1-Aryl-3-(dimethylamino)propenones: Strong Proton Acceptors for Hydrogen Bonds

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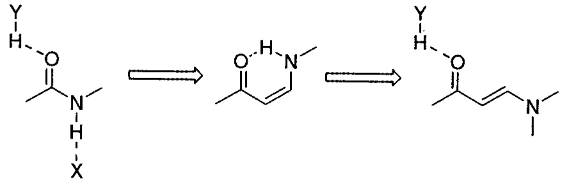
Because of the electron-donating effects of their terminal dimethylamino groups, the carbonyl units of 1-aryl-3-(dimethylamino)prop-2-en-1-ones are excellent proton acceptors. Intra- and intermolecular hydrogen bonds formed by these species were investigated by structural techniques (X-ray and neutron diffraction), spectroscopy, and density functional calculations. Co-crystallization of a derivative bearing three (dimethylamino)prop-2-en-1-one units attached at one center in the presence of different proton donors produced one- and two-dimensional H-bridged polymers.

Introduction

Intermolecular interactions such as hydrogen bonding, Lewis acid/base interactions, or aromatic π-stacking have for a long time attracted the attention of researchers in chemistry, biology, and materials sciences. Hydrogen bonds in particular have been found to be of fundamental relevance for the world we are living in. Starting from small molecules such as water[1] and extending to large biopolymers such as proteins[2] or DNA,[3] the chemical and physical properties of our environment are determined by hydrogen bonding. During the last few years, increasing efforts have been made to gain better understanding of these phenomena. An excellent review of hydrogen bonding in the solid state was recently published by Steiner.[4]

The secondary structures of proteins are governed mainly by the hydrogen-bonding properties of the amide units [−C(O)−N(H)−], the oxygen atom of the carbonyl group acting as a proton acceptor and the NH fragment as a proton donor. In this special case, the capability to form hydrogen bonds is enhanced by a cooperative effect, best described by a second mesomeric form carrying charges at both the oxygen (negatively polarized) and the nitrogen atom (positively polarized). Owing to their importance for the structural and functional features of proteins, the amide group and its hydrogen bonds have long been a matter of investigation. Switching from an amide to its vinylogue counterpart, a 3-aminoprop-2-enone, changes the situation completely. Whenever the nitrogen atom bears a proton, an intramolecular hydrogen bond will be favored, due to the formation of a stable six-membered ring (Scheme 1). Consequently, intermolecular hydrogen bonds are disfavored.



Scheme 1

Use of the 3-aminoprop-2-enone fragment for the formation of intermolecular hydrogen bonds requires substitution of the NH proton(s) by, for example, alkyl groups, which obviously kills the proton donor site but on the other hand enhances the proton-accepting properties of the carbonyl function through the σ-donating effect of the alkyl groups.

In this paper we present a study on the proton-bonding properties of 1-aryl-3-(dimethylamino)prop-2-en-1-ones and their application for the formation of polymeric structures built up by hydrogen bonds.

Results and Discussion

Aromatic 3-(dimethylamino)prop-2-en-1-ones can be obtained in high yields by heating the appropriate aromatic acyl derivatives with *N*,*N*-dimethylformamide diethyl or dimethyl acetals.[5] The reaction is best performed in a pressure tube with microwave heating.[5b] Carrying out this procedure with 2-hydroxyacetophenone (**1**) as the starting mat-

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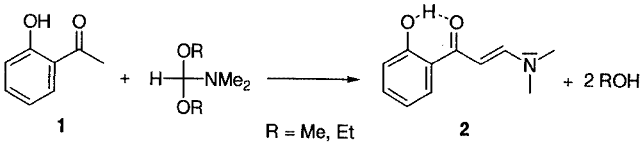
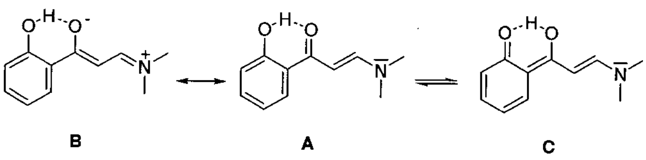
erial gives 1-(2-hydroxyphenyl)-3-(dimethylamino)prop-2-en-1-one (**2**, Scheme 2).



Scheme 2

The intense yellow compound **2** can be recrystallized from ethyl acetate, whereupon single crystalline needles of more than 1 cm length are formed. Initial investigation by X-ray diffraction[6] showed a relatively short distance between the proton of the aromatic OH group and the neighboring oxygen atom of the oxo function, indicating a strong intramolecular hydrogen bond. This is due to the electron-donating effect of the 3-(dimethylamino) group, which increases the electron density at the carbonyl oxygen atom according to the mesomeric form **B** (Scheme 3). For β-dioxo enols, equilibria between structures **A** and their tautomers **C** are usually observed, though this should play a minor role in our case, since it would destroy the aromaticity of the benzene ring.



Scheme 3

Further structural investigation of **2** by neutron diffraction, by which hydrogen positions can be elucidated with much higher accuracy than with X-ray diffraction, confirmed a long O1−H bond [1.032(3) Å], a very short H···O2 distance [1.500(3) Å], and a small C1−O1−H angle of 103.1(2)°. Figure 1 shows the molecular structure of **2** in the solid state as obtained from neutron diffraction data and a selection of characteristic bond lengths and angles.

Neither neutron nor X-ray diffraction experiments at different temperatures showed any significant temperature-dependent changes of the structural parameters for the atoms involved in hydrogen bonding.[6]

The molecules are packed in the unit cell by additional weak interactions between O1 and the hydrogen atoms of two C−H units of a neighboring molecule [H···O distances: C5a−H51a···O1 2.405(3) and C8a−H81a···O1 2.387(2) Å].[8] With these interactions, the solid-state structure of **2** can be described as an arrangement of parallel chains (Figure 2), within which the components are linked by C−H···O hydrogen interactions.

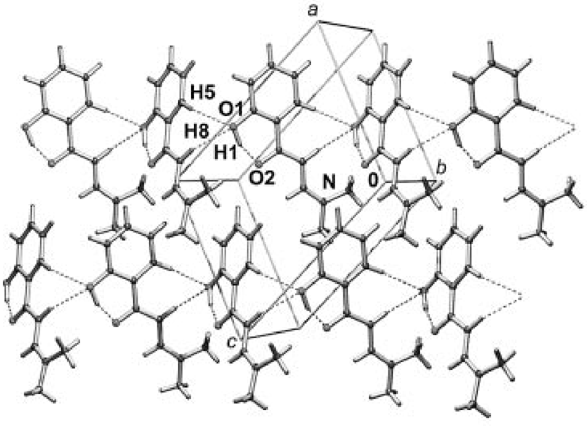


Figure 2. PLUTON[9] plot of the solid-state structure of **2**, showing the formation of parallel chains by C−H···O hydrogen bonds

Up to now, only a handful of solid-state structures of 1-aryl-3-(dimethylamino)prop-2-en-1-ones has been characterized by X-ray diffraction, and none by neutron diffraction.[5b,10] In all cases, hydrogen bonds between the carbonyl oxygen atom (acceptor) and sp^3 or sp^2 C−H moieties

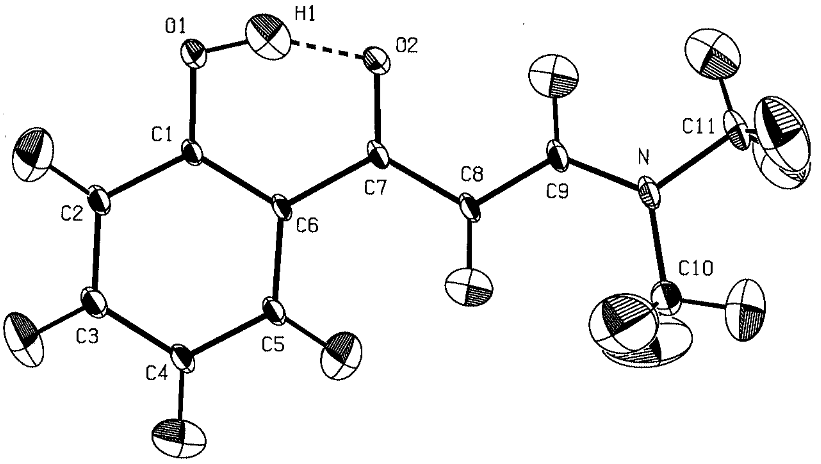


Figure 1. ORTEP[7] plot of the molecular structure of **2** in the solid state (from neutron diffraction); thermal ellipsoids are at the 90% probability level; selected bond lengths [Å] and angles [°]: O1−C1 1.346(2), O2−C7 1.273(2), O1−H1 1.032(3), O2···H1 1.500(3), O1···O2 2.474(2), C1−C2 1.406(2), C1−C6 1.420(2), C2−C3 1.390(2), C3−C4 1.403(2), C4−C5 1.390(2), C5−C6 1.411(1), C6−C7 1.486(2), C7−C8 1.428(2), C8−C9 1.384(2), N−C9 1.326(1), N−C10 1.458(1), N−C11 1.458(1); C1−O1−H1 103.1(2), O1−H1···O2 154.9(2)

resulted in the formation of one-, two-, or three-dimensional networks. The dominating influence of the electron-donating amino group on the distances in the O=C−C=C−N chain of **2** and related compounds becomes clear on comparison with 1-phenyl-3-[acetyl(phenyl)amino]prop-2-en-1-one.[10a] Owing to its electron-withdrawing acetyl group, the evidence of mesomeric structure **B** (Scheme 3) is reduced for this compound, as revealed by a pronounced shortening of the O=C and the C=C bonds and an elongation of the C−C and the C−N bonds [O=C: 1.228/*1.273(2)*, C−C: 1.474/*1.428(2)*, C=C: 1.327/*1.384(2)*, C−N: 1.392/*1.326(1)*; data for **2** in *italics*]. Only one compound {4-hydroxy-6-methyl-3-[3-(dimethylamino)acryloyl]-2*H*-pyran-2-one} forming an intramolecular O−H···O=C hydrogen bond as in **2** has so far been reported.[10b] However, the exact position of the OH proton could not be localized in this case, precluding any detailed discussion of the hydrogen bond.

To gain a deeper insight into the electronic situation of the charge distribution in such compounds, we carried out quantum chemical calculations on **2**, 1-phenyl-3-(dimethylamino)prop-2-en-1-one (**2a**), 2-hydroxyacetophenone (**1**), acetophenone (**1a**), and *N*-methylbenzamide (**1b**). Of a series of different methods (semiempirical, DFT, and ab initio) and basis sets, the B3LYP method in combination with a 6-311+G** basis set best reproduced the structural features of **2**.[11] The results are presented in Table 1, with the atom numbering according to Figure 1.

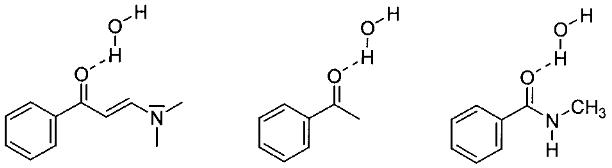
The results of the calculations are in agreement with the special situation in **2**, in which the hydrogen bond between O2 and H is promoted by the electron-donating effect of the dimethylamino group, as depicted in Scheme 3, increasing the negative charge at O2 (and even at O1). This results in a moderate elongation of the O1−H distance and a pronounced shrinkage of the distance between O2 and H (relative to compound **1**). However, the O−H distances obtained from the neutron diffraction structure of **2** are not completely reproducible by quantum chemical calculations. This might be due to the packing in the crystal, where the O1−H bond is weakened by the cooperative effects of two further hydrogen bonds between O1 and the hydrogen atoms of two C−H units of a neighboring molecule as described above.

Table 1. Data from quantum chemical calculations for **2**, 1-phenyl-3-(dimethylamino)prop-2-en-1-one (**2a**), 2-hydroxyacetophenone (**1**), and acetophenone (**1a**)

	2[a]	**2a**	**1**	**1a**
	Calcd. bond lengths [Å]			
O1−H	0.996, *1.032(3)*	−	0.988	−
O2···H	1.614, *1.500(3)*	−	1.686	−
O1−C1	1.339, *1.346(2)*	−	1.339	−
O2−C7	1.254, *1.273(2)*	1.232	1.236	1.217
C6−C7	1.486, *1.486(2)*	1.509	1.472	1.502
C7−C8	1.451, *1.428(2)*	1.461	1.513	1.518
C8−C9	1.365, *1.384(2)*	1.363	−	−
C9−N	1.349, *1.326(1)*	1.352	−	−
	Bond angles [°]			
C1−O1−H1	105.9, *103.1(2)*	−	107.0	−
O1−H1···O2	149.3, *154.9(2)*	−	146.8	−
	Mulliken charges			
H	+0.337	−	+0.319	−
O1	−0.337	−	−0.289	−
O2	−0.342	−0.297	−0.325	−0.265
C1	−0.405	+0.229	−0.647	+0.287
C6	+2.446	+1.783	+1.785	+1.214
C7	−1.267	−1.246	−0.075	−0.218
C8	+0.063	+0.092	−0.484	−0.483
C9	+0.276	−0.077	−	−
N	−0.018	+0.011	−	−
	Dipole moments [D]			
	6.890	5.318	3.494	3.248

[a] Bond lengths and angles from neutron diffraction in *italics*.

Additionally, the 3-(dimethylamino)prop-2-en-1-ones **2** and **2a** each show an increase in the charge at the carbonyl oxygen atom, of about 10% relative to **1** and **1a**. This, and the strong intramolecular hydrogen bond found in compound **2**, stimulated further investigations of the proton acceptor potential of other aromatic 3-(dimethylamino)prop-2-en-1-ones. For this purpose we carried out quantum chemical calculations on the hydrogen-bonded complexes of 1-phenyl-3-(dimethylamino)prop-2-en-1-one (**2a**), acetophenone (**1a**), and *N*-methylbenzamide (**1b**) with water as the proton donor (Scheme 4). The results are summarized in Table 2.



2a·H₂O **1a·H₂O** **1b·H₂O**

Scheme 4

Table 2. Data from quantum chemical calculations for the water adducts of 1-phenyl-3-(dimethylamino)prop-2-en-1-one (**2a**), acetophenone (**1a**), and *N*-methylbenzamide (**1b**)

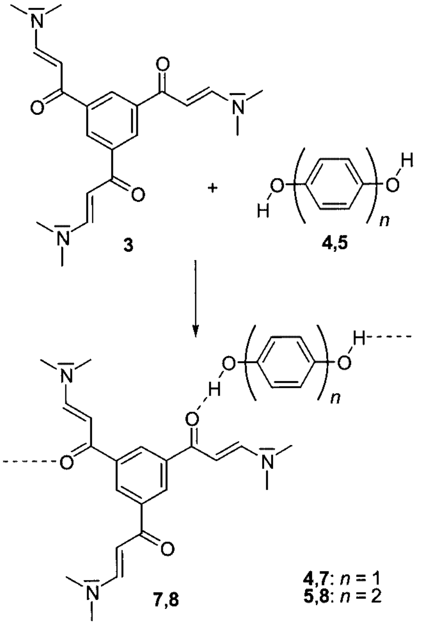
	2a·H_2O	**1a**·H_2O	**1b**·H_2O
	ΔH_R [kcal·mol^{-1}][a]		
	−7.45	−4.74	−5.57
	Calcd. bond lengths [Å]		
C=O1[b]	1.242, *1.232*	1.223, *1.217*	1.231, *1.224*
O1···H1	1.817	1.905	1.874
H1−O2[c]	0.979	0.973	0.974
H2−O2[c]	0.961	0.961	0.961
	Calcd. stretching frequencies [cm^{-1}][d]		
ν(C=O)[b]	1687, *1698*	1725, *1746*	1703, *1723*
ν_{sym}(O−H)[e]	3539	3648	3638
ν_{asym}(O−H)[e]	3893	3893	3892
	Mulliken charges		
C=O[b]	−1.222, *−1.246*	−0.530, *−0.218*	−0.517, *−0.427*
C=*O*[b]	−0.331, *−0.297*	−0.256, *−0.265*	−0.387, *−0.345*
H_2*O*[f]	−0.597	−0.542	−0.599
H1−O−H2	0.328	0.275	0.353
H1−O-*H2*	0.259	0.247	0.248

[a] For the reaction: A + H_2O → A···H_2O (A = acceptor) at 298 K. [b] In *italics*: values of pure compounds **2a**, **1a**, **1b**. [c] Calcd. bond length in water: 0.962 Å. [d] Without scaling. [e] Calcd. stretching frequencies of water: ν_{sym}(O−H) = 3816 cm^{-1}, ν_{asym}(O−H) = 3921 cm^{-1}. [f] Calcd. charges of water: H_2*O* −0.506, *H*$_2$O +0.253.

The strength of the hydrogen bond increases in the order **1a** < **1b** < **2a**, which is confirmed by the thermodynamic data, the C=O and O−H stretching frequencies, and the O···H distance. Additionally, there is an almost linear correlation between ΔH_R and the C=O distances of the proton acceptors, which might be usable in future for estimation of the proton-binding properties of unknown carbonyl compounds. In this context, it should not be forgotten that we are discussing calculations of isolated compounds/complexes in the gas phase, in which solvent or solid-state effects are excluded. Nevertheless, 1-aryl-3-(dimethylamino)-propenones such as **2a** seem to be better proton acceptors than arylcarboxamides such as **1b**, the aromatic model compounds for peptide bonds.

With these results in mind we investigated the proton acceptor potential of 1,3,5-tris[3-(dimethylamino)-1-oxoprop-2-enyl]benzene (**3**),[5b] which was expected to form hydrogen bonds with one, two, or three of its 3-(dimethylaminoprop)-2-en-1-one side chains. Depending on the nature of the proton donor used, this should give access to one- and two-dimensional supramolecular structures. Hydrogen-bonded polymers formed with **3** as the proton acceptor and *para*-hydroquinone (**4**), 4,4′-dihydroxybiphenyl (**5**), and water (**6**) are discussed below.

Treatment of **4** or **5** with **3** in different molar ratios (from 5:1 to 1:2) exclusively affords the chain-type arrangements **7** and **8**, with alternating proton donor and acceptor molecules (Scheme 5). Figures 3 and 4 show the molecular structures of **7** and **8** in the solid state.



Scheme 5

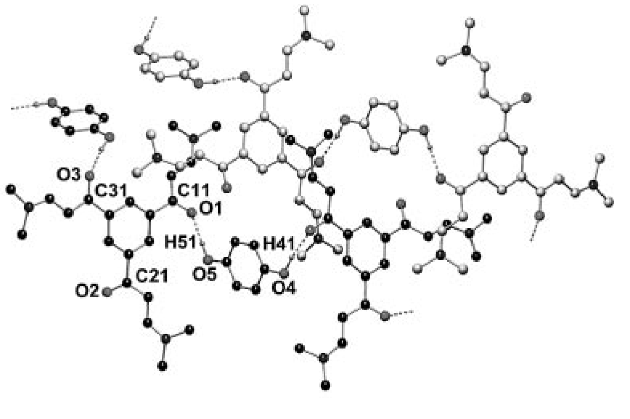


Figure 3. Hydrogen-bonded chains in the solid-state structure of **7** and packing of the chains (PLUTON[9] plot); all hydrogen atoms not involved in hydrogen bonds are omitted for clarity; selected bond lengths [Å]: O1−C11 1.252(2), O2−C21 1.243(2), O3−C31 1.252(2), O4−H41 0.94(2), O5−H51 0.93(2), O1···H51 1.75(2), O3···H41 1.75(2), O1···O5 2.676(2), O3···O4 2.685(2)

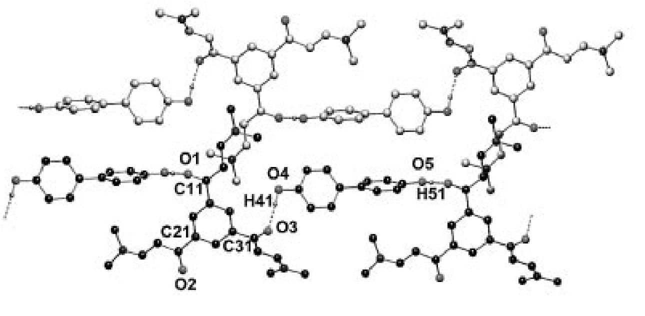


Figure 4. Hydrogen-bonded chains in the solid-state structure of **8** (PLUTON[9] plot); all hydrogen atoms not involved in hydrogen bonds are omitted for clarity; selected bond lengths [Å]: O1−C11 1.254(2), O2−C21 1.236(2), O3−C31 1.255(2), O4−H41 0.96(3), O5−H51 0.99(3), O1···H51 1.70(3), O3···H41 1.80(3), O1···O5 2.692(2), O3···O4 2.761(2)

Generally, the polymeric structures of **7** and **8** are produced by hydrogen bonding between two of the three carbonyl oxygen atoms (O1, O3) of **3** and the two OH protons of hydroquinone (**4**) and 4,4′-dihydroxybiphenyl (**5**), respectively. When examined carefully, however, the situation is a little more complicated. In **7**, two such chains, oriented parallel to the diagonal of the *ac* plane of the unit cell, form a zigzag arrangement. The resulting double chains are then packed into planes. The polymer chains in **8** do not cross each other, but form double layers parallel to the *bc* plane of the unit cell. Here, the phenyl rings of the 4,4′-dihydroxybiphenyl units are twisted by 60°. In all cases, hydrogen bonding increases the weight of the zwitterionic mesomeric structure **B** (Scheme 3), which increases the bond lengths O1−C11 and O3−C31 relative to O2−C21. The formation of hydrogen bonds is expressed by a slight shift of the C=O stretching frequency of the proton acceptor to lower energies and by a pronounced shift of the O−H stretching frequencies of the proton donors {KBr; ν_{O-H} = 3152 (**7**); 3203 [hydroquinone (**4**)]; 3225, 3134 (**8**); 3384 cm^{-1} [4,4′-dihydroxybiphenyl (**5**)]}.

To decrease the steric demand of the proton donor, water (**6**) was added. Crystallization of **3** from wet acetone results in the two-dimensional hydrogen-bonded arrangement **9**, in which all three 3-(dimethylamino)prop-2-en-1-one side chains are involved in hydrogen bonding (Figure 5).

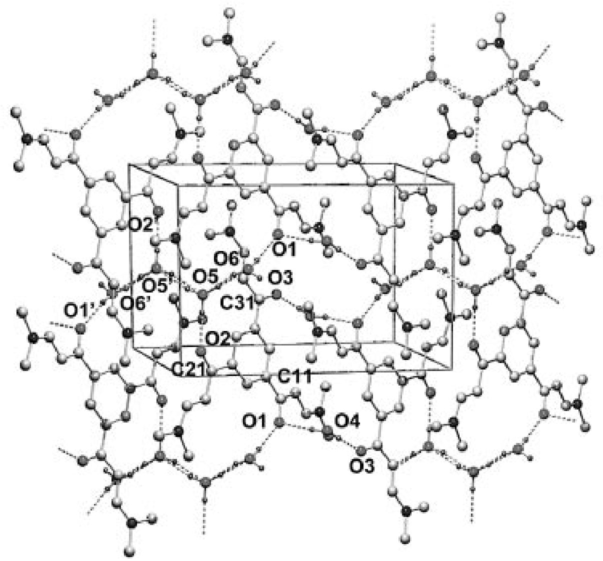
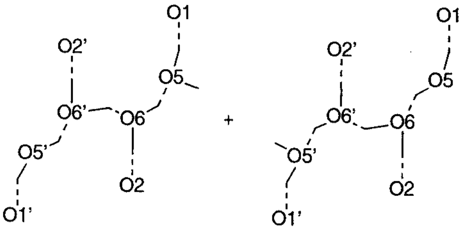


Figure 5. Hydrogen-bonded, two-dimensional polymeric structure of **9** (PLUTON[9] plot), including the disordering of two water molecules; all hydrogen atoms not involved in hydrogen bonds are omitted for clarity; selected bond lengths [Å]: O1−C11 1.259(2), O2−C21 1.246(2), O3−C31 1.242(2), O4−H1 0.91(2), H1···O1 1.92(2), O4···O1 2.826(2), O4−H2 0.94(2), H2···O3 1.85(2), O4···O3 2.790(2), O5−H3 0.87(3), H3···O2 1.88(3), O5···O2 2.751(2), O5−H4A 0.93(5), H4A···O6 1.89(5), O5···O6 2.811(2), O5−H4B 0.85(5), H4B···O5′ 1.92(4), O5···O5′ 2.759(2), O6−H5 0.85(3), H5···O1 1.97(3), O6···O1 2.808(2), O6−H6A 0.83(6), H6A···O5 1.99(6)

The two-dimensional hydrogen-bonded polymeric structure in **9**, in which the planes are oriented parallel to the *bc* plane of the unit cell, is formed by the interaction of three molecules of water with the three carbonyl oxygen atoms O1, O2, and O3. Several different types of hydrogen bonds are observed: while one water molecule (O4) acts as a proton-donating bridge between the carbonyl oxygen atoms O1 and O3, two further molecules of water (O5 and O6) build up a chain of four water molecules around a crystallographic center of inversion, bridging the proton acceptors O1, O2 and O1′, O2′ (due to crystal symmetry). This implies a disordering of the water molecules as depicted in Scheme 6.



Scheme 6

Mass spectrometric investigations (ESI-TOF) on compound **3** confirmed its tendency to bind positively charged species. For data acquisition, **3** was dissolved in THF containing a mixture of NaSCN and KSCN. The formation of three 1:1 adducts was observed [*m*/*z* (obsd./*calcd.*)]: [**3** + H^+] (370.253/*370.216*), [**3** + Na^+] (392.236/*392.195*), and [**3** + K^+] (408.210/*408.169*). The signals of a whole series of species containing more than one molecule of **3** in combination with one cation (charge +1) can be assigned: [(**3**)$_2$ + H^+] (739.515/*739.418*), [(**3**)$_2$ + Na^+] (761.501/*761.400*), [(**3**)$_2$ + K^+] (777.481/*777.374*), [(**3**)$_3$ + Na^+] (1030.765/*1130.605*), and [(**3**)$_4$ + Na^+] (1500.001/*1499.811*). In addition, low-intensity signals corresponding to dications of the type [(**3**)$_5$ + $(E^+)_2$] were detectable.

Conclusion

In this paper we have demonstrated that the carbonyl group of 1-aryl-3-(dimethylamino)prop-2-en-1-ones is a strong proton acceptor, a feature that can be used to build up hydrogen-bonded polymers. This is due to the π-donating effect of the dimethylamino group, which increases the electron density (basicity) of the carbonyl oxygen atom, as has been shown by quantum chemical calculations. Since aromatic acyl compounds are easily available by standard organic synthesis techniques, a broad range of 1-aryl-3-(dimethylamino)prop-2-en-1-ones bearing different types of arene groups are accessible. This may include dyes, electron-transferring groups such as ferrocene, or (transition)metal coordination complexes, and opens up the door to new hydrogen-bonded materials with interesting electronic or spectroscopic properties.

Experimental Section

General Information: The syntheses of compounds **2** and **3** are described elsewhere,[5b] hydroquinone (**4**) and 4,4′-dihydroxybiphenyl (**5**) are commercially available. The mass (Applied Biosystems Mariner System 5229), and infrared spectra (Perkin−Elmer FT-IR 1000), as well as the elemental analyses were carried out at the Institut für Chemie of the Technische Universität Chemnitz. Quantum chemical calculations were performed with the program Gaussian98W,[12] with the B3LYP gradient-corrected exchange-correlation functional[13] in combination with the 6-311+G** basis set.[14] Full geometry optimizations were carried out in C_1 symmetry by using analytical gradient techniques and the resulting structures were confirmed to be true minima by diagonalization of the analytical Hessian matrix.

1,3,5-Tris[3-(dimethylamino)-1-oxoprop-2-enyl]benzene−Hydroquinone and −4,4′-Dihydroxybiphenyl Adducts (7 and 8): 1,3,5-Tris[3-(dimethylamino)-1-oxoprop-2-enyl]benzene (**3**, 0.37 g, 1.00 mmol) was dissolved in $CHCl_3$ (15 mL). This solution was layered with a solution of 1 equiv. of the appropriate dihydroxy species (**4**: 0.11 g; **5**: 0.19 g), dissolved in 10 mL of acetone. Crystals formed by slow diffusion within a few days. Analytical data for **7**: Yield: 0.48 g (quant.), orange crystals. M.p. 220 °C. IR (KBr): see text. MS (ESI): see text. $C_{27}H_{33}N_3O_5$ (479.8): calcd. C 62.62, H 6.94, N 8.76; found C 67.32, H 7.10, N 8.67. Analytical data for **8**: Yield: 0.56 g (quant.), orange crystals. M. p. 206 °C. IR (KBr): see text. MS (ESI): see text. $C_{33}H_{37}N_3O_5$ (555.7): calcd. C 71.33, H 6.71, N 7.56; found C 77.11, H 6.62, N 7.06.

1,3,5-Tris[3-(dimethylamino)-1-oxoprop-2-enyl]benzene Trihydrate (9): 1,3,5-Tris[3-(dimethylamino)-1-oxoprop-2-enyl]benzene (**3**, 0.37 g, 1.00 mmol) was dissolved in acetone (15 mL), containing 5% water. This solution was left to concentrate slowly under ambient conditions, whereupon deep orange crystals were obtained. Yield: 0.42 g (quant.). M.p. 103 °C (dec.), 249 °C. IR (KBr): $\tilde{\nu}$ = 3395 m, 3139 m, 1636 vs, 1594 vs, 1532 vs, 1495 s, 1411 vs, 1359 m, 1272 vs, 1227 m, 1195 m, 1145 s, 1117 m, 1086 m, 692 cm^{-1} m. MS (ESI): see text. $C_{21}H_{33}N_3O_6$ (423.5): calcd. C 59.56, H 7.85, N 9.92; found C 59.54, H 8.00, N 9.81.

Single-Crystal Neutron Diffraction Study on 2: A single crystal suitable for the neutron diffraction study was grown at room temperature from a solution of **2** in ethyl acetate. A well-formed, yellow prism (3.6 × 3.5 × 1.8 mm) of the compound was fixed with a two-component glue (Kwikfill) on a vanadium pin and then mounted on the Eulerian cradle of the thermal neutron four-circle diffractometer D19, equipped with a 2-stage Displex cryorefrigerator[15] and a 64° × 4° position-sensitive detector.[16] A Ge(115) monochromator in reflection geometry was used to select a neutron beam of wavelength 1.308 Å. After indexing of three reflections at room temperature, the sample was slowly cooled (2 K/min) to 20 K, while a strong reflection was monitored. No splitting or change in mosaicity of the peak was observed. Intensity data [$\theta_{max} = 58.92°$, h (−11/11),k (−12/13),l (−14/7)] were measured by ω-scans in equatorial mode with a scan width between 2.4 and 3.2° and a measuring time of about 2.8 s per step (7500 monitor counts/point, 31 points). Three strong reflections were monitored regularly through the whole measurement and showed no significant variation. In addition, two ψ-scans clearly indicated that absorption ($\mu = 0.261\ mm^{-1}$) and also extinction effects [$\varepsilon = 0.070(2)$][17] had to be accounted for in the final refinement. In all, 3137 reflections were collected and integrated in three dimensions by use of the ILL program Retreat.[18] The final unit cell parameters $a = 8.8807(2)$, $b = 10.0998(2)$, $c = 11.4354(2)$ Å, $\beta = 109.6879(12)°$ were determined by use of the ILL program RAFD19. The data were corrected for absorption by using ψ-scan data.[19] After merging, with the program SHELXL-97,[17] a sum of 2225 independent reflections remained ($R_{int} = 0.0412$) and were used for a full-matrix, least-squares refinement by minimization of $\Sigma w(F_o^2 - F_c^2)^2$ with a SHELXL-97 weighting scheme. The initial atomic coordinates for the "heavy atoms" were taken from the X-ray structure determination and the neutron scattering lengths were taken as $bc(C) = 6.646$, $bc(H) = -3.739$, $bc(N) = 9.36$, $bc(O) = 5.803$ fm.[20] During the refinement, difference Fourier maps clearly revealed all of the hydrogen atom positions. All atoms of the asymmetric unit were refined anisotropically, giving a final R value of 0.0385 [$R1$, $I_o > 2\sigma(I_o)$] and 0.0948 ($wR2$, all data), respectively (GOF = 1.229). Details of the crystal data, intensity collection data, and refinement parameters are given in Table 3.

Single-Crystal X-Ray Structure Determinations. General Remarks: The preparation of the single crystals is described above. Selected crystals were coated with perfluorinated diethyl ether, fixed in a capillary, transferred to the diffractometer, and cooled in a nitrogen stream (Oxford Cryosystems). All structures were solved by a combination of direct methods[21] and difference Fourier syntheses. Full-matrix, least-squares refinements were carried out by minimization of $\Sigma w(F_o^2 - F_c^2)^2$ with SHELXL-97 weighting scheme and stopped at shift/err < 0.001. Neutral atom scattering factors for all atoms and anomalous dispersion corrections for the non-hydrogen atoms were taken from International Tables for Crystallography.[22] All calculations were performed with a DEC 3000 AXP workstation and an Intel Pentium II PC with the STRUX-V[23] system including the programs PLATON,[7] SIR92,[21] and SHELXL-97.[17] Details of the crystal data, intensity collection data and refinement parameters are given in Table 3. All hydrogen atoms were found in the difference Fourier maps and refined with individual isotropic thermal displacement parameters. Structure plots were generated by PLATON[7] and PLUTON.[9]

Data Collection and Refinement for 7: Intensity data were collected at 173 K. Preliminary examination and data collection were carried out with a kappa-CCD device (NONIUS MACH3) at the window of a rotating anode (NONIUS FR591) with graphite-monochromated Mo-K_α radiation ($\lambda = 0.71073$ Å). Data were corrected for Lorentz and polarization effects. Potential absorption effects and decay of the crystal were corrected during the scaling procedure.[24] Data collection was performed within the Θ range of 1.65° < Θ < 25.64° with an exposure time of 50 s per image (6 sets, 368 images, $\Delta\varphi/\Delta\Omega = 1.0°$). A total of 11656 reflections were integrated. After merging, a sum of 4684 independent reflections remained and were used for all calculations. All non-hydrogen atoms were refined anisotropically.

Data Collection and Refinement for 8: The intensity data were collected at 223 K. Preliminary examination and data collection were carried out with an imaging plate diffraction system (IPDS; Stoe & Cie.) at the window of a rotating anode (NONIUS FR591) with graphite-monochromated Mo-K_α radiation ($\lambda = 0.71073$ Å). Data were corrected for Lorentz and polarization effects.[25] No corrections for decay and absorption effects were applied. Data collection was performed within the Θ range of 2.10° < Θ < 25.72° with an exposure time of 900 s per image (oscillation scan mode from φ = 0° to 360° with $\Delta\varphi = 2.0°$). A total of 20191 reflections were collected. After merging, a sum of 5181 independent reflections remained and were used for all calculations. All non-hydrogen atoms were refined anisotropically. Disorder of the hydrogen atoms of two methyl groups (C15: two positions, 70:30; C25: two positions, 51:49) could be resolved clearly.

Data Collection and Refinement for 9: Intensity data were collected at 173 K. Preliminary examination and data collection were carried out with a kappa-CCD device (NONIUS MACH3) at the window of a rotating anode (NONIUS FR591) with graphite-monochromated Mo-K_α radiation ($\lambda = 0.71073$ Å). Data were corrected for Lorentz and polarization effects. Potential absorption effects and decay of the crystal were corrected during the scaling procedure.[24] Data collection was performed within the Θ range of 2.13° < Θ < 25.67° with an exposure time of 20 s per image (8 sets, 535 images, $\Delta\varphi/\Delta\Omega = 1.0°$). A total of 12627 reflections were integrated. After merging, a sum of 4030 independent reflections remained and were used for all calculations. All non-hydrogen atoms were refined anisotropically. Disorder of the hydrogen atoms of two methyl groups (C15: two positions, 50:50; C35: two positions, 50:50) could be resolved clearly. All three water molecules are involved in a two-dimensional hydrogen bonded network (see text). The hydrogen atoms of two water molecules (O4: two positions, 50:50; O5: two positions, 50:50) are disordered about a crystallographic center of inversion. The well-resolved disorder is a superposition of the two possible "homodromic" arrangements of the hydrogen bonds.[4]

CCDC-195156 (**2−100K**),[6] -195150 (**2−150K**),[6] -195154 (**2−200K**),[6] -195152 (**2−250K**),[6] -195155 (**2−300K**),[6] -195149 (**2−20K**), -195153 (**7**), -195148 (**8**) and -195151 (**9**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12

Table 3. Summary of the crystallographic data for compounds **2**, **7**, **8**, and **9**

	2[a]	**7**	**8**	**9**
Empirical formula	$C_{11}H_{13}NO_2$	$C_{21}H_{27}N_3O_3$, $C_6H_6O_2$	$C_{21}H_{27}N_3O_3$, $C_{12}H_{10}O_2$	$C_{21}H_{27}N_3O_3$, $3(H_2O)$
Formula mass	191.23	479.56	555.66	423.50
Crystal system	monoclinic	monoclinic	triclinic	triclinic
Space group	$P2_1/n$ (no. 14)	$C2/c$ (no. 15)	$P\bar{1}$ (no. 2)	$P\bar{1}$ (no. 2)
a [Å]	8.8807(2)	24.2378(3)	9.217(1)	7.6206(2)
b [Å]	10.0998(2)	14.4836(3)	11.838(2)	9.6569(2)
c [Å]	11.4354(2)	14.7336(3)	14.343(2)	15.1088(4)
α [°]	90	90	99.16(2)	95.449(1)
β [°]	109.6879(12)	105.512(1)	108.04(2)	92.491(2)
γ [°]	90	90	92.20(2)	96.848(2)
V [Å^3]	965.72(3)	4983.8(2)	1462.6(4)	1097.27(5)
Z	4	8	2	2
$\rho_{\text{calcd.}}$ [g cm^{-3}]	1.315	1.278	1.262	1.282
μ [mm^{-1}]	0.261	0.089	0.085	0.094
T [K]	20	173	223	173
Reflections collected	3137	11656	20191	12627
Independent reflections [$I_o > 2\sigma(I_o)$/all data/R_{int}]	2176/2225/0.0412	4265/4684/0.0239	4076/5181/0.0392	3401/4030/0.0217
Data/restraints/parameter	2225/0/245	4684/0/448	5181/0/528	4030/0/435
$R1$ [$I_o > 2\sigma(I_o)$/all data]	0.0385/0.0399	0.0379/0.0420	0.0366/0.0490	0.0397/0.0505
$wR2$ [$I_o > 2\sigma(I_o)$/all data]	0.0939/0.0948	0.1037/0.1067	0.0940/0.1029	0.0934/0.0986
GOF	1.229	1.037	1.027	1.012
Weights *a*/*b*	0.0422/4.8163	0.0579/2.8303	0.0637/0.1266	0.0407/0.3264
$\Delta\rho_{\text{max/min}}$ [e·Å^{-3}]	0.86/-0.94[b]	0.25/-0.19	0.20/-0.15	0.18/-0.18

[a] Neutron diffraction data. For X-ray experiments see ref.[6] [b] Unit: fm Å^{-3}

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