

INTRODUCTION

The importance of organic crystals in the technology advancement and development of materials such as drugs, catalytic, magnetic, electronic, and optical can not be over-emphasized owing to their unique properties.¹ The formation of good-quality crystals that will be useful has been a challenge since the discovery of X-ray diffraction. There is a general impression that salt molecules give good crystals than neutral, but the only report in the literature reveals that inorganic crystals with charge ions are larger, and the resultant crystallographic data are better than neutral organic crystals.² Here, we examined organic crystals with ionic or neutral species and their qualities.

The study aimed to investigate series of co-crystals and salts of substituted benzoic acid and substituted pyridine to assess the link (if any) between the electrostatic properties of the components and the quality of the crystals obtained experimentally. Selected molecules have series of pK_a values that will result in either co-crystal or salts of multi-components.

METHODOLOGY

Experimental

Synthesis of co-crystals and salts via slow evaporation crystallization technique.

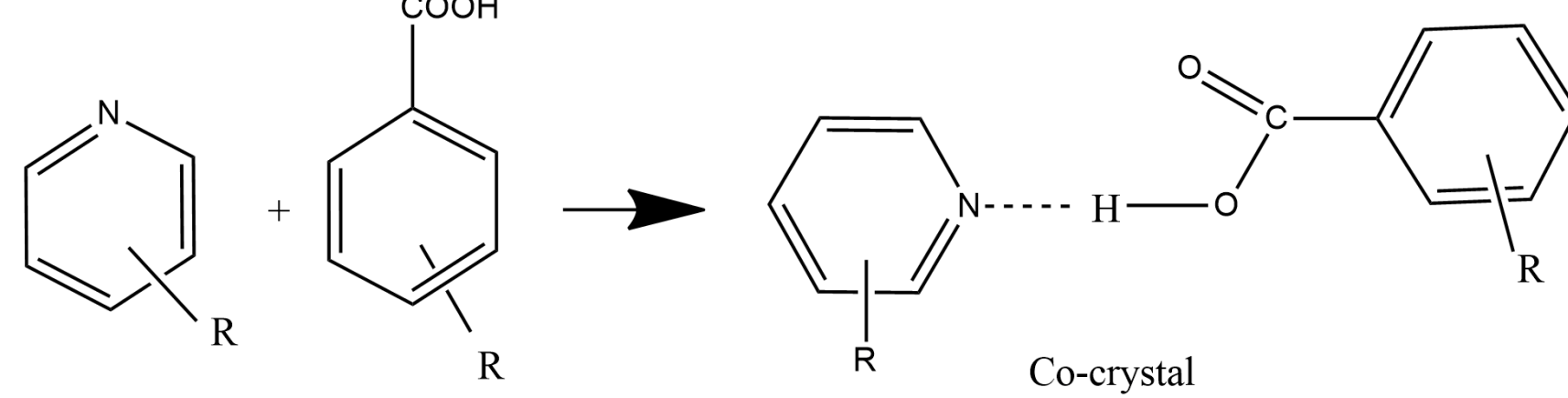


Figure 1: Synthesis of 1:1 of substituted pyridine and benzoic acid to give co-crystals

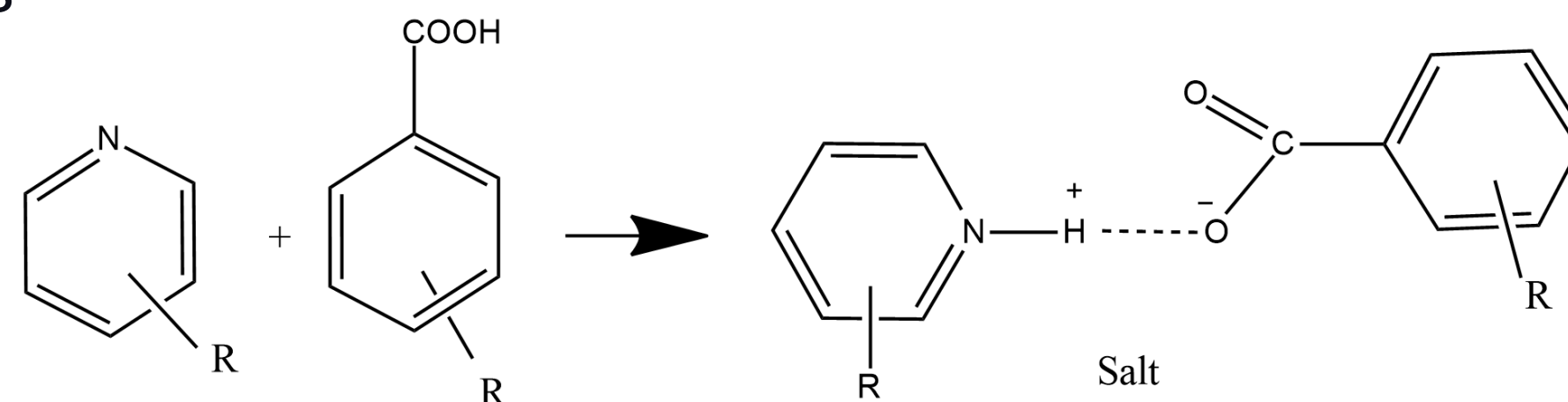


Figure 2: Synthesis of 1:1 of substituted pyridine and benzoic acid to give salt.

The mosaicity and R_{int} of crystal structure obtained from crystallographic data were used to establish the quality of the crystals.

Computational – Density Functional Theory (DFT)

-Interaction energy of crystal structure was calculated using Gaussian at, M06L/D3/def-2TZVP³ level of theory.

-Lattice energy: *CrystalExplorer*⁴ with B3LYP/6-31G(d,p)

-Molecular electrostatic surface potential: WFA-SAS suite.⁵ The surface statistics were mapped onto the molecular surface at an electron density of 0.001 au.⁶ The most positive and negative potentials (E_{max} and E_{min}) were selected for further analysis.

RESULTS

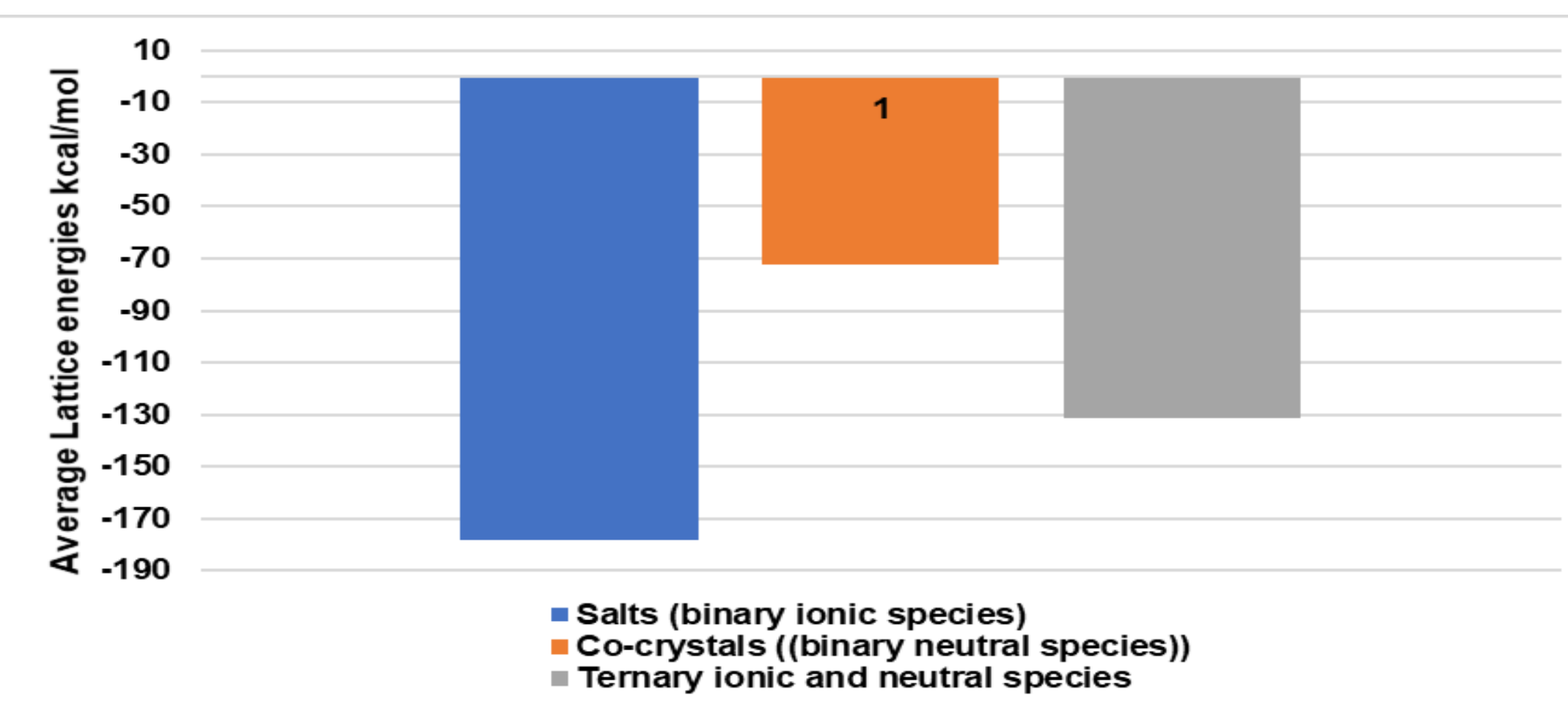


Figure 3: Average energy (kJ/mol) of co-crystals, salts and ternary components.

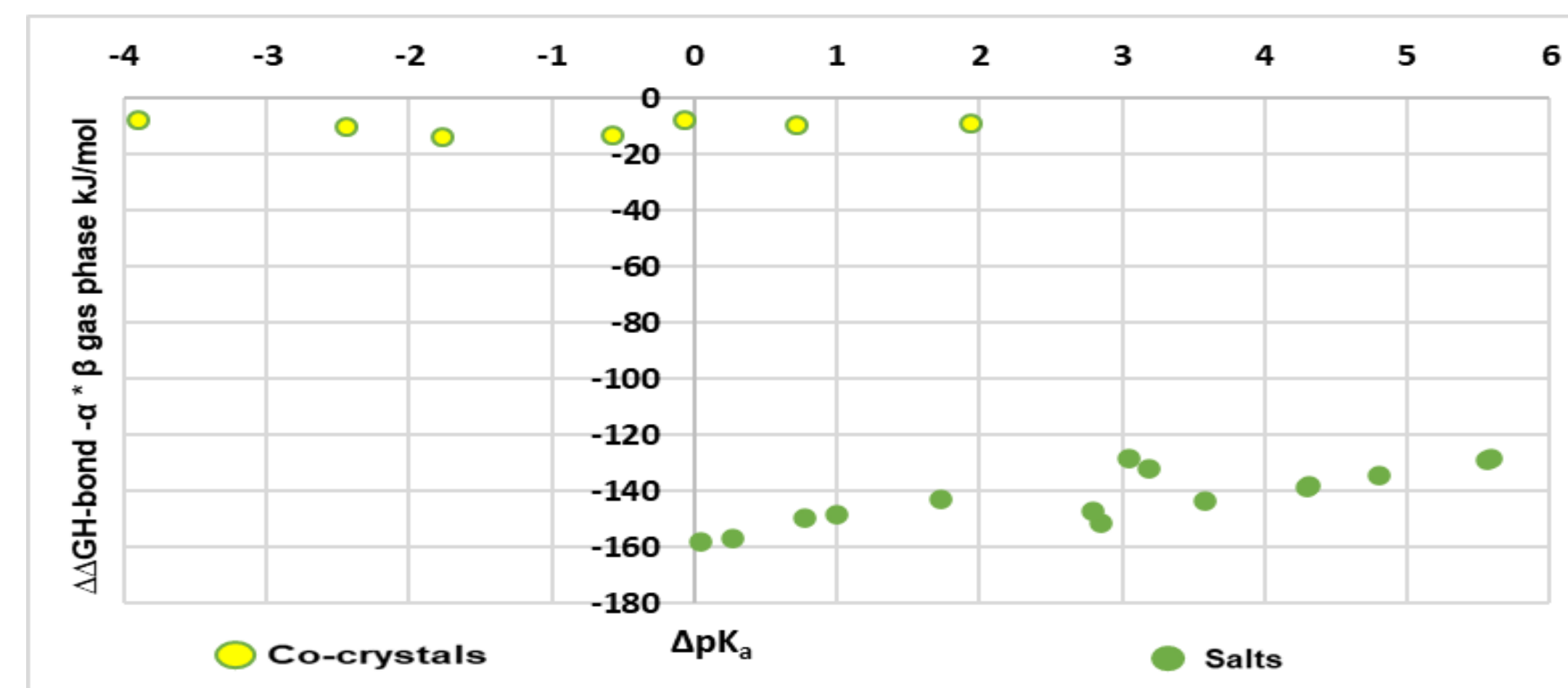


Figure 5: $\Delta\Delta G$ of salts and co-crystals in the gas phase

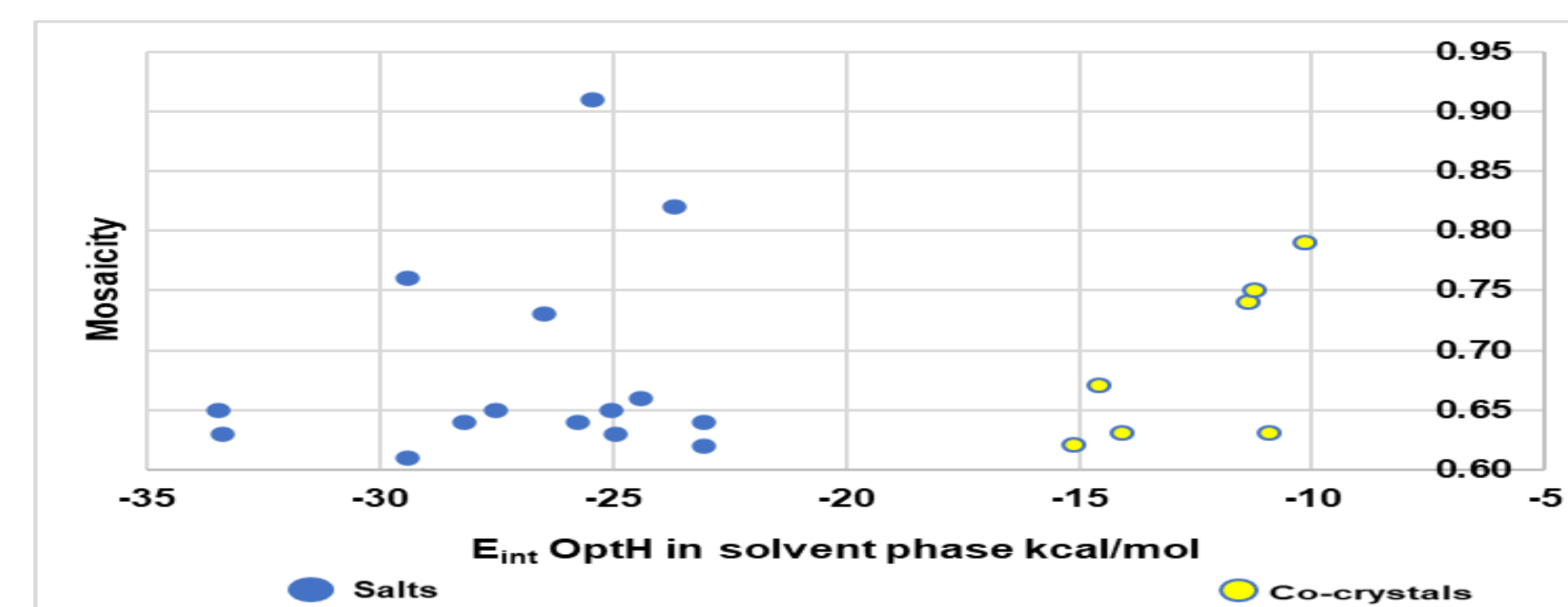


Figure 7: Mosaicity vs E_{int} of OptH in solvent phase

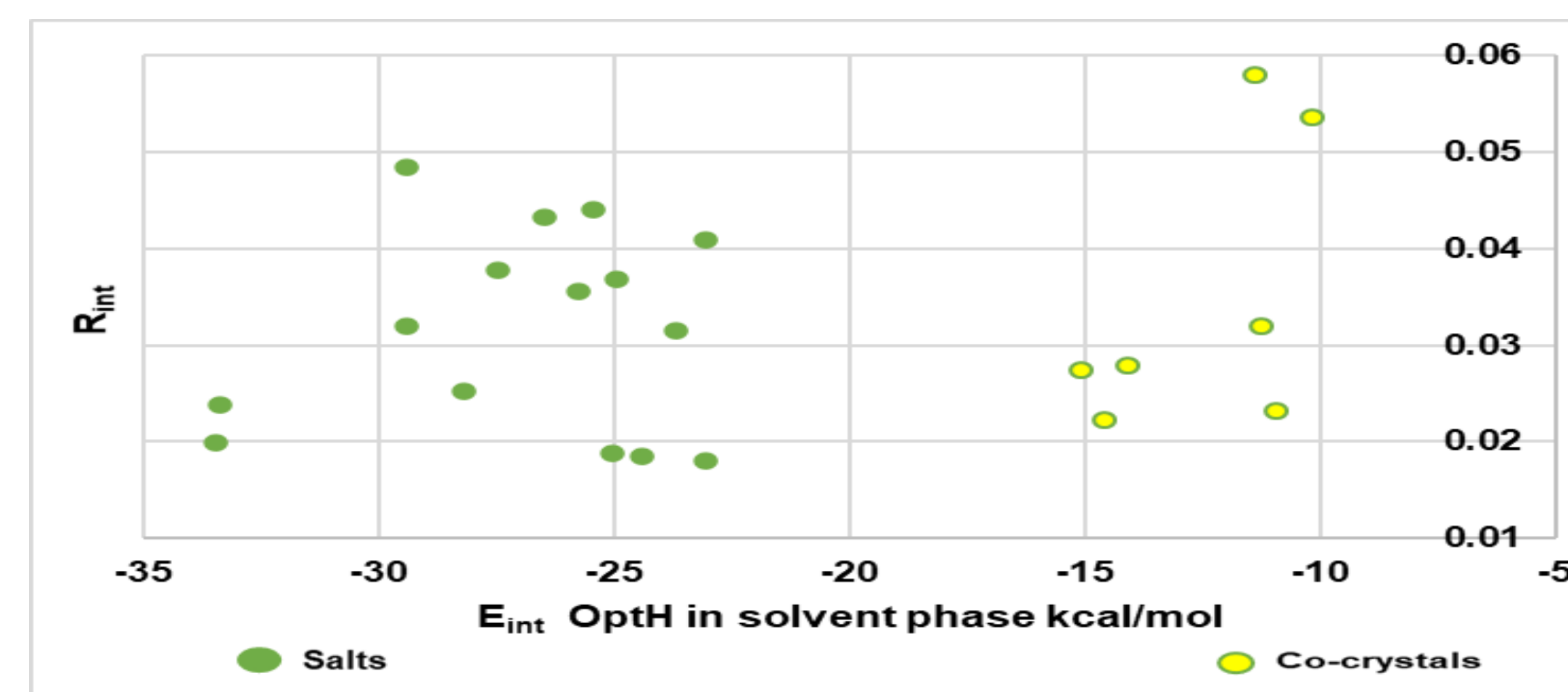


Figure 9: R_{int} vs E_{int} of OptH in solvent phase

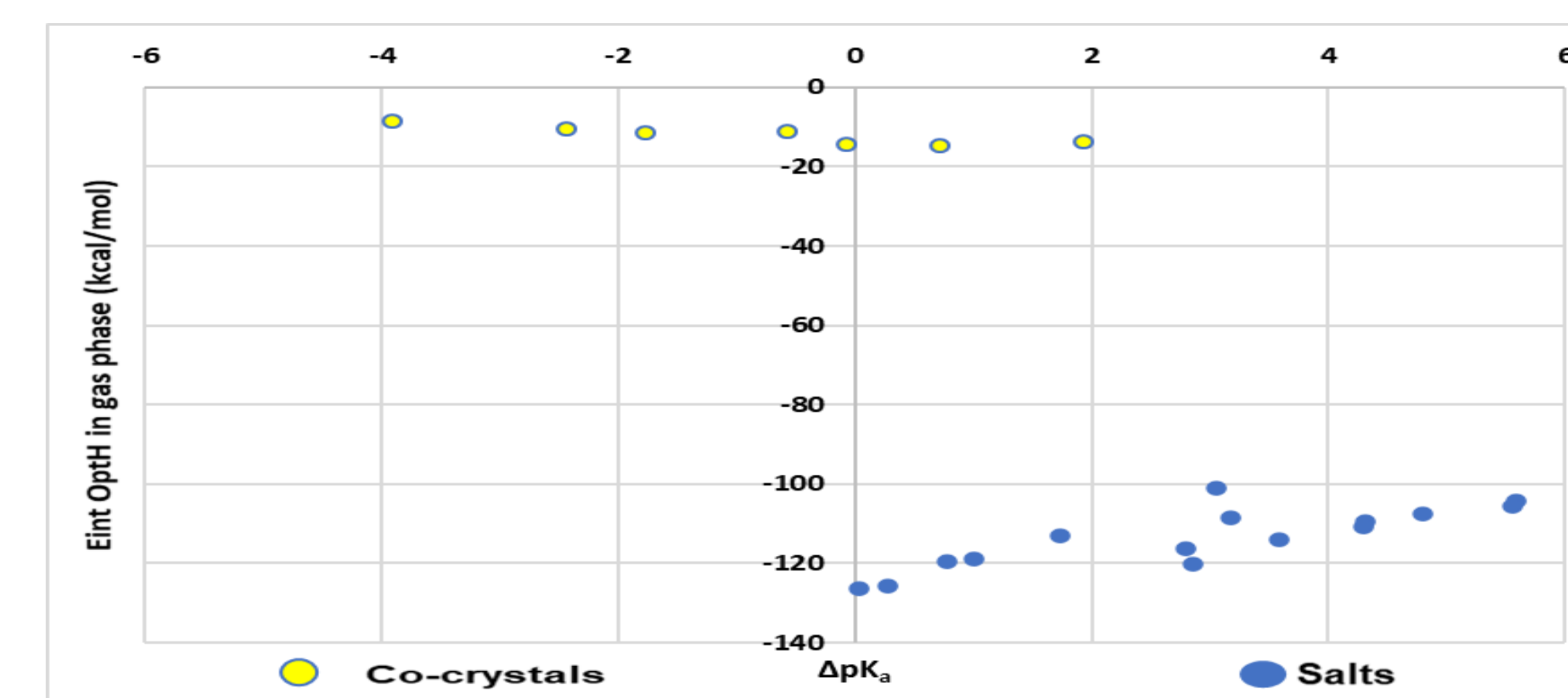


Figure 4: E_{int} (kcal/mol) in gas phase vs ΔpK_a

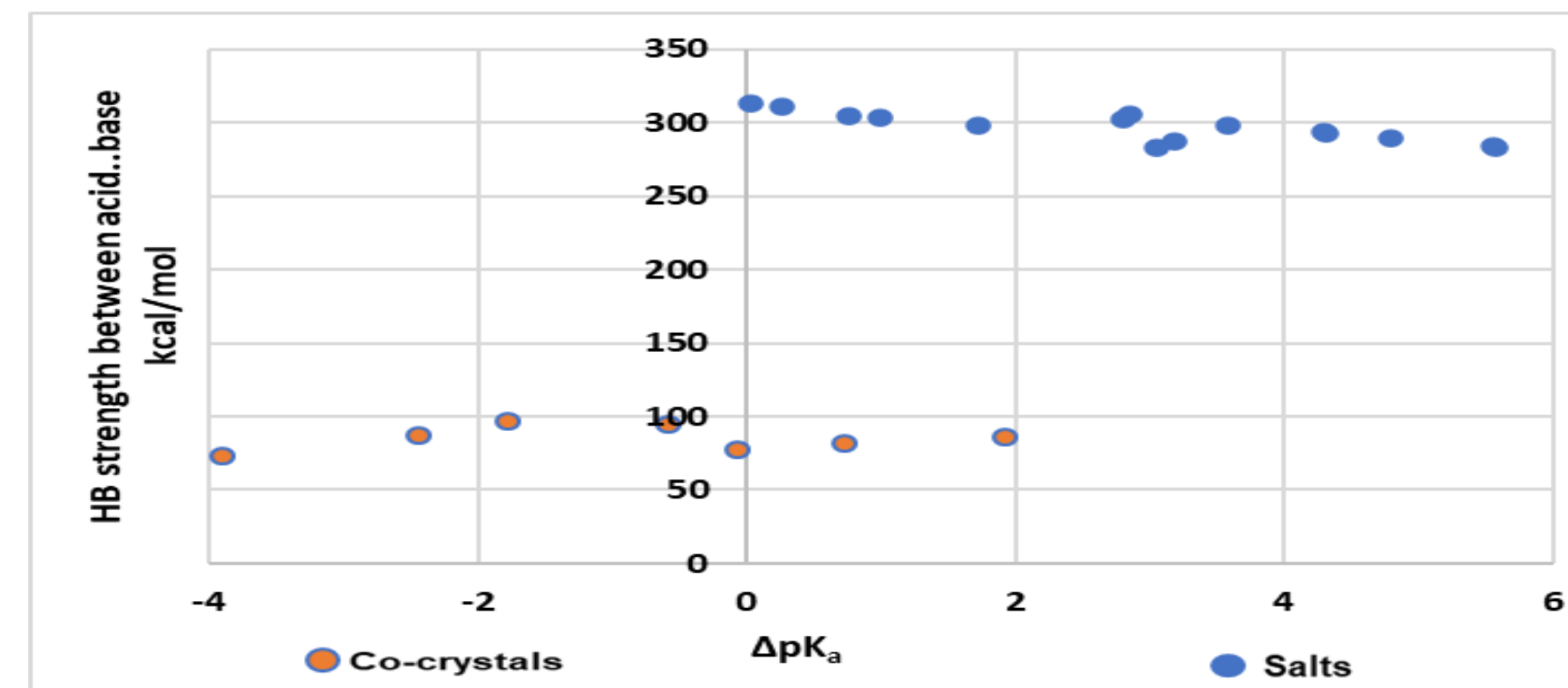


Figure 6: Difference between the E_{max} and E_{min} in co-crystals and salts against ΔpK_a . HB strength is the difference between the HBD and HBA of co-crystals and salts.

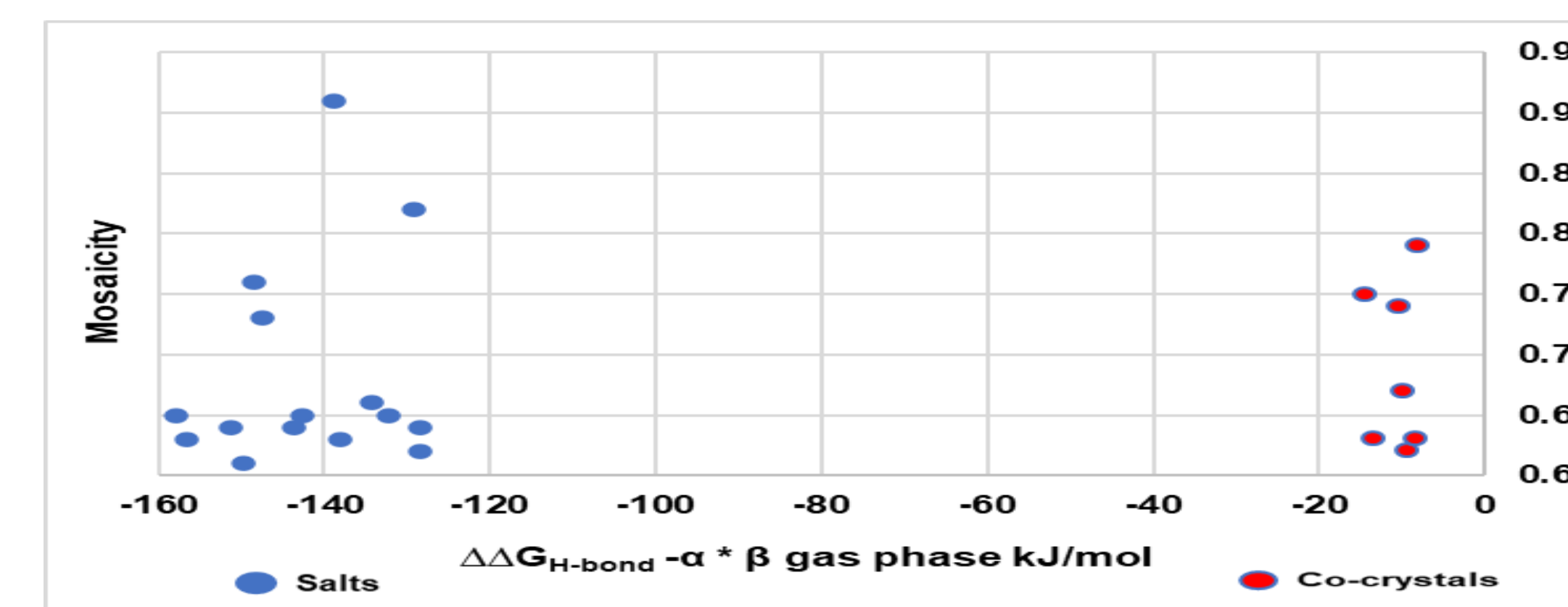


Figure 8: Mosaicity vs free energy of interaction in gas

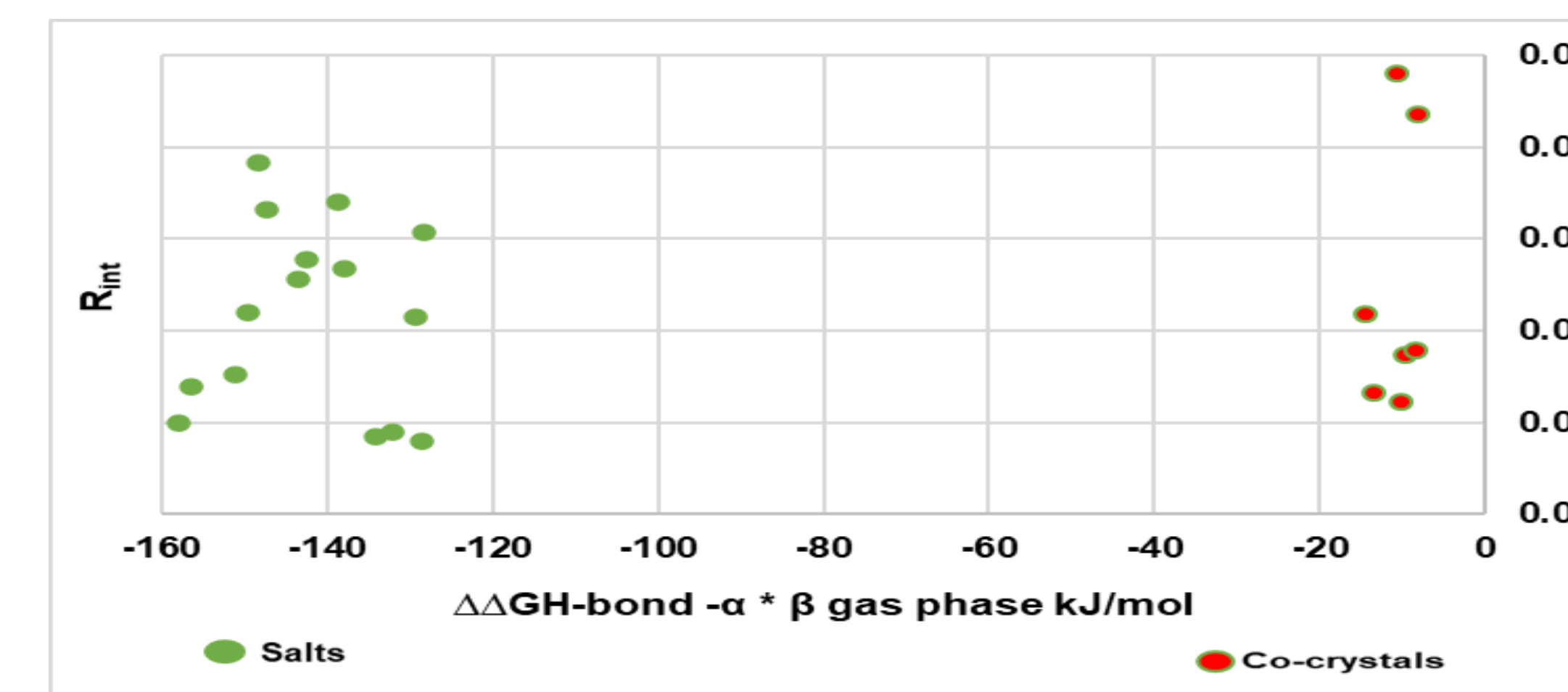


Figure 10: R_{int} vs free energy of interaction in gas

DISCUSSION

- ❖ The calculated lattice energies, interaction energies, and strength of HBD and HBA of the salts are higher than those of the co-crystals as shown in Figures 3 to 6, this means salts are more stable, their interactions are stronger, that is why it is difficult to break them into their individual molecules.
- ❖ Co-crystals and salts gave both low and high values of mosaicity and R_{int} . They were both found in the region of excellent crystallographic data (<0.04) and good-quality crystals (<0.7), and also found in the region of not-so-good crystallographic data (>0.04) and crystals (>0.7) as shown in Figures 7 to 10.
- ❖ The electrostatic, ionic character and strength of interactions of salts do not automatically translate into good-quality crystals of salts as we observed salt complexes at the region of bad crystals as well.
- ❖ The lattice energy, which is often used to predict the stability of crystal structure, does not correlate with the quality of crystals obtained experimentally.

CONCLUSION

- ❖ The formation of high-quality crystals may have been driven by the partial ionic character in the study conducted by Etter and Baure⁷ but, this is certainly not the case in the organic system.
- ❖ The quality of molecular organic crystals is not necessarily associated with the ionic nature or electrostatics of salts but rather with a combination of different factors.
- ❖ The findings in this study can be applied in the synthesis and design of quality crystalline molecules, which will be useful in the development of new technology and materials, that will improve the global economy. The development of materials that are self-reliant, environmentally friendly, and technically acceptable is one of the UN SDG.

REFERENCES

1. J. Hulliger, *Angew. Chem. Int. Ed. Engl.*, 1994, **33**, 143; A. Gavezzotti, *Solid State and Materials Science*, 1996, **1**, 501; E. Kemei, L. Yimin, L. Haiyang, *J. Mol. Struct.* 2003, **660**, 113.
2. M. Etter, D. Jahn, and B. Donahue, *J. Cryst. Growth*, 1986, **76**, 645.
3. F. Weigend, and R. Ahlrichs, *Phys. Chem. Chem. Phys.*, 2005, **7**, 329.
4. M. Turner, S. McKinnon, D. Wolff, P. Grimwood, D. Spackman, D. Jayatilaka, and M. Spackman, *CrystalExplorer17*, University of Western Australia. <http://hirshfeldsurface.net>, 2017.
5. F. Bulat, A. Toro-Labbé, T. Brinck, J. Murray, and P. Politzer, *J. Mol. Model.*, 2010, **16**, 1679.
6. R. Bader, M. Carroll, J. Cheeseman, and C. Cheng, *J. Am. Chem. Soc.*, 1987, **109**, 7968.
7. M. Etter, and P. Baures, *J. Am. Chem. Soc.*, 1988, **110**, 639.

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