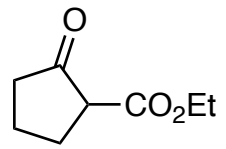
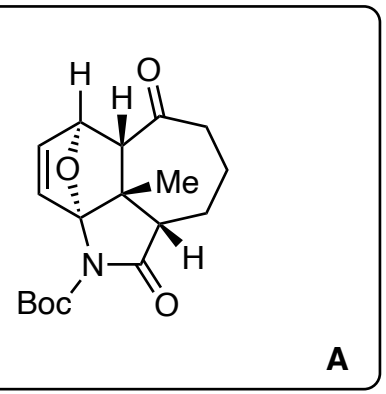
Total Synthesis of (–)-Himalensine A

Shi, H.; Michaelides, I. N.; Darses, B.; Jakubec, P.; Nguyen, Q. N. N.; Paton, R. S.; Dixon, D. J.

J. Am. Chem. Soc. **2017**, *139*, 17755–17758.



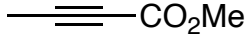
1-8



9-14

1) NaH, **1**, 60 °C
2) DMSO, HCl, 120 °C
3) TMSOTf, **2**
4) KOH (aq.)
5) cyanuric fluoride, pyr.
6) NaHMDS, **3**, *then* product from 5)
7) TsOH, acetone
8) **4** (cat.), PPh_3 (cat.) 60 °C

1



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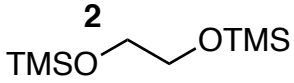

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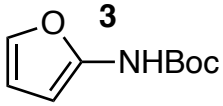
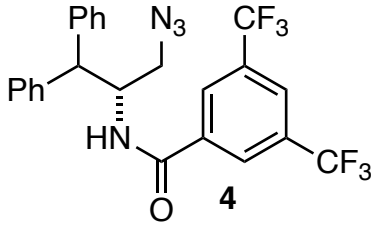


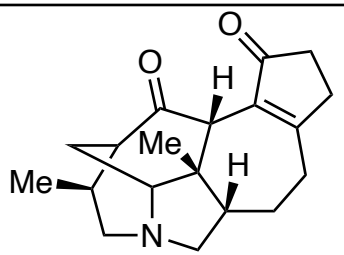


4

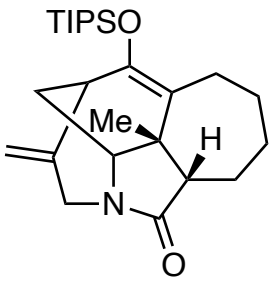
9) TFA, *then*, H_2, $Pd(OH)_2$, $NaHCO_3$
10) NaHMDS, propargyl bromide
11) $LiAlH_4$ *then* HCl, MeOH/H_2O
12) TIPSOTf, 2,6-lutidine
13) AIBN, Bu_3SnH, 90 °C
14) CSA, 0 °C

1) "Name" type reaction
Hint: ring expansion, 4-membered ring intermediate
Dieckmann type reaction
2) Name of the reaction?
Krapcho decarboxylation
8) Name the reaction, provide a mechanism and describe the role of the catalyst.
Diels-Alder / promoting prototropic shift
9) *Hint: 2 bonds are cleaved*

11) *Hint: only one carbonyl is affected.* One of the intermediate **11'** is not fully converted during the reaction. When subjected to MsCl, Et_3N, it can be converted to **12**. Give the structure of **11'.**

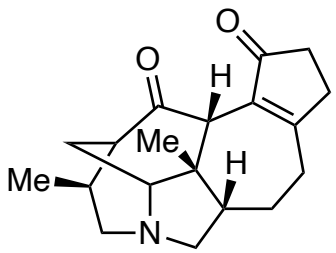


(–)-himalensine A



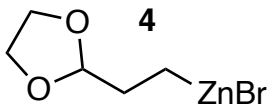
B

15-22



(–)-himalensine A

15) Crabtree's catalyst, H_2
16) NBS
17) pyr., TsOH, oxygen, reflux
18) NaHMDS, –78 °C, *then*, $PhNTf_2$
19) Pd_2dba_3, DTBPF, NMP, **4**
20) HCl (aq.)
21) **5** (cat.), Et_3N, 60 °C
22) Vaska's catalyst (cat.), TMDS
then MeOH, formic acid, 60 °C



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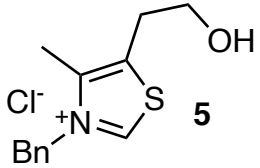
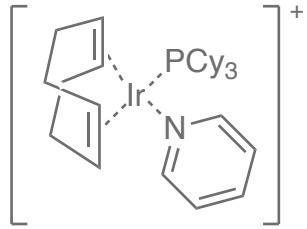


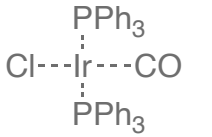
5

15) Structure of the Crabtree's catalyst?



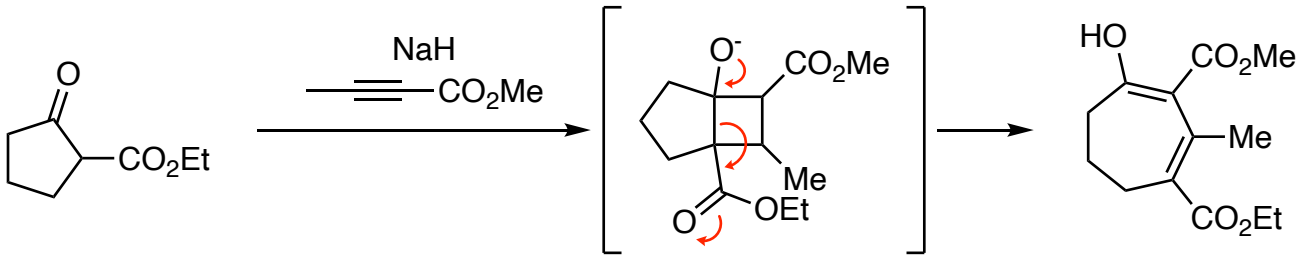
Crabtree's catalyst

17) Name the reaction and provide a mechanism.
Kornblum DeLaMare rearrangement
19) Name of the reaction?
Negishi coupling
21) Name the reaction and provide a mechanism.
Hint: cyclization and isomerization occured.
Stetter cyclization
22) Give the structure of Vaska's catalyst and provide a mechanism.



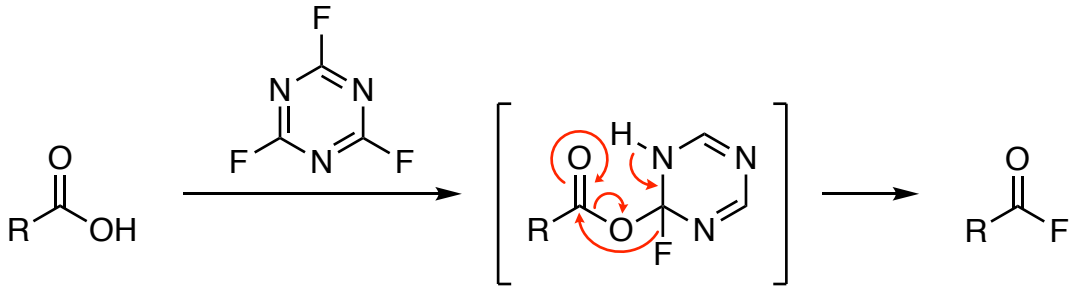
Vaska's catalyst

Solution to step 1



Org. Lett. **2011**, *13*, 4, 664–667

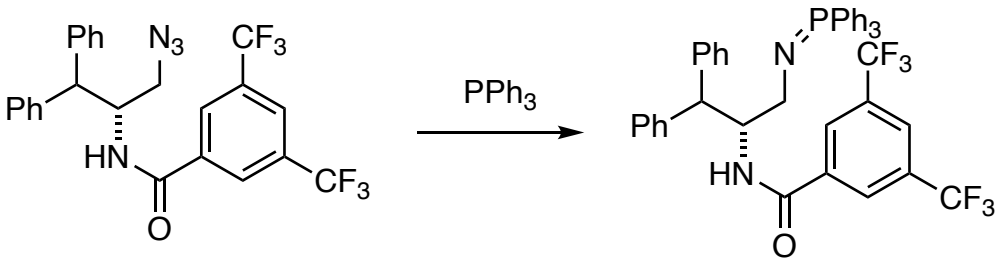
Solution to step 5



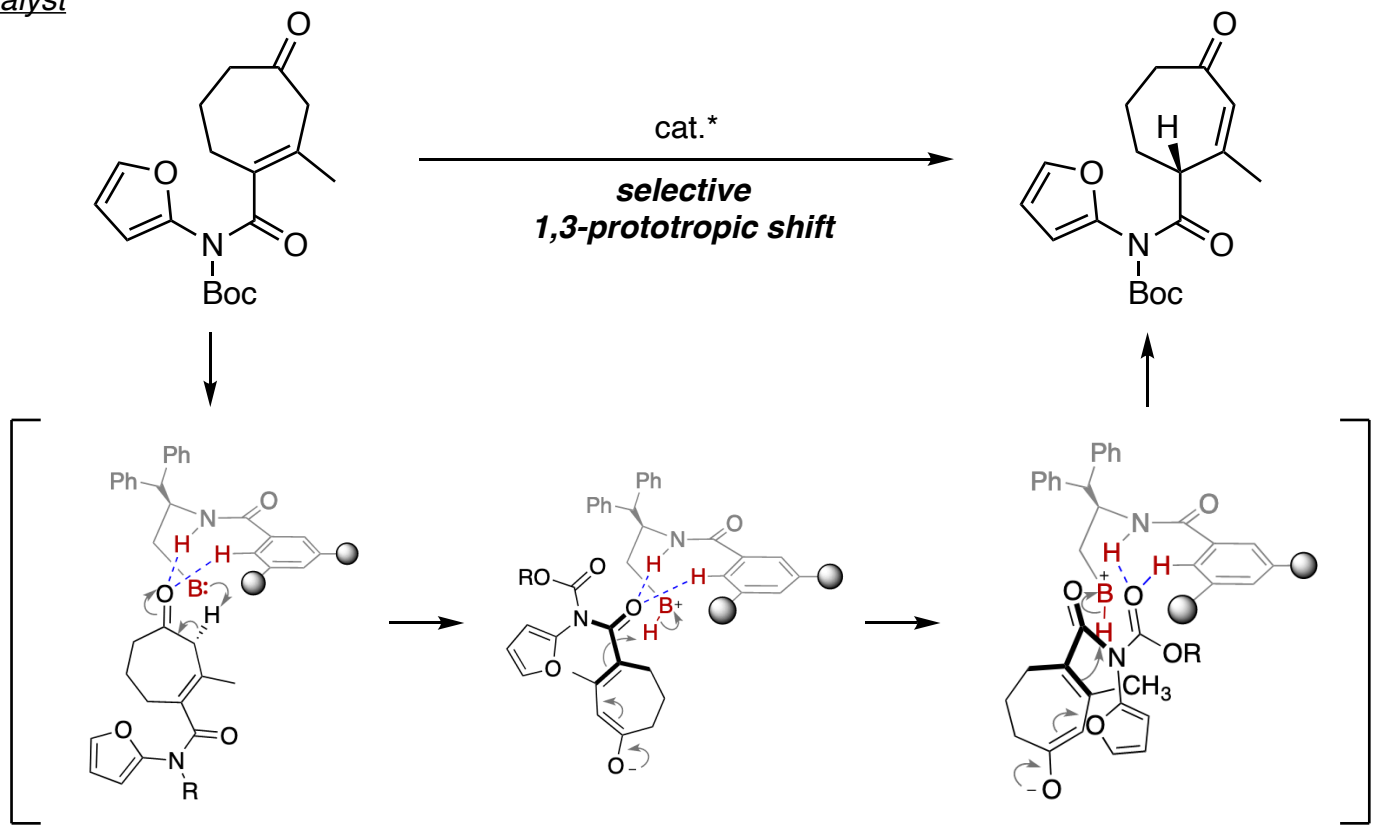
RSC Adv., **2015**, *5*, 48331–48362

Solution to step 8

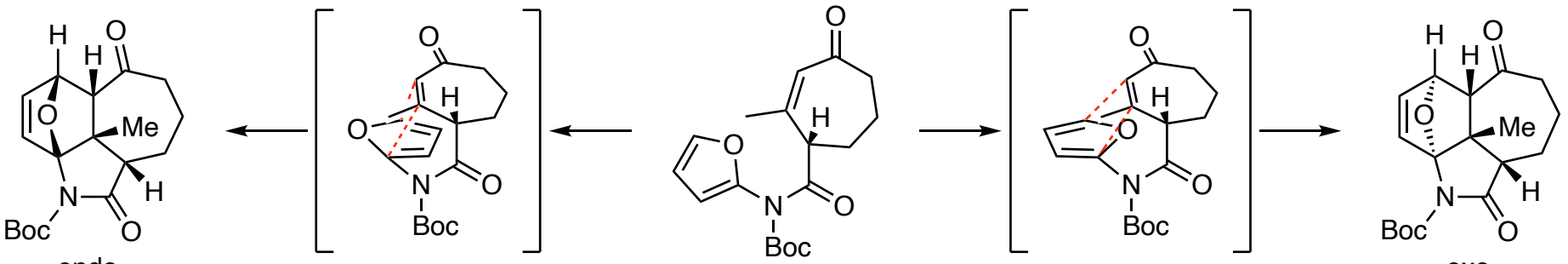
Catalyst formation in situ



Role of the catalyst

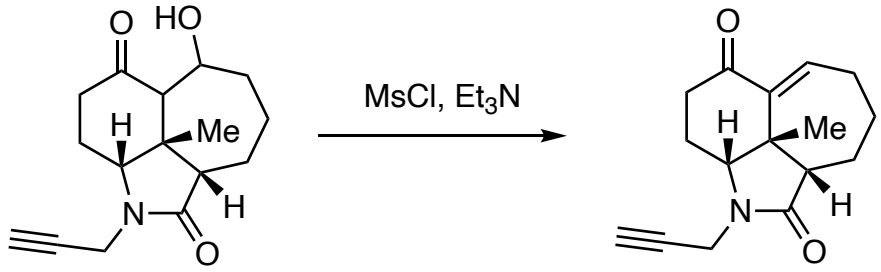


Diels-Alder reaction



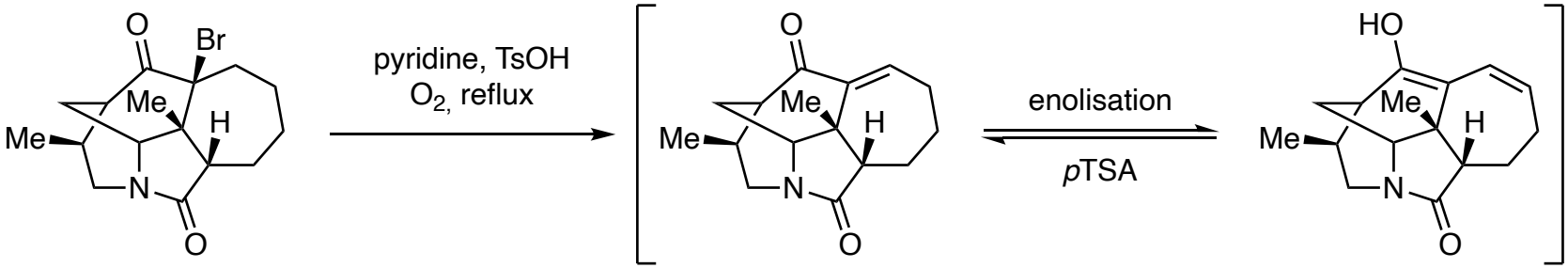
Solution to step 11

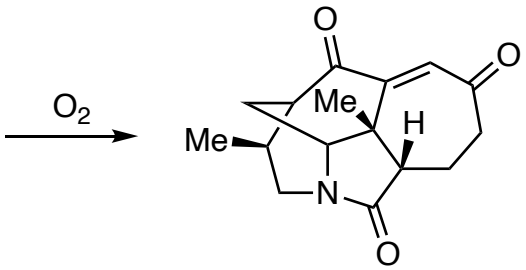
Intermediate 11'



11' **12**

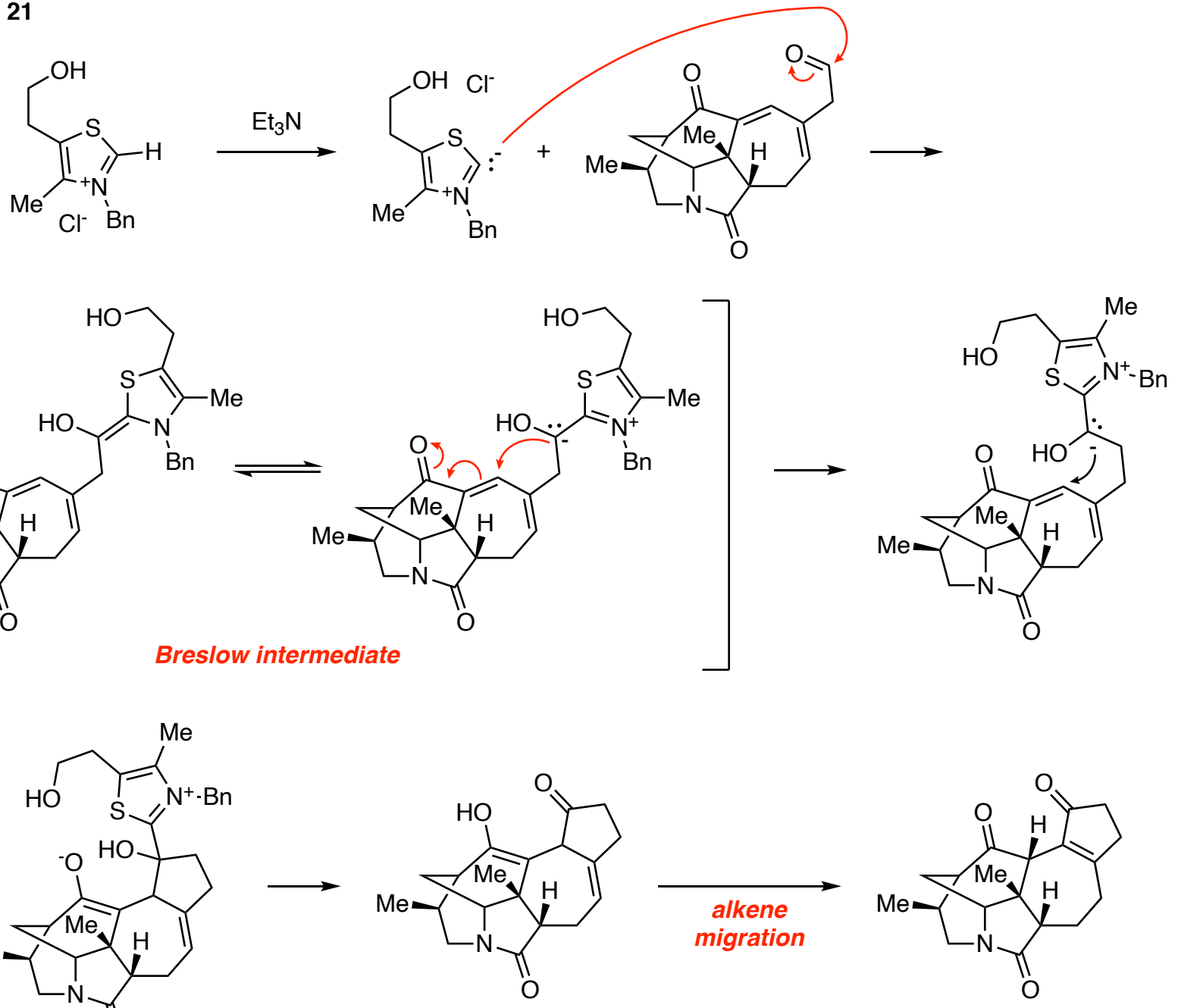
Solution to step 17





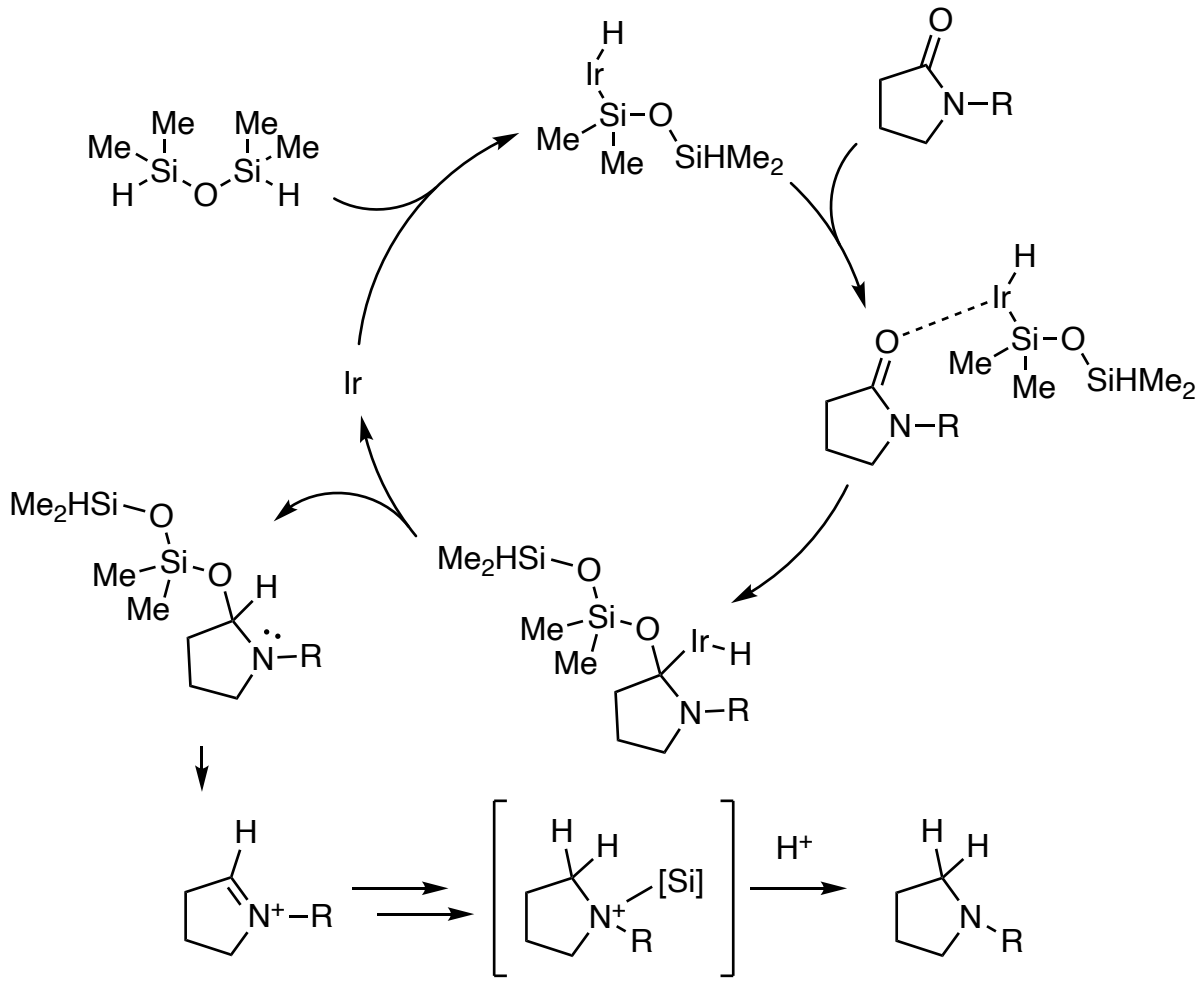
Solution to step 21

Stetter reaction



Stetter, H; *Angew. Chem. Int. Ed.* **1976**, *15*, 639.

Solution to step 22



Organometallics **2015**, *34*, 4895–4907