

Supporting Materials for Crystal Structure Optimization and Gibbs Free Energy Comparison of Five Sulfathiazole Polymorphs by the Embedded Fragment QM Method at the DFT Level

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The vibrational spectrum acts as a fingerprint to identify the crystal structure of the molecule. Here, we calculate the Raman and IR spectra to investigate the different forms of sulfathiazole (STZ) molecules. Figures S1-S2 show the calculated Raman and IR spectra of five forms of STZ from 0 to 4000 cm^{-1} , respectively. The five forms exhibit remarkable Raman and IR peaks in the range of 1-2000 cm^{-1} and 3000-4000 cm^{-1} , but the positions of the corresponding peaks are quite different for different forms. Such differences can be used to identify the five forms of sulfathiazole crystals. Based on the experimental work proposed by Munroe *et al.*, where they measured the Raman spectra of five STZ polymorphs in laboratory from 1100 to 1500 cm^{-1} , we pick the corresponding calculated Raman spectra and compare them with the experiment (as shown in Figure 4). Figure 4 not only provides an efficient method to distinguish the five STZ forms from the view of Raman spectra, but also verify the correctness of our proposed theoretical work since it matches the experimental results. However, the IR spectra for the five STZ polymorphs have not been measured in laboratory, hence we did not

pick the corresponding calculated IR bands to compare with the experiment. We hope the calculated results shown in Figure S2 can assist the IR spectral measurement in laboratory in the future. Table S1 shows the calculated Gibbs free energy differences of five polymorphs of STZ with reference to FIII. As shown in Table S1, the calculated stability order for five polymorphs of STZ is FI<FV<FIV<FII<FIII, which agrees well with the experimental results (see Figure 3).

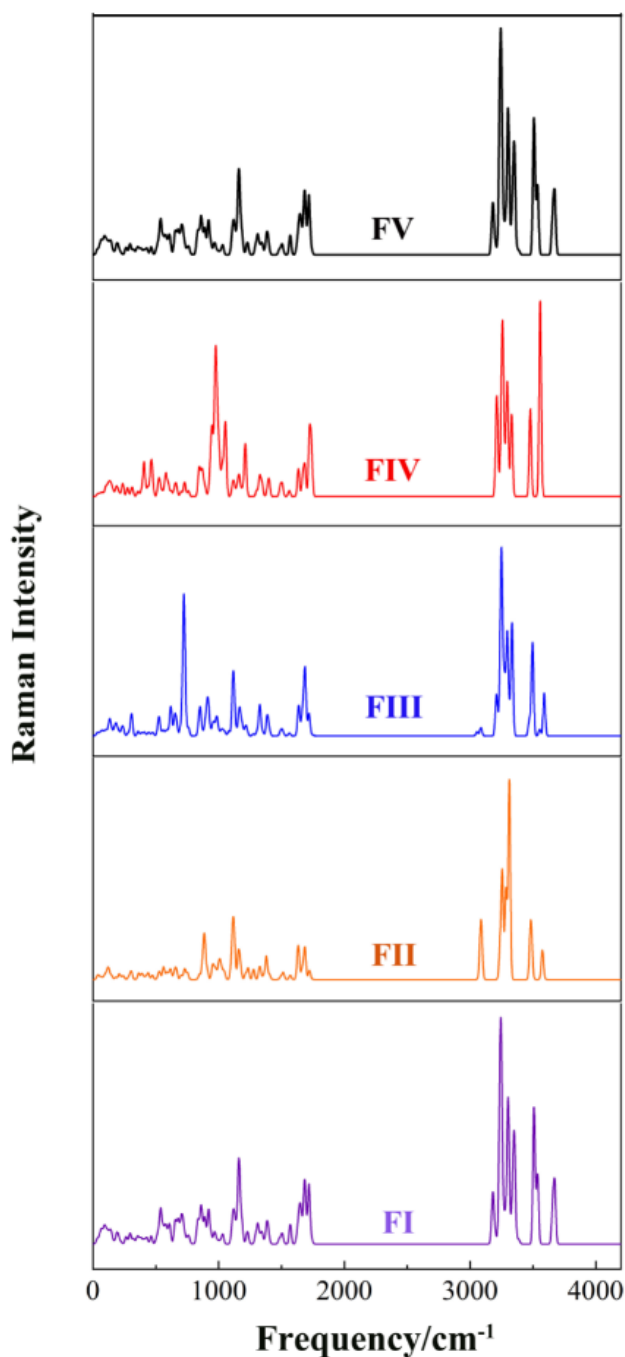


Figure S1 Calculated Raman spectra of five forms of STZ under standard atmospheric pressure.

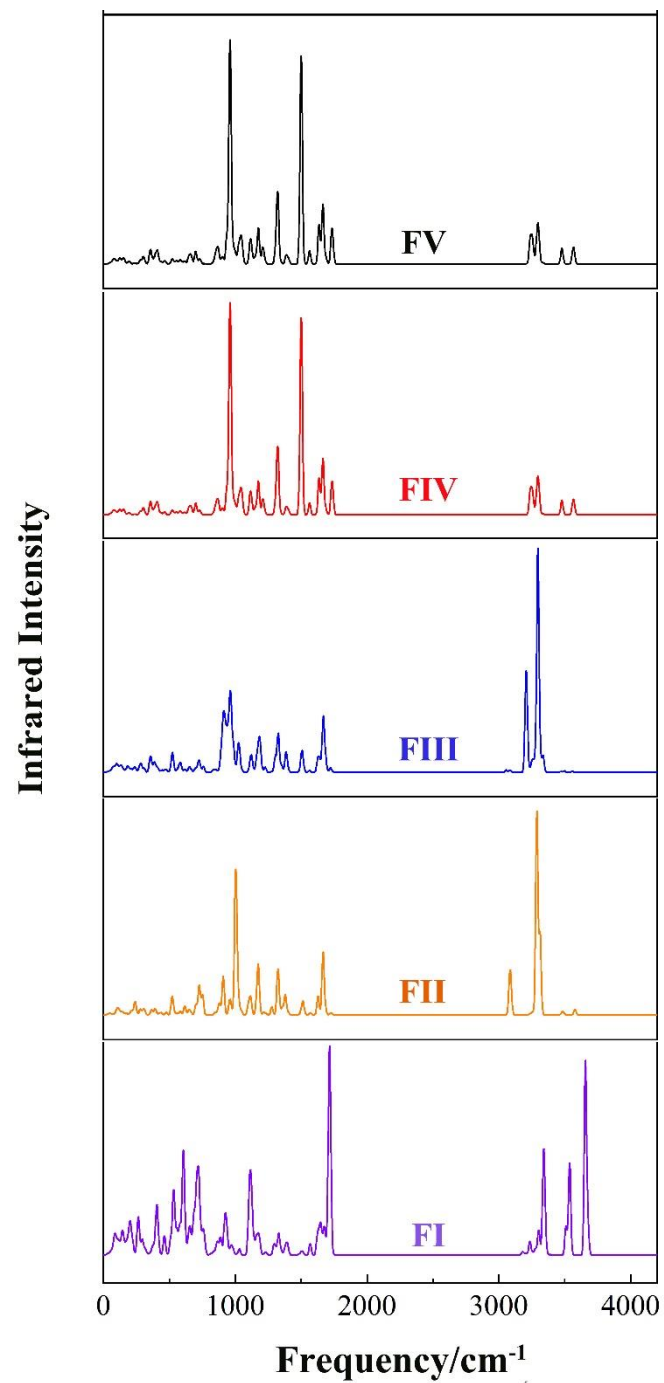


Figure S2 Calculated IR spectra of five forms of STZ under standard atmospheric pressure.

Table S1 The Gibbs free energy differences of five polymorphs of STZ. The calculated energy differences per molecule of STZ is for FI, FV, FIV, FII, with reference to FIII, respectively.

Polymorph	Gibbs free energy difference (kcal/mol)
FI	2.174
FII	0.255
FIII	0
FIV	0.292
FV	2.171