

The supplementary material contains a visual representation of guanosine and uridine samples before and after mechanochemical treatment, together with HPLC data from guanosine and uridine mechanochemical reactions with sodium chloride. Moreover, it comprises the optimized structures of guanosine and uridine for the DFT calculations.

### 1.0 Nickel and carbonate effect on mechanochemical treated guanosine and uridine samples

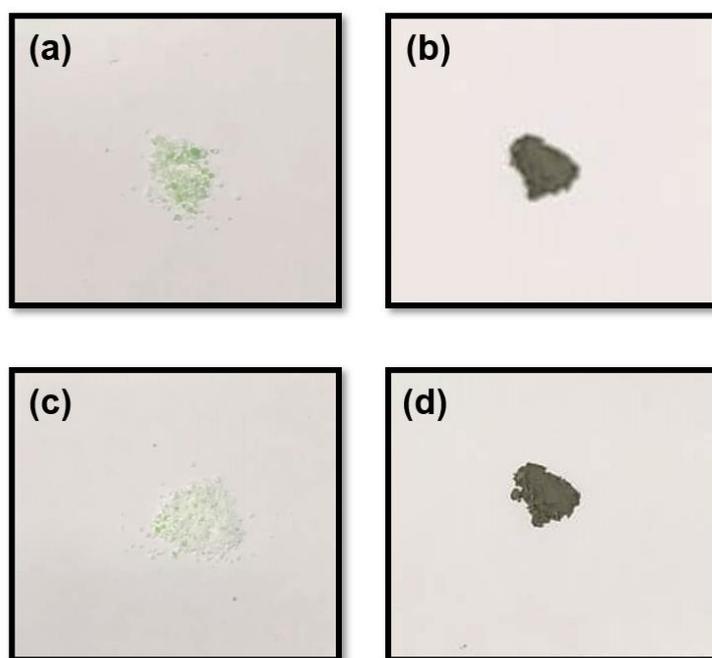


Figure S1 Ribonucleoside- $\text{Na}_2\text{CO}_3$ - $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$  samples before and after mechanochemical treatment (29 Hz, 6 h): (a) and (b) – Uridine sample before and after mechanochemical treatment, respectively; (c) and (d) – Guanosine sample before and after mechanochemical treatment, respectively

### 1.2 Sodium chlorine effect on ribonucleoside mechanochemical degradation

To understand the effect of sodium chlorine in the mechanochemical degradation of ribonucleosides, samples containing ribonucleoside (guanosine or uridine) and sodium chloride, were mechanochemically treated in a ribonucleoside-salt 1:4 ratio. S.2 reveals the HPLC analysis of the treated samples.

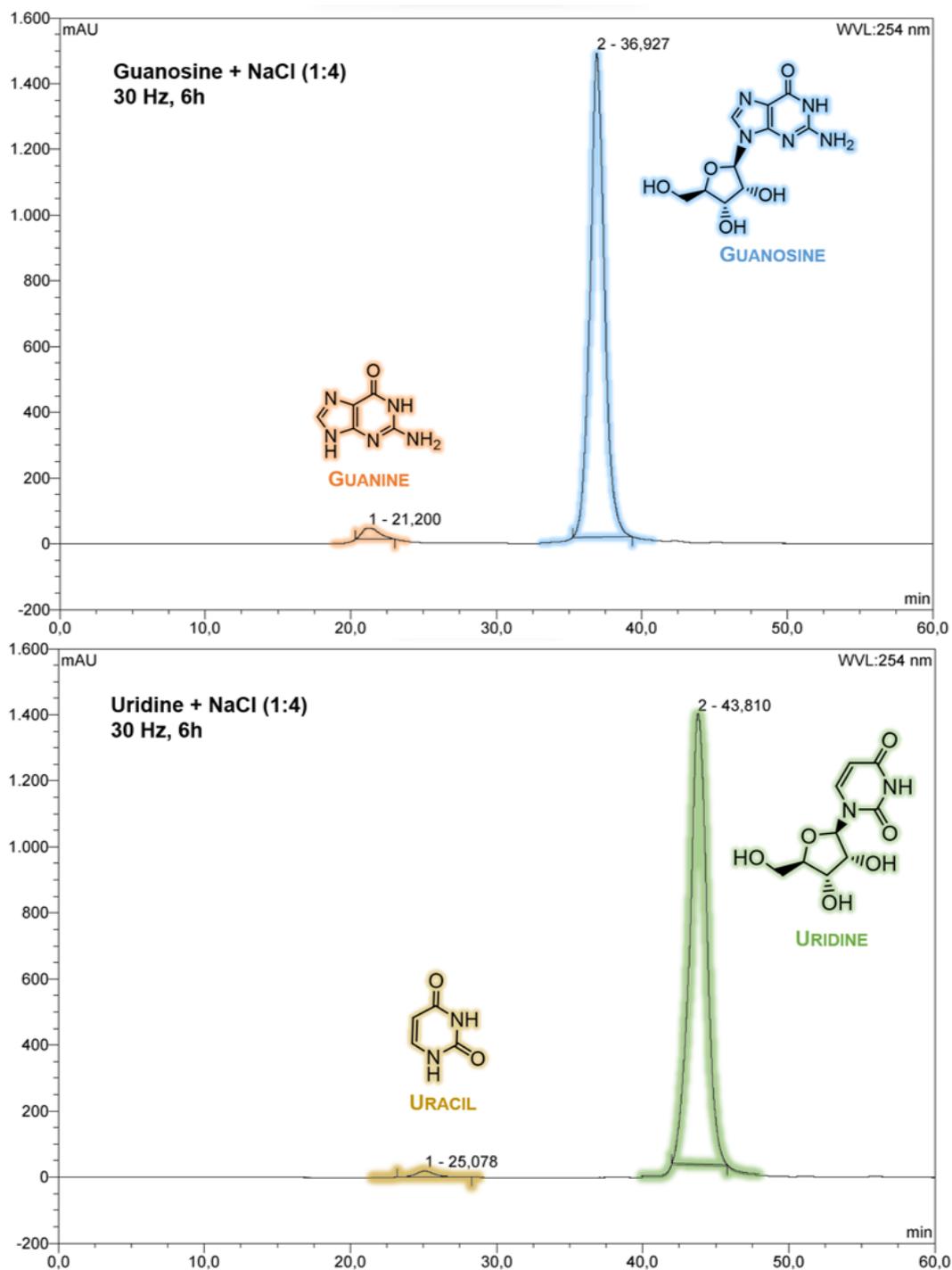


Figure S2 HPLC chromatogram from guanosine (above) and uridine (below) after mechanochemical treatment (29 Hz, 6h) with NaCl in ribonucleoside - NaCl proportion of 1:4. HPLC **Run 1** and **Run 2** conditions were applied for guanosine and uridine treated samples, respectively. Previously standard nucleobase/nucleoside solutions were run to identify their retention time.

## 1.2 DFT OPTIMISATIONS

Ribonucleosides are constructed by covalently bond ribose moiety with nucleobase (guanine and uracil for guanosine and uridine, respectively). Guanosine conformations were constructed based on X-rays geometries (S3, left and middle), which in solid state, exist in a  $\pi$ - $\pi$ -stacked dimer, as represented in S4.

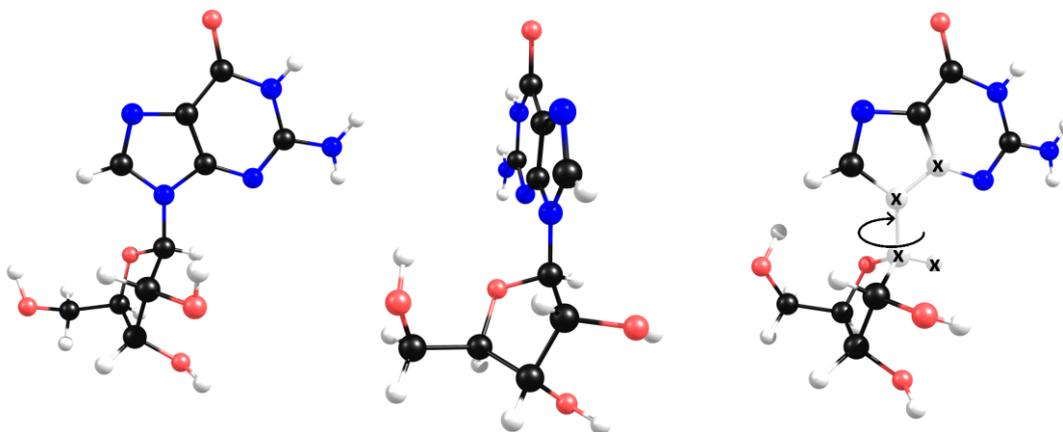


Figure S3 X-ray conformers for guanosine (left and middle). Definition of the twist angle for DFT calculations (right). X-ray experimental twist=300° (left) and twist=17° (middle).

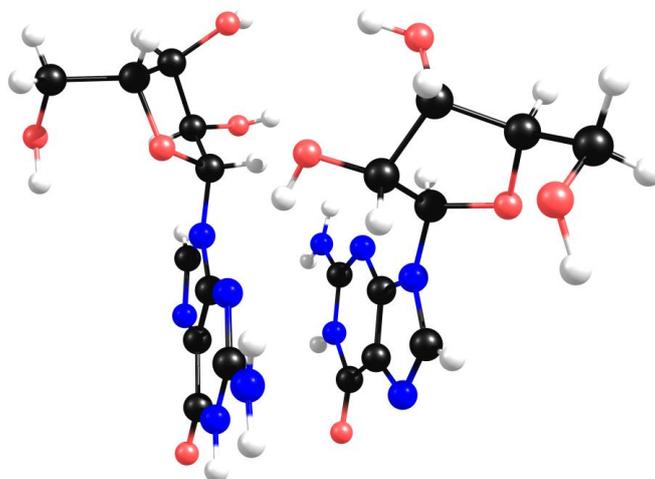


Figure S4 In x-ray, the geometries of the two conformers are  $\pi$ - $\pi$ -stacked forming a Van Der Waals dimer.

The conformational analysis was evaluated through the twist angle (S3, right). For uridine structures, a similar intramolecular H-bond interaction is observed, between 5'-hydroxyl and pyrimidine O2. The DFT calculations revealed that the stretching of the glycosylic bond seems to be enhanced in uridine leading to the prediction of an increased reactivity.

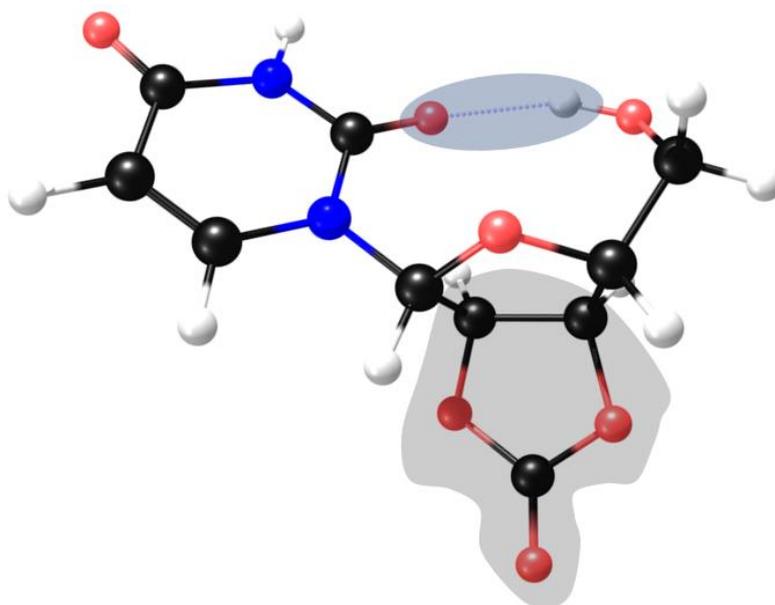


Figure S5 DFT calculated uridine neutral optimised conformers. Similar to guanosine, 5'-hydroxyl and O2 H-bonding is the predominant H-bond stabilization (blue). Carbonate moiety highlighted in grey.