Total Synthesis of Nakadomarin A

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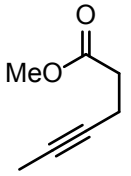
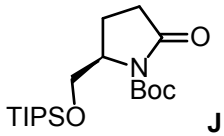


1 – 4

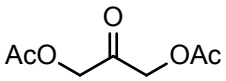
A



J

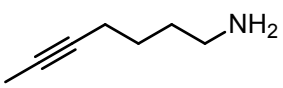
5 – 8

1) $PO(OMe)_2CH_2Li$
2) NaH, **1**
3) cat. HCl, MeOH, 50 °C
4) $(COCl)_2$, DMSO, NEt_3



1

5) $LiBHEt_3$ then *i*-Pr_2NEt, DMAP, TFAA
6) DMF, $(COCl)_2$ then sat. aq. Na_2CO_3
7) **2** then $NaBH_4$
8) **3**, NEt_3



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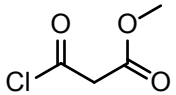
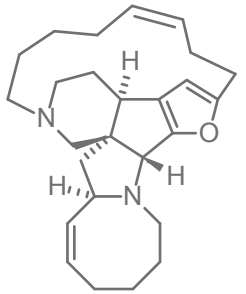


3

How would you make starting material **J**?



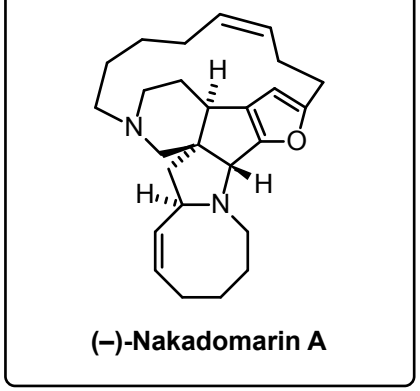
(–)-Nakadomarin A

B

9 – 14

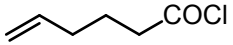
C

15 – 21



(–)-Nakadomarin A

9) **A**, $PhCO_2H$, piperidine, PhH, 80 °C
10) $InCl_3$ (10 mol%), DCM, 40 °C
11) KOH; acidic work up; PhMe, reflux
12) (*t*-BuO)$_3$W≡C-*t*-Bu (25 mol%), PhCl, 80 °C
13) H_2, Lindlar cat., quinoline, MeOH

14) TBAF
15) IBX, DMSO
16) Tebbe reagent
17) TFA
18) NEt_3, 
19) Grubbs I, DCM, 40 °C
20) Alane

What is the mechanism in step 10?

12) What other catalysts can be used for this transformation?

13) Name another system to accomplish this transformation.

16) How do you make the Tebbe reagent?

What other Ti-based methods to accomplish step 16 do you know?

20) How do you make the reagent?