

# *Cis* → *trans* and *trans* → *cis* isomerizations of styrylcoumarins in the solid state. Importance of the location of free volume in crystal lattices†‡

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We have examined the photobehavior of a set of isomers of 2-pyranone-annulated stilbenes (6-styrylcoumarin **1**, 7-styrylcoumarin **2**, 4-methyl-6-styrylcoumarin **3**, and 4-methyl-7-styrylcoumarin, **4**) in their crystalline phases. While the *cis* isomers of **1–3** undergo *cis* → *trans* photoisomerizations in the solid state, *cis-4* and the *trans* isomers of **1–3** do not; the *trans* isomer of **4** undergoes photo-induced intermolecular reactions. Solution-state irradiations of the *trans* isomers of **1–4** lead to the *cis* isomers quite readily, as does *cis-4* lead to *trans-4*, which suggests that the absence of geometric isomerization of the *trans* isomers and the lack of reactivity of *cis-4* in the solid state are due to molecular packing effects. X-Ray crystal structural analyses of **1–4** reveal interesting conformational preferences for the styrenic moieties and differences in the total ‘free’ volumes within the lattices, but neither factor explains satisfactorily why some of the molecules undergo geometric isomerizations in their single crystals and others do not. Using the PLATON program, we have located the sizes and positions of ‘void volumes’ within the crystal lattices, and identified trajectories necessary for atomic motions to lead to geometric isomerizations to understand the reactivities of **1–4**. The voids in the reactive *cis* isomers of **1–3** crystals are located along the trajectories needed for geometric isomerization. The relevant voids in the crystals of *cis-4* and the *trans* isomers of **1** and **2** (the non-isomerizing molecules for which suitable crystals could be grown for X-ray analyses) are located along a trajectory that does not permit isomerization. We hypothesize that the classical momentum gained from the initial motions that are facilitated due to the voids in the crystals of the *cis* isomers of **1–3**, as well as the heat dissipated to the local environment by internal conversions and vibronic cascade of the Franck–Condon states, helps to drive the system over potential energy barriers that would not be possible otherwise. *Cis-4* and the *trans* isomers of **1** and **2**, as well as other examples from the literature in which geometric isomerizations do or do not occur in the solid state, also follow the predictions based upon the PLATON analyses. On these bases, it is suggested that the methodology described may be generally applicable for predicting when geometric isomerizations (and possibly other reactive processes) in crystalline materials will occur.

## 1. Introduction

Although examples of organic reactions in crystalline media have been known for a century, they remained enigmatic until Schmidt’s systematic investigations led to empirical ‘rules’ concerning when to expect intermolecular photocycloadditions to occur.<sup>1</sup> Later, the same approach was used by Scheffer *et al.* to determine another set of empirical rules dealing with the prediction of the course of H-

atom abstractions during intramolecular photochemical processes in crystalline environments.<sup>2a,b</sup> Others, including Hollingsworth and McBride,<sup>2c</sup> McBride *et al.*,<sup>2d–e</sup> Zimmerman and Nesterov,<sup>2f</sup> Keating and Garcia-Garibay,<sup>2g</sup> Garcia-Garibay,<sup>2h</sup> Toda,<sup>2i–j</sup> and Toda and Tanaka,<sup>2k</sup> have extended these approaches to cover photoprocesses in which *cavity compression* is caused by expulsion of small molecular fragments, unimolecular photorearrangements, and photoreactions of guests in well-defined complexes and clathrates. Largely as a result of their seminal work, scientists working in the field of crystalline state photochemistry have made great strides in rationalizing why (or even predicting how) a crystalline lattice can control the selectivity of a reaction *based upon spatial orientation and proximity arguments*.<sup>2,3</sup> Here, we present evidence for control of crystalline lattices of photo-induced geometric isomerizations *based upon analyses of the proximity and orientation of specific groups of a molecule and pockets of free (i.e., ‘void’) volume*.

One paradigm of the predictions of solid-state reactions, the topochemical principle, is that they prefer to follow the minimum atomic motions in going from reactants to products.<sup>1,4</sup> However, reactions requiring large-scale motions of atoms in solid lattices are increasingly being discovered.<sup>5</sup> How and why such reactions

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‡ Electronic supplementary information (ESI) available: Cavity plots for *cis*-1,2-bis(1-naphthyl)ethylene, *Z*-2-benzylidenebutyrolactone, *E*-2-chlorocinnamic acid, *Z*-2-chlorocinnamic acid, *trans*-1,2-dibenzoyl-ethylene, *Z*-2-methylcinnamic acid and *cis*-1,2-bis(azulenyl)ethylene, and <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra for **1–4**. See DOI: 10.1039/b606027g

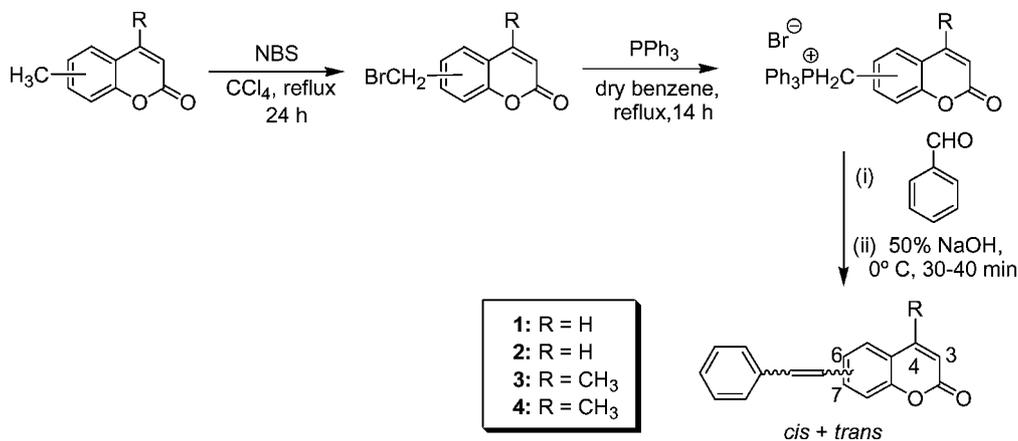
occur must be understood if solid state photoreactions are to be exploited in a rational manner. In that regard, geometric *cis* → *trans* isomerization processes in the solid state<sup>5d,6</sup> are of both fundamental and practical importance in view of their relationship to the mechanism by which the potential energy of light is converted to kinetic energy in rhodopsin and, therefore, to vision.<sup>7</sup>

Most structurally simple stilbenes are photostable in their solid state.<sup>8</sup> In an attempt to increase their reactivity,<sup>9</sup> we have synthesized and irradiated single crystals and solutions of the *cis* and *trans* isomers of a series of 2-pyrone-annulated stilbenes (i.e., 6- and 7-styrylcoumarins; *cis* and *trans* **1–4**; Chart 1 shows the *cis* isomers). Here, when there are no other photo-induced reactions, the occurrence or lack of *cis* → *trans* (or *trans* → *cis*) photoisomerizations in the initial *cis* (or *trans*) crystals can be rationalized on the basis of the availability of appropriately (or inappropriately) oriented void spaces, but not on the total free volume within the lattices.

## 2. Results

### (a) Syntheses of styrylcoumarins

The synthetic protocol for the preparation of styrylcoumarins **1–4** is shown in Scheme 1. The key starting materials, 7-methylcoumarin, 4,6-dimethylcoumarin, and 4,7-dimethylcoumarin, were prepared according to literature procedures;<sup>10</sup> 6-methylcoumarin was commercially available. Benzylic bromination of the coumarins with *N*-bromosuccinimide under standard conditions yielded the 6-/7-bromomethylated derivatives.<sup>11</sup> They were sub-

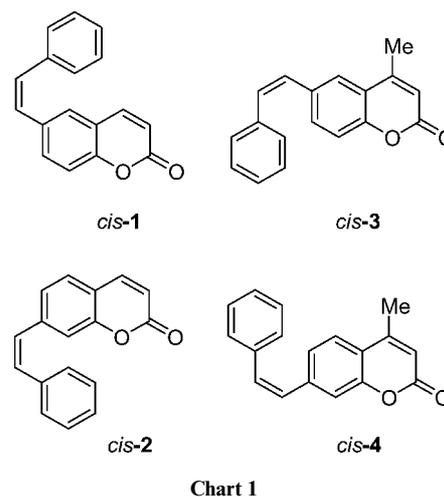


**Scheme 1** Synthetic route for the preparation of 6- and 7-styrylcoumarins **1–4**.

**Table 1** Irradiation of *cis*- and *trans*-styrylcoumarins **1–4** in their crystals and in benzene solutions; only results from experiments in which isomerization was observed are shown

Substrate	Solid state		Substrate	Solution state <sup>b</sup>	
	Duration of irradiation/h	Conversion to <i>trans</i> (%) <sup>a</sup>		Concentration/M	<i>Trans</i> : <i>cis</i> <sup>c</sup>
<i>Cis</i> - <b>1</b>	100	80	<i>Trans</i> - <b>1</b>	1 × 10 <sup>-3</sup>	28 : 72 <sup>d</sup>
<i>Cis</i> - <b>2</b>	80	68	<i>Trans</i> - <b>2</b>	1 × 10 <sup>-4</sup>	48 : 52 <sup>e</sup>
<i>Cis</i> - <b>3</b>	60	78	<i>Trans</i> - <b>3</b>	1 × 10 <sup>-3</sup>	17 : 83 <sup>d</sup>
<i>Cis</i> - <b>4</b>	100	0 <sup>f</sup>	<i>Trans</i> - <b>4</b>	1 × 10 <sup>-4</sup>	45 : 55 <sup>e</sup>
			<i>Cis</i> - <b>4</b>	1 × 10 <sup>-4</sup>	50 : 50 <sup>g</sup>

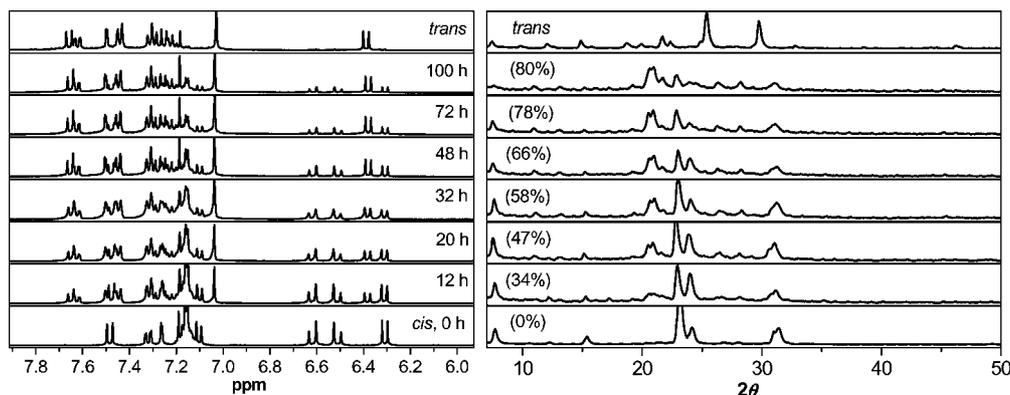
<sup>a</sup> From 400 MHz <sup>1</sup>H NMR analyses. <sup>b</sup> Solutions in nitrogen-saturated benzene were irradiated for 7 h at ca. 350 nm. <sup>c</sup> Based on GC analyses. <sup>d</sup> Ca. 15–18% cyclization. <sup>e</sup> Ca. 20% cyclization and dimerization. <sup>f</sup> No reaction observed. <sup>g</sup> Ca. 15% cyclization and dimerization.



jected to Wittig olefination with benzaldehyde to afford mixtures of the respective *cis*- and *trans*-styrylcoumarins **1–4** in 60–75% yields.

### (b) Solid-state irradiations

The crystals of *cis*- and *trans*-styrylcoumarins **1–4** were gently ground in a mortar and pestle and transferred to Pyrex test tubes. The samples were irradiated at ca. 350 nm under an N<sub>2</sub> atmosphere. The crystals of *cis*-styrylcoumarins **1–3** underwent ca. 68–80% conversion to their *trans* isomers after 60–100 h of irradiation (Table 1).



**Fig. 1** Left:  $^1\text{H}$  NMR spectra of *cis*–*trans* mixtures of initially *cis*-**1** after irradiation of its crystals for different periods. Notice the growth with increasing duration of irradiation of the doublet at *ca.*  $\delta$  6.35 due to the proton at C3 of the coumarin moiety. Right: powder XRD patterns of the irradiated samples of *cis*-**1** for which the  $^1\text{H}$  NMR spectra are shown on the left. Conversions are based on the ratios of integrated areas for peaks of the olefinic proton at the C3-position of the coumarin moiety in the *cis* and *trans* isomers.

By contrast, crystals of *cis*-**4** and the *trans* isomers of **1**–**3** showed no discernible reaction even after 100 h of irradiation under the same conditions that led to substantial *cis*  $\rightarrow$  *trans* isomerization.  $^1\text{H}$  NMR spectra of solutions of the irradiated crystals revealed no evidence for formation of any product. Irradiation of the crystals of *trans*-**4** afforded a highly insoluble material which could not be characterized, but probably was a result of intermolecular addition reactions.

Aliquots of the reactive *cis* isomers were also analyzed by  $^1\text{H}$  NMR for extent of isomerization after different periods of irradiation. Powder X-ray diffraction patterns of solid aliquots taken after the same irradiation times as those used for NMR analyses (and, therefore, at the same conversions) were used to determine crystallinity changes as isomerization progressed. The pertinent data for *cis*-**1**, a representative case, are shown in Fig. 1.

### (c) Solution-state irradiations

Irradiations at *ca.* 350 nm of *trans*-styrylcoumarins **1**–**4** were also examined in  $\text{N}_2$ -saturated benzene solutions (Table 1). Although a thorough study was not conducted, the conditions of the irradiations should have established *trans* : *cis* ratios that are near the photostationary states (PSS). In support of this, the *cis* : *trans* ratios obtained from irradiations of benzene solutions of the *cis* isomers of **1**–**4** were very near those found in Table 1 when starting from the *trans* isomers. The crude photoproduct mixtures (after removal of solvent) were analyzed by  $^1\text{H}$  NMR spectroscopy and gas chromatography (GC). The  $^1\text{H}$  NMR analyses revealed that all of the *trans* isomers undergo isomerization to their *cis* isomers, while *trans*-**1** and *trans*-**3** also cyclize somewhat (*ca.* 15–20%), and *trans*-**2** and *cis*- and *trans*-**4** appear to form some cyclobutane dimers. Even at concentrations as low as  $1 \times 10^{-4}$  M, 5–10% of the dimerization products of *trans*-**2** and *cis*- and *trans*-**4** were observed. The most important observation from these experiments is that *all* of the *trans* isomers, as well as *cis*-**4**, do isomerize in their excited-states in solution, even though they do not in their crystalline states. Their lack of photochemically-induced geometric isomerization in the crystals must be based

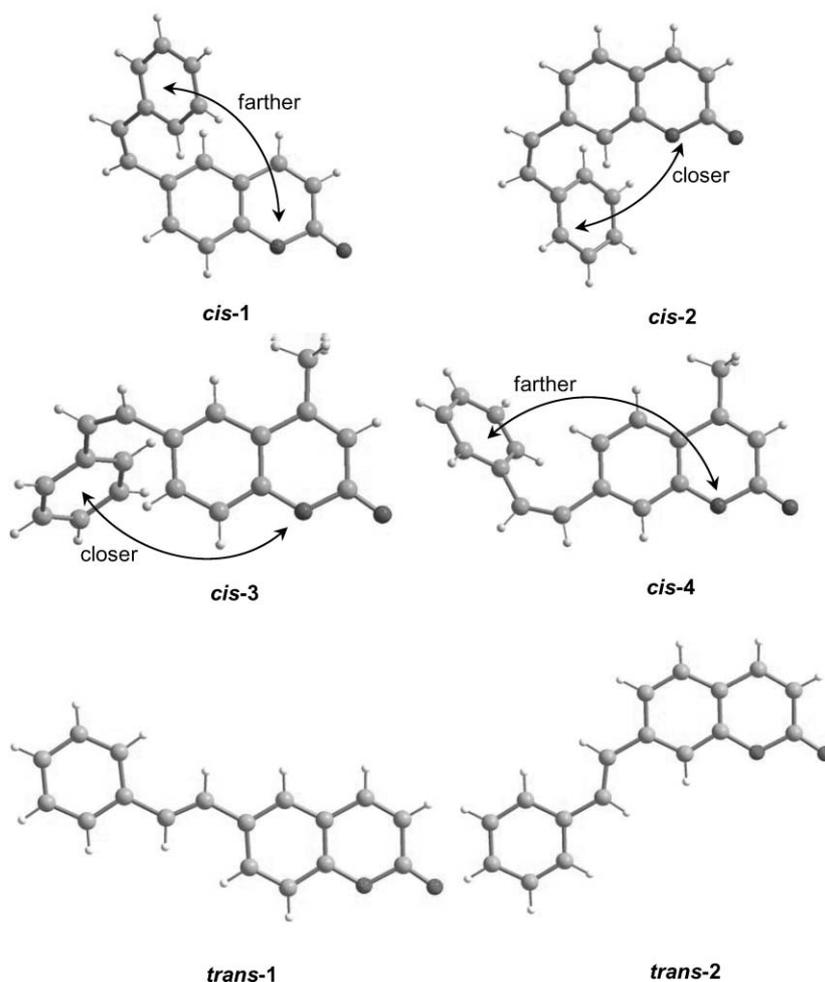
upon environmental constraints rather than intrinsic electronic or structural properties of the molecules.

### (d) X-Ray crystal structure analyses

Crystals of the *cis* isomers of **1**–**4** and the *trans* isomers of **1**–**3** suitable for X-ray diffraction were grown by slow evaporation of  $\text{CH}_2\text{Cl}_2$ –petroleum ether or  $\text{CHCl}_3$ –petroleum ether solutions at room temperature. Our attempts to grow crystals of *trans*-**4** suitable for X-ray studies have not been successful thus far. Although it would be useful to know its molecular packing, its lack of isomerization (and altogether different reactivity) in the crystalline state makes this information somewhat less important than the packing of the other molecules.

Each *cis* and *trans* isomer may, in principle, prefer conformations in which the phenyl ring is directed toward or away from the ether (lactone) oxygen of coumarin. In the extrema of these conformations, the styryl double bond is in the plane defined by the coumarin atoms, but the angle of rotation about the bond linking the double bond and the coumarin differs by  $180^\circ$ . The X-ray structures of the *cis* isomers of **1**–**4** from their single crystals reveal that **2** and **3** prefer closer and **1** and **4** prefer farther conformations (Fig. 2). In particular, it is noteworthy that substitution of hydrogen for methyl at C4 in the 6-styryl pair (*cf.* **1** and **3**) results in a change of conformation from ‘farther’ to ‘closer’. It cannot be attributed (solely) to intramolecular steric factors because the same change from hydrogen to methyl in the 7-styryl pair (*cf.* **2** and **4**) causes the opposite conformational change. It must depend on *intermolecular* factors associated with packing modes of molecules in the unit cells, such as van der Waals interactions, weak H-bonding, dipolar interactions, and limitations imposed by the *energetic preference to avoid large pockets of void volume*. It is the latter factor that we believe plays a crucial role in determining the reactivity of these molecules in their crystalline states (*vide infra*).

The X-ray determined structures for *trans*-**1** and -**2** are also shown in Fig. 2. The styryl moiety of *trans*-**3** was found to be disordered, which may lead to erroneous interpretation of the structure–reactivity correlations. For this reason, we will not discuss packing details of *trans*-**3** here.



**Fig. 2** The molecular structures of *cis*-styrylcoumarins **1–4** and *trans*-styryl coumarins **1** and **2**. There are two independent molecules in the asymmetric unit cell of *cis*-**3**. Since the conformations of the two molecules are similar and have no visually perceptible differences, only one is shown. The ‘closer’ and ‘farther’ conformations of **1–4** have been shown by arrows.

### 3. Discussion

The exceedingly important influence of molecular packing within the crystalline state on the reactivity of molecules is demonstrated clearly by the contrasting photochemical behavior of the very closely structurally-related *cis* and *trans* isomers of styrylcoumarins **1–4**. As noted, the crystals of *cis*-**1–3** undergo geometric isomerization, while those of *cis*-**4** and *trans*-**1–3** are unreactive photochemically and the crystals of *trans*-**4** yield photoproducts that are not easily characterized. Because all of the styrylcoumarins undergo at least some photoisomerization in benzene solutions, the origin of the different photoreactivities in the crystals must be based in larger part on molecular packing effects than on electronic factors. The challenge is to discern the specific features of the molecular packing arrangements that control reactivity.

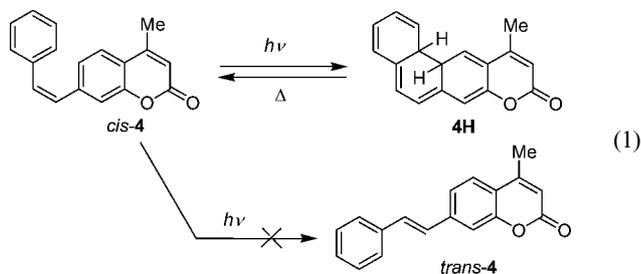
As mentioned, *cis*  $\rightarrow$  *trans* isomerization involves large displacements of the substituents on at least one of the carbon atoms of a carbon–carbon double bond. Yet, with the exception of **4**, the *cis* isomers of the styrylcoumarins do undergo significant *cis*  $\rightarrow$  *trans* isomerization in the solid state. The calculated densities of the crystals, which reflect the overall packing efficiencies for the

otherwise similar molecular systems, are 1.32 for *cis*-**1**, 1.27 for *cis*-**2**, 1.28 for *cis*-**3** and 1.26 g cm<sup>-3</sup> for *cis*-**4**. These values suggest that the molecular packing of the methylated styrylcoumarin which does *not* undergo isomerization, *cis*-**4**, is somewhat looser than that of the methylated styrylcoumarin which does, *cis*-**3**. Furthermore, the unmethylated coumarin which has the highest packing density, *cis*-**1**, undergoes efficient isomerization! Clearly, the reasons for the photoreactivity of these molecules or the lack thereof must involve much more subtle factors than bulk crystal density or, perhaps more appropriately, the fraction of volume that is ‘void’ within a crystal.

#### (a) Photostability of crystalline *cis*-4-methyl-7-styrylcoumarin, *cis*-**4**

We suggest two possible reasons for the lack of photoisomerization in solid *cis*-**4**. First, the excited states may be deactivated as they undergo a more facile, reversible photoprocess than geometric isomerization. One candidate for a competing process is the well-known formation of an unstable dihydrophenanthrene (**4H**) via a 6 $\pi$ -conrotatory closure (eqn (1)).<sup>12</sup> Thermal reversion of **4H** would be driven by the energy gained upon reestablishment of

the aromaticity of the affected rings. A second possible reason is that molecular packing may preclude the large-scale rotational motions necessary for geometric isomerization.



Ground crystals of *cis*-4 that had been irradiated (high-pressure Hg lamp,  $\lambda \approx 350$  nm) for 3 h under a nitrogen atmosphere at *ca.*  $-20$  °C (to retard thermal reversion of any **4H** that might have formed) developed a yellow color. However, the color persisted at room temperature for more than 30 h, even when the crystals were dissolved in  $\text{CDCl}_3$ . Coloration is a non-unique indicator of the presence of a dihydrophenanthrene.<sup>13</sup> However, a  $^1\text{H}$  NMR spectrum of the crystals (dissolved in  $\text{CDCl}_3$ ) immediately after irradiation revealed essentially unreacted *cis*-4, and no signals attributable to a **4H**-like intermediate. On these bases, the coloration is not from a dihydrophenanthrene; persistence of color is not consistent with the behavior expected of a species such as **4H**.

The feasibility of the formation of **4H** intermediates upon irradiation of the *cis* isomers of **1–4** in their crystals was assessed by analyzing the X-ray determined molecular structures in terms of the contact distances between the carbon atoms about which the cyclization might occur and the angle between the planes defined by the carbon atoms of the coumarin and phenyl rings (Table 2). Both of these parameters for unreactive *cis*-4 are similar to those for the *cis* isomers of **1–3**, which do undergo isomerization readily. In fact, since all four of the molecules are reasonably well disposed conformationally to yield **4H**-like intermediates, the structural factors in Table 2 do not appear to be the cause of the differences in photochemical reactivities among them. Indeed, *cis*-3 also developed a yellow color when its crystals were irradiated at *ca.*  $-20$  °C. Thus, we conclude that if reversible formation of **4H** is occurring, it is not the reason why *cis*-4 fails to isomerize to its *trans* isomer in the solid state.

**Table 2** Contact distances ( $d/\text{Å}$ ) between the atoms about which cyclization to yield dihydrophenanthrenes (indicated by asterisks) may occur and the plane-plane intersection angles ( $\theta/^\circ$ ) between the two aromatic rings of **1–4**

Substrate	$d/\text{Å}$	$\theta/^\circ$
<i>Cis</i> -1	3.33	60.5
<i>Cis</i> -2	3.22	54.8
<i>Cis</i> -3	3.27, 3.26 <sup>a</sup>	58.6, 73.9 <sup>a</sup>
<i>Cis</i> -4	3.21	54.2

<sup>a</sup> Two molecules in the asymmetric unit cell.

To test the second possibility, that matrix-imposed energy barriers do not allow the atoms of *cis*-4 to follow the trajectories required for isomerization, crystals of *cis*-4 were irradiated for 3 h at 80 °C, *ca.* 25 °C below their melting point. We hypothesized that the extra thermal energy might allow the matrix-imposed barriers to be overcome. A  $^1\text{H}$  NMR spectrum of the irradiated crystals dissolved in  $\text{CDCl}_3$  did reveal the presence of some *trans* isomer. However, other products, which appeared to include cyclobutane dimers (based on their diagnostic signals in the region between *ca.*  $\delta$  3.2 and 4.5<sup>8c,d,14</sup>), were also evident. Formation of cyclobutane dimers is unexpected based on the crystal packing because the intermolecular contacts about the styrenic C=C bond or the C3 and C4 atoms of the coumarin moiety are too long ( $>4.5$  Å).<sup>1,4a-c</sup> Since topochemically-controlled [2 + 2] cycloaddition is predicted not to be possible, we suggest that the crystal lattice is not retained as photo-induced reactions progress at 80 °C. Presumably, the initially-formed product(s) destroys the lattice or depresses the melting point of *cis*-4, allowing the reaction to proceed at defect sites or in a melt state.<sup>15</sup>

### (b) Correlation of the reactivity of the *cis* isomers of **1–4** and the *trans* isomers of **1** and **2** with their crystal structures

Photo-induced geometric isomerization about carbon–carbon double bonds has been observed in a number of cases in the solid state.<sup>6</sup> However, some aspects of the mechanism by which it occurs continue to be controversial (*vide infra*).<sup>16,17</sup> In their initial studies on the photoisomerization of cinnamic acids in the solid state, Bregman *et al.*<sup>18</sup> suggested the intermediacy of unstable cyclobutane dimers. The generality of such a mechanism is, however, questionable because many cyclobutane dimers are thermally quite stable,<sup>4a-c,8c,d,19</sup> and are transparent to the radiation wavelengths used to effect the photoreactions. In addition and as mentioned above, the interatomic distances between the olefinic atoms are too long to permit [2 + 2] photodimerizations.<sup>1,4a-c</sup> Thus, the intermediacy of cyclobutanes in the isomerization processes seems unfeasible here.

The more conventional mechanism for isomerization is a one-bond-flip (OBF)<sup>20</sup> involving torsional relaxation of a twisted excited state. A second mechanism, the so-called hula-twist (H-T),<sup>21</sup> has been invoked most often when isomerizations occur in confining environments. Whereas the former mechanism involves motion of a set of substituents attached to one of the two carbon atoms of the double bond along a conical potential energy surface, the latter is volume-conserving in that only one substituent attached to the olefinic carbon atoms needs to move significantly out of the original olefinic plane while the other substituents reorient more-or-less within it.

The crystal packing diagrams for the *cis* isomers of **1–4** and *trans* isomers of **1** and **2** are shown in Fig. 3. It is not apparent from the packing of **1–3** how the atomic motions that accompany *cis* → *trans* isomerization can be accommodated within these crystal lattices, and molecular packing of *cis*-3 ( $Z' = 2$ , space group:  $P\bar{1}$ ) appears to be as complex as that of the unreactive *cis*-4 ( $Z' = 1$ , space group:  $P2_1/c$ ). The molecules in the crystals of *trans*-1 ( $Z' = 1$ , space group:  $P2_1/c$ ) and *trans*-2 ( $Z' = 1$ , space group:  $Pc2_1b$ ) are associated *via* C–H...O and C–H... $\pi$  hydrogen bonds leading to mutually orthogonal layered structures.

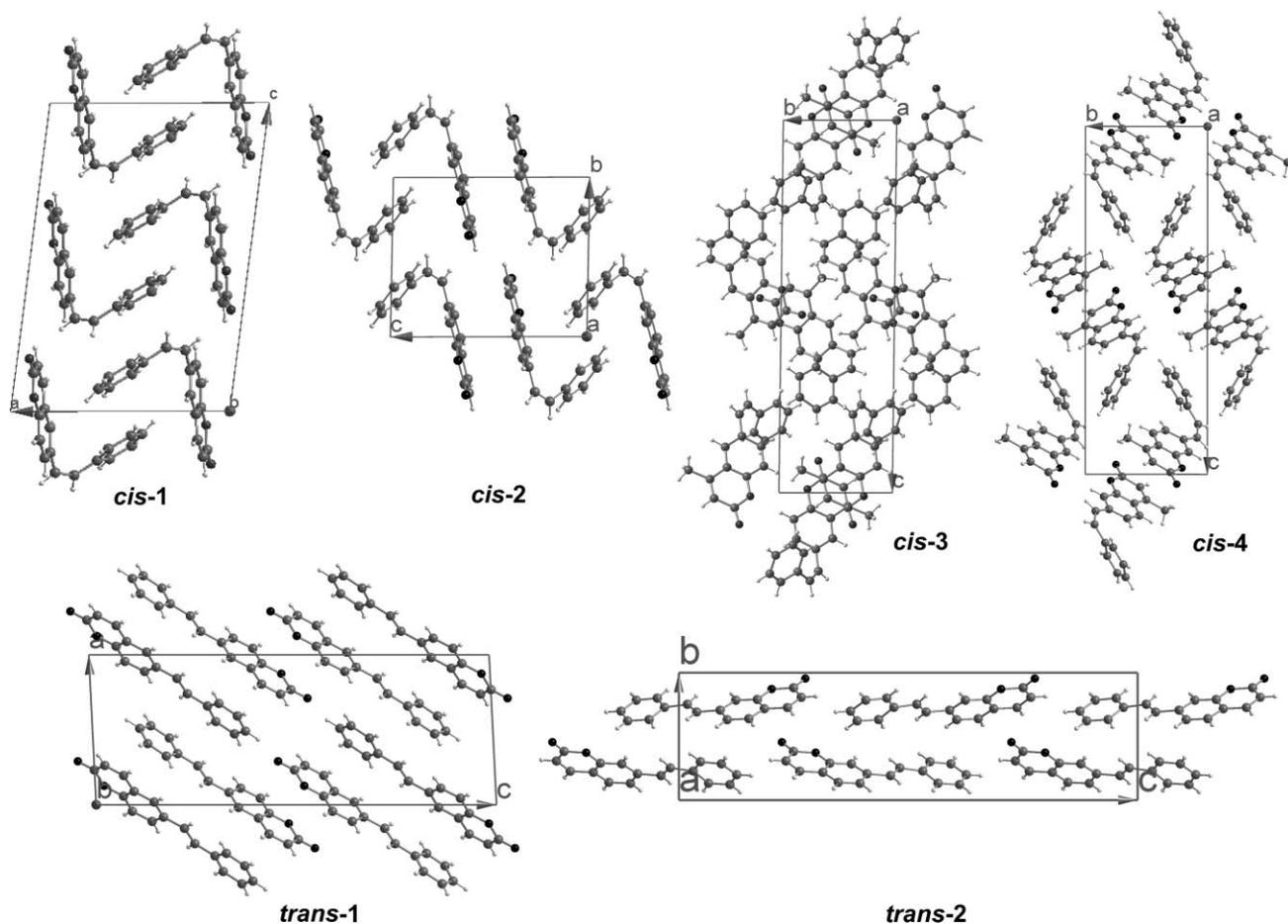


Fig. 3 Molecular packing diagrams of the *cis*-styrylcoumarins **1–4** and *trans*-styrylcoumarins **1** and **2**.

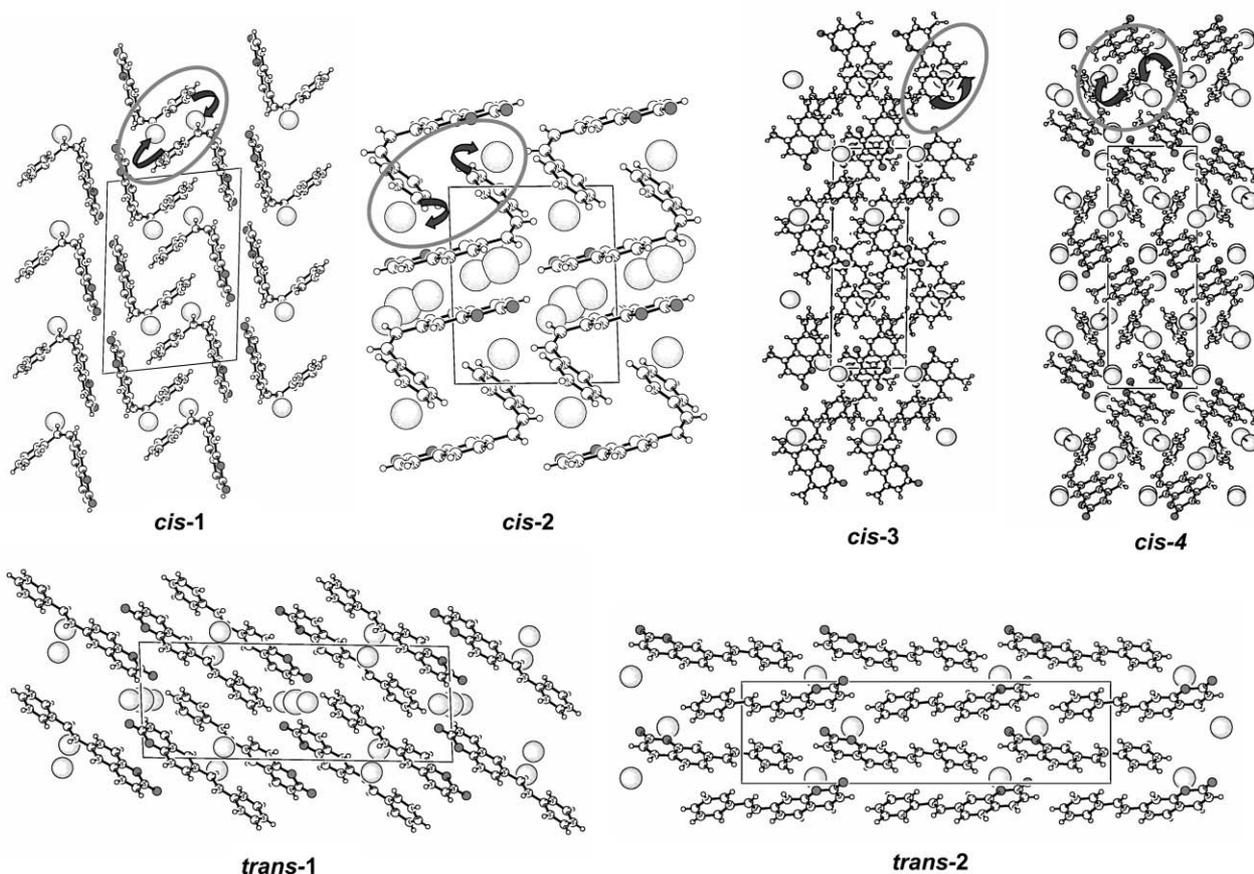
In a pioneering study, Gavezzotti has analyzed the relationship between molecular transformations and cavity volumes in crystal lattices.<sup>22</sup> Additionally, Ohashi has shown how X-ray and UV-induced racemization of chiral cobaloxime complexes can be rationalized by the cavity volumes near the chiral centers.<sup>23</sup> Recently, Natarajan *et al.* have also analyzed solid-state *cis* → *trans* isomerizations based on plots of the locations of cavities within lattices.<sup>24</sup> In hopes of gaining additional insights about the directions along which the atomic motions may occur most easily in the crystal lattices of the *cis* isomers of **1–4** and the *trans* isomers of **1** and **2**, we have generated their ‘cavity plots’ using the PLATON program.<sup>25</sup> In it, a ‘probe species’ with a defined radius ‘*r*’ explores the unit cell and outputs the available void spaces in the form of spheres corresponding to a particular radius (*R*, where  $R \geq r$ ). The plots generated with  $r = 0.80 \text{ \AA}$  are shown in Fig. 4 for the *cis* isomers of **1–4** and *trans* isomers of **1** and **2**. As  $r \rightarrow 0$ , the sum of the void volumes approaches a van der Waals limit. The approach to this limit was calculated per  $100 \text{ \AA}^3$  of crystal lattice of the *cis* isomers of **1–4** by decreasing ‘*r*’ progressively (Fig. 5). However, we did not continue the calculations to  $r = 0 \text{ \AA}$  because spaces smaller than a certain size are not useful in understanding dynamic processes.

In the well-accepted theory of Vrentas and Duda, void volumes are separated into ‘interstitial’ and ‘hole’ components.<sup>26</sup> The former is in very small pockets where the van der Waals shapes of abutting atoms do not permit them to occupy all of the vicinal

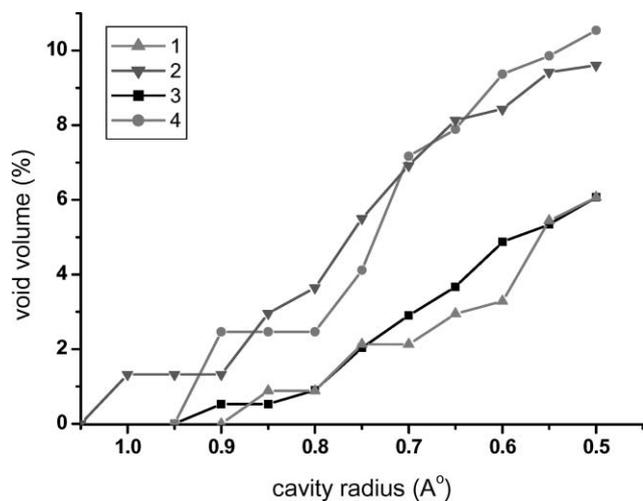
space. An analogy is the spaces between hard spheres of one size packed as tightly as possible in a box. As such, interstitial volume is not useful to explain dynamic processes, and it would be included in the void volumes of Fig. 5 if ‘*r*’ were allowed to go to  $0 \text{ \AA}$ ; arbitrarily, we have set a limit below which interstitial hole free volume would be included in the void volumes of Fig. 5 at  $r = 0.5 \text{ \AA}$ . Our focus is on the hole component of the void volume because it includes much larger spaces and occurs where groups of covalently attached atoms cannot pack with sufficient efficiency to leave only interstitial volume between them.

According to Fig. 5, both of the unmethylated and both of the methylated *cis* isomers have comparable amounts of void volume in their respective crystal lattices at least when  $r \geq 0.5 \text{ \AA}$ . On this basis, the total amount of void volume within a lattice is not a good indicator of why molecules in three of the crystals are able to undergo isomerization, but those in the fourth are not. We believe that the answer lies in the *specific location* of the hole free volume within a unit cell. Thus, a more careful inspection of Fig. 4 reveals that the voids detected in the crystals of the *cis* isomers of **1–3** are located over the phenyl rings and in a direction that can lead to the *trans* isomers. The locations of void spaces in the unreactive *cis*-**4** crystal are in the opposite direction, where rotation would lead to collision between the phenyl and coumarin parts of one molecule.

Obviously, real voids in a crystal are not spherical; this model provides only a useful indication of the sizes of the voids. Regardless, when  $r = 0.8 \text{ \AA}$ , the spherical void volume,  $2.14 \text{ \AA}^3$ ,



**Fig. 4** The PLATON-generated cavity plots with a probe radius of 0.80 Å. The spheres represent voids or empty spaces in the crystal lattices of *cis*-styrylcoumarins 1–4 and *trans*-styrylcoumarins 1 and 2. Notice that the spheres are located in the proximity of the phenyl rings and the olefinic carbons in the case of 1 and 2. In the case of 3, the voids are located closer to the phenyl rings, which may permit marginal rotational motions of the phenyl rings in crystal lattice. Observe that the void space present in 4 is, in contrast, not in the direction in which the motion of the phenyl ring may lead to the *trans* isomer. Curved arrows from the phenyl rings to the voids are included to show the expected direction of incipient motions of phenyl groups after electronic excitation. In the case of *trans* isomers 1 and 2, the voids are located at the unfavorable centers for *trans* → *cis* isomerization to happen.



**Fig. 5** The calculated void volumes (%) for *cis*-styrylcoumarins 1–4 with a decreasing cut-off limit of the probe radius.

should be sufficient to allow some atoms of a phenyl ring and the attached olefinic atoms of *cis*-1–3 to move in trajectories that are along the routes for isomerization; indeed, arguments

for trajectories along conical intersections have been hypothesized widely for other systems not necessarily within crystalline lattices.<sup>27</sup> The classical momentum gained from these initial motions, as electronically excited molecules move along their potential energy surfaces, may be sufficient to drive the system over barriers that would otherwise be inaccessible. In fact, Craig and co-workers emphasized long ago the importance of a particular type of *lattice instability* rendered by localized electronic excitation of a molecule in the crystal lattice.<sup>28</sup> They suggested that reactions not expected based on the ground-state structures may indeed occur if the *dynamic pre-formation* can be tolerated in the crystal lattice by the nearest neighbors. In this context, it is also noteworthy that Hollingsworth and McBride<sup>2c</sup> and McBride *et al.*,<sup>2d–e</sup> have advanced “local stress” to rationalize the reactivity of various azoalkanes and diacyl peroxides in the solid state.

As the initial (vibrationally and rotationally hot) Franck–Condon state of a styrylcoumarin that has been electronically excited with a 350 nm (81.7 kcal Einstein<sup>-1</sup>) photon relaxes to its 0th vibronic level, *ca.* 60 kcal mol<sup>-1</sup> above the ground state, >20 kcal of heat is dissipated to the lattice. Inoue and coworkers have demonstrated that specific dumping of excess excitation energy into the bonds of neighboring ground-state molecules can cause them to undergo specific reactions.<sup>29</sup> Here, the vibrational

and rotational excitation of bonds of neighboring ground-state molecules will make the reaction cavity more malleable. However, the attendant expansion and softening of the lattice will aid isomerization only if the time for transfer of energy to relevant modes of the immediate lattice is comparable to and persists as long as the excited state lifetimes of the styrylcoumarin.<sup>30</sup>

The unfavorable locations of the void cavities in *cis*-**4** do not aid the rotational motions that are essential for isomerization. They direct the phenyl rings along a trajectory that is not conducive to isomerization. To determine whether similar considerations can explain the lack of *trans* → *cis* isomerization in crystals of *trans*-**1** and **-2**, we have examined the locations of void cavities in their crystal lattices. The cavity plots (Fig. 4) show, as in the case of *cis*-**4**, that the locations of voids are not at appropriate regions for the motions of atoms or groups of atoms to lead to *trans* → *cis* isomerization.

Finally, in order to test the generality of these observations, we have constructed cavity plots for crystals of *cis*-1,2-bis(1-naphthyl)ethylene,<sup>6c</sup> *Z*-2-benzylidenebutyrolactone,<sup>6b</sup> *E*-2-chlorocinnamic acid,<sup>31a-b</sup> *Z*-2-chlorocinnamic acid,<sup>31b</sup> *trans*-1,2-dibenzoylethylene,<sup>6a,31c</sup> *Z*-2-methylcinnamic acid<sup>31b</sup> and *cis*-1,2-bis(azulenyl)ethylene.<sup>24</sup> Some of these crystals do and others do not undergo photo-induced *cis* → *trans* or *trans* → *cis* isomerization; see electronic supplementary information (ESI) for details.‡ *The actual results in all cases can be understood based on the locations of void cavities in the crystal lattices.* Thus, we hypothesize that the locations of individual pockets of void volume in a crystal are much more important than the sum of the void volumes within a unit cell. If placed appropriately, a void volume may act as a vector for the intramolecular motions of groups along pathways leading to geometric isomerizations (as well as other reactions). If, in addition, the excess vibronic energy from relaxation of the Franck–Condon to adiabatic excited state geometries can be dumped rapidly into the immediate space near the reacting molecule, the probability of overcoming the barriers to isomerization may be increased. Essentially, the matrix need not maintain a Boltzmann distribution of vibronic and rotational states during the excited state lifetime of a reactive molecule, and the pathway to isomerization (of a styrylcoumarin in our cases) can be facilitated.<sup>32</sup>

## 4. Conclusions

Our investigations of the reasons for the surprising observation that 3 *cis*-styrylcoumarins **1–3** can undergo photo-induced *cis* → *trans* isomerizations in their crystalline solid states, but crystals of a structurally-related *cis*-styrylcoumarin **4** and the *trans* isomers of **1–4** do not, have led us to hypothesize that the *locations* of voids are more important than the sum of the void volumes within a crystalline lattice, and that dumping excess energy of the electronic state into its immediate environment may increase the efficiency of the isomerizations as well. Clearly, these concepts need to be tested further before they can be placed on a reasonably firm footing. However, there are precedents for similar energy dumping modes, such as the use of excess vibronic energy from an electronically excited state of one molecule to facilitate hydrogen bond-breaking in another molecule in its electronic ground state.<sup>30</sup>

The ideas advanced here are amenable to experimental testing since there are many other systems that can be similarly examined.

In this regard, we have analyzed the cavity plots of the crystal structures of unreactive *trans*-**1–2** and several other systems in which geometric isomerization has been reported by others to occur readily or not at all in the solid state. Indeed, the reactivity/unreactivity patterns can be rationalized on the basis of the locations of void spaces within the crystal lattices. They lend support to our contention that the approach advanced here may be applicable generally. It will be interesting to determine whether exceptions exist.

## 5. Experimental

The commercially available chemicals were used as received. The starting materials for the syntheses of styrylcoumarins **1–4**, *viz.*, 7-methylcoumarin (mp 118–120 °C; lit.,<sup>10a</sup> mp 128–129 °C), 4,6-dimethylcoumarin (mp 151–153 °C; lit.,<sup>10b</sup> mp 150 °C), and 4,7-dimethylcoumarin (mp 134–136 °C; lit.,<sup>10a</sup> mp 131–132 °C), were prepared according to reported procedures.<sup>10</sup> 6-Methylcoumarin (Lancaster, 99%) was used as received.

### (a) Representative procedure for preparation of 6- and 7-bromomethylcoumarins

4,6-Dimethylcoumarin (4 g, 23.0 mmol) and *N*-bromosuccinimide (4.3 g, 24.2 mmol) were placed in a round-bottom flask containing 45 mL of carbon tetrachloride. The contents were heated at reflux for 24 h under a nitrogen atmosphere. After this period, the reaction mixture was cooled and the solvent removed *in vacuo*. The residue was treated with 10% aqueous potassium hydroxide (100 mL) and extracted with ethyl acetate (3 × 50 mL). The combined extracts were washed with brine, dried over anhydrous sodium sulfate and the solvent was removed *in vacuo*. The crude product was recrystallized from ethanol to give 3.9 g (67%) of colorless crystals, 4-methyl-6-bromomethylcoumarin (mp 180–182 °C; lit.,<sup>11</sup> 178–180 °C), 6-bromomethylcoumarin (mp 150–152 °C; lit.,<sup>11</sup> 148–149 °C), 7-bromomethylcoumarin (mp 168–170 °C; lit.,<sup>11</sup> 172–176 °C), and 4-methyl-7-bromomethylcoumarin (mp 195–196 °C; lit.,<sup>11</sup> 196 °C) were synthesized following similar procedures.

### (b) Preparation of phosphonium salts

Triphenylphosphine (3.2 g, 12.3 mmol) and 4-methyl-6-bromomethylcoumarin (3 g, 11.8 mmol) were dissolved in dry benzene (30 mL) and heated at reflux for 20 h under an N<sub>2</sub> atmosphere. Subsequently, the contents were cooled to afford a colorless solid material, which was filtered under suction, washed several times with petroleum ether, and dried to yield 5.7 g (94%) of crude product that was used without further purification.

### (c) General procedure for the synthesis of 6- and 7-styrylcoumarins (**1–4**)

To a stirred suspension of a mixture of a triphenylphosphonium salt of 6- or 7-bromomethylcoumarin (1.30 mmol) and benzaldehyde (1.00 mmol) in dichloromethane (5 mL) was added aqueous sodium hydroxide (50%, 1.2 mL) dropwise at 0 °C. The color of the solution turned orange-red immediately. After stirring the reaction mixture for 30–40 min, the reaction was quenched by adding water. The reaction mixture was extracted with chloroform

(3 × 30 mL) and the combined extracts were washed with brine, dried over anhydrous sodium sulfate and filtered. The solvent was removed *in vacuo* and the crude product was passed through a short silica-gel column using chloroform as the eluting solvent. Separation of *cis* and *trans* isomers was accomplished by radial chromatography technique using a Chromatotron apparatus and ethyl acetate-petroleum ether as the eluting solvent. Single crystals of the *cis* isomers were grown slowly by evaporating solutions with mixed solvents—dichloromethane and either petroleum ether or chloroform.

**Cis-1.** Colorless shiny crystals, mp 78–80 °C, IR (KBr)  $\text{cm}^{-1}$  3076, 2923, 1716, 1564;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  6.45 (d,  $J = 9.5$  Hz, 1H), 6.71 (dd,  $J_1 = 42.5$  Hz,  $J_2 = 12.2$  Hz, 2H), 7.25 (d,  $J = 8.6$  Hz, 1H), 7.23–7.35 (m, 5H), 7.41 (d,  $J = 2.0$  Hz, 1H), 7.47 (dd,  $J_1 = 8.7$  Hz,  $J_2 = 2.0$  Hz, 1H), 7.63 (d,  $J = 9.5$  Hz, 1H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  116.6, 116.7, 118.6, 127.5, 127.9, 128.1, 128.4, 128.7, 131.4, 132.5, 133.7, 136.6, 143.3, 152.9, 160.7; Anal. Calcd for  $\text{C}_{17}\text{H}_{12}\text{O}_2$  ( $M_r = 248.28$ ) C: 82.24; H: 4.87. Found C: 82.14; H: 4.96.

**Trans-1.** Pale yellow crystals, mp 132–134 °C, IR (KBr)  $\text{cm}^{-1}$  3027, 2362, 1741, 1617, 1566;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  6.38 (d,  $J = 9.5$  Hz, 1H), 7.04 (s, 2H), 7.22 (t,  $J = 7.5$  Hz, 1H), 7.26 (d,  $J = 8.6$  Hz, 1H), 7.31 (t,  $J = 7.3$  Hz, 1H), 7.45 (d,  $J = 7.3$  Hz, 2H), 7.50 (d,  $J = 2.2$  Hz, 1H), 7.62–7.67 (m, 2H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  117.0, 117.2, 119.0, 125.4, 126.5, 126.6, 128.0, 128.79, 129.69, 129.74, 134.0, 136.7, 143.3, 153.4, 160.6; Anal. Calcd for  $\text{C}_{17}\text{H}_{12}\text{O}_2$  ( $M_r = 248.28$ ) C: 82.24; H: 4.87. Found C: 82.10; H: 4.82.

**Cis-2.** Colorless crystals, mp 86–88 °C, IR (KBr)  $\text{cm}^{-1}$  3052, 1711, 1608, 1542;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  6.31 (d,  $J = 9.5$  Hz, 1H), 6.63 (dd,  $J_1 = 68.0$  Hz,  $J_2 = 12.4$  Hz, 2H), 7.08 (d,  $J = 8.4$  Hz, 1H), 7.14–7.21 (m, 6H), 7.25 (d,  $J = 8.0$  Hz, 1H), 7.58 (d,  $J = 9.5$  Hz, 1H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  116.1, 116.8, 117.7, 125.3, 127.4, 127.8, 128.4, 128.5, 128.7, 133.1, 136.3, 141.4, 143.0, 154.0, 160.9; Anal. Calcd for  $\text{C}_{17}\text{H}_{12}\text{O}_2$  ( $M_r = 248.28$ ) C: 82.24; H: 4.87. Found C: 82.29; H: 4.92.

**Trans-2.** Yellow crystals, mp 206–208 °C, IR (KBr)  $\text{cm}^{-1}$  3072, 3021, 1711, 1604;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  6.38 (d,  $J = 9.5$  Hz, 1H), 7.17 (dd,  $J_1 = 45.2$  Hz,  $J_2 = 16.3$  Hz, 2H), 7.29–7.46 (m, 6H), 7.54 (d,  $J = 7.6$  Hz, 2H), 7.68 (d,  $J = 9.5$  Hz, 1H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  114.2, 116.0, 118.1, 122.6, 126.9, 127.9, 128.0, 128.5, 128.8, 132.0, 136.4, 141.4, 143.0, 154.5, 160.9; Anal. Calcd for  $\text{C}_{17}\text{H}_{12}\text{O}_2$  ( $M_r = 248.28$ ) C: 82.24; H: 4.87. Found C: 82.32; H: 4.80.

**Cis-3.** Colorless shiny crystals, mp 79–81 °C, IR (KBr)  $\text{cm}^{-1}$  3008, 2922, 1722, 1568;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  2.20 (s, 3H), 6.25 (s, 1H), 6.68 (dd,  $J_1 = 45.4$  Hz,  $J_2 = 12.2$  Hz, 2H), 7.19 (d,  $J = 8.8$  Hz, 1H), 7.23–7.30 (m, 5H), 7.38 (d,  $J = 8.8$  Hz, 1H), 7.44 (s, 1H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  18.3, 115.0, 116.8, 119.6, 124.8, 127.4, 128.4, 128.5, 128.6, 131.3, 132.6, 133.1, 136.9, 152.28, 152.31, 160.7; Anal. Calcd for  $\text{C}_{18}\text{H}_{14}\text{O}_2$  ( $M_r = 262.30$ ) C: 82.42; H: 5.38. Found C: 82.38; H: 5.31.

**Trans-3.** Yellow crystals, mp 146–150 °C, IR (KBr)  $\text{cm}^{-1}$  3062, 3025, 2359, 1733, 1626, 1595, 1565;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  2.49 (s, 3H), 6.32 (s, 1H), 7.12 (dd,  $J_1 = 20.1$  Hz,  $J_2 = 16.6$  Hz, 2H), 7.27–7.40 (m, 4H), 7.53 (d,  $J = 7.6$  Hz, 2H), 7.66 (s, 1H),

7.71 (d,  $J = 8.5$  Hz, 1H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  18.7, 115.4, 117.4, 120.1, 122.4, 126.5, 126.9, 128.0, 128.7, 129.4, 129.5, 133.7, 136.8, 152.2, 152.9, 160.6; Anal. Calcd for  $\text{C}_{18}\text{H}_{14}\text{O}_2$  ( $M_r = 262.30$ ) C: 82.42; H: 5.38. Found C: 82.45; H: 5.46.

**Cis-4.** Colorless shiny plates, mp 110–114 °C, IR (KBr)  $\text{cm}^{-1}$ , 2920, 1728, 1610, 1382;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  2.42 (s, 3H), 6.26 (s, 1H), 6.69 (dd,  $J_1 = 65.5$  Hz,  $J_2 = 12.2$  Hz, 2H), 7.17 (d,  $J = 8.3$  Hz, 1H), 7.21–7.28 (m, 6H), 7.42 (d,  $J = 8.0$  Hz, 1H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  18.5, 114.6, 116.9, 118.7, 124.2, 125.0, 127.7, 128.3, 128.5, 128.7, 132.9, 136.4, 141.2, 152.1, 153.5, 160.9; Anal. Calcd for  $\text{C}_{18}\text{H}_{14}\text{O}_2$  ( $M_r = 262.30$ ) C: 82.42; H: 5.38. Found C: 82.31; H: 5.29.

**Trans-4.** Thick yellow plates, mp 194–198 °C, IR (KBr)  $\text{cm}^{-1}$  3056, 3026, 1712, 1607, 1546;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  2.42 (d,  $J = 1.2$  Hz, 3H), 6.24 (d,  $J = 1.2$  Hz, 1H), 7.15 (dd,  $J_1 = 44$  Hz,  $J_2 = 16.4$  Hz, 2H), 7.27–7.44 (m, 5H), 7.52–7.56 (t,  $J = 8.0$  Hz, 3H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  18.6, 114.3, 114.5, 119.1, 122.3, 124.7, 126.8, 126.9, 128.5, 128.8, 131.7, 136.4, 141.2, 152.1, 153.9, 160.9; Anal. Calcd for  $\text{C}_{18}\text{H}_{14}\text{O}_2$  ( $M_r = 262.30$ ) C: 82.42; H: 5.38. Found C: 82.36; H: 5.33.

#### (d) General procedure for the solid- and solution-state irradiations of 1–4

The crystals of styrylcoumarin (*ca.* 0.1 g) were crushed gently such that the crystallinity was preserved. They were spread evenly along the interior surface of a Pyrex test tube and rotated over a turn table during irradiation in a Luzchem photochemical reactor ( $\lambda \approx 350$  nm) for 60–100 h at room temperature (*ca.* 25 °C). The tubes were removed from the reactor from time to time and shaken thoroughly to maintain sample homogeneity.

For solution-state irradiations, *ca.*  $1 \times 10^{-3}$  to  $1 \times 10^{-4}$  M benzene solutions of a *trans* isomer of 1–4 in a Pyrex tube were purged with  $\text{N}_2$  gas for 30 min, closed, and irradiated for 7 h in a Luzchem photoreactor ( $\lambda \approx 350$  nm). Subsequently, the solvent was removed *in vacuo* by rotary evaporator and the remainder was analyzed by 400 MHz  $^1\text{H NMR}$  spectroscopy (JEOL-Lambda 400 MHz) and GC (Perkin Elmer-Clarus 500, Elite 1 column) to determine the photoproduct composition and extent of reaction.

#### (e) X-Ray crystal structure determinations

Intensity data were collected on Siemens P4 diffractometer (*cis*-1) and Bruker SMART/CCD diffractometers (*trans*-1–2, *cis*-2–4) using  $\text{MoK}\alpha$  ( $\lambda = 0.71073$  Å) radiation. The structures were solved by direct methods and were refined on  $F^2$  by a full-matrix least-squares technique using SHLEXL-97.<sup>33</sup> All atoms, except hydrogens, were refined anisotropically. Hydrogen atoms were placed in their idealized positions and refined by the riding model.

CCDC reference numbers 611803–611808.

For crystallographic data in CIF or other electronic format see DOI: 10.1039/b606027g

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