Convergent and Efficient Total Synthesis of (+)-Heilonine Enabled by C–H Functionalizations

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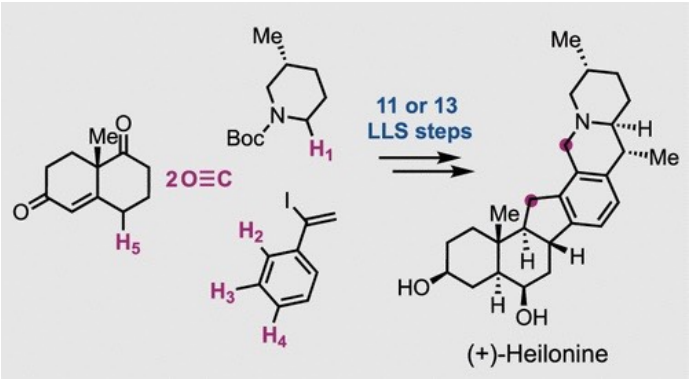
hexacyclic ring system, nine stereocenters, and a trans-hydrindane moiety.

four selective C–H functionalizations to form key C–C bonds and stereocenters,

longest linear sequence (LLS) steps.



A. Syntheses of fragments 17a/b and 26 via three C–H functionalizations and attempted carbonylative coupling and Nazarov cyclization

oxidative carbonylative C–H lactamization under Orito conditions

nitrogen-directed chelation model

carbonylative C–H lactamization

C–H borylation/iodination

Buchwald cat. CPhos Pd G3

Crabtree's cat.

17a + 27 / 17b + 28 → unsuccess due to the steric and electronic effects

facilitate the transmetalation step

model study

Wulff method

protection as ammonium salt

radical recombination

stabilized radical

Without HFIP, a 2.5/1 mixture of 33 (major, undesired) and 34

B. Convergent total synthesis of (+)-heilonine in 11 or 13 steps (LLS)

photoredox C–H oxidation Yue and Zheng conditions

carbon monoxide as a one carbon linchpin

crutial, DMSO unsuccess

optimized donditions

axial

13 lls steps

11 lls steps