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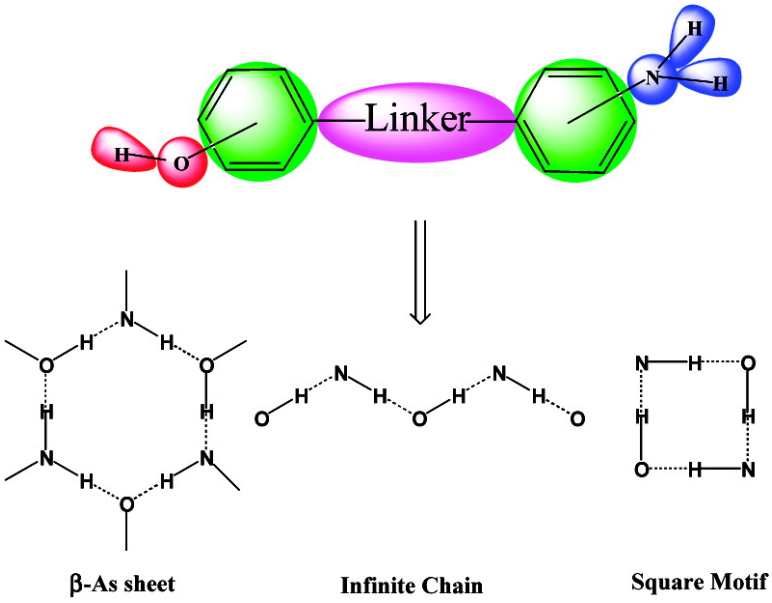

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Correspondence between Molecular Functionality and Crystal Structures. Supramolecular Chemistry of a Family of Homologated Aminophenols

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Abstract: The crystal structures and packing features of a family of 13 aminophenols, or supraminols, are analyzed and correlated. These compounds are divided into three groups: (a) compounds **1**−**5** with methylene spacers of the general type HO−C_6H_4−$(CH_2)_n$−C_6H_4−NH_2 (n = 1 to 5) and both OH and NH_2 in a *para* position; (b) compounds **1a**, **2a**, **2b**, **2c**, and **3a** in which one or more of the methylene linkers in **1** to **3** are exchanged with an S-atom; and (c) compounds **2d**, **1b**, and **6a** prepared with considerations of crystal engineering and where the crystal structures may be anticipated on the basis of structures **1**−**5**, **1a**, **2a**, **2b**, **2c**, and **3a**. These 13 aminols can be described in terms of three major supramolecular synthons based on hydrogen bonding between OH and NH_2 groups: the tetrameric loop or square motif, the infinite N(H)O chain, and the β-As sheet. These three synthons are not completely independent of each other but interrelate, with the structures tending toward the more stable β-As sheet in some cases. Compounds **1**−**5** show an alternation in melting points, and compounds with n = even exhibit systematically higher melting points compared to those with n = odd. The alternating melting points are reflected in, and explained by, the alternation in the crystal structures. The n = odd structures tend toward the β-As sheet as n increases and can be considered as a *variable series* whereas for n = even, the β-As sheet is invariably formed constituting a *fixed series*. Substitution of a methylene group by an isosteric S-atom may causes a change in the crystal structure. These observations are rationalized in terms of geometrical and chemical effects of the functional groups. This study shows that even for compounds with complex crystal structures the packing may be reasonably anticipated provided a sufficient number of examples are available.

Introduction

A major challenge in the crystal engineering of molecular solids[1] is the absence of a direct correspondence between molecular functionality and crystal structure. This arises from the complementary nature of molecular recognition so that the supramolecular behavior of a functional group in a molecule depends also on the position and location of the *other* functionalities, with the added caveat that *all* portions of a molecule including the hydrocarbon residues have supramolecular functionality. Crystal structures arise therefore from a complex convolution of recognition events.[2] In an attempt to simplify this complexity, the structural chemist identifies small structural units, known as *supramolecular synthons*,[3] that are associated with certain combinations of molecular functionality and that are reproduced from structure to structure within a family of molecules. When such synthons are identified, crystal design can become more straightforward. Supramolecular synthons are more representative of crystal packing features than individual interactions, and it is often more appropriate to describe struc-

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(1) Selected references on crystal engineering of organic molecular solids include the following. (a) Desiraju, G. R. *Crystal Engineering. The Design of Organic Solids*; Elsevier: Amsterdam, 1989. (b) *The Crystal as a Supramolecular Entity*. Perspectives in Supramolecular Chemistry, Vol. 2; Desiraju, G. R., Ed.; Wiley: Chichester, 1996. (c) *Comprehensive Supramolecular Chemistry*; Atwood, J. L., Davies, J. E. D., MacNicol, D. D., Vögtle, F., Eds.; Pergamon: Oxford, 1996; Vols. 6, 7, 9, 10. (d). *Design of Organic Solids*; Weber, E., Ed.; Topics in Current Chemistry; Springer: Berlin, 1998; Vol. 198. (e) *Crystal Engineering: From Molecules and Crystals To Materials*; Braga, D., Orpen, A. G., Eds.; NATO ASI Series Kluwer: Dordecht, The Netherlands, 1999. (f) *Crystal Engineering: The Design and Application of Functional Solids*; Seddon, K. R., Zaworotko, M. J., Eds.; NATO ASI Series Kluwer: Dordecht, The Netherlands, 1999. (g) Steed, J. W.; Atwood, J. L. *Supramolecular Chemistry*; Wiley: Chichester, 2000; Vol. 11, pp 389−463. (h) Desiraju, G. R. *Curr. Sci.* **2001**, *81*, 1038. (i) Sharma, C. V. K. *Cryst. Growth Des.* **2002**, *2*, 465. (j) *Crystal Design. Structure and Function*; Perspectives in Supramolecular Chemistry, Vol. 7; Desiraju, G. R., Ed.; Wiley: Chichester, 2003.

(2) That observed crystal structures cannot be predicted so easily is revealed in the difficulties encountered in crystal structure prediction. See: (a) Gavezzotti, A. *Acc. Chem. Res.* **1994**, *27*, 309. (b) Beyer, T.; Lewis, T.; Price, S. L. *CrystEngComm* **2001**, *3*, 178. (c) Desiraju, G. R. *Nature Materials* **2002**, *1*, 77. (d) Dunitz, J. D. *Chem. Commun.* **2003**, 545.

(3) (a) Desiraju, G. R. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2311. (b) Nangia, A.; Desiraju, G. R. *Top. Curr. Chem.* **1998**, *198*, 57.

10.1021/ja037227p CCC: $25.00

tural hierarchies[4] in terms of synthons rather than interactions or functional groups.

The family of aminophenols or supraminols, molecules that contain equal stoichiometries of hydroxyl and amino groups, offers sufficient structural consistency with enough supramolecular diversity to explore properly the interactions between molecular functionality in crystal packing. Ermer and co-workers[5] and Hanessian and co-workers[6] elaborated elegant principles of recognition for such molecules. According to these researchers, an −OH group with one hydrogen bond donor and two acceptors and an $-NH_2$ group with two hydrogen bond donors and one acceptor constitute a mutually compatible set of molecular functionality—one that permits the formation of one O−H···N and two N−H···O hydrogen bonds resulting in a complete saturation of the hydrogen bonding potential of both functional groups. In molecules such as 4-aminophenol (4AP), these hydrogen bonds form a N(H)O sheet structure in which the hydrogen bonds are arranged in a hexagonal manner, like the chair form of cyclohexane (Figure 1). We use the notation N(H)O in this paper to simultaneously refer to O−H···N and N−H···O hydrogen bonds. This arrangement is topologically equivalent to the sheet structure of β-arsenic and will be referred to as such in this paper. The β-As sheet and its variants have been noted in a number of N(H)O structures of supraminols.[7] Independently, Howard, Desiraju, and co-workers[8] recognized that factors other than N(H)O saturation need to be considered even for some simple aminols. In 2- and 3-aminophenol (2AP, 3AP), for example, the potential for the formation of strong O−H···N and N−H···O bonds is not completely fulfilled. Instead, there is the formation of a weak N−H···π hydrogen bridge[9] (Figure 2). These authors rationalized this behavior as being driven by the need to form herringbone interactions between phenyl residues. The change from the 4AP structure to the 2AP and 3AP structures is therefore a change from a more hierarchical arrangement to one where there is more *structural interference*[10] between molecular functionality. In effect, even with just three functional groups, hydroxy, amino, and phenyl, there are two quite distinct structural possibilities.

The present paper explores these ideas further and provides an analysis of the crystal structures of 13 supraminols (Scheme 1) that contain *four* molecular functionalities. These are respectively, the hydroxy group (phenolic), the amino group (anilino), phenyl rings, and a linker group, typically a polymethylene chain, which links phenyl rings. We attempt to find the correspondence between molecular structure and crystal structure for these compounds. We show that, in many cases, the observed crystal structures result from a fine balance between several factors leading to both hierarchic packing and to structures wherein interaction interference is more pronounced.

Experimental Section

General Methods. Melting points of compounds **1**−**5** were measured on a Perkin-Elmer Model DSC-4 melting point apparatus. All other melting points were recorded on a Fisher-Johns melting point apparatus and are uncorrected. All reactions were carried out using standard techniques and general literature procedures. The synthesis of the aminophenols in this study are given, whenever there is a significant variation from the literature procedures. Details of the synthetic procedures for compounds **1**−**5**, **1a**, **2a**, **2b**, **2c**, **3a**, **2d**, **1b**, and **6a** are given in the Supporting Information.

X-ray and Neutron Data Collections and Crystal Structure Determinations. Diffraction quality single crystals of all compounds were obtained by slow evaporation from various solvents. The X-ray data were collected on a Bruker SMART-1000 diffractometer (**1**−**5**, **2b**, **2c**, **3a**, **1b**) or the Bruker SMART-6000 diffractometer (**1a**, **2d**, and **6a**) using Mo Kα radiation. X-ray data for **2a** were collected on a Rigaku AFC6S diffractometer using Cu Kα radiation. The structure solution and refinements were carried out using SHELXTL programs.[11a] The neutron structure determination of **1** was carried out at the ISIS pulsed neutron source on the Laue time-of-flight diffractometer, SXD,[11b,c] using the multicrystal method:[11d] a sample of 4 crystals was mounted in the SXD ω−CCR and data collected at 12 K in a series of 10 frames with 25°ω steps. Intensities from all four crystals were extracted, resulting in 2403 unique, merged reflections. All interatomic distance and related calculations were carried out with PLATON2002.[12] For further details see Table 1 and the Supporting Information.

Results and Discussion

A. Methylene Spacer Structures. Ermer and Eling noted[5] that 4-(4-aminophenyl)phenol (4APP) forms a structure that is directly analogous to 4AP, consisting of parallel β-As sheets linked by a biphenyl spacer group—the phenyl group in 4AP is in effect replaced by the biphenyl group in 4APP (Figures 1b and 1c). Both molecules are in the same space group ($Pna2_1$) with similar dimensions for the *a* (∼8.1 Å) and *b* (∼5.3 Å) axes, and this is the plane of β-As sheets. The change in spacer is reflected in the length of the *c* axis, which at 12.95 Å for 4AP, and 21.22Å for 4APP, is approximately equal to the molecular length.

By examining these two β-As structures, the question arose as to whether this structure type could be reproduced with more extended linking units between the aniline and phenol moieties. To study this question, and to establish the requirements for β-As sheet formation in higher aminophenols, a series of 4-amino-4′-hydroxydiphenyl-*n*-alkanes (where $n = 1-5$) were synthesized. In effect, 4APP is the $n = 0$ compound. This series of homologated aminols also provides an opportunity for

(4) (a) Aakeröy, C. B.; Beatty, A. M.; Helfrich, B. A. *J. Am. Chem. Soc.* **2002**, *124*, 14425. (b) Vishweshwar, P.; Nangia, A.; Lynch, V. M. *Cryst. Growth Des*. **2003**, *3*, 783.
(5) Ermer, O.; Eling, A. *J. Chem. Soc., Perkin Trans. 2* **1994**, 925.
(6) (a) Hanessian, S.; Gomtsyan, A.; Simard, M.; Roelens, S. *J. Am. Chem. Soc.* **1994**, *116*, 4495. (b) Hanessian, S.; Simard, M.; Roelens, S. *J. Am. Chem. Soc.* **1995**, *117*, 7630. (c) Hanessian, S.; Saladino, R.; Margarita, R.; Simard, M. *Chem. Eur. J.* **1999**, *5*, 2169. (d) Hanessian, S.; Saladino, R. In *Crystal Design. Structure and Function*. Perspectives in Supramolecular Chemistry, Vol 7; Desiraju, G. R., Ed.; Wiley: New York; 2003, p 77.
(7) Selected references that describe the structural chemistry of supraminols include the following: (a) Loehlin, J. H.; Etter, M. C.; Gendreau, C.; Cervasio, E. *Chem. Mater*. **1998**, *6*, 1218. (b) Loehlin, J. H.; Franz, K. J.; Gist, L.; Moore, R. H. *Acta Crystallogr*. **1998**, *B54*, 695. (c) Toda, F.; Hyoda, S.; Okada, K.; Hirotsu. K. *J. Chem. Soc., Chem. Commun*. **1995**, 1531. (d) Roelens, S.; Dapporto, P.; Paoli, P. *Can. J. Chem.* **2000**, *78*, 723. (e) Dapporto, P.; Paoli, P.; Roelens, S. *J. Org. Chem.* **2001**, *66*, 4930. (f) Lewinski, J.; Zachara, J.; Kopec, T.; Starawiesky, B. K.; Lipkowski, J.; Justyniak, I.; Kolodziejczyk, E. *Eur. J. Inorg. Chem.* **2001**, *5*, 1123. (g) O'Leary, B.; Splading, T. R.; Ferguson, G.; Glidewell, C. *Acta Crystallogr*. **2000**, *B56*, 273.
(8) Allen, F. H.; Hoy, V. J.; Howard, J. A. K.; Thalladi, V. R.; Desiraju, G. R.; Wilson, C. C.; McIntyre, G. J. *J. Am. Chem. Soc.* **1997**, *119*, 3477.
(9) Desiraju, G. R. *Acc. Chem. Res.* **2002**, *35*, 565.
(10) (a) Desiraju, G. R. *Nature* **2001**, *412*, 397. (b) Madhavi, N. N. L.; Bilton, C.; Howard, J. A. K.; Allen, F. H.; Nangia, A.; Desiraju, G. R. *New J. Chem*. **2000**, *24*, 1.
(11) (a) SHELXTL version 5.1. Bruker AXS: Madison, WI, 2001. (b) Wilson, C. C. *J. Mol. Struct.* **1997**, *405*, 207. (c) Allen, F. H.; Howard, J. A. K.; Hoy, V. J.; Desiraju, G. R.; Reddy, D. S.; Wilson, C. C. *J. Am. Chem. Soc.* **1996**, *118*, 4081. (d) Wilson, C. C. *J. Appl. Crystallogr*. **1997**, *30*, 184.
(12) Spek, A. L. PLATON, A multipurpose Crystallographic Tool, Utrecht University, Utrecht, The Netherlands, 2002.

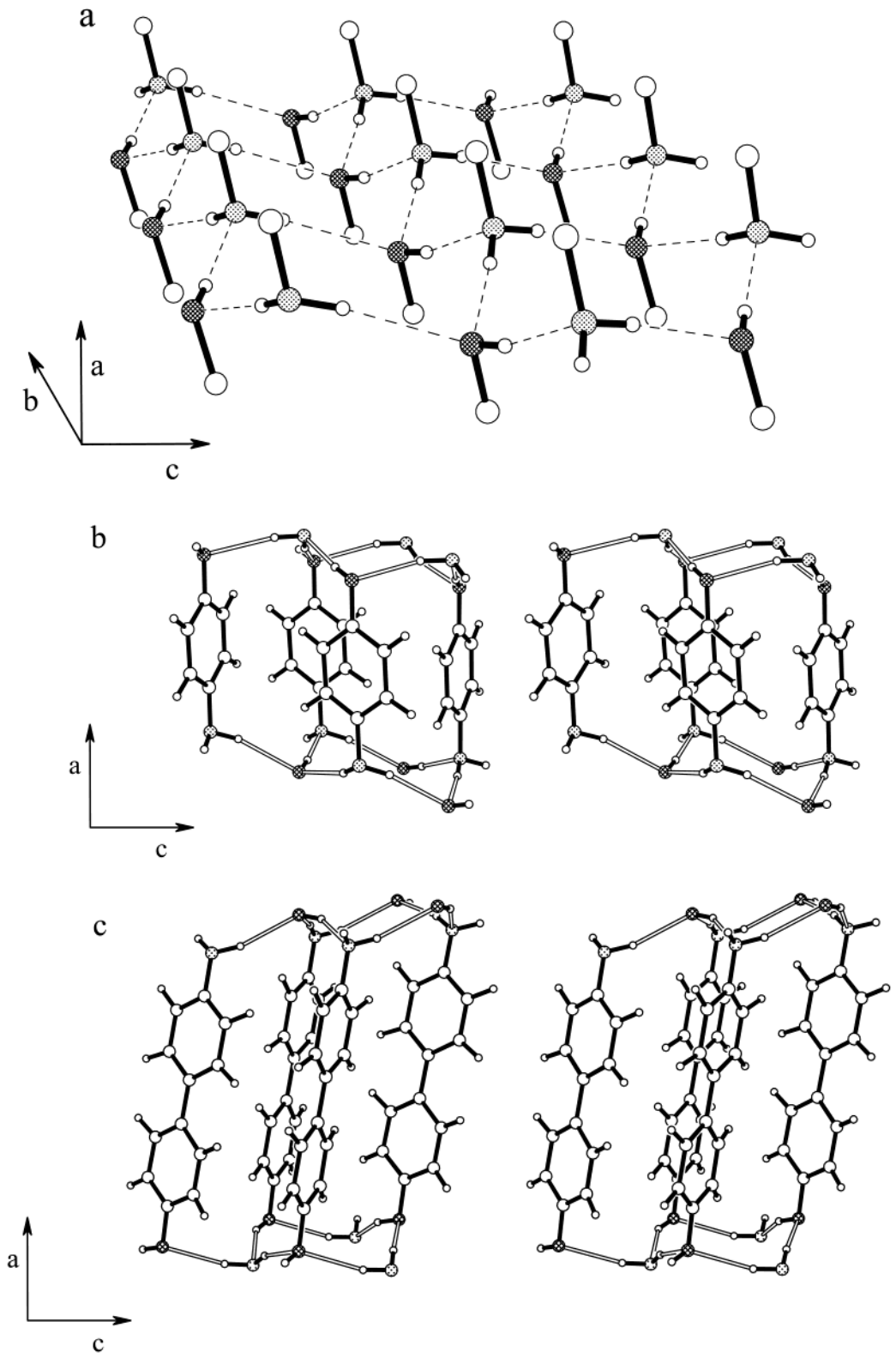


Figure 1. (a) β-As sheet, (b) stereoview of the β-As sheet structure in 4-aminophenol (4AP), (c) stereoview of the β-As sheet structure in 4-(4-aminophenyl)-phenol (4APP) (adapted from ref 5).

investigation into the even−odd effect in the alternation of melting points and other physical properties of *n*-alkanes and substituted *n*-alkanes.[13,14] These aminols also provided an interesting synthetic exercise, with each compound requiring a different multistep route. Details are given in the Supporting Information.

***n*-Even Structures.** 4-(4-aminophenethyl)phenol, **2**, forms crystals with a structure that is directly analogous to that of 4AP and 4APP. Parallel β-As sheets are linked by the rest of the molecule (Figure 3). The hydrogen bond distances within

(13) Baeyer, A. *Ber. Chem. Ges.* **1877**, *10*, 1286.

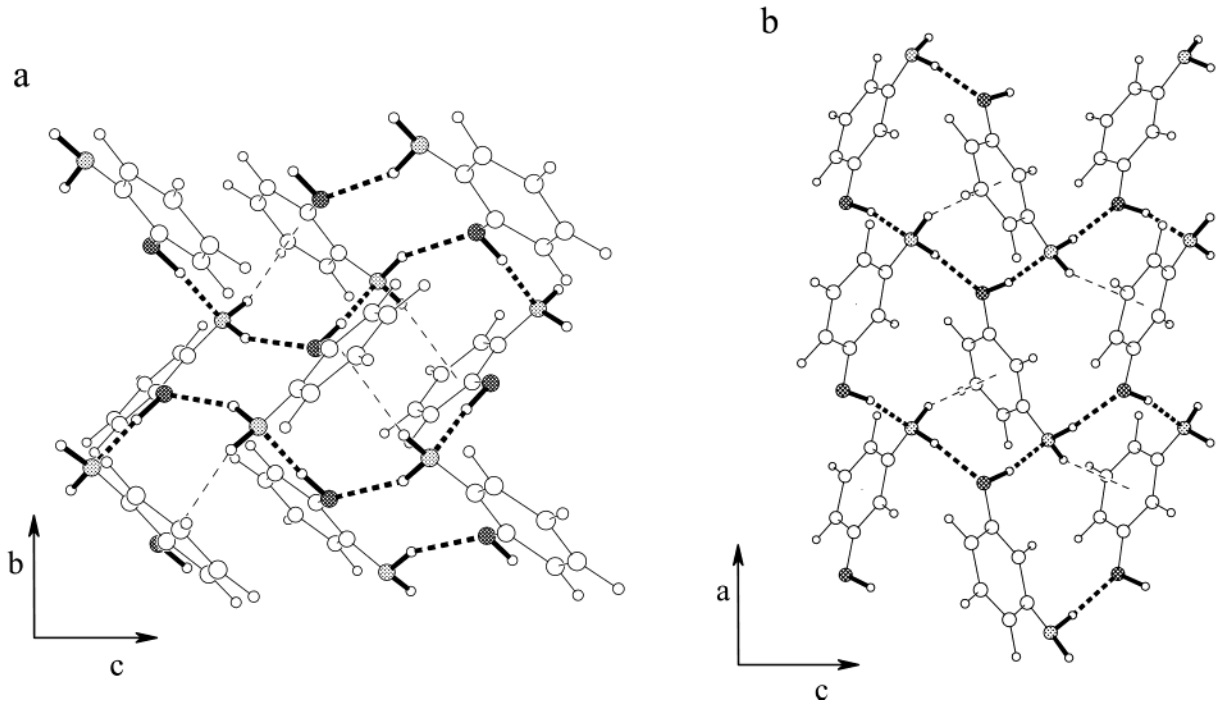
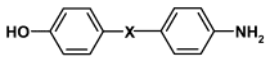
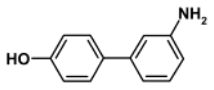


Figure 2. Hydrogen bridges in (a) 2-aminophenol (2AP) and (b) 3-aminophenol (3AP). The infinite chain N(H)O synthon is highlighted in both cases.

Scheme 1



X =	CH_2	1	S	1a	CH=CH	2d
	$(CH_2)_2$	2	S-CH_2	2a	O	1b
	$(CH_2)_3$	3	CH_2-S	2b		
	$(CH_2)_4$	4	S-S	2c		
	$(CH_2)_5$	5	S-$(CH_2)_2$	3a		



6a

the sheet are O−H···N (1.84 Å, 173.3°) and N−H···O (2.13 Å, 169.7°; 2.30 Å, 177.3°). The structure is further stabilized by herringbone interactions[15] with an angle of 67° between adjacent phenol rings and of 70° between adjacent anilino rings. There are subtle differences between this β-As sheet and those in 4AP and 4APP; first, there is a change in space group from $Pna2_1$ to Pc; second, while 4AP and 4APP are in a wurtzite-like structure, compound **2** is analogous to diamond.

The structure of 4-[4-(4-aminophenyl)butyl]phenol, **4**, is isostructural with that of **2** and β-As sheets are observed (Figure 4). The space group is Pc and the structure is diamond-like rather than wurtzite-like. The structure is further stabilized by herringbone interactions with ring plane−ring plane angles of 69° and 72°, respectively, for the phenol and anilino ring pairs.

***n*-Odd Structures.** Low-temperature X-ray and neutron data were collected for 4-(4-aminobenzyl)phenol, **1**, and are in good agreement. In the following discussion, the geometries derived from both the X-ray (X) and neutron (N) data sets are quoted. Complementary recognition of NH_2 and OH moieties to give a saturated N(H)O packing is not observed. Instead, an unsaturated arrangement of N(H)O hydrogen bonds is found. The structure is based on a 4-fold arrangement of N(H)O hydrogen bonds, a tetramer synthon, henceforth referred to as a square motif (Figure 5). The anilino hydrogen that is not involved in a hydrogen bond to the hydroxy group interacts with an adjacent phenol ring to form a N−H···π bridge[16] (2.43 Å, 156° (X), 2.39 Å, 155.5° (N)). A C−H···π interaction directed at the other face of the same phenol ring and another C−H···π bond with the anilino ring completes the packing.

With all π-bases there is some question as to where exactly the hydrogen bond accepting site is located. Questions of this kind can only be answered satisfactorily with neutron diffraction analysis. In X−H···π hydrogen bonds the X−H bond vector can be directed either toward the ring centroid or toward an individual carbon−carbon bond within the ring. In the $N_1-H_{1b}\cdots\pi_A$ interaction (interaction iv in Figure 5b), the N−H vector is directed toward one of the C−C bonds of the phenol ring but the $C_9-H_9\cdots\pi_A$ bond to the other face of the same ring (v in Figure 5b) is directed toward the ring centroid. In contrast, the C−H vector in the $C_5-H_5\cdots\pi_B$ interaction (iii in Figure 5a) is directed toward one of the C−C bonds. In all cases,

(14) (a) Thalladi, V. R.; Nüsse, M.; Boese, R. *J. Am. Chem. Soc.* **2000**, *122*, 9227. (b) Thalladi, V. R.; Boese, R. *New J. Chem.* **2000**, *24*, 579. (c) Thalladi, V. R.; Boese, R.; Weiss, H. C. *J. Am. Chem. Soc.* **2000**, *122*, 1186. (d) Thalladi, V. R.; Boese, R.; Weiss, H. C. *Angew. Chem., Int. Ed.* **2000**, *39*, 918. (e) Boese, R.; Weiss, H. C.; Bläser, D. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 988. (f) Bond, A. D. *Chem. Commun.* **2003**, 250.

(15) (a) Throughout this work the herringbone interaction has been described in terms of the angle between adjacent aromatic rings. This is not the only factor influencing the nature of this interaction, and the separation and the degree to which the rings are offset is also important; however, the relative ring plane angle gives a single value by which the interactions may be conveniently compared. (b) Zorkii, P. M.; Zorkaya, O. N. *J. Struct. Chem.* **1995**, *36*, 704. (c) Gavezzotti, A. *Chem. Phys. Lett.* **1988**, *161*, 67.

(16) (a) Malone, J. F.; Murray, C. M.; Charlton, M. H.; Docherty, R.; Lavery, A. J. *J. Chem. Soc., Faraday Trans.* **1997**, *93*, 3429. (b) Viswamitra, M. A.; Radhakrishnan, R.; Bandekar, J.; Desiraju, G. R. *J. Am. Chem. Soc.* **1993**, *115*, 4868. (c) Ciunik, Z.; Desiraju, G. R. *Chem. Commun.* **2001**, 703. (d) Hanton, L. R.; Hunter, C. A.; Purvis, D. H. *J. Chem. Soc., Chem. Commun.* **1992**, 1134. (e) Bond, A. D. *Chem Commun.* **2002**, 1664. (f) Nishio, M.; Hirota, M.; Umezawa, Y. *The CH/π Interaction*; Wiley-VCH: New York, 1998.

Table 1. Crystallographic Data and Structure Refinement Parameters for the Compounds in This Study

	1N	1X	2	3	4	5
emp. form.	$C_{13}H_{13}NO$		$C_{14}H_{15}NO$	$C_{15}H_{17}NO$	$C_{16}H_{19}NO$	$C_{17}H_{21}NO$
form. wt.	199.25		213.27	227.30	241.32	255.35
crystal system	monoclinic		orthorhombic	monoclinic	monoclinic	monoclinic
space group	$P2_1/n$		*Pc*	$Pca2_1$	*Pc*	Pc
T [K]	12(2)	100(2)	100(2)	100(2)	105(2)	100(2)
a [Å]	5.9180(12)	5.9820(3)	13.682(3)	23.9370(7)	15.7888(16)	14.9554(9)
b [Å]	19.213(4)	19.3670(9)	5.2619(11)	6.2160(2)	5.2088(6)	11.2370(8)
c [Å]	9.6510(19)	9.7390(4)	8.1916(2)	8.3970(3)	8.3399(8)	8.6841(6)
α [deg]	90	90	90	90	90	90
β [deg]	101.25(3)	100.860(2)	107.28(3)	90	100.912(5)	90.893(3)
γ [deg]	90	90	90	90	90	90
Z	4		2	4	2	4
V [Å^3]	1076.3(4)	1108.09(9)	563.1(2)	1249.41(7)	673.48(12)	1459.2(2)
D_{calc} [mg/m^3]	1.230	1.194	1.258	1.208	1.190	1.162
R_1 [$I > 2\sigma(I)$]	0.0791	0.0449	0.0405	0.0389	0.0418	0.0355
wR_2	0.2230	0.1049	0.1087	0.0856	0.0921	0.0885
GOF	1.081	1.030	1.034	1.016	1.030	1.033
structure	square motif		*β*-As	infinite chain	*β*-As	infinite chain
mp [°C]	147.59		222.46	141.96	185.97	106.56
C−O, C−N angle [deg][a]	117		174	124	174	129 (A) 125 (B)
herringbone angle [deg][b]	88		67 and 70	41	69 and 72	25 and 20
C_k* [%][c]	0.69	0.66	0.71	0.68	0.69	0.67
pyramidal factor[d]	0.305	0.278	0.320	0.284	0.304	A = 0.308 B = 0.347
lattice energies [kcal/mol][e]:						
van der Waals	−15.5103	−16.9782	−22.6960	−23.9593	−25.8799	−26.5133
electrostatic	−12.6148	−10.5619	−14.9624	−13.3021	−15.2413	−12.8726
hydrogen bond	−5.8331	−6.4404	−9.0674	−5.2543	−8.8910	−6.2596
total energy	−33.9582	−33.9805	−46.7258	−42.5157	−50.0122	−45.6455

	1a	2a	2b	2c	3a	2d	1b	6a
emp. form.	$C_{12}H_{11}NOS$	$C_{13}H_{13}NOS$	$C_{13}H_{13}NOS$	$C_{12}H_{11}NOS_2$	$C_{14}H_{15}NOS$	$C_{14}H_{13}NO$	$C_{12}H_{11}NO_2$	$C_{12}H_{11}NO$
form. wt.	217.28	231.30	231.30	249.34	245.33	211.25	201.22	185.22
crystal system	monoclinic	monoclinic	monoclinic	monoclinic	monoclinic	monoclinic	monoclinic	orthorhombic
space group	$P2_1/n$	*Pc*	*Pc*	$P2_1/c$	*Pc*	*Pc*	*Cc*	$Pca2_1$
T [K]	120(2)	100(2)	120(2)	100(2)	100(2)	120(2)	120(2)	120(2)
a [Å]	9.8597(3)	13.844(3)	13.7422(12)	10.4321(12)	12.6341(9)	12.951(8)	22.491(1)	19.2352(8)
b [Å]	10.0879(3)	5.1626(10)	5.1725(4)	8.1179(11)	5.8636(4)	5.226(3)	5.4647(2)	6.0039(3)
c [Å]	21.8081(7)	8.2485(16)	8.3055(7)	14.791(2)	8.5671(5)	8.046(3)	8.0466(4)	8.1627(4)
α [deg]	90	90	90	90	90	90	90	90
β [deg]	102.809(1)	107.22(3)	105.548(4)	109.633(6)	90.351(3)	98.12(3)	95.674(2)	90
γ [deg]	90	90	90	90	90	90	90	90
Z	8	2	2	4	2	2	4	4
V [Å^3]	2115.13(11)	563.07(21)	568.76(8)	1179.8(3)	634.65(7)	539.2(5)	984.14(8)	942.68(8)
D_{calc} [mg/m^3]	1.365	1.364	1.351	1.404	1.284	1.301	1.358	1.305
R_1 [$I > 2\sigma(I)$]	0.0464	0.0435	0.0402	0.0348	0.0322	0.0392	0.0329	0.0378
wR_2	0.1242	0.1170	0.0841	0.0836	0.0822	0.0996	0.0863	0.0930
GOF	1.034	1.095	1.021	1.078	1.055	1.045	1.047	1.033
structure	square motif	*β*-As	*β*-As	infinite chain	infinite chain	*β*-As	*β*-As	infinite chain
mp [°C]	147−148	211−212	205−207	113−115	116−118	272−275	155−157	180−182
C−O, C−N angle [deg][a]	106.93 (A) 100.16 (B)	171.9	174.7	91.184	115.6	173.8	141.6	121.4
herringbone angle [deg][b]	75 (A) 71 (B)	68 and 71	69 and 72	86	74 and 49	67 and 70	62 and 69	89.4
C_k* [%][c]	0.70	0.713	0.706	0.69	0.685	0.723	0.716	0.703
pyramidal factor[d]	0.262 (A) 0.315 (B)	0.328	0.300	0.290	0.318	0.300	0.337	0.300
lattice energies [kcal/mol][e]:								
van der Waals	−21.2104	−22.8127	−24.1992	−23.6826	−24.0041	−23.5826	−18.7798	−16.5686
electrostatic	−13.4020	−18.4422	−18.9782	−14.8522	−12.7148	−16.0236	−16.7818	−14.2359
hydrogen bond	−5.4285	−8.4105	−8.8847	−7.4514	−5.9412	−8.2482	−7.4019	−6.7081
total energy	−40.0409	−49.6654	−52.0621	−45.9862	−42.6601	−47.8544	−42.9635	−37.5126

[a] The angles between the C−O and C−N vectors in the compounds have been calculated using RPluto. This gives a measure of the linearity of the molecule. [b] The angles between two adjacent aromatic ring planes have been calculated using RPluto (phenol−phenol rings and anilino−anilino rings (2 values) or phenol−anilino rings (one value) depending on the relative orientation of the adjacent molecules head to head or head to tail. [c] C_k*, packing coefficient calculated with PLATON. [d] The perpendicular distance from the basal plane to the apex of the pyramid. [e]Lattice energies calculated using Cerius^2 from Accelrys.

the direction of the X−H vector with the closest approach is to the ring centroid and not to a specific C−C bond. Using the X−H···π categories defined by Malone et al.,[16a] $N_1-H_{1b}\cdots\pi_A$ and $C_9-H_9\cdots\pi_A$ are type I whereas $C_5-H_5\cdots\pi_B$ is a type III interaction. Full details of the geometries are given in the Supporting Information.

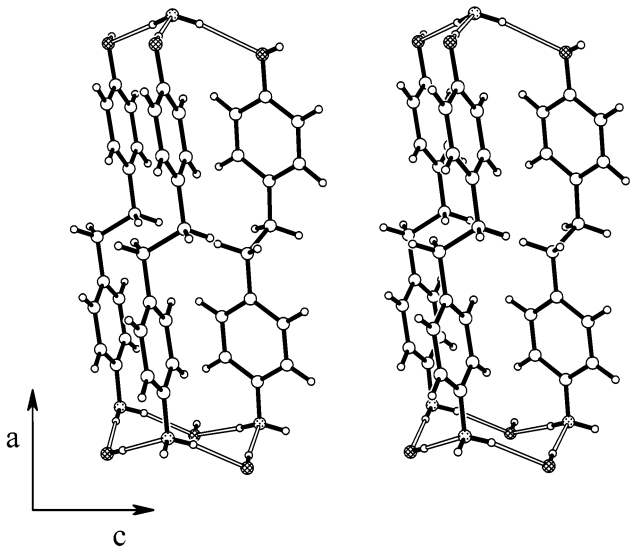


Figure 3. Stereoview of the β-As sheet in 4-(4-aminophenethyl)-phenol, **2**.

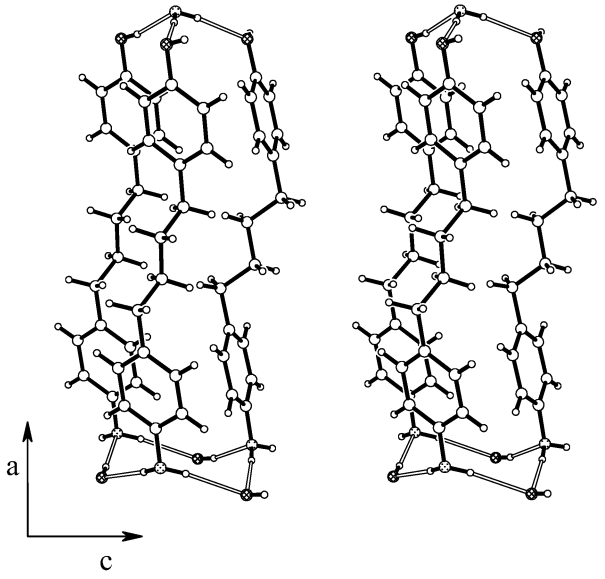


Figure 4. Stereoview of the β-As sheet in 4-[4-(4-aminophenyl) butyl]-phenol, **4**.

The most notable supramolecular synthon in 4-[3-(4-aminophenyl)propyl]phenol, **3**, is a chain of N(H)O hydrogen bonds. This motif (previously observed in 2AP and 3AP) is of major significance in this structural series and is henceforth referred to as the infinite chain. The moieties at both ends of a given molecule are involved in different chains, so that the molecule acts as a linker between chains, thus creating sheets. Once again, the amino hydrogen atom that is not involved in the chain forms an N−H···π hydrogen bridge (2.38 Å, 161.2°). This structure is directly comparable to 3AP (Figure 6), but not to 2AP.[8] Both **3** and 3AP are in the same space group $Pca2_1$ and the axial lengths along *b* and *c* are nearly equal.

There are two independent molecules in the asymmetric unit of 4-[5-(4-aminophenyl)pentyl]phenol, **5**, and these molecules have different geometries (Figure 7a). One is similar to **3** while the other is more twisted. The latter (A = $N_{(1)}O_{(1)}C_{(1-15)}$) is saturated in terms of N(H)O hydrogen bonds (forming 3 N(H)O hydrogen bonds at each oxygen and nitrogen), while the former (B = $N_{(21)}O_{(21)}C_{(21-35)}$) is unsaturated (forming only two hydrogen bonds at each O and N-atom and requiring N−H···π and C−H···O bonds to complete the supramolecular valence).

The structures of aminols **5** and **3** appear to be very similar; in both cases the major structural synthon is the infinite chain of N(H)O hydrogen bonds (compare Figures 6 and 7b). However, in **5** the infinite chains are partially cross-linked by additional N(H)O interactions so that they can be considered as running in two directions (Figure 8). For comparison, β-As sheets can be considered as fully cross-linked infinite chains. Therefore, **5** can be considered as bridging the β-As sheet (aminols **2** and **4**) and infinite chain structures (aminol **3)**, with molecules A and B in the β-As structure and the (single) infinite chain structure, respectively. As in **3** there is no evidence of stabilization by herringbone interactions; the ring plane (A)−ring plane (B) angle between adjacent molecules is 25° and 20°. One could say that **5** has the same basic structure type as **3**, but strives toward the β-As sheet structure.

General Discussion of *n*-Even and *n*-Odd Structures. This is a very interesting series and unusual in both the extent of the structural repetition and the degree to which the structural changes within the series can be understood and explained. The structures observed can be described by just three major synthons: the square motif, the infinite chain, and the β-As sheet. The best way to understand the relationship between these five structures is in terms of the infinite chain of N(H)O hydrogen bonds. The β-As sheet {4APP (or **0**), **2**, and **4**} can be considered as a very special case of the infinite chain wherein the chains run in two directions. In **3** only single or one-dimensional chains are found. In **5**, each symmetry-independent molecule has one of the above characteristics. The underlying reason for using the infinite chain as the basic structure motif can be seen from the unit cell dimensions: In all the cases where there is an infinite chain (**2** through **5**), the chain runs parallel to the *c* axis and the dimensions of the *c* axis are approximately equal (8.2−8.7 Å). In the β-As sheet structures, the *b* axis (in the plane of the β-As sheet) is also equal, and the *a* axis reflects the overall length of the molecule.

From this series it would appear that the driving force for the formation of β-As structures, over the (single) infinite chains, is the molecular geometry. While 4AP, 4APP, **2**, and **4** are approximately linear, 2AP, 3AP, **1**, **3**, and **5** are much more bent. A measure of molecular linearity can be obtained from the angle between the C−O and the C−N vectors (see Table 1). This angle is nearly 180° for the β-As structures and close to 120° for the other structures. The structures with n = odd can be considered as tending toward the β-As structure as the value of *n* increases: **1** has a structure that is far from the β-As structure, without any infinite chains, just square motifs. **3** is closer, with infinite chains, while **5** is still closer to the β-As structure with cross-linked infinite chains. The fact that **5** has two molecules in the asymmetric unit suggests that the structure is tending toward the β-As structure, preferring to assume a more intricate structure, involving two symmetry-independent molecules, that is more closely related to the β-As sheet rather than a simpler structure such as **3**.[17] An overlay of the sheets

(17) A very similar series that shows this sort of structural modulation is the 2,3-dicyano-5,6-dichloro-1,4-dialkoxybenzenes studied by Reddy, D. S.; Ovchinnikov, Y. E.; Shishkin, O. V.; Struchkov, Y. T.; Desiraju, G. R. *J. Am. Chem. Soc.* **1996**, *118*, 4085.

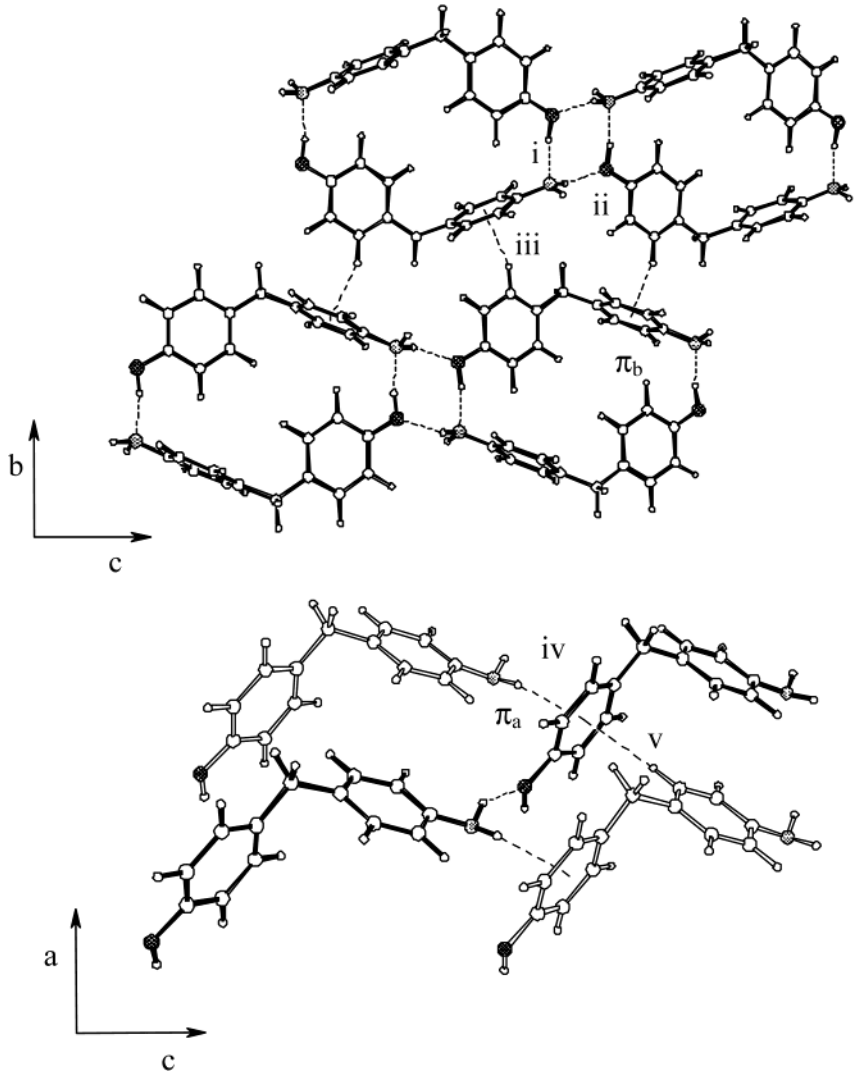


Figure 5. (a) Square motif synthon formed by O−H···N, (i) N−H···O (ii) hydrogen bonds and $C_5-H_5\cdots\pi_B$ (iii) interactions in the crystal structure of aminol **1**. (b) Notice $N_1-H_{1b}\cdots\pi_a$ (iv) and $C_9-H_9\cdots\pi_a$ (v) interactions to the same phenyl ring.

of the N(H)O interactions in **5** on the β-As sheet shows just how closely these two structures are related (Figure 8).

In summary, the n = odd series can be considered as a variable series, with the structure moving toward a β-As sheet structure as the length of the linker unit increases:

$$\mathbf{1} \rightarrow \mathbf{3} \rightarrow \mathbf{5} \rightarrow \rightarrow \beta\text{-As}$$

In comparison, the n = even series is a fixed series:

$$\mathbf{0} = \mathbf{2} = \mathbf{4} = \beta\text{-As}$$

This series also provides a good example of the even−odd effect in substituted *n*-alkanes. This effect was first studied by Baeyer in 1877, who noted that *n*-alkane dicarboxylic acids where n = even melt at higher temperatures than those where n = odd.[13] This phenomenon has since been observed in many other *n*-alkanes and end-substituted *n*-alkanes. In particular, detailed studies have been carried out by Boese and co-workers.[14] The phenomenon of alternation in solid-state properties has been attributed to crystal packing factors so that even *n*-alkanes pack more efficiently than odd *n*-alkanes. In our series, not only is the even−odd effect apparent from the alternation of the melting points but *also from the marked alternation of the crystal structure types*. The even structures take the β-As sheet structures, while the odd ones take infinite chain structures (or a square motif structure in **1**). This sort of structural modulation where the types of interactions and indeed the entire packing arrangements alternate, based on whether the member is even or odd, is very dramatic. Lattice energy calculations[18] confirm that the β-As structures are more stable. The decrease of melting points with an increase in chain length hint also at the importance of entropic factors (Figure 9).

This series shows good trends that can be clearly explained in terms of odd and even structures. However, it is still a series that consists of only five structures. To confirm the trends observed, structural analyses of more compounds are desirable. This is especially true at the lower end of the n = odd compounds where the square motif of **1** becomes the infinite chain motif in **3**. With this aim, a selection of S-substituted 4-amino-4′-hydroxybiphenyl-*n*-alkanes was synthesized. The

(18) Energy calculations were carried out on Indigo Solid Impact and Octane workstations from Silicon Graphics using the Dreiding 2.21 force field in the Cerius^2 program. Cerius^2, Accelrys Ltd., 334 Cambridge Science Park, Cambridge CB4 0WN, U.K. www.accelrys.com.

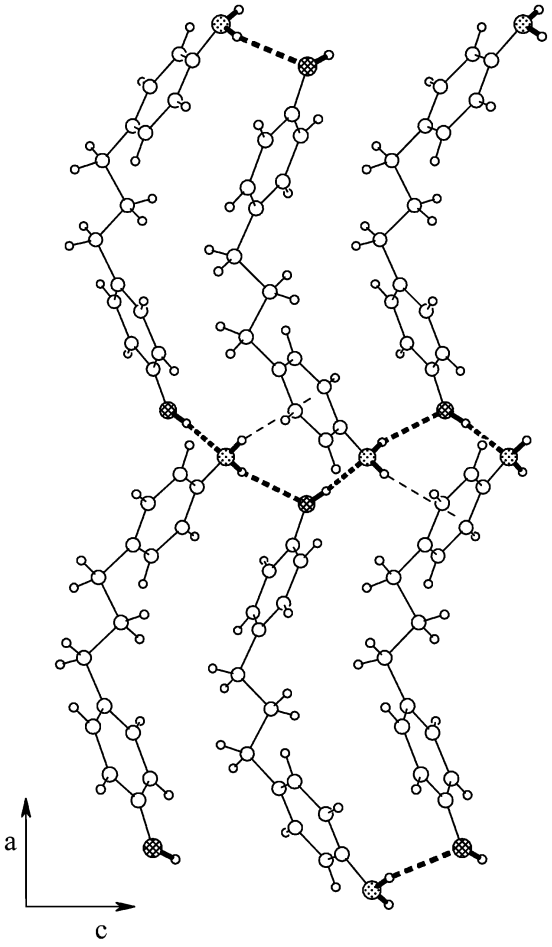


Figure 6. Infinite chain synthon in 4-[3-(4-aminophenyl)propyl]phenol, **3**. Note the similarity with the packing of 3AP shown in Figure 2.

method of exchanging one functional group with another of similar dimensions is a technique that has greatly furthered the field of crystal engineering. Whether the new structure is geometrically isostructural with the original or not can reveal a great deal about the ability and role of the exchanged group in determining the crystal structure.

B. Sulfur Spacer Structures. Kitaigorodskii[19] proposed that under appropriate circumstances interchanging a single functional group with another of comparable volume in a molecule, such as the S-atom and the $-CH_2-$ group, benzene−thiophene exchange,[20] or chloro−methyl exchange,[21] need not alter the crystal structure. A CSD search[22] was carried out for Ar−S−Ar/Ar−CH_2−Ar sets of compounds. A total of 21 pairs were found of which 8 are isostructural. The S-atom is approximately the same size as the CH_2 group (22.8 Å^3 and 19.1 Å^3, respectively), and the idealized C−S−C angle is 100°

(19) (a) Kitaigorodskii, A. I. *Molecular Crystals and Molecules*; Academic: New York, 1973. (b) Kitaigorodskii, A. I. *Mixed Crystals*; Springer: New York, 1984.
(20) Thallapally, P. K.; Chakraborty, K.; Carrell, H. L.; Kotha, S.; Desiraju, G. R. *Tetrahedron* **2000**, *56*, 6721.
(21) (a) Kálmán, A.; Argáy, Fábián, L.; Bernath, G.; Fulop, F. *Acta Crystallogr.* **2001**, *B57*, 539. (b) Muthuraman, M.; Le Fur, Y..; Beucher, M. B.; Masse, R.; Nicoud, J.-F.; George, S.; Nangia, A.; Desiraju, G. R. *J. Solid State Chem.* **2000**, *152*, 221.
(22) A search of the CSD (Version 5.23, April 2002) for error free Ar−S−Ar organic acyclic, nonionic, no polymeric with $R < 0.10$. Disordered, no coordinates present structures were excluded from the search. Of the 589 entries in the subset, 21 hits with corresponding Ar−CH_2−Ar were found of which eight are isostructural. Allen, F. H.; Kennard, O. *Chem. Des. Automat. News* **1993**, *8*, 31.

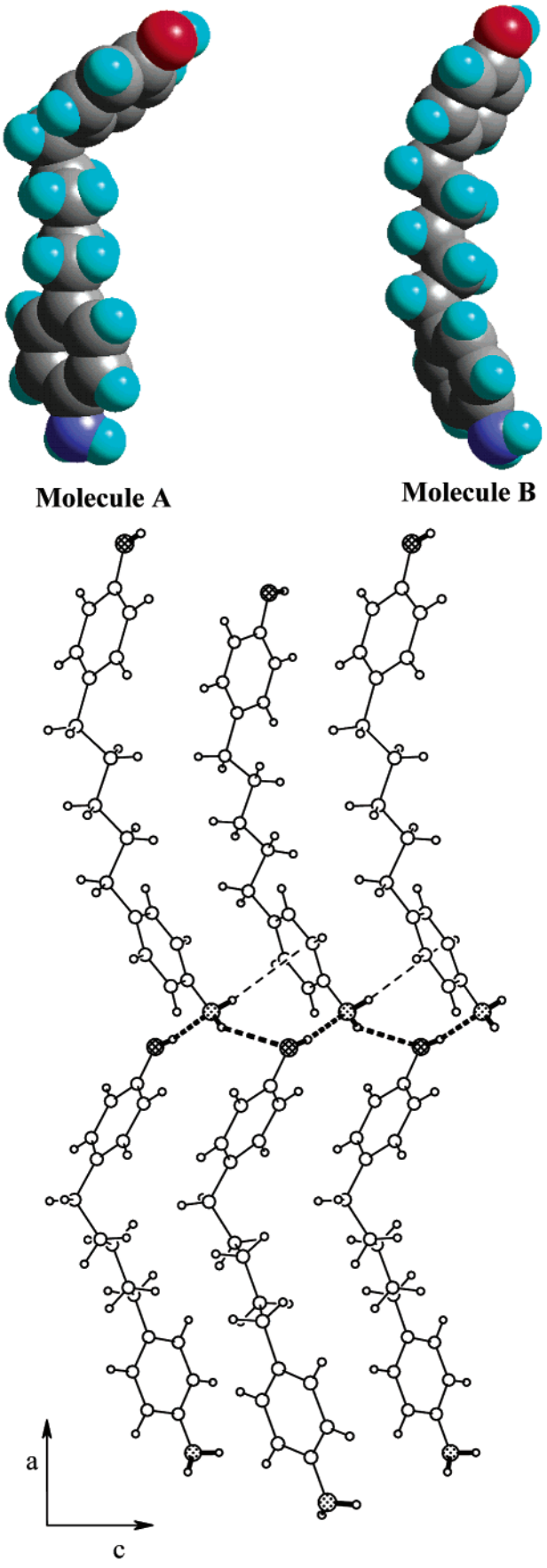


Figure 7. (a) Space-filling model of **5** showing the two symmetry-independent molecules. (b) Infinite chain in 4-[4-(4-aminophenyl)pentyl]-phenol, **5**. Compare this with Figure 6.

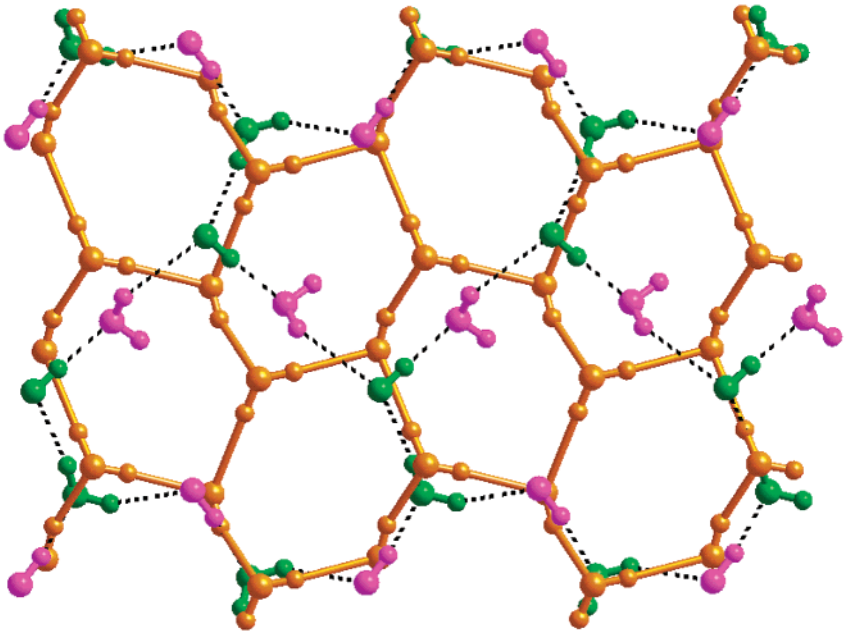


Figure 8. Showing how the cross-linked infinite chains in supraminol **5** relate to the β-As sheet in **4** (overlaid in orange). Symmetry-independent molecules A (green) and B (magenta) are color coded.

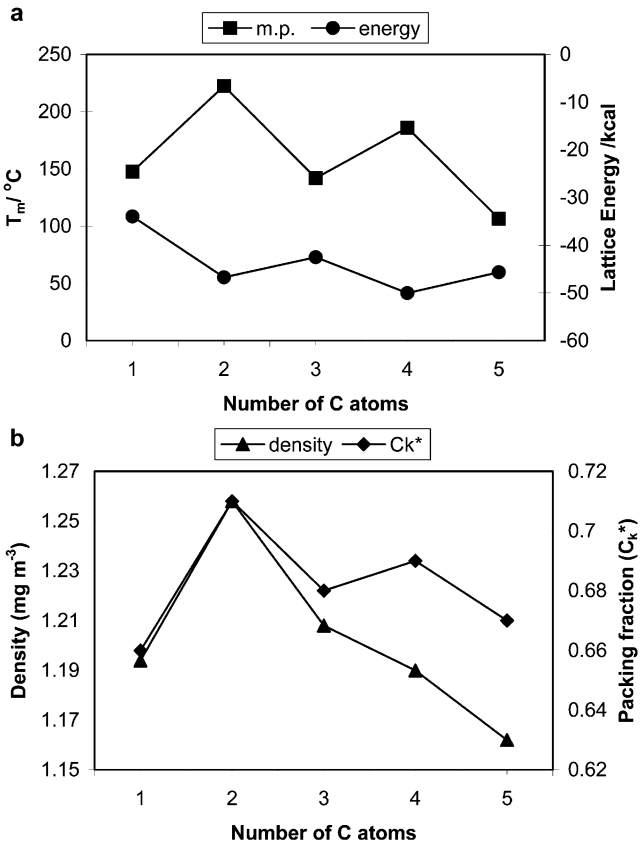


Figure 9. (a) Even−odd effect in aminols **1**−**5** of melting points and lattice energy.[18] (b) Alternation in density and packing fraction.

compared to a C−C−C angle of 109°. However, the geometry of Ar−S−S−Ar (torsion angle ~90°, see Supporting Information) is very different than that of Ar−C−C−Ar or Ar−S−C−Ar (torsion angle ~0°). Disulfide compounds are comparatively rare, with only a total of 51 CSD occurrences.[23]

Accordingly, we studied compounds **1a** (4-amino-4′-hydroxydiphenylsulfide), **2a** (4-amino-4′-hydroxydiphenylmethylsulfide), **2b** (4-amino-4′-hydroxydiphenylsulfide methane), **2c** (4-amino-4′-hydroxydiphenyldisulfide), and **3a** (4-amino-4′-hydroxydiphenylethylsulfide). It is noteworthy that all these compounds required a synthetic route for the preparation different from that used to obtain the parent compound. Details of the synthetic procedures are given in the Supporting Information.

Isostructural S-Spacer Supraminols. The substitution of one CH_2 group for an S-atom in compound **2** to give **2a** and **2b** has very little effect on the crystal structure (Figure 10).[24,25]The structure of **3a** is again very similar to that of **3** and the key synthon is the infinite chain. In **3** the molecules align head to tail. This allows the chains to be linked into sheets, with the molecule acting as a linker between adjacent N(H)O chains. In **3a** the molecules align head to head, preventing the formation of individual sheets (Figure 11).

Non-isostructural S-Spacer Supraminols. There are two independent molecules in the asymmetric unit of compound **1a** (molecule A = $N_{(1)}O_{(1)}S_{(1)}C_{(1-12)}$ and molecule B = $N_{(2)}O_{(2)}S_{(2)}C_{(21-22)}$) but the geometries of both molecules, and the way in which they interact within the crystal, are similar. The crystal structure consists of alternate sheets of A and B molecules. Both sheets are built up of square motifs of N(H)O hydrogen bonds. The difference between this structure and that of aminol **1** is that the four molecules spiral out from the square motif, in a windmill type arrangement (Figure 12). The reason for this difference appears to be the exchange of an N−H···π bond by an N−H···S bond.[26] Sheets of molecules A and B stack alternately, with herringbone interactions between the layers

(23) A search of the CSD (Version 5.23, April 2002) was done for error free Ar−S−S−Ar organic, aromatic, acyclic, nonionic, nonpolymeric structures with $R < 0.10$. Disordered structures and those without coordinates were excluded. Fiftyone hits with torsion angles of nearly 90° were found.

(24) (a) Fábián, L.; Kálmán, A. *Acta Crystallogr.* **1999**, *B55*, 1099. (b) Lowdin, P.-O. *J. Chem. Phys.* **1950**, *18*, 365.

(25) The near identity of the packing of **2**, **2a**, and **2b** molecules was also quantified with NIPMAT and simulated powder X-ray plots. For a description of the NIPMAT procedure, see Supporting Information.

(26) (a) Desiraju, G. R.; Steiner, T. *The Weak Hydrogen Bond in Structural Chemistry and Biology*; Oxford University Press: Oxford, 1999. (b) Vangala, V. R.; Desiraju, G. R.; Jetti, R. K. R.; Bläser, D.; Boese, R. *Acta Crystallogr.* **2002**, *C58*, 635.

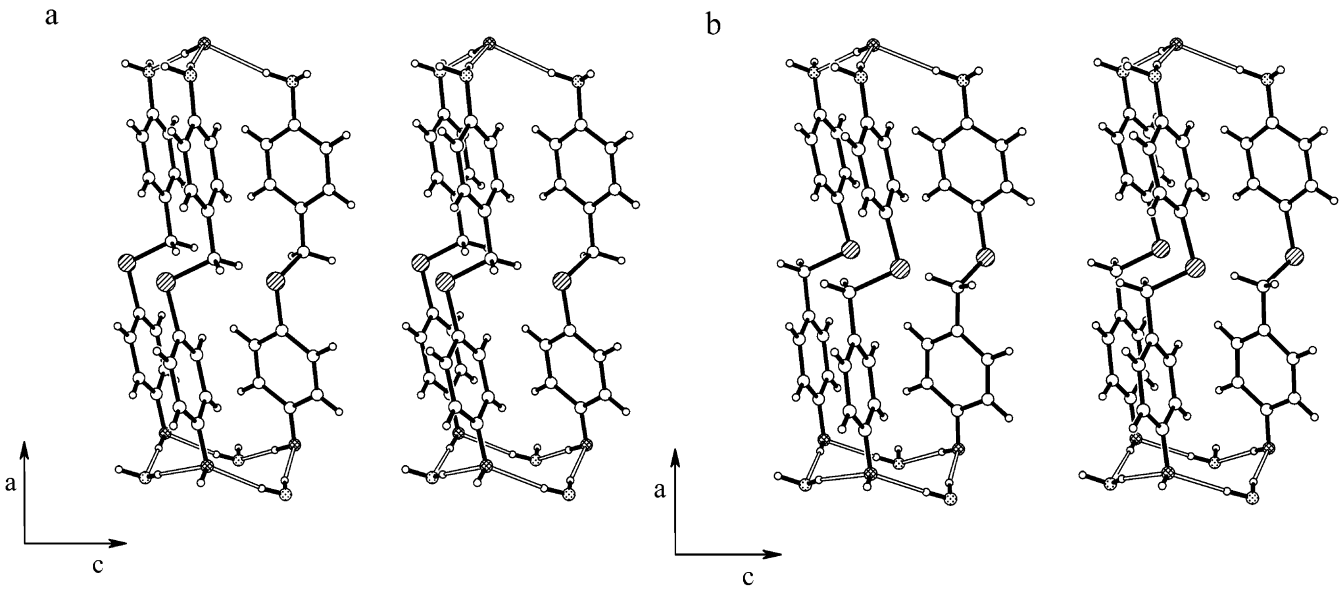


Figure 10. (a) Stereoview of the β-As sheet in 4-(4-aminobenzyl sulfamyl)phenol, **2a**, and (b) in 4-(4-aminophenylsulfamylmethyl)phenol, **2b**.

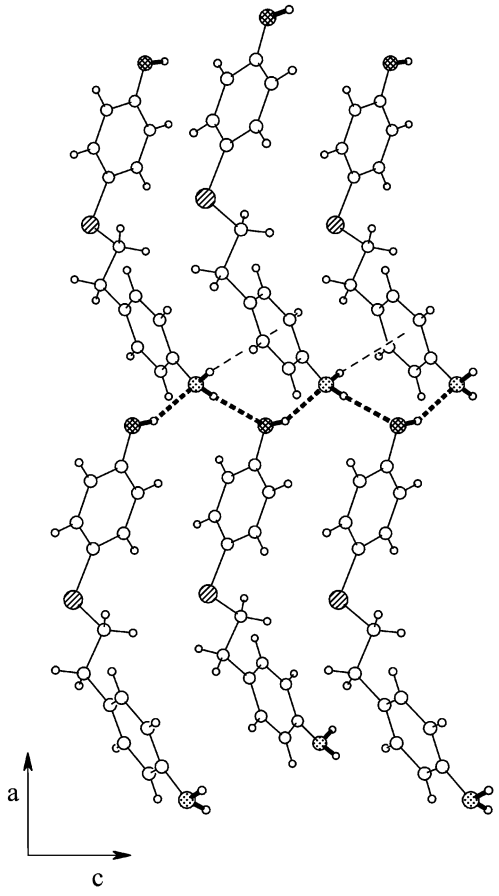


Figure 11. Infinite chain in 4-[2-(4-aminophenylsulfamyl)ethyl]phenol, **3a**. Note the head-to-head arrangement of the molecules within a row. This differs from the head-to-tail arrangement in aminol **3** (Figure 6).

(ring plane angle 75°), while C−H···O and C−H···π interactions also help to hold the sheets together.

Aminol **2c** adopts a very different crystal packing than that of **2**, **2a**, and **2b**. This could be expected, given the pronounced change in molecular geometry caused by the smaller torsion angle about C−S−S−C {83.3(1)°}[23], compared with the 0° torsion around C−C−C−C or C−S−C−C in **2**, **2a**, and **2b**. So **2c** is U-shaped while **2**, **2a**, and **2b** are linear. As in aminol **1**, **2c** can be considered in terms of dimers (Figures 13a and 5a); alternatively it can be considered in terms of the infinite chain. In effect, **2c** contains elements of both the square motif of **1** and the infinite chain of **3** and as such may be considered as bridging these two structural types.

General Discussion of S-Spacer Structures. Three examples of the infinite chain motif have now been observed, 3AP, **3**, and **3a**, as well as the partially cross-linked infinite chains of **5** and the fully cross-linked chains of the β-As sheet structures. The differences between these structures may be rationalized by analyzing the geometries and relative positions of the N(H)O infinite chains. In the following discussion a 2D schematic (Figure 14) of the infinite chains of N(H)O hydrogen bonds is drawn from two different perspectives: from side on (the infinite chain projected on to the *ac* plane of the crystal lattice) and from above (projected on to the *bc* plane). When considered in projection from either direction, the infinite chain takes the form of a zigzag chain of N(H)O bonds. The zigzag of the chain in **3** has twice the repeat unit of **3a** and **5**, with peaks and troughs of the zigzag occurring only at the O-atom, rather than peaks at O and troughs at N as in **3a** and **5**. This affects the relative orientation of the N−H···π hydrogen bonds. In **3**, they form on both sides of the chain, whereas in **3a** and **5**, they form only on one side. In the *bc* plane the situation is different. The repeat unit of the **3a** zigzag is now twice that of **3**. In both **3** and **3a**, the zigzag runs parallel with a peak coinciding with a peak of the chain below. In the β-As sheet, one zigzag chain is offset with relation to the next, allowing a close approach between the O- and N-atoms of adjacent layers and also to the formation of additional cross-linking hydrogen bonds.

The analysis of aminol **5** is complicated by the presence of two molecules in the asymmetric unit. In the *bc* plane two different infinite chains, running in the *c* direction, can be distinguished. Each chain is formed with both A and B molecules. One of the chains (on average consisting of weaker hydrogen bonds) is analogous to the infinite chain seen in **3a**,

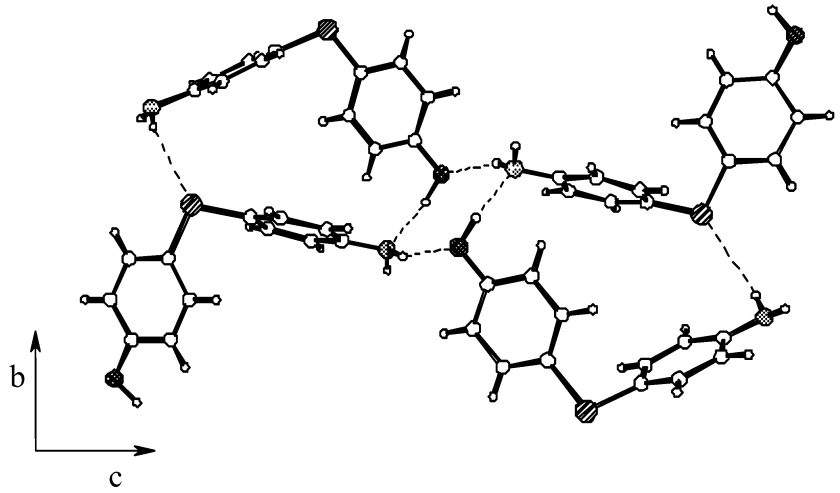


Figure 12. Square motif in 4-(4-aminophenylsulfamyl)phenol, **1a**. A sheet consisting of molecule type A is shown. B molecules form similar sheets, and sheets of type A and type B molecules stack, alternately. Note the windmill type arrangement.

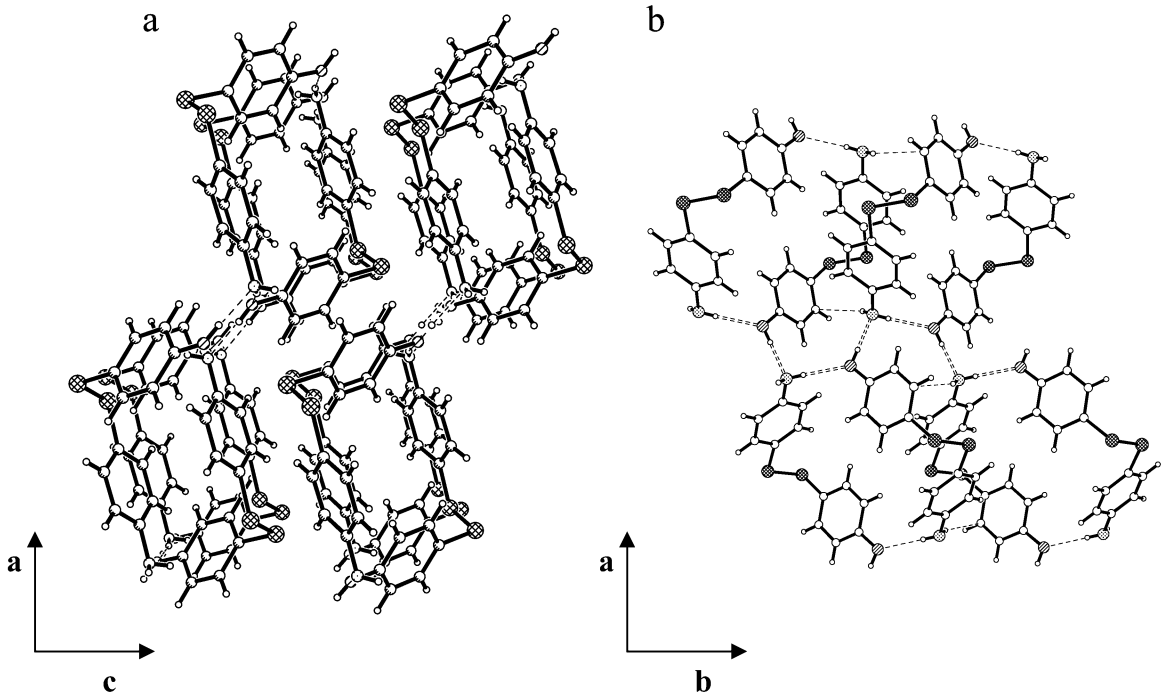


Figure 13. Crystal structure of 4-(4-aminophenyldisulfamyl)phenol, **2c** (a) *ac* plane. Compare this with Figure 5a. (b) *ab* plane showing helical infinite chain of hydrogen bonds.

while the other has a saw-tooth geometry and can be almost be directly mapped onto a section of the β-As sheet (Figure 8).

The length of the *b* axis is directly related to the distance between adjacent chains. The closest approach between two adjacent chains occurs in the β-As sheet where the adjacent chains are cross-linked by additional hydrogen bonds, creating a saturated system. The distance between two adjacent chains of the β-As sheet is approximately 5.2 Å. In **3** the separation between chains is greater at 6.2 Å. In **3a** the separation is closer to that seen in the β-As sheet, at 5.8 Å, while in **5** there is some cross linking between chains with the average separation being 5.6 Å. With two molecule in the asymmetric unit, the length of axis *b* is double the average separation ($2 \times 5.6 = 11.2$).

Two significant points emerge from the study of these sulfur-substituted compounds. First, the relationship between the square motif structure of **1** and the infinite chain structure of **3** can be understood by the study of aminol **2c**. All the compounds studied in this section can be included in either the variable or fixed series already identified. **2c** is considered as a bridging structure between **1** and **3**, and as such lies between them in the series. In the same way, **3a** lies between **3** and **5**.

$$\mathbf{1} \rightarrow \mathbf{2c} \rightarrow \mathbf{3} \rightarrow \mathbf{3a} \rightarrow \mathbf{5} \rightarrow \rightarrow \beta\text{-As:} \quad \text{variable series}$$

$$\mathbf{0} = \mathbf{2} = \mathbf{2a} = \mathbf{2b} = \mathbf{4} = \beta\text{-As:} \quad \text{fixed series}$$

Second, the differences between the infinite chain structures and the β-As sheets are demonstrated, as are the relationships between the unit cell dimensions and the structural synthons formed. Overall, good isostructurality[25] is observed between **2** and its S-analogues, while **3a** is similar to **5**. There is an interplay of geometrical and chemical effects. In **1** and **1a**, where

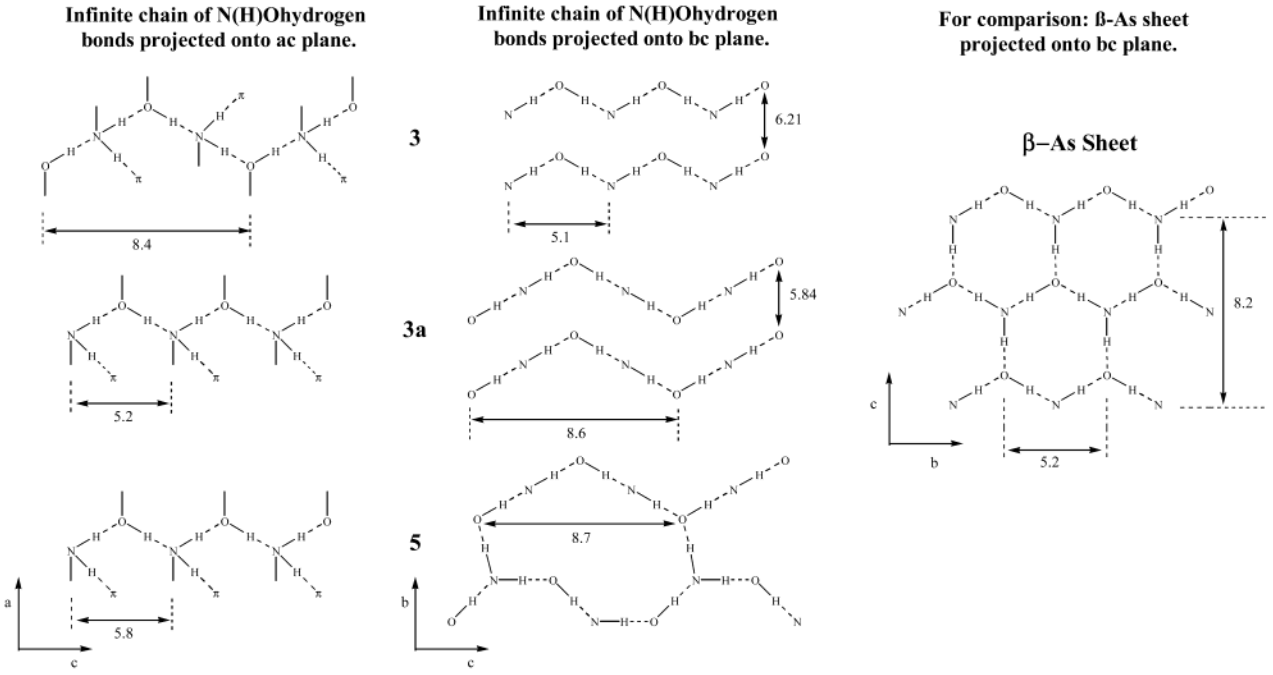


Figure 14. Schematic of the N(H)O infinite chains, showing the similarities and differences of chains in **3**, **3a**, and **5**. The β-As sheet is shown for comparison.

isostructurality is not observed, it is chemical effects that cause the change in structure, with the N−H···π interaction being replaced by an N−H···S. Similarly, the differences between **2** and **2c** can be attributed to the change in torsion angle resulting from the exchange of a CH_2-CH_2 for a S−S group. In the other isostructural cases, the geometrical factors are either consistent with or outweigh the chemical effects.

C. Design Strategies for Crystal Engineering. Crystals are composed of molecules but crystal structures cannot be easily derived or anticipated from molecular structures. Similar molecules can have dissimilar crystal structures and dissimilar molecules can have similar crystal structures. This is because the core constituents of a crystal, the synthons, result from complementary approaches of molecular functional groups. So, the exact pattern formed depends not only on the functional groups present in the molecules but also on their relative juxtapositioning. Successful strategies of crystal engineering are based on the supramolecular synthon approach, which simplifies the complex problem of structure prediction into the simpler problem of network architecture.

The patterns and trends observed so far provide a good understanding of the structural motifs possible for aminols and the geometrical and chemical reasons why one structural synthon is preferred over another. In this section three compounds have been synthesized that are related to, but intrinsically different from, those seen previously. Each compound explores a different aspect of the structural principles discussed above. These structures offer a chance for crystal engineering and, where the design strategy fails, provide further insight into the structural chemistry of these compounds.

(i) Effect of Molecular Shape To Give the β-As Sheet. 4-[(*E*)-2-(4-aminophenyl)-1-ethenyl]phenol, **2d**, and **2** are very similar and the saturated ethane bond of the linker is exchanged for an unsaturated ethene bond. This is but a small chemical change in supramolecular terms and it is not expected that the structure would deviate from the β-As sheet. Indeed, this was found to be the case. Equivalent synthons lead to virtually identical crystal structures. The unit cell dimensions of **2d** are comparable to those of compounds **2**, **2a**, **2b**, and **4**,[25] with the isostructurality parameter (Π) for **2** compared with **2d** of 0.027 (Figure 15).

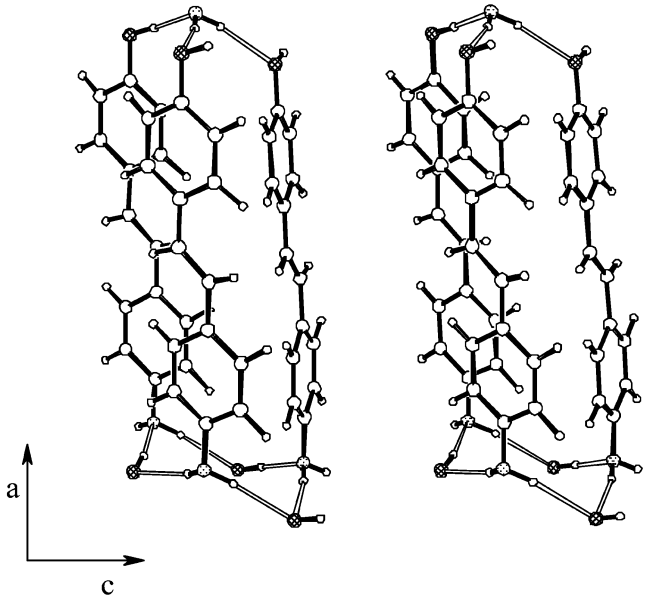


Figure 15. β-As sheet in 4-[(*E*)-2-(4-aminophenyl)-1-ethenyl]phenol, **2d**.

(ii) Substitution: Shape versus Electronic Factors. 4-(4-aminophenoxy)phenol, **1b**, is the O-analogue of **1** and **1a**, and as such it might be expected to form a square motif structure. However, while an S-atom can often be exchanged for a CH_2 group to form an isostructural crystal, the same cannot be said for exchange by oxygen.[27] When the structure of **1b** was determined, it was immediately apparent from the unit cell dimensions that the structural motif was neither that of a square motif nor that of an infinite chain, but the β-As sheet structure

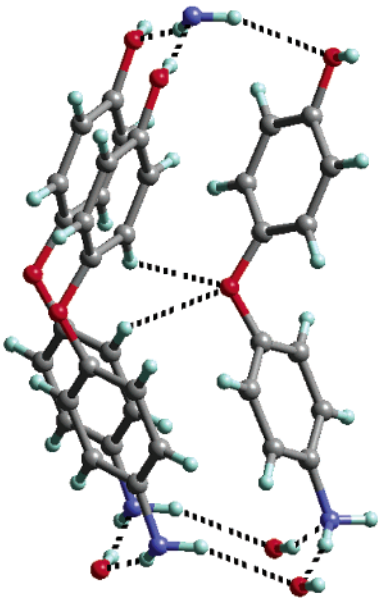


Figure 16. β-As sheet structure of 4-(4-aminophenoxy)phenol, **1b**.

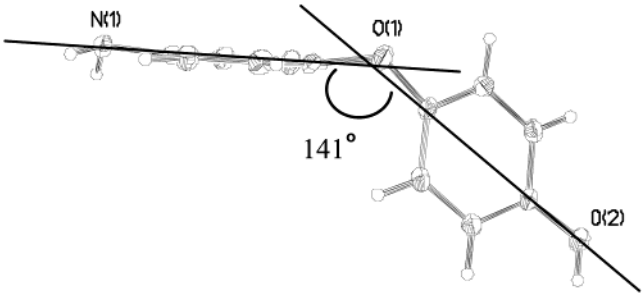


Figure 17. The flexing of **1b** to achieve a large C−O, C−N vector angle. Note that phenolic end of the molecule is also bent to a similar degree.

(Figure 16)! A closer study revealed why such an unlikely result was possible.

First, the geometry of the molecule shows that it has had to distort to obtain as large a C−O, C−N vector angle as possible; while the angle at the oxygen atom (C−O−C) is 120° as expected (for CSD search see Supporting Information), the C−O, C−N vector angle is 141° (Table 1), which is much larger than the corresponding angle seen in any of the infinite chains or square motif structures. To achieve this large C−O, C−N vector angle, the whole molecule is considerably bent (Figure 17). The O-atom is shifted about 0.2 Å out of the plane of each of the phenyl rings. The NH_2 and OH groups are also bent out of the plane of their respective phenyl rings but to a lesser extent (0.1 and 0.06 Å, respectively).

Second, the volume of the O-atom is much less than that of the $-CH_2-$ group or the S-atom (11 $Å^3$ compared to 19.1 $Å^3$ and 22.8 $Å^3$, respectively) and this allows the molecules to fit closer together. Further, while the molecules can pack better than would be possible for the S or CH_2 substituted structures, they cannot pack as closely as the more linear molecules that form β-As sheet structures. This gives rise to an elongation of the two N−H···O hydrogen bonds (and therefore the *b* axis) to

(27) The CSD (Version 5.23, April 2002) was searched for error free C−O−C organic acyclic, aromatic, nonionic, nonpolymeric structures with $R < 0.075$. Disordered structures and those without coordinates were excluded. Of the 418 entries in the subset, four hits with the corresponding C−C−C compounds in the CSD were found of which one set is isostructural (CAKGOK, GUHKUP).

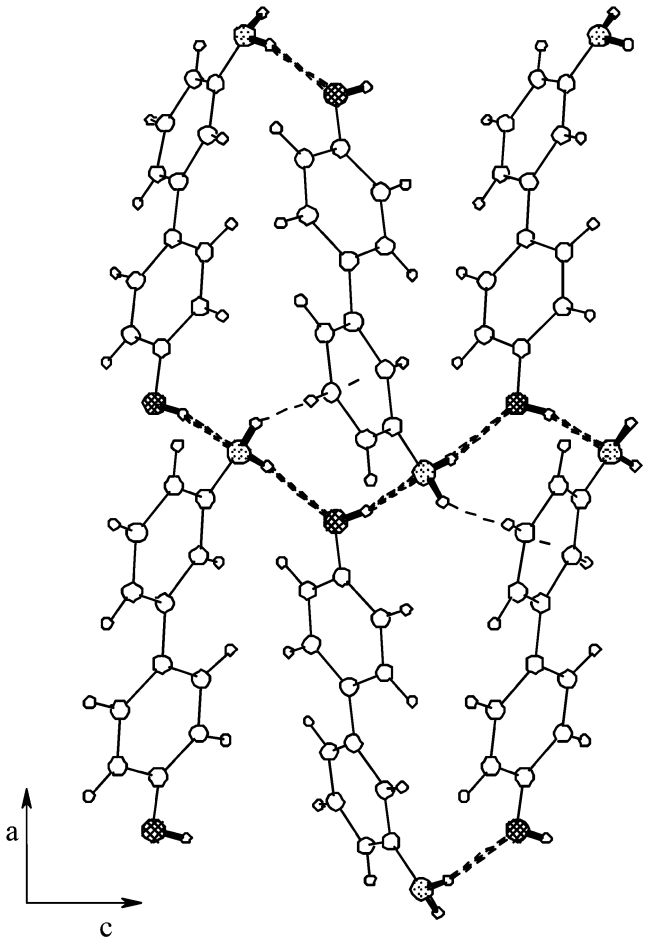


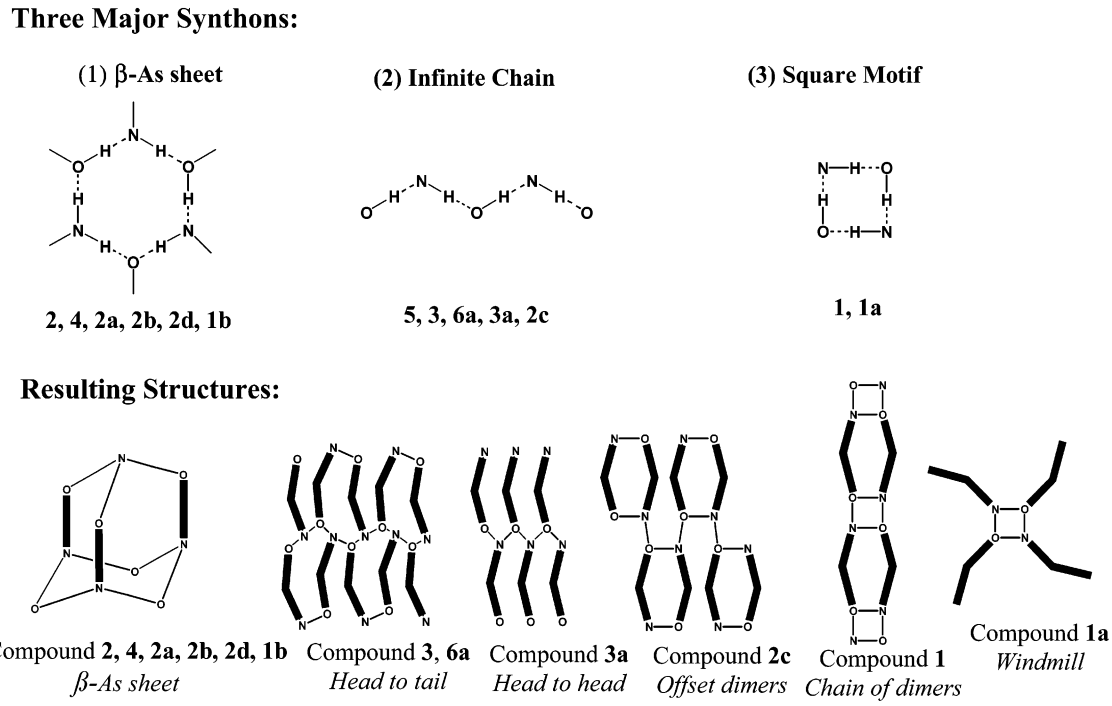
Figure 18. The Infinite chain motif in 4-(3-aminophenyl)phenol, **6a**.

2.3 Å and 2.4 Å, compared with an average value of 2.2 Å and 2.3 Å for the other β-As sheet structures.

Finally, the greater electronegativity of the O-atom relative to $-S-$ and $-CH_2-$ increases the donor ability of the adjacent phenyl hydrogen atoms (for Mulliken charges, see Supporting Information). This promotes the formation of bifurcated C−H···O hydrogen bonds. This is an additional factor in pulling adjacent molecules close together, and rather than being a consequence of the structure, it is more likely to be playing an important role in aligning the molecules so as to achieve the β-As structure (Figure 16). This illustrates the role of chemical influences. For example, if molecules of **1** were aligned in the same way, there would be repulsion between the methylene H- and aromatic H-atoms.

When chemical factors within the odd series are considered, the structures can be seen to tend toward the β-As sheet as the electronegativity increases. By replacement of $-CH_2-$ by an S-atom, i.e., a slight increase in electronegativity, the structure of compound **1a** is a square motif with additional C−H···S hydrogen bonds that change the motif to a windmill arrangement. This might suggest that aminol **1b** (with a greater increase in electronegativity) could be found as either a structure similar to **1a** or an infinite chain type structure. But interestingly, **1b** exceeded our predictions in achieving the target structure, i.e., a β-As sheet structure even within the $n =$ odd series. It is a matter of speculation whether extensions of the series **1** to **5** with $n = 7, 9$ would adopt the β-As sheet structure.

Scheme 2. β-As Sheet, Infinite Chain, and Square Motif Synthons[a]



0 = 2 = 4 = 2a = 2b = 2d = 1b ← ← 5 ← 3a ← 3 ~ 6a ← 2c ← 1 → 1a

[a] N−O represents the N(H)O hydrogen bond, i.e., either an O−H···N or an N−H···O hydrogen bond. Thick lines represent the hydrocarbon fragment of the molecule.

(iii) Effect of Molecular Shape To Give the Infinite Chain. Kitaigorodskii's close-packing principle[19] states that mutual recognition between molecular shapes is the key element in understanding the packing of molecular crystals. Given that 4-(3-aminophenyl)phenol, **6a**, has nearly the same shape as **3**, especially with respect to the all-important −OH and $-NH_2$ groups, we predicted that its crystal structure would contain the infinite chain motif. This prediction was borne out in practice. Aminol **6a** has a molecular geometry comparable with that of 3AP and **3**. The angle between the C−O and C−N vectors is 121° compared to 121° for 3AP and 124° for **3**. The value of Π for **6a** in relation to **3** is 0.15. The crystal packing motif is identical, and it is only the molecular length that varies. This is reflected in the change in length of *a* axis (Figure 18 cf. Figure 6). The N−H···π bond is slightly weaker than that seen for **3** (2.51 Å, 143.7°).

Conclusions

Scheme 2 summarizes the structural features in this family of compounds. A partial success has been achieved in the prediction of structural motifs of these aminols. The structures of two of the three compounds studied with crystal engineering considerations in mind (**2d**, **6a**) could be anticipated reasonably well. That the structure of **1b** could not be predicted is not particularly disappointing, and the observed structure actually provides more useful information. Aminol **1b** illustrates the geometric limits to which the β-As sheet structure can be pushed and a stable structure still obtained and demonstrates that molecular linearity is *not* a prerequisite for β-As sheet adoption. The lattice energy calculations (Table 1) indicate that **1b** is slightly less stable that the other β-As sheet structures but more stable than the square motif structures.

We feel that a good level of understanding has now been obtained for these supraminol systems. The infinite chain is the key synthon in this family. The way in which the fixed and the variable series relate to each other is also clearly understood:

1a ← 1 → 2c → 3 ~ 6a → 3a → 5 → → 1b = 0 = 2 = 2a = 2b = 2d = 4 = β-As

Variable → Fixed

It is noteworthy that the synthons discussed here are all constructed from a combination of O−H···N and N−H···O hydrogen bonds and that nowhere in these structures do O−H···O or N−H···N hydrogen bonds occur.

From this work a number of further avenues of exploration present themselves: (1) It would be interesting to extend the 4-amino-4′-hydroxybiphenyl-*n*-alkanes series to include the hexane and heptane derivatives (n = 6 and 7). The n = 6 compound would surely take the β-As structure, since it is the next compound in the fixed series. However, is the n = 7 compound flexible enough to obtain the β-As sheet structure, or will it form another bridging structure such as compound **5**? (2) A study of the 4-amino-3-hydroxy analogues of **6a** would be interesting. Would these compounds crystallize with the infinite chain motif? (3) The structure of **1b** raises the question of the effect of steric influences on the crystal structure obtained. Could a β-As sheet be disrupted by a sterically bulky group? If so, what structure would then be obtained? (4) In general it should be mentioned that polymorphism is a rare phenomenon in aminophenols. Why is this the case, and could polymorphism eventually be found in this family of structures? (5) In all the supraminols discussed in this paper, the N atoms of the anilino functionality are distinctly pyramidal (Table 1). Is this the driving force for the formation of both β-As sheet and N−H·

$\cdot\cdot\pi$ containing structure types? (6) With the correspondence between molecular and crystal structure now being understood for this group of compounds, we conclude that aminophenols are amenable to the principles of crystal engineering.

These issues are presently being studied.

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Supporting Information Available: Synthetic procedures, hydrogen bond geometries, additional structural details, additional figures, NIPMAT plots, simulated powder spectra, tables of crystal data, structure solution and refinement, atomic coordinates, bond lengths and angles, and anisotropic parameters for **1** (X and N), **2**−**5**, **1a**, **2a**, **2b**, **2c**, **3a**, **1b**, **2d**, and **6a** (PDF). This material is available free of charge via the Internet at http://www.pubs.acs.org.

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