Electronic Supplementary Information

Experimental Section

- Materials and Instruments

All reactants were purchased from: $K_2B_4O_7.4H_2O$ (BDH, 98.5%), K_2HPO_4 (BDH, 98%), urea (Fagron, 99.7%), Guanosine (Sigma, 98spectrometer%), Adenosine (Sigma-Aldrich, ≥99.7%), Cytidine (Sigma-Aldrich, 99%), H_3PO_4 (Sigma-Aldrich, ≥ 85%), HCl (Riedel-de-Haën 37%, puriss p.a.), KOH (Sigma-Aldrich, ≥ 90%), $Ca(OH)_2$ (Sigma-Aldrich, ≥ 95%) and D_2O (Sigma-Aldrich, 99.9%), and used without further purification.

Hydroxyapatite was prepared by addition of 0.35 g of $Ca(OH)_2$ in 400 cm^3 of water; then, with magnetic stirring, 0.71 cm^3 of H_3PO_4 4 M was added and the precipitate was filtered, washed with water and finally dried with acetone.[1] The product was characterised by FTIR with a Mattson Research Series 1 Fourier Transform (FTIR) spectrometer.

^1H, ^{11}B and ^{31}P NMR spectra were recorded on a 400 MHz Avance III Bruker spectrometers equipped with a 5 mm BBO probe at room temperature.

Mass spectra by EMI-MS (-) were carried out with LCQ Fleet equipment.

Studies to detect inorganic phosphorylated species

Sample was prepared by evaporation of an aqueous solution containing potassium hydroxidotrioxidophosphate(2−) (i.e., hydrogenphosphate) (72 mM) and urea (108 mM) at 90 ºC and dried during 1 day. Then, part of the solid was dissolved in water with two drops of D_2O to be analysed by ^{31}P NMR spectroscopy; one aliquot was dissolved in water (pH 8) and another adjusted to pH 1. Both were analysed by ESI-MS(-) as well as a sample of guanosine/cytidine (1:1) hydrogel after 10 wet/dry cycles of reaction at 90 ºC with K_2HPO_4 and urea adjusted to pH 5.

Studies with Hydrogels of Ribonucleosides and Borate

- Hydrogels synthesis

Hydrogels were prepared based on Peters at al.,[2] followed by addition of urea and a source of phosphate, potassium hydroxidotrioxidophosphate(2−) or hydroxyapatite. In some reactions half of guanosine was replaced by adenosine or cytidine.

Typically, 2.5 cm^3 of an aqueous solution (distilled water) of potassium borate (18 mM) was added to 90 μmol of guanosine (or 45 μmol of guanosine and an equivalent amount of other ribonucleoside) with magnetic stirring. Subsequently, the pH value was adjusted to 8-9, with solutions of KOH (1.2 M) and/or HCl (1.37 M), to obtain clear sols. Then, gelation was promoted by storing the

sample at 4 ºC. Afterwards, it was heated at 75 ºC to add urea (330 μmol) and 180 μmol of a phosphate source (K_2HPO_4 or hydroxyapatite). The soluble components were added in 0.1 cm^3 of water and hydroxyapatite as solid. Finally, the temperature of the sample was increased to 90 ºC and kept for some days (see experiments or captions of figures), while the phosphorylation reaction was carried out.

Typically, the samples at 90 ºC had two wet/dry cycles per day (addition of ca. 2.5 cm^3 of distilled water twice a day, i.e. each cycle with ca. 4 hours wet and ca. 8 hours dry). All the reactions were carried out without stirring (as is supposed to happen in the prebiological period), except for the sample with hydroxyapatite, due to its very slight solubility.

Experiments at 50 ºC, 60 ºC, 70 ºC and 90 ºC were carried out 2.5 cm^3 of aqueous solutions (distilled water) of potassium borate (9 mM) were added to 45 μmol of guanosine with magnetic stirring. Subsequently, the pH value was adjusted to 8-9, with solutions of KOH (1.2 M) and/or HCl (1.37 M), to obtain clear sols. Then, gelation was promoted by a similar procedure described above. Afterwards, they were heated to add urea (165 μmol) and 90 μmol of K_2HPO_4 in 0.1 cm^3 of water. All the reactions were done with 8 wet/dry cycles (in average at 50 ºC, 17 h wet and 22 h dry during 13 days; at 60 ºC, 14 h wet and 10 h dry during 8 days and at 70 ºC and 90 ºC 6 h wet and 6 h during 4 days – the rate of evaporation at 70 ºC, as compared to 90 ºC experiment, was increased with a higher contact surface of the sample with atmosphere).

The reaction yield was determined from the ^{31}P NMR spectrum of guanosine hydrogel after 12 wet/dry cycles at 90 ºC with K_2HPO_4 and urea, by adding $Cr(acac)_3$ and D_3PO_4 (58 μL of a solution 0.1 M) as relaxation agent and internal standard, respectively. The signals of guanosine-5'-phosphate and D_3PO_4 were integrated. The yield was calculated based on the initial number of moles of guanosine.

NMR samples were prepared with dry mixtures by adding heavy water; then, the solutions were transferred to a NMR tube to be analysed by ^{1}H, ^{11}B, ^{31}P and ^{1}H-^{31}P HMBC correlation at room temperature. In some cases the intensity of the ^{31}P signals corresponding to ribonucleotides were normalised to the absent phosphate signal (Figures 3, 4, ESI4 and ESI8). A capillary with neat $Et_2O.BF_3$ was used as external reference for ^{11}B and another capillary with H_3PO_4 for ^{31}P. ^{1}H chemical shifts are referenced to D_2O.

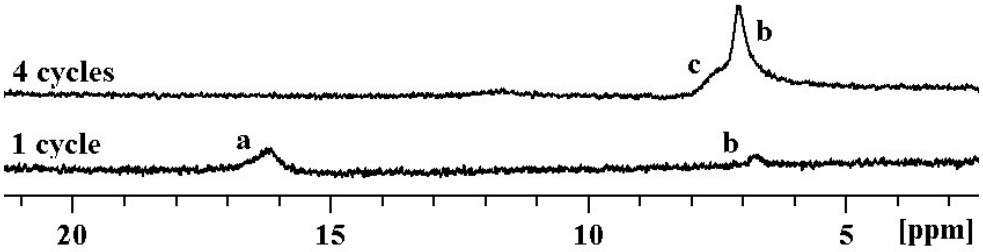

Figure ESI1 - ^{11}B NMR spectra of guanosine hydrogels after (from bottom to top): 1 and 4 wet/dry cycles of reaction at 90 ºC with K_2HPO_4 and urea, run in a 400 MHz spectrometer; (a) guanosine-borate diesters, (b) guanosine-borate monoesters and (c) unknown species (a phosphorylated nucleotide forming an ester with borate?).

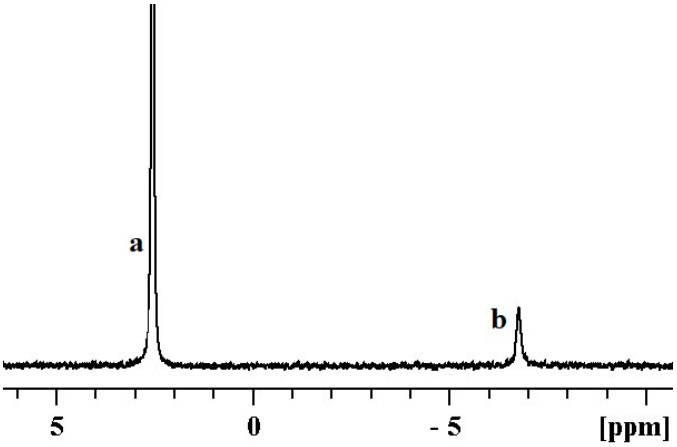

Figure ESI2 - ^{31}P NMR spectrum from a solution of K_2HPO_4 and urea after 1 day of dryness at 90 ºC, run in a 400 MHz spectrometer; (a) inorganic phosphate and (b) pyrophosphate.

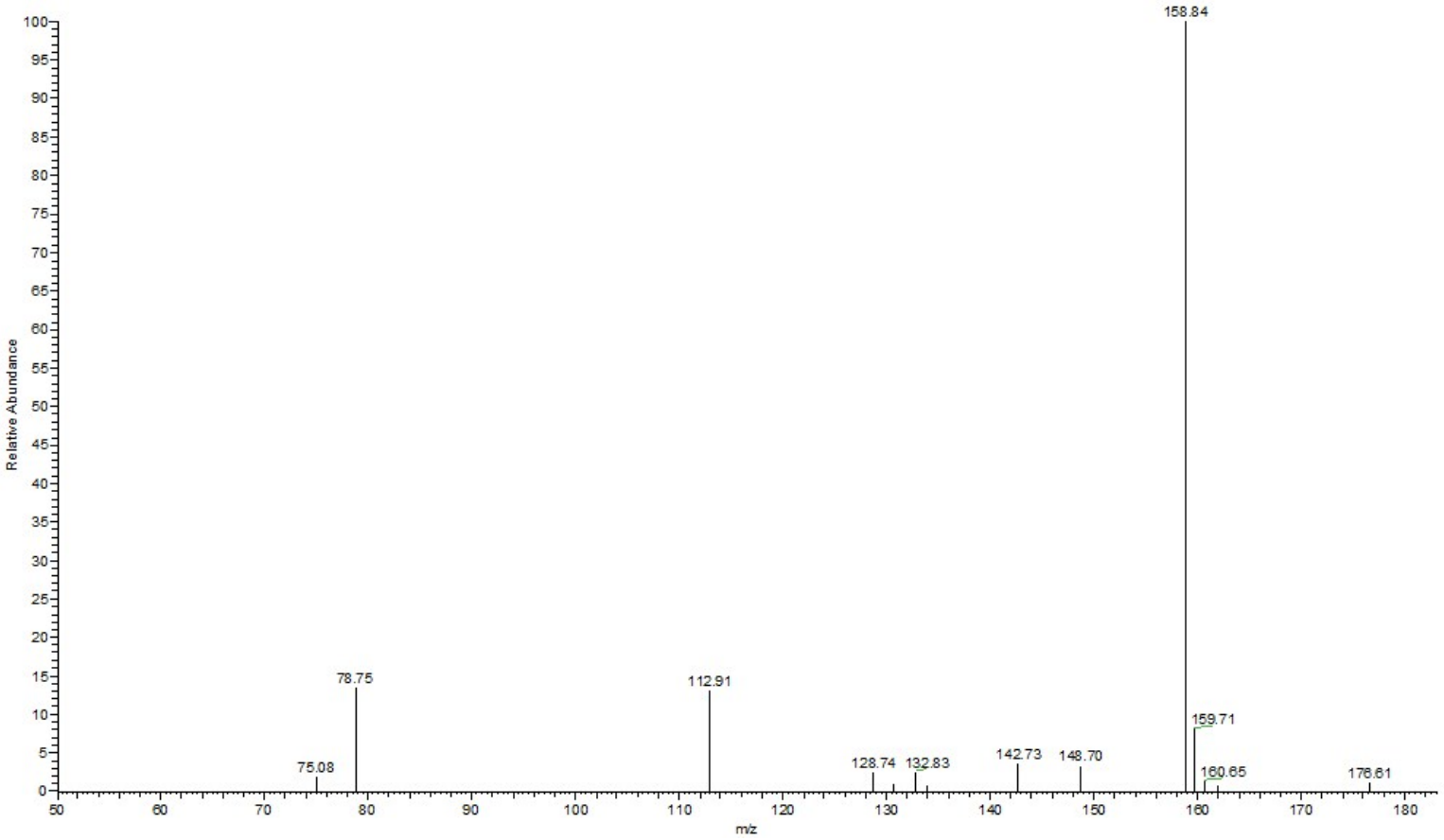

Figure ESI3 - ESI-MS/MS(-) from a solution of K_2HPO_4 and urea after 1 day of dryness at 90 ºC (adjusted to pH 1) showing the fragmentation pattern of *m*/*z* 177 species.

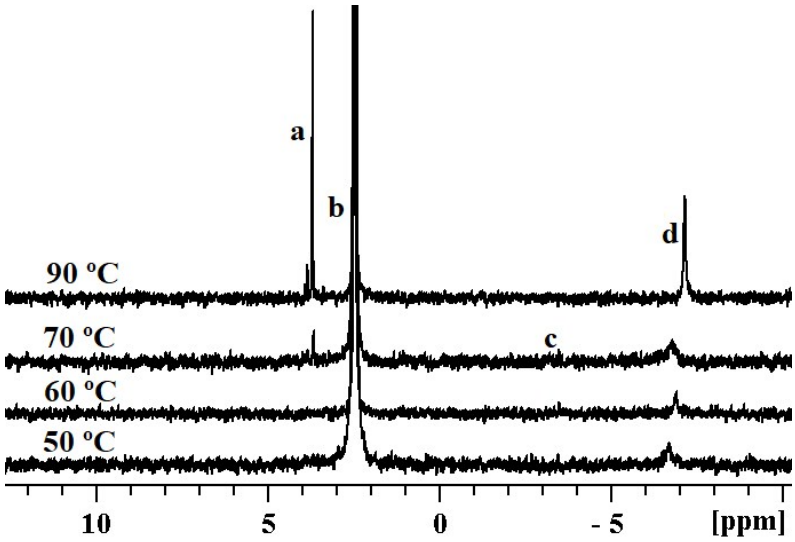

Figure ESI4 - ^{31}P NMR spectra of guanosine hydrogels after 8 wet/dry cycles of reaction at different temperatures with K_2HPO_4 and urea, run in a 400 MHz spectrometer. (a) guanosine-5'-phosphate; (b) inorganic phosphate; (c) diamidodiphosphate and (d) pyrophosphate.

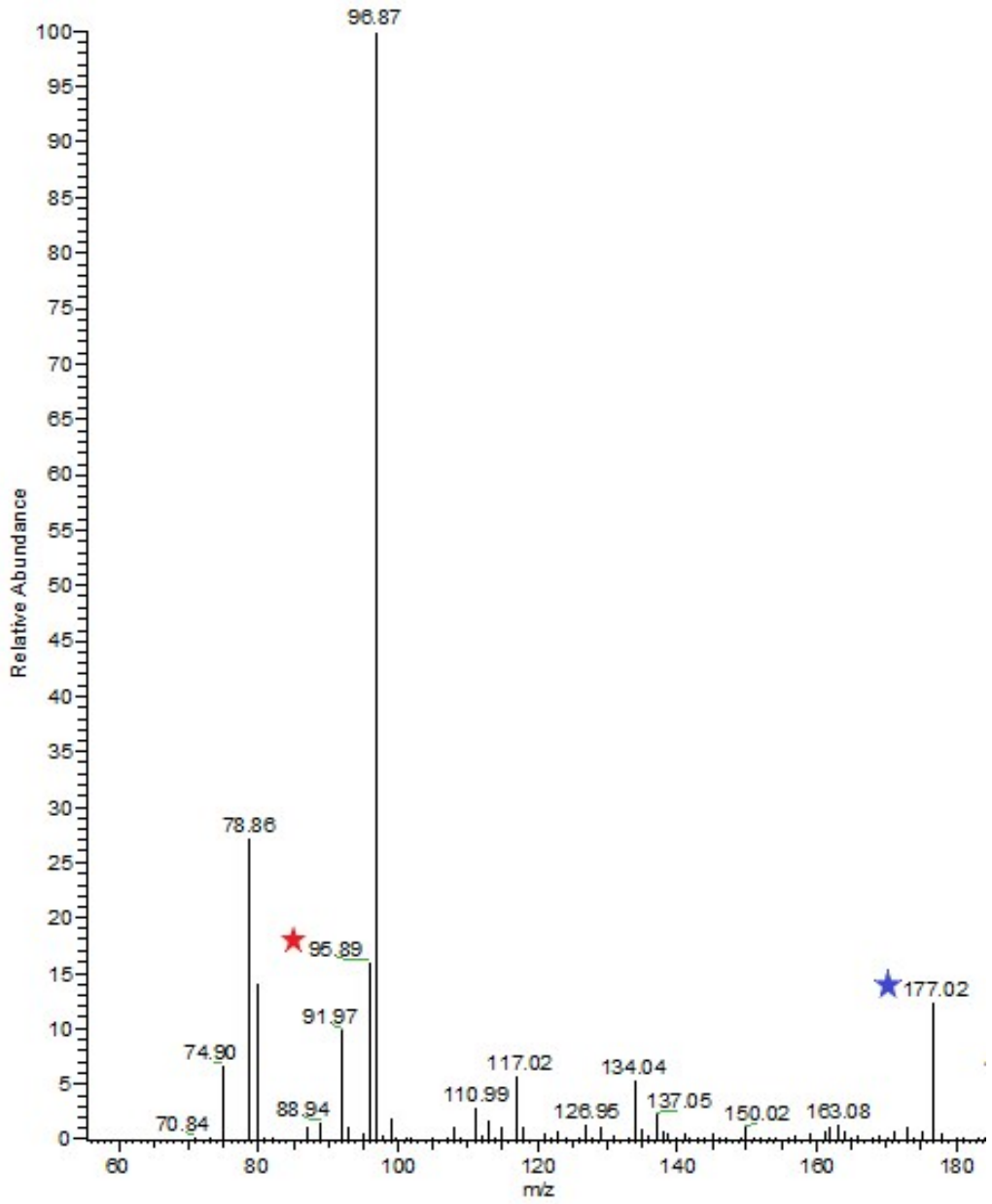

Figure ESI5 – ESI-MS(-) spectrum of a guanosine/cytidine (1:1) hydrogel after 10 wet/dry cycles of reaction at 90 ºC with K_2HPO_4 and urea (aliquot adjusted to pH 5); the red and blue stars indicate monoamidophosphate and pyrophosphate, respectively.

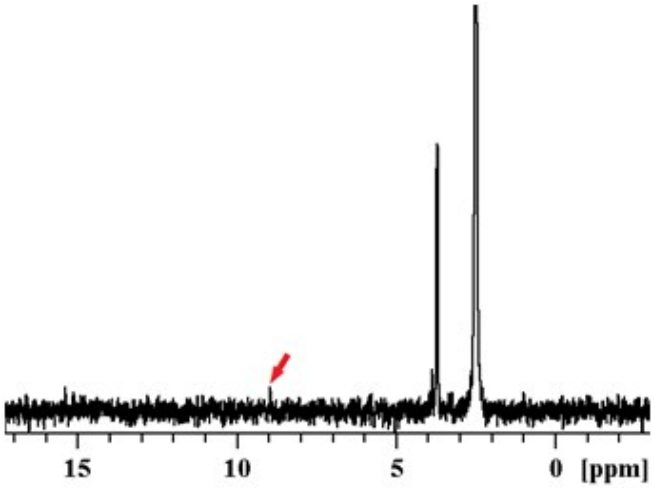

Figure ESI6 - ^{31}P NMR spectrum of a guanosine hydrogel after 20 wet/dry cycles of reaction at 90 ºC with K_2HPO_4 and urea, run in a 400 MHz spectrometer; the arrow indicates monoamidophosphate.

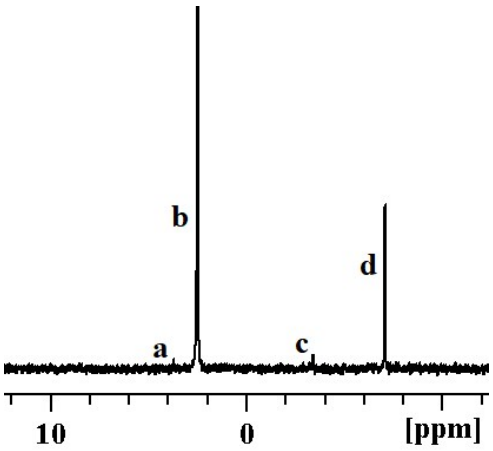

Figure ESI7 - ^{31}P NMR spectrum of a guanosine hydrogel after 1 wet/dry cycle of reaction at 90 ºC with K_2HPO_4 and urea, run in a 400 MHz spectrometer. (a) guanosine-5'-phosphate; (b) inorganic phosphate; (c) diamidodiphosphate and (d) pyrophosphate.

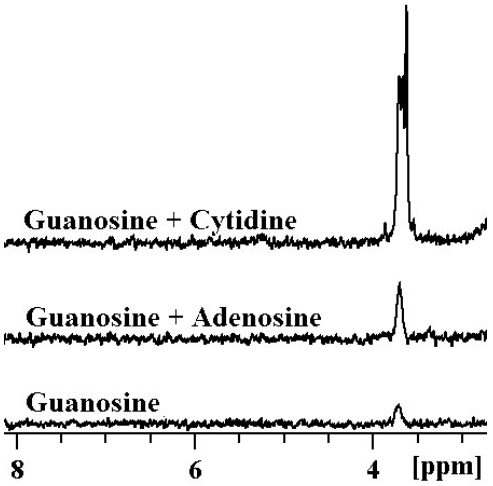

Figure ESI8 - ^{31}P NMR spectra of (from bottom to top) guanosine, guanosine/adenosine (1:1) and guanosine/cytidine (1:1) hydrogels, respectively, after 10 wet/dry cycles of reaction at 90 ºC with K_2HPO_4 and urea, run in a 400 MHz spectrometer.

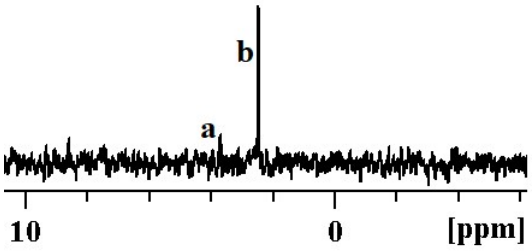

Figure ESI9 - ^{31}P NMR spectrum of a guanosine hydrogel after 30 wet/dry cycles of reaction at 90 ºC with hydroxyapatite and urea, run in a 400 MHz spectrometer; (a) traces of ribonucleotide; (b) inorganic phosphate.

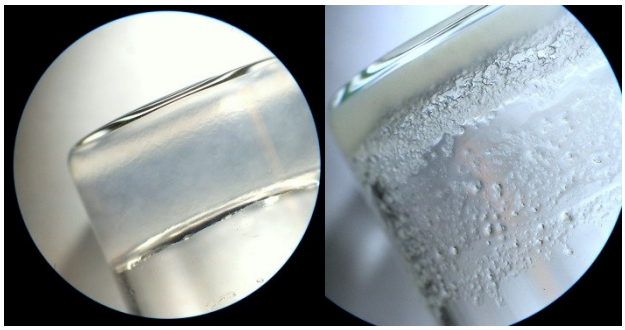

Figure ESI10 – Guanosine-borate hydrogel before addition of urea and K_2HPO_4 (left); the same sample after 4 wet/dry cycles of reaction and overnight storage at 4 ºC (right); both photos, amplified (4x), were taken with the samples at room temperature.

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[1] A. Paz, D. Guadarrama, M. López, J. E. González, N. Brizuelaand J. Aragón, *Quim. Nova*, 2012, **35**, 1724.

[2] G. M. Peters, L. P. Skala, T. N. Plank, B. J. Hyman, G. N. M. Reddy, A. Marsh, S. P. Brown and J. T. Davis, *J. Am. Chem. Soc.*, 2014, **136**, 12596.