Design and synthesis of macrocyclic ligands for specific interaction with crystalline ettringite and demonstration of a viable mechanism for the setting of cement

Jonathan L. W. Griffin,[a] Peter V. Coveney,*[b] Andrew Whiting *[a] and Roger Davey [c]

[a] *Department of Chemistry, Faraday Building, University of Manchester Institute of Science and Technology, PO Box 88, Sackville Street, Manchester, UK M60 1QD*
[b] *Centre for Computational Science, Queen Mary and Westfield College, London, UK E1 4NS*
[c] *Department of Chemical Engineering, University of Manchester Institute of Science and Technology, PO Box 88, Sackville Street, Manchester, UK M60 1QD*

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Cementitious materials are among those most widely used by mankind while being among the least well understood. The detailed physicochemical processes involved in the hydration and setting of cement slurries are very complex, and a clearly defined quantitative account is still lacking; indeed, even the composition of the cement powder itself is not known exactly. Still less has there been any understanding of the mechanism by which numerous known retarders of the cement setting process act. In this article, we detail the synthesis of novel macrocyclic organophosphonate retarders **1a** and **2a** which were developed by rational methods. Attempts to synthesise these compounds as phosphonate ester derivatives were universally unsuccessful, however direct modification of the parent hexaaza- (**3**) and trioxatriaza-18-crown-6 (**5**) derivatives was successful, to provide the phosphonic acids **1b** and **2b** respectively. Subsequent testing of these compounds showed their ability to inhibit the growth of crystalline ettringite and delay the setting of cement. These results support the hypothesis that the formation of crystalline ettringite is the rate determining step in the setting of cement.

Introduction

Cementitious materials have been used since Roman times and are still one of the most widely used materials today, and yet amongst the least well understood. They have proved essential to both the oil and construction industries, and although considered as being low-tech materials, they are essentially very complex.

In the oil industry, as part of the drilling process, it is necessary to strengthen the bore-holes before extraction of the oil commences. This is generally achieved using cement in very large quantities in order to line these bore-holes and maintain their structural integrity. Depending on the location of the oil reservoir beneath ground-level, the bore-holes will vary in depth from a few hundred metres to several kilometres. It follows that a deeper borehole will require more cement, and therefore it will take longer to pump the cement into place. The obvious problem associated with this is the premature setting of the cement before pumping is complete. It would therefore be of great importance to the oil industry[1] to discover an additive which was capable of delaying the setting time of cement, while, at the same time, leaving other properties, such as the speed of compressive strength development, unchanged.

The mechanism by which currently used additives work as cement retarders is not very well understood.[2] However, it has been established[3] that certain phosphonates are effective cement retarders. At the present time, however, the approach used to find effective cement retarders is purely empirical, and large amounts of time are expended in screening new additives. It would be highly beneficial if theoretical techniques could be used to evaluate the potential of new retarders, therefore reducing the amount of time spent designing new formulations.

The principal reaction leading to the setting of cement involves the hydration of tricalcium silicate (denoted by C_3S), present as a mass fraction of 50–70% of the cement grains, forming calcium hydroxide and hydrated calcium silicate gel (denoted by CSH) [eqn. (1)]. It is this gel which forms set cement.

$$C_3S + nH_2O \longrightarrow CSH + Ca(OH)_2 \qquad (1)$$

Also present in cement grains, but in smaller quantities, is tricalcium aluminate (C_3A), which is the fastest hydrating phase in cement. Gypsum is added to cement to slow this reaction down, thereby avoiding a 'flash set' of the material. Calcium aluminate then reacts with the sulfate ions from gypsum, forming the mineral called ettringite as shown in eqn. (2).

$$C_3A + \text{gypsum} \longrightarrow \underset{\text{Ettringite}}{[Ca_3Al(OH)_6]_2(SO_4)_3\cdot 26H_2O} \qquad (2)$$

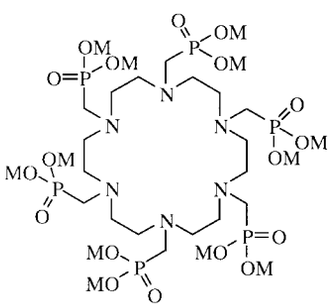
It is thought that ettringite forms initially as a gel, and over a period of time changes into its crystalline needle-like form.[2,4] Ettringite gel is impermeable to water and is deposited onto cement grains thus rendering them immune to hydrolysis. Once, however, crystallisation of ettringite commences, water can penetrate through to the cement grains and hydrolysis of the tricalcium silicate ensues and setting of the cement can then proceed. Using this information, it has been postulated[5] that if the nucleation and growth of crystalline ettringite, from its gelatinous precursor, can be retarded, then so can the setting of cement.

A paper recently published by Ramachandran[3] *et al.* considered the role of organic phosphonate retarders in the hydration of Portlandite cement. It was proposed that the powerful retarding effect of these phosphonates on the setting of cement is related to their complex formation with Ca and Si, both on the surface of the silicates and in the solution phase. However, no evidence is presented to support this theory. Nevertheless,

the main conclusion drawn from these studies was that phosphonates appear to be much more potent retarders than those normally used in cementing practice.

Organic phosphonates have also been studied extensively as barium sulfate inhibitors.[6–9] Davey *et al.* have shown that the techniques of molecular modelling and rational design can be used to evaluate the effectiveness of a particular retarder. In these papers it was proposed that the phosphonic acid groups are able to replace sulfate sites on a growing crystal face of barium sulfate, thus preventing any further deposition of inorganic matter and therefore inhibiting crystal growth. It was also shown that these inhibitors indeed work as barium sulfate crystal growth retarders. Coveney *et al.*[5] reasoned that since crystalline ettringite also contains sulfate groups, it was possible that organophosphonates might, in the same manner, also be able to inhibit the crystal growth of ettringite, and hence retard cement setting.

On the basis of modelling work[5] it was found that the most important structural motif associated with the efficiency of the inhibitor comprises of two aminomethylenephosphonic acid groups separated by an ethylene linkage. From the (001) face of ettringite (the fastest growing face in the crystal), it could be seen that six sulfate groups are situated in a hexagonal array around the octahedral $Al(OH)_6$ units. With this important structural motif, and the arrangement of sulfate ions on the crystal surface in mind, hexaaza analogue **1a** was designed,



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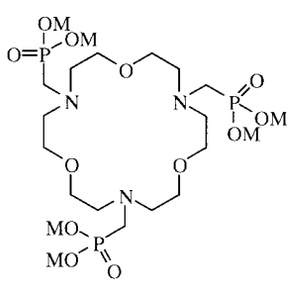
a; M = Na
b; M = H



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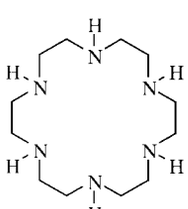
a; M = Na
b; M = H



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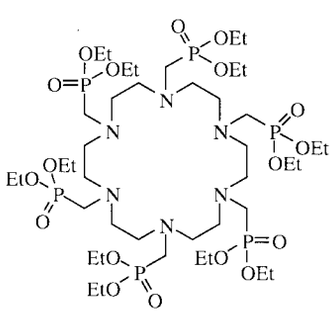

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together with trioxa derivative **2a**.[5,9] In this paper we fully discuss this work, including the synthesis of **2a** and comparative tests of **1a** and **2a** with ettringite and cement.

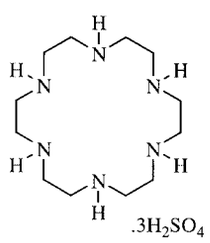
Results and discussion

During modelling studies of the docking of **1a** with ettringite,[5] a great deal of flexibility is required, however it was noted that hexaphosphonate **1a** was more conformationally rigid than was expected, and the phosphonate groups lie close to the plane of the macrocycle during molecular dynamics simulations. This rigidity, it was thought, may decrease the efficiency of **1a** as a cement retarder. In contrast, a similar molecule was studied, also based on the 18-crown-6 structure, but with the corresponding trioxatriaza ring system **2a**.[10] This compound possesses three methylene phosphonic acid moieties, as well as possessing a complementary geometric fit with the ettringite surface, and macrocycle **2a** also seemed to be more structurally flexible than the hexaaza analogue **1a**. It was capable of conformational flexing during the docking procedure and it was therefore predicted that triphosphonate **2a** would be a more effective retarder than hexaphosphonate **1a**.

It was therefore predicted that rationally designed additives could act as potential inhibitors of crystalline ettringite and may, as a consequence, inhibit the setting time of cement. Due to the immense complexity of cement systems, all studies to date have been purely theoretical, however, here was an opportunity to test the hypothesis of the mechanism of cement setting, starting with the synthesis of both retarders **1a** and **2a**, followed by an assessment of their performance as inhibitors of the crystal growth of ettringite, and retarders of the setting of cement.

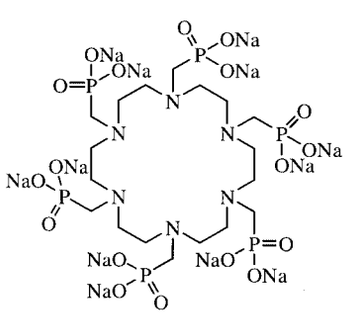
Macrocyclic synthesis

In order to access macrocycle **1a**, we started from the commercially available parent macrocycle (1,4,7,10,13,16-hexaazacyclooctadecane, or hexacyclen) **3**,[11,12] our first target being the ethyl ester analogue **4**. It was expected that simple alkylation of **3** could be achieved *via* reaction with diethyl iodomethylphosphonate. However, despite trying a wide variety of bases and solvents in this reaction, no reaction was observed. We then turned to an alternative method analogous to the Mannich reaction[13] using diethyl phosphite and formaldehyde diethyl acetal, however, neither boron trifluoride–diethyl ether nor titanium tetrachloride effected Lewis acid-catalysed formation of **4**. A more direct method to the phosphonic acid **1b** has however been reported,[14] involving similar methods to that reported by Moedritzer *et al.* [eqn. (3)].[15] Thus, the reaction of

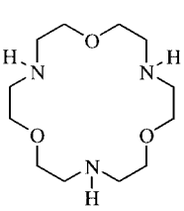


3

1) CH_2O
$HPO(OH)_2$
HCl
2) NaOH



1a



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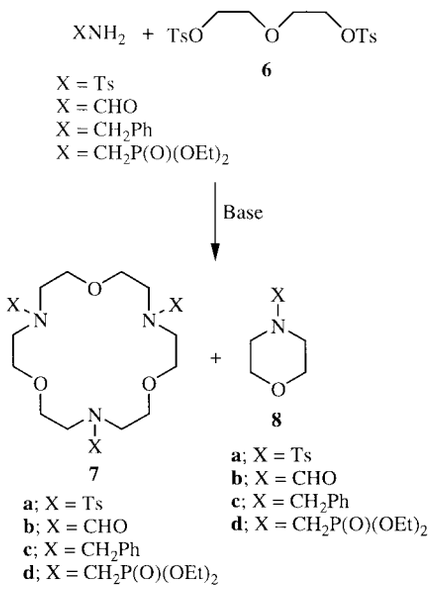
ammonium salt **3** with formaldehyde and phosphorous acid gave the required hexaphosphonic acid analogue of **1b** in high yield (86%). Simple buffering of the resulting acid with sodium hydroxide produced aqueous solutions of the required dodecasodium salt **1a** as required for testing (*vide infra*).

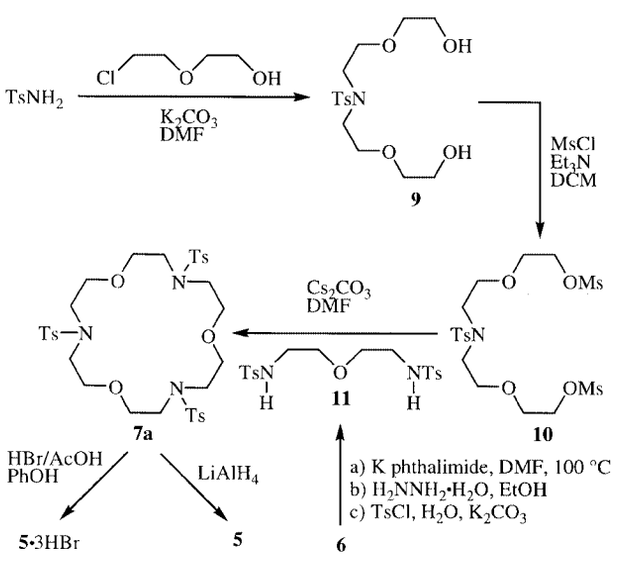
We then turned to the synthesis of triphosphonate **2a**. An

obvious starting point for the synthesis of this macrocycle would be the preparation of the parent macrocycle 4,10,16-triaza-18-crown-6 **5**,[10] followed by the alkylation of the ring nitrogens. Preliminary attempts to achieve a one-pot construction of macrocyles **7**, using the corresponding primary amide and amine derivatives as shown in eqn. (4), were unsucessful (the



only products being the corresponding morpholines **8**). The noteable exception to this was from attempted formation of phosphonoglycine derivative **7d**, which showed evidence for the formation of trace amounts of the larger ring **7d** (+ve ion CI mass spectrometry), together with the major N-alkylated morpholine derivative **8d**.

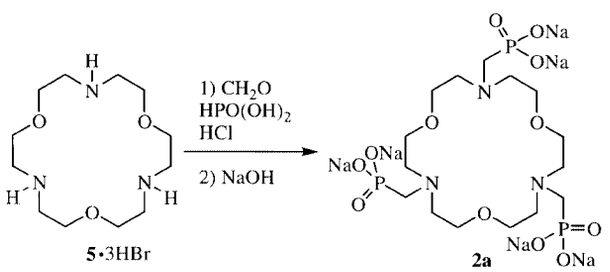
The problems associated with formation of the morpholines **8** meant that a stepwise synthesis of macrocycle **5** was required. We therefore adopted methods similar to those reported (Scheme 1),[16] but using the more reactive dimesylate **10** in



Scheme 1

place of the corresponding ditosylate. This was readily cyclised with ditosylamine **11** to provide the tritosylate **7a**, which was deprotected using literature methods[16] (HBr, AcOH, phenol) to provide **6** as the tri-HBr salt in 85% yield (Scheme 1). This procedure was more efficient than a reductive ($LiAlH_4$) detosylation (22% yield).

Once the parent macrocycle **5** was obtained it was necessary to alkylate the three ring nitrogens. Lazar *et al.*[17] have shown that macrocycles containing secondary nitrogen atoms in the ring can be alkylated to the appropriate diethylaminomethyl moiety using paraformaldehyde and diethyl phosphite in benzene. However, due to the insoluble nature of the tri-HBr salt of the parent macrocycle **5** in benzene, it was necessary to neutralise it to produce the free base using an anionic exchange resin IRA400.[18] Subsequent reaction on the basic form of **5** was found to produce the triphosphonate ester **7d**; however the yield of the reaction was low, the major product being diethyl hydroxymethylphosphonate. This by-product results from the competing reaction of diethyl phosphite with formaldehyde, which presumably occurs much faster than the intended Mannich-type reaction. Similarly, when the Arbuzov[19] type reaction was tried (with triethyl phosphite instead of diethyl phosphite) in the absence of any solvent,[20] diethyl hydroxymethylphosphonate was again produced. Despite many efforts, **7d** was difficult to separate[17] from diethyl hydroxymethylphosphonate. Hence, once again, direct conversion of cyclic triamine **5** into phosphonic acid **2b** would be more convenient, using the Mannich-type reaction.[15] Thus, reaction of **5**·3HBr with formaldehyde and phosphorous acid gave the required product **2b** after evaporation and precipitation with acetone in 58% yield. Buffering with sodium hydroxide gave solutions of the hexasodium salt **2a** (Scheme 2).



Scheme 2

Once that the synthesis of both **1a** and **2a** had been achieved, it was necessary to test them as inhibitors of the crystal growth of ettringite with a view to retarding the setting time of cement.

Testing on the ettringite system

It was necessary to find a highly reproducible and efficient synthesis of ettringite, yielding crystalline material which could then be observed under a scanning electron microscope (SEM). The reported method of synthesis[21] involves mixing six equivalents of calcium hydroxide with one equivalent of aluminium sulfate for 24 hours at 25 °C, and then leaving the sample to age for two weeks. It was found, however, that the mixing of these two solutions was only necessary for 30 minutes, and that ageing for 24 hours had no effect on the crystals of ettringite formed. Similarly, the reaction could then be repeated with the inhibitor present in the solution containing aluminium sulfate prior to mixing, in varying concentrations each time. The temperatures which cements generally experience down boreholes are often in the order of 70 °C. Therefore both of the solutions were heated to 70 °C and mixed in under five seconds, to ensure that the temperature remained constant. The ettringite crystals formed during these experiments were then separated from the reaction mixture *via* centrifugation, and the change in morphology of crystalline ettringite was observed by SEM. The resulting SEM pictures are shown in Figs. 1–5.

Ettringite grown in the absence of any additives is shown in Fig. 1, where the needles are long, thin and hexagonal and ranging from 15–50 μm in length. Figs. 2 and 3 show ettringite crystals grown in the presence of 1.0 and 4.1 mmol l^{-1} of hexaphosphonate **1a** respectively. As can be seen, at the former concentration, the needles are now shorter than those in Fig. 1, but

Fig. 1 SEM of pure ettringite.

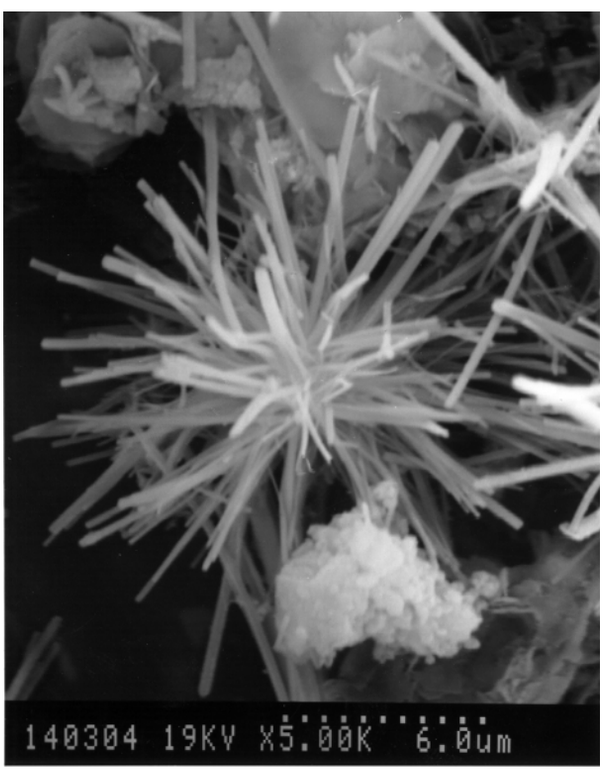


Fig. 2 SEM of ettringite grown in the presence of 1.0 mmol l^{-1} of **1a**.

are still needle-like. When the concentration of hexaphosphonate **1** is increased to 4.1 mmol l^{-1} (Fig. 3) the lengths of the crystals, on average, have been reduced significantly and are no longer needle-like. They are now short and stumpy, indicating to a certain extent that the retarders are preferentially inhibiting the growth of the once fastest-growing (001) face, over the sides of the growing crystal.

Figs. 4 and 5 show the crystals of ettringite grown in the presence of triphosphonate **2a** at concentrations of 1.0 and 4.1 mmol l^{-1}, respectively. Fig. 4 shows needles which are substantially shorter than those prepared without any inhibitor, and are still needle-like, but shorter than those formed in the presence of the same concentration of hexaphosphonate **1a**. At a concentration of 4.1 mmol l^{-1} (Fig. 5), the crystals are now very

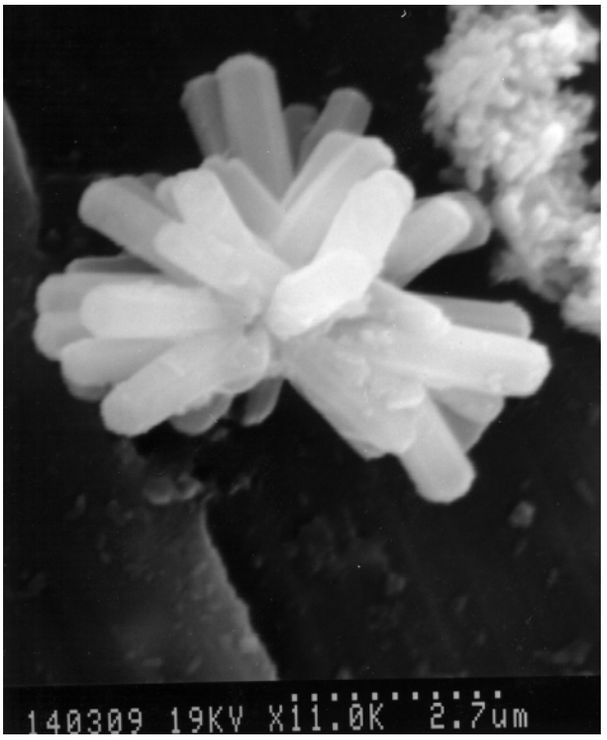


Fig. 3 SEM of ettringite grown in the presence of 4.1 mmol l^{-1} of **1a**.

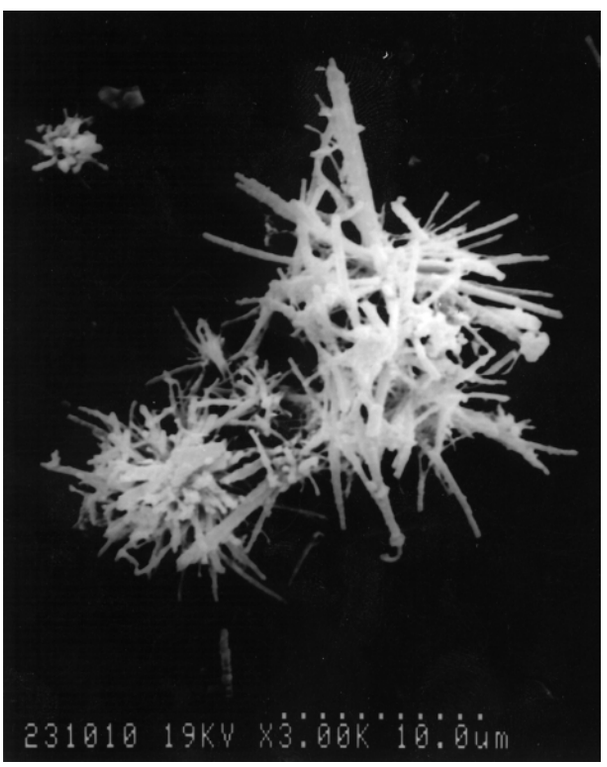


Fig. 4 SEM of ettringite grown in the presence of 1.0 mmol l^{-1} of **2a**.

short (shorter than those present in Fig. 2) and less thin in comparison to their width, indicating a selective inhibition of the (001) face.

Table 1 below shows the relationship between the concentration of inhibitors and the average crystal length of ettringite. The lengths were determined by measuring 20 crystals at each concentration of inhibitor and calculating the average length at that concentration. The aspect ratio of the crystals was found by dividing the length of the crystals by the width at each concentration. It follows therefore that a decrease in aspect ratio, with increasing concentration, indicates that the length of the

Table 1 Relationship between inhibitor concentration and average ettringite crystal length and aspect ratio

Concentration of inhibitor/ mmol l^{-1}	Length of crystals +**1a**/μm	Aspect ratio of crystals +**1a**	Length of crystals +**2a**/μm	Aspect ratio of crystals +**2a**
0	16.29	16.13	16.29	16.13
0.25	15.50	24.46	13.56	14.48
0.50	14.67	29.34	7.60	14.62
1.00	6.75	23.89	4.02	9.80
1.50	5.13	18.95	2.19	5.92
2.00	4.02	14.63	1.43	5.50
2.50	3.21	9.67	1.22	5.30
3.00	2.55	5.20	—	—
4.10	1.95	4.90	1.13	4.91
5.00	1.80	4.51	0.83	3.95

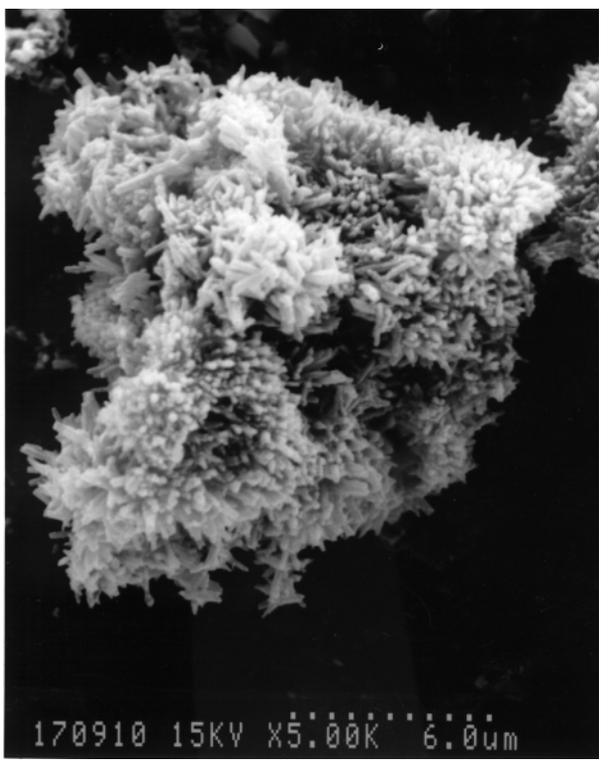


Fig. 5 SEM of ettringite grown in the presence of 4.1 mmol l^{-1} of **2a**.

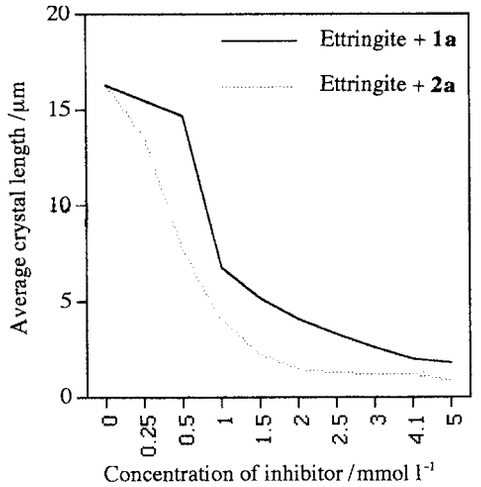


Fig. 6 Plot of average ettringite crystal length with varying inhibitor concentrations.

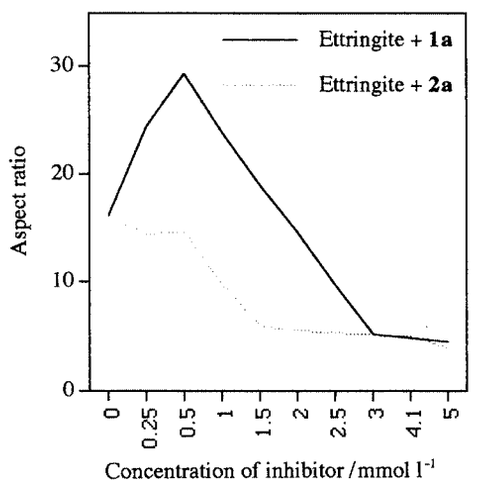


Fig. 7 Plot of aspect ratio for ettringite formed in the presence of varying concentration of inhibitors.

crystal is being reduced to a greater extent than the width. In order to clarify these data, Fig. 6 shows the average length of the ettringite crystals plotted against the concentration of each inhibitor, and Fig. 7 shows the aspect ratio of the crystals, also against concentration of each of the inhibitors **1a** and **2a**.

When growing ettringite crystals with increasing concentrations of hexaphosphonic acid **1a**, the length of the resulting crystals decreases, as predicted. However the aspect ratio (Fig. 6) increases initially, indicating that the inhibitor is attacking the sides of the crystal (and thus making them thinner) to a greater extent than the fastest growing face. With increasing concentration, above 0.5 mmol l^{-1}, the aspect ratio then drops in the predicted fashion. At a concentration of only 5 mmol l^{-1} the average length of the crystals is 1.80 μm, showing that this particular retarder is very effective at inhibiting the crystal growth of ettringite.

In the presence of increasing concentrations of triphosphonic acid **2a**, as predicted both the aspect ratio (Fig. 7) and the average length (Fig. 6) of the crystals decrease steadily, but at a faster rate than with hexaphosphonate **1a**, indicating that: (i) this particular retarder is more potent than hexaphosphonic acid **1a**; and (ii) the fastest growing face of the crystal is being inhibited to a greater extent than the sides of the crystal. Indeed this is what primarily the inhibitors were designed to achieve. The increased potency of inhibitor **2a** can be seen more clearly in Fig. 6, where between the concentrations of 0.5 and 1.0 mmol l^{-1} the average length of the crystals grown with **1a** appears to be about 15 μm, whereas in the presence of **2a**, the average size of the crystals is less than half that. Additionally, at a concentration of 5 mmol l^{-1} of **2a**, the average length of the crystals is 0.83 μm, indicating that this retarder is even more effective than **1a** as an inhibitor of crystalline ettringite. This is as predicted by the molecular modelling studies which suggests that the enhanced activity of the retarder is by virtue of the increased flexibility of triphosphonic acid **2a**, which is required during docking on to the crystal lattice.

These results are supported by X-ray powder diffractograms (shown in Figs. 8–10) of the solid products of ettringite crystallisations, carried out in the absence of additive and in the presence of 4.0 mM of additives **1a** and **2a**. Fig. 8 shows the diffractogram for a pure ettringite sample demonstrating the preferred orientation expected for *c*-axis needles, with all (*hkl*) reflections having significantly reduced intensities. In the presence of additive **1a** (Fig. 9), the relative intensities indicate significantly more equant crystal habits while at the same time the pattern indicates the presence of two other crystalline phases, calcium hydroxide ($2\theta = 47.28°$) and gypsum ($2\theta = 29.34°$), not normally seen as a product in these reactions. In the presence of additive **2a** (Fig. 10) the result is even more extreme, indicating significantly lower levels of ettringite ($2\theta = 22.9°$), some gypsum

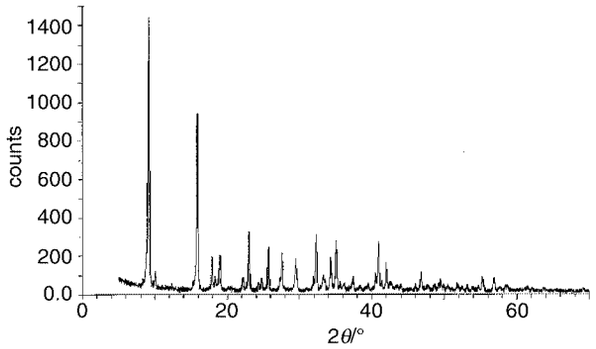


Fig. 8 X-Ray diffraction spectrum for pure ettringite.

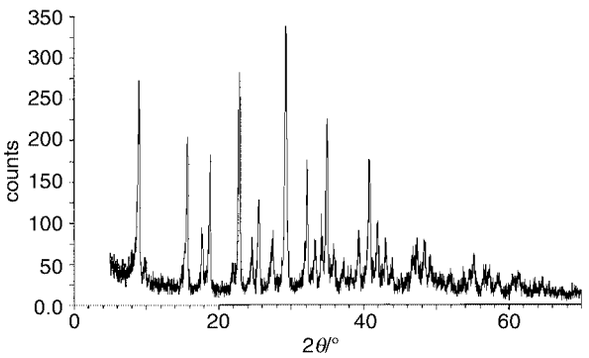


Fig. 9 X-Ray diffraction spectrum for attempted ettringite formation in the presence of 4.1 mmol l^{-1} of **1a**.

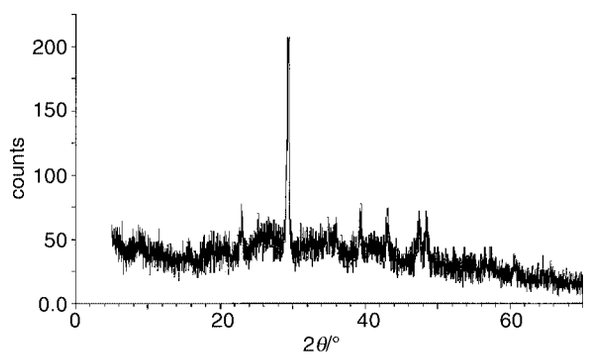


Fig. 10 X-Ray diffraction spectrum for attempted ettringite formation in the presence of 4.1 mmol l^{-1} of **2a**.

($2\theta = 29.4°$), and calcium hydroxide ($2\theta = 47.5°$), together with significant amounts of amorphous material. These data clearly confirm the observed morphological change in the ettringite crystals and also suggest that ettringite nucleation is indeed inhibited by these additives, leading to the production of amorphous material and crystalline gypsum together with a reduction in the overall reaction rate, resulting in unreacted calcium hydroxide. Again molecule **2a** is found to be the more active, as expected.

Testing on cement

In order to test the relative retardation capabilities of organophosphonates **1a** and **2a** on cements, heat calorimetry was employed, since the setting of cement is an exothermic process. In this case the start and the end of the set process can easily be detected by measuring the rate of heat evolution as a function of time.[22] All cement setting calorimetry experiments were carried out at 25 °C, a constant amount of class G cement was used (80 g), which was thoroughly mixed with 35.2 ml of water, which contained the dissolved inhibitors prior to transferring the resulting slurry to the calorimeter cells. The resulting heat

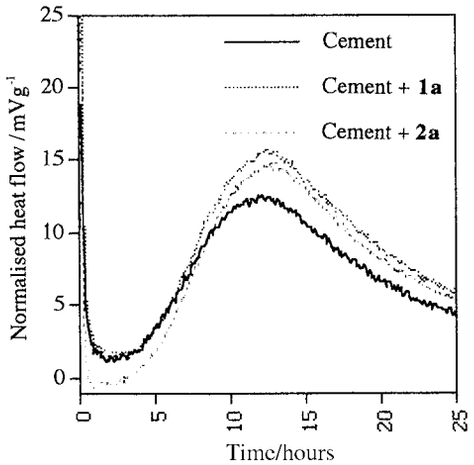


Fig. 11 Heatflow calorimetry results for neat cement and in the presence of 0.2 mmol l^{-1} of inhibitors **1a** and **2a**.

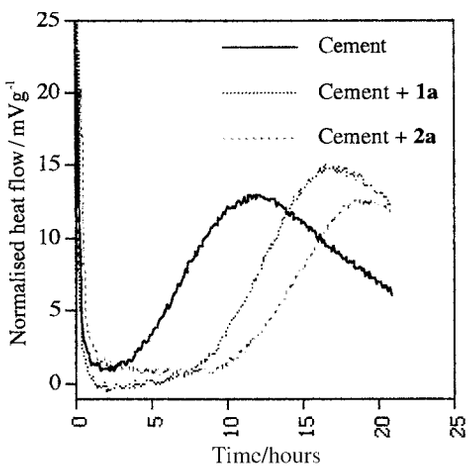


Fig. 12 Heatflow calorimetry results for neat cement and in the presence of 1.0 mmol l^{-1} of inhibitors **1a** and **2a**.

outputs (per gram of cement slurry) for retarders **1a** and **2a** (at a concentration of 0.2 mmol l^{-1}) are shown in Fig. 11.

The initial peak produced (to the left of Fig. 11) is due to the dissolution process, and, after a dormant period of about three hours, the growth of the main peak associated with the setting of cement begins. By looking at the graph it is evident that the retarders are not having the required effect on the cement at this concentration, since no delay in the setting time of the cement in the presence of the retarders is observed. The maximum exotherm produced by cement alone occurs at just over 10 hours, and in the presence of the inhibitors there is only a very small shift of the peaks to the right. As Coveney[5] previously added the inhibitors to the cement at a higher concentration, the experiment was repeated in the presence of 1.0 mmol l^{-1} of **1a** and **2a** (Fig. 12).

The resulting heat outputs (Fig. 12) show that, at this higher concentration, the retarders are having a profound effect on the setting time of cement. Again the maximum exotherm produced by neat cement can be located at about 11 hours. For the cement in the presence of hexaphosphonic acid **1a**, at a concentration of 1.0 mmol l^{-1}, the maximum exotherm occurs at around 17 hours. This equates to an increase of the setting time of about 55%. The more effective retarder therefore seems to be triphosphonic acid **2a** which, at a concentration of 1.0 mmol l^{-1}, produces a maximum exotherm at about 19 hours, indicating an increase in the setting time of 73%.

In addition to the remarkable delay in the setting time of the cement, it is evident that in both cases, the setting characteristics, as judged by the profile of the heat flow curves, remain unchanged compared with the case of neat cement, suggesting

that these compounds act to inhibit nucleation of ettringite and do not interfere with cement setting once nucleation has occurred. This is in marked contrast with the general behaviour of acyclic phosphonate cement setting retarders which both delay the onset of setting and inhibit the setting process once it has begun[5] (the maximum exotherms of these curves are substantially lower than that of neat cement). It is also noted that aged cements which have been exposed to atmospheric humidity for extended periods when treated with these additives show no delay in the onset of setting and display calorimetric profiles identical to neat cement. This result is consistent both with the specificity of these additives towards ettringite, which has presumably already formed in these aged materials, and their inability to influence other hydration products such as calcium silicate or hydroxide.

Summary

These results show that additives designed as selective inhibitors for the crystallisation of ettringite can be used to delay the onset of setting of cement slurries without interfering with the eventual setting process itself. This behaviour was discovered on the basis of two central concepts: firstly, that the formation of crystalline ettringite plays a rate determining role in cement setting, and secondly, that it is possible to rationally design compounds which are preorganised for molecular recognition at the surfaces of complex inorganic matrices, such as ettringite, and thus act as powerful crystallisation inhibitors.

Experimental

All reagents which were not prepared as detailed later were purchased from either Aldrich, Acros Chimica, Avocado or Lancaster. All were used without any further purification unless otherwise stated. Solvents were all distilled before use over either benzophenone–sodium (tetrahydrofuran) or calcium hydride (all remaining solvents) under an atmosphere of argon. TLC was performed on Merck plastic or aluminium sheets coated with silica gel 60 F_{254} (Art. 5735); the chromatograms were initially examined under UV light and then developed either with iodine vapour or a 10% ethanolic solution of molybdophosphoric acid and visualised by heating with a heat gun. Column chromatography was achieved under medium pressure, using Acros Chimica silica gel, 0.035–0.07 nm (pore diameter: *ca*. 6 nm). All anhydrous, low temperature reactions were carried out in glassware which was dried prior to use by storage in a glass oven maintained at 140 °C and cooled under a stream of argon. Evaporations were carried out using a Büchi rotary evaporator or Büchi cold-finger rotary evaporator. Kugelrohr distillations were carried out using a Büchi GKR-51 Kugelrohr apparatus. Melting points were determined using an Electrothermal melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded at 200 or 300 MHz on a Bruker AC200 or AC300 spectrometer. ^{13}C NMR spectra were recorded at 75.5 MHz on a Bruker AC300 spectrometer. Both ^{1}H and ^{13}C spectra were recorded using either $CDCl_3$ ($CHCl_3$) or DMSO as internal standards respectively. IR spectra were recorded on a Perkin-Elmer 783 equipped with a PE600 data station or a Perkin-Elmer 1605 FT-IR and UV spectra were recorded on a Perkin-Elmer 115 spectrometer. Electron impact (EI) (70 eV) and chemical ionisation (CI) spectra were recorded with a Kratos MS25. Fast atom bombardment (FAB) mass spectra were recorded on a Kratos MS50, using a *m*-nitrobenzyl alcohol matrix and accurate mass determinations were carried out on a Kratos Concept IS spectrometer.

Preparation of macrocycle 1a

A mixture of **3** (4.579 g, 8.18 mmol), phosphorous acid (4.025 g, 49.09 mmol) dissolved in water (18 ml) and concentrated hydrochloric acid (16 ml) was heated to reflux. To this mixture, formaldehyde (7.4 ml of a 37% solution in water, 98.57 mmol) was added dropwise over 1 h. After addition, the mixture was heated for a further 4 h and allowed to cool to rt. The mixture was concentrated and diluted with acetone (100 ml) and left at 0 °C overnight. The resulting off-white precipitate was removed by filtration and dried *in vacuo* for 8 h to give the phosphonic acid (7.52 g, 86%) as an extremely hygroscopic solid which was identical to that reported in the literature[14] and had satisfactory analytical properties consistent with the acid derivative of **1b**. Solutions of sodium salt **1a** were prepared prior to use by direct neutralisation of an aqueous solution of acid derivative.

Preparation of ditosylamide 11

To a stirring suspension of potassium phthalimide (21.45 g, 115.80 mmol) in *N*,*N*-dimethylformamide (150 ml), was added ditosylate **6** (20.00 g, 48.25 mmol) as a solution in *N*,*N*-dimethylformamide (50 ml) over a period of 5 minutes. After this addition, the reaction mixture was heated up to 100 °C and was left to stir for 7 hours. The contents of the flask were then poured into a beaker of ice (600 ml) which was stirred vigorously for an hour. The precipitated product was then filtered and washed with water (2 × 100 ml), and then recrystallised from acetic acid to yield the diphthalimide derivative as a white crystalline solid (12.42 g, 71%), which was identical to that reported in the literature:[23,24] mp 157–158 °C (lit.[24] 156 °C).

The diphthalimide (81.40 g, 0.22 mol) was dissolved in ethanol (300 ml) which was then heated to reflux with stirring. Then, hydrazine monohydrate (24.61 g, 0.49 mol) was dissolved in ethanol (100 ml) and added dropwise to the reaction mixture over a period of 20 minutes. The reaction mixture was then allowed to reflux overnight after which 6 M HCl (84 ml) was added. Further stirring for an hour was then followed by cooling and then filtering of the reaction mixture. The residue was washed with water (2 × 50 ml) and the ethanol was removed from the filtrate under reduced pressure, after which the precipitate was again filtered off and washed with water (2 × 20 ml). The aqueous fractions were then combined and the water removed under reduced pressure leaving an oily liquid from which the HCl salt of the diamine was precipitated with ethanol (200 ml) as a white crystalline solid (27.80 g, 70%) which was identical to that reported in the literature:[24] mp 168–170 °C.

The bis-HCl salt of the diamine (1.11 g, 6.29 mmol) and potassium carbonate (4.34 g, 31.43 mmol) were dissolved in water (30 ml) and the resulting solution was stirred. To this solution, toluene-*p*-sulfonyl chloride (2.42 g, 12.70 mmol) was added in small portions over 10 minutes. After the addition was complete, the mixture was heated to 60 °C and left for 6 hours. At this point the milky precipitate was filtered and washed with water (2 × 20 ml). The solid was dissolved in dichloromethane (50 ml) and dried ($MgSO_4$), filtered off and washed with dichloromethane (20 ml). The organic fractions were then combined and then removed under reduced pressure. The resulting white solid was then recrystallised from ethanol (20 ml) yielding **11** as a white solid (1.81 g, 70%) which was identical to that reported in the literature:[25] mp 106–108 °C (lit.[26] 118–119 °C).

Preparation of diol 9

Toluene-*p*-sulfonamide (5.00 g, 29.20 mmol) and potassium carbonate (16.14 g, 0.12 mol) were added to *N*,*N*-dimethylformamide (60 ml) and stirred. To this mixture 2-chloroethoxy ethanol (8.00 g, 64.20 mmol) was added dropwise over a period of 10 minutes. The reaction was then heated to 100 °C and left to stir for 3 days, after which the *N*,*N*-dimethylformamide was removed under reduced pressure and was replaced with dichloromethane (100 ml). The resulting slurry was then filtered through Celite, after which the remaining white solid was washed with

dichloromethane (2 × 50 ml). The organic fractions were combined and the solvent was removed to leave a viscous yellow oil. The product was purified *via* silica gel chromatography (the eluent being 9:1, EtOAc–*n*-hexane) yielding diol **9** as a colourless viscous oil (7.65 g, 76%), which was identical to that reported in the literature.[16]

Preparation of dimesylate 10

Diol **9** (2.00 g, 5.76 mmol) and triethylamine (7.00 g, 69.19 mmol) were dissolved in dichloromethane (60 ml) and stirred. To this solution methanesulfonyl chloride (1.78 g, 15.56 mmol) was added dropwise over a period of about 10 minutes. The reaction mixture was allowed to stir for 2 hours after which time TLC (8:2, EtOAc–*n*-hexane) indicated that the reaction had gone to completion. The reaction mixture was then washed with 1 M HCl (100 ml), and the organic layer was removed and the solvent removed under reduced pressure. The resulting viscous oil was purified *via* column chromatography using the above solvent system yielding **10** as a pale yellow oil (2.32 g, 80%), which was identical to that reported in the literature.[27]

Preparation of cyclic tritosylamide 7a

Ditosylamide **11** (4.92 g, 11.93 mmol) and dimesylate **10** (6.00 g, 11.93 mmol) were added to a suspension of caesium carbonate (15.55 g, 47.72 mmol) in *N*,*N*-dimethylformamide (300 ml). The reaction was heated to 100 °C and stirred for 20 hours, after which the *N*,*N*-dimethylformamide was removed under reduced pressure, and to the remaining slurry dichloromethane (100 ml) was added. The milky mixture was then filtered through Celite which was subsequently washed with dichloromethane (50 ml), the organic fractions were pooled and the solvent was removed under reduced pressure. To the resulting syrup, methanol (200 ml) was added to induce precipitation of the product which was then filtered and washed with methanol (100 ml) leaving **7a**[16] as a white crystalline solid (6.40 g, 74%); mp 130–132 °C; λ_{max}/nm (ε/dm^{-3} mol^{-1} cm^{-1}) 205.1 (26209), 231.0 (27613); ν_{max}/(KBr)/cm^{-1} *inter alia* 1330 (asym SO_2), 1155 (sym SO_2); δ_H(300 MHz; $CDCl_3$) 2.41 (9H, s, 3 × C*H*$_3$), 3.31 (12H, t, *J* 5.8, 6 × NC*H*$_2$), 3.55 (12H, t, *J* 5.8, 6 × OC*H*$_2$), 7.29 (6H, d, *J* 8.1, 6 × CH$_3$CC*H*), 7.66 (6H, d, *J* 8.1, 6 × SO$_2$CC*H*); δ_C(75.5 MHz; $CDCl_3$) 21.42 (3 × *C*H$_3$), 49.52 (6 × N*C*H$_2$), 70.61 (6 × O*C*H$_2$), 126.96 (12 × CH$_3$*C*CH), 129.68 (12 × SO$_2$*C*CH), 136.40 (3 × CH$_3$*C*), 143.37 (3 × SO$_2$*C*); *m*/*z* (FAB) *inter alia* 414 (M − 2 × ArSO$_2$ + H)$^+$, 568 (M − ArSO$_2$)$^+$, 724 (M + H)$^+$ [Found: M, 724.2404. Calc. for $C_{33}H_{45}N_3O_9S_3^+$, *M*: 724.2459].

Preparation of cyclic triamine 5

Cyclic tritosylamide **7a** (9.71 g, 13.40 mmol) and phenol (11.38 g, 0.12 mol) were dissolved in 33% HBr/AcOH (400 ml) and stirred. The reaction mixture was then heated to 80 °C and left for 60 h. After this time the reaction was cooled and the solvent was removed to a volume of 20 ml, when 100 ml acetone was then added to precipitate the HBr salt of **6**. This was then filtered, washed with acetone (3 × 50 ml) and dried under vacuum to yield the tri-HBr salt of triamine **5** (5.75 g, 85%). This could be easily neutralised to its basic form by dissolving it in water and adding portions of anionic exchange resin (IRA 400) until the pH of the solution remained constant. The water was then removed to yield a white solid which was recrystallised from hexane to form triamine **5** as long white crystals and which was identical to that reported in the literature:[24] mp 134–136 °C (lit.[10] 135–136 °C).

Preparation of cyclic triphosphonic ester 7d

Cyclic triamine **5** (0.10 g, 0.20 mmol), diethyl phosphite (0.08 ml, 0.70 mmol) and triethylamine (0.17 ml, 1.19 mmol) were dissolved in benzene (5 ml) which was then heated to reflux and left for 10 min. Then paraformaldehyde (27 mg, 0.90 mmol) was added in small portions in benzene over 45 minutes whilst azeotropically removing water. The distillation apparatus was then removed and replaced by a reflux condenser so that refluxing could continue overnight. The benzene was then removed and replaced by a mixture of water (5 ml) and dichloromethane (5 ml) the latter of which was removed and the water layer was washed again with dichloromethane (5 ml). The organic fractions were pooled and the solvent removed to leave colourless oil **7d** (52 mg, 37%): ν_{max}(thin film)/cm^{-1} *inter alia* 1039 (P–O-alkyl), 1226 (P=O); δ_H(200 MHz; $CDCl_3$) 1.31 (18H, t, *J* 7.1, 6 × C*H*$_3$), 2.93 (12H, t, *J* 5.7, 6 × NC*H*$_2$CH$_2$), 3.00 (6H, d, *J* 9.5, 3 × PC*H*$_2$), 3.53 (12H, t, *J* 5.7, 6 × OC*H*$_2$CH$_2$), 4.12 (12H, m, 6 × CH$_2$C*H*$_3$); δ_C (75.5 MHz; $CDCl_3$) 16.37 (6 × *C*H$_3$), 50.54 (d, *J* 158.9, 3 × *C*H$_2$P), 55.16 (6 × NCH$_2$CH$_2$), 61.76 (2 × OCH$_2$-CH$_2$), 69.44 (2 × POCH$_2$); m/z (FAB) *inter alia* 298 (M − 3PO(OEt)$_2$)$^+$, 436 (M − 2PO(OEt)$_2$)$^+$, 574 (M − PO(OEt)$_2$)$^+$, 712 (M + H)$^+$, 734 (M + Na)$^+$ [Found: M, 712.3477. Calc. for $C_{27}H_{61}N_3O_{12}P_3^+$, *M:* 712.3468].

Preparation of cyclic triphosphonic acid 2b

Cyclic triamine **5** (1.00 g, 1.98 mmol) and phosphorous acid (0.49 g, 5.95 mmol) were dissolved in a mixture of concentrated HCl (5 ml) and water (5 ml) and stirred. The mixture was then heated to reflux (~115 °C) and paraformaldehyde (0.36 g, 11.90 mmol) was then added in small portions over 45 minutes. After this was added, refluxing continued for a further 48 hours at which point the reaction mixture was cooled and the solvent removed. On adding ethanol (30 ml) with swirling, a white precipitate formed which could be separated from the liquid *via* centrifugation. The white solid was then dried *in vacuo* to yield the tri-HCl salt of **2b** (0.75 g, 58%): ν_{max}(KBr)/cm^{-1} *inter alia* 1135 (P=O); δ_H(200 MHz; D_2O) 3.54 (6H, d, *J* 12.5, 3 × PC*H*$_2$), 3.68–3.85 (12H, m, 6 × NC*H*$_2$CH$_2$), 3.96–4.10 (12H, m, 6 × OC*H*$_2$CH$_2$); δ_C(75.5 MHz; D_2O) 49.80 (d, *J* 139.0, 3 × P*C*H$_2$), 55.54 (6 × N*C*H$_2$CH$_2$), 64.82 (6 × O*C*H$_2$); δ_P(81 MHz; D_2O) 8.55 (3 × P); *m*/*z* (FAB) *inter alia* 544 (M + H)$^+$, 562 (M + H_2O) [Found: M, 544.1581. Calc. for $C_{15}H_{37}N_3O_{12}P_3^+$, *M:* 544.1590].

Solutions of sodium salt **2a** were prepared prior to use by direct neutralisation of an aqueous solution of acid derivative.

Preparation of ettringite

A stirring slurry of calcium hydroxide (0.50 g, 6.75 mmol) in water (40 ml) was heated to 70 °C in a jacketed vessel, to which a solution of aluminium hydroxide (0.71 g, 1.13 mmol) in water (60 ml), also at 70 °C, was added in under 5 seconds. The resulting mixture was then allowed to stir for 30 minutes after which time the mixture was centrifuged and the mother liquors removed. The resulting amorphous material was then washed three times with distilled water (40 ml), after each wash the water was removed after centrifugation. The product was then dried *in vacuo* leaving pure ettringite.[28] In experiments where ettringite was grown in the presence of the additives, these were dissolved in the aluminium sulfate solution, in a known concentration, prior to the mixing with the calcium hydroxide solution. All other experimental details were identical to that when preparing pure ettringite. The ettringite crystals were then mounted on 2.5 cm circular stubs, using ethanol which was then allowed to evaporate, before observation under a scanning electron microscope with fitted camera.

Preparation of cement

To class G cement (80 g), water (35.2 ml) was added with vigorous stirring. The slurry was allowed to stir for 20 seconds and then transferred to a calorimeter cell noting the exact weight of the slurry used. The cell was then sealed and placed in a calorimeter which measured the heat given out over a period of time, and left for 24 hours during monitoring. In experiments in the presence of the additives, these were added to the

water, in a known concentration, prior to mixing with the cement powder.

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