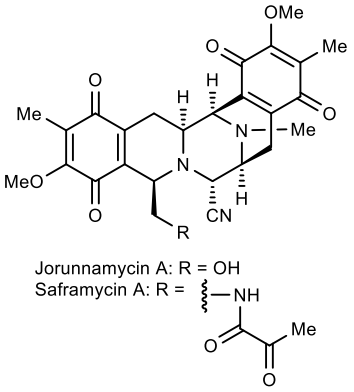
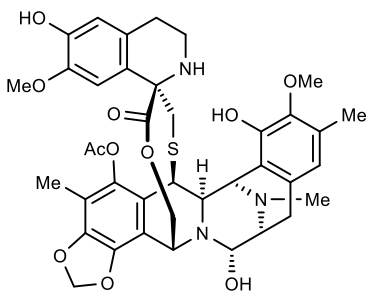
Jorunnamycin A; Saframycin A (Oguri 2018)





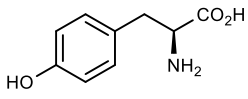
ecteinascidin 743 (Yondelis, trabectidin)

Introduction

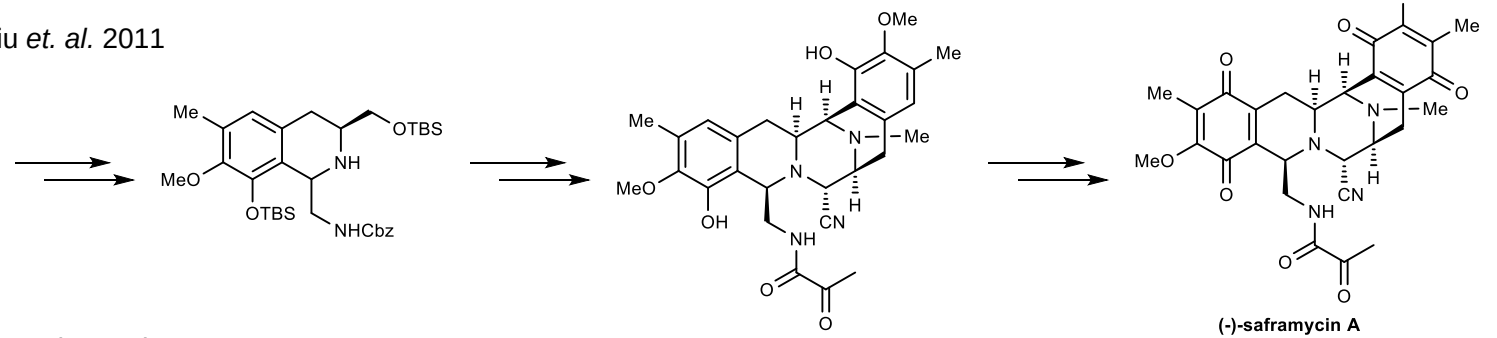
- The family of bis-tetrahydroisoquinoline (bis-THIQ) natural products have merited extensive study due to their potent anticancer properties. Within this family, Eceteinascidin 743 has been approved for the treatment of ovarian neoplasms and sarcoma.
- Towards both Jorunnamycin A and Saframycin A, the majority of previously reported total syntheses proceed through a biomimetic Pictet-Spengler or Bischler-Napieralski approach, although a route towards Jorunnamycin A has been reported using asymmetric catalysis and reductive cyclization.
- The 2018 route reported here entails chemoenzymatic synthesis of both compounds, giving the most concise routes to date.

Comparative Syntheses:

(-)-Saframycin A: Liu *et. al.* 2011

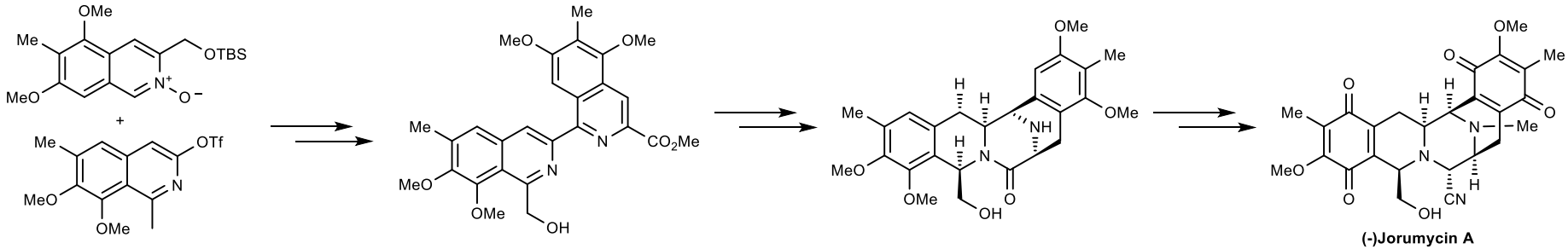


L-Tyrosine



(-)-saframycin A
24 steps, 9.7% Overall

(-)-Jorunnamycin A: Stolz *et. al.* 2019

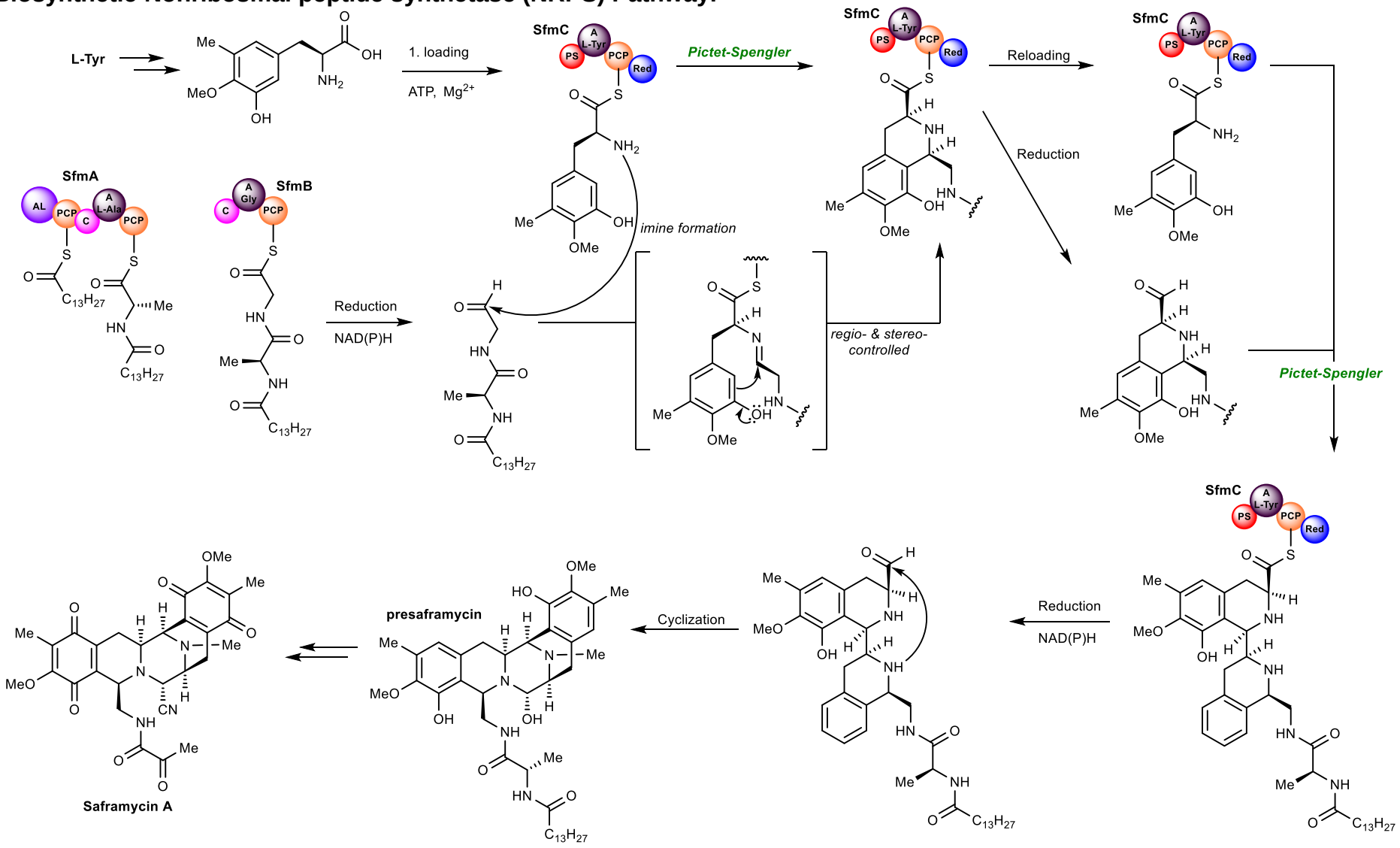


(-)Jorumycin A
15 steps, 0.24% Overall

J. Am. Chem. Soc. **2018**, *140*, 10705. http://doi.org/10.1021/jacs.8b07161
Science **2019**, *363,* 270. http://doi.org/10.1126/science.aav3421
J. Org. Chem. **2011**, *76*, 5363. http://doi.org/10.1021/jo200758r

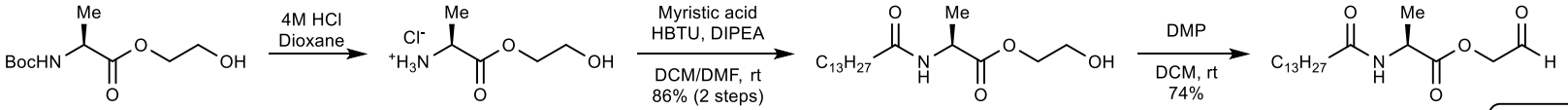
Jorunnamycin A; Safframycin A (Oguri 2018)

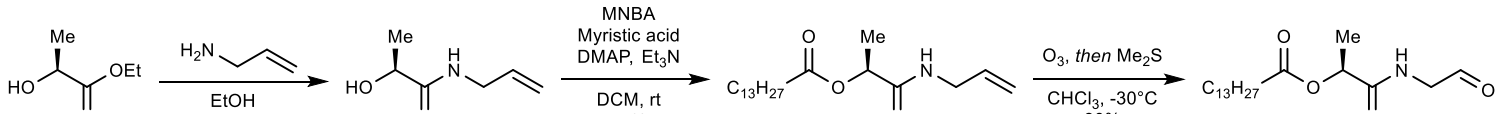
Biosynthetic Nonribosmal peptide synthetase (NRPS) Pathway:

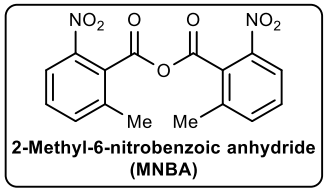


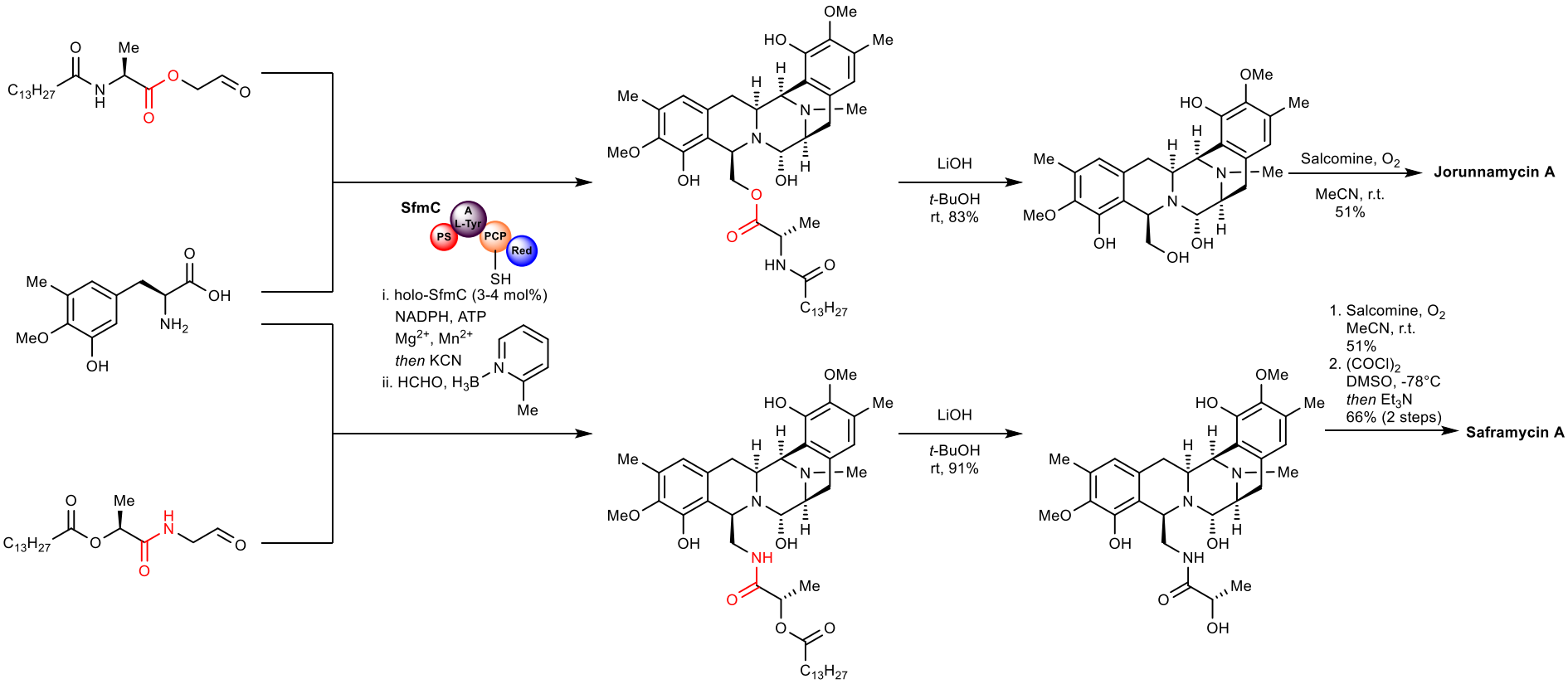
J. Am. Chem. Soc. **2018**, 140, 10705. https://doi.org/10.1021/jacs.8b07161

Jorunnamycin A; Saframycin A (Oguri 2018)









J. Am. Chem. Soc. **2018**, 140, 10705. https://doi.org/10.1021/jacs.8b07161