QUEST FOR ASYMMETRIC KULINKOVICH REACTION: FROM MECHANISM TOWARDS ENHANCED ENANTIOSELECTIVITY

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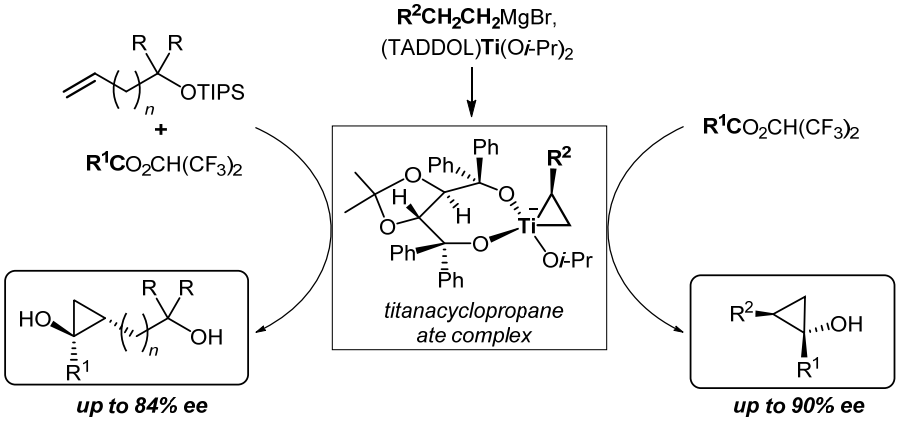
Discovery of titanium-catalyzed cyclopropanation of carboxylic esters in the late 1980s by the group of Kulinkovich commenced the era of titanacyclopropanes in organic synthesis. Despite the high synthetic value of the Kulinkovich reaction and its congeners, asymmetric version remains an unsolved challenge. The latest advances were possible due to ingenious insight that pentacoordinated titanium ate complexes, rather than tetracoordinated titanium species, mediate the process [1]. Mechanistic and solution NMR studies strongly support the idea of ate complex intermediates as a prerequisite of high enantiocontrol, while degradation of ate species result in dramatic erosion of enantioselectivity. Based on these findings, an improved protocol has been development for asymmetric Kulinkovich reaction, allowing preparation of (1*S*,2*S*)-cyclopropanols with up to 90% ee by using titanium (4*R*,5*R*)-TADDOLates. Expansion of the same methodology to hydroxycyclopropanation of prochiral olefins via a more convenient olefin ligand exchange method will be also presented [2].



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[1] Kulinkovich, O. G.; Kananovich. D. G.; Lopp, M.; Snieckus, V. *Adv. Synth. Catal*. **2014**, *356*, 3615.

[2] Iskryk, M.; Barysevich, M.; Ošeka, M.; Adamson, J.; Kananovich, D. *Synthesis* **2019**, DOI: 10.1055/s-0037-1611709