Electronic Supplementary Material (ESI) for CrystEngComm.


# pH-Dependent-Oiling-out During the Polymorphism Transformation of Disodium Guanosine 5′-Monophosphate

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# Supporting Information

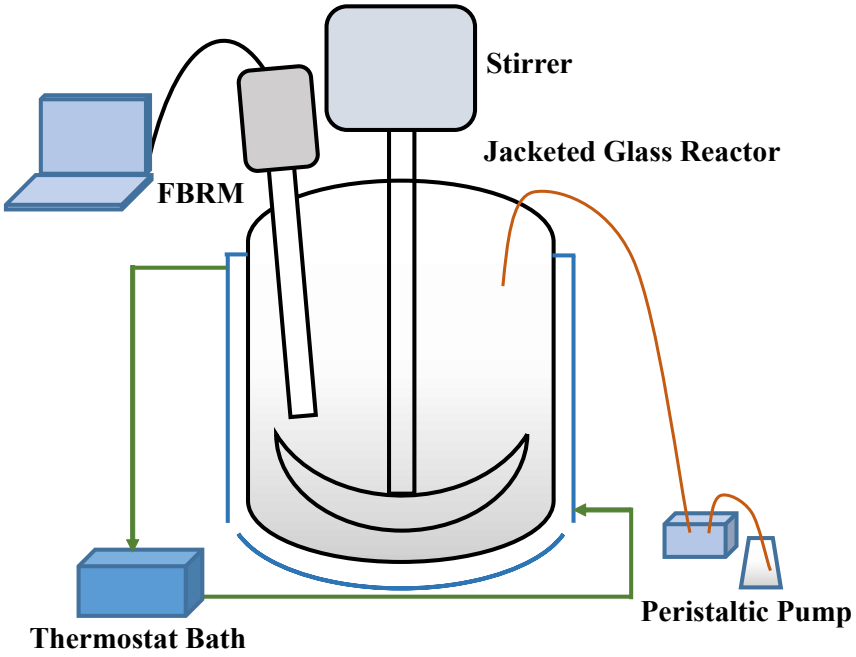
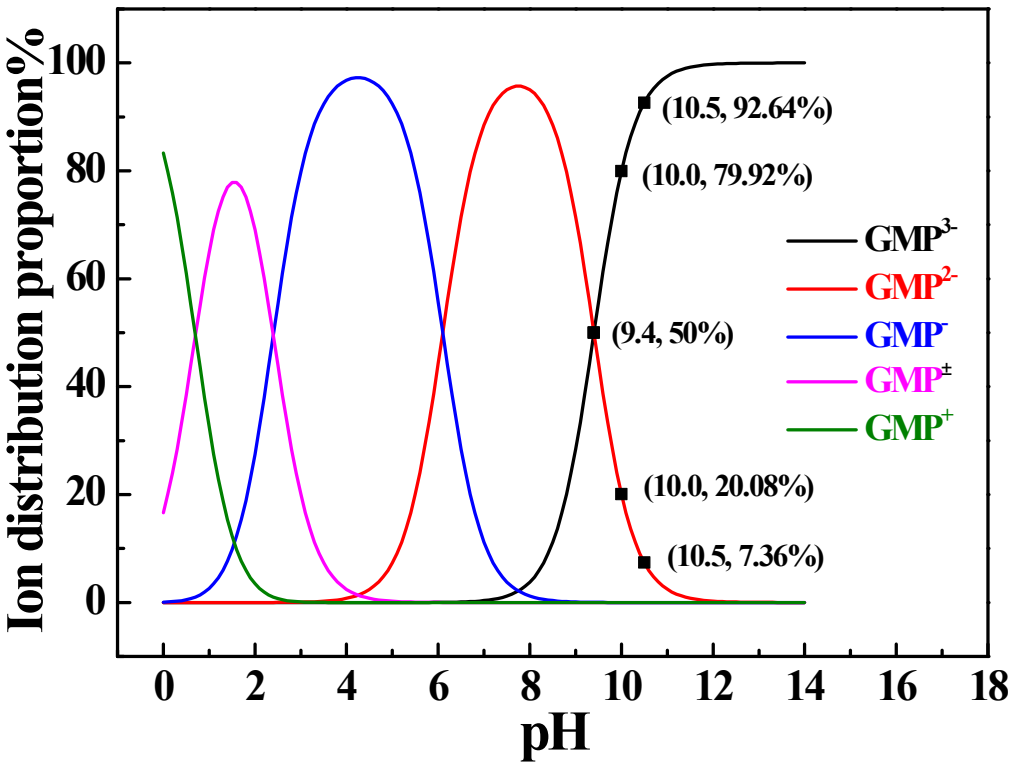



Fig. S1. Experimental device diagram of oiling-out process monitoring and control.

Table.S1 The $pK_a$ of 5′-GMP and location of hydrogen ions which can combine with Fig 1 to understand.

| 5′-GMP | $pK_a$ | location |
|---|---|---|
| $pK_{a1}$ | 0.7 | first phosphoric acid group |
| $pK_{a2}$ $pK_{a4}$ | 9.4(N-1) 2.4(N-7) | basic group |
| $pK_{a3}$ | 6.1 | second phosphoric acid group |




The

**Fig. S2** ion distribution of 5′-GMP in different pH aqueous solution.

**Verification Test**

**Experiment 2 --NaCl replace NaOH**

In order to verify alkaline environment contribute to oiling-out we design Experiment 2 what the NaOH were replaced by same mole NaCl, the remaining conditions are the same as Experiment 1, and the result of CLD with time was displayed in Fig. S3. The chaotic CLD shows that system can't complete transformation amorphous to crystal of 5′-GMP$Na_2$ before 5 h, and the crystal of 5′-GMP$Na_2$ and oil drop were not found with the addition of isopropanol until the end of Experiment 2. Which explains that $OH^-$ is important for crystalline transformation and oiling-out.

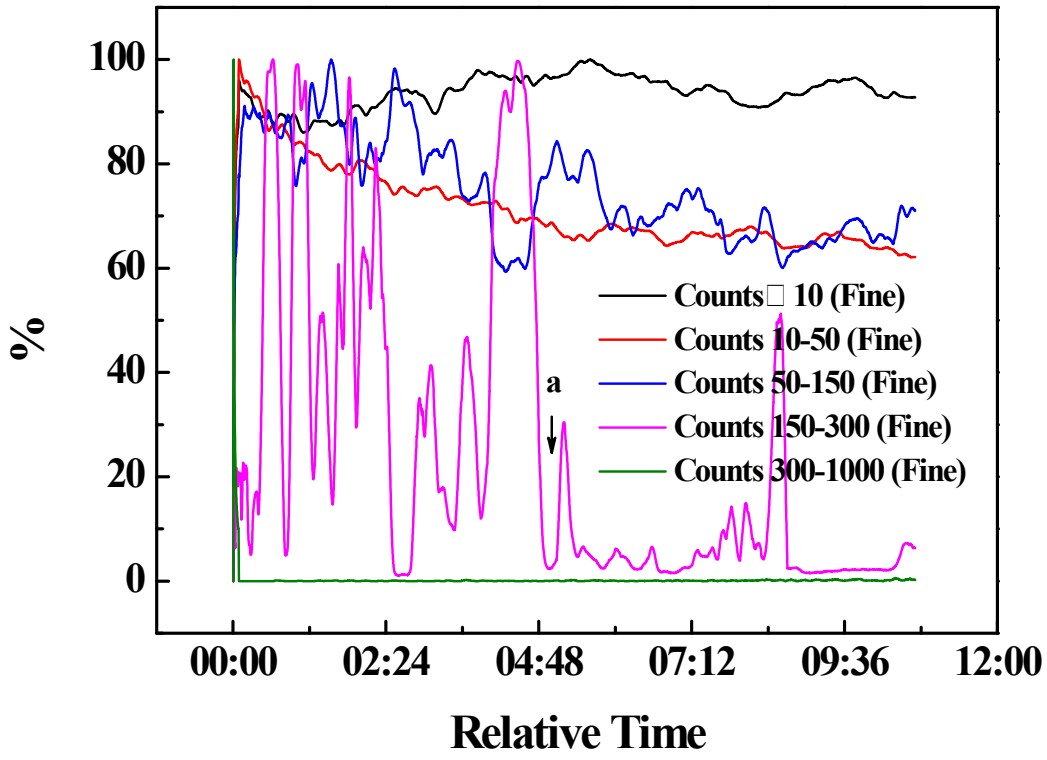



**Fig S3**. FBRM data monitor the crystallization of 5′-GMPNa$_2$ in Experiment 2. (a) the isopropanol solution were dropwise added to crystallizer.

**Experiment 3--Adding HCl**

In Experiment 3, the dilute HCl solution were added into system to control the alkaline of solution, and the remaining conditions are the same as Experiment 1, the result was displayed in Fig. S4. The order CLD shows that the system can complete transformation amorphous to crystal of 5′-GMPNa$_2$ before 5 h, the mixed liquid of the dilute HCl aqueous and isopropanol was slow entry system at 5 h. Then a sharp rise in the signal of FBRM, because HCl aqueous and isopropanol can reduce the solubility of 5′-GMPNa$_2$ respectively, which leads to a sharp increase in local supersaturation, and large number of amorphous 5′-GMPNa$_2$ were precipitate. The morphology of solid was showed in Fig.11a at 8 h. The amorphous particles gradually dissolve, and

crystal gradually growth, in other words amorphous transformed into crystal under the acceleration of supersaturation. Which leads to the counts $< 300$ gradually reduces, and the counts $> 300$ gradually increase. There were no oil droplets and amorphous were found at the end of the experiment as showed in Fig.11b.

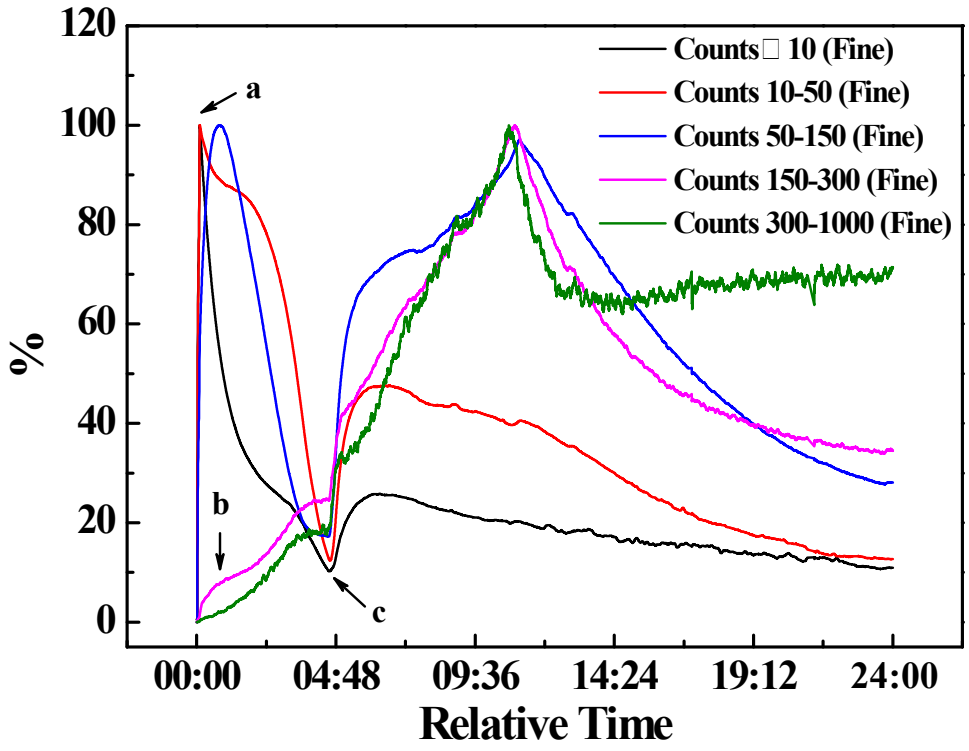



**Fig S4**. FBRM data monitor the crystallization of 5′-GMP$Na_2$ in Experiment 3. (a) the isopropanol solution were dropwise added to crystallizer.

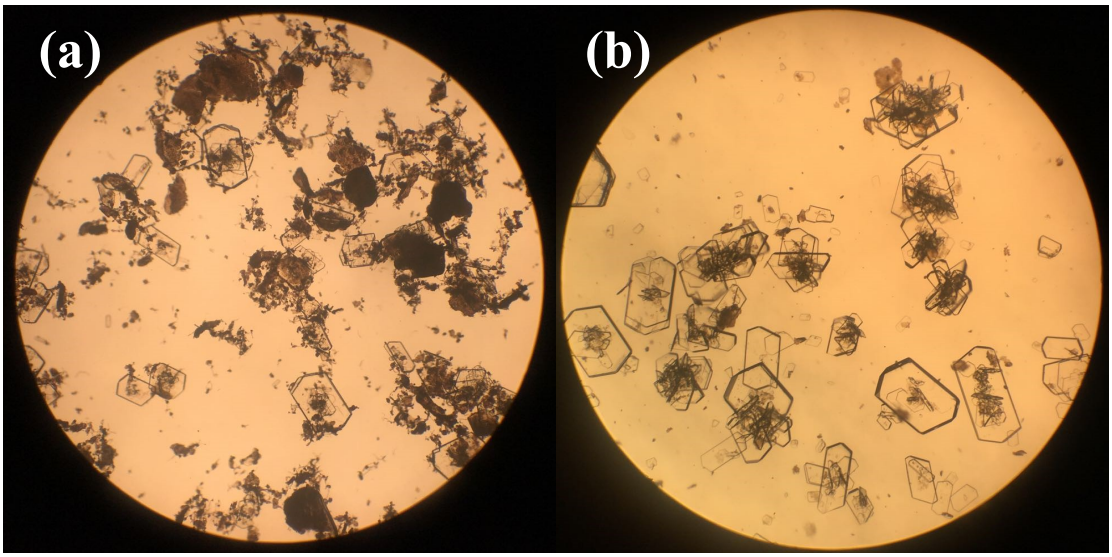


**Fig S5**. The process picture of crystallization Experiment 3 under a optical microscope ($16 \times 4$). The morphology of solid in Experiment 3 at 8 h (a), at 24 h (b).

**Simulation Test**

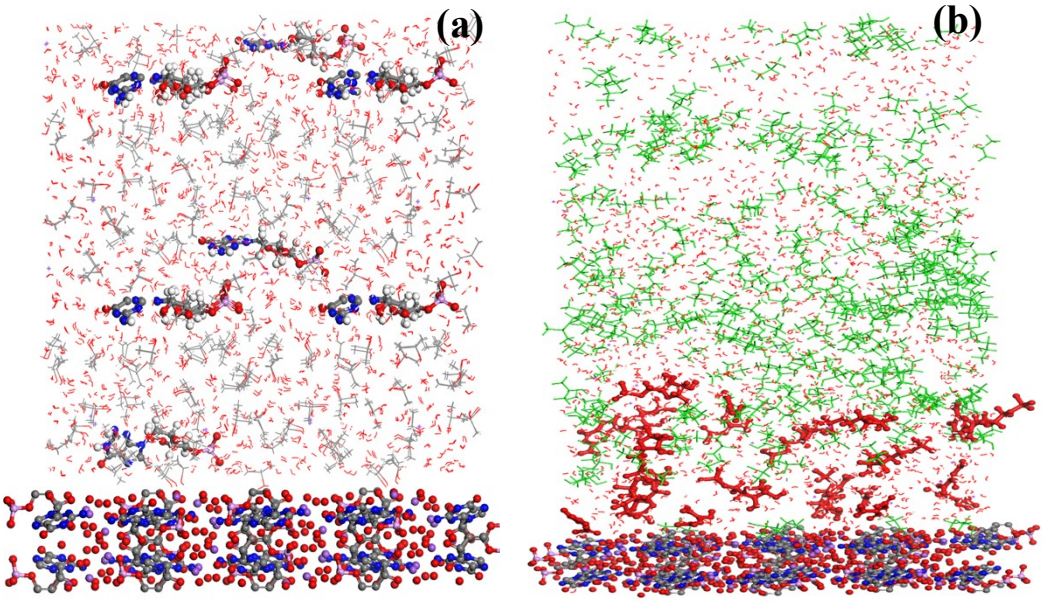



**Fig S6** the molecular crystal structure of in mixture solution, (a) is the initial state and (b) is the final state. Ball-and-stick model is GMP ($GMP^{2-}$and $GMP^{3-}$) and bases. Linear molecular is IPA and $H_2O$. Red in (b) is oil molecular while Green is IPA.

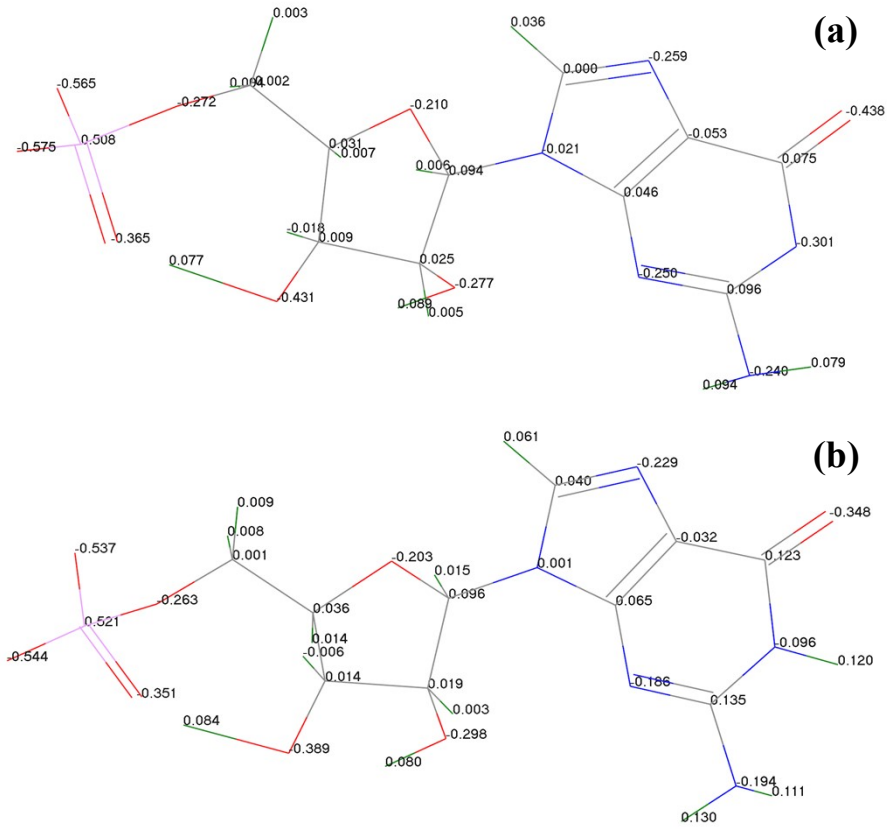



**Figure S7** Molecular charge profile of GMP, (a) is $GMP^{2-}$, (b) is $GMP^{3-}$

Dynamics of precise charge calculation is more accurate than universal charge field calculation.