

Hydroxyl-Benzene Hydrogen Bonding: an X-Ray Study

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THOUGH numerous spectroscopic studies of hydroxyl $\cdots \pi$ -electron hydrogen bonds have been published^{1,2} no crystal-structure examination of the geometry of such a complex appears to have been described. We now report that determination of the crystal structure of the cyclic peptide (I) reveals the presence of an intramolecular OH \cdots benzene hydrogen bond in the molecule

(see Figure 1) and permits some discussion of the distances involved.

The peptide crystallizes as the ethanol solvate with four units of $C_{24}H_{24}O_5N_3I, C_2H_5OH$ in an orthorhombic cell of dimensions $a = 15.48$, $b = 22.28$, $c = 7.52$ Å. The space group is $P2_12_12_1$. Three-dimensional intensity data were recorded by the equi-inclination Weissenberg technique and

¹ For reviews, see "The Hydrogen Bond", by G. C. Pimentel and A. L. McClellan, W. H. Freeman and Co., San Francisco, 1960; "Molecular Complexes in Organic Chemistry", by L. J. Andrews and R. M. Keefer, Holden-Day, San Francisco, 1964.

² R. E. Richards and H. W. Thompson, *J. Chem. Soc.*, 1947, 1260; W. Beckering, *J. Phys. Chem.*, 1961, 65, 206; G. Aulin-Erdtman and R. Sanden, *Acta Chem. Scand.*, 1963, 17, 1991.

were estimated visually; in all 2292 independent $|F_0|$ values were derived. The structure was elucidated by the heavy-atom method³ (the x -coordinate of the iodine atom is approximately 1/4, causing spurious symmetry in the first stage of the analysis⁴) and refined by Fourier and least-squares methods. The iodine atom was assigned an

anisotropic temperature factor, but the carbon, nitrogen, and oxygen atoms were assigned only isotropic values in order to conserve computer time. The present value of R is 11.1%.

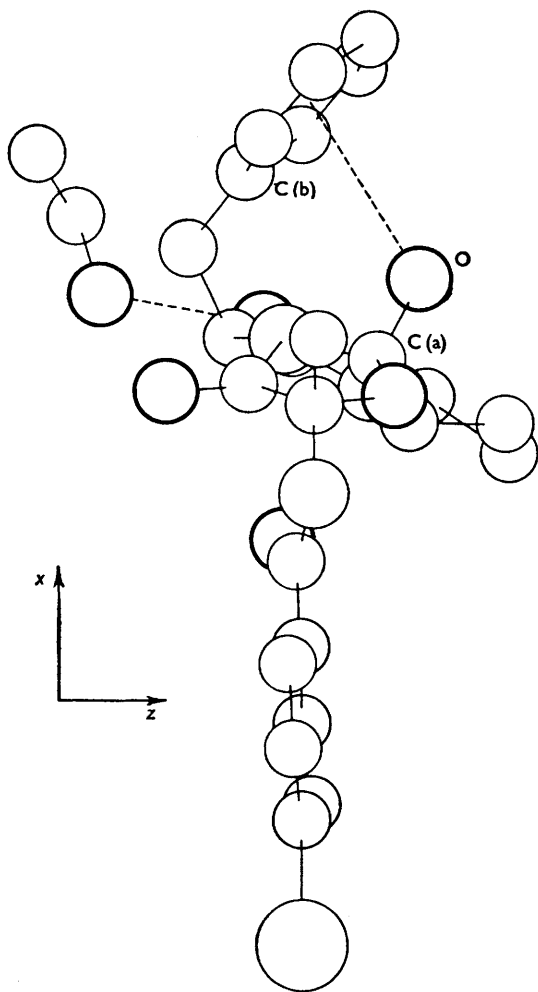
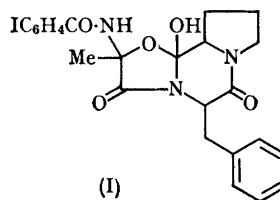


FIG. 1. The molecular structure as viewed along the b -axis.

The arrangement of atoms within the molecule as seen when viewed along the b -axis is shown in Figure 1. The molecule adopts a conformation in which the benzyl group approaches the hydroxyl group as closely as possible. The perpendicular distance from the benzene ring to the oxygen atom is 3.07 Å. The angle between the normal to the benzene plane and the C(a)-O bond is 106°, indicating that the hydroxyl proton probably lies on the normal to the benzene plane; in a difference three-dimensional electron-density distribution from which all the non-hydrogen atoms were subtracted a peak representing the hydroxyl hydrogen was located in the expected region between the oxygen atom and the benzene plane, just over 1 Å away from the oxygen. If we assume an O-H distance of about 1 Å the proton \cdots benzene distance is close to 2.1 Å. Because of the rigid molecular geometry elsewhere the O-H bond direction is not co-incident with the six-fold axis of the benzene ring, but is displaced by 0.84 Å towards C(b).

In a nuclear magnetic resonance study of the interaction of chloroform with benzene, the displacement of the chloroform proton signal relative to the signal in a non-complexing solvent has been attributed to hydrogen bonding and the H \cdots ring centre distance has been estimated⁵ as 3.1 Å, assuming that the C-H bond is coincident with the six-fold axis of the benzene molecule. In a similar study of the iodoform-toluene interaction the H \cdots ring centre distance has been assessed⁶ as 2.5 Å. The approximations involved in these calculations imply that the values quoted are probably larger than the real distances.

³ J. M. Robertson and I. Woodward, *J. Chem. Soc.*, 1937, 219; 1940, 36; G. A. Sim in "Computing Methods and the Phase Problem in X-Ray Crystal Analysis", ed. R. Pepinsky, J. M. Robertson, and J. C. Speakman, Pergamon Press, Oxford, 1961, p. 227.

⁴ J. D. M. Asher and G. A. Sim, *Proc. Chem. Soc.*, 1962, 111; *J. Chem. Soc.*, 1965, 1584.

⁵ L. W. Reeves and W. G. Schneider, *Canad. J. Chem.*, 1957, 35, 251.

⁶ R. J. Abraham, *Mol. Phys.*, 1961, 4, 367.

In the *p*-xylene-carbon tetrabromide⁷ and benzene-bromine⁸ complexes the C-Br and Br-Br bond directions are approximately perpendicular to the aromatic rings; the bromine...benzene distances are 3.34 and 3.36 Å, respectively. The covalent radii and the van der Waals radii of bromine and hydrogen are such that a bromine atom is 0.8 Å larger in radius than a hydrogen atom. Since we find that the H...ring distance

(2.1 Å) is 1.25 Å shorter than the Br...ring distance, it appears that the hydroxyl group interacts more strongly than bromine with the π -electrons of benzene.

After the discovery of the hydroxyl...benzene interaction in the crystal, we recorded the infrared spectrum of the solid (KCl disc) to confirm that the intramolecular hydrogen bond is indeed similar to other hydroxyl...benzene interactions. The hydroxyl stretching mode (see Figure 2) does not appear at the position expected for a free hydroxyl (~ 3620 cm.⁻¹) and the absorption band closest to this position (3520 cm.⁻¹) is similar in position and shape to infrared bands at 3550-3590 cm.⁻¹ which have been attributed to hydroxyl...benzene hydrogen bonding in a number of hydroxybiphenyls.²

The other hydrogen-bonded contacts in the crystal, OH...O 2.81 Å, NH...O 3.00 Å, are normal.

The calculations were performed on the DEUCE computer at the University of Glasgow and the IBM 7094 computer at the University of Illinois. Dr. A. J. Frey, Sandoz Pharmaceuticals, supplied the crystals.

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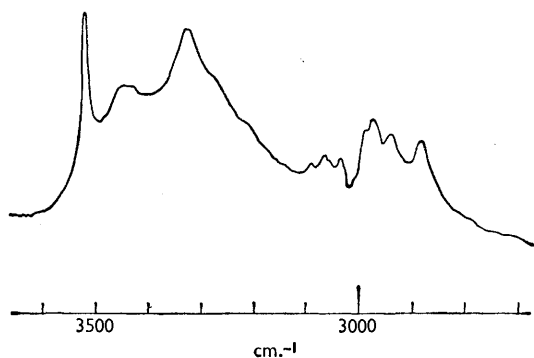


FIG. 2. The infrared spectrum (KCl disc) in the 3500 cm.⁻¹ region.

⁷ F. J. Strieter and D. H. Templeton, *J. Chem. Phys.*, 1962, **37**, 161.

⁸ O. Hassel and K. O. Strømme, *Acta Chem. Scand.*, 1958, **12**, 1146.