Reversing the code of a template-directed solid-state synthesis: a bipyridine template that directs a single-crystal-to-single-crystal [2 + 2] photodimerisation of a dicarboxylic acid†

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A linear template in the form of a bipyridine has been developed and is shown to direct a single-crystal-to-single-crystal [2 + 2] photodimerisation of a dicarboxylic acid.

The simplest way of transferring molecular information to form a covalent bond is to use a code based on a two-letter alphabet.[1] In Nature, molecular information is transferred through a four-letter alphabet involving nucleic acids (*i.e.* DNA), each letter being a purine or pyrimidine base.[2] In contrast, chemists have access to a virtually infinite number of such molecular letters that can be used to transfer information to code the formation of covalent bonds.[1]

In this context, chemists have recently utilised a two-letter code to direct light-driven reactions *via* ditopic molecules that act as linear templates.[3] The templates preorganize olefins in the solid state for [2 + 2] photodimerisations within hydrogen-bonded molecular assemblies. The assemblies have involved a code wherein templates that function as hydrogen-bond donors direct the synthesis of products that bear hydrogen-bond acceptors.[4]

In principle, the code of an existing template-directed solid-state synthesis can be reversed. In this context, we have described the ability of the bifunctional hydrogen-bond donor 1,8-naphthalene-dicarboxylic acid (1,8-nap) to direct a [2 + 2] photodimerisation of the bifunctional hydrogen-bond acceptor *trans*-1,2-bis(4-pyridyl)-ethylene (Scheme 1).[5] Moreover, it occurred to us that the code of this assembly process may be reversed, such that a bipyridine acts
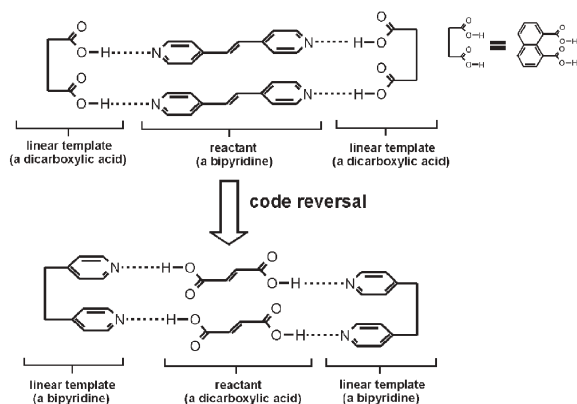
as a template and a dicarboxylic acid acts as a reactant. In contrast to the product obtained using 1,8-nap, the cyclobutane would be decorated with carboxylic acid groups, which could make the products readily amenable to postsynthetic transformations.[6]

Here, we report the application of code reversal to a template-directed solid-state synthesis that involves an assembly process based on pyridine and carboxylic acid groups. Specifically, we demonstrate the ability of 2,3-bis(4-methylenethiopyridyl)naphthalene (2,3-nap) to assemble fumaric acid (fum)[7] into the finite hydrogen-bonded molecular assembly 2(2,3-nap)·2(fum) for an intermolecular [2 + 2] photodimerisation (Scheme 2). We reveal that the reaction proceeds stereospecifically *via* a rare[8] single-crystal-to-single-crystal (SCSC) transformation and gives *rctt*-1,2,3,4-tetracarboxylic acid (*rctt*-cbta) in up to 70% yield. Our results are proof-of-principle that code reversal can be applied to an existing template-directed solid-state synthesis and suggest that the concept may be applied to future template-based systems.[3]

Our choice of 2,3-nap as a template stems from a report involving a related bipyridine that assembled two Ag(I) ions in the solid state in close proximity.[9] Specifically, reaction of the 4-thiopyridine framework with Ag(I) produced a dimer with two Ag(I) ions juxtaposed at 3.41 Å, a distance that meets the criterion of Schmidt for [2 + 2] photoreaction in a solid.[10] Thus, we anticipated that co-crystallization of 2,3-nap with fum would produce the four-component assembly 2(2,3-nap)·2(fum) with two diacids positioned, *via* O–H⋯N hydrogen bonds, for the photoreaction.
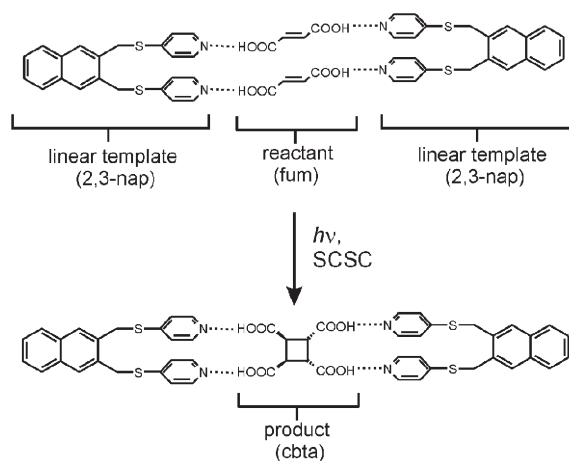

Scheme 1

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† Electronic supplementary information (ESI) available: Fig. S1. ^{1}H NMR spectrum of photoreacted 2(2,3-nap)·2(fum). See DOI: 10.1039/b510081j

Scheme 2

When 2,3-nap was co-crystallized with fum (ratio: 1 : 1) from a 2 : 1 (*v/v*) MeCN : CH$_3$OH solvent mixture, pale-yellow crystals of 2(2,3-nap)·2(fum) formed in a period of 10 minutes. The composition of 2(2,3-nap)·2(fum) was confirmed using ^{1}H NMR spectroscopy, as well as powder and single-crystal X-ray diffraction.‡

Perspectives of 2(2,3-nap)·2(fum) are shown in Fig. 1. As anticipated, the components assembled to form a four-component molecular assembly held together by four O–H···N hydrogen bonds [N···O separations (Å): N(1)···O(1) 2.550(4), N(2)···O(3) 2.584(4)] (Fig. 1a). The two 4-pyridyl groups adopt a *syn*§ and cofacial orientation (dihedral angle: 1.1°) while the diacids lie stacked in a face-to-face geometry. The carbon–carbon double (C=C) bonds of the diacids lie approximately parallel and separated by 3.84 Å. This arrangement conforms to the criteria of Schmidt for a [2 + 2] photoreaction in a solid.[10] C=C bonds of nearest-neighbour assemblies lie offset and separated by 8.97 Å (Fig. 1b). This means the olefins of the hydrogen-bonded complex are the sole C=C bonds arranged for reaction.

Ultraviolet (UV) irradiation of a powdered crystalline sample of 2(2,3-nap)·2(fum) using 300 nm light (Rayonet reactor) for 10 days produced *rctt*-cbta, stereospecifically, in 70% yield. The formation of the photoproduct was established *via* ^{1}H NMR spectroscopy (singlet 3.43 ppm; solvent: DMSO-d_6).[7] Optical microscopy also revealed that single crystals within the powdered solid maintained transparency during the photoreaction, which suggested that the reaction proceeded *via* a SCSC transformation.[8] To test this hypothesis, single crystals of 2(2,3-nap)·2(fum) were irradiated using 300 nm light for a period of 3 days. Indeed, a single-crystal X-ray analysis of 2(2,3-nap)·2(fum)¶ confirmed that the photoreaction proceeded *via* a partial[8a] SCSC transformation in which *rctt*-cbta was generated to a maximum of 36% yield. Similar to the reactants, the photoproduct interacts with the bipyridine template *via* four O–H···N forces [N···O separations (Å): N(1)···O(1) 2.52(1), N(2)···O(3) 2.86(2)] (Fig. 2).

It is important to note[13] that a single-crystal X-ray diffraction study of pure 2,3-nap (*i.e.* in the absence of fum)‖ reveals that the bipyridine adopts an *anti* conformation§ in which the 4-pyridyl units lie splayed from each other (dihedral angle: 82.7°) (Fig. 3). Molecular modelling[11] demonstrates that the splayed conformation (Fig. 3a) is 56 kJ mol^{-1} lower in energy than the cofacial conformation of 2(2,3-nap)·2(fum) (Fig. 3b). Although this difference in energy may be attributed to the O–H···N hydrogen
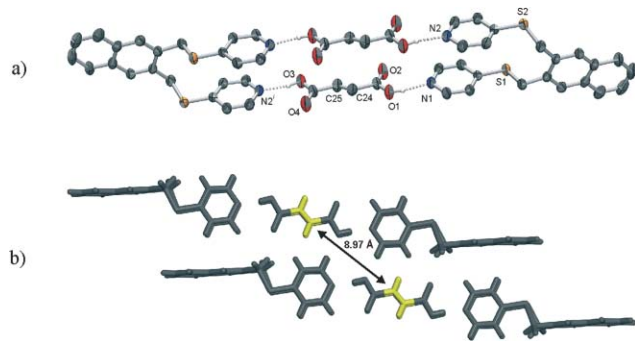

Fig. 1 Perspectives of 2(2,3-nap)·2(fum): a) four-component assembly and b) nearest-neighbour assemblies. Distances (Å): O(1)···N(1) 2.550(4), O(3)···N(2)^i 2.584(4). Symmetry operator *i*: x − 1, y, z.
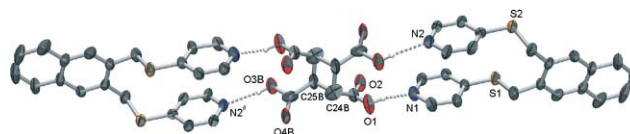

Fig. 2 Perspective of 2(2,3-nap)·(cbta). Distances (Å): O(1)···N(1) 2.523(7), O(3)···N(2)^{ii} 2.86(2). Symmetry operator *ii*: 3 − x, 1 − y, 1 − z.
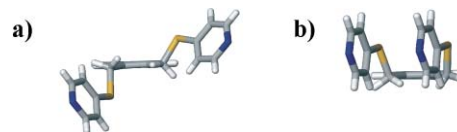

Fig. 3 Perspectives of 2,3-nap in: a) pure solid and b) 2(2,3-nap)·2(fum).

bonds of 2(2,3-nap)·2(fum),[12] it is likely that structure effects of close packing also play a role in determining the conformation of the thiopyridine.[13] Studies are underway to identify those factors that determine the conformation of the bipyridine framework and its ability to direct the [2 + 2] photoreaction in a solid.

In summary, we have employed principles of supramolecular synthesis and molecular self-assembly to reverse the code of a template-directed solid-state synthesis.[5] We believe that such code reversal expands the scope of employing linear templates to direct solid-state reactivity and may be used to decorate products obtained from the solid state with functional groups of synthetic and materials science interests.

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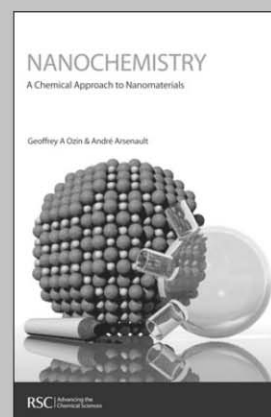13 For effects of conformation in crystalline assemblies, see: G. S. Papaefstathiou and L. R. MacGillivray, *Org. Lett.*, 2001, **3**, 3835.