

Significant contribution of phenyl centroid...I-C(sp^2) Coulombic donor–acceptor attractions to the buildup of a crystal structure

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The X-ray crystallographic analysis of racemate **5** revealed distinct phenyl centroid...I-C(sp^2) Coulombic donor–acceptor attractions, which are responsible for the inhibition of a certain mode of polymorphic transition inducing Preferential Enrichment.

In 1996, we reported the first instance where an enantiomeric resolution by simple recrystallization of a racemic crystal was feasible and this unusual enantiomeric resolution phenomenon was referred to as Preferential Enrichment (Figure 1).^{1,2} Thus far, more than ten structurally analogous racemic samples have been found to exhibit this phenomenon capable of giving both enantiomers in high ee and in quantity by a simple operation.³ Mechanistically, Preferential Enrichment has been shown to

be a secondary, dynamic enantiomeric resolution phenomenon caused by a solvent-assisted solid-to-solid transformation of a metastable γ -polymorphic form into a thermodynamically stable δ -form (or ϵ -form in a specific case) during crystallization from the supersaturated solution of a certain kind of racemic mixed crystals composed of two enantiomers (Figure 2).^{4–6}

During our investigation on the relationship between the molecular structure and the occurrence of Preferential Enrichment, we have encountered an unexpected result that *p*-iodobenzenesulfonate derivative (\pm)-**5** of a series of sulfonium sulfonates (\pm)-**1**–(\pm)-**4**, which could show Preferential Enrichment,^{1,7–10} has failed to show the same phenomenon. To clarify this cause, the crystal structure of the stable form of (\pm)-**5** was solved by X-ray crystallographic analysis.

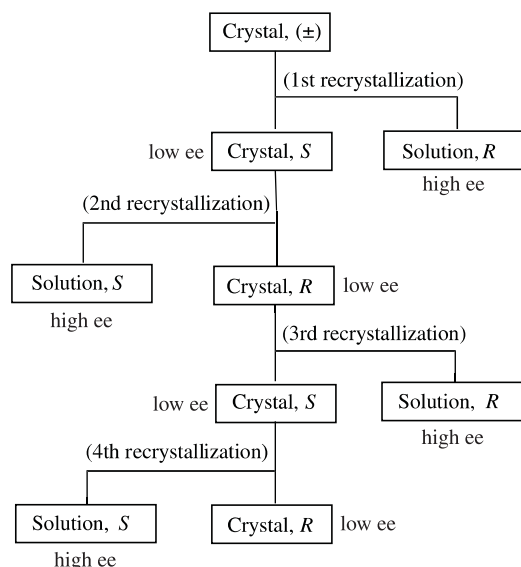
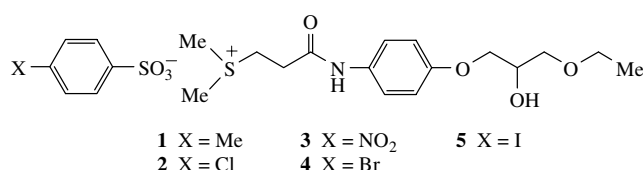


Figure 1 Principle of Preferential Enrichment in the case of an enrichment of the *R* enantiomer in solution after the first recrystallization of the racemic sample. Actually, the probability for either the *R* or *S* enantiomer to be enriched in solution after recrystallization of an exactly racemic sample was 50%.



The single crystal of (\pm)-**5** suitable for X-ray analysis was obtained from an about twofold supersaturated solution in isopropanol followed by slow evaporation of the solvent at 20 °C. The powder X-ray diffraction pattern of (\pm)-**5** crystallised from ethanol was identical to that simulated from the X-ray crystallographic data of the same compound obtained from isopropanol, indicating this crystalline phase to be a stable form.^{4,5} The crystal structure is quite different from a δ -form, which is commonly observed for the compounds showing Preferential Enrichment, but rather similar to a γ -form, which is a metastable key-intermediate polymorph and easily undergoes the subsequent polymorphic transition inducing Preferential En-

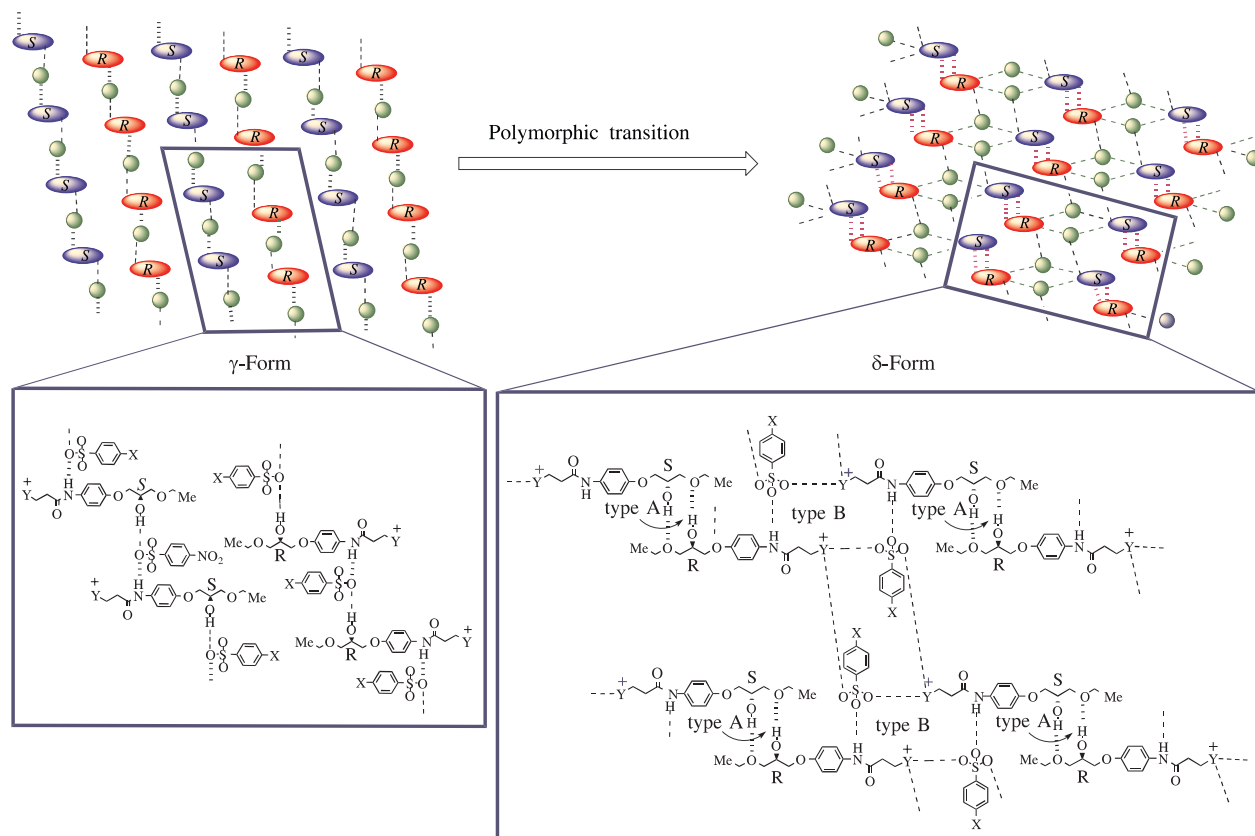


Figure 2. A mode of the polymorphic transition of the metastable γ -form into the stable δ -form inducing Preferential Enrichment. The crystal structure of the γ -form is characterised by the alternating alignment of the homochiral *R* and *S* 1-D chains in an antiparallel direction, while that of the δ -form is characterised by the heterochiral 2-D sheet structure composed of two types of centrosymmetric cyclic dimers (types A and B). The ellipsoids and circles indicate the long-chain cation and the sulfonate ion, respectively.

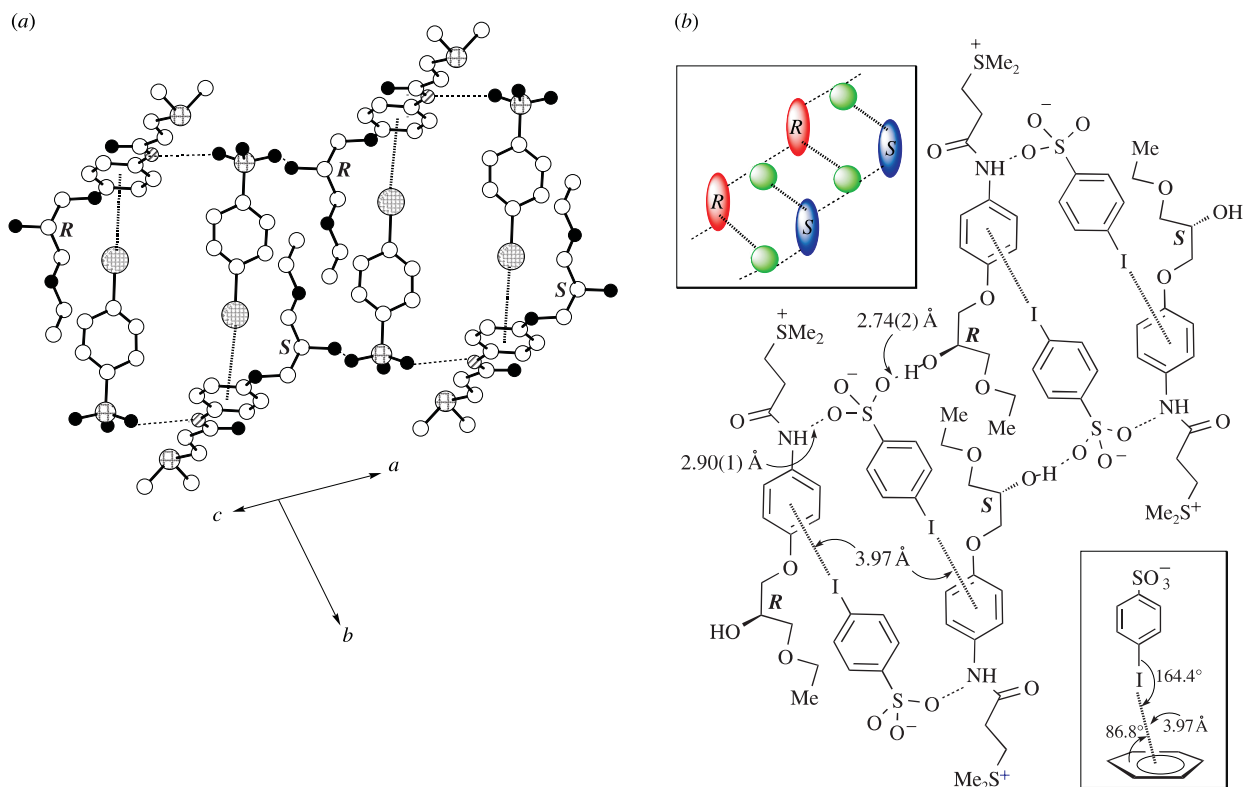


Figure 3 (a) Crystal structure of (\pm) -**5** and (b) its schematic representation. The carbon, nitrogen, oxygen, sulfur and iodine atoms are represented by open, crosshatched, closed, coarse grid and fine grid circles, respectively. All hydrogen atoms are omitted in (a). The ellipsoid and circle in the inset of (b) indicate the long-chain cation and the sulfonate ion, respectively.

richment.^{4,5} We call this new crystal structure a γ_1 -form (Figure 3).[†]

This γ_1 -form crystal is composed of an alternating alignment of homochiral *R* and *S* 1D chains in an antiparallel direction, each of which is formed by two kinds of hydrogen bonds along the *a* axis; one is between an oxygen atom of the sulfonate ion and the hydroxy group [O...O distance of 2.74(2) Å] of the neighbouring long-chain cation, and the other is between another oxygen atom of the same sulfonate ion and the amide NH [O...N distance of 2.90(1) Å] of another neighbouring molecule (Figure 3).

The decisive difference in crystal structure between this γ_1 -form and a metastable γ -form lies in the mode of interchain interactions between analogous homochiral 1D chains; in the crystal structure of the γ_1 -form, the phenyl centroid...I- $C(sp^2)$ Coulombic donor–acceptor interchain interactions between the iodine atom of the *p*-iodobenzenesulfonate ion and the benzene ring of the neighbouring long-chain cation are observed, eventually forming the heterochiral 1D ribbon structure (Figure 3), while there is no appreciable interchain interaction in the γ -form (Figure 2).^{1,2} Although in the γ_1 -form crystal the distance (3.97 Å) between the iodine atom and the centroid of the benzene ring is ~0.1 Å longer than the sum of the van der Waals radii of iodine (2.15 Å) and the sp^2 carbon atom (1.7 Å), the phenyl centroid–I- $C(sp^2)$ angle of 164.4° and an angle of 86.8° between the phenyl centroid–I line and the phenyl plane, both of which are consistent with the phenyl centroid...I- $C(sp^2)$ donor–acceptor interaction, implies its significant contribution to the buildup of the γ_1 -form crystal structure of (\pm)-**5** (Figure 3). In fact, the electrostatic potential calculated using the MNDO/d program in Spartan'02 Windows shows the highly positive cap

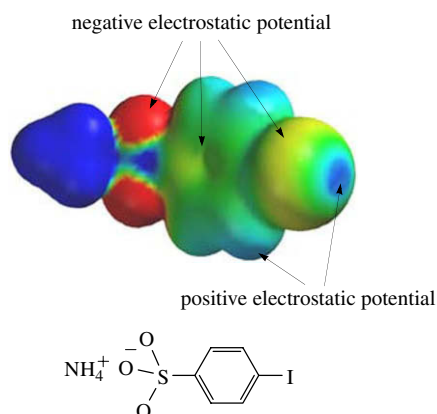


Figure 4 Electrostatic potentials of ammonium *p*-iodobenzenesulfonate calculated using the MNDO/d program in Spartan'02 Windows. The positive cap on the iodine atom is distinctly seen.

[†] Crystallographic data for (\pm)-**5** at 23 °C: $C_{27}H_{30}NO_7S_2I$, triclinic, crystal size 0.40×0.20×0.20 mm, space group *P*1 (#2), $a = 11.55(1)$, $b = 14.89(3)$ and $c = 8.602(8)$ Å, $\alpha = 101.7(1)^\circ$, $\beta = 107.06(8)^\circ$, $\gamma = 69.7(1)^\circ$, $V = 1318(3)$ Å³, $Z = 2$, $d_{\text{calc}} = 1.541$ g cm⁻³, $\mu(\text{MoK}\alpha) = 14.135$ cm⁻¹, $F(000) = 620$. The intensities of 10082 reflections were measured on a Rigaku AFC5S diffractometer at 23 °C [MoK α ($\lambda = 0.71073$ Å) radiation, $\omega/2\theta$ scans, $2.7^\circ < \theta < 27.5^\circ$], and 4740 independent reflections were used for further calculations and refinement. The structure was solved by a direct method and refined using the full-matrix least-squares method against F in the anisotropic–isotropic approximation. The refinement is converged to $R = 0.093$, $R_w = 0.126$ and GOF = 1.002 for all independent reflections is calculated against F for 1938 observed reflections with $I > 3\sigma(I)$. The number of refined parameters is 327. All calculations were performed using the Crystal-Structure crystallographic software package.

Atomic coordinates, bond lengths, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336 033; or deposit@ccdc.cam.ac.uk). Any request to the CCDC for data should quote the full literature citation and CCDC reference number 248611. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2004.

on the iodine atom in ammonium *p*-iodobenzenesulfonate as depicted in Figure 4.¹¹

In conclusion, the reason why Preferential Enrichment does not occur with respect to (\pm)-**5** can be well understood in terms of the weak phenyl centroid...I- $C(sp^2)$ Coulombic donor–acceptor attractions, which were found to play a pivotal role in building up the γ_1 -form crystal structure of (\pm)-**5**. Consequently, the polymorphic transition of the metastable γ -form into the δ -form inducing Preferential Enrichment does not proceed, but instead the γ_1 -form has been produced as a stable crystal. From a different angle, such a donor–acceptor phenyl centroid–iodine interactions may serve as a viable synthon in crystal engineering.[‡]

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[‡] The Cambridge Structural Database (version 5.25) search carried out under the defined conditions, where (i) the phenyl centroid...I distance is less than 4.0 Å, (ii) the phenyl centroid–I- $C(sp^2)$ angle is between 160° and 180°, and (iii) the angle between the phenyl centroid–I line and the phenyl plane is $90^\circ \pm 10^\circ$, indicates that the similar phenyl centroid...I- $C(sp^2)$ interactions are observed for 24 crystal structures; these CSD Refcodes are as follows: ACIGAU, ADUDAE, BANWIX, BOLWAA, CABMAT, COWTEN, DOQYUD, GAPWUP, HEYZUG, JADBIZ, JAJZID, JINCAK, KOGBEN, LAPIYK, LUNDIH, MACMEJ, PIPQUA, QADQIW, QOMYOG, TYRREA10, WIKPAH, ZIKYOH, AQUMUU and ATEQIZ.