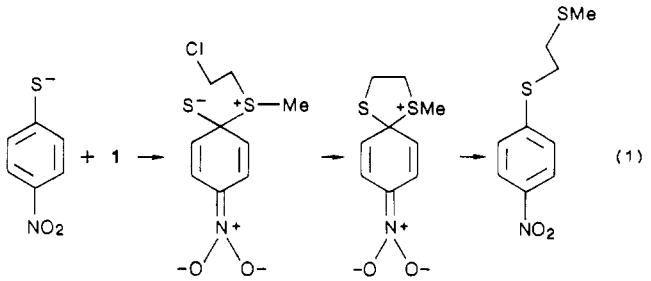
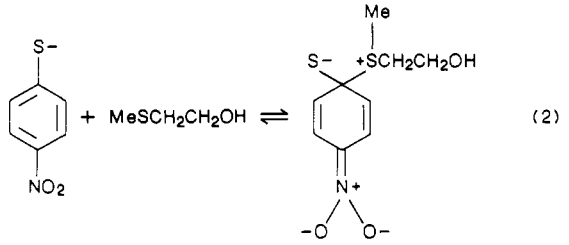
the anomalous reaction only occurs when strong electron-withdrawing groups are substituted on the aryl nucleus, involvement of the aryl ring is suggested. Recent studies have reminded us of the high nucleophilicity of the sulfur atom in 1.[3-5] Thus a *possible* mechanism for the anomalous nucleophiles involves attack by the sulfur of 1 on the electrophilic thiophenoxide aromatic ring by an S_NAr mechanism,[6] eq 1. Provided that the first step of



(1)

the mechanism is rate-determining, this mechanism predicts the observed reactivity trend of faster rates as the thiophenoxide anions are substituted with stronger electron-withdrawing groups. A rapid second step is anticipated since it involves a favorable ring closure to a five-membered ring.[7] The rate of the third step is more difficult to estimate. We attempted to find evidence for the mechanism by substituting $MeSCH_2CH_2OH$ for the chloride 1 in the reaction with *p*-nitrothiophenoxide in DMSO, but we observed no UV evidence for complex **2**, eq 2. This



(2)

may be because it is reversibly formed in a fast reaction, which, of course, would be consistent with a fast third step in eq 1.[8]

Alternatively, we have considered rate-limiting formation of the dimer of 1,[3,4] i.e., $MeSCH_2CH_2S^+(Me)$-$CH_2CH_2Cl^-$, which could subsequently react with the thiophenoxide ions by displacement of 1 and give the observed S_N2 product. However, in the absence of thiophenoxide ion, 1 (at a concentration of 0.4 M) is stable at 25 °C in DMSO-d_6 for at least 12 h as determined by NMR.

A third mechanistic possibility is a shift to a single electron transfer (SET) process involving the sulfonium ion formed by the k_Δ mechanism.[9-12] Bordwell and Harrelson have shown[13] that primary alkyl chlorides have reduction potentials which are too low for SET reaction with ArS^-, but the intermediate sulfonium ion could well have a sufficiently positive reduction potential. Two problems are apparent with this proposed mechanism. First, one would expect the oxidation potentials of the thiophenoxides to be roughly proportional to Hammett σ values of the ring substituents, so that the *p*-nitro and pentachloro derivatives would probably have less negative oxidation potentials than the trichloro derivative and should thus react more slowly by the SET mechanism. Secondly, this mechanism would appear to require rate-limiting formation of the sulfonium ion, a fact we ruled out above.

Future work will concentrate on elucidating this previously unobserved mechanism for reaction of nucleophiles with 2-(alkylthio)ethyl derivatives.

Acknowledgment. Financial support from the U.S. Army Research Office (DAAL03-86-K-0026) and helpful discussions with Drs. F. G. Bordwell and J. M. Dust are gratefully acknowledged.

(3) Yang, Y.-C.; Szafraniec, L. L.; Beaudry, W. T.; Ward, J. R. *J. Org. Chem.* **1987**, *52*, 1637.
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(5) Toward methyl iodide in methanol, diethyl sulfide has a *n* value about 4 units less than thiophenoxide (cf. Pearson, R. G.; Sobel, H.; Songstad, J. *J. Am. Chem. Soc.* **1968**, *90*, 319). In DMSO, pentachlorothiophenoxide is about 3 orders of magnitude less nucleophilic than thiophenoxide (cf. Table I). Thus, we can estimate that 1 is only slightly less nucleophilic than the highly deactivated thiophenoxide ions.
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(7) Capon, B.; McManus, S. P. *Neighboring Group Participation*; New York: Plenum Press, 1976, Chapters 2 and 5.
(8) We are not aware of an example of an attack of a neutral nucleophile on a aromatic anion to form a Meisenheimer complex (e.g. see, Terrier, F. *Chem. Rev.* **1982**, *82*, 77). However, there is evidence for Meisenheimer complex formation by attack of a dianionic nucleophile on a trianionic aromatic substrate, cf. Crampton, M. R. *J. Chem. Soc., Perkin Trans 2* **1978**, 343. The referees have suggested that the pentachloro derivative ought to show steric retardation to ring attack. Also, the slight excess of thiol used in these reactions may provide a pathway for attack by 1 on the neutral thiol in addition to attack on thiophenoxide anion.
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Dual Hydrogen Bond Association of (*R*,*R*)-*N*,*N*'-Diisopropyltartramide with (*S*,*S*)-9,10-Dimethyl-9,10-dihydrophenanthrene-9,10-diol

Summary: (*S*,*S*)-9,10-Dimethyl-9,10-dihydrophenanthrene-9,10-diol (**2**) associates more strongly with (*R*,*R*)-*N*,*N*'-diisopropyltartramide (**1**) than its enantiomer through dual hydrogen bonds in nonaqueous media. The X-ray crystal structure of the 1:1 complex of (*S*,*S*)-**2** and (*R*,*R*)-**1** identified the interaction of these species as two sets of hydrogen bonds between the gauche hydroxyls of (*S*,*S*)-**2** and two amide carbonyls of (*R*,*R*)-**1**.

Sir: The enantiomers of 1,2-diols undergo enantioselective association with (*R*,*R*)-*N*,*N*'-diisopropyltartramide (**1**) through hydrogen bonds in nonaqueous media. In our previous resolution of a series of enantiomers of 1-phenyl-2-alkyl-1,2-ethanediols using (*R*,*R*)-**1** as the chiral mobile-phase additive in silica gel chromatography, dual hydrogen bonds of (*R*,*R*)-**1** and gauche hydroxyls of diol enantiomers were proposed as the mode of association responsible for the observed enantioselection although the bonding sites in (*R*,*R*)-**1** remained obscure.[1] In the present study, the dual hydrogen bond association of (*R*,*R*)-**1** with a 1,2-diol is clearly demonstrated by an X-ray crystal analysis of the complex of (*R*,*R*)-**1** with (*S*,*S*)-9,10-dimethyl-9,10-dihydrophenanthrene-9,10-diol (**2**)[2] and the

(1) Dobashi, Y.; Hara, S. *J. Am. Chem. Soc.* **1985**, *107*, 3406.

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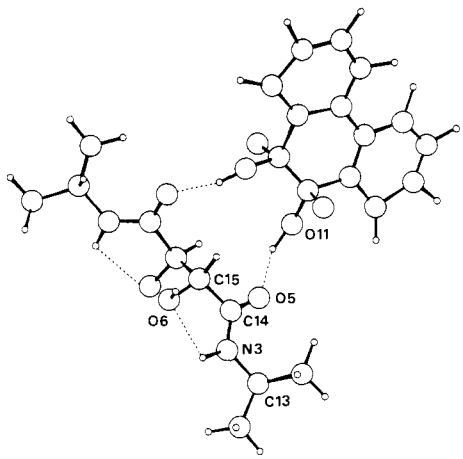
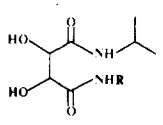
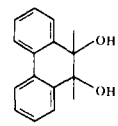


Figure 1. X-ray crystal structure of the associate of (*R,R*)-**1** with (*S,S*)-**2**. The hydrogen bonds are shown as dashed lines. The methyl protons of (*S,S*)-**2** have been omitted. Selected structural parameters: O(5)–O(11) = 2.56 (1) Å, O(6)–HN(3) = 2.15 (6) Å, O(6)–O(6′) = 2.768 (5) Å, ∠C(14)–C(15)–C(15′)–O(6′) = +67.5 (4)°, ∠O(6)–C(15)–C(15′)–O(6′) = −54.0 (4)°, ∠O(6)–C(15)–C(14)–N(3) = −8.2 (5)°, ∠O(6)–C(15)–C(14)–O(5) = +175.5 (6)°, ∠C(13)–N(3)–C(14)–O(5) = +0.7 (7)°. Primes denote symmetry related atoms.

observed association is considered to be the probable cause for enantioselectivity in solution.



1, R = i-Pr



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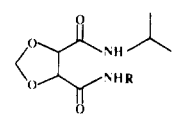
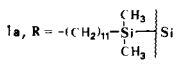
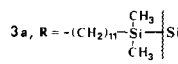


3, R = i-Pr



1a, R = -(CH$_2$)$_{11}$-Si(CH$_3$)$_2$-Si



3a, R = -(CH$_2$)$_{11}$-Si(CH$_3$)$_2$-Si

(*S,S*)-**2** exhibits greater retentivity on a chiral stationary phase (CSP) **1a**[3] and thus forms a more stable hydrogen bond associate with the (*R,R*)-**1** analogue on CSP **1a** than its enantiomer. The downfield shift for the resonance of two hydroxyl protons of (*S,S*)-**2** in the ^{1}H NMR spectra is greater than that for the corresponding resonance of the *R,R* isomer following the addition of (*R,R*)-**1** to a $CDCl_3$ solution of racemic **2**.[4] It thus follows that hydrogen bonding of the two hydroxyls of (*S,S*)-**2** with (*R,R*)-**1** is stronger.

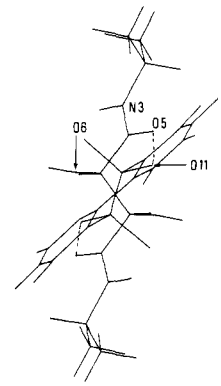


Figure 2. X-ray crystal structure of the associate of (*R,R*)-**1** with (*S,S*)-**2** as viewed along the C_2 axis from the (*R,R*)-**1** side. The methyl protons of (*S,S*)-**2** have been omitted for clarity. The intermolecular hydrogen bonds are shown as dashed lines.

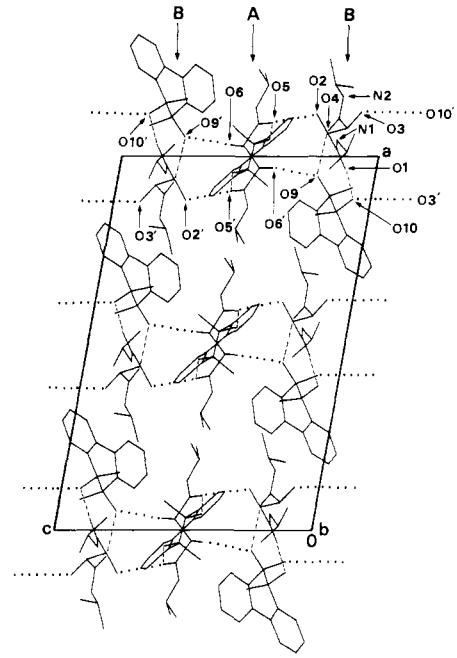


Figure 3. Packing of the complex of (*R,R*)-**1** with (*S,S*)-**2** in the crystal lattice as viewed along the C_2 axis. The hydrogen bond network is shown as dotted lines, and dual hydrogen bonds in complexes A and B are shown as dashed lines. Selected structural parameters: O(5)–O(2) = 2.799 (6) Å, O(6)–O(9′) = 2.685 (5) Å, O(3)–O(10′) = 2.687 (6) Å. Primes denote symmetry related atoms. The unit cell contains 6 molecules of the complex; four complex molecules are at general 4-fold sites and each of the remaining two (*R,R*)-**1** and two (*S,S*)-**2** molecules has a 2-fold rotation axis coinciding with the crystallographic diad. Thus, the asymmetric unit contains one and a half complex molecules. Half molecules of (*R,R*)-**1** and (*S,S*)-**2** are related to the other half by a diad axis lying at (0, *y*, $^1/_2$). Complex A is also shown in Figures 1 and 2. For details of complex B, see ref 6.

Crystals of a 1:1 complex of (*S,S*)-**2** and (*R,R*)-**1** were grown by the slow evaporation of a 1:1 mixture of these species in $CHCl_3$. The X-ray crystal structure[5] of this complex shows two sets of hydrogen bonds between gauche hydroxyls of (*S,S*)-**2** and two amide carbonyls of (*R,R*)-**1**. A perspective view of this associated species is shown in Figure 1. The associate possesses a C_2 axis identical with that of each component. In this bimolecular associate, the (*S,S*)-**2** molecule is not eclipsed by the (*R,R*)-**1** molecule but rotates about the C_2 axis so as to minimize steric interactions between these molecules, as shown in Figure 2. Each hydroxyl proton of (*R,R*)-**1** in the associate participates in hydrogen bonding with the other (*S,S*)-**2** molecule so that a network in the crystal packing is constructed (O(9)···HO(6′) and O(9′)···HO(6)) as illustrated in Figure

(2) Each enantiomer of **2**, whose absolute configuration had not yet been established, was obtained by preparative scale resolution on CSP **1a**[3] using 50% (v/v) $CHCl_3$ in *n*-hexane as the mobile-phase solvent. The most retained enantiomer showed a specific rotation of −234.5° (*c* 0.54, MeOH). The *S,S* configuration of (−)-**2** was established from relative stereochemistry in the X-ray crystal structure of a (−)-**2**:(*R,R*)-**1** complex.

(3) Dobashi, Y.; Hara, S. *J. Org. Chem.* **1987**, *52*, 2490. In this literature, 9,10-dihydroxy-9,10-dimethylphenanthrene should read 9,10-dimethyl-9,10-dihydrophenanthrene-9,10-diol. The capacity factor for the most retained enantiomer and the separation factor were 3.31 and 1.47, respectively when 50% (v/v) $CHCl_3$ in *n*-hexane was used as the mobile-phase solvent at 20 °C.

(4) The resonance for the two hydroxyl protons appearing at 2.25 ppm as a singlet in 0.12 M $CDCl_3$ solution of racemic **2** at 25 °C shifted downfield and split into two singlets with essentially the same intensity at 2.87 ppm and 3.03 ppm when the solution was 0.18 M (*R,R*)-**1**. The downfield singlet is assigned to the resonance of (*S,S*)-**2** based on the correlation of the relative intensity of the signals with the enantiomeric composition of **2**.

(5) Crystal data for (*S,S*)-**2**:(*R,R*)-**1** complex ($C_{10}H_{20}N_2O_4 \cdot C_{16}H_{16}O_2$, M_r 472.6): crystal system monoclinic; space group C_2; lattice constants, a = 21.832 (11), b = 12.268 (7), and c = 15.032 (8) Å, β = 100.54 (5)°, V = 3958 Å^3, Z (number of molecules of complex per cell) = 6, D_{calc} = 1.190 g cm^{-3}; μ for Cu Kα radiation = 6.5 cm^{-1}. A total of 4007 reflections was observed out of 4343 within the 2θ range of 6° through 156°. The structure was determined by direct methods and refined by the block-diagonal least-squares method to an *R* value of 0.082; 51 out of 54 hydrogen atoms were located on the difference electron density map and refined including their isotropic temperature factors. Some atoms of (*S,S*)-**2** showed extraordinarily large anisotropic thermal vibrations.

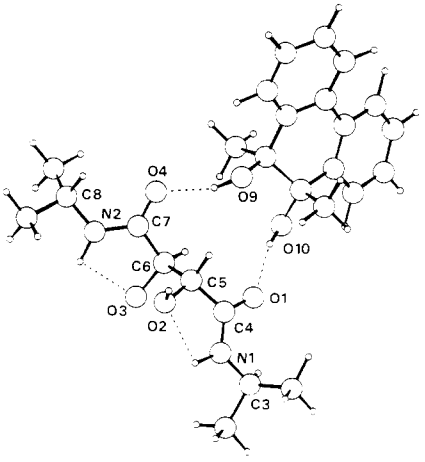
3.[6] Two amide carbonyls, as bonding sites for dual hydrogen bonds with (*S,S*)-**2**, also contribute to the formation of this network through hydrogen bonding with hydroxyls of other (*R,R*)-**1** molecules (O(5)···HO(2) and O(5′)···HO(2′)).

In solution, (*R,R*)-**1** may adjust its conformation to allow for dual hydrogen bonding with 1,2-diol enantiomers, resulting in enantioselective association. Such adjustment may possibly come about through a combination of intramolecular hydrogen bonds in (*R,R*)-**1**. The X-ray study indicates the following features of the conformation of (*R,R*)-**1** induced by dual hydrogen bond association with (*S,S*)-**2** in the solid state: (1) The relationship between the two hydroxyls and between two amide units are gauche (∠O(6)–C(15)–C(15′)–O(6′) = −54.0°) and anti (∠C(14)–C(15)–C(15′)–C(14′) = +189.0°), respectively. (2) The intramolecular hydrogen bond of an amide proton with a hydroxyl oxygen adjacent to the amide unit (O(6)–HN(3) = 2.15 Å) forms a planar five-membered ring (∠O(6)–C(15)–C(14)N(3) = −8.2°). (3) The relative orientation of two planar rings thus formed displays a propeller-like twist, and the rotation sense of one ring to the other is counterclockwise, thus reflecting the absolute stereochemistry of the two hydroxyl-bearing carbons.[7] In this conformation, (*R,R*)-**1** provides two amide carbonyls as sites for dual hydrogen bond association with (*S,S*)-**2**, whose gauche hydroxyls display clockwise rotation.[7] These association sites are probably mismatched with those of the *R,R* isomer. It should be noted that the gauche relationship between the two hydroxyls of (*R,R*)-**1** could also be caused by intramolecular hydrogen bonding of these groups although such bonding interaction has not been observed in the crystal. That is, the conformational adjustment of (*R,R*)-**1** observed in the crystal may also arise from three simultaneous intramolecular hydrogen bonds, i.e., one set of hydroxyls (O(6)···HO(6′) or O(6′)···HO(6)) and two sets of amide protons and hydroxyl oxygens (O(6)···HN(3) and O(6′)···HN(3′)). As a result, the conformational structure of the associate in the crystal is expected to be reproduced in solution as well. In solution, the three intramolecular hydrogen bonds should stabilize not only (*R,R*)-**1** itself but also the associate. The anti relationship between two bulky amide units is also favorable. In addition, steric interactions between each component of the associate are minimal as discussed above. It is thus reasonable to consider that the dual hydrogen bond association observed in the crystal is responsible for the enantioselection of **2** by (*R,R*)-**1** in solution.

The methylenated derivative (**3**)[8] was designed and synthesized in order to confirm that the association mode in the crystal elicits enantioselectivity in solution. (*R,R*)-**3** was considered to be an analogue of the conformer of (*R,R*)-**1**, in which there would be intramolecular hydrogen bonding between two hydroxyls. Due to the planarity of the 1,3-dioxolane ring, the dihedral angle of two C–O bonds at asymmetric carbons is less than that of two hydroxyls in the gauche relationship. However, (*R,R*)-**3** can provide two amide carbonyls as suitable sites for dual hydrogen bonding with (*S,S*)-**2** since the sense of rotation between two five-membered rings formed by two sets of intramolecular hydrogen bonds between amide protons and oxolane oxygens remains counterclockwise.[7] Thus (*R,R*)-**3** should associate enantioselectively with (*S,S*)-**2** through dual hydrogen bonding between two amide carbonyls and two hydroxyls to give rise to the same sense of chiral recognition observed for the system of **2** and (*R,R*)-**1**. As expected, the resonance for the two hydroxyls of (*S,S*)-**2** appears downfield relative to that of its enantiomer in the ^{1}H NMR spectrum of a $CDCl_3$ solution of racemic **2** containing (*R,R*)-**3**, indicating stronger hydrogen bonding of two hydroxyls of (*S,S*)-**2** with (*R,R*)-**3**.[9] The formation of a more stable associate between (*R,R*)-**3** and (*S,S*)-**2** is warranted by the fact that the most retained enantiomer of **2** on CSP **3a** derived from the (*R,R*)-**3** analogue has the *S,S* configuration.[10]

Supplementary Material Available: Crystallographic details for the complex of (*R,R*)-**1** with (*S,S*)-**2** including atom-numbering scheme, atomic coordinates, thermal parameters, bond lengths, and bond angles (29 pages). Ordering information is given on any current masthead page.

(6) There are two independent complexes (A and B) per asymmetric unit as shown in Figures 3. In this paper, our discussion is focused on complex A since this complex has a C_2 axis identical to that of each component. A perspective view of complex B is shown below.



Selected structural parameters are as follows: O(1)–O(10) = 2.629 (6) Å, O(4)–O(9) = 2.669 (5) Å, O(2)–HN(1) = 2.22 (9) Å, O(3)–HN(2) = 2.23 (6) Å, O(2)–O(3) = 2.750 (6) Å, ∠O(3)–C(6)–C(5)–C(4) = +69.5 (4)°, ∠O(2)–C(5)–C(6)–C(7) = +70.9 (4)°, ∠O(3)–C(6)–C(5)–O(2) = −53.1 (4)°, ∠O(2)–C(5)–C(4)–N(1) = +8.3 (6)°, ∠O(3)–C(6)–C(7)–N(2) = +9.8 (6)°, ∠O(4)–C(7)–C(6)–O(3) = −171.5 (6)°, ∠O(2)–C(5)–C(4)–O(1) = −172.7 (1)°, ∠C(3)–N(1)–C(4)–O(1) = −2.0 (7)°, ∠C(8)–N(2)–C(7)–O(4) = +2.8 (7)°. As can be seen from these parameters and the above figure, (*R,R*)-**1** and (*S,S*)-**2** in complex B also form dual hydrogen bonds between two amide carbonyls and two hydroxyls although the conformation of complex B is slightly different from that of complex A. Even if the structure of complex B is used to discuss the enantioselectivity of (*R,R*)-**1**, our conclusion is unchanged.

(7) The sense of rotation was determined from the following criteria: For (*R,R*)-**1** and **3**, the sense of rotation is that of the far ring with respect to the one that is near when viewed along the long axis of the molecule; For (*S,S*)-**2**, the sense of rotation is that of the far C–O bond with respect to the one that is near when viewed along the C–C bond between two carbons each bearing a hydroxyl.

(8) This derivative was prepared according to the method reported by Kim and Szarek. Kim, K. S.; Szarek, W. A. *Synthesis* **1978**, 48.

(9) The resonances of two hydroxyls of (*R,R*)- and (*S,S*)-**2** in a $CDCl_3$ solution 0.15 M in racemic **2** and 0.11 M in (*R,R*)-**3** at 25 °C appeared at 2.706 and 2.750 ppm as singlets, respectively.

(10) The capacity factor for the most retained enantiomer and the separation factor were 5.91 and 1.06, respectively, on using 25% (v/v) $CHCl_3$ in *n*-hexane as the mobile-phase solvent at 20 °C. The details will be published elsewhere.

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