Laboratory of Polymer Chemistry
Department of Chemistry
University of Helsinki
Helsinki, Finland

Multi-stimuli responsive polymers based on calix[4]arenes and dibenzo-18-crown-6-ethers

Szymon Wiktorowicz

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FOR THE DEGREE OF DOCTOR OF PHILOSOPHY**

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Supervisor

Professor Heikki Tenhu
Laboratory of Polymer Chemistry
Department of Chemistry
University of Helsinki
Finland

Opponent

Professor Stefan Hecht
Department of Chemistry
Humboldt-Universität zu Berlin
Germany

Reviewers

Professor Kalle Levon
Department of Chemical and Biological Sciences
Polytechnic Institute of New York University
United States of America

&

Professor Carl-Eric Wilén
Department of Chemical Engineering
Åbo Akademi University
Finland

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Abstract

The possibility to respond to external stimuli with change in physicochemical properties of a polymeric system is appealing to a broad range of scientists as it may result in the preparation of exciting new ‘smart’ materials. Whilst numerous reports exist on polymers which respond to single stimulus such as temperature, light, pH, redox, etc., the examples of multiple stimuli responsive polymers are limited.

This study deals with the preparation and characterisation of polymers comprising of calix[4]arene or dibenzo-18-crown-6-ether units, which have been joined by azo-bridges. The objectives and synthetic pathways towards monomer and polymer formation are evaluated and the best methods are highlighted as being versatile and promising for the synthesis of a wide range of main chain azopolymers.

As a result of their intricate design, the polymers are capable of response to irradiation by means of reversible *trans*-to-*cis* photo-isomerization of the azo-linkages. The extent of the photo-switchability in various solvents is evaluated by UV-Vis spectroscopy and the structural changes upon isomerization are resolved with ^1H NMR analysis.

The choice of the calix[4]arene and crown ether units as major chemical components enables interaction of the polymers with low molar mass guests (evidenced by titration experiments monitored by means of ^1H NMR, UV-Vis spectroscopy). This supramolecular activity is shown to be influenced by the photo-stationary state of the polymers in the case of poly(azocalix[4]arene)s and thus a serial photo-tuning of the extent of the host-guest interaction is possible. For the poly(azodibenzo-18-crown-6-ether)s addition of guests leads to phase separation of the polymers from certain solutions.

By incorporating tetraethyleneglycol monomethyl ether chains into the lower rim of the calixarene units, thermo-responsive behaviour could be induced onto the poly(azocalix[4]arene) framework. Lower critical solution (LCST) type transitions in water and upper critical solution (UCST) type transitions in alcohols were observed, which are strongly dependent on the degree of polymerization, concentration and choice of solvent. The latter was also demonstrated for the poly(azodibenzo-18-crown-6-ether)s. In both cases, the UCST type behaviour may be influenced by irradiation. The reversible *trans*-to-*cis* photo-isomerization decreases the demixing temperature of the solutions proportionally to the *trans* content of the samples. Thermal relaxation reverts the isomerization and the cloud point values from prior to irradiation are regained. For the tegylated poly(azocalix[4]arene)s the isomerization may also be induced in the phase separated state, leading to dissolution of the polymers, as the UCST value is shifted. This may be done locally in a thin 1 mm quartz cuvette, yielding areas of translucency in the polymer dispersion upon irradiation and a possible photo-writing application.

The thermo-responsive properties of the crown ether polymers may also be influenced by the addition of barium ions, which act as dynamic intermolecular crosslinkers increasing the cloud point values. These polymers are also shown to be solvatochromic and pH-sensitive.

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List of original publications

This thesis is based on the following publications:

- I** Wiktorowicz, S., Aseyev, V., Tenhu, H.
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- II** Wiktorowicz, S., Tenhu, H., Aseyev, V.
Influence of Photo-isomerization on Host-Guest Interactions in Poly(azocalix[4]arene)s.
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- III** Wiktorowicz, S., Tenhu, H., Aseyev, V.
Using Light To Tune Thermo-Responsive Behavior and Host-Guest Interactions in Tegylated Poly(azocalix[4]arene)s.
Macromolecules **2013**, 46(15), 6209-6216.
- IV** Wiktorowicz, S., Duchêne, R., Tenhu, H., Aseyev, V.
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The publications are referred to in the text by their roman numerals.

Author's Contribution to the Publications

For all publications (**I-IV**) S.Wiktorowicz has designed the research plan, created and characterised the polymers and written the manuscripts.

Publication related to the thesis:

- V** Pulkkinen, P.M.S., Wiktorowicz, S., Aseyev, V., Tenhu, H.
Complexation of calix[4]arene protected gold nanoparticles with pyridinium and bipyridinium compounds.
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Abbreviations

ATRP	Atom transfer radical polymerization
C16Py+	Hexadecylpyridinium chloride
CTADC	Cetyltrimethylammonium dichromate
DMF	N,N-dimethylformamide
DMSO	Dimethylsulfoxide
LAH	Lithium aluminium hydride
LCST	Lower critical solution temperature
LS	Light scattering
NLO	Non-linear optics
NMP	Nitroxide-mediated polymerization
NMPI	N-methyl pyridinium iodide
NMR	Nuclear magnetic resonance spectroscopy
NOESY	Nuclear Overhauser effect spectroscopy
OLED	organic light emitting diode
OPV	organic photovoltaics
PAAc	Poly(acrylic acid)
PDEAEMA	Poly(diethylaminoethyl methacrylate)
PDMAEMA	Poly(dimethylaminoethyl methacrylate)
PMAAc	Poly(methacrylic acid)
PMMA	Poly(methyl methacrylate)
PNAGA	Poly(N-acryloylglycinamide)
PNIPAM	Poly(N-isopropylacrylamide)
POEGMA	Poly(oligoethyleneglycol methacrylate)
POF	Polymer optical fibers
PPP	poly(paraphenylene)
PSS	Photo-stationary state
PVIm	Poly(vinyl imidazole)
PVP	Poly(vinylpyridine)
RAFT	Reversible Addition Fragmentation Chain Transfer
Red-Al	Reducing aluminium, sodium bis(2-methoxyethoxy aluminium hydride)
SEC	Size exclusion chromatography
TEMPO	Tetramethylpiperidine-1-oxyl
THF	Tetrahydrofuran
UCST	Upper Critical Solution Temperature
UV-Vis	Ultraviolet-visible spectroscopy

1 Introduction

With the substantial progress in the field of polymer science over the previous century, the modern day chemist has acquired an extensive tool-kit, which allows for preparation of a variety of advanced structures and the creation of new technological processes. This would not have been possible without understanding the processes of synthesis, physicochemical theory, structure-property relationships and identifying the applications. To date, different mechanisms of polymerization have been studied, which can be divided into step-growth and chain-growth (cationic, anionic, radical) polymerization. All these synthetic methods have their advantages and drawbacks and the choice of technique is related to the design of the end polymer, whether based on chemical composition, architecture and/or reaction conditions.

In the past two decades living polymerization (anionic, cationic, free radical, ring opening) has taken to the spotlight, offering the possibility of producing complicated architectures (block, comb, brush, star, ring (co) polymers). Furthermore, the evolution of controlled radical polymerization methods¹ (Nitroxide Mediated Polymerization (NMP), Atom Transfer Radical Polymerization (ATRP), and Reversible Addition-Fragmentation Chain Transfer (RAFT)) has greatly improved the control over structure and polydispersity. The possibility to tailor the polymer properties by modifying the monomers prior to or post polymerization is further enhanced by the reaction portfolio derived from organic chemistry. The most popular of which include high yielding ‘click’ protocols² such as 1,3-Huisgen dipolar cycloaddition between an azide and alkyne species, thiol-ene³ and thiol-yne⁴, as well as Diels-Alder cycloaddition reactions⁵.

Along with the development in synthetic methods, new processing techniques and applications have emerged. Self-assembly of block copolymers⁶ has attracted attention in the field of nanotechnology as a means of patterning surfaces in the sub 50 nm region. This could potentially provide further reduction in size of microcircuits and thus contribute to higher performance nanoelectronics. This self-assembled patterning (bottom-up approach) is being explored as an alternative to the traditional photoresists⁷ (top-down approach), which utilize radiation induced solubility change as a means for patterning. The current limitations in this technology include the current irradiation sources, as shorter wavelengths than 193 nm are difficult to realize and diffusion of acid as a result of using chemical amplification processes. Patterning of surfaces may also be applied to three dimensional structures⁸. This is especially useful in the preparation of prototypes and personalized items, medical devices or mechanical components. The current methods of photopolymerization, extrusion, powder solidification and lamination all have features which make them interesting for various applications. The most commercially promising is the 3D printing (3DP) powder-based process developed by Sachs and Co-workers in 1986 at MIT, which allows for easy fabrication of components and has been extended from polymer powders to ceramics and even metal. In recent years, the computer-assisted printing of systems has also been applied to ink-jet printing⁹ onto paper and flexible polymer substrates resulting in production of microcircuits, organic light emitting diodes (OLEDs) and organic photovoltaics (OPVs). The resolution of this method is strongly dependent on the flow properties of the ink and other printing parameters.

Conjugated polymers have been extensively explored as a means of producing advanced functional materials which harvest energy and translate it into an output signal. Several strategies for the preparation of OLEDs and OPVs have been employed the latter however needs more efforts to be competitive in terms of efficiency with the inorganic analogues. They have also been used in the preparation of sensors and photonics.

In 1985, Harold Kroto, James R. Heath, Sean O'Brien, Robert Curl and Richard Smalley paved the way for all-carbon π -rich systems with their discovery of C₆₀ (0D)¹⁰ and other fullerenes. In 1990s the possibility to obtain 1D carbon materials was elucidated with the introduction of carbon nanotubes¹¹ and more recently the development of a 2D carbon allotrope - graphene has been gaining interest of the scientific community. The latter has been exhibiting superior properties to all other carbon-based conjugated materials and is a promising candidate for optoelectronics¹². Other interesting applications of various polymers for advanced materials include the preparation of membranes¹³, modern adhesives and sealants¹⁴, polymer optical fibres¹⁵ for data communication (POFs), nanocomposites and hybrid materials¹⁶. An exciting class of functional materials which offer the possibility of external control of their function is stimuli-responsive polymeric systems¹⁷.

Nature has long been relying on processes which differ in their outcome based on the conditions of the environment. Following this inspiration, scientists have attempted to create structures capable of response to external stimuli (single or multiple) with change in physicochemical properties. As a result of these efforts numerous systems have been invented and the field of 'smart' polymers is experiencing a recurring surge of interest¹⁸.

Generally, these systems can be divided based on the nature of the environmental stimulus: physical (temperature, ionic strength, electromagnetic radiation, electric or magnetic fields, solvents, mechanical stress, etc.), chemical (pH, specific ions and chemical agents) or biomedical (enzyme substrates, other biochemical agents, affinity ligands)¹⁹. Considering the substantial investigations into various systems, another classification is possible and entails the response of the polymer to single or multiple stimuli.

1.1 Single-stimulus responsive polymers

Studying the outcome of applying a stimulus, may be performed in bulk (polymer films) or solution. Majority of the investigations rely on the most abundant solvent source - water. But also other solvent systems have been used. For the purpose of this overview and relevance to the author's contributions, the focus will be primarily on temperature, light and pH-responsive macromolecules.

1.1.1 Thermo-responsive polymers

In terms of approach, temperature change is the most commonly applied stimulus for smart materials. It is relatively easy to realize and control and a large effort has gone into understanding the processes involved in the response of the system in solutions. An application-based explanation for this interest in thermo-sensitive systems may be that the immune system of the body relies on temperature changes in affected areas and hence site-specific drug delivery should be possible.

In some cases, the interaction of the polymer with the solvent may be influenced by change in temperature. Depending on the mode of response, the polymers may exhibit a demixing behaviour that is typical for lower critical solution (LCST) or upper critical solution (UCST) - type transitions. The first of which involves the phase separation from a soluble to insoluble state with increase in temperature and the latter undergoes the opposite.

One of the most extensively studied thermo-responsive polymers is poly(*N*-isopropyl acrylamide), PNIPAM. The LCST behaviour in aqueous solutions²⁰ relies on the hydrogen bonding between the water molecules and the polar groups on the polymer. Upon increase in temperature, those bonds are cleaved resulting in possibility of the nonpolar groups to interact leading to a coil-to-globule transition (Fig 2a).

The LCST-type transition in water which relies on the balance between hydrophilic and hydrophobic contributions of the polymer chain may be tuned by modifying the chemical composition. Other important thermo-responsive polymers include polyacrylamides, polyoxazolines, polyvinyl ethers and poly(oligoethylene oxide) methacrylates. In their review, Aseyev et al.²¹ showcase the vast library of neutral water-soluble polymers, which exhibit this transition along with the studies on tuning their behaviour. Chain length²², tacticity²³, nature of the end group, addition of (co)monomer²⁴ and salt²⁵ also play an important role in the process of adjusting the critical temperature depending on the polymer.

In sharp contrast to the literature available for LCST polymers in aqueous media, only few reports exist on the UCST-type transitions of polymers, predominantly in different water-alcohol solvent mixtures²⁶. This may be attributed to the fact, that the transitions are seldom observed for practically relevant conditions²⁷. Few recent examples of polymers exhibiting UCST based on thermally reversible hydrogen bonding (HB-UCST) in water include poly(*N*-acryloylglycinamide) (PNAGA) and its derivatives^{27,28}, poly(allylurea) copolymers²⁹ and copolymers of *N*-vinylimidazole and 1-vinyl-2-(hydroxymethyl)imidazole³⁰. In the past, systems based on poly(methyl methacrylate), PMMA³¹, poly(2-oxazolines)³² and copolymers of hydroxyethyl methacrylate and acetoacetoxyethyl methacrylate in ethanol/water mixtures have also demonstrated the UCST-behaviour. Recently, poly(oligoethyleneglycol) methacrylate, POEGMA has been shown to undergo the UCST-type transitions in alcohols, which are strongly dependent on the degree of polymerization, concentration, alcohol and end groups³³.

Dual thermo-responsive systems have also been prepared in the past³⁴. Copolymers of 3-[*N*-(3-methacrylamidopropyl)-*N,N*-dimethyl]ammoniopropane sulfonate, (SPP) and

PNIPAM³⁵, as well as 2-hydroxyethyl methacrylate (HEMA) and N,N-dimethylaminoethylmethacrylate, (DMAEMA) or [2-(methacryloyloxy)ethyl]trimethylammonium chloride (MOETAC)³⁶ exhibit both LCST and UCST response in water. Triple thermo-responsive systems have also been reported³⁷.

By crosslinking the polymers, hydrogels³⁸ may be obtained, in which hydration/dehydration is controlled by means of temperature (Fig. 2d). In the case of self-assembled block copolymers (Fig. 2b), thermo-responsive micelles⁴¹ and microgels³⁹ may be prepared. The polymers may also be grafted onto surfaces (Fig. 2c), thus enabling the tuning of their wettability⁴⁰. Depending on the morphology, these systems may be used for e.g. drug delivery⁴¹, membranes⁴², smart coatings⁴³, etc.

Fig. 1 Examples of thermo-responsive polymers; PNIPAM (LCST in water $\sim 32^{\circ}\text{C}$); Poly(methylvinyl ether), PVME (LCST in water $\sim 34\text{--}38^{\circ}\text{C}$); Poly(vinylcaprolactam), PVCl (LCST in water $\sim 32\text{--}40^{\circ}\text{C}$) PDMAEMA (LCST in water $\sim 50^{\circ}\text{C}$, pH-responsive); POEGMA (LCST in water, UCST in alcohols); PNAGA (HB-UCST in water).

Fig. 2 (a) coil-to-globule transition of a thermo-responsive polymer; (b) micelle formation in a diblock copolymer (c) thermo-responsive grafts on a surface (d) shrinking of a thermoresponsive hydrogel.

1.1.2 Photo-responsive polymers

Another stimulus, which is easy to realize is irradiation. The offered range of specific wavelengths (from UV to deep infrared) alongside with control of intensity, exposure time, as well as irradiation site (area/volume), makes it a very promising candidate for stimulus-responsive systems. The most universally explored photo-switchable systems⁴⁴ include azobenzene and diarylethene derivatives, spiropyran, spirooxazine, fulgide units (Fig. 3). A variety of molecules undergoing dimerization (cinnamic acid⁴⁵, coumarin⁴⁶, dimethylmaleimide⁴⁷) may also be termed as photo-responsive.

Fig. 3 Examples of known photo-switches; (a) azobenzene; (b) spiropyran; (c) fulgide; (d) diarylethene

By far the most commonly used photo-switch is azobenzene⁴⁸. The structural transition which the molecule experiences upon irradiation is a great platform for the design of smart materials⁴⁹. Though the mechanism of this transition still remains under investigation⁴⁸, the result of the *trans*-to-*cis* photo-isomerization may easily be followed by means of UV-Vis spectroscopy. The maximum of absorption in the UV region (typically ~320-380 nm) corresponds to the π - π^* transitions, whereas a low intensity maximum at ~450 nm is indicative of the n - π^* transitions. Upon irradiation from the *trans* to the *cis* form, the absorption at shorter wavelengths decreases, whilst a slight increase for the 450 nm maximum can be observed. The *trans* form is thermodynamically more stable

and thus *cis* to *trans* isomerization occurs spontaneously in the dark following a relaxation process. Many factors influence the photo-isomerization behaviour and it is now perceived as an interplay of conditions of substituents, mobility, solvent (or lack thereof), temperature, intensity of irradiation source, etc. Azo derivatives have also been utilized for their chromophoric properties as dyes, pH or metal ion indicators, and in non-linear optical devices (NLOs).

Numerous azopolymers have been prepared in the past⁵⁰. The typical strategies employ the use of azobenzene derivatives in the main chain⁵¹ or as side⁵² groups. They have also been applied in the preparation of block copolymers⁵³, hyperbranched polymers and dendrimers⁵⁴. Amphiphilic azopolymers⁵⁵ have been used in self-assembly processes to produce thin films, micelles, vesicles and manufacture surface relief gratings. An interesting example of translation of the change in structure upon *trans* to *cis* photo-isomerization towards change of size in a main chain azopolymer has been demonstrated by Bléger et al.⁵⁶ The azobenzene-containing poly(paraphenylene)s, (PPPs) had been decoupled by means of distorted twisted angles on the phenylene unit as a result of its substitution with long aliphatic chains, thus enabling a *cis*-rich state of the chromophores upon irradiation in this rigid system. This strategy is promising towards preparation of new photoactuators.

In many cases, the use of a photo-switch (azobenzene⁵⁷, spirobenzopyran⁵⁸) in solution is accompanied by changes in solubility upon photo-isomerization. This is attributed to the difference in polarity of the azo moiety in its *cis* state, and the spirobenzopyran heterolytic cleavage of the bond, which leads to formation of a charged species. This is often used as a means of changing the thermo-responsive properties in a multi-stimuli responsive system which will be discussed later.

1.1.3 pH-sensitive polymers

The possibility to tune the characteristics of a polymeric system upon change in pH has been the subject of exhaustive research and remains relevant in terms of biological applications⁵⁹. Proton donating (polyacids) or accepting groups (polybases) upon change in the pH value undergo protonation/deprotonation resulting in generated charges and thus ionic interaction. This leads to swelling behaviour (extending of the polymer chain) when the charge is introduced. The balance between the hydrophobicity of the polymer and the ionizability of the chain will determine the conformation and phase separation behaviour of the system. In majority of the studies⁶⁰, weak polyacids include poly(acrylic acid), (PAAc), poly(methacrylic acid), (PMAAc), polysulfonamide derivatives. Some examples of polybases are poly(N,N-dimethylaminoethyl methacrylate), (PDMAEMA), poly(N,N-diethylaminoethyl methacrylate), (PDEAEMA), poly(4 or 2-vinylpyridine), (PVP), poly(vinyl imidazole), (PVIIm). In order to enhance the abruptness of phase separation, in many cases, hydrophobic modification is introduced (addition of comonomer). Furthermore the pH-response may be used to achieve degradation in the case of e.g. poly(ortho ester)s and poly (β -aminoester)s. Many biological polymers are pH responsive (chitosan, alginate). The applications of pH-responsive polymers include systems for oral drug-delivery, smart coatings, hydrogels, sensors, bioconjugates, and degradable materials.

Fig. 4 Examples of pH-responsive polymers; Poly(acids): PAAc, PMAAc; Poly(bases): PDEAEMA, P4VP, P2VP and PVIIm

1.1.4 Other stimuli responsive polymers

Apart from controlling the temperature, irradiation or pH and thus tuning the physicochemical properties, other means of stimulus-induced sensitivities are possible⁶¹.

Ferrocene and tetramethylpiperidine-1-oxyl (TEMPO) have been used in polymer based redox-active systems⁶². An external electric field may be used to tune the transmittance of liquid crystals in a polymer matrix⁶³. Immobilizing finely dispersed magnetite particles in a hydrogel of poly(N-isopropylacrylamide-co-vinyl alcohol), (PNIPAM-co-PVA)⁶⁴ results in magnetoelastic properties. Systems responsive to specific molecules (CO₂⁶⁵, glucose^{61,66}) as well as based on host-guest inclusion complexes⁶⁷ can also be produced.

1.2 Multi-stimuli responsive polymers

With the development of modern controlled radical polymerization, new modification and functionalization methods which enable precise tailoring of molecular architecture and composition, the preparation of systems, which respond to multiple stimuli changes in the environment, has been gaining considerable interest in recent years⁶⁸.

When two or more stimuli responsive groups are combined within a polymer, the interplay of those is a base for classification and is referred to as parallel, serial or causal⁶⁸. The first of which depicts a situation in which the stimuli responses are independent of each other. In the case of serial interplay, control of one stimuli-derived effect amplifies the other. Causal effect describes a system in which manipulation of one stimuli-responsive group generates a new stimulus, which influences the outcome of the second responsive group. Another approach is to divide the polymers according to their combinatorial stimuli-responses.

1.2.1 Double-stimuli responsive polymers

Temperature and light responsive systems⁶⁹ are most often studied. The vast library of thermoresponsive polymers and toolkit of photo-switchable molecules enables construction of numerous serial systems, majority of which result in photo-tuning of the thermal response. The first example of a photo-controlled LCST was reported by Kungwachakun in 1988⁷⁰. In a typical example of photo-tuning of LCST, Akiyama and Tamaoki prepared copolymers of NIPAM and acrylamides derived with azo moieties⁷¹. The polymers exhibited photo-induced changes of the transition temperature and wettability of polymer films. The same team also showed the effect of azo-end groups on linear PNIPAM⁷². Many other photo-tunable LCST polymers have been prepared by other groups over the years⁷³, however the investigation of photo-tunable UCST has been limited to random copolymers of PNIPAM and 4-phenylazophenyl methacrylate (AzoMA) in an ionic liquid⁷⁴. The concept of controlling either temperature or irradiation state to produce double stimuli-responsive materials⁶⁹ has been applied to more complicated block copolymers, hydro and nanogels, nanocomposites.

By manipulating the pH of a polymer solution, the outcome of its thermal response may be controlled. Poly(N,N-dimethylaminomethylmethacrylate), PDMAEMA⁷⁵ is a prime example of a pH and thermo-responsive polymer - upon increase in pH, the cloud point decreases. This property has been utilized by many groups⁷⁶ and provides an easy solution for the incorporation of dual responsiveness onto a system. Other strategies may involve synthesis of novel polymers⁷⁷ or introducing pH-sensitive moieties (e.g. poly(acrylic acid)) alongside a thermo-responsive backbone⁷⁸. Because both pH and temperature control are biocompatible stimuli changes, the smart polymers based on this dual response have potential for biomedical applications⁷⁹. It is also possible to control the LCST-type transitions of a ferrocene⁸⁰ or disulfide-containing⁸¹ polymers by means of a redox process.

1.2.2 Triple-stimuli responsive polymers

Though possessing a higher level of complexity, systems which are capable of response to more than two stimuli (light, temperature and pH) are interesting candidates for smart precision materials. By combining units that are photo-switchable (e.g. azo derivatives) with thermo- and pH-sensitive PDMAEMA, polymers, which are triple-stimuli responsive, can be prepared⁸². The LCST is affected by the protonation levels and irradiation. When PNIPAM is functionalized with spirobenzopyran, the thermal response is provided by the polymer chain and the spirobenzopyran acts as the photo and pH-sensitive unit⁸³. In the case of using spiropyran and PDMAEMA⁸⁴, both the polymer and the photo-switch contribute to the pH stimulus. Plamper et al.⁸⁵ used hexacyanocobaltate(III) as a trivalent counterion, which induces a UCST transition for aqueous solutions of PDMAEMA (apart from the LCST, which is controllable by pH). Irradiation of the polymer-counterion mixture diminishes the transition. Klaikherd et al.⁸⁶ have prepared an amphiphilic diblock copolymer of NIPAM and THP-protected HEMA joined by a disulphide linkage. The self-assembled micellar system could then be disassembled by means of temperature, pH and redox activity. Redox-active TEMPO molecules may be embedded into copolymers of NIPAM and aminofunctionalized azobenzene moieties⁸⁷. It was shown that the TEMPO and azo units contribute to increase of the LCST of the NIPAM polymer upon persistence of the corresponding stimuli. (redox and irradiation). Temperature and pH-sensitive hydrogels, which were responsive to glucose⁸⁸ have been reported. Other examples include triple stimuli-sensitive polypeptide nanoparticles⁸⁹.

In summary, the stimuli-responsive behaviour in smart materials may be attributed to specific design features within a polymer and the choice of its architecture. Random and block copolymers will differ in their responsive behaviour. Thermal response may be induced by using specific polymers described earlier (PNIPAM, POEGMA, etc.). Photoswitchability is provided by low molar mass molecules capable of photo-isomerization (azobenzene, spiropyran) or photochromism (fulgide). By introducing functional groups capable of protonation/deprotonation, pH-sensitivity is tailored onto the system. By careful consideration of these design factors along with processing conditions, smart materials capable of precise, targeted response may be prepared.

1.3 Complexing structural units of the polymers

1.3.1 Calixarenes

The onset of phenol-formaldehyde chemistry which was studied by Adolph von Baeyer, had laid grounds for the discovery of calixarenes⁹⁰. Though early suggestions on the cyclic nature of some of the products of condensation were made by Zinke in the 1950s, it was only in 1978 that structure proof was obtained by Gutsche⁹¹ and in 1979 by Andreotti⁹². Calixarenes are prepared in the acid (resorcinarenes) or base (calixarenes) - catalysed condensation of phenol and formaldehyde and the resulting cyclic oligomers (typically $n=4-8$) comprise of phenolic units that are joined by methylene bridges. The latter are responsible for the flexibility of the structure and as a result different conformations are possible. The hydroxyl groups make up the 'lower/narrow rim' of the calixarene and the para-positions are referred to as the 'upper/wider rim'.

In the case of calix[4]arenes (4 phenolic units joined by 4 methylene bridges, Fig. 5) the accessible conformations⁹³ include the *cone*, *partial cone*, *1,2-alternate* and *1,3-alternate*. In many cases, the hydrogen bonding in the lower rim, renders the *cone* conformation preferred ('chalice-like' [gr. *calix*] shape, from which the name is derived), however this is not straightforward and in solution, the persistence of the conformation also relies on the choice of solvent, substituents in the upper rim and temperature. This means, that interconversion between the species is possible.

Fig. 5 Structure and possible conformations of calix[4]arenes.

In 1982 Donald J. Cram⁹⁴ introduced the option to immobilize this inversion by means of modifying the lower rim with substituents which are larger than ethyl groups. As a result shape-defined molecules could be prepared.

Much of the appeal of calixarenes comes from the difference in chemical structure of the upper and lower rim which translates to different reaction protocols being used⁹⁰. The lower rim is prone to etherification and esterification reactions due to the hydroxyl group being present. The upper rim may undergo electrophilic substitution reactions upon removal of tert-butyl groups from the parent calix[4]arene. Furthermore, the modification of the lower rim may be done partially (mono, di or tri-), which results in a dissimilar reactivity of the upper rim (tri-, di- and mono-substitution). Many protective routes for the hydroxyl groups may be used and bridging of the lower or upper rim is synthetically feasible. These factors contribute greatly to the vast availability of structures and reactions and make calixarenes one of the best known cavitands in host-guest chemistry.

The interaction with low molar mass guests is enhanced by the cyclic array of aromatic groups which allow for a π -rich cavity in the *cone* conformation. The strength of the interaction may be enhanced by addition of specific functional groups enhancing hydrogen bonding in the upper or lower rim, crown ether linkages or metal-specific moieties. Calixarenes have been used in metal ion recognition⁹⁵ and complexation⁹⁶, interaction with low molar mass guests⁹⁷, film forming⁹⁸, biomolecular recognition⁹⁹, catalysis¹⁰⁰, and drug delivery¹⁰¹.

In terms of polymer science, calixarenes have been immobilized on polymer supports¹⁰², introduced as side groups¹⁰³ or into the main chain¹⁰⁴. They have also been used as core molecules for the preparation of star polymers¹⁰⁵ and dendrimers¹⁰⁶, as well as in the preparation of alternating copolymers with tetrathiophene¹⁰⁷.

Different azocalixarenes have been prepared in the past, where the azo unit is introduced into the upper¹⁰⁸ or lower rim¹⁰⁹ in most cases with the purpose of metal ion detection¹¹⁰. However, systems incorporating more than one azocalixarene are rare¹¹¹.

Our group was the first to report on a main chain azopolymer comprising exclusively of calixarenes (Fig.6). To the best of our knowledge, this is also the first example of a ‘smart’ stimuli-responsive polymer based on calixarenes.

Fig.6 Illustration of tegylated poly(azocalix[4]arene) in the *trans* form

1.3.2 Crown ethers

The discovery of crown ethers by Pedersen in 1967¹¹² contributed greatly to the establishment and understanding of supramolecular chemistry. These cyclic molecules, typically comprising of ethyleneoxy units, have been investigated over the years¹¹³ for numerous applications which include extraction¹¹⁴ of metal, non-metal and neutral molecules, phase transfer catalysis¹¹⁵, probing of biological processes¹¹⁶, chromatography¹¹⁷, etc. Their affinity for cations is determined by the denticity of the crown, which is related to size¹¹⁸, but also on the presence of heteroatoms (as is the case in azacrowns). The nomenclature of crown ethers (x-crown-y-ether) indicates the size of the macrocycle, where x-crown-y where x denotes the total number of atoms in the cyclic backbone and y denotes the number of oxygen atoms.

Fig. 7 Examples of crown ethers: (a) with increasing ring size: 12-crown-4, 15-crown-5 and 18-crown 6 ether. (b) benzo-18-crown-6 and dibenzo-18-crown-6-ether. (c) different azacrowns.

The available synthetic manipulation is defined by the unit used for closing the ring. In the case of benzocrown ethers, the introduction of a functional group may be done prior to ring closure or by means of electrophilic substitution reactions (bromination, nitration). Further post modification enables the synthesis of more complicated structures.

Crown ether polymers have been studied in the past, with the primary motivation of using them for extraction. The employed strategies included immobilization on polymer supports¹¹⁹ and incorporation into the backbone or side chain¹²⁰. They have also been used in the formulation of supramolecular polymers¹²¹.

Azocrown ethers¹²² capable of photo-induced isomerization have been extensively studied by Shinkai and incorporated as pendant groups¹²³ onto polymeric frameworks. However, prior to our report, main chain azopolymers with crown ether units composing the backbone (Fig. 8) have not been reported.

Fig.8 *Structure and illustration of poly(azodibenzo-18-crown-6-ether) in the trans form.*

2 Objectives of the study

The primary goal of this study was to understand the interplay between stimuli responses in multi-stimuli responsive systems and how intricate molecular design contributes to the fabrication of a desired response (light, temperature, host-guest interactions).

With regards to structure, the polymers were to contain molecules capable of host-guest interactions (calixarenes and crown ethers), which were connected by photo-switchable azo bridges.

In terms of synthesis and characterization, the key objectives were:

- (I) The preparation of calix[4]arene monomers locked in the *cone* conformation. The development and evaluation of the available coupling methods for polymerization.
- (II) The fractionation of the polymers, understanding their response to irradiation and their interactions with low molar mass guests. Evaluation of the influence of photo-isomerization on the host-guest interaction.
- (III) The preparation of polymers with tegylated chains in the lower rim of the calix[4]arene units. Studying their thermo-responsive behaviour and the influence of photo-isomerization on host-guest interactions and thermal responsiveness.
- (IV) The synthesis of poly(azodibenzo-18-crown-6-ether)s and highlighting the versatility of the reductive coupling method. Evaluating their pH-sensitivity, photo-isomerization and its effect on thermo-responsive properties. Furthermore, depicting the interaction with low molar mass guests and the influence of water on the observed UCST in alcohols.

3 Experimental

This section briefly describes the synthesis of monomers, different polymerization procedures and characterization methods used within the study. Detailed descriptions, conditions and synthesis of model compounds are presented in the papers attached (*I-IV*).

3.1 Synthesis of monomers

3.1.1 5,17-di(*tert*)butylcalix[4]arenes (*Papers I-III*)

The common intermediate compound, 5,17-di(*tert*)butylcalix[4]arene for the synthesis of the monomers was prepared according to Scheme 1. Parent *tert*butylcalix[4]arene, was subjected to a diametric protection of the lower rim hydroxyl groups (2) with benzoyl chloride and potassium carbonate in acetonitrile. In a following step, a reverse Friedel Crafts dealkylation of the upper rim employing aluminium trichloride and phenol in toluene selectively yielded the di(*tert*)butylcalix[4]arene derivative (3). The benzoyl groups were removed (4) by hydrolysis using sodium hydroxide in a mixture of tetrahydrofuran, THF water and ethanol.

Scheme 1 Synthesis of 5,17-di(*tert*)butylcalix[4]arenes.

Scheme 2 Synthesis of 5,17-dinitrocalix[4]arenes with aliphatic chains.

3.1.1.1 5,17-dinitrocalix[4]arenes with aliphatic chains (Papers I, II)

In the case of aliphatic substitution of the lower rim (n-butyl and n-dodecyl chains), the etherification was carried out using 1-butylbromide or 1-dodecylbromide and sodium hydride in DMF (5). Upon crystallization, the *cone* conformer was used in an *ipso* nitration employing a mixture of nitric and acetic acid in dichloromethane, to yield the desired 5,17-dinitrocalix[4]arene species (6) upon crystallization from 2-propanol.

3.1.1.2 5,17-dinitrocalix[4]arenes with tetraethyleneglycol monomethyl ether chains (Paper III)

Etherification of the di(*tert*)butylcalix[4]arene (4) using ethyl bromoacetate and potassium carbonate in acetone, yielded the spacer intermediate (7), which was reduced using lithium aluminium hydride in THF. The resulting *cone* calix[4]arene (8) was then etherified by means of a mesylated triethyleneglycol monomethyl ether and sodium hydride in THF. *Ipso* nitration of the tegylated calix[4]arene (9) using nitric and acetic acid in dichloromethane resulted in the tegylated 5,17-dinitrocalix[4]arenes (10) upon purification by means of column chromatography.

Scheme 3 Synthesis of tegylated 5,17-dinitrocalix [4]arenes.

3.1.2 4',4'' (5'') – dinitrodibenzo-18-crown-6-ethers (*Paper IV*)

The nitration of dibenzo-18-crown-6-ether (11) was done using nitric acid and acetic acid in chloroform. The 4',4''-species (12) precipitates from the reaction mixture first and has a higher melting temperature ($m_p=236^\circ\text{C}$), followed by the 4',5''-dinitrodibenzo-18-crown-6-ether (13) ($m_p=206^\circ\text{C}$) after stirring overnight.

Scheme 4 *Synthesis of 4',4'' (5'') – dinitrodibenzo-18-crown-6-ethers.*

3.2 Polymerizations

3.2.1 Reductive coupling of monomers

The following methods were studied to prepare the azopolymers from the nitroderivatives through a reductive coupling protocol. The conditions were adjusted (temperature, solvent, concentration, coupling agent/monomer ratios) to obtain highest molecular weights possible.

Lithium Aluminium Hydride, LAH (*Paper I*)

In a typical procedure, lithium aluminium hydride (LAH, 25 eq.) was suspended in a solvent (diethyl ether, dimethoxyethane or THF) at room temperature. The 5,17-dinitrocalixarene, (6, 1 eq) was dissolved in THF, THF/diethyl ether or dimethoxyethane. The reaction was stirred for 5 days. Quenching was done by slow addition of ethyl acetate

(CAUTION! exothermic reaction), followed by water and the extraction was subsequently done to dichloromethane.

Sodium bis(2-methoxyethoxyaluminium hydride), Red-Al (*Papers I-IV*)

The general procedure for the preparation of the azopolymers was as follows. Sodium bis(2-methoxyethoxyaluminium hydride), Red-Al (10 eq.) solution in toluene (65% v/v), maintained under argon was cooled to 0°C. The monomer (1 eq.) in toluene (2 mL/mmol) was added dropwise to the reaction mixture. Stirring was continued for 2-5 days. The reaction was quenched by careful addition of methanol (CAUTION! exothermic reaction). The residue was washed with 10% hydrochloric acid and extraction was done into dichloromethane, followed by washing with water (and/or brine).

Scheme 5 Reductive coupling of 5,17-dinitrocalix[4]arenes using Red-Al in toluene.

3.2.2 Oxidative coupling of oligomers

Cetyltrimethylammonium dichromate (CTADC) (*Paper I*)

Oligomers (1 eq.) from the reductive coupling procedures (3.2.1) were dissolved in chloroform (10mL/mmol) and subsequently CTADC (1 eq) was added to the reaction mixture followed by heating at reflux for 5 days. Evaporation of the solvent *in vacuo* was done upon cooling to room temperature and the purification was done by column chromatography.

Iron (II) sulphate heptahydrate and potassium permanganate (*Paper I*)

The oxidant mixture (4 eq.) of equal amounts of $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ and KMnO_4 (ground by means of mortar and pestle) was added to a solution of oligomers (1 eq) dissolved in chloroform and heated at reflux for 5 days. The mixture upon cooling was filtered through a pad of celite.

3.3 Fractionation of the polymers

The previously described coupling methods (3.2) result in the preparation of species with high polydispersity, as was evidenced by size exclusion chromatography of the crude reaction samples. As a consequence, fractionation needed to be performed before studies on the characterization of the polymers could commence.

The polymer crude samples were dissolved in THF at a high concentration (approx. 25 g/L) and left stirring overnight to ensure complete solubilisation. Fractionation was done by careful addition of a precipitating solvent. 2-propanol was used in the case of aliphatic poly(azocalix[4]arene)s and hexane for the tegylated counterparts and poly(azodibenzo-18-crown-6-ether)s. When the cloud point was reached, the addition was stopped and the stirring was continued overnight. The samples were then collected by filtration or upon centrifugation. The resulting filtered solution, was then subjected to a subsequent addition of the precipitant. And the procedure was repeated until large addition of the non-solvent did not yield phase separation of the mixture. If a selected fraction had too high polydispersity, the procedure was also repeated. The molecular weight characteristics for the polymers which have been studied are collected in Table 1.

Table 1. *Molecular weight characteristics of the selected polymers.*

Fraction Name	Chains	M _n [g/mol]	M _w [g/mol]	PDI	DP (M _n)	DP (M _w)
A13C4	C4	9000	12000	1.29	13	18
A13C12	C12	14000	20000	1.36	13	18
A19C4	C4	13000	15000	1.24	19	22
A25C12	C12	28000	40000	1.42	25	36
A37C4	C4	25000	39000	1.56	37	57
A35C12	C12	38000	59000	1.56	35	54
AZTEGOMe20	TEGOMe	18000	28000	1.55	15	24
AZTEGOMe10	TEGOMe	10000	15000	1.5	11	13
PADBCE-F1	crown	8000	11500	1.46	18	26
PADBCE-F2	crown	5000	7000	1.38	12	17

3.4 Characterization

All the intermediate reaction products were evaluated by means of ^1H NMR spectroscopy (200 MHz Varian Gemini 2000 NMR or 500 MHz Bruker Avance III) and where applicable by FTIR (PerkinElmer Spectrum One). The final products (monomers and polymers) were also studied by MALDI ToF mass spectrometry (Bruker Microflex equipped with 337 nm N_2 laser) and ^{13}C NMR spectra (500 MHz Bruker Avance III).

The molecular weight characterization of the polymers was done with size exclusion chromatography (Waters instrument equipped with Waters Styragel HR6, HR4 and HR2 columns (7.8x300 mm each), with UV and RI detectors (Waters 2487 UV and 2410 RI). Poly(styrene) standards in THF (Scientific Polymer Products, Inc.) were used as reference for poly(azocalix[4]arene)s and poly(methylmethacrylate) in DMF in the case of poly(azodibenzo-18-crown-6-ether)s (Polymer Standards Service-USA, Inc.).

UV-Vis spectra of all the polymers were recorded on a Shimadzu UV-1601 PC spectrometer. All samples were thermally relaxed prior to measurement to induce highest photo-stationary levels (*trans* content). To study the photo-isomerization, two different irradiation sources were used. The internal xenon lamp of a Fluoromax-4 Spectrofluorometer from HoribaJobin Yvon was used for samples of low polymer concentration. For concentrated samples (as for ^1H NMR relaxation experiments, photo-assisted writing) a High Power fibre-coupled LED, Black-LED-365, from Prizmatix was used.

For light scattering measurements a set up comprising of a Brookhaven Instruments goniometer BIC-200SM, a BIC—TurboCorr digital auto/crosscorrelator, a BIC-CrossCorr detector combining two BIC-DSI detectors and a light source of a BIC Mini-L30 diode laser operating at 637 nm wavelength was used.

Host-guest interactions were evaluated by means of ^1H NMR, 2D NOESY, as well as UV-Vis spectroscopy.

All turbidity measurements were performed on a JASCO J-815 CD spectrometer, the temperature range dependent on the sample and with varying the heating and cooling rates, where applicable.

4 Results and Discussion

4.1 Synthesis of monomers (*Papers I, III and IV*)

The availability of two sites for modification (the upper and the lower rim) which utilize different chemical reactions makes calixarenes a great candidate for derivatization. The key synthetic factors in the design of our calix[4]arene-based systems, included the locking of the cone conformation, whilst maintaining specific location of functional groups in the upper rim (5,17-positions, Fig. 9).

Fig. 9 *Structure of 25,26,27,28-tetrahydroxycalix[4]arene.*

In order to achieve this, different synthetic strategies needed to be explored (Fig. 10). Electrophilic substitution of a 25,26,27,28-tetrahydroxycalix[4]arene, may lead to complete substitution on all four aromatic rings and despite stoichiometric control, a mixture of products will be obtained resulting in low yields. The diametrical placement of functional groups (in our case – nitro groups in the 5,17-positions) may be achieved by selective etherification/esterification of the lower rim. By using potassium carbonate in acetonitrile and controlling the stoichiometry, the etherification proceeds in 25,27-positions. As a result, the remaining unsubstituted phenolic rings (26,28-positions) have a higher reactivity towards electrophilic substitution reactions and nitration yields a 5,17-dinitrocalix[4]arene with substituents in 25,27-positions in the lower rim. This calix[4]arene is still conformationally flexible and derivatization of the 26,28-positions would be desired to lock the conformation. As was mentioned earlier, the interconversion between the 4 different conformations of calix[4]arenes (Fig. 5) is possible and the preferred conformation is governed by the choice of solvent, temperature and substituents in the upper rim. Locking of the *cone* conformation occurs when that particular structure is favoured in solution. The nitro groups present in a diametrically (25,27-positions) substituted calix[4]arene distort the *cone* conformation and the presence of bulky substituents results in yield loss. To enhance the synthesis yields, a new synthetic route was studied.

Several groups have reported on successful *ipso* nitration of tert-butylcalix[4]arene derivatives. The tert-butyl groups are less prone to distortion of conformation in the final locking step. Once again, relying on the difference in reactivities of substituted and unsubstituted phenols, the pathway involved the benzylation of diametrical 26,28-positions of a tert-butylcalix[4]arene (parent compound). The reversed Friedel Crafts on the product yielded the removal of tert-butyl groups from 11,23-positions, while retaining the functionalities in 5,17-positions. Benzoyl groups are easily removed by base (sodium hydroxide) hydrolysis. The obtained 5,17-di(tert)butylcalix[4]arene is then subjected to etherification reactions with 1-bromoalkyl chains and *cone* conformers may be prepared in relatively high yield. However, in the case of the tegylated calix[4]arenes, direct reaction with mesylated tetraethyleneglycol monomethyl ether, leads to a mixture of conformers. The introduction of a spacer by means of reaction with ethyl bromoacetate and subsequent hydrolysis towards 2-hydroxyethoxy derivative allows for locking of the *cone* conformation. Thus, the tegylation reaction that follows does not influence the conformation. The *ipso* nitration that takes place in the next step follows a colour change (purple to dark yellow), which allows for easy depiction of the end of the reaction and thus translates to high nitration yields. The alkylated calixarenes were isolated (Fig. 11a-b) upon crystallization from 2-propanol and the tegylated species (Fig. 11c) were subjected to column chromatography (10% methanol in chloroform).

Fig. 10 Strategies for selective nitration of calix[4]arenes; (a) nitration on unsubstituted phenols. (b) *ipso* nitration on substituted tert-butylcalix[4]arene derivatives.

The preparation of dinitrodibenzo-18-crown-6-ethers (Fig. 11d) was done according to known literature procedures by means of nitric and acetic acid in chloroform. The separation of the 4',4''- and 4',5''- species (Scheme 4) proceeds *via* precipitation of the first early on in the reaction and the 4',5''-counterpart remains in the reaction mixture. The ^1H NMR spectra do not discern the difference, but the differentiating parameter is their melting point.

Fig. 11 ^1H NMR spectra of (a) cone 5,17-dinitrocalix[4]arene with *n*-butyl chains, (b) *n*-dodecyl chains, (c) tetraethyleneglycol monomethyl ether chains in CDCl_3 and (d) magnification of ^1H NMR spectrum of 4',4''-dinitrodibenzo-18-crown-6-ether in $\text{DMSO}-d_6$.

4.2 Polymerization (*Papers I, III and IV*)

In the early stages of the study, trial reactions on the reductive coupling of 5,17-dinitrocalixarenes using lithium aluminium hydride as the coupling agent showed potential in the preparation of the azopolymers. However the molecular weight obtained was indicative of only short oligomers being formed ($n < 10$), which meant that optimising the conditions was necessary. A series of polymerizations in which the concentration, solvent and temperature were varied (*Paper I, ESI, Table S1*), showed that best results are obtained for concentrated conditions in which diethyl ether is used with minimal amount of THF at room temperature. In all cases, short oligomers were formed, leading us to believe that the end groups may be unreactive in the coupling conditions. FTIR measurements of the oligomers showed disappearance of strong Ar-NO₂ signals at 1524, 1347, and 745 cm⁻¹. If we consider the possible pathways (Fig.12) of reduction and the coupling towards azo-formation, we see that the nonreactive group would be the amino functionality. If the reduction towards the amine proceeds faster than the dimerization of nitroso groups, coupling of nitrosobenzene (15) and phenylhydroxylamine (16) or nitrosobenzene and aniline (17), then the preparation of short oligomers may be expected.

Fig. 12 Possible reduction of nitrobenzene (14) to aniline (17) and azobenzene (18).

Two different procedures for oxidative coupling of aniline-derivatives were investigated, one employing cetyltrimethylammonium dichromate in chloroform and the other iron(II)sulphate heptahydrate with potassium permanganate in chloroform or dichloromethane. The SEC eluograms of the oligomers prior to and after the reactions (*Paper I, ESI, Fig. S1 and S2*) indicated the development of larger polymers with simultaneous decrease in oligomer content. This strategy however would require a two-

step process and the purification of the polymers and subsequent yield loss would favour a one-step procedure.

Given the difference in reactivity of the lithium aluminium hydride process based on the solvent choice, the partial solubility of the LAH agent was called into question. An industrial stable equivalent of LAH, sodium bis(2-methoxyethoxy)aluminium hydride in toluene, Red-Al was thus used for coupling reactions (Scheme 5). This route allows for more control over the agent, as it is completely soluble in the reaction mixture. When analysing the SEC traces (Fig. 13), larger molecular weight polymers were produced (when referenced to the LAH reactions) though short oligomers were also present in the crude mixtures. Upon precipitation, polymers with DP of 50 could be isolated.

As a general remark, we observed that using low temperature, high concentration and adjusting the coupling agent-to-monomer ratios leads to efficient azo-bridge formation and this resulted in the preparation of main chain azopolymers (*Papers I, III and IV*) in good yields.

Fig. 13 Comparison of SEC traces of 5,17-dinitrocalix[4]arene with butyl chains (black line); crude polymerization reaction (red line) and *n*-butyloxy poly(azocalix[4]arene) precipitate (blue line). Source: Paper I.

The coupling reaction which results in the preparation of polymers is a step growth process and the polymerization mixture contains a broad distribution of molecular weights. A way to overcome this problem would be to fractionate the crude mixtures and thus derive polymers with moderate polydispersity. Preliminary attempts at fractionation of aliphatic poly(azocalix[4]arene)s using methanol from chloroform or membrane dialysis (*Paper II*) proved to be unsuccessful. However, when the polymers were dissolved in a good solvent (THF) and 2-propanol was used as the precipitating agent, the collected fractions for both the n-butoxy and n-dodecyloxy (Fig. 14) poly(azocalix[4]arene)s showed a significant decrease in polydispersity.

Fig. 14 (a): Fractions collected from crude reaction mixture. Monomer, DNcalixC12 (—), Crude reaction, AZ2C12 (—), Fraction 1 (—), 2 (—), 3 (—); (b): Fractions collected from reprecipitation of Fraction 1. Monomer, DNcalixC12 (—), Fraction 1 (—), Precipitate 1 from Fraction 1 (—), 2 (—), 3 (—) from Fraction 1 (Source: *Paper II*).

The same fractionation approach was used for tegylated poly(azocalix[4]arene)s (*Paper III*) and the poly(azodibenzo-18-crown-6-ether)s (*Paper IV*). In both studies, the precipitating solvent was hexane from solutions of the polymers in THF. The molecular weight characteristics of the polymers, which have been studied in Papers I-IV have been collected in Table 1.

Upon fractionation, the polymers were analysed by ^1H NMR spectroscopy (Fig. 15). For all samples, (*Papers I-IV*) the formation of an azo-bridge (proton signal between 7.5-7.85 ppm) could be observed as was a broadening of the signals indicative of reduced mobility, which is characteristic of polymeric systems. In the case of poly(azocalix[4]arene)s (*Papers I-III*), the conformation of the calix[4]arene unit is influenced by the coupling. The *cone* conformation becomes pinched (C_{2v} -symmetry, referenced to monomer) which is evidenced by an upfield shift of the proton signals (6.73 to 6.29 ppm, b to b', Fig. 15) corresponding to the unsubstituted aromatic rings, which are now in closer proximity to each other. This is further supported by an enhanced difference in chemical shifts of the signals corresponding to the methylene bridge (c' and f', Fig. 15).

Fig. 15 Comparison of ^1H NMR spectra in CDCl_3 of monomer, *n*-butoxy 5,17-dinitrocalix[4]arene (above) and *n*-butoxy poly(azocalix[4]arene (below).

4.3 Photo-isomerization (*Papers II- IV*)

Apart from using calix[4]arenes and dibenzo-18-crown-6-ethers as the framework for the polymers, an important feature in the design of these systems is the azo-bridges, which are incorporated into the backbone. The reversible *trans*-to-*cis* photo-isomerization of the linkages could potentially influence the conformation of the polymer and thus translate to other properties which needed to be studied. Low molar mass model azocompounds were prepared to serve as a reference in these investigations (*Papers II- IV*). The polymers were first studied by means of UV-Vis spectroscopy to determine the extent of the photo-isomerization (Fig. 16), which was dependent on the choice of solvent and concentration. Lowest photo-stationary states (PSS) were obtained for solutions of the polymers in THF (Fig. 17).

Fig. 16. Example of photo-isomerization study on tegylated poly(azocalix[4]arene), DP=10 in THF ($c=0.2$ g/L). (a) *trans*-to-*cis* photo-isomerization; (b) *cis*-to-*trans* photo-isomerization; (c) thermal relaxation at 20°C; (d) thermal relaxation at 50°C.

As can be seen from Fig. 17, the dependence of the photo-isomerization on the degree of polymerization is negligible. The model compounds have a higher isomerization rate and reach very low photo-stationary states (photo-induced chemical equilibrium of isomers), indicating that the molecules are predominantly in the *cis* state. The higher values for the polymers, suggest that despite long irradiation times, several (approx. 20%) *trans* bonds are present and the systems are never all *trans* or all *cis*. This may be due to

steric hindrance. When the quality of the solvent is reduced, the PSS levels are proportionally higher.

The *cis*-to-*trans* photo-isomerization also bears the same pattern. Upon irradiation with 450 nm, a plateau region is reached at approximately 85-95% of initial maximum absorption (prior to irradiation), however given enough time (12-24h), the polymers regain their absorption intensity from before irradiation.

The *cis*-to-*trans* isomerization may also be driven by means of thermal relaxation in absence of irradiation, as the *trans* form of the azo-bridge is preferred. The higher the temperature, the faster the isomerization process.

Fig. 17. Comparison of the absorption decays $A_{\max}(t)/A_{\max}(0)$ upon *trans*-to-*cis* photo-isomerization in THF of (a) *n*-butoxy poly(azocalix[4]arene)s; (b) *n*-dodecyloxy poly(azocalix[4]arene)s; (c) tegylated poly(azocalix[4]arene)s and (d) poly(azodibenzo-18-crown-6-ether)s in various solvents.

To further understand the photo-induced transition, ^1H NMR studies were performed to evaluate the structural changes which the molecules undergo upon irradiation/relaxation. Firstly the model compounds (for poly(azodibenzo-18-crown-6-ether)s see *Paper IV, ESI, Fig. S14*) were subjected to irradiation and comparing the spectra in deuterated chloroform prior and post irradiation (Fig. 18) showed differences in chemical shifts characteristic of the azobenzene photo-isomerization.

Fig. 18 ^1H NMR spectrum in CDCl_3 of model compound, MC4, before (red) and after (black) irradiation (Source: Paper II).

The signals at 7.85 ppm (Fig. 18 - a), corresponding to the protons adjacent (*ortho*) to the azo-bridge are shifted upfield to the value of 6.88 ppm. The *meta* protons experience a smaller shift (from 6.98 to 6.76 ppm) as do the signals derived from the aliphatic chain. Both samples contain traces of the other isomer. In a subsequent step, the photo-isomerization of the polymers was evaluated by ^1H NMR (Fig. 19).

Fig. 19 Example of photo-isomerization of poly(azocalix[4]arene)s: ^1H NMR spectrum of A35C12 before (red) and after (black) irradiation (Source: Paper II).

The ^1H NMR spectra of *trans*-rich poly(azocalix[4]arene)s with n-dodecyl chains gives proton signals at 7.92 ppm (*ortho* to azo-bridge, a), and the peak of the unsubstituted aromatic rings (11,23 – positions) of the calixarene moiety at 6.24 ppm (Fig. 19, b). The

large upfield shift of the latter indicates that the opposing aromatic groups are oriented in close proximity to each other, and thus a pinched *cone* conformation of the calixarene unit is proposed¹²⁴. The methylene bridge protons (c and c*) appear at 4.56 and 3.36 ppm.

Upon irradiation, the *ortho*-position a' protons are shifted to 6.92 ppm and the unsubstituted aromatic group signals (Fig. 19, b') are split. Furthermore the methylene bridge protons experience an upfield shift, (4.40 and 3.04 ppm, c' and c*''). And the separation of the methylene bridge protons changes from 1.20 ($\Delta\delta_{c-c^*}$) to 1.36 ($\Delta\delta_{c'-c''}$) ppm. The aliphatic chain protons (d' and e') show a decrease in separation and an upfield shift. These changes in the spectrum led us to believe, that in order to accommodate the *trans*-to-*cis* photo-isomerization, the calixarene units, which still retain a bit of flexibility, adopt a more flattened pinched cone conformation (Fig. 20). This is supported by simultaneous splitting of the 11,23-position proton signals, increase in the separation of the methylene bridge protons ($\Delta\delta_{c'-c''}$), decrease in the separation of the OCH₂ aliphatic protons ($\Delta\delta_{d'-e''}$) and an overall upfield shift.

Fig. 20 Graphic depiction of the flattening of the pinched cone conformation of the calix[4]arene unit in poly(azocalixa[4]arenes upon photo-isomerization.

Additionally to the conformational analysis, the relaxation of the polymers may be followed by ¹H NMR (Paper II, ESI, Fig. S9-S11; Paper III, SI, Fig. S7).

In the case of the poly(azodibenzo-18-crown-6-ether)s, the crown ether unit remains flexible. The structural transition and relaxation (Fig. 21) is evidenced by the proton signals at 7.6, 7.52 and 7.08 ppm for the *trans*-rich polymers, which upon irradiation are shifted to 7.15, 6.7 and 6.4 ppm. The intensity of the crown ether peaks changes, but no upfield shifts are observed.

Fig. 21 Comparison of ^1H NMR spectra of PADBCE-F1 in CDCl_3 (2.5 g/L at 20°C) upon relaxation from (a) *cis* to (j) *trans* state. (b) 0.5 h; (c) 1 h (d) 1.5 h (e) 2 h (f) 3 h (g) 4 h (h) 6 h (i) 8 h from irradiation (Source: Paper IV).

The effect of the transition on the size of the polymers was studied by SEC (Paper II, ESI, Fig. S18; Paper IV, ESI, Fig. S15) and LS (Paper II, ESI, Fig. S19). Samples in THF (poly(azocalix[4]arene)s) and DMF (poly(azodibenzo-18-crown-6-ether)s) in the *trans* and *cis* rich state were prepared and eluograms were recorded with UV-detection set to 365 (or 369) nm to monitor the PSS values upon elution. Only minimal changes in the retention time could be observed, indicating that there is no significant change in the size of the macromolecules upon irradiation. This may be attributed to the relative flexibility of both the calixarene and crown-ether units in the polymers, as well as presence of distortive *trans* bonds. The photo-response can thus be classified as a reversible structural, isomeric change of the azo-bridge, which may influence the conformation of the polymeric units and induce local mobility in the polymer backbone, change the absorption properties but does not translate to a difference in size.

4.4 Host-Guest Interactions (*Papers II- IV*)

The idea behind using calixarenes and crown ethers as the structural components in our polymers was to produce systems capable of host-guest interactions. Both calixarenes and crown ethers have been shown to interact with low molar mass cationic organic guests. In the latter case, the size and denticity of the crown enables complex formation with alkali metal ions.

The advantage of using pyridinium-based low molar mass guests lays in the fact, that the large downfield chemical shifts of the aromatic groups may easily be monitored by ^1H NMR (*Paper V*). Upon complex formation, upfield shift of the proton signals may be observed, indicative of the extent of interaction. In the first studies (*Paper II*) hexadecylpyridinium chloride, C16Py^+ , was used as the guest compound. The chemical shifts of the aromatic ring (H_α , H_β , H_γ) in free solution appear at 9.55, 8.14 and 8.50 ppm (Fig. 22). When the monitoring is done for the H_γ (*para* to the nitrogen atom), titration in the presence of the host polymer, n-butyloxy poly(azocalix[4]arene) results in the evolution of a signal at 8.28 ppm (0.32 ppm difference). Subsequent additions of the guest shift the signals downfield, indicating that the interaction is strong enough to be observed, even in the absence of free hydroxyl groups on the calix[4]arene.

Fig. 22 Magnification of the ^1H NMR spectra (7.7-10 ppm) of the pyridinium-based guest, C16Py^+ upon titration of the host A19C4 in CDCl_3 : (a) A19C4 before addition, (b to i) subsequent additions, and (j) C16Py^+ in the absence of host (Source: *Paper II*).

2D NOESY experiments however did not yield relevant data suggesting a spatially fixed complex of the guest with the host, as the lifetime of the interaction is short compared to the NMR timescale. Diffusion measurements for the guest ($D_G=6.8\times10^{-10}\text{m}^2\text{s}^{-1}$) and host ($D_H=1.54\times10^{-10}\text{m}^2\text{s}^{-1}$) were referenced to the supposed complex ($D_{\text{comp}}=1.58\times10^{-10}\text{m}^2\text{s}^{-1}$) and showed no significant change in the values. The conclusion from these experiments was that the complex is a short lived one, dynamic in terms of the NMR timescale, in which the pyridinium guest ‘senses’ the presence of the calixarene units, but no distinction into bound and free guests can be made.

If the same titration conditions are applied to n-dodecyloxy poly(azocalix[4]arene)s, the guest signals are shifted, but to a smaller extent (Fig. 23a). This is not surprising, as the bulkier dodecyl chains render the cavity of the calixarenes less accessible.

Fig. 23 (a) Comparison of the chemical shifts monitored for H_γ of the pyridinium guest in the absence ($\blacktriangle$) and presence of A19C4 ($\blacksquare$) and A25C12 ($\bullet$) poly(azocalix[4]arene) fractions in CDCl_3 . (b) Chemical shifts monitored for H_γ of the pyridinium guest in the absence ($\blacktriangle$) and presence of the A19C4 poly(azocalix[4]arene) fractions in the trans ($\blacksquare$) and cis form ($\bullet$) in CDCl_3 (Source: Paper II).

Furthermore, if the titration of the polymers is done in the presence of the guest in the *trans* or *cis* rich state, the complex formation is shown to be diminished in the case of the *cis* polymers (Fig 23b). A possible explanation of this decrease in interaction may be the change in the conformation of the calixarene unit upon photo-isomerization. The more flattened pinched *cone* conformation in the *cis* form leads to a weaker interaction with the guest. A following experiment was performed to evaluate the photo-tuning of preformed complexes (Fig. 24). The *trans* rich polymers were complexed with the C16Py⁺ guests, and the chemical shift for the H_α protons of the pyridinium gave a signal at 9.20 ppm. Upon irradiation to the *cis* rich state, the signals were shifted to 9.31 ppm. Relaxation of the samples (70% *trans*/30% *cis* PSS) gave an intermediate value of 9.25 ppm before complete relaxation to the *trans* form and regaining of the 9.20 ppm signal.

Fig. 24 Magnification of the ¹H NMR spectra (7.5-10 ppm) of the pyridinium-based guest, C16Py⁺ (*c*=1.0 mmol/L) upon titration of the host A19C4 (*c*(calix)=3.6 mmol/L) in CDCl₃: (a) *trans* A19C4 before addition, (b) *trans* A19C4 in presence of guest, (c) *cis* A19C4 after irradiation with 365 nm (d) intermediate state A19C4 – 450nm irradiation (e) after irradiation with 450 nm (f) upon thermal relaxation, (g) C16Py⁺ in absence of host (Source: Paper II).

It is noteworthy that the model compound, MC_{azo} (Paper II, ESI, Fig. S20-S23) which was prepared for complexation studies: a 5,17-diazoarylcalix[4]arene with *n*-butyl chains in the lower rim did not show any interaction with the guest in either the *trans* nor the *cis* forms. The reason for this may be the inaccessibility of the cavity as a result of interpenetration of the azoaryl moieties or aggregation.

For the tegylated poly(azocalix[4]arene)s, the guest was exchanged. N-methyl pyridinium iodide, NMPI, was used to maximize the interaction with the cavity, as long tetratethyleneglycol monomethyl ether chains required a less bulky guest than C16Py⁺ for titration experiments. As was the case for the aliphatic poly(azocalix[4]arene)s, the polymers showed large difference in interaction with the guest in the *trans* and the *cis* forms (*Paper III*, Fig. 3).

NMPI was also used to evaluate host-guest interactions by ¹H NMR spectroscopy for poly(azodibenzo-18crown-6-ether)s. The pyridinium aromatic signals (H_α, H_β, H_γ) in free solution (CDCl₃) appear at 9.32, 8.15 and 8.53 ppm. When titration is performed on the solutions containing the *trans*-rich polymers, a large upfield shift of the H_α protons from 9.32 to 8.65 ppm can be observed (Fig. 25). However, no significant change in the interaction can be seen when the titration is done in the presence of *cis* polymers. A significantly weaker interaction is observed for the dimeric model compounds, both in the *trans* and *cis* state. The difference in interaction between the polymers and reference compounds, may indicate that in the case of the polymers, the NMPI guests interact with more than one crown ether unit.

Fig. 25 Comparison of the chemical shifts monitored for H_α of the pyridinium guest in free solution (♦); in the presence of *trans*-rich (●) and *cis*-rich (●) host model compound, MC, and *trans*-rich (▲) and *cis*-rich (▼) host polymer). *c*=6.5 mmol/L as calcd per crown ether unit (Source: *Paper IV*).

We also wanted to study the complex formation of the polymers with alkali metal ions (K⁺ and Ba²⁺). The limited solubility of the KClO₄ salt in common organic solvents led us to focus on the barium counterpart. The UV-Vis spectra of the polymers were recorded before and after addition of the guests. The formed complexes were then

subjected to irradiation and spectra were compared to the photo-isomerization results of the pure polymers. In highly polar DMSO, no shifts of absorption maxima could be observed. For DMF solutions a slight hypsochromic shift for the K^+ and in THF for Ba^{2+} could be observed, no significant effect on photo-isomerization could be deduced. Addition of minimal amount of the barium salt to chloroform solutions of the polymers led to a large 12 nm hypsochromic shift and phase separation of the polymers (*Paper IV, ESI, Fig. S18*). The phase separation could be overcome by addition of more than 15% (v/v) of a cosolvent (acetonitrile). Irradiation of 25% acetonitrile-chloroform solutions demonstrated restricted photo-isomerization behaviour which was diminished in 50% acetonitrile-chloroform (ACN- $CHCl_3$) solutions.

Transmittance measurements (Fig. 26) were done for samples of the polymers and model compounds with NMPI in chloroform and Ba^{2+} in 50% ACN- $CHCl_3$. Addition of a low amount of barium to the polymers results in a rapid precipitation, which is not observable for the dimeric model compounds. Upon exceeding of a 1:2 (guest: host) molar ratio of NMPI to polymer in chloroform, the transmittance in the polymer solution decreases slowly, leading to complete phase separation at higher ratios. No effect of guest addition on the model compound solutions could be observed. The phase separation suggests that upon addition, the ions act as intermolecular crosslinkers for the polymers in these (co)solvent systems.

Fig. 26 Transmittance measurements (600 nm) as a function of added guest.

Incorporating calixarene or crown ether units into the backbone of a polymer results in systems capable of host-guest interactions. Additionally, in the case of poly(azocalix[4]arene)s the extent of the interaction with low molar mass guests may be controlled by photo-isomerization. For crown-ether containing azopolymers, this photo-tuning is absent, but the added guests may act as crosslinkers between the polymers.

4.5 Thermo-responsiveness (*Papers III and IV*)

Recently, poly[oligo(ethylene glycol methyl ether) methacrylate], POEGMA has been shown to undergo LCST-type transitions in water¹²⁵ and UCST-type behaviour in alcohols³³. Building on these studies, we wanted to prepare poly(azocalix[4]arene)s derivatized with tetraethylene glycol monomethyl ether in the lower rim and investigate their thermo-responsiveness in the above mentioned solvents.

The tegylated poly(azocalix[4]arene)s showed temperature-dependent solubilisation in water and alcohols. The aqueous solutions were subjected to turbidity measurements (Fig. 27). At low temperatures the polymers are soluble in water. Upon increase in temperature, phase separation occurs. This LCST-type behaviour is strongly dependent on the degree of polymerization, as only oligomers ($DP < 7$) could be readily solubilized under the applied concentration conditions (1.5 g/L). When the degree of polymerization exceeds 10, the samples are turbid (68% transmittance). Diluting the sample (0.5 g/L) leads to increase in transmittance, however at a cost of broadening of the transition range. A possible way to overcome this decreased solubility for larger polymers, will be to use longer ethylene glycol chains ($n > 4$) in the future. The monomer used in the preparation of the polymers (tegylated 5,17-dinitrocalix[4]arene) is not soluble in water at any temperature.

Fig. 27 Transmittance plots as a function of temperature for aqueous solutions of AZTEGOMe10 ($DP=10$) at $c=0.5$ g/L (—), $c=1.5$ g/L (—) and AZTEGOMe 7($DP<7$) at $c=1.5$ g/L (—) done with a heating rate of $1^{\circ}\text{C}/\text{min}$. Photographic inserts represent the solution of AZTEGOMe7 before (left) and after (right) the LCST phase transition (Source: Paper III).

In a subsequent study, samples of the polymers in alcohols (varying DP, concentration and alcohol) were prepared and investigated for their thermo-responsive properties. At low concentrations (0.5 g/L) only the polymers in 2-propanol showed UCST-type transitions. Increasing the concentration to 1.5 g/L yielded the occurrence of the UCST also for the samples in ethanol and n-propanol. In the case of methanol solutions, the transition takes place at approximately -20°C, which is not in the measuring range of the instrumental set up. This suggests that the longer, branched alcohol chain gives a higher UCST-transition. The demixing temperatures are also strongly dependent on the degree of polymerization and the concentration of the samples (Fig. 28 and Table 2).

Fig. 28 Transmittance vs. temperature plots for samples AZTEGOMe10 and AZTEGOMe20 at different concentration in ethanol done with a cooling rate of 1°C/min (Source: Paper III).

Table 2 Summary of UCST cloud point characteristics of polymer samples AZTEGOMe10 and AZTEGOMe20 in alcohol solutions (Source: Paper III).

Sample	$\overline{DP}$	Solvent	Concentration (g/L)	Cloud Point (°C)
AZTEGOMe10	10	EtOH	1.5	-5
AZTEGOMe10	10	nPrOH	1.5	-5
AZTEGOMe10	10	iPrOH	1.5	27
AZTEGOMe20	20	MeOH	1.5	-20*
AZTEGOMe20	20	EtOH	1.5	7
AZTEGOMe20	20	EtOH	1.8	11
AZTEGOMe20	20	EtOH	2.5	23
AZTEGOMe20	20	nPrOH	1.5	7
AZTEGOMe20	20	iPrOH	1.5	38

* discerned for refrigerated sample

To further understand the transition, LS measurements (Fig. 29) were done on a *trans* AZTEGOME20 (DP=20) polymer in ethanol (2.5 g/L). The sample was equilibrated at each temperature step until intensity of scattered light at 90° angle was constant. For temperatures above UCST, most of the polymers were dissolved on a molecular level (d_h =8-9 nm). Upon reaching the temperature at which the phase separation takes place, the intensity of scattered light increases. However the hydrodynamic diameter, d_h of the particles left in solution decreases, which would indicate that larger species undergo the phase separation prior to the smaller, resulting in a thermally driven fractionation.

Fig. 29 Intensity of scattered light at 90°angle (left axis) and the hydrodynamic diameter (right axis) as function of temperature for solution of *trans*- rich AZTEGOME20 in ethanol ($c=2.5$ g/L) (Source: Paper III).

Irradiation of the polymers in alcohols leads to high photo-stationary states (Paper III, SI, Fig.S15-S18), but the photo-isomerization is nevertheless possible. Inducing lower PSS values was possible when a higher intensity irradiation source was used.

We then wanted to evaluate the influence of the photo-isomerization on the thermo-responsive behaviour of the polymers in alcohols. A sample of the *trans*-rich AZTEGOME20 in ethanol (2.25 g/L) gave a cloud point of 21°C. Upon irradiation at 25°C with 365 nm wavelength, the PSS was determined from UV-Vis spectra and the sample was subjected to turbidity measurements. Interestingly, a decrease in the cloud point temperature could be observed, which was proportional to the decrease in the *trans* content of the sample (Fig. 30-31).

Fig. 30 *Transmittance vs. Temperature plots for AZTEGOMe20 in ethanol ($c=2.5$ g/L) upon irradiation to different photo-stationary states (trans content). Cooling rate = $1^{\circ}\text{C}/\text{min}$.*

Fig. 31 *Plot of the cloud point as a function of photo-induced trans content from measurements done with cooling rate of $1^{\circ}\text{C}/\text{min}$ (Source: Paper III).*

It is noteworthy, that as the photo-isomerization is a reversible process, either by means of irradiation with 450 nm wavelength or *via* thermal relaxation, the observed decrease in cloud point is also reversible. Thus the photo-isomerization becomes a convenient tool for the control and tuning of the UCST.

Irradiation of the polymer alcohol solutions below the UCST (in the phase separated state) also induces photo-isomerization and subsequent decrease in the *trans* content resulting in redissolution of the polymers in the alcohol. When this irradiation is done locally on a suspension of the polymer in a thin 1mm quartz cuvette (Fig. 32), translucent regions corresponding to lower *trans* content could be produced offering us a possibility to write on the liquid samples with the wavelength characteristic of the *trans*-to-*cis* photo-isomerization. As a result of the competing thermal relaxation, the images disappear given enough time (dependent on temperature, concentration, alcohol and irradiation exposure time), in the present case after 2-3 h at 20°C.

Fig. 32 Photographs of AZTEGOMe20 in ethanol ($c=2.5$ g/L) (a) at 20°C before irradiation; (b) after photo-assisted printing at 20°C; (c) at 40°C and (d) at 20°C after thermal relaxation/erasing (Source: Paper III).

In the case of the *trans*-rich polymers, the alternating orientation of the chains along the rigid polymer backbone (Fig. 33) may promote intermolecular interaction between the polymers. Upon photo-isomerization, the orientation of the chains in the *cis*-rich species changes and intermolecular interactions may be favoured. Another explanation may be attributed to changes in polarity of the azo-bridges upon isomerization.

Fig. 33 *Illustration of tegylated poly(azocalix[4]arene)s in the (a) trans and (b) cis form*

When looking at the structure of the poly(azodibenzo-18-crown-6-ether)s, we see that the ethylene oxide units are arranged in a cyclic crown ether moiety which has been joined by azobenzene-derivatives (Fig. 34). Early on in the studies, we could observe that the polymers become soluble in alcohols upon increase in temperature, and thus they demonstrate UCST-type transitions.

Fig. 34 *Structure of poly(azodibenzo-18-crown-6-ether)s*

The thermo-responsive properties were studied for samples with varying degree of polymerization (DP=12 and 18), concentration (0.5, 1 and 2 g/L) and alcohol (methanol, ethanol, 2-propanol). The same polymer fraction (DP=12) at a concentration of 2 g/L gave a cloud point in methanol at 52°C and for ethanol and 2-propanol at 57°C. Much larger dependence of the demixing temperature was observed for concentration change. At 1 g/L the cloud point was shifted to 46°C, which was further reduced to 35°C for 0.5 g/L. A similar dependence was observed when varying the degree of polymerization of the samples in methanol at 0.8 g/L. The UCST-type transitions in the case of poly(azodibenzo-18-crown-6-ether)s can thus be tuned by means of concentration, degree of polymerization and alcohol choice.

Drawing from our previous experience with tegylated poly(azocalixa[4]arene)s, we proceeded to studying the influence of photo-isomerization on the thermal responsiveness of our crown ether azopolymers. A sample of the polymer (DP=18) in methanol (0.8g/L) was kept at 50°C prior to the study to induce the highest possible photo-stationary state. UV-Vis spectra were recorded after each irradiation step and before the consecutive turbidity measurement (Fig. 35). A significant shift of the cloud point from 45°C in the *trans* rich state to 15°C at 35% of the initial *trans* content was observed and the relationship between the demixing temperature and *trans* content was shown to be proportional (Fig. 36). Thermal relaxation back to the *trans* form results in the polymers regaining their cloud point from prior to irradiation within 24h.

Fig. 35 Transmittance vs. temperature plots for PADBCE-F1 in methanol (0.8 g/L) upon irradiation to different photo-stationary state (*trans* content) (Source: Paper IV).

Fig. 36 Plot of the cloud point as a function of photo-induced trans content for PADBCE-F1 in methanol (0.8 g/L) (Source: Paper IV).

Similarly to reports by Roth et al³³, our tegylated poly(azocalix[4]arene)s and poly(azodibenzo-18-crown-6-ether)s showed strong dependence of the cloud point on water content within the alcohol sample. In the first case, minimal addition (0.5% v/v) of water to a polymer fraction AZTEGOMe20 in ethanol (2.5 g/L) resulted in a shift of the demixing temperature by 10°C. Subsequent additions lead to further shifts and for the 98% alcohol solution no cloud point can be detected (*Paper III, SI, Fig. S20*). The strong hydrogen bonding activity of water results in increased solubility of the tegylated units.

The crown ether polymers have a more robust response to changes in water content. The polymer fraction (DP=12) in 100% ethanol (0.5 g/L) gives a cloud point at 26°C. Addition of 2% (v/v) of water to the resulting 98% ethanol solution decreases the demixing temperature to 18°C. Subsequent measurements for 87.5% and 75% samples did not yield a detectable cloud point, however when the alcohol content was further lowered to 62.5%, the UCST reappeared at 11°C. At 50% ethanol: water, the cloud point occurred at 30°C and further decrease of alcohol content (40% and 30%) gave a transition at 50°C and 62°C respectively (Fig. 37). It is noteworthy, that in both polymers, the photo-tuning of the UCST could be observed, when the transition occurred in the measurable range of the instrumental set up. We can thus add another means of controlling the thermo-responsiveness of the polymers by simple adjusting of solvent composition.

Fig. 37 (a) Transmittance vs. temperature plots for PADBCE-F2 (0.5 g/L) in various ethanol: water mixtures. (b) Cloud point temperature vs. ethanol: water content (values for 87,5% and 75% have been estimated from extrapolation) (Source: Paper IV).

In the case of the poly(azodibenzo-18-crown-6-ether)s, the effect of alkali metal addition was also evaluated. Barium ions were added to the alcohol solutions of the polymers and an increase in cloud point could be observed (Fig. 38). At the same time, the extent of photo-tuning of the UCST is decreased upon subsequent additions of the salt. However, the photo-isomerization takes place (*Paper IV*, *ESI*, Fig. S23), which indicates that the diminished photo-tuning of the UCST is a result of strong, yet dynamic interaction with the barium ions rather than restricted photo-isomerization.

Fig. 38 Transmittance vs. temperature plots for PADBCE-F2 (0.5 g/L) in ethanol upon titration with barium ions (Ba^{2+} : polymer = 1:4, 1:1.5 and 4:1) at different PSS (Source: Paper IV).

4.6 Solvatochromism and pH-sensitivity (*Paper IV*)

The azobenzene derivatives in the structure of the poly(azodibenzo-18-crown-6-ether)s act as chromophores which are capable of sensing changes in the environment of the polymer. One of the simplest ways to highlight this property is by looking into the UV-Vis spectra of the free polymers in various solvents. Depending on the polarity of the solvent¹²⁶, different shift of the maximum absorption corresponding to the π - π^* transitions can be observed (Fig. 39a). In DMSO the transition occurs at 373 nm, for DMF that value is shifted to 369 nm, in THF at 365 nm and chloroform at 363 nm.

Changes in the pH of the solutions also generate a spectral output (Fig. 39b). Lowering the pH of the THF solutions of the polymers results in the appearance of an absorption maximum at 530 nm, which is increased upon further addition of acid. This may be attributed to protonation of one of the nitrogen atoms of the azo-bridge¹²⁷. The photo-isomerization on these protonated species could not be induced despite long irradiation times. It is noteworthy, that this pH-sensitivity is valid for all the main chain azopolymers we have prepared.

Fig. 39 (a) UV-Vis spectra of PADBCE-F2 (c=0.08g/L) in different solvents; (b) UV-Vis spectra of PADBCE-F1 (c=0.2 g/L) in THF upon addition of HCl.

5 Conclusions

New main chain azopolymers comprising aliphatic and tegylated calix[4]arenes as well as dibenzo-18-crown-6-ethers have been successfully prepared. The key synthetic steps of locking of the *cone* conformation of the calixarene units, whilst maintaining specific location of functional groups on the upper rim (5,17-positions) of the monomers has been achieved by means of a lower rim substituted, preformed intermediate, 5,17-di(tert)butylcalix[4]arene, which was subjected to *ipso* nitration. The dinitrodibenzo-18-crown-6-ethers have been synthesized according to known literature procedures.

Different polymerization approaches have been examined which involved reductive coupling of nitro-monomers and oxidative coupling of the resulting oligomers. Owing to the enhanced solubility of sodium bis(2-methoxyethoxy) aluminium hydride, Red-Al, over lithium aluminium hydride, larger polymers and better reproducibility of the reaction could be achieved. However, this being a step growth polymerization and as a consequence exhibiting a broad size distribution, all the polymers were further subjected to fractionation to obtain samples with moderate polydispersity.

The reversible *trans*-to-*cis* photo-isomerization was evaluated in different solvent for all polymers. In good solvents, photo-stationary states of 20% *trans* (80% *cis*) could be achieved and when referenced to model azobenzene compounds, the isomerization rate is lower. The structural changes upon irradiation and relaxation could be visualized with ¹H NMR spectroscopy. In the case of the poly(azocalix[4]arene)s, in order to accommodate the structural transition from the *trans* to the *cis* form, the calixarene units adopt a flattened pinched cone conformation.

NMR monitoring of titration of all polymers with pyridinium-based low molar mass compounds showed that a dynamic interaction was possible. For poly(azocalix[4]arene)s, the longer the chain in the lower rim the more hindered the interaction. The extent of the interaction was larger for poly(azodibenzo-18-crown-6-ether)s than the corresponding model dimeric model compounds.

Tegylated poly(azocalix[4]arene)s also exhibited thermo-responsive properties. A lower critical solution temperature (LCS) type transition occurred in water, which was strongly dependent on degree of polymerization and concentration. The same dependence was observed for the upper critical solution (UCST) type transitions of the polymers in alcohols. This behaviour was also dependent on the choice of alcohol as well as water content in the sample. The poly(azodibenzo-18-crown-6-ether)s demonstrated UCST-type demixing in alcohols, governed by concentration, degree of polymerization, alcohol choice and water content. These polymers were further shown to be solvatochromic and pH-sensitive.

The effect of one stimuli-response on the outcome of the other in these multi-stimuli responsive systems was evaluated. Firstly irradiation of the poly(azocalix[4]arene)s with monitoring of host-guest interactions showed a serial interplay in which the photo-stationary state of the polymers determined the extent of the interaction. This photo-tuning was shown to be completely reversible. The *trans*-to-*cis* photo-isomerization also allows for serial control over the UCST-type transitions in alcohols of the tegylated poly(azocalix[4]arene)s and the poly(azodibenzo-18-crown-6-ether)s. The lower the *trans*

content in the sample, the lower the cloud point temperature. This could further be translated onto samples in the phase separated state, resulting in solubilisation of the polymers upon sufficient irradiation. Thermal relaxation will revert the phenomenon.

The influence of alkali metal addition on the UCST behaviour of the crown ether polymers, showed an increase in the cloud point temperature with simultaneous diminishing of the photo-tuning of the UCST. The barium ions act as intermolecular crosslinkers in the system. Furthermore, when these polymers were protonated, the photo-isomerization could not be induced despite long irradiation times.

In conclusion, we have shown how through intricate molecular design different multi-stimuli responsive polymers may be prepared. The serial interplay of the stimuli responses allows for discrete control over the remaining stimuli-derived effects and thus results in the possibility to produce systems which respond differently under various changes in the environment. This work may hence contribute to better understanding and design of smart materials.

6 References

- 1 Matyjaszewski, K.; Spanswick, J. *Materials Today* **2005**, 8, 26.
- 2 (a) Binder, W. H.; Sachsenhofer, R. *Macromol. Rapid Commun* **2007**, 28, 15 (b) Binder, W. H.; Sachsenhofer, R. *Macromol. Rapid Commun* **2008**, 29, 952.
- 3 Lowe, A. B. *Polym. Chem.* **2010**, 1, 17.
- 4 Lowe, A. B.; Hoyle, C. E.; Bowman, C. N. *J. Mater. Chem.* **2010**, 20, 4745.
- 5 Tasdelen, M. A. *Polym. Chem.* **2011**, 2, 2133.
- 6 Bosworth, J. K.; Ober, C. K. In *Polymer Science: A Comprehensive Reference*; Matyjaszewski, K., Möller, M., Eds.; Elsevier: Amsterdam, 2012.
- 7 Henderson, C. L. In *Polymer Science: A Comprehensive Reference*; Matyjaszewski, K., Möller, M., Eds.; Elsevier: Amsterdam, 2012.
- 8 Gurr, M.; Mülhaupt, R. In *Polymer Science: A Comprehensive Reference*; Matyjaszewski, K., Möller, M., Eds.; Elsevier: Amsterdam, 2012.
- 9 Perelaer, J.; Schubert, U. S. In *Polymer Science: A Comprehensive Reference*; Matyjaszewski, K., Möller, M., Eds.; Elsevier: Amsterdam, 2012.
- 10 Kroto, H. W.; Heath, J. R.; O'Brien, S. C.; Curl, R. F.; Smalley, R. E. *Nature* **1985**, 318, 162.
- 11 De Volder, M. F. L.; Tawfick, S. H.; Baughman, R. H.; Hart, A. J. *Science* **2013**, 339, 535.
- 12 Bonaccorso, F.; Sun, Z.; Hasan, T.; Ferrari, A. C. *Nat Photon* **2010**, 4, 611.
- 13 Robeson, L. M. In *Polymer Science: A Comprehensive Reference*; Matyjaszewski, K., Möller, M., Eds.; Elsevier: Amsterdam, 2012.
- 14 Pocius, A. V. In *Polymer Science: A Comprehensive Reference*; Matyjaszewski, K., Möller, M., Eds.; Elsevier: Amsterdam, 2012.
- 15 Koike, Y.; Koike, K. In *Polymer Science: A Comprehensive Reference*; Matyjaszewski, K., Möller, M., Eds.; Elsevier: Amsterdam, 2012.
- 16 Grothe, J.; Kaskel, S.; Leuteritz, A. In *Polymer Science: A Comprehensive Reference*; Matyjaszewski, K., Möller, M., Eds.; Elsevier: Amsterdam, 2012.
- 17 Stuart, M. A. C.; Huck, W. T. S.; Genzer, J.; Muller, M.; Ober, C.; Stamm, M.; Sukhorukov, G. B.; Szleifer, I.; Tsukruk, V. V.; Urban, M.; Winnik, F.; Zauscher, S.; Luzinov, I.; Minko, S. *Nat. Mater.* **2010**, 9, 101.
- 18 (a) Roy, D.; Cambre, J.N.; Sumerlin, B.S. *Prog. Pol. Sci.* 2010, 35, 278. (b) Kumar, A.; Srivastava, A.; Galaev, I.Y.; Mattiasson, B. *Prog. Pol. Sci.* **2007**, 32, 1205. (c) Stuart, M.A.C.; Huck, W.T.S.; Genzer, J.; Muller, M.; Ober, C.; Stamm, M.; Sukhorukov, G.B.; Szleifer, I.; Tsukruk, V.V.; Urban, M.; Winnik, F.; Zauscher, S.; Luzinov, I.; Minko, S. *Nat. Mater.* **2010**, 9, 101. (d) Plamper, F.; Schmalz, A.; Ballauff, M.; Müller, A. *J. Am. Chem. Soc.* **2007**, 129, 47, 14538. (e) Liu, F.; Urban, M. W. *Prog. Polym.Sci.* **2010**, 35, 3.
- 19 D.Kuckling, A.Doering, F.Krahl, and K-F Arndt in *Polymer Science: A Comprehensive Reference, Volume 8: Polymers for Advanced Functional Materials*, Elsevier, **2012**, 377-415.
- 20 Schild, H. G. *Prog. Pol. Sci.* **1992**, 17, 163-249.
- 21 Aseyev, V.; Tenhu H.; Winnik, F., *Adv. Pol. Sci.* **2011**, 1.

- 22 (a) Hoogenboom, R.; Thijs, H. M. L.; Jochems, M. J. H. C.; van Lankvelt, B. M.; Fijten, M. W. M.; Schubert, U. S. *Chem. Comm.* **2008**, 5758. (b) Lutz, J.-F.; Akdemir, Ö.; Hoth, A. *J. Am. Chem. Soc.* **2006**, *128*, 13046.
- 23 Katsumoto, Y.; Kubosaki, N.; *Macromolecules*, **2008**, *41*, 5955
- 24 (a) Feil, H.; Bae, Y. H.; Feijen J. and Kim, S. W. *Macromolecules* **1993**, *26*, 2496-2500. (b) Lutz, J.-F., *J. Polym. Sci. Part A: Polym. Chem.* **2008**, *46*, 3459.
- 25 Zhang, Y.; Furyk, S.; Bergbreiter D. E. and Cremer, P. S. *J. Am. Chem. Soc.* **2005**, *127*, 14505.
- 26 Hoogenboom, R.; Thijs, H. M. L.; Wouters, D.; Hoeppener, S.; Schubert, U. S. *Soft Matter* **2008**, *4*, 103.
- 27 Seuring, J.; Agarwal, S. *Macromol. Rapid Commun.* **2012**, *33*, 1898
- 28 (a) Seuring, J.; Agarwal, S. *ACS Macro Lett.* **2013**, *2*, 597.
(b) Seuring, J.; Agarwal, S. *Macromolecules* **2012**, *45*, 3910.
- 29 Shimada, N.; Ino, H.; Maie, K.; Nakayama, M.; Kano, A.; Maruyama, A. *Biomacromolecules* **2011**, *12*, 3418.
- 30 Meiswinkel, G.; Ritter, H. *Macromol. Rapid Commun.* **2013**, *34*, 1026.
- 31 (a) Pietsch, C.; Hoogenboom, R.; Schubert, U. S. *Polym. Chem.* **2010**, *1*, 1005. (b) Zhang, Q.; Schattling, P.; Theato, P.; Hoogenboom, R. *Polym. Chem.* **2012**, *3*, 1418.
- 32 Hoogenboom, R.; Lambermont-Thijs, H. M. L.; Jochems, M. J. H. C.; Hoeppener, S.; Guerlain, C.; Fustin, C.-A.; Gohy, J.-F.; Schubert, U. S. *Soft Matter* **2009**, *5*, 3590.
- 33 Roth, P. J.; Jochum, F. D.; Theato, P. *Soft Matter* **2011**, *7*, 2484.
- 34 (a) Pietsch, C.; Mansfeld, U.; Guerrero-Sanchez, C. ; Hoeppener, S. ; Vollrath, A.; Wagner, M. ; Hoogenboom, R. ; Saubern, S. ; Thang, S. H. ; Becer, C. R. ; Chiefari J.; Schubert, U. S., *Macromolecules* **2012**, *45*, 9292 (b) Cheng, C. ; Schmidt, M. ; Zhang A. ; Schlüter, A. D., *Macromolecules* **2007**, *40*, 220 (c) Tang X. , Pan, C.-Y., *J. Biomed. Mater. Res., Part A* **2008**, *86*, 428 (d) Roth, P. J.; Davis T. P.; Lowe, A. B., *Macromolecules* **2012**, *45*, 3221 (e) Yuen F.; Tam, K. C.; *J. Appl. Polym. Sci.* **2013**, *127*, 4785.
- 35 Arotçaréna, M. ; Heise, B. ; Ishaya S. ; Laschewsky, A., *J. Am. Chem. Soc.* **2002**, *124*, 3787
- 36 Longenecker, R.; Mu, T.; Hanna, M. ; Burke N. A. D. ; Stöver, H. D. H., *Macromolecules* **2011**, *44*, 8962.
- 37 Weiss, J.; Laschewsky, A. *Langmuir* **2011**, *27*, 4465.
- 38 Klouda, L.; Mikos, A. G. *European J. Pharm. Biopharm.* **2008**, *68*, 34.
- 39 Lyon, L. A.; Meng, Z.; Singh, N.; Sorrell, C. D.; St. John, A. *Chem. Soc. Rev.* **2009**, *38*, 865.
- 40 Yakushiji, T.; Sakai, K.; Kikuchi, A.; Aoyagi, T.; Sakurai, Y.; Okano, T. *Langmuir* **1998**, *14*, 4657.
- 41 Rapoport, N. *Prog. Polym. Sci.* **2007**, *32*, 962.
- 42 Xu, F. J.; Li, J.; Yuan, S. J.; Zhang, Z. X.; Kang, E. T.; Neoh, K. G. *Biomacromolecules* **2007**, *9*, 331.
- 43 (a) Brun-Graeppe, A. K. A. S.; Richard, C.; Bessodes, M.; Scherman, D.; Merten, O.-W. *Prog. Polym. Sci.* **2010**, *35*, 1311. (b) da Silva, R. M. P.; Mano, J. F.; Reis, R. L. *Trends in Biotechnology* **2007**, *25*, 577.

- 44 Russew, M.-M.; Hecht, S. *Adv. Mater.* **2010**, *22*, 3348.
- 45 (a) Enkelmann, V.; Wegner, G.; Novak, K.; Wagener, K. B. *J. Am. Chem. Soc.* **1993**, *115*, 10390. (b) Nakayama, Y.; Matsuda, T. *Polym. Sci. Part A: Polym. Chem.* **1992**, *30*, 2451. (c) Shi, D.; Matsusaki, M.; Akashi, M. *Bioconj. Chem.* **2009**, *20*, 1917.
- 46 Jiang, J.; Qi, B.; Lepage, M.; Zhao, Y. *Macromolecules* **2007**, *40*, 790.
- 47 Vo, C. D.; Kuckling, D.; Adler, H. J. P.; Schönhoff, M. *Colloid Polym. Sci.* **2002**, *280*, 400.
- 48 Bandara, H. M. D.; Burdette, S. C. *Chem. Soc. Rev.* **2012**, *41*, 1809.
- 49 Yager K. G. ; Barrett, C. J. in *Smart Light-Responsive Materials*, John Wiley & Sons, Inc., **2008**, 1-46.
- 50 Natansohn, A.; Rochon, P. *Chem. Rev.* **2002**, *102* , 4139.
- 51 (a) Xue, X.; Zhu, J. ; Zhang, Z.; Zhou, N.; Tu Y.; Zhu, X.; *Macromolecules* **2010**, *43*, 2704. (b) Izumi, A. ; Nomura, R. ; Masuda, T.; *Macromolecules* **2001**, *34*, 4342.
- 52 Zhao Y.; He. J., *Soft Matter* **2009**, *5*, 2686.
- 53 Zhao, Y. *J. Mater. Chem.* **2009**, *19*, 4887.
- 54 (a) Nardele, C. G.; Asha, S. K. *J. Phys. Chem. B* **2014**, *118*, 1670. (b) Shi, Z.; Lu, H.; Chen, Z.; Cheng, R.; Chen, D. *Polymer* **2012**, *53*, 359. (c) Nguyen, T.-T.-T.; Türp, D.; Wang, D.; Nölscher, B.; Laquai, F.; Müllen, K. *J. Am. Chem. Soc.* **2011**, *133*, 11194. (d) Hernández-Ainsa, S.; Alcalá, R.; Barberá, J. n.; Marcos, M.; Sánchez, C.; Serrano, J. L. *Macromolecules* **2010**, *43*, 2660.
- 55 Wang, D.; Wang, X. *Prog. Polym. Sci.* **2013**, *38*, 271.
- 56 Bléger, D.; Liebig, T.; Thiermann, R. ; Maskos, M. ; Rabe, J. P. ; Hecht, S. ; *Angew. Chem. Int. Ed.* **2011**, *50*, 12559.
- 57 Howley, C.; Marangoni, D. G.; Kwak, J. C. T. *Colloid Polym. Sci.* **1997**, *275*, 760.
- 58 Ivanov, A. E.; Ereemeev, N. L.; Wahlund, P. O.; Galaev, I. Y.; Mattiasson, B. *Polymer* **2002**, *43*, 3819.
- 59 Dai, S.; Ravi, P.; Tam, K.C. *Soft Matter* **2008**, *4*, 435
- 60 Gil, E. S.; Hudson, S. M. *Prog. Polym. Sci.* **2004**, *29*, 1173.
- 61 Roy, D.; Cambre, J. N.; Sumerlin, B. S. *Prog. Polym. Sci.* **2010**, *35*, 27
- 62 Huo, M.; Yuan, J.; Tao, L.; Wei, Y. *Polym. Chem.* **2014**, *5*, 1519.
- 63 Lanzo, J.; Nicoletta, F. P.; De Filpo, G.; Chidichimo, G. *J. Appl. Phys.* **2002**, *92*, 4271.
- 64 Zrínyi, M. *Colloid Polym. Sci.* **2000**, *278*, 98.
- 65 (a) Lin, S.; Theato, P. *Macromol. Rapid Commun.* **2013**, *34*, 1118. (b) Quek, J. Y.; Roth, P. J.; Evans, R. A.; Davis, T. P.; Lowe, A. B. *J. Polym. Sci. Part A: Polym. Chem.* **2013**, *51*, 394. (c) Yan, Q.; Zhou, R.; Fu, C.; Zhang, H.; Yin, Y.; Yuan, J. *Angew. Chem. Int. Ed.* **2011**, *50*, 4923. (d) Han, D.; Tong, X.; Boissière, O.; Zhao, Y. *ACS Macro Lett.* **2011**, *1*, 57. (e) Guo, Z.; Feng, Y.; He, S.; Qu, M.; Chen, H.; Liu, H.; Wu, Y.; Wang, Y. *Adv. Mater.* **2013**, *25*, 584.
- 66 (a) Pasparakis, G.; Vamvakaki, M.; Krasnogor, N.; Alexander, C. *Soft Matter* **2009**, *5*, 3839. (b) Traitel, T.; Cohen, Y.; Kost, J. *Biomaterials* **2000**, *21*, 1679. (c) Vancoillie, G.; Pelz, S.; Holder, E.; Hoogenboom, R. *Polym. Chem.* **2012**, *3*, 1726.
- 67 Masaki, N.; Yoshinori, T.; Hiroyasu, Y.; Akira, H. *Nature Comm.* **2011**, *2*, 511.
- 68 Schattling, P.; Jochum, F. D.; Theato, P. *Polym. Chem.* **2014**, *5*, 25.
- 69 Jochum, F. D.; Theato, P. *Chem. Soc. Rev.* **2013**, *42*, 7468.
- 70 Kungwachakun, D.; Irie, M. *Makromol. Chem., Rapid Commun.* **1988**, *9*, 243–246.

- 71 Akiyama, H.; Tamaoki, N. *J. Polym. Sci. Part A: Polym. Chem.* **2004**, 42, 5200.
- 72 Akiyama, H.; Tamaoki, N. *Macromolecules* **2007**, 40, 5129.
- 73 (a) Kroger, R.; Menzel, H.; Hallensleben, M. L. *Macromol. Chem. Phys.* **1994**, 195, 2291–2298. (b) Menzel, H.; Kroger, R.; Hallensleben, M. L. *Macromol. Rep.* **1995**, A32, 779–787. (c) Desponds, A.; Freitag, R. *Langmuir* **2003**, 19, 6261. (d) F. D. Jochum and P. Theato, *Polymer*, 2009, 50, 3079–3085 (e) Jochum, F. D.; zur Borg, L.; Roth, P. J.; Theato, P. *Macromolecules* **2009**, 42, 7854. (f) Lee, H.-i.; Pietrasik, J. Matyjaszewski, K., *Macromolecules* **2006**, 39, 3914 (g) Ishii, N.; Mamiya, J.-i.; Ikeda T.; Winnik, F. M., *Chem. Commun.* **2011**, 47, 1267 (h) Ueki, T.; Yamaguchi, A.; Ito, N.; Kodama, K.; Sakamoto, J.; Ueno, K.; Kokubo H.; Watanabe, M., *Langmuir* **2009**, 25, 8845 (i) Ogoshi, T., Kida, K., Yamagishi, T.-a. *J. Am. Chem. Soc.* **2012**, 134, 20146.
- 74 Ueki, T.; Nakamura, Y.; Yamaguchi, A.; Niitsuma, K.; Lodge, T. P.; Watanabe, M. *Macromolecules* **2011**, 44, 6908.
- 75 Bütün, V.; Armes, S. P.; Billingham, N. C., *Polymer*, **2001**, 42, 5993.
- 76 (a) Ma, L.; Liu, R.; Tan, J.; Wang, D.; Jin, X.; Kang, H. ; Wu, M. ; Huang, Y., *Langmuir* **2010**, 26, 8697.
(b) Mao, J.; Bo S.; Ji, X., *Langmuir* **2011**, 27, 7385.
(c) Plamper, F. A.; Steinschulte, A. A.; Hofmann, C. H.; Drude, N.; Mergel, O.; Herbert, C.; Erberich, M.; Schulte, B.; Winter R.; Richtering, W., *Macromolecules* **2012**, 45, 8021. (d) Niskanen, J.; Wu, C.; Ostrowski, M.; Fuller, G. G.; Hietala, S.; Tenhu, H.; *Macromolecules* **2013**, 46, 2331. (e) Zhang, B.-Y.; He, W.-D.; Li, W.-T.; Li, L.-Y.; Zhang, K.-R.; Zhang, H. *Polymer* **2010**, 51, 3039. (f) Liu, Y.; Cao, X.; Luo, M.; Le, Z.; Xu, W. *J. Colloid Interf. Sci.* **2009**, 329, 244. (g) Liu, F.; Urban, M. W. *Macromolecules* **2008**, 41, 6531. (h) Zhang, Q.; Hong, J.-D.; Hoogenboom, R. *Polym. Chem.* **2013**, 4, 4322.
- 77 Jung, S.-H.; Song, H.-Y.; Lee, Y.; Jeong, H. M.; Lee, H.-i., *Macromolecules* **2011**, 44, 1628.
- 78 (a) Schilli, C. M.; Zhang, M.; Rizzardo, E.; Thang, S. H.; Chong, Y. K.; Edwards, K.; Karlsson, G.; Müller, A. H. E. *Macromolecules* **2004**, 37, 7861. (b) Mu, B.; Liu, P. *React. Funct. Polym.* **2012**, 72, 983.
- 79 Mano, J. F. *Adv. Eng. Mater.* **2008**, 10, 515.
- 80 Kuramoto, N.; Shishido, Y.; Nagai, K. *J. Polym. Sci. Part A: Polym. Chem.* **1997**, 35, 1967.
- 81 (a) Phillips, D. J.; Gibson, M. I. *Chem. Comm.* **2012**, 48, 1054.
(b) Chan, N.; An, S. Y.; Yee, N.; Oh, J. K. *Macromol. Rapid Commun.* **2014**, n/a.
- 82 (a) Tang, X.; Liang, X.; Gao, L.; Fan, X.; Zhou, Q. *J. Polym. Sci. Part A: Polym. Chem.* **2010**, 48, 2564. (b)
- 83 Sumaru, K.; Kameda, M.; Kanamori, T.; Shinbo, T. *Macromolecules* **2004**, 37, 4949.
- 84 Achilleos D. S.; Vamvakaki, M.; *Macromolecules* **2010**, 43, 7073.
- 85 Plamper, F. A.; Schmalz, A.; Müller, A. H. E.; *J. Am. Chem. Soc.* **2007**, 129, 14538.
- 86 Klaiherd, A.; Nagamani, C.; Thayumanavan, S. *J. Am. Chem. Soc.* **2009**, 131, 4830.
- 87 Schattling, P.; Jochum, F. D.; Theato, P. *Chem. Comm.* **2011**, 47, 8859.

- 88 Wang, L.; Liu, M.; Gao, C.; Ma, L.; Cui, D. *React. Funct. Polym.* **2010**, *70*, 159.
- 89 Callahan, D. J.; Liu, W.; Li, X.; Dreher, M. R.; Hassounh, W.; Kim, M.; Marszalek, P.; Chilkoti, A. *Nano Letters* **2012**, *12*, 2165.
- 90 (a) Gutsche, C.D. "Calixarenes", 1989, Royal Society of Chemistry.
(b) Manodolini, L.; Ungaro, R. "Calixarenes in action", 2000, Imperial College Press.
(c) Sliwa, W.; Kozłowski, C.; "Calixarenes and Resorcinarenes", 2009, Wiley-VCH.
- 91 Gutsche, C. D.; Muthukrishnan, R., *J.Org.Chem.* **1978**, *43*, 4905.
- 92 Andreotti, G.D.; Ungaro, R.; Pochini, A.; *J.Chem. Soc., Chem. Commun.* **1979**, 1005.
- 93 Gutsche C. D.; Bauer, L. J.; *J.Am.Chem.Soc.* **1985**, *107*, 6052.
- 94 Moran, J. R.; Karch, S.; Cram, D. J.; *J. Am. Chem. Soc.* **1982**, *104*, 5826.
- 95 (a) Ishikawa, Y.; Kunitake, T.; Otsuka, T.; Shinkai, S.; *J. Chem. Soc., Chem. Commun.* **1989**, 736. (b) Mandolini, L.; Ungaro, R. In 'Calixarenes in action'; A.Casnati; R.Ungaro, Imperial College Press, London, **2000**, p.62
- 96 Wieser, C.; Dieleman, C.B.; Matt, D., *Coordination Chem. Rev.* **1997**, *165*, 93.
- 97 (a) Ishihara, S.; Takeoka, S.; *Tetrahedron Lett.*, **2006**, *47*, 181 (b) Ciesa, F.; Plech, A.; Mattioli, C.; Pescatori, L.; Arduini, A.; Pochini, A.; Rossi, F.; Secchi, A.; *J. Phys. Chem. C*, **2010**, *114*, 13601 (c) Pescatori, L.; Arduini, A.; Pochini, A.; Rossi, F.; Secchi, A.; Massera C., Ugozzoli, F., *Org. Biomol. Chem.* **2009**, *7*, 3698. (d) Pulkkinen, P.; Wiktorowicz, S.; Aseyev, V.; Tenhu, H., *RSC Advances*, **2013**, *3*, 733
- 98 Fujimoto, T; Shimizu, C; Hayashida, O.; Aoyama, Y., *J. Am. Chem. Soc.*, **1997**, *119*, 6676.
- 99 Sansone, F.; Baldini, L.; Casnati, A. Ungaro, R., *New J. Chem.* **2010**, *34*, 2715.
- 100 Homden, D. M.; Redshaw, C. *Chem. Rev.* **2008**, *108*, 5086.
- 101 de Fatima, A.; Fernandes, S. A.; Sabino, A. A. *Current Drug Discovery Technologies* **2009**, *6*, 151.
- 102 (a) Barata, P. c. D.; Costa, A. I.; Granja, P.; Prata, J. V. *React. Funct. Polym.* **2004**, *61*, 147. (b) Deligöz, H.; Yilmaz, M. *J. Polym. Sci. Part A: Polym.Chem.* **1995**, *33*, 2851. (c) Memon, S.; Akceylan, E.; Sap, B.; Tabakci, M.; Roundhill, D. M.; Yilmaz, M. *J.Polym & Env.* **2003**, *11*, 67.
- 103 Barata P.D.; Costa,A.I.; Ferreira, L.F.; Prata, J.V.; *J.Pol.Sci. A:Pol. Chem.* **2010**, *48*, 22, 5040..
- 104 (a) Yang, Y., Swager, T. *Macromolecules* **2006**, *39*, 2013
(b) Yang, Y., Swager, T. *Macromolecules* **2007**, *40*, 7437.
- 105 (a) Angot, S; Murthy, K. S; Taton, D; Gnanou, Y.; *Macromolecules* **1998**, *31*, 7218
(b) Angot, S; Murthy, K. S; Taton, D; Gnanou, Y.; *Macromolecules* **2000**, *33*, 7261
- 106 (a) Baklouti, L.; Cheriaa, N.; Mahouachi, M.; Abidi, R.; Kim, J. S.; Kim, Y.; Vicens, J. *J Incl Phenom Macrocycl. Chem.* **2006**, *54*, 1. (b) Lalor, R.; Gunning, A. P.; Morris, V. J.; Matthews, S. E. *Chem. Comm.* **2010**, *46*, 8665.
- 107 (a) Yu, H-h; Xu, B.; Swager, T.M.; *J.Am.Chem.Soc.* **2003**, *125*, 1142; (b) Yu, H-h.; Pullen, A.E.; Büschel, M.G; Swager, T.M.; *Angew. Chem. Int. Ed.* **2004**, *43*, 3700.

- 108 (a) Deligöz, H.; Ercan, N.; *Tetrahedron* **2002**, 58, 2881 (b) Oueslati, F.; Dumazet-Bonnamour, I.; Lamartine, R.; *Tetrahedron Letters* **2001**, 42, 8177.
- 109 Vögtle, F.; Udelhofen, D.; Abramson, S.; Fuchs, B.; *J. Photochem. Photobiol. A : Chem.* **2000**, 131, 41.
- 110 (a) Ma, Q.; Ma, H.; Su, M.; Wang, Z.; Nie, L.; Liang, S.; *Anal. Chim. Acta*, **2001**, 439, 73.
(b) Chawla H; Singh, S.; Sahu, S.; Upreti, S., *Tetrahedron* **2006**, 62, 7854.
(c) Lu, L.; Zhu, S.; Liu, X.; Xie, Z.; Yan, X.; *Anal. Chim. Acta* **2005**, 535, 183
- 111 (a) Galán, H.; Hennrich, G.; de Mendoza, J.; Prados, P., *Eur. J. Org. Chem.* **2010**, 1249.; (b) Arduini, A.; Pochini, A.; Secchi, A., *Eur. J. Org. Chem.* 2000, 2325. (c) Tilki, T.; Şener, İ. ; Karci, F.; Gülce, A.; Deligöz, H., *Tetrahedron* **2005**, 61, 9624.
- 112 (a) Pedersen, C. J., *J. Am. Chem. Soc.*, **1967**, 89, 7017. (b) Pedersen, C. J.; *J. Am. Chem. Soc.*, **1967**, 89, 2495.
- 113 Cragg P. J. ; Vahora, R. in *Supramolecular Chemistry*, John Wiley & Sons, Ltd, **2012**.
- 114 Gokel, G. W.; Leevy W. M.; Weber, M. E.; *Chem. Rev.* **2004**, 104, 2723.
- 115 Ooi, T.; Maruoka, K. *Angew. Chem. Int. Ed.* **2007**, 46, 4222.
- 116 Tsukube, H.; Yamada, T.; Shinoda, S. *J. Heterocyclic Chem.* **2001**, 38, 1401.
- 117 (a) Mohammadzadeh Kakhki, R.; *J. Incl. Phenom. Macrocycl. Chem.* **2013**, 75, 11.
(b) Cavazzini, A.; Pasti, L.; Massi, A.; Marchetti N.; Dondi, F., *Anal. Chim. Acta* **2011**, 706, 205.
- 118 Hancock, R. D. *J. Chem. Edu.* **1992**, 69, 615.
- 119 Alexandratos S. D.; Stine, C. L.; *React. Funct. Polym.* **2004**, 60, 3.
- 120 Tunca U.; Yagci, Y.; *Prog. Pol. Sci.* **1994**, 19, 233.
- 121 Zheng, B.; Wang, F.; Dong, S.; Huang, F. *Chem. Soc. Rev.* **2012**, 41, 1621.
- 122 Shinkai, S. In *Molecular Switches*; Wiley-VCH Verlag GmbH, **2001**.
- 123 (a) Shinkai, S.; Kinda, H.; Ishihara, M.; and Manabe, O. *J. Pol. Sci: Pol. Chem. Ed.*, 1983, **21**, 3525. (b) Shinkai, S.; Ishihara, M.; Manabe, O. *Polym. J.*, 1985, **17**, 1141. (c) Kimura, K.; Sakamoto, H.; Nakamura, T. *J. Nanosci. Nanotechnol.* 2006, **6**, 1741.
- 124 Struck, O.; Verboom, W.; Smeets, W.J.J.; Spek, A.L.; Reinhoudt, D.N.; *J. Chem. Soc., Perkin Trans.*, **1997**, 2, 223.
- 125 Lutz, J.-F. *J. Polym. Sci. Part A: Polym. Chem.* 2008, **46**, 3459.
- 126 Rusu, E.; Dorohoi, D.-O.; Airinei, A., *J. Mol. Struct.* **2008**, 887, 216.
- 127 Hofmann, K.; Brumm, S.; Mende, C.; Nagel, K.; Seifert, A.; Roth, I.; Schaarschmidt, D.; Lang H.; Spange, S., *New J. Chem.*, **2012**, 36, 1655.