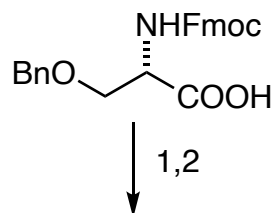


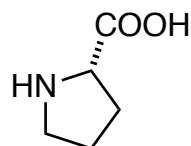
Scalable total synthesis of saxitoxin and related natural products

Guo, Y.; Li, Y.; Chen, S.; Wu, Y.; Poll, O.; Ren, Z.; Liu, Z.; Vlkolinsky, R.; Bajo, M.; Prier, C. K.; Xiao, K.; Cravatt, B. F.; Roberto, M.; Baran, P. S.

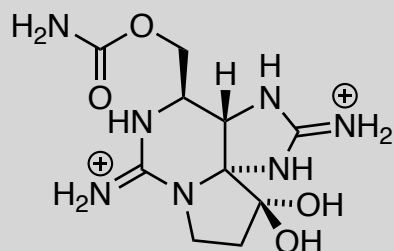
Nature **2025**, DOI: 10.1038/s41586-025-09551-5



1,2

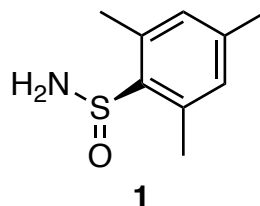


3-9

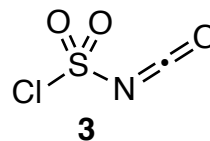
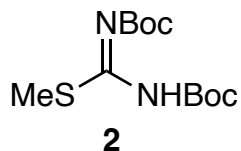


(+)-Saxitoxin

- 1) CDI (1.1 eq) *then* DIBAL-H, -78 °C
- 2) **1**, Ti(OEt)₄



- 3) FrbA-Rd10bb, α -ketoglutarate ascorbate, (NH₄)₂Fe(SO₄)₂, air *then* Na₂CO₃, Boc₂O
- 4) TBSCl, imid., DMAP *then* DIC, DMAP, NHPI
- 5) **A**, NiCl₂•glyme, Zn
- 6) HCl *then* HgO, TEA, **2** (2.5 eq) *then* piperidine
- 7) TEMPO, NaOCl, KBr *then* PIFA
- 8) BCl₃
- 9) **3**, HCOOH *then* MeOH



- 3) FrbA-Rd10bb is an engineered enzyme. *Hint*: C3-hydroxylation.
- 4) NHPI is *N*-hydroxyphthalimide

- 7) What are the conditions in the first part of this reaction called (TEMPO, NaOCl)?