The Bis-Barium Complex of a Butterfly Crown Ether as a Phototunable Supramolecular Catalyst

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Abstract: Reversible phototuning of the catalytic efficiency of the bis-barium complex of azobis(benzo-18-crown-6) in the basic ethanolysis of anilide derivatives has been achieved by light-induced cis ⇌ trans interconversion of the azobenzene spacer unit of the catalyst. The geometry of the productive catalyst—substrate complex is more favorable when the concave cis form of the catalyst is involved. Continuous photoregulation of the catalytic activity at any intermediate value between the "HIGH" and "LOW" levels was achieved by proper adjustment of the excitation wavelength or the irradiation time. The complete and relatively fast interconvertibility of photostationary states allowed the activity of the catalyst to be repeatedly photoswitched "HIGH" and "LOW" in the course of the same run.

Introduction

Light-induced changes in molecular geometry, e.g., cis ⇌ trans isomerization of suitable photochromics, have been widely used to control the shape and, consequently, the properties and functions of molecules, macromolecules, and biomaterials.[1]
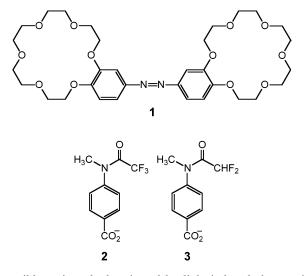
Among the various functions which are worth triggering by external stimuli, catalysis plays an important role. Fairly numerous reports are available on the photoregulation of the catalytic activity of enzymes and related systems chemically modified with photoisomerizable units.[2] However, surprisingly little work has been carried out on the photocontrol of catalysis by artificial systems. A pioneering report on photocontrol of the catalytic activity of an azobenzene-capped β-cyclodextrin dates back to 1981,[3] and a few years later Balzani et al. clearly defined the essential machinery of a *photocoreceptive catalyst*: i.e., a photochemical molecular device capable of performing the function of a photoswitchable supramolecular catalyst.[4] Yet, to the best of our knowledge, only one more paper on the subject has been published ever since.[5]

Recently, we have shown[6] that dinuclear alkaline-earth (Ba, Sr) metal ion complexes of bis-crown ether ligands selectively catalyze the basic ethanolysis of esters and anilides, which can

bind to the catalyst through a distal carboxylate anchoring group, as schematically depicted in Figure 1.

This work deals with the bis-barium complex of the azobis-(benzo-18-crown-6) ether **1**, whose catalytic properties can be
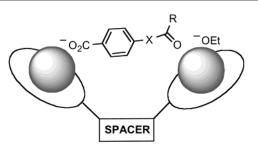

1

2   **3**

reversibly activated—deactivated by light-induced changes in molecular geometry. The azobenzene unit is a well-known photochromic,[7] whose use in the construction of molecular switches was pioneered by Shinkai[8] and Ueno[3,9] more than two decades ago.

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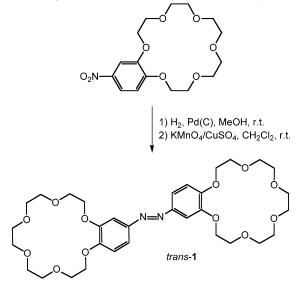(7) Balzani, V.; Scandola, F. *Supramolecular Photochemistry*; Ellis Horwood: Midsamer Norton, Avon, U.K., 1991; p 199.
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Figure 1. Productive catalyst−substrate complex for the basic ethanolysis of esters and anilides. One of the metal ions serves as a binding unit for the carboxylate anchoring group, and the other delivers an activated ethoxide ion to the substrate carbonyl.

Scheme 1. Synthesis of *trans*-Azobis(benzo-18-crown-6)

Results and Discussion

Pure *trans*-azobis(benzo-18-crown-6) was easily prepared[10] by starting from the commercially available 4′-nitrobenzo-18-crown-6 (Scheme 1). *trans*-**1**·[Ba]₂[11] exhibits the photoisomerization behavior typical of an azobenzene.[7] The composition of the fully interconvertible photostationary equilibria depends on the wavelength chosen. Irradiation of a 0.10 mM *trans*-**1**·[Ba]₂ solution in EtOH−CH₃CN (65/35 v/v)[12] at 370 nm leads after 40 s to a photostationary state, heretofore referred to as quasi-*cis*-**1**·[Ba]₂, in which the cis/trans ratio is estimated to be as high as 95/5 (Figure 2). Thus, apart from a small residual absorption of the trans isomer in a narrow region centered about its absorption maximum at 370 nm, the absorption spectrum of quasi-*cis*-**1**·[Ba]₂ reproduces well the main features of that of the pure cis isomer: namely, two absorption maxima centered at 320 and 450 nm. Upon irradiation at 480 nm the quasi-cis mixture is converted to a new photostationary state, hereafter

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(10) The synthetic procedure described in ref 8f (reported yield 1.6%) did not work in our hands.
(11) *trans*-**1**·[Ba]₂ was obtained in situ by addition of 2 equiv of Ba(SCN)₂ to *trans*-**1**. Spectrophotometric titrations have shown that the ternary complexes *trans*-**1**·[Ba]₂ and quasi-*cis*-**1**·[Ba]₂ are almost completely formed in EtOH−CH₃CN (65/35) even at a concentration as low as 0.10 mM.
(12) The solvent mixture EtOH/CH₃CN (65/35) was dictated by the low solubility of *trans*-**1** in absolute EtOH.
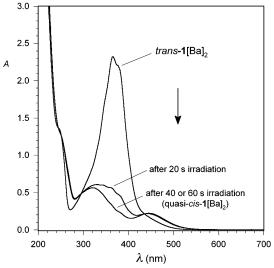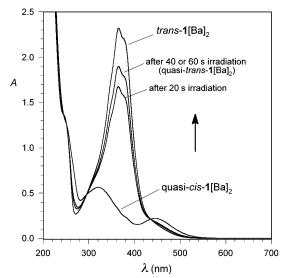
Figure 2. UV−vis spectra of 0.10 mM *trans*-**1**·[Ba]₂ before and after irradiation at 370 nm.

Figure 3. UV−vis spectra of 0.10 mM quasi-*cis*-**1**·[Ba]₂ before and after irradiation at 480 nm. The spectrum of 0.10 mM *trans*-**1**·[Ba]₂ is shown for comparison.

referred to as quasi-*trans*-**1**·[Ba]₂, whose composition is 19/81 cis/trans (Figure 3).

The computer-generated molecular models of interswitchable cis and trans forms shown in Figure 4 illustrate well the figurative expression *butterfly crown ethers* coined by Shinkai[8] for bis-crown ethers of this kind.
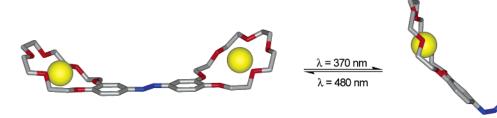
The photostationary mixtures are slowly converted in the dark to the pure trans isomer with a half-life of 7.9 h at 25 °C. Thus, the thermal cis → trans isomerization had a negligible influence on the outcome of the catalytic experiments reported below, yet its rate was not low enough for the pure cis isomer to be isolated by ordinary column chromatography. Therefore, pure *trans*-**1**·[Ba]₂ was used as the starting material in all kinetic experiments.

The effect of the complex **1**·[Ba]₂ on the rate of basic ethanolysis of anilides **2** and **3** (Me₄N⁺ salts) is shown in Table 1. It is apparent that the cis form of the dinuclear complex is a better catalyst than the trans form with both substrates, which is in line with a previous report on the catalytic activity of isomeric dinuclear barium complexes of *cis*- and *trans*-stilbeno-
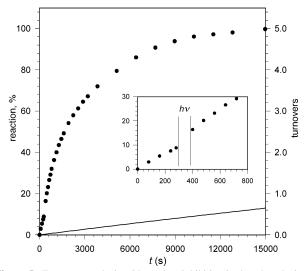
Figure 4. Computer-generated structures of interswitchable trans and cis forms of **1**·[Ba]₂.

Table 1. Catalysis of the Basic Ethanolysis of Anilides **2** and **3** in EtOH–CH₃CN (65/35 v/v) at 25 °C[a]

substrate	additive (0.10 mM)	k_{obs}[b] (s⁻¹)	k_{rel}
2	none	3.93×10^{-5}	1
	trans-**1**·[Ba]₂	1.09×10^{-2}	280
	quasi-*trans*-**1**·[Ba]₂	1.84×10^{-2}	470
	quasi-*cis*-**1**·[Ba]₂	4.89×10^{-2}	1240
3	none	1.85×10^{-6}	1
	trans-**1**·[Ba]₂	4.26×10^{-4}	230
	quasi-*trans*-**1**·[Ba]₂	7.82×10^{-4}	420
	quasi-*cis*-**1**·[Ba]₂	2.36×10^{-3}	1280

[a] Experiments carried out on 0.025 mM substrate solutions in the presence of 1.00 mM Me₄NOEt. [b] Clean first-order time dependence was observed in all cases. Error limits are on the order of ±5%.

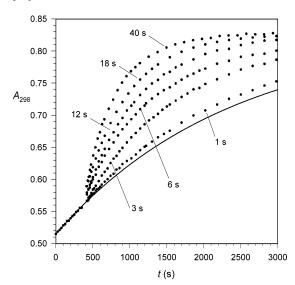
Figure 5. Turnover catalysis with product inhibition in the ethanolysis of a 5-fold molar excess of **3** in the presence of 5.00 mM EtONMe₄ and 0.10 mM *trans*-**1**·[Ba]₂ irradiated at 370 nm for 40 s after 5 min from the start. The line represents the background ethanolysis. The inset shows the early stages of the reaction.

bis(18-crown-6).[6c] The geometry of the productive complex (Figure 1) is clearly more favorable and leads to a closer proximity of the two reactants when the concave cis form of the catalyst is involved.
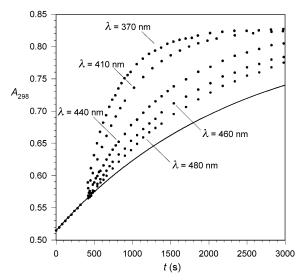
The kinetic experiments listed in Table 1 were carried out in the presence of excess catalyst to avoid complications arising from product inhibition, obviously due to the fact that the reaction product p-NHMeC₆H₄CO₂⁻ still has a carboxylate for binding to the catalyst. Five catalytic turnovers have been seen in an experiment in which a 5-fold molar excess of **3** was ethanolyzed (Figure 5), but the shape of the reaction profile clearly suggests that product inhibition becomes effective in the late stages of the reaction.

Because of the incomplete one-sidedness of the photostationary equilibria obtained by irradiation at 370 and 480 nm,
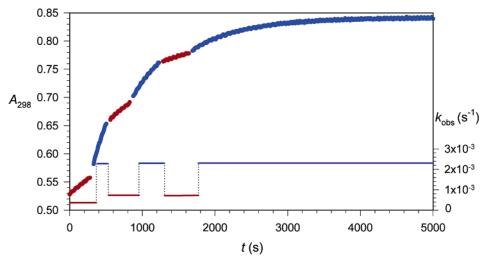

Figure 6. Basic ethanolysis of 0.025 mM **3** in the presence of 0.10 mM *trans*-**1**·[Ba]₂ and 1.00 mM EtONMe₄. The reaction was monitored at 298 nm, where the absorptions of *trans*-**1**·[Ba]₂ and *cis*-**1**·[Ba]₂ exhibit an isosbestic point. In each experiment the reaction mixture was irradiated after 6 min from the start at 370 nm for the given irradiation times.
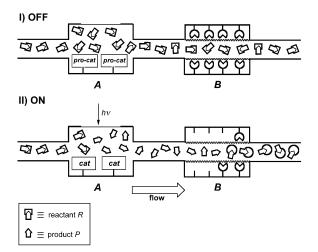

Figure 7. Basic ethanolysis of **3** (reaction conditions as in Figure 6). In each experiment the reaction mixture was irradiated at the given wavelengths for 40 s after 6 min from the start.

and because of the moderate cis/trans selectivity due to the adaptability of the flexible crown ether moieties, the switched-off state of the catalyst reveals substantial residual activity. Hence, our catalytic system exhibits incompletely photoswitchable "ON/OFF" activity, and the expression photoswitchable "HIGH/LOW" activity is more appropriate.

Figure 8. Basic ethanolysis of **3** (reaction conditions as in Figure 6). Repeated photoconversions into quasi-*cis*-**1**·[Ba]₂ and quasi-*trans*-**1**·[Ba]₂ were obtained upon alternate irradiation at 370 or 480 nm for 40 s. Specific rates are reported on the right-hand ordinate axis.

Figure 9. Schematic representation of a stirred-flow reactor system involving an immobilized photoswitchable catalyst: (I) the inactive form *pro-cat* contained in the upstream reactor *A* does not catalyze the conversion of *R* into *P*; (II) light-induced conversion into the active form *cat* liberates *P*, which in turn triggers a chemical process in a downstream reactor *B*. With a phototunable catalyst all of the possible situations between the two limiting ON and OFF states can be achieved.

Virtually continuous photoregulation of the catalytic activity at any intermediate value between the "HIGH" and "LOW" levels was achieved in either of the following ways: (i) the wavelength was fixed at 370 nm and the irradiation time was changed in the range of 0–40 s (Figure 6) or (ii) the irradiation time was fixed at 40 s and the wavelength was varied in the range of 370–480 nm (Figure 7). Thus for any time/wavelength combination a different state is obtained, whose cis/trans composition and catalytic activity can be precisely predetermined.

Finally, the complete interconvertibility of photostationary states is well illustrated by an experiment in which the activity of the catalyst was varied a number of times in the time course of the reaction (Figure 8).

The development of supramolecular catalysts is still at the stage of basic research, and none of them appears to have reached the degree of ripeness for practical applications. Nevertheless, one might envisage a flow system in which the concentration level of effluents is light-controlled. The flow system consists of a stirred-flow reactor in which a photoswitchable catalyst is immobilized by attachment to a solid material

or by other means. A reactant (*R*) solution enters the reactor, where the catalyzed reaction *R* → *P* takes place. The concentrations of liberated *P* and unreacted *R* in the outlet flow will depend, other things being equal, on the activity of the catalyst, which, in turn, depends on the irradiation time/wavelength.

Furthermore, the reaction product *P*, generated in the stirred-flow reactor *A* (Figure 9) by the photoconversion of the inactive *pro-cat* into the active *cat* form, could be a chemical messenger that can trigger a chemical process occurring in a second stirred-flow reactor *B* that is downstream with respect to *A*. In this way a regulatory strategy is realized through remote photocontrol of the chemical activity in *B*, triggered by the light-induced secretion of a chemical messenger in *A*.

Experimental Section

Instruments and Techniques. UV–vis spectra and kinetic measurements were carried out in the thermostated cell compartment of a double-beam spectrophotometer. Monochromatic light irradiations of the solutions were performed on a spectrofluorimeter equipped with a 150 W xenon lamp (5 nm spectral bandwidth).

Materials. Acids **1**·H⁺ and **2**·H⁺ were prepared as previously described[6c] and converted in situ into their Me₄N⁺ salts by neutralization with EtO⁻⁺NMe₄.

***trans*-Azobis(benzo-18-crown-6) (*trans*-1).** Commercially available 4′-nitrobenzo-18-crown-6 was reduced with H₂ and 10% Pd(C) in MeOH at room temperature to give 4′-aminobenzo-18-crown-6 (80% yield), which was then dissolved in CH₂Cl₂ and selectively oxidized to *trans*-**1** with KMnO₄ on CuSO₄·5H₂O at room temperature according to a literature procedure.[13] The crude product was recrystallized from absolute ethanol (38% yield; mp 176–178 °C, lit.[8f] mp 173–174 °C). ¹H NMR (200 MHz, CDCl₃, TMS): δ 7.64 (dd, 2H, J^{ortho} = 8.5 Hz, J^{meta} = 2.2 Hz), 7.48 (d, 2H, J^{meta} = 2.2 Hz), 6.97 (d, 2H, J^{ortho} = 8.5 Hz), 4.29–4.22 (m, 8H), 3.99–3.93 (m, 8H), 3.77–3.69 (m, 24H). ¹³C NMR (75 MHz, CDCl₃, TMS): δ 151.25, 149.27, 147.12, 119.99, 70.94, 70.79, 70.69, 70.66 69.46, 69.03, 68.86. ES-MS (M_r = 650.31): m/z 651 [M + H⁺], 673 [M + Na⁺], 689 [M + K⁺], 348 [(M + 2Na⁺)/2], 364 [(M + 2K⁺)/2]. Anal. Calcd for C₃₂H₄₆N₂O₁₂: N, 4.31; C, 59.06; H, 7.13. Found: N, 4.26; C, 58.83; H, 7.52.

Other techniques, apparatus, and materials were as previously reported.[6a]

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