Explanation and prediction of nucleophilic reaction's facial selectivity of cyclic ketones by calculating steric and orbital factor.

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We have developed a new method to explain and predict the facial selectivity of nucleophilic reactions by evaluating the difference between the steric factor and the lowest unoccupied molecular orbital (LUMO) electron density (orbital factor) of both π planes of cyclic ketones. We quantified the steric and orbital factors of various cyclic ketones using this method, and regression analysis of the facial selectivity for each nucleophile yielded interesting results: while the orbital factors contribute relatively more to the facial selectivity for NaBH4 and LiAlH4, the steric factors dominate for LiAl(OMe)3H, MeLi, MeMgX and PhMgX. The parameters of the space in which the steric and orbital factors are evaluated (evaluation space) were optimized, and it was found that the evaluation space is larger in the PhMgX system than in the MeLi and MeMgX systems, reflecting the size of the nucleophile. This method is not only simple and easy to understand, but also reasonable and reflects experimental facts. We think this method will be an effective tool for organic chemists to understand the facial selectivity of nucleophilic reactions.