Supramolecular Chemistry

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Heteroditopic Rebek's Imide Directs the Reactivity of Homoditopic Olefins within Desolvated Quaternary Assemblies in the Solid State**

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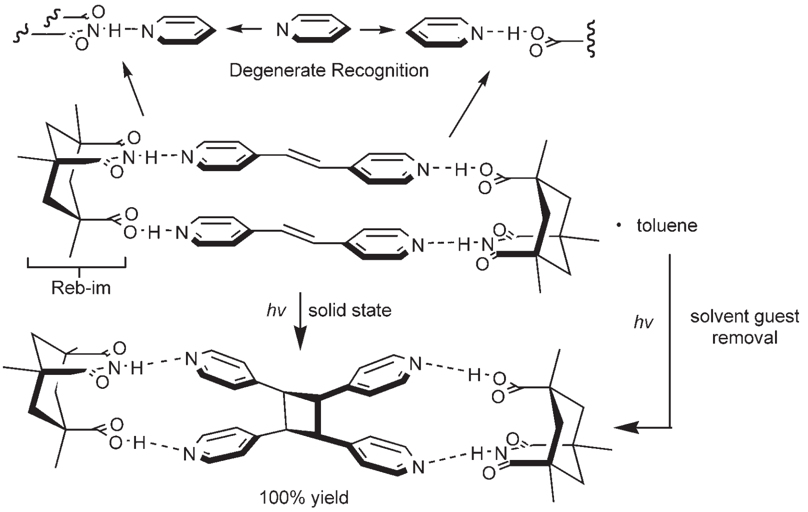
Molecules with two different binding sites are important constructs in supramolecular chemistry.[1] Such heteroditopic molecules are designed, a priori, to assemble two different molecules and/or ions within ternary complexes, a process which is exploitable in areas such as separations,[2] nucleobase recognition,[3] and replication.[4] Whereas recent studies involving heteroditopic molecules have focused largely on the binding of ion pairs[2,5] and the programmed assembly of metallosupramolecular architectures,[6] the application of heteroditopic molecules as "artificial enzymes"[7] that direct the formation of covalent bonds[8] remains a worthy goal. Indeed, since the work of Kelly et al. that described a heteroditopic molecule that employed hydrogen bonds to orient two different molecules in solution for an S_N2 reaction,[9] advances have been made in our understanding of self-assembly such that complexes that transcend the ternary level are now viable targets in supramolecular syntheses[8] and may be used to direct the formation of covalent bonds.[8]

With this in mind, we report here the ability of a heteroditopic molecule, in the form of Rebek's imide (Reb-im),[11] to direct a solid-state reaction in which a covalent bond is formed (Scheme 1). Specifically, we reveal that Reb-im assembles two molecules of *trans*-1,2-bis(4-pyridyl)ethylene (4,4′-bpe) within a solvated quaternary complex, in **1**·toluene (where **1** = {(Reb-im)·(4,4′-bpe)}$_2$), which reacts through an intermolecular [2+2] photodimerization[12] and a rare single crystal to single crystal (SCSC) transformation[13] to give *rctt*-tetrakis(4-pyridyl)cyclobutane (4,4′-tpcb) stereospecifically in up to 100% yield. We demonstrate that Reb-im assembles two identical olefins with two identical recognition sites and, thus, exhibits a novel and unusual form of degeneracy[14] in its recognition abilities. We also provide evidence that supports the structures of such hydrogen-bonded complexes being remarkably robust, being able to operate in the wake of an induced desolvation and phase transition of the solid.[15,16] To our knowledge, Reb-im is the first example of a heteroditopic molecule that directs a chemical reaction in the solid state.[17–19]

Our choice of Reb-im as a heteroditopic molecule that directs a [2+2] photodimerization stems from the nature and positioning of the imide and carboxylic acid functionalities.[11] The two groups lie approximately parallel and separated by 3.5 Å—positions that conform to the geometry criteria of Schmidt for [2+2] photodimerization.[12] Moreover, studies involving the use of Reb-im to serve as a receptor in the solid state,[20] and reports on the ability of derivatives to act as photoreceptors in solution,[21] suggested that the two functionalities could act as hydrogen-bond donor sites that juxtapose two ditopic molecules with complementary acceptor sites in a quaternary complex for reaction in a solid.



Scheme 1.

To test our hypothesis, Reb-im was dissolved in toluene/tetrahydrofuran (60:40 v/v) by heating. A solution of 4,4′-bpe in tetrahydrofuran was added to the resulting solution. Colorless crystals of **1**·toluene suitable for X-ray analysis were obtained in 95% yield by slowly cooling the solution for approximately 6 h. The formulation of **1**·toluene was confirmed by ^{1}H NMR spectroscopy and IR spectroscopy, as well as powder and single-crystal X-ray diffraction data.

A single-crystal X-ray diffraction study of **1**·toluene reveals a quaternary complex, which sits around a crystallographic center of inversion, held together by N−H···N (N···N 2.84(1) Å) and O−H···N (O···N 2.59(1) Å) hydrogen bonds (Figure 1). In this arrangement, Reb-im juxtaposes two molecules of 4,4′-bpe such that the two C=C bonds lie parallel and separated by 3.78 Å (Figure 1a). This position is favorable for a [2+2] photodimerization.[12] The complexes self-

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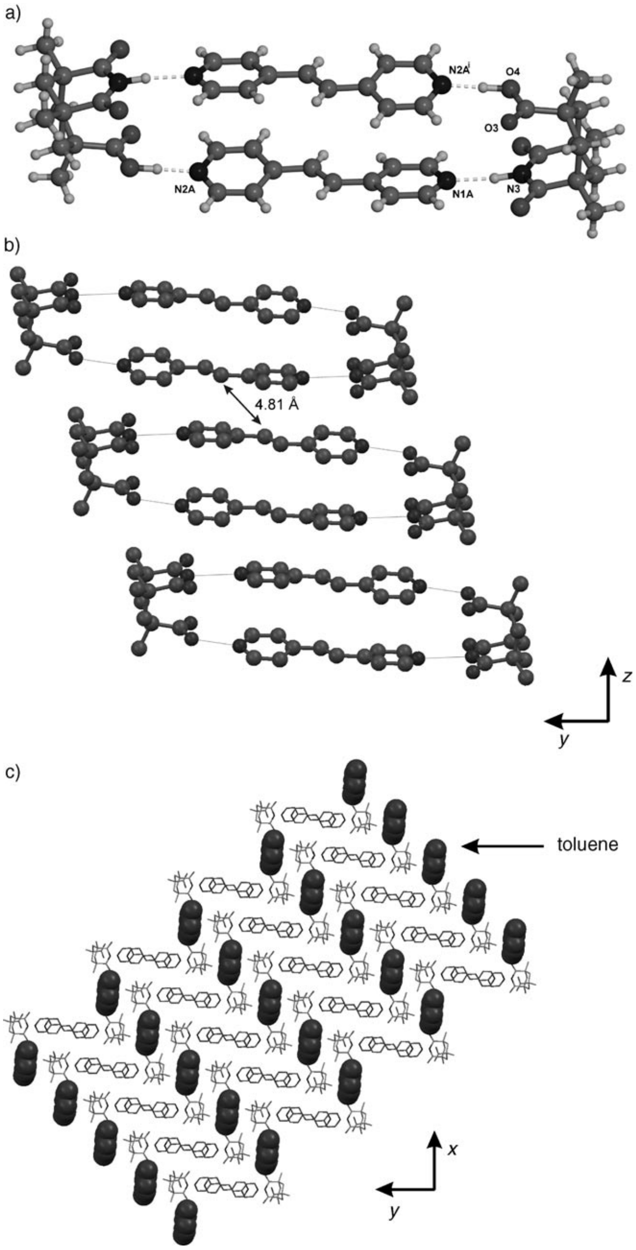


Figure 1. X-ray crystal structure of **1**: ball-and-stick views of a) the quaternary complex **1**, b) nearest-neighbor assemblies, and c) included solvent toluene (space filling model). Selected interatomic distances [Å]: N3⋯N1A 2.84(1), O4⋯N2A^i 2.59(1). Symmetry operator i: $-x-1$, $-y$, $-z+1$.

assemble along the crystallographic z-axis to form 1D columns with nearest-neighbor assemblies separated by 4.81 Å (Figure 1 b). The columns lie offset and parallel to form layers segregated by the included solvent molecules (Figure 1 c). This arrangement means that the olefin units of the quaternary complexes are the sole olefins of **1**·toluene organized for photoreaction.

The quaternary complexes of **1**·toluene are photoactive. Specifically, electron density that corresponds to 4,4′-tpcb (yield: 10 %), the result of a [2+2] photodimerization between the two olefins of 4,4′-bpe, is observed. The reaction presumably occurred under ambient UV light. Moreover, irradiation of **1**·toluene with UV light (Hg lamp of Rayonet reactor, 350 nm) for approximately one hour produced 4,4′-tpcb in 100 % yield, as confirmed by ^{1}H NMR spectroscopic analysis. Thermal gravimetric analysis revealed that the material lost 15 % of the toluene solvent during the photoreaction. The loss of the solvent guest was accompanied by a partial loss of crystallinity, as indicated by X-ray powder diffraction analyses (Figure 2 a→b).

The observation that **1**·toluene retained its crystallinity upon irradiation with UV light suggested that the reaction could proceed by a rare SCSC transformation.[13] To test this hypothesis, **1**·toluene was irradiated with light of wavelength 419 nm (Rayonet reactor)[13a] for a period of 15 h. Optical microscopy demonstrated that the crystals maintained their transparency. An X-ray diffraction analysis revealed that the photoreaction proceeded by a partial[13b] SCSC transformation (Figure 3). Specifically, 4,4′-tpcb was generated to a maximum of 24 % during the transformation and the toluene molecules were retained in the channels. Similar to the reactants, the product interacts with Reb-im through N−H⋯N (N⋯N 2.94(1) Å) and O−H⋯N (O⋯N 2.75(1) Å) hydrogen bonds. Further irradiation of the solid with UV light for a period of eight days produced 4,4′-tpcb in 100 % yield. During this time, the single crystals turned opaque, while 65 % of the toluene was lost from the solid. The slow progress of the photoreaction can be attributed to low absorption of the UV light with a wavelength of 419 nm.[13a]

The observation that **1**·toluene maintained its reactivity upon loss of the solvent guest motivated us to determine whether the quaternary assemblies can operate upon removal, and therefore in the complete absence, of the guest.[15,16] Given the fragile nature of organic solids,[16] we anticipated that removal of the guest prior to the photoreaction would likely induce a phase transition or complete collapse of the structure. Such changes to structure, as a result

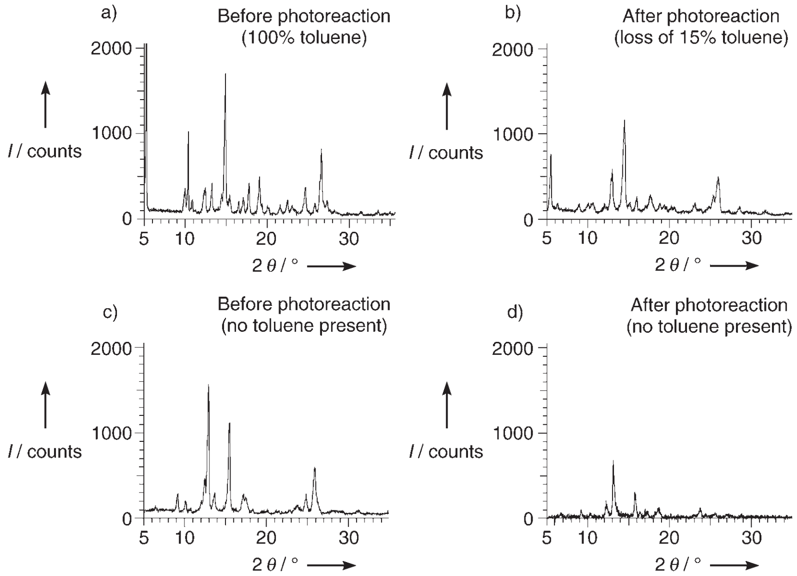


Figure 2. X-ray powder diffraction patterns of **1**·toluene: a) before photoreaction, b) after photoreaction (loss of 15 % toluene), c) before photoreaction (no toluene present), and d) after photoreaction (no toluene present).

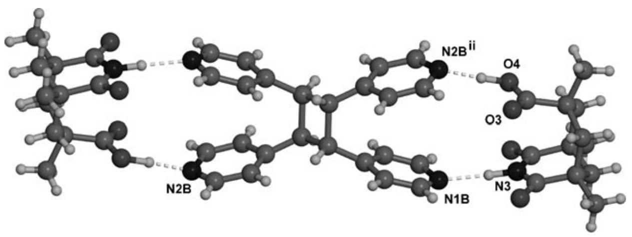


Figure 3. X-ray crystal structure of **1**·toluene (24% 4,4′-tpcb, SCSC): Selected interatomic distances [Å]: N3···N1B 2.90(1), O4···N2B^{ii} 2.65(1). Symmetry operator ii: $-x$, $-y-1$, $-z+1$.

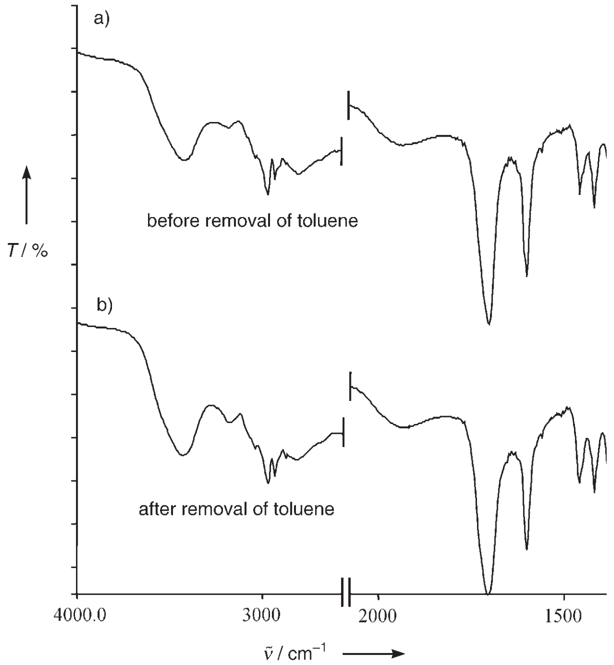
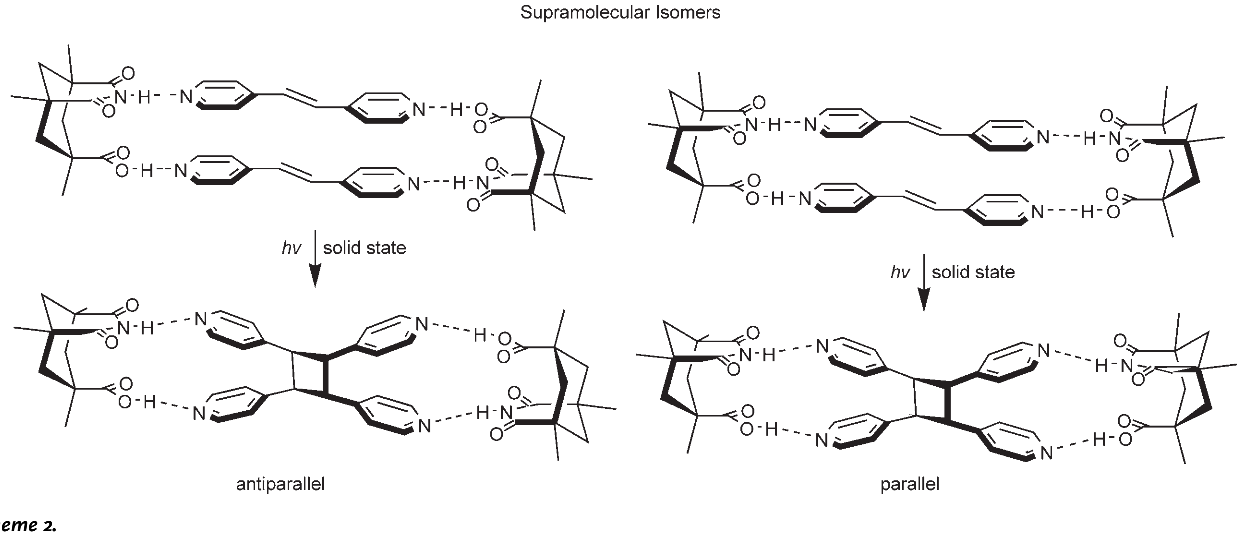


Figure 4. FTIR spectra of the hydrogen-bonding region of **1**·toluene (O–H···N, N–H···N 3100–3600 cm^{-1}; C=O 1600–1750 cm^{-1}): a) in the presence of toluene and b) upon complete removal of toluene.

of the relative weakness of hydrogen bonds, could destroy the self-assembled complexes and thereby render the components of the solid photostable. Thus, **1**·toluene was heated at 90 °C in a vacuum for a period of 10 h.[22] A ^{1}H NMR spectrum indicated that the toluene was completely liberated from the solid. Unsurprisingly, the desolvation induced a phase transition and partial loss of crystallinity (Figure 2a→c).[16] The FTIR spectra of the solid, however, revealed the hydrogen bonding to be the same before and after the phase transition (Figure 4).[23] This observation supports the structures of the quaternary complexes being maintained during removal of the solvent guest and phase transition of the solid. Moreover, irradiation of the desolvated solid with UV light produced 4,4′-tpcb in 100% yield, as confirmed by ^{1}H NMR spectroscopic analysis. An X-ray powder diffraction analysis of the fully reacted solid (Figure 2c→d) demonstrated a further loss of crystallinity, as evidenced by the diffraction pattern exhibiting further line broadening. The fact that 4,4′-tpcb was generated following the phase transition is indicative of the structures of the self-assembled complexes being remarkably robust[16] and suggests that such hydrogen-bonded assemblies may be developed to operate in less organized media (for example, amorphous solids).[24]

The degeneracy[14] of the recognition properties of Reb-im in **1**·toluene is unusual and can be considered counterintuitive.[25] Heteroditopic molecules are designed to bind two different guests, which means the ability of such molecules to bind two identical guests has remained virtually unexplored.[1–6] In the case of **1**·toluene, the quaternary nature of the complex, coupled with the degeneracy of the recognition, presents an opportunity for the self-assembly process to exhibit a unique form of supramolecular isomerism[26] in which Reb-im is oriented either antiparallel or parallel in the complex and solid (Scheme 2). Reb-im is oriented antiparallel in **1**·toluene.[27] The same photoproduct, however, would be expected to form in each solid.

In this study, we identified a role of heteroditopic molecules, in the form of Reb-im, to direct a [2+2] photodimerization within a hydrogen-bonded quaternary complex in the solid state. The reaction proceeded by a SCSC reaction[13] in which the complexes operate upon an induced desolvation and phase transition of the solid. We are now investigating the behavior of Reb-im with other olefins and in



Scheme 2.

the presence of additional guests. We are also studying such unsymmetrical environments to control the reactivity of two different olefins, where such reactivity may be achieved in amorphous phases,[24] as well as solution.

Experimental Section

Preparation of cocrystals of **1**·toluene: Reb-im was prepared according to the literature.[28] 4,4′-Bpe was commercially available (Aldrich Co.). Reb-im (15 mg) was dissolved in toluene and tetrahydrofuran (3 mL, 60:40 v/v) by heating at 40–50 °C for 2–3 mins. A clear solution of 4,4′-bpe (22 mg) in tetrahydrofuran (0.5 mL) was added to this solution, and stirred for 1 min. Colorless crystals of **1**·toluene suitable for single-crystal X-ray analysis were obtained in 95 % yield upon slow cooling of the solution over approximately 6 h.

Solid-state photodimerizations: The UV-irradiation experiments were performed by placing either single crystals or finely ground samples of **1**·toluene between two pyrex plates and turning the sample to ensure uniform irradiation.

^{1}H NMR spectra of **1**·toluene (300 MHz, [D$_6$]DMSO): before UV irradiation: $\delta = 12.17$ (br s, 1 H), 10.33 (s, 1 H), 8.60 (dd, 4 H), 7.60 (dd, 4 H), 7.54 (s, 2 H), 7.20 (m, 5 H), 2.38 (d, 1 H), 2.29 (s, 3 H), 1.89 (br d, 1 H), 1.37 (d, 1 H), 1.14 ppm (d, 12 H); after UV irradiation (100 % yield of 4,4′-tpcb): $\delta = 12.17$ (br s, 1 H) 10.33 (s, 1 H), 8.34 (dd, 4 H), 7.18 (dd, 4 H), 7.20 (m, 5 H), 4.65 (s, 2 H), 2.38 (d,1 H), 2.29 (s, 3 H), 1.89 (br d, 1 H), 1.37 (d, 1 H), 1.14 ppm (d, 12 H).

X-ray crystallography: Crystal data for **1**·toluene: triclinic, space group $P\bar{1}$, $a = 8.003(1)$, $b = 9.093(1)$, $c = 17.061(2)$ Å, $\alpha = 94.33(1)$, $\beta = 89.93(1)$, $\gamma = 101.95(1)°$, $V = 1210.9(2)$ Å^3, $\rho_{\text{calcd}} = 1.28$ g cm^{-1} for $Z = 1$ and $R = 0.059$. Crystal data for **1**·toluene(SCSC): triclinic, space group $P\bar{1}$, $a = 7.974(1)$, $b = 9.115(1)$, $c = 17.088(2)$ Å, $\alpha = 94.39(1)$, $\beta = 89.60(1)$, $\gamma = 101.97(1)°$, $V = 1211.4(1)$ Å^3, $\rho_{\text{calcd}} = 1.28$ g cm^{-1} for $Z = 1$ and $R = 0.056$. Mo$_{K\alpha}$ radiation ($\lambda = 0.71070$ Å). All crystal data were measured on a Nonius Kappa CCD single-crystal X-ray diffractometer at liquid-nitrogen temperature. After anisotropic refinement of all non-hydrogen atoms, the aromatic, methylene, and methyl hydrogen atoms were placed in idealized positions and allowed to ride on the atom to which they are attached. All hydroxy and imide hydrogen atoms were located from the final Fourier difference electron density map and refined according to the riding isotropic model. The 4,4′-bpe units of **1**·toluene and **1**·toluene(SCSC) were found disordered with 4,4′-tpcb. The occupational parameters for 4,4′-bpe and 4,4′-tpcb in **1**·toluene and **1**·toluene(SCSC) were determined to be 0.90 and 0.10, and 0.76 and 0.24, respectively. The toluene solvent molecule was found to be disordered over two positions (relative occupancies 0.50/0.50) in each solid. The non-hydrogen atoms of the six-membered ring based on N2B in **1**·toluene(SCSC) was refined with a model based on N1A, with the atoms being forced into planarity (average deviation 0.025 Å). All crystallographic calculations were conducted using SHELXL-97[29] locally implemented on an IBM-compatible pentium-based PC. CCDC-263613 (**1**·toluene) and CCDC-263614 (**1**·toluene(SCSC)) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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