Collective total synthesis of stereoisomeric yohimbine alkaloids
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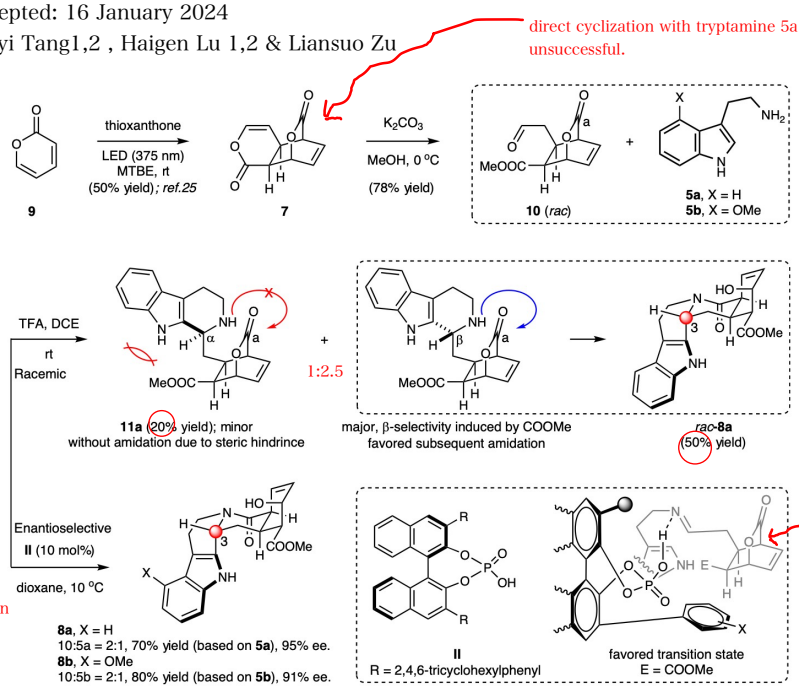
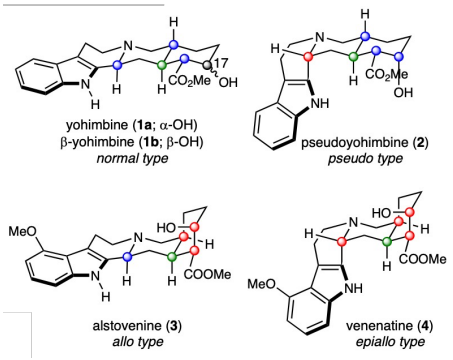
direct cyclization with tryptamine 5a unsuccessful.




optimization

the matched half of 10

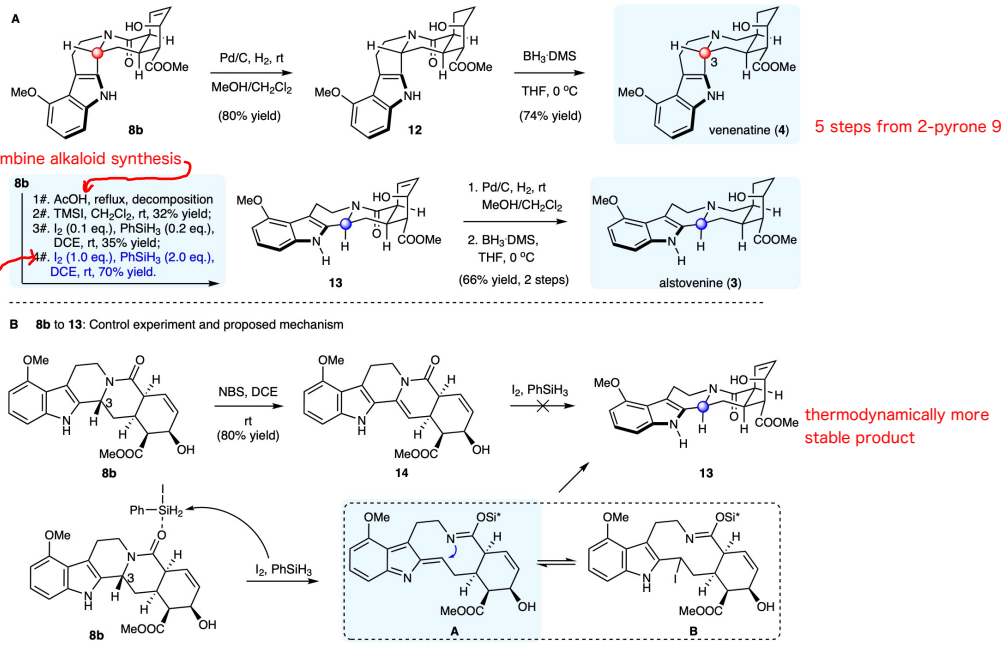



setting up the desired C3-stereochemistry of this type has been a long-standing challenge;

**Bioinspired Coupling**
- achiral synthetic surrogate **7**
  easily accessible from pyrone in a single step
- enantioselective control all five chiral centers
- rapid skeleton construction (**8**)

Pictet-Spengler/amidation cascade.

**Fig. 2 | Three-step construction of the pentacyclic skeleton.** Racemic version used trifluoroacetic acid (TFA) as the promotor. Enantioselective version used chiral phosphoric acid catalyst **II**. MTBE: methyl *tert*-butyl ether.




5 steps from 2-pyrone 9

previously used for yohimbine alkaloid synthesis

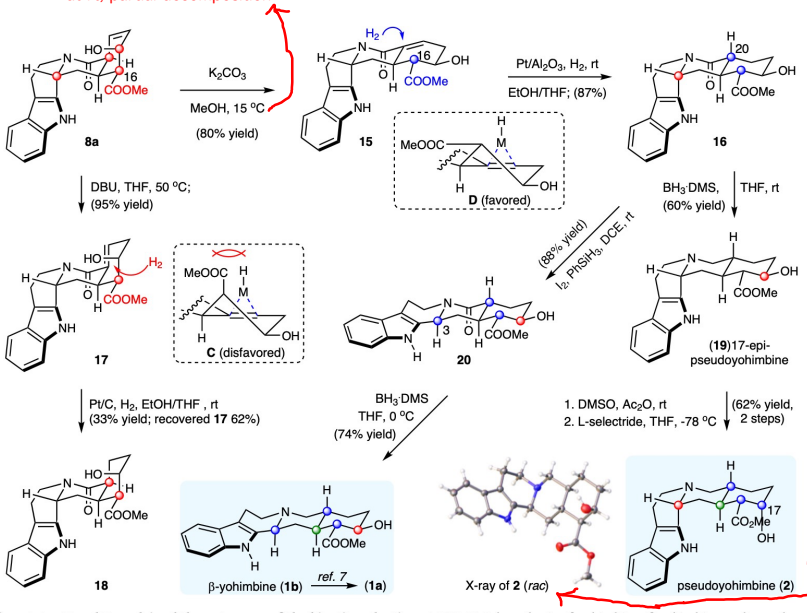
bioinspired coupling and stereochemical diversification

stoichiometric due to the presence of the free hydroxy group

thermodynamically more stable product

**Fig. 3 | Total synthesis of alstovenine and venenatine. A**: synthetic route to alstovenine and venenatine. **B**: control experiment and proposed mechanism for the C3-epimerization.

at 0 °C, no epimerization;
at rt, partial decomposition




using only tryptamine and pyrone as the starting materials in an enantioselective, atom-efficient , step-efficient , protecting-group-free, concise and divergent manner.

The1H-NMR data : inconsistencies

**Fig. 4 | Transition states C and D explained the outcomes of the kinetic reduction at C20.** Total synthesis of yohimbine, *β*-yohimbine and pseudoyohimbine.