Diastereoselective cyclization of a dithienylethene switch through single crystal confinement†

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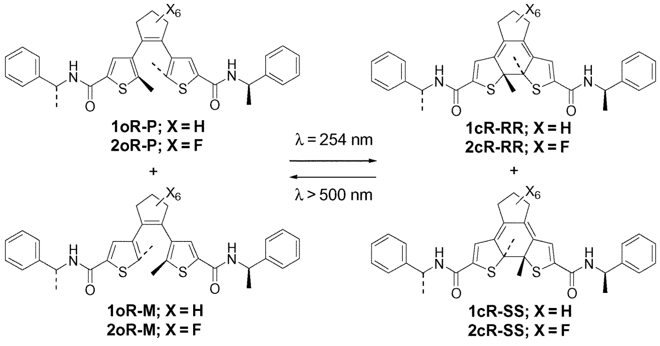
Upon UV irradiation of the hydrogen-bond confined crystal state of a dithienylhexafluorocyclopentene with (*R*)-*N*-phenylethylamide substituents, the photochemical cyclization reaction proceeds diastereoselectively to form the coloured, closed-ring isomer with 97% de.

Photochromism is defined as the reversible transformation of a single molecule between two states having different absorption spectra. Hence, photochromic molecules often hold considerable potential towards application as molecular switches and as control elements in molecular devices.[1]

Diarylethenes are among the most promising of photochromic compounds,[2] not only as memory materials but also as switching units for molecular devices and in supramolecular systems.[3] Some of us (Feringa, van Esch and co-workers) have demonstrated recently that a diarylethene **1oR** with chiral, (*R*)-*N*-phenylethylamide groups at both ends of the molecule engages in self-assembled gels through the formation of multiple hydrogen bonds between the amide groups (Scheme 1). The supramolecular chirality of the gel was translated into molecular chirality through the hydrogen-bonding networks formed and upon photochemical ring closure the molecular chirality of the gel was 'locked' by the stereoselectivity of the photochemical transformation. This example demonstrates the potentially useful interplay of molecular and supramolecular chirality.[4]



Scheme 1 Diarylethene **1oR** and **2oR** in the open form are in rapid equilibrium between *P*- and *M*-helicity, which upon irradiation with UV light lead to the closed form in *RR* and *SS* configuration, respectively.

In the present contribution, we report the synthesis of the perfluorocyclopentene derivative **2oR** to explore the effect of the fluorinated cyclopentene on the self-assembly process, the intermolecular hydrogen-bonding networks formed and the stereoselectivity of the photochromism in hydrogen-bond confined states.

Diarylethene **2oR** was prepared in one step starting from 1,2-bis(5-carbonyl-2-methylthien-3-yl)perfluorocyclopentene. The carboxylic acid was first deprotonated by *N*-methylmorpholine and subsequently activated by 2-chloro-4,6-dimethoxytriazine, followed by a reaction of the activated ester with (*R*)-α-phenylethylamine.[5] The compound **2oR** was prepared as colourless plates in 48% yield.[6] **2oR** shows reversible photochromism in acetonitrile solution. Fig. 1 illustrates the absorption and CD spectral changes of **2oR** in acetonitrile upon photo-irradiation. Upon irradiation at λ_{exc} 254 nm, the colourless solution turned blue and absorption bands assigned to **2cR** appeared at 576 nm (ε: 1.02×10^4 M^{-1} cm^{-1}) and 369 nm (ε: 7.00×10^3 M^{-1} cm^{-1}). Concomitantly the absorption of **2oR** at 258 nm (ε: 3.91×10^4 M^{-1} cm^{-1}) decreased in intensity. Upon irradiation at $\lambda >$ 500 nm, the blue colour was bleached and the open-ring isomer **2oR** was regenerated as confirmed by UV/Vis spectroscopy. The isosbestic points were observed at 206, 232, and 299 nm in Fig. 1(a).

In contrast to **1oR**, which forms gels with organic solvents, **2oR** did not engage in gelation and, indeed, formed colourless crystals from ethanol which were suitable for X-ray analysis. The difference in gelation behaviour between **1oR** and **2oR** may arise from the formation of (F···H) hydrogen bonds between diarylethene molecules. The availability of **2oR** as single crystals, nevertheless, allows for examination of the stereoselectivity of photochemical ring closure in a crystalline state.

In order for the photocyclization reactions to take place in the single crystalline phase, the diarylethene molecules should be in an *anti*-parallel conformation with the distance between the reactive carbon atoms being less than 4.2 Å.[7,8] In the crystal, **2oR**[9] was present in two different conformational states in a 1 : 1 ratio, the distances between the reactive carbon atoms being 3.546(10) and 3.686(8) Å, respectively (Fig. 2). The presence of two conformers is due to the presence amide substituents in two different conformations. Nevertheless, the separation of

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† Electronic supplementary information (ESI) available: X-ray crystallographic details for the compound **2oR** and ^{1}H NMR spectrum of compound **2cR**. See DOI: 10.1039/b517370a

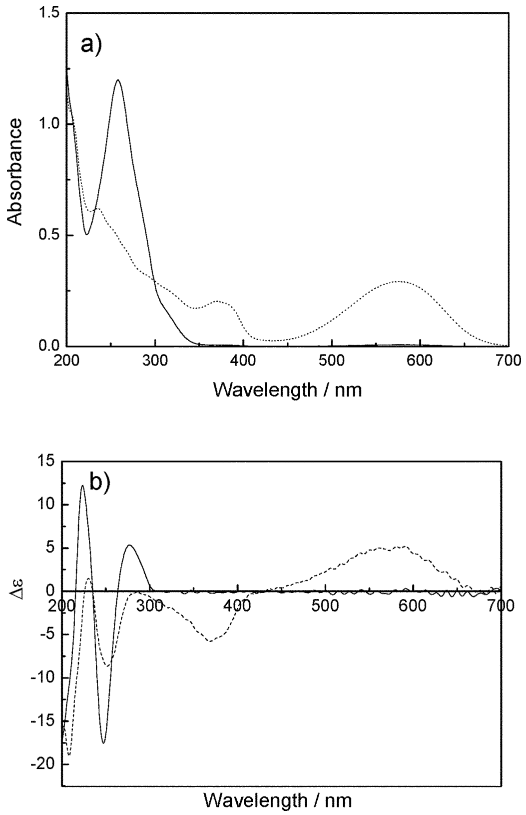

Fig. 1 UV/Vis absorption (a) and CD (b) spectral changes of **2R** in acetonitrile solution (3.07×10^{-5} M^{-1} cm^{-1}). Solid line (**2oR**), and dotted line [photostationary state (**2oR** : **2cR** = 7 : 93) under UV (254 nm) light irradiation].

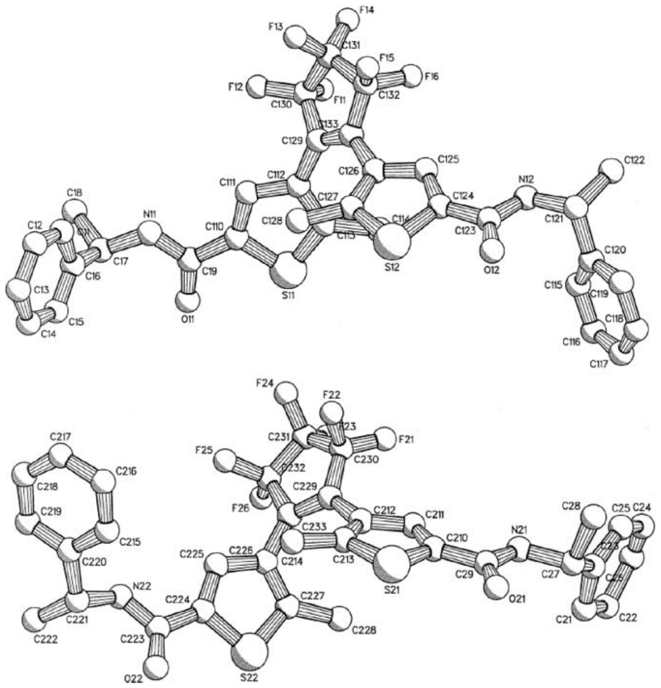

Fig. 2 PLUTO drawing of the two conformers of **2oR** present in the single crystal.

the reactive carbons of both conformers is less than 4.2 Å, which suggests that both conformers are capable of engaging in photochemical ring-closure. In addition, the central hexatriene moieties of both conformers are in the *M*-helicity configuration as shown in Fig. 2; therefore, the photocyclization reaction in the crystal is expected to give only one diastereoisomer of the closed-ring isomer, *i.e.* **2cR**-*SS*.

In the single crystal, these two conformers form a ladder-like structure through multiple intermolecular hydrogen bonding (Fig. 3). Each molecule participates in four hydrogen bonds that connect it to four (perpendicularly orientated) other molecules of different conformation. The amide moieties, linked by hydrogen bonds, form an infinite two-dimensional network along the base vectors [100] and [010], *i.e.* in the plane (001).

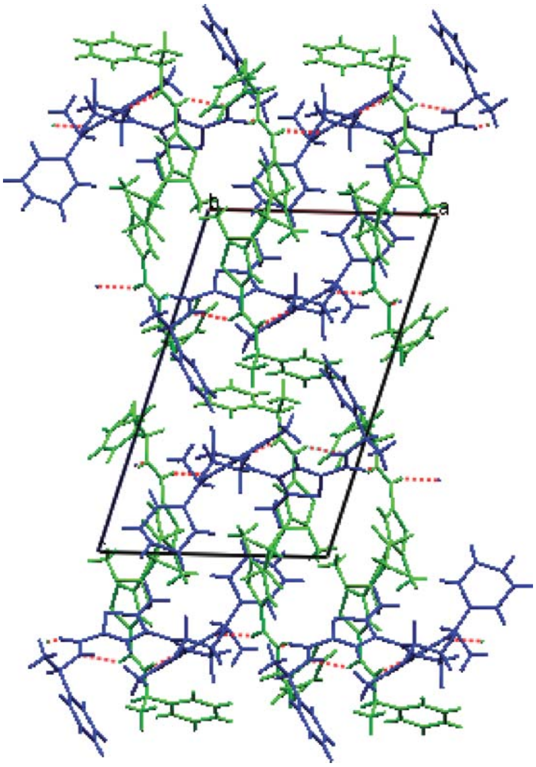

Fig. 3 Molecular packing of **2oR**. Conformers A and B, drawn in green and blue, respectively, are hydrogen bonded (red dotted line).

The absorption spectra of the coloured crystal, prepared by photolysis of a single crystal (Fig. 4) of **2oR** were monitored while rotating the crystal sample under linearly polarized light [Fig. 5(a)].

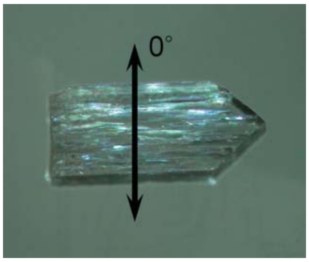

Fig. 4 Appearance of the single crystal of **2oR** (0.6 × 1.5 mm).

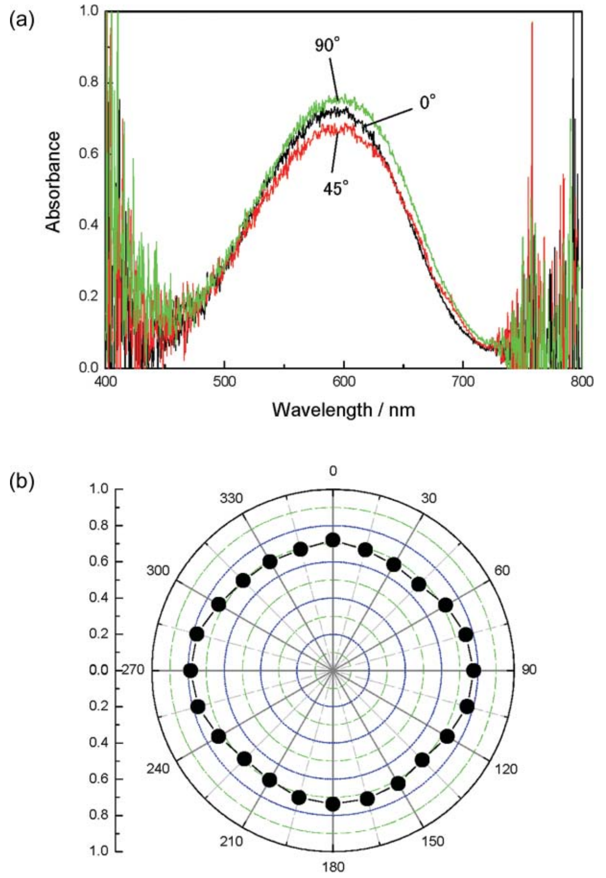

Fig. 5 Absorption spectra (a) of the photochemically coloured crystal of **2oR** at several orientations, and polar plots (b) of the absorbance at 598 nm.

The absorption maximum of the closed-ring isomer in the crystalline state is 22 nm (576 to 598 nm) red-shifted compared with that in solution. This is attributed to the restricted structure of the closed-ring isomer in the crystal lattice.[10] The dependence of the absorption of the changes of the closed-ring isomer was plotted against the angle of orientation of the crystal with respect to the linearly polarized light [Fig. 5(b)]. In this case, when the direction of the polarized light was rotated through 90°, the absorbance was almost equal to that at 0°, indicating that the molecules in the crystal have orientations which are nearly perpendicular to each other (Fig. 6).[11]

As shown in Fig. 2, diarylethene molecules **2oR** are fixed to form **2cR**-*SS*, and hence upon UV light irradiation, diastereoselective cyclization is expected. To verify that stereoselective photochemical ring closure occurs, the coloured crystal obtained by UV irradiation was dissolved in chloroform and the closed-ring isomer was separated by preparative TLC using a chloroform–methanol [96 : 4 (v/v)] mixture as the eluent. A CD spectrum of the closed-ring isomer **2cR** obtained in this way (Fig. 7) is significantly different from that of **2cR** formed upon UV irradiation in solution [Fig. 1(b)], especially in the 200–350 nm region of the spectrum.

The origin of the difference of the CD spectra of **2cR** prepared by irradiation of **2oR** in the single crystal and in solution was investigated through ^{1}H NMR spectroscopy (see ESI†). In the spectrum of **2cR** generated in solution, two signals for the protons on the thienyl moiety were observed at 6.74 and 6.75 ppm in CDCl$_3$ with the ratio of 1 : 1. In contrast, **2cR** generated in the crystalline phase showed only one signal at 6.74 ppm. The incomplete resolution of the two signals prohibited de determination accurately by ^{1}H NMR spectroscopy. Hence, the de was determined by chiral HPLC,[12] as shown in Fig. 8. The CD spectra of the diastereomeric closed-ring isomers **2cR**-*RR*, **2cR**-*SS* were obtained after isolation by HPLC. Interestingly, in such closed-ring isomers having two (*R*)-*N*-phenylethylamide groups, the CD spectra of both diastereomers have the same sign in the 450–700 nm region, but opposite signs at shorter wavelengths caused by the chirality of the central cyclohexadiene moiety. The tendency is very different with other enantiomeric and diastereomeric closed-ring isomers of diarylethenes which show the opposite Cotton effect over the entire wavelength region.[13,14] The sum of these CD spectra (solid line in Fig. 9) maches with that of Fig 1(b), indicating the lack of diastereoselectivity in the photocyclization in solution.

In the crystal, the conversion to the closed-ring isomer **2cR** was very low (2.3%) compared with that (95%) in solution. The low conversion in the crystal is due to inner filter effects with photoreaction proceeding only on the surface and in the thin

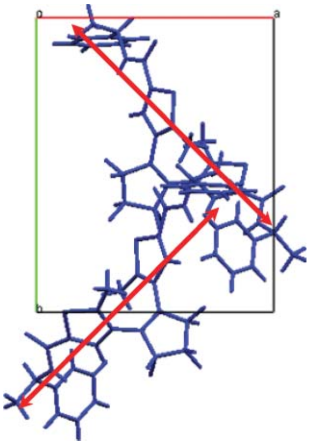

Fig. 6 Molecular packing of two conformers from the (001) face. The long axes of the molecules are oriented perpendicular to each other. The packing pattern is in agreement with the polar plot in Fig. 5(b).

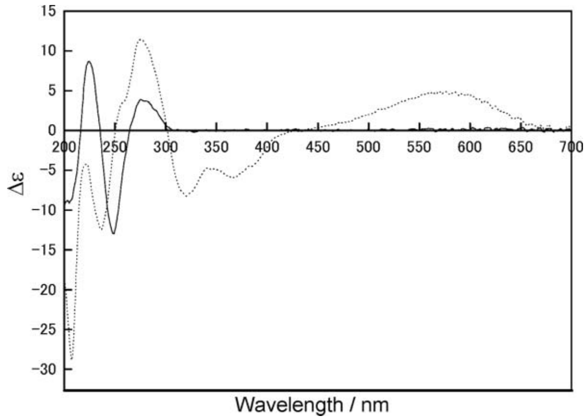

Fig. 7 CD spectrum of the closed-ring isomer **2cR** in acetonitrile (dotted line) dissolved after irradiation of a single crystal of **2oR** and that of the open-ring isomer **2oR** (solid line) obtained upon visible light ($\lambda > 500$ nm) irradiation.

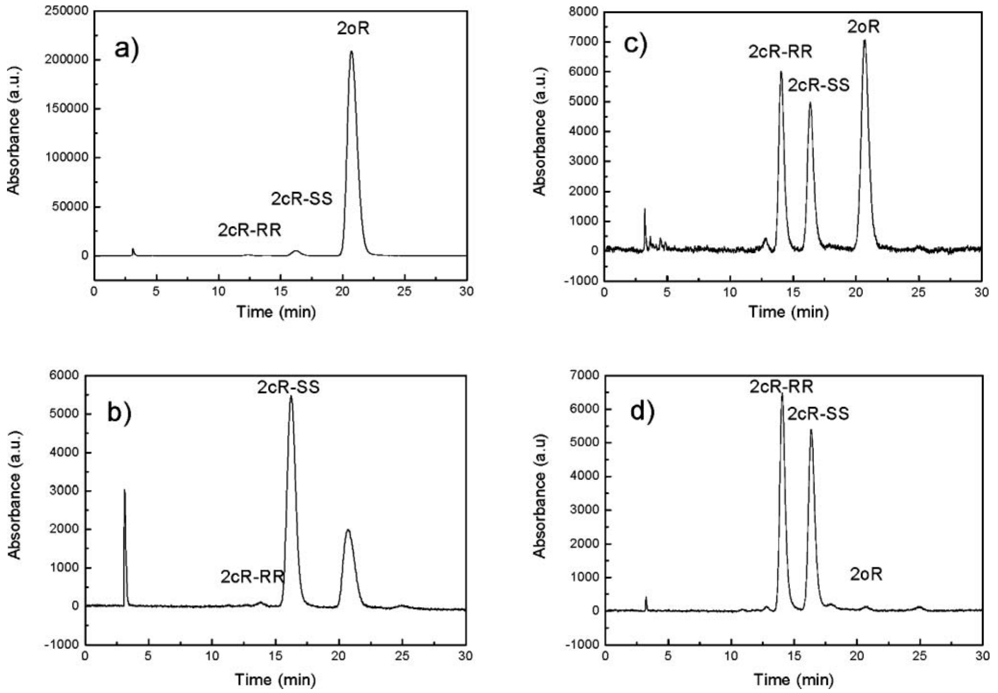

Fig. 8 HPLC chromatograms of **2R** after 254 nm light irradiation: (a) and (b) are the chromatograms of **2R** irradiated in the crystalline state; (c) and (d) are those of **2R** irradiated in acetonitrile solution; (a) and (c) were monitored at 299 nm (isosbestic point); (b) and (d) were monitored at 576 nm (λ_{max} of **2cR**). The retention times of **2cR**-*RR*, **2cR**-*SS*, and **2oR** are 14.05, 16.36, and 20.67 min, respectively.

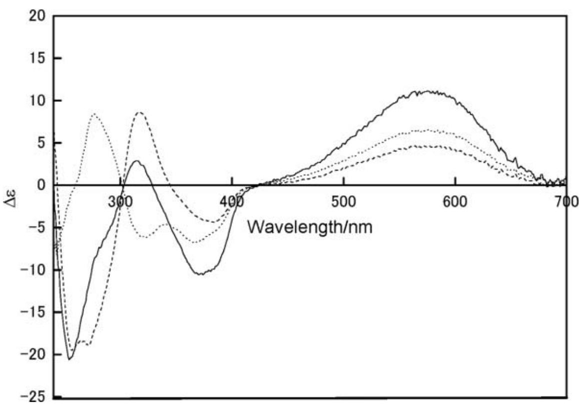

Fig. 9 CD spectra of the isolated closed-ring isomers **2cR**-*RR* (dashed line) and **2cR**-*SS* (dotted line) and the sum of these spectra (solid line).

subsurface layer. Nevertheless, the diastereomeric excess of **2cR**-*SS* was 97%, while no selectivity in the cyclization was observed in solution.

Similar diastereoselective cyclization (82%) in the crystalline state was reported for a diarylethene having one (*S*)-*N*-phenylethylamide group in each molecule.[15] The higher diastereoselectivity of the present system is attributed to the stronger intermolecular interactions through the double intermolecular hydrogen bonds, which lock the chiral helical conformation more efficiently. The distances between the amide hydrogen and the amide oxygen of the neighbouring molecule in the crystal are 2.744(6), 2.822(6), 2.890(5), and 2.966(6) Å, for each of the four hydrogen bonds present, which are all sufficiently short to form hydrogen bonds.

In order to achieve a large surface area for photocyclization, single crystals of **2oR** were ground to powder form. For the powders, conversions of up to 40% were achievable; however, the diastereoselectivity decreased to as low as 30%. This result indicates the importance of the crystal packing on the diastereoselectivity of the cyclization. Once the lattice is broken, molecules gain conformational freedom and selectivity drops considerably.

In conclusion, diarylethene **2oR** crystallizes due to strong intermolecular hydrogen bonds. In the single crystal, diarylethene **2oR** forms a ladder structure consisting of the molecules in two different conformations being oriented perpendicular to each other. Upon UV irradiation, the open-ring isomer with the *M*-form cyclizes to yield only one diastereoisomer of the closed form **2cR**-*SS* in excellent (97%) diastereoselectivity.

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6 1,2-Bis(5′-carboxy-2′-methylthien-3′-yl)perfluorocyclopentene (2.3 g, 5.04 mmol) was suspended in CH_2Cl_2 (30 ml) and cooled in an ice bath. Subsequently *N*-methylmorpholine (1.02 g, 10.1 mmol) was added and the suspension dissolved. Then 2-chloro-4,6-dimethoxytriazine (1.68 g,

10.1 mmol) was added, forming a white precipitate immediately. The reaction mixture was stirred for 2 h at 0 °C, and then another two equivalents of *N*-methylmorpholine (1.02 g, 10.1 mmol) were added followed by (*R*)-phenylethylamine (1.22 g, 10.1 mmol). Stirring was continued for 1 h at 0 °C, followed by stirring overnight at room temperature. To the reaction mixture, CH_2Cl_2 (200 ml) was added and the solution was washed with 1 M HCl (2 × 100 ml), brine (1 × 100 ml), saturated aqueous sodium bicarbonate solution (1 × 100 ml) and H_2O (1 × 100 ml), respectively. The organic phase was dried (Na_2SO_4) and after evaporation of the solvent gave a solid product. Purification was carried out by chromatography on silica gel (hexane–ethyl acetate = 80 : 20) to afford 1.6 g of 1,2-bis(2′-methyl-5′-{[((*R*)-1-phenylethyl)amino]carbonyl}-thien-3′-yl)perfluorocyclopentene **2oR** (48%). Mp 273–274 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.61 (d, J = 7.0 Hz, 6H), 1.91 (s, 6H), 5.27 (dq, J = 7.7, 7.0 Hz, 2H), 6.06 (d, J = 7.7 Hz, 2H), 7.35–7.40 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.06, 21.69, 29.83, 49.66, 56.03, 115.90, 125.27, 126.50, 127.26, 127.86, 128.99, 137.58, 142.68, 146.64, 160.0; MS (EI) m/z = 662 (M^+, 9.7), 557 (8.0), 438 (39.5) and 120 (100%); HRMS calc. for $C_{33}H_{28}N_2F_6O_2S_2$ 662.150, found 662.150. Anal. calc. for $C_{33}H_{28}N_2F_6O_2S_2$: C, 59.81; H, 4.26; N, 4.23; 9.66. Found: C, 59.70; H, 4.27; N, 4.21; S, 9.71%.

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9 *Crystal data* for **2oR**: $C_{33}H_{28}F_6N_2O_2S_2$, monoclinic, space group $P2_1$, a = 12.358(1), b = 14.623(1), c = 19.349(2) Å, β = 106.678(1)°, V = 3349.5(5) Å^3, Z = 4, D_x = 1.314 g cm^{-3}, $F(000)$ = 1368, μ = 2.24 cm^{-1}, λ(MoKα) = 0.71073 Å, T = 170(1) K, 24 172 reflections measured, GoF = 1.035, $wR(F^2)$ = 0.1700 for 11 628 unique reflections and 819 parameters, 1 restraint and $R(F)$ = 0.0667 for 8556 reflections obeying the $F_o \geqslant 4.0\sigma(F_o)$ criterion of absorbability. The absolute structure was determined by Flack's x-refinement [x = 0.07(9)]. The asymmetric unit consists of two molecules of the title compound, which are linked into a two-dimensional framework by N–H · · · O intermolecular bonds. CCDC reference number 291880. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b517370a.

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