Enantioselective Total Synthesis of (+)-Stephadiamine *J. Am. Chem. Soc.* **2023**, *145*, 5001–5006. DOI: https://doi.org/10.1021/jacs.3c00884 Baochao Yang, Guang Li, Qian Wang, and Jieping Zhu*. (Ecole Polytechnique Fédérale de Lausanne, Switzerland.)



Key Steps:

- Enantioselective dearomatizative Michael addition to generate a quaternary stereocenter.
- Domino sequence involving reductive generation of nitrone from γ-nitro ketone followed by a highly regio- and diastereo-selective intramolecular [3 + 2] cycloaddition.
- Curtius rearrangement of the sensitive α,αdisubstituted malonic acid mono ester.

Significance:

- An enantioselective total synthesis of (+)stephadiamine (1) has been accomplished.
- A strategically designed domino sequence involving reductive generation of nitrone from γnitro ketone followed by a highly regio- and diastereo-selective intramolecular dipolar cycloaddition afforded not only the aza[4,3,3]propellane core with concurrent generation of two contiguous quaternary stereocenters.