Constitutional Dynamic Chemistry

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Structural and Functional Evolution of a Library of Constitutional Dynamic Polymers Driven by Alkali Metal Ion Recognition**

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Dedicated to Professor C. N. R. Rao on the occasion of his 75th birthday

Adaptive materials, which are capable of responding to physical triggers or chemical effectors by modification of their very constitution, represent an intriguing class of "smart" materials that are of both basic and applied interest. Their development rests on the implementation of constitutional dynamic chemistry (CDC),[1] which is based on the lability of either molecular and supramolecular entities that are derived from the formation of reversible covalent bonds or through noncovalent interactions between their components, respectively. This lability ensures the thermodynamic control of the dynamic libraries of constituents, which are represented by all possible combinations of the components present, as well as the rapid response of such libraries to changes in imposed conditions.[2] Dynamic polymers (dynamers[3]) are constitutionally dynamic polymeric entities based on monomers that are linked through reversible connections at either the molecular or supramolecular levels, and have the capacity to undergo spontaneous and continuous changes in their constitution by exchange, reshuffling, incorporation, and decorporation of their monomeric components. A constitutional dynamic polymer library (CDPL) is expected to have the ability to respond to interacting species or to environmental conditions by shifts in equilibria towards the preferred "fittest" dynamer(s). Thus, the properties that are displayed may evolve in response to a variety of external factors, so that constitutional variation by component exchange in a CDPL offers a basis for a new class of adaptive, "intelligent" materials.

The understanding, design, and control of the folding of molecular strands has attracted great interest in both chemistry and biology.[4–8] In the area of biopolymers, such as double-stranded DNA and proteins, folding is a crucial aspect of the development and expression of specific functions. In materials science, especially polymer science, an understanding of folded forms and of folding processes should enable the design of foldamers on the nanoscale and thus allow for control of macroscopic properties such as electrical and optical features.[5,7]

Herein, we describe the combined adaptation and folding behavior of a CDPL[2,3,4d,6] that is generated by condensation polymerization through the reversible formation of imine bonds. The bond formation occurs between α,ω-diamines and dialdehydes, which are functionalized with various groups that potentially give rise to the supramolecular interactions expected to induce or favor particular folded forms. We show that these dynamic libraries can undergo driven evolution under the double effect of donor–acceptor stacking[7] and metal-ion binding.[8] In the presence of alkali metal ions, the specific binding modes of these metal ions induce an adaptation behavior, which is associated with specific constitutional changes and with different optical characteristics that reflect the presence and the positioning of donor and acceptor units within the folded dynamer.[7,8]

Scheme 1 shows the monomer units used in this study: the diamines AmD and AmSi, the dialdehydes AlA and AlSi, the four different imine links that may form during the polycondensation reaction L1–L4, and the four possible generated dynamers **P1**–**P4**. Key features of the design are the presence of 1) C=N, N, and ether O sites, which are suitable for the binding of alkali metal ions, and 2) electron-rich 1,5-dialkoxynaphthalene and electron-deficient 1,4,5,8-naphthalene-tetracarboxylic diimide units, which can associate by charge-transfer interactions, in the diamines and the dialdehydes, respectively. These groups were chosen as their features are well-documented.[4e,7a,b] Only the dynamer **P3** involves both the donor and acceptor components, which are connected by a heteroatom-containing chain. The chain is capable of binding metal cations and is sufficiently flexible to allow folding, which results in stacking and thus in CT interactions.

The dynamers **P1**–**P4**, which are formed from reversible imine bonds of only one type, were obtained separately by polycondensation of equimolar amounts of the relevant diamine and dialdehyde monomers in $CHCl_3$ in the presence of anhydrous $MgSO_4$. As a prelude to the study of the full CDPL, the folding behavior of dynamer **P3**, which was derived from AmD and AlA, was examined in organic solvents. Addition of the alkali metal salts LiOTf, NaOTf, and KOTf to 3 mM **P3** in an CD_2Cl_2/CD_3CN mixture (8:2) led, in the first two cases, to folding that brought the donor and acceptor units into proximity, as indicated by the correlation of Hb, Hc, and Hd of the donor with Ha of the acceptor in the 2D NOESY ^1H NMR spectrum (Figure S1 (left) in the

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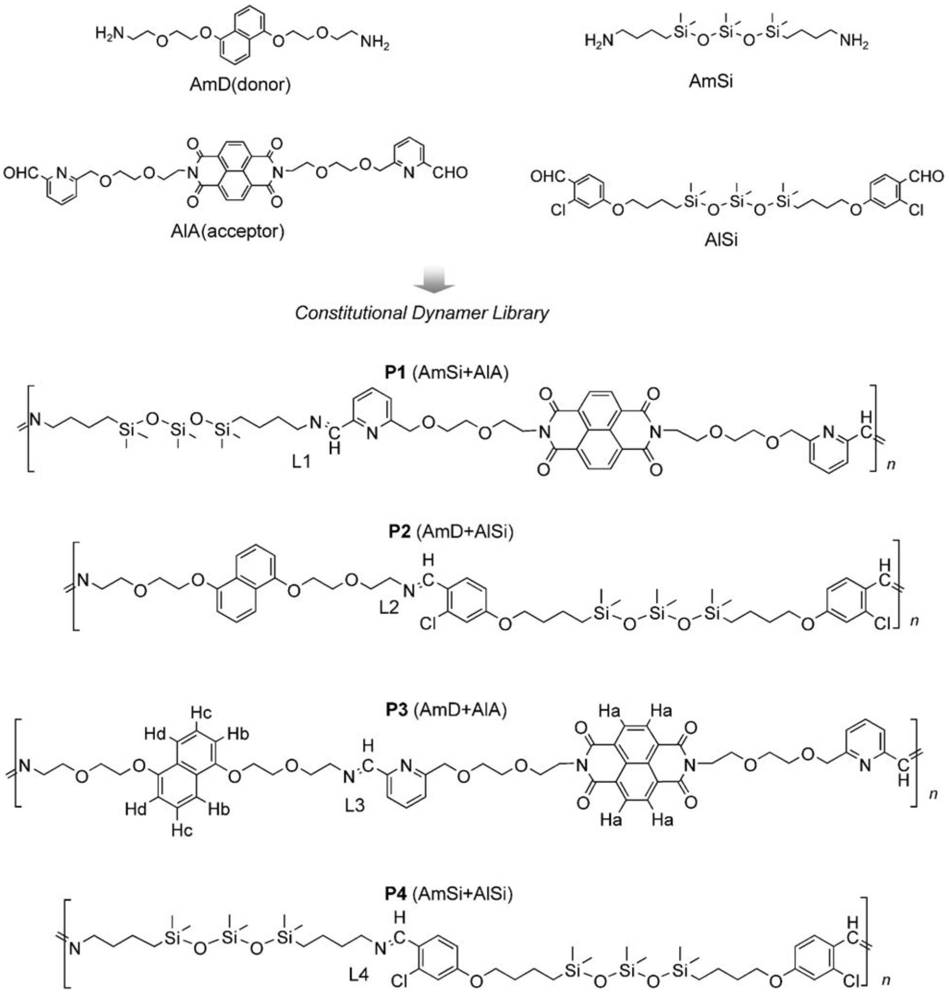

Scheme 1. Molecular structures of the donor diamines AmD and AmSi, of the acceptor dialdehydes AlA and AlSi and of the constitutional dynamic polymers (dynamers) obtained by polycondensation: **P1** (AmSi + AlA), **P2** (AmD + AlSi), **P3** (AmD + AlA), and **P4** (AmSi + AlSi) that contain the different imine links L1–L4.

Supporting Information), as well as by color changes. Binding of the larger K^+ ion to the polymer seems to be less compatible with close approach of the donor and acceptor units. An absorption band indicative of the charge-transfer (CT) interaction that occurs in the Na^+ complex appears at 517 nm (Figure S1 (right) in the Supporting Information).[7a,8] In the experimental range of concentrations from 0.3 mM to 3.0 mM, adherence to Beer's Law was observed, which indicated that a single species was present over this range and that the interaction must be intra- and not intermolecular.

The solid-state molecular structures of the NaOTf and KOTf complexes of a model oligomer for **P3**, which was formed by reaction of a monoamine analogue of AmD[9] with AlA in a 2:1 molar ratio, were determined by X-ray crystallography (Figure 1). The structures are indeed folded; the two donor and one acceptor units form a stack, and two equivalent ions are bound to the connecting chains. Each ion is hexacoordinated to pyridine N, imine N, two ether O and one carbonyl O sites of the oligomer (Figure 1), as well as to one triflate O site (not shown in Figure 1). The preference for Na^+ (and Li^+) complexation with respect to K^+ may be related to the size as well as to the adaptability of the binding cavity that is defined by the strands of the stacked folded form of the ligand, in analogy to the selectivity shown by macrocyclic polyethers of different sizes. The average Na^+–O and K^+–O distances are 2.6 Å and 2.75 Å, compared to 2.44 Å in [15]crown-5[11a] and 2.80 Å[11b] in [18]crown-6, respectively.

Addition of NaOTf to the dynamer **P3**, which was obtained from AmD and AlA, also resulted in the formation of Na^+ complexes. Gel permeation chromatography indicated that the detected species showed a mean molecular weight M_n = 45 000 and dispersivity M_w/M_n = 1.2. These data indicate that addition of NaOTf to the dynamer **P3** does not result in a small oligomer such as a macrocycle, but a polymeric chain is formed (Figure 1).

A CDPL was generated from a mixture of equimolar amounts of preformed[9] **P1** and **P2** (each 3 mM in CD_2Cl_2/CD_3CN 8:2) in the presence of 2 mol% CF_3COOD as the acid catalyst for the imine equilibration. The integrations (Σ^1H) of the imine and the residual terminal aldehyde proton signals in the ^1H NMR spectrum were used in Equation (1) to estimate the degree of polymerization DP and polymer weight M_n (see Table S1 in the Supporting Information).[12]

$$[\mathrm{DP}n] = 1/2[\sum \mathrm{Imine}\,^1\mathrm{H}/\sum \mathrm{Aldehyde}\,^1\mathrm{H} + 1] \qquad (1)$$

The mean molecular weight of the dynamers did not show a significant change throughout the CDPL study. Thus, the addition of the different metal triflate salts caused only a minor effect in the overall degree of polymerization of the dynamic library.

To ensure equilibration, the dynamer mixture was stirred for 12 hours at room temperature. After this time, the ^1H NMR spectrum of the mixture showed the four sets of characteristic imine proton signals of the link units L1–L4 in the **P1**–**P4** dynamers that resulted from exchange and recombination of the monomer constituents of **P1** and **P2** (Figure S2e in the Supporting Information). The ratio L1/L2/L3/L4 was determined to be 22:22:28:28 from the peak integration in the ^1H NMR spectrum. The nearly statistical

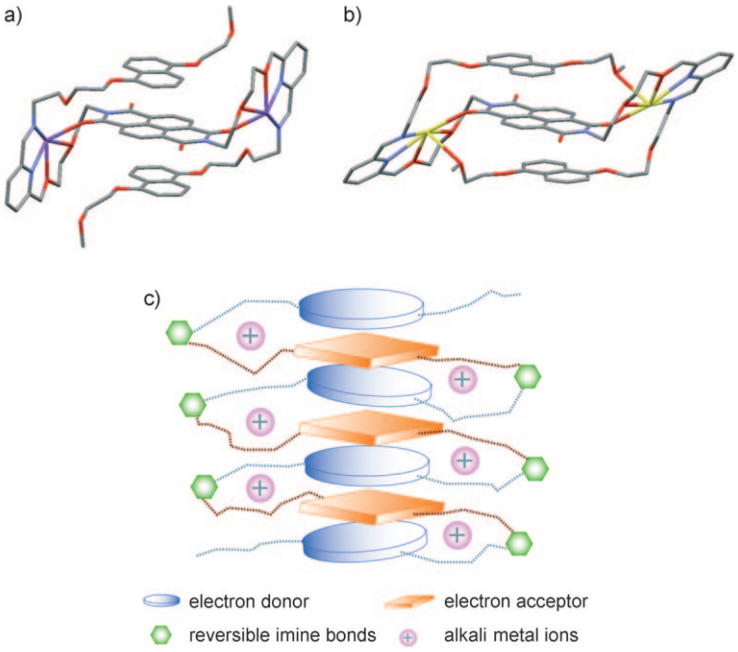

Figure 1. a) Solid-state structure of the NaOTf complex of the model compound for dynamer **P3** generated by condensation of two molecules of a monoamine analogue of AmD with one molecule of AIA. The stacking of the donor and acceptor units, which result from the folding of the chains and the binding of two Na^+ ions, are shown (triflate counteranions omitted). b) Solid-state structure of the corresponding KOTf complex. c) Schematic representation of the folded dynamer **P3** as its Na+ complex based on the crystal structure of the model compound.

link distribution at equilibrium reflects the essentially isoenergetic nature of the links under the given conditions. Subsequent addition of alkali metal triflate salts (2 mol per mol of imine) led to shifts in the initial equilibrium distribution, which were dependent upon the nature of the cation and were reflected not only in the NMR spectra but also in color changes that arise from modification of CT interactions. Consistent with expectations based on the structural characterization of the NaOTf complex of the model bis(imine) (Figure 1), and with the observation of color development from CT interactions, addition of NaOTf (as well as LiOTf) resulted in a strong increase in the fraction of link **L3** and therefore in the **P3** constituent (or **P3** blocks) of the polymer mixture. The L1/L2/L3/L4 ratios in presence of LiOTf and NaOTf were around 8:8:42:42 and 7:7:43:43, respectively (Figure 2). It is noted that the enhanced formation of L3 must necessarily result in the release of the components of L4, so that the increase of **L4** and therefore of **P4** (blocks) can be regarded as an agonistic[10] consequence of the formation of L3. The data obtained from ^1H NMR measurements and GPC analyses indicate consistently that the overall degree of polymerization in the dynamic library is hardly affected by the addition of the different metal triflate salts.

As noted previously, the constitutional evolution of the CDPL gives rise to changing optical characteristics. The differing abilities of the metal ions to bring donor and acceptor units into proximity through folding are conveniently illustrated by the colors of the library mixture in the presence of the various metal triflate salts (Figure 3). A marked color change, from the light brown of the initial equilibrium state to a much deeper purple tint, was observed for LiOTf and NaOTf, while KOTf produced a weaker effect and the color decreased further for RbOTf and CsOTf. The color observed for LiOTf and NaOTf corresponds to the same absorption spectrum as that observed for pure **P3** in presence of NaOTf (Figure S1 in the Supporting Information). The amplification of L3 decreased with increasing ion size (L1/L2/L3/L4 = 12:12:38:38, 17:17:33:33, and 20:20:30:30, for KOTf, RbOTf, and CsOTf, respectively; Figure 2). This observation is consistent with the association of these effects with the preferred binding of the smaller metal ions in the fold provided by the link L3 (generated in the course of the constitutional evolution of a mixture of **P1** and **P2**).

The behavior of this CDPL as a function of the size of alkali metal ions demonstrates a self-sensing property,[3i] which results from an adaptation of the CDPL through the constitutional evolution of the system that is driven by the recognition of each alkali metal ion. The system displays the ability to respond to external factors by selective amplification of specific constituents in an adaptive system.

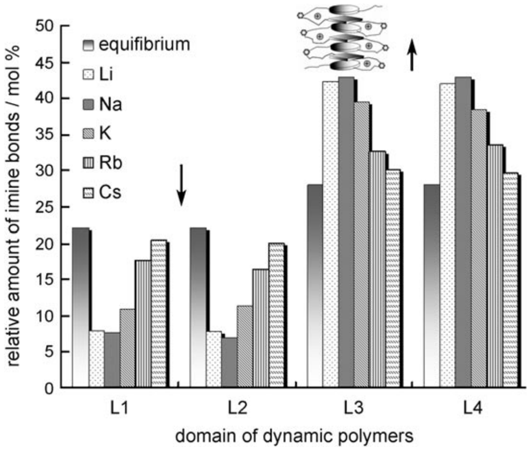

Figure 2. Representation of the distribution of the imine link domains L1–L4 generated from the library of **P1**, **P2**, **P3**, and **P4** dynamers. The distribution results from the addition of different alkali metal cations after the library has reached equilibrium, and is determined by integration of the imine proton signals in the ^1H NMR spectra in Figure S2 (see the Supporting Information).

In conclusion, the CDPL reported here exhibits adaptive behavior by constitutional recombination in response to the addition of alkali metal ions. A given metal ion induces the formation of its binding site by synergistic 1) selection of the optimal components, 2) chain folding, and 3) donor–acceptor stacking interactions. Moreover, this system is capable of recognizing alkali metal ions with generation of different

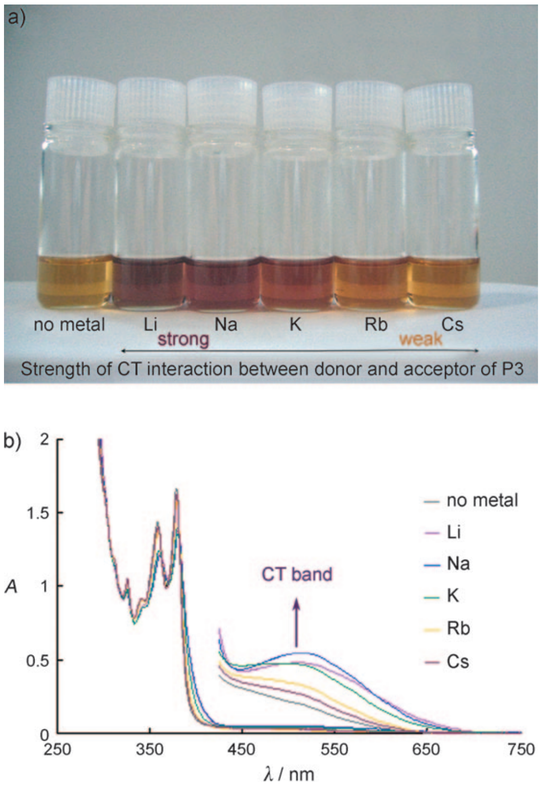

Figure 3. Optical evolution of the dynamer library (as in Figure 2) in the presence of the different alkali metal ions. a) Photographs showing the color changes; b) corresponding UV/Vis spectra (with expansion of the CT band).

optical signals, thus displaying a sensing function that arises from constitutional modification. Numerous variations may be envisaged, such as extensions to other types of metal ions or to organic guests, incorporation of other components, and induction of novel properties. In general terms, a CDPL may display various features that evolve under the pressure of external factors, thus defining a new type of smart material based on change in chemical constitution. Such materials should be able to generate specific responses to external stimuli and thereby exhibit several different kinds of functions through the implementation of dynamic constitutional variation and adaptation. The development of these materials represents a significant step in the emergence of adaptive materials technologies.

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