

Studies in crystal engineering: crystal packing, topological photodimerization and structure–reactivity correlations in fluoro-substituted styrylcoumarins



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In continuation of our studies on the influence of fluoro substitution on the solid state photobehaviour and packing pattern of styrylcoumarins, the results obtained for 4-(3-fluorostyryl)coumarin **1**, 4-styryl-6-fluorocoumarin **2** and 4-styryl-7-fluorocoumarin **3** are presented. The configuration of the dimers was established on the basis of crystal packing of **1** and **2** (α -packed). A rationale for the significantly lower dimer yield in the crystal for **2** is proposed. In the observed centrosymmetric arrangement of the reactants the C=O $\cdots \pi$ (phenyl) contacts seem to provide additional attractive interactions. C–H \cdots O and C–H \cdots F hydrogen bonding seems to provide stability in these structures.

It is well known that if potentially reactive double bonds are orientated parallel to each other and separated by approximately 4 Å, then [2 + 2] photocycloaddition takes place with a minimum of atomic and molecular motion.¹ In general, the environment of olefinic double bonds in these crystals conforms to one of the three principle types: (a) the α -type crystal, in which the double bonds of neighbouring molecules make contact at a distance of *ca.* 3.7 Å across a centre of symmetry to give a centrosymmetric dimer; (b) the β -type, characterized by a lattice having one axial length of 4.0 ± 0.1 Å yielding a dimer of mirror symmetry, and (c) the photochemically inactive γ -type crystal in which double bonds of neighbouring molecules are more than 4.2 Å apart.

It has been observed that the parent styrylcoumarin crystallizes as dimorphs, namely prisms and needles and both yield centrosymmetric [α -mode; *anti*-head–tail (HT)] photodimers in the solid state.² The cycloaddition in prismatic crystals is across the styrenic double bond whereas in needles the dimerization is through the pyrone double bond. Substituted (*e.g.* –OH and –Cl) styrylcoumarins also produce *anti*-HT photodimers.² On the other hand our studies on the structure–reactivity relationship of 4-(2-fluorostyryl)coumarin and 4-(4-fluorostyryl)coumarin lead to the β -packing mode,³ demonstrating the steering capability of fluorine. With a view to further investigating the effect of fluorine substitution at different positions in the molecule on the packing mode, we have now studied the photobehaviour and molecular organization in **1–3**.

Results and discussion

The crystal data and details of the refinement of compounds **1–3** are given in Table 1. Structures **1** and **2** consist of two molecules in the asymmetric unit designated hereafter as **A** and **B**. The perspective views of compounds **1–3** along with the atomic numbering scheme (the same atom numbering is used for molecule **B** in compounds **1** and **2**) drawn using the program XPLA/ZORTEP⁴ are shown in Figs. 1–3 (thermal ellipsoids are given at 40% probability level) and their perspective view packing diagrams⁵ are presented in Figs. 4–6, respectively. Both **1** and **2** produce centrosymmetric (*anti*-HT) photodimers **1a** and **2a** (Scheme 1), when subjected to irradiation in the solid state for *ca.* 35–40 h, similar to the observation in the styrylcoumarins parent as well as –OH and –Cl substituted molecules.² However, in both **1** and **2**, the [2 + 2] cycloaddition is

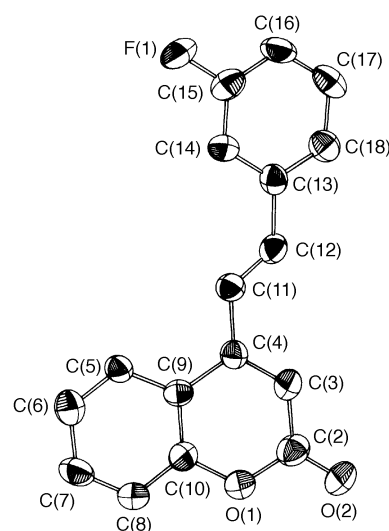


Fig. 1 ORTEP diagram of 4-(3-fluorostyryl)coumarin **1** (molecule **A**)

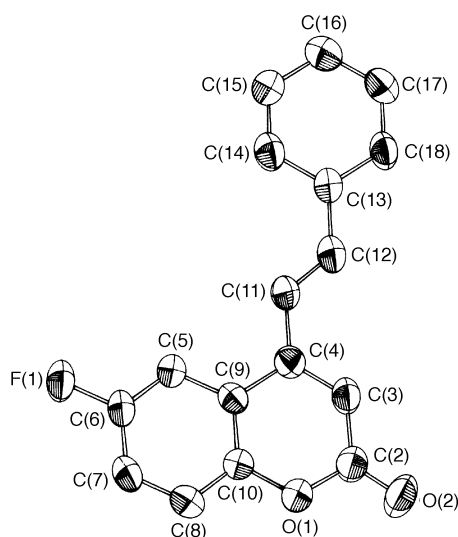
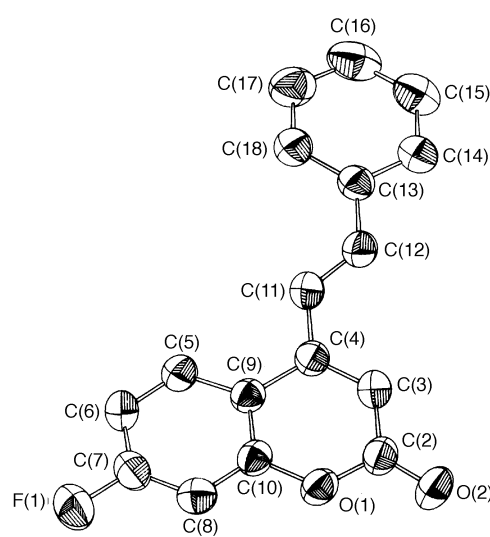
only across the styrenic double bond. It is noteworthy that 4-(2-fluorostyryl)coumarin and 4-(4-fluorostyryl)coumarin are β -packed.³

The powder samples of **1–3** were irradiated simultaneously using Rayonet lamps for *ca.* 35–40 h. During irradiation care was taken to expose samples uniformly by shaking the containers at regular intervals. The progress of the reaction was monitored by ¹H NMR and thin layer chromatography (TLC). Compound **3** remained unchanged even after 10 d of continuous irradiation. The IR stretching frequencies of carbonyl carbon in **1** and **2** are at 1725 and 1720 cm⁻¹ and those for the corresponding dimers **1a** and **2a** are also in the same region to ± 5 cm⁻¹ suggesting that the dimerization is about the styrenic double bond only (dimerization across the pyrone double bond results in deconjugation). The formation of dimers (**1a** and **2a**) has been interpreted only on the basis of molecular arrangement of monomer crystal structures (Scheme 1) (Figs. 4 and 5). The yield of the photodimers as determined from ¹H NMR spectra was 78–83% in **1** and 48–50% in **2**.

In the crystal of **1**, the distance between the two reactive partners [C(11)=C(12)] of molecule **A** (**A** and its centrosymmetrically related partner **A'**) generated across the centre of

Table 1 Crystal data and details of refinement

	1	2	3
Molecular formula	C ₁₇ H ₁₁ FO ₂	C ₁₇ H ₁₁ FO ₂	C ₁₇ H ₁₁ FO ₂
<i>M</i>	266.26	266.26	266.26
Crystal system	Triclinic	Triclinic	Monoclinic
<i>a</i> /Å	7.358(1)	7.318(2)	6.843(2)
<i>b</i> /Å	7.652(1)	12.816(2)	20.452(4)
<i>c</i> /Å	23.829(3)	13.849(2)	9.079(1)
<i>a</i> ^o	97.04(1)	95.97(2)	
<i>β</i> ^o	96.03(1)	94.26(2)	96.23(2)
<i>γ</i> ^o	101.78(1)	95.17(2)	
<i>V</i> /Å ³	1291.8(3)	1282.0(4)	1263.1(5)
<i>TK</i>	293	293	293
Radiation	Cu-Kα	Mo-Kα	Cu-Kα
Space group	<i>P</i> $\bar{1}$	<i>P</i> $\bar{1}$	<i>P</i> 2 ₁ / <i>n</i>
<i>Z</i>	4	4	4
<i>D</i> _c /mg m ⁻³	1.369	1.380	1.400
Crystal size/mm ³	0.9 × 0.3 × 0.2	0.6 × 0.21 × 0.3	1 × 0.3 × 0.4
<i>μ</i> /cm ⁻¹	0.818	0.099	0.836
<i>F</i> (000)	552	552	552
<i>θ</i> ^o	1.8–60.1	1.48–25.1	4.32–59.92
Mode of data collection	<i>ω</i> -2 <i>θ</i>	<i>ω</i> -2 <i>θ</i>	<i>ω</i> -2 <i>θ</i>
No. of unique reflections/those with <i>I</i> > 4 <i>σ</i> (<i>I</i>)	3843/1125	4519/2685	1768/1328
Final <i>R</i>	0.046	0.072	0.045
Final <i>R</i> _w	0.052	0.199	0.120
Residual electron density/e Å ⁻³	0.16	0.27	0.14

**Fig. 2** ORTEP diagram of 4-styryl-6-fluorocoumarin **2** (molecule **A**)**Fig. 3** ORTEP diagram of 4-styryl-7-fluorocoumarin **3**

inversion at 1/2,0,0) is 3.93 Å (Fig. 4). Interestingly, the atomic positions corresponding to the molecule **B** in **1** are such that the molecules generated by the centre of inversion at (0,0,1/2) as well as (1/2,0,1/2) are both favourably juxtaposed with the distance of separation being 3.62 and 3.79 Å, respectively (Fig. 4). In the crystal of **2** the situation is different. In molecule **A**, centre-to-centre distances of the reacting partners are 3.66 and 3.68 Å and hence favourable for photocycloaddition. Molecule **B** is not favourably positioned for the reaction (Fig. 5) as the distance of separation is as large as 6.94 Å. The lower yield in **2** (ca. 50%) in comparison with compound **1** (yield ca. 80%) may be due to the fact that only one of the molecules in the asymmetric unit is in a reacting situation. In the crystal of **3** the distances between the styrenic and pyrone double bonds and their centrosymmetrically related counterparts are as large as 5.79 and 5.40 Å, respectively and it is therefore photostable. It must be stressed that all factors except the particle size which influence the product yield are the same as the irradiation was carried out under identical experimental conditions. Therefore it is reasonable to attribute the much larger dimer yield in **1** to the fact that both the independent molecules in the asymmetric

unit are involved in the dimerization reaction whereas in **2** only one of the two molecules is reacting.

In a topochemical reaction, the geometrical parameters (θ_1 , θ_2 , θ_3 and *d*) of the reactive partners C(11)=C(12) (Fig. 7) parameters should ideally be 0, 90, 90° and 0 Å, respectively. The calculated values for styrenic double bonds are given in Table 2. The deviation of these parameters from the ideal values has been observed in many other photolabile crystals.⁶

It has been recognized that the role of the C=O... π interaction between centrosymmetrically reactive partners assists the α -packing mode in the solid state.^{2,7} The relative orientation of the centrosymmetrically related molecules **A** in **1** is shown in Fig. 8. The relevant geometrical parameters of the carbonyl group with respect to the phenyl ring of the centrosymmetrically related partner are defined² using α_1 , d_1 and d_2 (Fig. 9). From the calculated values² of these parameters, benzilidene-DL-piperitone is expected to be photolabile but is in fact photoinert.⁸ The values of these parameters for crystals **1–3** are given in Table 3 and are found to be similar to those reported in a few other structures.² As discussed earlier, crystal

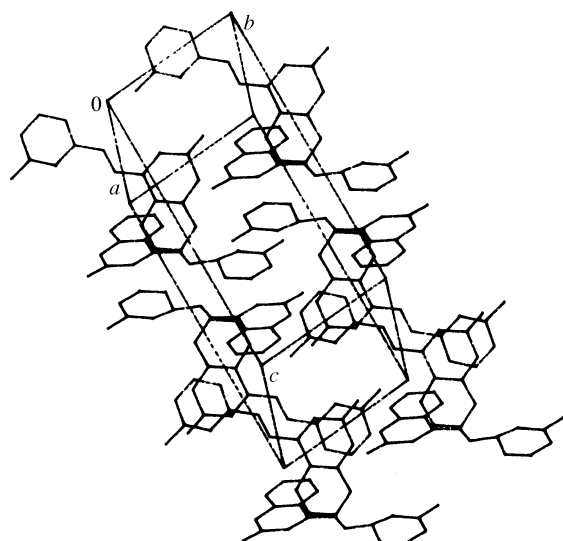


Fig. 4 A perspective view of the crystal packing of 4-(3-fluorostyryl)coumarin **1**

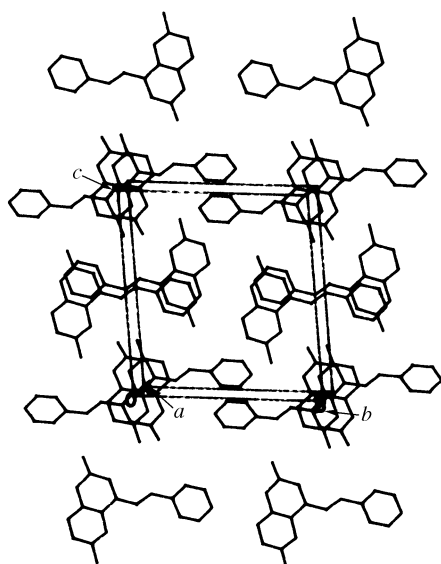


Fig. 5 A perspective view of the crystal packing of 4-styryl-6-fluorocoumarin **2**

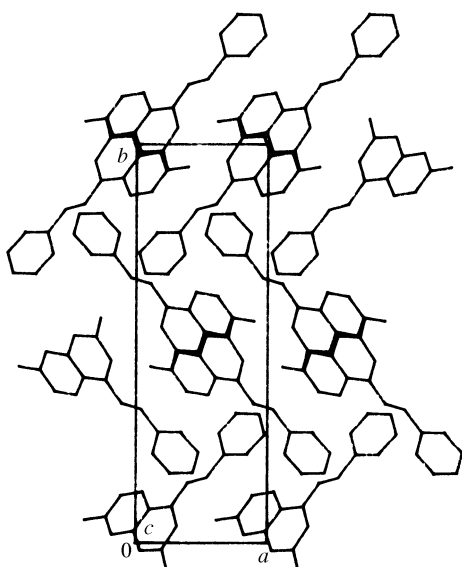
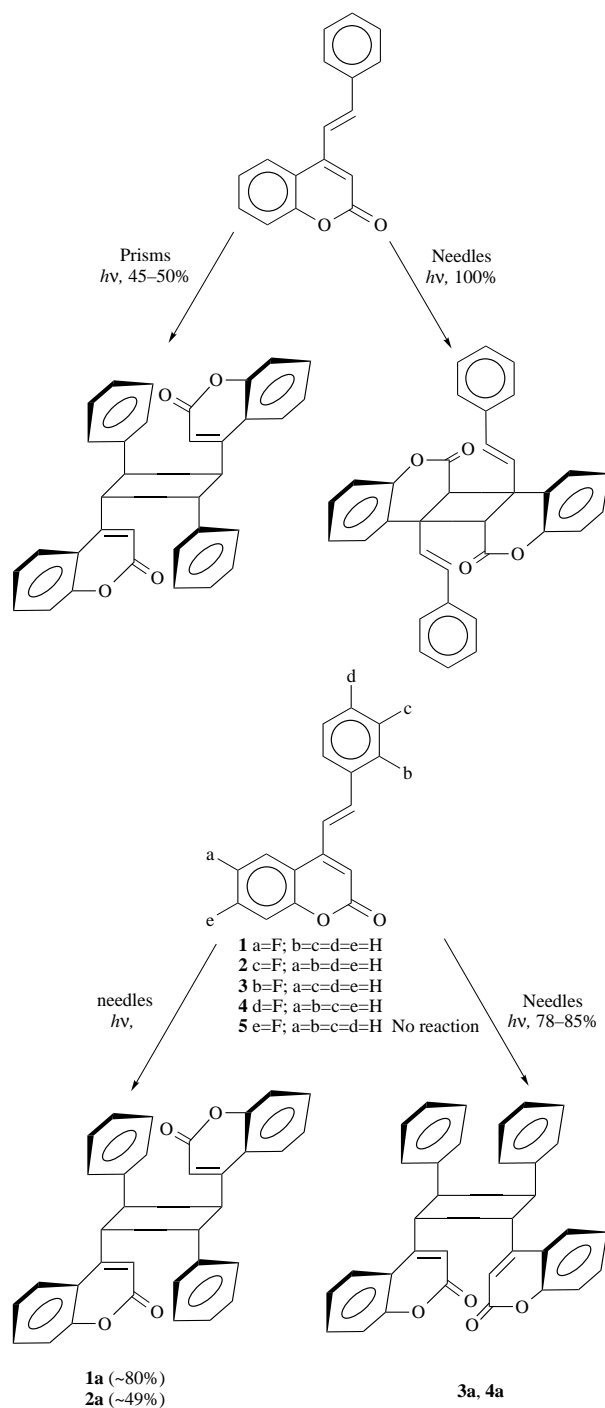


Fig. 6 A perspective view of the crystal packing of 4-styryl-7-fluorocoumarin **3**



Scheme 1

3 and molecule **B** in crystal **2** are photostable. The very large values of the displacement distance d_3 for these cases seem to be relevant.

The crystal densities of **1–3** (1.369, 1.380 and 1.400 Mg m⁻³, respectively) are significantly larger than those of the parent styrylcoumarin (needles 1.288; prisms 1.303 Mg m⁻³).³ This could be partly due to closer packing of the molecules on fluoro substitution. Table 3 shows the relevant intermolecular contacts in structures **1–3**. In **1** and **2**, there are a few C–H···F contacts in addition to C–H···O interactions. In **3** there is a F···F short contact (2.80 Å) of less than the sum of the van der Waals radius of fluorine atom (1.47 Å). The influence of the fluorine atom on steering the molecules in a predictable manner may not be as effective as that of the chlorine atom. For example 6- and 7-fluorocoumarins, 4-(4-fluorostyryl)coumarin and 4-(2-fluorostyryl)coumarin have β-packing.^{3,9} In contrast, *p*-fluorobenzylidene-DL-piperitone¹⁰ and compounds **1** and **2**

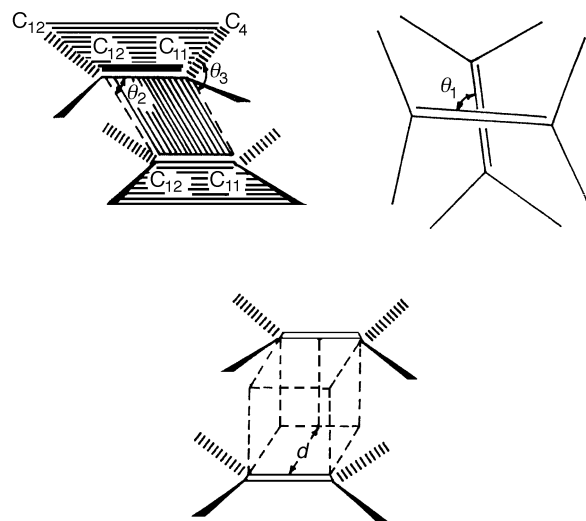
Table 2 Geometrical parameters (θ_1 , θ_2 , θ_3 and d) of the π -orbitals of the styrenic C(11)=C(12) double bond

Compound		Distance/Å	$\theta_1/^\circ$	$\theta_2/^\circ$	$\theta_3/^\circ$	$d/\text{Å}$
4-(3-Fluorostyryl)coumarin	A	3.93	0	63.9	91.5	0.1
	B	3.79	0	96.0	87.7	0.2
		3.62	0	74.3	79.0	0.4
4-Styryl-6-fluorocoumarin	A	3.66	0	103.2	91.0	0.1
		3.68	0	79.9	85.2	0.1

Table 3 Geometrical parameters for carbonyl oxygen with respect to phenyl ring

Compound		$a_1/^\circ$	$d_1/\text{Å}$	$d_2/\text{Å}$
4-(3-Fluorostyryl)coumarin	A	13.98	4.12	1.30
	B	5.74	4.32	2.45
4-Styryl-6-fluorocoumarin	A	7.19	4.05	1.67
	B	16.31	7.62	6.21
4-Styryl-7-fluorocoumarin		6.20	7.90	5.16

Geometrical parameters for carbonyl carbon with respect to phenyl ring				
Compound		$a_1/^\circ$	$d_1/\text{Å}$	$d_2/\text{Å}$
4-(3-Fluorostyryl)coumarin	A		3.73	0.67
	B		3.83	1.36
4-Styryl-6-fluorocoumarin	A		3.64	0.80
	B		7.54	6.33
4-Styryl-7-fluorocoumarin			7.93	3.71

**Fig. 7** Pictorial representation of θ_1 , θ_2 , θ_3 and d parameters

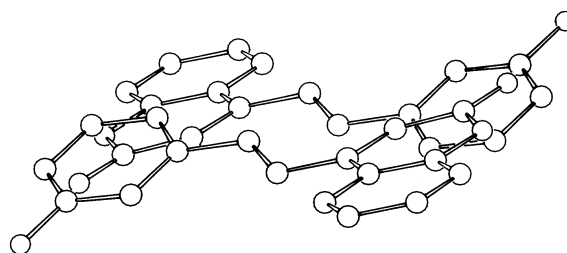
have α -packing. All these are photolabile while compound **3** is photoinert. It is also obvious from our studies that the replacement of a hydrogen atom by a fluorine atom alters the packing mode dramatically. But the exact nature of the interactions responsible for the observed changes are not easily discernible. It appears that the high electronegativity of the fluorine atom and electrostatic interactions between the electron-rich carbonyl group and the electron-deficient phenyl group assist α -packing mode. Apart from C-H \cdots O interactions, C-H \cdots F, $\pi\cdots\pi$ and C=O $\cdots\pi$ (phenyl) interactions also contribute towards the stability of α -packing mode in these structures.

Experimental

Compound **1–3** were prepared¹¹ by condensation of the corresponding fluoro-2'-hydroxychalcone with the Wittig reagent Ph₃P=CHCOOEt and purified by column chromatography using 10% EtOAc in light petroleum as eluent. Crystallization from 1:2 chloroform and ethanol gave pale-yellow crystals. The

Table 4 Geometrical parameters of the C-H \cdots O and C-H \cdots F hydrogen bonds

Atom	bonded to	C \cdots O/F(Å)	H \cdots O/F(Å)	C-H \cdots O/F($^\circ$)
Compound 1				
AO(2)	AC(11)H	3.40	2.53	167.1
AO(2)	AC(5)H	3.37	2.48	147.0
BO(2)	BC(12)H	3.49	2.35	166.1
AF(1)	AC(12)H	3.44	2.47	160.2
BF(1)	BC(14)H	3.48	2.46	166.3
Compound 2				
AO(1)	AC(8)H	2.75	2.55	122.9
AO(2)	BC(14)H	3.60	2.65	150.3
BO(1)	BC(16)H	3.49	2.49	164.1
AO(2)	BC(12)H	3.48	2.58	157.7
BO(2)	AC(12)H	3.47	2.59	151.2
BF(6)	AC(14)H	3.49	2.62	157.2
BF(6)	AC(5)H	3.39	2.57	149.9
Compound 3				
O2	C(12)H	3.41	2.52	160.1
	F \cdots C		F \cdots F	F-C \cdots F
F1	C(7)F1	3.63	2.80	117.4

**Fig. 8** Relative orientation of the centrosymmetrically related molecules **A** of **1**

powder samples of **1** and **2** were irradiated with UV-light in a Rayonet photochemical reactor (λ_{max} 320 nm) at room temperature. The progress of the reaction was monitored by ¹H NMR spectroscopy and TLC. Corresponding photodimers were purified by column chromatography using 10% EtOAc in light petroleum.

X-Ray structural analysis and refinement

Single crystals of **1–3** were obtained by slow evaporation from chloroform and ethanol (1:2 ratio). Three-dimensional intensity data were collected on an Enraf-Nonius CAD4 diffractometer using Ni-filtered Cu-K α for **1** and **3** and graphite monochromated Mo-K α for **2** in ω - 2θ mode at 293 K. The intensity of three standard reflections 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 **1–3** were solved using direct methods (SHELXS-86).¹² Use of the default options of the program furnished the E-map from which all the positions corresponding to the non-hydrogen atoms could be identified. Full matrix least-squares refinement,

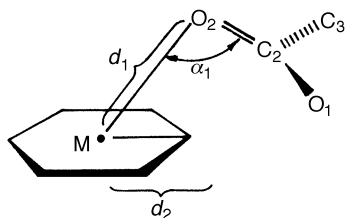


Fig. 9 Pictorial representation of the geometrical parameters a_1 , d_1 and d_2

using SHELXL-93,¹³ of scale factors, positional and thermal parameters of non-hydrogen atoms converged to final R values of 0.046, 0.072 and 0.045 for **1**, **2** and **3**, 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 collection and refinement are summarized in Table 1. Anisotropic thermal parameters of non-hydrogen atoms, atomic coordinates, bond lengths and bond angles involving hydrogen atoms will be deposited at the Cambridge Crystallographic Data Centre (CCDC).[‡]

Acknowledgements

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[‡] For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 2*, 1997, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 188/44.

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