

This article was downloaded by:

On: 29 January 2011

Access details: *Access Details: Free Access*

Publisher *Taylor & Francis*

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



## Supramolecular Chemistry

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713649759>

### Crystalline $\beta$ -cyclodextrin hydrate is non-stoichiometric with 10.5-12 waters per cyclodextrin molecule

John A. Ripmeester<sup>a</sup>

<sup>a</sup> Steacie Institute for Molecular Sciences, National Research Council of Canada, Ottawa, Ontario, Canada

**To cite this Article** Ripmeester, John A.(1993) 'Crystalline  $\beta$ -cyclodextrin hydrate is non-stoichiometric with 10.5-12 waters per cyclodextrin molecule', *Supramolecular Chemistry*, 2: 2, 89 – 91

**To link to this Article:** DOI: 10.1080/10610279308038301

**URL:** <http://dx.doi.org/10.1080/10610279308038301>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

# Crystalline $\beta$ -cyclodextrin hydrate is non-stoichiometric with 10.5–12 waters per cyclodextrin molecule

JOHN A. RIPMEESTER

*Steacie Institute for Molecular Sciences, National Research Council of Canada, Ottawa, Ontario K1A 0R9 Canada*

*(Received January 5, 1993)*

Solid-state  $^{13}\text{C}$  NMR spectroscopy was used to follow the dehydration of  $\beta$ -cyclodextrin hydrate from 12 to 10.5 waters per cyclodextrin. The process takes place without loss of crystalline order, or the presence of a phase transition. The water molecules involved can best be described as space-filling guests enclathrated in the cyclodextrin cavity. Hence the hydrate is non-stoichiometric within the limits of 10.5–12 waters per cyclodextrin molecule. On the other hand, dehydration of crystalline  $\alpha$ -cyclodextrin hexahydrate involves a phase transition.

## INTRODUCTION

The cyclodextrins, macrocycles comprised of 6–8 anhydroglucose units, are extremely versatile host molecules which form inclusion complexes in the solid state as well as solution.<sup>1,2</sup> In the solid state, guest-free cyclodextrins exist in several hydrated forms, with some water molecules in the host cavity, others forming hydrogen bonding networks between macrocycles.

$\alpha$ -Cyclodextrin, with 6 anhydroglucose units is known to form at least three different hydrates at room temperature,<sup>3</sup> the structures for some of which are known.<sup>4–6</sup> For  $\beta$ -cyclodextrin, with 7 anhydroglucose units, the structure of a high hydrate is known.<sup>7,8</sup> Recent work has shown that under ambient conditions this hydrate with 12 waters per cyclodextrin reversibly dehydrates to a 10.5-hydrate with only slight structural changes,<sup>10</sup> and one is left with the impression that  $\beta$ -cyclodextrin forms two stoichiometric hydrates. One concern is that the composition of samples prepared for physical measurements will depend on the preparation method and conditions of storage, and that there is no easy way to monitor the hydration state of the material.<sup>10</sup> In this contribution it is shown that solid-state  $^{13}\text{C}$  NMR can give exact information on the hydration state, and that in fact there is just a

single, non-stoichiometric hydrate, rather than two hydrates of fixed stoichiometry. Also some suggestions are given as to the correct description of the water that is easily lost and regained.

## EXPERIMENTAL

$\alpha$ - and  $\beta$ -cyclodextrins were obtained as commercial products and recrystallized from distilled water. For some samples water contents were checked by using Karl Fischer titration. CP/MAS  $^{13}\text{C}$  NMR spectra were obtained as previously described<sup>11</sup> on a Bruker CXP-180 NMR spectrometer.

## RESULTS AND DISCUSSION

When  $\beta$ -cyclodextrin is recrystallized from water, the 12-hydrate is obtained, and it can be preserved intact by keeping it in contact with mother liquor. The  $^{13}\text{C}$  CP/MAS NMR spectrum, shown in Fig 1a, shows partially resolved septets, for the C1 and C4 carbons, as all 7 anhydroglucose units in the asymmetric unit are inequivalent.<sup>7–9</sup> Some years ago, it was reported that the lower hydrate could be prepared in a consistent way by heating the recrystallized  $\beta$ -cyclodextrin to constant weight at 60 °C.<sup>12</sup> The  $^{13}\text{C}$  CP/MAS NMR spectrum for this material is shown in Fig 1b. It is clear that this spectrum is quite distinct from that of the higher hydrate, and that therefore the NMR spectrum is quite diagnostic of the hydration state of the material. Again the spectrum consists of partially resolved septets, as the asymmetric unit still contains one entire  $\beta$ -cyclodextrin molecule. It should be mentioned that the spectra shown in Fig 1 have been reported before in a number of different

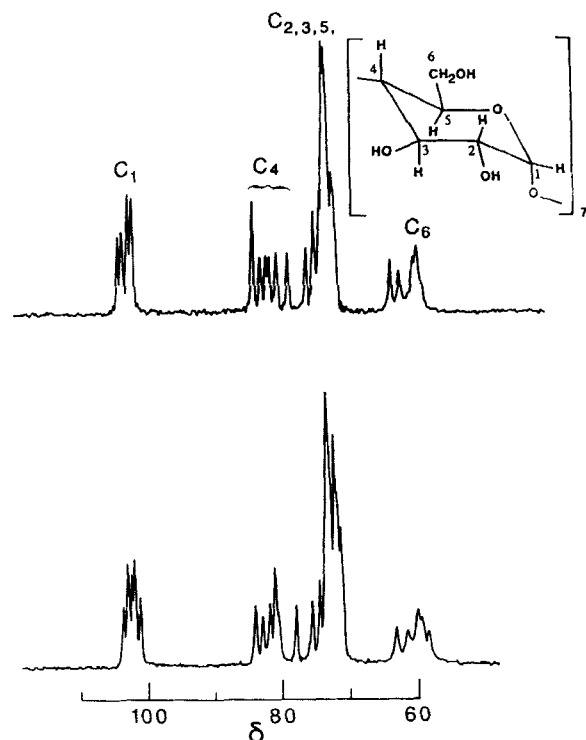


Figure 1  $^{13}\text{C}$  CP/MAS NMR spectra of  $\beta$ -cyclodextrin hydrates; 12-hydrate (top), 10.5 hydrate (bottom).

publications,<sup>13-16</sup> but their relationship and assignment to a specific hydration state have not been remarked upon so far.

One remarkable aspect of the dehydration process was revealed during a prolonged spectral run on a freshly prepared sample of the 12-hydrate. The spectrum changed continuously as a function of time until it became identical to that of the lower hydrate. This sequence of events is shown in Fig 2, where a detail of the C4 carbon region is given. The remarkable feature is that the individual lines remain sharp and distinct, and shift slightly as time progresses and water is lost. There are no lines which disappear from the spectrum, and no new lines are added, as one might expect if a phase transition accompanied the loss of water. This latter case is illustrated explicitly below for the dehydration of  $\alpha$ -cyclodextrin hexahydrate.

From crystallographic work it is known that the water molecules which are lost during the dehydration from the 12 to the 10.5 hydrate reside in the cyclodextrin cavity where there are 7 partially and 2 fully occupied sites.<sup>10</sup> However, the NMR experiment shows that crystalline order is maintained in the lattice during hydration, as all of the spectral lines remain sharp. Since there are only 7 C4 lines, this means that all cyclodextrin molecules are equivalent. This may be difficult to understand in light of the partial occupancy of the water positions, and the fact that these

occupancies must change in a continuous way as the water content changes. The only way that this is possible is if there is dynamic averaging, that is at least some of the water molecules must move from one cyclodextrin cavity to another, and the motion must be rapid on an NMR timescale. If we can estimate the changes in  $^{13}\text{C}$  chemical shift associated with the different static hydration states at no more than a few ppm, the maximum correlation time for the water exchange is  $\sim 0.001$  sec. Of course it is likely that this intercavity exchange of water molecules involves water molecules outside the cyclodextrin cavity as well. The presence of relatively rapid water reorientation is known from dielectric<sup>17</sup> and  $^2\text{H}$  NMR measurements,<sup>18</sup> although as used, these methods did not give information on exchange between intra and intercavity water.

A good description for the easily exchanged water molecules in the cavity would be one of enclathrated guest molecules, as they seem to play a space-filling rather than an important structural role. The variable composition of the  $\beta$ -cyclodextrin hydrate has an analogy with the non-stoichiometric clathrate hydrates where the water molecules form a host lattice for a large variety of guest molecules.<sup>19-20</sup> For the clathrate hydrates, especially those belonging to the class of cubic structures known as type I, the exact composition

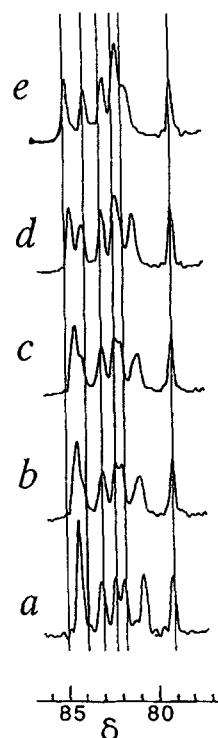


Figure 2  $^{13}\text{C}$  CP/MAS NMR spectra of  $\beta$ -cyclodextrin; detail of C4 region a) 12 hydrate; b)-d) intermediate hydration states; e) 10.5 hydrate.

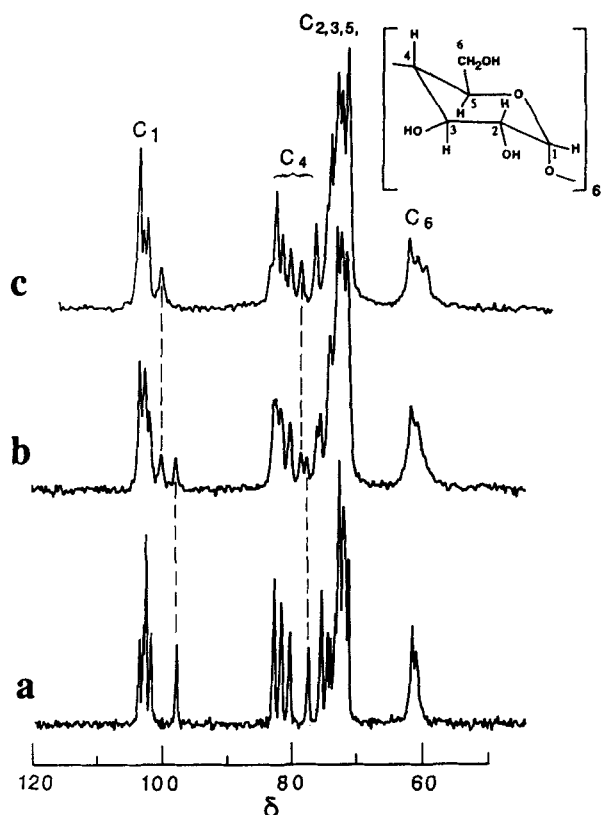


Figure 3  $^{13}\text{C}$  CP/MAS NMR spectra of  $\alpha$ -cyclodextrin; a) hexahydrate; b) mixed phases; c) lower hydrate.

varies between certain limits, which at a constant temperature depends on the vapour pressure of the guest.<sup>19</sup>

The other case, that is, the initiation of a phase change by the loss of water, is illustrated in Fig 3a-c.  $\alpha$ -Cyclodextrin was dried over calcium chloride and the  $^{13}\text{C}$  NMR spectrum was recorded as a function of time the sample was kept over the drying agent. It is quite clear that as water is lost from the sample, new lines appear in the spectrum, and the characteristic hexahydrate spectrum lose intensity. The spectrum in

Fig 3c is that of a new, lower hydrate which again appears to have one complete cyclodextrin molecule in the asymmetric unit, as the C1 and C4 carbon lines still are more or less resolved sextets. The spectrum shown in Fig 3b is then a weighted sum of the spectra shown in Figs 3a and 3c.

## REFERENCES

- 1 Saenger, W.; in *Inclusion Compounds*, Vol 2 (Atwood, J.L., Davies, J.E.D. and MacNicol, D.D. eds), Academic Press, London, 1984.
- 2 Szejtli, J.; *Cyclodextrins and Their Inclusion Compounds*, Akademiai Kiado, Budapest, 1982.
- 3 Wiedenhoff, N. and Lammers, J.N.J.J.; *Carbohydrate Res.* 1967, 4, 318.
- 4 Klar, B., Hingerty, B. and Saenger, W.; *Acta Crystallogr.* 1980, B36, 1154.
- 5 Chacko, K.K. and Saenger, W.; *J. Am. Chem. Soc.* 1981, 103, 1708.
- 6 Lindner, K. and Saenger, W.; *Acta Crystallogr.* 1982, B38, 203.
- 7 Lindner, K. and Saenger, W.; *Carbohydrate Res.* 1982, 99, 103.
- 8 Zabel, V., Saenger, W. and Mason, S.A.; *J. Am. Chem. Soc.* 1986, 108, 3664.
- 9 Betzel, C., Saenger, W., Hingerty, B.E. and Brown, G.M.; *J. Am. Chem. Soc.* 1984, 106, 7545.
- 10 Steiner, T., Koellner, G., Ali, S., Zakim, D. and Saenger, W.; *Biochem. Biophys. Res. Comm.* 1992, 188, 1060.
- 11 Ripmeester, J.A.; *J. Inclusion Phenom.* 1988, 6, 31.
- 12 Hanabata, H., Matsuo, T. and Suga, H.; *J. Incl. Phenom.* 1987, 5, 325.
- 13 Gidley, M.J. and Bociek, S.M.; *J. Chem. Soc. Chem. Comm.* 1986, 1223.
- 14 Veregin, R.P., Fyfe, C.A., Marchessault, R.H. and Taylor, M.G.; *Carbohydrate Res.* 1987, 160, 41.
- 15 Veregin, R.P., Fyfe, C.A. and Marchessault, R.H.; *Macromolecules* 1987, 20, 3007.
- 16 Furo, I., Pocsik, I., Tompa, K., Teeaar and Lippmaa, E.; *Carbohydrate Res.* 1987, 166, 27.
- 17 Pathmanathan, K., Johari, G.P. and Ripmeester, J.A.; *J. Phys. Chem.* 1989, 93, 7491.
- 18 Usha, M.G. and Wittebort, R.J.; *J. Am. Chem. Soc.* 1992, 114, 1541.
- 19 Davidson, D.W.; in *Water, A Comprehensive Treatise*, Vol 2 (Frank, F., ed.), Plenum Press, N.Y., 1973.
- 20 Davidson, D.W. and Ripmeester, J.A.; in *Inclusion Compounds*, Vol 3 (Atwood, J.A., Davies, J.E.D. and MacNicol, D.D. eds), Academic Press, London, 1984.