π Facial Hydrogen Bonding in the Chiral Resolving Agent (*S*)-2,2,2-Trifluoro-1-(9-anthryl)ethanol and its Racemic Modification

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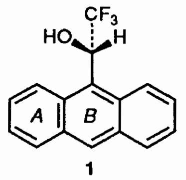
Single crystal X-ray analysis reveals that although molecules of pure (*S*)-and racemic (*R,S*)-2,2,2-trifluoro-1-(9-anthryl)ethanol **1** differ significantly in their intermolecular packing; in each case a strong hydrogen bond is formed between the OH group of one molecule and a specific π-face of one benzo ring of **1** which PM3 derived molecular electrostatic potentials show to arise *via* stereoelectronic assistance from the OH group.

2,2,2-Trifluoro-1-(9-anthryl)ethanol **1** in its pure enantiomeric forms has been extensively used as a chiral solvating agent in NMR spectroscopy and forms the basis of several commercially available chiral stationary phases in HPLC.[1]



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Pirkle[2] has previously discussed three point models[3] of chiral recognition in which **1** might interact with a substrate *via* hydrogen bonds formed to the OH group and possibly the

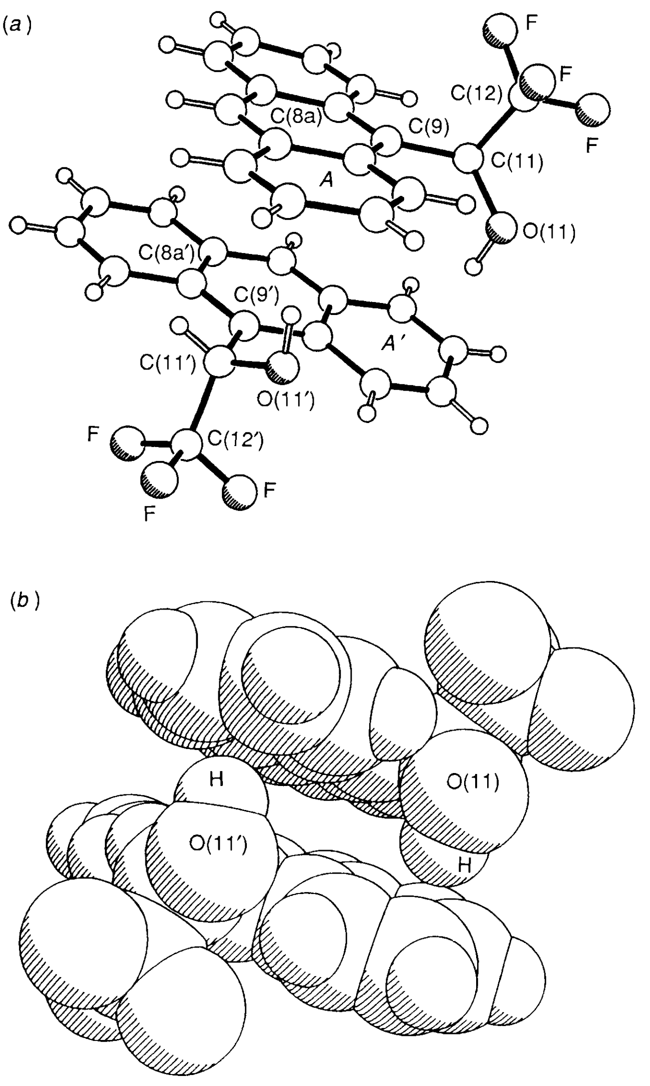


Fig. 1 (*a*) Ball and stick and (*b*) edge-on space-filling representation of the packing of a pair of crystallographically independent molecules of enantiomerically pure (*S*)-**1** showing the directing of the O–H bonds of each molecule into the π-face of the *A* ring of the other. The mean interplanar separation is 3.61 Å and the *A*–*A'* ring centroid-ring-centroid distance is 3.66 Å.

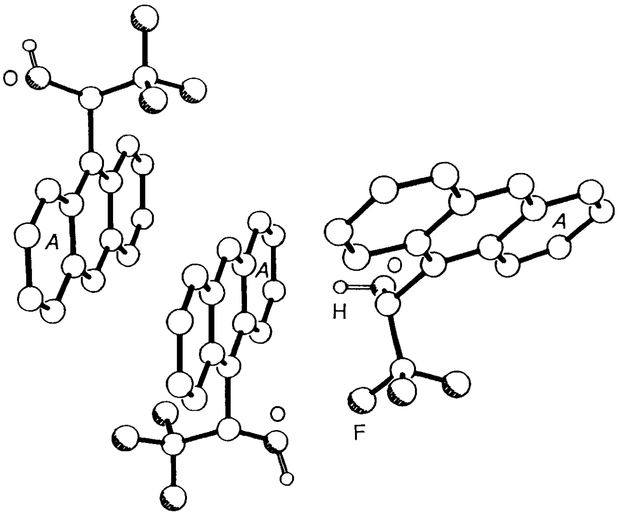
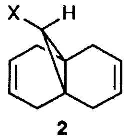


Fig. 2 The principal stacking interactions in racemic (*R*,*S*) crystals of **1**, showing the π–π facial and π-face ··· HO interactions. The mean interplanar separation between the parallel anthracene rings is 3.54 Å.



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methine hydrogen,[4] and by aromatic π-stacking interactions. Recently, however, the crystal structure of racemic **1** was reported[5] as showing an apparent intermolecular O–H ··· F_3C hydrogen bond. We report here crystallographic data for both enantiomerically pure and racemic crystals of **1** which instead reveals an unusual perpendicular close approach of the O–H group to the π face of an adjacent unit of **1** in both crystal forms.

The pure (*S*) enantiomer crystallises† with two crystallographically independent molecules in the asymmetric unit, the pair being related by a non-crystallographic C_2 axis. In each molecule, the C–CF_3 bond is directed almost perpendicular to the anthracene axis with the C(8a)–C(9)–C(11)–C(12) torsion angle being 93°. Rotation about the C(9)–C(11) bond results in significant *peri* interactions, a process for which variable-temperature lineshape analysis[6] on 1-H and 8-H of the approximate ABCD spin system indicates activation parameters of *ca.* $\Delta G^{\ddagger}$ 61, $\Delta H^{\ddagger}$ 68 kJ mol^{-1} and $\Delta S^{\ddagger}$ +23 J mol^{-1} K^{-1}. This barrier, which has previously been shown to be essential for chiral discriminatory ability,[7] clearly differentiates between the OH and CF_3 π-faces of **1**.

The packing of the (*S*) crystal shows that the two anthracene rings are nearly parallel to each other, with the O–H bond of each molecule directed into the *A* ring π face of the other (Fig. 1). The O(11)–H and O(11')–H' bonds subtend angles of 81 and 86° to the plane of the *A'* and *A* rings respectively, the hydrogen atoms lying only *ca.* 2.2 Å from these planes. We believe this constitutes a novel form of OH ··· π-facial hydrogen bonding characterised in the solid state, which coupled with the π–π interactions of the central rings must play a significant role in determining the face-to-face dispositions of these molecules and the properties of **1** as a chiral resolving agent.

The packing of the racemic crystal† reveals two further types of intermolecular interactions.[5] A pair of *R*,*S* molecules stack with their CF_3 faces towards each other and with the rings parallel. Their exposed OH π-faces are approached at an angle by additional molecules so as to form an OH bond perpendicular to ring *A* (one such additional molecule is shown in Fig. 2).‡ This packing must be the stable form since spontaneous resolution into (*R*) and (*S*) crystals does not occur, and indeed the racemate is significantly less soluble in *e.g.* dichloromethane than the pure enantiomers. Unambiguous location of the OH hydrogen atom shows that the previously proposed OH ··· F interaction does not occur.[5]

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† *Crystal data* for (*S*)-**1**: $C_{16}H_{11}F_3O$, M = 276.3, monoclinic, a = 9.764(3), b = 10.603(2), c = 12.529(3) Å, β = 96.35(2)°, V = 1289 $Å^3$, space group $P2_1$, Z = 4 (2 crystallographically independent molecules), D_c = 1.42 g cm^{-3}, μ = 10 cm^{-1}. Data for both structures were measured on a Nicolet R3m diffractometer with Cu-Kα radiation (graphite monochromator) using ω-scans. The (*S*) structure was solved by direct methods and refined anisotropically to give R = 0.048, R_w = 0.047 for 1830 independent observed reflections [$|F_o| > 3\sigma(|F_o|)$, $2\theta \leq 116°$]. For (*R*,*S*)-**1**: $C_{16}H_{11}F_3O$, M = 276.3, orthorhombic, a = 9.267(3), b = 16.258(6), c = 16.608(8) Å, V = 2502 $Å^3$, space group *Pcab*, Z = 8, D_c = 1.47 g cm^{-3}, μ = 10 cm^{-1}. The (*R*,*S*) structure was solved by direct methods and refined anisotropically to give R = 0.044, R_w = 0.057 for 1514 independent observed reflections [$|F_o| > 3\sigma(|F_o|)$, $2\theta \leq 116°$]. The positions of the hydroxy protons in both structures were located from ΔF maps and refined isotropically. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

‡ The OH hydrogen atom lies 2.3 Å from the plane of the adjacent aromatic ring, the OH bond subtending an angle of 87° to the ring plane.

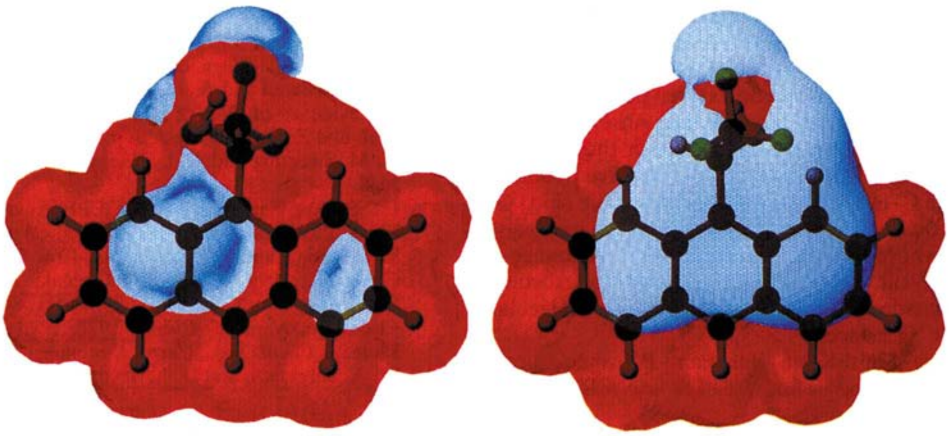

Fig. 3 PM3 molecular electrostatic isopotential at ± 0.03 au and a resolution of 0.4 Å for the two faces of **1**, with blue representing negative and the red positive values of the potential. The OH bond orientation corresponds to that in the racemic (*R*,*S*) crystal.

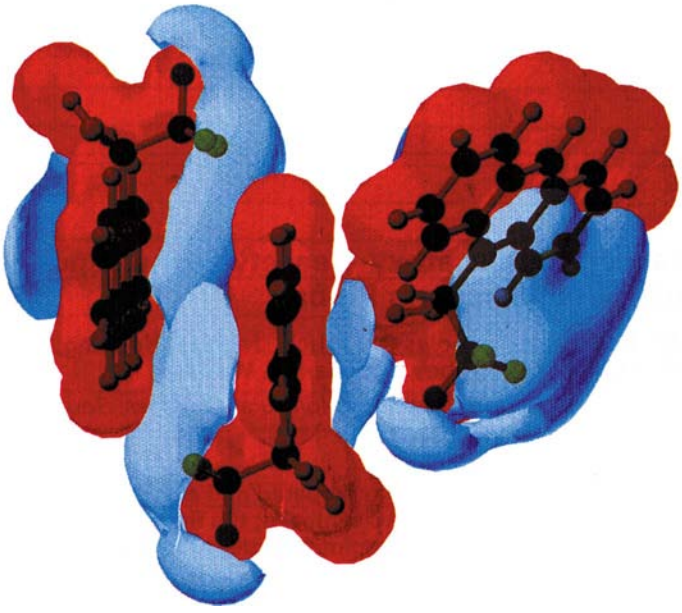

Fig. 4 The stacking of three molecules of **1** in the racemic crystal, showing the overlap of the electrostatic potentials of **1** calculated as an isolated molecule

Two further structural differences between the (*S*) and (*R*,*S*) crystals are noteworthy. In the former form, the perpendicular projected from the O–H bond to the plane of the anthracene is displaced towards the outside of ring *A*, whilst in the latter it is shifted towards the bond common to rings *A* and *B*. Secondly, the dihedral angle between the O–H and the methine C–H bonds in the (*R*,*S*) crystal corresponds to a partially eclipsed orientation (γ = 17°).

To seek explanations for both this behaviour and the π-facial selectivities[8] revealed in the aromatic stacking,[9] we investigated the use of PM3 analytically derived molecular electrostatic potentials (MEP).§ The isopotential surface[10] for isolated **1** with the OH group orientated as found in the racemic crystal reveals a major negative peak on the ring *A*/*B* boundary of the π-face *syn* to the OH group (Fig. 3), corresponding closely to the observed position of the hydrogen bond. The eclipsed orientation of the OH bond orientates the lone pairs on the oxygen in such a manner as to enhance the basicity of one π-face of rings *A*/*B*. This allows the π-face to act as the electron donor to the OH group from an adjacent molecule. To achieve this interaction the acceptor OH group in turn adopts what would otherwise be an unfavourable eclipsed conformation with the adjacent CH bond, hence setting up the next hydrogen bond and allowing the effect to be continued through the crystal lattice. The stereoelectronic nature of the π-facial basicity is revealed by the sensitivity of the calculated electrostatic potentials in rings *A*/*B* to the OH group orientation, and this further implies that mesomeric interaction with substituents in *e.g.* ring *A* may significantly influence the hydrogen bonding occurring in this reagent. With the OH group orientated as found in the (*S*) crystal, a smaller electrostatic discrimination in favour of ring *A* was calculated, the negative centroid being located further away from ring *B* as was indeed revealed in the crystal structure.

An antiperiplanar electron-withdrawing effect of the C–CF_3 bond is manifested through a decreased volume for the

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§ The PM3 derived isopotential surface for molecule **2** (X = Cl) as a model for **1** shows an increase in the volume of the MEP associated with the π-bond *endo* to the chlorine substituent and a decrease in the corresponding *exo* MEP, in apparent agreement with the known selectivity of the *endo* bond in **2** towards electrophilic reagents such as dichlorocarbene or peracid (S. G. G. Russell, PhD Thesis, Victoria University of Wellington, New Zealand, 1990). The substituent X = CF_3 is predicted to display even greater π selectivity, which we attribute to an *anti*-periplanar stabilisation of the *exo* π bond by interaction with the C–X σ* orbital. We do note, however, that the conformations of the two 6-rings in **2** are different, which might result in differential steric effects. We thank Professor B. Halton for bringing this example to our attention.

calculated negative MEP on the π-face *anti* to the CF_3 group,§ particularly prominent on ring *C* which is not perturbed by the oxygen lone-pairs, and an increase in volume on the π-face *syn* to the CF_3 group (Fig. 3). This second stereoelectronic effect enhances the dislocated face-to-face stacking observed in the racemic crystal by increasing overlap between the negative potential associated with the π-face and the positive potential associated with the C–H region of a second molecule (Fig. 4).

We conclude that strong hydrogen bonds to aromatic π-faces can form where suitable stereoelectronic assistance is possible, and that calculated PM3 molecular electrostatic potentials can provide valuable models for intermolecular interactions involving π-faces.[11]

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