PERKIN 2

Studies in crystal engineering: effect of fluorine substitution in crystal packing and topological photodimerization of styryl coumarins in the solid state

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Styryl coumarins generally yield centrosymmetric (α-mode, *anti*-HT) photodimers when subjected to irradiation in the solid state. However, the substitution of fluorine dramatically alters the packing mode and steers the molecules 4-(4-fluorostyryl)coumarin 1 and 4-(2-fluorostyryl)coumarin 2 to form a stereospecific photodimer, β-mode, *syn*-HH across the styrenic double bond (yield 78–85%). The stereochemistry of the photodimer 2a has been established by X-ray crystallography. There is no evidence for the presence of C–H · · · F interactions. The true nature of the weak atom–atom interactions called into play when fluorine is substituted is not clear. It is observed that the fluoro substituted compounds have greater crystal density than the corresponding unsubstituted ones.

The correlation between the reactive molecular arrangement in the reactant crystals and the configuration of the photoproduct was discovered by Schmidt and co-workers.[1–3] The photoproducts are classified as α, β and γ based on the geometrical disposition of the individual monomers. The α-modification has centrosymmetric related double bonds and yields upon irradiation, a centrosymmetric dimer. The β-modification has reactive double bonds related by a translational symmetry and upon irradiation gives a photoproduct with a mirror plane. In both these modifications the distance between the reactive double bonds is <4.2 Å. The γ-form has a double bond separation distance of >4.2 Å and is photostable. With the aim of pre-organizing the reactants into a packing mode favourable for photoreactions, the steering ability of chloro,[4,5] bromo,[6] methoxy[7] and acetoxy[8] groups has been extensively examined. However, studies using fluorine as a steering group have been carried out only to a limited extent, *e.g.* it has been reported that in a planar molecule like coumarin, fluoro substitution leads to the β-packing mode,[9] whereas in benzylidene-DL-piperitone, α-packing is observed.[10] This difference between the two classes of molecules is attributed to the closer packing that is attainable in the α-mode when the molecule is non-planar. The photobehaviour of unsubstituted and substituted (*e.g.* –OH and –Cl) styrylcoumarins examined previously in our laboratory yield centrosymmetric dimer (*anti*-HT) upon irradiation.[11,12] In this context, it seemed worthwhile to investigate other molecular frameworks containing fluorine as a substituent and to delineate the mode of packing in such moieties and also identify the possible intermolecular interactions of crucial importance. We report here the crystal packing and the photobehaviour of reactants 1 and 2. The influence of fluorine substitution on crystal packing is discussed.

Results and discussion

The crystal data and details of the refinements of **1**, **2** and **2a** are given in Table 1. The perspective views of compounds **1**, **2** and **2a** along with the atomic numbering scheme drawn by using the program XPMA/ZORTEP[13] are shown in Figs. 1–3 and the stereo packing diagrams[14] of **1** and **2** in Figs. 4 and 5. respectively. After an irradiation of 35–45 h both molecules **1** and **2** gave [in total contrast to the photobehaviour of unsubstituted and substituted (*e.g.* –OH and –Cl) styrylcoumarins] a single stereospecific *syn*-HH dimer **1a** and **2a** (Scheme 1) which is consistent with a short *a* axis of *ca.* 3.85 Å in both **1** and **2**.

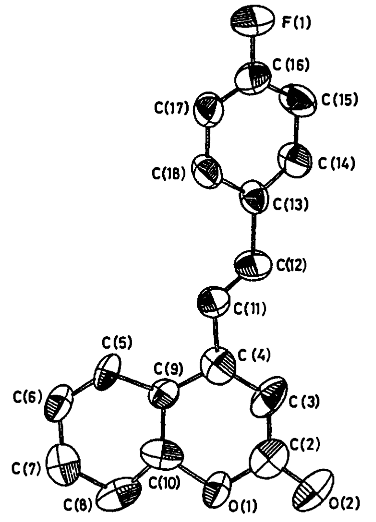


Fig. 1 ORTEP diagram of **1**. Thermal ellipsoids are at 40% probability level.

The progress of the photochemical reaction was monitored by thin layer chromatography (TLC) and ^{1}H NMR spectroscopy. The NMR pattern corresponds to the cyclobutyl protons in both cases showing that the photoproduct is *syn*-HH. The carbonyl stretching frequency ($>$C=O 1720 cm^{-1}) of both the monomer and the product are identical indicating that the [2+2] photocycloaddition is across the styrenic double bond. Note that these fluoro derivatives give mirror symmetric products in contrast to the centrosymmetric photoproducts obtained from the parent styrylcoumarin and with substituents other than fluorine.[11,12] A similar observation has been made previously for 6- and 7-fluorocoumarins.[9]

To achieve a [2+2] topochemical photocycloaddition, the centre-to-centre distance between the potentially reactive double bonds should be less than *ca.* 4.2 Å, and the best overlap

Table 1 Crystal data and details of refinement

	1	**2**	**2a**
Molecular formula	$C_{17}H_{11}FO_2$	$C_{17}H_{11}FO_2$	$C_{34}H_{22}F_2O_4$
M	266.26	266.26	532.52
Crystal system	Monoclinic	Orthorhombic	Monoclinic
a/Å	3.846(2)	3.853(1)	8.085(4)
b/Å	11.670(2)	6.853(2)	13.250(4)
c/Å	28.215(2)	46.785(10)	23.356(8)
β/°	93.15(2)		97.46(5)
V/Å^3	1264.5(7)	1235.4(5)	2481(2)
T/K	293	158	158
Radiation/Å	Cu-Kα, 1.5418	Mo-Kα, 0.7107	Mo-Kα, 0.7107
Space group	$P2_1/c$	$P2_12_12_1$	$P2_1/n$
Z	4	4	4
D_x/mg m^{-3}	1.399	1.432	1.426
Crystal size/mm^3	0.6 × 0.3 × 0.14	0.85 × 0.16 × 0.08	0.4 × 0.25 × 0.06
μ/cm^{-1}	0.836	0.103	0.103
F(000)	552	552	1104
θ/°	3.1–60.3	2.6–22.5	2.3–22.5
Mode of data collection	ω–2θ	ω–2θ	ω–2θ
No. of observed reflections	1797	1033	3247
Final R	0.110	0.046	0.069
Final R_w	0.205	0.053	0.109
No. of variables	181	225	361
Residual electron density, ρ/Å^{-3}	0.35	0.17	0.27

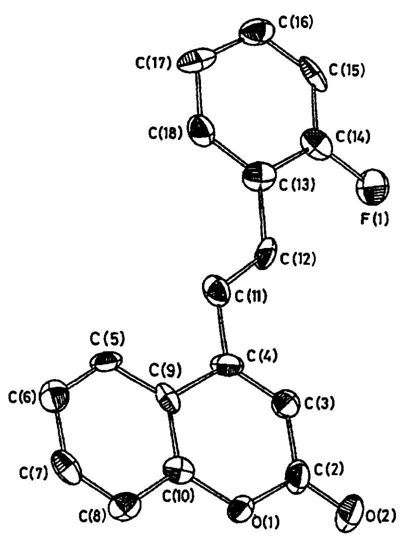


Fig. 2 ORTEP diagram of **2**. Thermal ellipsoids are at 40% probability level.

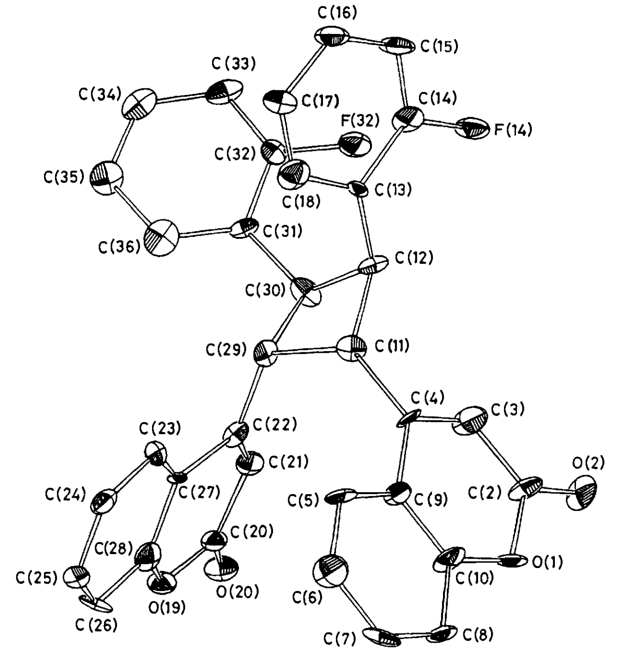


Fig. 3 ORTEP diagram of photodimer **2a**. Thermal ellipsoids are at 40% probability level.

of the π-orbital of the reactive partners can be identified through the geometrical parameters θ_1, θ_2, θ_3 and d, as proposed in our recent publications[11,12] (Fig. 6). The ideal values of these parameters are 0, 90, 90° and 0 Å. The centre-to-centre distance between the styrenic double bonds [C(11)=C(12)] of translated molecules along the a axis is 3.846 and 3.853 Å in **1** and **2**, respectively. The calculated values of θ_1, θ_2, θ_3 and d for the styrenic double bonds of **1** are 0, 73.8, 72.9° and 1.1 Å, respectively, and those for **2** are 0, 74.1, 99.2° and 0.44 Å, respectively. The observed deviation of θ_1, θ_2, θ_3 and d from the ideal values are encountered in many other photolabile crystals.[15] In both crystals **1** and **2**, we found that there are C–H···O interactions and the parameters of these bonds are provided in Table 2. There are neither F···F intermolecular contacts less than the sum of the van der Waals radius of the fluorine atom (1.47 Å) nor are there any significant C–H···F interactions. However, the fluorine substitution has a dramatic effect on the organization of the molecules in the crystal lattices resulting in a mirror symmetric product. The ultimate crystal structure that we observe is an interplay between the various interactions such as F···F, F···H, π···π and C–H···O, all of which contribute to different degrees in stabilizing the crystal structure. It is remarkable that the crystal densities of **1** and **2** are significantly greater than those of the parent compounds (Table 3), showing that the fluoro substitution leads to closer packing of the molecules. Indeed comparison of the values of the densities of the crystals of other fluoro substituted molecules with those of the parent molecules shows the fluoro ones are packed closer.

Conclusions

It is remarkable that replacement of a hydrogen atom at *ortho* and *para* positions by a fluorine atom leads to a dramatic change in the assembly of styrylcoumarin molecules which results in the β-packing mode as against the α-packing mode in the parent and substituted (–OH and –Cl) styrylcoumarins. It is interesting that molecules **1** and **2**, despite being similar,

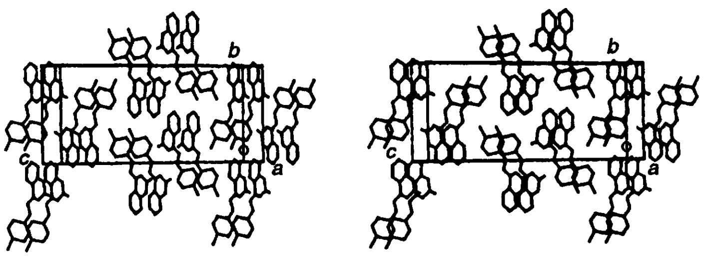


Fig. 4 Stereospecific view of crystal packing of 1

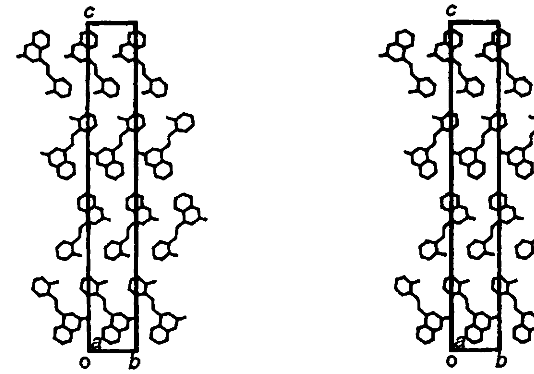
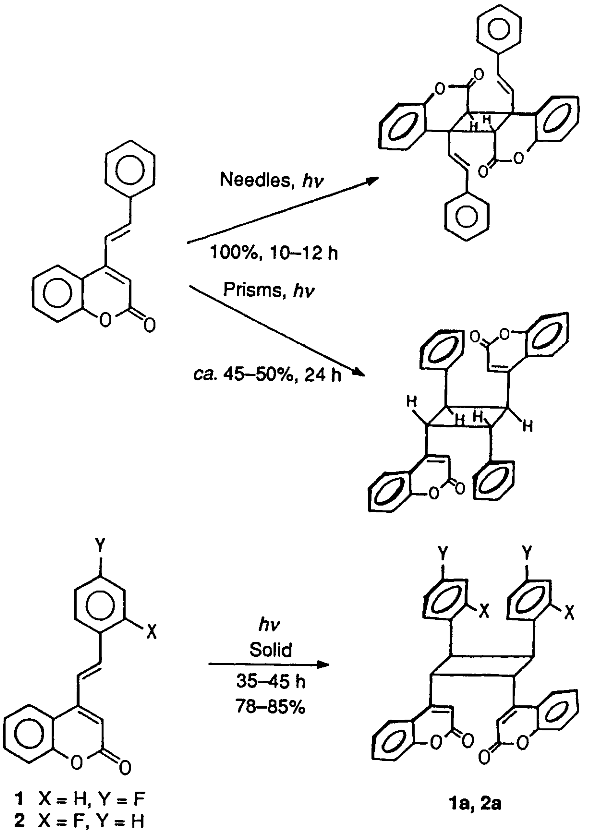


Fig. 5 Stereospecific view of crystal packing of 2



Scheme 1

crystallize in different crystal symmetries; **1** in centrosymmetric and **2** in non-centrosymmetric space groups, $P2_1/c$ and $P2_12_12_1$, respectively, with one crystallographic axis as short as *ca.* 3.85 Å. The C–H···F interaction first recognized in the crystal structures of 6- and 7-fluorocoumarins and *p*-fluorobenzylidenepiperitone is absent in the structures discussed here. The exact nature of the weak intermolecular interactions which come into play in the fluoro derivatives needs to be understood. In addition to interactions such as C–H···O and π···π, long range electrostatic attractive interactions are likely to be important in orientating the monomers. The greater values of the crystal densities of the fluoro derivatives as against the parent styrylcoumarin (Table 3) is suggestive of the closer molecular packing on substitution. Further investigations with fluorine substitution at different positions of styrylcoumarins are underway with a view to examining further the steering ability of fluorine and to unravel the intermolecular interactions operating in these crystals.

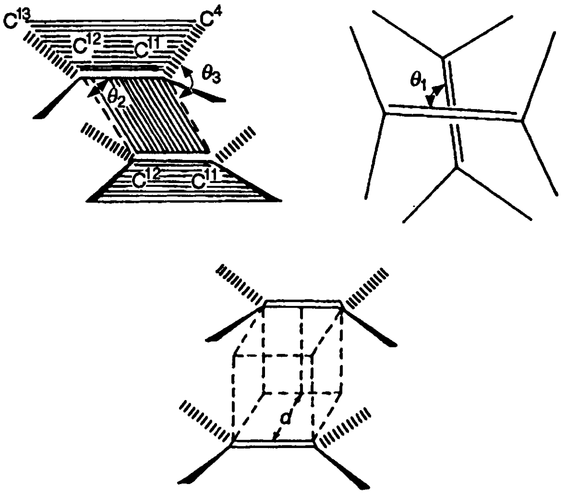


Fig. 6 Pictorial representation of θ_1, θ_2, θ_3 and d.

Table 2 Geometrical parameters of the C–H···O hydrogen bonds

Atom	Bonded to	C···O/Å	H···O/Å	C–H···O/°
Compound 1				
O(2)	C(3)H	3.58	2.65	177.9
O(2)	C(14)H	3.47	2.59	158.4
O(1)	C(8)H	3.19	2.65	127.2
Compound 2				
O(2)	C(5)H	3.24	2.45	150.7
O(2)	C(18)H	3.48	2.58	174.9
O(2)	C(11)H	3.48	2.34	167.5

Experimental

Compounds **1** and **2** were prepared[17] by condensing the corresponding fluoro-2′-hydroxychalcone with the Wittig reagent $Ph_3P{=}CHCOOEt$ and purified by 10% EtOAc in hexane. A 1 : 2 ratio of chloroform and ethanol gave pale yellow crystals. The powder samples of **1** and **2** are irradiated with UV light in Rayonet photochemical reactors (λ_{max} = 320 nm) at room temperature. The progress of the reaction was monitored by ^1H NMR spectroscopy and TLC. After an irradiation period of 35–45 h, **1** and **2** gave the β-symmetric dimer (yield 78–85%),

Table 3 Crystal densities of compounds with and without fluorine

Compound[a]	D_x/mg m^{-3}	Compound	D_x/mg m^{-3}
4-(4-Fluorostyryl)coumarin	1.399	4-(Styryl)coumarin[b]	
4-(2-Fluorostyryl)coumarin	1.432	Needles	1.288
		Prisms	1.303
6,7-Difluorobenzimidazol-2-one	1.654	Benzimidazol-2-one	1.410
3,5-Difluorophenol	1.566	Phenol	1.071
6-Fluorocoumarin[c]	1.530	Coumarin	1.397
7-Fluorocoumarin[c]	1.521		
p-Fluorobenzoic acid	1.437	Benzoic acid	1.266
1,2-Bis(2,3,4,5,6-pentafluorophenyl)ethane	1.851	1,2-Diphenylethane	1.120
Hexafluorobenzene	2.100	Benzene	1.060

[a] Ref. 16. [b] Ref. 11. [c] Ref. 9.

in total contrast to the photoproduct of parent and substituted (*e.g.* –OH and –Cl) styrylcoumarins. Corresponding photodimers were purified by column chromatography using 10% EtOAc in hexane.

X-Ray structural analysis and refinement

Single crystals of **1**, **2** and **2a** were obtained by slow evaporation from a solution of chloroform and ethanol (1 : 2), respectively. Three dimensional intensity data were collected for **1** on an Enraf–Nonius CAD-4 diffractometer using Ni-filtered Cu-Kα at 293 K, and for **2** and **2a**, on a Siemens diffractometer using graphite monochromated Mo-Kα radiation at 158 K, in ω–2θ mode. The highly mosaic nature of the crystals of **1** did not permit good quality data to be collected. However, with the main focus being the details of the molecular packing only the structural analysis was carried out. The intensity of the three standard reflections used for checking the stability of the crystals showed only statistical variations. The orientation of the crystal in each case was monitored with the aid of three reflections after the measurement of every 400 reflections. The data were corrected for Lorentz and polarization factors, but not for absorption. The structures of **1**, **2** and **2a** were solved by using direct method SHELXS-86.[18] Using the default options of the program, the E-map was given from which all the positions corresponding to the non-hydrogen atoms could be identified. Full matrix least-squares refinement using SHELXL-93[19] of scale factor, positional and thermal parameters of non-hydrogen atoms converged to give final *R* values of 0.110, 0.046 and 0.069 for **1**, **2** and **2a**, respectively. In the final cycles of the refinements the hydrogen atoms were fixed using the option HFIX in SHELXL-93 and were allowed to refine as riding hydrogens. The details of data collections and refinement are summarized in Table 1. Anisotropic thermal parameters of non-hydrogen atoms, atomic coordinates and bond lengths and bond angles involving hydrogen atoms have been deposited at the Cambridge Crystallographic Data Centre (CCDC).†

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† For details of the deposition scheme see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 2*, 1996, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the ref. no. 188/5.