PREDICTION OF SOLID SOLUTION FORMATION AMONG CHEMICALLY SIMILAR MOLECULES USING CALCULATION OF LATTICE AND INTERMOLECULAR INTERACTION ENERGY

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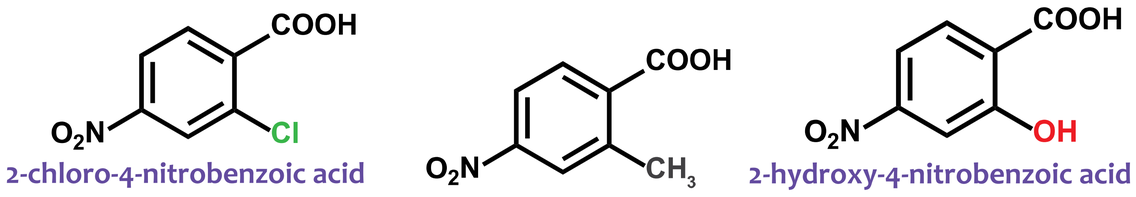
Introduction

Several 2-substituted 4-nitrobenzoic acid (**NBA**) derivatives (see below) were selected as model compounds because of their availability and chemically similar structures, in which the different group/atom (**-Cl, -CH_3 or -OH**) does not significantly affect the dominant intermolecular interactions.



2-chloro-4-nitrobenzoic acid | 2-methyl-4-nitrobenzoic acid | 2-hydroxy-4-nitrobenzoic acid

Molecular structures of studied 2-substituted 4-nitrobenzoic acid derivatives

Crystal structures of nitrobenzoic acid derivatives

	2C4NBA	2$CH_3$4NBA	2OH4NBA
	I	I	I
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	$P2_1/c$	$P2_1/c$	$P2_1/c$
a / Å	10.833(3)	4.9248(10)	3.8015(1)
b / Å	5.8573(14)	11.8428(2)	11.6936(4)
c / Å	13.497(3)	13.6012(2)	16.2761(5)
α / °	90	90	90
β / °	105.734(4)	92.036(2)	94.506(2)
γ / °	90	90	90
V / Å^3	824.32	792.76	721.28
$\rho_{calc.}$ / g·cm^{-3}	1.624	1.518	1.687
Z, Z′	4, 1	4, 1	4, 1
Temperature / K	297	293	290
Sample type	Single crystal	Single crystal	Single crystal
CSD identifier	VOLZEC	1945316	1945319
$E_{Lattice}$ / kJ·mol^{-1} [c]	-144.1	-140.6	-139.9
$E_{Inter.}$ / kJ·mol^{-1} [d]	-114.2	-118.2	-114.6

The commercially available 2OH4NBA, 2C4NBA and 2$CH_3$4NBA all correspond to polymorph I of the respective compound. All of these structures correspond to monoclinic system $P2_1/c$ space group with one independent molecules in the asymmetric unit.

Crystallization results

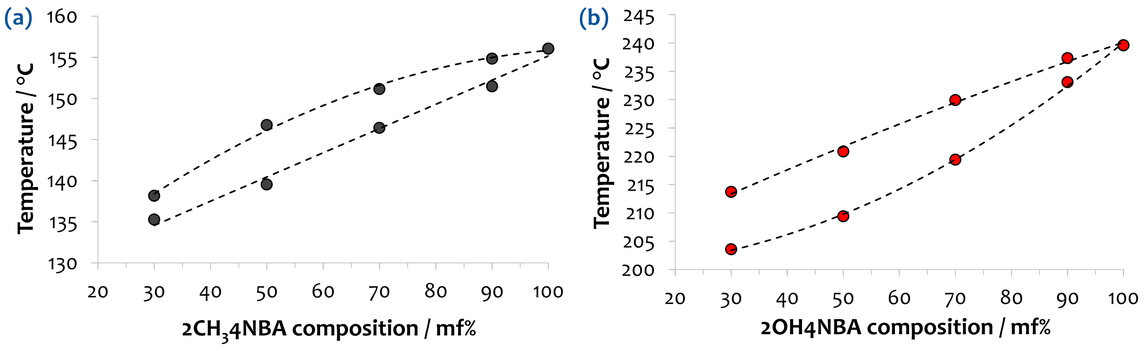
The preparation of the solid solutions of **2OH4NBA$_{100-x}$2C4NBA$_x$**, **2$CH_3$4NBA$_{100-x}$2C4NBA$_x$** and **2OH4NBA$_{100-x}$2$CH_3$4NBA$_x$** was based on crystallization from solvent (in this case from ethanol), in different proportions (%), from *100-x* to *x*, where $0 \le x \le 100$.

Experimentally obtained crystalline phases from different nitrobenzoic acid mixtures[a]

Substance ratio / %	Series of nitrobenzoic acid derivatives		
	2OH4NBA$_{100-x}$2C4NBA$_x$	2$CH_3$4NBA$_{100-x}$2C4NBA$_x$	2OH4NBA$_{100-x}$2$CH_3$4NBA$_x$
0:100	2C4NBA|	2C4NBA|	2$CH_3$4NBA|
10:90	Mixture	Mixture	SS[2$CH_3$4NBA]|
25:75	Mixture	SS[2$CH_3$4NBA]|	Mixture
30:70	SS[2OH4NBA]|	SS[2$CH_3$4NBA]|	Mixture
50:50	SS[2OH4NBA]|	SS[2$CH_3$4NBA]|	Mixture
70:30	SS[2OH4NBA]|	SS[2$CH_3$4NBA]|	SS[2OH4NBA]|
75:25	SS[2OH4NBA]|	SS[2$CH_3$4NBA]|	SS[2OH4NBA]|
90:10	SS[2OH4NBA]|	SS[2$CH_3$4NBA]|	SS[2OH4NBA]|
100:0	2OH4NBA|	2$CH_3$4NBA|	2OH4NBA|

[a] – 2OH4NBA = 2-hydroxy-4-nitrobenzoic acid, 2Cl4NBA = 2-chloro-4-nitrobenzoic acid, 2$CH_3$4NBA = 2-methyl-4-nitrobenzoic acid, I = polymorph, SS = solid solution

Structural aspects of solid solution formation



Melting points *vs.* mole fraction of (a) 2$CH_3$4NBA in 2$CH_3$4NBA$_{100-x}$2C4NBA$_x$ and (b) 2OH4NBA in 2OH4NBA$_{100-x}$2C4NBA$_x$ solid solutions

Solid solution formation can be confirmed by means of melting phase diagram. It precisely demonstrate that the 2-substituted 4-nitrobenzoic acid derivatives form solid solutions between each other.

Conclusions

- A prediction of the different experimental phase behaviors observed for these systems has been achieved meaning that the computational studies could be used to predict the solid solution formation for binary systems of various 2-substituted 4-nitrobenzoic acid derivatives.
- The results show that the lattice and intermolecular interaction energy could be used to determine if the respective solid solution will form, but do not allow prediction of solid solution formation having specific maximum ratios.

Acknowledgments

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Background

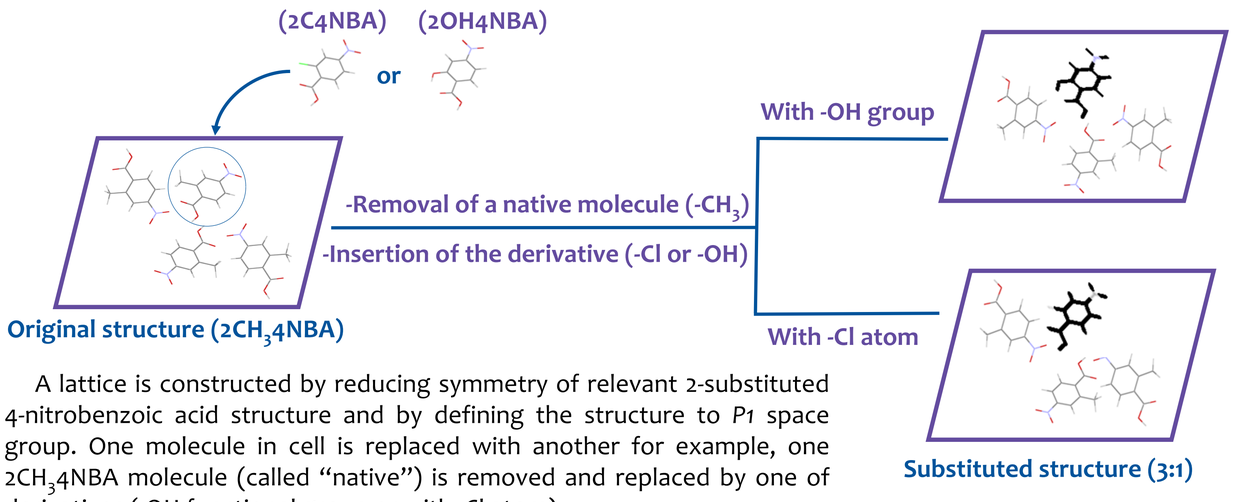
Organic solids are able to form very wide range of crystalline structures of different compositions – including polymorphs, solvates, co-crystals and solid solutions (SS). Both geometric and chemical aspects, such as molecule dimensions, symmetry, and intermolecular interactions, are important in understanding solid state properties of all these phases. In last decade research of solid solutions has increased significantly and has become common in crystal engineering. While analysing solid solutions and their molecular packing, more and more attention is paid to structural aspects that promotes and are responsible for the formation of solid solutions in two-component systems.

Aims

- To perfrom crystallization experiments between binary systems of various 2-substituted 4-nitrobenzoic acid derivatives (such as 2OH4NBA, 2$CH_3$4NBA and 2C4NBA) to experimentally determine the information about formation of solid solutions
- To identify possible factors which could be used in prediction of the formation of solid solutions between chemically similar molecules

Molecular modelling

Lattice as well as intermolecular interaction energies were calculated for original, isostructural and substituted structure (schematic example see below).



A lattice is constructed by reducing symmetry of relevant 2-substituted 4-nitrobenzoic acid structure and by defining the structure to *P1* space group. One molecule in cell is replaced with another for example, one 2$CH_3$4NBA molecule (called "native") is removed and replaced by one of derivatives (-OH functional group or with -Cl atom).

Crystalline lattice cell volume

The volume of cells (see below) and each individual molecule (**2$CH_3$4NBA = 124.2 cm^3·mol^{-1}**, **2C4NBA = 126.6 cm^3·mol^{-1}** and **2OH4NBA = 110.3 cm^3·mol^{-1}**) were estimated as known the fact that when replacing a "native" molecule in a crystalline structure, attributable to a substituted structure (as it is in the case of a solid solution), the cell must expand, resulting in a volume change.

Volumes of crystalline structures (original, substituted, and isostructural)[b]

Molecule	Substituted with	V / Å^3 Original	Subst.	Isostr.	Molecule	Substituted with	V / Å^3 Original	Subst.	Isostr.
2OH4NBA	**-Cl**	636.5	▲ **648.1**	▲ **682.5**	**2C4NBA**	**-OH**	784.9	▲ **786.3**	▼ 742.0
2C4NBA	**-CH_3**	784.9	▲ **785. 0**	▼ 777.6	**2$CH_3$4NBA**	**-Cl**	742.3	▲ **744.7**	▼ 740.5
2$CH_3$4NBA	**-OH**	742.3	▲ **744.1**	▼ 707.7	**2OH4NBA**	**-CH_3**	636.5	▲ **651.0**	▲ **684.7**

[b] – Crystal structures were used after full geometry optimization in *Quantum ESPRESSO*

Analysis of the molecular modelling results

Lattice energies of various structures of 2-substituted 4-nitrobenzoic acid derivatives[c]

Molecule	Substituted with	$E_{Lattice}$ / kJ·mol^{-1} Original	ΔE / kJ·mol^{-1} Subst.	Isostr.	Molecule	Substituted with	$E_{Lattice}$ / kJ·mol^{-1} Original	ΔE / kJ·mol^{-1} Subst.	Isostr.
2OH4NBA	**-Cl**	-139.9	1.0	1.0	**2C4NBA**	**-OH**	-144.1	1.7	28.6
2C4NBA	**-CH_3**	-144.1	0.4	**-0.4**	**2$CH_3$4NBA**	**-Cl**	-140.6	0.2	4.7
2$CH_3$4NBA	**-OH**	-140.6	0.2	10.4	**2OH4NBA**	**-CH_3**	-139.8	1.2	1.7

[c] – Calculation of lattice energy was performed in *Quantum ESPRESSO* using *SCF* and *VC-relax* calculations

Intermolecular interaction energies of various structures of 2-substituted 4-nitrobenzoic acid derivatives[d]

Molecule	Substituted with	$E_{Inter.}$ / kJ·mol^{-1} Original	ΔE / kJ·mol^{-1} Subst.	Isostr.	Molecule	Substituted with	$E_{Inter.}$ / kJ·mol^{-1} Original	ΔE / kJ·mol^{-1} Subst.	Isostr.
2OH4NBA	**-Cl**	-114.6	3.2	**-1.3**	**2C4NBA**	**-OH**	-114.2	4.6	0.5
2C4NBA	**-CH_3**	-114.2	**-4.9**	**-7.5**	**2$CH_3$4NBA**	**-Cl**	-118.2	**-1.0**	0.6
2$CH_3$4NBA	**-OH**	-118.2	0.9	**-0.4**	**2OH4NBA**	**-CH_3**	-114.6	2.9	0.9

[d] – The *CrystalExplorer 17.5* was used for calculation of intermolecular interaction energy between molecule pairs at the B3LYP-D2/6-31G(d,p) level

Notes and references

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