

Halogen Bonding and $\pi\cdots\pi$ Stacking Control Reactivity in the Solid State

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The ultimate goal of supramolecular chemistry is to gain control over the noncovalent self-assembly of molecules in order to direct their functions.¹ Solid-state synthesis is one of the most fascinating and rapidly emerging fields of supramolecular chemistry.² Noncovalent interactions have recently proven fruitful in dictating the regioselectivity of solid-state reactions.³ For instance, hydrogen bonding has been used to pin olefins to linear templates⁴ and to form discrete supramolecules meeting Schmidt's requirements for UV-induced [2 + 2] cycloaddition reactions.⁵ A full utilization of this innovative approach requires the successful exploitation of new and effective noncovalent interactions for the self-assembly of architectures geometrically tailored to preestablished reactions.

In this contribution we describe the first case wherein halogen bonding, namely the charge-transfer interaction between Lewis bases and halogen atoms,⁶ drives the assembly of a template with an olefins' carrier, orienting double bonds for photocyclization in the crystal. To achieve this result, we engineered and synthesized the tetratopic halogen-bonding donor **3** (Scheme 1).⁷

The pentaerythritol ether **3** is obtained by a S_NAr attack of oxygen sites in **1** on iodopentafluorobenzene **2**. The reactions occur with a very high regioselectivity on the sites occupied by the para fluorine atoms. This S_NAr reaction, previously used for the preparation of ditopic halogen-bonding donors,⁸ is here proven as an effective strategy to new tectons⁹ for halogen-bonding-driven crystal engineering.

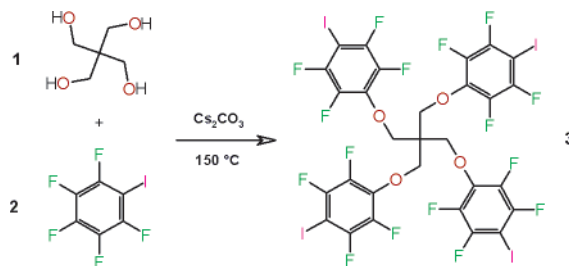
Iodoperfluoroarenes are very good halogen-bonding donors, and they easily self-assemble with nitrogen-substituted hydrocarbons.¹⁰ To test the ability of the tetratopic tecton **3** to be involved in halogen-bonding-driven intermolecular recognition processes, we challenged it with 1,2-diaminoethane **4a** (Scheme 2). Single crystals of **5a**, melting at 435 K, were grown under isothermal conditions ($T = 298$ K) by using the diffusion technique within a chloroform–tetrachloromethane system.

The X-ray diffraction analysis of those cocrystals gave details about their supramolecular organization (Figure 1).^{7,11}

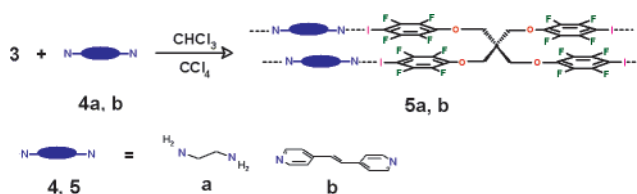
Modules **3** and **4a** are present in the cocrystal **5a** with a 2:1 ratio, and they form infinite 1D halogen-bonded ribbons.

As expected, the pentaerythritol derivative **3** behaves as a tetratopic halogen-bonding donor, while the dinitrogen module **4a** is a ditopic acceptor. The structure presents two different halogen bonds with $N\cdots I$ distances of 2.811 and 2.960 Å. These are, respectively, 20 and 16% shorter than the sum of the van der Waals radii for N and I (3.53 Å).¹² The $N\cdots I-C$ angles are 174.99 and 168.20°. This is consistent with the $n \rightarrow \sigma^*$ character of the halogen bonding¹³ and confirms its high directionality.¹⁴ The tecton **3** differs from the other pentaerythritol derivatives¹⁵ in that it does not show either a planar or a tetrahedral conformation. Instead, the four arms

Scheme 1



Scheme 2



of **3** point two by two to the opposite sides. The tetrafluorophenyl rings lying on the same side are paired in a quasi-parallel fashion due to remarkable face-to-face $\pi\cdots\pi$ intramolecular interactions¹⁶ (distances ranging from 3.551 to 3.915 Å; typical cutoff distance 3.9 Å¹⁵). The wider distances are observed between the carbon atoms closer to the iodine atoms. In fact, the rings slightly open up. This is probably caused by the steric hindrance of the iodine atoms, which do not show any reciprocal attraction. Thanks to the $\pi\cdots\pi$ stacking interaction forces, the iodine atoms in the periphery of module **3** stay at a distance of about 4 Å. Thus, tetratopic tecton **3** looks ideally pre-organized for enforcing topochemical alignment of the electron donor module by means of a double supramolecular control: intramolecular $\pi\cdots\pi$ stacking interaction and intermolecular halogen bonding.

With this in mind, we tried to obtain halogen-bonded adducts between **3** and *trans*-1,2-bis(4-pyridyl)ethylene (**4b**), which is a strong halogen-bonding acceptor and easily self-assembles with iodo- and bromoperfluoroarenes.¹⁷ Colorless cocrystals **5b** were obtained upon a slow diffusion of the volatiles in a chloroform–tetrachloromethane crystallizing system (Scheme 2).⁷ The thermal analysis of **5b** gave very interesting information. The melting endotherms of the source compounds (**3**: 439 K, **4b**: 426 K) were both missing in the thermograph of **5b**, while a new endotherm, corresponding to the sample melting, appears at 494 K. This behavior is consistent with the formation of new well-defined crystalline species. The dramatic melting-point increase demonstrates the robustness of the crystal matrix of **5b**.¹⁰ Suitable crystals of **5b** were submitted to single-crystal X-ray analysis (Figure 2).¹⁸

The supramolecular architecture of **5b** was also characterized by infinite 1D halogen-bonded ribbons. The similarities between

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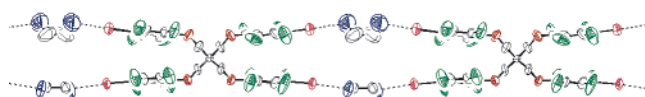
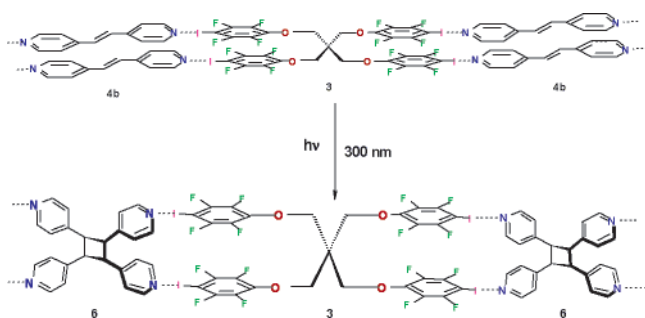


Figure 1. Infinite 1D halogen-bonded ribbons **5a** formed by self-assembling modules **3** and **4a**. Hydrogen atoms are omitted for clarity.



Figure 2. Infinite 1D halogen-bonded ribbons **5b** formed by self-assembling modules **3** and **4b**. Hydrogen and disordered atoms are omitted for clarity.

Scheme 3



the organization of the interacting modules in cocrystals **5a,b** are impressive and confirm the validity of our supramolecular design. The arms of the pentaerythritol derivative **3** show the same parallel arrangement with $\pi\cdots\pi$ distances ranging from 3.524 to 3.897 Å. Two different halogen bonds are present here, too, with $N\cdots I$ distances of 2.795–2.819 Å, about 21% shorter than the sum of the van der Waals radii for N and I (3.53 Å).¹² The $N\cdots I-C$ angles are 177.09 and 176.72°, respectively. In cocrystal **5b**, $\pi\cdots\pi$ stacking interactions determine the pre-organization of module **3** and the high strength and directionality of the halogen bonding transfer this topochemical information to the olefins that are pinned in the ribbons in a parallel fashion with a distance of less than 4.5 Å between the olefins' centroids. In **5b**, the olefins present the typical disorder of stilbene derivatives, which has also been observed in the structures of related supramolecules.^{4b}

A powdered crystalline sample of **5b**, placed between two glass plates, was irradiated using a Rayonet at 300 nm. The cocrystal **5b** readily underwent a photochemical cycloaddition under topochemical control, producing tetrakis(4-pyridyl)cyclobutane **6** (Scheme 3). As confirmed by ¹H NMR spectroscopy of the crude reaction mixture and FAB-MS spectrometry, the reaction occurs stereospecifically and with high yields. After 3 h a 100% conversion of **5b** occurred, yielding 100% the *rc*tt isomer only (GC analysis).^{4a,7} No byproducts were revealed; in **5b**, the olefin ethylene bonds are always parallel, while the apparent cross-like feature is only due to long-range statistical disorder of these pairs (see Supporting Information). Moreover, cross-plane photoreactions are prevented by the absence of any short contacts between the olefins belonging to adjacent ribbons in the crystal stacking (inter-ribbons distance > 7 Å).¹⁹

In summary, we present a means to achieve supramolecular control on reactivity in the solid state using a template⁴ that operates via halogen bonding. It is based on noncovalent interactions and operates at two levels. The intramolecular $\pi\cdots\pi$ interactions pre-organize the template. The intermolecular halogen bonding assembles template and olefin carrier in ribbons. As a result of the remarkable strength and directionality of the halogen bonding, the

alignment of the arms of the template is translated into alignment of olefins at the distance needed for the photoreaction. Only occasional precedents have been reported wherein the halogen bonding affects solid-state photoreactions. A paper describes a chlorodiazirine that packs in infinite chains and photodecomposes with low selectivity due to intermolecular $N\cdots Cl$ interactions.²⁰ Schmidt reports how weak $Cl\cdots Cl$ contacts align polyenes in discrete assemblies that undergo photocyclization to cyclobutanes.²¹ In contrast to Schmidt, we have used for the first time the halogen bonding in the context of a template/cocrystal system, thus inducing stereoselective photocyclization of olefins. The limited flexibility of template **3**, the strength of $\pi-\pi$ interactions between perfluorophenyl rings,^{16a} and the directionality of the $N\cdots I$ halogen bonding^{14a} suggest that the impact of the templated synthesis here described may extend to a variety of solid-state photoreactions involving nitrogen substituted partners.

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Supporting Information Available: Crystallographic Information Files (CIFs) for **5a,b**. Experimental data for **3**, **5a,b**, and **6**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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