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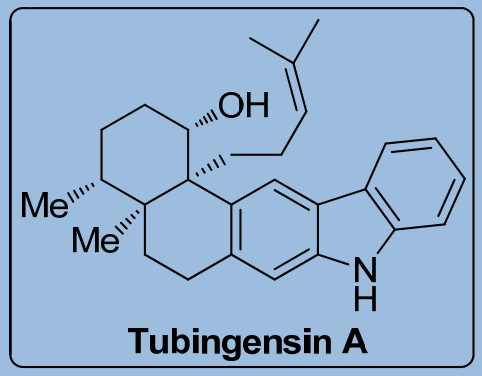
Total Synthesis of Tubingensin A

Adam E. Goetz , Amanda L. Silberstein , Michael A. Corsello , and **Neil K. Garg** *J. Am. Chem. Soc.*, **2014**, *136* (8), 3036–3039.

Bian, M.; Wang, Z.; Xiong, X.; Sun, Y.; Matera, C.; **Nicolaou, K. C.; Li, A.** *J. Am. Chem. Soc*., **2012**, 134 , 8078



Tubingensin A

Current literature
Gong Xu
09.10.2014

About Tubingensin A

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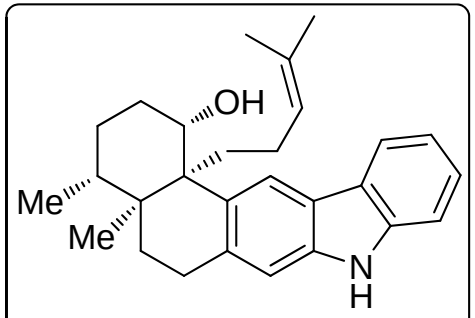
- Initially isolated from the fungus ***Aspergillus tubingensis*** by Gloer and co-workers in 1989;
- Shown to display **antiviral, anticancer, and insecticidal** activity;
- Structurally, **Tubingensin A** possesses a disubstituted **carbazole** that is fused to a densely functionalized ***cis*-decalin** framework. Moreover, the decalin core contains four contiguous stereocenters, two of which are vicinal quaternary centers.



Tubingensin A

Postulated Biosynthetic Relationship

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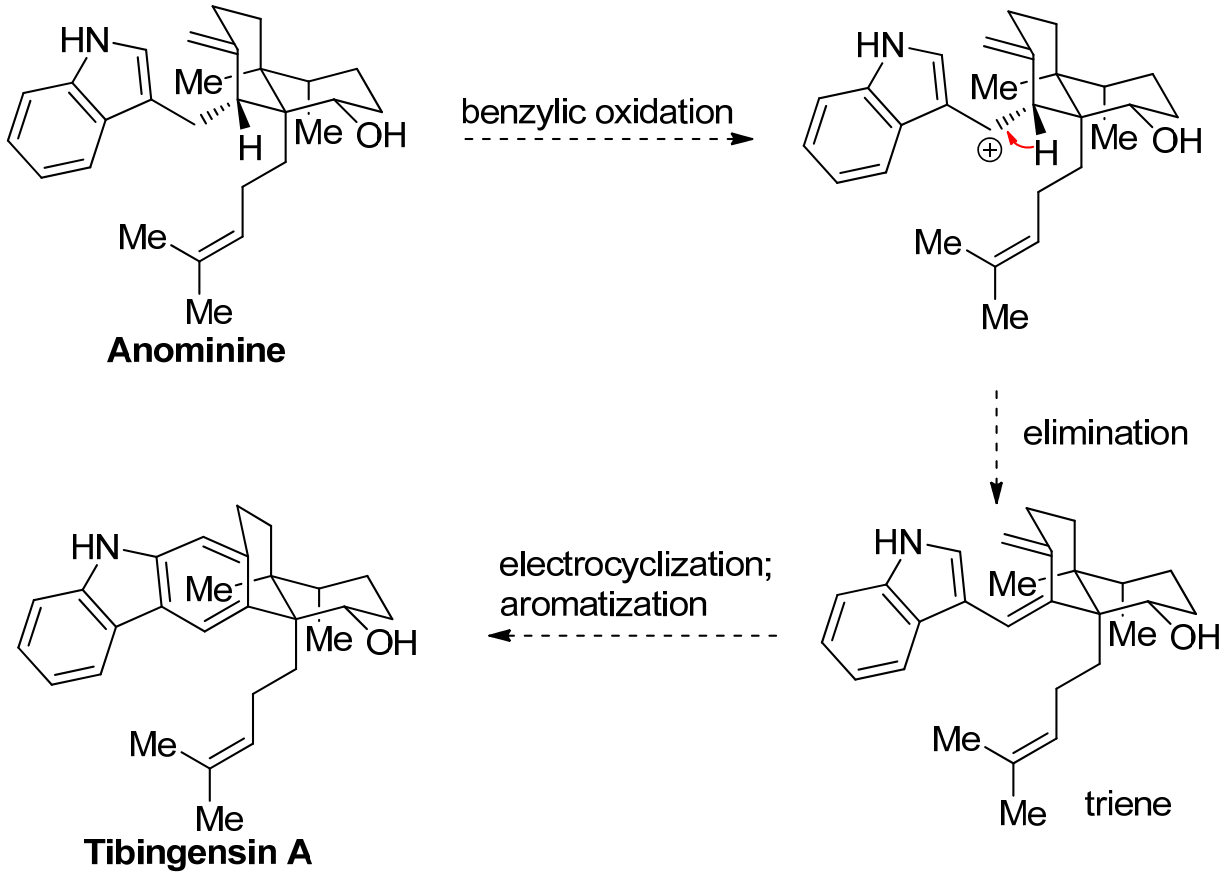
> Postulated to arise biosynthetically from the indole diterpenoid **anominine**:



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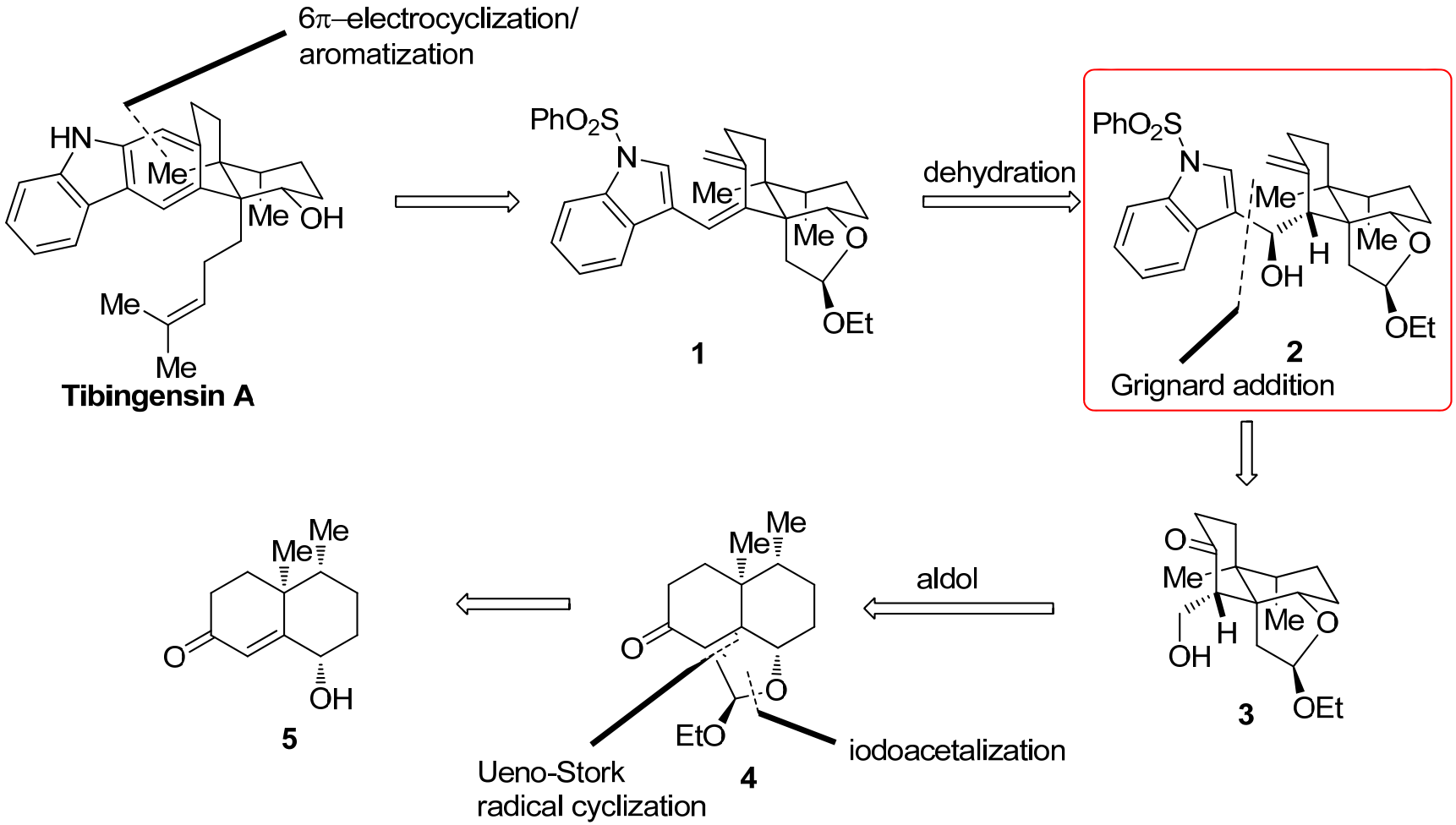
First approach to Tubingensin A
---retrosynthesis



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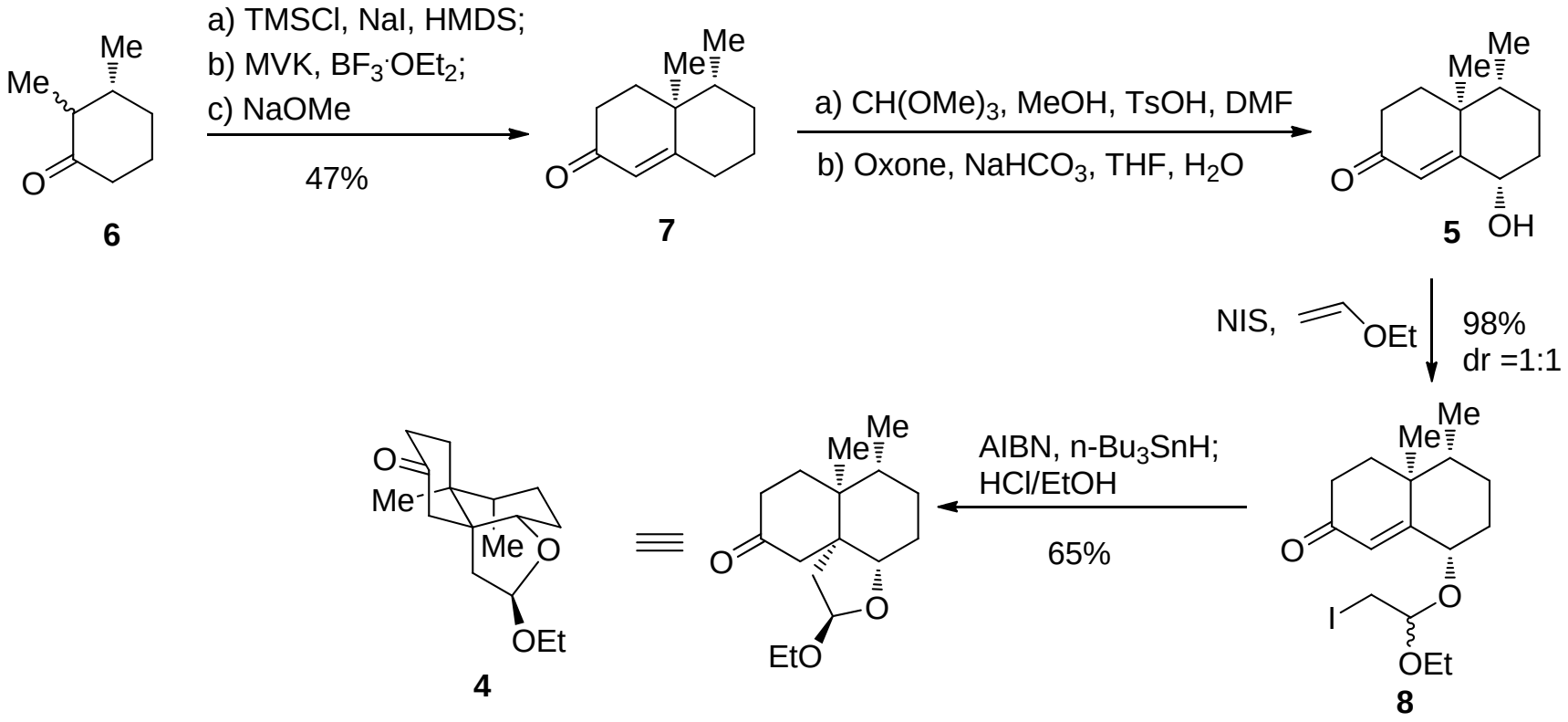
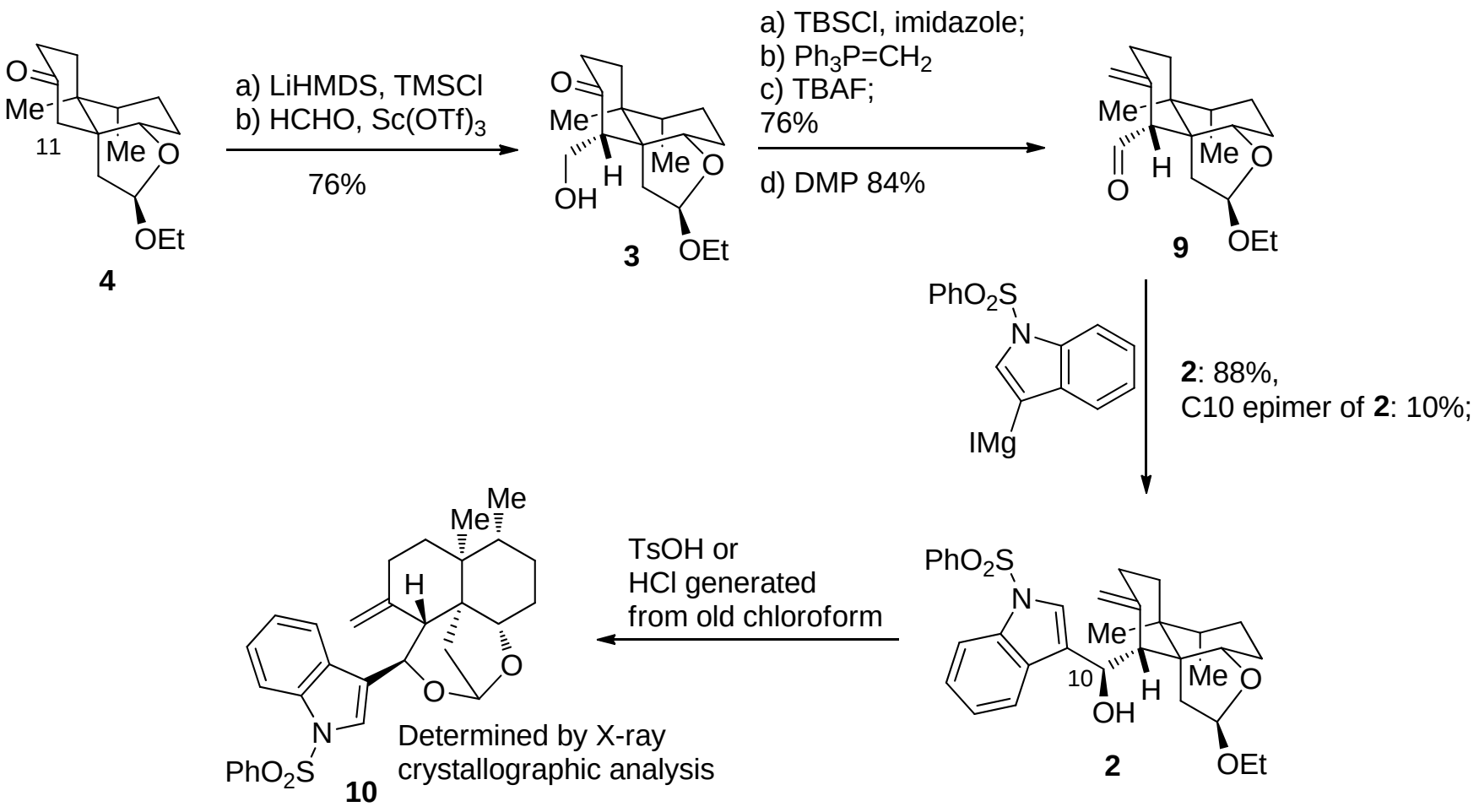
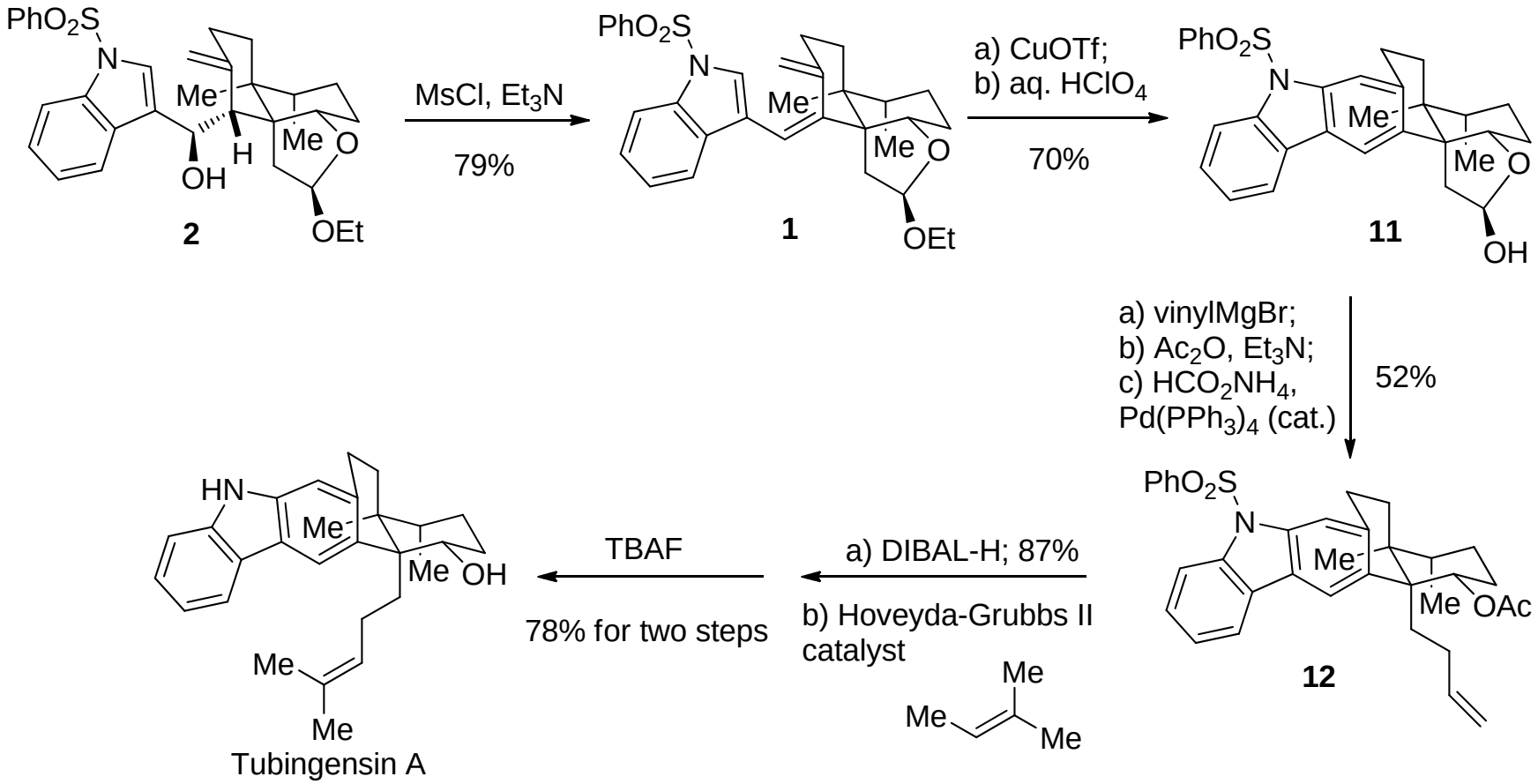
First approach to Tubingensin A
---construction of tricyclic ketone **4**



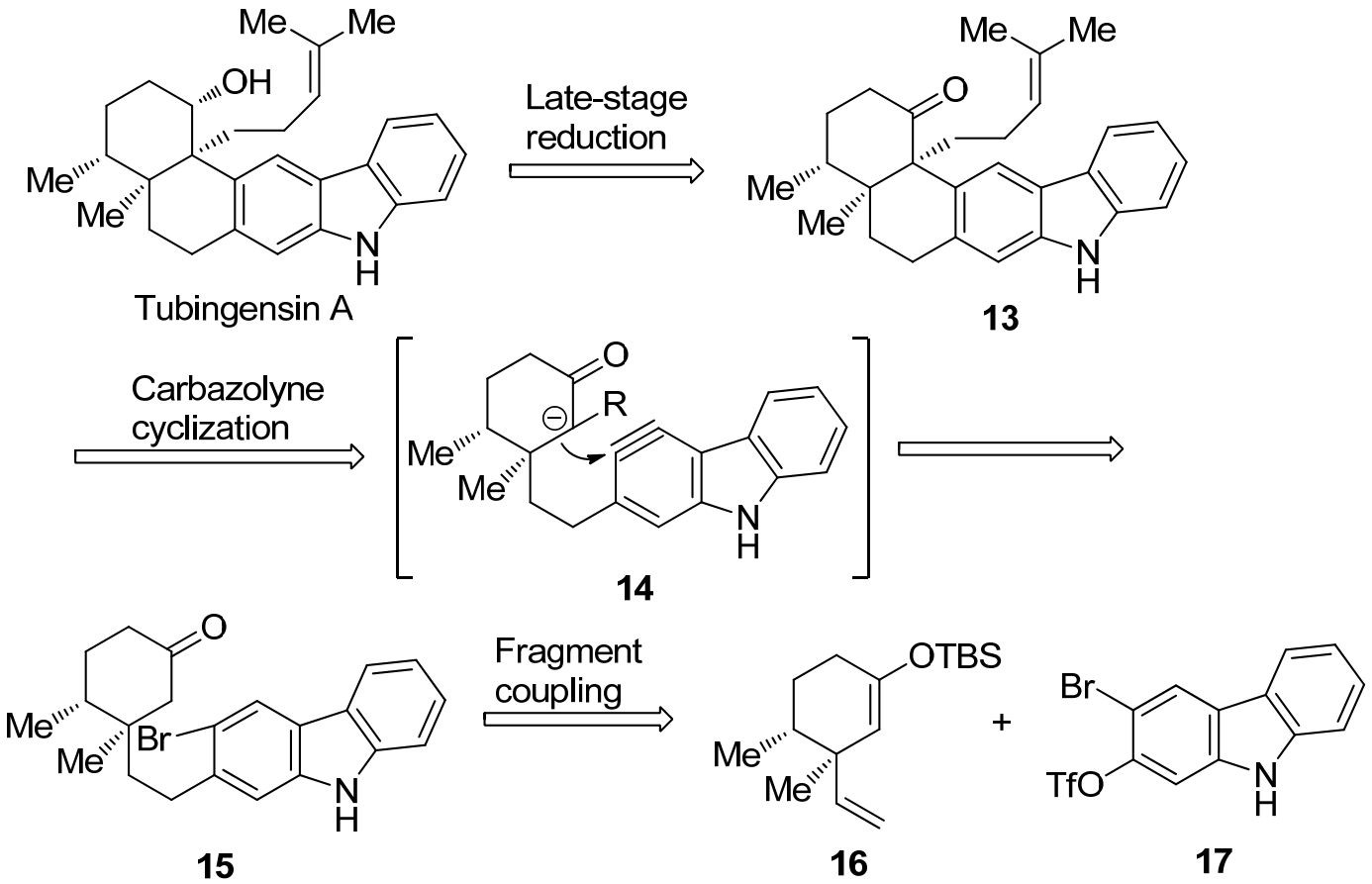
First approach to Tubingensin A
---assembly of key intermediate **2**



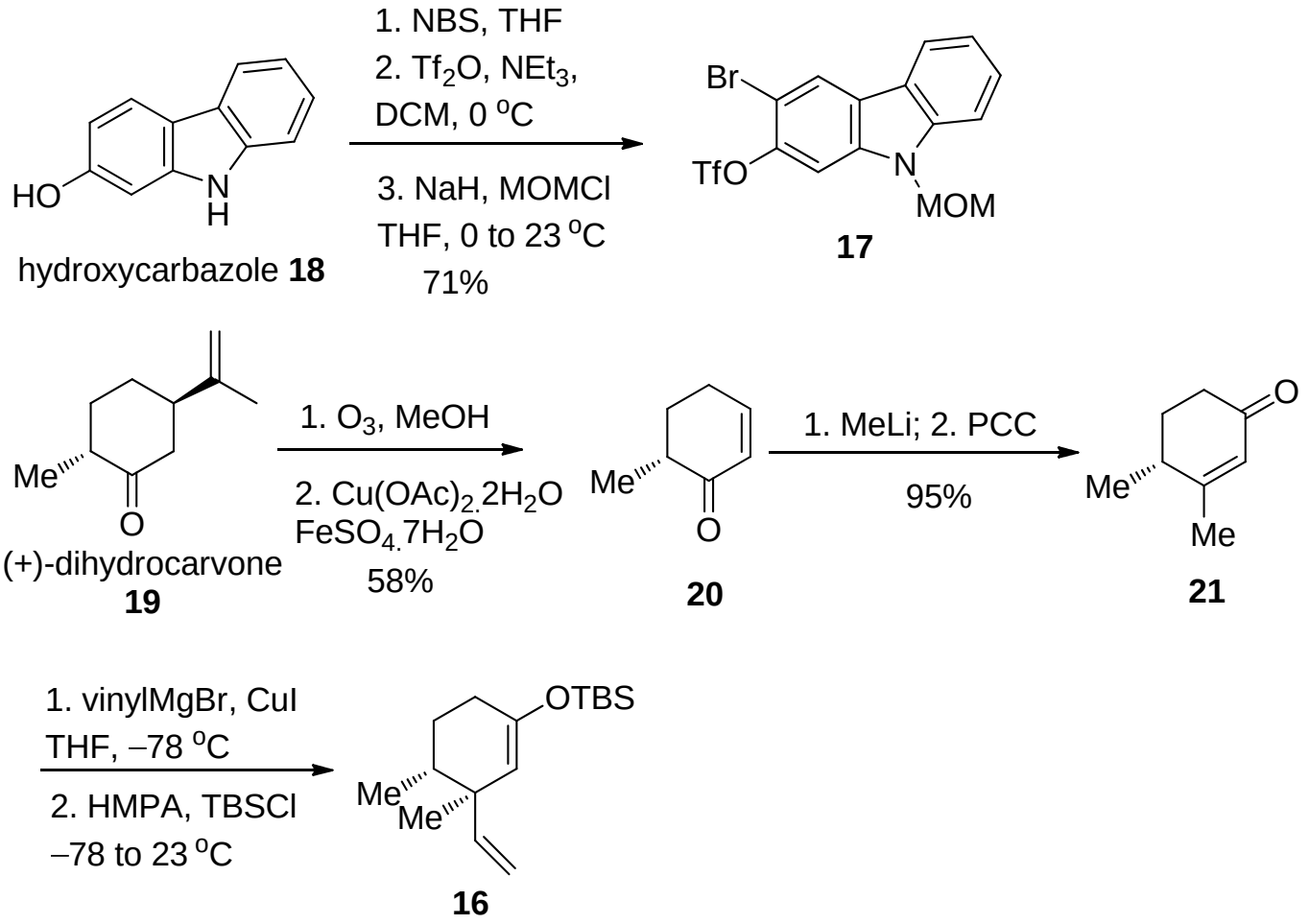
First approach to Tubingensin A
---Furnishing



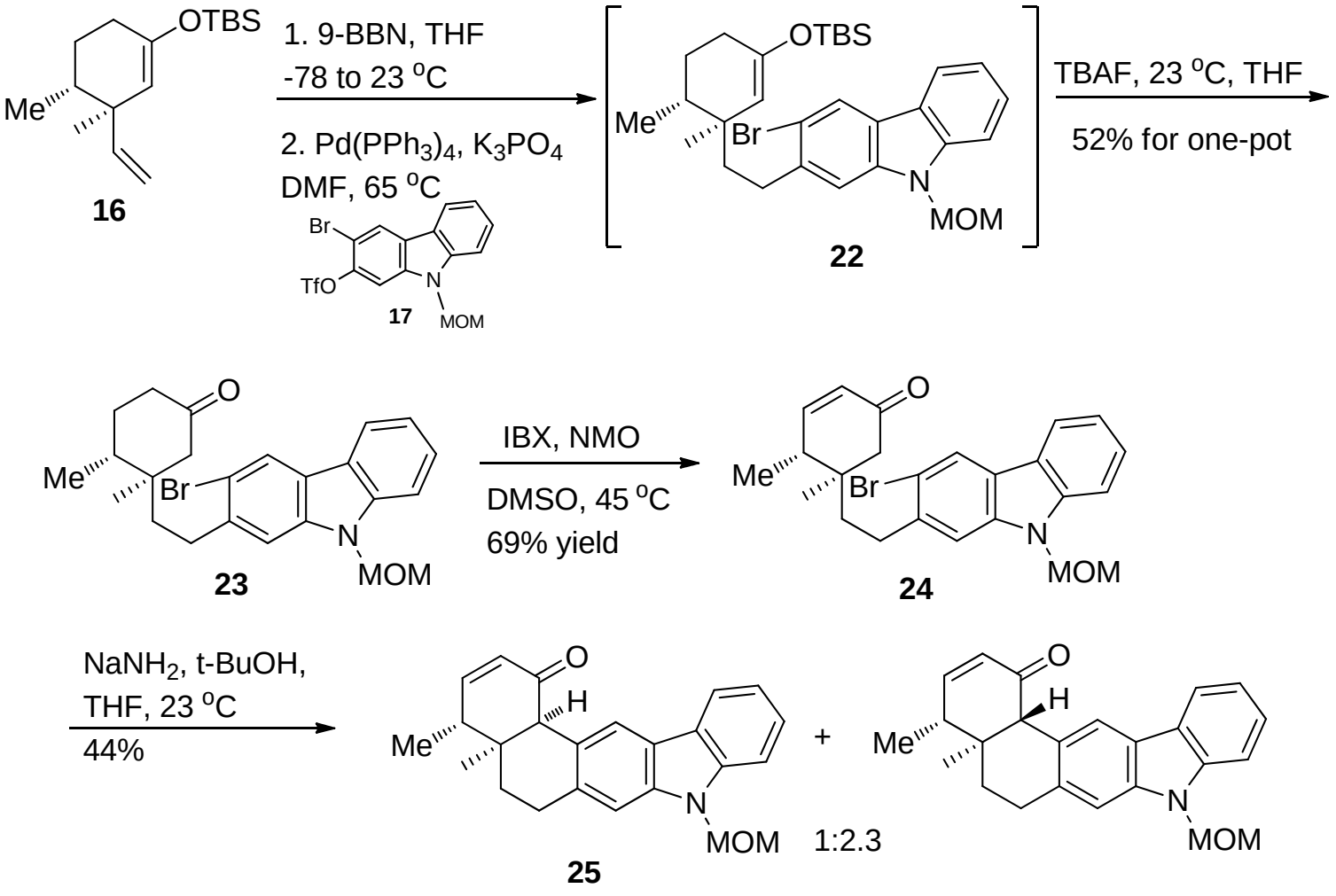
New approach to Tubingensin A
---retrosynthetic analysis



New approach to Tubingensin A
---synthesis of carbazole and cyclohexyl parts



New approach to Tubingensin A
---coupling and carbazolyne cyclization



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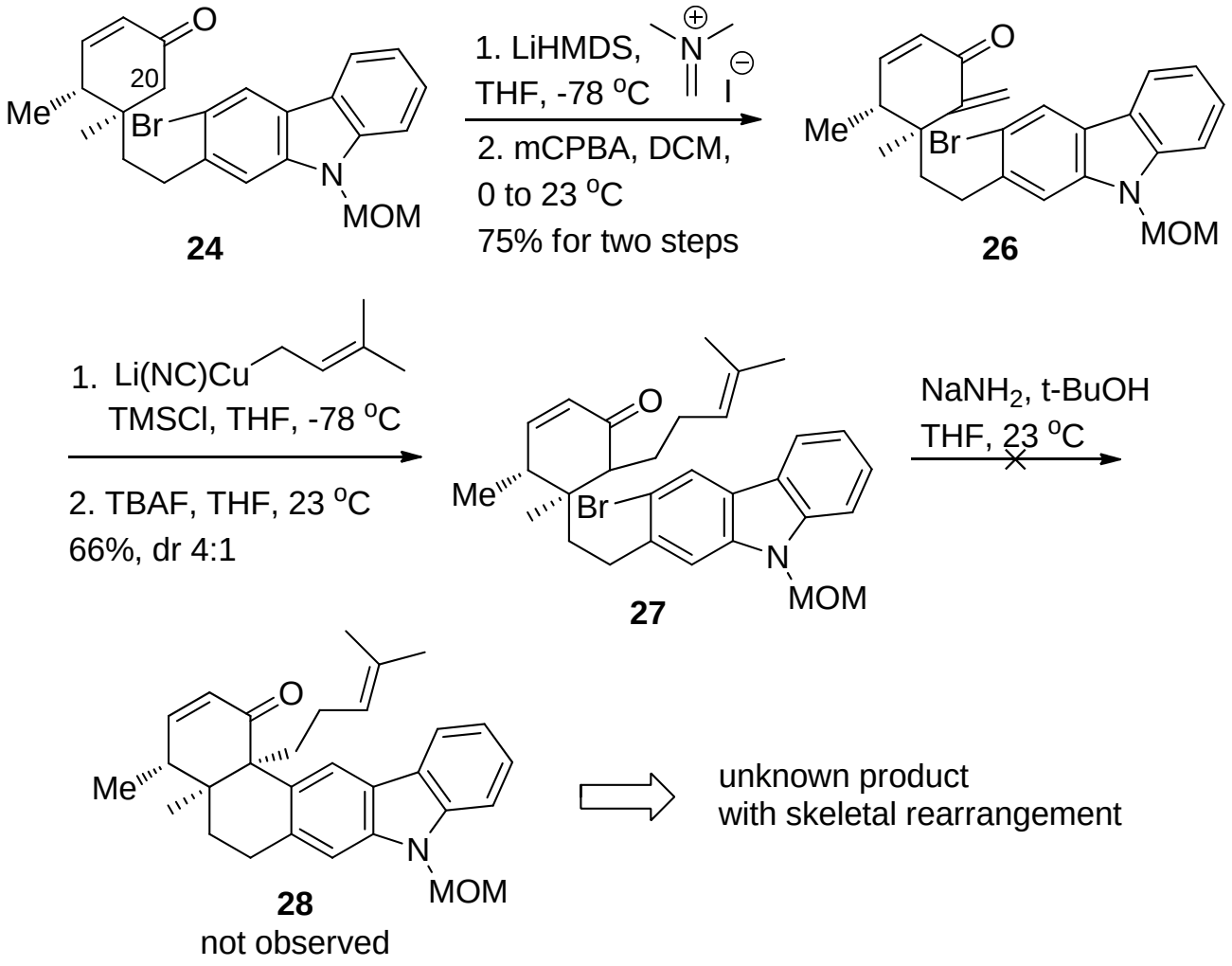
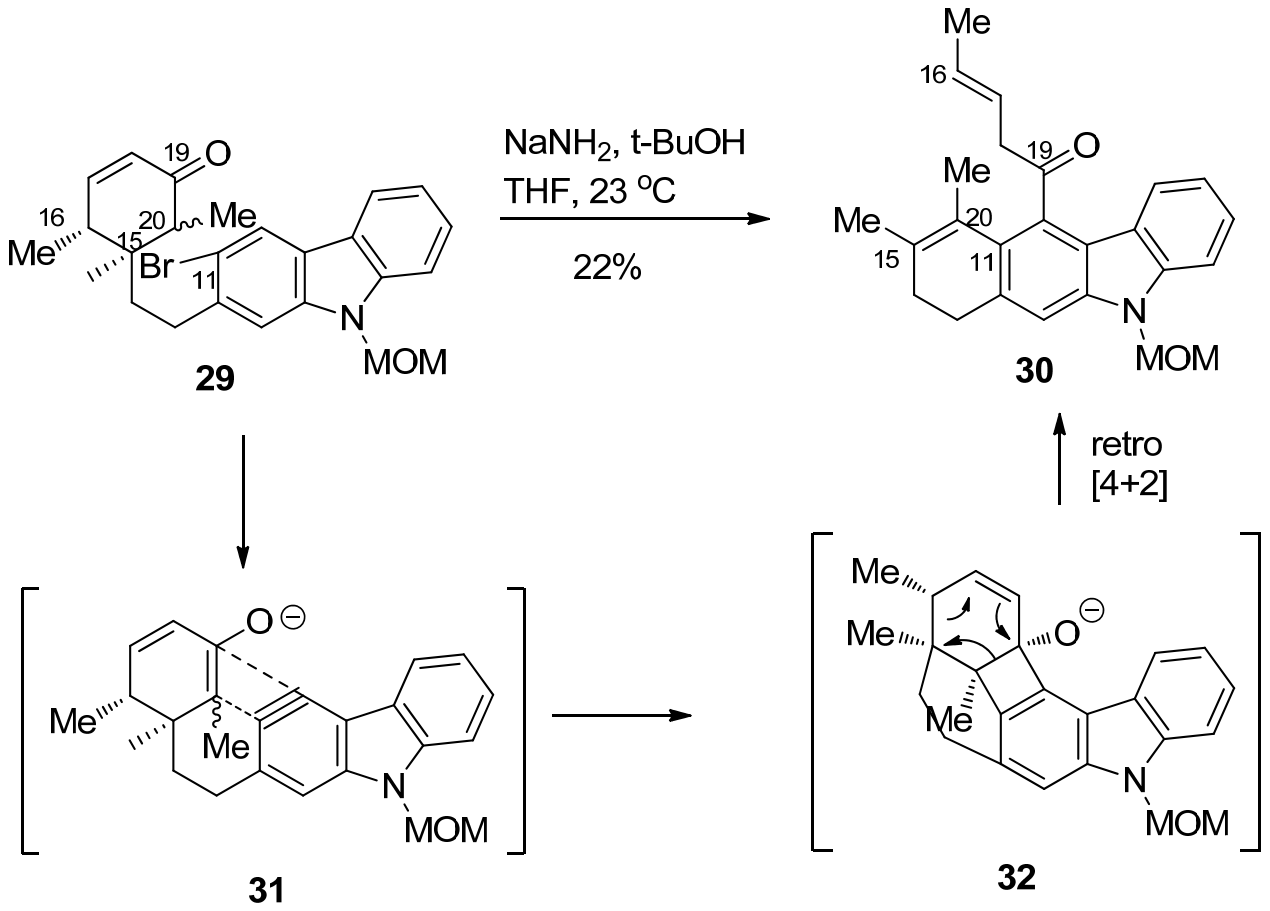
New approach to Tubingensin A
---test with C20-substituted substrate



New approach to Tubingensin A
---test with C20-substituted substrate



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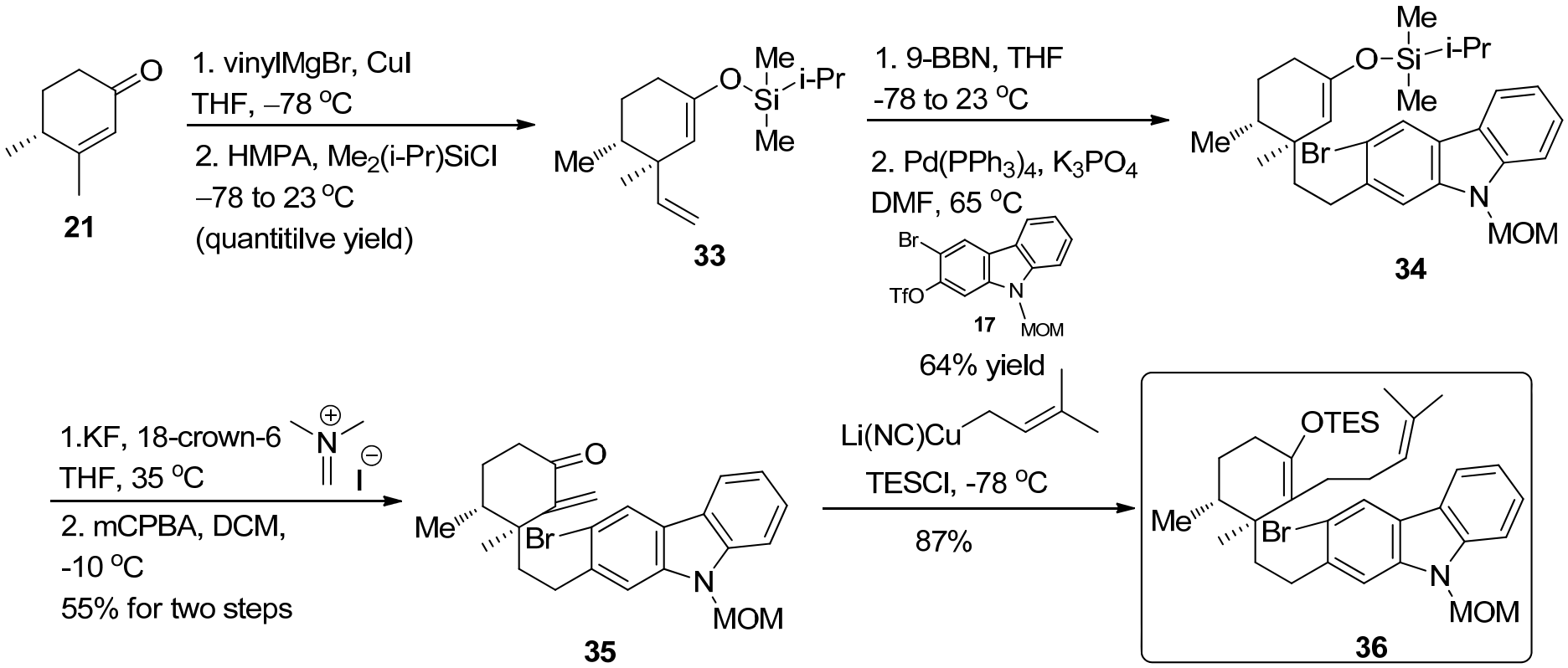
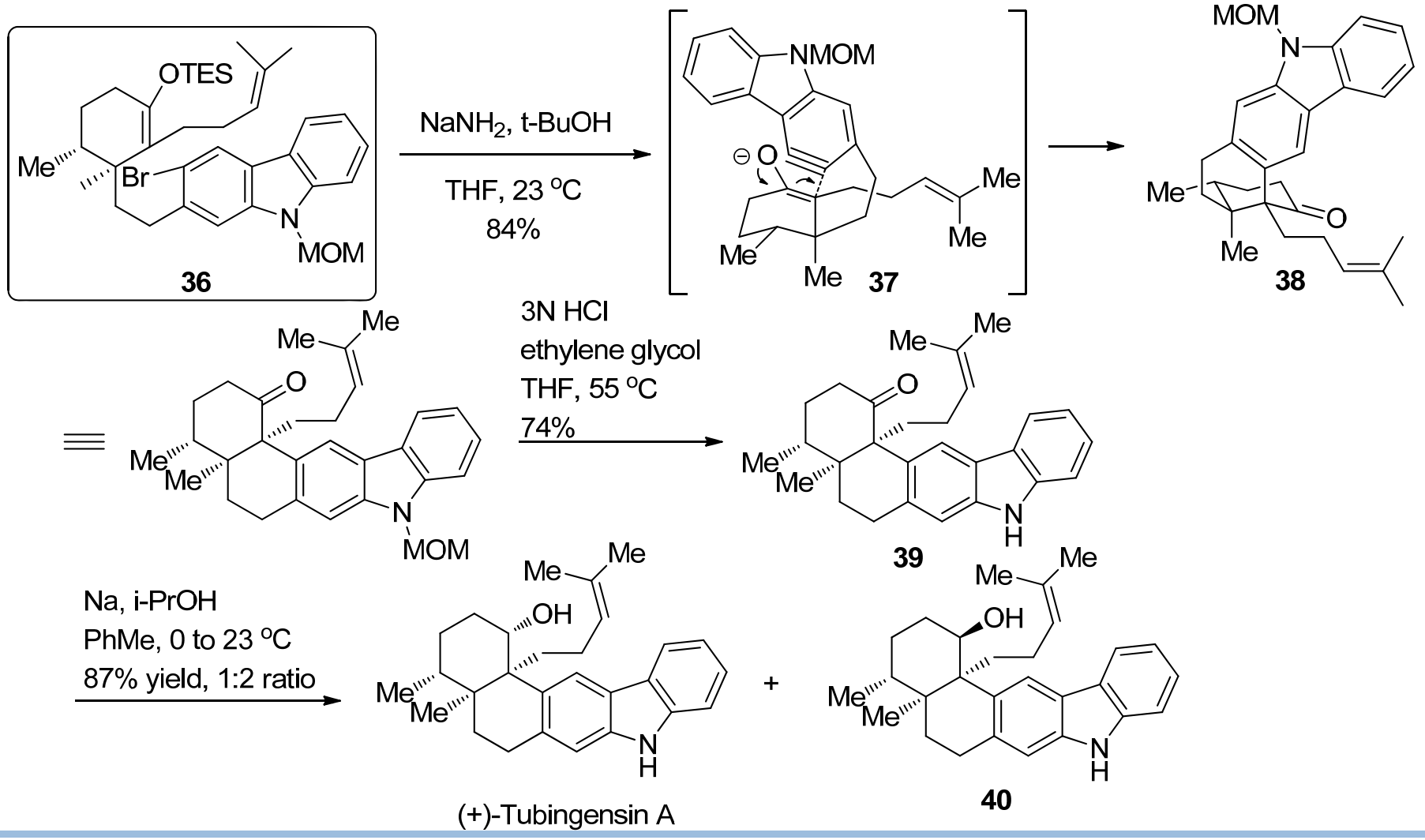
New approach to Tubingensin A
---modified substrate



New approach to Tubingensin A



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Summary

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First approach: key step --- an **Ueno-stork radical cyclization** to form C-C bond in a stereocontrolled manner. It proceeds in **23** steps from cyclohexyl precursor.

New approach: key step --- an **aryne cyclization** to efficiently introduce the vicinal quaternary stereocenters of the natural product and proceeds in only **9** steps from known compounds.