

Evolution of Organized Lariat Ether Alcohol and Diol Hydrate Macrostructures in the Solid State

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Abstract

Lariat ether alcohols and diols derived from dibenzo-14-crown-4 crystallize in the anhydrous form or as hydrogen-bonded monohydrates or networks depending upon the polyether ring substituents and the composition of the aqueous organic crystallization solvent. Supramolecular structures are created when the lariat ether alcohol *sym*-(hydroxy)dibenzo-14-crown-4 (**1**) with “sticky ends” of ether oxygens and hydroxyl protons, hydrogen bond to each other via bridging water molecules to form three-dimensional networks. For crystallization of **1** from 30% aqueous acetonitrile, this self-association is sufficiently strong to spontaneously generate a supramolecular structure with water channels.

Introduction

Earlier, we reported an unusual crystal structure of *sym*-(hydroxy)dibenzo-14-crown-4 (**1**) (Figure 1) as a monohydrate tecton with a water-methanol channel that was grown from aqueous methanol [1]. The tendency of **1** to form a monohydrate allows it to be used as “sticky sites” that compel molecules to associate, thereby driving the self-assembly of aggregates joined together by an extended network of hydrogen bonds. This suggests that incorporation of multiple sticky sites into a rigid framework might induce the self-assembly of three-dimensional networks with internal channels.

In other studies performed with lariat ether alcohol **1**, acetonitrile [2] and aqueous acetonitrile solutions [3] were employed as crystal growth media. From the former, crystals of anhydrous **1** were formed. However, from aqueous acetonitrile, crystals of anhydrous **1** were obtained in some instances and of **1**-monohydrate in others. The same phenomena was observed when *sym-trans*-(dihydroxy)dibenzo-14-crown-4 (**2**) was crystallized from acetonitrile and aqueous acetonitrile solutions [2, 3]. On the other hand, when *sym-cis*-(dihydroxy)dibenzo-14-crown-4 (**3**) was crystallized from the same media, only **3**-monohydrate was obtained [3]. These results suggest a dependence of the crystallization process on the structure of the lariat ether alcohol or diol and the presence or absence of water in the crystallization solvent.

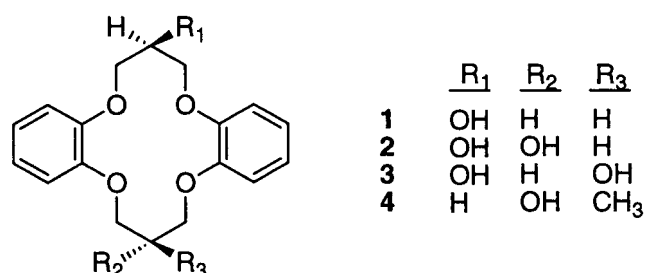


Figure 1. Structures of lariat ether alcohols **1** and **4** and diols **2** and **3**.

To probe the role of solvent composition on crystal growth for such small organic molecules, we have conducted a series of experiments in which two lariat ether alcohols and two lariat ether diols were crystallized from organic solvents and aqueous-organic solvent solutions. Herein we report the solid-state compositions of dibenzo-14-crown-4 alcohol (**1**), dibenzo-14-crown-4 diols **2** and **3**, and *sym*-(hydroxy)(methyl)dibenzo-14-crown-5 (**4**) as crystallized from acetonitrile and aqueous organic solvent solutions in which the organic solvent component was acetonitrile, ethanol, ethylene glycol, and methanol.

Experimental

Lariat ether alcohols **1** [1] and **4** [2] and diols **2** [4] and **3** [4] were prepared by reported methods. Reagent-grade organic solvents from Fluka were dried over 4 Å molecular

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Table 1. Crystal data and refinement results for **1**-(water channel)

Formula	C ₁₈ H ₂₂ O ₅
Formula weight	342.36
Crystal system	Tetragonal
Space group	I $\bar{4}$
Crystal size/mm	0.3 × 0.3 × 0.1
Crystal color	Colorless
<i>a</i> , <i>b</i> /Å	16.406(4)
<i>c</i> /Å	13.164(5)
<i>V</i> /Å ³	3545
<i>Z</i>	8
Density/mg m ⁻³	1.287
Independent data	1750 (<i>R</i> _{int} = 0.0556)
Data/restraints/parameters	1744/0/228
<i>R</i> , <i>ωR</i> ² (<i>I</i> = 2σ(<i>I</i>)) ^a	0.0650, 0.1497
GOF on <i>F</i> ²	0.996
Largest diff. peak and hole/eÅ ⁻³	0.318, -0.193

$$^a R = \sum \| |F_0| - |F_c| \| / \sum |F_0|, \omega R^2 = [\sum [\omega(F_0^2 - F_c^2)^2] / \sum [\omega(F_0^2)^2]]^{1/2}.$$

sieves. Crystals were grown from solutions of the lariat ether alcohols and diols at ambient temperature.

The X-ray data were obtained using a Nicolet R3 automated diffractometer with MoK α radiation ($\lambda = 0.71073$ Å). Solid-state compositions for the lariat ether alcohols and diols crystallized from various solvents were established by determination of the lattice parameters for their crystals and comparison with those of known structures [2, 3], except with **1**-(water channel) for which a complete structure determination was performed.

The structure for **1**-(water channel) was solved using the direct methods program contained in the SHELXTL program package [5]. Final refinement and display of the structures were performed using the SHELXTL-PC program package [6]. Crystal data and refinement results for **1**-(water channel) are presented in Table 1. Complete crystallographic data have been deposited with the Cambridge Crystallographic Data Centre (CCDC, 12 Union Road, Cambridge, CB2 1E2, UK) [7].

Results

Compositions for lariat ether alcohols **1** and **4** and diols **2** and **3** crystallized from acetonitrile and from aqueous acetonitrile, ethanol, ethylene glycol, and methanol solutions of varying water contents are presented in Table 2.

To investigate the influence of water content in acetonitrile solutions upon the solid-state structure, a systematic study of crystal growth of lariat ether alcohols **1** and **4** and diols **2** and **3** from aqueous acetonitrile solutions was undertaken in which the water content was increased stepwise in the order 5, 10, 15, 20, 25, and 30% (v/v). The results presented in Table II reveal a different composition pattern for each of the four hydroxy lariat ether compounds. From acetonitrile and 5% aqueous acetonitrile, crystals of the anhydrous forms of lariat ether alcohols **1** and **4** and diol **2**

Table 2. Crystal compositions for lariat ether alcohols **1** and **4** and diols **2** and **3** as a function of the aqueous-organic solvent composition of the crystallization solvent

Organic solvent	Percent water by volume	Crystal structure ^a for:			
		1	2	3	4
Acetonitrile	0	A	A	M	A
Acetonitrile	5	A	A	M	A
Acetonitrile	10	M	M	M	A
Acetonitrile	15	M	M	M	A
Acetonitrile	20	M	M	M	A
Acetonitrile	25	M	M	M	A
Acetonitrile	30	WC	M	M	A
Ethanol	2	A	M	M	A
Ethanol	5	A	M	M	A
Ethanol	10	M	M	M	A
Ethylene glycol	2	M	U	U	U
Methanol	2	M	M	M	A
Methanol	5	WMC	M	M	A

^a A = anhydrous, M = monohydrate, WC = water channel, U = unsuitable crystals, WMC = water-methanol channel.

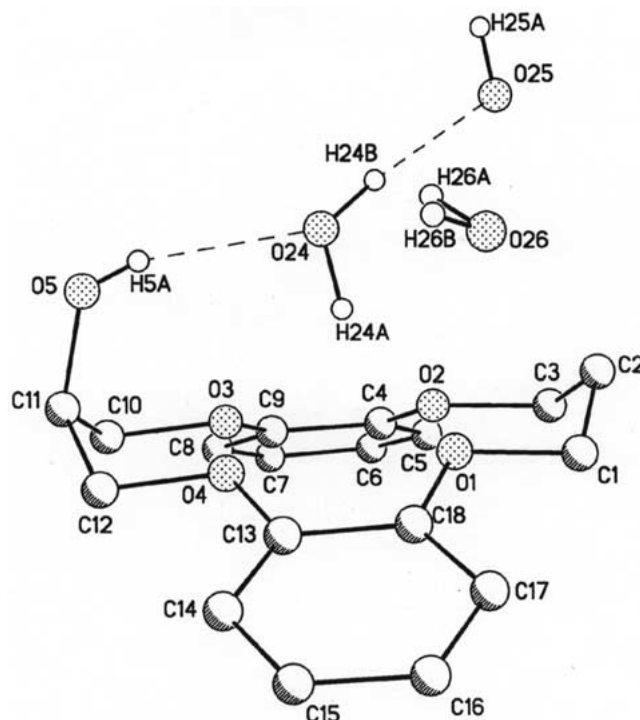


Figure 2. Conformation of the lariat ether alcohol unit in **1**-(water channel).

were obtained. On the other hand, diol **3** gave a monohydrate structure. Increasing the water content to 10, 15, 20 and 25% aqueous acetonitrile, gave crystals of **1**-monohydrate, **2**-monohydrate, and **3**-monohydrate. In contrast, only the anhydrous form of lariat ether alcohol **4** was evident for this solvent variation. Although the crystal compositions remained the same for the change to 30% aqueous acetonitrile with lariat ether alcohol **4** and diols **2** and **3**, a very different situation was observed with **1**. For this lariat ether alcohol, additional hydrogen bond interactions between **1** and water molecules produced crystals of **1**-(water channel) from 30% aqueous acetonitrile within an hour. Structures of an

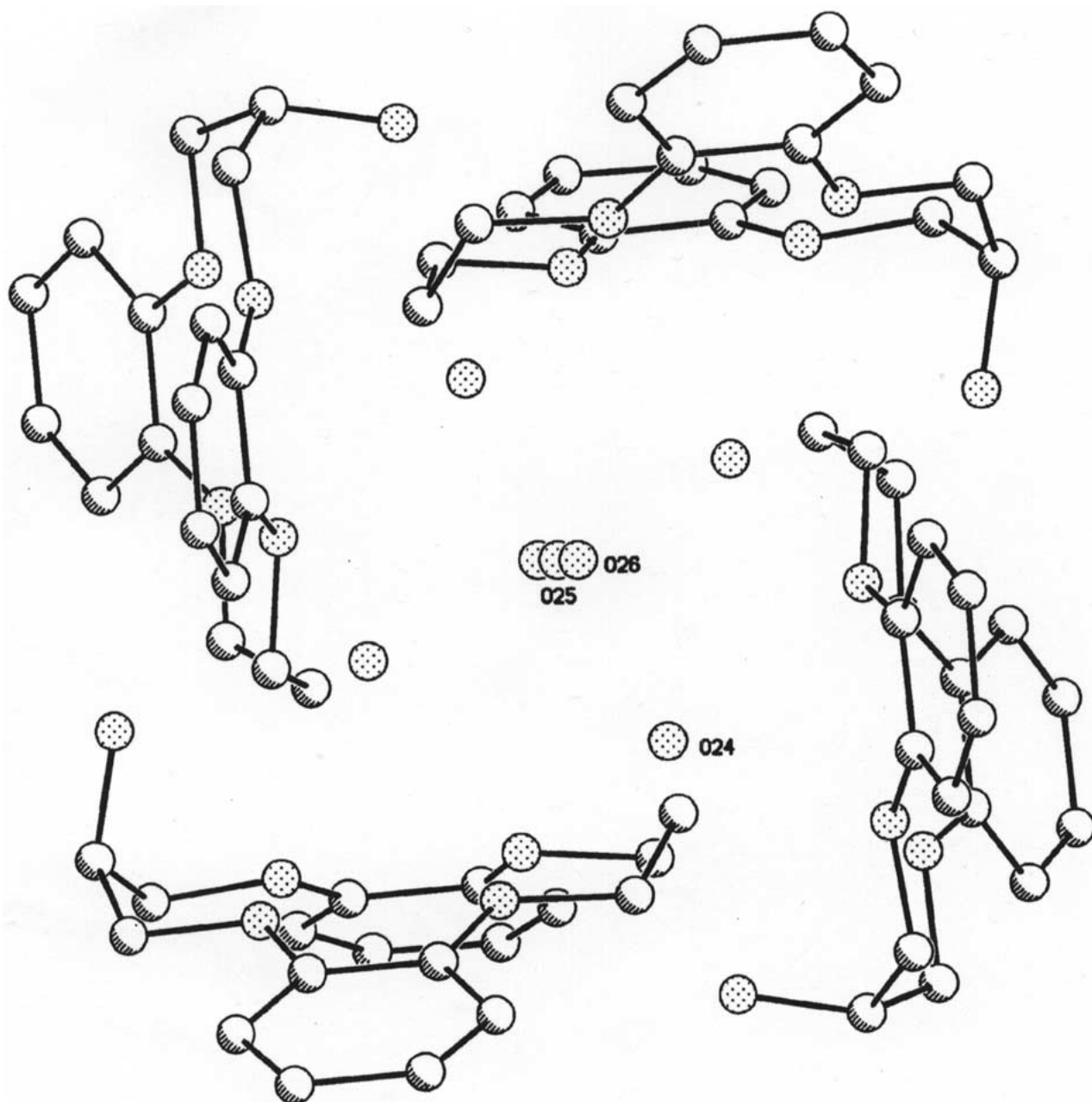


Figure 3. The water channel formed by four lariat ether alcohol units in **1**-(water channel).

individual hydrogen-bonded lariat ether alcohol unit, of four cooperating molecules of **1** that form the water channel, and of the packing diagram for the water channel structure are shown in Figures 2–4, respectively.

Lariat ether alcohol **1** was also crystallized from aqueous ethanol, ethylene glycol, and methanol solutions. The composition results for crystal growth from aqueous ethanol were very similar to those obtained from aqueous acetonitrile with low water content. Thus, anhydrous **1** was isolated from 2 and 5% aqueous ethanol, but **1**-hydrate was formed in 10% aqueous ethanol. From 2% aqueous ethylene glycol, **1**-monohydrate was isolated. Crystals suitable for structure determination could not be obtained when the water content of aqueous ethylene glycol was increased. From 2% aqueous methanol, **1**-monohydrate was formed. From 5%

aqueous methanol, crystals of **1**-(water-methanol channel) were obtained. This solvent composition is similar to that from which the **1**-(water-methanol channel) crystals were grown initially [1].

For the lariat ether alcohol **4** and diols **2** and **3**, crystallization from 2, 5 and 10% aqueous ethanol and from 2 and 5% aqueous methanol gave the same solid-state compositions as were observed for 10% aqueous acetonitrile and higher water contents. Thus, the monohydrate forms of lariat ether diols **2** and **3** and the anhydrous form of lariat ether alcohol **4** were produced. It was not possible to obtain suitable crystals from hydroxyl group-containing lariat ethers **2–4** from aqueous ethylene glycol solutions of any proportions.

Thus each of the four lariat ether alcohols and diols exhibits a unique pattern for incorporating water from the

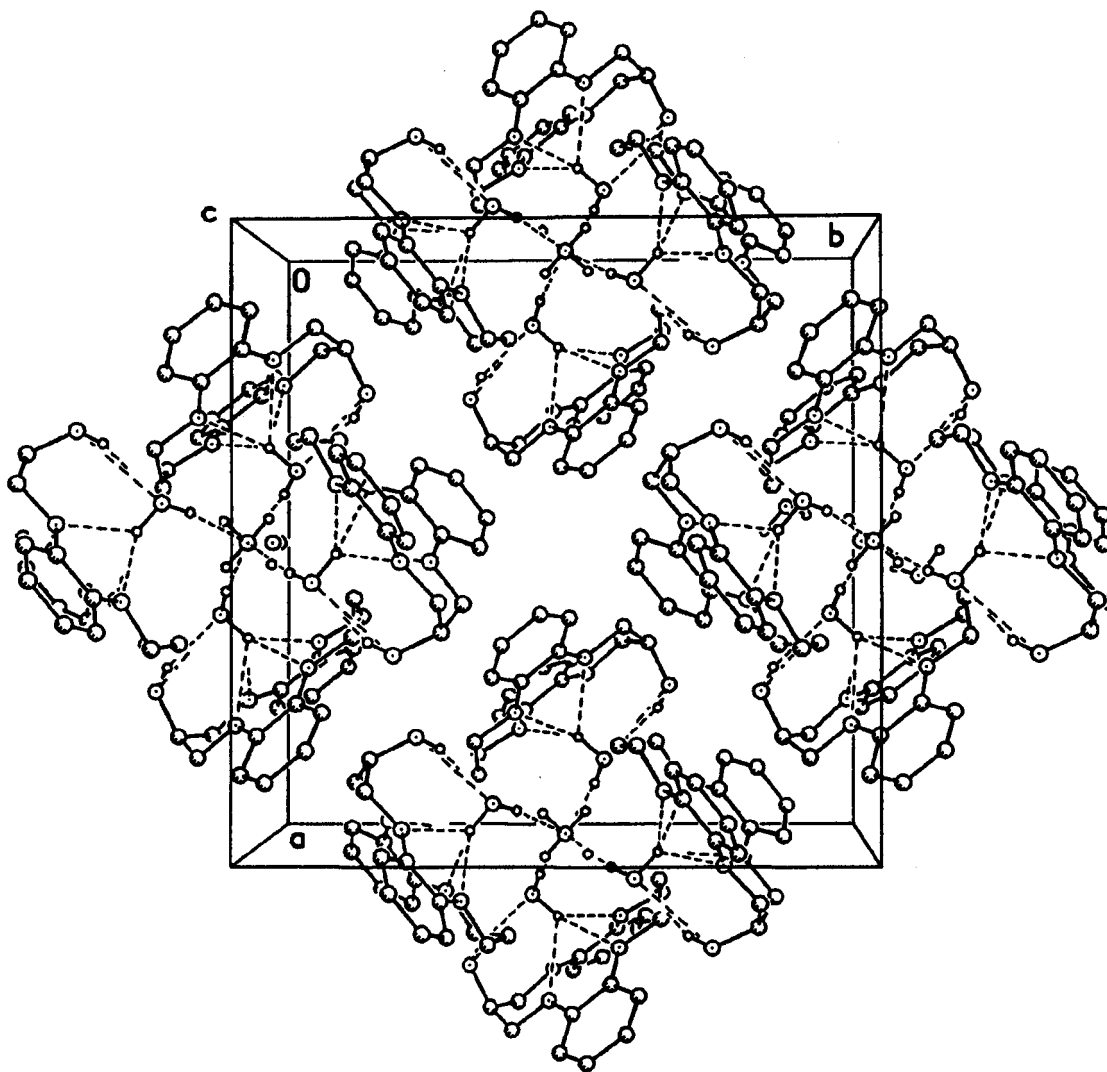


Figure 4. Packing diagram of 1-(water channel) that shows the hydrogen bond network.

solvent into the crystals or rejecting it. Substituents on the central carbon of the three-carbon bridge in dibenzo-14-crown-4 compounds can either occupy a pseudoequatorial position in which the substituent lies approximately in the plane of the crown ether ring or a pseudoaxial position with the substituent approximately perpendicular to that plane [1–4]. Formation of a solid-state monohydrate structure involves hydrogen bonding of a pseudoaxial hydroxyl group with the oxygen atom of a water molecule positioned over the crown ether cavity [3].

Lariat ether diol **3** crystallized as a monohydrate from aqueous acetonitrile, ethanol, and methanol solutions. Since **3**-monohydrate was also formed from acetonitrile with no added water, some structural feature of this lariat ether diol must strongly favor monohydrate formation. This is attributed to the *cis* arrangement of the two hydroxyl groups attached to the central carbons of each three-carbon bridge. These two pseudoaxial hydroxyl groups provide an optimal cage for a water molecule in which there is hydrogen bonding of the hydrogen of one hydroxyl group to the oxygen of the water molecule and hydrogen bonding of one hydrogen

of the water molecule to the oxygen of the second hydroxyl group [3, 4].

Crystallization of *sym*-(hydroxy)(methyl)dibenzo-14-crown-4 (**4**) from acetonitrile and aqueous acetonitrile, ethanol, and methanol gave only the anhydrous form. Although the solid-state structure of **4** shows a pseudoaxial hydroxyl group [2], it is proposed that the presence of the geminal methyl group promotes strong intramolecular hydrogen bonding of the alcohol group hydrogen with an adjacent polyether ring oxygen. Furthermore, it is suggested that for lariat ether alcohol **4** in solution, this strong intramolecular hydrogen bonding locks the conformation and prevents inversion of the dibenzo-14-crown-4 ring [2]. Thus, the intramolecular hydrogen bond blocks formation of a potential intermolecular hydrogen bond with a water molecule.

From acetonitrile, 5% aqueous acetonitrile, and 2 and 5% aqueous ethanol, *sym*-(hydroxy)dibenzo-14-crown-4 (**1**) crystallized in the anhydrous form. Increasing the water content to 10% aqueous acetonitrile and 10% aqueous ethanol produced **1**-monohydrate. On the other hand, crystallization of **1** from 2% aqueous methanol and 2% aqueous

ethylene glycol gave **1**-monohydrate. Since acetonitrile and ethanol form azeotropes with water while ethylene glycol and methanol do not, some type of stripping mechanism is suggested that reduces the tendency for hydrate formation in acetonitrile and ethanol. For *sym-trans*-(dihydroxy)dibenzo-14-crown-4 (**2**), crystallization from acetonitrile and 5% aqueous acetonitrile gave the anhydrous form. In contrast, crystallization of **2** from 10% aqueous acetonitrile or greater water content and from aqueous ethanol and methanol produced **2**-monohydrate. The apparent greater tendency for monohydrate formation from *trans*-diol **2** than alcohol **1** may be rationalized by their solid-state structures [2]. In the disordered solid-state structure for lariat ether alcohol **1**, there is 70% partial occupancy by a conformation with the hydroxyl group pseudoequatorial and 30% partial occupancy by a conformation with the hydroxyl group pseudoaxial. On the other hand, lariat ether diol **2** has one hydroxyl group pseudoaxial and one pseudoequatorial at all times.

With the change to 25 to 30% aqueous acetonitrile as the crystallization solvent for lariat ether alcohol **1**, the solid-state composition changes from **1**-monohydrate to **1**-(water channel) (Figure 4). Thus additional hydrogen bonding interactions of water generate a network. The structure of **1**-(water channel) is isomorphous with **1**-(water-methanol channel) [1] with the methanol molecule in the latter replaced by a disordered water molecule. In the present study, it was found that changing from 2 to 5% aqueous methanol as the crystallization solvent altered the solid-state morphology from **1**-monohydrate to **1**-(water-methanol channel).

Central to the question of association in aqueous and aqueous-organic solvent solutions is the debate over the relative importance of solute-solute vs. solute-solvent interactions [9]. In this research, a dependence of crystal composition on both the water content of the organic solvent and the properties of the organic solvents is demonstrated. Water molecules organize the structure of organic solute molecules via hydration and vice-versa. Results from this study of crystal growth from aqueous organic solvents and those published by other researchers [10] demonstrate a requirement for a minimal number of water molecules to promote formation of a three-dimensional structure in the crystals of a hydrated organic solute. By providing that minimal number of molecules, we are able to change the crystal structure gradually from an anhydrous form of lariat ether alcohol **1** to highly organized hydrated structures. This phenomenon is controlled by the water [11–14] and organic solvent [14, 15] properties and, in particular, by enhancement of hydrogen bond strength due to cooperativity effects of the hydrogen bonds [16, 17].

Formation of water channels for **1** from aqueous acetonitrile and of water-methanol channels from aqueous methanol is a clear manifestation of their function in architecture at the molecular level. Thus, it is not that water molecules occupy channels formed in the lattice, but rather that these channels are formed around the water molecules. The water channel structure represents a self-assembly based on the lariat ether

alcohol-water lattice and is an unusual demonstration of molecular tectonics [2, 3, 18, 19]. The current systematic study of the anhydrous and monohydrate forms of **1** and its water channel and water-methanol channel forms reveals that these hydrogen bond patterns are predictable. This will enable us to design new macro structures based on lariat ether monohydrate building blocks. By choice of an appropriate binary solution, it may be possible to propagate from anhydrous to highly organized hydrate structures.

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