Total Synthesis of (+)-Granatumine A and Related Bislactone Limonoid Alkaloids via a Pyran to Pyridine Interconversion

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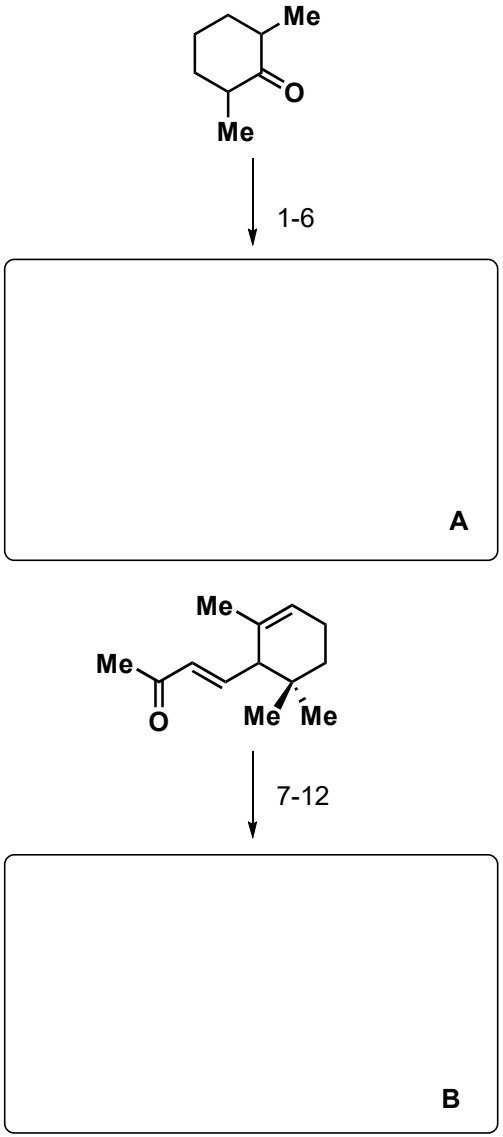
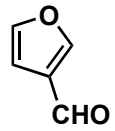


1) LDA(1.5 eq), ZnCl, THF, -40°C,
then allyl acetate, $[Pd(Allyl)Cl]_2$, 60°C
2) LDA, **1,** THF, -78 °C
3) Ac_2O, **2** (cat.), PhMe
4) LiHMDS, then Burgess reagent
5) SeO_2, Na2HPO4, 1,4-dioxane, 100°C
6) DMP



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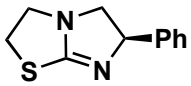

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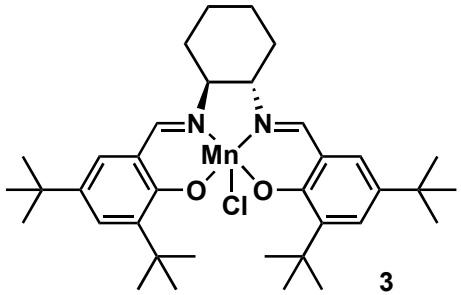
7) **3** (cat.), 4-PPNO, NaOCl
8) $[Rh(cod)(OH)]_2$, $PhMe_2SiH$
9) O_3, *then* Jones reagent
10) $Pd(TFA)_2$, DMSO, O_2, 80°C
11) urea•H_2O_2, DBN, H_2O
12) $Pd(OAc)_2$, XPhos, toluene



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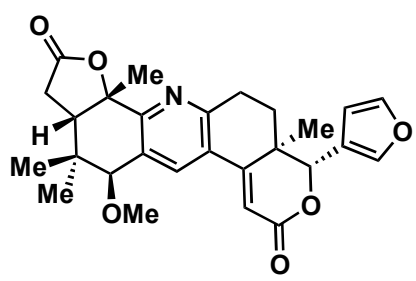
Step 1: Please provide a mechanism and two alternative approaches.

Step 9: A heterocycle is formed, please provide a mechanism.

Step 12: Please provide a plausible mechanism



(+)-Granatumine A

13-14

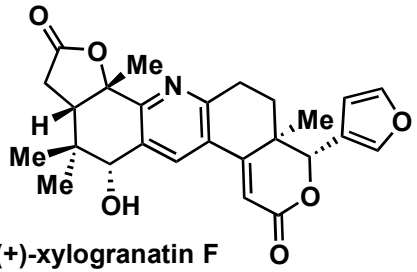
C

13) ethyldiammonium diacetate, **A**, 65°C
14) $LiBH_4$, $CeCl_3$, TFE/THF

15) $HO\text{-}NH_2 \bullet HCl$, $LiOAc \bullet 2H_2O$, 80°C

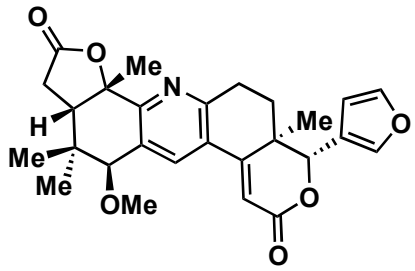
15

34%



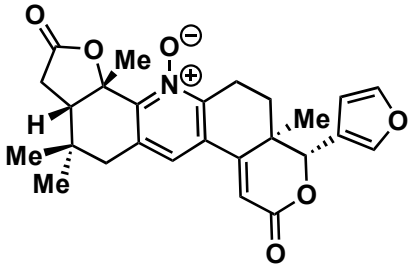
(+)-xylogranatin F
[misassigned structure]

16



(+)-Granatumine A

35%



D

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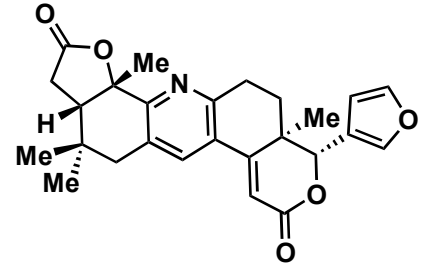

(+)-3-deoxy-xylogranatin F

Step 13: A cyclization occurs. Provide a mechanism for it and classify it.

Step 15: Yields two products. Propose mechanisms for the formation of each.

Step 16 and 17: Propose conditions for the convertions.