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Site-directed regiocontrolled synthesis of a 'head-to-head' photodimer *via* a single-crystal-to-single-crystal transformation involving a linear template†

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Co-crystallisation of 1,8-naphthalenedicarboxylic acid (1,8-nap) with *trans*-1-(3-pyridyl)-2-(4-pyridyl)ethylene (3,4-bpe) gives a discrete molecular solid-state assembly, 2(3,4-bpe)·2(1,8-nap) 1, that is held together by four O–H···N hydrogen bonds wherein the diacid directs a regiocontrolled [2 + 2] photodimerization; the reaction occurs by way of a single-crystal-to-single-crystal transformation.

One of the main goals of synthetic organic chemistry is to make covalent bonds regioselectively.[1] Such control of reactivity enables chemists to dictate directionality of a covalent-bond-making-process thereby reducing formation of undesired single and/or multiple side-products.[2] In the ideal case, a chemist will strive to control a reaction such that one regioisomer forms, preferably in quantitative yield.

Whereas the idea of achieving regiocontrol of covalent bond formation is established in the context of synthetic chemistry at the molecular level,[1,2] the concept at the supramolecular level is less explored.[3] Although Nature routinely utilizes molecular templates (*e.g.* enzymes, deoxyribonucleic acid) to organise reactants, by way of directional noncovalent forces (*e.g.* hydrogen bonds), to achieve regiocontrolled syntheses supramolecularly, problems of entropy and solvent-effects encountered in the liquid phase have largely hindered chemists from mimicking such synthetic behaviour.[3,4] A general ability of chemists to direct the regiocontrolled formation of covalent bonds supramolecularly may, in principle, provide ready access to molecules, and materials, with properties that, similar to Nature, may be less accessible, or not attainable using more traditional chemical methods.[3]

We have recently reported an ability to control reactivity supramolecularly in the organised environment of the solid state using linear templates.[5] Co-crystallization of either resorcinol[5d] or 1,8-naphthalenedicarboxylic acid[5b] (1,8-nap) with a symmetrically substituted *trans*-1,2-bis(*n*-pyridyl)ethylene (*n*,*n*′-bpe) (*n* = 2 or 4) was shown to give a discrete four-component molecular assembly, 2(*n*,*n*′-bpe)·2(resorcinol) and 2(*n*,*n*′-bpe)·2(1,8-nap), respectively, held together by four O–H···N hydrogen bonds wherein two stilbenes are preorganised for a UV-induced [2 + 2] cycloaddition reaction. UV-irradiation of each solid produced the desired photoproduct, *rctt*-tetrakis(*n*-pyridyl)cyclobutane (*n*,*n*′-tpcb), stereospecifically (yield: 100%).

With a realisation that linear templates enable the stereocontrolled synthesis of molecules in solids,[5,6] it has occurred to us that it should be possible to employ this approach to conduct the [2 + 2] cycloaddition reaction regioselectively.[2] Whereas the reaction is controlled stereoselectively by connecting two identical pyridyl units (*i.e.* hydrogen bond acceptor sites) to the C=C linkage,[5] we anticipated that it should be possible to control the reaction regioselectively by attaching two different pyridyl units to the C=C bond. Owing to the ability of the templates to organise identical acceptor site linearly, we anticipated the template to preorganise such unsymmetrical reactants for a regiocontrolled 'head-to-head' [2 + 2] photoreaction.[7] Since different combinations of hydrogen bond acceptor sites may, in principle, be employed to direct the solid-state reaction (*i.e.* 1-(*n*-pyridyl)-2-(*m*-pyridyl)ethylene, where *n*,*m* = 2,3; 2,4; 3,4), a general means to direct the photoreaction regioselectively, using principles of supramolecular chemistry, may be achieved. A general ability to control the [2 + 2] photoreaction regioselectively in the solid state has, to our knowledge, not been realised,[8] an observation that may be attributed to the difficulty in dictating the arrangement of molecules in solids.[9]

Here we report an entry to establishing regiocontrol of the UV-induced [2 + 2] cycloaddition reaction in the solid state using an unsymmetrical dipyridyl ethylene as a reactant and a dicarboxylic acid as a linear template. Specifically, 1,8-nap, in 2(3,4-bpe)·2(1,8-nap) **1** (where: 3,4-bpe = *trans*-1-(3-pyridyl)-2-(4-pyridyl)ethylene), is employed to direct a regiospecific [2 + 2] reaction wherein the product, *rctt*-1,2-bis(3-pyridyl)-3,4-bis(4-pyridyl)cyclobutane (3,4-tpcb), forms in quantitative yield. Additionally, we reveal that the designed reaction occurs *via* a single-crystal-to-single-crystal (SCSC) transformation,[10,11] **1** being the first example in which a discrete multicomponent molecular assembly occurs *via* such a conversion.

Addition of 1,8-nap (0.017 g) to methanol (2 mL) in the presence of 3,4-bpe (0.015 g) yielded, upon standing for a period of approximately 3 days, colourless crystals of **1** suitable for X-ray analysis. The formulation of **1** was confirmed by ^{1}H NMR spectroscopy and single-crystal X-ray diffraction.‡

An ORTEP perspective of **1** is shown in Fig. 1. The components of **1** have assembled, similar to 2(*n*,*n*′-bpe)·(1,8-nap) (*n* = 2 or 4) **2**,[5b] to form a discrete molecular assembly held together by four O–H···N hydrogen bonds [O···N separations (Å): O(1)···N(1) 2.646(4), O(3)···N(3) 2.547(4),

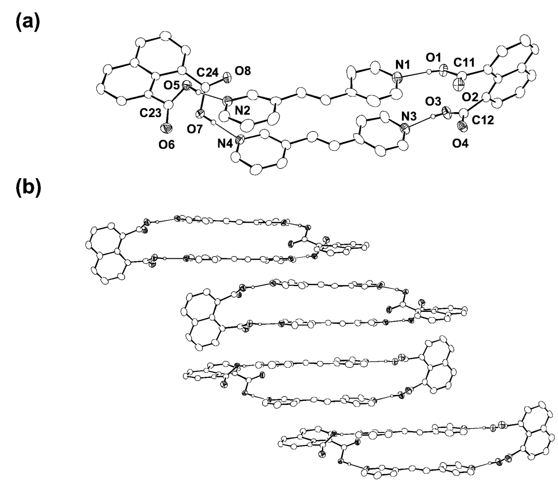

Fig. 1 Perspective of **1**: (a) discrete assembly and (b) stacked array. Interatomic distances (Å): O(1)···N(1) 2.646(4), O(3)···N(3) 2.547(4), O(5)···N(2) 2.632(4), O(7)···N(4) 2.598(4). Twist angles of carboxy groups (°): 55.7 (C11), 53.9 (C12), 41.6 (C23), 39.3 (C24).

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† Electronic supplementary information (ESI) available: X-ray crystal structure data, ^{1}H NMR spectra and X-ray powder pattern of **1**. See http://www.rsc.org/suppdata/cc/b2/b204542g/

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O(5)$\cdots$N(2) 2.632(4), O(7)$\cdots$N(4) 2.598(4)] (Fig 1a). As anticipated, the bipyridines are organised within the assembly in a 'head-to-head' fashion, each diacid interacting with either a 3-pyridyl or a 4-pyridyl unit. In this arrangement, each carboxyl group is twisted out of the plane of each naphthalene moiety such that the two carboxy groups associated with one of the pyridyl units (*i.e.* 3-pyridine), in contrast to **2**, adopt a staggered, rather than an eclipsed, conformation, the naphthalene unit being twisted approximately coplanar (twist angle: 11°) with respect to the bipyridines. As a consequence of these forces, the two C=C bonds, one of which lies disordered across two positions (relative occupancies: 72 : 28), are separated by 3.58 Å. The disordered olefin is, notably, aligned within the assembly such that the major site lies parallel with the ordered olefin, a position that satisfies the two geometry criteria of Schmidt for [2 + 2] photoreaction.[12] Adjacent complexes of **1** assemble to form stacked arrays held together by face-to-face π–π interactions (repeat pattern: nap$\cdots$bpe$\cdots$bpe$\cdots$nap) such that olefins of nearest-neighbour assemblies lie offset and separated by 3.92 Å (Fig. 1b).

Further examination of **1** suggests the hydrogen-bonded assembly to be photoactive. Specifically, electron density consistent with a cyclobutane ring the result of a regioselective [2 + 2] photoreaction involving 3,4-bpe to give 3,4-tpcb (yield: 9%) is observed between the two bipyridines. Indeed, generation of 3,4-tpcb in **1** is confirmed by ^{1}H NMR spectroscopy, the methine protons of the unsymmetrical cyclobutane appearing as two doublets at 4.67 and 4.69 ppm. Such conversion of 3,4-bpe to 3,4-tpcb has presumably occurred by way of ambient UV-light. Moreover, UV-irradiation of **1** for a period of 7 hours (broad-band Hg lamp) gives 3,4-tpcb, as determined by ^{1}H NMR spectroscopy, in quantitative yield. Although optical microscopy reveals single crystals of **1** become opaque during the photoreaction, X-ray powder diffraction, despite line broadening, indicates that irradiated **1** maintains crystalline order similar to the unreacted solid.

The observation that 3,4-tpcb may be generated in **1** suggested that the photoreaction may be induced to occur by way of a SCSC transformation.[10,11] During such a reaction, the product would interact with the template within a discrete complex analogous to the reactants. Although single crystals of **1** become opaque upon being exposed to the broad-band Hg source, irradiation of crystals with UV-energy that corresponds to the absorption tail of the reactants could result in such a conversion.[10]

When crystals of **1** were exposed to 400 nm light (Rayonet reactor), quantitative conversion of 3,4-bpe to 3,4-tpcb occurred, as determined by ^{1}H NMR spectroscopy. Moreover, optical microscopy indicated that the transparency of the single crystals was maintained during the photoreaction. As shown in Fig. 2, a single-crystal X-ray study§ (Fig. 2a) confirms SCSC conversion of 3,4-bpe to 3,4-tpcb (yield: 100%) (Fig. 2a). The photoproduct has been generated within **1** such that the product interacts with the template within a discrete complex, similar to the reactants, held together by four O–H$\cdots$N hydrogen bonds [O$\cdots$N separations (Å): O(1)$\cdots$N(1) 2.663(4), O(3)$\cdots$N(3) 2.591(4), O(5)$\cdots$N(2) 2.710(4), O(7)$\cdots$N(4) 2.591(4)]. To accommodate the product, the diacids undergo a change in conformation and orientation in **1** such that an acid group of each template (C12 and C23) rotates approximately 4° to accommodate splaying of the pyridyl groups and each template rotates approximately 3° to accommodate a 0.4 Å translation of the reactants to form the cyclobutane ring, respectively (Fig. 2b). To our knowledge, **1** is the first example where a linear template has been observed to guide a reaction involving its reactants.[3]

In this report, we have presented an approach to achieving regiocontrol of the [2 + 2] photoreaction supramolecularly in the solid state. The approach relies upon utilising a C=C bond with two different hydrogen bond acceptor sites where linear templates preorganise an unsymmetrical bipyridine for a 'head-to-head' photodimerization. With such observations achieved, we are expanding the approach to the remaining homologues of this series of compounds.[12] In principle, the method may also be applied to additional unsymmetrical reactants, and additional reactions, organised supramolecularly. That the reaction occurs *via* a SCSC transformation also suggests that the approach may be applied to the design of crystalline switches and devices.[13]

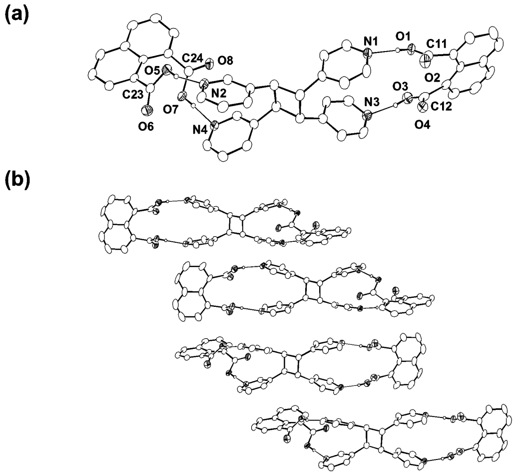

Fig. 2 Perspective of **1** (SCSC): (a) discrete assembly and (b) stacked array. Interatomic distances (Å): O(1)$\cdots$N(1) 2.663(4), O(3)$\cdots$N(3) 2.591(4), O(5)$\cdots$N(2) 2.710(4), O(7)$\cdots$N(4) 2.591(4). Twist angles of carboxy groups (°): 54.4 (C11), 50.0 (C12), 38.1 (C23), 41.4 (C24).

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Notes and references

‡ *Crystal data* for **1**: monoclinic, space group $P2_1/n$, a = 10.168(2), b = 33.916(7), c = 11.277(2) Å, β = 98.58(3)°, U = 3845(1) Å^3, D_c = 1.38 g cm^{-3}, Mo-Kα radiation (λ = 0.71070 Å) for Z = 4. Least-squares refinement based on 3930 reflections with $I_{\text{net}} > 2.0\sigma(I_{\text{net}})$ (out of 4946 unique reflections) led to a final value of R = 0.058. CCDC 186038.

§ *Crystal data* for **1** (SCSC): monoclinic, space group $P2_1/n$, a = 10.169(2), b = 34.357(7), c = 11.181(2) Å, β = 100.32(3)°, U = 3843(1) Å^3, D_c = 1.38 g cm^{-3}, Mo-Kα radiation (λ = 0.71070 Å) for Z = 4. Least-squares refinement based on 3714 reflections with $I_{\text{net}} > 2.0\sigma(I_{\text{net}})$ (out of 4994 unique reflections) led to a final value of R = 0.056. CCDC reference number 186039. See http://www.rsc.org/suppdata/cc/b2/b204542g/ for crystallographic data in CIF or other electronic format.

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