384. *A Molecular Addition Compound of* α-D-*Glucopyranose and Urea.*

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THE ability to form an addition compound can be an important factor in deciding whether D-glucose crystallizes from solution as the α- or as the β-anomer. From water below 50° the hydrate of the α-form is most likely to separate, whereas from pyridine the solvated β-form crystallizes. Quehl[1] reported that glucose forms an addition compound with urea, but he gave little information other than that it formed small needles which melted sharply at 117°. No analysis was given and as, in its preparation by fusion, he used 198 parts of glucose (m. p. 85°) and 60 parts of urea, its composition could well correspond with the formula $C_6H_{12}O_6,CO(NH_2)_2,H_2O$. Quehl claimed the existence of addition compounds of either the 2 : 1 or 1 : 1 type between urea and many mono-, di-, and poly-saccharides, and, although he stated that " identification was effected in the crystalline material only," the compound of urea and glucose was the only crystalline one described and he emphasized that " the compound of urea with lævulose . . . cannot be obtained in crystalline form." It is thus not surprising that, in a review article,[2] these compounds of Quehl were termed " merely physical mixtures of urea and D-glucose in the form of ' molecular compounds '."

From concentrated aqueous solutions of urea and various sugars, we have obtained, after several months, a crystalline equimolecular addition compound of urea and glucose, but so far of no other sugar. When inoculation is possible this compound crystallizes with ease and is readily prepared. It can be made by mixing cold concentrated aqueous solutions of glucose and urea, followed by inoculation, but because of its high solubility the yields are then small unless the solution is concentrated further, for example in a desiccator. It is prepared more rapidly and in much better yield by commencing with hot concentrated solutions: Urea (60 g.) is dissolved in water (40 g.) at 65°, and powdered anhydrous α-D-glucose (180 g.) is added. The resulting solution is, if necessary, filtered from impurities at 70°, inoculated with the powdered *addition compound*, stirred, and set aside overnight. The well-formed crystals are filtered off, washed successively with 50% aqueous acetone (25 ml.), 80% aqueous acetone (50 ml.), and acetone, and dried at 50°; yield 150 g., m. p. 112—114° (Kofler) (Found: C, 35·0; H, 6·6; N, 11·6. $C_6H_{12}O_6,CO(NH_2)_2$ requires C, 35·0; H, 6·7; N, 11·7%). By slower crystallization large crystals several mm. across can be obtained.

Dr. J. Fridrichson, of the Division of Chemical Physics, has kindly obtained the following crystallographic information: $M = 240{\cdot}22$, orthorhombic, $a = 6{\cdot}915$, $b = 9{\cdot}157$, $c = 16{\cdot}518$ (all $\pm 0{\cdot}003$) Å, $U = 1045{\cdot}9 \pm 1{\cdot}0$ Å^3, $D_m = 1{\cdot}525$ (by flotation in carbon tetrachloride–bromobenzene), $Z = 4$, $D_c = 1{\cdot}526 \pm 0{\cdot}002$. Space group $P2_12_12_1$.

The addition compound is of α-D-glucose and urea, and was also the only crystalline compound when β-D-glucose and urea were the starting materials. Hot ethanol extracted the urea preferentially and left behind some two-thirds of the D-glucose in the pure crystalline α-form. There was no evidence that the compound existed in solution. The initial optical rotation of an aqueous solution, obtained by extrapolation, was that calculated from its α-D-glucose content, and, after mutarotation, the value of $[\alpha]_D^{20}$ (+39·5°; *c* 6·4) agreed with that calculated from the probable content of equilibrated D-glucose. In water (100 g.) its solubility was 145·7 g. at 15°, 206·8 g. at 25°, and 251 g. at 35°. The water-vapour pressure over a saturated solution at 25°, measured in an isoteniscope, was 16·7 mm. Hg, which corresponds to a relative humidity of 70·3. At a relative humidity of 58, crystals of the addition compound remained anhydrous, whereas an intimate

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[1] Quehl, U.S.P. 2,116,640 (1938); Quehl and Rotta, B.P. 467,749 (1937).

[2] Goodman, *Adv. Carbohydrate Chem.*, 1958, **13**, 215.

equimolecular mixture of urea and α-D-glucose absorbed 21% by weight of water. At a relative humidity of 76 the addition compound slowly absorbed water and at equilibrium it absorbed 45% (the same as that absorbed by an equimolecular mixture of its components).

The infrared spectrum of the addition compound in a Nujol mull differs from that of each of its components and from an intimate mixture of them; it is much sharper than that of the mixture. The strong band at 914 cm.$^{-1}$ of α-D-glucose is shown by both the addition compound and the mixture, but that at 837 cm.$^{-1}$, which the mixture also shows, is absent for the addition compound and is replaced by a band of like intensity at 862 cm.$^{-1}$. Other characteristic bands occur at 1270, 1505, and 1645 cm.$^{-1}$, the last being in addition to the expected band for urea at 1675 cm.$^{-1}$.

That it is possible to extract the urea of the addition compound preferentially with ethanol at temperatures 30° or more below the melting point of the compound and to leave behind pure crystalline α-D-glucopyranose, indicates that this ring form of glucose is present essentially unchanged in the addition compound. This is supported by the agreement of the initial optical rotation of the addition compound in solution with that which would be shown by the glucose it contains if it alone were present in solution as the α-anomer. The strong absorption bands at 914 and at 862 cm.$^{-1}$ in the infrared spectrum further imply that the α-glucose is present in much the same condition as that in which it exists in its crystalline hydrate.

It follows that, in the addition compound, the α-D-glucopyranose and urea molecules are not linked covalently, but retain their "molecular individuality" and are held principally by hydrogen bonding and by weak van der Waals forces. The fact that in aqueous solution there is mutarotation to a value which scarcely differs from that which would be shown by a solution of equilibrated glucose of comparable concentration, indicates that the addition compound is probably completely dissociated in solution.

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