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Supramolecular detection of geometrical differences of azobenzene carboxylates

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ABSTRACT

In dynamic combinatorial chemistry, the geometry of a template can be translated into the composition of a library of interchanging components. In this study, such a dynamic combinatorial library was used for the first time to detect and evaluate differences in the geometry of isomers of photoswitchable azobenzene based templates.

The modus operandi of molecular machines consists in utilising switchable moieties which change their geometry when an appropriate stimulus is applied.[1] Among the various triggers that can be used for this purpose, light has unique features that render it particularly useful, i.e. its unmatched spatial resolution and electrically neutral character.[2] Moreover, light-triggered transformations are generally reversible and can easily be fine-tuned to selectively affect only the chosen molecules. The photoactive moieties that are often applied in such transformations include diaryl- and dithienylethene, spiropyrane, and azobenzene (AB) derivatives.[2b,3] Among these, the latter appear to be the most useful owing to their synthetic availability and robustness.[4] One challenging aspect of such light-induced changes in geometry lies in accurately detecting and evaluating them. Simple UV–vis and ^{1}D NMR measurements are typically employed to track such isomerisation, but they do not measure changes in the molecule geometry directly, usually providing information only about chromophore moiety and its close proximity.[5] Such geometrical changes are indeed difficult to spot and quantify, and this is even more troublesome when one isomer is thermodynamically unstable, e.g. *(Z)*-isomer of AB. There are few examples in the literature that deal with the detection of such differences in the geometry of photoisomers, the methods used being limited to NOE[6] and diffusion-based[7] NMR, conducting atomic force microscopy[8] (*c*-AFM), FRES, and in rare cases single crystal X-ray diffraction.[9]

In this Letter we present a novel concept for sensing photochemical isomerisation phenomena using dynamic combinatorial chemistry (DCC).[10] A dynamic combinatorial library (DCL) consists of species that interchange via reversible reactions. The composition of such a DCL is a consequence of the thermodynamic stability of its components, which can be modified through the addition of a template. The template may bind to selected components, resulting in the amplification of their abundances. In general, the content of a library component exhibiting the highest affinity towards the template is increased at the cost of all other DCL members.[11] Binding usually occurs between two compatible groups, enabling weak non-covalent interactions, the most important of these being hydrogen bonds (H-bonds). The strongest binding and therefore amplification are obtained when there is a good geometrical match between the anchoring points in the template and in the DCL member. If the template is a switchable molecule the spatial arrangement of the anchoring groups can be changed upon isomerisation, and different amplification profiles will be obtained for each isomer. Thus, the composition of the DCL can be translated into the geometrical parameters of the template.

Recently, we described a DCL relying on disulfide bond exchange, composed of cyclooligomers ($\mathbf{1_n}$) incorporating dipicolinic acid diamide subunits equipped with H-bond donors suitable for anion complexation (Fig. 1).[12] Under basic conditions these macrocycles are in equilibrium, which can be altered through the introduction of anionic guests. This library proved to be strongly

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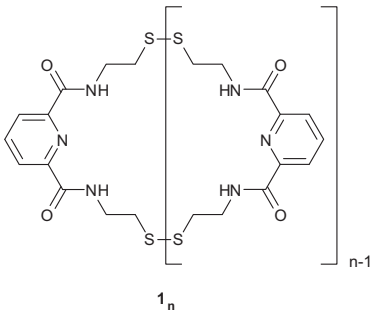


Figure 1. Dynamic combinatorial library $\mathbf{1_n}$.

influenced by the shape and size of the various carboxylates acting as templates. For example, benzene-1,3,5-tricarboxylate predominantly amplifies the tetrameric $\mathbf{1_4}$ whereas structurally related cyclohexane-1,3,5-tricarboxylate increases mainly the abundance of trimeric $\mathbf{1_3}$.

For the present study, we decided to use as template model photoswitchable carboxylates **2**, **3**, and **4** in the form of tetra-*n*-butylammonium (TBA) salts equipped with two, three and four carboxylic groups, respectively (Scheme 1).

The corresponding compounds were synthesised according to known procedures (see ESI for details). Upon irradiation of compounds **2**–**4** with light, a photostationary state (PSS) is established between the near planar *(E)*-isomer and the more compact V-shaped *(Z)*-isomer.

The corresponding *(E)*→*(Z)* and *(Z)*→*(E)* isomerisation for a diluted solution ($5 \cdot 10^{-5}$ M) of templates was completed within 1 min by irradiation with UVA light (368 nm, 60W) or blue light (410 nm, 5W LED), respectively. In UVA light driven PSS, the majority of each template exists in the respective *(Z)*-form. Relevant data describing *(Z)*→*(E)* isomerisation of the templates studied are shown in Table 1.[13] The rates of the thermal *(Z)*→*(E)* isomerisation indicate that the number of carboxylate groups is just as important as their substitution pattern in the arene ring. For example, the symmetrical di-*para*-substituted **2** back-isomerises faster than the unsymmetrical di-*meta*- and *para*-substituted **3**, whereas the symmetrical tetra-meta-substituted **4** is situated in between. Reports in the literature indicate that thermal-isomerisation of

Table 1
Kinetic data for thermal *(Z)*→*(E)*[a]

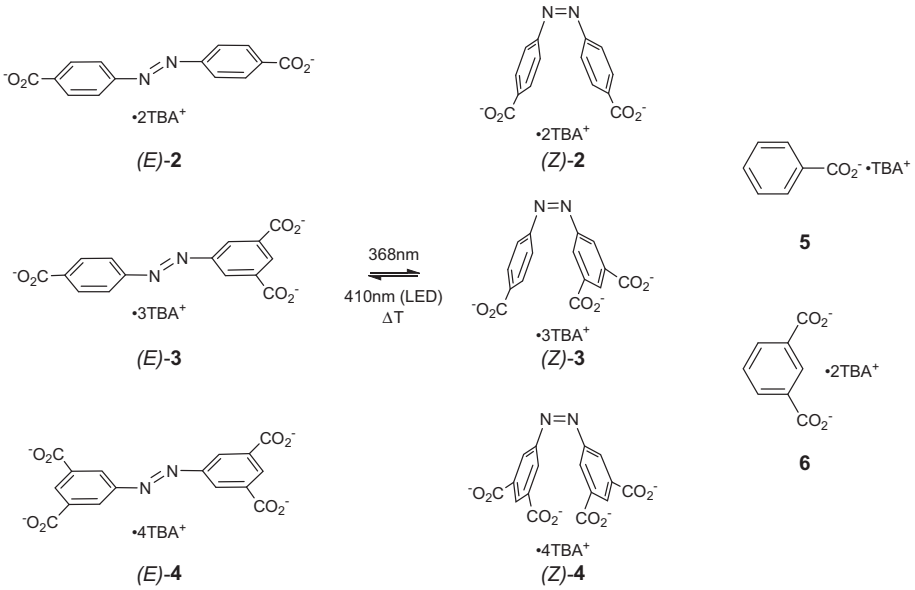
Compound	%$Z_{@PSS}$	$k_{\Delta T} \cdot 10^{-6}$ (s)	$\tau_{1/2}$ (h)
2	85 (68)	8.4	23.0
3	89 (70)	2.7	71.5
4	90 (82)	5.1	37.8

[a] Measured at $T = 298 \pm 0.1$ K; PSS are given for host concentration $5 \cdot 10^{-5}$ M and $5 \cdot 10^{-2}$ M (in parentheses), respectively; $k_{\Delta T}$ was predicted using $\Delta G^{\ddagger}$ derived from thermodynamic data (see ESI‡).

meta-substituted AB derivatives should resemble that of the parent AB, due to weak π-conjugation of substituents with an azo group. Surprisingly, however, template **3** most resembles the parent AB. Notably, the rates of isomerisation $k_{\Delta T}$ for the corresponding carboxylic acids are 2.2–8 times higher (see ESI), which supports the recently published hypothesis that increased electron density in the π-system of the AB scaffold accelerates this process.[14] For our purposes, the rates of thermal isomerisation of all templates are sufficiently low. The degree of thermal *(Z)*→*(E)* isomerisation was negligible ($\tau_{1/2} > 20$ h @ 25 °C) during the templation experiment, since the equilibration of the library takes only 3 h. Templation experiments with a library of $\mathbf{1_n}$ were conducted using tetrabutylammonium (TBA) salts of **2**–**4** in *(E)*-form and their PSS mixtures of *(E)*- and *(Z)*-isomers (further named in the text as *(Z)*-form). TBA salts of benzoic (**5**) and isophthalic acids (**6**), as well as their equimolar mixture, were used as references, as they resemble in terms of their structure the appropriate halves of templates **2**–**4**. Templation experiments were run in DMSO (+0.5% H_2O), with a total concentration of **1** being 0.01 M. Compositions of the library were determined by HPLC analyses. For each template and each library component we calculated a normalised amplification factor (AF_n), a useful parameter introduced recently by Otto and co-workers,[15] which we modified in the range of negative values to limit and normalise its range to −1.

$$AF_n = \begin{cases} \frac{A_n - A_0}{A_{max} - A_0} & \text{for} \quad A_n > A_0 \\ \frac{A_0 - A_n}{A_0} & \text{for} \quad A_n < A_0 \end{cases}$$

where A_0 is the concentration of library component, A in the absence of template, A_n – in the presence of template, and Amax



Scheme 1. Structures of templates **2**–**6** and isomerisation of **2**–**4**.