Striking Example of a Contact Chloride Ion Pair with Bridging Water Molecules in the Solid State

Edward F. Kleinman,*,† Jon Bordner,†,‡
Bradley J. Newhouse,† and Kurtis MacFerrin§

Central Research Division, Pfizer Inc.
Department of Medicinal Chemistry
Groton, Connecticut 06340
Department of Chemistry, Harvard University
12 Oxford Street, Cambridge, Massachusetts 02138

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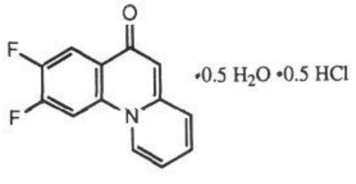
Recent theoretical studies of ion solvation that treat the medium as a molecular ensemble rather than as a dielectric continuum have led to the startling prediction that chloride ions in water are *attracted* to each other in the neighborhood of contact distance, forming ion pairs with bridging water molecules (CIPBWs) which stabilize the Coulombic repulsion through the formation of simultaneous hydrogen bonds.[1-4] While there is experimental



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support for the phenomenon of halide aggregation,[5-7] direct evidence for the existence of CIPBWs in aqueous solution is lacking and could be difficult to obtain because CIPBWs are predicted to be in equilibrium with solvent-separated species and with the dissociated ions. If CIPBWs do have inherent stability in aqueous solution, they should also have stability in the solid state, making direct observation possible through X-ray analysis. A recent search of the Cambridge Structural Database (CSD)[8] for the existence of CIPBWs in the solid state by Gao et al.[9] prompts us to disclose a most striking example discovered serendipitously in the X-ray structure of 8,9-difluoro-6-oxo-6*H*-benzo[*c*]quinolizine hemihydrate hemihydrochloride (**1**),[10] which is unique from several

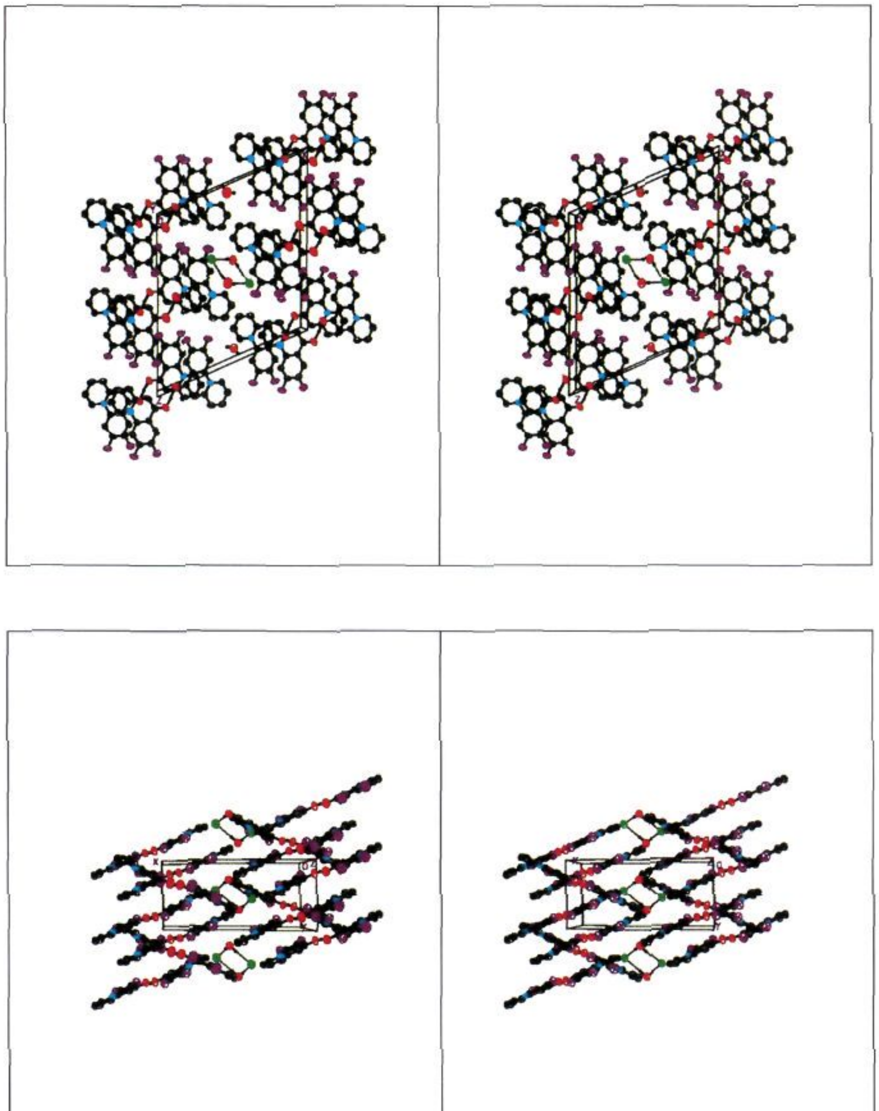

Figure 1. Two perpendicular stereoviews of the X-ray packing diagram of **1** containing the CIPBW. The box marks the unit cell.

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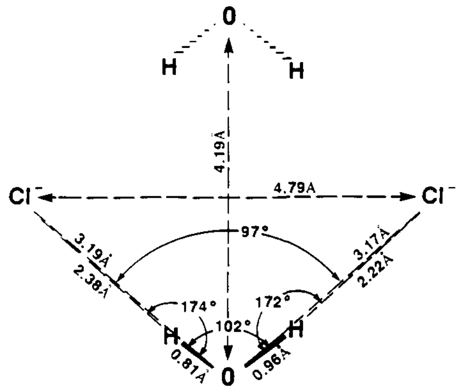

Figure 2. Schematic diagram of the ClPBW in the X-ray structure of **1**. The hydrogens protrude slightly out of plane by 5°, as indicated by the solid and dashed wedged lines.

perspectives in that it features (1) two simultaneously bridging waters, (2) a C_i axis of symmetry, (3) a strict *hydrophobic* environment, and (4) dimensions very similar to theoretical predictions by Buckner and Jorgensen.[4]

As shown in two views of the X-ray packing diagram (Figure 1), the ClPBW is interwoven among a complex network of pairs of 8,9-difluoro-6-oxo-6*H*-benzo[*c*]quinolizines (linked unsymmetrically at their carbonyls by a proton), where it appears as a distinct, rectangular-like aggregate. A schematic diagram (Figure 2) illustrates that the chlorides and water oxygens are arranged symmetrically at opposite corners of a parallelogram with protons along its side which are simultaneously hydrogen bonded to the chlorides in near-linear fashion. The two pairs of protons within the individual water molecules protrude together very slightly out of the plane of the parallelogram in opposite fashion, respectively, by 5°. The chloride–chloride distance is 4.79 Å, which is in excellent agreement with the 4.8–5.0 Å value predicted by Buckner and Jorgensen in a study of the hydration of tetramethylammonium chloride using statistical perturbation theory and Monte Carlo simulations.[4] Also, the chloride–water distances, 3.17 and 3.19 Å, match the optimal distance of 3.2 Å calculated for the chlorides and waters that are linearly hydrogen bonded.

Perhaps the most interesting feature of the ClPBWs in the crystal structure of **1** is that, in contrast to those found in the CSD, there are no unsymmetrical hydrogen-bonding contacts with the organic component of the unit cell, which would distort its internal structure and symmetry and thereby make it a less effective model for ClPBWs in solution or in the gas phase. In fact, no external hydrogen-bonding contacts are observed, as the ClPBW interacts with the benzo[*c*]quinolizine not at the hydrophilic protonated carbonyl region but at the opposite lipophilic side spanning the C10–N–C4 periphery of the benzo[*c*]quinolizine ring.[11] That ClPBWs do not require external stabilization by external polar forces other than the Coulombic attraction to the positive charge, which in this case is extensively delocalized over a region of nearly 10 Å spanning the proton and the nitrogen of the two benzo[*c*]quinolizines, suggests that such species can exist in aprotic solvents.

The failure of CSD searches to detect ClPBWs which so markedly match those predicted in aqueous solution is not entirely unexpected. CSD entries are generated using the minimum number of symmetry operations required to fully account for the molecular formula of the compound. Hence, ClPBWs between cells may be missed. While the CSD GEOSTAT program ostensibly will locate such interactions, in our experience it failed. Our own search (supplementary material) has thus given results similar to those of Gao et al.,[9] with the further observation that the proximity and geometry of chloride pairs is less likely to be a result of a random orientation in the crystal when water molecules are present.

In conclusion, we have provided graphic evidence that ClPBWs have inherent stability in the solid state and display dimensions similar to those predicted in aqueous solution. Clearly, further experimental work is needed to prove the existence of such species in solution, and we hope that this disclosure will stimulate such efforts.

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Supplementary Material Available: Complete descriptions of the X-ray crystallographic determination of **1** and our search of the CSD for other examples of ClPBWs (11 pages). Ordering information is given on any current masthead page.

[†] Pfizer Central Research.

[‡] To whom correspondence should be sent concerning details of the X-ray structure determination.

[§] Harvard University.

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(10) Compound **1** was prepared by hydrolysis and decarboxylation in refluxing aqueous hydrochloric acid of the known 8,9-difluoro-6-oxo-6*H*-benzo[*c*]quinolizine-5-carboxylic acid ethyl ester (see: Ziegler, C. B., Jr.; Moran, D. B.; Fenton, T. J.; Lin, Y.-i. *J. Heterocycl. Chem.* **1990**, *27*, 587). Crystals of **1** suitable for X-ray analysis were obtained by slow evaporation in a methanol–water solution.

(11) All nearest-neighbor-type interactions within 3 Å are made with the C1, C2, C3, C4, and C10 hydrogens of the benzo[*c*]quinolizines. The distances between the aromatic fluorines and the hydrogens of the ClPBW are well beyond hydrogen-bonding contact distance.