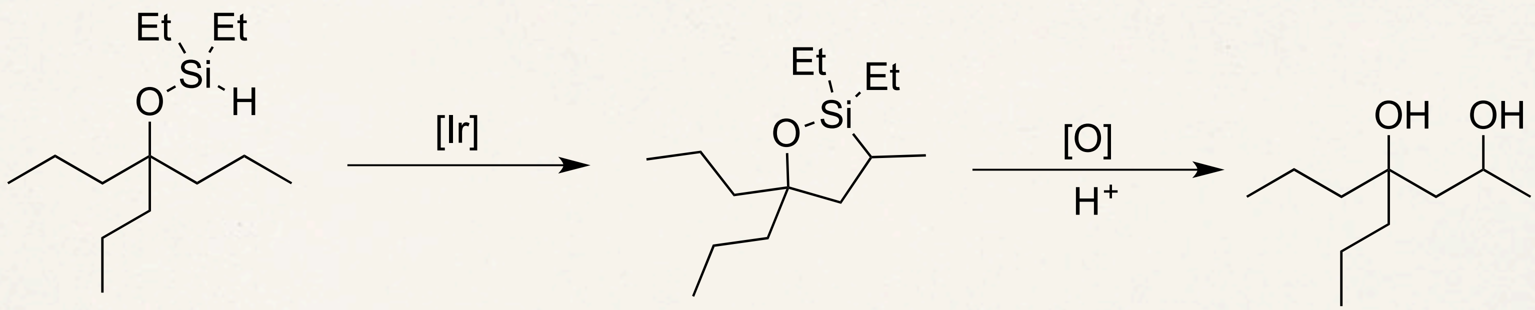


Iridium-Catalyzed Regioselective Silylation of Secondary Alkyl C−H Bonds for the Synthesis of 1,3-Diols

Bijie Li, Matthias Driess, and John F. Hartwig.

J. Am. Chem. Soc. 2014, ASAP.

dx.doi.org/10.1021/ja5026479

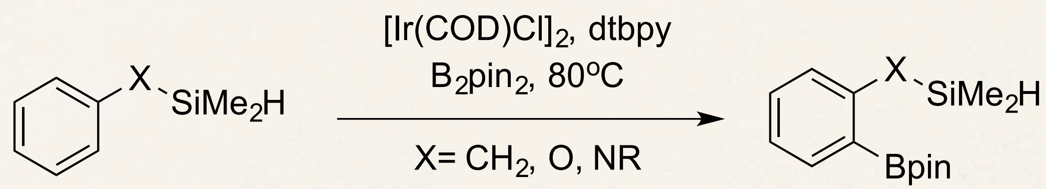
Aliphatic C-H Activation

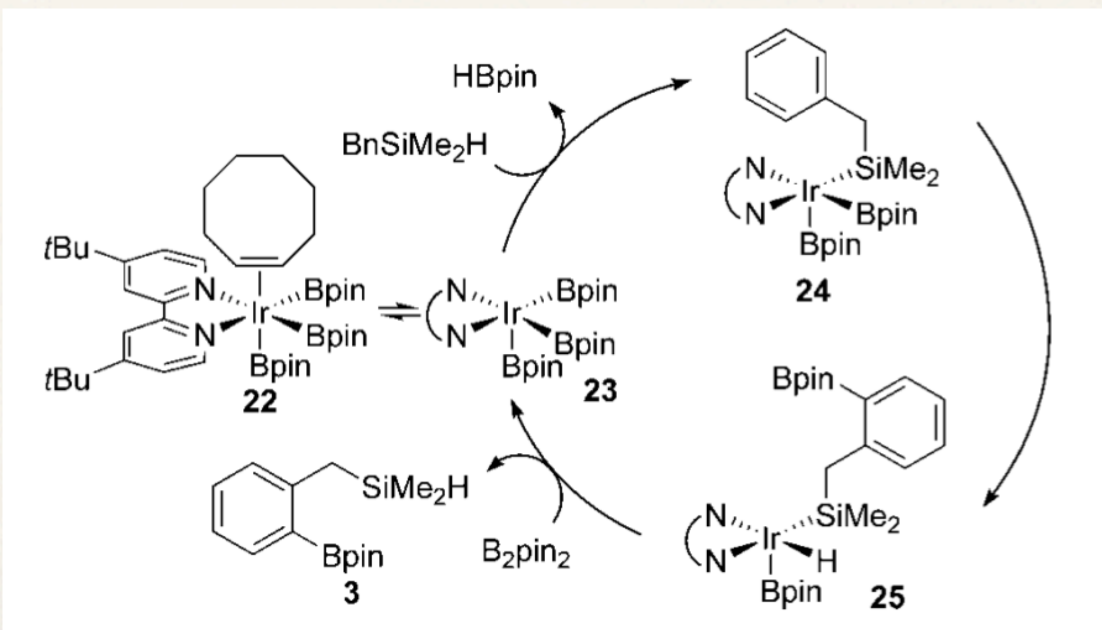
- One the greatest challenges in complex-molecules synthesis
- Inherently reactive C-H bond (Benzylic position and etc.)
- Directing group not present in desired target.

1. Chen, M. S. & White, M. C. *Science* **318**, 783–787 (2007).
2. Lyons, T. W. & Sanford, M. S. *Chem. Rev.* **110**, 1147–1169 (2010)
3. Newhouse, T. & Baran, P. S. *Angew. Chem. Int. Ed.* **50**, 3362–3374 (2011).

Si-H Directing Group

- Hydrosilane as a directing group.



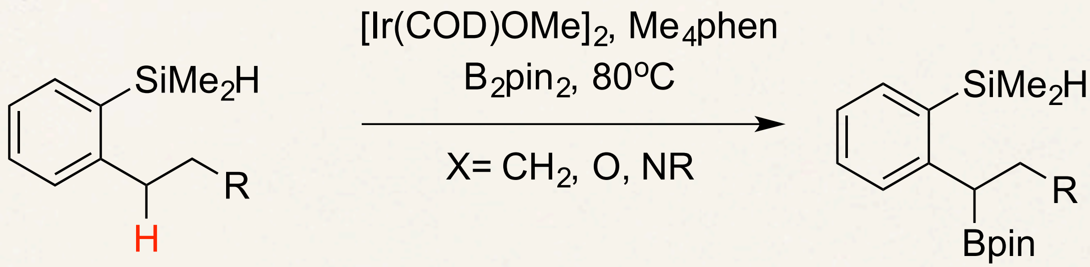


Meta selectivity

1. Boebel, T. A. & Hartwig, J. F. *J. Am. Chem. Soc.* **130**, 7534–7535 (2008).

Si-H Directing Group

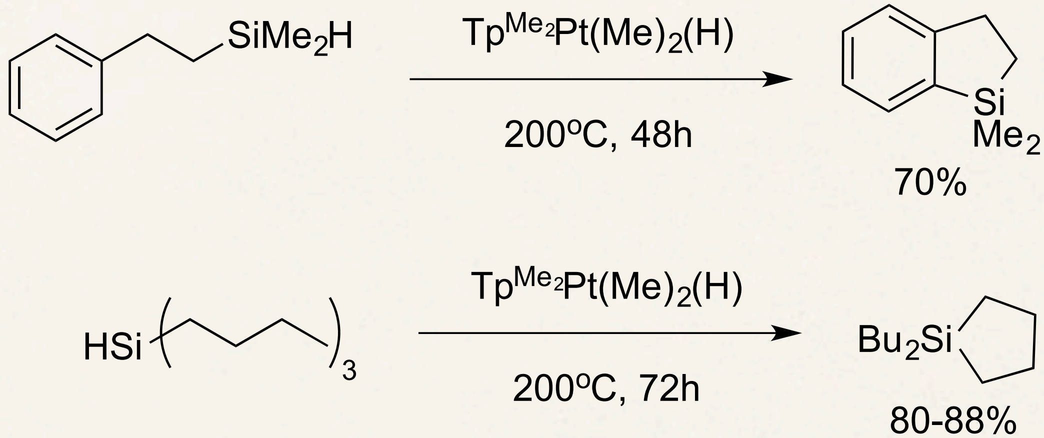
- Recent example:



1. Cho, S. H.; Hartwig, J.F., *J. Am. Chem. Soc.*, **2013**, *135*, 8157-8160

Intramolecular C-H Silylation

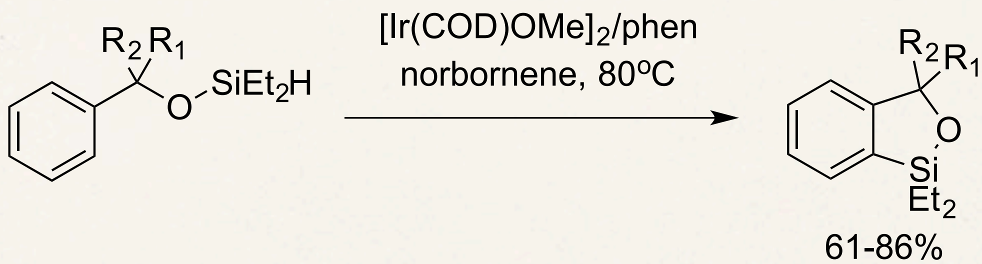
- Platinum as catalyst:

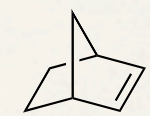


1. Tsukada, N.; Hartwig, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 5022–5023.

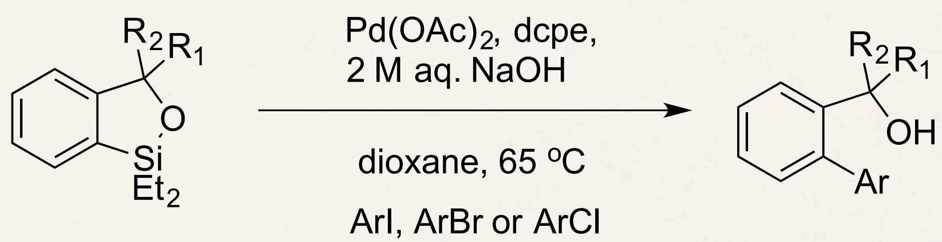
Intramolecular C-H Silylation

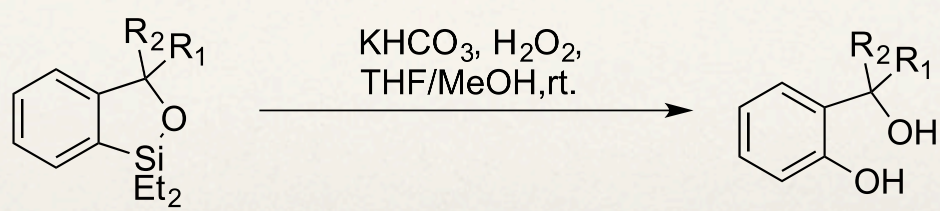
- Iridium catalyzed *ortho*-silylation





norbornene



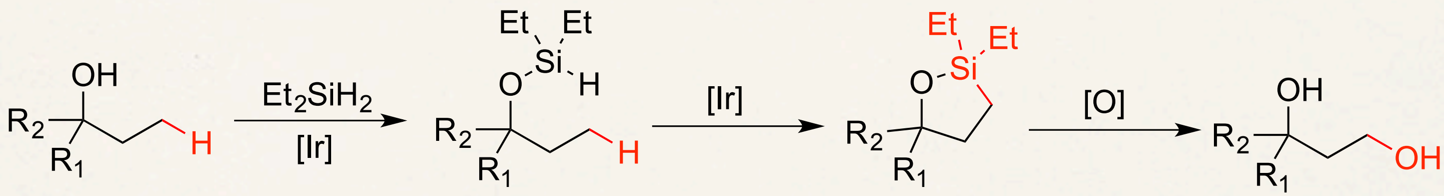


Norbornene H2 absorbant

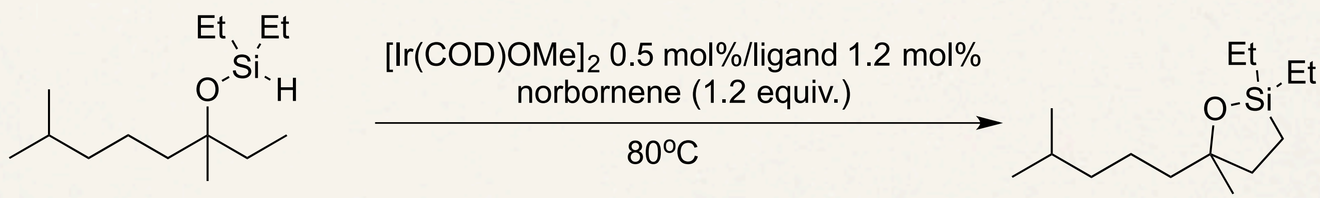
1. Simmons, E. M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, 132, 17092-17095.

Aliphatic C-H Silylation

- 1,3-diol formation sequence

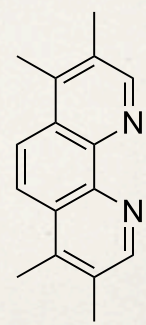


- Ligand screening



Gc yield

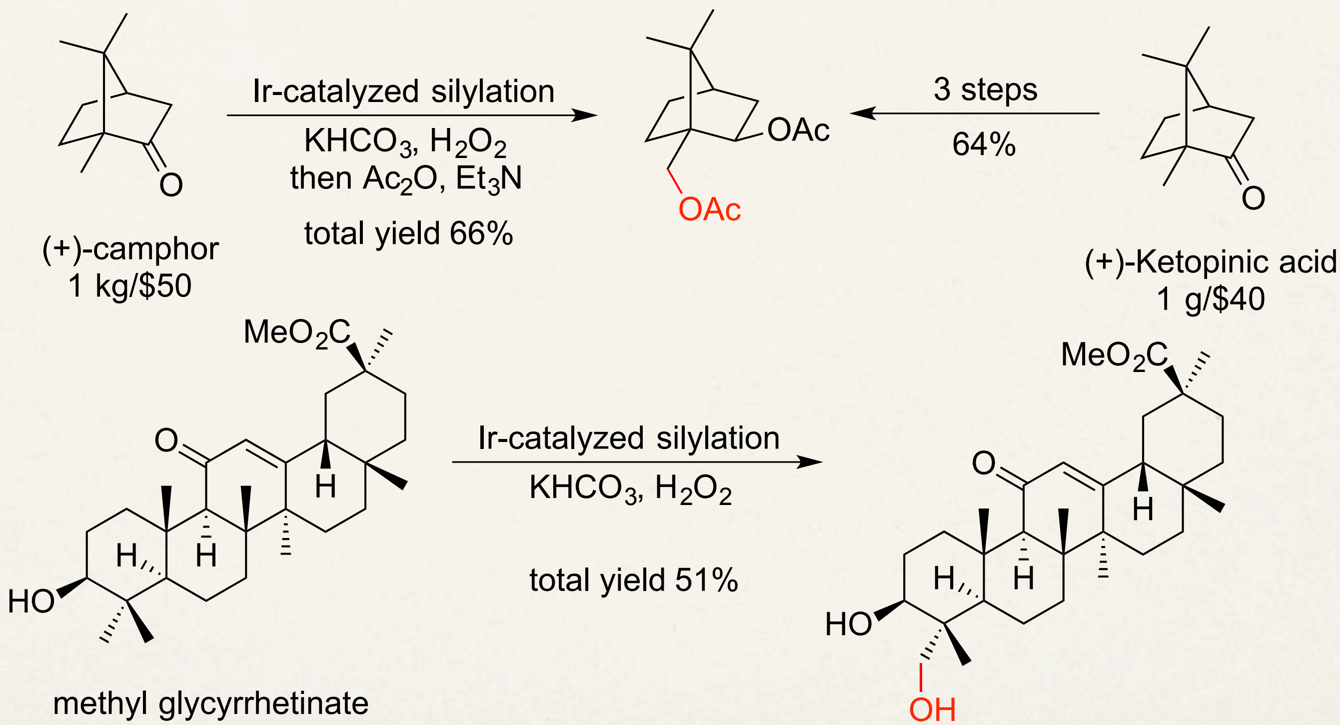
	Ligand, *L*	Conversion	Yield
a	phen	77%	68%
b	dtbpy	83%	76%
c	4,7-Cl_2phen	13%	<2%
d	4,7-$(HO)_2$phen	33%	19%
e	4,7-Ph_2phen	82%	72%
f	4,7-Me_2phen	94%	85%
g	4,7-$(MeO)_2$phen	94%	87%
h	3,4,7,8-Me_4phen	100%	99%



1. Simmons, E. M.; Hartwig, J. F. *Nature* **2012**, *483*, 70.

Aliphatic C-H Silylation

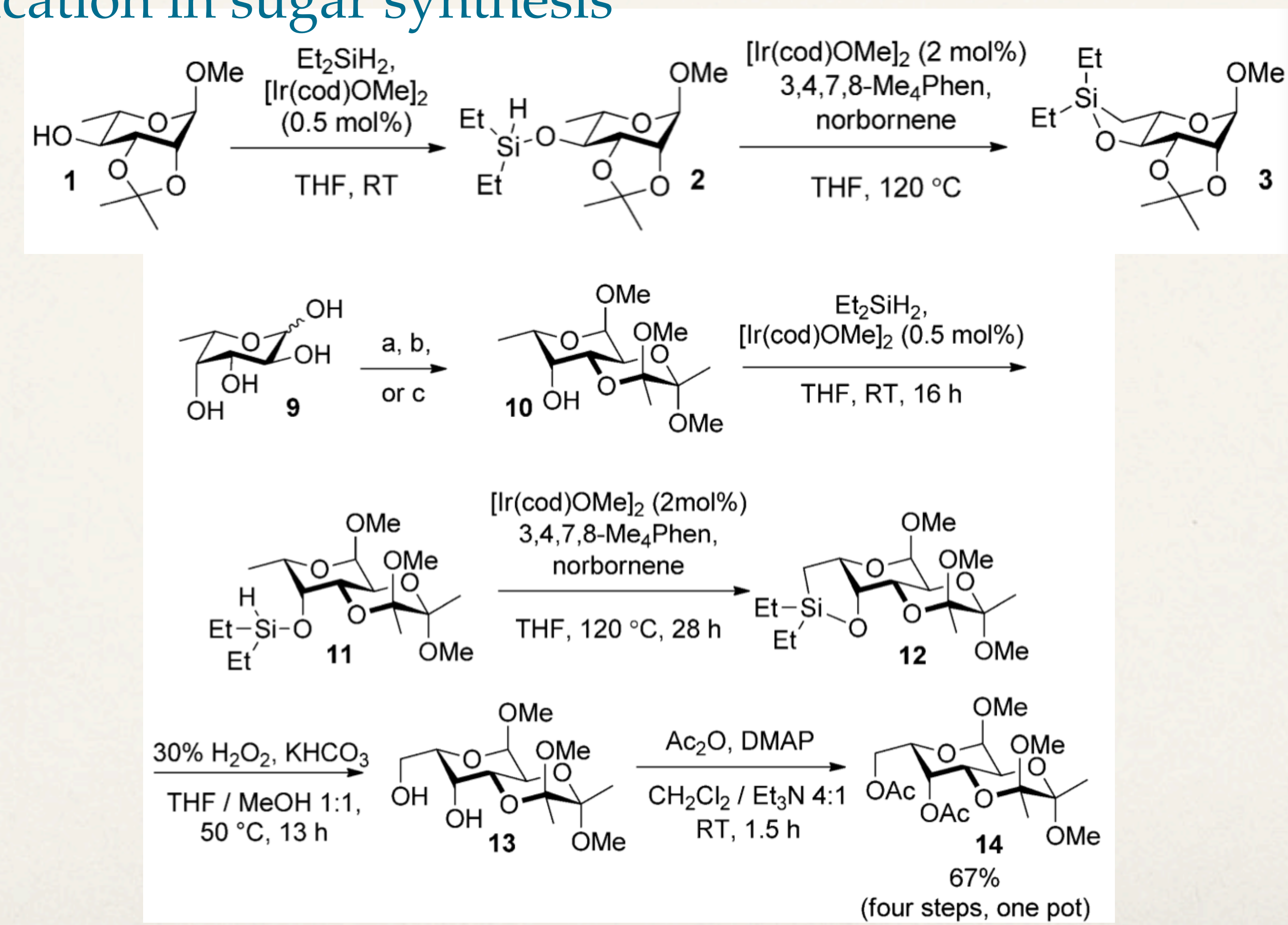
- Examples in complex molecules synthesis



1. Simmons, E. M.; Hartwig, J. F. *Nature* **2012**, *483*, 70.

Aliphatic C-H Silylation

- Application in sugar synthesis

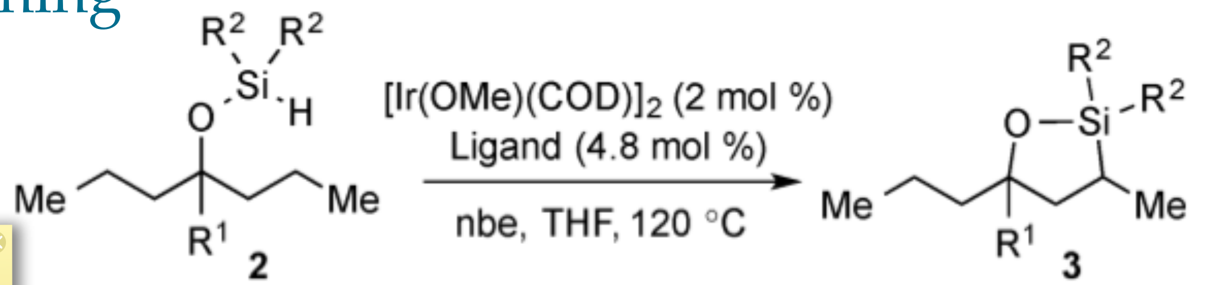


1. Frihed, T. G.; Heuckendorff, M.; Pedersen, C. M.; Bols, M. *Angew. Chem., Int. Ed.* **2012**, *51*, 12285.

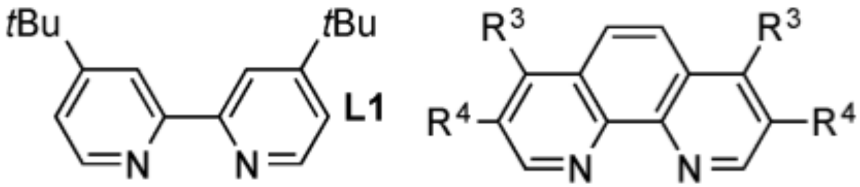
Silylation of Secondary Alkyl C-H

- Ligand screening

120oC higher than 80oC



entry	R^1	R^2	ligand	conv (%)	yield (%)
1	*n*-Pr	Et	**L1**	83	76
2	*n*-Pr	Et	**L2**	62	55
3	*n*-Pr	Et	**L3**	88	82
4	*n*-Pr	Et	**L4**	100	94
5	H	Et	**L4**	92	< 10
6	*n*-Pr	Me	**L4**	100	89
7	*n*-Pr	*i*-Pr	**L4**	12	< 10



R^3 = Cl, R^4 = H, **L2**
R^3 = R^4 = H, **L3**
R^3 = R^4 = Me, **L4**