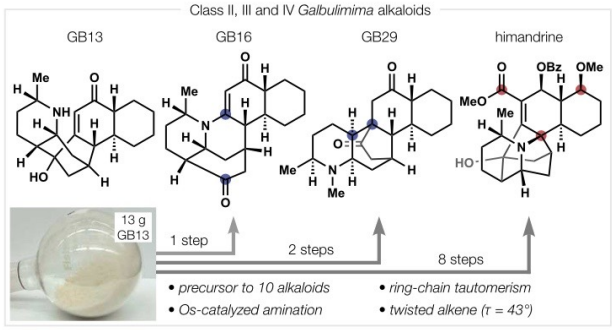
Decagram-Scale Synthesis of GB13 and Remodeling to the Galbulimima Alkaloids

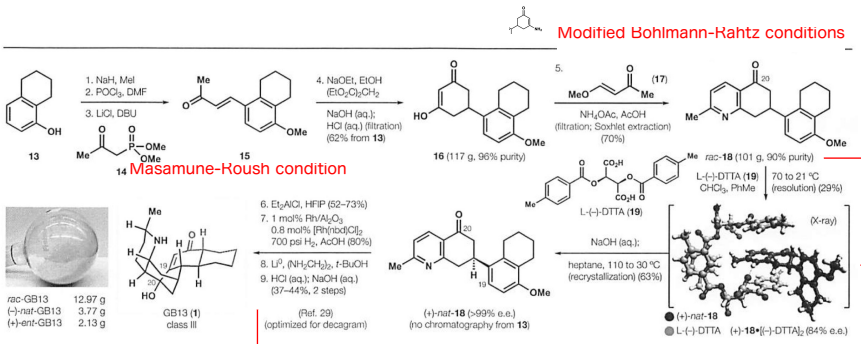
Stephan M. Freeman, Eleanor M. Landwehr, Riku Tanaka, Juan J. Rojas, Jake B. Bailey, Milan Gembicky, Ryan A. Shenvi

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late-stage functionalization and scaffold remodeling of 12.97 g of GB13,



Modified Bohlmann-Rahtz conditions



Masamune-Roush condition

Filtration of 16, precipitation of 18 from DMF, and continuous Soxhlet extraction of 18 with heptane eliminated column chromatography.

stacking interactions between the cationic pyridinium of 18-H* and the relatively electron-rich arenes of two DTTA monomers

Figure 2. Synthesis of the class III GB alkaloid GB13 on decagram scale. Both L-(−)-DTTA and D-(+)-DTTA are inexpensive (<$0.06/g, Ambeed).

only 3 chromatographic purifications

Friedel-Crafts reaction, pyridine hydrogenation, Birch reduction, and hydrolysis

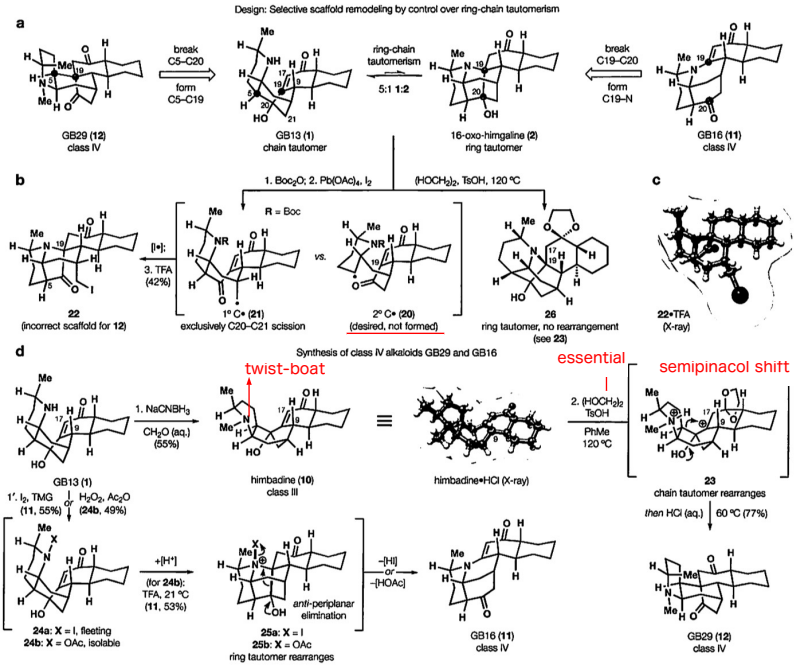
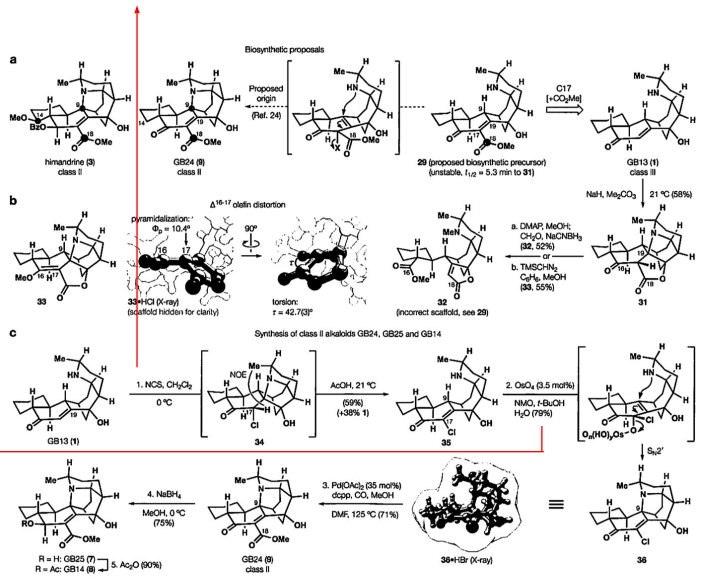


Figure 3. Synthesis of class IV alkaloids from GB13. (a) Design: each class IV scaffold could arise from either ring or chain tautomers of GB13. (b) β-scission occurred with incorrect scaffold-selectivity, and ketalization of GB13 did not induce cationic rearrangement. (c) X-ray crystal structure of fragmentation product 22·TFA. (d) Synthesis of class IV alkaloids GB29 and GB16 by scaffold remodeling.

Incorporation of bromine or iodine at C17 failed because oxidative rearrangement to GB16 (11) becomes competitive



Os(VIII) rarely oxidizes amines because the reverse reaction is rapid

Figure 4. Synthesis of class II alkaloids from GB13. (a) Early carboxylation leads to a lactone trap, 31, which locks the piperidine. (b) Core intractability is illustrated by O-methylation to a twisted (τ = 42.7°) alkene. (c) A chloride placeholder enables osmium-catalyzed amination and late-stage carboxylation.

Yu's bifunctional ligands to accelerate the concerted metalation-deprotonation
:robust methylene C-H activation, avoided iodine(III) oxidants

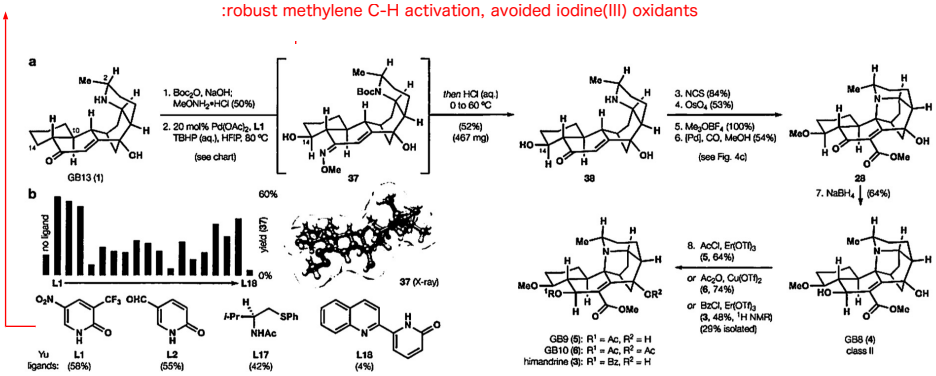


Figure 5. C–H oxidation: templated synthesis of himandrine. (a) A site-selective, catalytic C–H hydroxylation enables simple syntheses of GB8, GB9, GB10 and himandrine. (b) Ligand acceleration of C–H activation.