Co-operative and Competitive Hydrogen Bonding in Sucrose determined by SIMPLE ^{1}H N.M.R. Spectroscopy

John C. Christofides and David B. Davies*

Department of Chemistry, Birkbeck College, Malet Street, London WC1E 7HX, U.K.

SIMPLE ^{1}H n.m.r. measurements of isotope-shifted resonances for hydroxy groups in sucrose show that hydrogen bonding in solution is different from that observed in the solid state *viz.* there are two inter-residue hydrogen bonds in competition for one acceptor group (*i.e.* OH1′ · · · O2 *vs.* OH3′ · · · O2) and an intramolecular hydrogen-bond network that is nucleated by the inter-residue hydrogen bonds.

Observations of carbohydrate crystals by neutron diffraction have shown that most hydroxy groups are involved in intermolecular hydrogen bond interactions with other hydroxy groups, with ring oxygen atoms, or with water of crystallisation to form infinite chains of hydrogen bonds through the crystal lattice.[1] In some crystal structures of oligosaccharides intramolecular hydrogen bonds are also observed between hydroxy groups (*e.g.* OH1′ · · · OH2 in sucrose[2]) or between hydroxy groups and ring oxygen atoms (*e.g.* OH6′ · · · O5 in sucrose[2]). Such detailed information about hydrogen bonds is generally not available for molecules in solution, though a number of n.m.r. methods have been used to indicate the presence of hydrogen bonds *e.g.* chemical shifts, temperature and solvent dependence of chemical shifts, H/D exchange rates.[3] Recently high field ^{1}H n.m.r. observations of H/D isotopomers in the slow exchange condition (*i.e.* SIMPLE n.m.r.; Secondary Isotope Multiplet n.m.r. spectroscopy of Partially Labelled Entities[4]) have shown that hydrogen bonds between hydroxy groups are manifested by isotope-shifted signals *e.g.* cyclodextrin,[5] sucrose,[6] and some sucrose derivatives.[7,8]

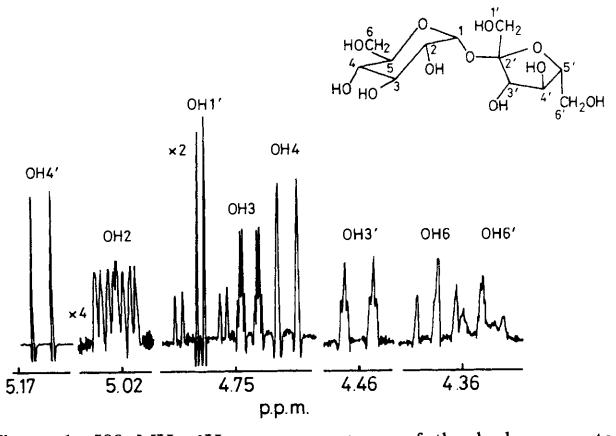

Figure 1. 500 MHz ^{1}H n.m.r. spectrum of the hydroxy proton resonances of sucrose in [$^2H_6$]Me_2SO solution at a deuteriation ratio of OH : OD *ca.* 1 : 1; T = 305 K. Chemical shifts given with respect to δ ([$^2H_5$]Me_2SO) = 2.49.

In the present work the 500 MHz SIMPLE ^{1}H n.m.r. spectrum of sucrose (Figure 1, OH : OD *ca.* 1 : 1) shows that the negative isotope effect observed for OH1′ is similar to that observed previously by Lemieux and Bock[6] but the number of isotope effects on other hydroxy signals is quite different, *viz.* three effects for OH3 (++−) and two resolved effects for OH2 (++) and OH3′ (+−). Small isotope effects that lead to line broadening are also observed for the OH2, OH4, OH3′, OH6, and OH6′ signals by comparison with the sharp lines of the other signals or by comparison with the normal spectrum of sucrose.

The large positive isotope effect on OH2 (+70 × 10^{-4} p.p.m., acceptor) and the negative isotope effect on OH1′ (−43 × 10^{-4} p.p.m., donor) correspond to the presence of the OH1′ · · · O2 inter-residue hydrogen bond previously found in [$^2H_6$]Me_2SO solutions of sucrose[6] and a 3′-sucrose derivative (3,3′,4′,6′-tetra-*O*-acetylsucrose).[7] The medium-sized isotope effect on OH2 (+32 × 10^{-4} p.p.m., acceptor) and the isotope effect on OH3′ (−22 × 10^{-4} p.p.m.) correspond to the presence of the novel inter-residue OH3′ · · · O2 hydrogen bond recently observed for 1′-sucrose derivatives.[9] Observation of these isotope effects is consistent with either a bifurcated hydrogen bond in which OH2 simultaneously acts as acceptor for both the OH1′ and OH3′ donors (excluded because of unfavourable steric interactions as shown by molecular models) or, more likely, the two inter-residue hydrogen bonds exist in competitive equilibrium, as shown in Figure 2. Assuming that the magnitudes of isotope shifts reflect the relative 'strengths' of hydrogen bonds, it is found that the equilibrium favours the OH1′ · · · O2 compared to the OH3′ · · · O2 hydrogen bond. The smaller isotope effects observed for most hydroxy signals correspond to very weak hydrogen bonds between neighbouring hydroxy groups which are nucleated by the presence of a relatively strong and predominantly unidirectional inter-residue hydrogen bond; such isotope effects are not observed for the corresponding

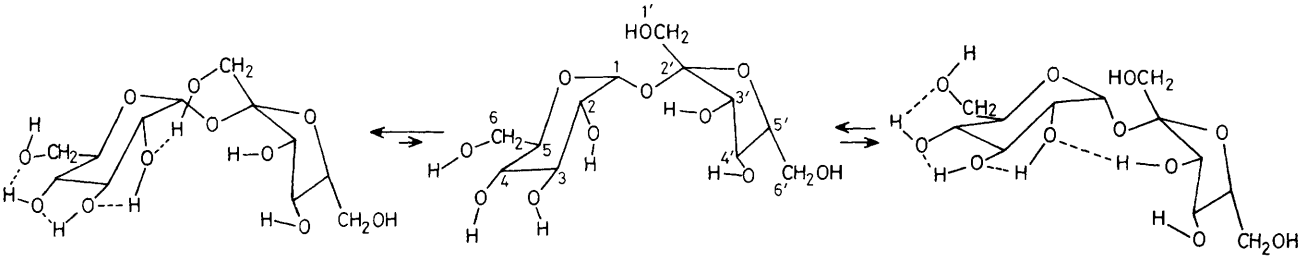

Figure 2. Conformational equilibrium of sucrose showing two inter-residue hydrogen-bonded forms in solution and the hydrogen-bond network in the glucose residue nucleated by the inter-residue hydrogen bonds. Hydrogen bonds in the fructose residue have not been characterised completely.

hydroxy resonances of the monomer units of sucrose. The hydrogen-bond network in the glucose residue is similar to that observed previously for 1′- and for 3′-sucrose derivatives.[8,9]

Despite the conformational flexibility of the molecule and the exocyclic carbinol and hydroxy groups, it is found that hydrogen-bond interactions between hydroxy groups are sufficiently stable to be manifested as isotope shifts. The number and magnitudes of the isotope shifts observed for sucrose in solution can be understood in terms of an intramolecular hydrogen-bond network between hydroxy groups that is quite different from the intermolecular hydrogen-bond network observed in the solid state. For molecules dissolved in $[^2H_6]Me_2SO$ solution it is likely that the solvent acts as a hydrogen-bond acceptor for each hydroxy group[10] whereas crystal packing is likely to be dominant for molecules in the solid state. Crystal packing constraints may also account for the different glycosidic bond conformations observed for sucrose (with its OH1′ · · · O2 hydrogen bond)[2] and the sucrose unit in raffinose (with no inter-residue hydrogen bond)[11] whereas, in solution, our SIMPLE ^1H n.m.r. studies show that the two competitive inter-residue hydrogen bonds (OH1′ · · · O2 *vs.* OH3′ · · · O2) found for sucrose are also observed for the sucrose residue in the trimer raffinose and the tetramer stachyose.

We thank the S.E.R.C. for a studentship (to J. C. C.) and the M.R.C. for access to 500 MHz n.m.r. facilities (NIMR, London) and n.m.r. computing facilities (Birkbeck College, London).

Received, 8th July 1985; Com. 967

References

1 G. A. Jeffrey and S. Takagi, *Acc. Chem. Res.*, 1978, **11**, 264.
2 G. M. Brown and H. A. Levy, *Acta Crystallogr., Sect. B*, 1973, **29**, 790.
3 J. W. Emsley, J. Feeney, and L. H. Sutcliffe, 'High Resolution Nuclear Magnetic Resonance Spectroscopy,' Vol. 1, 1966, Pergamon Press, Oxford.
4 J. C. Christofides and D. B. Davies, *J. Am. Chem. Soc.*, 1983, **105**, 5099.
5 J. C. Christofides and D. B. Davies, *J. Chem. Soc., Chem. Commun.*, 1982, 560.
6 R. U. Lemieux and K. Bock, *Jpn. J. Antibiot.*, Supplement XXXII, 1979, S163; K. Bock and R. U. Lemieux, *Carbohydr. Res.*, 1982, **100**, 63.
7 D. B. Davies and J. C. Christofides, in 'Natural Products Chemistry', eds. R. I. Zalewski and J. J. Skolik, 1985, Elsevier, Amsterdam, pp. 305—317.
8 J. C. Christofides and D. B. Davies, *Magn. Reson. Chem.*, 1985, **23**, 582.
9 J. C. Christofides, D. B. Davies, J. A. Martin, and E. B. Rathbone, *J. Am. Chem. Soc.*, submitted for publication.
10 R. U. Lemieux and A. A. Pavia, *Can. J. Chem.*, 1969, **347**, 4441.
11 H. M. Berman, *Acta Crystallogr., Sect. B*, 1970, **26**, 290.