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Stereoselective Total Synthesis of Eburnane-Type Alkaloids Enabled by Conformation-Directed Cyclization and Rearrangement


Synthesis of Eburnane-Type Alkaloids

Significance: Zhu and co-workers present their recent efforts to access eburnane-type alkaloids using a highly divergent approach. The presented route features an \( \alpha \)-iminol rearrangement to access the trans-fused core in intermediate \( D \). The conformational bias allowed to close the remaining six-membered ring of the eburnane core in a diastereoselective fashion. The divergent design of the route uses key intermediates \( D \) and \( E \) to access four different eburnane alkaloids with good yields.

Comment: \( \alpha \)-iminol rearrangement of \( C \) led to key intermediate \( D \). Oxidative cleavage of the diol and reduction yielded hexacyclic aminal \( F \) as a single diastereomer. Lewis acid induced 1,2-alkyl shift of \( F \) furnished (±)-terengganensine B. Reduction to alcohol \( G \) and Brønsted acid mediated rearrangement allowed synthesis of (±)-larutensine. Oxidation of diol \( D \) to the corresponding diketone and subsequent oxidative bond cleavage gave pentacyclic amide \( I \). (±)-Melokhanine E was obtained in five additional steps and was then converted into (±)-eburnamonine by means of an aza-pinacol rearrangement.