THE FORMATION OF CYANOBORATE LIQUID CLATHRATES

WITH WATER OR CRESOL AS PROMOTERS

Dissertation submitted for the degree of Master of Science

by Bridgit Davis

CHEMISTRY DEPARTMENT

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ABSTRACT

If host and guest components form a liquid clathrate only when a third component is present, the third component is a promoter of liquid clathrate formation. The importance of promoters was verified by promoting liquid clathrate formation in guest-host combinations which do not form liquid clathrates without a promoter.

The validity of the conventional definition of liquid clathrates was probed with respect to the absence of host in the excess guest layer and with respect to the fixed maximum guest to host ratio. A model which allows for the effect of promoters on liquid clathrates was proposed. The Π electron rich nature of the guest is important in the model, so the guests, furan, thiophene and benzene, were used to probe the dependence of cyanoborate liquid clathrate formation on the Π electron rich nature of the guest. Differences in the electronic nature of the promoters, water and cresol, caused differences in the ease of promoting cyanoborate liquid clathrate formation, in the stability and composition of the liquid clathrates formed, and in the interactions between the promoter and the components of the liquid clathrate (host anion, host cation and guest).

In promoting liquid clathrate formation, the promoter separated the host cation-anion pairs so that the guest interacted favourably with the host cation. The guest to host ratio was dependent on the amount of promoter present in the liquid clathrate, and favourable interactions of the promoter with liquid clathrate components caused the liquid clathrate to expand as it accommodated increased amounts of promoter and guest. Favourable interaction of the promoter with the components of the liquid clathrate compensated for the energy required to separate the host cation-anion pairs.

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R. Mohamed performed the thermogravimetric analyses.

N. Hendriks ran the VXR 200 NMR spectra.

M. Nair ran the Varian Unity 400 NMR spectra.

P. Benincasa performed the elemental analyses.

W. Coetzer and R. Hunter assisted with figure drawing.

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APPENDICES

Abbreviations

1	bis(methyltriphenylphosphonium) 1,6-bis(B-cyano-9-boratabicyclo[3.3.1]non-9-yl)hexane
2	bis(benzyltriphenylphosphonium) 1,6-bis(B-cyano-9-boratabicyclo[3.3.1]non-9-yl)hexane
9-BBN	9-borabicyclo[3.3.1]nonane
G/H	the guest per host ratio in the liquid clathrate
DMSO-d_6	[$^2H_6$]-dimethylsulfoxide
DET	diethyl-(L)- tartrate
dma	N,N-dimethylaniline
mand	mandelic acid
2-mf	2-methoxyfuran
pyra	methyl-α-D-glucopyranoside

CHAPTER 1

Introduction to liquid clathrates

1.1 Clathrates

In 1969 the first liquid clathrate was made[1] by adding excess toluene to $K[Al_2Me_6N_3]$ crystals. Two immiscible liquid layers formed with the top layer being pure toluene. The more dense, bottom layer was $K[Al_2Me_6N_3]\bullet 3.8C_6H_5Me$. This phenomenon was called a liquid clathrate by Atwood in which he extended nomenclature of solid host-guest chemistry into the liquid phase, proposing that the toluene guest molecules were trapped in the $K[Al_2Me_6N_3]$ host in the same way that guests are trapped in solid clathrates.

Solid clathrates are inclusion compounds which form host-guest lattices. A clathrate lattice[2] has two distinguishing features.

(1) The guest is found in spaces in the lattices.
(2) The guest is held in place by crystal lattice forces.

A consequence is that clathrate structure disintegrates on dissolution of the host-guest lattice. Other inclusion compounds, such as cavitates and complexes, do not disintegrate in solution as they are fundamentally different from clathrates.

(1) A cavitate guest molecule is found within its host molecule, not in a lattice.
(2) A complexed guest is held in place by co-ordination between host and guest, not by crystal lattice forces.

According to Weber[2], host - guest compounds cannot be classified without knowledge of crystal structure or a structural assignment using, for example, spectroscopy.

1.2 Definition of liquid clathrates

Each liquid clathrate has a fixed, maximum guest to host ratio which is unaltered by addition of excess guest. The liquid clathrate is immiscible with excess guest[1]. Although this diagnostic definition was formulated without knowledge of the fundamental nature and structure of liquid clathrates, it is crucial for identifying a solution as being a liquid clathrate. Biochemistry text books[3,4] have described and diagrammed the clathrate structure of water molecules around hydrophobic molecules. Although these clathrates are liquid, they are not liquid clathrates as defined above. A liquid clathrate in the laboratory appears as two immiscible liquid layers. Analysis of the two layers shows that one layer is pure excess guest and the other layer is host•nguest, where n is the maximum number of guest molecules (maximum G/H). G/H is the guest per host ratio in the liquid clathrate. Liquid clathrate literature does not always report an estimate of error[5-20] for the maximum G/H, leaving the reader in doubt about the range within which the maximum G/H is fixed. Atwood[1] estimated the standard deviation of G/H as *ca*± 0.2. Gaudet, Peterson and Zaworotko[21] obtained G/H values reproducible to within *ca*5%.

1.3 Composition of liquid clathrates

1.3.1 Liquid clathrate hosts

A liquid clathrate host consists of a cation and an anion. Atwood's prototype liquid clathrate hosts[1] were species related geometrically to $M^+[Al_2R_6X]^-$ in which:

M^+ = alkali metal, Ba^{2+}, tetra-alkylammonium cation, tetra-alkylphosphonium cation, $(C_6H_6)_2Cr^+$, Me_2Tl^+

R = Me, Et, Pr^n, Bu^n

X = halide, N_3^-, SCN^-, $SeCN^-$, NO_3^-, NO_2^-, $HCOO^-$, $MeCOO^-$, O_2^-, OH^-, O^{2-}, SO_4^{2-}, CO_3^{2-}, $C_2O_4^{2-}$

Additional liquid clathrate cations were developed, including the cation in the first selenium-based liquid clathrate host[14], $[(CH_3)_3Se][ClAl(CH_3)_2(Cl)Al(CH_3)_3]$. Some

cation-anion combinations formed liquid clathrates when a crown ether co-ordinated to the cation[1,8], altering the size of the cation, for example[10,11,17] [K^+•18-crown-6], [Na^+•15-crown-5], [Li^+•12-crown-4]. The oxonium ion, H_3O^+, has been used as a liquid clathrate cation in the forms[7,17,18], [H_3O^+•18-crown-6], and $(H_3O^+)_2$[222-$2H^+$][20] and the higher hydrated species [$H_5O_2^+$•21-crown-7][19]. (222 Is a large flexible macrobicyclic, cryptand222.)

Structurally similar but chemically different anions can be components of liquid clathrates[1,21], indicating that the geometry of a host anion is more important than its chemical reactivity. Because the shape of the ion separates the charge from the organic portion of the liquid clathrate, angular geometry of anions was considered a prerequisite for liquid clathrate formation[1]. An increased range of liquid clathrate hosts brought this assumption into question[9]. Liquid clathrate anions which differ from Atwood's $[Al_2R_6X]^-$ include the silicon-based $[N(SiMe_3)_2]^-$. Halides took the form[7,15,18,21], $[(HX)_nX]^-$ (X = Cl, Br and n = 1-3), $[I_3^-]$ and $[I_7^-]$. Anions of transition metal salts included[11,17,19] $[Mn(CO)_5]^-$, $[Cr(CO)_5Cl]^-$, $[W(CO)_5Cl]^-$, $[W(CO)_4Cl_3]^-$ and $[WOCl_5]^-$. The first indium-based liquid clathrate was[8] [K•18-crown-6]$_2$[$InClI_2(CH_3)$][$InClI(CH_3)_2$]. The anions[9,10], $[InCl_3X]^-$ (X = Cl, Br, I) have been used in liquid clathrates. Boron-based liquid clathrates have been synthesised with anions[5,12], $[BF_4]^-$, $[(Bu^s)_3B(Bu^n)]^-$ and the cyanoborate[16] used in this project, 1,6-bis(B-cyano-9-boratabicyclo[3.3.1]non-9-yl)hexane^{-2}. The counter ions used in this project were the methyltriphenyl- or the benzyltriphenylphosphonium cations.

According to Atwood[1], when the host interacts with the guest to form a liquid clathrate, host cation-anion interactions have to be strong enough, despite the geometry of the ions and the presence of organic portions in the ions, to prevent dissolution of the liquid clathrate in the excess guest. Gaudet, Zaworotko and White[13], however, have suggested that the liquid clathrate behaviour and low melting points of chloroaluminate salts could be the result of insignificant cation-anion attractions as weak as the molecular interaction of non-polar covalent compounds, with the liquid

clathrate guest dissolved in the melt of the host. The separation of excess guest would occur when the melt is saturated with the guest.

Regardless of the potential strength and importance of the interactions between the ions in the liquid clathrate, geometrical constraints determine how closely ions can pack in the solid host[1]. Pure liquid clathrate hosts tend to be low melting point solids or room temperature melts[1,10,13,15]. The low lattice energy directly affects the ability of a host to form a liquid clathrate with an aromatic guest as described as follows by Atwood[1].

KN_3 is insoluble in an aromatic and does not form a liquid clathrate as there are sufficient sites around the azide for strong interaction between the azide and the potassium cation. $K[AlMe_3N_3]$ does not form a liquid clathrate with an aromatic as the reduced number of sites around the azide is still sufficient for strong interaction between the azide and the cation. $K[Al_2Me_6N_3]$, however, forms liquid clathrates with aromatic guests because the two $AlMe_3$ groups restrict the strong interaction between the azide and the cation. Support for this interpretation is found in the crystal structure of $K[Al_2Me_6N_3]$ with potassium cations being found in two crystallographic environments[1]. Although the position near two azide ions is electrostatically favoured, the other position is amongst the methyl groups. These groups prevent the potentially strong interaction between the azide and the cation and prevent close packing of the lattice. $K[Al_2Me_6N_3]$ thus readily forms a liquid clathrate with aromatic guests. The inability to close pack thus results in the formation of space for the guests to fit into. The elasticity of this type of model is a crucial aspect addressed in this dissertation.

1.3.2 Liquid clathrate guests

Liquid clathrate guests are usually aromatic with Π excessive electron density for interaction with the host. The most frequently used liquid clathrate guests are benzene and toluene[1,5,7,10,11,14,17,18,19,21]. Also used are ethylbenzene[1,10,11], propylbenzene[1], o-, m- and p-xylene[1,10,11,12], mesitylene[1] and 1,2,3,5-tetramethylbenzene[1]. The guest can be a heteroaromatic, such as furan and thiophene[16]. Non-aromatic guests are unusual, but a range of tetra-alkylammonium borate salts, $[NR_4]^+[(Bu^s)_3B(Bu^n)]^-$ (R = Bu^n, n-C_6H_{13}

or n-C_6H_7), have been shown to form liquid clathrates[12] with aromatic and non-aromatic guests, namely benzene, toluene, p-xylene, p-cymene, cyclohexane, cyclohexene, n-hexane and 1,4-dioxane. A portion of non-aromatic guests can be substituted for aromatic guests already present in a liquid clathrate[1]. Guest molecules travel freely across the interface between the excess guest and liquid clathrate layers[8].

Aromatic guests interact favourably with host cations because of their Π electron rich character. Evidence of interaction between aromatic guests and host cations is found from X-ray crystallography. Examples[1] include a cation sandwiched between two aromatics, an aromatic sandwiched between two cations, and a crown ether co-ordinated cation interacting with an isolated aromatic. Aromatic guests can influence the size of the space they fill[1] and reduce host cation-cation repulsion[10], and presumably through this interaction they influence host cation-anion interactions as well as host anion-anion interactions, which have been found in solid state ordering of two liquid clathrate hosts[15]. An indication of the structural importance of the guest is that liquid clathrates with small G/H are particularly prone to precipitation of the host[10].

Benzene and the heteroaromatic guests, furan and thiophene, have been used in this project. Thiophene, and furan in particular, are more electron-rich than benzene and less stabilised by delocalisation of electrons than benzene[22]. Interaction between host and guest based solely on the electron density of the guest would therefore be of strength:

furan >> thiophene > benzene.

Guests such as 2-methoxyfuran and N,N-dimethylaniline are as electron-rich as furan but are sterically more bulky than furan and, in a comparative study with benzene, thiophene and furan, could indicate the importance of the electron density of the guest.

1.3.3 The G/H of liquid clathrates

1.3.3.1 The size of the maximum G/H in liquid clathrates

Although aromatic guests reduce host cation-cation repulsion[10] and influence the size of the space they fill[1], Atwood's investigation into the influence of closely related guests, C_6H_6, C_6H_5Me and C_6H_5Et, on the G/H of hosts, $[NR_4][Al_2(CH_3)_6I]$, R = CH_3, C_2H_5, C_3H_7, C_4H_9 and C_5H_{11}, lead to the conclusion that the host's cavity size is independent of the (specific) nature of the guest. Host cavity size depends on the host ions, for example, $[Bu_4N][Al_2Me_6I]$ forms a liquid clathrate with 9.4 benzene guests[1] whereas $[Bu_4N][InCl_4]$ forms a liquid clathrate with only 1.8 benzene guests[10].

The G/H depends on all three components, namely the host cation, the host anion and the guest, and G/H tends to increase for larger cations, larger anions and smaller guests[1]. For guests C_6H_6, C_6H_5Me, C_6H_5Et and $C_6H_4(Me)_2$, and hosts of composition, $[NR_4][Al_2Me_6I]$ and $[NR_4][Al_2Et_6I]$, R = CH_3, C_2H_5, C_3H_7, C_4H_9 and C_5H_{11}, the trend is true for cations, anions and guests, except for R = CH_3 in $[NR_4][Al_2Et_6I]$. This liquid clathrate has a higher G/H than liquid clathrates with R = C_2H_5 or C_3H_7 in $[NR_4][Al_2Et_6I]$. Atwood[1] proposed that because of the relative sizes of the cation-anion combinations, $[N(CH_3)_4][Al_2Et_6I]$ is the only host in this group which can form oligomeric units. The liquid clathrate consequently has regions where these units are surrounded by large numbers of guests, as they would be in solution. The G/H is thus higher than the trend requires.

Liquid clathrate literature comments on the non-stoichiometric values of G/H[1,15], but does not always include an estimate of the error for the non-integral G/H value[5-20]. The reader cannot judge the significance of the non-stoichiometric G/H value. The value might be integral if a different analysis is used. By contrast, a survey of structural aspects of solid clathrates[23] reports stoichiometric G/H for solid clathrates. A structure-activity study of organic ammonium clathrates similarly reports only stoichiometric G/H[24].

1.3.3.2 Perturbation of the fixed maximum G/H of a liquid clathrate

There are four conditions under which the G/H of a liquid clathrate is not equal to the maximum G/H. Firstly, if the liquid clathrate is made with too little guest present for the amount of host, the G/H is less than maximum G/H and there is no excess guest layer. A liquid clathrate has[1] a minimum G/H in addition to its maximum G/H and the liquid clathrate can only form when the available amount of guest is in the range of minimum to maximum amount of guests per host, but the liquid clathrate cannot form if less than the minimum amount of guest is available[1]. This behaviour can be written as:

pure host

↓ guest

pure host + pure guest

↓ guest

liquid clathrate with minimum G/H

↓ guest

liquid clathrate with minimum G/H < G/H < maximum G/H

↓ guest

liquid clathrate with maximum G/H

↓ guest

excess guest layer +

liquid clathrate with maximum G/H

^{1}H NMR spectra of liquid clathrates have resonances for the host and for the guest, not for some product of reaction between the host and guest. Formation of a liquid clathrate with fixed G/H is therefore not the result of chemical reaction between host and guest (although some liquid clathrates are prepared *in situ* by synthesis of the host using the guest as solvent[1,8,9,14,15,21]). The interactions in the liquid clathrate which keep the maximum G/H constant are therefore weak enough to make the fixed maximum G/H susceptible to change, leading to the remaining three conditions under which the G/H of a liquid clathrate is not equal to the maximum G/H.

Firstly, the formation of the liquid clathrate can be a temperature dependent equilibrium[1,5].

$$H + G = \text{liquid clathrate}$$

In these cases, heat is required to force the equilibrium to the right, so the equilibrium is endothermic and can be written as:

$$H + G = \text{liquid clathrate} \qquad \Delta H > 0 \qquad \text{G/H of the liquid clathrate is fixed}$$

Loss of heat by the liquid clathrate causes a change in G/H as the liquid clathrate reverts to pure host and guest. Once the liquid clathrate has formed, heating the liquid clathrate does not alter the G/H, up to the decomposition of the liquid clathrate (excluding liquid clathrates with more than about forty guest molecules per host[1]) as all the host has already been used to form the liquid clathrate with fixed G/H, and the equilibrium therefore cannot shift further to the right to diminish the effect of heating this endothermic equilibrium.

Secondly, the liquid clathrate can crystallise to form a solid clathrate instead of pure host and guest[16]. This solid clathrate, called a salt of the liquid clathrate, has a lower G/H than its liquid clathrate. This behaviour can be written as:

$$\text{liquid clathrate with G/H} = b$$
$$\downarrow$$
$$\text{solid clathrate with G/H} = q \qquad \text{and } b > q$$

The ions of the solid clathrate are more closely packed than the ions of the liquid clathrate, thus providing less space for the guest.

Finally, an additional component can affect the G/H. For example, HCl in contact with a benzene solution of 1-methylpyrrolidine was absorbed[21] to form liquid clathrates with host anions, $[(HCl)_nCl]^-$ (n = 1-3). The more HCl absorbed, the greater the G/H of the

liquid clathrate up to a point where the liquid clathrate and excess benzene became a single solution[21]. The ratio of the components therefore affected the G/H. This behaviour can be written as:

liquid clathrate with G/H = x

↓ HCl

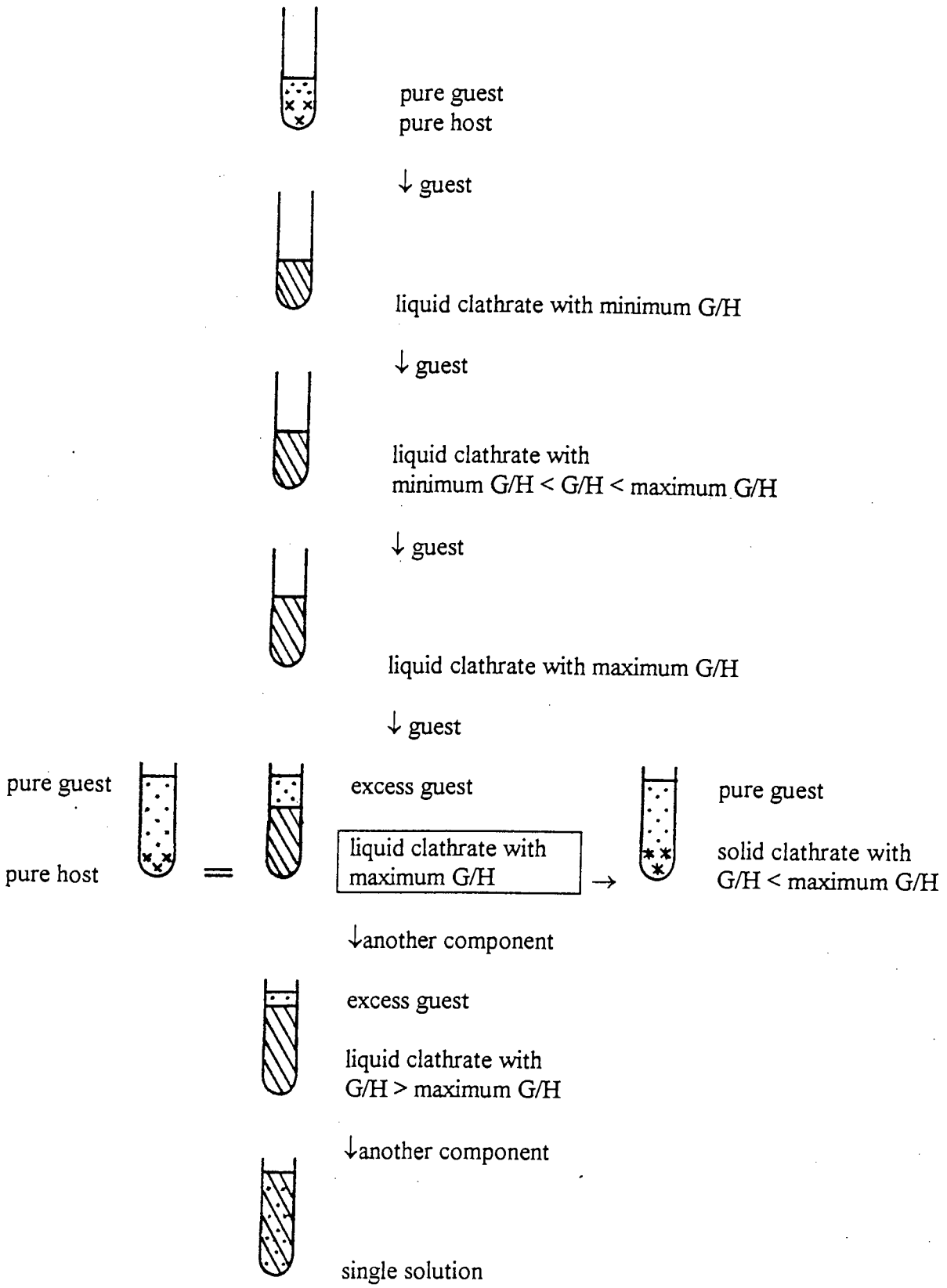
liquid clathrate with G/H = y and x < y

↓ HCl

single solution

These four variations of a fixed maximum G/H are diagrammed in figure 1.3.3.2 and indicate that there is more to a liquid clathrate than a fixed structure with fixed maximum G/H. The liquid clathrate expands from minimum G/H to form a maximum G/H which, with an additional component, can expand via increased G/H liquid clathrates to form a single solution. The liquid clathrate with maximum G/H can contract to form a solid clathrate with reduced G/H or to form pure host and guest with no G/H.

FIGURE 1.3.3.2 Formation and perturbation of a liquid clathrate with a fixed maximum G/H



1.4 Promoters of liquid clathrate formation

If host and guest components form a liquid clathrate only when a third component is present, the third component can be called a promoter of liquid clathrate formation. This will be the term used throughout this dissertation. For example, neither $Na[N(SiMe_3)_2]$ nor $Li[N(SiMe_3)_2]$ form liquid clathrates with aromatics unless a crown ether is present[1]. The crown ether therefore promotes the formation of the liquid clathrate. Without crown ether present, the sodium salt formed a dimer in solution and the lithium salt forms a trimer in solution and in the solid state[1]. A crown ether complexed cation is too large to form dimer or trimer structures with its anion, leaving the host free to make a liquid clathrate with the aromatic guest.

Insight about the role promoters might play in liquid clathrate formation can be gained from general host-guest chemistry, although a liquid clathrate's intermolecular forces are likely to be less rigid than a solid host-guest inclusion complex. Diederich[25] reports that two factors are important for strong binding between host and guest molecules.

Firstly, the host must be preorganised for guest complexation[25]. If the host is not correctly organised, complexation of the guest causes the host to reorganise. Reorganisation requires energy and no complexation between host and guest occurs if the reorganisation energy is greater than the free complexation energy. Applied to liquid clathrates, a promoter could reorganise the host so that the liquid clathrate obtains maximum stabilisation from the interaction between guest and reorganised host, without some of the energy being used to organise the host.

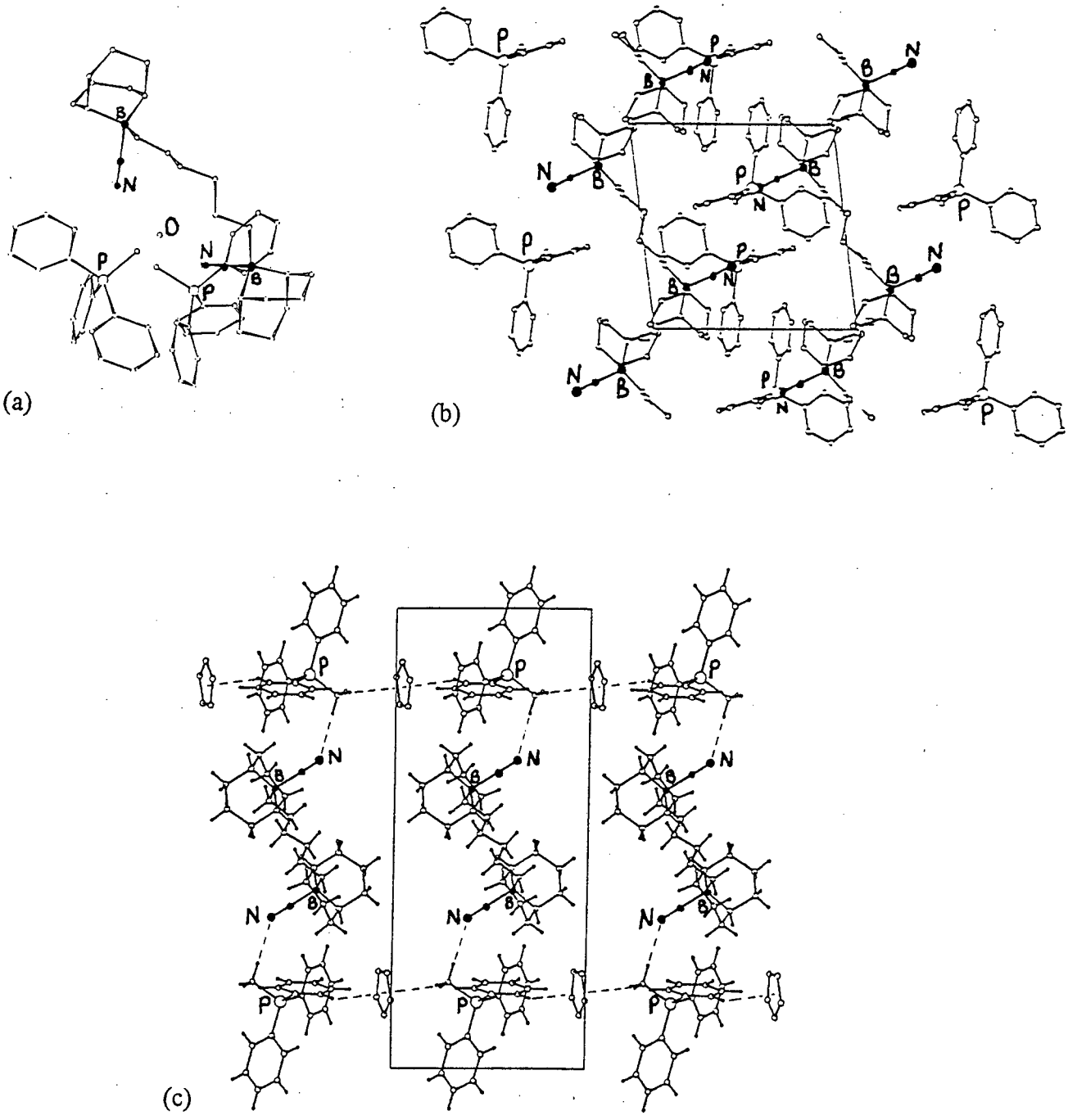
The crown ether[1] mentioned above disrupted the dimer or trimer structure of the host and thus promoted liquid clathrate formation by reorganising the host so that the interaction between the host and guest could form a liquid clathrate. The host-guest interaction, without promoter present, could not supply enough energy to reorganise the host to allow a liquid clathrate to form.

The second requirement for strong host-guest interaction involves the arrangement of orbitals in space to ensure stereoelectronic complementarity[25] between host and guest.

Applied to liquid clathrates, the interaction of a hydrogen-bonding promoter with, for example, the host anion, could enhance the interaction between the guest and the host cation, thus promoting the formation of the liquid clathrate.

The cyanoborate host used in this project forms a liquid clathrate with furan as guest only if water was present[16]. Water is thus a promoter of formation of this liquid clathrate. The anhydrous cyanoborate, **1**, does not form a liquid clathrate with furan[16]. Water affects the conformation and the hydrogen bonding of the host as shown in Figure 1.4.

FIGURE 1.4 Crystal structures[26] showing the conformation and hydrogen bonding of (a) **1**•H_2 O (b) anhydrous **1** and (c) **1**•(furan)$_2$



The anhydrous cyanoborate, **1**

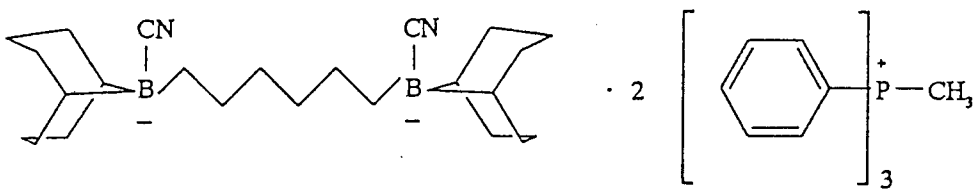


Figure 1.4(a) shows that the hexamethylene chain of the anion of **1**•H_2O is cisoid with respect to the boron-boron axis[26]. The two cyano groups of the anion are hydrogen bonded to water, resulting in a 1:1 ratio of water:cyanoborate[26]. **1**•H_2O does form a liquid clathrate with furan.

By contrast, anhydrous **1** (figure 1.4(b)) does not form a liquid clathrate with furan, and **1**•$(furan)_2$ (figure (1.4(c)), which does not contain water, has crystallised from a liquid clathrate. In both these structures the hexamethylene chain is transoid (zigzag conformation) with respect to the boron-boron axis and each cyano group of the anion is hydrogen bonded to the methyl group of a cation[26].

Water interacts with the anion of the host leading to the anion taking the cisoid conformation and altering the arrangement of the host orbitals in space. (The methyl group of the cation is not hydrogen bonded to the cyano group of the anion.) The hydrogen bonding of water could thus promote liquid clathrate formation by organising the host to allow maximum liquid clathrate stabilisation from the guest-host interaction and by maximising the orbital complementarity of the guest and portions of the host.

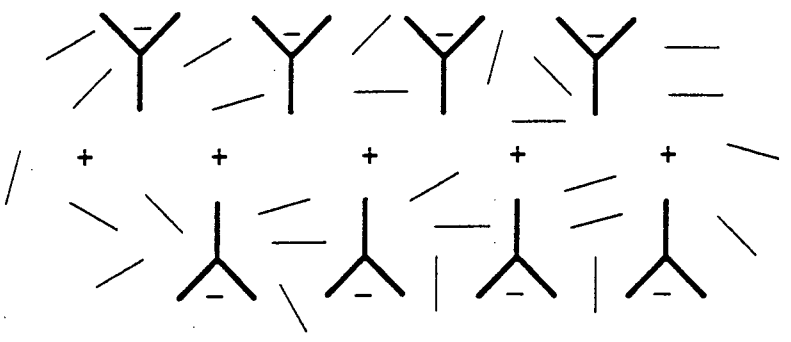
As water is involved in hydrogen bonding, a comparative study of the promotion of the furan/cyanoborate liquid clathrate would usefully include the alcohol closest in structure to water, which is methanol; an aromatic phenol such as cresol; a saturated cyclohexanol such as menthol; compounds with more than one site for hydrogen bonding such as diethyl tartrate and methyl glucopyranoside; a compound with phenyl, hydroxyl and carboxylic acid groups such as mandelic acid; and a range of nitrogen bases. Moreover, many of these potential promoters are chiral which introduces the exciting possibility of making chiral liquid clathrates.

1.5 Models of liquid clathrate structure

1.5.1 Atwood's model of liquid clathrate structure[1]

Ions of the host interact co-operatively. One cation is associated with two or more anions and *vice versa* in a layered structure as diagrammed.

Figure 1.5.1 Atwood's two dimensional diagram of liquid clathrate structure[1]



Interaction of cation and anion is strong so that ions do not separate to form a solution. Despite the strong ionic interaction in the host, unfavourable packing of the ions causes a low lattice energy of the host which is crucial to liquid clathrate formation.

Aromatic molecules are necessary components of liquid clathrate structure as guests. They provide stabilisation through favourable interaction with the cation as well as organic groups on both cation and anion. They fill in space between host ions, with the space being partly of the guests own making. The aromatic influences the amount of space between the cation-anion layered structure and influences cation-anion interaction.

1.5.2 Liquid clathrates as saturated solutions of hydrocarbon in melts[13]

Gaudet, Zaworotko and White[13] suggest that the physical properties of room-temperature melts favoured high hydrocarbon solubility and liquid clathrate behaviour. In heptachlorodialuminate and tetrachloroaluminate salts, the anions are weak hydrogen bond acceptors and the weaker hydrogen bond acceptor (heptachlorodialuminate salt) forms room temperature melts and liquid clathrates more easily than the slightly stronger hydrogen bond acceptor (tetrachloroaluminate salt). The lack of cation-anion attraction is therefore identified as the physical property which causes low melting points and high hydrocarbon solubility of chloroaluminate salts. If the cation-anion attractions approach the magnitude of the intermolecular attractions in non-polar covalent compounds, liquid clathrates can be seen as saturated solutions of hydrocarbons in the melts, without significant cation-anion attractions in the ordering of the liquid phase.

1.5.3 Liquid clathrates as binary liquid/liquid systems

A liquid clathrate with excess guest has the appearance of two immiscible liquids. Two liquids which are essentially immiscible are considered to have negligible mutual solubility. In other words, the solubility of one component in the other is limited. A liquid clathrate might be an extension of this, with limited or negligible solubility of host in the excess guest layer, but significant solubility of guest in the host layer.

The comparison of liquid clathrates with the binary liquid/liquid solvent systems widely used in liquid/liquid extraction is useful because the behaviour of such systems has been defined and documented in detail. The early literature in this field might have described those systems as liquid clathrates. Atwood[1] has mentioned liquid clathrates found in literature preceding the coining of the name, "liquid clathrate". Research for this project yielded no additional examples in the literature from 1947 to 1971. Some liquid clathrates might have been created and disregarded because they were irrelevant. For example, Hildebrand[27] explained the mutual insolubilities of seven liquid phases in equilibrium with each other. His work might have encountered a combination which would be called a liquid clathrate today. The seven insoluble liquid phases he discussed

were heptane, aniline, water, perfluorokerosene (~ $C_{12}F_{26}$), supercooled phosphorus, gallium and mercury.

Although searching the literature did not reveal any liquid clathrate between 1947 and 1971, it did provide rigorous and diverse theoretical and practical treatment of liquid/liquid extraction systems. Extension of this work to include liquid clathrates would increase present understanding of liquid clathrate structure, but would only be valid if some connection could be made between the binary liquid/liquid systems used in extractions and the binary liquid/liquid systems found in liquid clathrates.

The liquid clathrate definition maintains that no host is found in the excess guest layer. If liquid clathrates are similar to liquid/liquid systems used in extractions, the amount of host in the excess guest layer would be limited or negligible rather than absolutely zero. It is possible that the reason for no host being detected in the excess guest layer is the insensitive detection limit of ^{1}H NMR spectroscopy rather than its real absence.

A liquid/liquid solvent system which is not a liquid clathrate, could appear to be a liquid clathrate by ^{1}H NMR analysis. Consider a water/diethyl ether system. If this binary liquid/liquid system were a liquid clathrate and if water were a guest in the diethyl ether (ether) layer, ^{1}H NMR analysis of the two liquid layers would reveal water present in the ether layer and no ether present in the water layer.

At 20°C, the solubility by weight of water in ether is 18.8%[28]. The mole ratio is calculated to be 1 water : 1.3 ether and the proton ratio is 2 : 13. A water peak should therefore be detectable by running a ^{1}H NMR spectrum of ether which has been in equilibrium with water. At 20°C the solubility by weight of ether in water is 0.986%[28]. The calculated mole ratio is 1 ether : 417 water and the proton ratio is 10 : 800. It is therefore unlikely that ^{1}H NMR spectroscopy could be used to detect ether in this case. ^{1}H NMR analysis of a binary ether/water system would therefore indicate that the system might be a liquid clathrate with water as guest and ether as host.

A difference between a liquid clathrate and a water/ether system would be that the composition of the liquid clathrate at maximum G/H and the excess guest layer would not change on addition of guest, whereas the composition of the water/ether layers would change on addition of water, because each component is dissolved in the other in a fixed ratio. The liquid clathrate layer is close to saturation with the guest, so an increase in the G/H of the liquid clathrate with increased excess guest, might be small enough to fall in the range within which the G/H is considered fixed. This emphasises the need for estimated errors for G/H reported in literature. Changes in the composition of the excess guest layer cannot be detected as no host is found in this layer. A valid statement about the presence of host in the guest layer is that the host is not present in concentrations above the detection limit of the analytical method.

1.6 Possible methods for investigation into liquid clathrate structure

Except for nuclear magnetic resonance spectroscopy, I have not encountered any of the following methods applied to elucidation of liquid clathrate structure in the literature.

1.6.1 XAFS spectroscopy[29]

X-ray absorption spectroscopy (XAFS spectroscopy), which determines element specific local structure, is applicable to almost any mixture in any physical state. Crystalline samples are analysed with realistic confidence in the results, but spectra of amorphous materials are difficult to analyse, require extensive spectral simulation and the results can be ambiguous. XAFS spectroscopy could provide information about liquid clathrate structure and host-guest interactions by revealing the immediate short-range order around atoms in the liquid clathrate but, for the effort involved, the amount of reliable information obtained is likely to be minimal.

1.6.2 UV/VIS spectroscopy

Ultraviolet/visible (UV/VIS) spectroscopy can probe the type of interaction between the host and guest in a liquid clathrate. For example, Haueisen[26] mixed the guest, furan, with the cyanoborate host dissolved in tetrahydrofuran and ascribed the resultant

colour changes (purple to red to orange to yellow) to the components finding the best relative orientation in Π-Π interactions of furan (electron donor) with the aromatic rings of the host (electron acceptors) in charge-transfer complexes. This result should be treated with caution as charge-transfer is an excited state interaction. A charge-transfer absorption band in the liquid clathrate spectrum does therefore not necessarily mean that charge-transfer is the most significant interaction between the host and the guest in the ground state of the liquid clathrate[30].

1.6.3 Fluorescence spectroscopy

Fluorescence spectroscopy could be used to study liquid clathrates if the guests are fluorophores. For example, furan is a fluorophore[31], making the furan/cyanoborate liquid clathrate a candidate for study with fluorescence spectroscopy. Water, which promotes the formation of this liquid clathrate would, however, quench the fluorescence. In a suitable liquid clathrate, fluorescence lifetime could provide information about the guest environment. For instance, multiple decay constants could indicate that the fluorophore (the guest) is in several environments unless excited state processes are occuring[32]. Unfortunately, fluorescence lifetime is difficult to measure because of its brevity[32].

Excited state energy can be transferred from donor to acceptor without photon emission if there are dipole-dipole interactions between the donor and acceptor[32]. The rate of transfer depends *inter alia* on the relative orientation of donor and acceptor transition dipoles and on the distance between the molecules[32]. Energy transfer could therefore provide information about the relative orientation of host and guest in the liquid clathrate and the intermolecular distances between them.

1.6.4 Infrared spectroscopy

Infrared (IR) spectroscopy could be useful for investigating the interaction between host and guest in hydrogen bond-rich liquid clathrates. For example, the cyano stretch of the cyanoborate host would be sensitive to hydrogen bonding and a comparative

study could indicate whether this functional group is involved in structuring the liquid clathrate.

1.6.5 NMR spectroscopy

Comparison of nuclear magnetic resonance (NMR) spectra of the host, the guest, the liquid clathrate and the liquid clathrate in solution can provide information about the structure of a liquid clathrate, especially if spectra of the free components differ from the spectra of the components in the liquid clathrate. Liquid clathrates made using the cyanoborate as host could be studied with ^{1}H, ^{13}C, ^{11}B, ^{15}N and ^{31}P spectroscopy. ^{1}H NMR spectroscopy is invariably used to determine the maximum G/H of liquid clathrates[1,5-21].

Spectra obtained using Nuclear Overhauser Effect Spectroscopy (NOESY) have cross peaks for nuclei that are in close spatial proximity. The NOESY of a liquid clathrate could contribute to understanding liquid clathrate structure by indicating how the host and guest molecules arrange themselves in space. For example, intermolecular Nuclear Overhauser Effects (NOEs) were detected[12] in liquid clathrates with hosts $[NR_4]^+[(Bu^s)_3B(Bu^n)]^-$. The guest molecules were thought to lie between the arms of the host cation as substantial NOE was observed between host cation and guest protons and no NOE was observed between host anion and guest protons.[12]

NOESY signals require time to be collected, the signal of a viscous sample decays quickly and as no solvent can be used for the liquid clathrate sample, NOESY is limited to non-viscous liquid clathrates. The signal of a viscous liquid clathrate would decay before the host-guest interaction could be detected by NOESY. In addition, NOESY of a liquid clathrate cannot be attempted until some other method is used to get an indication of which protons interact with each other in the sample.

Information about the structure of liquid clathrates can be obtained from measuring the longitudinal relaxation time, T_1, and the transverse relaxation time, T_2, of the protons in the host, in the guest and in the liquid clathrate. The protons which experience the

host-guest interaction the most, will show the greatest change in T_1 and T_2 on formation of the liquid clathrate from the free host and the free guest. This information could contribute to understanding liquid clathrate structure by indicating the locality of the interaction between the host and guest. For example, the guest might interact more with the cation than with the anion of the host.

The measurement of T_1 and T_2 of a solid host would involve NMR of a solid or of the host in solution. Measurement of T_1 and T_2 of the guest would involve NMR of a pure liquid of low viscosity. Measurement of T_1 and T_2 of the liquid clathrate would involve NMR of a liquid which would probably be more viscous than the pure guest. Changes observed in T_1 and T_2 of the host and guest on formation of the liquid clathrate would arise from solvent effects and differences in sample viscosity as well as from the host-guest interaction in the liquid clathrate.

This method therefore cannot be used for probing the structure of the liquid clathrate, but information has been obtained from the T_1 of a benzene/$[N(CH_3)_4][Al_2(CH_3)_6I]$ liquid clathrate[6]. The shorter T_1 of the liquid clathrate benzene than the T_1 of the excess benzene indicates that the guest benzene is held in a more rigid environment in the liquid clathrate than the free benzene.

1.6.6 Equilibrium constants between host and guest in a liquid clathrate

All conventional methods for equilibrium constant measurement require change in concentration of at least one component of the equilibrium[33]. The methods considered for investigating liquid clathrate structure by determining equilibrium constants between host and guest at fixed maximum G/H could not be applied to liquid clathrates for two reasons.

(1) Clathrate structure is destroyed in solution[2]. This was confirmed by Haueisen for the furan/cyanoborate liquid clathrate[26].

(2) As the maximum G/H is fixed regardless of how much excess guest is added[1], the relative concentrations of the liquid clathrate components cannot be

varied without use of a solvent or one of the perturbations of the maximum G/H (section 1.3.3.2 of this chapter).

Equilibrium constants between host and guest in liquid clathrates therefore could not be measured without destroying the structure of the liquid clathrate either in solution or by perturbing the fixed maximum G/H. A point to note is that the fixed composition of a liquid clathrate cannot be perturbed by adding guest, so the host and guest of a liquid clathrate are not in normal equilibrium. Measurement of equilibrium constants between the host and the guest of a liquid clathrate at a fixed maximum G/H cannot be achieved.

1.7 Uses of liquid clathrates

Solid clathrates are used[2], *inter alia*, in chemical analysis and molecular separation, in the formation of stereoregular inclusion polymers, and in the alteration of physical properties and reactivity of chemical species. Liquid clathrates could perform the same function as solid clathrates, and in some contexts, liquids are easier to manipulate than solids. For example, a solid clathrate[23] has separated m-cresol from a mixture of cresols in 98.5% purity and 55% yield. (Cresol is a guest with 1:1 G/H ratio.) This separation method involves repeated crystallisation. A liquid clathrate which interacts selectively with the different isomers of cresol would provide a simpler method for the separation of cresol isomers, based on liquid/liquid extraction methodology. The isomers of cresol have close boiling points, which hinders the separation of cresol isomers by distillation. The development of an efficient separation of cresol isomers is desirable as cresol has commercial significance in South Africa. Cresol is recovered from depitched tar acids by SASOL Chemical Industries. In 1994 SASOL was the largest cresol producer in the world and entered a contract to supply Japan and other East Asian countries with m-cresol and p-cresol[34].

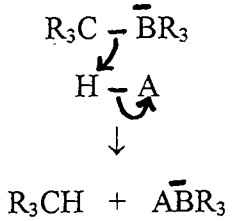
Liquid clathrates have been useful as catalyst supports, and in coal liquefaction and hydrocarbon separation[35]. For example, aromatic and aliphatic separation is possible[12]. Pickett proposes that the liquid clathrate, $[NBu^n_4][BF_4]\bullet 3$toluene could be used in

electrosynthesis, in electrochemistry spanning the macro- to ultra - microelectrode domains and in spectroelectrochemistry[5].

1.8 Liquid clathrate hosts used in this project

The host, bis(methyltriphenylphosphonium) 1,6-bis(B-cyano-9-boratabicyclo[3.3.1]non-9-yl)hexane, **1**, was first made by Haueisen[26] in a synthetic search for an electrolyte for the Zebra car battery. NMR was used to characterise the structure of **1**. The structure of **1** and the ^{1}H and ^{13}C NMR spectra of **1** obtained in this project are shown in figure 1.8a. The most labile bond in **1** is that between carbon (C) and negatively charged boron (B^-), and it should be susceptible to protonolysis by an acid (HA) (Scheme 1.8).

SCHEME 1.8 Protonolysis of the boron-carbon bond in **1**

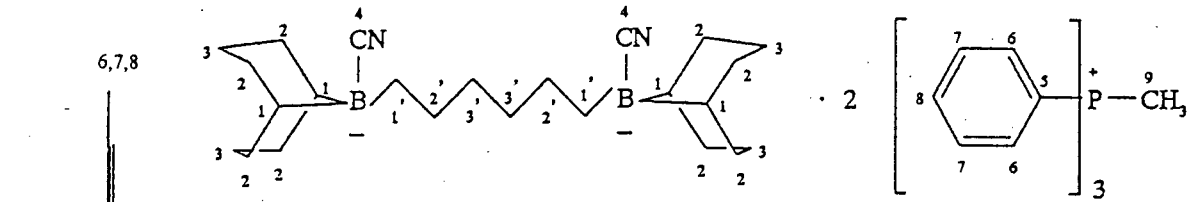


R = an alkyl group

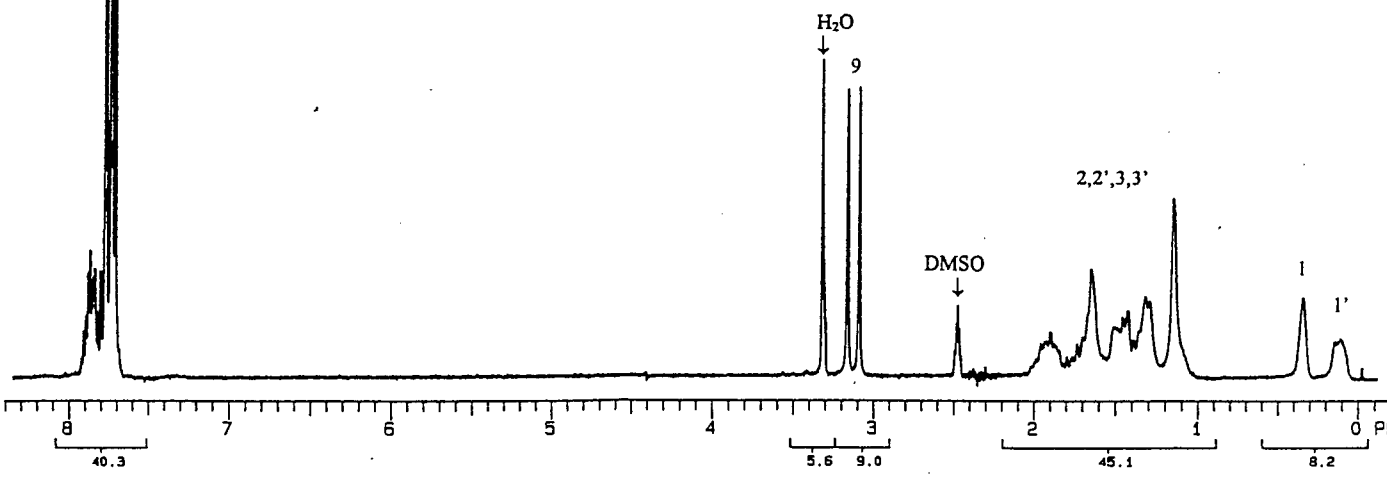
FIGURE 1.8a Structure and assignment of **1**•nH_2O

(i) ^{1}H NMR (200MHz, DMSO-d_6, 25°C)

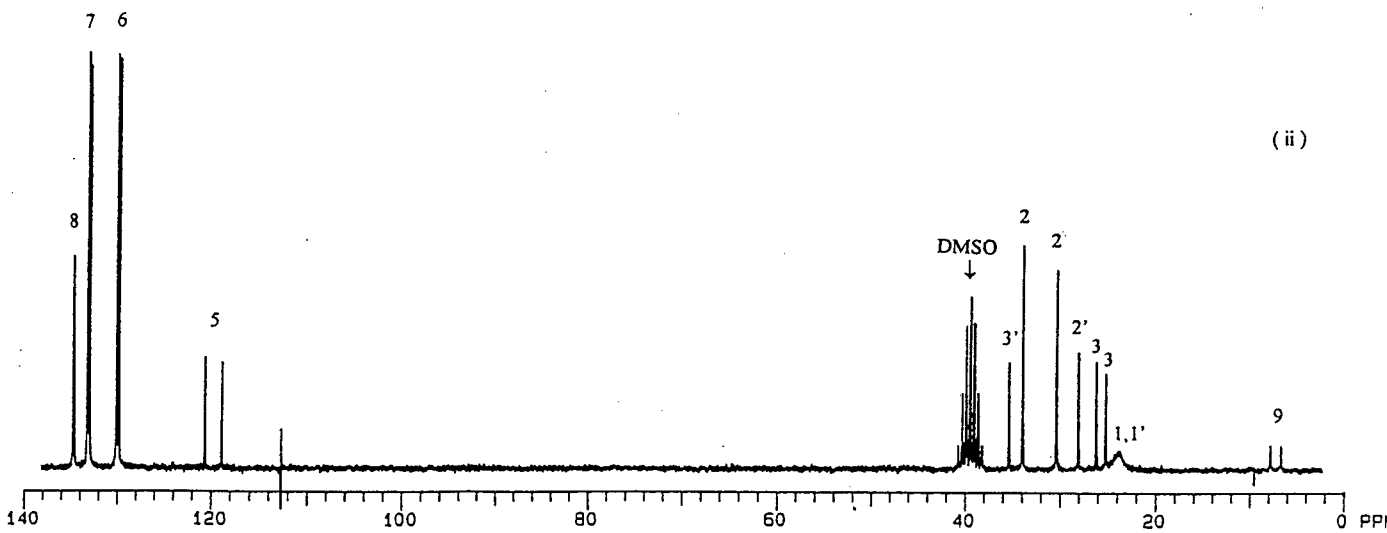
(ii) ^{13}C NMR (50MHz, DMSO-d_6, 25°C)



(i)

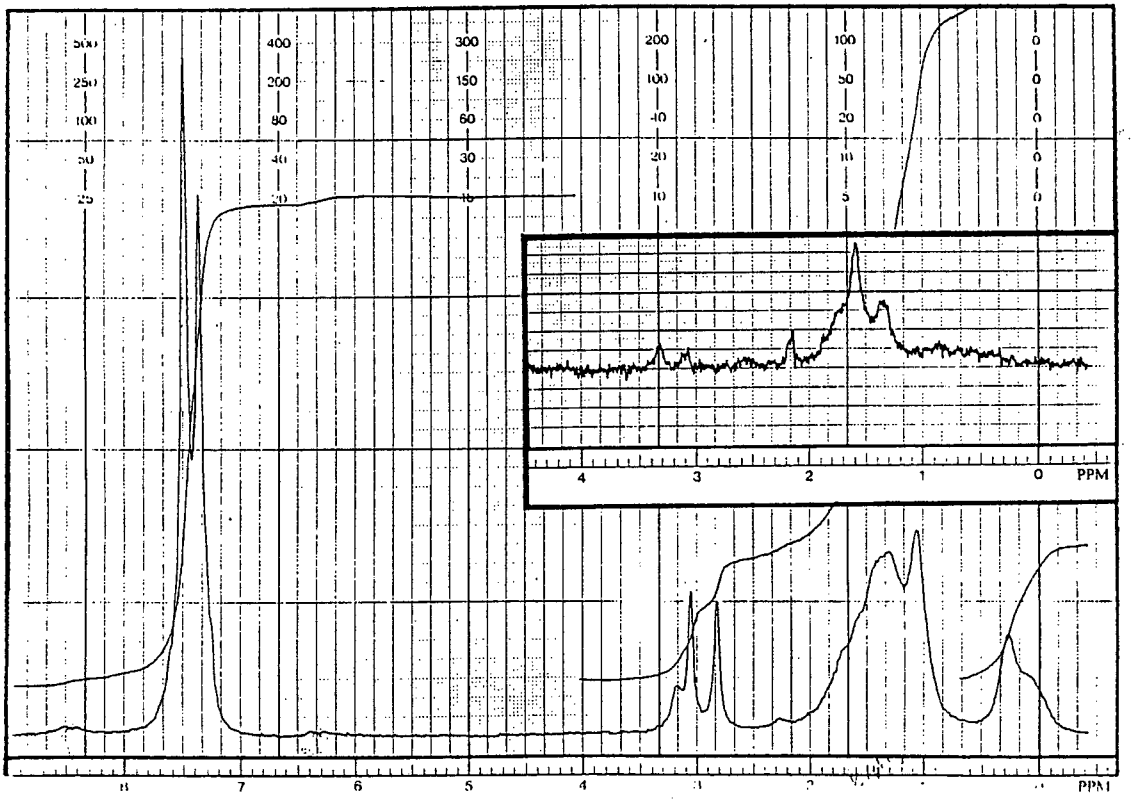


(ii)



^{1}H NMR is particularly sensitive to the decomposition of **1** via boron-carbon bond heterolysis. The upfield peaks between 0 and 0.5ppm are characteristic of shielded hydrogens on a carbon bonded to negatively charged boron[26]. The formal negative charge on boron is partially transmitted to the methylene and methine protons adjacent to boron (α position), resulting in their shielding. If the boron-carbon bond breaks and boron loses its negative charge, the α-methylene peaks (αB peaks) lose their upfield positions as shown in figure 1.8b. αB peaks can integrate incorrectly with boron-carbon bonds still intact. The cation, Na^+, close enough to the borate anion, $^-BBu_3CN$, decreases the αB peaks because Na^+ cancels the effect of the negative charge without breaking the boron-carbon bond[26].

FIGURE 1.8b ^{1}H NMR (60MHz) spectrum of **1**•nH_2O. Inset shows protonolysis by HCl causes the αB peaks to lose their upfield position.



The liquid clathrate formed with furan as guest was singled out for this project for two reasons. Firstly, Haueisen's preliminary studies indicated that the colour changes from purple to red to orange to yellow can be used to study thermodynamic and kinetic features of liquid clathrate formation[26]. This aspect had to be abandoned because the colour changes resulted from impurities in the furan interacting with the liquid clathrate instead of liquid clathrate host-guest interactions *per se*.

Secondly, the promotion of the formation of the furan/**1** liquid clathrate by water was an attractive avenue of study. Promotion of liquid clathrate formation extends the guest-host combinations of existing liquid clathrate hosts and increases the parameters available for the design of liquid clathrates.

Haueisen found[26] that the host, **1**, does not form liquid clathrates with 2-methoxyfuran, N,N-dimethylaniline and toluene as guests and does form water dependent liquid clathrates with furan, thiophene and benzene. The G/H of the benzene and thiophene liquid clathrates varies depending on the amount of water present in the host. Water promotes formation of the furan/**1**•nH_2O liquid clathrate if $0.8 < n < 1$. The water is found in the liquid clathrate layer and the G/H is approximately eight. A mixture of furan and **1**•nH_2O with $n > 1$ forms three immiscible layers, one of which is water. When the liquid clathrate crystallises to form a solid clathrate with a G/H = 2, no water is present in the solid clathrate.

In a structure-activity study, Haueisen made[26] various compounds by modifying the cation and anion of **1**. For this project, bis(benzyltriphenylphosphonium) 1,6-bis(B-cyano-9-boratabicyclo[3.3.1]non-9-yl)hexane, (**2**) was chosen from these modifications of **1** for two reasons. Firstly, **2** has the same anion as **1**, but has a benzyl instead of a methyl group in the cation. A difference in cation rather than anion was chosen because of the importance of cation and guest interactions in this liquid clathrate[26]. Evidence of interaction between furan and the cation of **1** was found in an X-ray crystallographic study[26] of the **1**•$(furan)_2$ clathrate salt of the furan/**1** liquid clathrate. Two different phosphonium cations hold a furan molecule in place with

C-H---Π(furan)---H-C bonds. A methyl and a phenyl group on different cations supply the hydrogens involved in this interaction (figure 1.4(c)).

The second reason for choosing **2**, was that although **2** formed a solid clathrate with diethyl ether, **2** did not form a liquid clathrate with any of the guests Haueisen[26] tested (*inter alia* furan, thiophene, benzene, toluene, N,N-dimethyl aniline and 2-methoxyfuran). The host, **2**, was therefore ideal for comparison with **1** with respect to promotion of liquid clathrate formation.

1.9 The aims of this research

The aims of this research were to:

1. Use general experimental methods which:

   (1) accurately and realistically analyse the G/H and P/H ratios in cyanoborate liquid clathrates and nH_2O in $\mathbf{1}\bullet nH_2O$.

   (2) Avoid spurious promotion of liquid clathrate formation in experiments investigating the promotion of liquid clathrate formation.

2. Investigate the validity of the definition of liquid clathrates with respect to the absence of host in the excess guest layer and with respect to the existence of a fixed maximum G/H.

3. Propose a model of liquid clathrates which allows for the effect of promoters of liquid clathrate formation.

4. Verify the importance of promoters in liquid clathrate work.

5. Use promotion of cyanoborate liquid clathrate formation by water or cresol to investigate:

   (1) The importance of the Π electron rich nature of the guest in the formation of cyanoborate liquid clathrates.

   (2) The interaction between the promoter and the cyanoborate liquid clathrate.

   (3) The interaction of cresol with host anion and with the guest.

   (4) The outcome of competition between water and cresol in a liquid clathrate.

   (5) The effect of the interaction of two components prior to the addition of the third component to form a three component (promoter, guest, host) liquid clathrate.

   (6) The differences between cresol and water as promoters with respect to the ease of promotion of liquid clathrate formation and the stability of the liquid clathrates formed.

   (7) Uses of the interaction between cresol and the liquid clathrate.

CHAPTER 2

Experimental methods

The details of section 2.1 are presented in the appendices as the details are relevant for repetition or continuation of the work described in chapters 3 and 4, rather than for evaluation of chapters 3 and 4. Sections 2.2 - 2.4 are general methods presented in detail because they affect the results presented in chapters 3 and 4 and are fundamental to evaluating these results. The specific methods for obtaining the results in chapters 3 and 4 are presented with the results in the chapters.

2.1 Elimination of spurious promotion of liquid clathrate formation

The work in this project involved the promotion of liquid clathrate formation with water or cresol as promoters. Precautions were taken to eliminate spurious promotion of liquid clathrate formation by contaminants, decomposition products and water. Synthesis of **1** using Haueisen's method[26] did not invariably produce pure **1** as evidenced by yellow discoloration of the crystals. This method was adapted until pure white **1** was invariably produced. This improved synthesis of **1**•nH_2O, the purification of yellow **1**•nH_2O and the manipulation of the value of nH_2O is described in appendix 1. The synthesis of **2** is described in appendix 2. Components of the liquid clathrate and components mixed with the liquid clathrate were purified to prevent impurities promoting liquid clathrate formation, and dried to prevent water promoting liquid clathrate formation. This work is described in appendix 3. The investigation into whether cresol and other alcohols mixed with **1**•nH_2O caused protonolysis of **1**•nH_2O is described in appendix 4. Cresol did not destroy **1**•nH_2O.

2.2 Sampling of the liquid clathrate

Formation of the liquid clathrate with excess guest resulted in two layers. The bottom, liquid clathrate layer was sampled with a glass Pasteur pipette. Positive pressure was applied to the pipette as its tip passed through the top, excess guest layer to prevent excess guest entering the pipette.

Improved sampling of the bottom layer was achieved by using a tap in the base of a test tube. The contents of the test tube could be stirred evenly with a magnetic stirrer bar. No solid **1**•nH_2O was caught in the tap during formation of the liquid clathrate and the bottom layer could be sampled with no direct contamination from the top layer.

Nevertheless, excess guest was invariably found in the liquid clathrate layer because **1**•nH_2O and excess guest were mixed vigorously and sometimes refluxed to form the liquid clathrate. The liquid clathrate was therefore normally an emulsion of excess guest droplets in the liquid clathrate. The emulsion was sometimes unstable and separated into two pure layers within a few minutes. More often, the emulsion was stable and the droplets of excess guest were removed from the liquid clathrate sample by filtering the sample through cottonwool.

If the liquid clathrate was being sampled for NMR, the sample was filtered into an NMR tube containing [$^2H_6$]-dimethylsulfoxide (DMSO-d_6). The DMSO-d_6 prevented the precipitation of the liquid clathrate in the NMR tube. Solids in the sample would have caused line broadening because of local magnetic field inhomogeneities and disturbed molecular tumbling[36]. DMSO-d_6 added to a precipitated sample of liquid clathrate would have dissolved the sample, but for analysis of G/H in a liquid clathrate, precipitation was prevented by adding the sample to DMSO-d_6. G/H decreased when the clathrate changed from liquid to solid. As the guests were volatile, some of the released guest would have escaped when the DMSO-d_6 was added to the precipitated sample, resulting in a diminished observed G/H of the liquid clathrate.

2.3 Analysis of the amount of water in a solid or a liquid clathrate sample

2.3.1 Karl Fisher titrations[37] as a method for analysis of water

With suitable sample preparation and control of experimental conditions, the versatile Karl Fisher method of water analysis can be used for a wide variety of solid, liquid or gaseous samples. Samples include, *inter alia* quaternary ammonium chlorides, paper, plastics, paints, hydrogen fluoride, cigarette smoke and gaseous fuels. Karl Fisher titrations are so versatile that they can be used to determine parts per million to almost one hundred percent amounts of water in almost any sample. The unsuitability of Karl Fisher titrations for the analysis of water in **1**•nH_2O and cyanoborate liquid clathrates formed with water or cresol as promoters, is discussed in appendix 5.

2.3.2 Thermogravimetric analysis of water in **1**•nH_2O and the cyanoborate liquid clathrate

Thermogravimetric analysis (TGA) was initially used for determination of nH_2O in **1**•nH_2O.

$$nH_2O = \frac{xM_{HOST}}{(1 - x)M_{H2O}}$$

x = (TGA %mass loss)/100 M = molar mass

The molar mass of anhydrous host is 932.866, which is large compared to the molar mass of water, which is 18.015. The %mass loss due to water in a TGA of **1**•nH_2O is therefore relatively small. This decreases the precision of the analysis, leading to results such as nH_2O = 0.8 or 1.4 in repeat analyses of a sample of **1**•nH_2O. The accuracy might also have been compromised by the relatively small mass loss, but the accuracy was not easy to define as the true amount of water was not known. For most of this project TGA was used only to check that an anhydrous sample of **1** did not display any weight loss due to water loss.

Conversely, a liquid clathrate losing its guest molecules shows relatively large weight loss on TGA. Assignment of the steps in the weight loss of a liquid clathrate sample to

loss of guest or loss of water is not easy as the temperature of the weight loss is not necessarily the boiling point of the component. The temperature of a sample in TGA is not known accurately and can lag behind the furnace temperature by up to 30°C[38]. Ambiguous TGA of liquid clathrate samples therefore prevented the simultaneous determination of nH_2O and G/H in a liquid clathrate using TGA.

An advantage of TGA is that TGA uses less sample than NMR spectroscopy does. The size of a solid sample could affect the outcome of analysis of nH_2O as water could be unevenly distributed in **1**•nH_2O. A large sample for NMR spectroscopy would give an average for nH_2O, whereas a small sample could show local variation in nH_2O. Appendix 6 describes an experiment investigating the effect of sample size and sample site on the analysis of nH_2O in **1**•nH_2O.

2.3.3 Analysis of water using ^{1}H NMR spectroscopy

NMR spectroscopy was chosen in preference to chromatography for analyses in this project because NMR samples are contained in an inert glass tube instead of running the risk of reacting with or poisoning a chromatographic column in, for example, high performance liquid chromatography.

The relative amounts of components in an NMR sample is easily obtained from the integration of the area under a correctly adjusted NMR spectrum as the area is proportional to the corresponding nuclei in the sample[39]. IR measurement of the amount of water in a sample agrees to within 0.03% with ^{1}H NMR analysis[40], but the results are less easily obtained than NMR results. IR and all optical spectroscopic methods require measurement of absorption coefficients at known concentrations of analyte to obtain quantitative results.

NMR spectroscopy was found to be the most suitable analytical tool for this project. The analysis of water using NMR spectroscopy is covered in the detailed discussion of the use of NMR spectroscopy in section 2.4.

2.4 ^{1}H NMR analysis of n in 1•nH_2O, and of G/H and P/H in the liquid clathrate

2.4.1 Obtaining accurate integration of continuous wave ^{1}H NMR spectra in this project

60 MHz ^{1}H NMR spectra were run on a continuous wave (CW) VarianEM 360A machine. CW NMR spectroscopy means the nuclei of the sample are successively brought into resonance by varying the magnetic field. Accurate analysis of nH_2O, G/H or P/H required accurate integration. Integration of a peak would have been inaccurate if its frequency were saturated. Frequency saturation was avoided during integration by scanning the integration rapidly (scan collected over one minute). The phase and the drift of the integration also affected its accuracy. For each spectrum, the phase had to be adjusted carefully to ensure absorption peaks instead of dispersion signals. (The integration of the area under a dispersion signal is zero[39].) The high integration sweep speed minimised the effect of the drift in the integration baseline so the integrator balance required only minor adjustments for each spectrum. In CW NMR spectroscopy, the integration scan and the spectrum scan are collected separately. The spectrum was scanned slowly (five minutes) to increase peak resolution. The spectrum amplitude and sample spin rate were adjusted for each sample.

Error in the integration of NMR spectra is approximately 10% of peak size and the relative integration of peaks in a spectrum is not affected by spectrum amplitude, concentration of sample and tube spin rate. Repeated spectra (60MHz) of a sample of 1•nH_2O confirmed this as follows. Integration of peaks was repeatable within 10% of peak size (10 spectra, 1 sample). Relative peak size was not affected by spectrum amplitude (5 different amplitudes, 1 sample, relative peak size within 10%). The more concentrated a sample was, the easier it was to balance and phase the integration (3 concentrations of sample, different amplitudes, unbalanced and badly phased integration increased uncertainty in integration of peaks). Relative peak size was not affected by sample tube spin rate if the tube was spinning and if the spinning did not cause a vortex in the sample (4 different spin rates, 1 sample, relative peak sizes within 10%).

The sample tube is spun by a rotor attached to an air driven turbine[39]. There were periods in this project when build up of oil from the compressed air disrupted adjustment of sample tube spinning. At these times it was not always possible to eliminate spinning side bands in the spectra. Care was taken to identify the spinning side bands and to minimise their effect on the accuracy of the integration.

Integration of peaks depends on the relaxation times of the nuclei. Different nuclei in a sample may have a wide range of relaxation times. The high integration sweep speed on the CW EM 360A ensured that the difference in the relaxation times was not significant in the integration error[39].

2.4.2 Obtaining accurate integration of Fourier transform 1H NMR spectra in this project

200MHz and 400MHz ^{1}H NMR spectra were run on the Fourier transform VXR 200 and Varian Unity 400 machines respectively. In Fourier transform NMR spectroscopy, the spectrum and the integration are obtained from the same set of scans. An accurate integration must therefore accommodate the relaxation times of the nuclei by allowing at least five times the longest relaxation time between scans[41].

The transverse relaxation time, T_2, can never be longer than the longitudinal relaxation time, T_1. It was therefore not necessary to measure T_2. The sample was not degassed for measurement of T_1 because oxygen was present in all NMR spectrum samples. The VXR 200 was shimmed and the 90° pulse width was calibrated for the NMR solvent. The T_1 were measured in an inversion-recovery experiment. The nuclei were given decreasing lengths of time to recover from a 180° pulse. The peak with the longest T_1 shrunk the most as the experiment progressed, whereas a peak with a short T_1 maintained its height. Five times the longest T_1 of a sample nucleus was used as relaxation time between scans for accurately integrated spectra on the Fourier transform machines.

2.4.3 Int% as a check of the validity of each NMR result

For a ratio of the integration of two peaks of a compound, the observed ratio, int_{OBS}, was written as a percentage, Int%, of the theoretical ratio, int_{CALC}.

$$Int\% = int_{OBS}/int_{CALC} \times 100\%$$

For example, the methyl and the phenyl groups in **1** might integrate as 9.0 and 40.3 respectively. $int_{OBS} = 9/40.3 = 0.22$

$int_{CALC} = 6/30 = 0.20$ (6 methyl : 30 phenyl protons)

$Int\% = 0.22/0.20 \times 100\% = 110\%$

Int% was calculated for ratios of all the peaks of a compound. A spectrum was discarded if the integration percentages were greater than 125% or less than 75%. The proportion of the spectra which had to be discarded emphasises that in this project NMR spectroscopy was used at or beyond its limits as an analytical tool. Int% not only checked that the integration of the spectra was correct. Correct Int% of a spectrum, particularly Int% involving the peaks α to boron, confirmed the chemical integrity of the NMR sample. The convenient Int% calculation to check the validity of each NMR result added to the suitability of NMR spectroscopy as an analytical tool in this project.

2.4.4 Analysis of the amounts of components relative to the amount of host in a liquid clathrate (n)

^1H NMR was used to analyse the amounts of various components relative to the amount of host (**1**). The ratios were calculated as equivalents of component per single equivalent of **1** and were abbreviated as n.

nH_2O = the number of H_2O molecules per **1**

ncresol = the number of cresol molecules per **1** = cresol/**1**

nguest = G/H

A computer spreadsheet was created to facilitate evaluation of ^1H NMR spectra. The simple task of entering the integration of the peaks of a spectrum into the spreadsheet resulted in the calculation of the Int% of **1** and the calculation of n of up to three other components in the spectrum.

2.4.5 Calculated uncertainty in n

As the quality of the NMR spectra varied and the integration of **1** was seldom 100%, a 10% error on the analysis of n was not assumed and the uncertainty was estimated as follows. For a single analysis of n, four different values of n were calculated from the four different peaks of **1**. The peaks corresponded to:

(i) protons α to boron in the anion (8 protons, αB)

(ii) protons in the anion not α to boron (32 protons, hB)

(iii) methyl protons of the cation (6 protons, me)

(iv) phenyl protons of the cation (30 protons, ph)

The value of n and the uncertainty in n was taken as

$$n = n_S + (n_B - n_S)/2 \quad \pm \quad (n_B - n_S)/2$$

out of the four values of n in a single analysis,

n_S = smallest n

n_B = biggest n

For a spectrum with Int% far from 100%, the uncertainty in n would be large whereas a spectrum with correct integration would cause a smaller uncertainty in n. The uncertainty in n is therefore a useful reflection of the quality of the NMR spectrum used to determine n. No attempt was made to estimate the contribution of sampling and systematic errors to the uncertainty of results.

2.4.6 NMR solvent used to dilute samples of 1•nH_2O and cyanoborate liquid clathrates

Chloroform ($CHCl_3$) is not a guest of **1** and does not destroy **1**. $CDCl_3$ (D = ^2H) was therefore used as a solvent for NMR until certain problems became apparent. Solid 1•nH_2O did not dissolve readily in $CDCl_3$, crystals sometimes formed while the spectrum was being run, and mixtures of liquid clathrate samples and $CDCl_3$ occasionally formed a small immiscible liquid layer of unknown composition. The water peak sometimes overlapped the peaks of **1**, which prevented accurate determination of nH_2O by comparison of peak integration. All the peaks in **1** were used

to determine nH_2O, P/H or G/H. $CDCl_3$ and the methyl group of **1** exchanged ^2H and ^1H, making the methyl peak integration too small and introducing a $CHCl_3$ peak. As the extent of the ^1H-^2H exchange was unpredictable, $CDCl_3$ was unsuitable as a solvent for determining the amount of a component in a sample.

Acetone dissolved **1** readily, was not a guest of **1** and did not destroy **1**. A spectrum of **1**•nH_2O in deuterated acetone normally had a free standing water peak. When the water peak did overlap the methyl peak of **1**, nH_2O could be calculated if the methyl peak integration was accurate. The methyl peak, however, became diminished by ^1H-^2H exchange occurring between **1** and the deuterated acetone, so deuterated acetone was unsuitable as an NMR solvent in this project.

[$^2H_6$]-dimethylsulfoxide, (DMSO-d_6), was chosen as the solvent for NMR as it does not destroy **1**, dissolves samples readily and keeps them in solution. The water peak in the spectrum is often free standing and DMSO-d_6 does not undergo ^1H-^2H exchange with **1**. Unfortunately, DMSO-d_6 is hygroscopic. Activated 4Å molecular sieves kept 99.9% deuterated DMSO-d_6 dry enough for the solvent water peak to be undetectable in 200MHz ^1H NMR spectra and in 60MHz ^1H NMR spectra with amplitude higher than the amplitude of sample spectra. Vials of greater percentage deuterated DMSO were not used because of their expense. The higher deuteration percentage did not mean the solvent contained less water than the 99.9% solvent. The DMSO peak did not interfere significantly with analysis of nH_2O or other components.

The DMSO-d_6 was syringed out of a bottle sealed with a rubber septum. As the supply of DMSO-d_6 was limited for this project, experiments were planned carefully. Aliquots of the minimum possible amount of DMSO-d_6 were syringed into pill vials containing solid samples and as many as eight dry NMR tubes for liquid clathrate samples. This decreased wasting DMSO-d_6 in the syringe and prevented contamination of the stock DMSO-d_6 by a syringe needle not properly dried. The tubes with DMSO-d_6 were sealed (lids and Parafilm) until a liquid clathrate sample was added directly to the DMSO-d_6. The DMSO-d_6 could be left in the sealed NMR tubes for at least a week without absorbing enough water for the water to be detected in a ^1H NMR spectrum.

2.5 Linear regression of data

For the graphs presented in chapters 3 and 4, linear regressions of y against x were performed at 95% confidence level. The strength of the straight line relationship was obtained from the coefficient of determination, r^2, which reflects what percentage of the variation in y is accounted for by the fitted regression[42]. The correlation coefficient is equal to one for perfect correlation of the data. Simple linear regressions are made with the assumption that there is no error in x values and the error in y values is independent of the size of y[43]. This assumption is incorrect for the data in chapters 3 and 4, but a weighted regression, which gives approximately the same result as an unweighted regression[43], is not necessary as this data is not being used further as, for example, a calibration graph.

Visual inspection of the graphs in chapter 3 and 4 revealed trends which were not necessarily confirmed by statistical analysis. Emphasis was therefore placed on the trends observed visually, and the results of the linear regression of y against x were reported only if r^2 was greater than 80%.

CHAPTER 3

Formation of cyanoborate liquid clathrates

The validity of the definition of liquid clathrates was probed with respect to the absence of host in the excess guest layer. As no host was detected in the excess guest layer by ^{1}H NMR, an ether/water system, which was not considered a liquid clathrate, was tested for this behaviour and the limit of detection of the cyanoborate host in a solvent was investigated using infrared spectroscopy. The validity of the definition of liquid clathrates was probed with respect to the fixed maximum G/H. The maximum G/H of cyanoborate liquid clathrates formed with water as a promoter was determined, to see if the maximum G/H was constant (within ± 0.2 or 5% of the value)[1,21] and the G/H was determined when the available guest was less than excess. A model which allows for the effect of promoters on liquid clathrates was proposed. The importance of promoters was verified by promoting liquid clathrate formation in guest-host combinations which do not form liquid clathrates without a promoter. The formation of two immiscible liquid layers was used as the criterion for liquid clathrate formation.

3.1 The maximum G/H of furan/1 and thiophene/1 liquid clathrates formed with the promoter, water

3.1.1 Method

Special precautions to eliminate contamination by atmospheric moisture were not taken. The G/H ratio was obtained using ^{1}H NMR, with the error of each analysis estimated as described in chapter 2.4.5. TGA and gravimetric analysis were used for comparison with the ^{1}H NMR analysis of G/H. The error in the TGA results was not estimated although it was certainly present. In gravimetric analysis, **1**•nH_2O was weighed, a liquid clathrate was made with furan as guest, the excess guest layer was removed with a Pasteur pipette, the liquid clathrate layer was weighed and the G/H was calculated. The weighed liquid clathrate was heated to 86°C at 1.5mmHg for an hour to remove the furan, the remaining host was weighed, ^{1}H NMR (60MHz) was used to confirm that no furan remained in the host, and the G/H was calculated. The

error in these two analyses was estimated using a propagation of error calculation which accommodated the uncertainty in weighing (±0.0005g) and the uncertainty in the molecular mass of **1**•nH_2O (the error in n was taken as 10% of n).

The G/H results obtained by ^1H NMR (60MHz) for the furan/**1** liquid clathrate were regrouped according to batch of **1**•nH_2O and the G/H was plotted against nH_2O in **1**•nH_2O (table 3.1.2b and figure 3.1.2).

3.1.2 Results

TABLE 3.1.2a Maximum G/H with H = **1**•nH_2O

G = furan	G = thiophene
$5.8^{1,a}$	$6.9 \pm 0.2^{(1)}$
$5.9^{1,(a)}$	7.5 ± 0.5^{m}
$6.6^{1,(a)}$	$7.6^{1,n}$
$6.6 \pm 0.4^{(b)}$	$12.4 \pm 0.7^{2,n}$
7.2 ± 0.4^{c}	13.4 ± 0.1^{n}
7.3 ± 0.2^{d}	13.7 ± 0.1^{n}
7.3 ± 0.4^{b}	$13.8 \pm 4.8^{2,n}$
7.3 ± 0.5^{e}	13.8 ± 0.3^{n}
7.6 ± 0.4^{b}	13.8 ± 0.2^{n}
7.7 ± 0.4^{c}	14.0 ± 0.1^{n}
7.7 ± 0.7^{d}	15.8 ± 0.2^{n}
8.4 ± 0.1^{c}	$<16.3^{5,n}$
8.7 ± 0.4^{f}	17 ± 1^{p}
$8.7 \pm 0.7^{2,g}$	
9.1 ± 1^{f}	
$9.2 \pm 0.1^{3,h}$	
9.3 ± 0.4^{i}	
9.7 ± 0.5^{f}	
9.8 ± 0.7^{j}	
9.9 ± 0.3^{k}	
10.3 ± 0.6^{k}	
$10.8 \pm 0.1^{4,h}$	

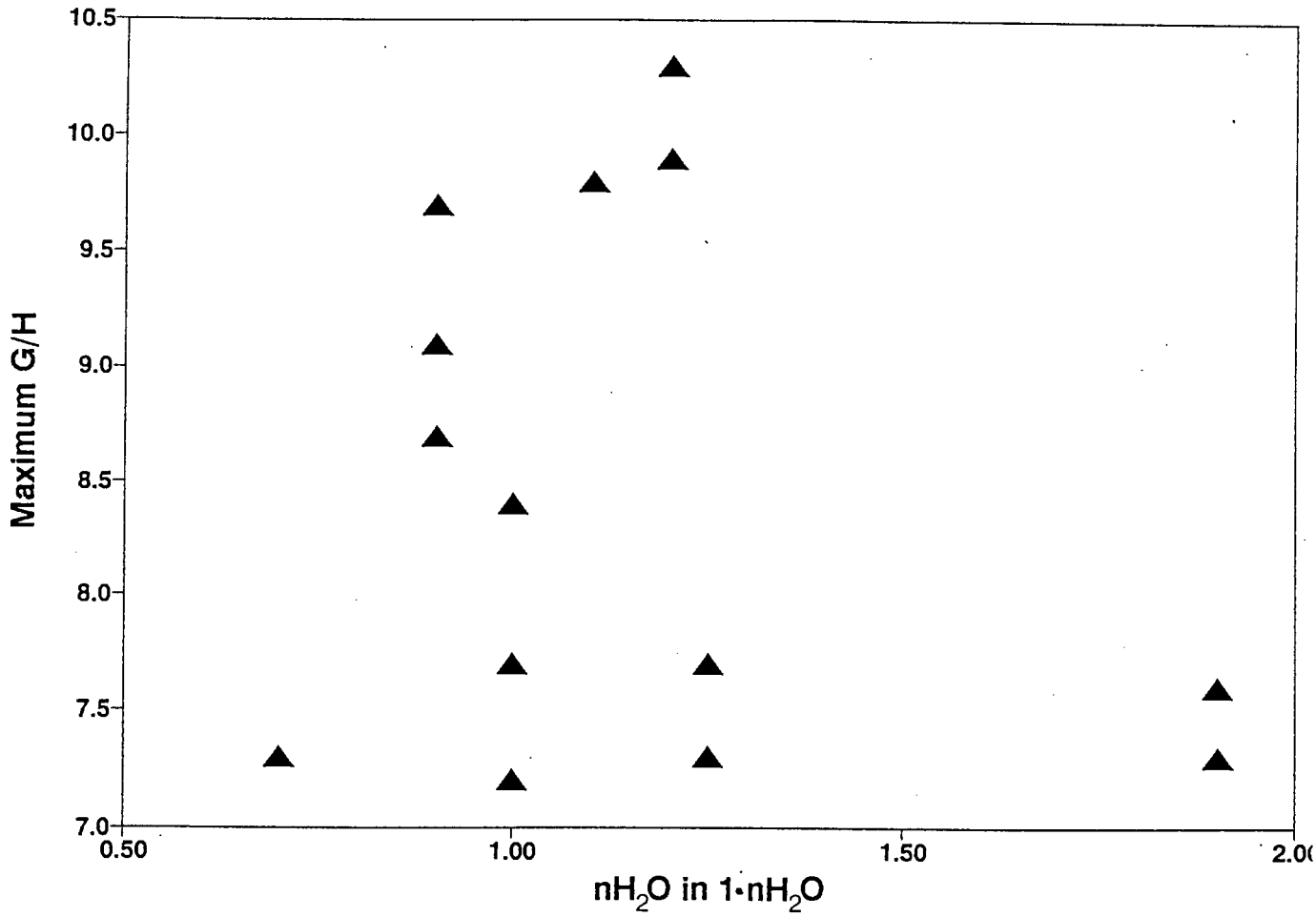
a - p different batches of **1**; ( ) sample has been dried in vacuum pistol
1 TGA
2 200MHz ^{1}H NMR
3 gravimetric analysis
4 gravimetric analysis using distillation Other values 60MHz ^{1}H NMR
5 two immiscible layers observed when only 16.3 equivalents of thiophene were available

Assuming a Gaussian distribution of the values in table 3.1.2a, the G/H in the furan/**1** liquid clathrate is 8.2 ± 0.6 (number of repeats = 22) and the G/H in the thiophene/**1** liquid clathrate is 12.5 ± 2.1 (number of repeats = 12).

TABLE 3.1.2b Maximum G/H of the furan/**1**•nH_2O liquid clathrate and the amount of water, nH_2O, in **1**•nH_2O (^1H NMR, 60MHz)

nH_2O	Maximum G/H
1.0	7.2 ± 0.4
	7.7 ± 0.4
	8.4 ± 0.1
1.25	7.3 ± 0.2
	7.7 ± 0.7
1.9	7.3 ± 0.4
	7.6 ± 0.4
0.7	7.3 ± 0.5
0.9	8.7 ± 0.4
	9.1 ± 1
	9.7 ± 0.5
5.2	9.3 ± 0.4
1.1	9.8 ± 0.7
1.2	9.9 ± 0.3
	10.3 ± 0.6

FIGURE 3.1.2 The effect of nH_2O on the maximum G/H of the furan/1•nH_2O liquid clathrate



3.2 The G/H of thiophene/1 mixtures with G/H ≤ maximum G/H

3.2.1 Method

Thiophene was chosen as guest because it was less volatile, formed a liquid clathrate more easily and formed a more stable liquid clathrate than furan. Thiophene and **1** were weighed, mixed, stirred overnight and analysed by ^{1}H NMR (60MHz).

3.2.2 Results

TABLE 3.2.2 Different amounts of thiophene mixed with **1** and analysed with ^{1}H NMR (60 MHz); n = moles of thiophene per mole of **1**

mixture	n added[a]	n analysed[b]
1	16.3 ± 0.6	13.8 ± 0.2[c]
2	6.5 ± 0.6	5.5 ± 0.2
3	4.9 ± 0.6	4.3 ± 0.2
4	3.2 ± 0.6	3.5 ± 0.2

a Error obtained from propagation of error calculation.

b NMR error calculated as described in chapter 2.4.5

c A small separate top layer formed. The bottom layer was analysed.

3.3 ^{1}H NMR (60MHz) analysis of water/ether systems

3.3.1 Method

Different ratios of water and diethyl ether (ether) dried with sodium wire were mixed vigorously overnight and then allowed to settle into two immiscible layers. ^{1}H NMR (60MHz) spectra were taken of the two layers of the mixtures.

3.3.2 Results

In all the mixtures of ether and water, no water was detected in the ether layer and no ether was detected in the water layer.

3.4 Limits of detection of 1 using IR spectroscopy

3.4.1 Method

Although the C≡N stretch was not the strongest signal in the IR spectrum of **1**, the cyano stretch was not overlapped by other signals of the host or of the guests, and was therefore chosen as the unambiguous signal to follow in this experiment.

An IR spectrum was taken of the excess thiophene layer of a thiophene/**1** liquid clathrate. **1** was quantitatively dissolved in dichloromethane, and successive dilutions were made of this solution. IR spectra were taken of these solutions to find the minimum concentration of **1** detectable by looking for the C≡N stretch. All the IR spectra were run in NaCl cells on a Perkin Elmer Paragon 1000 spectrometer.

3.4.2 Results

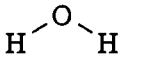
Using IR spectroscopy, no C≡N stretch of **1** was detected in the excess thiophene layer of the thiophene/**1** liquid clathrate. The C≡N stretch of **1** was detected down to a disappointingly high and inconsistent concentration of $0.001 moldm^{-3}$ in dichloromethane.

3.5 Promotion of liquid clathrate formation in guest-host combinations which did not necessarily form liquid clathrates without a promoter

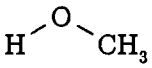
3.5.1 Method

The promoters shown in figure 3.5.1 were chosen from those discussed in chapter 1.4.

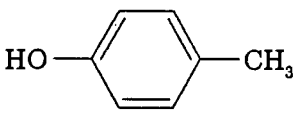
Figure 3.5.1 The hydroxyl functional group in promotion of liquid clathrates



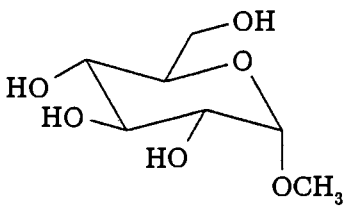
Water



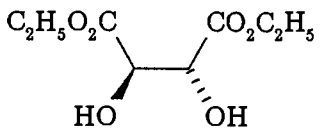
Methanol



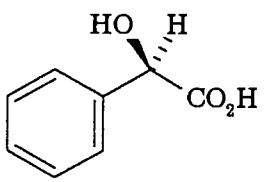
p - Cresol



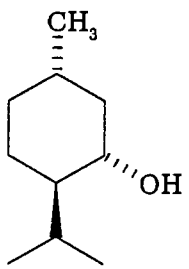
Methyl - α - D - glucopyranoside



Diethyl - (L) - Tartrate



(S) - Mandelic Acid



(1S, 2R, 5S) - Menthol

The hosts, guests and possible promoters were dried as described in appendix 3. Three to five equivalents of promoter per host were mixed with excess guest and added to the host. The methyl-α-D-glucopyranoside and mandelic acid did not dissolve in the guests. The appearance of a second liquid immiscible with the excess guest liquid indicated that a liquid clathrate was forming. (Further study of any liquid clathrates formed in this experiment would require assessment of the two immiscible liquids to check that one layer is the liquid clathrate layer and the other layer is excess guest.) If no second liquid layer formed, the mixture was heated with a hairdryer for up to two minutes. The results with **1** or **2** as host were compared with respect to promoters and guests.

3.5.2 Results

TABLE 3.5.2a The promotion of liquid clathrate formation in different guest/host combinations

		GUESTS					
promoter	host	thiophene	furan	benzene	toluene	N,N-dma	2-mf
none	1	lc	$S^{\Delta}\rightarrow S$	$S^{\Delta}\rightarrow S$	$S^{\Delta}\rightarrow lc^{\Delta}\rightarrow ppt$	$S^{\Delta}\rightarrow D$	D
none	2	$S^{\Delta}\rightarrow S,G$	$S^{\Delta}\rightarrow S$	$S^{\Delta}\rightarrow S$	$S^{\Delta}\rightarrow S$	$S^{\Delta}\rightarrow D$	$S^{\Delta}\rightarrow D$
water[a]	1	lc	$S^{\Delta}\rightarrow lc$	lc	$S^{\Delta}\rightarrow G$		D
ether[b]	2	$S^{\Delta}\rightarrow S$	$S^{\Delta}\rightarrow S$	$S^{\Delta}\rightarrow S$	$S^{\Delta}\rightarrow S$		$S^{\Delta}\rightarrow D$
methanol	1	lc	lc	$S^{\Delta}\rightarrow lc$	lc	D	
methanol	2	$S^{\Delta}\rightarrow lc$	$S^{\Delta}\rightarrow S$	$G^{\Delta}\rightarrow ppt$	$S^{\Delta}\rightarrow S$	D	
p-cresol	1	lc	lc	lc	lc		
p-cresol	2	lc	lc	lc	lc		
pyra	1	lc	$S^{\Delta}\rightarrow G$	$S^{\Delta}\rightarrow lc$	$S^{\Delta}\rightarrow S$		
pyra	2	$S^{\Delta}\rightarrow lc$	$S^{\Delta}\rightarrow S$	$S^{\Delta}\rightarrow S$	$S^{\Delta}\rightarrow S$		
mand	1	lc	lc	$S^{\Delta}\rightarrow lc\rightarrow G$	$lc^{\Delta}\rightarrow lc$		
mand	2	lc	$S^{\Delta}\rightarrow G$	$G^{\Delta}\rightarrow lc$	$S^{\Delta}\rightarrow G$		
menthol	1	lc	$G^{\Delta}\rightarrow lc$	$S^{\Delta}\rightarrow lc$	$S^{\Delta}\rightarrow S$		
menthol	2	$S^{\Delta}\rightarrow S$	$S^{\Delta}\rightarrow S$	$S^{\Delta}\rightarrow S$	$S^{\Delta}\rightarrow S$		
DET	1	lc	lc	$G^{\Delta}\rightarrow lc$	$lc^{\Delta}\rightarrow ppt$		
DET	2	lc	$G^{\Delta}\rightarrow ppt$	$G,lc^{\Delta}\rightarrow lc$	$S^{\Delta}\rightarrow S$		

$^{\Delta}$	heat with stirring for ~two minutes	dma	N,N-dimethylaniline
a	water of crystallisation in host	2-mf	2-methoxyfuran
b	diethyl ether of crystallisation in host	pyra	methyl-α-D-glucopyranoside
lc	formation of two immiscible liquid layers	mand	mandelic acid
S	suspension of solid in liquid	DET	diethyl-(L)- tartrate
G	gum or sticky solid		
ppt	precipitation after formation of two liquid layers		
D	solid dissolved in liquid forming a single solution		

TABLE 3.5.2b Comparison of promoters and guests in liquid clathrate formation with **1** or **2** as host. lc = stable liquid clathrate forms, x = not tested

promoter	**1**				**2**			
	thio	furan	benzene	toluene	thio	furan	benzene	toluene
none	lc							
water	lc	lc	lc		x	x	x	x
ether	x	x	x	x				
methanol	lc	lc	lc	lc	lc			
cresol	lc	lc	lc	lc	lc	lc	lc	lc
pyra	lc		lc		lc			
mand	lc	lc		lc	lc		lc	
menthol	lc	lc	lc					
DET	lc	lc	lc		lc		lc	

thio thiophene

pyra methyl-α-D-glucopyranoside (unpurified)

mand mandelic acid

DET diethyl-L- tartrate

3.6 Discussion

3.6.1 The definition of liquid clathrates and the formation of liquid clathrates with cyanoborate hosts

G/H was not fixed within[1,21] ±0.2 or 5% for the furan/**1** and thiophene/**1** liquid clathrates (table 3.1.2a). These liquid clathrates are therefore not strictly liquid clathrates according to the definition[1] of liquid clathrates in chapter 1. The range of G/H for the furan/**1** liquid clathrate was smaller for a single batch of **1** (table 3.1.2b) than for the G/H from all the batches. G/H values determined by TGA or ^{1}H NMR for a single batch of **1** all fell within one unit of each other, with the exception of batch *c* which ranged from 7.2 to 8.4 (1.2 units). G/H of batch *h* was determined gravimetrically and ranged from 9.2 to 10.8 (1.6 units). The most obvious difference between different batches of **1**•nH_2O was the value of n (table 3.1.2b). As water

promoted the formation of the furan/**1** liquid clathrate, the amount of water present could have affected G/H.

Haueisen[26] found that the G/H of the thiophene/**1** and benzene/**1** liquid clathrates depended on the amount of water present, so the G/H of these cyanoborate liquid clathrates depended on the amount of water present. Similarly, Gaudet, Peterson and Zaworotko[21] found that the G/H of the benzene/1-methyl pyrrolidine/$[(HCl)_nCl]^-$ (n = 1 - 3) liquid clathrate depended on the amount of HCl present. Atwood[1] reported that the maximum G/H of a liquid clathrate depended on cavity size and that the guest can affect the size of the volume it fills. A promoter could affect the size of the volume the guest fills, thus making the maximum G/H dependent on the amount of promoter present.

Atmospheric water could have been responsible for the lack of a relationship between nH_2O in **1**•nH_2O and the G/H of the liquid clathrate (figure 3.1.2). The interaction of the furan/**1** liquid clathrate with water is the subject of chapter five. The effect of cresol on G/H in the furan/1 liquid clathrate is described in chapter four.

The G/H is expected to differ from the maximum G/H either when the liquid clathrate crystallises to form a salt[26] or when less than the maximum amount of guest is available for liquid clathrate formation[1]. The latter was confirmed for mixtures of thiophene and **1** (table 3.2.2). The formation of two immiscible liquid layers characteristic of liquid clathrates indicated that the maximum G/H of the thiophene/**1** liquid clathrate was less than 16.3 ± 0.6. Within experimental error, all the available thiophene interacted with **1** to form the solutions of thiophene in **1**. The interaction between **1** and thiophene did not demand that the maximum G/H amount of guest was present. The interaction of liquid clathrate host and guest below the maximum G/H involved a structure which expanded to accommodate all available guest.

This increase in G/H up to maximum G/H implies that each increased G/H is more stable than its predecessor, with maximum G/H being the most stable. The interaction between the guest and the host stabilises the structure of the liquid clathrate. The

importance of the guest in the liquid clathrate structure is reflected by the propensity of liquid clathrates with low G/H to precipitate[10]. When a liquid clathrate forms a solid with lower G/H, the interaction between the ions of the host become more important than the stabilising effect of the interaction between the guest and the host. Promotion of liquid clathrate formation could result from the promoter enhancing expansion of the structure to accommodate the guest, and from the promoter decreasing the interaction of the host cations and anions. This ionic interaction tends to form a closely packed solid lattice with less space for the guest.

Another important aspect of the definition of a liquid clathrate is that no host is present in the excess guest layer. This is usually verified with ^{1}H NMR, and could be a detection limit phenomenon which would make a system which is not considered a liquid clathrate appear to be a liquid clathrate. This possibility was investigated for a water/ether system. As expected (chapter 1.5.3), no ether peak was observed in the ^{1}H NMR (60MHz) spectrum of the water layer. Unexpectedly (chapter 1.5.3), no water peak was observed in the ^{1}H NMR (60MHz) spectrum of the ether layer. The water/ether system therefore did not display liquid clathrate behaviour. Use of 200MHz or 400MHz ^{1}H NMR would have been more appropriate for this experiment, which was designed to investigate whether the absence of host in the excess guest layer is an intrinsic feature of a liquid clathrate system, or is a detection limit phenomenon which is observable in a binary liquid/liquid system which is not a liquid clathrate.

The infrared studies lead to the conclusion that the thiophene/**1** liquid clathrate has less than 0.001moldm^{-3} host in the excess guest layer. This conclusion, which accommodates the limits of detection methods, is preferable to concluding that the absence of host in the excess guest layer of a liquid clathrate is an absolute fact.

3.6.2 Proposal of a model of liquid clathrates which allows for the effect of promoters on liquid clathrate behaviour

The guests are electron rich aromatics and are therefore concentrated around the cations of the host and resist interactions with the anions of the host. Before the maximum amount of guest is added, the structure of the guest-host interaction changes and expands to accommodate more guest as guest is added, without guest molecules having to interact closely with the anions of the host. There is enough space for the guest molecules around the cations.

When the maximum amount of interaction between the guest and cation is reached, additional guest is forced to interact with the anion unless the guest is expelled from the liquid clathrate structure or the excess guest in effect never interacts with the liquid clathrate structure (although exchange of guest between the layers occurs[8]). The excess guest layer is thus formed. As the interaction between host and guest is saturated when the excess guest layer forms, the excess guest does not interact with the host and host molecules are not detectable in the excess guest. The maximum G/H and the absence of host in the excess guest layer is thus explained by the limit to the space around the cation for the guest to interact with an electron poor region, and by the limit to the interaction between the electron rich guest and the anion.

If the interactions between the ions of the host are strong enough, a liquid clathrate solidifies to form either the pure host with no guest present or a solid clathrate with G/H lower than the G/H of the liquid clathrate. The decreased amount of guest in the solid results from the decrease in electron poor space around the host cation. The electron rich guest molecules concentrated around the cation in the liquid clathrate are forced out of the structure by the proximity of the cation and anion to each other in the solid structure.

Formation of liquid clathrates from some guest-host combinations requires the presence of a promoter. A promoter enhances liquid clathrate formation by extending the space available for interaction of the guest with electron poor regions of the

structure. The promoter achieves this by separating the host cation and anion, thus physically extending the available space around the cation, and by diminishing the effect of the negative charge of the anion.

The maximum G/H of a guest-host combination is not fixed if a promoter is present. Two explanations would accommodate this effect of a promoter on the maximum G/H. Each guest-host-promoter combination with a different amount of promoter could be considered a different liquid clathrate with a fixed G/H. Alternatively, the amount of guest in the electron poor space in a guest-host combination could be considered fixed, with the promoter altering the size of this space. In this case the guest per (electron poor) volume is fixed, not the G/H.

The electronic nature of a promoter affects the extent of interaction between the promoter and the host anion, host cation, liquid clathrate guest and excess guest. In the extreme case of enough promoter present and favourable interaction between promoter, guest and host, the liquid clathrate and excess guest layer form a single solution of host ions in guest and promoter molecules.

3.6.3 The promotion of liquid clathrate formation in guest-host combinations which did not necessarily form liquid clathrates without a promoter

In the following discussion of table 3.5.2, "formation of a liquid clathrate" means two immiscible liquid layers were observed; the liquid clathrate nature of these layers was not confirmed. The thiophene/**1** liquid clathrate formed without a promoter present, so thiophene was used in studies of promoters only for comparison. The unifying feature of the promoters chosen (figure 3.5.1) in this experiment is that they are capable of hydrogen bonding. Cresol was a particularly strong promoter as cresol promoted liquid clathrate formation in all guest-host combinations tested. The spread of the remaining results indicated that promotion of liquid clathrate formation requires a contribution from host, guest and promoter as none of these hosts, guests or promoters formed a liquid clathrate without fail. Except for the water-dependent liquid clathrates of

thiophene/**1**, furan/**1** and benzene/**1**, all the liquid clathrates formed in this experiment have never been reported before and, with the exception of the thiophene liquid clathrates, do not form without a promoter. Promoters can therefore be used to form liquid clathrates from combinations of guests and hosts which do not form liquid clathrates without a promoter.

This exciting result justifies the research (presented in chapter 4), which probes the interactions between promoters and liquid clathrates. A thorough understanding of the promotion of liquid clathrate formation will provide an additional and useful parameter in the design of liquid clathrates. Use of chiral promoters to form chiral liquid clathrates could become important in the separation of chiral isomers using liquid/liquid extraction methodology.

CHAPTER 4

Liquid clathrate formation promoted by water or cresol

Water is historically[16] the promoter of cyanoborate liquid clathrate formation (with guests furan, thiophene and benzene). Out of the promoters tested, cresol promoted liquid clathrate formation for the widest range of guest-host combinations (chapter 3.5). Water is a stronger dipole than cresol as Π electrons can be delocalised in the cresol ring. The electronic nature of the liquid clathrate components was thought to be important in liquid clathrate formation, so water and cresol were chosen for this study. Neither water nor cresol are liquid clathrate guests of the cyanoborate host, **1**.

As the Π electron rich nature of the guest is fundamental to the model proposed in chapter 3.6.2 (model 3.6.2), the importance of the Π electron rich nature of the guest was probed by comparing the formation of the cyanoborate liquid clathrates, with and without water as a promoter, using the three guests, furan, thiophene and benzene. The interaction between promoter and the cyanoborate liquid clathrate was investigated by examining the amount of promoter (water or cresol) in the liquid clathrate layer compared with the total amount of promoter present in the liquid clathrate/excess guest system. For cresol as a promoter, the interaction between promoter and liquid clathrate was examined in greater detail through concentrating on the interaction of cresol with the host anion and on the interaction of cresol with the guest. In probing the promoter-anion interactions, the effect of cresol on the protons α to the negatively charged boron was observed, to provide evidence that cresol decreased the effect of the negative charge of the host anion. In probing the promoter-guest interaction, the effect of cresol in the liquid clathrate on the G/H of the furan/**1** liquid clathrate was determined. The composition of liquid clathrates formed with water and cresol present was used to compare which, if any, of these promoters is favoured in the interaction of the liquid clathrate with two promoters in competition with each other.

By changing the order of mixing the three components of a promoter-guest-host system, the effect of interaction of two components prior to the addition of the third component to form a liquid clathrate was probed with respect to the ease of liquid clathrate formation and the stability of the liquid clathrate formed. The length of time taken for liquid clathrate formation was used to compare the ease with which water or cresol promote liquid clathrate formation. The length of time taken for a liquid clathrate to precipitate was used to compare the stability of the liquid clathrates formed with water or cresol as promoters.

Use of the interaction of cresol with the liquid clathrate was considered for:

(1) Measuring equilibrium constants between host and guest in an expanding host-guest-promoter liquid clathrate system,

(2) Investigating whether cresol partitions between the excess guest and liquid clathrate layers, and

(3) Investigating whether the different isomers of cresol partition selectively between the excess guest and liquid clathrate layers so that cresol isomers can be separated using liquid clathrates in liquid/liquid extraction methodology.

4.1 Formation of cyanoborate liquid clathrates with furan, thiophene and benzene as guests

4.1.1 Method

Appendix 3 describes how liquid clathrate components were dried. Excess dry guest (furan, thiophene, benzene) was added to anhydrous **1** and to **1**•$3H_2O$. If the two immiscible liquid layers characteristic of liquid clathrates did not form after at least two minutes of vigorous mixing, the mixture was heated with a hairdryer for at least one minute.

4.1.2 Results

TABLE 4.1.2 Formation of cyanoborate liquid clathrates[a] with and without water as promoter

Host	Guest	Result of stirring	Result of heating
anhydrous **1**	furan	no liquid clathrate	no liquid clathrate
anhydrous **1**	thiophene	liquid clathrate	
anhydrous **1**	benzene	no liquid clathrate	no liquid clathrate
1•$3H_2O$	furan	no liquid clathrate	liquid clathrate
1•$3H_2O$	thiophene	liquid clathrate	
1•$3H_2O$	benzene	liquid clathrate	

a two immiscible liquid layers observed

4.2 The amount of water in the cyanoborate liquid clathrate compared with the available amount of water

4.2.1 Method

nH_2O was analysed by ^1H NMR (scheme 4.2.1). nH_2O in the host, **1**• nH_2O, was determined (analysis **A**). A liquid clathrate was formed with the host and freshly distilled guest (furan, thiophene, benzene) and sampled for NMR (analysis **B**). To investigate whether the amount of water in the liquid clathrate changed with increased availability of water once the liquid clathrate formed, the liquid clathrate and excess guest were mixed vigorously with excess water, which, on settling, formed a third liquid layer immiscible with the liquid clathrate and excess guest layers. The liquid clathrate layer was sampled for NMR (analysis **C**).

SCHEME 4.2.1 Analyses of the amount of water in the host, in the liquid clathrate and in the liquid clathrate after mixing with excess water

Solid **1**•nH_2O analysis **A**

↓ guest

Excess guest layer
Liquid clathrate layer analysis **B**

↓ water

Excess guest layer
Excess water layer
Liquid clathrate layer analysis **C**

4.2.2 Results

TABLE 4.2.2 The amounts of water in the liquid clathrate. **A** = solid **1**•nH_2O, **B** = liquid clathrate after mixing with excess guest, **C** = liquid clathrate after mixing with excess guest and excess water.

Guest	nH_2O in **A**	nH_2O in **B**	nH_2O in **C**
furan	2.9 ± 0.2	1.1 ± 0.1	
	2.5 ± 0.3	1.0 ± 0.1	1.1 ± 0.1
	2.5 ± 0.3.	1.2 ± 0.1	1.1 ± 0.1
	2.0 ± 0.1[a]	1.1 ± 0.1[a]	
	1.1 ± 0.1	1.1 ± 0.1	
	1.0 ± 0.1	1.0 ± 0.1	0.9 ± 0.1
	1.0 ± 0.1	1.1 ± 0.1	0.9 ± 0.1
	0.9 ± 0.1	0.9 ± 0.1	0.9 ± 0.1
	0.6 ± 0.1		1.4 ± 0.2
	0.3 ± 0.1[b]	0.3 ± 0.1	1.3 ± 0.2
thiophene	4.2 ± 0.7	1.4 ± 0.1	0.7 ± 0.1
	0.9 ± 0.1	0.8 ± 0.1	1.0 ± 0.2
	0.1 ± 0.1	0.2 ± 0.1	0.9 ± 0.1
benzene	4.2 ± 0.7	1.3 ± 0.1	1.6 ± 0.1
	1.2 ± 0.1	1.1 ± 0.1	
	0.1 ± 0.1		

a 200MHz ^{1}H NMR. (Other results: 60MHz ^{1}H NMR)

b **1**•nH_2O slightly yellow. Undetectable impurity might have promoted liquid clathrate formation.

4.3 The amount of cresol in the furan/1 liquid clathrate compared with the total amount of cresol added

4.3.1 Method

Weighed cresol was quantitatively transferred to weighed **1**•H_2O using excess furan. The mixture was stirred vigorously for five minutes and was then left stirring overnight in a closed container to equilibrate. ^{1}H NMR (60MHz) was used to look for the presence of **1** and of cresol in the excess furan layer. Integration of ^{1}H NMR (200MHz, DMSO-d_6) spectra of the liquid clathrate layer was used to calculate the amount of cresol in the liquid clathrate layer. The amount of cresol in the liquid clathrate was plotted against the total amount of cresol added .

4.3.2 Results

TABLE 4.3.2 The amount of cresol found (^{1}H NMR, 200MHz, DMSO-d_6) in the furan/**1** liquid clathrate after mixing cresol, **1**•H_2O and excess furan[a]

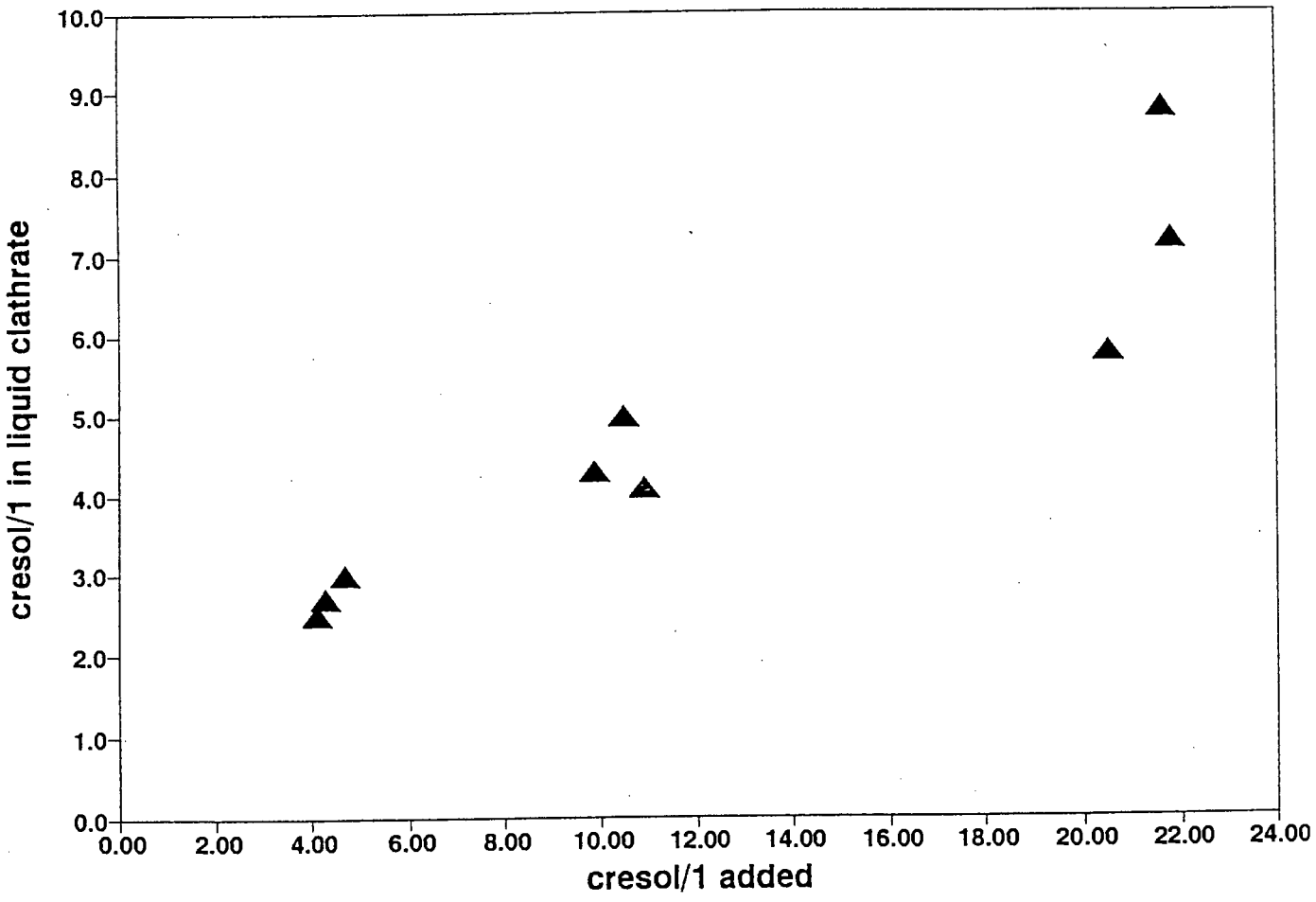
Cresol isomer	cresol/**1** added	cresol/**1** in liquid clathrate
ortho	4.3	2.7 ± 0.2
ortho	10.9	4.1 ± 0.3
ortho	20.5	5.8 ± 0.4
ortho	101	14.9 ± 1.8
meta	4.1	2.5 ± 0.2
meta	9.9	4.3 ± 0.3
meta	21.8	7.2 ± 0.1
meta	100	solution[b]
para	4.7	3.0 ± 0.3
para	10.5	5.0 ± 0.5
para	21.6	8.8 ± 1.0
para	100	solution[b]

a cresol, but not **1** was found in the excess furan layer(^{1}H NMR, 60MHz)

b The mixture formed a single solution instead of two immiscible layers. Addition of furan and **1** caused the solution to form two immiscible layers

FIGURE 4.3.2 The increase of cresol in the furan/1 liquid clathrate with increased cresol added to 1 and excess furan

Correlation coefficient = 0.94, r^2 = 88% (95% confidence level)



4.4 The effect of cresol in the furan/1 liquid clathrate on the NMR integration of protons α to negatively charged boron (αB peaks) in the cyanoborate anion

4.4.1 Method

Liquid clathrates were made by adding mixtures of excess furan and cresol to **1**•H_2O. ^1H NMR (200MHz, DMSO-d_6) spectra of the liquid clathrate samples were obtained with pulse delays of five times the longest T_1 (chapter 2.4.2). Integration of the spectra was used to calculate the equivalents of cresol in the liquid clathrate (cresol/**1**). The estimated error of cresol/**1** was calculated (chapter 2.4.5) using all peaks of the spectrum except the αB peak. The range of the estimated error of cresol/**1** was therefore an indication of the correctness of the integration of **1** except for the integration of the protons α to boron. Int% of αB peaks relative to peaks corresponding to phenyl (ph) protons and to the protons in the anion not α to boron (hB) were used to estimate the percentage decrease in the αB peaks by assuming that the hB and ph peaks were correctly integrated and that:

$$\% \text{ decrease in } \alpha B \text{ peak integration} = 100 - (\text{Int}\% \ \alpha B/ph + \text{Int}\% \ \alpha B/hB)/2$$

The calculated % decrease in the αB peaks was written with one significant digit only, to emphasise that the % decrease was an approximation. The relationship between the amount of cresol in the liquid clathrate and the integration of the αB peaks was investigated graphically.

4.4.2 Results

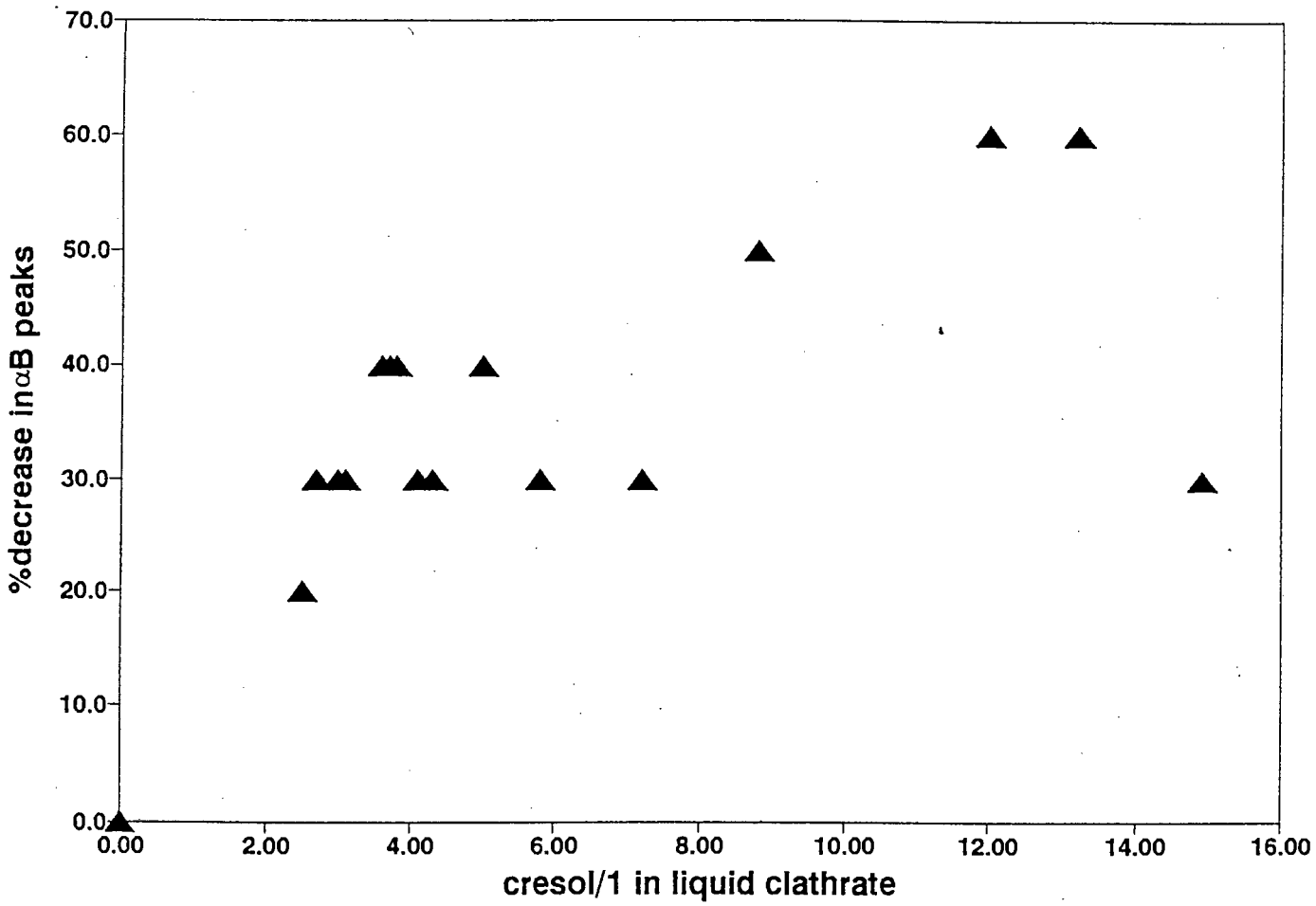
TABLE 4.4.2 Int% involving αB peaks (^{1}H NMR, 200MHz, DMSO-d_6) used to approximate the percentage decrease in αB peaks of furan/1 liquid clathrates containing cresol

Cresol isomer	cresol/1 in liquid clathrate	Int% αB/ph	Int% αB/hB	%decrease in αB peak integration[b]
	none[a]	100	101	0
ortho	2.7 ± 0.2	64	68	30
ortho	4.1 ± 0.3	67	68	30
ortho	5.8 ± 0.4	70	68	30
ortho	14.9 ± 1.8	68	75	30
meta	2.5 ± 0.2	83	82	20
meta	4.3 ± 0.3	65	68	30
meta	7.2 ± 0.1	70	73	30
meta	13.2 ± 1.6	35	37	60
para	3.0 ± 0.3	67	73	30
para	5.0 ± 0.5	57	64	40
para	8.8 ± 1.0	47	57	50
para	12 ± 0.5	39	40	60
ortho,meta,para	3.1 ± 0.4	66	65	30
ortho, para	3.6 ± 0.5	62	63	40
ortho, meta	3.7 ± 0.4	63	64	40
meta, para	3.8 ± 0.5	60	63	40

a ^{1}H NMR (60MHz, DMSO-d_6) spectrum of a furan/1•nH_2O liquid clathrate

b one significant digit used for 100 - (Int% αB/ph + Int% αB/hB)/2

FIGURE 4.4.2 Approximate decrease in the αB peaks (^{1}H NMR, 200MHz, DMSO-d_6) in furan/1 liquid clathrates with cresol present



4.5 The effect of cresol on the G/H of the furan/1 liquid clathrate

4.5.1 Method

Cresol, **1**•H_2O and excess furan were stirred vigorously for five minutes and then stirred overnight in a closed container to equilibrate. Integration of ^1H NMR (200MHz, DMSO-d_6) spectra of the liquid clathrate layer was used to calculate the amount of cresol and furan in the liquid clathrate layer. The relationship between the amount of cresol and the amount of furan in the liquid clathrate layer was plotted.

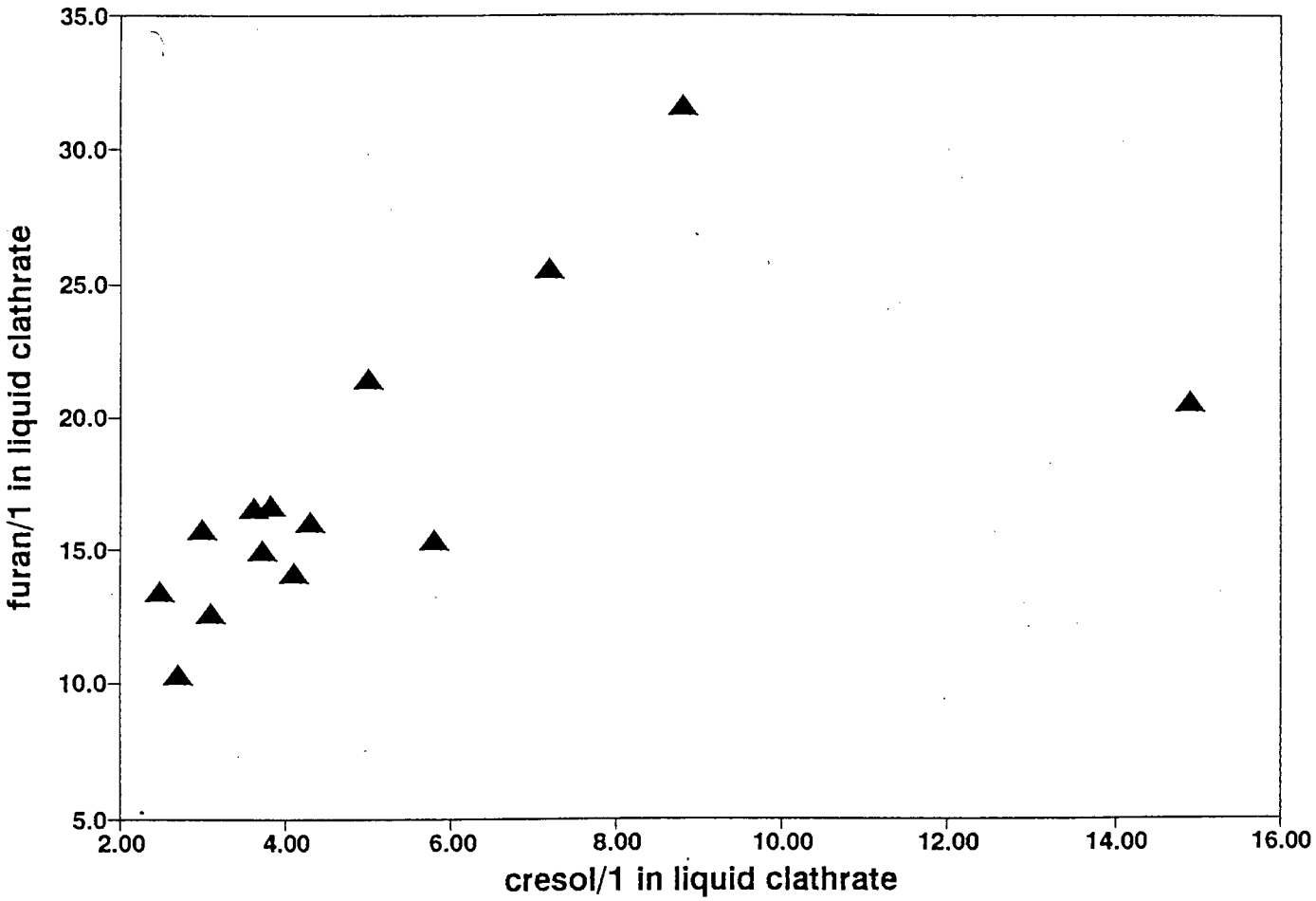
4.5.2 Results

TABLE 4.5.2 The amounts of cresol and furan in the liquid clathrate layer after mixing cresol, **1**•H_2O and excess furan

cresol/**1** in the liquid clathrate	furan/**1**[a] in the liquid clathrate
2.5 ± 0.2	13.4 ± 0.7
2.7 ± 0.2	10.3 ± 0.7
3.0 ± 0.3	15.8 ± 1.5
3.1 ± 0.4	12.6 ± 1.3
3.6 ± 0.5	16.6 ± 2.3
3.7 ± 0.4	15.0 ± 1.5
3.8 ± 0.5	16.7 ± 1.9
4.1 ± 0.3	14.1 ± 1.2
4.3 ± 0.3	16.1 ± 1.2
5.0 ± 0.5	21.5 ± 1.9
5.8 ± 0.4	15.4 ± 0.9
7.2 ± 0.1	25.6 ± 0.4
8.8 ± 1.0	31.6 ± 3.5
14.9 ± 1.8	20.6 ± 2.5

a same batch of **1** used throughout this experiment

FIGURE 4.5.2 The effect of cresol in the furan/1 liquid clathrate on the furan/1 G/H



4.6 The composition of furan/1 liquid clathrates made in the presence of both water and cresol

4.6.1 Method

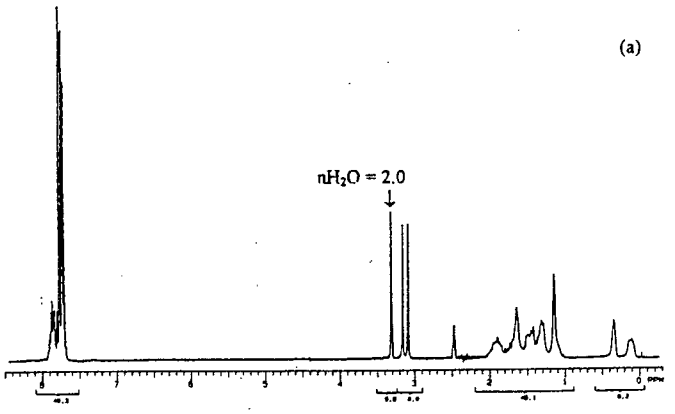
Liquid clathrates were made by adding excess furan to **1**•nH_2O and by adding a mixture of cresol and excess furan to **1**•nH_2O. ^1H NMR (200MHz, DMSO-d_6) spectra were taken of **1**•nH_2O, the liquid clathrate layer of furan added to **1**•nH_2O and the liquid clathrate layer of cresol and furan added to **1**•nH_2O.

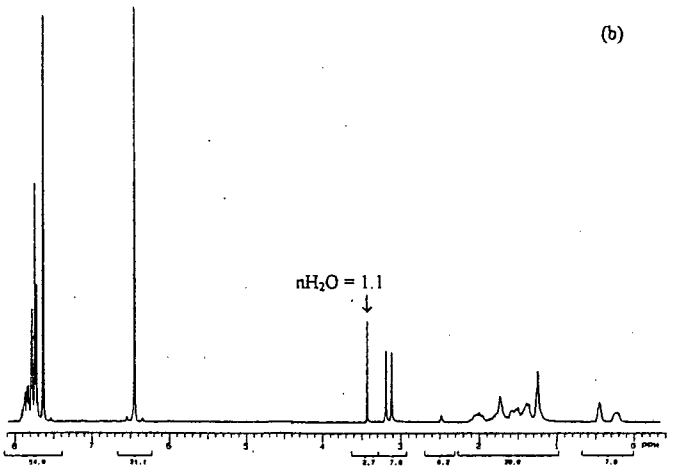
4.6.2 Results

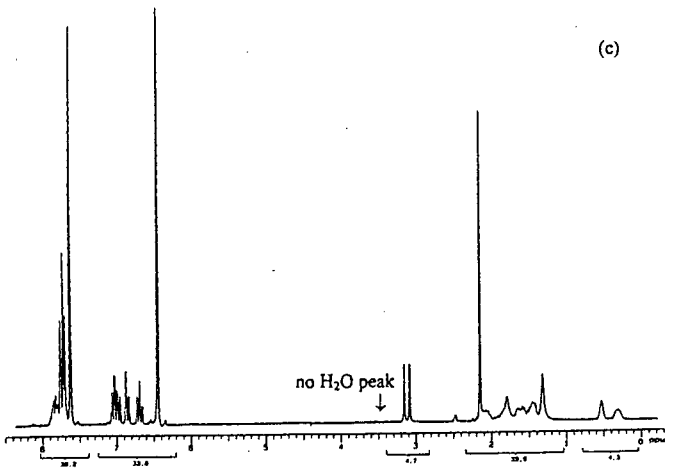
TABLE 4.6.2 The amounts of water, furan and cresol relative to the amount of host (n) determined by the ^1H NMR (200MHz, DMSO-d_6) spectra in figure 4.6.2

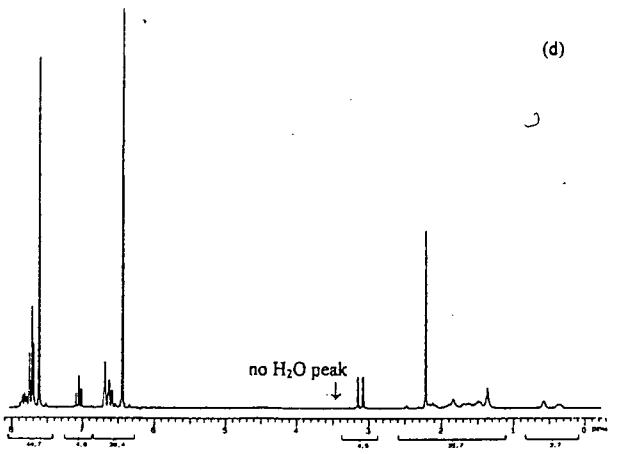
Sample	nH_2O	nfuran	ncresol
1•nH_2O	2.0 ± 0.1		
furan/**1**•nH_2O liquid clathrate	1.1 ± 0.1	8.7 ± 0.7	
o-cresol/furan/**1**•nH_2O liquid clathrate	no peak	15.2 ± 2.8	5.6 ± 1
m-cresol/furan/**1**•nH_2O liquid clathrate	no peak	23.7 ± 5.6	7.3 ± 1.8
p-cresol/furan/**1**•nH_2O liquid clathrate	no peak	22.8 ± 3.9	7.3 ± 1.5

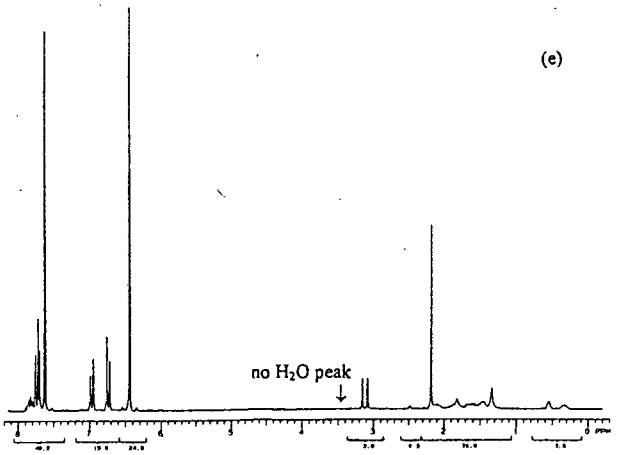
FIGURE 4.6.2 ^{1}H NMR spectra (200MHz, DMSO-d_6)
(a) 1•nH_2O
(b) Liquid clathrate of furan added to 1•nH_2O
(c) Liquid clathrate of furan and o-cresol added to 1•nH_2O
(d) Liquid clathrate of furan and m-cresol added to 1•nH_2O
(e) Liquid clathrate of furan and p-cresol added to 1•nH_2O











4.7 The effect of the order of mixing cresol, guest and 1 on the promotion of liquid clathrate formation (guest = furan, thiophene, benzene)

4.7.1 Method

Liquid clathrates were made with anhydrous **1**, guest and cresol by adding guest to a mixture of cresol and **1**, by adding cresol to a mixture of guest and **1** and by adding a mixture of guest and cresol to **1**.

The amount of host and guest used in each experiment was identical (within experimental error), so the length of time needed to form the liquid clathrate from the host and guest was used as an indication of how easily the liquid clathrate formed. The time was measured from addition of the guest until all the crystals of **1** had formed a liquid layer immiscible with the excess guest layer. The time taken by the liquid clathrate to precipitate or form crystals was taken as an indication of the stability of the liquid clathrate.

4.7.2 Results

TABLE 4.7.2 Times taken for liquid clathrates to form when cresol, anhydrous **1** and guest (furan, thiophene, benzene) were mixed in different orders, and the times taken for these liquid clathrates to precipitate

Initial components	Components added	Stirring time/minute[a]	Precipitation time/days[b]
1/cresol	furan	4	>22
1/furan	cresol	0.5	>22
1	furan/cresol	1	>22
1/cresol	thiophene	10	>22
1/thiophene	none	6	>22
1	thiophene/cresol	2	>22
1/cresol	benzene	2	>22
1/benzene	cresol	3	>22
1	benzene/cresol	5	>22

a length of time the mixture of components was stirred to form the liquid clathrate completely
b length of time the liquid clathrate took to start forming crystals

4.8 Comparison of water and cresol as promoters, using time as an estimate of the ease of formation of furan/1, thiophene/1 and benzene/1 liquid clathrates and of the stability of the resultant liquid clathrates

4.8.1 Method

Using **1**•$3H_2O$ or anhydrous **1** mixed with ten equivalents of cresol, liquid clathrates were made with anhydrous furan, thiophene or benzene.

The amount of host and guest used in each experiment was identical (within experimental error), so the length of time needed to form the liquid clathrate from the host and guest was used as an indication of how easily the liquid clathrate formed. The time was measured from addition of the guest until all the crystals of **1** had formed a liquid layer immiscible with the excess guest layer. The time taken by the liquid clathrate to precipitate or form crystals was taken as an indication of the stability of the liquid clathrate.

4.8.2 Results

TABLE 4.8.2 Times taken for liquid clathrates to form and to precipitate with water or cresol as promoters

Guest	Promoter	Stirring time/minutes[a]	Precipitation time/days[b]
furan	$H_2O^c + \Delta$	3.5	8
furan	cresol	4	>22
thiophene	none	6	>22
thiophene	(H_2O^c)	1	3
thiophene	(cresol)	10	>22
benzene	H_2O^c	1	3
benzene	cresol	2	>22

a length of time the mixture of components was stirred to form the liquid clathrate completely

b length of time the liquid clathrate took to start forming crystals

c water from **1**•3H_2O; anhydrous **1** used when water was not the promoter

Δ 2minutes stirring without heating + 1.5minutes stirring with heating

( ) thiophene does not need a promoter to form a liquid clathrate with pure anhydrous **1**

4.9 Discussion

4.9.1 The importance of the Π electron rich nature of the guest in the formation of cyanoborate liquid clathrates

The thiophene/**1** liquid clathrate formed without a promoter (table 4.1.2). The benzene/**1** liquid clathrate formed (without heating) if water was present and did not form without water present. The furan/**1** liquid clathrate did not form without water present and required heating of the furan/**1**•3H_2O mixture before a liquid clathrate was formed. The ease of liquid clathrate formation therefore increased from furan to benzene to thiophene, but the excess of Π electrons increases from benzene to thiophene to furan. Thus the ease of liquid clathrate formation does not depend solely on the degree of electron excess of the guest. Model 3.6.2 depends heavily on the Π electron excessive nature of the guest in explaining the interaction of the guest with the host and promoter to form the liquid clathrate. Amendment of model 3.6.2 to accommodate factors other than the promoter and the electron rich nature of the guest was not attempted. Model 3.6.2 was, however, useful for understanding the interaction between promoters and the cyanoborate liquid clathrate.

4.9.2 Interaction between water and the **1**•nH_2O liquid clathrate (guest = furan, thiophene, benzene)

For all three guests, **1**•nH_2O with n >> 1 formed a liquid clathrate with greatly reduced nH_2O (table 4.2.2). If furan was guest, the liquid clathrate had n≈1. This amount of water in the liquid clathrate did not increase when additional excess water was mixed with the liquid clathrate and excess furan.

Using guests, furan, thiophene and benzene, **1**•nH_2O with n≈1 formed a liquid clathrate with n≈1. This amount of water in the liquid clathrate did not increase when additional excess water was mixed with the liquid clathrate and excess guest.

With furan or thiophene as guests, **1**•nH_2O with n << 1, formed a liquid clathrate which contained all the available water. The discoloration of **1**•0.3H_2O might have resulted from an impurity which promoted this nearly anhydrous host to form a liquid

clathrate with furan. Thiophene/**1** did not need a promoter to form a liquid clathrate. Even though the liquid clathrate had already formed, nH_2O in both these water deficient liquid clathrates went up to $n \approx 1$ when more water was available.

When enough water was available, therefore, water interacted with the host in a 1:1 ratio and additional water was not required for the interaction between the promoter and host. For simplicity in the rest of this discussion, the thiophene/**1** liquid clathrate is going to be considered to require water for (optimal) liquid clathrate formation as the amount of water increased to $nH_2O = 1$ when water was available.

In the crystal structure[26] of the solid **1**•H_2O, one water molecule is equidistant from and hydrogen bonded to the two cyano groups of one host anion (figure 1.4a). The favoured 1:1 ratio of the host and water in the liquid clathrate might be the result of the hydrogen bond between water and the host anion persisting in the liquid clathrate. In this case, and using model 3.6.2, water promotes the formation of the liquid clathrate by allowing the host cation and anion to separate so that the electron rich guest interacts with the cation sufficiently to form a liquid clathrate.

In the crystal structure[26] of the anhydrous **1** solid, the two cyano groups of the anion interact with methyl groups of two different cations (figure 1.4b). When an electron rich guest is mixed with the anhydrous host, it is reasonable to propose that the electron rich guest encounters unfavourable interactions with the anion's cyano groups, preventing liquid clathrate formation. Using model 3.6.2, water promotes liquid clathrate formation by providing more space for electron rich guest molecules to interact with the cation before the limit is reached at which the guest has to form a separate layer to avoid coming into close contact with the anion.

4.9.3 Interaction between cresol and the furan/1 liquid clathrate

When water promoted liquid clathrate formation, the limited interaction between water and the host meant that not all the water present was found in the liquid clathrate layer, and the excess water formed a third layer immiscible with the excess guest and liquid clathrate layers. With cresol as promoter, not all of the cresol present was found in the

liquid clathrate layer (table 4.3.2) but for a different reason. Cresol and furan are miscible and the favourable interaction between cresol and furan is strong enough for cresol to be found in the excess furan layer as well as in the liquid clathrate layer. Although the amount of cresol in the liquid clathrate layer correlated strongly with the amount of cresol present in the liquid clathrate/excess guest system (figure 4.3.2), the interaction of cresol with each layer distributed the cresol between the two layers. The interaction of cresol with the liquid clathrate must be favourable because a high concentration of cresol in the liquid clathrate can be reached (table 4.3.2). Confirmation of cresol's interaction with the liquid clathrate components, specifically the host anion and the guest, is discussed below.

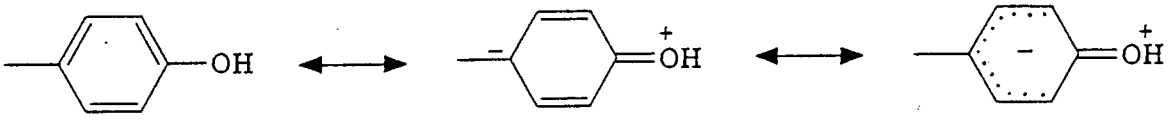
4.9.4 Interaction between cresol and the host anion in the furan/1 liquid clathrate

According to the model 3.6.2 the interaction of cresol with the anion of **1** is important in the functioning of cresol as a promoter of liquid clathrate formation in the furan/**1** liquid clathrate. The integration of the αB peaks in the furan/**1** liquid clathrate decreased if cresol was present in the liquid clathrate (table 4.4.2 and figure 4.4.2). These upfield αB peaks decrease because the protons experience less of the shielding effect of the negative charge of the boron in the anion. Cresol's interaction with the anion, which is reflected in the integration of the αB peaks, diminishes the negative effect of the anion probably via hydrogen bonding between the hydroxyl group of cresol and the cyano group of the borate (Similar to figure 1.4a). The hydrogen bond between the cyano group of the anion and cresol could replace a hydrogen bond between the cyano group of the anion and the methyl group of the cation (figure 1.4b), thus liberating the cation for interaction with the guest. Furthermore, the hydrogen bond could alter the conformation of the anion. In terms of model 3.6.2, cresol promotes liquid clathrate formation by increasing the space for electron rich furan to interact with the cation without feeling the unfavourable effect of the negative charge of the anion.

The amount of cresol found in the liquid clathrate (P/H up to 15) is higher than the 1:1 water:host ratio of water in the liquid clathrate. Two factors contribute to this

difference. Firstly, cresol is larger in size than water and cresol therefore creates more space than water when inserted in the liquid clathrate structure. Secondly, the amount of cresol in the liquid clathrate is not limited to a 2cresol:1host ratio by the hydroxyl groups of two cresols hydrogen bonding to the two cyano groups of the anion. It is feasible that the methyl group and the ring of cresol interact with the 9-BBN portion of the host anion as well as with the guest and the methyl and phenyl groups of the host cation. The methyl group of cresol provides van der Waal's interactions with the liquid clathrate components. The delocalisation of electrons in the cresol ring provides more contact points with organic groups in the anion, cation and guest (particularly δ^+ protons) than the polarised water dipole provides. The delocalisation of electrons in p-cresol, shown in figure 4.9.4, spreads the negative charge of cresol over the ring and contrasts with the polarised concentration of electrons on the oxygen in water.

FIGURE 4.9.4 Resonance structures of p-cresol showing delocalisation of electrons in the cresol ring



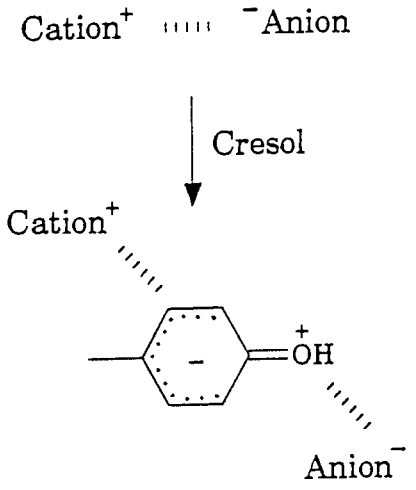
4.9.5 Interaction between cresol and the guest in the furan/1 liquid clathrate

An increase in the amount of cresol present in the liquid clathrate resulted in an increase in the G/H (table 4.5.2 and figure 4.5.2). Cresol, miscible with furan, is found in both the excess furan and the liquid clathrate layers. In the extreme case of enough cresol present, the excess furan and liquid clathrate layers formed a single solution (table 4.3.2) of host ions in an organic mixture of cresol and furan. The expansion by cresol of the G/H of the furan/1 liquid clathrate and the formation of a single solution of the liquid clathrate and excess furan by cresol do not comply with the conventional definition[1] of liquid clathrates (chapter 1.2) but do agree with model 3.6.2.

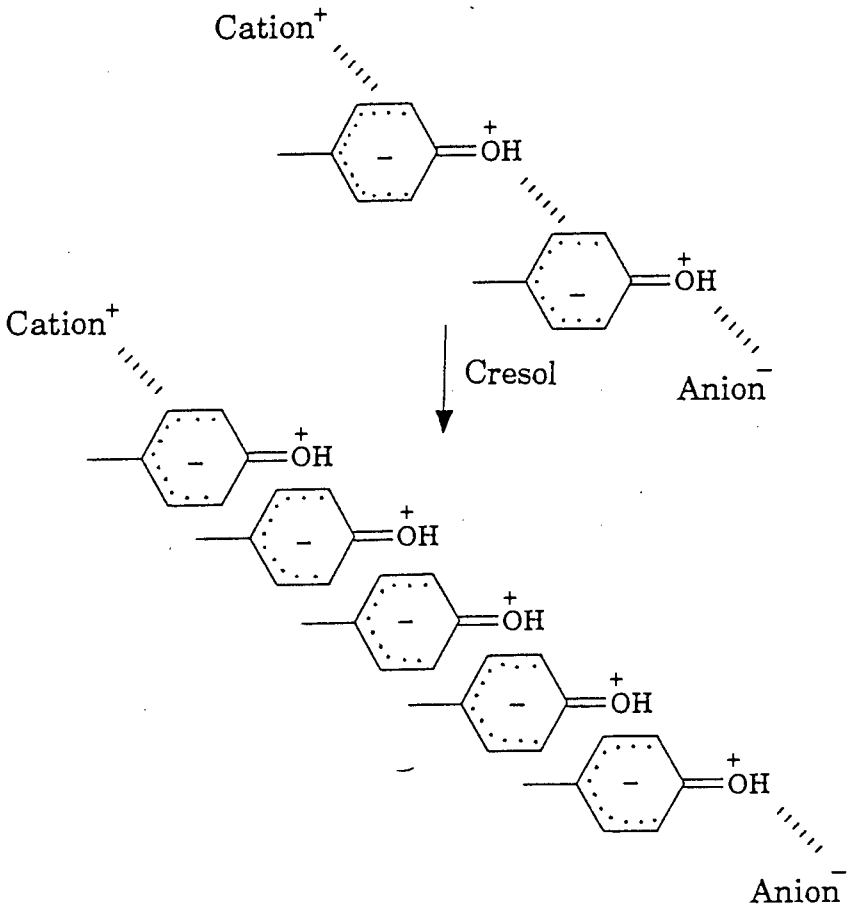
Cresol inserted between the host cations and anions effectively increases anion-cation separation, creating more space for the guest (figure 4.9.5a). Increased amounts of cresol in the liquid clathrate means that additional cresol is inserted between the host anions and cations (figure 4.9.5b) until a limit is reached at which the separation between ions in an anion-cation pair is so great, and the electrostatic interaction so diminished that the liquid clathrate structure breaks down and the excess guest and liquid clathrate layers form a single solution.

FIGURE 4.9.5 (a) Cresol inserted between host cation and anion in the liquid clathrate separates the ion pair (b) Cresol expands the liquid clathrate further by interacting with itself as well as with a cation-anion pair

(a)



(b)

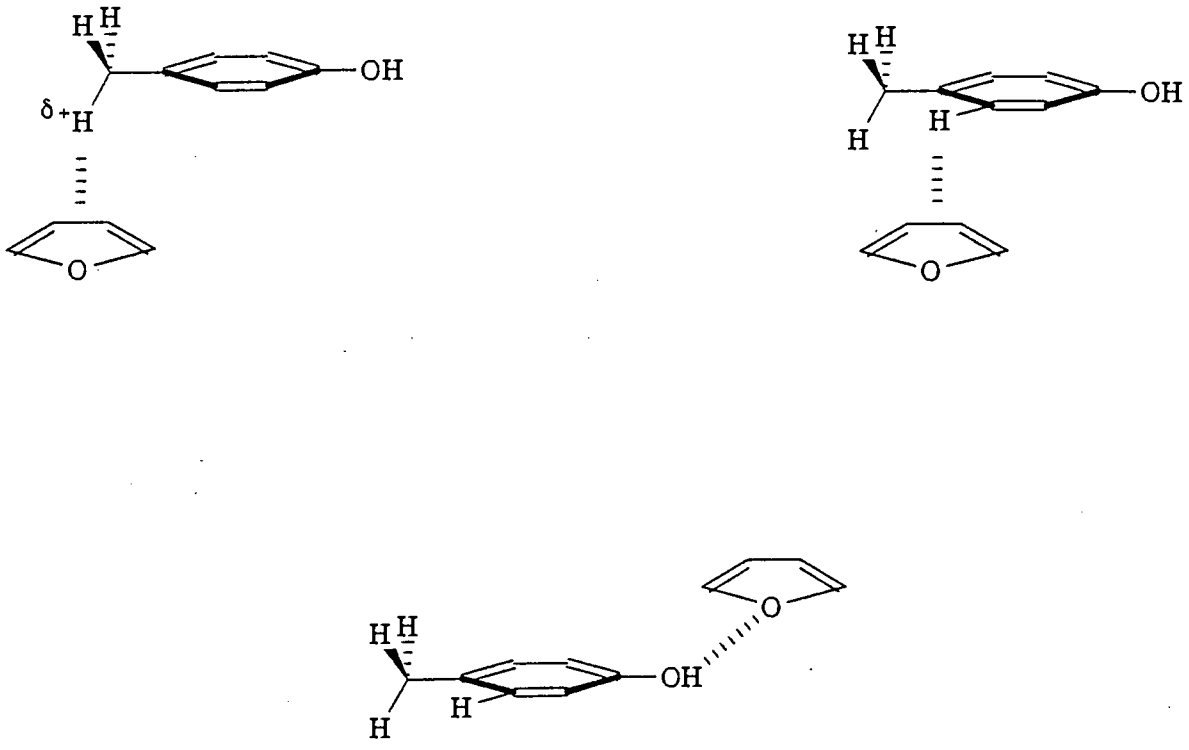


Water, as a stronger dipole than cresol, would solvate the cation-anion pair more easily than cresol does. In a liquid clathrate, however, water is limited to a 1:1 ratio with the host whereas the P/H of cresol in the liquid clathrate can be as high as P/H = 15 (table 4.3.2). The interaction of furan with the promoter is important here. Water and furan are immiscible, so the interaction between these components is unfavourable. Cresol and furan are miscible, so these two components interact favourably.

Although water can expand the separation of host cations and anions in a similar manner as cresol (in figure 4.9.5b), the interaction between water and furan is unfavourable so water does not provide additional contact points for furan in the liquid clathrate. The amount of furan in the liquid clathrate is limited by the space available for furan's interaction with the cation. Because of delocalisation of the negative charge in cresol, cresol provides weaker cation-anion charge separation in the liquid clathrate than water does, but cresol and furan interact favourably so cresol provides additional contact points for furan in the liquid clathrate.

The crystal structure[26] of the **1**•(furan)$_2$ salt of the furan/**1** liquid clathrate (no cresol present) shows that furan is held in place by hydrogen bonding interactions with both faces of the delocalised Π electron ring (figure 1.4c) The ring interacts on one face with a methyl proton and on the other face with a phenyl proton (two different methyl triphenylphosphonium cations). The interaction of furan with cresol molecules in a liquid clathrate could make use of the same hydrogen bonding interactions. Figure 4.9.5c shows the interaction of cresol methyl, ring and hydroxyl protons with furan.

FIGURE 4.9.5 (c) Interactions between cresol and furan



4.9.6 Water and cresol in competition with each other in liquid clathrate formation

Liquid clathrates made with cresol and water present contained cresol but no water (table 4.6.2 and figure 4.6.2), so water was expelled from the liquid clathrate structure. The formation of the furan/1 liquid clathrate therefore involved selective incorporation of cresol as promoter. Energy is required for both water and cresol to increase the charge separation of the host cation-anion pairs. Favourable interactions of the components of the liquid clathrate have to compensate for the energy of separating the host ions. With water as promoter, the guest interacts with the cation. With cresol as promoter, however, the guest interacts with the cation and with cresol, so cresol provides a greater number of favourable interactions to compensate for the increased energy required to separate the host cations and anions. Cresol is thus incorporated into the liquid clathrate structure in preference to water.

4.9.7 The effect of the interaction of two components prior to the addition of a third component to form a liquid clathrate in a three component system

Cresol interacts with the host and with the guest, and the guest interacts with the host. Changing the order of mixing these three components to form a liquid clathrate probed whether interaction of two components affected the interaction of the third component to form the liquid clathrate. Equal amounts of components were used in each run of this experiment so that the time taken for the liquid clathrate to form was a rough estimate of the ease of liquid clathrate formation. Time taken for these liquid clathrates to precipitate was a rough estimate of the stability of the liquid clathrates. Table 4.7.2 shows that although the guests, furan, thiophene and benzene, do not follow the same trend, the order in which the components interact with each other does affect the ease of liquid clathrate formation. On addition of the third component, the first two components rearrange their interactions so that all three components can interact to form a liquid clathrate. This might affect the structure of liquid clathrates by imposing a hierarchy of interactions between the components on a first come, first served basis, but liquid clathrate formation is probably under thermodynamic control, forming the same structure regardless of the order of addition of components. The stability of liquid clathrates is unaffected by the order of addition of components as the interaction of cresol with the anion, cation and guest is sufficient to prevent the cation and anion forming a solid.

4.9.8 The ease with which water and cresol promote liquid clathrate formation and the stability of the liquid clathrates formed with water or cresol as promoters

A comparison of the efficiency of water and cresol as promoters was obtained by comparing how easily the liquid clathrate formed using the two promoters, and by comparing how stable the resultant liquid clathrates were (table 4.8.2). Water as a promoter (or water and heat in the furan/1 liquid clathrate) formed liquid clathrates more easily than cresol did. Water is more efficient than cresol in overcoming the lattice energy of the host to separate the host cations and anions for the guest to interact with this reorganised host to form a liquid clathrate. Cresol as a promoter stabilised the liquid clathrate more efficiently than water did because the interactions of cresol with all the components of the liquid clathrate prevented the ion pairs of the host

from approaching each other closely enough for the ionic attraction to become the dominant interaction, causing precipitation of the liquid clathrate.

4.9.9 Use of the interaction between cresol and the cyanoborate liquid clathrate

Experiments to ascertain that cresol partitioned between the excess furan and liquid clathrate layers, and to ascertain whether the partitioning was selective enough to separate cresol isomers using liquid /liquid extraction methodology, were inconclusive. These experiments were based on the incorrect assumption that the maximum G/H of a liquid clathrate is fixed.

Equilibrium constants between the host and guest of a liquid clathrate cannot be measured unless the concentration of at least one component is changed (chapter 1.6.6). Promoters in expanding liquid clathrates as described in chapter 4.5 (and 4.9.5) can be used to alter the concentrations of the components of a liquid clathrate and force the liquid clathrate into a normal equilibrium situation (chapter 1.6.6), opening the way for measurement of equilibrium constants in the liquid clathrate. Measurement of equilibrium constants in a liquid clathrate have to be of undiluted liquid clathrate samples (chapter 1.6.6). The aromatic nature of liquid clathrate guests and of the promoter, cresol, made UV/VIS spectroscopy worth investigating as an alternative method to, for example, solvent free NMR spectroscopy. The experiment is described in appendix 7. This investigation of UV/VIS spectroscopy of undiluted liquid clathrates indicated that UV spectroscopy was not a feasible method for measuring equilibrium constants in solvent free liquid clathrates.

CHAPTER 5

Conclusions

Liquid clathrates are conventionally defined as having a fixed maximum G/H. Guest in excess of the maximum G/H is found as a separate layer which is immiscible with the liquid clathrate and which contains no host. Reasonable modifications to this definition are to consider the maximum G/H fixed within an uncertainty range and to evaluate the limiting concentration of detection of host in the excess guest layer.

The uses of liquid clathrates are found mostly in separation technology. The structure of liquid clathrates can be probed, but many methods are not applicable to liquid clathrates. For instance, the equilibrium constant between host and guest cannot be measured in a liquid clathrate with fixed G/H without diluting the liquid clathrate but this destroys the liquid clathrate structure.

The fixed maximum G/H of a liquid clathrate is, however, subject to variation. A liquid clathrate with G/H less than the maximum G/H expands to accommodate all the guest available. The liquid clathrate can contract to form a solid clathrate with G/H less than the maximum G/H of the liquid clathrate, or to form a pure solid host. An additional component in the liquid clathrate can cause the liquid clathrate to expand beyond the maximum G/H, to a point where the excess guest and liquid clathrate layers form a single solution. An example of an additional component is the promoter, cresol.

If a host and guest form a liquid clathrate only when a third component is present, the third component is a promoter of liquid clathrate formation. A range of promoters capable of hydrogen bonding via their hydroxyl groups promoted liquid clathrate formation in guest-host combinations which do not form liquid clathrates without promoters. The formation of these liquid clathrates depends on all three components (guest, host and promoter). The study of promotion of liquid clathrate formation must be free of spurious promotion of liquid clathrate formation.

Promoters affect liquid clathrate behaviour so that a liquid clathrate with a promoter present does not necessarily conform to the conventional definition of liquid clathrates. A model accommodating the presence of a promoter in the liquid clathrate emphasizes the Π electron rich nature of the guest, which causes the guest to favour interaction with the cation and disfavour interaction with the anion of the host. A promoter increases the space for the guest to interact favourably with the host cation by separating the host cation-anion pairs and by decreasing the effect of the anion's negative charge through hydrogen bonding to the host anion and/or changing the conformation of the anion. The Π electron rich nature of the guest is not the only factor in liquid clathrate formation but the model can be used to explain the interaction between host, guest and promoter in the liquid clathrate.

The electronic nature of the promoter affects the interaction of the promoter with the liquid clathrate. Water is a stronger dipole than cresol, whose electron density is delocalised in the ring. Water is immiscible with furan. Even with water in excess, the cyanoborate liquid clathrate has a P/H = 1. The solid state structure of **1**•H_2O indicates that this 1:1 ratio in the liquid clathrate reflects a 1H_2O:1host anion ratio. The polarized dipole of water does not provide as many contact points for interaction with the guest as cresol's resonance structure provides.

Cresol probably interacts with furan through its hydroxyl, phenyl and methyl groups. The G/H of the liquid clathrate increases as P/H in the liquid clathrate increases. Cresol and furan are miscible and cresol distributes between the excess guest and liquid clathrate layers. The P/H of cresol in the cyanoborate liquid clathrate depends on the total amount of cresol present in both layers and can be as high as P/H = 15, before additional cresol causes the two layers to form a single solution.

Cresol's hydroxyl group interacts with the anion of the host, decreasing the shielding effect of the negative charge on the protons α to boron. It is feasible that the methyl group and the ring of cresol interact with the 9-BBN groups of the host anion and the methyl and phenyl groups of the cation.

The favourable interactions of cresol with the guest, the host anion and the host cation compensate for the energy used in promotion of liquid clathrate formation by increasing the space between host cation-anion pairs so that the electron rich guest is not forced into close interaction with the host anion. By contrast, water does not interact as favorably with all the components of the liquid clathrate, but water's strong dipole results in water separating the host lattice to promote liquid clathrate formation more easily than cresol does. Nevertheless, cresol's interaction with all the components of the liquid clathrate is more important than the interaction of water with the anion of the host. Cresol promotes liquid clathrate formation in a wide range of liquid clathrates. Liquid clathrates formed with cresol as promoter are stable as they do not precipitate. When water and cresol are in competition, the furan/1 liquid selects cresol as promoter.

Selective interaction between the liquid clathrate and the different isomers of cresol would be useful for separation of cresol isomers using liquid clathrates in liquid/liquid extraction methodology. Experiments used to investigate this possibility must incorporate the promoter's perturbation of the fixed maximum G/H of the liquid clathrate. Continued study of the interactions in guest-host-promoter liquid clathrate systems and the effect of such interactions is thus important for facilitating use of liquid clathrates. The perturbation of the fixed maximum G/H by a promoter can be put to good use in solvent free measurement of equilibrium constants between host and guest. NMR spectroscopy would be more suitable for analysis of solvent free liquid clathrates than UV/VIS spectroscopy.

Promoters are a useful tool in the design of liquid clathrates as they extend the range of guest-host combinations which form liquid clathrates. More importantly, the electronic nature of the promoter affects the nature of the liquid clathrate formed. The design of liquid clathrates is thus further extended to the fine tuning of liquid clathrates for specific purposes. For example, a promoter might form a liquid clathrate quickly and reversibly, whereas with the same guest-host combination, a different promoter slowly forms a stable liquid clathrate. Given the importance of the nature of the promoter, useful future study of promoters would extend the range of hydroxyl containing

promoters and would investigate other potentially useful promoters such as nitrogen containing compounds and chiral compounds.

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APPENDIX 1

Synthesis and purification of $1 \bullet nH_2O$ and manipulation of nH_2O in $1 \bullet nH_2O$

A1.1 Synthesis of $1 \bullet nH_2O$

Bis(methyltriphenylphosphonium) 1,6-bis(B-cyano-9-boratabicyclo[3.3.1]non-9-yl)hexane, 1

1,5-Hexadiene was distilled. Dimethylformamide was distilled from calcium hydride and stored over 4Å molecular sieves. Water was glass distilled deionised water.

9 - Borabicyclo[3.3.1]nonane (0.5M in tetrahydrofuran, 40cm^3, 20mmol) was syringed into a nitrogen-flushed flask and brought to 0°C. 1,5 - Hexadiene (1.2cm^3, 10mmol) was syringed in. The solution was allowed to reach room temperature and most of the tetrahydrofuran was then removed by distillation under nitrogen. The temperature was brought to 0°C, dry dimethylformamide (5cm^3) syringed in and solid sodium cyanide (1.2g, 25mmol) was added. The solution was allowed to reach room temperature before methyltriphenylphosphonium bromide (7.15g, 20mmol) was added, followed by methanol (35cm^3). The mixture was stirred until all the methyltriphenylphosphonium bromide had dissolved. The solution was decanted from the excess sodium cyanide. The methanol was removed under reduced pressure. The viscous liquid was poured into a separating funnel containing water (50cm^3), sodium chloride (0.1g) and diethylether (30cm^3). The water layer was washed twice with diethyl ether (2x15cm^3). All diethyl ether fragments and **1** were added to water (50cm^3) and stirred vigorously for at least ten minutes before being refrigerated overnight to produce a crystalline suspension. The crystals were filtered, washed with diethyl ether (3x25cm^3) and vacuum dried (yield 73 - 82%, m.p.128-136°C). Found C 79.8, H 8.4, N 3.0%. $C_{62}H_{76}B_2N_2P_2$ requires C 79.8, H 8.2, N 3.0%. ^{1}H NMR (200MHz, DMSO-d_6, 25 °C) δ = 0.11 (m, 4H), 0.34 (br.s., 4H), 1.10 - 1.96 (m, 32H), 3.13 (d, ^{2}J (P,H) = 14.6Hz, 6H), 7.78 (m, 30H). ^{13}C NMR (50Hz, DMSO-d_6, 25 °C) δ = 7.3 (^{1}J (C,P) = 57Hz),

24.0, 25.2, 26.2, 28.1, 30.4, 34.0, 35.4, 119.8 (^{1}J (C, P) = 88.2Hz), 130.0 (^{2}J (C, P) = 12.8Hz), 133.1 (^{3}J (C,P) = 10.6Hz, 134.7 (^{4}J (C, P) = 2.3Hz). The assignment[10] of the spectra is shown in figure 1.8a.

A1.2 Purification of 1•nH_2O

This variation of Haueisen's method consistently produced white crystals. The final steps of this modification were used for purification. Yellow crystals produced in alternative syntheses were purified by dissolving them in methanol, removing the methanol under reduced pressure and extracting and washing **1** as described in section A1.1. **1** was reclaimed from experiments which involved mixing **1** with furan and/or water. The mixture was dissolved in methanol, forming a yellow solution which was purified as described. **1** was washed off glassware using acetone. **1** was stable in acetone (deuterated acetone used as NMR solvent did not destroy **1**). Intact **1** could thus be retrieved from the acetone used to wash **1** off glassware. The acetone was removed under reduced pressure, and the extraction and washing of **1** was performed as described. The retrieved **1** was then purified if necessary.

A1.3 Manipulation of nH_2O in 1•nH_2O

Experiments required $nH_2O = 0$, $0 < nH_2O < 1$, $nH_2O = 1$ and $nH_2O > 1$ in **1**• nH_2O. Methods had to be developed to increase or decrease nH_2O at will. Quantitative addition of water to experiments using anhydrous host was open to large relative error because sample sizes were kept as small as possible.

A1.3.1 Decrease nH_2O in 1•nH_2O

Haueisen[26] reported that water is tightly hydrogen bonded in **1** as removal of the water required drying *in vacuo* (0.5mmHg) for three hours at 134°C or for sixteen hours at 70°C. Table A1.3.1 shows that the results of drying **1**•nH_2O in a vacuum pistol (~0.5mmHg) for a certain time at a certain temperature are unpredictable.

TABLE A1.3.1 **1**•nH_2O dried in a vacuum pistol.

drying temperature/ °C	drying time/ hour	end nH_2O[a]
46	2.5	0.5
45	3	0.6
49	3	0.7
48	3	0.8
134	3[b]	0
70	16[b]	0
71	16	0.2
82	16	0
105	16	0
95	64	0.2
95	64	
125	24	
129	24	0[c]

a end nH_2O evaluated with thermogravimetric analysis

b Haueisen's result[26]

c evaluated after drying at three different temperatures, 95,125 and 129°C

Variation in pressure, sample size, initial nH_2O and thermogravimetric analyses (TGA) could account for the inconsistent results. A consequence was that a sample of **1** could not be considered anhydrous because it had been dried *in vacuo* at a certain temperature for a certain length of time. The sample was only be considered anhydrous if analysis of nH_2O found n equal to zero.

A second consequence was that a desired value of n could not be obtained at will, but required careful alternating drying of **1**•nH_2O and analysis of n. Similarly, increasing n in **1**•nH_2O was possible but the end value of n could not be predetermined.

A1.3.2 Increase nH_2O in $1 \bullet nH_2O$

For $1 \bullet nH_2O$ left open to the atmosphere for 22 hours, nH_2O increased from n = 0.2 to n = 1.0 (TGA). This change in nH_2O was not necessarily uniform throughout the crystals. Two methods were developed for increasing nH_2O.

$1 \bullet 4H_2O$ (TGA) was stirred vigorously overnight with diethylether and water. The mixture was ultrasonicated for seven minutes and immediately filtered and dried on the filter. nH_2O had increased to $1 \bullet 8H_2O$ (^{1}H NMR, 60MHz). For this method, the increased nH_2O was not necessarily uniform throughout the crystals, so the second method involved dissolving **1** and the added water. Acetone was chosen as the solvent because it evaporates easily, dissolves **1** and water, and does not destroy **1**.

$1 \bullet 4H_2O$ (TGA) was dissolved in minimum acetone (analytical grade), forming a clear viscous solution which remained clear on addition of water. The mixture was stirred vigorously. A sticky gum formed when the acetone was removed under reduced pressure. The gum was left overnight and some crystals formed. The gum and crystals were washed repeatedly with diethylether until $1 \bullet nH_2O$ had crystallised completely. nH_2O had increased to $1 \bullet 8H_2O$ (^{1}H NMR, 60MHz).

Synthesis of $1 \bullet nH_2O$ in twenty one different batches yielded nH_2O varying from 0.8 to 5.4, with a strong median at nH_2O = 1. A judicious combination of increasing n and decreasing n extended the range to $0 \leq n \leq 8$. The exact value of nH_2O, however, was not totally adjustable.

APPENDIX 2

Synthesis of 2

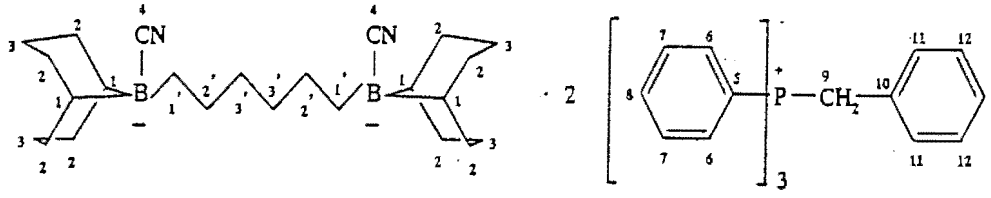
Bis(benzyltriphenylphosphonium) 1,6-bis(B-cyano-9-boratabicyclo[3.3.1]non-9-yl)hexane, **2**

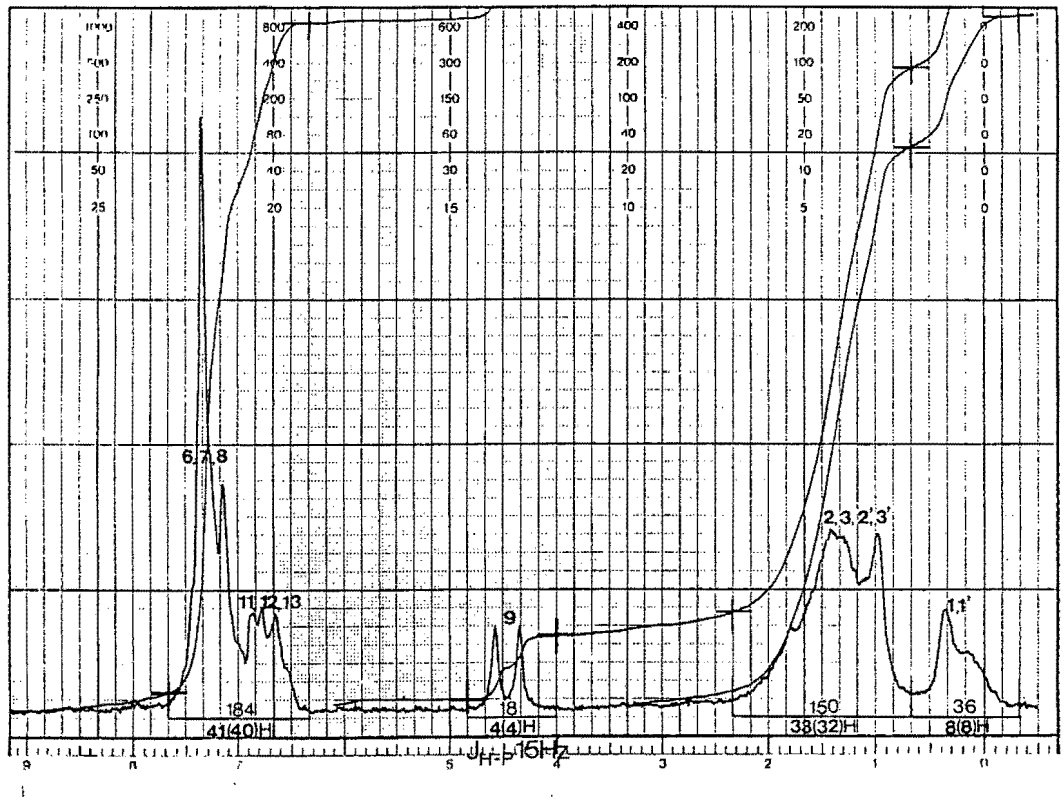
Benzene was distilled from sodium wire. Benzyltriphenylphosphonium bromide was made by adding benzylbromide ($5cm^3$, 42mmol) to triphenylphosphine (10g, 38mmol) dissolved in benzene ($20cm^3$). The mixture was refluxed overnight, left stirring for more than 24 hours and filtered. The white crystals were washed with benzene and dried under vacuum (16.1g, 97.4%).

Benzyltriphenylphosphonium bromide (8.76g, 20mmol) was used instead of methyltriphenylphosphonium bromide in the method described for synthesis of **1** (section A1.1). The white crystalline product was **2**•n$CH_3CH_2OCH_2CH_3$ (10.025g, 92%). After drying for four hours at 1mmHg, n = 0.2 (TGA and ^{1}H NMR). The diethylether ($CH_3CH_2OCH_2CH_3$) was removed in the vacuum pistol (~0.5mmHg, 100°C for 19 hours and 129°C for 29 hours). The assignment of the ^{1}H NMR spectrum of this product is shown in figure A2.

Figure A2 Assignment of ^{1}H NMR (60 MHz, $CDCl_3$) spectrum of **2**.

. ( ) Theoretical number of protons





APPENDIX 3

Purification and drying of liquid clathrate components

A3.1 Drying of hosts

Anhydrous **1** and **2** were obtained by drying the samples in the vacuum pistol (~0.5mmHg) at elevated temperatures (up to 129°C) until TGA confirmed that n = 0.

A3.2 Purification and drying of guests

Furan was distilled and used within one to two days of distillation. Liquid clathrate made from **1** and freshly distilled furan was colourless and did not exhibit the colour changes observed by Haueisen[26]. The furan/**1** liquid clathrate's lack of colour was taken as a mark of purity of furan. Furan which formed a pink or yellow test liquid clathrate was redistilled before being used for an experiment.

Furan, thiophene and N,N-dimethylaniline were considered dry after they had been stirred overnight with calcium hydride and distilled. Benzene and toluene were stored over and distilled from sodium wire. 2-Methoxyfuran was dried with 4Å molecular sieve. The dried guests were used immediately after distillation.

A3.3 Purification and drying of promoters

Methanol was stirred overnight with calcium hydride and distilled. The cresols were distilled under reduced pressure.

Methyl-α-D-glucopyranoside showed a single spot on thin layer chromatography, but its melting point was 159 - 165°C (literature 169 - 171°C). The integration of the ^1H NMR (60MHz) spectrum was not acceptable. Methyl-α-D-glucopyranoside (pyra) was therefore used with the reservation that any positive result involving pyra had to be repeated after purifying pyra.

Pyra and mandelic acid (mand) were dried in the vacuum pistol (~0.5mmHg, 100°C for 19 hours and 129°C for 29 hours).

^{1}H NMR (60MHz) indicated that diethyl-L-tartrate (DET) had decomposed during a drying method which involved magnesium sulphate and distillation. 4Å molecular sieves were used as an alternative drying method for drying DET.

All the dried promoters were stored in a dessicator over silica gel and P_2O_5 powder.

APPENDIX 4

Investigation of the possible protonolysis of 1•nH_2O by cresol and other alcohols mixed with 1•nH_2O

A4.1 Method

The alcohols and phenols selected were methanol, ethanol, n-propanol, i-propanol, t-butanol, menthol, o-, m- and p-cresol, and p-(t-butyl)phenol. Methanol, ethanol, n-propanol, i-propanol, menthol and p-(t-butyl)phenol were analytical grade reagents. Tertiary butanol and o-, m- and p-cresol were purified by distillation.

1 was dissolved in the alcohol, with refluxing if necessary. Dichloromethane (CH_2Cl_2) was used as a solvent for solid or viscous liquid alcohols. CH_2Cl_2 is not a guest of **1**, but was a good solvent for dissolution and evaporated off easily. After approximately a month, the mixtures which had not solidified were washed repeatedly with diethylether (ether) until they precipitated. Ether is not a guest of **1**, nor does it dissolve **1**. It readily dissolved all the alcohols and phenols. All the solids were filtered and washed thoroughly with ether to remove free alcohol. Solids which were still discoloured or sticky were further washed repeatedly with ether until the crystals were white and dry (table A4.2). The melting point and the ^1H NMR (60MHz, $CDCl_3$) spectrum of each solid was used as an indication of whether or not the alcohol had destroyed **1**, with correct relative integration of protons α to boron (αB peaks) used as evidence that protonolysis had not occurred (chapter 1.8).

A4.2 Results

TABLE A4.2 **1** mixed with alcohols

alcohol	appearance[1]	ppt[2]	wash[3]	m.p.[a]/ °C	m.p.[b]/ °C	NMR[4]
methanol	cream crystals	0	3	102 -113	127 - 134	reasonable[a]
ethanol	solid gum	0	5	133 - 143	130 - 142	dubious[a,b]
n-propanol	crystals/ gum	0	5	129 - 152	127 - 134	dubious[a,b]
i-propanol[b]	yellow/ white crystals	0	3	142 - 147	127 - 134	dubious[a,b]
t-butanol[b]	yellow crystals	0	3	140 - 148	127 - 134	reasonable[a]
menthol[c]	white crystals/ yellow gum	0	3	136 - 144	102 - 127	correct[a]
o-cresol[c]	yellow liquid	2	3	139 - 150	133 - 138	correct[a]
m-cresol[c]	yellow liquid	3	4	141 -147	131 - 137	correct[a]
p-cresol[c]	sticky orange gum	5	7	144 - 153	138 - 141	correct[a]
t-butylphenol[c]	pink gum/crystals	6	3	140 - 151	127 - 133	correct[a]
none	reference: anhydrous **1**			133 - 136	128 - 134	correct[a]

a,b two separate experiments
c CH_2Cl_2 was added
d **1**/ alcohol mixture refluxed to dissolve **1** in the alcohol
1 appearance of **1**/ alcohol mixture after ~ 1 month (b)
2 number of ether washes to obtain a solid (b)
3 number of ether washes to obtain dry white crystals (b)
4 integration of ^1H NMR (60MHz, $CDCl_3$) spectrum of solid white **1**

reasonable	spectrum not totally correct because of $^2H/^1H$ exchange between $CDCl_3$ and CH_3
dubious	αB integration too small
correct	αB integration correct

Table A4.2 shows that all the alcohol was not necessarily washed away as the melting points showed variation between experiments. The reference melting points of two different batches of anhydrous **1** also showed variation. **1** was not destroyed by contact with cresol for a month. Further experiments would be needed to test the stability of **1** in the presence of ethanol, n - propanol, i - propanol and t - butanol.

APPENDIX 5

The unsuitability of Karl Fisher titrations[37] for the analysis of water in $1 \bullet nH_2O$ and in the cyanoborate liquid clathrates formed with water or cresol as promoters

The Karl Fisher titration is based on the equilibrium,

$$I_2 + SO_2 + 2H_2O = 2HI + H_2SO_4.$$

This equilibrium is used in the quantitative analysis of water by addition of a base, such as pyridine, to the sulphuric acid and hydrogen iodide, thus shifting the equilibrium completely to the right.

If Karl Fisher titrations had been used to analyse nH_2O in $\mathbf{1} \bullet nH_2O$, the sulphuric acid might have broken the boron-carbon bond in protonolysis of $\mathbf{1} \bullet nH_2O$ (chapter 1.8). The products of this side reaction, however, would only have affected the analysis of water if these products included water, which would not happen in protonolysis of the boron-carbon bond of **1**.

Methanol, which is an acceptable solvent for $\mathbf{1} \bullet nH_2O$, is the traditional solvent for Karl Fisher titrations. Karl Fisher titration end points occur when all the water present has reacted with the iodine and sulphur dioxide. The end points are marked by the appearance of excess iodine, or, in back titrations, by the disappearance of iodine excess.

In coulometric titrations, electrochemical oxidation of iodide produces iodine *in situ*.

$$2I^- \rightarrow I_2 + 2e^-$$

The amount of iodine produced depends on the strength of the current and for how long the current flows between the electrodes. The number of moles of iodine reacting

with water can be calculated precisely using Faraday's constant, but only if no side reactions occur. In a coulometric Karl Fisher analysis of the amount of water in **1**•nH_2O, the cyanoborate anion might have been oxidised. Volumetric Karl Fisher analysis of n would therefore have been more appropriate, but the volumetric Karl Fisher titration is not as precise as the coulometric method, especially in analysis of trace amounts of water.

The volumetric titration endpoint of excess iodine is detected visually, photometrically or electrometrically. The electrometric endpoint detection relies on the iodine/iodide redox couple and could thus have been affected by side reactions of **1**•nH_2O in the analysis of n. Both photometric and visual detection rely on changes in the visible spectrum at the endpoint. Before the endpoint is reached, the solution is yellow, or colourless if buffered at ~pH 7. The solution turns yellow-brown at the endpoint. Liquid clathrate samples, however, turn yellow in methanol. This discoloration would have interfered with the analysis of the amount of water in the liquid clathrate using visual or photometric detection of the endpoint in a volumetric titration.

Solvents other than methanol are used for Karl Fisher titrations. Protic solvents such as methanol participate in the chemistry of the titration, so in protic solvents the water to iodine ratio is 1 : 1, whereas the ratio in Karl Fisher titrations using aprotic solvents is the expected $2H_2O$: 1 I_2. This dichotomy of ratios would have biased the analysis of the amount of water in samples containing alcohols mixed with the liquid clathrate, especially for phenols with acidic protons, such as cresol.

The Karl Fisher options include coulometric or volumetric titrations, electrometric, photometric or visual endpoint detection, and protic or aprotic solvents. These options all seemed to be unsuitable for determining the amount of water in samples in this project although the difficulties described could have been dealt with if no alternative analyses of water were available. The acquisition of Karl Fisher titration equipment, and time-consuming adaptation of the Karl Fisher method were also considered negative aspects. Instead, two less conventional methods of water analysis, TGA and ^{1}H NMR, were chosen.

APPENDIX 6

The effect of sample size and sample site on the analysis of nH_2O in $1 \bullet nH_2O$

^1H NMR (60MHz) gave results inconsistent with TGA for analysis of nH_2O in $1 \bullet nH_2O$. The sample size of ^1H NMR (60MHz) was 100 - 150mg whereas for TGA it was 5 - 11mg. The inconsistency could have resulted from the different sample size in that TGA on a small sample might be influenced by uneven distribution of water in a batch of $1 \bullet nH_2O$. NMR of a higher mass sample would reflect an average value for nH_2O in a batch of $1 \bullet nH_2O$. Since ^1H NMR (400MHz) in DMSO-d_6 only needs a sample size of ~5mg, the TGA and 400MHz ^1H NMR of a 5mg sample were recorded in order to address this problem. These analyses were compared with large sample size ^1H NMR (60MHz) analysis of nH_2O. The small samples were sub-samples of larger samples, so these samples were taken from a single site in a batch of $1 \bullet nH_2O$.

The comparison between ^1H NMR (60MHz) and TGA was repeated on samples from a different site in the batch of $1 \bullet nH_2O$. ^1H NMR (400MHz) was not repeated because of expense. These comparisons were all repeated for a different batch of $1 \bullet nH_2O$. The effect of sample site on the analysis of nH_2O seemed greater for analysis by ^1H NMR (60MHz, large sample) than by TGA (small sample). As this was unexpected, nH_2O in samples from two additional sites was analysed using ^1H NMR (60MHz). The results are presented in table A6.

TABLE A6 Effect of sample size and sample site on analysis of nH_2O in $\mathbf{1}\bullet nH_2O$

sample site	nH_2O	nH_2O	nH_2O
	100mg $\mathbf{1}\bullet nH_2O$ $0.4cm^3$ dry[a] DMSO-d_6	8mg $\mathbf{1}\bullet nH_2O$ $0.7cm^3$ dry[a] DMSO-d_6	8mg $\mathbf{1}\bullet nH_2O$
	^{1}H NMR (60MHz)	^{1}H NMR (400MHz)[b]	TGA
X[c]	0.8 ± 0.1	13.5 ± 1	1.0
Y[c]	1.4 ± 0.1		1.0
A[d]	1.2 ± 0.1	8.4 ± 0.5	0.9
B[d]	2.8 ± 0.1		1.0
C[d]	3.2 ± 0.1		
D[d]	2.9 ± 0.1		

a dried with 4Å molecular sieve

b relaxation time = 5 x longest T_1 measured on VXR200

c and d are different batches of **1**

^{1}H NMR (400MHz) analysis of nH_2O was inflated compared to the TGA analysis of the same sized sample and compared to ^{1}H NMR (60MHz) analysis of a larger sample. The water content of the dry DMSO-d_6 was not negligible in analyses using 400MHz ^{1}H NMR. The relatively high NMR solvent to sample ratio in the 400MHz analysis exacerbated this error. This error prevented the detection of an uneven distribution of water within a batch of $\mathbf{1}\bullet nH_2O$, but clarified the cause of inconsistency between TGA and ^{1}H NMR results.

The variation in nH_2O analysed at *X* and *Y*, and *A*, *B*, *C* and *D* by ^{1}H NMR (60MHz) could have resulted from experimental error. The relative amount of water from the DMSO-d_6 might have varied, depending on the accuracy of weighing 100mg $\mathbf{1}\bullet nH_2O$ and syringing $0.4cm^3$ DMSO-d_6. This is unlikely, however, as the amount of water in the dried DMSO-d_6 could not have been high enough to account for the nH_2O being two and a half times lower in *A* than in *B*, *C* and *D*. It is also unlikely that ^{1}H NMR (60HMz) detected local variation in nH_2O instead of analysing an average for nH_2O. *A* might be an inaccurate result, but it agrees most closely with the TGA results.

In this experiment, TGA of nH_2O was internally consistent, showing no variation with sample site. TGA was therefore insensitive to variation in water content within a batch

of **1**•nH_2O. Alternatively, there was no local variation in nH_2O, or the two sample sites in a batch had identical nH_2O.

According to TGA for a different experiment, nH_2O in batch c of **1**•nH_2O was 0.4, not 1.0 so inconsistency does exist in TGA results. As the weight loss ascribed to water was small and gradual, the analysis depended to some extent on the judgement of the operator. This could have contributed to the discrepancy in nH_2O analysed with TGA or ^1H NMR. The use of TGA in this project was therefore limited to looking for zero weight loss up to 200°C in anhydrous samples of **1**.

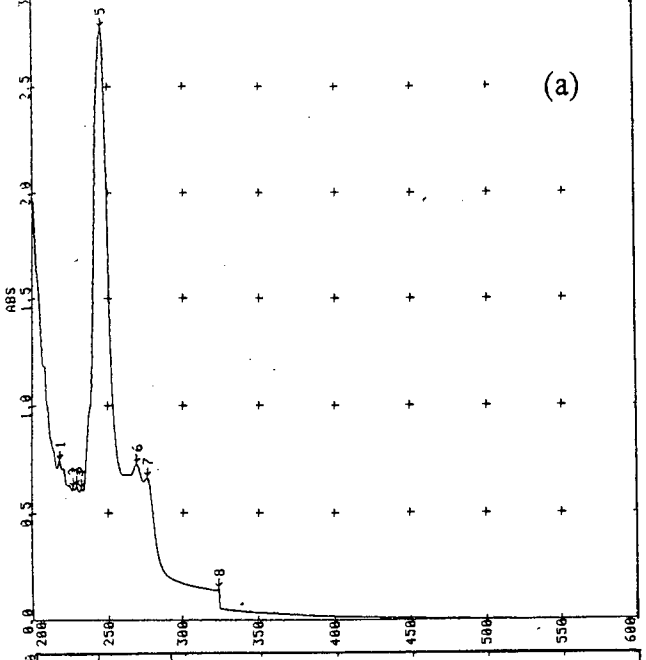
APPENDIX 7

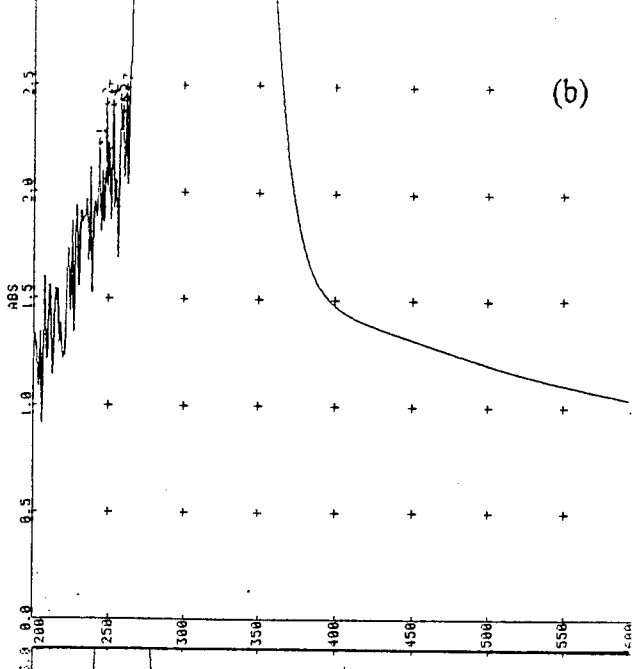
UV/VIS spectroscopy of undiluted liquid clathrates

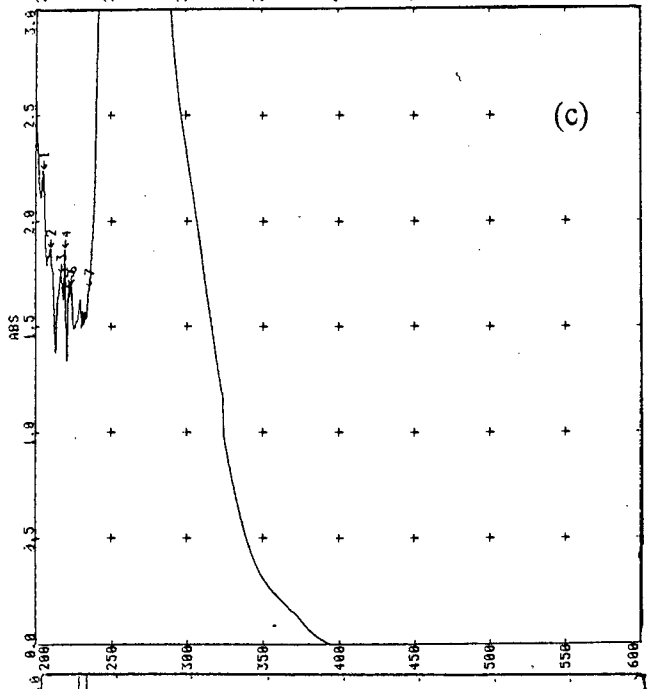
As the absorbance of undiluted liquid clathrates was beyond the range of the spectrometer, the possibility of obtaining UV/VIS spectra of undiluted liquid clathrates was investigated.

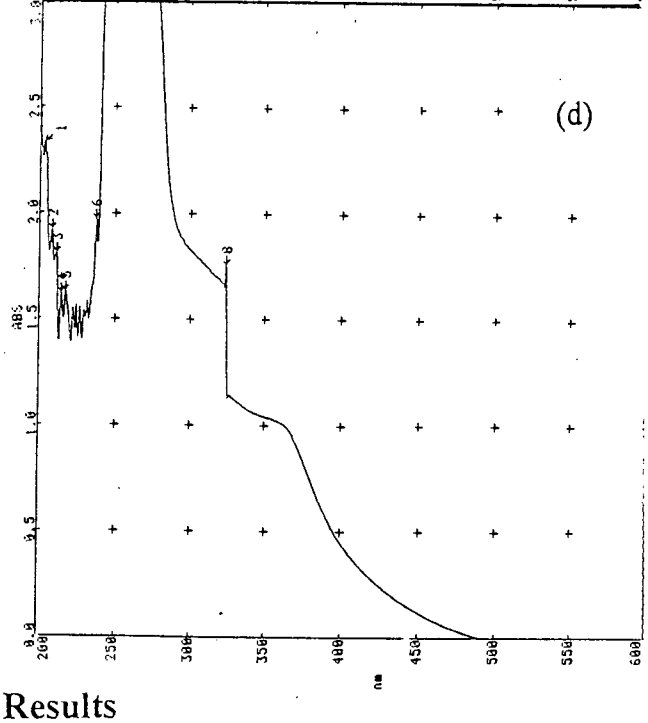
A7.1 Method

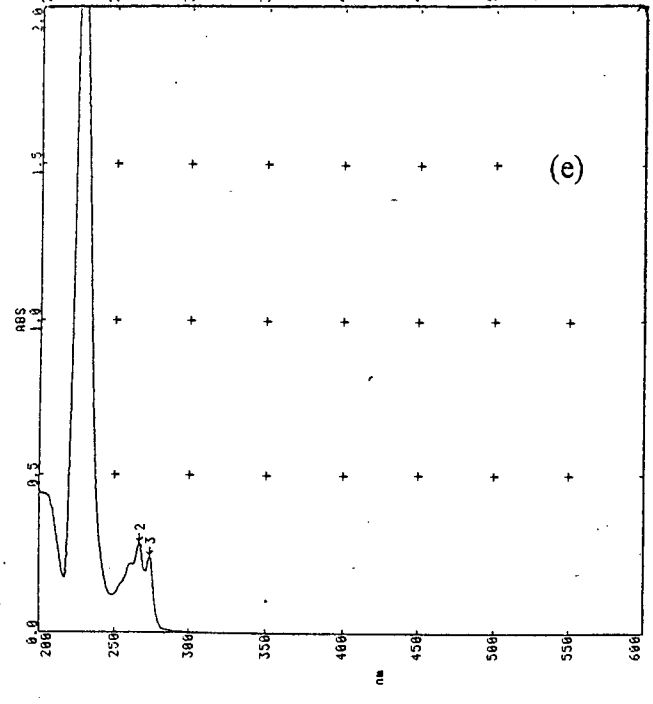
A cuvette length of 1mm was used to decrease the absorbance to a tenth of the absorbance of a sample path length of 1cm. The absorbance remained off scale, so the position of the cuvette, the volume of sample (cuvette a quarter or half full instead of three quarters full) and the background reference (guest instead of air) were manipulated to decrease the absorbance of the undiluted liquid clathrate to ≤ 3. The spectra were run on a Philips PU 8700 spectrophotometer.











A7.2 Results

FIGURE 7.2. UV/VIS spectra of a thiophene/**1** liquid clathrate, no solvent, cell path 1mm, thiophene reference.

(a) best spectrum obtained

(b) no 323.8nm peak detected

(c) hint of a shoulder at ~375nm

(d) sample made with stringently dry **1** and thiophene, prominent shoulder at ~375nm

Figure 7.2(e). UV/VIS spectrum of **1** dissolved in 96% ethanol, cell path 1cm, ethanol reference.

A7.3 Discussion

The manipulations to decrease the absorbance improved the peak resolution of the spectra, but some of the peaks could have been artefacts of the manipulations, instead of chemical in origin. For example, the 323.8nm peak in figure A7.2a was persistent through most of the manipulations but was not found in all the spectra, which indicated it was spurious as the same sample was used for these spectra. Alternatively, the 323.8nm peak could have been present but hidden as in figure A7.2b, and there was a hint of a 323.8nm peak in figure A7.2c, so the peak could have been chemical in origin. A spectrum of thiophene (with air as background reference) had a peak at 319.8nm. The 4nm difference could have been a result of the host-guest interaction.

Figures A7.2a, b and c were spectra of the same sample of thiophene/**1**•nH_2O liquid clathrate, but figure A7.2d was the spectrum of the intensely yellow liquid clathrate formed from strictly anhydrous thiophene and strictly anhydrous **1**. There was a hint of a shoulder at ~375nm in figure A7.2c. The ~375nm shoulder on the 323.8nm peak in figure A7.2d was more prominent and could have been pursued further as a probe of liquid clathrate structure as this liquid clathrate sample was promoter-free. Although this sample was intensely yellow, the spectrum had no peak at 500 - 600nm, probably as a result of manipulations to decrease the absorbance of the spectrum.

The spectrum of the solvent-free liquid clathrate in figure A7.2a (λ 227.2, 269.5, 276.3nm) compared well with the spectrum of **1** dissolved in 96% ethanol in figure A7.2e (λ 227.4, 267.1, 274.1nm). This, however, was no indication of the validity of the solvent-free spectra in general. Figure A7.2a was the best spectrum out of a range of spectra with decreased absorbance but with poor sensitivity, reproducibility and peak definition. Attempts to obtain repeated spectra of the calibre of figure A7.2a failed.

UV/VIS studies of undiluted liquid clathrates were not feasible because repeatable results could not be obtained, spectra had reduced sensitivity and the validity of results obtained was not established.