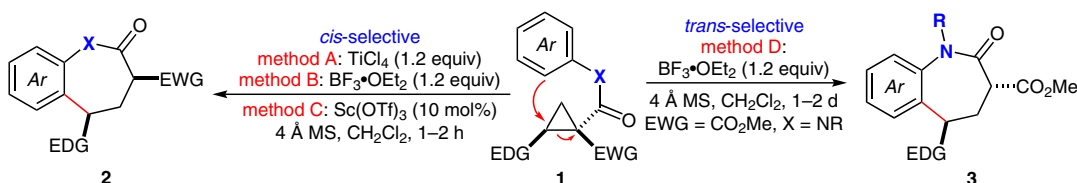


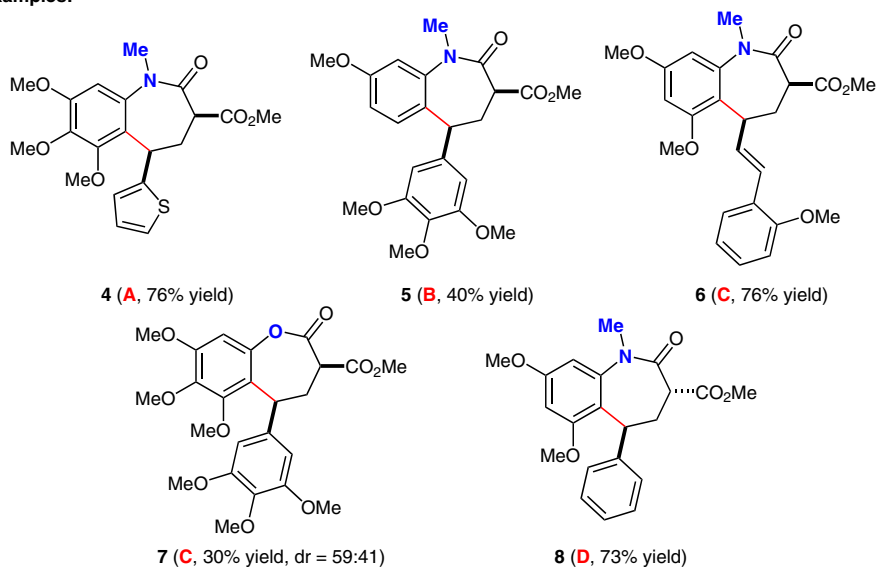
A. E. VARTANOVA, A. Y. PLODUKHIN, N. K. RATMANOVA, I. A. ANDREEV, M. N. ANISIMOV, N. B. GUDIMCHUK, V. B. RYBAKOV, I. I. LEVINA, O. A. IVANOVA*, I. V. TRUSHKOV*, I. V. ALABUGIN* (FLORIDA STATE UNIVERSITY, USA; N. D. ZELINSKY INSTITUTE OF ORGANIC CHEMISTRY, MOSCOW AND MOSCOW STATE UNIVERSITY, RUSSIAN FEDERATION) Expanding Stereoelectronic Limits of *endo-tet* Cyclizations: Synthesis of Benz[*b*]azepines from Donor–Acceptor Cyclopropanes *J. Am. Chem. Soc.* **2021**, *143*, 13952–13961, DOI: 10.1021/jacs.1c07088.

Demonstrated 6-*endo-tet* Cyclizations!

Transformation of cyclopropanes to benzazepinones:



Examples:



Significance: Baldwin's rules represent established dogma when considering the chances of a specific cyclization reaction occurring, and are based on the geometric restraints within the cyclic transition states (TSs) associated with the ideal trajectories for engagement of the reacting centers. These constraints are particularly strong when the attack of a nucleophile at an electrophilic sp^3 -carbon atom takes place to break a bond inside a cyclic TS (an *endo-tet* cyclization) that has fewer than eight atoms, and although there is some debate regarding 7-*endo-tet* reactions, the 5-*endo-tet* and 6-*endo-tet* TSs are clearly disfavored. The current report describes a genuine 6-*endo-tet* process to form a seven-membered ring through intramolecular ring opening of donor–acceptor cyclopropanes to form biologically significant tetrahydro-benz[*b*]azepin-2-ones.

Comment: Optimization experiments focused on the screening of Lewis acids, a number of which were identified as capable of promoting the reaction, leading to several general methods being developed, the best of which, in terms of yield and diastereoselectivity, depended on the nature of the substrate. These experiments also showed that under otherwise constant conditions, increasing the reaction time led to the formation of the *trans* isomers through isomerization of the kinetically controlled *cis* products. The S_N2 nature of the process was confirmed through the observed inversion of stereochemistry at the electrophilic carbon atom in the formation of **8**, thereby proving that the reaction constituted a genuine *endo-tet* cyclization, while DFT calculations supported this hypothesis in demonstrating that the proposed mechanism does not involve carbocationic intermediates.

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Category

Synthesis of
Heterocycles

Key words

Lewis acids

Baldwin's rules

endo-tet cyclization

benzazepines

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