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Achieving a series of solid-state [2 + 2] cycloaddition reactions involving 1,2-bis(2-pyridyl)ethylene within halogen-bonded co-crystals†

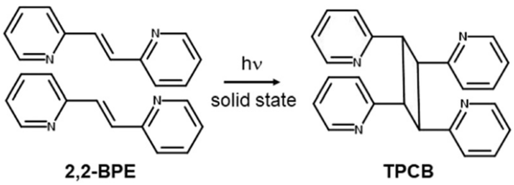
Max Andren,[a] Eric Bosch,[b] Herman R. Krueger Jr.[a] and Ryan H. Groeneman*[a]

The solid-state [2 + 2] cycloaddition reaction of *trans*-1,2-bis(2-pyridyl)ethylene through both co-crystallization and mechanical grinding is reported. The photoreaction is achieved by using iodoperchlorobenzene as a molecular template. The co-crystal is sustained primarily by I⋯N halogen bonds and homogeneous face-to-face π–π stacking interactions. The combination of these non-covalent forces ultimately places the reactant in a suitable position to photoreact. In addition, a pair of photoreactive solids were also achieved through a solvent-free mechanical grinding approach with similar yields.

Halogen bonding is a well established and important non-covalent interaction in the formation of molecular solids.[1] In particular, halogen bonding has been extensively utilized in the formation of co-crystals where it influences not only the structure, but the overall physical and chemical properties of these multicomponent solids.[2] In the domain of the light-induced [2 + 2] cycloaddition reaction, co-crystallization has proven to be a reliable approach to prepare photoreactive solids from otherwise unreactive alkenes.[3] In these co-crystals, one component acts as a molecular template to align a pair of carbon–carbon double bonds (C═C) on neighbouring reactants in a suitable position to photoreact. These co-crystal formers can utilize halogen bonding, as well as other non-covalent interactions, to generate these photoreactive solids.

A continued focus within our research groups has been the formation of halogen-bonded co-crystals that undergo the solid-state [2 + 2] cycloaddition reaction.[4] In particular, we have reported on the ability of various chlorine-substituted iodobenzenes, that reliably π-stack in a homogeneous manner, to act as a halogen-bond donor and thereby template photoreactions with various olefin-containing reactants. Initially, we reported the ability of 1,4-diiodoperchlorobenzene to engage in both I⋯N halogen bonds along with a homogeneous and face-to-face π–π stacking arrangement, which is essential to generate a photoreactive co-crystal as the reactant molecule must also participate in this type of stacking pattern.[5] Originally, a halogen-bonded co-crystal was reported based upon *trans*-1,2-bis(4-pyridyl)ethylene (**4,4-BPE**), since it remains the gold standard and most investigated reactant for this type of cycloaddition reaction.[5] Curiously, the remaining two symmetric bipyridines, namely *trans*-1,2-bis(3-pyridyl)ethylene and *trans*-1,2-bis(2-pyridyl)ethylene, are not nearly studied as frequently, in terms of their photochemical reactivity, even though these cyclobutanes are attractive building blocks for metal–organic materials.[6]

Using this as inspiration, we report here the ability to achieve a nearly quantitative photoreaction for a series of co-crystals that contain *trans*-1,2-bis(2-pyridyl)ethylene (**2,2-BPE**) (Scheme 1). A slow evaporation approach yielded a photoreactive halogen-bonded co-crystal based upon iodoperchlorobenzene (**C_6ICl_5**) along with **2,2-BPE**, namely 2(**C_6ICl_5**)·(**2,2-BPE**). As expected, molecules of **2,2-BPE** are able to accept I⋯N halogen bonds from **C_6ICl_5** that again stack in a homogeneous and face-to-face pattern that



Scheme 1 Rendering of the solid-state [2 + 2] cycloaddition reaction of **2,2-BPE** forming the photoproduct **TPCB**.

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[a] Department of Natural Sciences and Mathematics, Webster University, St. Louis, MO, 63119, USA. E-mail: ryangroeneman19@webster.edu

[b] Department of Chemistry and Biochemistry, Missouri State University, Springfield, MO, 65897, USA

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position the C═C on the reactant in a suitable orientation to photoreact and generate *rctt*-tetrakis(2-pyridyl)cyclobutane (**TPCB**) in the solid state (Scheme 1). In addition to this traditional solvent method for generating reactive co-crystals, a pair of photoreactive solids was also realized by employing a mechanochemical synthesis using a vortex grinder. In these solids, the halogen-bond donors were **C_6ICl_5** and 1,2,4,5-tetrachloro-3-iodobenzene (**C_6HICl_4**) that along with **2,2-BPE** produced two photoreactive co-crystals. To the best of our knowledge, these are the first reported examples of achieving a photoreactive co-crystal containing **2,2-BPE** *via* a solvent-free approach.

Both halogen-bond donors **C_6ICl_5**[7] and **C_6HICl_4**[8] were prepared by previously reported methods. The reactant **2,2-BPE** was purchased from a commercial source and was used without any purification. The co-crystal 2(**C_6ICl_5**)·(**2,2-BPE**) was realized by combining 103 mg of **C_6ICl_5** in 2 mL of toluene and 25 mg of **2,2-BPE** also in 2 mL of toluene (2 : 1 ratio) and allowed to slowly evaporate. Within two days along with some loss of solvent, single crystals suitable for X-ray diffraction were formed. It is important to note, the co-crystal 2(**C_6ICl_5**)·(**2,2-BPE**) was also attained from a 1 : 1 molar ratio based upon 52 mg of **C_6ICl_5** and 25 mg of **2,2-BPE** again using toluene as the solvent. The formation of 2(**C_6ICl_5**)·(**2,2-BPE**) was confirmed from the 1 : 1 ratio synthesis by using unit cell data determined from single-crystal X-ray diffraction data.

Single-crystal X-ray diffraction data determined that the components of 2(**C_6ICl_5**)·(**2,2-BPE**) crystallize in the centrosymmetric monoclinic space group $P2/c$. The asymmetric unit contains one molecule of **C_6ICl_5** and half of **2,2-BPE** where inversion symmetry generates the remainder of the molecule. The co-crystal is sustained by I⋯N halogen bonds [I⋯N 2.886(8) Å; C–I⋯N 175.6(3)°] to generate a three-component solid (Fig. 1). The ethylene bridge within **2,2-BPE** is found to be ordered at 300 K (Fig. 1). The aromatic ring on **C_6ICl_5** is slightly rotated from the planarity of the pyridine ring on **2,2-BPE** by 18.3(3)°. The halogen-bonded three-component units are found to engage in Type I Cl⋯Cl contacts[9] [Cl⋯Cl 3.328(4) Å; C–Cl⋯Cl 143.4(3)°; $|\theta_1 - \theta_2| = 0°$] with a nearest neighbour using the *ortho*-chlorine atoms with respect to the iodine (Fig. 2). The combination of these non-covalent interactions yields a wave-like one-dimensional chain that runs along the crystallographic *c*-axis.

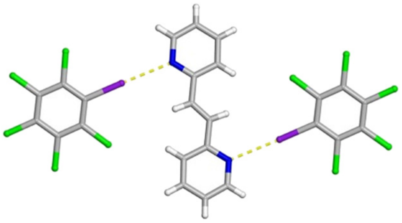

Fig. 1 X-ray structure of 2(**C_6ICl_5**)·(**2,2-BPE**) illustrating the I⋯N halogen bonds between the components. The I⋯N halogen bonds are shown with yellow dashed lines.

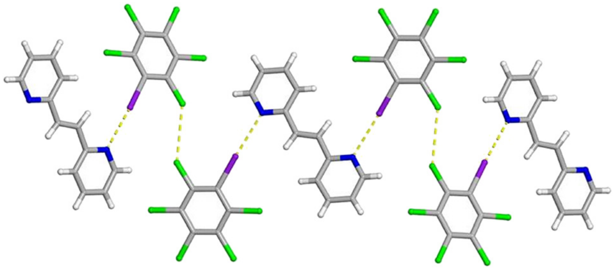

Fig. 2 X-ray structure of 2(**C_6ICl_5**)·(**2,2-BPE**) illustrating both the I⋯N halogen bonds and Type I Cl⋯Cl contacts to yield a wave-like one-dimensional chain. The I⋯N halogen bonds and Type I Cl⋯Cl contacts are shown with yellow dashed lines.

As expected, the halogen-bond donor **C_6ICl_5** stacks in a homogeneous and face-to-face π–π stacking pattern (Fig. 3). Due to crystal symmetry, the aromatic rings of both the donor and acceptor molecules are found parallel with a centroid-to-centroid distance of 3.9776(1) Å which is equal to the crystallographic *b*-axis. As a result, the reactant **2,2-BPE** is found in a suitable position to undergo a solid-state [2 + 2] cycloaddition based upon the requirements defined by Schmidt.[10]

In order to determine if a photoreaction would occur within 2(**C_6ICl_5**)·(**2,2-BPE**), crystals of the solid were dried and placed between glass plates and put into a photoreactor and exposed to broadband ultraviolet radiation from a 450 W medium-pressure mercury bulb. A photoreaction was confirmed in 2(**C_6ICl_5**)·(**2,2-BPE**) by ^{1}H NMR spectrometry which indicated the nearly complete loss of the olefin peak at 7.70 ppm (Fig. S1†) with the concomitant appearance of the cyclobutane peak at 4.93 ppm that corresponds to the stereoselective photoproduct **TPCB** (Fig. S2†).[11] The overall yield for the [2 + 2] cycloaddition reaction was determined to be 98% after 80 hours of exposure. The infinite stacking of the **2,2-BPE** reactant molecules could explain the near

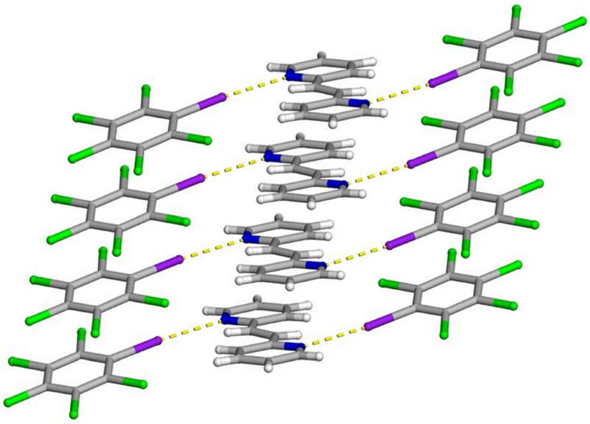

Fig. 3 X-ray structure of 2(**C_6ICl_5**)·(**2,2-BPE**) illustrating the I⋯N halogen bonds and the homogenous face-to-face π–π stacking pattern of both the halogen-bond donor and acceptor. The I⋯N halogen bonds are shown with yellow dashed lines.

quantitative yield for this co-crystal, since similar yields have been observed in other infinite and homogeneous π-stacked co-crystals.[4b,c,5]

Based on the observed ability of $\mathbf{C_6ICl_5}$ to halogen bond to **2,2-BPE** and form homogeneous face-to-face π–π stacks, we anticipated that a photoreactive co-crystal could also be achieved using a solvent-free approach. To this end, a mechanochemical synthesis was attempted again using a 2 : 1 ratio of these halogen-bond donor and acceptor. In particular, 103 mg of $\mathbf{C_6ICl_5}$ and 25 mg of **2,2-BPE** were ground together. The components were placed in a SmartSnap Grinding Jar along with 2 ball bearings (5 mm diameter) and were dry vortex ground using a VWR Vortex Genie 2. The molecules were ground for a total of 15 minutes where at both the 5 and 10 minute marks the resulting solid was scraped from the edges before continuing grinding. As before, the resulting solid was then placed in a photoreactor and exposed to ultraviolet light. A photoreaction was again detected by the appearance of the cyclobutane peak within **TPCB** by ^{1}H NMR spectroscopy at 4.93 ppm (Fig. S3†).[11] Similar to the solvent co-crystallization approach, the dry grinded solid also reached a yield of 98% for the [2 + 2] cycloaddition reaction after 40 hours.

With the goal to determine the bulk properties and possibly the structure of the ground solid the resulting material was investigated by powder X-ray diffraction. The diffractogram determined that the grinded solid created a new phase when compared to the expected powder pattern of **2,2-BPE** (Fig. S5†).[12] More importantly, the observed powder pattern for the dry ground sample is in good agreement with the calculated pattern for $2(\mathbf{C_6ICl_5})\cdot(\mathbf{2,2\text{-}BPE})$ (Fig. S6†). This diffraction data confirms that both the solvent and solvent-free synthesis resulted in the formation of the photoreactive halogen-bonded co-crystal. This reasonably explains why the overall yields for the cycloaddition reaction were 98% for each synthetic approach.

In the attempt to achieve another high yielding [2 + 2] cycloaddition reaction, *via* a solvent-free approach, a second donor was investigated, namely $\mathbf{C_6HICl_4}$. Unlike before, a 1 : 1 ratio for the donor to acceptor, namely 47 mg of $\mathbf{C_6HICl_4}$ and 25 mg **2,2-BPE**, were ground using the Vortex Genie 2. This molar ratio was selected due to the ability of $\mathbf{C_6HICl_4}$ to form both halogen and hydrogen bonds with the hope to yield a chain-like structure rather than a discrete assembly.[4b] The components were vortex grinded for 15 minutes with scraping after the 5 and 10 minute marks. The resulting solid was then transferred to glass plates and exposed to radiation. Again, a photoreaction was detected by the nearly complete loss of the olefin peak at 7.70 ppm along with the concomitant appearance of a cyclobutane peak at 4.93 ppm indicating the formation of **TPCB** (Fig. S4†).[11] The solid reached an overall yield of 99% for the cycloaddition reaction within 80 hours of exposure.

Powder X-ray diffraction pattern for this vortexed sample confirmed a new phase was formed when compared to the expected powder pattern for both **2,2-BPE** (Fig. S7†) and $2(\mathbf{C_6ICl_5})\cdot(\mathbf{2,2\text{-}BPE})$ (Fig. S8†), since the observed to calculated patterns did not match. In terms of the photoreactivity, the resulting solid must place the reactive C=C in a suitable position due to the observed [2 + 2] cycloaddition reaction. It is therefore reasonable to conclude that $\mathbf{C_6HICl_4}$ acts as a molecular template and interacts with **2,2-BPE** *via* non-covalent interactions to overcome the photostability of the reactant as a single-component solid.[12]

With the goal to calculate the homogeneous face-to-face π–π stacking interaction energy and to determine if that is preferred over a hypothetical heterogeneous pattern a theoretical study utilizing density functional theory at the M062X/aug-cc-pVTZ level was undertaken. The homogeneous π-stacking energy of $\mathbf{C_6ICl_5}$ was calculated by using atomic positions based upon the single-crystal X-ray diffraction data of $2(\mathbf{C_6ICl_5})\cdot(\mathbf{2,2\text{-}BPE})$ (Fig. S9a†). The theoretical calculation returned a value of −34.2 kJ mol^{-1} for the homogenous π–π stacking energy for two $\mathbf{C_6ICl_5}$ molecules. To estimate the hypothetical heterogeneous π-stacking energy an additional computation was performed where one of the $\mathbf{C_6ICl_5}$ members of the pair was replaced with a pyridine molecule at identical atomic positions for the carbons (Fig. S9b†). In this case, a value of −19.9 kJ mol^{-1} was obtained for the heterogeneous π–π stacking energy. The difference in these interaction energies illustrates the preference of the homogenous π-stacking pattern observed within $2(\mathbf{C_6ICl_5})\cdot(\mathbf{2,2\text{-}BPE})$ which along with the I⋯N halogen bond are the important non-covalent interactions that aided in the formation of a photoreactive co-crystal.

Conclusions

In this communication, we report the formation of a halogen-bonded co-crystal that undergoes a nearly quantitative yield for the [2 + 2] cycloaddition reaction. This photoreactive co-crystal contains *trans*-1,2-bis(2-pyridyl) ethylene along with iodoperchlorobenzene. In particular, the co-crystal $2(\mathbf{C_6ICl_5})\cdot(\mathbf{2,2\text{-}BPE})$ was attained by utilizing both a solvent-based and solvent-free approach with similar yields for the solid-state photoreaction. In addition, a second high yielding cycloaddition reaction was observed within a co-crystal using 1,2,4,5-tetrachloro-3-iodobenzene as the donor using a mechanochemical approach. The formation and photoreactivity of additional co-crystals containing **2,2-BPE** with other halogen- and hydrogen-bond donors are currently being investigated.

Author contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Conflicts of interest

There are no conflicts to declare.

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