Journal Name

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Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

ARTICLE TYPE

The Chemistry of Low Dosage Clathrate Hydrate Inhibitors

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Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
DOI: 10.1039/b000000x

This review aims to introduce the chemistry of low dosage inhibitors of clathrate hydrate formation within the context of their role in the oil and gas industry. The review covers both kinetic hydrate inhibitors and anti-agglomerants from the point of view of structure-function relationships, focussing on recent refinements in mechanistic understanding and chemical design, and the consequently evolving and increasingly fine-tuned properties of these fascinating compounds.

Clathrate hydrates

Clathrate hydrates are crystalline, non-stoichiometric host-guest compounds comprising a hydrogen bonded water framework, into which small molecular guest species such as methane are included within cavities formed by the water cages. Because there are no strong directional interactions between guest and host the guests are free to vibrate and rotate but possess limited translational motion.[1] Typically common clathrate hydrates comprise 85 mol% water and 15 mol% guest(s) when all of the cavities are occupied.[2] These materials form when the components are subjected to ambient temperatures (generally less than 300 K) and moderate pressures (>0.6 MPa); conditions frequently found in oil and gas pipelines.[3]

The initial reporting of gas hydrates is accredited to Sir Humphrey Davy in 1811, who focussed upon the crystallisation of a cold aqueous solution of chlorine (known as oxymuriatic gas at the time).[4] In 1934 a pivotal report by Hammerschmidt acted as a catalyst for stimulating research in this area, by confirming that clathrate hydrates are responsible for the plugging of gas and oil pipelines and thereby dramatically increasing industrial investment and research on the topic.[5]

Today clathrate hydrates pose a major problem to the oil and gas industry with pipeline blockage causing many safety concerns in addition to requiring the shutdown of the pipeline for a time whilst the plug is removed. This shutdown period results in reduced field site performance and may cause significant financial loss. Avoidance of pipeline shutdown is a priority to many oil and gas companies, and as such considerable investment is being made into research into clathrate hydrate inhibition to circumvent such potentially catastrophic effects. Problems associated with gas hydrate formation reached the headlines in 2010 due to their destructive effects during BP's efforts to contain the oil spillage after the Deepwater Horizon blowout, thereby illustrating the importance of research in this area.[6]

While the petrochemical industry is working towards chemistries which circumvent the formation of clathrate hydrates, other research is underway into utilising methane hydrate in particular, as a potential fuel reserve.[2, 7] Gas hydrates located in the Earth's permafrost and deep sea regions may hold much potential as an alternative energy source, although due to difficulties in extraction of such icy masses this reserve remains largely untapped at present.[8] There is much discussion into other potential benefits and drawbacks associated with clathrate hydrates[8], for example in energy storage.[9] One significant concern is the potential global warming effect of methane clathrate hydrate dissociation with increasing climate temperature, and the consequential release of vast quantities of methane into the atmosphere; this may have run-away consequences to global climate change.[2, 8, 10, 11]

As a result of such practical interest, considerable work has been undertaken in the broad area of clathrate hydrates. This review focuses in particular on the emerging molecular design and chemistry of low dosage clathrate hydrate inhibitors, their mechanism of action and the constraints placed upon performance by regulatory and environmental factors.

Clathrate hydrate structures

Three common clathrate hydrate structures exist: structure I (cubic); structure II (cubic) and structure H (hexagonal); with the structure adopted being dependent predominantly upon the size of the guest(s).[12] Typically each cavity will accommodate one guest molecule, although when exposed to higher pressures (500 bar) multiple occupancy can be reached.[13] A fourth general structure type has been reported, known as structure T (trigonal), which forms in the presence of dimethyl ether. In addition, an unusual complex structure is known comprising alternating stacks of structure H and structure II.[14] However, only structure I and structure II will be discussed in detail herein, as these are the two most frequently observed within pipelines and hence are of importance in the context of inhibition chemistries. The cavities present within clathrate hydrates are supported by the repulsion

forces imparted on the water molecules by the guest species.[15] Rodger has argued that such repulsion forces prevent the collapse of the expanded cavities (relative to ice, Ih), and that the attractive dispersion forces are unimportant in this context.[15]

The formalism A^B is frequently used to describe the cage structure of each water host cavity within a clathrate hydrate structure, where A represents the number of OH···O hydrogen-bonded edges of the face (*i.e.* the face shape) and B represents the number of faces with A sides.[16] The faces are made from hydrogen bonded rings of water molecules, with arrangements such as those in Fig. 1.[13]

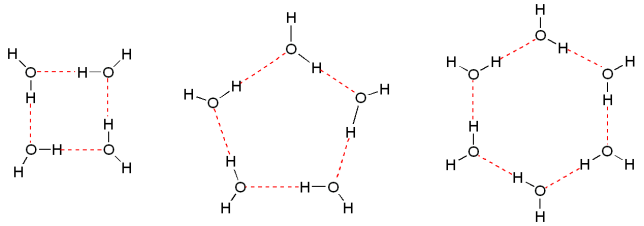


Fig. 1 Hydrogen bonded water motifs comprising the faces in clathrate hydrate cages (reproduced with permission from ref.[13])

The structure I and structure II crystal structures were first elucidated by von Stackelberg and coworkers following the interpretation of several earlier hydrate crystal diffraction experiments.[17-20] This work was followed by Mak, McMullan and Jeffrey in 1965 who completed additional diffraction studies, providing more conclusive evidence for these structures.[21, 22] Later work in 1987 by Ripmeester *et al.* resulted in the discovery and characterisation of structure H through use of solid state NMR spectroscopy and diffraction.[23]

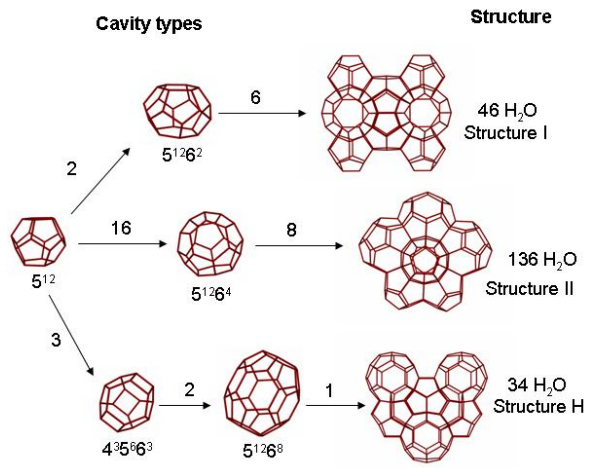


Fig. 2 Common clathrate hydrate structures (reproduced with permission from ref.[13])

Fig. 2 shows a simplistic representation of the cavity composition found in structures I, II and H, with the 5^{12} cavity common to each. The pentagonal dodecahedral 5^{12} results from the combination of 12 pentagons to form the basic building block cavity. When these 5^{12} cavities are linked by their vertices the result is structure I hydrate, whilst those with face-sharing 5^{12} cavities result in structure II.[24] The difference in linkages allows for the formation of the larger voids within the structure I and structure II cavities ($5^{12}6^2$ and $5^{12}6^4$ respectively).

Structure I hydrate comprises two 5^{12} cavities and six $5^{12}6^2$ cavities (tetrakaidecahedron), with the unit cell containing 46 water molecules.[25] The tetrakaidecahedral cavity ($5^{12}6^2$) has an average radius of 4.33Å which can include molecules with a diameter of up to about 6.0Å.[24] In contrast, the unit cell of structure II hydrate contains sixteen 5^{12} and eight $5^{12}6^4$ cages (forming a hexakaidecahedron) which are larger and can accommodate molecules with a diameter of up to 6.6Å.[24] Therefore, small hydrocarbon guests such as methane and ethane occupy structure I cavities, whilst the larger hydrocarbons, such as iso-butane and propane occupy the larger structure II cavities. Methane hydrate, for example, is a structure I compound with average composition $CH_4{\cdot}5.75H_2O$. Structure H, which has significantly larger cavities, forms in the presence of larger guest molecules such as some of the heavier components of crude oil in conjunction with a light gas (*e.g.* methane).[24, 26]

Many inhibition studies involve THF hydrate as a means to test the performance of new compounds. Use of this model hydrate system is due to the low solubility of natural gas within water. Whilst THF hydrate is known to form a structure II hydrate, further testing may be necessary to ensure the relevance of THF hydrate based model studies and appropriate performance in the field.

Importance to the oil industry

Water is frequently present during the extraction of gas and oil, and due to the close proximity of an abundance of hydrocarbon species it comes as no real surprise that clathrate hydrate species can form within pipelines particularly under high pressure, low temperature environments' such as the sea bed. Fig. 3 shows an example pipeline plug, illustrating the true immensity of disruption that may result by the formation of an icy mass in this context. Moreover, pressure build-up behind the blockage is a significant safety concern.

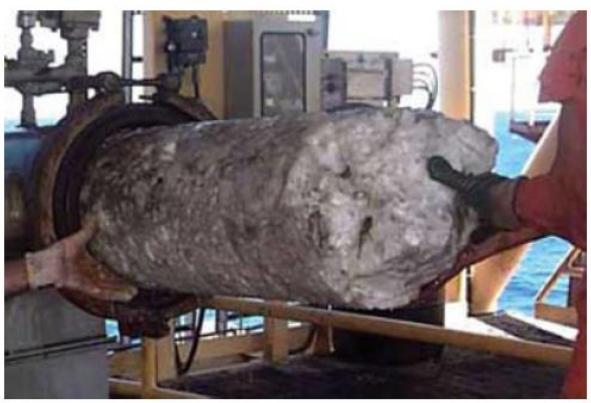


Fig. 3 Clathrate hydrate plug (reproduced with permission from ref.[27])

The oil industry continues to research inhibitor species to prevent or delay this kind of large scale clathrate hydrate formation problem. Broadly, clathrate hydrate inhibitors can be split into two categories; thermodynamic inhibitors (THI) typically used in very large quantities and the potentially more cost effective low-

dosage hydrate inhibitors (LDHI).

Traditionally, inhibition has been performed through the addition of methanol or ethylene glycol, thermodynamic inhibitors, which shift the phase boundary for the formation of gas hydrates to lower temperatures and higher pressures, preventing hydrate formation under the prevailing conditions in the pipeline.[16] However, while the addition of thermodynamic inhibitors is effective, 20-50wt% of the THI is generally required.[28] This brings with it significant financial implications, exacerbated by the difficulty in recovering or recycling the methanol post-addition. In addition to the treatment costs, transportation costs associated with supplying considerable volumes of methanol, for example, to an oilfield site are highly significant. LDHIs, which can be added in much smaller quantity, therefore, have markedly reduced transportation costs,[29] and hence industry has seen a large push into the development of LDHIs, which can be added in concentrations as low as 0.01-5wt%; it is these species that form the focus of this review.

Low-dosage hydrate inhibition

LDHIs can be split broadly into two categories; kinetic hydrate inhibitors (KHI) and anti-agglomerants (AA). KHIs and AAs offer slightly different properties in terms of their mode of action and factors such as the degree of subcooling and cloud point (the temperature at which the inhibitor becomes cloudy in solution due to polymer aggregation), thereby dictating the preference for a particular type of species at a given field site. Of great importance to oilfield considerations is the deposition temperature, this is the temperature at which the inhibitor polymer precipitates out of solution, thereby becoming ineffective. Deposition temperature is typically 5 – 15 ^{o}C above the cloud point but can be much higher depending on conditions.[30] Broadly, KHIs inhibit the rate of nucleation and growth of clathrate hydrate crystals while AAs prevent the aggregation of small hydrate crystals into large, pipeline-blocking masses. Within the context of gas pipelines, the application of AAs is not possible since they require a liquid hydrocarbon phase, therefore KHIs are essential in this field context.[28]

The subcooling (ΔT_{sub}, Fig. 4) is an important property for comparing the performance of different inhibitor species, and can be defined as the difference between the hydrate equilibrium temperature and the operating temperature at a given pressure.[28] It is advantageous for an LDHI to have a high subcooling, since this in principle allows lower operating temperatures (as is necessary for extraction in some field sites).

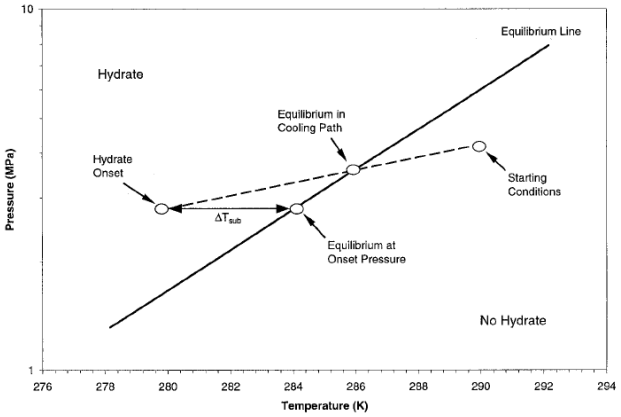


Fig. 4 The subcooling (ΔT_{sub}) is the temperature difference between the hydrate equilibrium temperature and the operating temperature (reproduced with permission from ref.[31])

Kinetic Hydrate Inhibitors

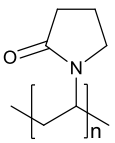
KHIs are water-soluble polymers that can either effectively delay the onset of hydrate nucleation or can delay the growth of hydrate crystals for periods long enough to ensure transport of the fluid without pipeline blockage.[28] This review aims to consider the variety of different KHIs that have been reported, looking at their synthesis, their practical application including adaptations to the chemical structure that can enhance performance in extreme conditions, and proposals for the inhibitors' mode of action. In the oilfield business KHIs are often used in conjunction with synergists, such as 2-butoxyethanol, which are generally added at the same time as the polymer and effectively enhance the performance of the inhibitor. Such synergists will be introduced where their presence is important to the KHI mode of action, however they do not form a primary focus.

Development of KHIs

Nature provides some clues into the kinds of structures that might inhibit the crystallization of ice and ice-like materials in the form of natural antifreeze proteins. Fish such as Winter Flounder which live in or near to the polar regions possess an interesting mixture of proteins to prevent them from freezing in the often extreme cold temperatures. These proteins have two categories (i) antifreeze glycoproteins (AFGP) and (ii) antifreeze proteins (AFP).[32] The proteins exhibit structural features such as a regular array of hydrophilic amino acid residues that are thought to interact with the growing surface of an ice crystal.[33] The ability of anti-freeze proteins to prevent the freezing of arctic fish by inhibiting ice crystallization provokes the question as to whether it is possible to artificially synthesise analogues of such proteins and whether these would exhibit similar antifreeze properties with gas hydrates.[28] The synthesis of glycoproteins has been undertaken and proven to be successful at interfering with hydrate crystal growth, however it did not prove to be an economically viable inhibition methodology.[34] Several studies have been reported which compare the efficacy of AFPs with synthetic KHIs such as poly(N-vinyl pyrrolidone) (PVP, **1**), indicating that AFPs may hold advantages in prolonging induction periods by having a more pronounced effect upon

nucleation.[35] There has been considerable work probing the mechanism of action of AFPs at inhibiting ice growth, reporting a surface adsorption mechanism and the resulting Kelvin effect.[36, 37] The mechanism of action for type-I anti-freeze proteins is believed to occur through hydrogen bond formation between four threonine residues with oxygen atoms from the ice lattice.[38] In conjunction, an alanine rich surface is present adjacent to the threonine residues.[33] The use of antifreeze proteins for hydrate inhibition is an interesting area, and the interested reader is directed to the work of Ripmeester and Walker.[35, 39, 40]

It was these concepts which led Shell to investigate alternative water-soluble amides in connection with clathrate hydrate inhibition, and the discovery of hydrate inhibition by PVP, independently to the Colorado School of Mines.[28] PVP was first synthesised in 1939, and has found application as a flocculant and sorbents amongst many others.[41] The clathrate hydrate inhibition activity of PVP was first reported by the Colorado School of Mines (CSM) in the early 1990s, with a molecular weight in excess of 20,000 being particularly effective.[42]



1

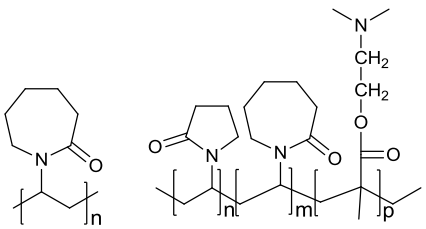
This polymeric species is particularly appealing due to its low toxicity, thereby reducing any associated risks if accidental pipeline leakage were to occur. Testing of the inhibition properties was completed by CSM through use of a ball-stop rig in which PVP successfully prevented formation of THF hydrate for a period in excess of 24 hours.[42]

Ball-stop rig testing is a popular methodology for analysing the inhibition performance of LDHIs; this technique measures the time taken for a metal ball to cease movement when located within a cooled cell containing a hydrate-forming liquid (frequently THF and water in a 1:17 ratio) and inhibitor species.[28] The cessation of ball movement is indicative of hydrate plug formation. Obviously the longer time period over which ball movement is possible, the more efficient the inhibitor is at preventing the plug appearance.

CSM conducted further work on the effect of PVP molecular weight upon the inhibitor performance, again utilising ball-stop rig testing, and comparing the ball-stop time and induction times for an array of different molecular weight polymers.[43] With a molecular weight of 360,000 the ball did not stop moving throughout the testing period (6 hours).[43] Higher molecular weight polymer adsorbs more strongly to the hydrate surface and hence acts as an effective crystal growth inhibitor.[44] However, it has also been shown that low molecular weight PVP has a more pronounced effect on perturbing the water structure, and hence has a greater effect upon gas hydrate nucleation.[44] So it seems that regardless of the molecular weight chosen, PVP is able to function to some extent as a KHI. As a result of its efficacy, PVP is now commercially available and is sold in large quantities by Ashland Inc. (Ashland Speciality Ingredients, ASI, formerly International Specialty Products, ISP) and BASF, amongst others.[45]

The cavities of clathrate hydrates possess some pentagonal faces (5^{12}) and it has been speculated that a 5-membered ring upon a polymer backbone might enable optimum interaction with clathrate hydrate pentagonal faces and hence prevent those pentagonal faces from participating in the formation of a larger clathrate hydrate mass.[46] It is difficult to see the logic in such a parallel since it does not explain the efficacy of seven-membered caprolactam KHIs and even pyrrolidone derivatives do not possess five-fold symmetry because of the presence of the carbonyl group and polymer backbone.

Whilst this first generation inhibitor species (PVP) is effective at a temperature of 285.6 K, upon reducing the temperature to 277 K the inhibition performance is exceeded by the use of alternative second generation inhibitors such as polyvinylcaprolactam (PVCap, **2**) and a terpolymer of vinyl pyrrolidone (VP), vinyl caprolactam (VCap) and dimethylaminoethyl methacrylate (**3**, marketed commercially as Gaffix VC-713).[47] Inhibition performance can be monitored and compared through use of high pressure apparatus in which gas consumption indicates hydrate formation (an increased gas consumption is indicative of hydrate formation and therefore an ineffective inhibitor).[47] Inhibitors **2** and **3** are found to have significantly reduced gas consumption relative to **1** (when analysed at 277.2 K).[47]



2 **3**

As a continuation of their work in this field, CSM investigated the inhibition properties of **3** which at the time was being synthesised for alternative application within the hair-care industry.[28, 48] The optimal composition for polymer **3** is reported as: VCap (65-80wt%), VP (17-32wt%) and dimethylaminoethyl methacrylate (3-6wt%).[49] Ball stop testing of inhibition performance using an aqueous solution containing sodium chloride (3.5 wt%), THF (20wt%) and **3** (0.5wt%) at 0 ^{o}C showed no hydrate formation during the 8 hours of monitoring.[46] Inhibitor **3** is reported as having a subcooling of 8-9 ^{o}C.[24]

It has been suggested that the inclusion of a small non-cyclic organic group such as dimethylaminoethyl methacrylate may further enhance the inhibition properties by providing an additional group to which "free" water molecules may cluster.[48] If the water molecules are clustered around the inhibitor pendant arm, this would reduce the likelihood of their being incorporated into a hydrate mass, thereby enhancing the inhibitor performance.

The improvement on including the vinyl caprolactam component

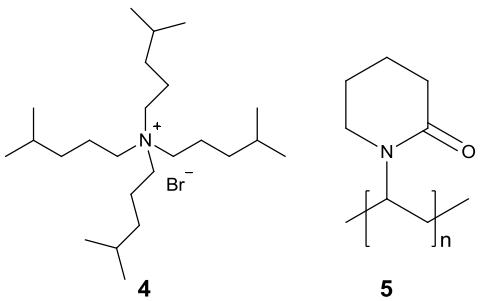
suggests that this functionality may hold some benefits as a KHI and indeed the homopolymeric species, PVCap, has become an industry leading inhibitor. PVCap can be prepared by the addition of a monomer premix of vinyl caprolactam with di-t-butyl peroxide initiator to pre-heated 2-butoxyethanol at 150 °C, with the later addition of some additional di-t-butyl peroxide.[50] This synthetic methodology is used for the production of low molecular weight polymers, with a molecular weight in the range of 500 to 2000. Carrying out the polymerisation in a mixture of 2-butoxyethanol and water (80:20), at a pH of about 8-12, enables the formation of PVCap with molecular weight in the range 500 to 4000.[51] Alternatively, a significantly higher average molecular weight ($2.1x10^4$) can be achieved through use of azobisisobutyronitryl (AIBN) as the radical polymerisation initiator, with reaction proceeding in isopropanol.[52] Dependent upon the field application there may be preference for a specific molecular weight; with low molecular weight PVCap exhibiting a markedly higher cloud point than the higher molecular weight analogue.[53] In warmer waters, such as the Gulf of Mexico, the inhibitor cloud point can be a significant concern and high cloud point inhibitors are an active area of research (*vide infra*). PVCap is a thermoresponsive polymer undergoing a phase transition to globules at its lower critical solution temperature of 31-38 °C.[54] At lower temperature, however, it is a very efficient and effective hydrate inhibitor, and is now the industry standard to which new KHIs are compared.

Within PVCap the oxygen atom of the lactam carbonyl group possesses a significant negative partial charge of approximately –0.4[52] making this functional group a good hydrogen-bond acceptor. As a result, the polymer is expected to interact strongly with water and this interaction has been implicated in the mechanism of hydrate inhibition by this species. Hydrogen bond formation, between the C=O of PVCap and water, was confirmed by IR spectroscopy and results in a considerable shift in the frequency of the carbonyl stretching mode.[52] Comparison of the C=O stretching band for PVP versus PVCap (1685 *vs* 1640 cm^{-1})[52] shows that PVP has more carbonyl double bond character whilst PVCap shows greater enolate character. The greater carbonyl double bond character in PVP results from the increased strain within the 5-membered ring. The carbonyl oxygen atom within PVCap is a particularly good hydrogen acceptor due to the greater contribution to the enolate resonance form as a result of the less strained 7-membered ring.[55]

Lederhos *et al.* carried out KHI testing on PVP, PVCap and **3**.[47] The work initially used a ball-stop rig and subsequently a high pressure autoclave with gas consumption an indicator of hydrate formation using a typical Gulf of Mexico natural gas mixture.[47] Performance was affected by high pressure, low temperature and inhibitor concentration.[47] Compound **3** and PVCap were found to perform well at moderate pressures (6.89 MPa) whilst performance at higher pressures (10.3 MPa) was significantly reduced.[47] Copolymers of VP/VCap were also studied. The work showed that when the ratio of VP/VCap is equal to or less than 1:3, copolymer inhibitor performance is equal to that of PVCap or **3**. This suggests that it is reasonable to speculate that the caprolactam ring is crucial for inhibition properties.[47]

There appears to be a potential problem with dissolving in water a polymer containing an organic ring functionality in that the presence of this hydrophobic residue enhances the probability of polymer self-association as opposed to effective interaction of the polymer with liquid water or the growing clathrate hydrate crystal surface (as would be desirable for inhibition).[48] If the polymer molecules self-associate then this will likely reduce their efficiency as inhibitors by restricting the dispersion of the polymer within solution. Moreover, some polymers may adopt a compacted form in water. In order to prevent transition to this compacted conformation, it has been proposed that modifications to the polymer to provide steric hindrance may ensure that the extended conformation is maintained.[48] Alternatively, there is report of the inclusion of ionic groups, which, through enhancing charge repulsions, may also prevent the transition to the compacted form.[56]

The efficacy of PVCap is further enhanced through the use of synergists, which are believed to work in conjunction with the polymer. There are several reports as to the use of quaternary ammonium or phosphonium salts such as tetrabutylammonium bromide (TBAB) and tetrapentylammonium bromide (TPAB) as crystal growth inhibitors for structure II hydrates when used in conjuction with PVCap.[57, 58] Inhibition enhancement results from the differing geometries of PVCap and TPAB (or TBAB) enabling attachment at different hydrate crystal sites.[57, 58] It has been postulated that a pentyl group present on the TPAB will embed within a cavity on the hydrate surface and hence hinder hydrate growth, with this embedding mode of action explaining the reduced synergistic performance for analogues containing *n*-hexyl or *n*-propyl pendant arms.[57, 58] In addition to acting as KHI synergists, quaternary salts can also function as anti-agglomerants upon transformation into surfactants, *vide infra*.[57] Recently, there has been report of the use of tetra(*iso*-hexyl) ammonium bromide (TiHexAB, **4**), which shows improvement in slowing THF hydrate growth rate in comparison to TBAB and TPAB, and is believed to be the most powerful synergist and crystal growth inhibitor studied to date.[57] Combining TiHexAB with PVCap results in an average hydrate onset temperature of 4.3 °C, as measured through use of a rocker rig (at a concentration of 2500ppm of PVCap and 2500ppm TiHexAB) which is an improvement on 9.2 °C and 5.6 °C for PVCap plus TBAB and TPAB, respectively.[57]

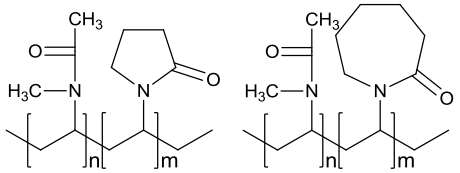


4 **5**

The use of PVP (5-membered ring) and PVCap (7-membered ring), provokes the question as to the performance of polyvinyl piperidone (PVPip, **5**) which contains a 6-membered ring. Vinyl piperidone monomer is not currently readily available

commercially which limits studies on PVPip. However, recently, O'Reilly *et al.* have compared the relative performance of all three poly vinyl lactam species at inhibiting structure II hydrate formation.[44] It was concluded that PVPip functions as a clathrate hydrate inhibitor with efficacy intermediate between PVP and PVCap and hence PVCap is the most effective of the three. As a result further research into PVPip seems to be of low priority.[44]

Following on from the suggestion that the inclusion of small organic amide functionalities upon the polymer backbone, alongside the vinyl lactam groups, may further enhance inhibition performance, work has been carried out on further copolymers of this type. One example is the copolymer of *N*-methyl-*N*-vinylacetamide (VIMA) and VCap (or VP), with an average molecular weight ranging 1000 to approximately 6,000,000 (**6** and **7**).[59]



6 **7**

Synthesis of the VIMA/VCap copolymer can be achieved by heating a reaction mixture comprising VIMA, VCap and AIBN in ethanol, at 78 °C for 8 hours.[59] The procedure also works well for the VP and VPip analogues.[59] The mini-loop testing of VIMA/VCap showed an improvement in subcooling relative to PVCap (PVCap subcooling = 12.4 °C; VIMA/VCap 3:1 ratio subcooling = 14.7 °C); thereby confirming that VIMA has a synergist effect upon VCap, and may indicate that investigation into copolymers of vinyl lactam / *N*-vinyl amides are worth additional consideration.[59]

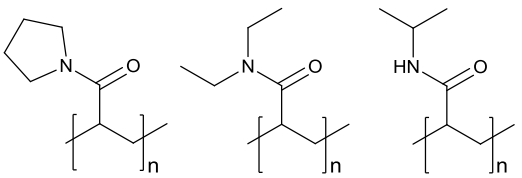
This copolymeric inhibitor has been trialled in field application (in the West Pembina field, near Alberta, Canada), and was found to inhibit formation of hydrates in a 4-in, 2.8mi-long oil flowline.[60] The low dosage required for application of KHI in contrast to THI is highlighted in this field trial, where originally methanol was used to treat hydrate formation often requiring 130-260 gallons of methanol per week, while only 0.5 gallons per day of the KHI are required for inhibition.[60] This significant reduction in the quantity of chemical required will impart a reduction in costs, and should make this the economically advantageous choice; Table 1 shows the comparison for approximate cost of different inhibitors at the West Pembina field.

Inhibitor	Dose Rate (gal/day)	Chemical cost (C$/day)
Methanol (130 litre batch treatment every 3 days)	43	$68.50
Methanol (calc. requirement for continuous injection)	34.6	$53.67
7	0.5	<$20

Table 1 Economic comparison for costing of different inhibitors at the West Pembina Field.[60]

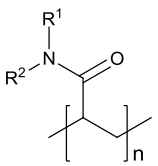
Prior to application, poly(VIMA/VCap) is premixed with a carrier solvent, which may be methanol or water, dependent upon likely operation temperatures. Preferably, the carrier solvent is water as this reduces safety implications for the handling and storage of the inhibitor species.[61] In addition, due to stringent safety regulations, testing of the environmental impact resulted in poly(VIMA/VCap) being awarded the most environmentally friendly rating (E) by the UK Offshore Chemical Notification Scheme (OCNS).[61] Whilst this species may appear to be the ideal KHI, unfortunately, due to difficulties in obtaining the VIMA monomer, this copolymer is no longer commercially available.[28]

Investigation into polyalkylacrylamides and polydialkylacrylamides yielded pleasing results, particularly for polyacryloylpyrrolidine (polyAP, **8**), polydiethylacrylamide (polyDA, **9**) and polyisopropylacrylamide (polyIP, **10**).[28]



8 **9** **10**

The design of these species is consistent with the postulation made by Exxon that the presence of amide functionality attached to a hydrophobic group is integral for KHI performance[28] and a broad range of polyalkylacrylamides of type **11** have been patented.[62]



11

Kelland proposed the mode of action of the polyalkylacrylamides to be similar to that of PVCap or PVP, whereby there is interaction between the hydrate surface and the pendant groups of the inhibitor.[30] It is postulated that the alkyl groups fit within an available cavity on the hydrate surface, while the carbonyl group hydrogen bonds to the surface.[30] The cloud point (T_{cl}) for polymeric acryloylpyrrolidine (polyAP) is appreciably higher than that for PVCap, as shown in Table 2, where T_{cl} for PVCap (in 3.6% synthetic sea water (SSW)) is 30 °C (when M_n = 1300), in comparison to 53 °C for polyAP (M_n = 1200).[30]

Inhibitor	M_n	T_{cl}/°C in DI H_2O	T_{cl}/°C in 3.6% SSW
2	1300	33	30
3	4500	33	30
VP/VCap	4000	70	60
7	2000	74	62
8	1200	60	53

Table 2 Cloud points for an array of different inhibitor species.[30]

It is advantageous for an inhibitor species to have an increased cloud point as this will enable application of such species in field

sites such as the Gulf of Mexico wherein the high temperatures may circumvent the use of some low T_{cl} inhibitor species as clouding out of the inhibitor results in decreased efficiency.

Inhibitor	Conc. (ppm)	M_n	T (°C)	t_i (min)	S_{t-1} (min)	Total (min)
None			7.6	<2	<2	<2
2	5000	7500	7.6	49	70	119
2	5000	1300	3.7	72	136	208
3	5000	4500	5.8	28	32	60
3	5000	4500	3.9	3.9	0.6	3.9
7	5000	2000	3.9	1.3	4.5	5.8
8	5000	1200	5.7	33	148	181
8	6000	1200	5.7	250	120	370
8	5000	1200	3.7	2	22	24
8	6000	43000	5.5	14	3	17
8	5000	6100	5.5	620	180	800
8	5000	6100	3.9	158	73	231

Table 3 Data table from showing the performance tests for comparison between PVCap and polyAP; where T=constant temperature, t_i = induction time and S_{t-1} = crystal growth delay time.[30]

The results from sapphire cell testing indicate that polyAP and polyIP are particularly promising KHIs, with some showing a performance to equal or exceed that of the PVCap tested, although performance is largely dependent on molecular weight (Table 3).[30] Additionally, the blend of a large amount of low molecular weight alkylacrylamide polymer with small amounts of PVCap results in significant improvements in induction time (>1347 mins at 5.7 °C).[30] Whilst the induction times appear very encouraging for these species, the reproducibility error of these data ranges between 30-50%.[30] Sapphire cell testing requires an arrangement comprising sapphire cells (manufactured using sapphire crystals) a cooling bath and a data centre, and simulates a North Sea well stream through use of synthetic natural gas, condensate and synthetic sea water (Fig. 5 shows the general arrangement for sapphire cell testing).[63]

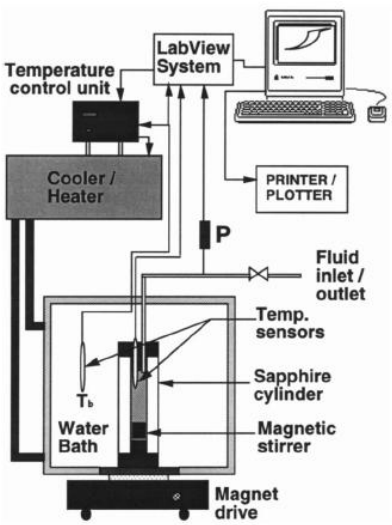
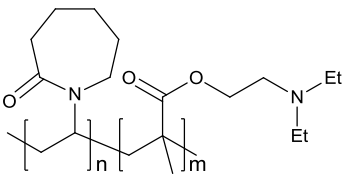


Fig. 5 Sapphire Cell Testing equipment (reproduced with permission from ref. [30])

An alternative performance testing methodology is the use of a mini-loop system. This comprises stainless steel tubing through which fluid (often synthetic sea water with hydrocarbon condensate) is circulated.[59] Inhibitor species are injected as an aqueous solution into the fluid, with careful monitoring of the system pressure.[59] The loop is placed in a water bath, wherein the temperature is reduced at a constant rate to test for hydrate formation.[59] The system is carefully monitored for any changes in temperature or pressure.

A copolymer comprising 80-95wt% VCap and 5-20wt% *N*,*N*-diethylaminoethyl(meth)acrylate (DEAEMA, **12**) has been found to have good inhibition performance.[64] In particular, using a polymer comprising 13wt% DEAEMA results in hydrate inhibition in excess of 24 hours.[64]



12

Synthesis of this copolymer is performed through the addition of weighed amounts of VCap and DEAEMA into a flask containing 2-butoxyethanol, with the addition of di-t-butyl-peroxide (initiator). The reaction mixture is purged with nitrogen throughout and heated to 150°C, with the addition of further boosts of initiator to yield the desired product.[64] Alongside the maximum subcooling of 10.5 °C, as measured in autoclave cells containing Green Canyon gas, the VCap/DEAEMA copolymer also has corrosion inhibition properties and is commercially available.[65]

The development of synergists has allowed further optimisation of the efficiency of KHI species, with some solvents having a significant effect upon improving the inhibition performance. The use of glycol ethers is common, in particular 2-butoxyethanol (butyl glycol ether), although an array of glycol ethers comprising at least three carbon atoms in the alkoxy group result in a significant improvement in performance with respect to compound **3**.[66, 67] The significant effect that altering the solvent may have upon inhibition was clearly shown by Young and coworkers who conducted a study using gas consumption as the indicator of the extent of inhibition (reduced gas consumption implies good inhibitor performance as less hydrate has formed).[67] Using synthetic sea water and Green Canyon gas the performance for 0.5wt% **3** in 0.75wt% ethanol was compared to that for 0.5wt% **3** in 0.75wt% 2-butoxyethanol. The results show that after 40 minutes there is rapid hydrate formation in the mixture containing ethanol, whilst the mixture with 2-butoxyethanol remains hydrate free throughout the testing period (20 h).[67] In addition, the same test procedure was used to assess the performance of PVCap with ethanol versus 2-butoxyethanol, where a significant reduction in gas consumption resulted when using only 0.3wt% 2-butoxyethanol in comparison to 0.75wt% ethanol, as shown in Fig. 6.[67]

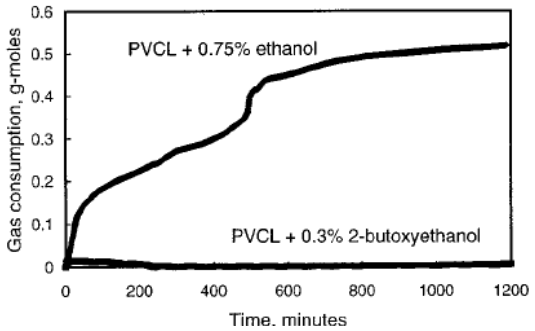
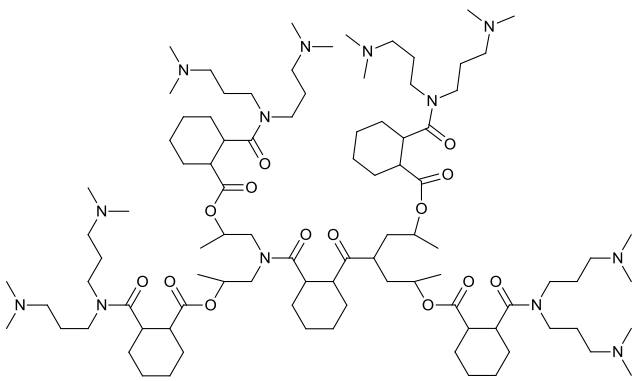


Fig. 6 Gas consumption comparison for PVCap plus ethanol (0.75wt%) *versus* 2-butoxyethanol (0.3wt%) measured at 4 °C, 1000 psig in 3.5wt% sea saltwater (reproduced with permission from ref. [66])

Shell has patented the use of an array of hyperbranched poly(esteramide)s such as **13** as KHIs (and also as AAs), which are trademarked and commercially available under the name of HYBRANES.[68] These species possess a common functionality, in that they each have at least one hydroxyalkylamine end group. Species of this type can typically be synthesised through the self-condensation of a cyclic anhydride with a dialkanolamine.[69] Similarly to the application of vinyl lactam inhibitors, it is generally only necessary to use between 0.5 and 3.5wt%, with the addition of such species being either as a dry powder, or more commonly as a concentrated solution.[69]



13

The amide groups are expected to form hydrogen bonds with the hydrate crystal (as suggested for vinyl lactam polymers) whilst the hydrophobic functionality will form van der Waals interactions with the surface.[28] Overall, the cumulative effect of the hydrogen bond and the van der Waals interactions offers a qualitative explanation for the mode of action of these species as KHIs and results in the retardation of the crystal growth rate. Studies on THF hydrate indicate that inhibition is not an inherent property of these compounds, and that inhibitor performance is dependent upon the size of the hydrophobic groups.[69] When considering the size of the structure II cavities in THF hydrate, the efficiency of an inhibitor may depend in part upon the ability of such a polymer to fit within the hydrate cavity.[69] Optimal inhibition results are obtained from a hyperbranched polymer comprising isobutyl groups attached to the 2-carbon of the succinyl units.[69] Test results for the inhibition of THF hydrate show that whilst the investigated poly(esteramide)s do function as KHIs (efficiency being size dependent), complete inhibition is not achieved, even when used in concentrations as high as 8000 ppm.[69]

Use of a bimodal molecular weight distribution for VCap and IPMA polymers has been used to excellent effect, and gives good subcoolings (ranging from 10 °C to 24.2 °C dependent upon the polymer).[70] This concept is based upon the blending of both a low molecular weight (LMW) polymer with a high molecular weight (HMW) polymer, wherein the LMW fraction has a weight average molecular weight between 500 and 10,000, whilst the HMW fraction ranges 10,000 to 1,000,000.[70] Improved performance is seen for bimodal PVCap with a reported subcooling of 18.9 °C at 20 hour hold time.[70]

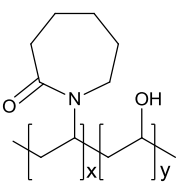
Most recent developments in KHIs

Whilst the use of PVCap is industry leading due in part to the long induction time and economic benefits in comparison to thermodynamic inhibitors, there is still room for further development in improving the biodegradability and performance under extremes of temperature and salinity. Issues such as the salt and temperature tolerance become significant on application of KHIs in challenging environments such as high salt conditions, or in the warm waters as found in the Gulf of Mexico. The deposition temperature and cloud point may be crucial considerations as the clouding out of the inhibitor will result in reduced performance and may leave the system vulnerable to plugging. As a result of these additional considerations, recent research has resulted in a number of next-generation lactam type KHIs that address these industry drivers.

In recent years strict regulations have been imposed with regard to the biodegradability required prior to large-scale application of an inhibitor. The restrictions posed for application in the North Sea can be split into three categories:[71]

1. Green: >60% degradability in 28 days
2. Yellow: 20-60% degradability in 28 days
3. Red: <20% degradability in 28 days

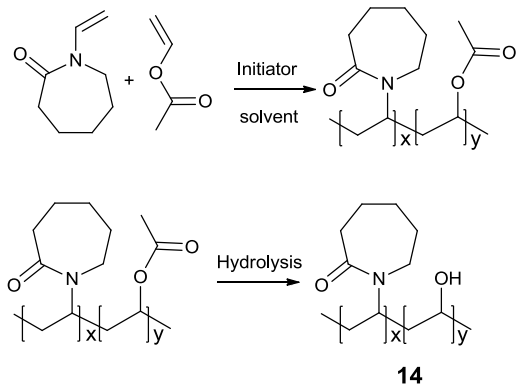
Clearly, it is desirable to produce an inhibitor possessing green category biodegradability (>60%), but there is a fine balance with altering the properties to achieve the green status without compromising on KHI performance. Recent work at ASI has resulted in the development of new polymeric inhibitors offering performance similar to that of PVCap whilst also possessing improved biodegradability. One such species is a copolymer of PVCap with polyvinyl alcohol (VOH) (**14**), asdeveloped by Musa and co-workers.[72]



14

This copolymer exhibits an induction time in excess of two days

and has a subcooling of 10.5 °C, as tested using an autoclave with Green Canyon gas.[72] Synthesis of **14** proceeds *via* a two-step reaction process; involving firstly the synthesis of a copolymer of VCap and vinyl acetate, and subsequently the hydrolysis of this intermediate to yield inhibitor **14** (Scheme 1).[72]

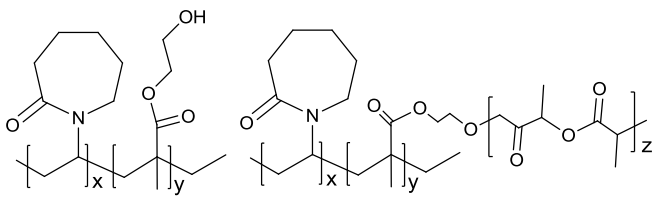


14

Scheme 1 Synthesis of PVCap/VOH copolymer.[72]

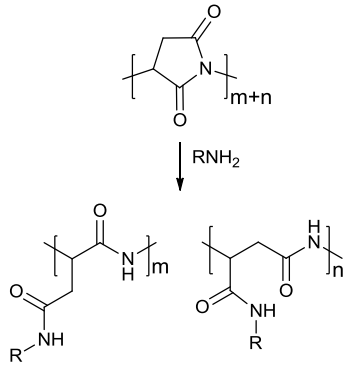
A variety of solvent systems have been trialled for the copolymer synthesis including methanol/water, 2-butoxyethanol/water, 2-butoxyethanol and IPA/water, all yielding a copolymer comprising 82% VCap and 18% VOH.[72] In all cases an induction time in excess of 2800 minutes resulted at a low inhibitor dosage (0.3 – 0.6%).[72] In addition to this high performance, the inclusion of the alcohol functionality enables improved biodegradability relative to the PVCap homopolymer. Biodegradability testing of inhibitor **14** as supplied to site (within 2-butoxyethanol) reports an impressive 76% in 28 days.[72]

The incorporation of a hydrolysable ester linkage further enhances the biodegradability of the polymer, as seen with the copolymer of VCap and hydroxyethylmethacrylate (VCap-HEMA) (**15**).[72] A composition of 95% VCap and 5% HEMA results in a high subcooling (9.5-10.5 °C) with induction times in excess of 48 hours.[72] The inclusion of the alcohol functionality in compound **15** allows for post-modification of the compound, for example with the grafting of poly(lactide) onto **15** to formulate an inhibitor with an extended pendant arm (**16**).[73]



15 **16**

Polyaspartamides are an alternative polymeric inhibitor believed to possess improved biodegradability, high cloud point and good inhibition performance.[74] Such inhibitors can be synthesised by the ring opening of polysuccinimides using alkylamines, an example of such is shown in Scheme 2.[75]

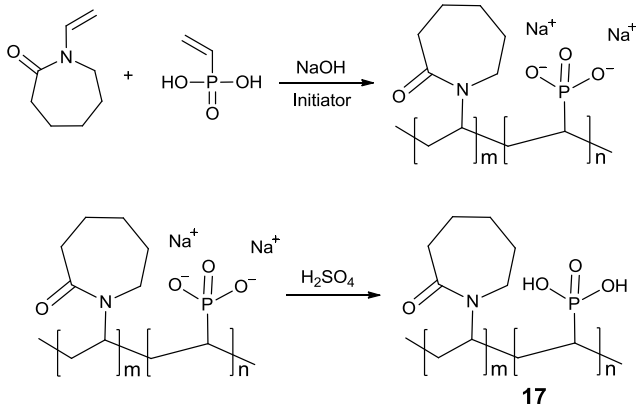


Scheme 2 Synthesis of polyaspartamides from polysuccinimide.[75]

The inclusion of 75-80% isobutyl groups and 20-25% methyl groups provides good inhibition performance, as tested through use of a high pressure autoclave (using a titanium cell) with an average induction time of 313 minutes.[75] However, while this species does have some desirable biodegradability (>20% in 28 days) the inhibition performance is exceeded by vinyl lactam KHIs.[75] More recently, it has been noted that incorporation of a high percentage of isopentyl groups is advantageous to the inhibition performance, although this does also require the inclusion of minor amounts of very hydrophilic alkylamines to circumvent water-insolubility issues.[74] While there is still room for further improvement of the inhibition performance to exceed that of currently used vinyl lactam KHIs, these results seem very encouraging.

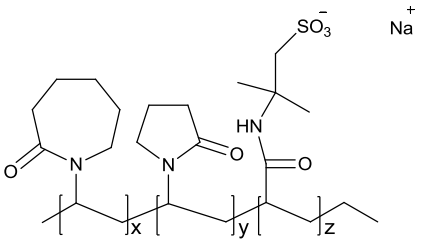
Within the oil and gas industry, scale inhibitors (SI) and corrosion inhibitors (CI) are frequently added to pipelines in addition to KHIs. Some polyaspartamides/polyaspartates will act as inhibitors for both carbonate and sulphate scale in addition to functioning as a KHI, therefore use of inhibitors such as **16** may circumvent the need for the addition of two inhibitor species with differing functionalities to the pipeline.[74] Such dual functionality may increase the benefits with use of such a polymer, although this area is still awaiting further clarification of performance.[74] There has been report of the potential problems with the addition of both a KHI and a CI, in that the combination may reduce the KHI performance due to an incompatibility of some CIs in conjunction with a KHI.[76]

Combining corrosion inhibition with KHI performance has been achieved in copolymers comprising both vinylcaprolactam and phosphoric acid functionality, as in inhibitor **17**.[77] This material exhibits a high subcooling (10.5 °C at a temperature of 7 °C and 9.5 °C at a temperature of 4 °C) with an induction time >48 h. Synthesis of **17** occurs via a two-step reaction in 2-butoxyethanol/water (Scheme 3).[77]



Scheme 3 Synthesis of vinylcaprolactam phosphoric acid copolymer **17**.

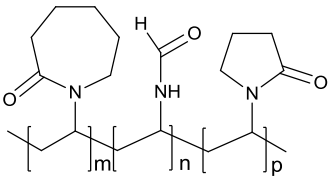
As gas and oil extraction moves deeper and further afield, industry has seen an increased demand for KHIs with improved salt tolerance and improved tolerance when subjected to a high injection temperature. If a polymer has little temperature tolerance it may precipitate out of the solution upon injection, thereby reducing performance. PVCap has a cloud point of 40 °C, but a cloud point in excess of 70 °C is required for some field applications. Musa and coworkers have reported a terpolymer (**18**) of PVCap/PVP and 2-acrylamide-2-methyl-1-propane sulfonate (AMPS) which possesses an increased salt and temperature tolerance. Inhibitor **18** contains vinyl lactam functionalities to provide KHI performance, whilst the incorporation of the AMPS group increases the water affinity of the polymer and enables high salt tolerance to be achieved.



18

Autoclave testing has confirmed that at a polymer dosage of 0.5% gas hydrate formation is prevented over the 48 hours of monitoring at a subcooling of 10.3 °C representing excellent performance for a low dosage.[78] Testing of the salt and temperature tolerance concluded that a maximum injection temperature of 85 °C can be reached without polymer precipitation whilst using a 15wt% brine solution.[78] In addition to high performance in seawater, this terpolymer possesses a cloud point of 89 °C for freshwater sites.

The high cloud point criterion is also achieved by a terpolymer comprising *N*-vinyl formamide (20%), VCap (50%) and VP (30%) (**19**).[79] Synthesis within ethylene glycol yields an alternating or block copolymer having a molecular weight between 500 and 5,000,000 amu. Inhibitor **19** has a high cloud point of 89 °C in addition to good KHI performance (induction time >48 h at a subcooling of 10.3 °C).[79]



19

These recent developments highlight the considerable work being undertaken in order to meet the increasingly demanding conditions and regulatory requirements.

Formation mechanism of clathrate hydrates

Clathrate hydrate nucleation and growth has received considerable attention in recent years, both from a thermodynamic and kinetic perspective. A full understanding of the formation process will enable clearer insight into the inhibition mechanisms. In order to introduce fundamental concepts we will first provide a brief description of crystal nucleation and growth, followed by an overview of current mechanistic understanding of gas hydrate formation.

Crystal nucleation and growth

Crystallisation can be defined as the phase change from solution, melt or vapour to the solid phase, and for a solution is achieved through supersaturation. Classically, the formation of a crystal mass (and in this context a clathrate hydrate mass) proceeds *via* nucleation followed by crystal growth. As the solute concentration increases (towards supersaturation) dissolved molecules begin to aggregate, enabling the formation of a critical nucleus; an essential precursor for further growth.

The process of nucleation can be artificially induced (*i.e.* through introduction of crystal seeds, a process termed secondary nucleation) or can occur spontaneously (primary nucleation).[80] In order for nucleation to occur, it is necessary to overcome the interfacial energy barrier, which is the difference between the free energy of the molecule within the bulk ΔG_v and the surface ΔG_s; it has a positive value and in effect represents the instability of the growing, sub-critical nucleus in comparison to liquid or solution phase species.[80] Once the critical size is achieved, the interfacial energy becomes small relative to the bulk crystal energy and hence provides no further hindrance to crystal growth. As a result dissipation of supercritical nuclei is disfavoured and crystal growth continues until the supersaturation is depleted to the solubility limit. The time taken for the formation of a critical size nucleus is known as the induction time. The free energies associated with this process are plotted on the graph shown in Fig. 7, which shows the free energy associated with achieving a nucleus of critical size, and the energetic favourability of growth once the critical radius has been met.

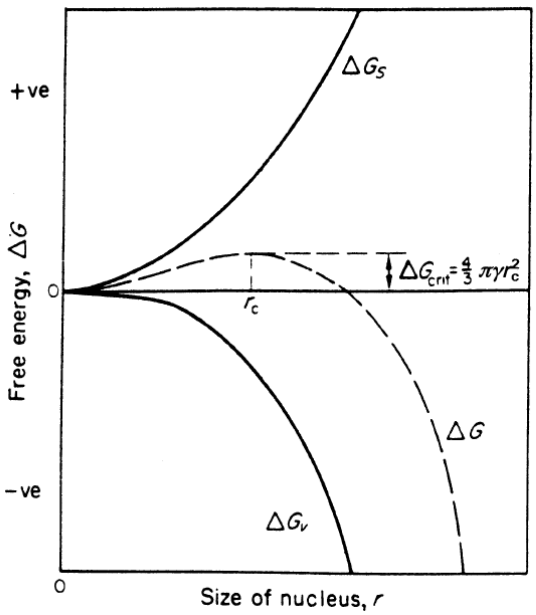


Fig. 7 Gibbs free energy of a crystal nucleus as a function of particle radius (reproduced with permission from ref.[81])

While homogeneous nucleation can occur in ultrapure systems, there have been reports as to the difficulties in achieving such a pure system.[24] In fact, heterogeneous nucleation is far more commonly encountered, on substrates such as a surface (*e.g.* pipe wall) or foreign body (*e.g.* a dust particle).[81] Kashchiev and Firoozabadi have reported kinetics of gas hydrate nucleation (both heterogeneous and homogeneous nucleation), and the effects of inhibition additives upon both nucleation pathways.[82]

Following nucleation, crystal growth can occur by the diffusion and incorporation of growth units or "building blocks" onto the critical nucleus surface.[80] There are two proposals for the site of crystal growth, these being the Terrace-Ledge Kink theory or growth at screw dislocation sites.[80] The Terrace-Ledge Kink theory (also known as the Kossel-Stranski model) assumes the pre-existence of steps on a crystal surface, whereby it is preferable for maximisation of contact sites. The kink site is most preferable for the growth of the crystal, as this provides the site with the highest degree of coordination to an incoming growth unit and therefore imparts the greatest stability.[80] A plausible source of steps and kinks is through the formation of dislocations (many dislocations may pre-exist on crystal surfaces due to their imperfect nature).[80] Screw dislocations result in a spiral growth pattern and are the consequence of atom displacement along the dislocation line.[81]

Gas hydrate nucleation and growth

Clathrate hydrate formation is known to be stochastic (randomly determined), which makes the conclusive determination of a mechanism very challenging. Hydrate nucleation is believed to occur at the water-hydrocarbon interface, as this is the site of the necessarily high concentrations of both guest and host species, thereby making the attainment of a critically sized nucleus more likely.[24, 83] The site of hydrate nucleation was investigated by Long and Sloan in 1996, studying mixtures of deionised water and Green Canyon gas in a sapphire tube.[84] They observed that upon dissolving gas molecules in liquid water, small needles of hydrate crystals formed at the interface (at 277 K and 6.9 MPa); whilst the induction time was not reproducible between experimental runs, the investigation seems conclusive that hydrate nucleation originates at the interface.[84]

Recently, Ohmura and coworkers used videographs to study the growth of crystals at the liquid-gas interfaces for systems containing gaseous methane, ethane or propane.[85] A water droplet was held on a Teflon stage placed within a test cell, wherein the temperature and pressure could be monitored and maintained.[85] The air environment within the test cell was replaced with hydrocarbon gas (*e.g.* methane) and the temperature reduced to promote hydrate formation.[85] By examining the sequential videograph images it was concluded that nucleation occurred at a random point upon the water droplet, and was followed by growth to cover the surface with a polycrystalline layer (Fig. 8).[85] Additionally, a relationship between subcooling and crystal morphology was observed, with high subcooling resulting in small sword-like crystals, and low subcooling leading to larger polygon crystals.[85]

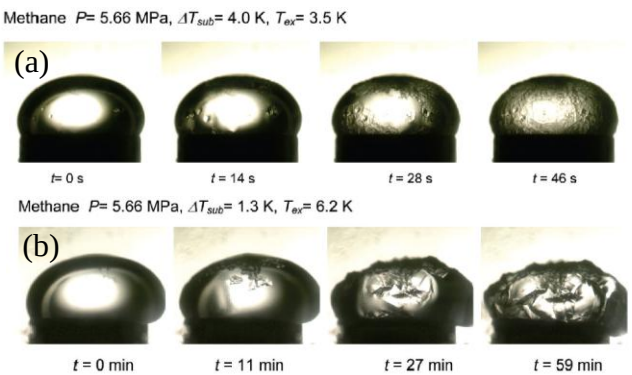


Fig. 8 Videographs showing the growth of methane hydrate on the surface of a water droplet (a) high subcooling and (b) low subcooling (reproduced with permission from ref. [85])

There exist several suggestions as to the hydrate nucleation mechanism, including the "labile cluster" hypothesis, interfacial nucleation and local structuring nucleation; these will be addressed in more detail below.

(1) The "labile cluster" hypothesis was proposed by Sloan and Christiansen in 1994 (Fig. 9), identifying the clustering of water molecules when the appropriate temperature and pressure conditions occur.[86] Once gas molecules (guests) are dissolved within the water, labile clusters form, which are metastable species of below critical size which can either dissipate or agglomerate. Upon agglomeration, and the attainment of a critical size, growth of the hydrate may then begin.[86]

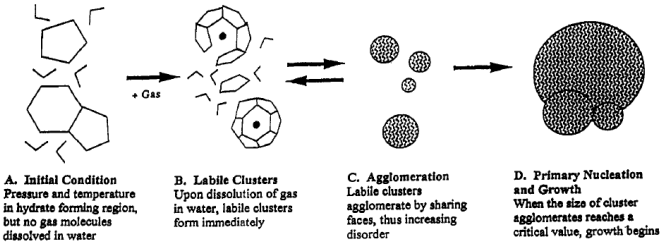


Fig. 9 Labile cluster hypothesis (reproduced with permission from ref. [86])

(2) The interfacial nucleation mechanism hypothesis was proposed by Long and Kvamme, wherein the gas molecules are transported to the interface. Surface diffusion allows the migration of the gas molecules to the desired site where cage formation of water molecules can occur.[24]

(3) There are a few reports into the local structuring nucleation postulate, obtained through molecular simulation studies. Baez and Clancy used Molecular Dynamics (MD) to obtain snapshots of the molecular configurations within the bulk phase both during the dissolution of a hydrate crystal and during the growth of a hydrate crystal.[87] More recently, Radhakrishnan and Trout have used Monte Carlo simulations with the Landau free energy method (using the Landau-Ginzburg formalism) in order to provide some further simulated evidence for the local structuring hypothesis, and also to disprove the labile cluster hypothesis.[88] The hydrate of choice for study in this instance was the CO_2 hydrate, which is known to nucleate at the liquid-liquid interface.[88] Guest molecules arrange themselves in a configuration similar to the clathrate hydrate, as a result of thermal fluctuation. Consequently, water molecule structuring is perturbed relative to the bulk phase and providing the number of guest molecules is high enough, a critical nucleus may be attained, and the growth of a hydrate cluster may then result.[88] MD simulations of methane hydrate nucleation were undertaken by Moon *et al.* in 2003, studying the nucleation at the water-methane interface.[89] Whilst full crystallisation was not observed during the timescale of the investigation, it was noted that at moderate subcooling rapid ordering (with clusters of 280 water molecules) occurs within 10 ns.[89]

In further Molecular Dynamic studies, Walsh *et al.* have simulated the nucleation and growth of methane hydrate, with the resulting structure being a combination of structure I and structure II.[90] Following nucleation and growth the crystal is believed to comprise both structure I and structure II cages, linked by $5^{12}6^3$ cages. In this simulation, small face-sharing cages (structure II) form initially, but sterics and thermodynamics favours the later formation of the structure I cages.[90]

In situ neutron diffraction has provided insight into hydrate formation, for carbon dioxide hydrate (from deuterated ice)[91], propane hydrate[92] and methane hydrate[93]. Henning *et al*. used neutron powder diffraction between 230 – 290 K to study the formation of CO_2 hydrate from deuterated ice crystals.[91] Whilst initially fast conversion of ice to hydrate is observed, this is followed by a diffusion-limited stage.[91] Conclusions of this work propose that the formation of hydrate proceeds in the quasi-liquid layer.[91] H/D isotopic substitution was used in the methane hydrate study in order to probe the environment of dissolved methane molecules, concluding that even within the liquid phase water clusters are formed around methane.[16, 93]

There is a plethora of work investigating whether nucleation of hydrates occurs directly to yield the thermodynamic species or whether it goes *via* a metastable intermediate.[94] Several MD studies have suggested that nucleation proceeds *via* an amorphous intermediate, which then undergoes a solid-solid rearrangement to yield the familiar crystalline clathrate species.[95-97] In contrast, recent work examining multiple MD simulations for methane clathrate hydrate nucleation indicates that nucleation occurs predominantly *via* a set of seven Eulerian cages which can interconvert and form solids with long-range order.[94] The results imply that templates for the exclusive growth of the thermodynamically preferred crystalline phase can form almost immediately upon nucleation.[94]

Monte Carlo algorithms have been used to model the interactions between PVP and gas hydrates (simulating a structure II hydrate), concluding that the effects of PVP upon the incorporation of gas at the hydrate crystal surface determines the inhibition effects.[98]

Once a critically sized nucleus is formed, growth of the clathrate hydrate crystal may proceed. To enable nucleus growth a continuous supply of both water and hydrocarbon gas must reach the growing crystal surface.[83] There have been many attempts to model post-nucleation growth of clathrate hydrates, and several detailed growth models have been developed.[24] In one such model, Englezos *et al*. proposed that clathrate hydrate crystal growth occurs *via* a two-step process: (1) dissolved gas diffuses from the solution bulk to the crystal-liquid interface; (2) gas molecules are adsorbed into the water network therein stabilising the hydrate lattice.[99] Whilst these studies go some way to understanding the nucleation and crystal growth of clathrate hydrates, there is still the need for experimental verification of such results, but due to the stochastic nature of hydrate formation this remains a challenge.[16] A detailed discussion of post-nucleation growth is beyond the present scope and the interested reader is directed to excellent discussions by Ribeiro and Lang[83] and Sloan and Koh[24] for more information.

Thermodynamics of hydrate formation

Van der Waals and Platteeuw developed the first thermodynamic model for the formation of gas hydrates in 1958, through the use of statistical thermodynamics.[100] Several assumptions were made in the development of this model, including: (1) the gas molecule moves within a spherical cavity; (2) each cavity can only hold one guest molecule; (3) no interactions exist between the guest molecules; (4) guests are small enough so as no distortion to the hydrate lattice results; (5) guest-host interactions are limited to weak van der Waals forces and extend only to the first shell of water molecules surrounding each guest.[100]

Further developments have been made to this thermodynamic model due to slight inaccuracies upon moving away from the ice point of water, however, this model provided the fundamental

concepts for further study. Since 1958, there have been a great deal of work into extensions of the van de Waals and Platteeuw model, for example to incorporate multi-component mixtures as in the work of Parrish and Prausnitz in 1972.[101] Also, there has been argument that in order to calculate guest-host interactions, the effects of the second and third shells should be taken into account, along with changes in the cell parameters upon guest binding; both of these concepts were not considered in the original thermodynamic model.[102] The more recent model by Klauda and Sandler removes the assumption of a constant lattice, and uses published Kihara cell potential parameters to improve accuracy of predictions.[102]

KHI Mode of Action

The mode of action of KHIs is a subject of much debate and current research and presumably depends to a considerable extent on the particular KHI in question. While the mode of action of kinetic inhibitors is not currently fully understood, there are a number of interesting reports concerning the solvation of KHIs, and their mode of interaction with a growing clathrate hydrate crystal surface that shed some light onto plausible inhibition mechanisms.

Broadly speaking there are three proposed mechanisms for the inhibition of clathrate hydrates, namely (1) adsorption of the inhibitor onto the growing crystal surface; (2) binding to a pre-critical nucleus preventing it from reaching critical size; (3) structuring of water molecules in order to prevent nucleation.

A plethora of techniques are used in order to gain insight into gas hydrate nucleation and growth, and also as to the potential mode of action of KHIs on the macroscopic and microscopic scale.[27, 103, 104] There have been several recent developments in this area, with the introduction of high-pressure powder X-ray diffraction (PXRD),[105] NMR and high-pressure calorimetry[106] to probe inhibition using chemical KHIs or anti-freeze proteins by enabling characterisation of resulting gas hydrate phases.[104] To enable the close simulation of pipeline conditions, Englezos and coworkers have recently reported the development of a small-scale stirred reactor, which allows for study of nucleation and decomposition of mixed gas hydrates when using KHIs or AFPs, whilst providing a more "real-world" environment.[107]

Macroscopic studies of KHIs

One theory, favoured by many, is that pendant functionalities upon KHIs enable the adsorption of the inhibitor to the growing crystal surface, generally through hydrogen bonding. This adsorption will effectively restrict further growth of the hydrate because of the hydrophobic backbone on opposite face of the polymer, thereby reducing the likelihood of large scale hydrate formation and hence pipeline plugging. In the case of the vinyl lactam homologues (PVP, PVCap *etc*.) it is postulated that hydrogen bonding between the amide functionality (through the carbonyl) and the hydrate surface allows for the adsorption of the KHI.[108]

The adsorption hypothesis has been tested through a consideration of the crystal growth and morphology of uninhibited and inhibited systems of THF hydrate, which crystallises as structure II, and ethylene oxide, a structure I complex.[108] When the THF hydrate is allowed to form in an uninhibited melt, the crystals adopt a regular octahedral morphology with predominantly {111} crystallographic faces. In the same uninhibited melt conditions ethylene oxide hydrate crystals are dodecahedral with rhombic {110} faces. When applied in low concentration (<0.1wt%) inhibitors **1**, **2** and **3** result in the alteration in the growth of the crystal from the regular octahedral shape to a 2-dimensional hexagonal morphology (Fig. 10). Upon use of a higher concentration of inhibitors **2** or **3** the crystal growth is completely inhibited.[108] It is believed that the hydrate is unable to grow between the polymer strands at these high concentrations and hence crystal growth halts.[108]

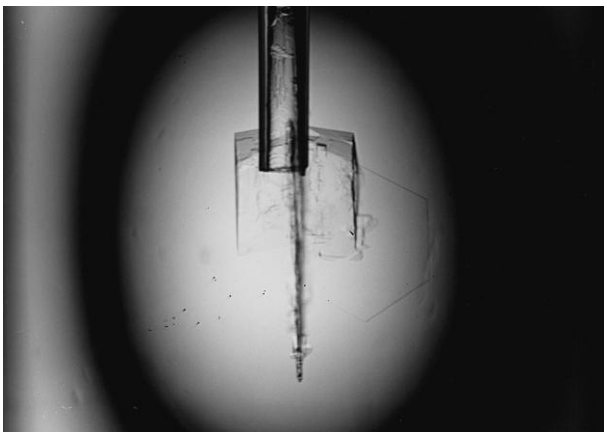


Fig. 10 Plate morphology THF hydrate crystal following transfer to solution containing 0.025wt% PVCap (reproduced with permission from ref. [108])

As a true test for this hypothesis, a hydrate crystal from an inhibited solution was transferred to an uninhibited mixture; crystal growth did not recommence, thereby indicating that inhibition is irreversible in practical terms, and lending support to the theory that the inhibitor is bound to the hydrate surface.[108] When considering the adsorption of the inhibition polymer to the hydrate, there will be many pendant groups along the length of the polymer, so it may not be too surprising that the adsorption is irreversible because in order to fully desorb this would require the many pendant groups to all simultaneously desorb from the surface.[108] This concept is an example of the principle of multivalency in supramolecular chemistry.[109]

Adsorption studies conducted by Lee and coworkers have provided evidence for the superior performance of PVCap relative to PVP, by studying the adsorption on cyclopentane hydrates.[110] Calculation of the adsorption isotherms for both vinyl lactam polymers has concluded that PVP follows the Langmuir isotherm whilst PVCap follows the BET-type; the combination of the increased molecular size and multilayer adsorption as seen for PVCap results in inhibition performance exceeding that for PVP.[110]

The superior performance of PVCap was further investigated through a study into the adsorption onto silica (with a THF water

mixture), wherein PVCap forms a rigid and compact film whilst PVP forms a loose film.[111] Silica was chosen in the study by Ripmeester and coworkers as it is known to be an ice-nucleating species, with the adsorption being monitored using a quartz crystal microbalance.[111] In order for hydrate nucleation to occur, the THF and water molecules must reach the nucleating surface, in this case the silica. The stronger adsorption of PVCap to the silica surface reduces the ability of the THF and water molecules to reach the surface, and thereby reduces the likelihood of hydrate formation; thus PVCap is the more effective inhibitor species due to its ability to adsorb more strongly.[111]

Small-angle neutron scattering studies for poly(ethylene oxide) (PEO), PVP, PVCap and a copolymer of VIMA/VCap on a model THF hydrate surface suggests that as the adsorption to the surface increases, more growth sites are blocked.[112] By studying the THF hydrate system containing inhibitor polymer both above and below the hydrate forming temperature, King *et al.* were able to observe conformational changes in the inhibitor polymers believed to be associated with the adsorption of the inhibitor to the hydrate surface.[112] By making the assumption that majority of low-*q* scattering is the result of adsorbed polymer, comparisons between the different KHIs are possible, confirming the increased efficiency of PVCap and VIMA/VCap over the PEO species.[112]

Yang and Tohidi used ultrasonic testing with attenuation analysis and fast Fourier transform analysis to probe the inhibition performance of PVCap.[113] In doing so, they concluded that gas hydrate formation occurs via a three step process; (i) nucleation, (ii) initial formation and (iii) catastrophic growth.[113] PVCap had a significant effect upon hydrate growth, which was accredited to the adsorption of inhibitor onto the growth sites.[113]

Microscopic Studies of KHIs

Raman spectroscopy can be used to gain insight as to the degree to which gas molecules are enclathrated within the hydrate lattice, and also as a means to identify the hydrate crystal structure attained.[114] The υ_1 band acts as a signature to enable the identification of the structure, with differences in υ_1 peak position observed for different hydrate structures and for "free" methane (in the gas phase), as shown in Table 4.[114]

Condition	Structure		
	I	II	H
Small Cavity	5^{12}	5^{12}	5^{12}
Position (cm^{-1})	2915.04±0.58	2913.73±0.76	2912.76±0.30
Large Cavity	$5^{12}6^2$	$5^{12}6^4$	$4^3 5^6 6^3$
Position (cm^{-1})	2904.85±0.33	2903.72±0.28	2905

Table 4 Raman peak positions (cm^{-1}) corresponding to methane in different hydrate crystal structures.[114]

The ability to calculate the relative occupancy of the hydrate cages, when coupled with information on the hydration number, can allow for the determination of the absolute occupancies, and thereby allow elucidation of the chemical potential, which is very difficult to obtain by other methodologies.[114] The Raman spectrum for enclathrated methane (as shown in Fig. 11) comprises a split band indicating the partitioning between the small and large cavities of structure I hydrate.[114] The differences between the free and enclathrated species are evident from the figure.

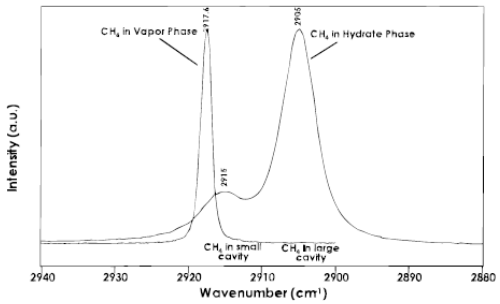


Fig. 11 Raman Spectra for υ_1 of methane vapour incorporated in the structure I hydrate. Two peaks are seen for the hydrate phase, showing that CH_4 is incorporated into both cavities of the structure I hydrate (reproduced with permission from ref. [114])

Raman spectroscopy has been utilised to provide further insight into the inhibition methodologies, and there is report of the associated shifts in Raman frequency upon methane hydrate formation (from dissolved methane), in both an uninhibited and inhibited solution system (as shown in Figs. 12 and 13, using PVCap inhibitor).[31]

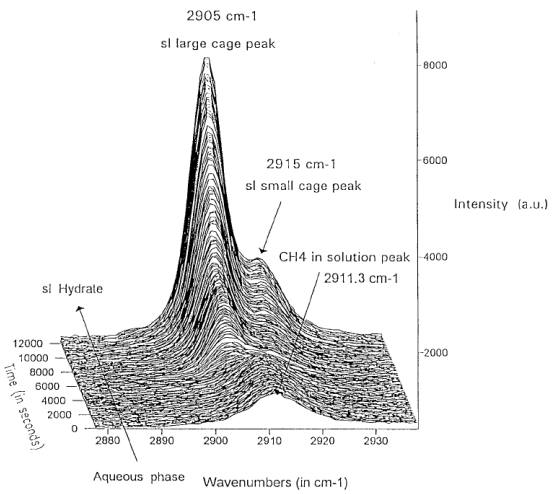


Fig. 12 Raman spectra for the uninhibited system for the transition from dissolved methane to methane hydrate, taken at a pressure of 31.7 MPa, with an initial T of 24.0 °C and final T of 2.5 °C (using a cooling rate of 0.1 °C/min) (reproduced with permission from ref. [31])

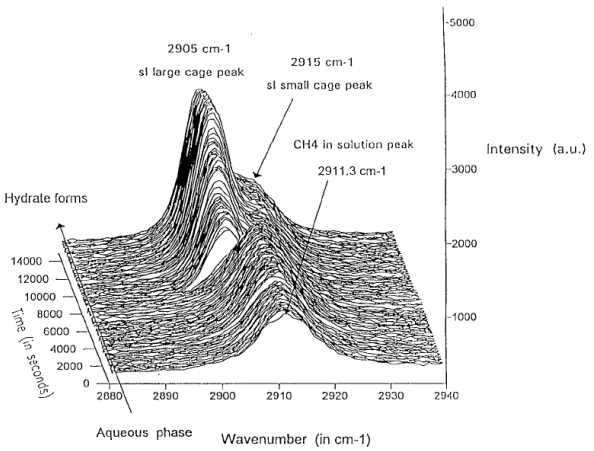


Fig. 13 Raman spectra for the inhibited system for the transition from dissolved methane to methane hydrate, taken at a pressure of 31.7 MPa, with an initial T of 24.0 °C and final T of -1.9 °C (using a cooling rate of 0.1 °C/min) (reproduced with permission from ref. [31])

The ratio between large and small cage occupancy differs between the two systems. Hydrate signals first appear 4 °C lower in the inhibited system than in the uninhibited system, and as a result a discontinuity is observed at 8500 seconds in the spectra of the inhibited system due to catastrophic hydrate nucleation.[31]

Computational modelling of KHI inhibition

As a development to their initial MD simulations for methane hydrate nucleation, Rodger and coworkers incorporated an octamer of PVP into the simulation as an initial probe for mechanism of action.[115] The model used atactic PVP and rapid incorporation of the inhibitor onto the water surface was observed, including the almost complete immersion of the pyrrolidone rings.[115] Snapshots were taken throughout the simulation clearly showing that without PVP there is evidence of water clustering, with 2D sheets of fused rings after 0.6 ns and aggregates of cages by 1.5 ns.[115] In comparison, the analogous simulation in the presence of PVP did not show such clustering, therein illustrating how PVP is believed to disrupt the process and function as a KHI.

Trout and co-workers have reported an interesting computational simulation of inhibitor binding, proposing that the process of inhibition occurs via two steps: (1) the inhibitor disrupts the organisation of the water and guest molecules increasing the barrier to nucleation, (2) the inhibitor can then bind to the surface of the hydrate crystal, thereby retarding the growth along that plane.[116] This work provides further rationale for the efficacy of PVCap compared to PVP, through consideration of the free energy of binding for the inhibitor to the hydrate surface.[116] For PVCap the binding free energy is -9.4±3.8 kcal mol^{-1} whilst for PVP it is only 0.5±3.7 kcal mol^{-1}; these results indicate that PVCap favours being bound to the hydrate surface, with the equilibrium shifted toward the bound state.[116]

The radial distribution functions (rdf) derived from MD simulations have been examined, both for monomers of PVCap and PVP, when bound to the hydrate surface and when away in the bulk solution.[116] The rdf for the interaction between the oxygen atoms of the inhibitor and oxygen atoms of water is compared to the rdf for interaction between oxygen atoms in two water molecules. There is significantly stronger correlation between the PVCap monomer-water rdf and the water-water rdf (O-O interaction), than for the PVP analogue.[116] Consequently, the carbonyl oxygen of the PVCap appears to readily locate itself in a water molecule lattice position, and thereby ensures a strong binding energy.[116]

Monte Carlo simulations have been reported for the inhibition of methane hydrate using PVP and are in agreement with the adsorption postulation.[117] Using a model of methane hydrate (structure I), the interaction of PVP with two different {001} surfaces was observed; these surfaces being at {001;0} and {001;¾}.[117] Due to great difficulties that would be associated with trying to model the entire polymer, it is necessary to consider smaller subunits of the inhibitor, and observe the interaction of these subunits with the hydrate surface. To this end, Rodger and co-workers report the calculations and results for the interaction of the monomer (*N*-ethyl pyrrolidone), dimer and analogous tetramer and octamer with the hydrate surface. The results obtained for the monomer and dimer allow for the identification of potential adsorption sites with the formation of two hydrogen bonds between the pendant hydrogen atoms on the hydrate surface and one pyrrolidone oxygen atom (Fig. 14).[117]

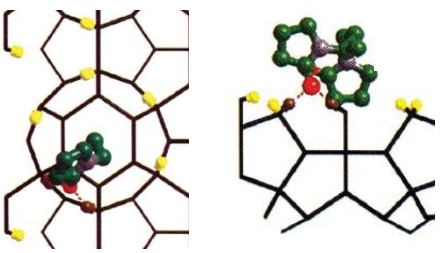


Fig. 14 Simulation result showing the formation of two hydrogen bonds between the pyrollidone oxygen atom and hydrogen atoms on the hydrate surface (brown = H of hydrogen-bonding hydrate) for (i) monomer binding and (ii) dimer binding (reproduced with permission from ref. [117])

Other studies

Recently the mode of binding for PVCap to bulk water has been probed through consideration of a dimeric model compound and use of experimental and DFT computational analysis.[55] It was proposed that by producing a dimeric model compound of PVCap and comparing it with a more rigid, unsaturated analogue, insight may be gained into the KHI mode of action. Comparisons of solution IR spectroscopic data for the dimeric model and for PVCap suggest that this model compound behaves in a similar way to the polymeric KHI. DFT calculations on the interaction of water with the model compounds suggest the presence of OH···O and CH···O hydrogen bonding within a unique pocket complementary to the water molecule. This research offers a possible rationalisation for the increased ability for the VCap oxygen atoms to function as hydrogen bond acceptors on the

basis of the high contribution to the enolate resonance form, as a result of the less strained 7-membered ring.[55] The DFT results from this work are shown in Fig. 15, highlighting the binding of the saturated and unsaturated forms to water. An X-ray crystal structure of the model dimer revealed it to be of particularly low density and lacking stabilising intermolecular interactions, suggesting a reason for the compound's hydrophilicity.

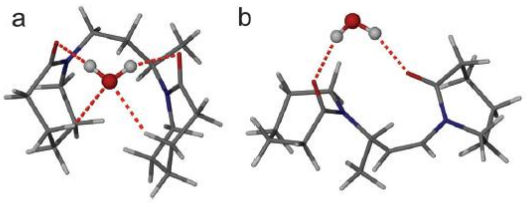


Fig. 15 DFT structures of (a) hydrogenated and (b) unsaturated dimeric model compounds derived from VCap showing binding to H_2O (reproduced with permission from ref. [55])

Investigations using Differential Scanning Calorimetry (DSC) as a means to ascertain the effectiveness of PVCap as an inhibitor, through use of an "emulsified system", concluded that an increased concentration of PVCap enhances the inhibition properties of the polymer.[118] Analysis of the thermogram obtained from use of the emulsion system both with and without the PVCap inhibitor indicates that inclusion of the inhibitor is effective at delaying the hydrate nucleation time; this is observed by a broadening of the peak in the DSC thermogram.[118]

Anti-agglomerants

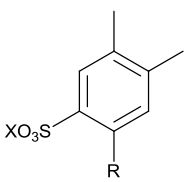
Anti-agglomerants are species which interact with the liquid hydrocarbon phase and rather than inhibiting the crystallisation of clathrate hydrates, they prevent the agglomeration of small clathrate hydrate crystallites and ensure that a free-flowing slurry is maintained. The main advantage associated with the use of AAs is that performance at high subcooling is superior to that of KHIs. There is the necessity for the presence of a liquid hydrocarbon phase for AAs to function, and as such they are not suitable for all field site applications. In general, it is possible to split AAs into two types: (1) products forming a water-in-oil emulsion as produced by the French Petroleum Institute (IFP) and (2) species comprising hydrophobic tail(s) and hydrate-philic head group(s) as identified by Shell.[24] As expected, these species have different modes of action, which can be addressed through a consideration of the chemistries involved.

In the late 1980s, Conoco reported that surface active agents comprising phosphonates, phosphate esters and polymers such as polyacrylamide and polyacrylates inhibit the agglomeration of clathrate hydrates.[119] In general, a high concentration of such surface active agent is required for good inhibition performance,[119] thereby reducing the economic viability of such species. Inhibition performance has since been exceeded at lower concentrations using alternative AAs, and as such further work in this area has not been reported.

IFP exploited the observation that upon mixing gas, fluid and specific amphiphilic compounds under conditions at which hydrates typically form, the mixture will thicken but no plugging occurs.[120] Thickening is due in part to the presence of dispersed hydrate particles within the fluid, with dispersion resulting from the presence of the amphiphilic compound, but key to their functionality as an anti-agglomerant is that no blockage results.[120] To this end, IFP explored the use of non-ionic, anionic and cationic amphiphilic compounds as a means to ensure that any hydrate crystals which do form remain dispersed within the fluid mixture and thereby remain transportable.[120] Optimisation of such species concluded that non-ionic amphiphilic compounds containing amide functionality were highly successful, for example the inclusion of 0.25wt% of coconut diethanolamide results in hydrate formation occurring at 7.5 ^{o}C with no blockage observed during the test which extended to -10 ^{o}C. These results indicate that while these species allow hydrates to form, they effectively ensure that agglomeration into a plug does not occur.[121] Addition of amphiphilic compounds is economically advantageous, as less than 0.5wt% (relative to the water phase) has proven successful.[120]

Application of amphiphilic compounds results in a water-in-oil emulsion, with the hydrates confined to water droplets.[28] The confinement of hydrate particles within water droplets effectively prevents their agglomeration, a mechanism utilised to great effect by IFP.

Shell has identified that alkylarylsulfonates function successfully as gas hydrate anti-agglomerants when 0.1-3 wt% (based on the water content) of such species is added to the pipeline fluid.[122] Compound **20** shows the general structure of such species, where X represents H, Na or K and R is an alkyl group.[122]



20

Whilst these compounds do act to inhibit agglomeration, inhibitor performance has since been exceeded by current AAs (*e.g* quaternary ammonium surfactants), and thus these species are not of current application.

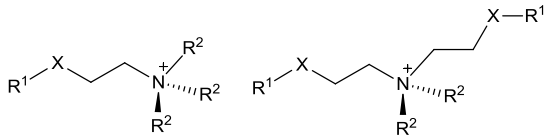
Use of quaternary tri- or tetraalkylammonium, or phosphonium, salts for inhibition activity has proved very fruitful for the petrochemical industry. Preliminary investigations into performance was undertaken through the monitoring of deformation of hydrate crystals upon addition of the inhibitor, whereby addition of 0.5wt% of such salts to a THF-water model system resulted in the severe deformation of crystals from perfectly hexagonal plates to crumpled sheets.[34]

In the case of the tetraalkyl species further modification of the water structure at the hydrocarbon-water interface may further

enhance inhibitor performance.[34] AAs containing an alkyl chain arm can effectively attach to the pipeline walls, thereby preventing the adhesion of hydrate particles to such surface; this will reduce the likelihood of full pipeline blockage.

Continuing with their postulate of inhibition by emulsification, IFP have synthesised an array of polymeric emulsifiers[123-125] such as compounds containing the product of the reaction of derivatives of polyalkenylsuccinic anhydride (or acid) with polyethylene glycol monoether. More specifically, the focus was on obtaining an amphiphilic compound with a hydrophilic lipophilic balance (HLB) of between 2 and 7 (maximum of 8) with molecular weights chosen in order to achieve such balance.[124] Such amphiphilic compounds can be added in concentrations ranging 0.1-5wt% (based on water content), thereby minimising cost. The reaction between polyisobutenyl succinic anhydride with polyethylene glycol monomethyl ether (in xylene) yields a product with a hydrophilic lipophilic balance of 4.9, which effectively inhibits the formation of a hydrate plug for a period in excess of the 24 hours of monitoring in a mini-loop testing system.[124]

At the same time, work was being undertaken into optimising the use of quaternary AAs.[28] Due to the hydrophobicity of alkyl chain arms, it is possible to affect the solubility of the anti-agglomerant species; attachment of two "tails" leads to a more oil-soluble species, whilst one "tail" leads to increased water solubility (*e.g.* compounds **21** and **22**).[28]



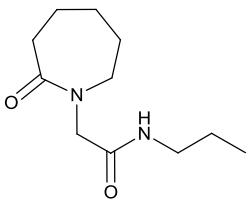
21 **22**

Where R_1 = long chain; R_2 = *n*-butyl, *n*-pentyl or isopentyl; X = spacer group.[28]

Single tails AAs comprising a tail of 10-14 carbon atoms, a tributylammonium or tripentylammonium headgroup and an anion are reported as being very effective in saline conditions (subcoolings of greater than 20 ^{o}C have been achieved), however efficiency is significantly reduced in freshwater applications.[28] Whilst single-tailed AAs may appear to be the ideal species for application there are concerns with regard the toxicity and biodegradability of these compounds; the low biodegradability would result in the persistence of these toxic compounds in the environment for a prolonged time period.[28]

In an attempt to overcome the shortfalls of the single-tailed AAs, the twin-tailed analogues formed the focus of research by the Dutch Shell team.[28, 126] Inhibition performance, as measured through hydrate recirculation testing, was very encouraging for dibutyldicocylammonium bromide, with the conversion of hydrates into a very fine powder and thereby the prevention of agglomeration.[126] An important consideration for industry is whether an inhibitor remains functional following a restart if pipeline flow has been interrupted (whether scheduled or not).[127] The use of the di-ester of di-butyl-di-ethanol ammonium bromide and coconut fatty acid offers advantages as it enables pipeline flow post-restart whilst also decreasing the temperature of formation for hydrates.[127]

An array of commercially available surfactants, under the trademark name of Span^{TM} have been found to function successfully as hydrate inhibitors, although a concentration of 3wt% is required to achieve the desired response.[128] Span^{TM} compounds are surfactants based on natural fatty acids and sorbitol. Sloan and coworkers explored the performance of Span 20, Span 40, Span 60 and Span 80 in contrast to analogous synthetic surfactants in order to monitor the ability to suspend hydrate particles.[128] As a measure of performance, high pressure apparatus was used with a change in the stirrer motor current being indicative of plug formation.[128] In the case of anti-agglomerants, simply measuring the gas consumption does not give a good representation of the inhibitor performance, as hydrates are allowed to form and thus gas consumption will increase, but this does not necessarily mean that a plug has resulted.[128] Of the species synthesised by the group, the performance of dodecyl-2-(2-caprolactamyl) ethanamide (**23**) was most promising due to its efficacy at very low concentration (0.75wt%), however there are some concerns with regard the commercial viability due to the cost of synthesis of such species.[128]



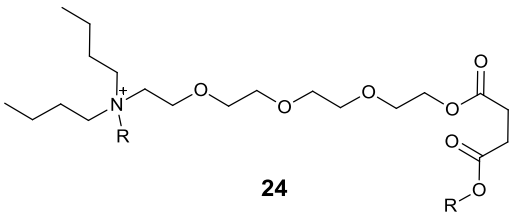
23

It seems unsurprising that this compound would act successfully as a hydrate inhibitor as we have seen earlier that the caprolactam ring functionality provides good performance (as a KHI).

By the end of the 1990s the best high performing surfactant AAs were the quaternary surfactants with 2 or 3 butyl (or pentyl) groups, as initially discovered by Shell. Whilst other species were reported, the inhibition performance was exceeded by the quaternary ammonium surfactants (QAS) and so there has been an influx of new compounds of this type reported which perform effectively as inhibitors.[28]

The main issue associated with the use of QAS is the associated environmental impact, with toxicity remaining a concern.[28] Shell proposed that addition of an inorganic salt (with a second polar phase) could be added to the effluent in order to enforce a phase separation whereby ionic surfactants or polymeric surfactants could be recovered.[129] The recovery of surfactants effectively reduces the associated environmental impact, although this requires the addition of further chemicals to the effluent which brings additional cost, so preference is for modification of the QAS prior to addition rather than the later recovery. Alternatively, anionic polymers such as polycarboxylic acids, polysulfonic acids, polyphosphoric acids and polyphosphonic acids have been found to successfully detoxify onium compounds

with the compound remaining in the aqueous phase.[130] The potential to reduce the toxicity associated with QAS compounds further enhances their potential application and unsurprisingly a number of field trials have been reported, particularly in the Gulf of Mexico.[131] The incorporation of an ether linkage within the inhibitor compound also improves the water dispersibility.[132] Clariant have more recently patented an array of alternative gas hydrate inhibitors such as **24**, where R is a long alkyl chain.[133, 134]



24

There have been many developments in the area of AAs over the past 15 years, with optimisation of performance a current topic. The application of AAs seems an encouraging research area with many companies maintaining considerable research investment in the development of new compounds.

For a comprehensive overview of LDHI developments, including species developed which failed to reach field site application, the interested reader is directed to an excellent review by Kelland.[28]

Conclusions

Due to the many problems associated with the plugging of pipelines as a result of clathrate hydrate formation, the development of inhibitor compounds is paramount. Application of LDHIs circumvents the need for large concentrations of chemical species, as is necessary when using thermodynamic inhibitors. KHIs are highly utilised inhibitors after significant research development has been undertaken, with use of such species prevalent when subcooling is below 10 ^{o}C. Current research is focussed on improving KHI design for application in increasingly challenging and highly regulated environments, with issues such as biodegradability, salt tolerance and high cloud point receiving increasing prominence. The mechanism of action of KHIs has not been conclusively determined at present; work in this area would be highly advantageous to enable identification of optimal functionalities for future KHI development. With drilling for gas and oil going to greater depths and further afield, there is a need for species active at higher subcooling, and as such there has been a large rise in interest in AAs over recent years.

Notes and references

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† Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/b000000x/

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Jonathan W. Steed was born in London, UK in 1969. He obtained his B.Sc. and Ph.D. degrees at University College London. He graduated in 1993 winning the Ramsay Medal. After two years as a NATO postdoctoral fellow at the Universities of Alabama and Missouri with Jerry Atwood he was appointed as a Lecturer at Kings College London in 1995. He moved to Durham University in 2004 where he is currently Professor of Inorganic Chemistry. He is the recipient of the RSC Meldola Medal (1998), the Bob Hay Lectureship (2008) and the RSC Corday-Morgan Prize (2010). His interests are in molecular materials and supramolecular gels.

Table of Contents Entry

This review introduces the chemistry of low dosage clathrate hydrate inhibitors, focussing on recent refinements in mechanistic understanding and chemical design, and the consequently evolving and increasingly fine-tuned properties of these fascinating compounds.