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# Mechanochemical deracemization : Study of the impact of a chiral impurity

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During the last decades, separation of enantiomers became of paramount importance since more than 50% of the marketed drugs are chiral.<sup>[1]</sup> Several methods have been developed to isolate pure enantiomers, aiming at highest yield, productivity and lowest cost. Methods using crystallization are generally preferred for economic reasons. Among them, deracemization is an attractive procedure that permits to convert 100% of a racemic conglomerate into a pure enantiomer by combining dissolution, solution racemization and recrystallization. The enantiomeric conversion at the solid state relies on the disappearance of one enantiomeric population by using constant energy input (either using abrasion or temperature cycling). Deracemization processes exhibit high yields and can be easily scaled-up.<sup>[2]</sup> However, the use of solvent is an important drawback of deracemization: in addition to potential toxicity, solvent needs to be recycled, increasing the cost and the carbon footprint of the process.

Besides, mechanochemistry refers to the use of high energy milling to overcome the energy barrier required by several chemical reactions.<sup>[3]</sup> A mechanochemical process requires only few amount of solvent, while maintaining a similar (or even better) yield of reaction compared to solutions. Thus, we managed to transfer deracemization to high energy milling conditions, improving process productivity and providing a greener approach to enantiomeric separation.<sup>[4]</sup>

However, such processes imply equals probability to obtain R or S enantiomers. Orientation of the outcome towards the desired enantiomers is possible by starting with an enantioenriched media. Yet, it implies the constraint to own the pure enantiomer of the studied compound. A part of our work is based on the orientation of mechanochemical deracemization by using a chiral impurity. Despite the success of this project, some questions remain regarding the implied mechanisms. How two species that share no particular solid/solid interactions succeed to interact together in a milling media? More than that, what kind of interactions permit to orientate the deracemization?

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