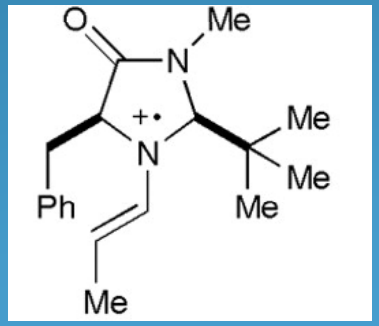
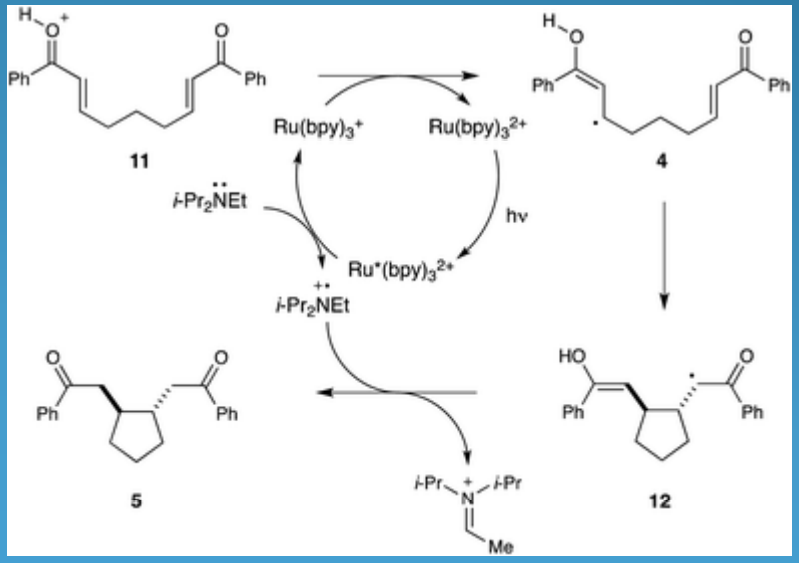
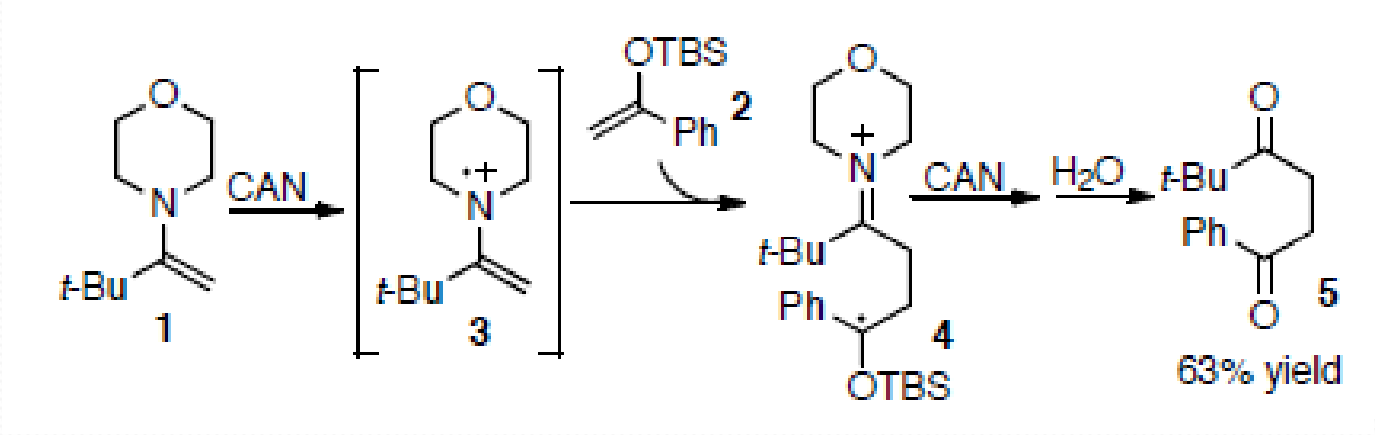
Christian Gloor
Topic Review
17.10.2013

Radicals in Organocatalysis and Photocatalysis



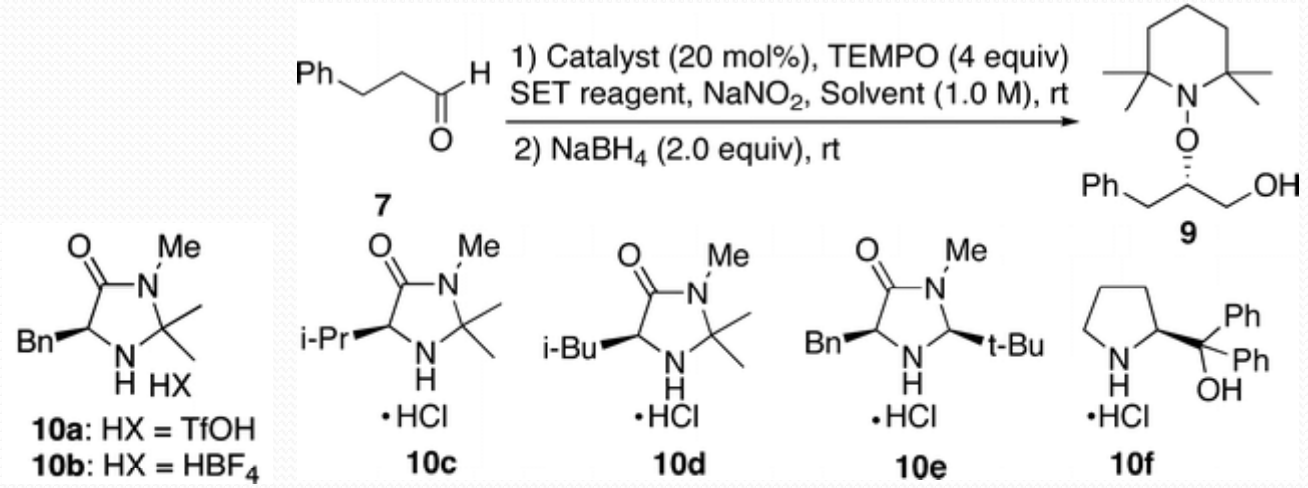


SOMO activation



Narasaka, K.; Okauchi, T.; Tanaka, K.; Murakami, M. *Chem. Lett. (Jpn.)* **1992**, *21*, 2099

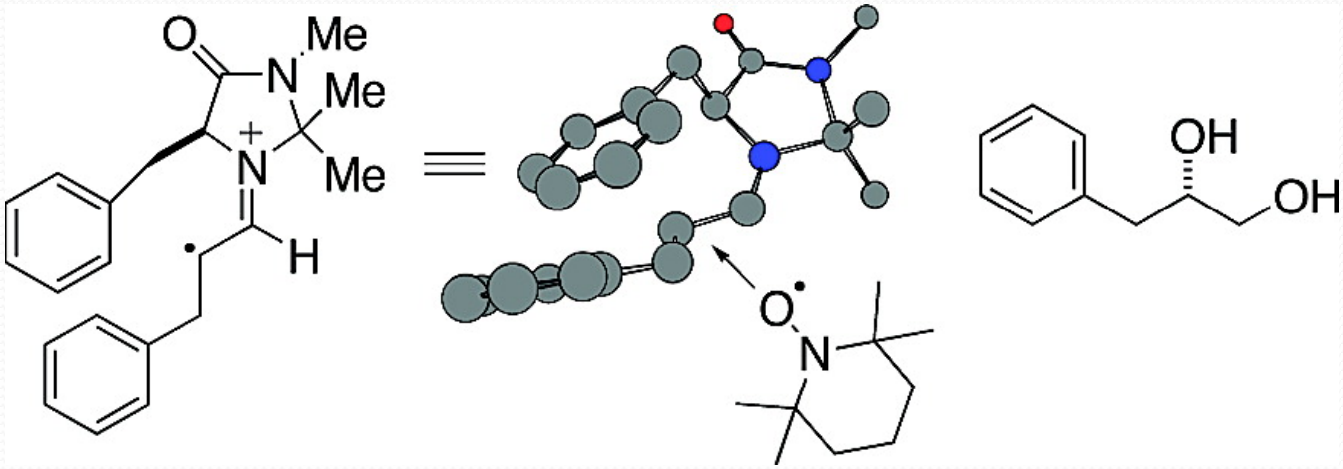
SOMO catalysis



entry	SET reagent (mol %)	ligand	$NaNO_2$ (equiv.)	solvent	Yield (%)	ee (%)
1	$FeCl_3$ (10)	**10b**	0.3	DMF	83	72
2	$FeCl_3$ (10)	**10c**	0.3	DMF	75	5
3	$FeCl_3$ (10)	**10d**	0.3	DMF	64	46
4	$FeCl_3$ (10)	**10e**	0.3	DMF	26	0
5	$FeCl_3$ (10)	**10f**	0.3	DMF	33	17

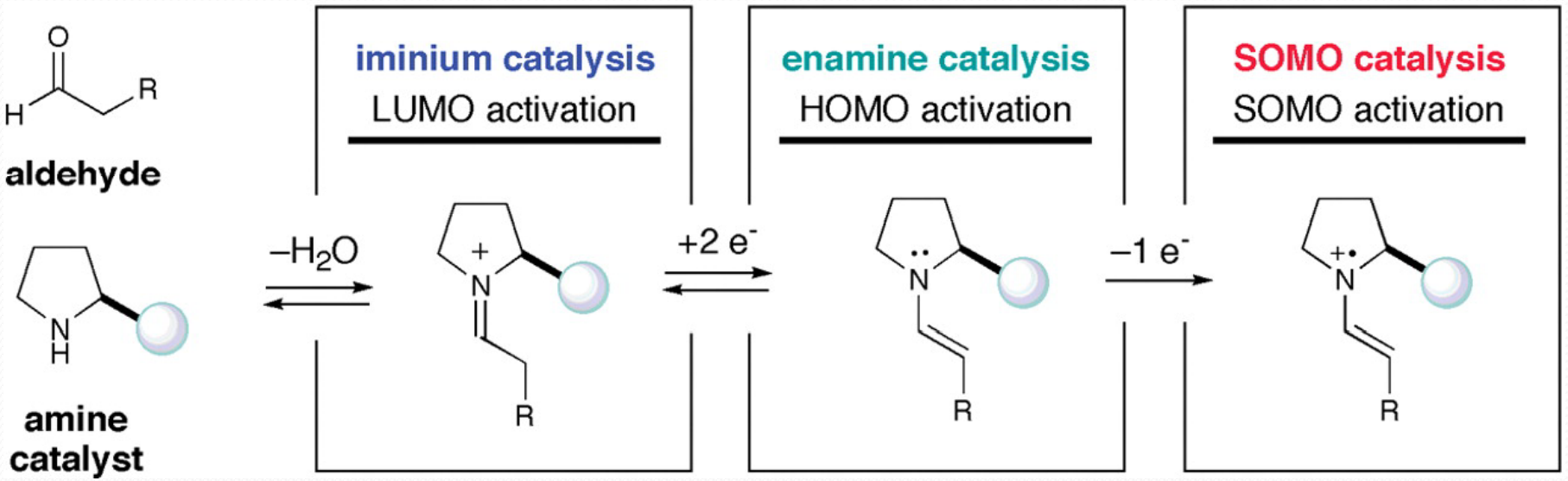
Sibi, M. P.; Hasegawa, M. *J. Am. Chem. Soc* **2007**, *129*, 4124

SOMO catalysis



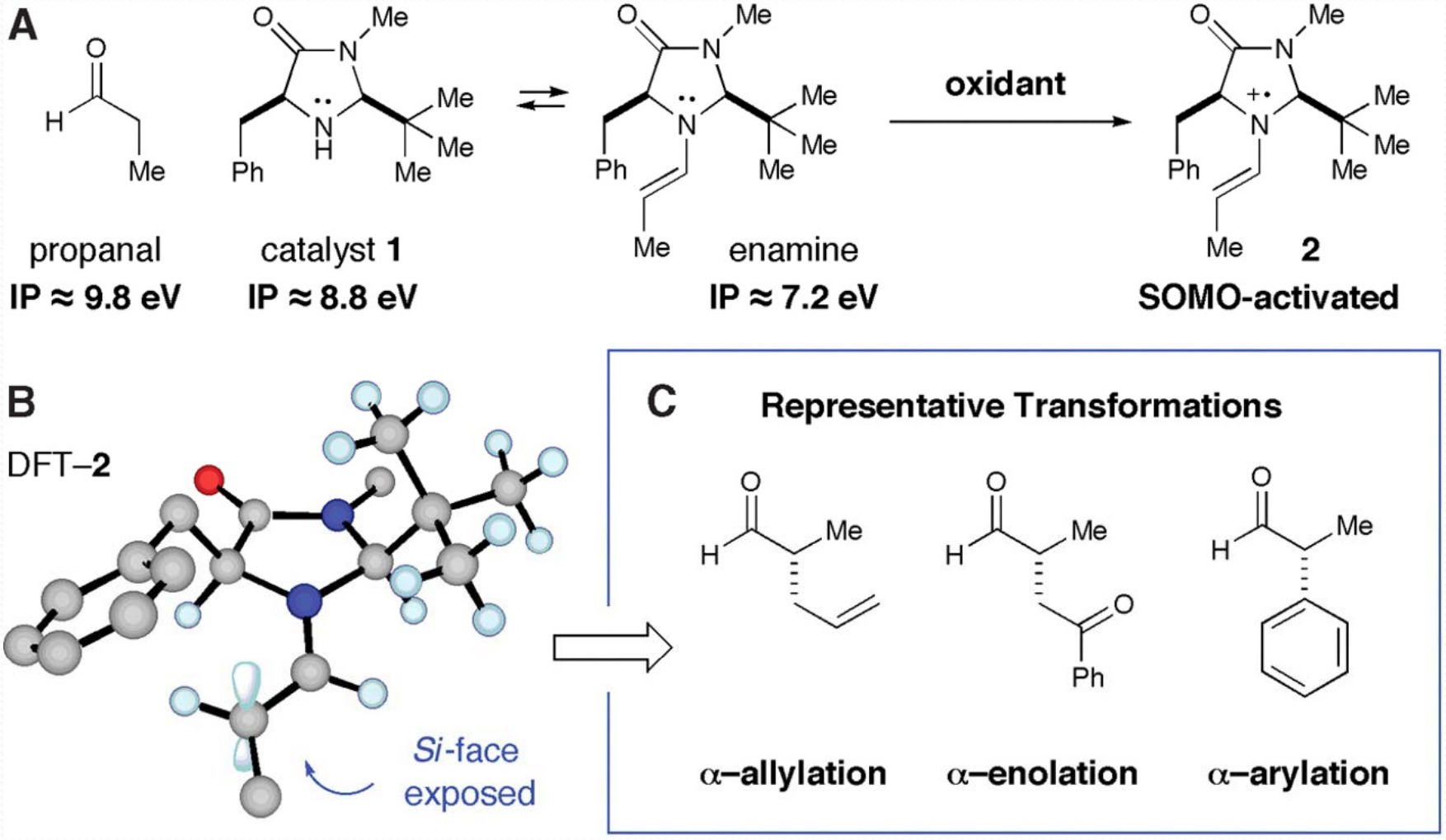
Sibi, M. P.; Hasegawa, M. *J. Am. Chem. Soc* **2007**, *129*, 4124

SOMO catalysis



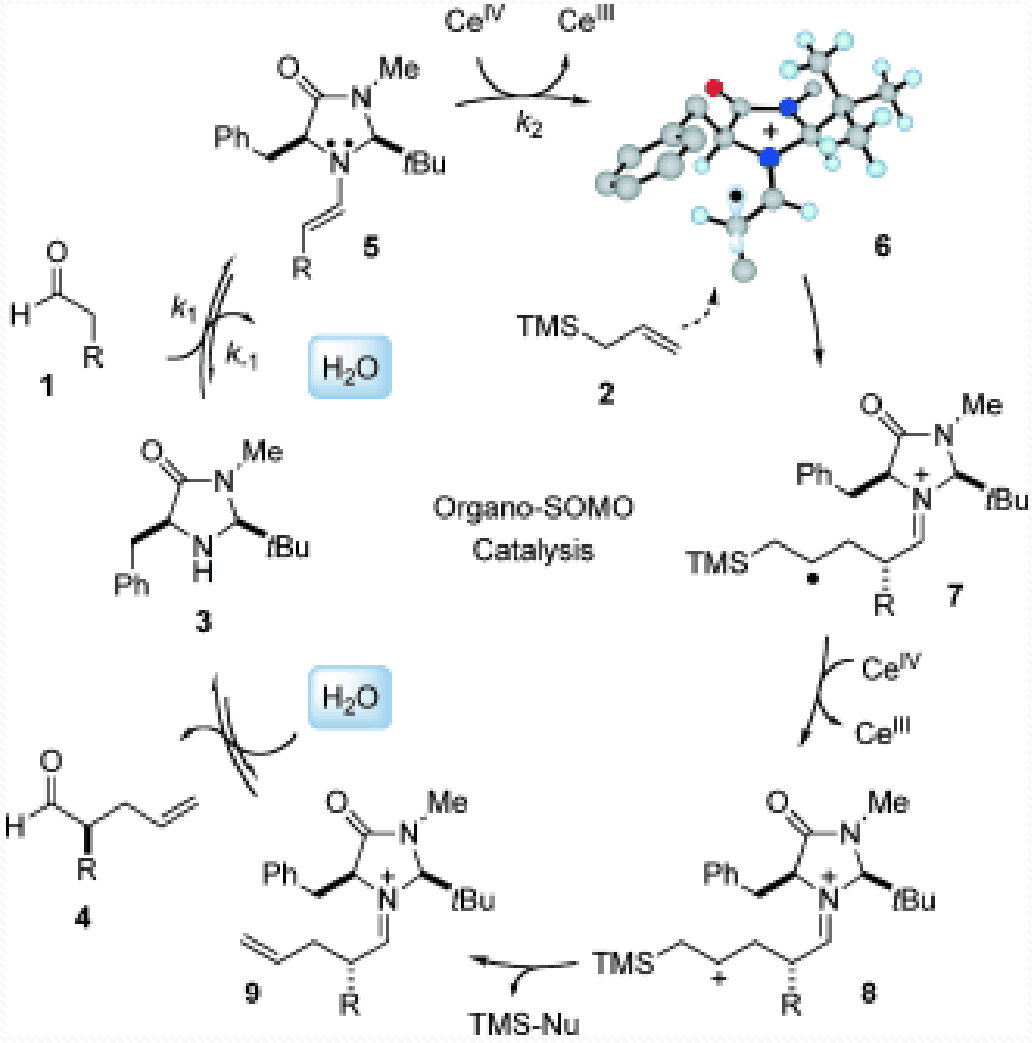
Beeson, T.D.; Mastracchio, A.; Hong, J.-B.; Ashton, K.; MacMillan, D.W.C. *Science* **2007**, *316*, 582

SOMO catalysis



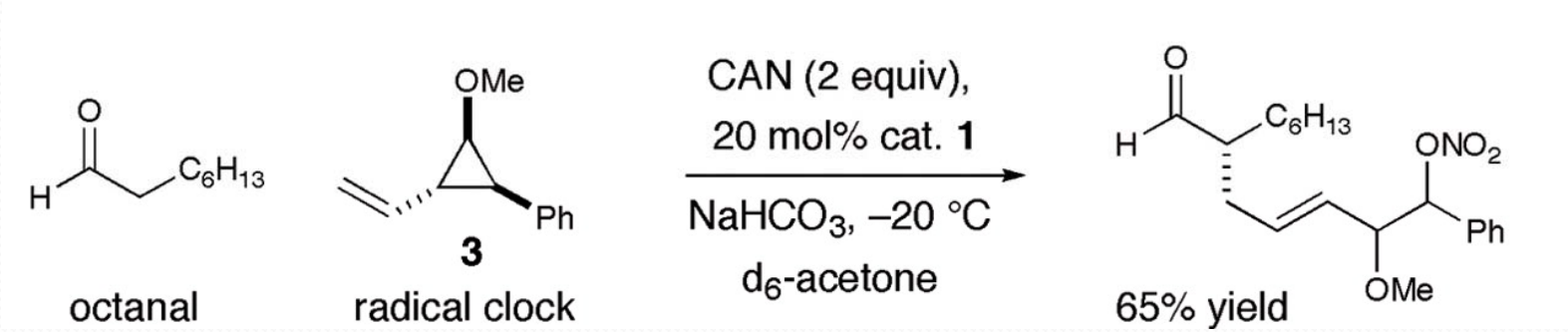
Beeson, T.D.; Mastracchio, A.; Hong, J.-B.; Ashton, K.; MacMillan, D.W.C. *Science* **2007**, *316*, 582

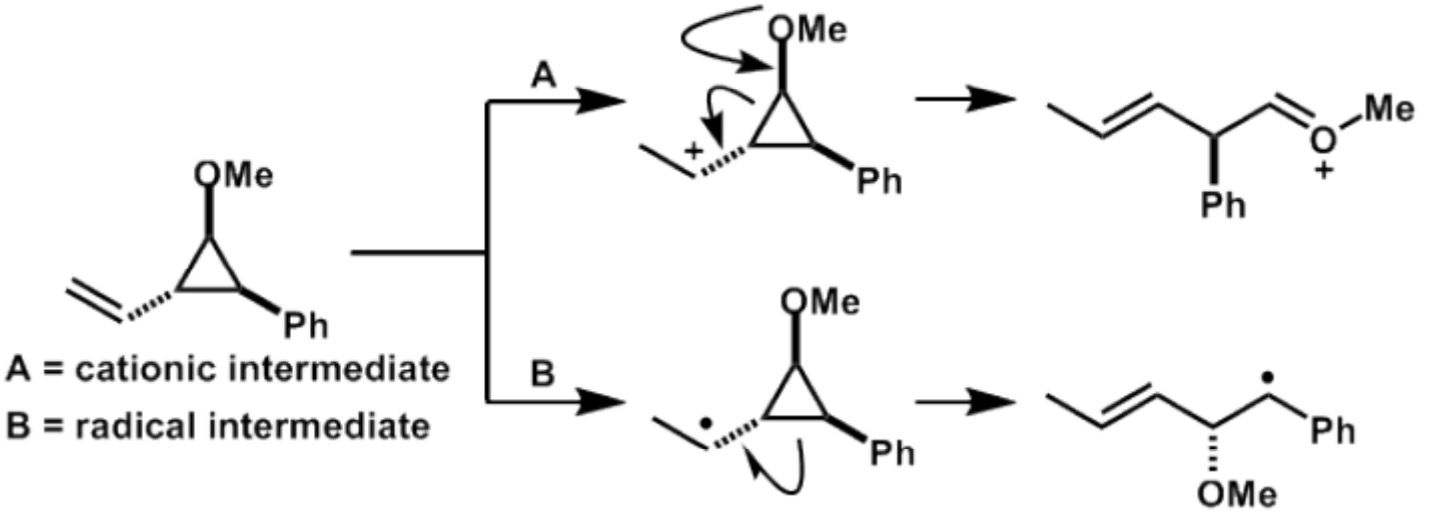
SOMO catalysis



Devery, J.J., Conrad, J.C., MacMillan, D.W.C.; Flowers, R.A. *Angew. Chem. Int. Ed.* **2010**, *49*: 6106

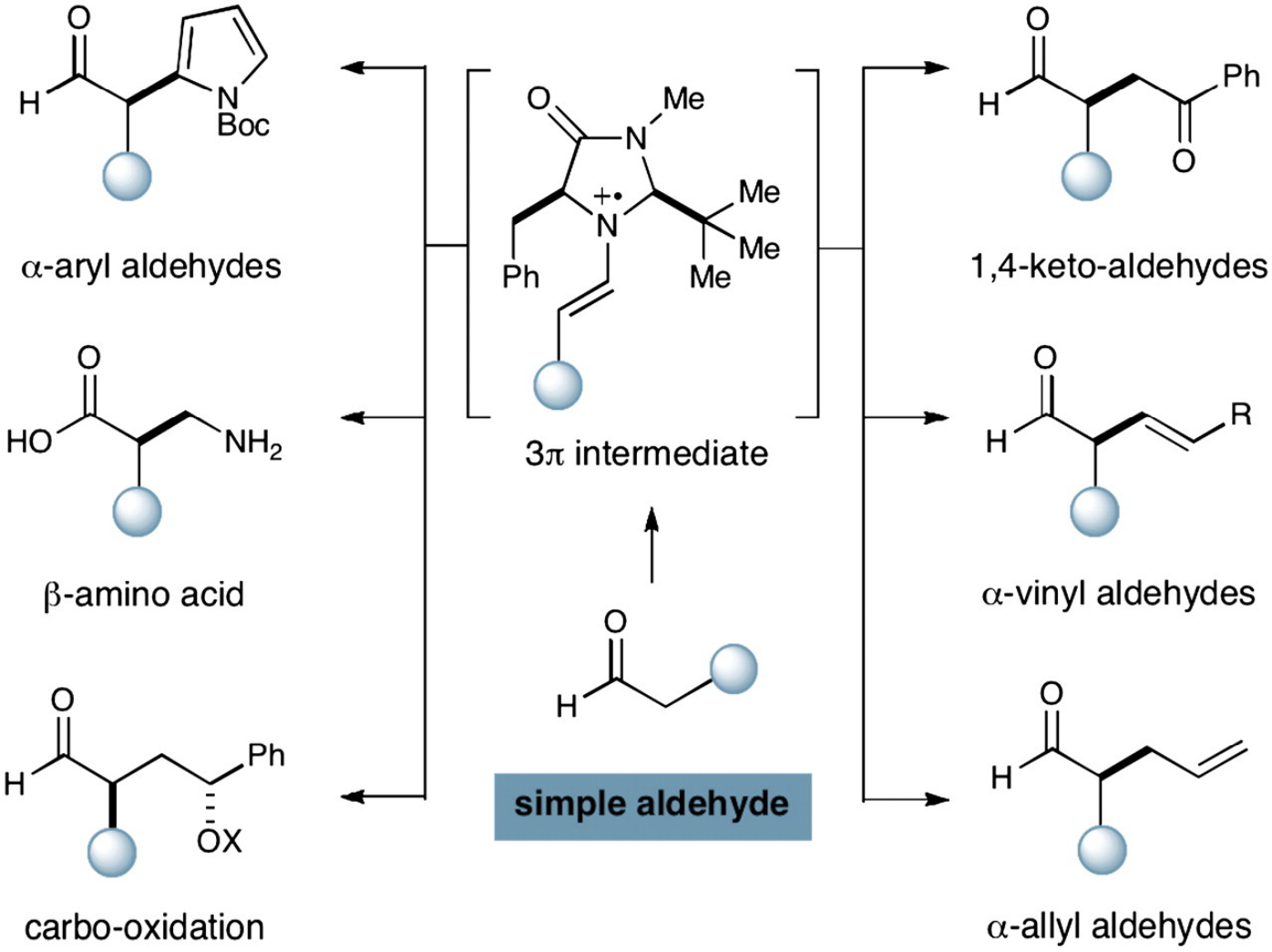
SOMO catalysis





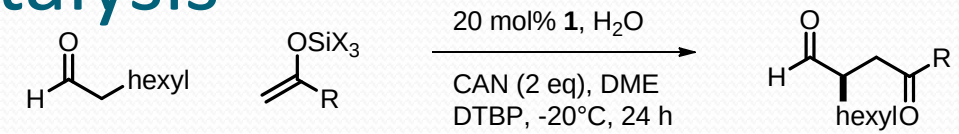
Beeson, T.D.; Mastracchio, A.; Hong, J.-B.; Ashton, K.; MacMillan, D.W.C. *Science.* **2007**, *316*, 582

SOMO catalysis

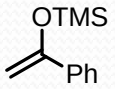
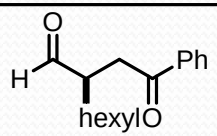
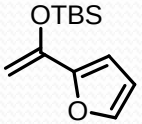
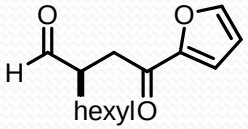
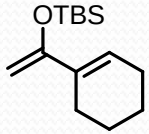
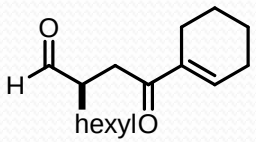
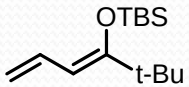
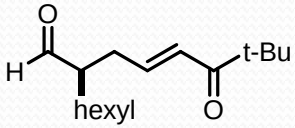
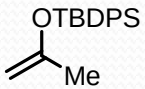
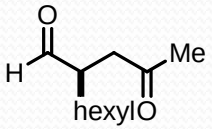
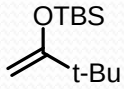
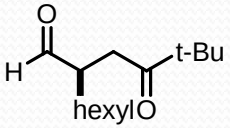


Mastracchio, A.; Warkentin, A.A.; Walji, A.M.; MacMillan, D.W.C. *PNAS* **2010**, *107*, 20648

SOMO catalysis

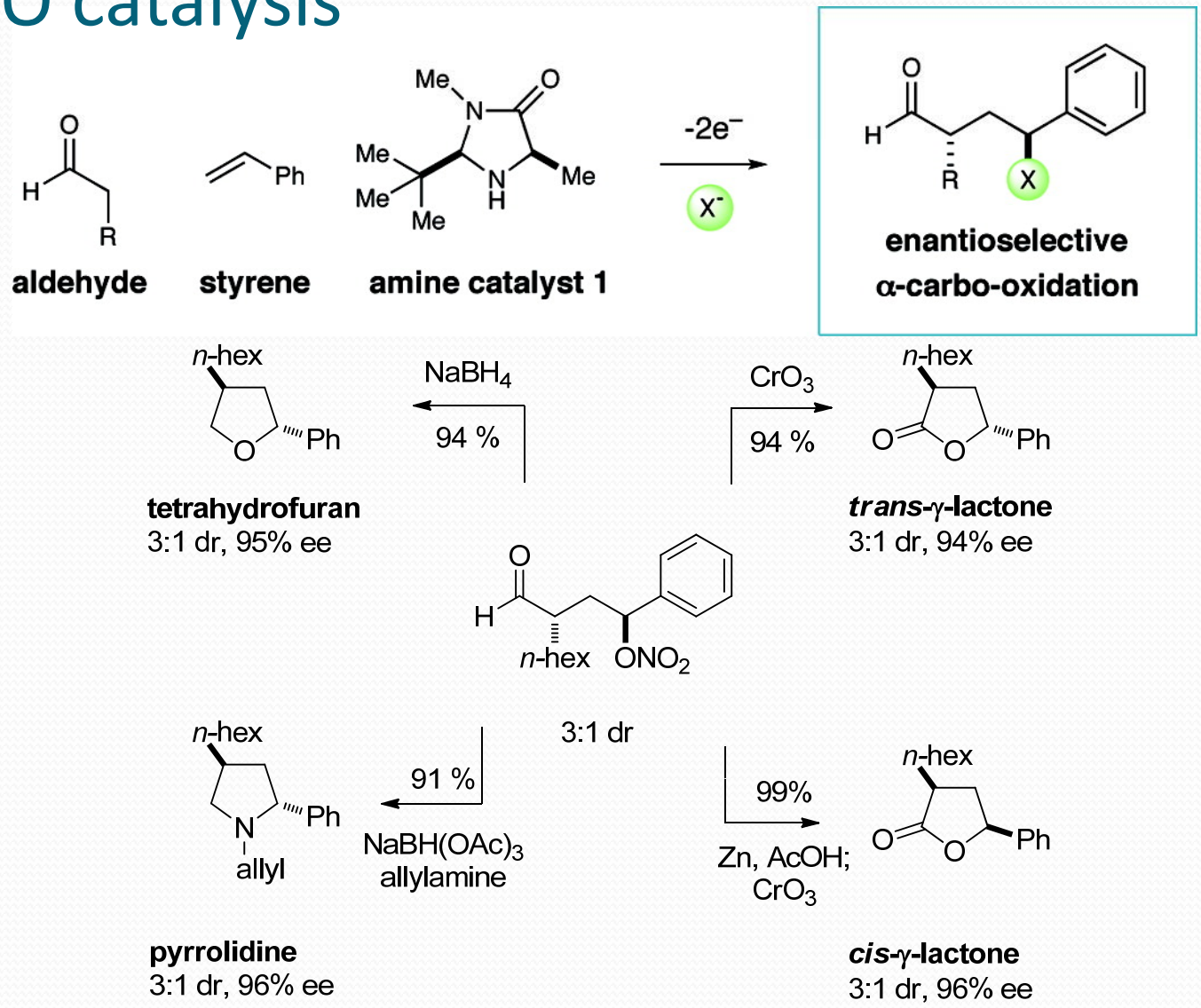


octanal enolsilane γ-ketoaldehydes

entry	enolsilane	product	% yield	% ee
1			**85**	90
2			**77**	92
3			**71**	92
4			**74**	96
5			**67**	86
6			**55**	92

Jang, H.-Y.; Hong, J.-B.; MacMillan, D.W.C. *J. Am. Chem. Soc.* **2007**, *129*, 7004

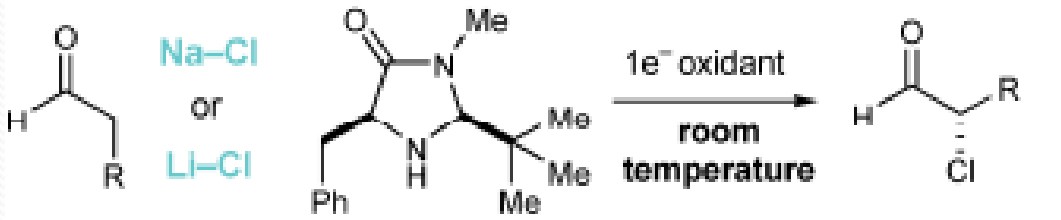
SOMO catalysis



Graham, T. H.; Jones, C. M..; Jui, N. T.; MacMillan, D.W.C. *J. Am. Chem. Soc.* **2008**, *130*, 16494

SOMO catalysis

SOMO Catalysis: Ambient Temp., Inexpensive Chlorine Source



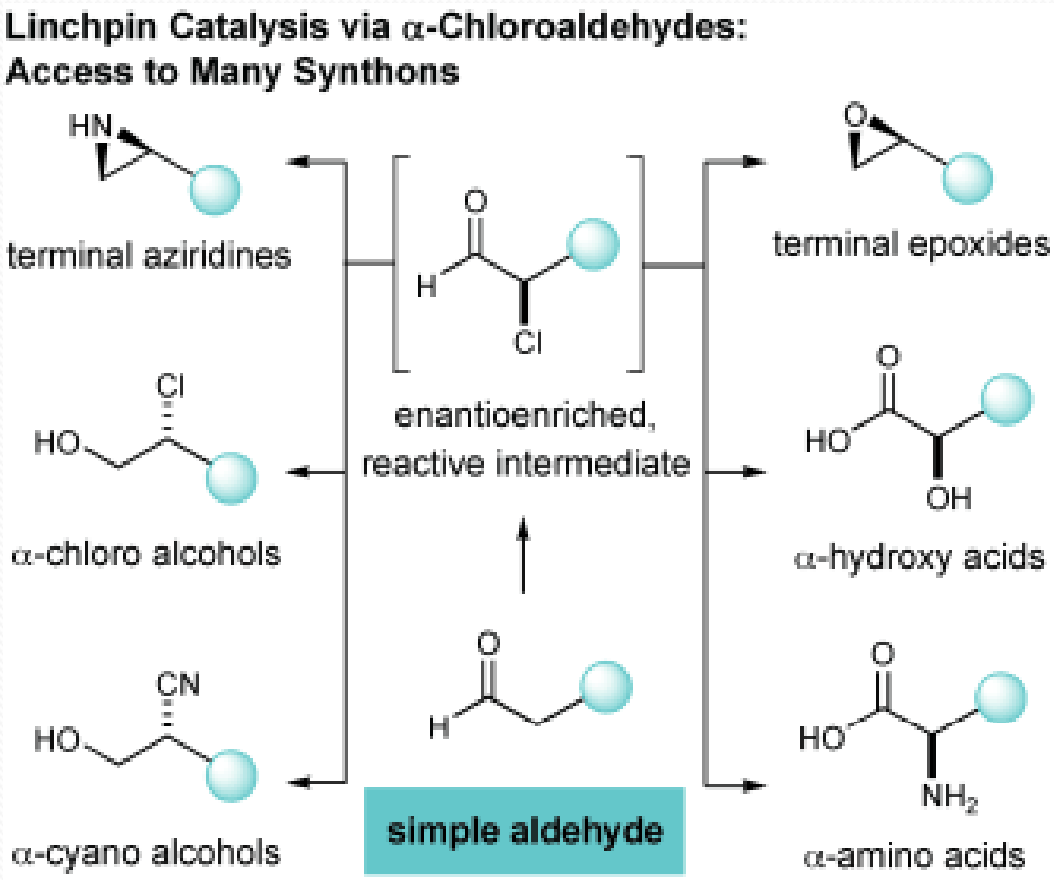
feedstock amine catalyst **1** enantioenriched

R = *n*-Hex (1.5 equiv), LiCl (2.2 equiv), $Ce(NH_4)_2(NO_3)_6$, catalyst **1**, $NaHCO_3$

–40 °C = 95% yield, 92% *ee* **23 °C** = 27% yield, 47% *ee*

Amatore, M.; Beeson, T. D.; Brown, S. P.; MacMillan, D.W.C. *Angew. Chem. Int. Ed.* **2009**, *48*, 5121

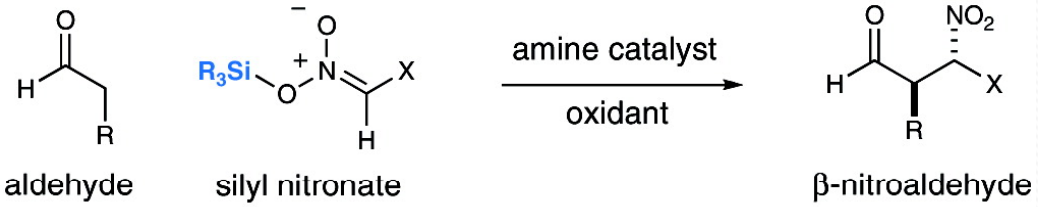
SOMO catalysis



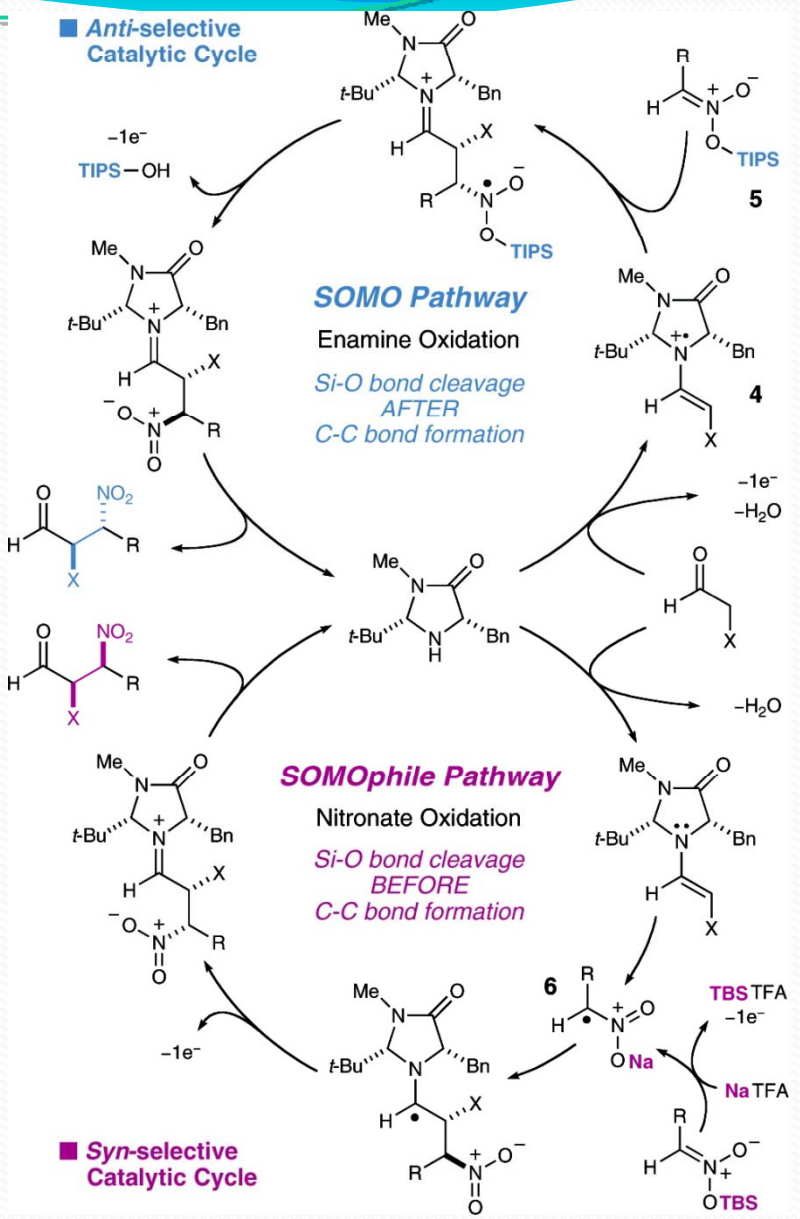
Amatore, M.; Beeson, T. D.; Brown, S. P.; MacMillan, D.W.C. *Angew. Chem. Int. Ed.* **2009**, *48*, 5121

SOMO catalysis

Oxidative Organocatalytic Enantioselective Aldehyde Nitroalkylation

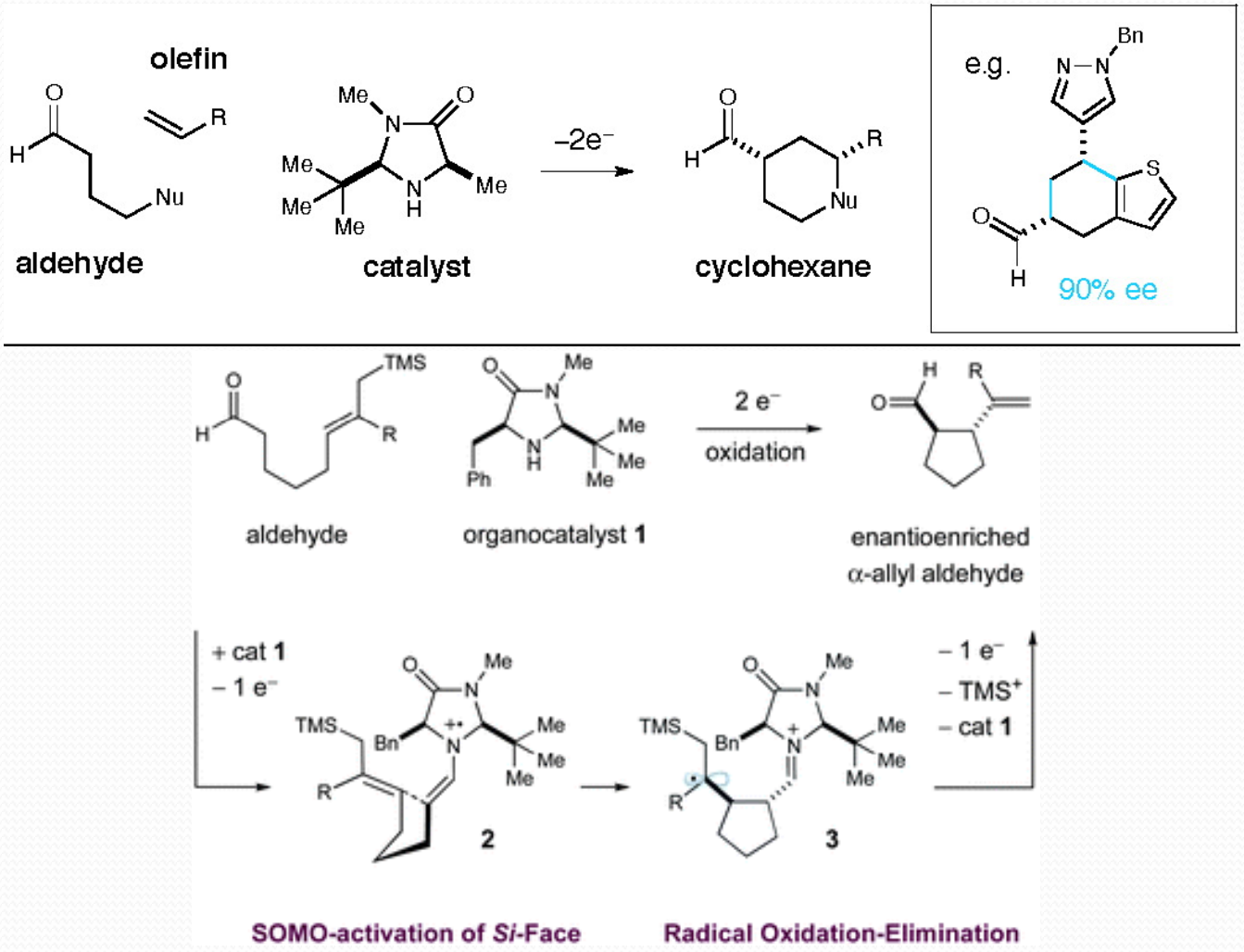


- ***SOMO Catalysis or Enamine Catalysis***
- ***Mechanism Controlled by Silyl Group***



Wilson, J. E.; Casarez, A. D.; MacMillan, D.W.C. *J. Am. Chem. Soc.* **2009**, *131*, 11332

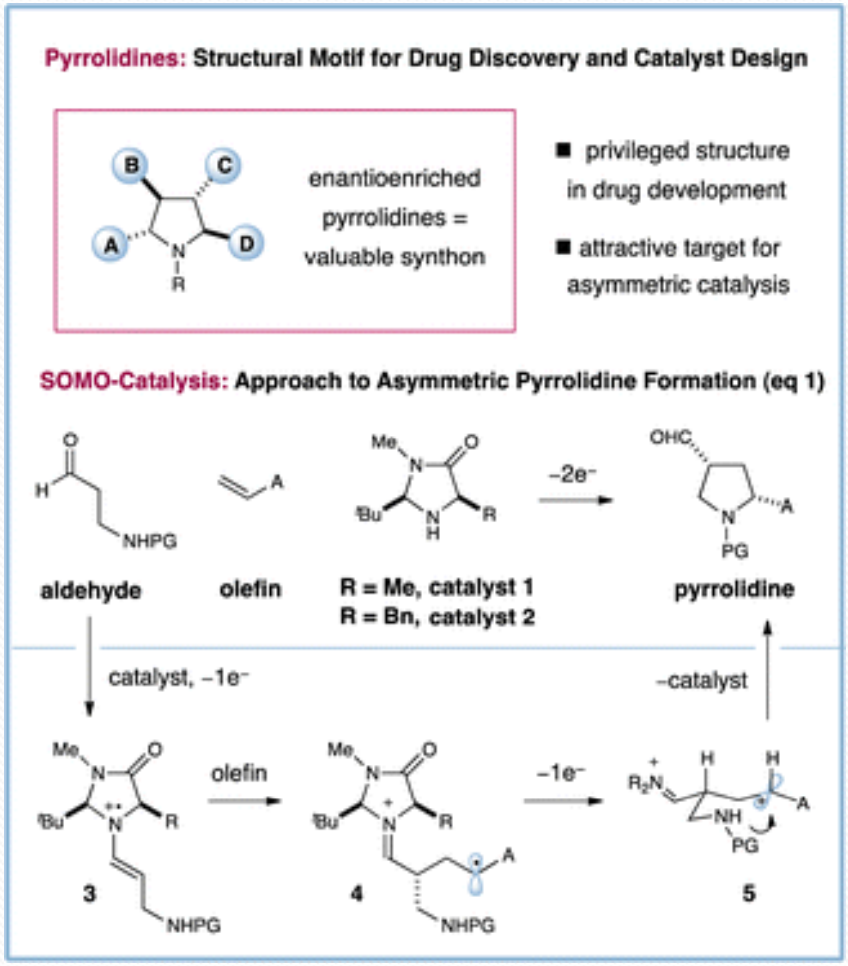
SOMO catalysis

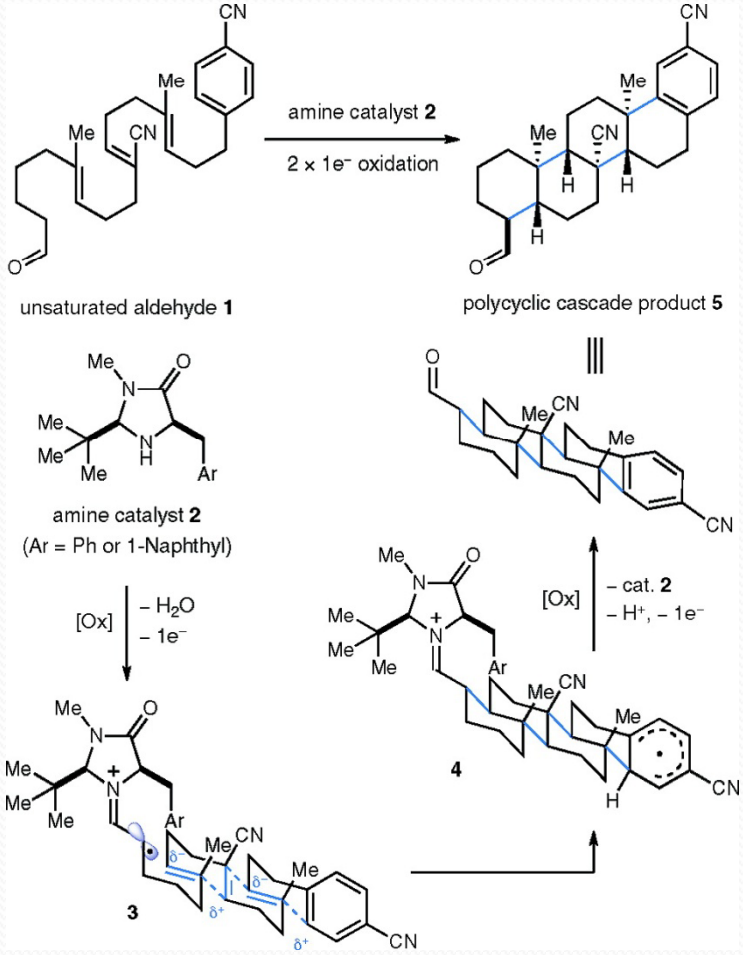


Jui, N. T.; Lee, E. C. Y.; MacMillan, D.W.C. *J. Am. Chem. Soc.* **2010**, *132*, 10015

Pham, P. V.; Ashton, K.; MacMillan, D.W.C. *Chem. Sci.* **2011**, *2*, 1470

SOMO catalysis



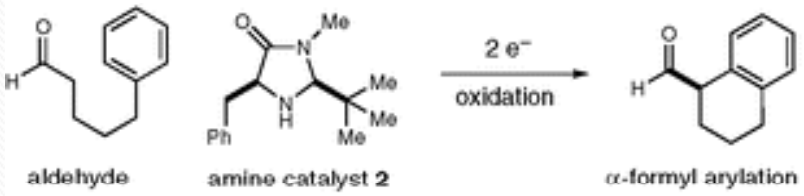


Jui, N. T.; Garber, J. A. O.; Finelli, F. G.; MacMillan, D.W.C. *J. Am. Chem. Soc.* **2012**, *134*, 11400

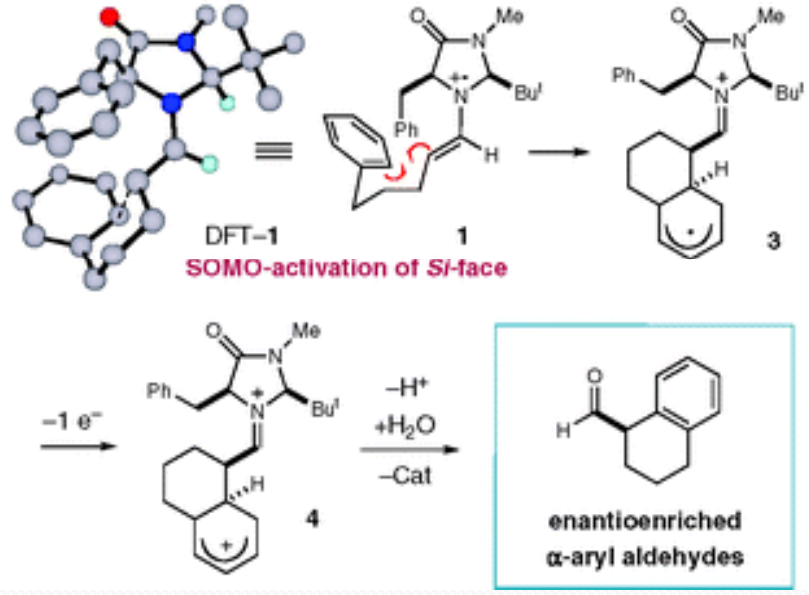
Rendler, S.; MacMillan, D.W.C. *J. Am. Chem. Soc.* **2010**, *132*, 5027

SOMO catalysis

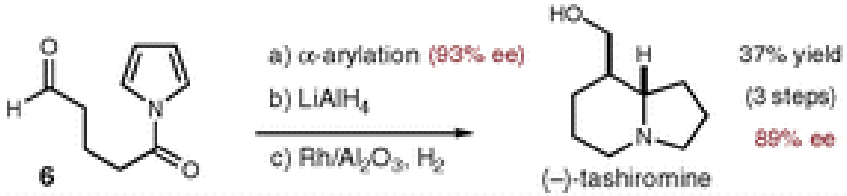
Enantioselective α-Arylation of Aldehydes via SOMO Catalysis (eq 1)



Mechanism of Organo-SOMO Catalyzed Aldehyde α-Arylation (eq 2)

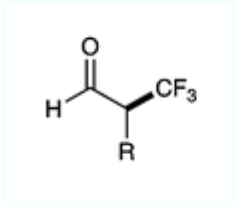


Enantioselective Synthesis of (–)-Tashiromine via Formyl α-Arylation

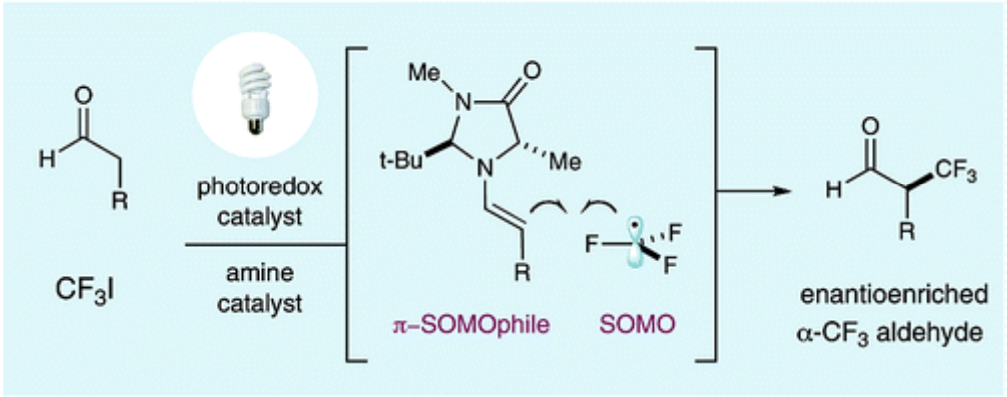


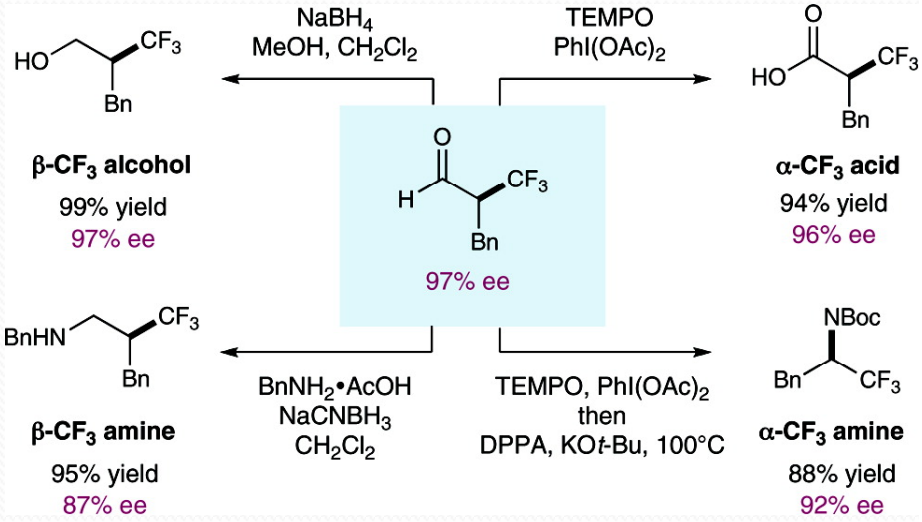
Conrad, J. C.; Kong, J.; Laforteza, B. N.; MacMillan, D.W.C. *J. Am. Chem. Soc.* **2009**, *131*, 11640

Photoredox SOMO catalysis



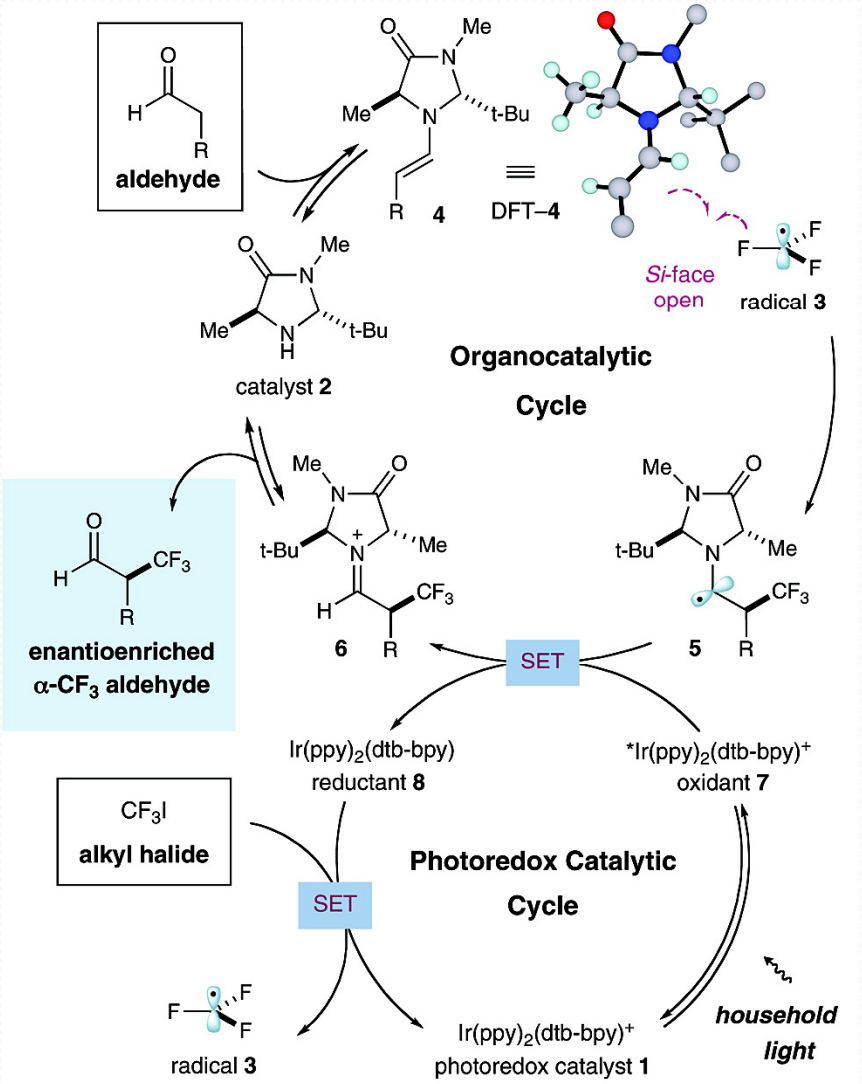
- Versatile synthon for medicinal agent synthesis
- Allows trivial access to enantioenriched CF_3-containing building blocks
- No known catalytic routes to α-formyl CF_3

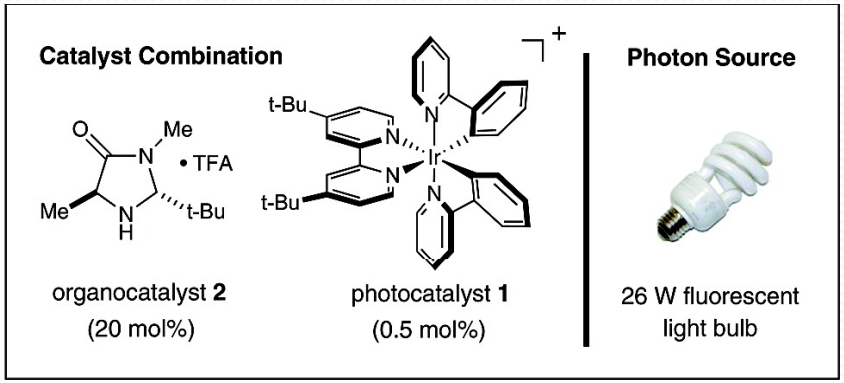




Nagib, D. A.; Scott, M. E.; MacMillan, D.W.C. *J. Am. Chem. Soc.* **2009**, *131*, 10875

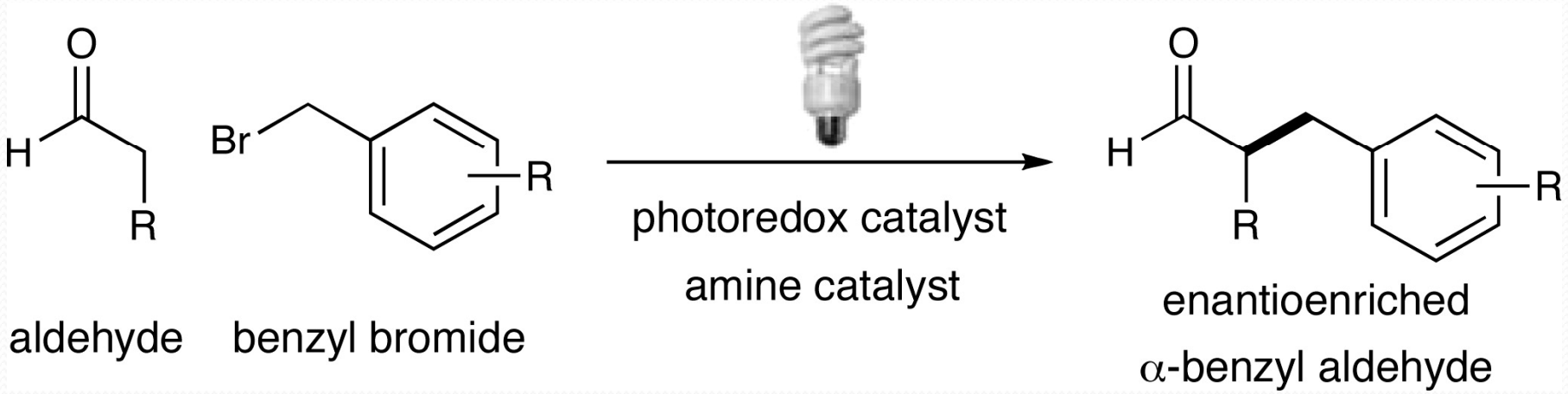
Photoredox SOMO catalysis





Nagib, D. A.; Scott, M. E.; MacMillan, D.W.C. *J. Am. Chem. Soc.* **2009**, *131*, 10875

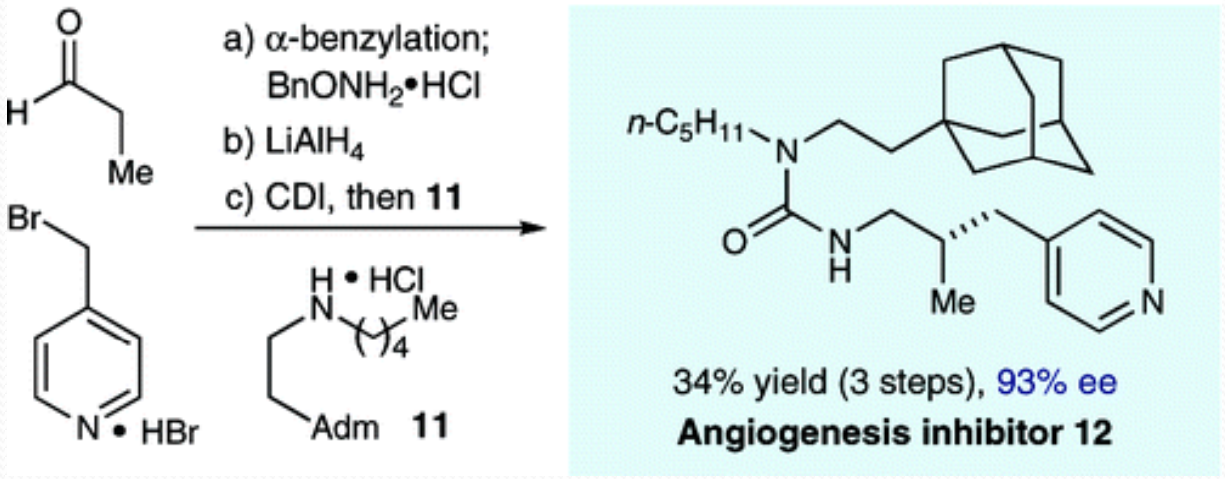
Photoredox SOMO catalysis



Shih, H.-W.; Vander Wal, M. N.; Grange, R. L.; MacMillan, D.W.C. *J. Am. Chem. Soc.* **2010**, *132*, 13600

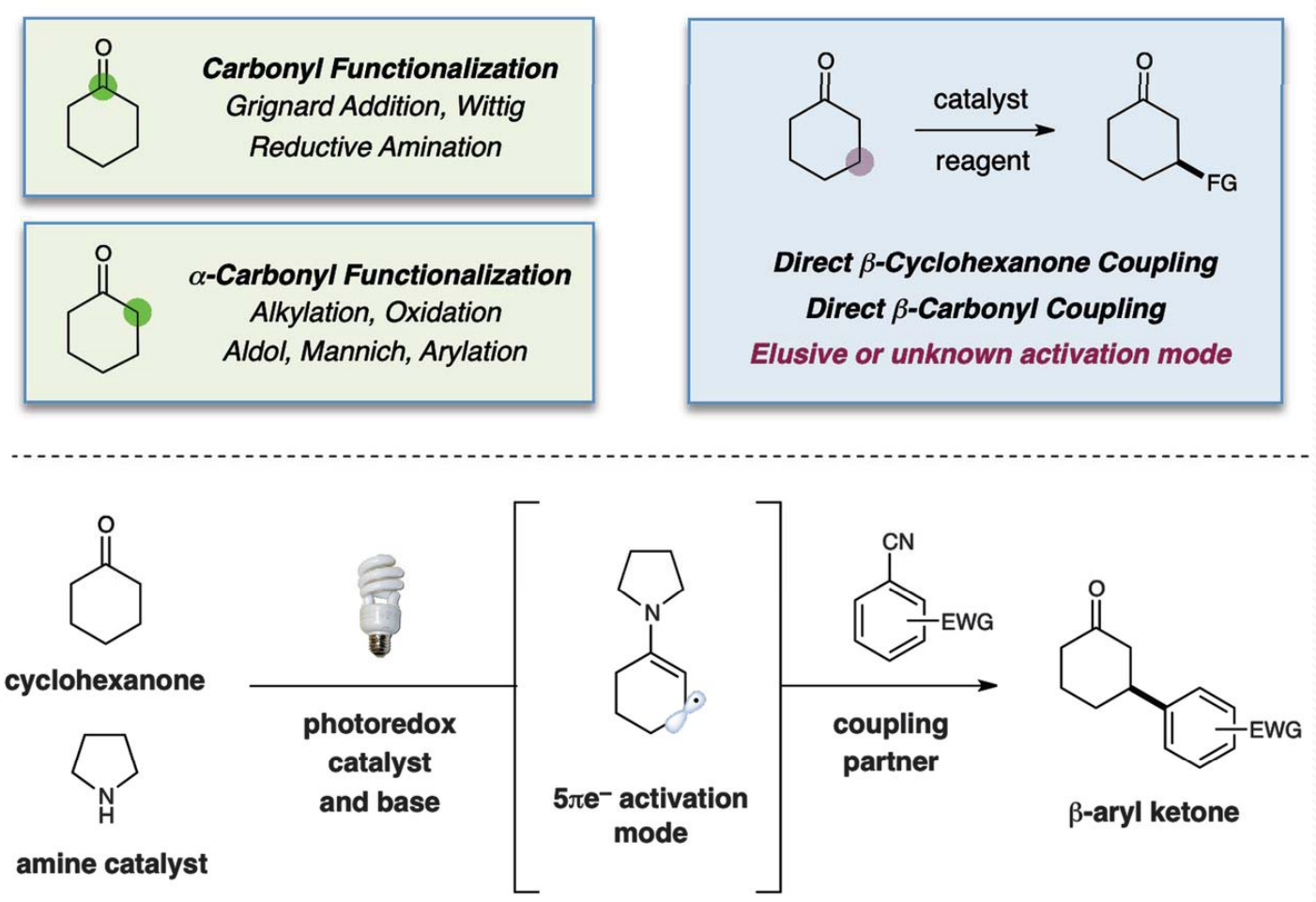
Photoredox SOMO catalysis

Enantioselective synthesis of a bioactive drug candidate



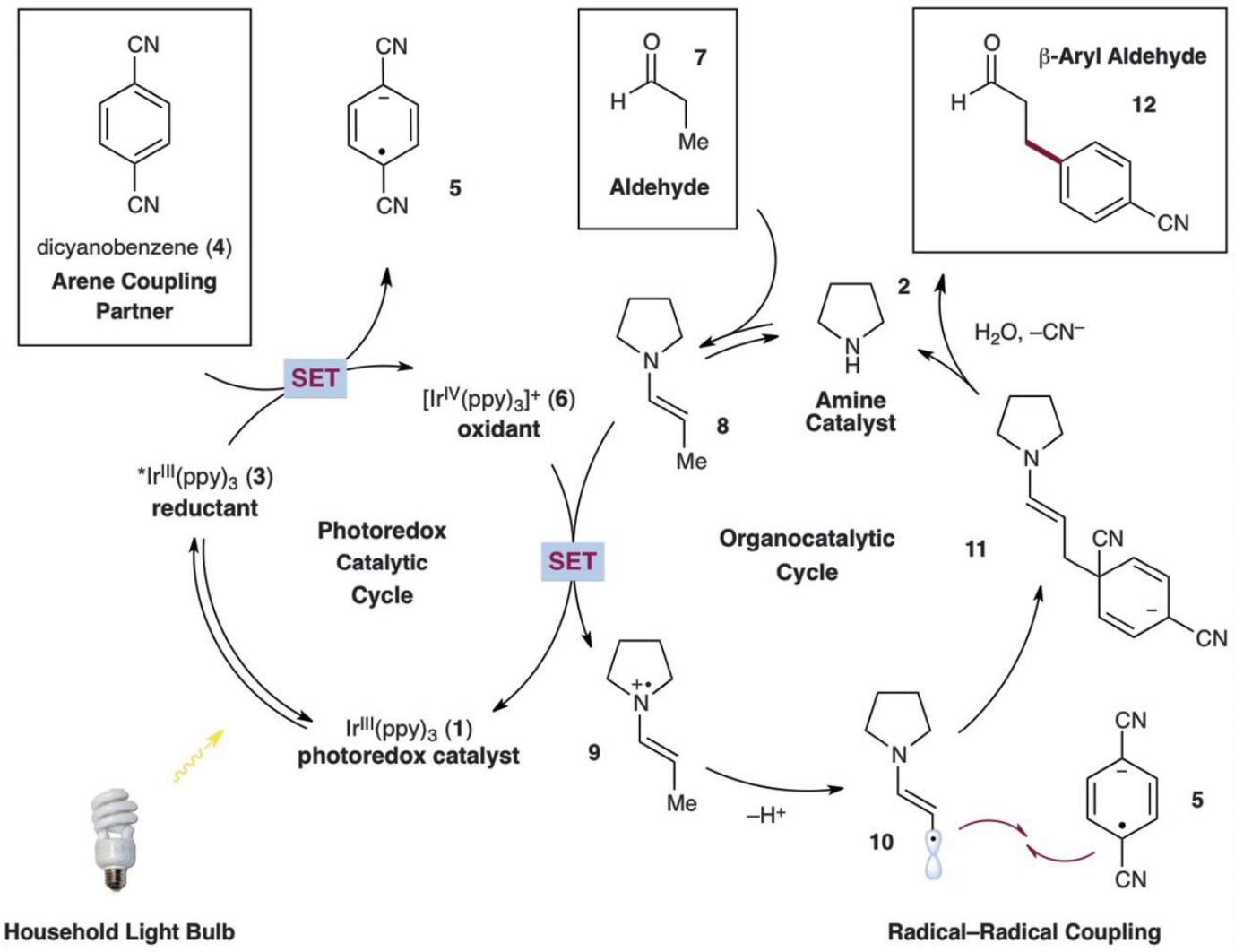
Shih, H.-W.; Vander Wal, M. N.; Grange, R. L.; MacMillan, D.W.C. *J. Am. Chem. Soc.* **2010**, *132*, 13600

Photoredox SOMO catalysis



Pirnot, M. T.; Rankic, D. A.; Martin, D. B. C.; MacMillan, D.W.C. *Science.* **2013**, *339*, 1593

Photoredox SOMO catalysis



Pirnot, M. T.; Rankic, D. A.; Martin, D. B. C.; MacMillan, D.W.C. *Science.* **2013**, *339*, 1593

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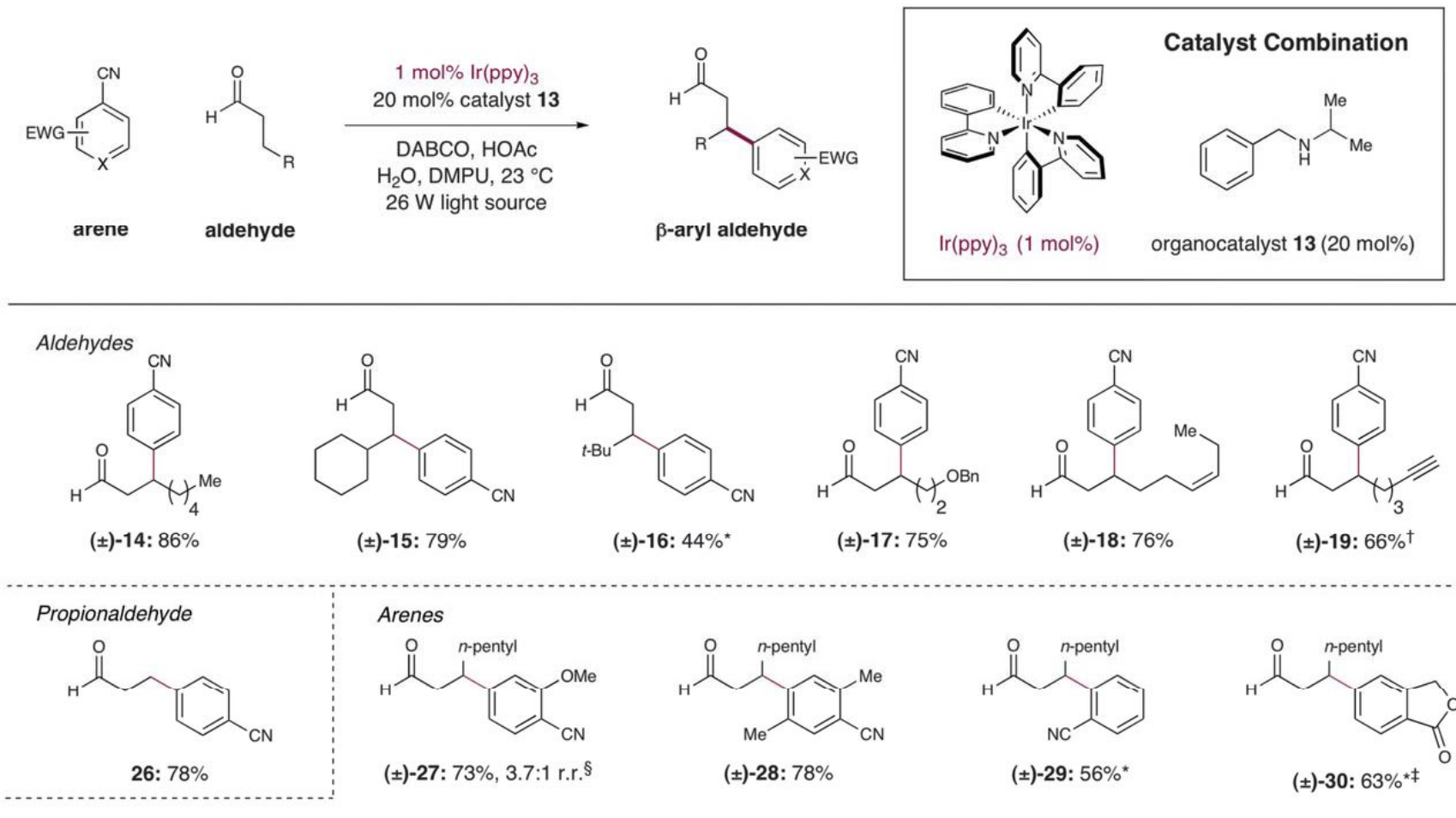

Pirnot, M. T.; Rankic, D. A.; Martin, D. B. C.; MacMillan, D.W.C. *Science.* **2013**, *339*, 1593

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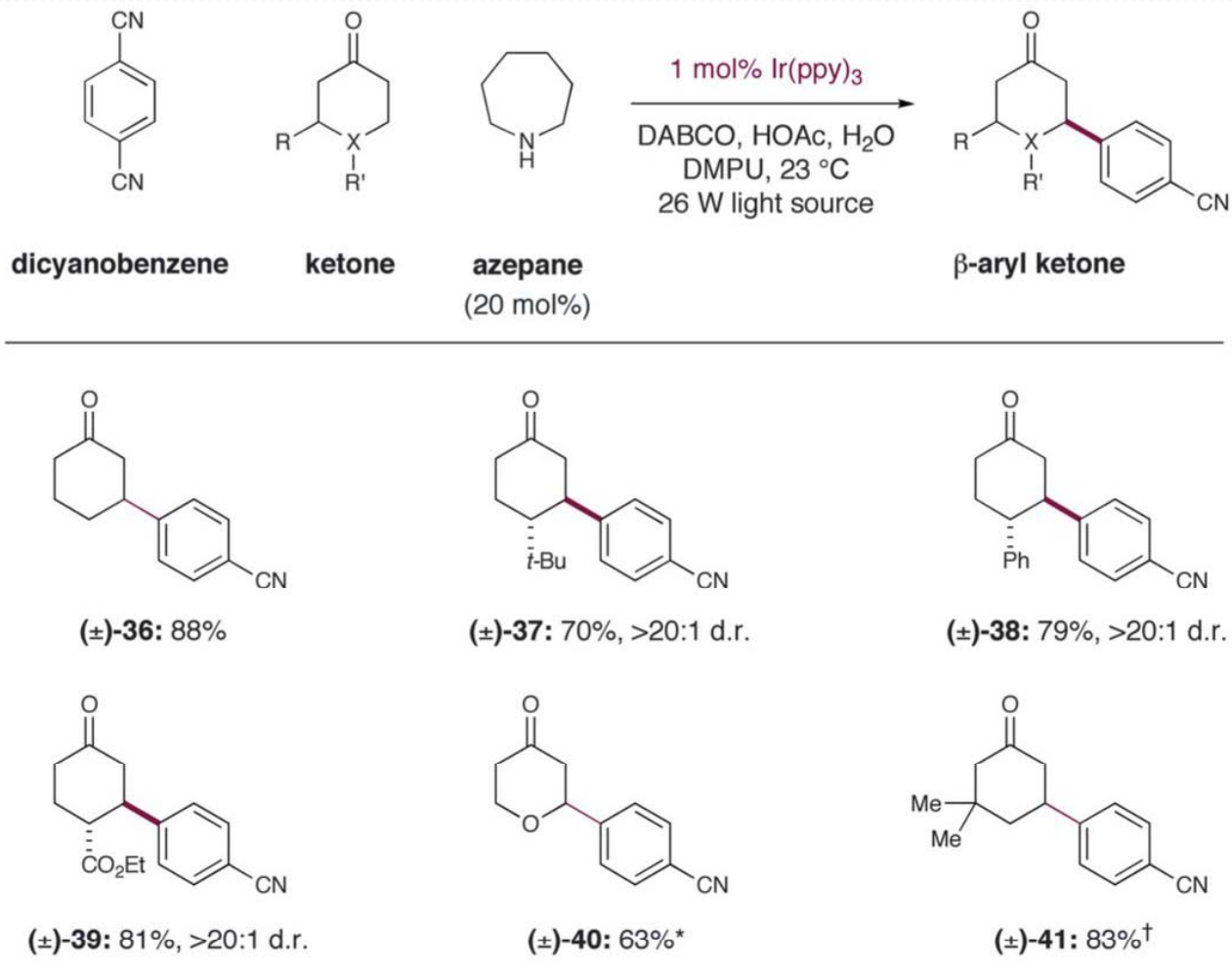
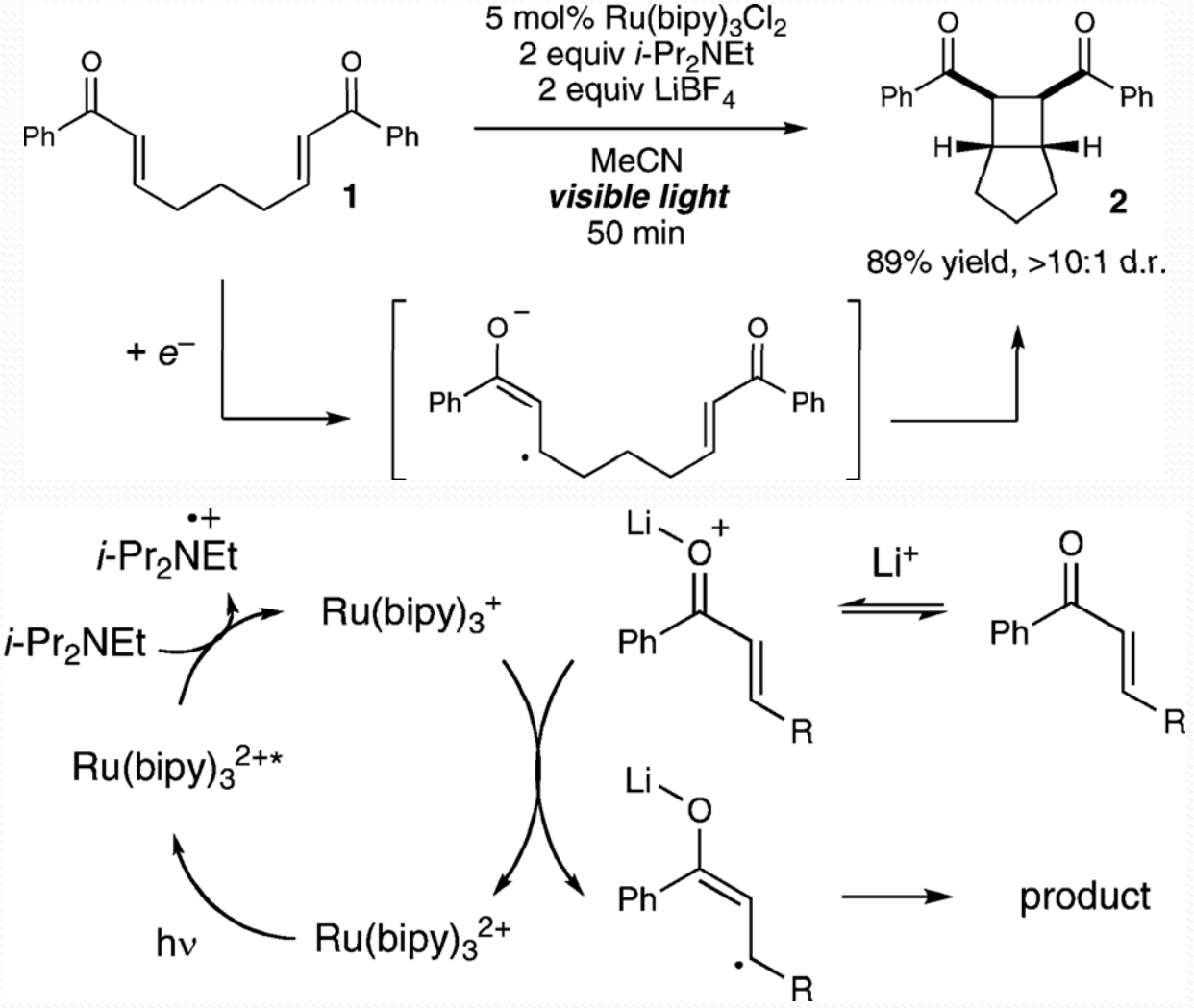


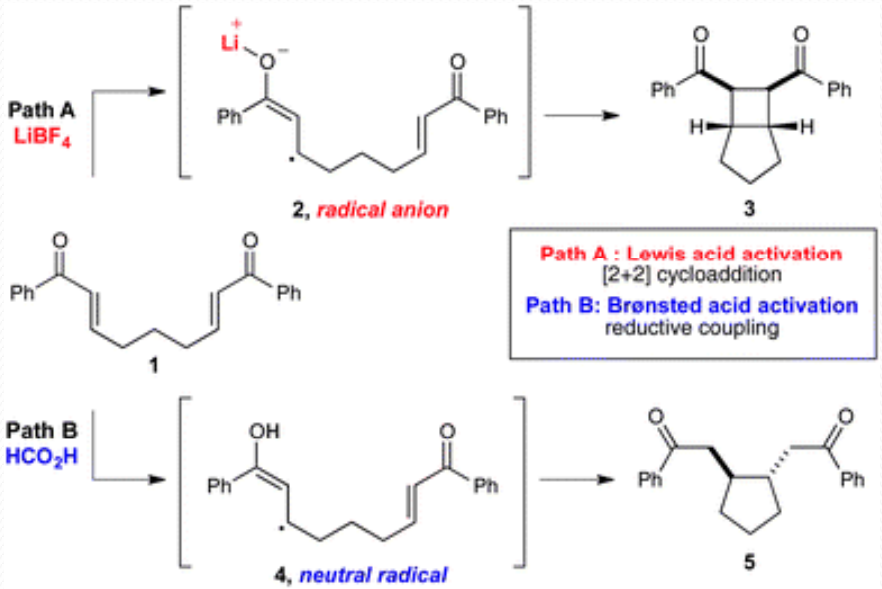
Pirnot, M. T.; Rankic, D. A.; Martin, D. B. C.; MacMillan, D.W.C. *Science.* **2013**, *339*, 1593

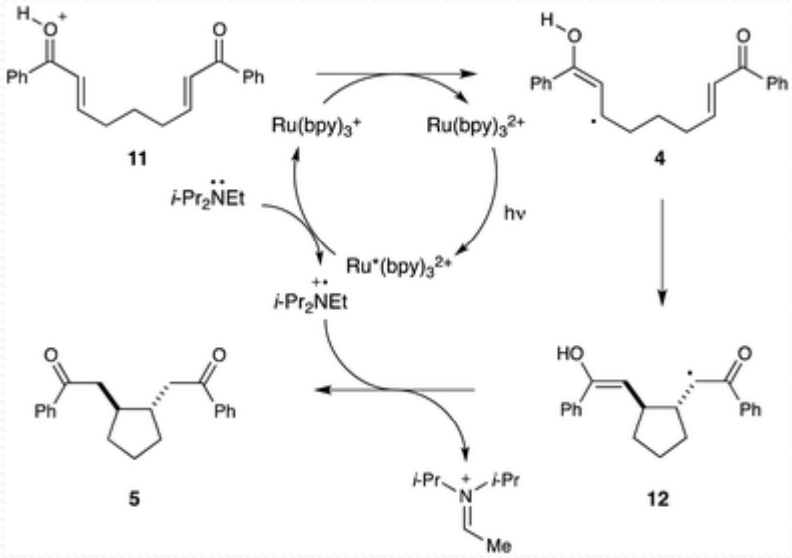
Photoredox catalysis



Ischay, M. A.; Anzovino, M. E.; Du, J.; Yoon, T. P. *J. Am. Chem. Soc.* **2008**, *130*, 12886

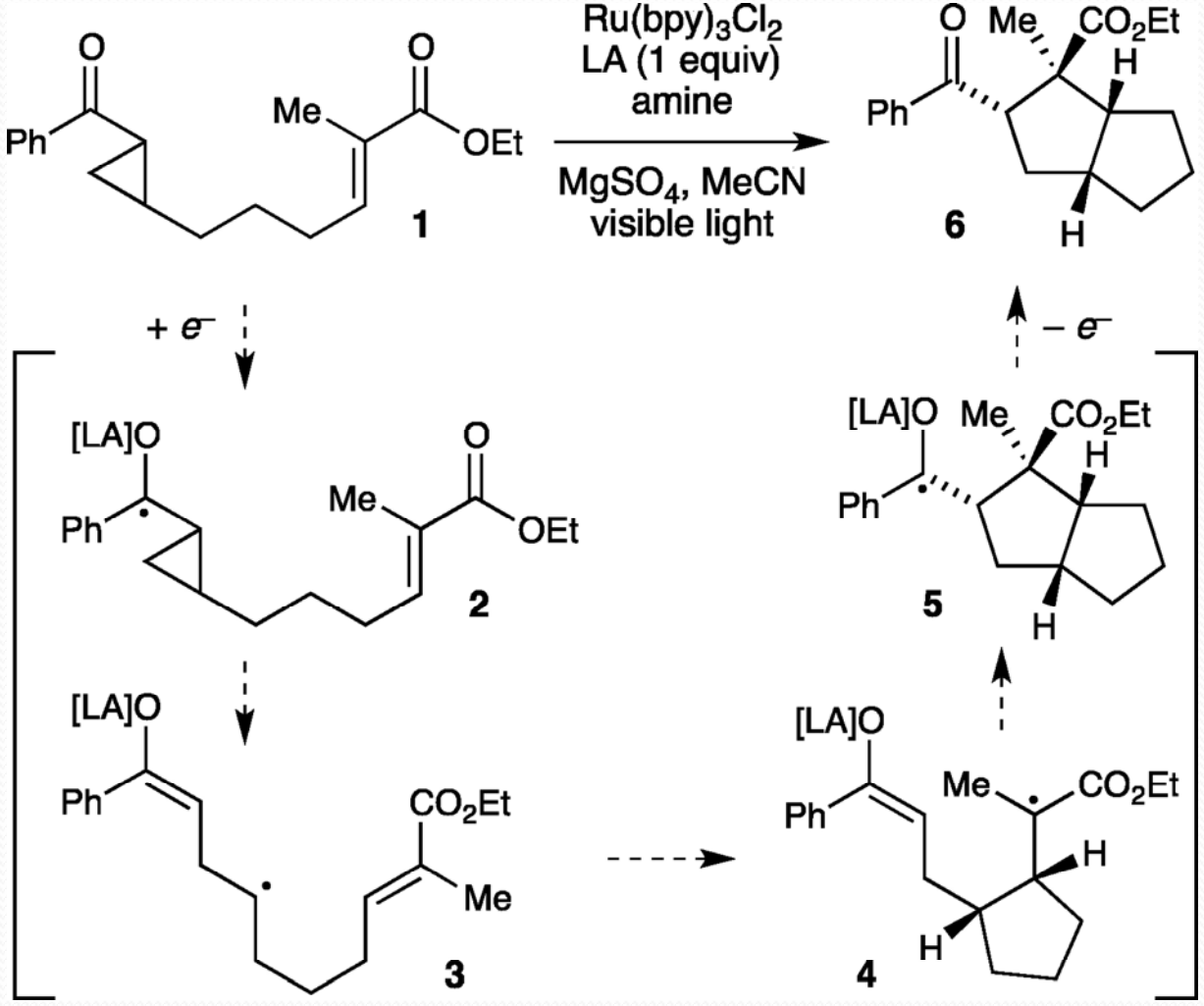
Photoredox catalysis





Du, J.; Ruiz Espelt, L.; Guzei, I. A.; Yoon, T. P. *Chem. Sci.* **2011**, *2*, 2115

Photoredox catalysis



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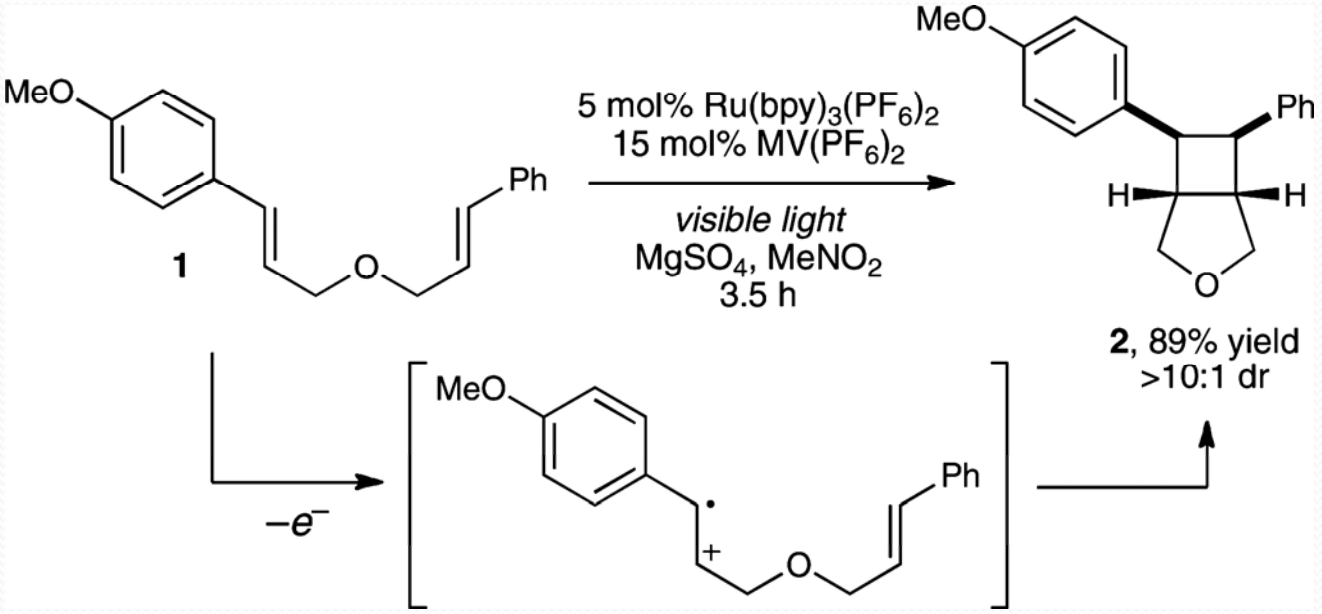
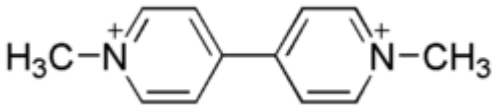


MV = Methyl viologen = 

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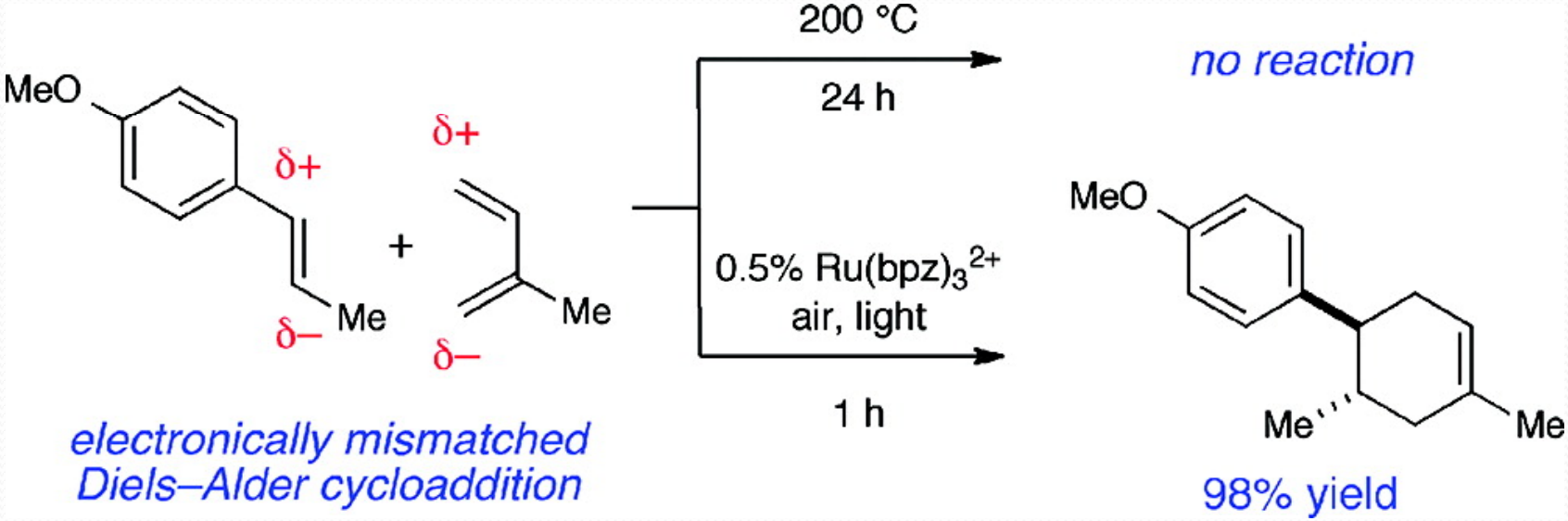

Lin, S.; Ischay, M. A..; Fry, C. G.; Yoon, T. P. *J. Am. Chem. Soc.* **2011**, *133*, 19350

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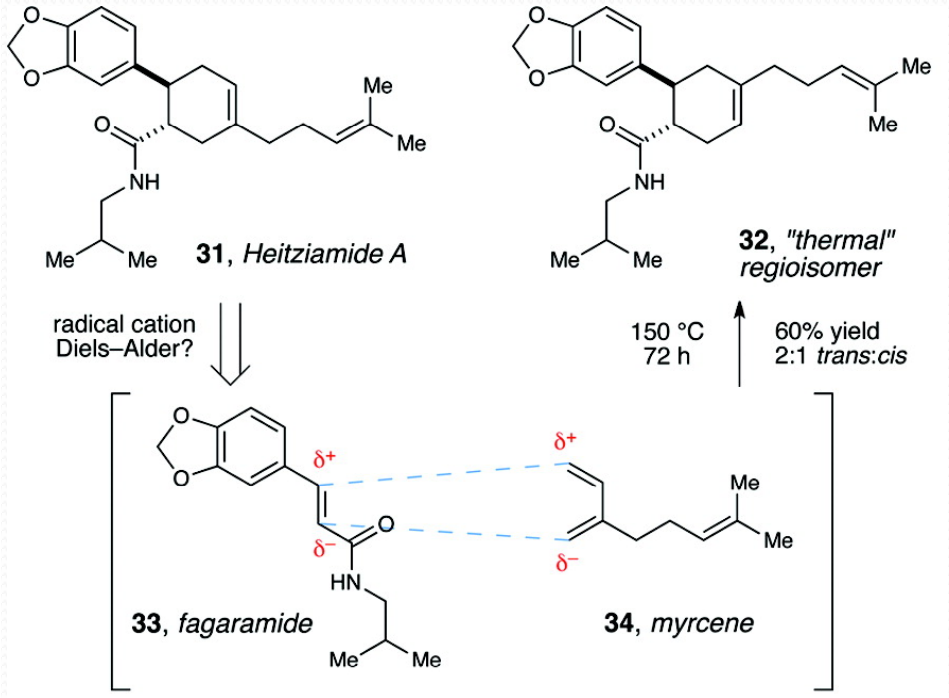

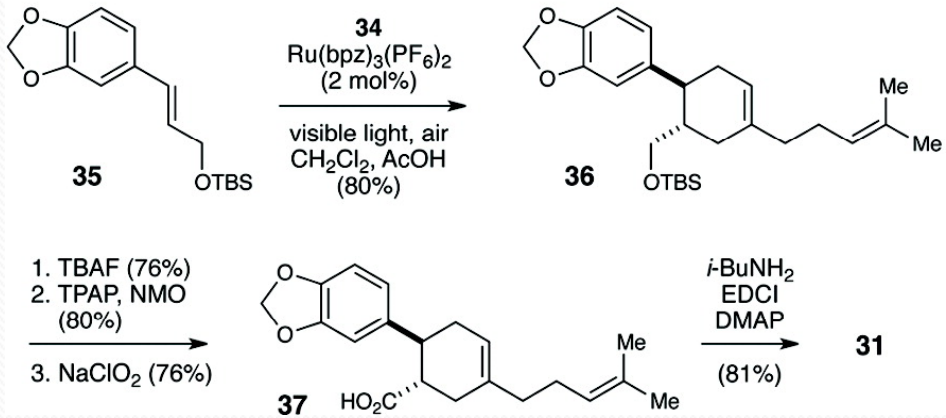

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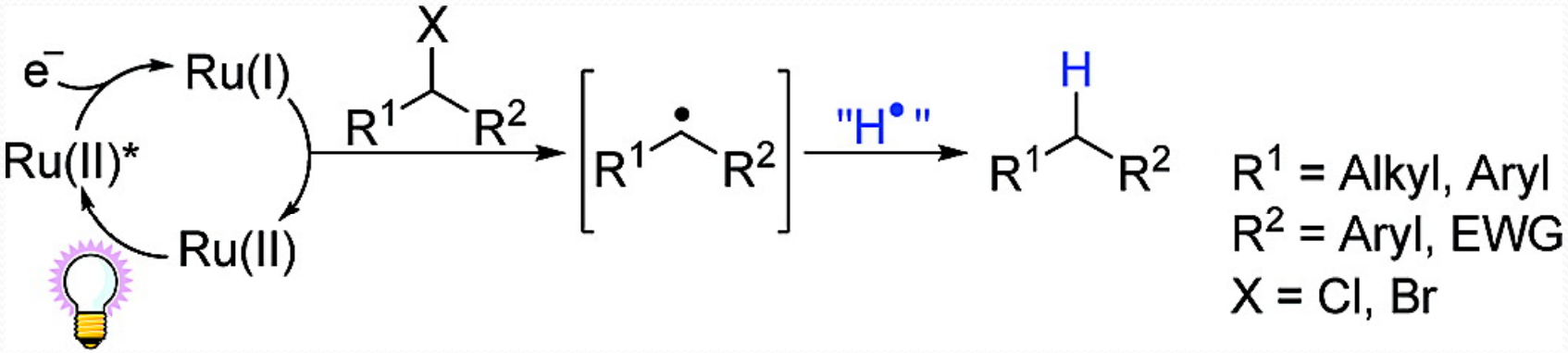

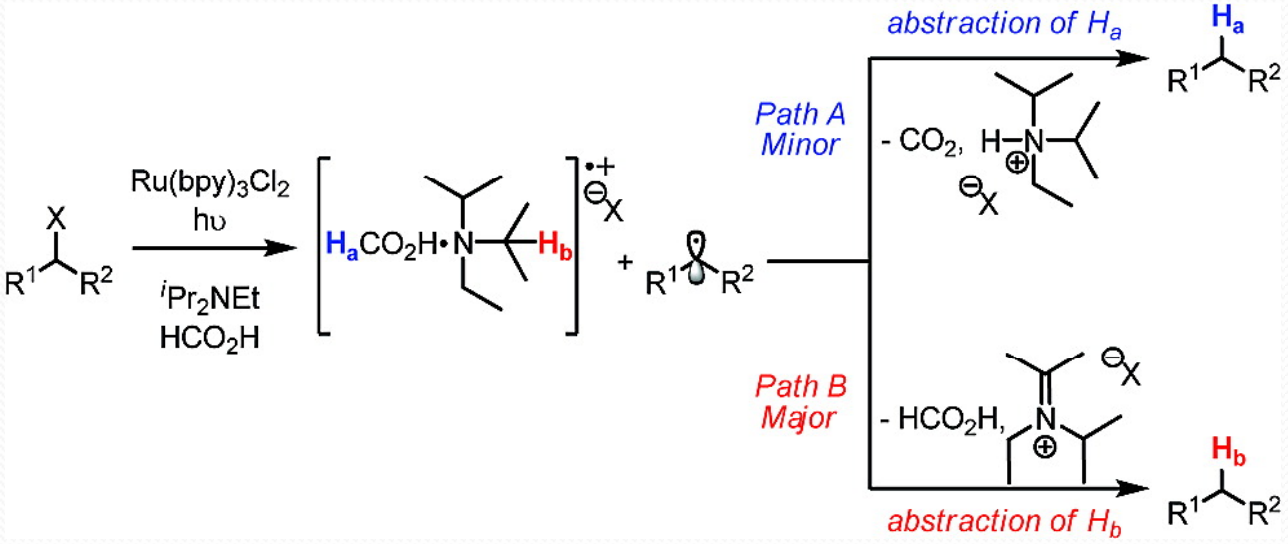

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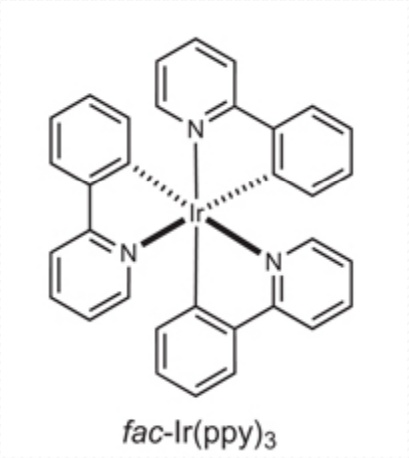
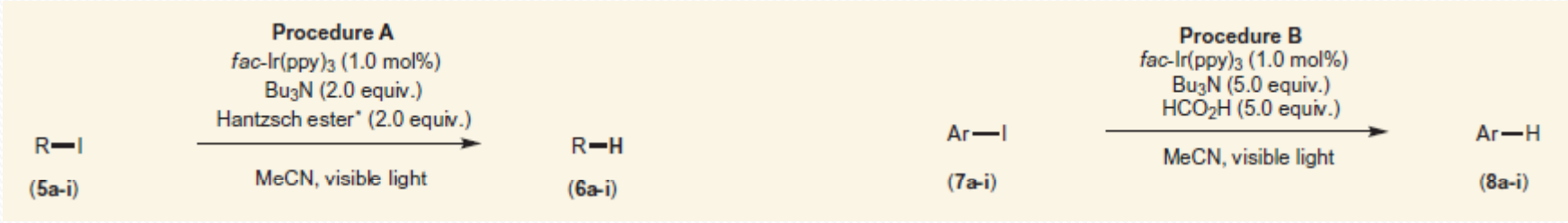
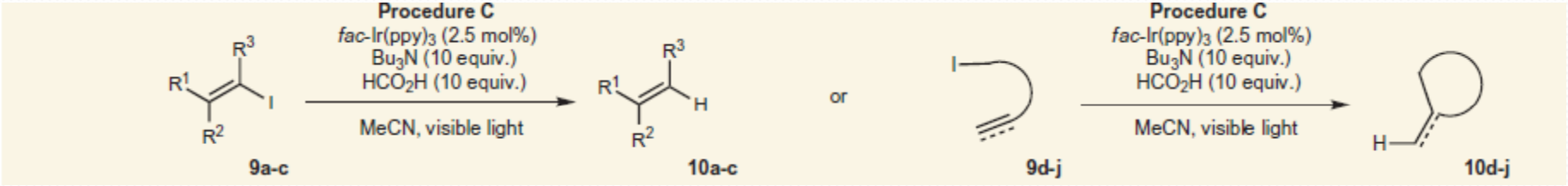


fac-Ir(ppy)$_3$





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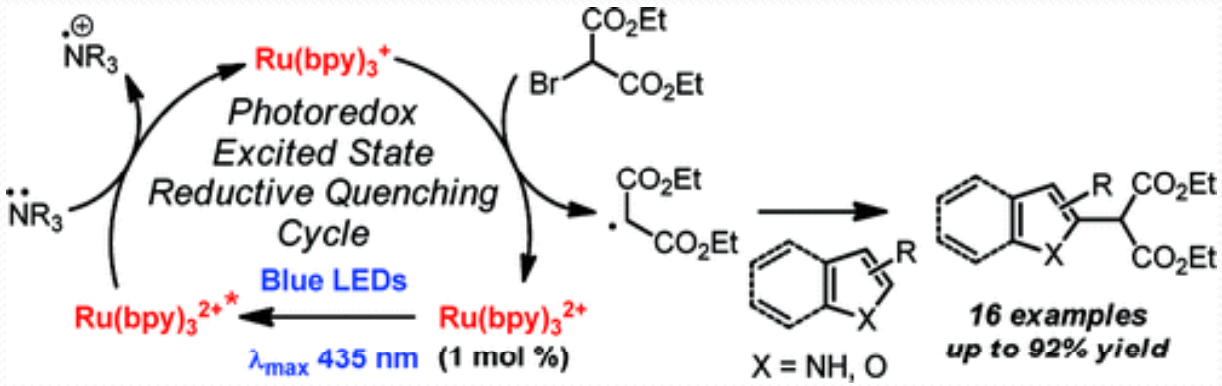

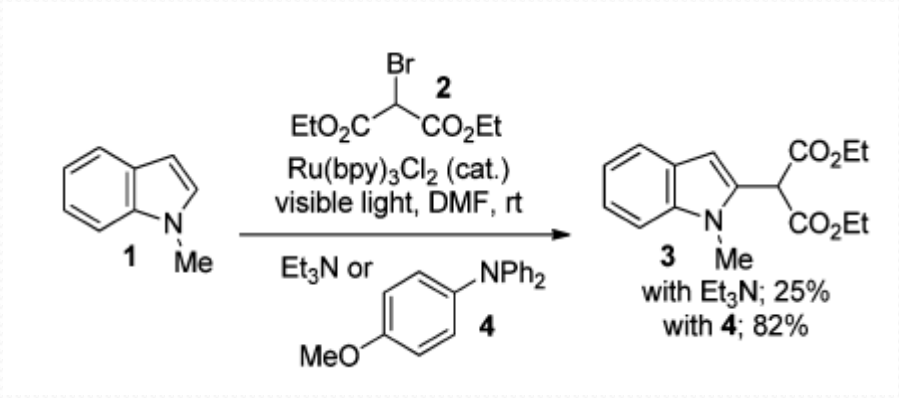

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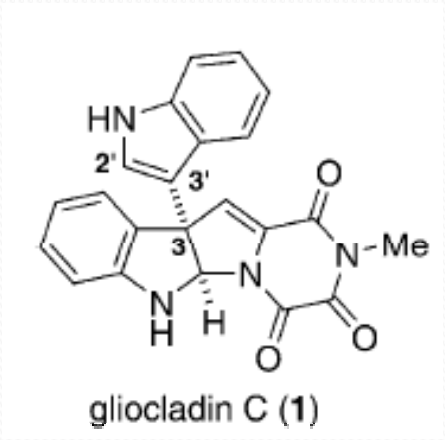
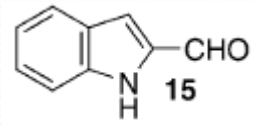
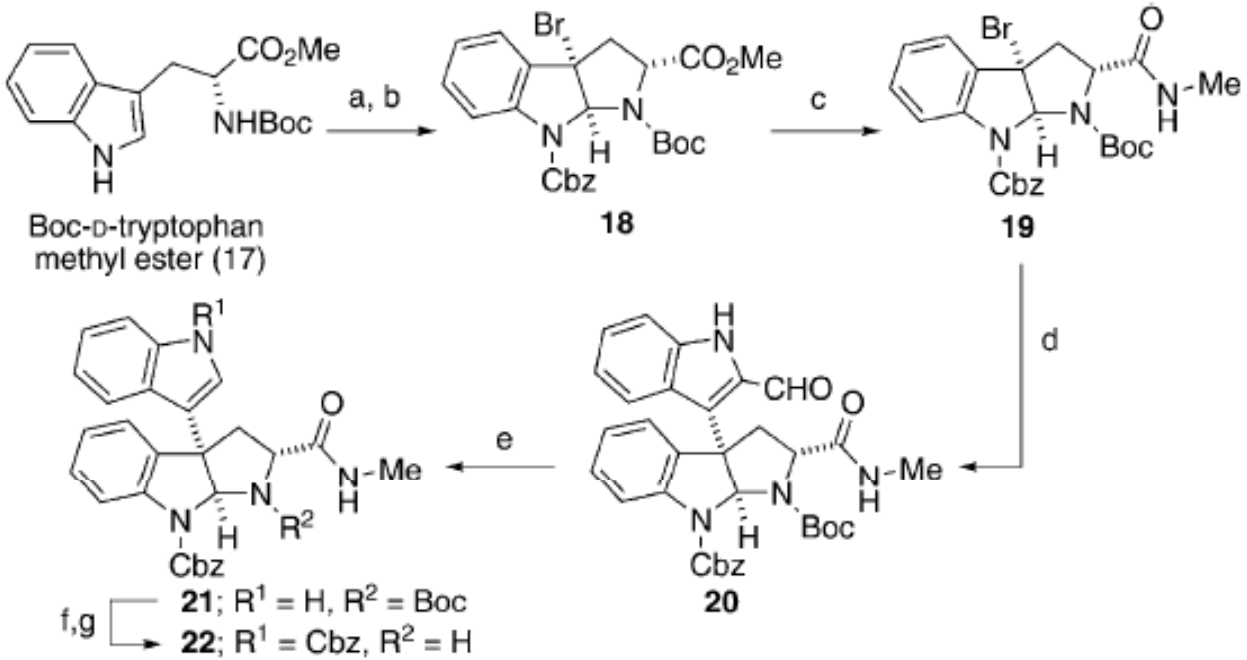


gliocladin C (**1**)





Boc-D-tryptophan methyl ester (17)

Scheme 3. a) CbzCl, NaOH, Bu_4NHSO_4, CH_2Cl_2, 12 h; b) NBS, PPTS, CH_2Cl_2, 23 °C, 12 h, 91% (two steps); c) $MeNH_2$, THF, 23 °C, 3 d, 87%; d) $[Ru(bpy)_3Cl_2]$ (1.0 mol%), Bu_3N (2 equiv), **15** (5 equiv), DMF, blue LEDs, 12 h, 82%; e) $[Rh(Ph_3P)_3Cl]$ (1 equiv), xylenes, 140 °C, 12 h, 86% or $[Rh(CO)(Ph_3P)_2Cl]$ (20 mol%), dppp (44 mol%), DPPA (2 equiv), xylenes, 140 °C, 85%; f) CbzCl, NaOH, Bu_4NHSO_4, CH_2Cl_2, 12 h, 98%; g) TMSI, CH_3CN, 0 °C, 1 h, 91%. Cbz = benzyloxycarbonyl;

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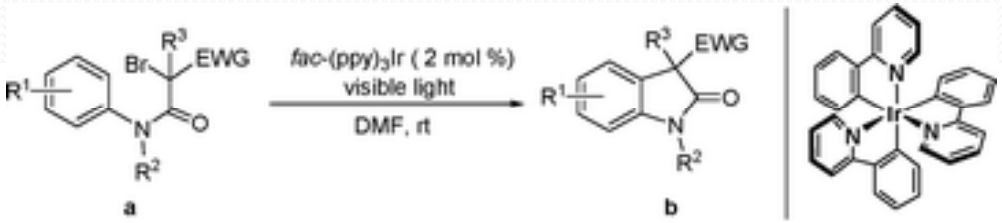
Photoredox catalysis



Entry	Catalyst	Additive (equiv.)	Conversion (%)	Yield (%)[b]
1	$Ru(bpy)_3Cl_2$	Et_3N (2)	70	35
2	$Ru(bpy)_3Cl_2$	$^iPr_2NEt$ (2)	100	60
3	$Ru(bpy)_3Cl_2$	Ph_3N (2)	17	14
4	$Ru(bpy)_3Cl_2$	none	<1	N.D.[c]
5	$Ir(ppy)_2(dtbpy)PF_6$	Ph_3N (2)	80	71
6	*fac*-$(ppy)_3Ir$	2,6-lutidine (2)	100	95
7	***fac*-$(ppy)_3Ir$**	**none**	**100**	**95**
8	*fac*-$(ppy)_3Ir$	none	<1[d]	N.D.[c]
9	none	none	<1	N.D.[c]

[a] A solution of 0.12 mmol of **1a** and 2.4×10^{-3} mmol of catalyst in DMF (2.4 mL) was irradiated at room temperature under argon atmosphere for 12 h. [b] Isolated yield. [c] Not determined. [d] Control experiment without irradiation under the otherwise same conditions.

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Conclusion

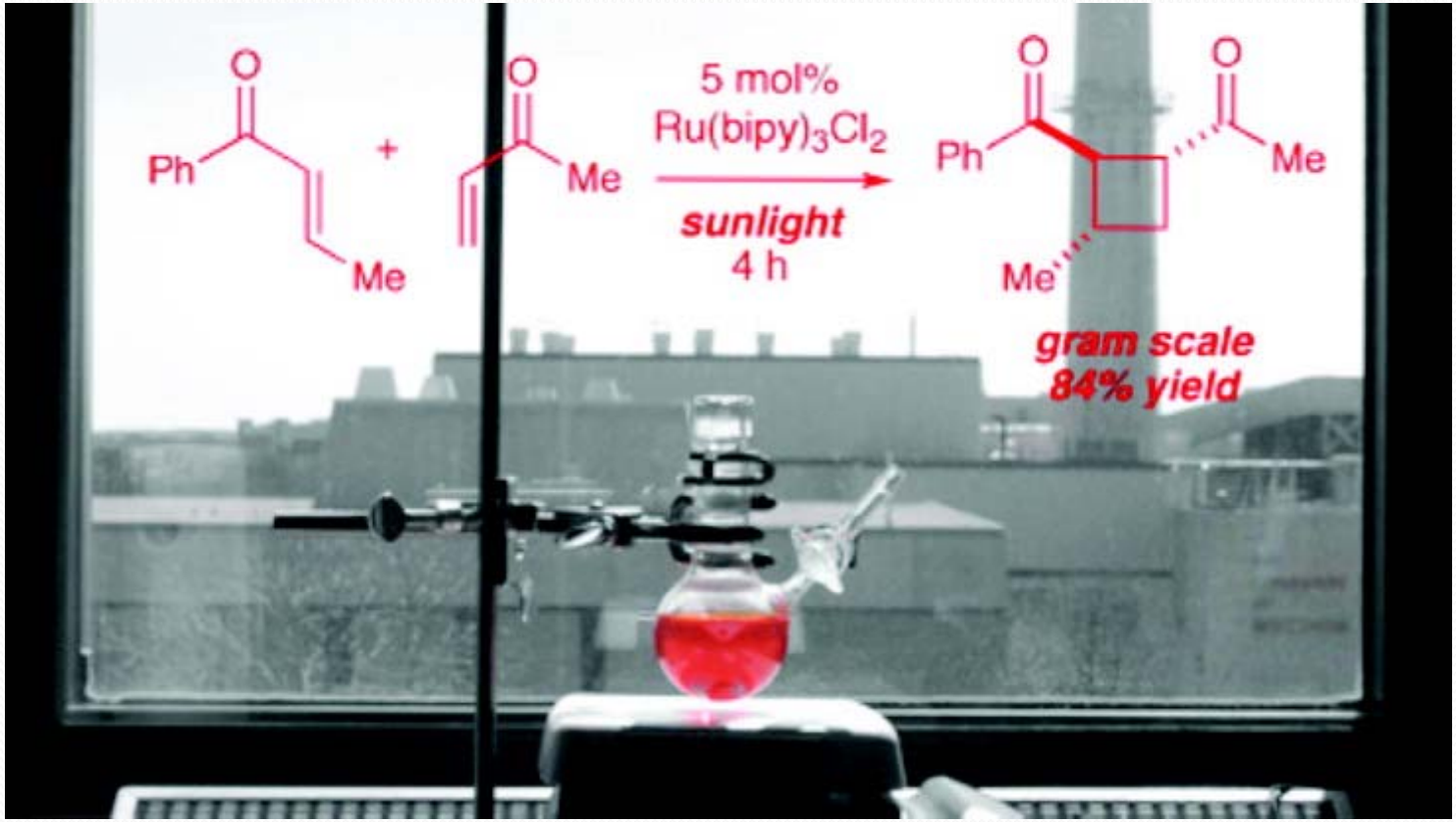
-Using SOMO catalysis many different building blocks for pharmaceutical and medicinal chemistry could be synthesised

- Photocatalyst such as Ru complexes can be used as one electron oxidizer

- Radicals are the most present intermediates in photocatalysis

Thank you for your attention

Photoredox catalysis



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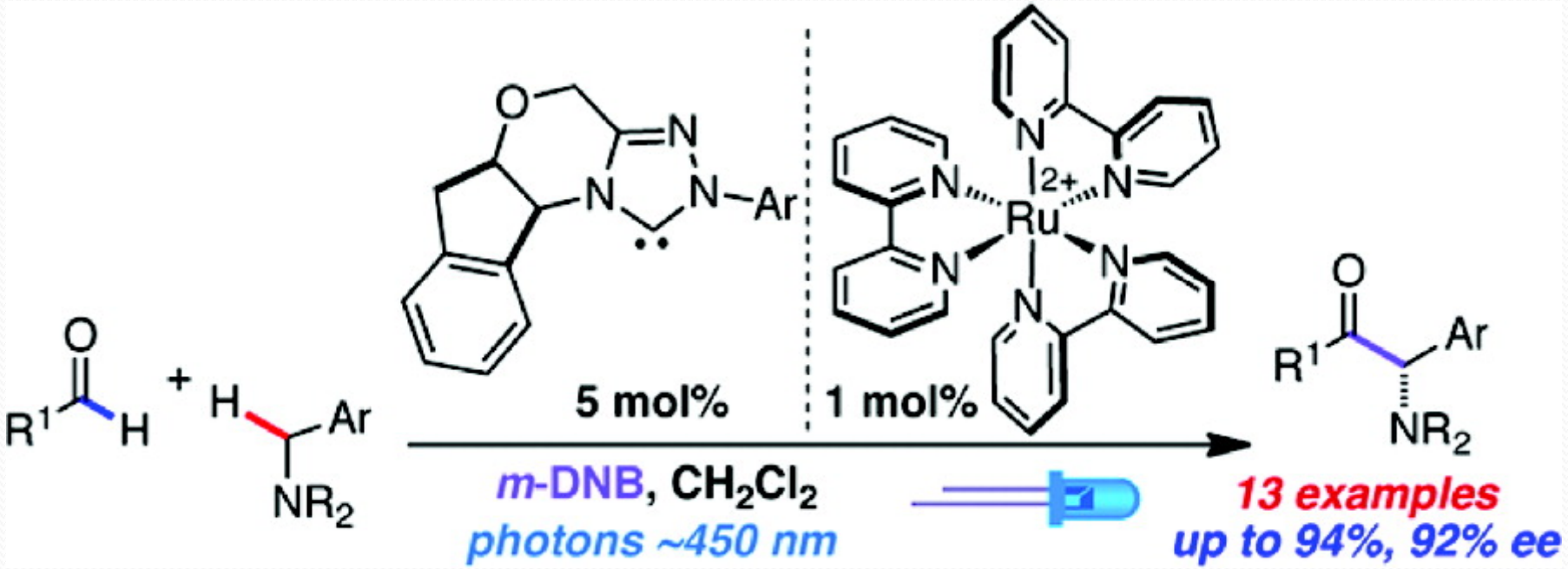
Photoredox catalysis



DiRocco, D. A.; Rovis, T. *J. Am. Chem. Soc.* **2012**, *134*, 8094

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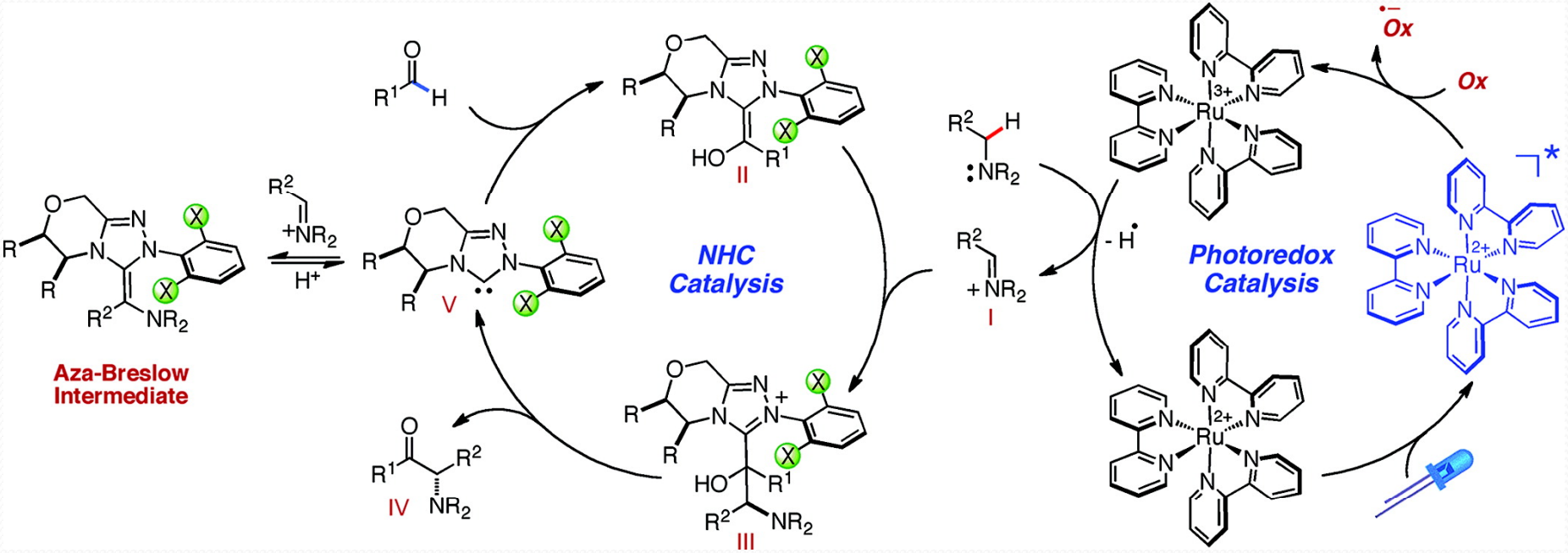

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