MODELING IN TARGETED SYNTHESIS

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The studies on the modeling of active structures both in the targeted synthesis of biologically active compounds with given properties and in catalysis are considered. The methodology is divided into 3 parts according to the complexity and accuracy of the calculations:

1) Discrete (common), where the total binding energy is the sum of the interactions between functional groups of the ligand and the target.

2) Dynamically optimized – showing the fluctuations of the total energy of the components and allowing for conformational filtering and solvent participation. This method, in addition to modeling kinase inhibitors: PARP[1], Syk[2] and ABL[3], was used to predict the configuration of products of asymmetric synthesis in the presence of an inducer[4], as well as in calculations of the Suzuki reaction mechanism[5]. Using quantum chemical methods[6] all possible transition states (TS) in the Diels–Alder reaction catalyzed by SpnF were analyzed and it was established that this reaction preferably proceeds through (6+4)-bis-pericyclic TS rather than (4+2)-TS[7].

3) In 2019, we found that the accuracy of calculating the binding of a molecule (ligand) to a protein in the framework of the docking approaches is significantly increased if the interaction energy with the active center is normalized to that with the protein surface. To take this effect into account, a 'over-the-hood docking', or 'OTH-docking', algorithm has been developed, which increases the accuracy of virtual screening by 35–50% ROC AUC.

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