Oral presentation

A predictive tool for estimating the melting point of a binary mixture for mechanochemical syntheses and cocrystallizations

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The prediction of the phase behaviour of a mixture of solid components when the materials come into contact is attracting a high interest in fastly growing research fields such mechanochemistry (MC) and deep eutectic solvents (DES). In MC processes, reactions implying breaking and forming covalent bonds or supramolecular aggregation occur by grinding dry components together; the mechanism of MC reaction paths is far to be understood, but it has been suggested that in some cases proceeding through liquid intermediates may facilitate the activation of the process.

Some examples where cocrystal formation occurs through metastable liquid eutectics have been published recently [1].

A prior knowledge of the possibility that the reaction mixture could give a low melting eutectic [2] would be greatly advantegeous for the experimental design of more efficient MC protocols. Analogously, the estimation of the effect of intermolecular interactions in depressing the melting point for DES has been approached with computational methods, but simple guidelines are not available. The estimation of the effect of intermolecular interactions in depressing or raising the melting point of eutectic mixtures is not straigtforward, and for deep eutectic solvents (DES) several parameters have been proposed for defining the depression gap of binary mixtures from ideality [3] but calculations are often considerably time-consuming.

This paper provides some easily usable guidelines and quantitative references to estimate the decrease of melting point for a DES or of a mixture of reactants for a MC process relatively to the separate components. An empirical model relating intermolecular interactions and departure from ideality is presented, allowing to design synthetic procedures for solventless cocrystallization processes.

As a working example we here consider how to design a cocrystal containing thymol as the active ingredient, combined with possible coformers taken from the GRAS list, in case we desire that cocrystallization proceeds through a metastable liquid phase (Fig. 1).

	EUTECTIC TEMPERATURE									
$T_c/\Delta H_c$	10	14	18	22	26	30	34	38	42	46
320	277	283	287	291	293	295	297	298	299	301
335	279	286	290	293	296	298	300	301	303	304
350	281	288	292	296	298	301	303	304	305	307
365	283	290	294	298	301	303	305	307	308	309
380	285	291	296	300	303	305	307	309	310	311
395	286	293	298	301	304	307	309	311	312	313
410	287	294	299	303	306	308	310	312	314	315
425	288	296	301	304	307	310	312	314	315	316
440	289	297	302	306	309	311	313	315	316	317
455	290	298	303	307	310	312	314	316	317	318

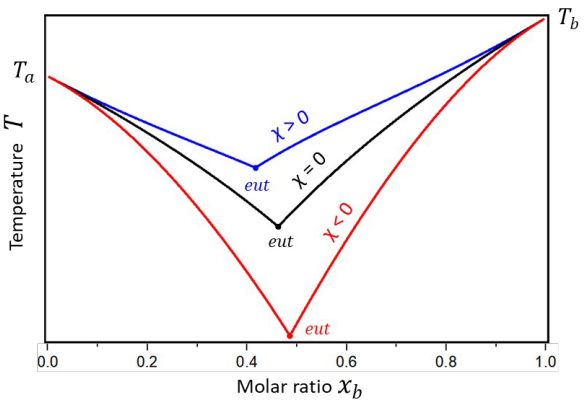

Figure 1. Left: Estimate of eutectic melting temperature for an array of hydrogen bonding coformers combined with thymol; right: eutectic depression departing from ideality (χ=0) at different levels of intermolecular interactions (X<0, X>0).

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