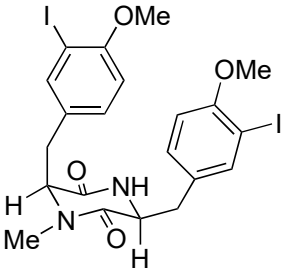
Problem Session (1) **2020.7.4 Risa Yoshinaga**

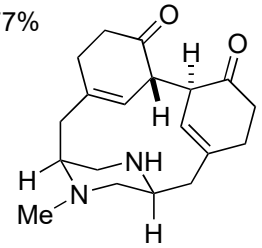
Please explain the reaction mechanisms.

problem 1



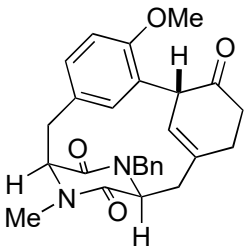
1-1

1. $Pd(dppf)Cl_2•CH_2Cl_2$ (0.2 eq.), $B_2(Pin)_2$ (4.0 eq.), K_2CO_3 (6.0 eq.), DMSO/H_2O (100/1), 90 °C; air, 60%
2. Li (15 eq.), NH_3, 2,2,2-trifluoroethanol (8.0 eq.), THF, -78°C, 77%
3. $[Ir(COE)_2Cl]_2$ (0.2 eq.), Et_2SiH_2 (10 eq.), toluene, reflux, 86%
4. *p*-toluenesulfonic acid (0.5 eq.), ethylene glycol (15 eq.), benzene, reflux
5. Li (30 eq.), NH_3, *t*-BuOH/THF (1/10), -78 °C; THF/MeOH/1 M HCl (3/3/2); DBU (2.0 eq.), toluene, rt, 28% (over 4 steps)



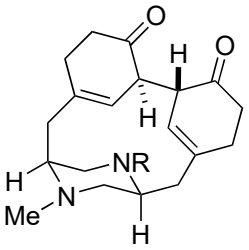
(+)-herquline B (1-2)

problem 2

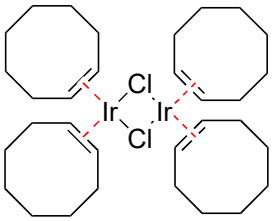


2-1

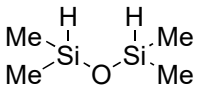
1. **A** (120 eq.), $Fe_3(CO)_{12}$ (15 mol%), toluene, 100 °C; 1 M HCl, acetone, 60%
2. $NaBH_4$ (5.0 eq.), MeOH, 0 °C to rt, 80% (single diastereomer)
3. Na (100 eq.), NH_3 (excess), THF, -78 °C, 55%
4. 1 M HCl, acetone, rt, 90%
5. $(COCl)_2$ (4.0 eq.), Et_3N (8.0 eq.), DMSO (16 eq.), CH_2Cl_2, -78 °C, 82%



1 step → **2-2**: R = Bn; **(+)-herquline C (2-3)**: R = H



$[Ir(COE)_2Cl]_2$

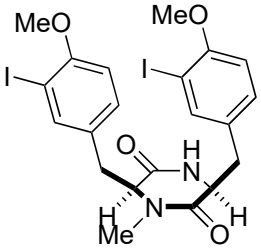


A

Problem Session (1) **2020.7.4 Risa Yoshinga**

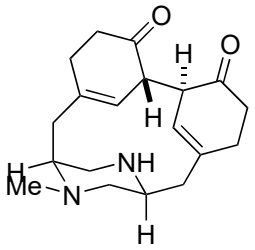
Please explain the reaction mechanisms.

problem 1



1-1

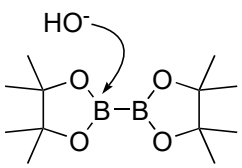
1. $Pd(dppf)Cl_2•CH_2Cl_2$ (0.2 eq.), $B_2(Pin)_2$ (4.0 eq.), K_2CO_3 (6.0 eq.), DMSO/H_2O (100/1), 90 °C; air, 60%
2. Li (15 eq.), NH_3, 2,2,2-trifluoroethanol (8.0 eq.), -78°C, 77%
3. $[Ir(COE)_2Cl]_2$ (0.2 eq.), Et_2SiH_2 (10 eq.), toluene, reflux, 86%
4. *p*-toluenesulfonic acid (0.5 eq.), ethylene glycol (15 eq.), benzene, reflux
5. Li (30 eq.), NH_3, *t*-B*u*OH/THF (1/10), -78 °C; THF/MeOH/1 M HCl (3/3/2); DBU (2.0 eq.), toluene, rt, 28% (over 4 steps)



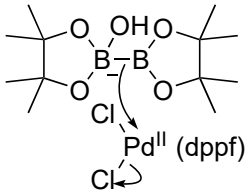
(+)-herquline B (1-2)

He, C.; Stratton, T. P.; Baran, P. S. *J. Am. Chem. Soc.* **2019**, *141*, 29.

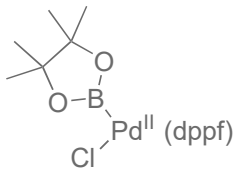
Formation of palladium(0) complex



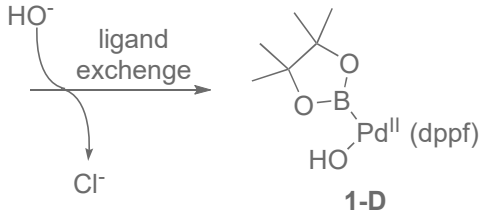
1-A



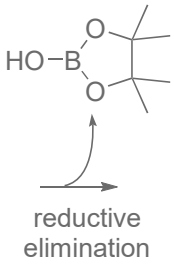
1-B



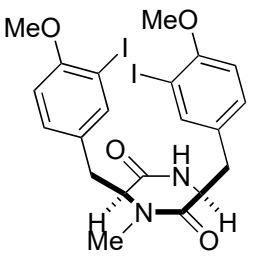
1-C



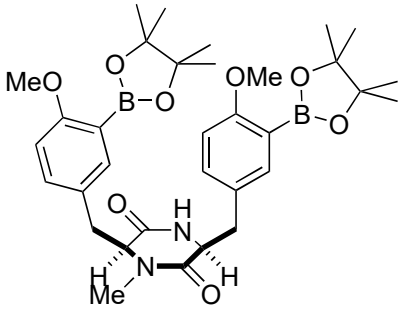
1-D



1-E



1-1



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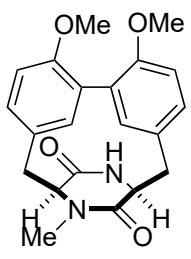

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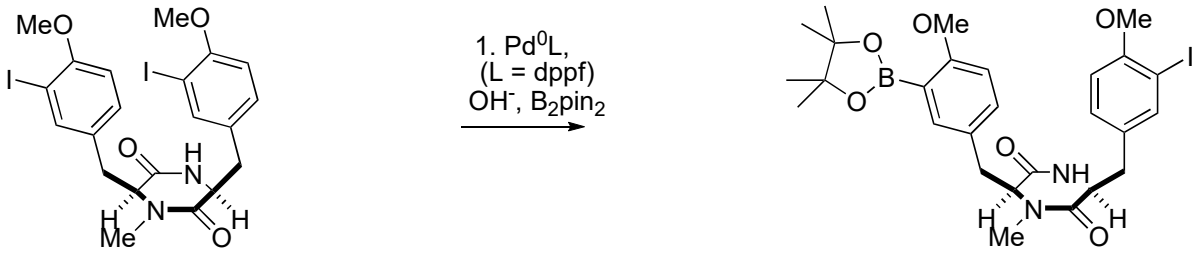
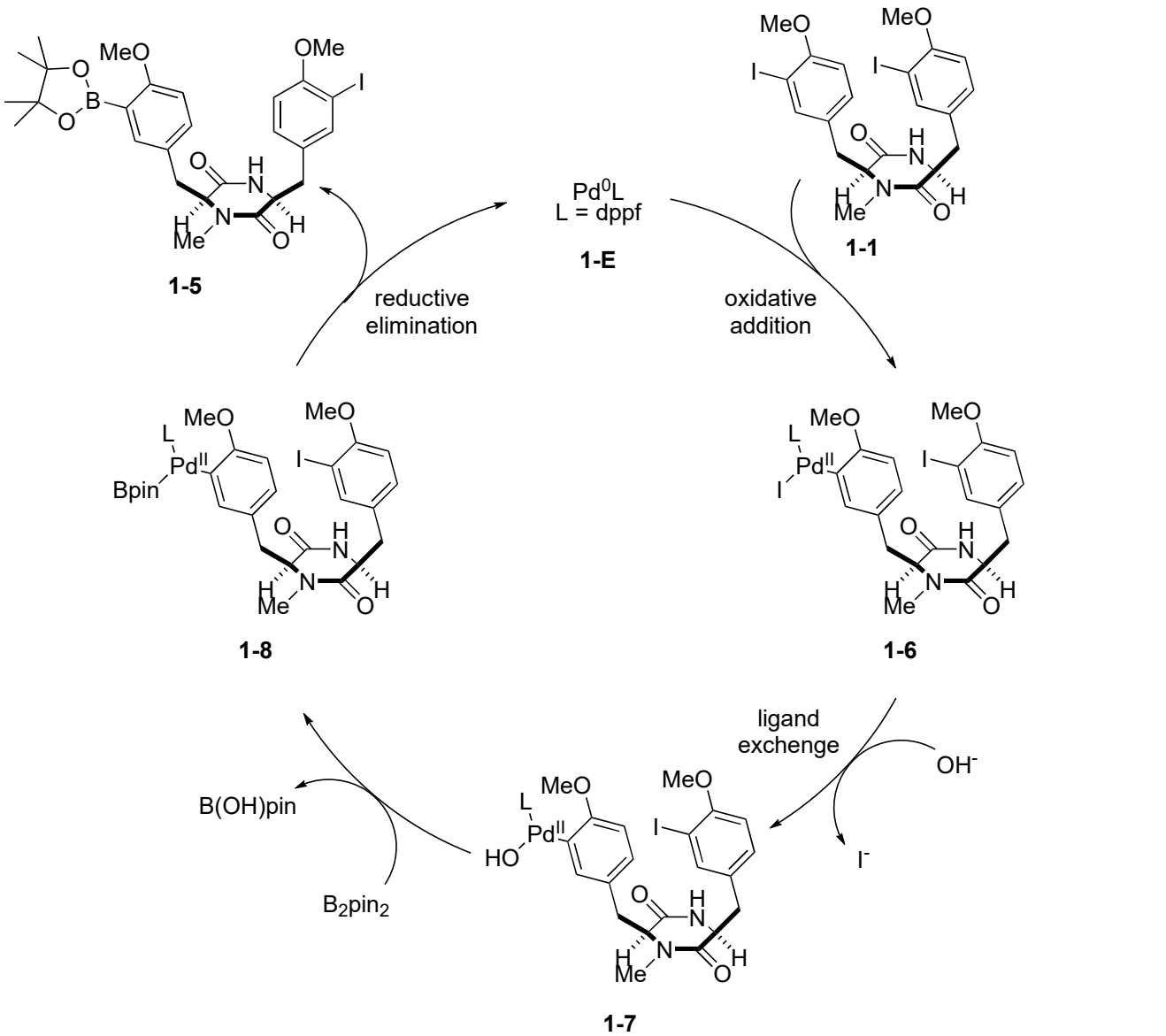
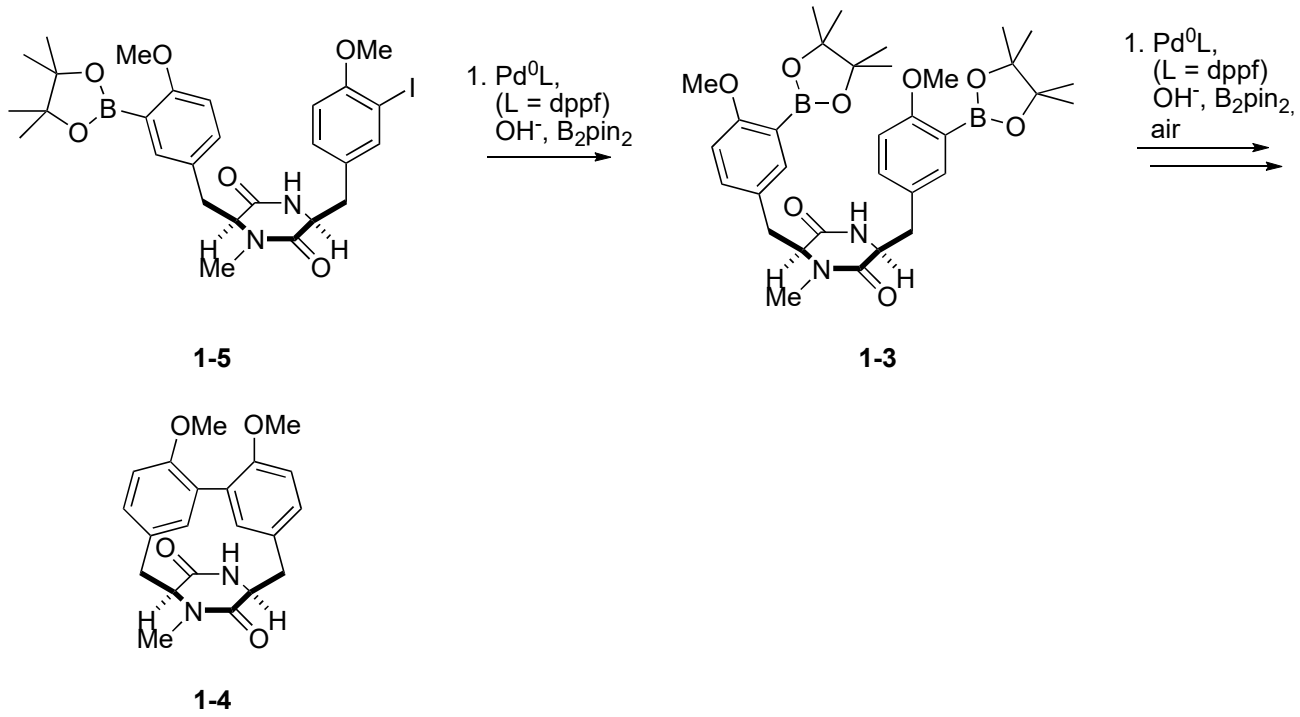

1. Pd0L,
(L = dppf)
OH-, B2pin2

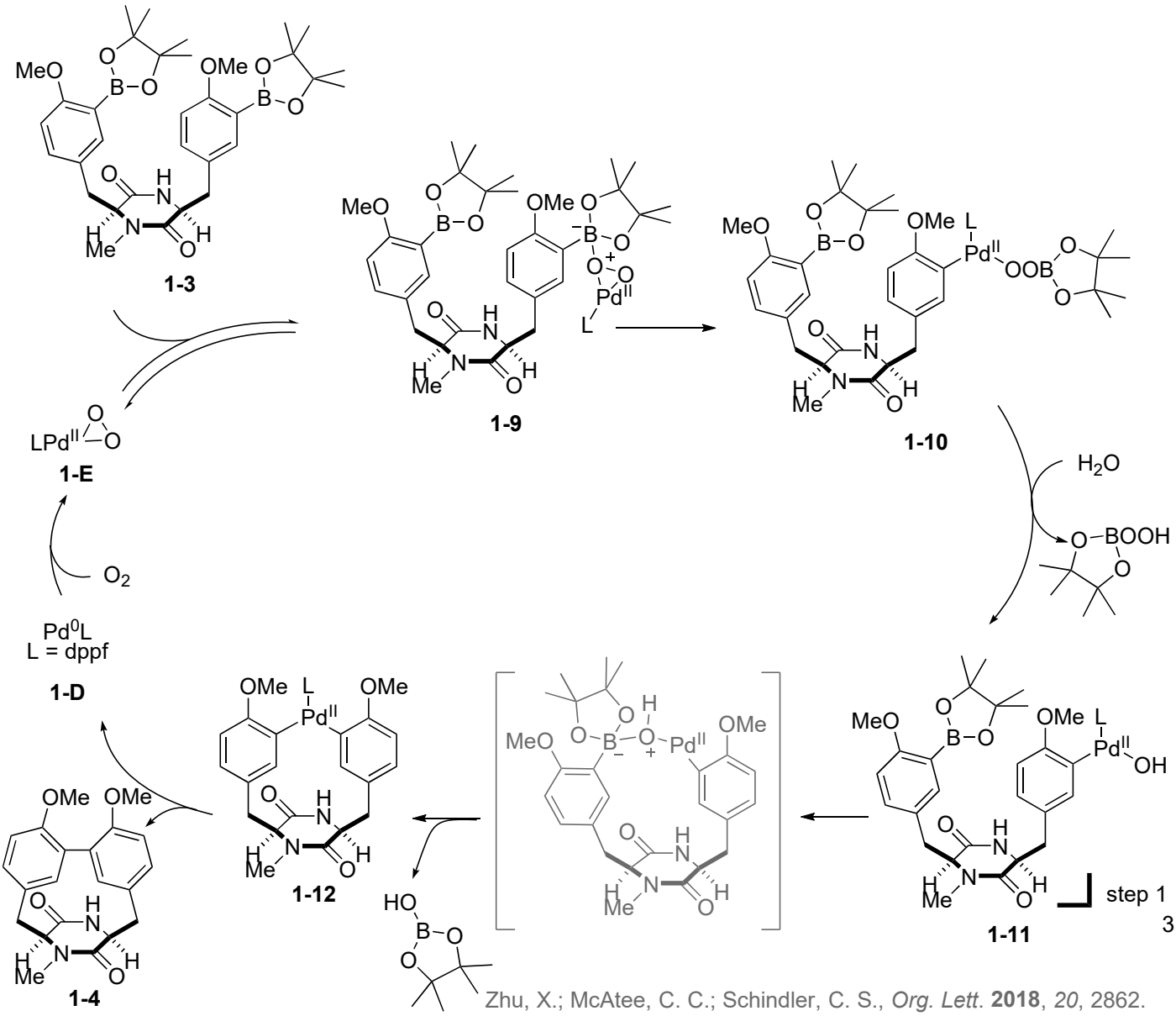
1-1 **1-5**


Pd0L
L = dppf
1-E
reductive
elimination
oxidative
addition
ligand
exchenge
OH-
I-
B(OH)pin
B2pin2
1-5
1-1
1-8
1-6
1-7

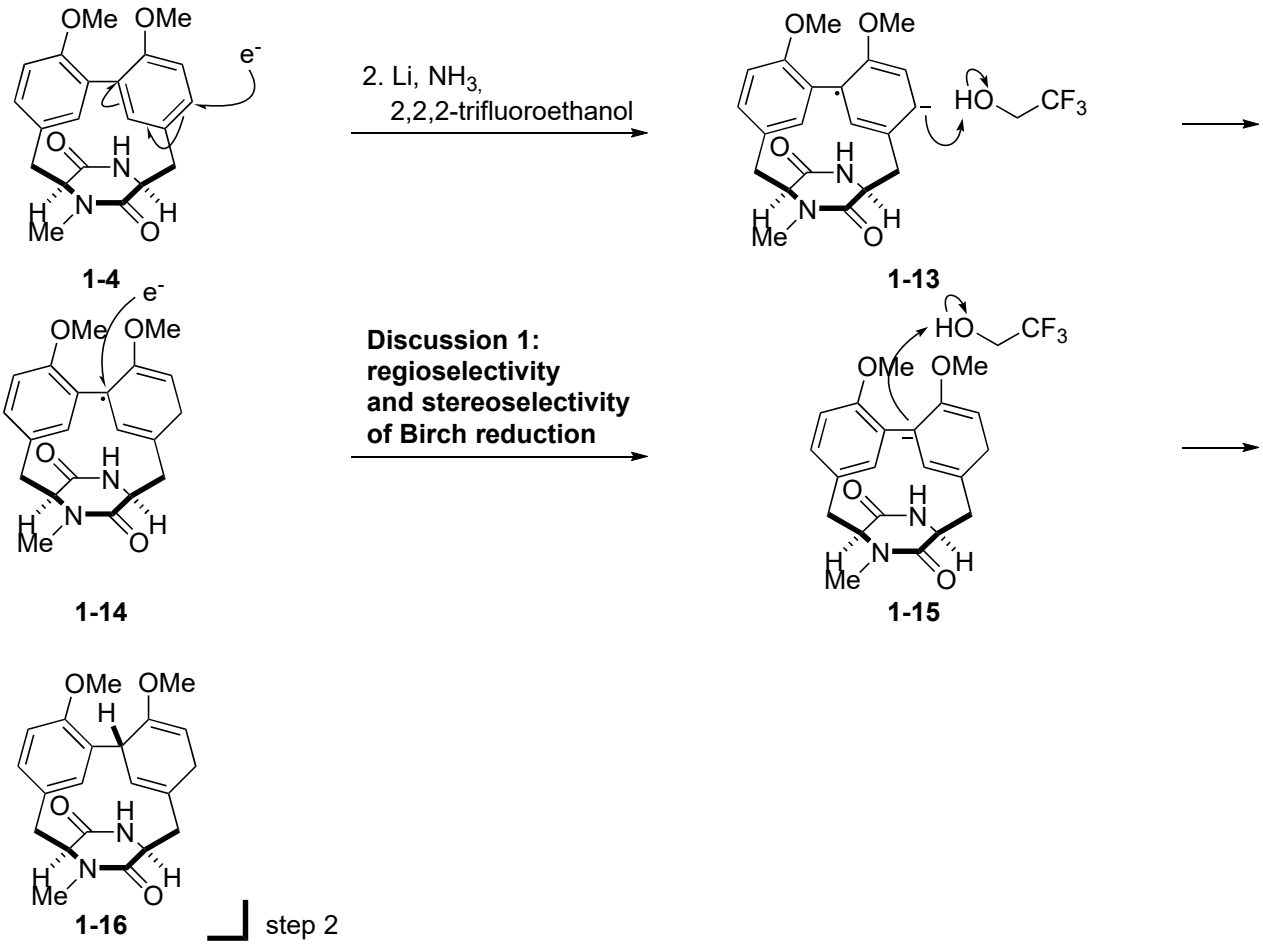


1-5 **1-3**

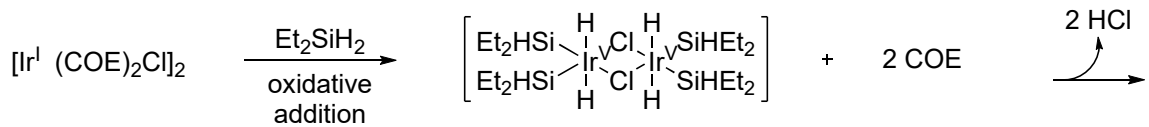
1-4



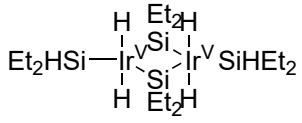
Zhu, X.; McAtee, C. C.; Schindler, C. S., *Org. Lett*. **2018**, *20*, 2862.



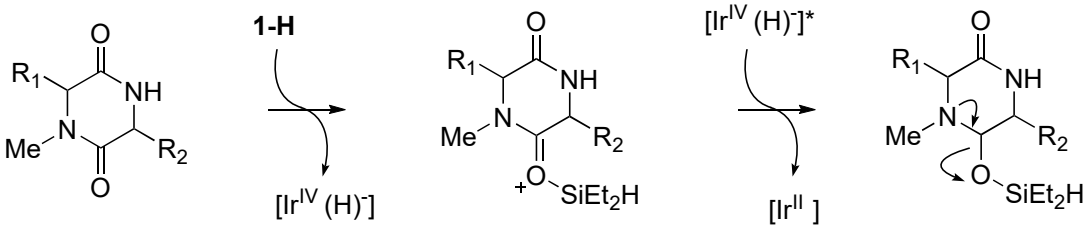
Formation of the proposed catalyst resting state



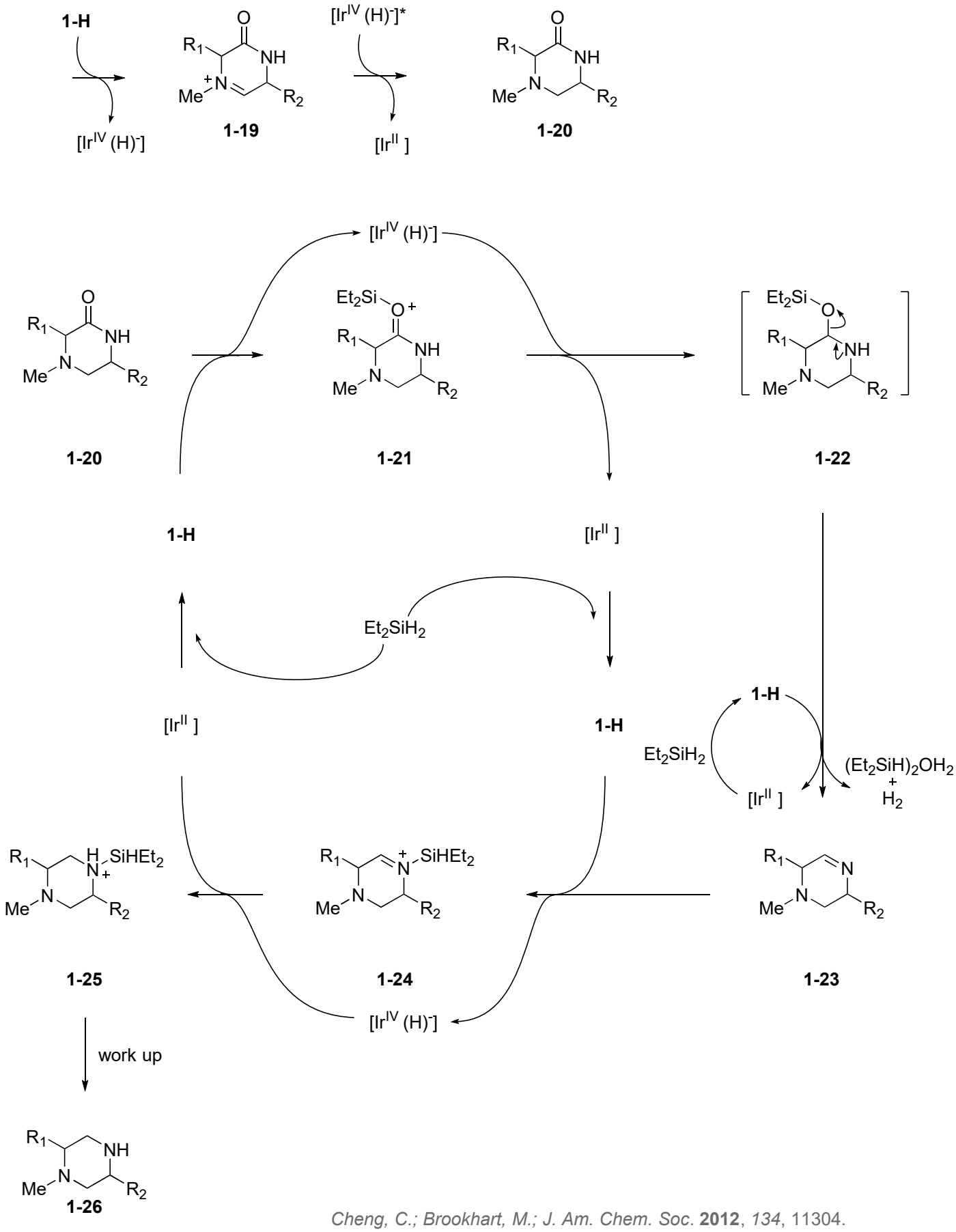
1-F 1-G



1-H

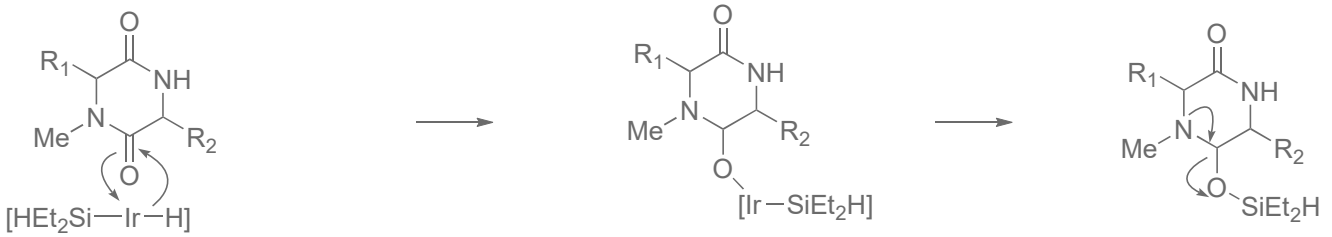


1-16 1-17 1-18

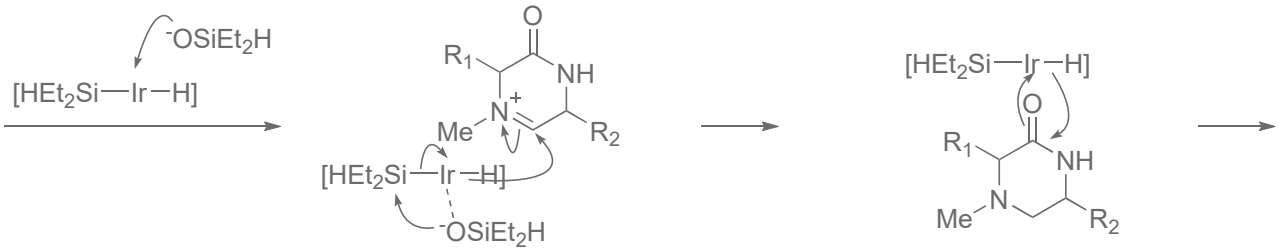


Cheng, C.; Brookhart, M.; J. Am. Chem. Soc. **2012**, *134*, 11304.

another plausible pathway



1-16 **1-27** **1-18**



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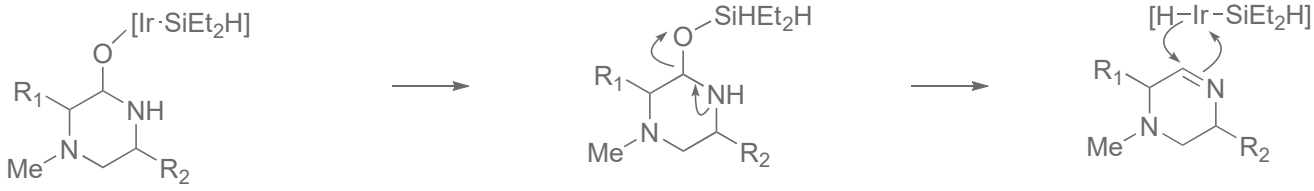

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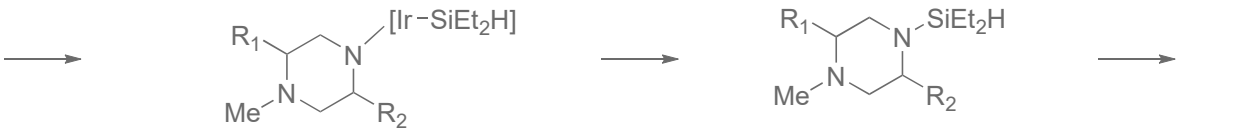
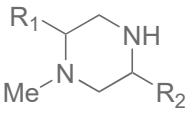


1-29 **1-30**



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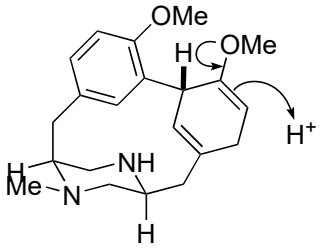

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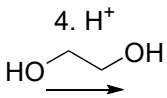

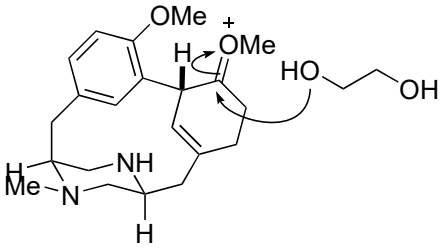

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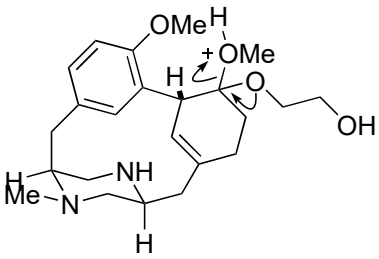

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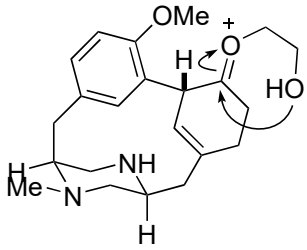

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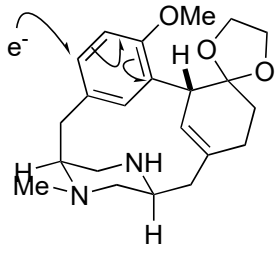

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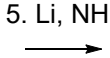
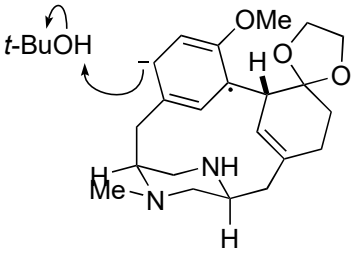
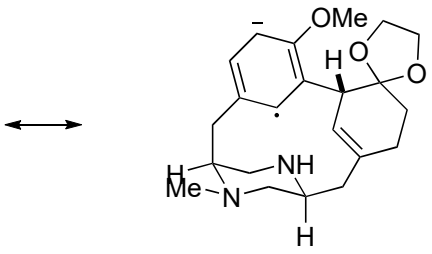


step 4



1-35
more stable



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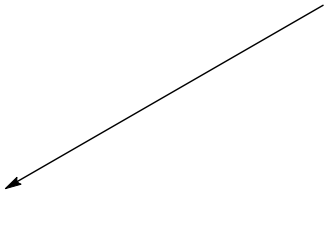

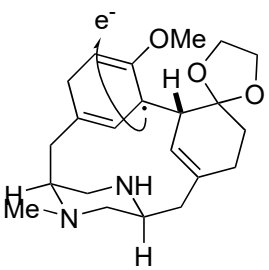

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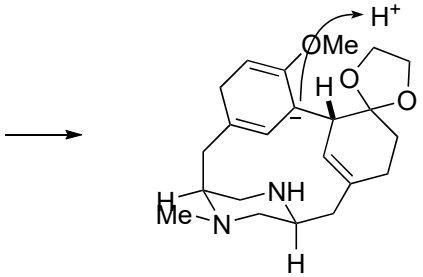

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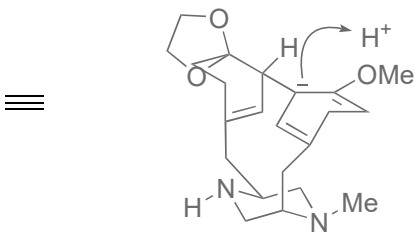

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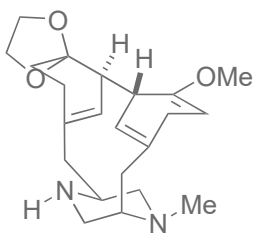

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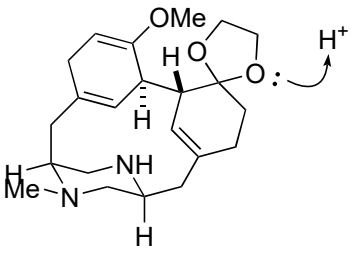

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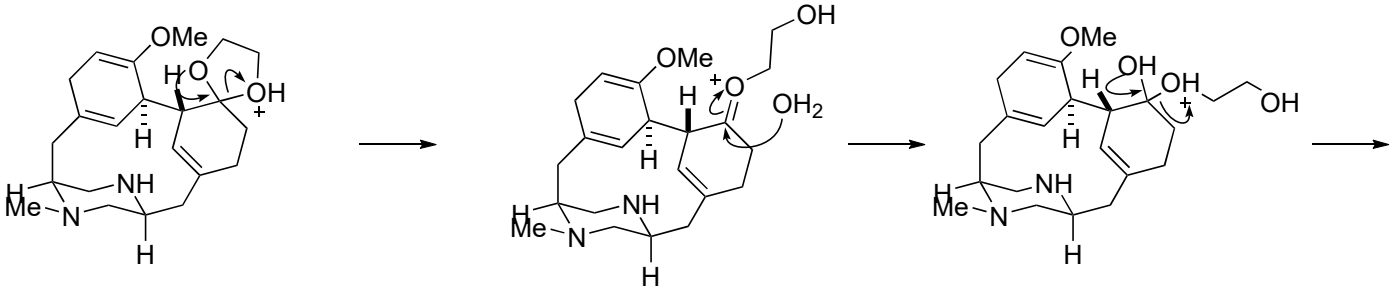
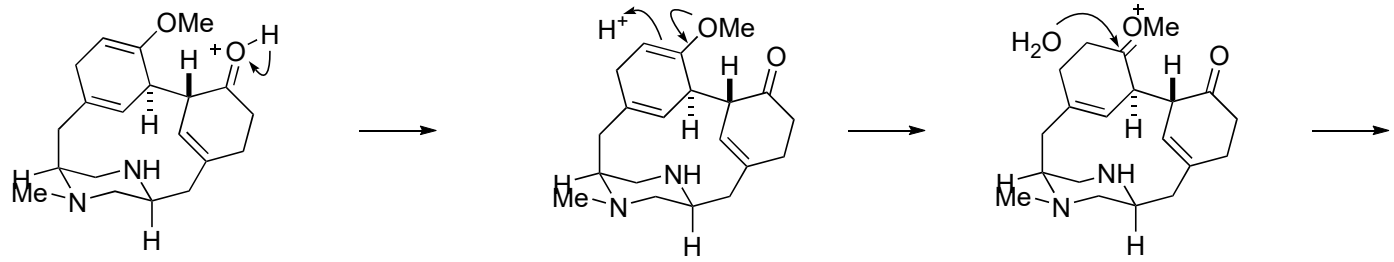
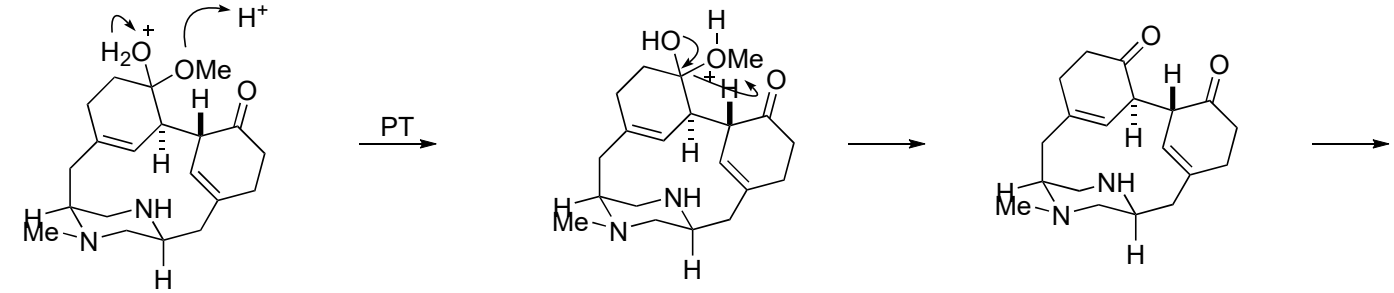


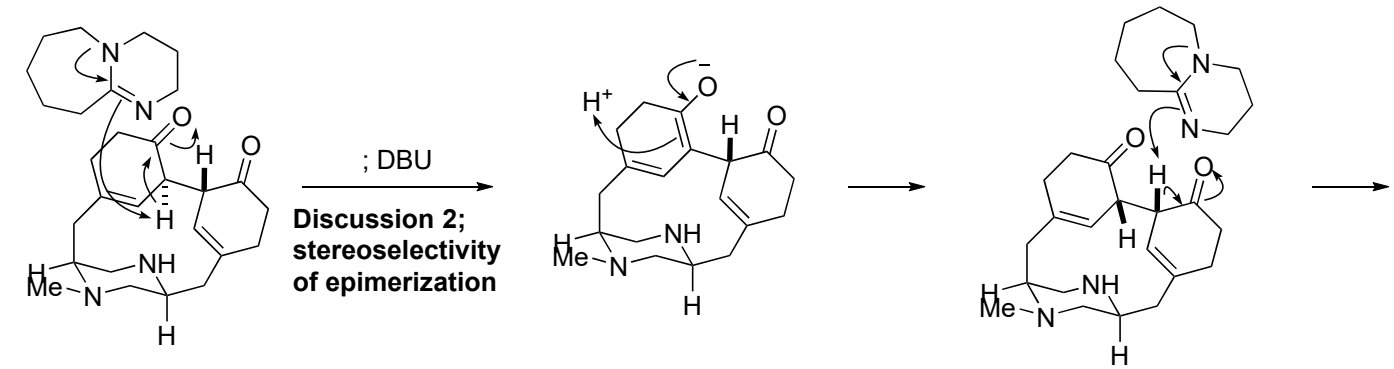
1-40 **1-41** **1-42**



1-43 **1-44** **1-45**

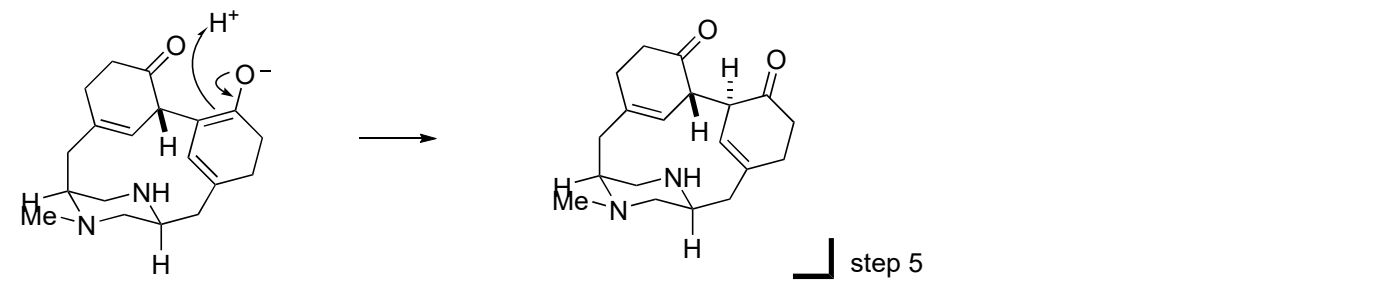


1-46 **1-47** **1-48**



Discussion 2; stereoselectivity of epimerization

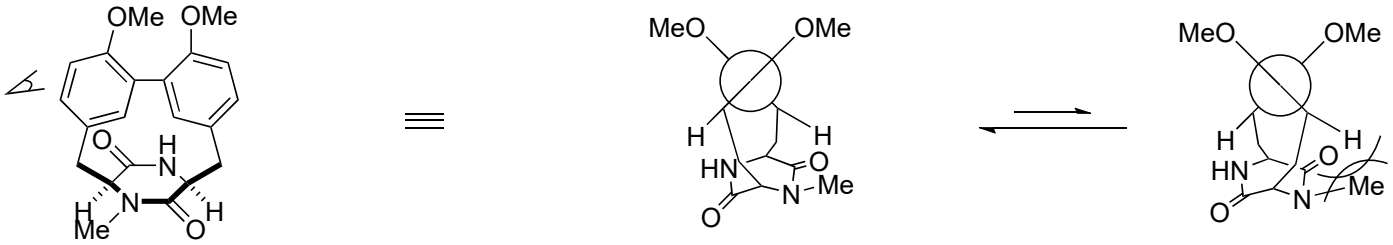
herquline C (2-2)* **1-49** **1-50**



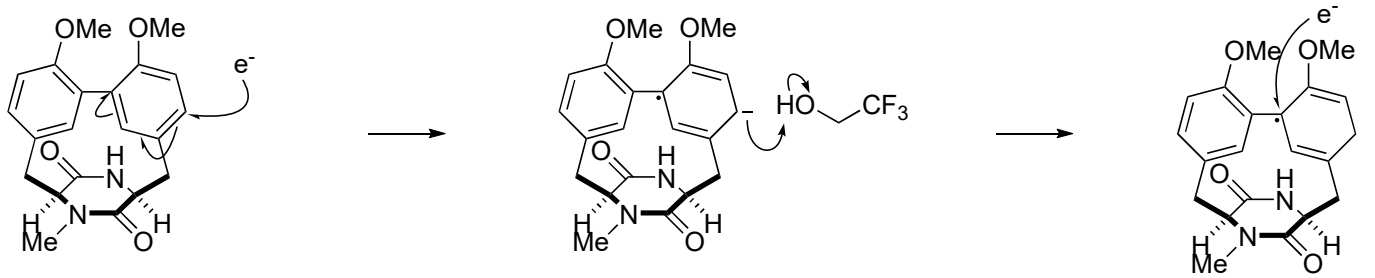
1-51 **herquline B (1-2)**

* This clude was 1 : 5 mixture of **herquline B (1-2)** and **C (2-2)** and directly subjected to the next reaction without purification.

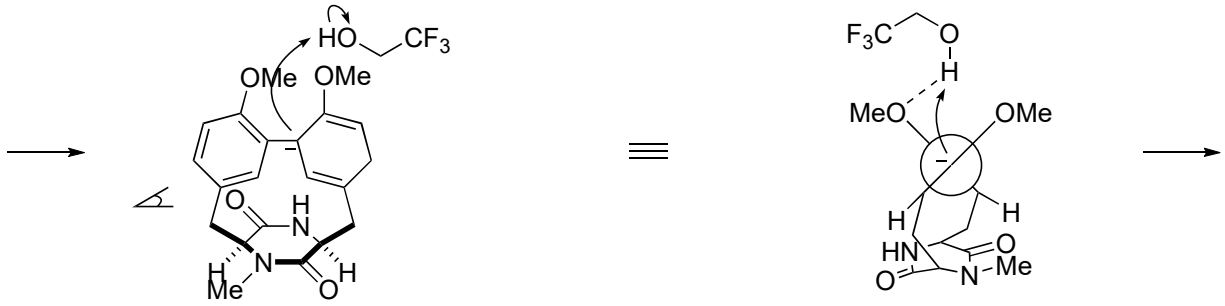
Discussion 1; regioselectivity and stereoselectivity of Birch reduction



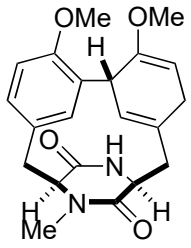
1-4 **1-4** more stable **1-4'**



1-4 **1-13** **1-14**



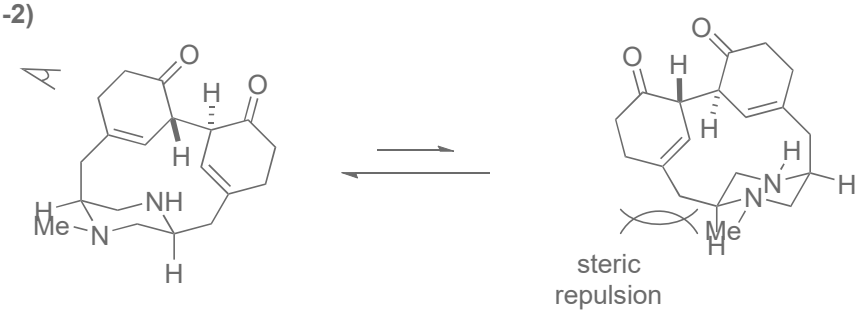
1-15 **1-15**



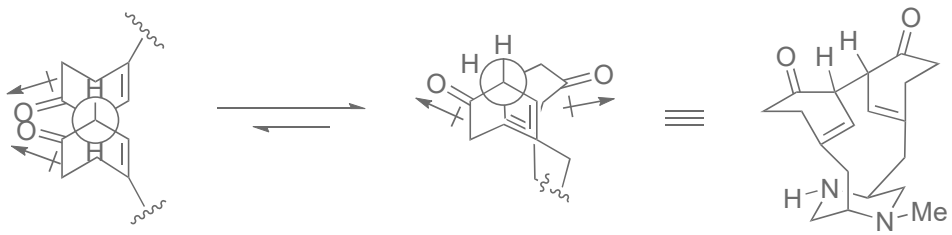
1-16

Discussion 2; stereoselectivity of epimerization

herquline B (1-2)



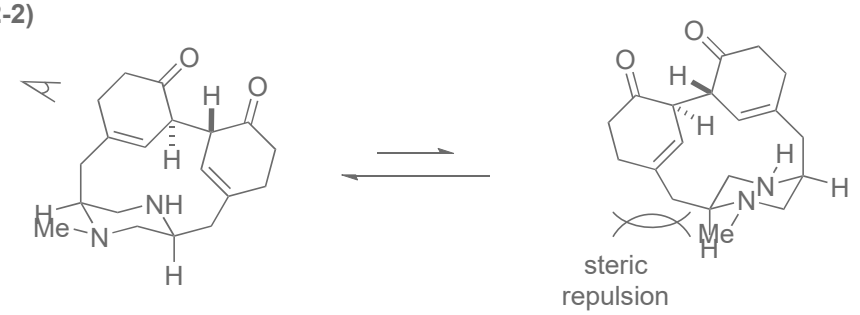
1-2 **1-2'**



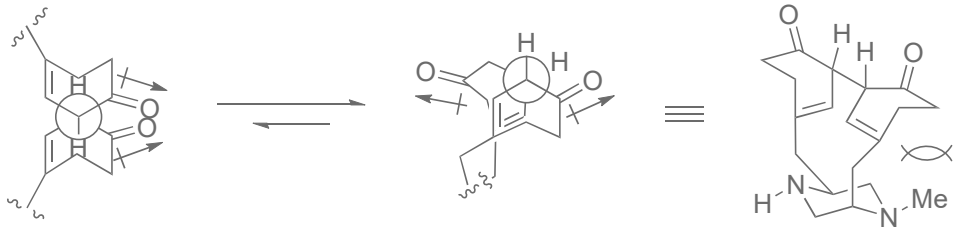
1-2a **1-2b** **1-2b**

1-2b is more stable because of smaller dipole moment.

herquline C (2-2)



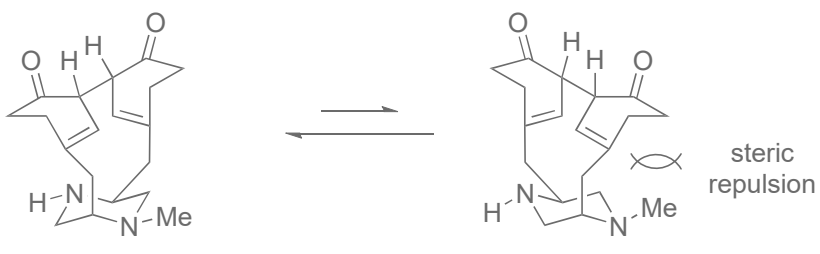
2-2 **2-2'**



2-2a **2-2b** **2-2b**

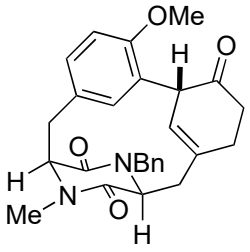
2-2b is more stable because of smaller dipole moment.

Comparison of herquline B (1-2) and herquline C (2-2)



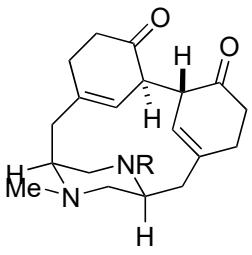
herquline B (1-2)
more stable **herquline C (2-2)**

problem 2

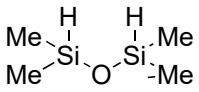


2-1

1. **A** (120 eq.), $Fe_3(CO)_{12}$ (15 mol%), toluene, 100 °C; 1 M HCl, acetone, 60%
2. $NaBH_4$ (5.0 eq.), MeOH, 0 °C to rt, 80% (single diastereomer)
3. Na (100 eq.), NH_3 (excess), THF, -78 °C, 55%
4. 1 M HCl, acetone, rt, 90%
5. $(COCl)_2$ (4.0 eq.), Et_3N (8.0 eq.), DMSO (16 eq.), CH_2Cl_2, -78 °C, 82%

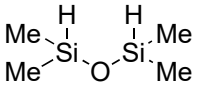


1 step → **2-2**: R = Bn; **(+)-herquline C (2-3)**: R = H



2-A

Zhu, X.; McAtee, C. C.; Schindler, C. S. *J. Am. Chem. Soc.* **2019**, *141*, 3409.

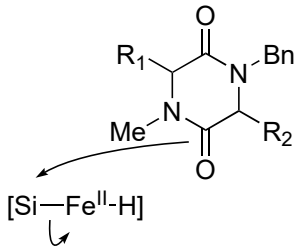


2-A

$[Fe^0]$ — **2-B**

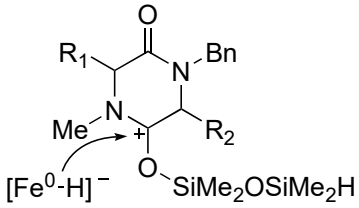
oxidative addition

$[Si—Fe^{II}-H]$ — **2-C**



2-1

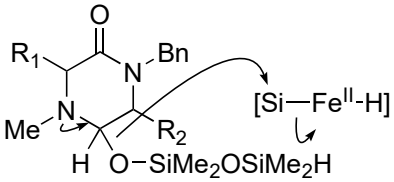
1. **2-A**, $Fe_3(CO)_{12}$



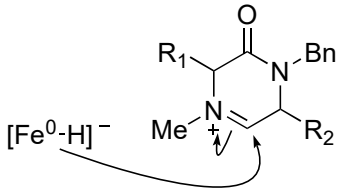
2-4

$[Fe^0]$

$O(SiMe_2OSiMe_2H)_2$

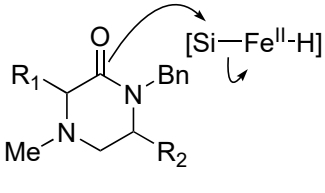


2-5

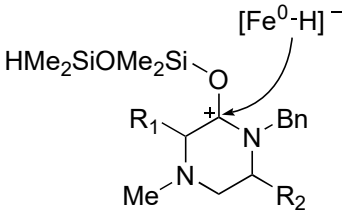


2-6

$[Fe^0]$

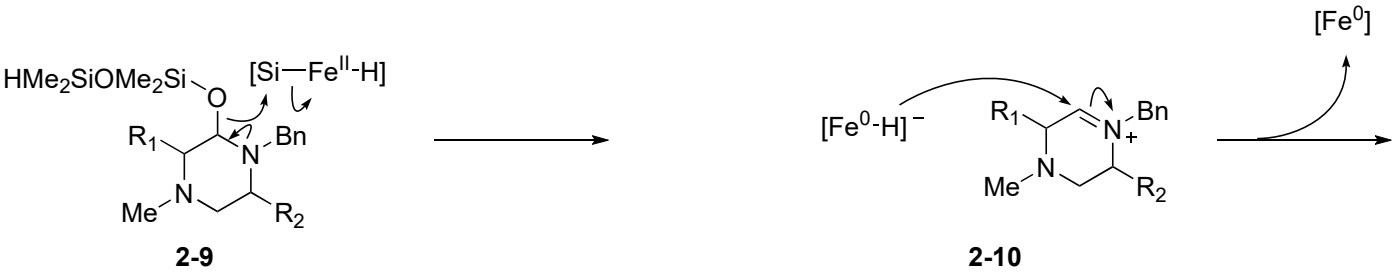


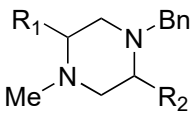
2-7



2-8

$[Fe^0]$



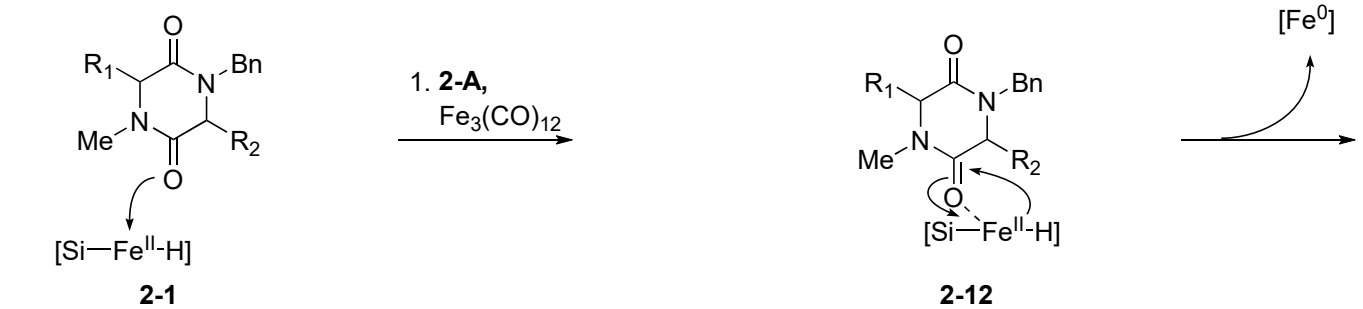


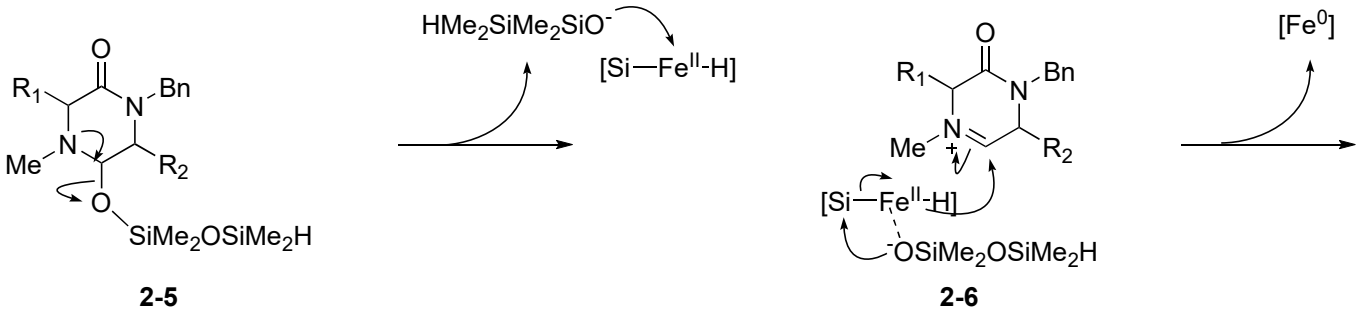
2-11

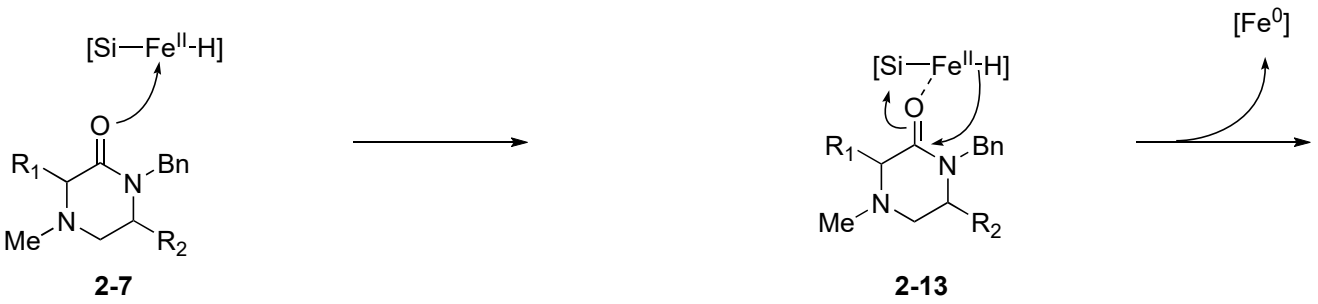
step 1

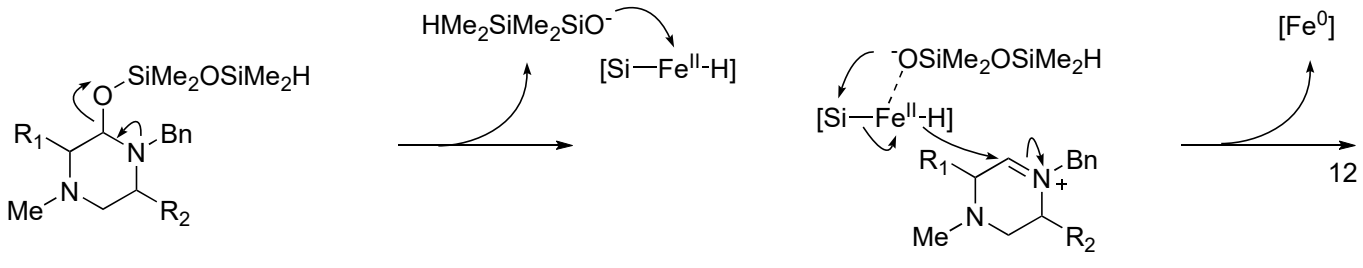
Hanada, S.; Ishida, T.; Motoyama, Y.; Nagashima, H. *J. Org. Chem.* **2007**, *72*, 7551.

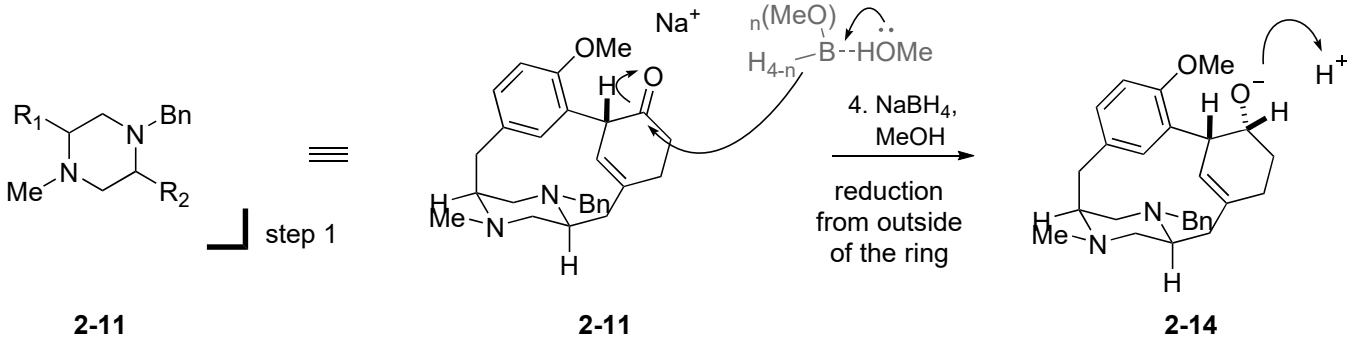
another pathway



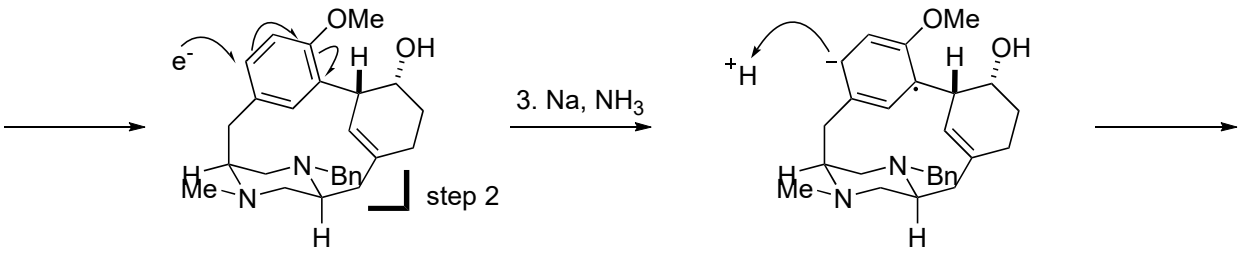




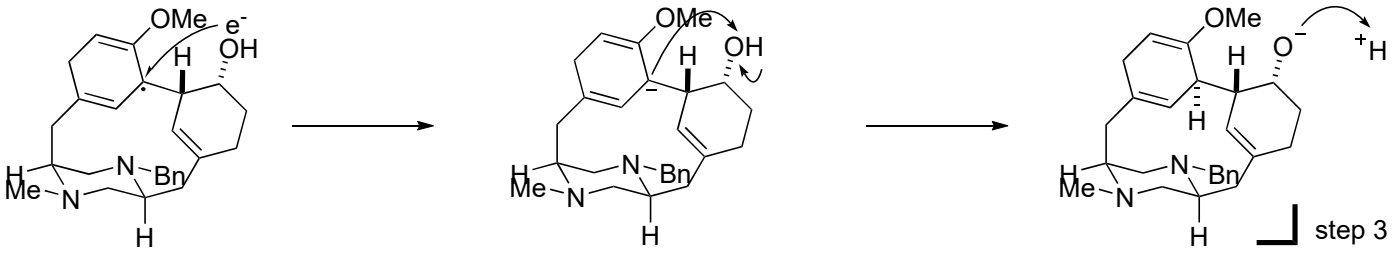




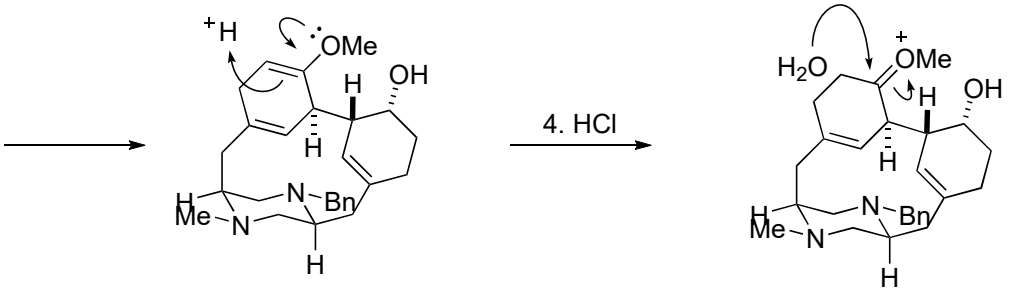
2-11 **2-11** **2-14**



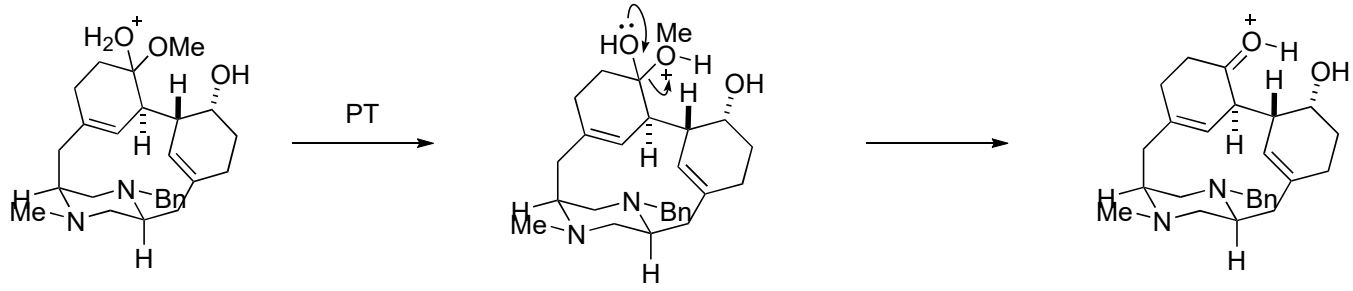
2-15 **2-16**



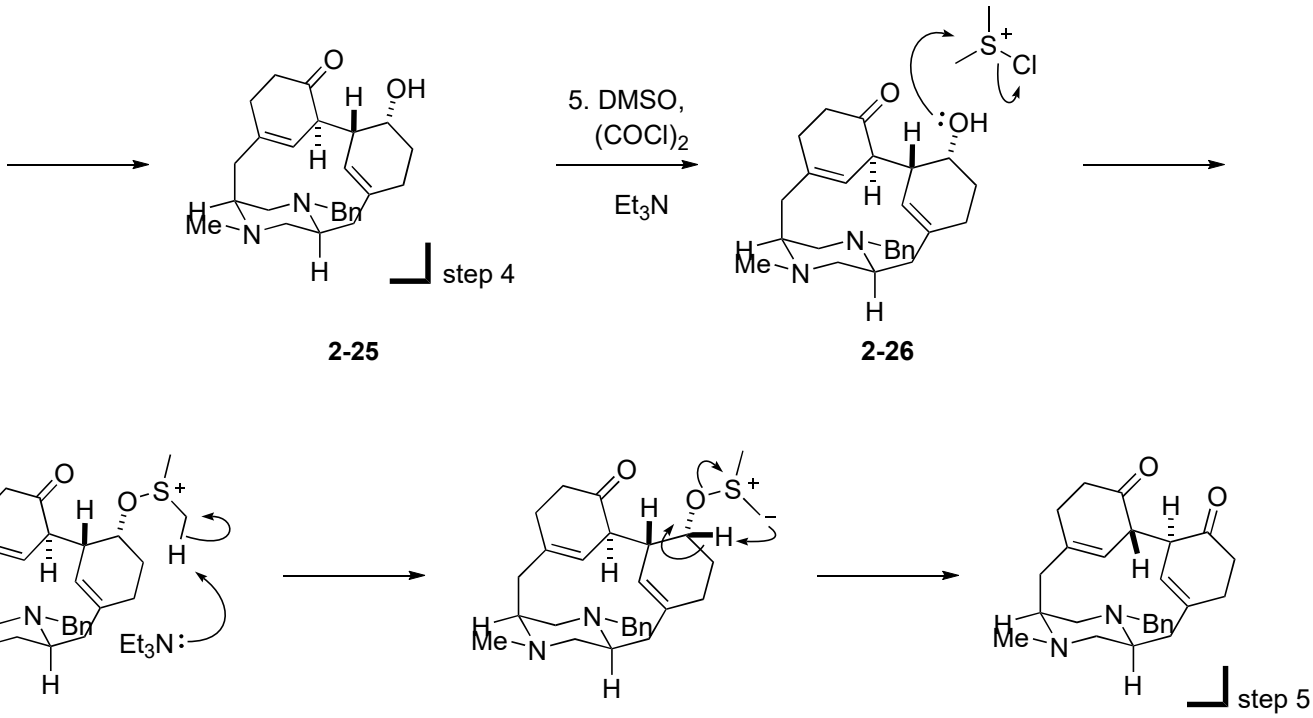
2-17 **2-18** **2-19**



2-20 **2-21**



2-22 **2-23** **2-24**


step 4
5. DMSO,
(COCl)2
Et3N
2-25
2-26
step 5
2-27
2-28
2-29
1 step
Harquline C (2-2)