Angewandte
International Edition Chemie

DOI: 10.1002/anie.201403331

Supramolecular Switches

Photoresponsive Switches at Surfaces Based on Supramolecular Functionalization with Azobenzene–Oligoglycerol Conjugates**

*Olaf Nachtigall, Christian Kördel, Leonhard H. Urner, and Rainer Haag**

Dedicated to Professor Armin de Meijere on the occasion of his 75th birthday

Abstract: *The synthesis, supramolecular complexation, and switching of new bifunctional azobenzene–oligoglycerol conjugates in different environments is reported. Through the formation of host–guest complexes with surface immobilized β-cyclodextrin receptors, the bifunctional switches were coupled to gold surfaces. The isomerization of the amphiphilic azobenzene derivatives was examined in solution, on gold nanoparticles, and on planar gold surfaces. The wettability of functionalized gold surfaces can be reversibly switched under light-illumination with two different wavelengths. Besides the photoisomerization processes and concomitant effects on functionality, the thermal cis to trans isomerization of the conjugates and their complexes was monitored. Thermal half-lives of the cis isomers were calculated for different environments. Surprisingly, the half-lives on gold nanoparticles were significantly smaller compared to planar gold surfaces.*

The light-directed switching of molecules on surfaces has great potential for interfacial changes, such as hydrophobicity and bio-fouling behavior. The light-induced isomerization of azobenzene is a paragon for a molecular switch.[1] The *trans* to *cis* isomerization of the N=N-double bond is triggered by UV light, whereas back-switching can be realized either by heat or visible light. Azobenzenes have been used in a variety of applications and more recently were also investigated to switch the function of genes or proteins.[2–5] Self-assembled monolayers (SAM) on gold are an excellent method to study functional surfaces and sense changes on the surface with many experimental techniques.[6,7] However, molecular switching of azobenzenes on planar gold surfaces is often problematic owing to the excellent packing of alkanethiol SAM on gold.[8] Therefore, a new approach to immobilize functional switches on surfaces is required. Supramolecular reversible switches are quite promising for establishing a switchable surface.[9] Additionally, characterizing the switching mechanism as well as the stability of the switching states in different environments are important for possible applications.

Herein, we examined the switching dynamics and thermal half-life of amphiphilic azobenzene–glycerol conjugates as well as their host–guest complex with a cyclodextrin derivative, in different polar solvents, which were immobilized on gold surfaces. For this purpose, we synthesized three different bifunctional azobenzene–glycerols, which contained an adamantane and different generations of oligoglycerol dendrons G1-AB-Ad, G2-AB-Ad, and G3-AB-Ad (Figure 1). The oligoglycerol dendrons were attached to induce water solubility and for potential bioapplications. A thiol-functionalized β-cyclodextrin compound (β-CD-SH) and its protected version prot. β-CD-SR were synthesized as a host molecule (see the Supporting Information).[10] The formation of the host–guest complex of G3-AB-Ad and prot. β-CD-SR was carried out in an equimolar D_2O solution for 24 h and was confirmed by NMR spectroscopy (Figure 2a). The NMR spectrum of the complex exhibited changes in the chemical shifts compared to the spectra of the single compounds, which indicated a significant host–guest interaction. Moreover, NOESY experiments showed cross-peaks between the protons in the cavity of cyclodextrin and adamantane. The nuclear Overhauser effect confirmed the successful formation of the complex.[11] The absence of cross-peaks between the azobenzene and cyclodextrin indicated that there was no interaction between these molecular parts.

Subsequently, the complex was formed on gold nanoparticles (AuNPs). Therefore, functionalized AuNPs were synthesized by the reduction of tetrachloroauric(III) acid $HAuCl_4$ with sodium borohydride in DMSO in the presence of β-CD-SH.[12] Pure CD-coated nanoparticle solutions were collected by centrifugation. Comparative NMR measurements of the free β-CD and the β-CD functionalized AuNPs ensured the successful coating of the nanoparticles. The host–guest complex formed in aqueous solution except for G1-AB-Ad, which was due to its poor solubility in water. For G1-AB-Ad a mixture of DMSO/water (1:3) was used. Again, the complexation step was monitored by NMR-spectroscopy for the inclusion of G3-AB-Ad and β-CD functionalized particles (Figure 2b). NOESY spectra showed cross-peaks between β-CD-SH and G3-AB-Ad on AuNPs. Moreover, dynamic light scattering (DLS) was used to determine the particle sizes of the CD-coated AuNPs and the corresponding complexes with the glycerol–azobenzene conjugates. For CD-coated AuNPs the observed size of 2.7 nm was in good agreement with the work of Kaifer and Huskens et al.[12,13] Upon the formation of the host–guest complex with G1-AB-Ad, the size increased

---

[*] O. Nachtigall, Dr. C. Kördel, L. H. Urner, Prof. Dr. R. Haag
Institut für Chemie und Biochemie, Freie Universität Berlin
Takustrasse 3, 14195 Berlin (Germany)
E-mail: haag@chemie.fu-berlin.de
Homepage: http://www.polytree.de

[**] This work was funded by the DFG within the SFB 658 and SFB 765. O.N. thanks Dr. Matthew J. Webb for his kind support and the Friedrich-Ebert-Stiftung for a scholarship.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201403331.

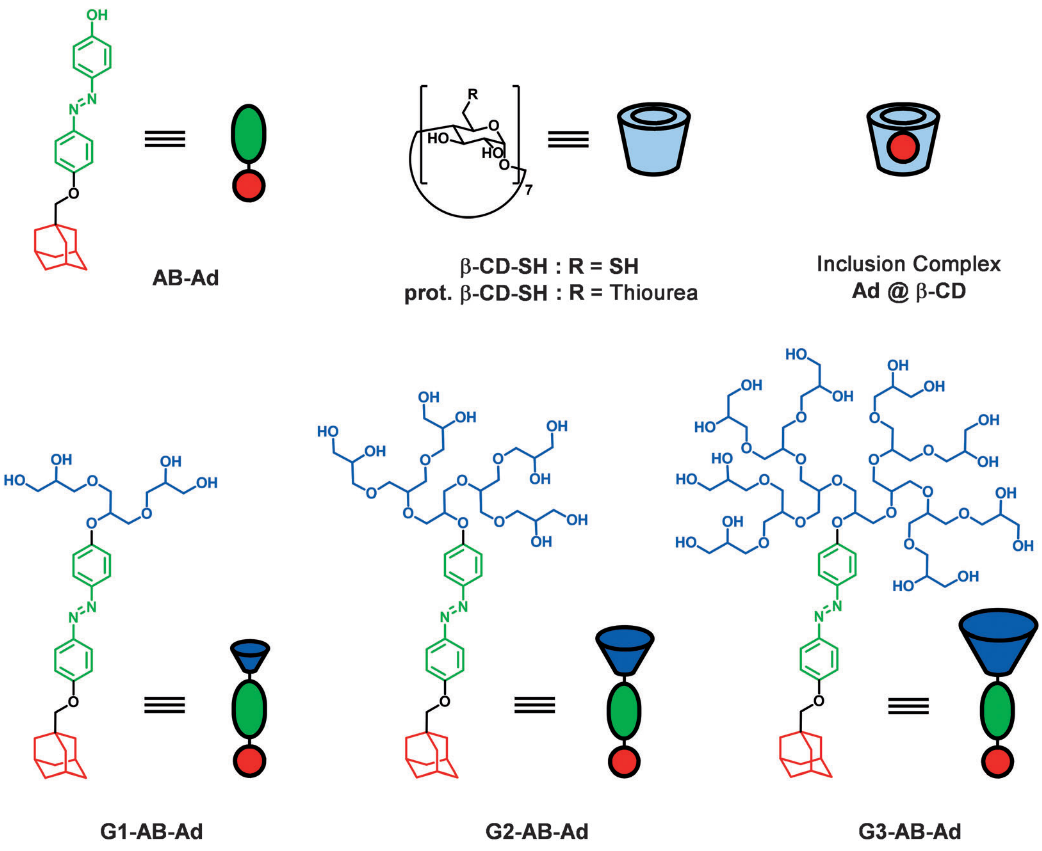

Figure 1. Amphiphilic azobenzenes (guest) and cyclodextrins (host) for supramolecular architectures.

due to the additional contribution of the supramolecular nanoparticle complex. Upon complexation of larger oligoglycerol dendrons, the particle size increased up to 8.7 nm for G3-AB-Ad at β-CD AuNPs, and was clearly dependent on the size of the guest.

The functionalization of planar gold surfaces was performed on three different types of surfaces. The first were semi-transparent surfaces with a 20 nm gold layer on glass for UV/Vis spectroscopy; the second were gold chip sensors for quartz crystal microbalance (QCM) for the online monitoring of the host–guest complex formation. QCM measurements were widely used in the detection of thin film formation.[14,15] The third were gold (111) surfaces on glass with a 200 nm metal layer for contact angle measurements. At first, the gold sensor slides for QCM measurements were coated with the thiol-functionalized β-CD in a 1 mM solution in DMSO in the presence of sodium borohydride to prevent disulfide formation. Subsequently, the guest molecule G3-AB-Ad was rinsed with a flow rate of 50 μL min^{-1} over the receptor-functionalized surfaces. During this process the frequency response was recorded (Figure 3). The frequency decreased, which showed the formation of the inclusion complex at the surface until a saturation was achieved (I–II). In region III the surface was equilibrated to Millipore water, which caused a slow but steady increase in frequency. In region IV the host–guest-functionalized surface was rinsed with sodium dodecylsulfate (SDS) to induce decomplexation.[16] After this treatment the initial frequency was observed. With this host–guest chemistry on surfaces, a modular functional surface was established for reversible coating with bifunctional molecular switches.

Adsorption spectra were recorded for all three systems: inclusion complex in solution, grafted on gold nanoparticles, and on planar gold surfaces (Figure 4). Samples were illuminated with 366 nm to trigger the photo-isomerization of the azobenzene moiety. The lamp we used was a long-wave UV lamp. The first spectrum was assigned to the host–guest complex formed by G3-AB-Ad and prot. β-CD-SH in an aqueous solution. Upon illumination with 366 nm the adsorption spectrum changed (blue dotted line). The initial absorbance band for the π–π*-transition at 360 nm, 365 nm for gold nanoparticles of the *trans*-azobenzene decreased upon illumination showing the isomerization. The increase at 450 nm could be assigned to the n–π*-transition of the formed *cis* isomer.

Back-switching was induced by illumination with 450 nm using a high-pressure mercury lamp (100 W) with an optical band-pass filter, which triggered the isomerization from the *cis* to the *trans* form. The absorption spectrum changed, which was caused by the switch. The π–π* absorption band increased again but only to a certain point. This photo-isomerization reached its photo-stationary state at the given wavelength.

Similar observations were made for the complex on gold nanoparticles. For *trans*-G3-AB-Ad complexed with CD functionalized AuNPs, a spectrum was received with the typical absorption of the π–π* transition at 360 nm of the azobenzene and a broad absorption at 520 nm, which is normal for the surface plasmon resonance of gold nanoparticles.[12] These solutions were illuminated with UV light to induce the isomerization process. The ππ*-transition band decreased again, whereas the n–π* transition band at 450 nm increased. As a result, the azobenzene was able to undergo the isomerization immobilized on gold nanoparticles.

To ensure that the switching process worked on planar gold surfaces, the host–guest system was transferred to semi-transparent gold chips. Therefore, the chips were coated with β-CD-SH before the inclusion complex was formed in a 1 mM solution of the corresponding guests. For the UV/Vis meas-

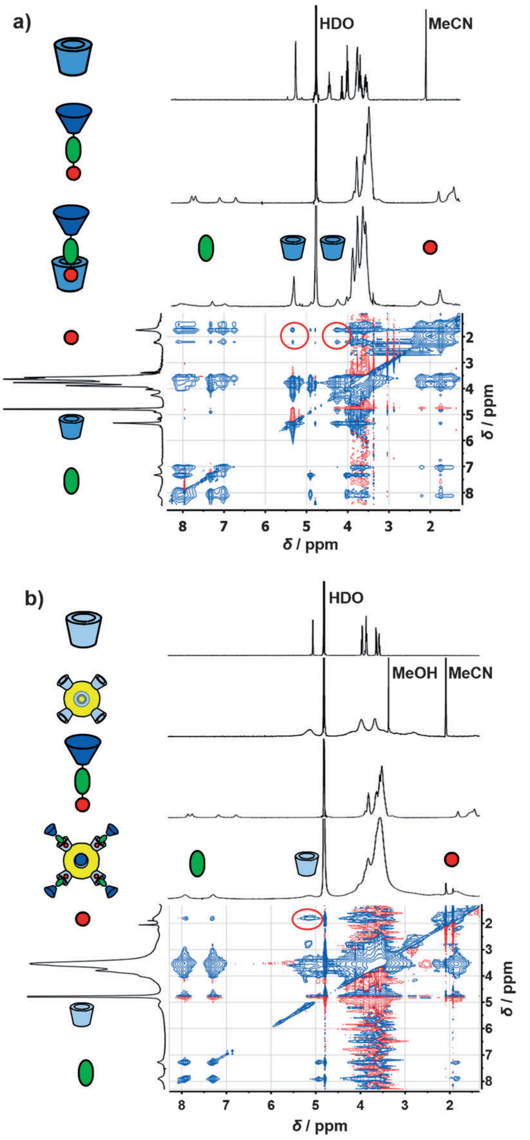

Figure 2. a) ^{1}H NMR spectra of the host cyclodextrin and guest G3-AB-Ad and a 2D-NMR (NOESY) of the corresponding inclusion complex; b) NMR spectra of β-CD, β-CD on AuNPs, G3-AB-Ad, and the 2D-NMR (NOESY) of the corresponding inclusion complex on gold nanoparticles. NOE: circled in red.

urements the gold chips were put upright in a cuvette and the spectrum was recorded in transmission (Figure 4). We could detect the transition at 350 nm as a small shoulder, which decreased upon illumination. The overall absorption was weak because the measurement was carried out in transmission of the monolayer. To clarify the isomerization process the polynomial fits of the adsorption difference are shown in the spectrum as green lines. The continuous green line represents the *trans* isomer at the surface, whereas the dotted line refers to the switched *cis* isomer. Back-switching is shown by the dashed green line, which did not reach the initial intensity because of the photo-stationary state at this wavelength. The G1/2/3-AB-Ad was able to switch reversibly on semi-transparent surfaces. Additionally, we confirmed the switching process by contact angle measurements. Upon isomerization from *trans* to *cis*, the hydrophilic glycerol head groups tilted sideward and the hydrophobic azobenzene was presented to the interface. Hence, an increase of the contact angle could be expected by switching from *trans* to *cis*, whereas a decrease of the contact angle should happen upon back-isomerization. We measured an advancing contact angle of 60° for the *trans*-G2-AB-Ad monolayer, which widened to 72° in the switched *cis* state (Figure 5). No significant change in contact angle was observed for the G3 bearing azobenzene owing to the large glycerol dendron. When the G3-oligoglycerol dendron was tilted to the side, the steric demand did not alter the hydrophobicity in the switched state.

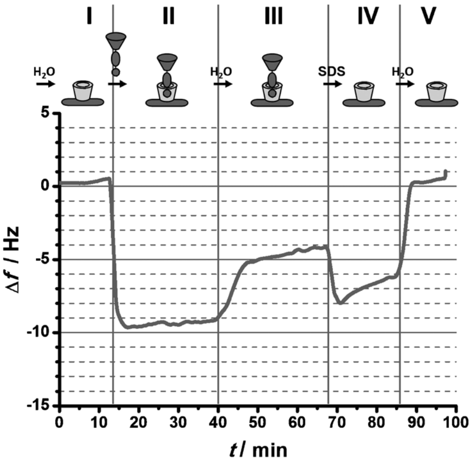

Figure 3. QCM sensogram of the online complexation of G3-AB-Ad on planar gold surfaces coated with β-CD-SH.

High thermal stability is important for applications of these systems. Therefore, we determined the thermal half-lives of the *cis* isomers for all the synthesized azobenzenes in different solvents, for the G3-AB-Ad cyclodextrin inclusion complex in solution, on gold nanoparticles, and on planar gold surfaces (Table 1). A large thermal half-life ensures stable switching states. All values were calculated from the corresponding UV/Vis spectra. A half-life of six minutes in acetonitrile was measured for the simple *cis*-azobenzene–adamantyl conjugate. In a protic polar solvent such as methanol, the half-life was much shorter and was smaller than one minute. Here the solvent effect provoked a reduced energy barrier for the *cis* to *trans* isomerization. Such solvent dependency illustrates a dipolar transition state and thus a rotational mechanism of the isomerization moiety.[17,18]

The half-life increased dramatically by attaching the glycerol dendrons. G1-AB-Ad had the highest half-life of 1773 min in methanol. Upon increasing glycerol dendron generation, the half-lives of the respective *cis* isomers were lower: G2-AB-Ad with 1223 min and G3-AB-Ad 702 min. The increasing steric demand of the growing generations is responsible for the lower half-life because the complexed *cis* isomer is less favorable compared to smaller generations. After changing to water as solvent, the half-life of G3-AB-Ad was doubled to 1523 min. This opposite solvent effect implied a stabilization of the *cis* isomer by water. The thermal half-life of the host–guest-complex of G3-AB-Ad and β-CD was significantly smaller with 478 min than for the free azoben-

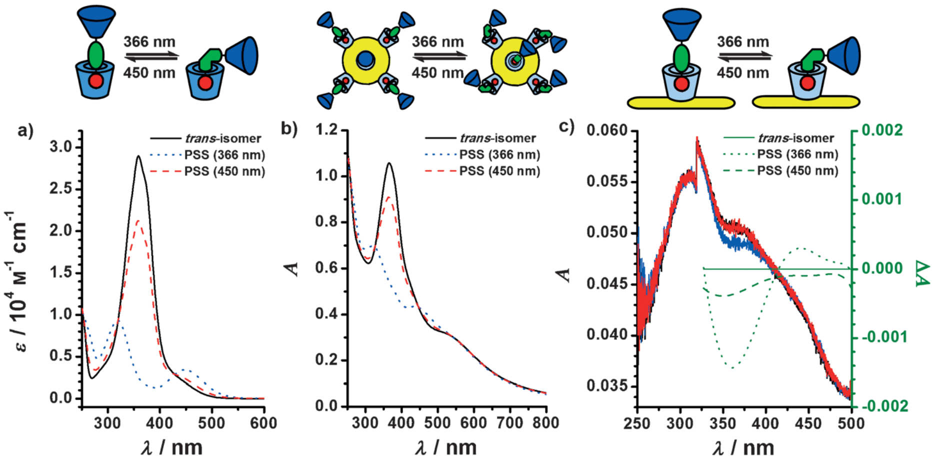

Figure 4. UV/Vis spectra of the switching process of complexed β-CD/G3-AB-Ad of a) in solution, b) on nanoparticles, and c) a planar surface

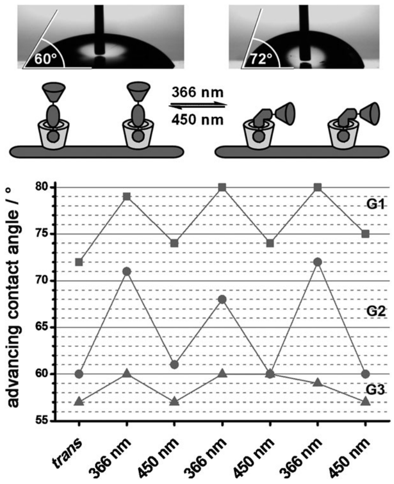

Figure 5. Switching process of the inclusion complexes G1/2/3-AB-Ad monitored by contact angle measurements on gold surfaces for three cycles.

Table 1: Half-lives of different azobenzenes and their complexes with β-CD in various solvents and substrates.

compound	environment at 20 °C	$\tau_{1/2}$ [min]
Z-AB-Ad	acetonitrile	6
Z-AB-Ad	methanol	< 1
Z-G1-AB-Ad	methanol	1773
Z-G2-AB-Ad	methanol	1223
Z-G3-AB-Ad	methanol	702
Z-G3-AB-Ad	water	1523
Z-G3-AB-Ad @ prot. β-CD-SH	water	478
Z-G1-AB-Ad @ β-CD-S-AuNP	water	20
Z-G2-AB-Ad @ β-CD-S-AuNP	water	26
Z-G3-AB-Ad @ β-CD-S-AuNP	water	33
Z-G1-AB-Ad @ β-CD-S-Au	air	613
Z-G2-AB-Ad @ β-CD-S-Au	air	517
Z-G3-AB-Ad @ β-CD-S-Au	air	465

zene. The solvent effect was reduced by the inclusion complex. The solvent molecules did not have the space for interacting with the azobenzene moiety. Therefore, the solvent effect is reduced. However, the other oligoglycerol azobenzene derivatives were not water soluble and therefore the half-lives could not be measured.

The situation changed dramatically on gold nanoparticles. The *cis*-azobenzenes complexed on CD-coated gold nanoparticles had significant lower half-lives. A half-life of 20 min was measured for G1-AB-Ad on nanoparticles, which increased only slightly for the higher generation dendrons. The *cis*-G2-AB-Ad switched in 26 min back to the *trans* isomer, whereas *cis*-G3-AB-Ad needed 33 min. This surprising trend was not observed for light-induced back-switching, where the process on nanoparticles was as fast as in solution. Two different explanations for this phenomenon are possible. On the one hand, plasmonic effects of the gold nanoparticles could lead to higher isomerization rates. The plasmon resonance of the nanoparticles interacted with excitons and enhanced the dissipation of exciton–hole pairs. On the other hand, the isomerization catalyzed by gold nanoparticles by an electron-transfer mechanism, which was discussed by Scaiano et al.[19] The half-lives of the AB-complex on planar gold surfaces were in good agreement with the observations made in free solution. This would imply the dark back-switching independent from solvent and is governed only by the interaction of the host–guest. The half-life here decreased on planar surfaces with the size of the dendrons, which was also observed in solution (Table 1).

We investigated whether the guest molecule decomplexed by switching from *trans* to *cis* using DOSY NMR and QCM experiments. DOSY NMR measurements of the host–guest complex in D_2O for the *trans* isomer and after illumination with UV-light (*cis* isomer) showed no change of the diffusion coefficient (Supporting Information, Figure S12), which indicates there is no free guest. QCM measurements with illumination were performed similar to the above mentioned experiments. The complexation was confirmed by a decrease in frequency. Over the period of the whole measurement the functionalized chip was constantly rinsed with Milli-Q water. After addition of the *trans*-azobenzene guest and equilibration, the sensor was illuminated with 366 nm for 30 min to induce the *cis* isomerization. During this procedure the frequency slightly increased for 2 Hz. A control experiment with a blank sensor chip was performed the same way. After starting the lamp und during the illumination with 366 nm the frequency increased for 2 Hz. This identical small frequency change indicates that no desorption occurs during switching from *trans* to *cis*. The small frequency increase can be explained by a local temperature change on the sensor surface.

In summary, we have introduced a new supramolecular amphiphilic switch that can readily be applied in solution as well as on surfaces. The switching behavior of the host–guest complex was carefully analyzed by different methods and revealed an efficient process with a strong environment dependence upon both solvent as well as the kind of surface (curved vs. planar). This is in contrast to self-assembled monolayers of densely packed azoswitches that cannot be switched readily on planar gold surfaces. Furthermore, we could demonstrate a clear switching behavior of the contact angle and hence the hydrophobicity of the surface. Particularly the contact angles around 65° are discussed as transitions between fouling and non-fouling surfaces.[20] Therefore, the G2-switch on gold is a potential candidate for light-controlled bioadhesion.

Received: March 14, 2014
Revised: April 30, 2014

Keywords: azobenzene · half-life · host–guest chemistry · molecular switches · surface chemistry

---

[1] J. Griffiths, *Chem. Soc. Rev.* **1972**, *1*, 481 – 493.
[2] A. Beharry, G. A. Woolley, *Chem. Soc. Rev.* **2011**, *40*, 4422 – 4437.
[3] M. Petr, P. T. Hammond, *Macromolecules* **2011**, *44*, 8880 – 8885.
[4] A. Natansohn, P. Rochon, *Chem. Rev.* **2002**, *102*, 4139 – 4176.
[5] M. A. Kienzler, A. Reiner, E. Trautman, S. Yoo, D. Trauner, E. Y. Isacoff, *J. Am. Chem. Soc.* **2013**, *135*, 17683 – 17686.
[6] P. E. Laibinis, J. J. Hickman, M. S. Wrighton, G. M. Whitesides, *Science* **1989**, *245*, 845 – 847.
[7] S. Wagner, F. Leyssner, C. Kördel, S. Zarwell, R. Schmidt, M. Weinelt, K. Rück-Braun, M. Wolf, P. Tegeder, *Phys. Chem. Chem. Phys.* **2009**, *11*, 6242 – 6248.
[8] C. Gahl, R. Schmidt, D. Brete, E. R. McNellis, W. Freyer, R. Carley, K. Reuter, M. Weinelt, *J. Am. Chem. Soc.* **2010**, *132*, 1831 – 1838.
[9] R. Klajn, J. F. Stoddart, B. Grzybowski, *Chem. Soc. Rev.* **2010**, *39*, 2203 – 2237.
[10] M. T. Rojas, R. Königer, J. F. Stoddart, A. E. Kaifer, *J. Am. Chem. Soc.* **1995**, *117*, 336 – 343.
[11] B. Hakkarainen, K. Fujita, S. Immel, L. Kenne, C. Sandström, *Carbohydr. Res.* **2005**, *340*, 1539 – 1545.
[12] J. Liu, W. Ong, E. Roma, M. J. Lynn, A. E. Kaifer, *Langmuir* **2000**, *16*, 3000 – 3002.
[13] O. Crespo-Biel, A. Jukovic, M. Karlsson, D. N. Reinhoudt, J. Huskens, *Isr. J. Chem.* **2005**, *45*, 353 – 362.
[14] Z. Cao, B. Du, T. Chen, H. Li, J. Xu, Z. Fan, *Langmuir* **2008**, *24*, 5543 – 5551.
[15] B. Du, D. Johannsmann, *Langmuir* **2004**, *20*, 2809 – 2812.
[16] C. David, F. Hervé, B. Sébille, M. Canva, M. C. Millot, *Sens. Actuators B* **2006**, *114*, 869 – 880.
[17] F. Serra, E. M. Terentjev, *Macromolecules* **2008**, *41*, 981 – 986.
[18] T. Asano, T. Okada, *J. Org. Chem.* **1984**, *49*, 4387 – 4391.
[19] G. L. Hallett-Tapley, C. D'Alfonso, N. L. Pacioni, C. D. McTiernan, M. González-Béjar, O. Lanzalunga, E. I. Alarcon, J. C. Scaiano, *Chem. Commun.* **2013**, *49*, 10073 – 10075.
[20] N. Schwierz, D. Horinek, S. Liese, T. Pirzer, B. N. Balzer, T. Hugel, R. R. Netz, *J. Am. Chem. Soc.* **2012**, *134*, 19628 – 19638.