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Head-to-tail photodimerization of a thiophene in a co-crystal and a rare adipic acid dimer in the presence of a heterosynthon

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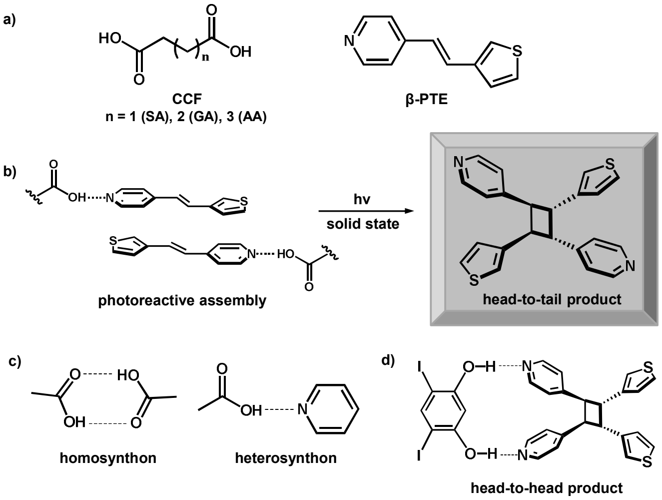
A saturated dicarboxylic acid is employed to achieve a photoreactive hydrogen-bonded assembly based on a thiophene that reacts to generate a head-to-tail photoproduct. A co-crystal that exhibits both a homo- and heterosynthon in the same co-crystal based on adipic acid and the thiophene is also presented.

Control of solid-state packing of molecules is of great interest to design functional solids and direct [2+2] photodimerizations in crystals.[1] To date, two general approaches have emerged to achieve [2+2] photoreactions in the solid state; namely, covalent- and auxiliary-based methods. While a covalent approach involves carefully varying substituents attached to olefins to control packing,[2] the auxiliary method relies on using a second component to modify supramolecular packing to achieve a photodimerization, often in the form of a co-crystal.[3] The auxiliary approach has been reliable when using a ditopic template (*i.e.* resorcinol).[4] Ditopic templates preorganize olefins into favourable geometries for photoreactions *via* spatially-oriented hydrogen-bond-donor and -acceptor groups.[5] Ditopic templates have been particularly successful in generating head-to-head photoproducts. A second component can also be used, however, to interact with an olefin so as to effectively 'fill space' in a solid to support reactivity. Indeed, such a method may be attractive to generate a head-to-tail cyclobutane where a ditopic template is already known to direct the formation of the corresponding head-to-head photoproduct.[6] To generate head-to-tail regioisomers, such a 'trial-and-error' approach using a second component would be beneficial when prerequisite packings and assemblies using different co-crystal formers (**CCF**s) are achieved.

Here, we apply a co-crystallization to direct the formation of head-to-tail *rctt*-1,3-bis(4-pyridyl)-2,4-bis(3-thienyl)cyclobutane (**4p3tc**) regiospecificallly and in high yield (Schemes 1a,b). A **CCF** in the form of a saturated dicarboxylic acid is used to achieve the photoreactive assembly *via* a co-crystal of 2(**β-PTE**)·succinic acid (**SA**) (where **β-PTE**: = 1-(4-pyridyl)-2-(3-thienyl)ethylene (Scheme 1a). Additional **CCF**s were also used to afford co-crystals of 2(**β-PTE**)·glutaric acid (**GA**) and (**β-PTE**)·adipic acid (**AA**). In one solid, we demonstrate a rare occurrence wherein both the carboxylic acid dimer of adipic acid and O-H···N heterosynthon are present in the same co-crystal (Scheme 1c).

Using a ditopic template in the form of 4,6-diiodoresorcinol, we have very recently reported the solid-state photodimerization of **β-PTE**, which is photostable as a pure solid, to give the corresponding head-to-head photoproduct (Scheme 1d).[6] Our interests in the olefin relate to the integration of thiophenes as component of electronic materials and devices.[6] In efforts to generate the head-to-tail cyclobutane, we have discovered that **SA** in a co-crystal with **β-PTE** affords **4p3tc**. We have also systematically modified the chain length of the dicarboxylic acid in efforts to determine how packings of **β-PTE** are affected by changing the **CCF**.



Scheme 1. Structures of: (a) dicarboxylic acid **CCF**s and β-substituted thiophene, (b) photoreactive assembly that yields head-to-tail cyclobutane, (c) synthons achieved via co-crystallization, and (d) head-to-head photoproduct of **β-PTE**.

Initially, we focused on a dicarboxylic acid with a chain length of four carbons in the form of **SA**. **β-PTE** was co-crystallized with **SA** in a 2:1 ratio in tetrahydrofuran. Colorless plate-shaped crystals formed upon slow solvent evaporation over a period of 2 days. The formulation of 2(**β-PTE**)·(**SA**) was confirmed using ^{1}H NMR spectroscopy and single-crystal X-ray diffraction.

A crystal structure analysis revealed the O-H···N heterosynthon [O···N separation (Å): O(1)···N(1) 2.619(4), O(3)···N(2) 2.642(4)] that defines a discrete three-component assembly with the hydrogen bonds extending in the *bc* plane. The assembly is accompanied by close S···S contacts (3.46 Å) that effectively serve to link thiophenes of neighboring assemblies (Fig 1). The assemblies stack in offset layers, producing a head-to-tail arrangement of the olefins (C=C 3.99 Å), which are canted at 15° to one another (Fig 1b). Each olefin and **CCF** are disordered over two sites [site occupancies: 0.908(2) and 0.092(2)]. The extended packing of 2(**β-PTE**)·(**SA**) consists of isolated olefin pairs arranged head-to-tail, surrounded above and below by a **SA** molecule (Fig 1c).

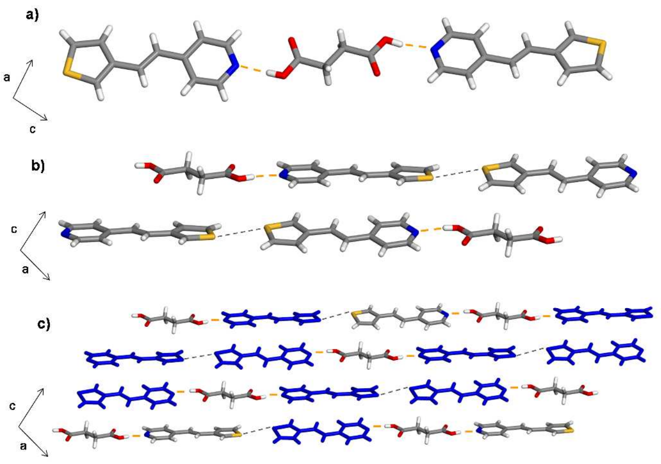


Figure 1. X-ray structures of 2(**β-PTE**)·(**SA**): (a) heterosynthon assembly, (b) head-to-tail arrangement of olefins, and (c) extended packing highlighting olefin pairs. Dotted grey lines show S···S contacts. Highest occupancies are shown for all structures.

Since the thiophenes lie in a suitable geometry for a [2+2] photodimerization,[7] a powdered crystalline sample (50 mg) of 2(**β-PTE**)·(**SA**) was irradiated with UV light (medium pressure Hg). Photodimerization was confirmed by an upfield shift in the pyridine peaks (0.2 ppm) in the ^{1}H NMR spectrum. Furthermore, two cyclobutane peaks (4.45 and 4.65 ppm) emerged, which contrasts a single peak for the reported head-to-head photoproduct.[6] The photodimerization proceeded to 86% yield upon irradiation for 110 h. To confirm the stereochemistry of the photoproduct, **SA** was removed from the product (See SI) and single crystals of **4p3tc** were grown from a solution of acetonitrile and toluene (3:2 *v*/*v*).

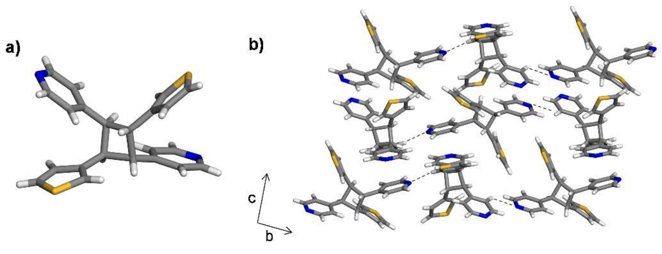


Figure 2. X-ray structure of **4p3tc**: (a) asymmetric unit and (b) extended packing. Dotted grey lines show C-H···N interactions. Highest occupancies shown for disordered thiophene ring.

A crystal structure analysis confirmed head-to-tail **4p3tc** [C-C bond lengths (Å): C(6)-C(7) 1.54(1), C(6)-C(18) 1.58(1), C(7)-C(17) 1.58(1), C(17)-C(18) 1.55(1)] (Fig 2). One thiophene ring of the cyclobutane lies disordered over two sites [site occupancies: 0.648(3) and 0.352(3)]. The cyclobutanes interact *via* C-H(thiophene)···N and C-H(pyridine)···N forces (3.55 and 3.46 Å, respectively).

Among the three **CCF**s studied here, the reactivity is specific to 2(**β-PTE**)·(**SA**). When **β-PTE** was co-crystallized with **GA** in a 2:1 ratio in acetonitrile, colorless prism-shaped crystals formed upon slow solvent evaporation over a period of 1 day. The formulation of 2(**β-PTE**)·(**GA**) was confirmed using ^{1}H NMR spectroscopy and single-crystal X-ray diffraction.

A single-crystal X-ray analysis revealed the O-H···N heterosynthon [O···N separation (Å): O(2)···N(1A) 2.728(5), O(4)···N(2) 2.652(2)] (Fig 3) that define, similar to 2(**β-PTE**)·(**SA**), a three-component assembly. The hydrogen bonding extends in the *ab* plane accompanied by S···S contacts (3.58 Å) that link thiophenes of neighboring assemblies also akin to 2(**β-PTE**)·(**SA**). The assemblies in 2(**β-PTE**)·(**GA**) stack in offset layers, producing a head-to-tail arrangement of closest olefin pairs (C=C 4.37 Å) with one olefin being disordered over two sites [site occupancies: 0.633(1) and 0.367(1)]. Whereas the layers in 2(**β-PTE**)·(**SA**) stack such that two reactive olefins are surrounded by acids, the packing in 2(**β-PTE**)·(**GA**) effectively consists of olefin pairs surrounded by olefins (Fig 3b). The mean planes of the olefin pairs are canted at 33° with the outer olefins being canted at 59°.[7] Upon UV irradiation for 30 h, 2(**β-PTE**)·(**GA**) was determined to be photostable.

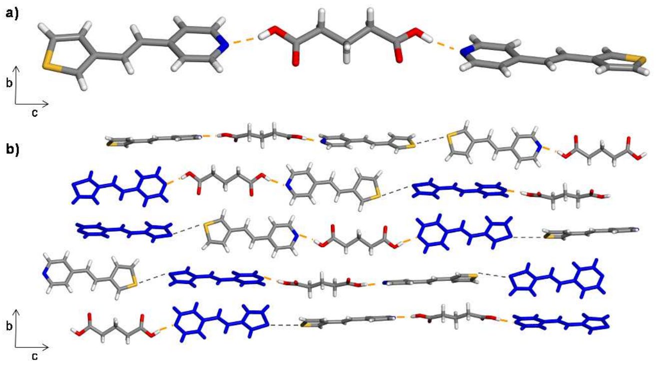


Figure 3. X-ray structure of 2(**β-PTE**)·(**GA**): (a) heterosynthon assembly and (b) extended packing highlighting olefin pairs. Dotted grey lines show S···S contacts. Highest occupancies shown for disordered olefin.

When **β-PTE** was co-crystallized with **AA** in a 2:1 ratio in ethyl acetate, colorless plate-shaped crystals formed upon slow solvent evaporation over a period of 1 day. The formulation of (**β-PTE**)·(**AA**) was confirmed using ^{1}H NMR spectroscopy and single-crystal X-ray diffraction. Moreover, rather than co-crystallizing in a 2:1 ratio, a solid based on a 1:1 ratio in (**β-PTE**)·(**AA**) formed.

A crystal structure analysis revealed the presence of the O-H···N heterosynthon [O···N separation (Å): O(1)···N(1) 2.623(5)]. Whereas the O-H···N heterosynthon dominates in the co-crystals based on **SA** and **GA**, the acid dimer O-H···O homosynthon also defines the hydrogen bonding in (**β-PTE**)·(**AA**) [O···O separation (Å): O(3)···O(4) 2.667(4)] so as to generate, in contrast to 2(**β-PTE**)·(**SA**) and 2(**β-PTE**)·(**SA**), a four-component assembly (Fig. 4). The hydrogen bonding extends in the *ac* plane accompanied by longer S···S contacts (3.63 Å) that link thiophenes of neighboring assemblies. In the arrangement, the acid dimer synthons are effectively surrounded by thiophene rings. The assemblies stack offset such that **β-PTE** molecules do not overlap (closest C=C 8.56

Å). Upon UV irradiation for a period of 30 h, (**β-PTE**)·(**AA**) was photostable.

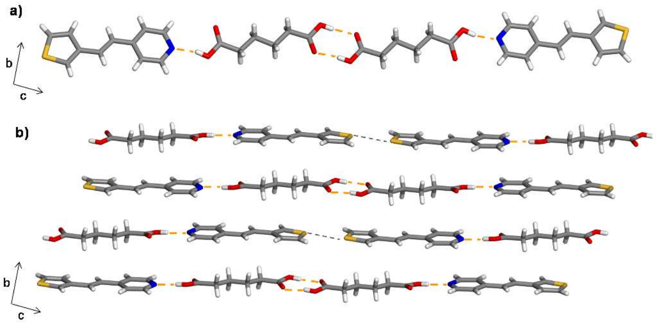


Figure 4. X-ray structure of (**β-PTE**)·(**AA**): (a) acid dimer and heterosynthon and (b) extended packing in neighboring layers. Dotted grey lines show S···S contacts.

There are few reported co-crystals involving pyridine-based acceptors that possess both a homo- and heterosynthon present in the same solid.[8] Price *et al.* have addressed the issue involving caffeine and 4-hydroxybenzoic acid where the formation of an acid dimer is calculated to be more stable than the C(O)OH···N heterosynthon.[9] While extended stacking of the components, intermolecular forces, and molecular flexibility can all play a role in determining hydrogen bonds that dominate,[9, 10] that **AA** is similar in size to **β-PTE** could also allow for such favourable overlap of components[11] to support the co-existence of the two synthons in the solid.

Conclusions

In this report, we have used an auxiliary approach in the form of a co-crystallization to support the formation of a head-to-tail cyclobutane of a thiophene. We also describe a rare occurrence wherein both a homo- and hetero-synthon are present in the same co-crystal. We are currently investigating additional auxiliary approaches to reliably direct [2+2] photodimerizations in thiophenes, with a goal to design complex molecules for applications in organic materials.

Notes and references

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† Electronic Supplementary Information (ESI) available: [experimental details, ^{1}H NMR, and single-crystal X-ray data]. CCDC 989758-989761 contains the supplementary crystallographic data for this paper. See DOI: 10.1039/c000000x/

‡ Crystal data for 2(**β-PTE**)·(**SA**): 2($C_{11}H_9NS$)·($C_4H_6O_4$), M = 492.59, monoclinic, space group P2$_1$/c, a = 9.283(1), b = 19.692(2), c = 13.665(2), β = 108.704(5), V = 2365.9(4), T = 298(2) K, Z = 4, MoKα radiation (λ = 0.7107 Å), 15445 reflections measured, 2713 reflections for I >2σ(I) with R$_1$ = 0.0591. Crystal data for **4p3tc**: $C_{22}H_{18}N_2S_2$, M = 374.5, monoclinic, space group P2$_1$/c, a = 11.689(1), b = 15.176(2), c = 12.166(1), β = 117.334(5), V = 1917.1(3), T = 298(2) K, Z = 4, MoKα radiation (λ = 0.7107 Å), 10820 reflections measured, 2218 reflections for I >2σ(I) with R$_1$ = 0.0443. Crystal data for 2(**β-PTE**)·(**GA**): 2($C_{11}H_9NS$)·($C_5H_8O_4$), M = 506.61, monoclinic, space group P2$_1$/c, a = 15.935(2), b = 7.3782(7), c = 21.823(3), β = 100.382(5), V = 2523.8(5), T = 190(2) K, Z = 4, MoKα radiation (λ = 0.7107 Å), 43736 reflections measured, 3525 reflections for I >2σ(I) with R$_1$ = 0.0408. Crystal data for (**β-PTE**)·(**AA**): ($C_{11}H_9NS$)·($C_6H_{10}O_4$), M = 333.39, triclinic, space group P $\bar{1}$, a = 5.6534(6), b = 8.1587(8), c = 18.996(2), α = 83.851(5), β = 83.879(5), γ = 74.142(5), V = 835.2(2), T = 298(2) K, Z = 2, MoKα radiation (λ = 0.7107 Å), 3741 reflections measured, 1190 reflections for I >2σ(I) with R$_1$ = 0.0610.

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11 The size of the diacid is ultimately determined by the length of the -CH_2- chain, which can also evoke arguments related to odd/even effects in crystal packing. See: (a) G. R. Desiraju *et al.*, *J. Am. Chem. Soc.*, *2013*, **135**, 8121; (b) C. B. Aakeröy *et al.*, *Cryst. Growth Des.*, *2012*, **12**, 2579.

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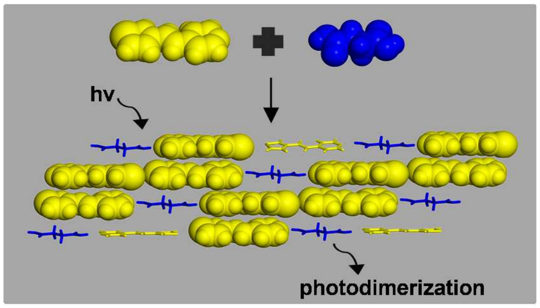

Head-to-tail photodimerization of thiophene is achieved in a co-crystal while a co-crystal with an acid dimer and heterosynthon is also described.