inversion and the incorporation of a sterically demanding terphenyl blocking group for efficient shielding of the catalytically active site, were adopted from the parent catalyst system. Thereby, reactivity differences observed in homogeneous solution should be transferred to the immobilized system.

Starting from methyl 5-bromosalicylate **1** (Scheme 1), alkylation with ω-undecenyl bromide proceeded smoothly to give the desired alkylated methyl ester, which was hydrolyzed to give ω-undecenyl 5-bromosalicylic acid.[2] Synthesis of spiroannulated piperidine **2** was possible by lithiation of ω-undecenyl 5-bromosalicylic acid employing 2 equiv of LTMP and subsequent reaction with *N*-*tert*-butyl piperidone.[3] *N*-Arylation of terphenyl-based hydrazine **3**[1] with spiroannulated piperidine **2** proceeded in relatively low yields yet allowed for isolation of a Boc-protected diarylhydrazine intermediate,[4] which was subsequently oxidized to obtain sufficient amounts of immobilization precursor **4**.[5]

Considering hydroxyl-functionalized substrates, in particular, oxidized silicon wafers or (quartz) glass slides, a suitable way of immobilization is the reaction of surface hydroxyl groups with suitable monochlorosilanes, which can conveniently be derived from precursors carrying a C═C double bond on a flexible linker. Hydrosilylation of immobilization precursor **4** was achieved by reaction with excess chlorodimethylsilane in the presence of catalytic amounts of Karstedt's catalyst (Scheme 2).[6] The azobenzene chromophore is not destroyed under the conditions employed, as judged from persistent orange-red coloration of the solution throughout the entire reaction. To avoid hydrolysis of monochlorosilane **5**, the orange material obtained was directly used without further characterization. Subsequent immobilization on a solid support was carried out by reacting monochlorosilane **5** with conventional silica gel in the presence of triethylamine.[6] Again, the red color of the solution, remaining throughout the entire reaction, was indicative of the stability of the azobenzene chromophore toward the conditions employed. After repeated washing/sonication cycles, the supported catalyst **6** was isolated as a gray powder. The use of conventional silica gel as solid support with a high surface area and hence high loading capacity offers the advantage to use conventional UV/vis absorption spectroscopy in solution/suspension to character-

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(4) Lim, Y.-K.; Lee, K.-S.; Cho, C.-G. *Org. Lett.* **2003**, *5*, 979–982.

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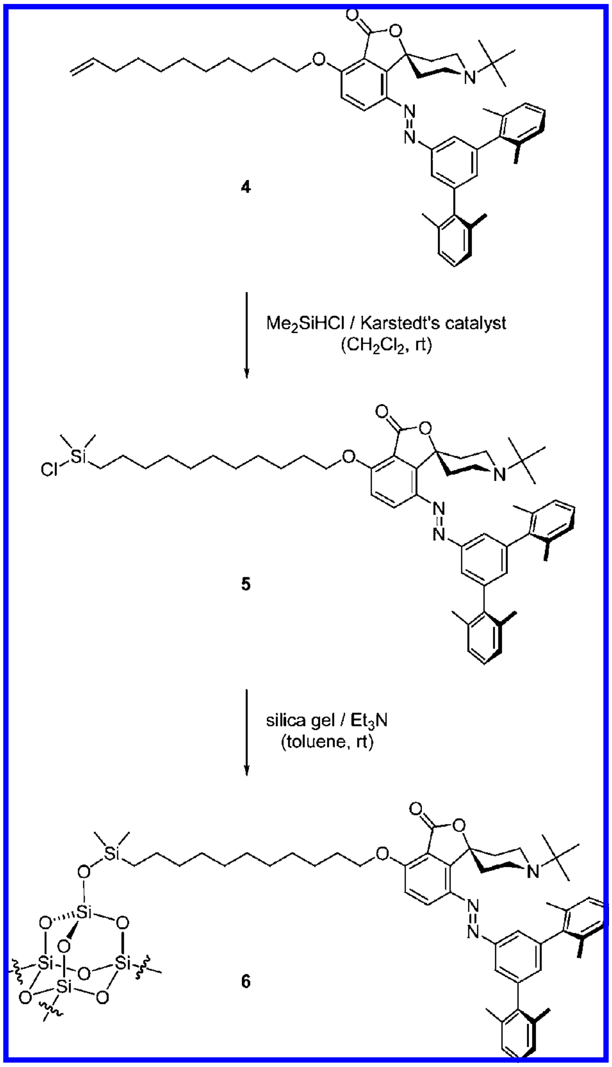
Scheme 2. Synthesis of Piperidine-Functionalized Silica Gel



ize the materials obtained, thereby circumventing common problems associated with the characterization of monolayers on planar substrates, for example, (quartz) glass slides or silicon wafers. Note that silica gel in this case serves as a convenient model system to mimic silicon oxide surfaces as immobilization on planar substrates will be necessary to truly exploit the advantages of the surface-confined systems.

The photochromic behavior of immobilization precursor **4** in solution was investigated in detail. Irradiation of (*E*)-**4** with light of 365 nm wavelength causes isomerization of the azobenzene moiety, leading to a remarkable photostationary state composition containing 98% (*Z*)-**4** (Figure 2). The photochemical *Z* → *E* reversion can be affected by irradiation with light of wavelengths >400 nm and proceeds cleanly until a photostationary state comprising 77% (*E*)-**4** is reached. No evidence for degradation of the photochrome upon light-induced switching was observed, neither by inspection of the absorption spectra nor by UPLC analysis of the irradiated mixtures.

The *Z* isomer of immobilization precursor **4** thermally reverts to the *E* isomer with prolonged half-lifes of $\tau_{1/2} = 248$ h at 20 °C, clearly exceeding the value known for the parent azobenzene ($\tau_{1/2} = 16$ h in benzene).[7] However, the thermal half-life is decreased by almost a factor of 2, when comparing $\tau_{1/2}$ to a structurally related piperidine base without the *para*-alkoxy substituent.[1] Such a decrease is expected for azobenzenes carrying an additional donor substituent in conjugation to the N═N double bond.[8] Activation parameters for the thermal isomerization of (*Z*)-**4** were determined as $\Delta G^{\ddagger}_{298\mathrm{K}} = 25$ kcal mol^{-1}, with $\Delta H^{\ddagger} = 23$ kcal mol^{-1} and $\Delta S^{\ddagger} = -6$ kcal mol^{-1} K^{-1}, by monitoring the *Z* → *E* isomerization by UV/vis spectroscopy at different temperatures. These values are comparable to values reported previously for the parent piperidine bases not carrying the anchor group.[1]

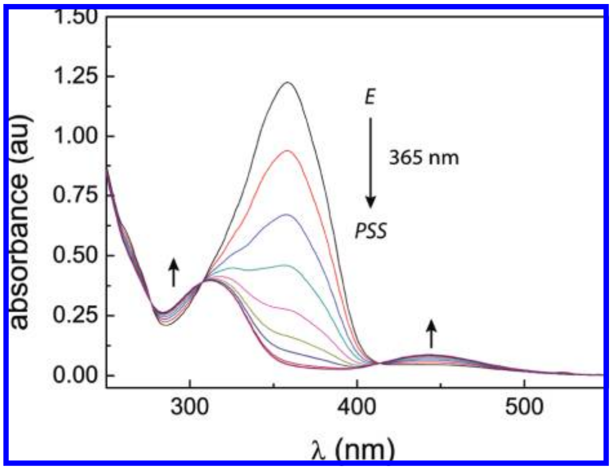


Figure 2. Irradiation of immobilization precursor **4** inducing (*E*)-**4** → (*Z*)-**4** isomerization ($\lambda = 365$ nm, 2 min 30 s irradiation time, 4.76×10^{-5} M in CH_3CN) to obtain a photostationary state mixture comprising 98% (*Z*)-**4** (the remaining 2% being (*E*)-**4** according to UPLC analysis).

The photoswitching behavior of supported catalyst **6** was investigated by UV/vis absorption spectroscopy of suspensions of **6** in methylene chloride (Figure 3). Use of methylene chloride as solvent is crucial for obtaining satisfying results as the comparable refractive indices of this solvent and silica gel diminish detrimental diffraction at the solid−liquid interface. A distinct absorption around 360 nm is attributed to the $\pi \rightarrow \pi^*$ transition of (*E*)-**6**. The symmetry forbidden and hence weak $n \rightarrow \pi^*$ transition cannot be resolved due to the increased background absorption of the suspensions. Compared to homogeneous solutions, the spectra obtained from suspensions of **6** exhibit a substantial amount of noise, which is attributed to unavoidable scattering on large silica particles. Irradiation of (*E*)-**6** with light of 365 nm wavelength induces *E* → *Z* isomerization, as evident from the bleaching

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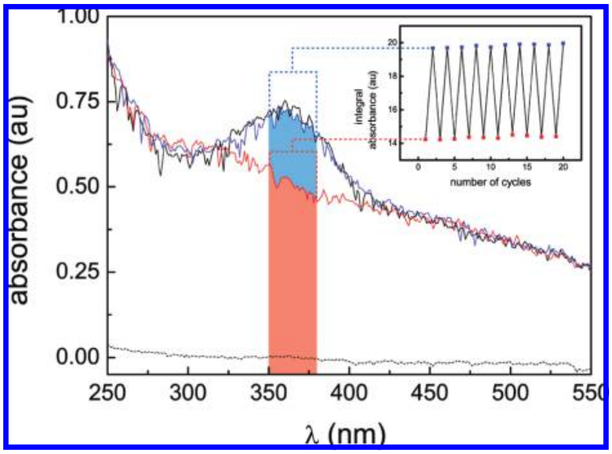

Figure 3. Switching of silica gel supported piperidine base **6** (black, (*E*)-**6**; red, PSS for (*E*)-**6** → (*Z*)-**6**, $\lambda = 365$ nm, 2 min 30 s irradiation time; blue, PSS for (*Z*)-**6** → (*E*)-**6**, $\lambda > 400$ nm, 1 min irradiation time; 6.14 mg of **6** in 3 mL of CH_2Cl_2). Inset shows the highlighted integral absorption between 350 and 380 nm during subsequent cycles of irradiation. The dotted line (bottom) shows the residual absorption after filtration of the silica gel, illustrating the absence of catalyst leaching.

of the absorption band at around 360 nm. The expected increase of the $n \rightarrow \pi^*$ absorption attributed to (*Z*)-**6** can only be anticipated from a very slight increase of the absorbance around 450 nm. Again, this is attributed to the increased background absorbance of the suspension. As expected, irradiation of (*Z*)-**6** with light of wavelengths >400 nm induces $Z \rightarrow E$ isomerization, leading to a photostationary state mainly containing (*E*)-**6**. Most importantly, the initial spectrum obtained from a nonirradiated sample is almost completely restored, demonstrating the efficiency and reversibility of the overall switching process. The exact composition of the PSS at the silica support is currently not known.

Supported catalyst **6** exhibits noticeable fatigue resistance. Switching was affected many times without any detectable sign of degradation, as evident from the practically constant integral absorbance in the range of 350−380 nm during several irradiation cycles (Figure 3, inset). The integral absorbance over a wavelength range was plotted rather than at a single wavelength to compensate for the enhanced scattering of the suspension. Furthermore, no evidence for catalyst leaching from the solid support was found after repeated switching, as confirmed by the absence of any detectable absorption around 360 nm after filtration of the suspension.

First experiments comparing the basicity difference of the two switching states of **6** on the solid support were carried out by direct measurement of the associated pH values of suspensions in water. Indeed, after irradiation of (*E*)-**6**, the pH value increased by 0.26 units ($pH_{PSS} = 6.89$ vs $pH_{(E)\text{-}\mathbf{6}} = 6.63$). Considering the rather low loading of approximately 10^{-5} mol/g (see supporting information), this pH change in water is remarkable and not only verifies basicity switching on the silica gel support but also illustrates a general way to photomodulate pH in aqueous systems.

In summary, we have described the synthesis of a photoswitchable piperidine base and its immobilization on silica gel particles. The photochromic behavior of the immobilization precursor **4** was thoroughly studied in homogeneous solution. Suspensions of piperidine-functionalized silica gel particles **6** exhibited the desired switching behavior upon exposure to light, and hence the concept of photoswitchable bases could successfully be transferred from solution to solid substrates. Ongoing research in our laboratories is directed toward the immobilization on planar oxidized silicon wafers and quartz slides and the thorough characterization of the obtained monolayers. Subsequently, we want to exploit these smart surfaces (Figure 1) to locally control polymerization reactions as well as pH values for surface patterning as well as (bio)sensor applications.

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Supporting Information Available: Detailed experimental procedures and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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