# Nornicotine enantiomers and their salts – crystallographic cases on the way to the synthesis and enantioseparation of pure (S)-nicotine

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Nicotine related industry is still under development and methods for efficient synthesis of (*S*)-nicotine enantiomer are still wanted [1]. To fulfil this need a crystallization process as an intermediate step was proposed [2]. The studies on the crystal forms obtained during these experiments only mentioned previously are discussed here in details. The nornicotine was crystallized with N-lauroyl-(*S*)-alanine to yield a few crystallographic forms. The results of crystallization experiments are shown in Fig. 1. The number of hydrogen bonds and their architecture decided on the success of efficient enantioseparation process in certain conditions. This approach proved to be more economical and efficient than previously used multistep synthesis methods of (*S*)-nicotine. Additional advantage of this method is the lack of contamination with nitrosamines. Detailed crystallographic analysis of crystal structures of these salts is presented along with Hirshfeld surface and energy framework analysis.

a) b) c)

d) e) f)

###### **Figure 1**. Crystal structures of obtained salts of nornicotine enantiomer *S* (a, d), *D* (b, e) and racemate (c, f) with N-lauroyl-(S)-alanine.

#### [1] Agarthimoole, R.K.; Gagan, S.; Parida, S.; Dimesh, T.K.; Karatholuvhu, M.S.; Palani, N.; Mukherjee, S. (2022) A novel approach for the synthesis of (*R*) and (*S*)-nicotine. Int. J. Org. Chem. ***12***, 189–199.

#### [2] Trotsko, N., Miroslaw, B., Jasiński, R., Długosz, M., Sadczuk, M., & Demchuk, O. M. (2024). Efficient Method of (*S*)-Nicotine Synthesis. *Molecules*, ***29***(23), 5731.

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