GEOMETRY OF HYDROGEN-BONDED WATER MOLECULES IN ORGANIC CRYSTALS

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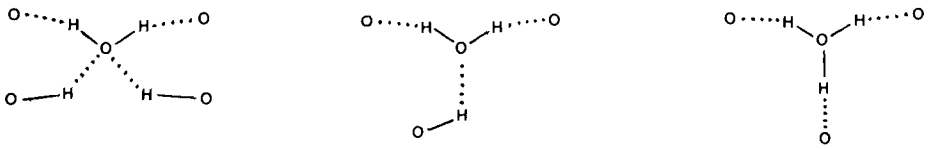
Hydrogen bonding contributes to the stability of many crystalline drugs. In procaine penicillin monohydrate, for example, an intricate network of hydrogen bonds, most of them involving water, holds the crystal together (Dexter & van der Veen 1978; Lowe & Schwalbe 1978). Because of its particular importance the geometry of hydrogen-bonded water molecules was surveyed and classified (FFA) by Ferraris and Franchini-Angela (1972). Since then, however, many additional structure determinations have been carried out, and a new survey appears desirable. We have therefore searched the Cambridge Crystallographic Data File for appropriate data, restricting our attention to neutron diffraction studies for accuracy, to organic crystals for relevance to drugs, and to O-H···O bonds for adequacy of sample size.

Water molecules always share their protons in hydrogen bonds, but they differ in the involvement of their oxygen atom. Thus they may be crudely classified as 4-coordinate or 3-coordinate. For many purposes the hydronium ion may be considered as an extension of the 3-coordinate case in which the third proton has moved closer to the water oxygen than to its original donor. The three situations are illustrated from left to right:



The best correlation (coefficient r = 0.95) found by FFA was between the H···O and O···O distances. We find that this good correlation extends to hydronium ions as well, obtaining r = 0.94 for all cases of proton donation by water or hydronium. This correlation would be perfect if all hydrogen bonds were linear, but they are not: the O-H···O angles span a 50° range, the variation being greater for the longer hydrogen bonds. Thus the hydrogen bonds can adjust to the requirements of crystal packing. The H-O-H bond angle also responds to crystal packing, but a trend with hydrogen bond length is still discernible. A plot of H-O-H angle (in hydronium ions the angle between the two shortest O-H bonds) versus O···H distance (in hydronium ions the longest O-H bond) gives r = -0.5 . The average H-O-H angles of 113° in hydronium ions, 108° in 3-coordinate water, and 106° in 4-coordinate water all exceed the 104° in free water. A measure of the bonding at oxygen is the sum of three H-O-H and/or H-O···H angles; this would be 360° for trigonal planar and 328° for tetrahedral geometry but is concentrated near 335-340° for hydronium ions, either 335-340° or nearly 360° for 3-coordinate water, and evenly distributed between 300° and 360° for 4-coordinate water. Clearly the water molecule is a very flexible "glue" for holding organic crystals together.

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