Regiospecific topochemical reactions controlled by trifluoromethyl directing groups†

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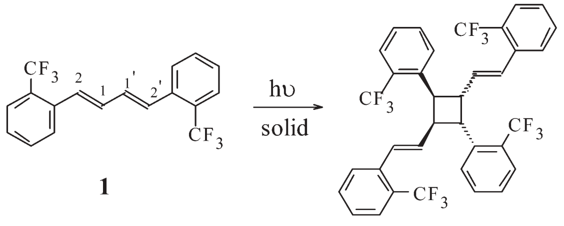
A parallel, offset-stacked orientation was found in the crystal packing of *E,E*-1,4-di(*o*-trifluoromethyl)phenyl-1,3-butadiene. UV-irradiation of the powered crystalline sample resulted in a quantitative conversion to a single [2 + 2] cycloaddition product.

A classic example of topochemical reaction control in the solid state is the photodimerization of cinnamic acid discovered by Schmidt *et al.* in the 1960s.[1] Through their pioneering work[2] as well as many other studies,[3,4] a topochemical principle for the [2 + 2] cycloaddition reactions of olefinic molecules in the solid state was outlined. According to Schmidt's topochemical principle, products can be formed only if the reactants lie parallel and are separated by 3.5–4.2 Å. With this ordering principle in mind, chemists have used a variety of innovative approaches to organize molecules to allow such a reaction to occur. Chloro,[5] fluoro,[6] and acetoxy[3] were found to have the topochemical controlling effects on the crystal lattices of some olefinic reactants. Also, $\pi\cdots\pi$ stacking interactions[7] were used to construct ideal architectures for [2 + 2] photodimerization and photopolymerization.[6,8] Moreover, during the past ten years, templates have been successfully designed to organize *all-trans*-bis(4-pyridyl)polyenes[9,10] and other short polyenes[11] for [2 + 2] cycloaddition. However, it is still a challenge to use a template to assemble *E,E*-1,4-diphenyl-1,3-butadiene (DPB) that contains no charged ring systems and is photostable in the solid state.[3] Herein, we report the first application of a trifluoromethyl group as a new handle to direct DPB molecules in arrangements suitable for [2 + 2] cycloaddition reactions.



1

2

Although non-covalent $\pi\cdots\pi$ interactions between perfluorophenyl rings have been reported in different cases,[12,13] very little is known about substituent effects in $\pi\cdots\pi$ stacking, either theoretically or experimentally.[14] It is notable that fluorine plays a critical role in the formation of $\pi\cdots\pi$ stacking orientations. It has occurred to us that a trifluoromethyl group may have the same attractive prospect as fluorine. Therefore, we chose to examine the crystal packing of *E,E*-1,4-di(*o*-trifluoromethyl)phenyl-1,3-butadiene **1**. To synthesize **1**, *E*-(*o*-CF_3)–$C_6H_4CH{=}CHCHO$, which was prepared by the C_2-extension of *o*-CF_3–C_6H_4CHO with $(C_6H_5)_3P{=}CHCHO$, was coupled in a Horner–Wadsworth–Emmons olefination with *o*-CF_3–$C_6H_4CH_2P(O)(OC_2H_5)_2$ using sodium hydride as a base. The colorless crystals of **1** were obtained from ethyl acetate in an overall yield of 50%.

A view of the X-ray crystal structure of **1** determined at 173 K (Fig. 1a) indicates that the molecule is related by an inversion center so that only half the structure is crystallographically unique.‡ The crystal structure shows that the diene unit is coplanar with the absolute torsional angles ranging from 179 to 180°, and the two phenyl rings are slightly twisted from the conjugated 1,3-butadiene unit with a torsional angle (~4.0°, C1–C2–C3–C8). As expected, the offset-stacked orientation between the phenyl rings of neighboring molecules has been found in the crystal packing (Fig. 1b). Compound **1** crystallizes to a layered structure in which olefins of neighboring layers are separated by 3.50 Å. As a result, the double bonds of the diene units conform to the topochemical principle. Further analysis of the crystal structure (**1**) suggests that the shortest distance of H$\cdots$F bonds (C_9–F$\cdots H_7$: 2.67 Å) is identical to the sum of the van der Waals radii for H and F (H = 1.20 Å, F = 1.47 Å).[15] Thus, hydrogen bonding is considered to be negligible in this case. Also, the trifluoromethyl groups of the neighboring molecules in the crystal lattice tend to come closer to

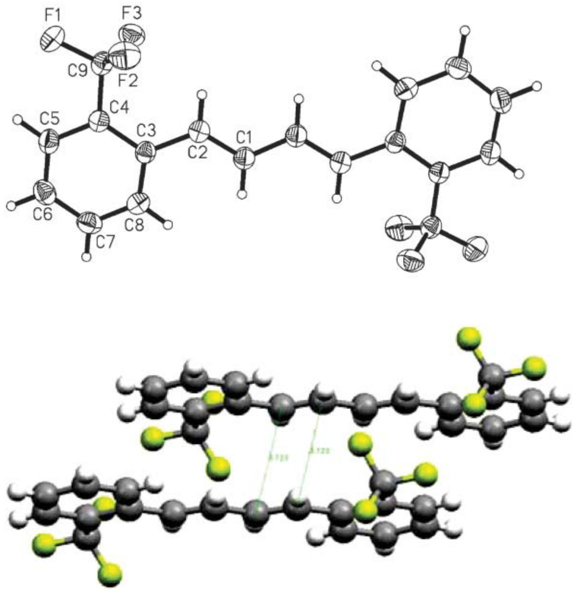


Fig. 1 (a) An ORTEP diagram of **1** (top); (b) the molecules (**1**) stack in an offset arrangement along the unique (*b*) axis, and the distance between the layers of the molecules is 3.50 Å.

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† Electronic supplementary information (ESI) available: spectroscopic data. See http://www.rsc.org/suppdata/cc/b4/b413898h/

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each other at a distance of 2.93 Å ($F_1 \cdots F_3$), due to the weak F···F interactions.[6] Because of the weakness of the short-distance contacts, we believe that the noncovalent π···π stacking interaction is mainly responsible for the observed self-assembling of **1**.

UV-irradiation of **1** in solution using a 200 W Hg medium-pressure lamp with a Pyrex filter resulted in the conversion of **1** to its *Z*,*E* isomer in >95% yield. On the other hand, UV photolysis of the powdered crystalline sample **1** using the same light source at room temperature for 15 h afforded a single product (**2**) in 100% yield. The cyclobutane ring of **2** was characterized by two proton signals at 4.45 and 4.15 ppm (^{1}H NMR). Also, as evidenced by a doublet (d) and a doublet of doublets (dd) at 6.71 and 5.91 ppm, respectively, the existence of carbon–carbon double bonds was suggested in **2**. The spectroscopic data indicated that two DPB molecules underwent a single [2 + 2] addition reaction to form **2**. This observation is in accordance with reactivity studies involving 1,3-butadienes in solid.[2] In addition, it was noticed, interestingly, that photoisomerization of the C=C bonds in **2** was undetected in solution[16] upon direct irradiation (Pyrex). To unequivocally elucidate the stereochemistry of **2**, crystallographic data was obtained (Fig. 2). The central four-membered ring of **2** was found to be the crystallographic centre of inversion. Examination of the crystal structure indicates that the C2–C1 double bond of **1** (see structure of **1** and Fig. 1b) reacted with the C1′–C2′ double bond of the neighboring molecule. The regiospecific addition is due to the closest distance (3.72 Å) between the C2–C1 and C1′–C2′ bonds, while the distance (4.92 Å) between two neighboring C2–C1 double bonds is exceeded for the topochemical reaction. It appears that the π···π stacking interaction produced by trifluoromethyl groups directed the geometry of crystallization to yield photoactive crystals of **1**.

To further probe the generality of trifluoromethyl in exerting direct control of the crystal packing of DPB molecules, we prepared *E*,*E*-1,4-di(*m*-trifluoromethyl)phenyl-1,3-butadiene **3** and *E*,*E*-1,4-di(*p*-trifluoromethyl)phenyl-1,3-butadiene **4** by the procedure described above. UV irradiation of powdered crystalline samples **3** and **4** for 15 h at 25 °C afforded a single photoproduct in 50–60% yield, respectively. The yields remained the same after irradiation for 15 h. Each photoproduct isolated from the unreacted starting material by way of silica-gel column chromatography (hexanes as an eluant) was suggested by MS to be a dimer from a single [2 + 2] reaction (see ESI†). Also, as evidenced by a broad proton signal at around 4.00 ppm and two carbon signals in the range of δ = 47.0–45.0 ppm, the cyclobutane ring in each photoproduct was confirmed. Moreover, in the ^{1}H NMR spectrum of each photoproduct, the appearance of a pair of d and dd in the range of δ = 6.60–6.00 ppm showed a strong resemblance to the proton absorptions characterized for the olefinic hydrogens of **2**. All the structural data strongly supports that **3** and **4** indeed undergo a single [2 + 2] cycloaddition, analogous to **1**. The results further corroborate that trifluoromethyl is capable of juxtaposing DPB molecules in a parallel fashion for an intermolecular [2 + 2] cycloaddition by means of a π···π stacking interaction. We are now investigating potential applications of the trifluoromethyl group to other systems for stereo-controlled reactions in the solid state.

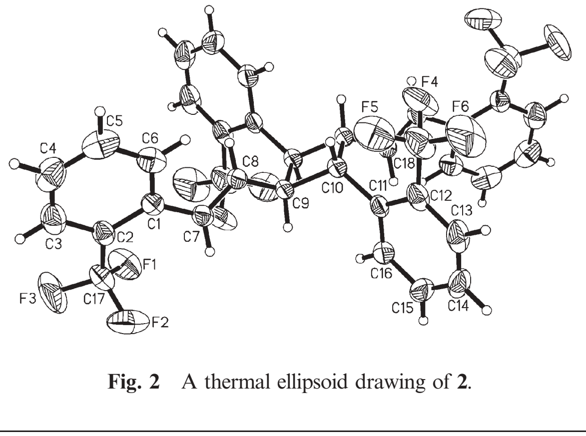

Fig. 2 A thermal ellipsoid drawing of **2**.

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Notes and references

‡ *Crystal data.* Compound **1**, $C_{18}H_{12}F_6$, M = 342.28, monoclinic, a = 10.3758(19), b = 4.9215(9), c = 15.280(3) Å, α = 90, β = 107.108(2), γ = 90°, U = 745.8(2) Å^3, T = 173(2) K, space group: $P2_1/c$, Z = 2, μ(Mo–Kα) = 0.140 mm^{-1}, 6437 reflections measured, 1690 unique (R_{int} = 0.0285) which were used in all calculations. The final $wR(F^2)$ = 0.1131 (all data). Compound **2**, $C_{36}H_{24}F_{12}$, M = 684.55, triclinic, a = 7.9904(9), b = 10.0114(11), c = 10.6547(12) Å, α = 73.214(2), β = 68.806(2), γ = 84.573(2)°, U = 760.77(15) Å^3, T = 173(2) K, space group: $P\bar{1}$, Z = 1, μ(Mo–Kα) = 0.138 mm^{-1}, 7718 reflections measured, 2700 unique (R_{int} = 0.0368) which were used in all calculations. The final $wR(F^2)$ = 0.1257 (all data). CCDC 249913 and 249914. See http://www.rsc.org/suppdata/cc/b4/b413898h/ for crystallographic data in .cif or other electronic format.

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