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Hydrogen-Bond Patterns in Several 2:1 Amine–Phenol Cocrystals

James H. Loehlin,* Margaret C. Etter, Christina Gendreau,[1] and Erika Cervasio[2]

Departments of Chemistry, Wellesley College, Wellesley, Massachusetts 02181, and University of Minnesota, Minneapolis, Minnesota 55455

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This is a report on the structures of four cocrystals containing a difunctional amine or phenol with phenol or aniline, respectively. Three different hydrogen-bond patterns are observed and analysed. The materials are piperazine·2phenol, $C_4H_{10}N_2\cdot 2(C_6H_6O)$, $P2_1/n$, $a = 6.750(1)$ Å, $b = 16.651(2)$ Å, $c = 7.017(3)$ Å, $\beta = 100.49(3)°$, $Z = 2$; *trans*-2,5-dimethylpiperazine·2phenol, $C_6H_{14}N_2\cdot 2(C_6H_6O)$, $P2_1/c$, $a = 6.481(9)$ Å, $b = 19.371(9)$ Å, $c = 7.270(3)$ Å, $\beta = 104.2(1)°$, $Z = 2$; ethylenediamine·2phenol, $C_2H_8N_2\cdot 2(C_6H_6O)$, *Pbca*, $a = 18.125(5)$ Å, $b = 7.842(3)$ Å, $c = 9.815(7)$ Å, $Z = 4$; hydroquinone·2aniline, $C_6H_6O_2\cdot 2(C_6H_7N)$, $P2_1/c$, $a = 18.744(4)$ Å, $b = 5.386(1)$ Å, $c = 8.219(2)$ Å, $\beta = 102.49(3)°$, $Z = 2$.

Introduction

This study was initiated as an exploration of host–guest compounds in which a polyfunctional central "host" molecule organized "guest" molecules around it via hydrogen bonding. This is essentially the inverse of the usual host–guest situation in which the guests are accommodated in a cavity created by the host. Although separate clusters are conceivable, most of the combinations tried, including those reported here, appear to find ways to link into a larger network. The materials in the present study all have only amine or hydroxyl groups, each of which participates as both donor and acceptor in hydrogen bonding. If these functional groups hydrogen bond in a linear chain arrangement, they have the potential to allow proton transfer along the chain and through the crystal.[3] These crystals are part of a study of materials which might form proton-transfer chains.[4] Analysis of the hydrogen-bond patterns can also serve as a guide when attempting to control the arrangement of molecules in the solid state for this or other purposes, such as attempts to design acentric structures with nonlinear optical properties.

Experimental Section

All the components of the cocrystals and the solvents used were commercially available and used without further purification as starting materials, except as indicated. Since all of these cocrystals seemed to degrade slowly when left in the open, all data were gathered from crystals sealed into glass capillaries. Both crystal growth and data collection were carried out at room temperature.

Piperazine·2phenol ($C_4H_{10}N_2\cdot 2(C_6H_6O)$). Crystals were grown by slow evaporation following mixing stoichiometric amounts of separate acetone solutions of the two components.

***trans*-2,5-Dimethylpiperazine·2phenol ($C_6H_{14}N_2\cdot 2(C_6H_6O)$).** Upon recrystallization from acetone of commercially available *cis-,trans-* mixed-isomer 2,5-dimethylpiperazine, small prisms and large hexagonal plates were obtained. Cocrystals were obtained by placing a hexagonal plate and phenol crystals separately in a closed vial. Long chains of linked diamond-shaped crystals grew overnight by dual vapor diffusion nearer the less volatile piperazine; mp = 86–88 °C.

Ethylenediamine·2phenol ($C_2H_8N_2\cdot 2(C_6H_6O)$). Stoichiometric amounts of the components were mixed forming a solution which then solidified at room temperature. Single crystals were grown by slow evaporation from a diethyl ether solution of the solid. The cocrystals melted at about 55 °C.

Hydroquinone·2aniline ($C_6H_6O_2\cdot 2(C_6H_7N)$). Crystals were grown from stoichiometric mixture which was dissolved in 3:1 diethyl ether:toluene and allowed to evaporate slowly. Sample was cut from a hexagonal plate; mp = 90–93 °C.

Structure Determination and Refinement. Data were collected for crystals **1–3** on an Enraf-Nonius CAD-4 diffractometer, while **4** used a Siemans R3m/V diffractometer, using graphite-monochromated Mo Kα radiation $\lambda = 0.710\,73$ Å. Data were corrected for Lorentz and polarization effects and in the case of **4** for crystal degradation of 10%. The structures were solved using direct methods and refined utilising TEXSAN,[5] SHELX,[6] and XTAL[7] program packages. The final weighting of reflections used $1/w = \sigma^2(F) + n(F_{obs})^2$, with n values shown along with refinement results in Table 1.

In each of these structures, except **2**, all non-hydrogen atoms were refined with anisotropic displacement parameters in the final stages of refinement. All hydrogen atoms were found in difference maps, but those on phenyl rings were put in at calculated positions 1.08 Å from carbon and not refined. All hydrogen atom displacement parameters were held fixed. Because of the paucity of data for **2** and the focus of interest, its phenyl group was refined as a rigid body (C–C = 1.395 Å) with isotropic carbon displacement parameters. All but hydrogen-bonding hydrogen atoms were in calculated positions, riding model (C–H = 0.95 Å).

Discussion of Structures and Hydrogen-Bond Patterns

In each of these structures, the difunctional moiety is located at a center of inversion. The only unusual feature of the covalent bonding in the molecular constituents is that the aniline amine hydrogens are further than previously reported from the plane of the molecule, in an

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* To whom correspondence should be addressed at Wellesley College.

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(1) Present address: Stonehill College, North Easton, MA.

(2) Present address: Intel Corp., San Jose, CA.

(3) Vanderkooy, J.; Cuthbert, J. D.; Petch, H. E. *Can. J. Phys.* **1964,** *42,* 1871–1878.

(4) Loehlin, J. H. *Acta Crystallogr.* **1985,** *C41,* 210–212.

(5) *TEXSAN-TEXRAY Structure Analysis Package,* Molecular Structure Corp., 1985.

(6) Sheldrick, G. M. *Acta Crystallogr.* **1990,** *A46,* 467–473.

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0897-4756/94/2806-1218$04.50/0

Table 1. Crystallographic Refinement Parameters

	1	2	3	4
crystal size (mm)	0.40 × 0.50 × 0.28	0.30 × 0.30 × 0.15	0.50 × 0.50 × 0.30	0.35 × 0.50 × 0.50
color	colorless	colorless	pale yellow	tan
independent reflns	1364	1388	1459	1803
used in refinement	1064	550	684	1191
($F_{obs} > n(\sigma_F)$), n	3	2	2	4
params refined	109	64	91	109
R, wR	0.055, 0.065	0.072, 0.082	0.054, 0.057	0.052, 0.056
all reflns	0.069, 0.069		0.105, 0.070	0.094, 0.076
n (wt eqn)	0.0025	0.0025	0.0025	0.0008
goodness of fit	1.20	2.03	1.32	1.38
shift/error (max)	0.02	0.01	0.03	0.0003
difference map (max/min, e/Å^3)	0.2, −0.3	0.30, −0.36	0.20, −0.31	0.3, −0.6

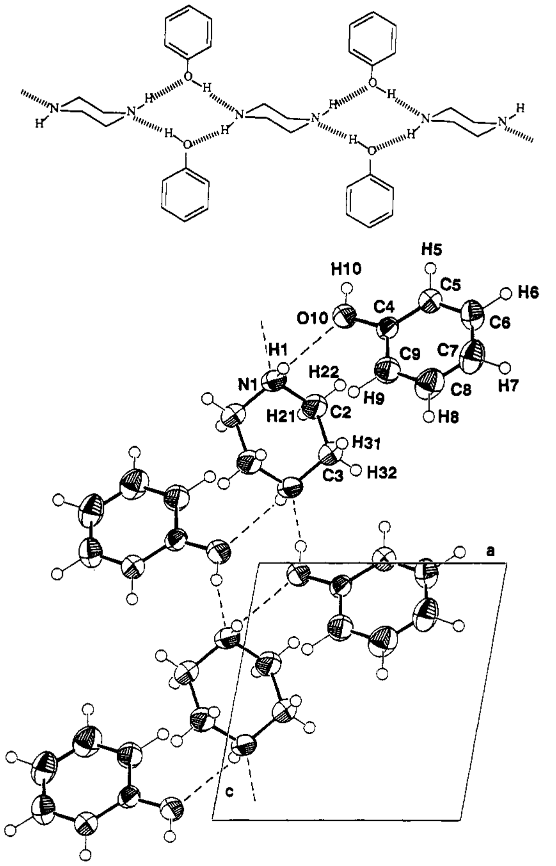

Figure 1. (a) Hydrogen-bond pattern for piperazine·2phenol. (b) ORTEP plot showing the molecular packing and the atomic numbering system used.

approximately tetrahedral orientation consistent with an sp^3 hybrid model.

In the two piperazine/phenol cocrystals (**1**, **2**), two phenols hydrogen bond to each nitrogen atom, one acting as proton donor and the other as an acceptor for the amine hydrogen. Each phenol then forms a second hydrogen bond with the next piperazine ring. The resulting structure is a chain of piperazine rings linked by phenol molecules in hydrogen-bonded rings. The amine hydrogens are in axial orientations on the piperazine rings with the lone-pair acceptor in equatorial orientation. In the dimethylpiperazine, the methyl groups are in equatorial positions. These chains parallel *c* in **1** and *a* in **2** and are almost identical. The direction of the glide operation which relates the chains to each other, however, differs by about 55°, so that the way the chains pack together in the two structures is quite different. The hydrogen bonds in cocrystals **1** and **2** are, respectively, OH- -N 2.682(3) and 2.685(8) Å, and NH- -O 3.075(4) and 3.115(8) Å. The graph sets[8] for these two cocrystals are identical: $N_1 = D_2^2(7)\ D_2^2(5)$, $N_2 = R_4^4(8)\ 2C_2^2(7)$. See Figures 1 and 2 and Tables 2 and 3 for the numbering systems, hydrogen-bond patterns, and atomic coordinates for **1** and **2**, respectively. For all experimentally determined parameters, in tables and text, the estimated standard deviation in the last given digit is shown in parentheses following the value.

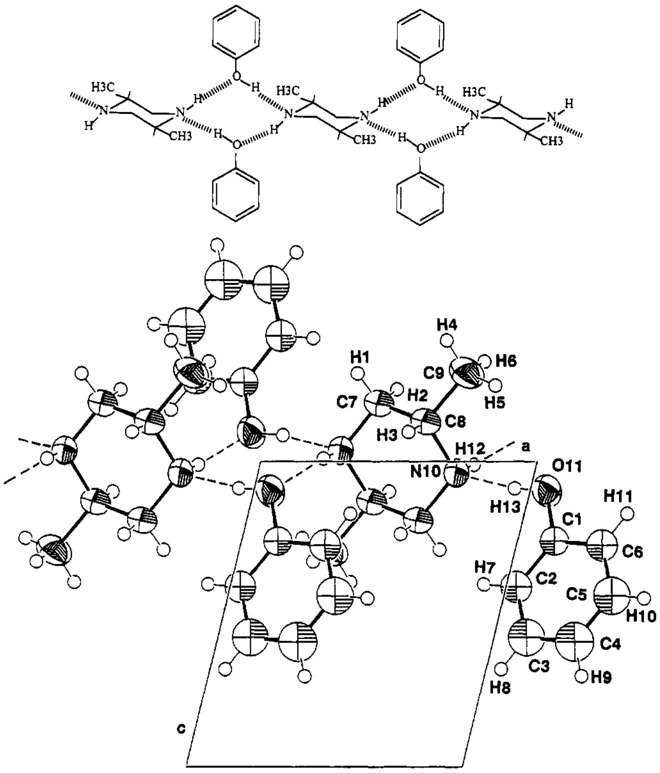

Figure 2. (a) Hydrogen-bond pattern (dashed line) for dimethylpiperazine·2phenol. (b) ORTEP plot of the crystal showing the molecular packing and the atomic numbering system used.

The ethylenediamine/phenol cocrystal **3** also has each amine hydrogen bonded as both donor and acceptor to two separate phenol molecules using only one of its hydrogens as a donor, but in this case the two phenols bridge to the ends of adjacent ethylenediamine molecules along the *b* axis. The infinite, NH- -OH- - chains form a spiral around a 2_1 axis parallel to *b* and are linked by alternating diamine "rungs" to form a hydrogen-bonded sheet perpendicular to *a*. Hydrogen bond lengths are OH- -N = 2.681(4) Å and NH- -O = 3.135(4) Å. The graph sets are $N_1 = D_2^2(7)\ D_2^2(5)$, $N_2 = R_8^8(22)\ C_2^2(7)\ C_2^2(4)$. Figure 3 and Table 4 show the hydrogen-bond pattern, crystal packing, numbering system, and atomic coordinates for **3**.

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[8] Etter, M. C.; MacDonald, J. C.; Bernstein, J. *Acta Crystallogr.* 1990, *B46*, 256–262.

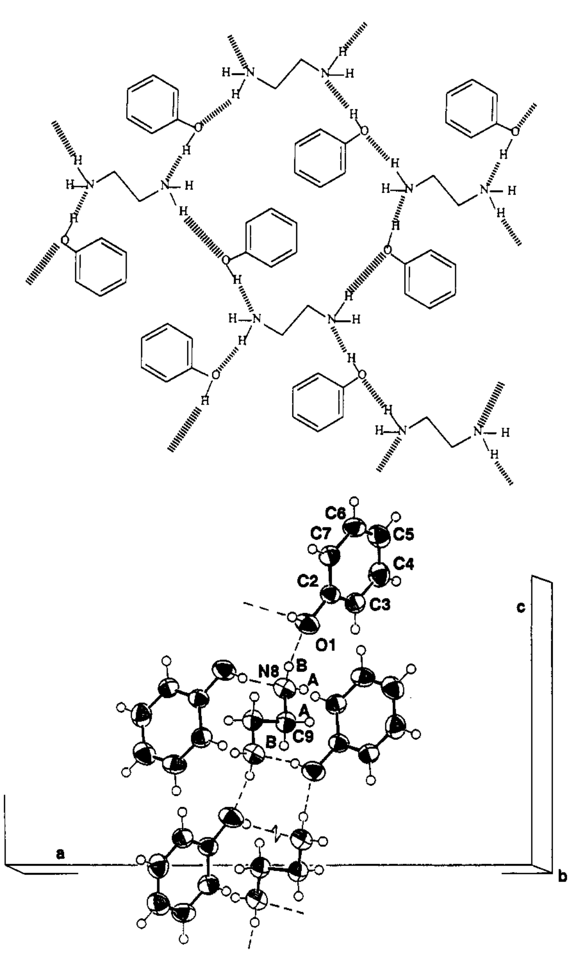

Figure 3. (a) Diagram of the hydrogen-bond pattern for ethylenediamine·2phenol. (b) ORTEP plot of the structure showing the unit cell, molecular packing, and the atomic numbering system. Hydrogen atoms use the number of the attached atom.

Table 2. Atomic Positional and Isotropic Displacement Parameters for Piperazine·2phenol

atom	*x*/*a*	*y*/*b*	*z*/*c*	*U*
N1	0.0723(3)	0.5095(1)	0.7077(2)	*0.0473(6)
C2	−0.1126(4)	0.5488(2)	0.6082(3)	*0.0563(9)
C3	−0.2112(3)	0.5048(2)	0.4260(3)	*0.0516(8)
C4	0.3501(3)	0.6268(1)	0.0900(3)	*0.0403(6)
C5	0.5034(3)	0.6176(1)	−0.0153(3)	*0.0458(7)
C6	0.6835(3)	0.6586(2)	0.0397(3)	*0.0572(9)
C7	0.7115(4)	0.7084(2)	0.2009(4)	*0.066(1)
C8	0.5585(4)	0.7167(2)	0.3052(4)	*0.0660(9)
C9	0.3785(3)	0.6766(1)	0.2517(3)	*0.0538(8)
O10	0.1699(2)	0.5889(1)	0.0433(2)	*0.0551(6)
H1	0.042(3)	0.460(1)	0.755(3)	0.045
H21	−0.071(3)	0.604(1)	0.579(3)	0.045
H22	−0.199(3)	0.558(1)	0.691(3)	0.045
H31	−0.251(3)	0.451(1)	0.466(3)	0.045
H32	−0.326(3)	0.537(1)	0.361(3)	0.045
H10	0.158(3)	0.563(1)	−0.065(4)	0.045
H5	0.4822	0.5788	−0.1401	0.045
H6	0.8025	0.6515	−0.0430	0.045
H7	0.8516	0.7402	0.2438	0.045
H8	0.5799	0.7554	0.4306	0.045
H9	0.2596	0.6839	0.3348	0.045

Table 3. Atomic Positional and Isotropic Displacement Parameters for Dimethylpiperazine·2phenol

atom	*x*/*a*	*y*/*b*	*z*/*c*	*B*(eq)
O11	0.4393(7)	0.1052(2)	0.4042(6)	4.6(2)
C1	0.3677(7)	0.1390(2)	0.2399(5)	3.7(2)
C2	0.4628(6)	0.1332(2)	0.0880(6)	4.4(2)
C3	0.3818(8)	0.1703(3)	−0.0785(5)	6.0(2)
C4	0.2057(8)	0.2133(2)	−0.0931(5)	6.7(2)
C5	0.1107(7)	0.2191(2)	0.0588(7)	6.2(2)
C6	0.1917(7)	0.1819(2)	0.2253(6)	4.5(2)
N10	0.781(1)	0.0220(3)	0.4631(8)	3.7(3)
C7	0.877(1)	0.0030(4)	0.3086(9)	4.1(3)
C8	0.938(1)	0.0468(3)	0.631(1)	4.0(3)
C9	0.832(1)	0.0609(4)	0.791(1)	5.9(4)
H1	0.7713	−0.0180	0.2107	4.9
H2	0.9271	0.0438	0.2614	4.9
H3	0.9927	0.0893	0.5986	4.8
H4	0.9336	0.0795	0.8964	7.1
H5	0.7192	0.0929	0.7497	7.1
H6	0.7768	0.0190	0.8274	7.1
H7	0.5827	0.1039	0.0979	5.3
H8	0.4465	0.1664	−0.1820	7.2
H9	0.1505	0.2386	−0.2065	8.1
H10	−0.0092	0.2483	0.0489	7.4
H11	0.1269	0.1859	0.3287	5.5
H12	0.72(1)	−0.012(3)	0.49(1)	4.5
H13	0.56(1)	0.078(3)	0.413(9)	5.5

Table 4. Atomic Positional and Isotropic Displacement Parameters for Ethylenediamine·2phenol

atom	*x*/*a*	*y*/*b*	*z*/*c*	*B*(eq)
O1	0.5691(1)	0.0930(3)	0.1628(2)	4.8(1)
C2	0.6150(2)	0.0377(4)	0.0632(2)	3.5(1)
C3	0.6670(2)	−0.0833(5)	0.0971(3)	4.1(2)
C4	0.7155(2)	−0.1436(5)	0.0011(4)	5.0(2)
C5	0.7127(2)	−0.0829(5)	−0.1310(4)	5.0(2)
C6	0.6609(2)	0.0370(5)	−0.1651(3)	4.4(2)
C7	0.6116(2)	0.0979(4)	−0.0701(3)	3.8(2)
N8	0.5359(2)	−0.1760(4)	0.3911(3)	4.1(1)
C9	0.5337(1)	−0.0551(4)	0.5049(3)	3.8(1)
H1	0.537(2)	0.178(4)	0.138(3)	4.8
H3	0.6692	−0.1256	0.1877	5.0
H4	0.7512	−0.2270	0.0255	5.9
H5	0.7463	−0.1243	−0.1976	6.0
H6	0.6591	0.0791	−0.2559	5.3
H7	0.5755	0.1802	−0.0953	4.6
H8A	0.574(2)	−0.240(4)	0.396(3)	5.0
H8B	0.542(2)	−0.121(4)	0.314(3)	5.0
H9A	0.5764	0.0152	0.5021	4.6
H9B	0.5327	−0.1162	0.5884	4.6

The hydroquinone/aniline cocrystal 4 also forms infinite hydrogen-bonded sheets, but in this case they are double layered, in the *bc* plane with the hydroquinone molecules linking the layers. In this structure each $-OH$ and $-NH_2$ participates in three hydrogen bonds to neighboring N and O atoms. Thus each oxygen uses both lone pairs and its hydrogen, and each amine uses both hydrogens and its lone pair and each hydroquinone is linked to six different aniline molecules. This arrangement with three hydrogen bonds to every nitrogen and oxygen is quite unusual. It approaches the complexity of the hydrogen-bond network in ice, where each oxygen atom participates in four hydrogen bonds, the maximum possible number. The hydrogen bonds are OH- -N = 2.804(4) Å, NH- -O = 3.142(4) Å and 3.349(9) Å. This structure's graph sets are $N_1 = 2D_2^2(7)\ D_2^2(9)$, $N_2 = 3R_4^4(18)\ R_6^6(12)\ 2C_2^2(4)$.[9] Near the final model, one of the largest peaks in the Fourier difference map was near the position which would be expected for the third hydrogen on an anilinium ion. Attempts to model this structure did not refine satisfactorily, though there were hints that this third position might be populated at 25% or less. Whether or not this is real and, if real, whether it is the result of proton transfer or of orientational disorder of the amine hydrogens is not clear.

With the exception of the hydrogen-bonding hydrogen and the nitrogen atoms, all atoms of both the hydroquinone

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(9) Several aspects of the graph-set analysis of this structure are not adequately addressed by the original set of guidelines.[8] Several modifications to the original rules to deal with some of the shortcomings discovered to date are being proposed in a paper currently in preparation by J. Bernstein, R. E. Davis, L. Shimoni, and N. L. Chang.

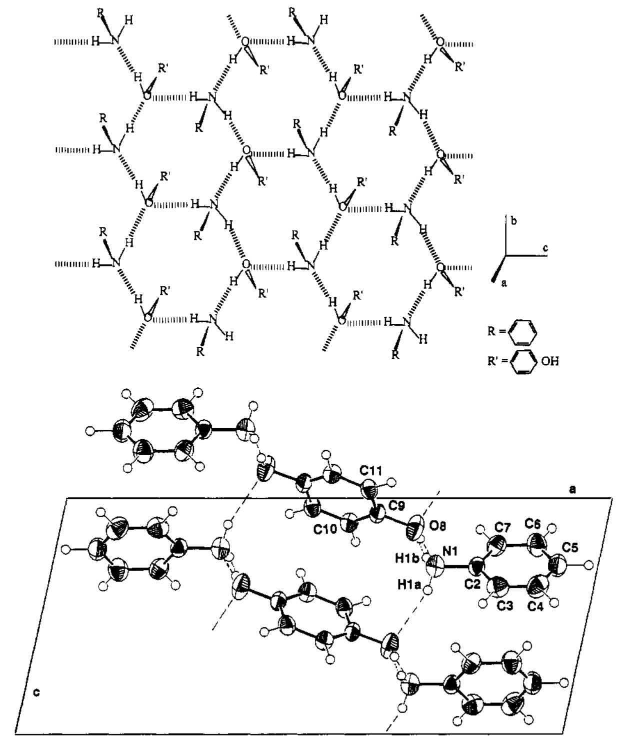

Figure 4. (a) Diagram of one layer of the hydrogen-bond pattern for hydroquinone·2aniline. Hydroquinones lie below this plane and form a parallel, symmetric plane with other anilines. The anilines shown lie with their phenyl rings above this plane. (b) ORTEP plot perpendicular to 4a showing the unit cell, packing arrangement and numbering system used. Hydrogen atoms have the number of the attached atom.

and aniline molecules lie within about 0.002 Å of the least-squares molecular planes. The hydroxyl hydrogen is 0.19(4) Å and the amine hydrogens lie 0.23(4) Å and 0.44(4) Å opposite the nitrogen −0.033(7) Å from the planes in hydroquinone and aniline. Figure 4a shows the hydrogen-bond pattern in one layer. Figure 4b shows the numbering system used and an a–c projection of the crystal packing. The longest hydrogen bond is in the *b* direction and might be questioned on the basis of length alone. The geometry, however, clearly shows that the amines as well as the hydroxyls are in an almost ideal tetrahedral pattern of hydrogen atoms with nearly linear hydrogen bonds. Table 5 shows the atomic coordinates for this cocrystal. The aniline molecule, with nitrogen having tetrahedral geometry and a 1.436(4) Å C–N bond, appears significantly different from other reported aniline structures.

Cocrystals of 1,4-phenylenediamine with two molecules of phenol have also been made. This material is identical except for the interchange of amine and hydroxyl groups. It appears essentially isostructural with hydroquinone·2aniline, but detailed crystallographic structure determination has not yet been completed.

Fukuyo et al.[10] have determined the aniline structure at 252 K. It has two independent molecules with nitrogen atoms acting both as hydrogen-bond donor and acceptor, graph set $C_2^2(2)$. The carbon–nitrogen bond lengths are shorter (1.398(6) and 1.386(6) Å); the molecules are midway between tetrahedral and trigonal planar geometry with nitrogen further and hydrogen atoms much closer to the least-squares plane of the phenyl ring than we observe. The aniline cocrystals with substituted phenols studied by Van Bellingen et al.[11] show none of the hydrogen atoms. The cocrystal with pentachlorophenol they interpret as that of an anilinium ion, with C–N = 1.48(2) Å, forming an almost symmetrical and planar chain of -HNH- -O- hydrogen bonds (N- -O = 2.72, 2.60 Å) but suitable locations for the anilinium hydrogen atoms present a problem. Their trichlorophenol aniline cocrystal, with C–N = 1.44(1) Å, forms individual $R_4^4(8)$ rings similar to our piperazine/phenol cocrystals (NH- -O = 3.13 Å, OH- -N = 2.78 Å).

Table 5. Atomic Positional and Isotropic Displacement Parameters for Hydroquinone·2aniline

atom	*x*/*a*	*y*/*b*	*z*/*c*	*U*
N1	0.7010(2)	0.5113(7)	0.2886(5)	*0.0567
O8	0.6485(1)	0.9533(6)	0.1259(4)	*0.0610
C2	0.7778(2)	0.5067(8)	0.2901(5)	*0.0410
C3	0.8238(2)	0.6831(9)	0.3759(6)	*0.0526
C4	0.8972(2)	0.6800(9)	0.3731(6)	*0.0613
C5	0.9253(2)	0.5023(9)	0.2848(6)	*0.0567
C6	0.8793(2)	0.3249(9)	0.1974(6)	*0.0563
C7	0.8055(2)	0.3285(8)	0.2009(6)	*0.0490
C9	0.5740(2)	0.9712(8)	0.0650(5)	*0.0401
C10	0.5251(2)	0.7993(8)	0.1030(5)	*0.0407
C11	0.5490(2)	1.1704(8)	−0.0371(5)	*0.0426
H3	0.8026	0.8245	0.4458	0.040
H4	0.9331	0.8196	0.4412	0.040
H5	0.9828	0.5012	0.2838	0.040
H6	0.9005	0.1845	0.1267	0.040
H7	0.7695	0.1896	0.1325	0.040
H10	0.5443	0.6440	0.1838	0.040
H11	0.5875	1.3038	−0.0658	0.040
H1a	0.696(2)	0.569(6)	0.390(4)	0.040
H1b	0.681(2)	0.353(6)	0.252(4)	0.040
H8	0.662(2)	0.803(6)	0.171(4)	0.040

Though all of these materials form linear or two-dimensional aggregates linked by hydrogen bonds across which protons might be transferred from donor to acceptor in a concerted manner, **1** and **2** with closed-loop $R_4^4(8)$ arrangement would not allow macroscopic proton transfer. Long-range proton transfer might be possible along the $C_2^2(4)$ chains in cocrystals **3** and **4**.

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Supplementary Material Available: Lists of bond distances and angles and anisotropic displacement parameters for compounds 1, 2, 3, and 4 (includes least squares planes and hydrogen-bond geometry) (14 pages); list of observed and calculated structure factors (36 pages). Ordering information is given on any current masthead page.

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[10] Fukuyo, M.; Hirotsu, K.; Higuchi, T. *Acta Crystallogr.* **1982**, *B38*, 640–643.

[11] Van Bellingen, I.; Germain, G.; Piret, P.; Van Meerssche, M. *Acta Crystallogr.* **1971**, *B27*, 553–559, 560–563.