

Predicting formation of hydrate inclusion compounds: furan clathrate hydrate

T. H. PLUMRIDGE, G. STEELE * AND R. D. WAIGH

*Department of Pharmaceutical Sciences, University of Strathclyde, 204 George Street, Glasgow G1 1XW, and *Astra Charnwood, Bakewell Road, Loughborough, LE11 5RH*

Hydrate inclusion compounds are solid crystalline complexes in which various types of guest molecule are accommodated inside regular cage structures formed by hydrogen-bonded water molecules. Clathrate hydrates are the simplest hydrate inclusion compounds with about 90 compounds known to form clathrates of the most common structure -I and -II types. We are using a combination of molecular modelling studies of the hydrate cavities enclosing various guest molecules and regression equations developed from a databank of structural and physico-chemical properties of all the molecules which had been reported to form clathrate hydrates, in order to identify guest molecules which will form more stable hydrates than those currently known.

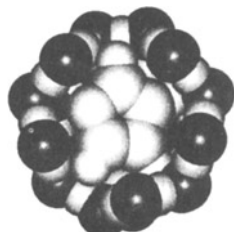


Fig.1 : A molecule of furan inside the large cavity of the structure-II clathrate.

Using these techniques we have predicted a number of molecules which we believe will form clathrate hydrates of either structure-I or -II. From this list we chose furan clathrate for a detailed practical investigation.

Furan was chosen because

- the predicted clathrate melting point from the regression equation below was 14°C.
 $b.p. = 7.27 m.p. - 71.30.$
(Plumridge & Waigh, 1997)
where *b.p.* is the boiling point of the pure guest (32 °C for furan) and *m.p.* is the melting point of the clathrate, for structure-II clathrates.
- the furan molecule appears to fit well inside the large structure-II cavity (see Fig.1)
- furan had been reported to form a hydrate but no further work had been carried out (von Stackelburg, 1951).
- a neutron diffraction study of the structurally related tetrahydrofuran clathrate hydrate has been reported (Yamamuro et al., 1995).

The furan hydrate was prepared by stirring a stoichiometric mixture of 4.5g water and 1g furan at constant temperature. The resulting crystals were analysed by DSC scans between -5 and 15°C, which revealed the amount of ice contamination in the sample by the size of the peak with onset *ca.* 0°C. The DSC information was used to refine the preparative procedure. The onset of the melting of the clathrate occurred at *ca.* 4.4°C, which is not in very good agreement with

prediction. Various formation temperatures in the range 0 °C < T < 4.4 °C were tried with an optimum at 3.8 °C. The mixtures were also seeded with small amounts of previous samples which facilitated crystallisation. DSC plots of an early product (Fig.2a), showed a large ice peak; a purer sample (Fig.2b) showed a shoulder peak due to slight ice contamination and a large clathrate peak.

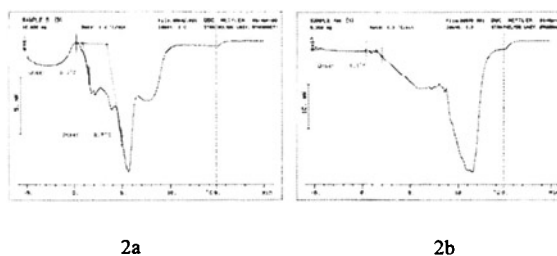


Fig.2 : DSC plots for impure (2a) and almost pure (2b) samples of furan clathrate hydrate.

Once the samples were sufficiently pure, the next stage of the work involved a more detailed structural study. As single crystals of the clathrate proved impossible to prepare, it was decided to use a microcrystalline powder diffraction technique. Because of the extensive hydrogen-bonding in clathrate systems, neutron diffraction is preferred, and to investigate the hydrogen atom positions it was necessary to produce a fully deuterated clathrate using deuterated water and deuterated furan. The melting point of pure D₂O is 3.8°C. The melting point of fully deuterated furan clathrate was found to be 7.4°C, and the optimal reaction temperature was found to be 6.9°C.

The resulting sample will be analysed on the high resolution powder diffractometer at the *ISIS* facility of the Rutherford Appleton Laboratory.

We would like to thank Astra Charnwood and EPSRC for financial support for T. H. Plumridge.

Plumridge, T. H. & Waigh, R. D. (1997) *J. Pharm. Pharmacol.* **49**, S4, 67
von Stackelburg, M. & Müller, H. R. (1951) *J. Chem. Phys.* **16**, 1319
Yamamuro, O., Matsuo, T., Suga, H., David, W. I. F., Ibberson, R. M., & Leadbetter, A. J. (1995) *Physica B* **213&214**, 407.