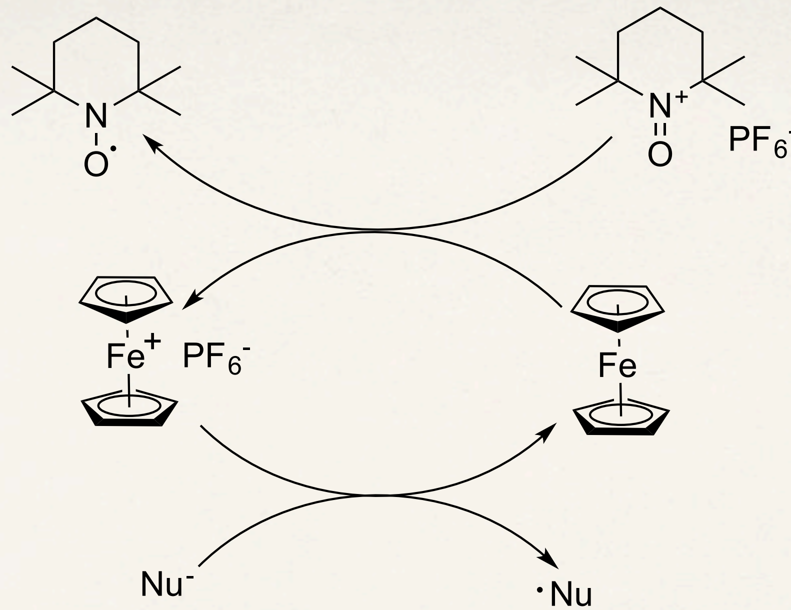


An Efficient Strategy Single-Electron-Transfer-Induced Tandem Anion–Radical Reactions

Frantisˇek Kafka, Martin Holan, Denisa Hidasovµ, Radek Pohl, Ivana Císarˇova,

Blanka Klepetµrˇovµ, and Ullrich Jahn*

Angew. Chem. Int. Ed. **2014**, *53, 9944 –9948*

DOI: 10.1002/anie.201403776

Yongzhao Yan *Wipf Group Current Literature* *9-5-2014*

SET-Mediated Transformation

- Radicals are generated from neutral precursors.
- Overall reactions are classified as neutral, oxidative and reductive.
- Stoichiometric amounts of SET agents.

主要是oxi reduc
两步set最后产生中性
的产物

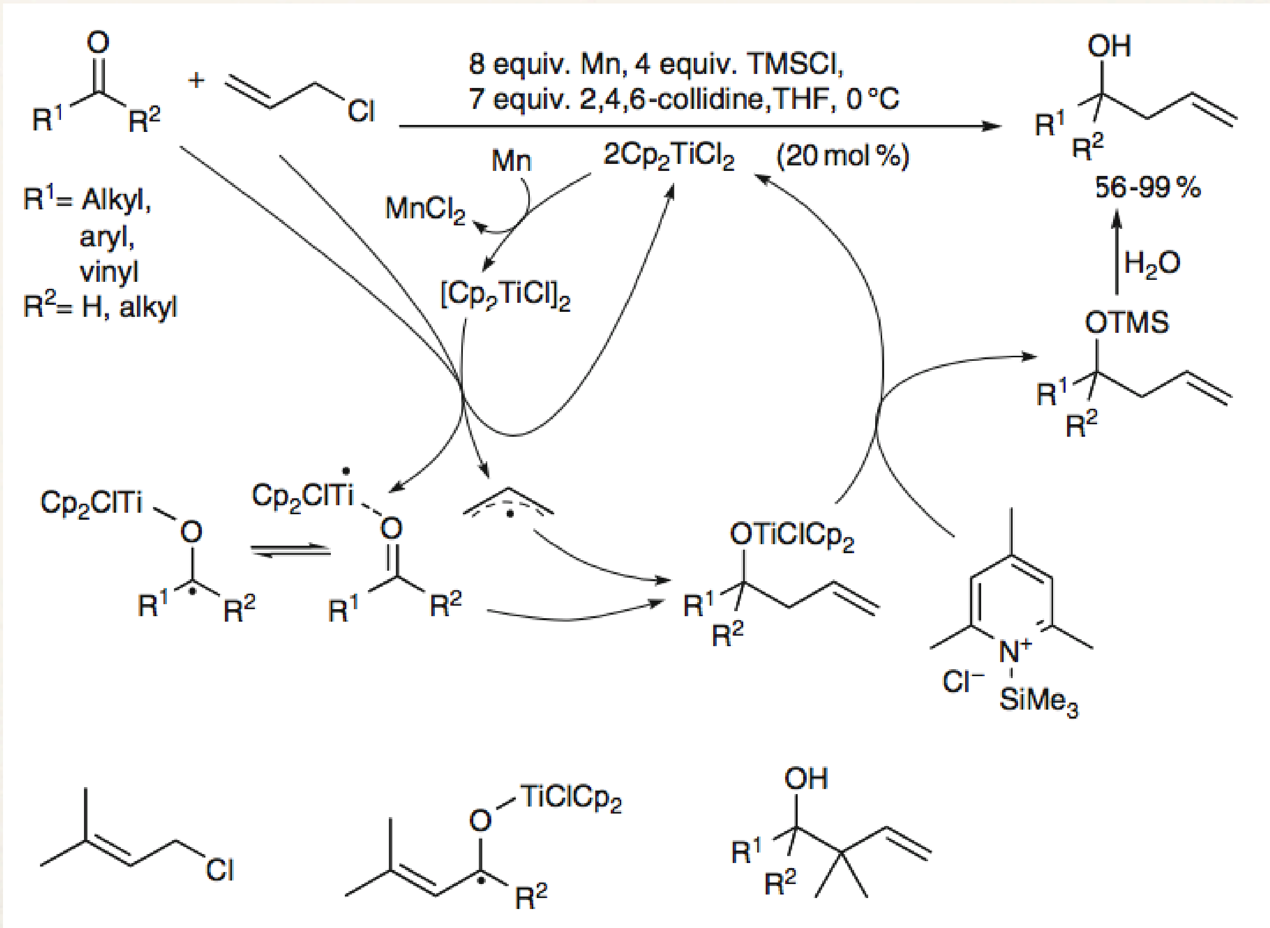
alkyl halides or sulfur electrophiles,

transition-metal-catalyzed atom-transfer radical reactions,

1. *Top. Curr. Chem.* **2012**, *320*, 121–452

Catalytic SET-Mediated Reactions

- Reductive Titanium(III)-catalyzed reaction



Ti promotes 2 SET

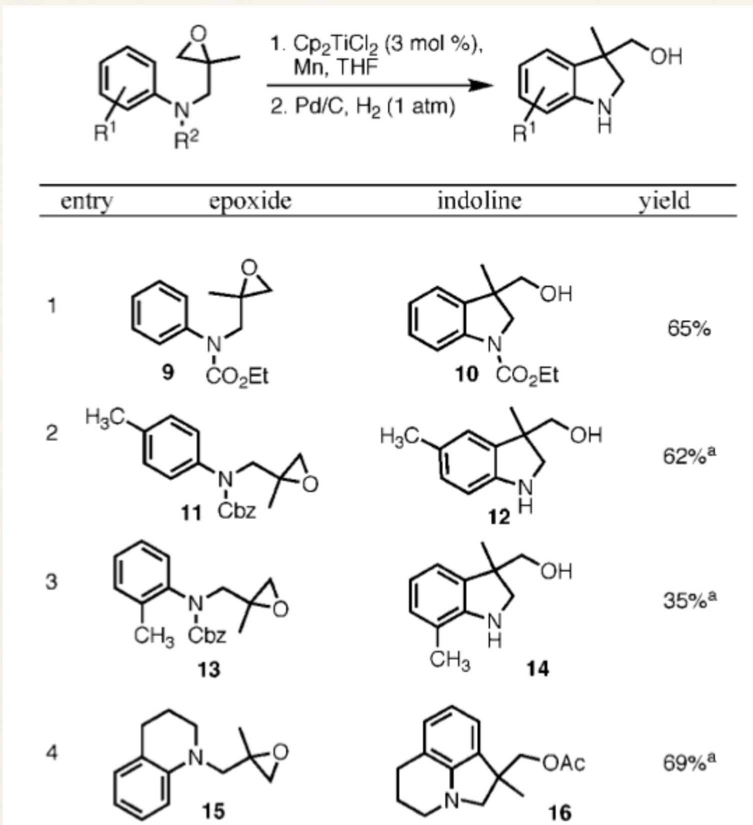
1. *Top. Curr. Chem.* **2012**, *320*, 121–452

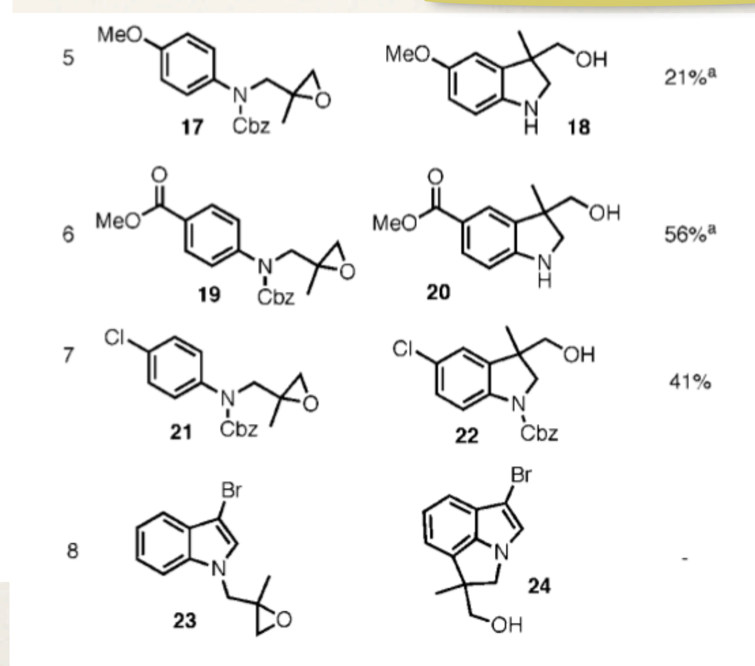
Catalytic SET-Mediated Reactions

- Reductive Titanium(III)-catalyzed reaction

john maciejsiki
indoline scaffold
synthesis

3mol%



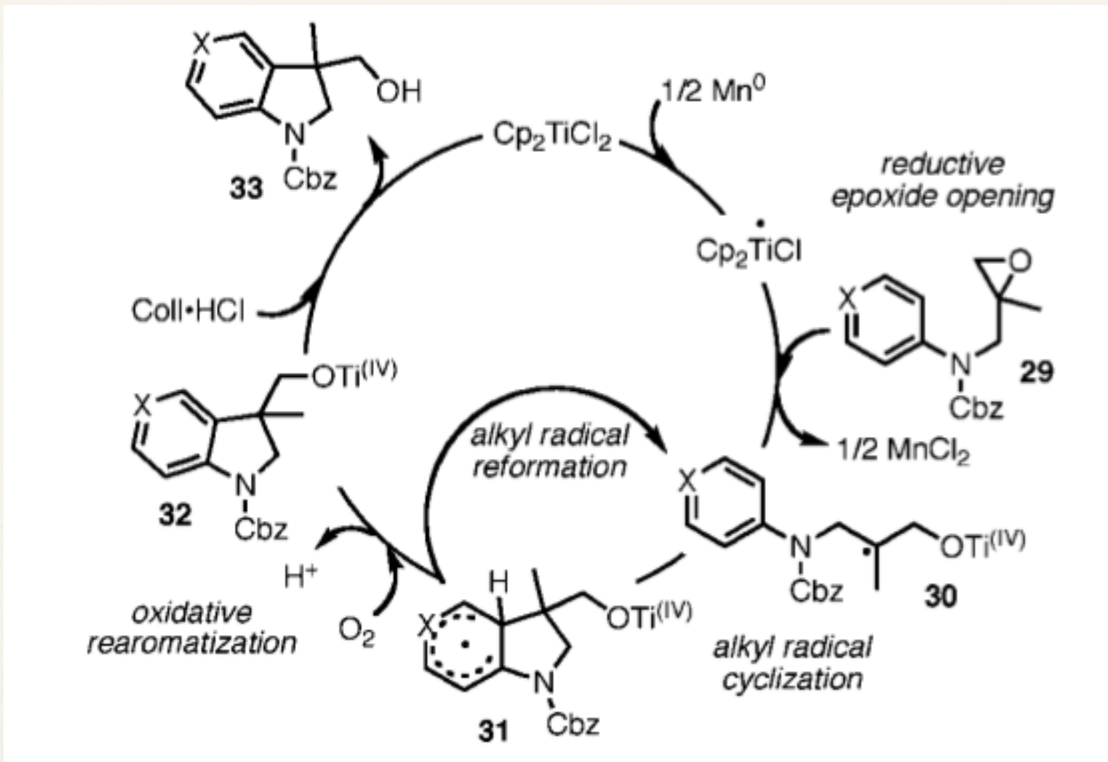


1. *Org. Lett.*, **2008**, *10* (19), pp 4383–4386

Catalytic SET-Mediated Reactions

- Reductive Titanium(III)-catalyzed reaction

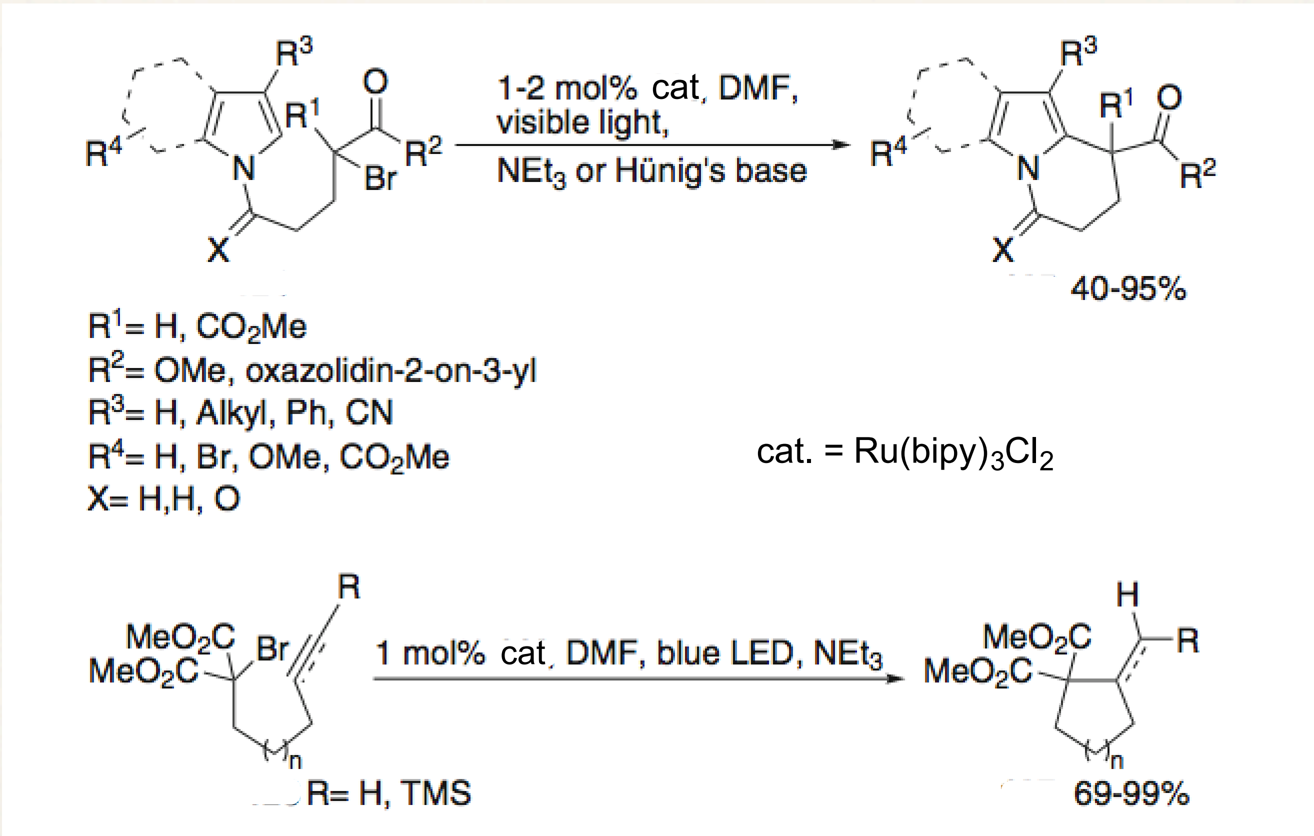
trace O2 or H+ oxidize back



1. *Org. Lett.*, **2008**, *10* (19), pp 4383–4386

Catalytic SET-Mediated Reactions

- Ru(II) catalyzed photoredox reactions



1. *Top. Curr. Chem.* **2012**, *320*, 121–452

Ferrocene/Ferrocenium Couple

Table 2. Formal Potentials (V *vs* Fc) of Selected Oxidizing Agents

oxidant	solvent	$E^{\circ\prime}$	correction	ref
$[N(C_6H_2Br_3\text{-}2,4,6)_3]^+$	MeCN	1.36	*a*	228
Ce(IV)	$HClO_4$	1.30	*b*	*c*
	H_2O	0.88	*b*	*c*
$[N(C_6H_3Br_2\text{-}2,4)_3]^+$	MeCN	1.14	*a*	228
$[WCl_6]$	CH_2Cl_2	*ca.* 1.1	*d*	132
$[NO]^+$	CH_2Cl_2	1.00	none	195
$[Ru(phen)_3]^{3+}$	MeCN	0.87	*e*	108
$[NO]^+$	MeCN	0.87	none	195
$[thianthrene]^+$	MeCN	0.86	*f*	*g*
$[N(C_6H_4Br\text{-}4)_3]^+$	CH_2Cl_2	0.70	*d*	*h*
	MeCN	0.67	*i*	*j*
$[Fe(bipy)_3]^{3+}$	MeCN	0.66	*e*	111
Ag^+	CH_2Cl_2	0.65	*d*	63
$[Mo(tfd)_3]$	MeCN	0.55	*f*	*k*
$[IrCl_4(PMe_2Ph)_2]$	MeCN	*ca.* 0.5	*l*	123
$[Fe(\eta\text{-}C_5H_4COMe)_2]^+$	CH_2Cl_2	0.49	none	*h*
$[CuTf_2]$	MeCN	0.40	*f*	88
Ag^+	THF	0.41	*m*	63
$[Ni(tfd)_2]$	CH_2Cl_2	0.33	none	*h*
$[PtCl_6]^{2-}$	H_2O	0.31	*b*	*n*
$[Fe(\eta\text{-}C_5H_4COMe)Cp]^+$	CH_2Cl_2	0.27	none	*h*
Ag^+	acetone	0.18	*o*	63
Cl_2	MeCN	0.18	*b*	*p*
DDQ	MeCN	0.13	*i*	308
Br_2	MeCN	0.07	*b*	*p*
$[N_2C_6H_4NO_2\text{-}4]^+$	sulfolane	*ca.* 0.05	*f*	*q*
Ag^+	MeCN	0.04	*f*	63
$[C_3\{C(CN)_2\}_3]^-$	MeCN	0.03−0.06	*r*	304
$[FeCp_2]^+$		0.0		
$[N_2C_6H_4F\text{-}4]^+$	MeCN	−0.07	*f*	*q*
$[CPh_3]^+$	MeCN	−0.11	*f*	*s*
I_2	MeCN	−0.14	*f*	*t*
TCNE	MeCN	−0.27	*f*	*u*
TCNQ	MeCN	−0.30	*f*	*u*
$[FeCp^*_2]^+$	MeCN	−0.59	none	*h*
	CH_2Cl_2	−0.48	none	*h*
$[C_7H_7]^+$	MeCN	−0.65	*f*	*s*

Table 3. Formal Potentials (V *vs* Fc) of Selected Reducing Agents

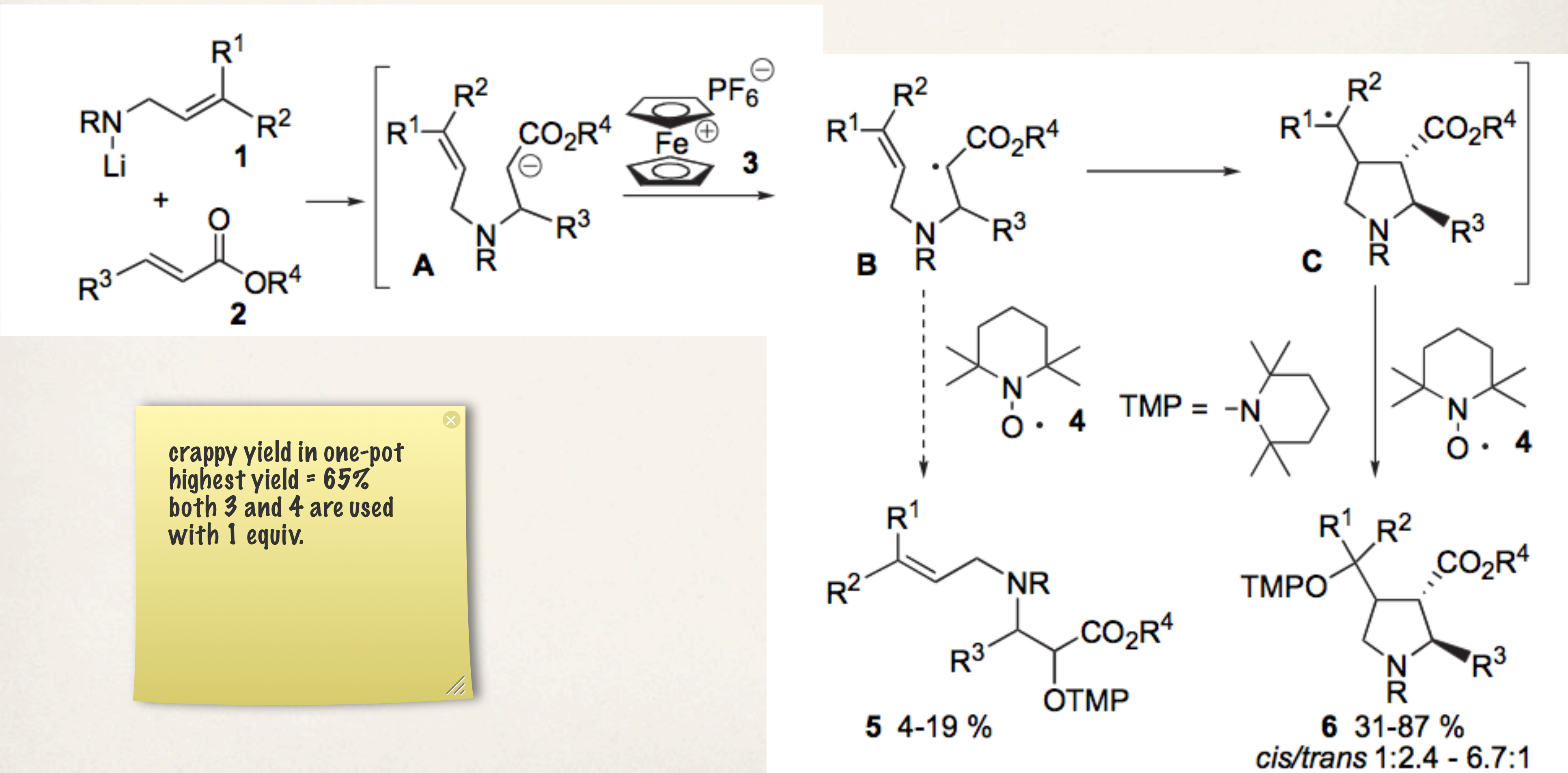
reductant	solvent	$E^{\circ\prime}$	correction	ref
$[C_{10}H_8]^-$	THF	−3.10	*a*	366b
	glyme	−3.05	*a*	366b
	DMF	−2.95	*b*	*c*
Na	THF, glyme	−3.04	*a*	*d*
Li	NH_3	−2.64	*e*	*f*
Li(Hg)	H_2O	−2.60	*e*	*g*
K	NH_3	−2.38	*e*	*f*
Na(Hg)	nonaqueous	−2.36	*e*	*h*
$[anthracene]^-$	glyme	−2.47	*i*	*j*
$[FeCp^*(\eta\text{-}C_6Me_6)]$	dmf	−2.30	*b*	437
Na	NH_3	−2.25	*e*	*f*
$[benzophenone]^-$	THF	−2.30	none	*k*
	DMF	−2.17	*b*	*l*
$[acenaphthalene]^-$	THF	−2.26	*a*	366b
	glyme	−2.17	*i*	*i*
$[FeCp(\eta\text{-}C_6Me_6)]$	glyme	−2.09	*m*	402
$[CoCp^*_2]$	CH_2Cl_2	−1.94	*n*	*o*
	MeCN	−1.91	*p*	*q*
$[Fe(CO)_2Cp]^-$	THF, MeCN	*ca.* −1.8 (irr)	*p, r*	448, 449
$[CoCp_2]$	CH_2Cl_2	−1.33	none	*k*
	glyme	−1.31	*m*	404a
$[Cr(\eta\text{-}C_6H_6)_2]$	CH_2Cl_2	−1.15	none	8
$[FeCp^*_2]$	CH_2Cl_2	−0.59	*n*	*q*
	MeCN	−0.48	*p*	*s*
hydrazine	DMSO	−0.41	*t*	357
$[FeCp_2]$		0.0		
NEt_3	MeCN	*ca.* 0.47	*u*	393

mild Oxidant
weak reductant
recommended by IUPAC
for standard

0.40 V in MeCN

1. *Chem. Rev.* **1996,** *96*, 877–910

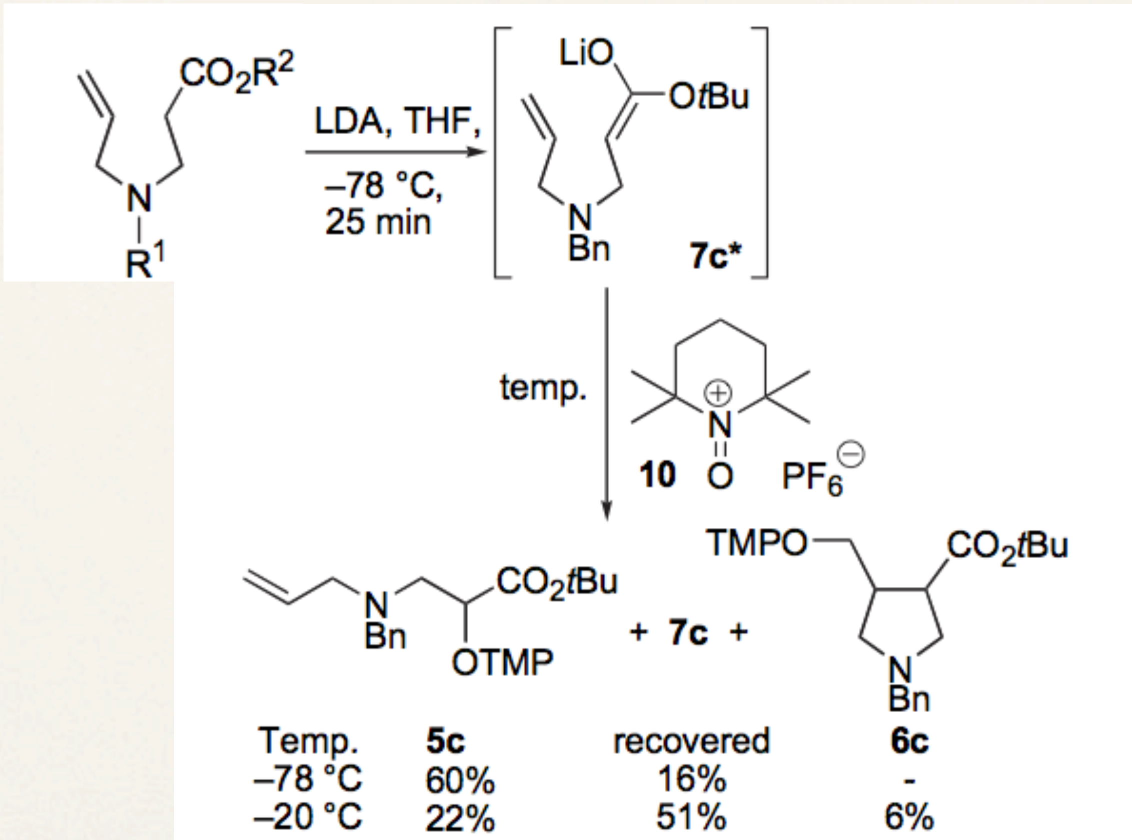
Ferrocene/TEMPO Combination



crappy yield in one-pot
highest yield = 65%
both 3 and 4 are used
with 1 equiv.

1. *Tetrahedron* **2009**, *65*, 10917–10929

Ferrocene/TEMPO Combination



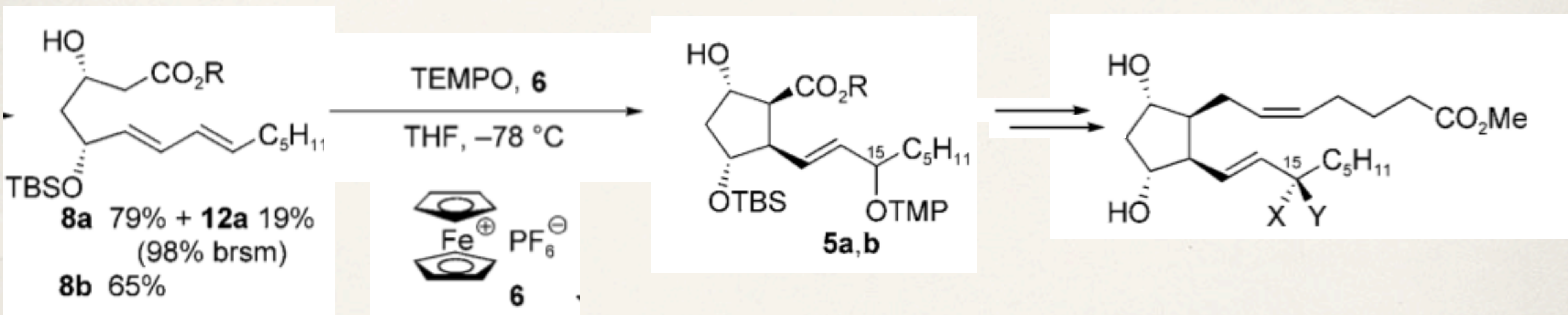
Radical recombination faster than radical addition to alkene

without FeCp2

1. *Tetrahedron* **2009**, *65*, 10917–10929

Applications in Total Synthesis

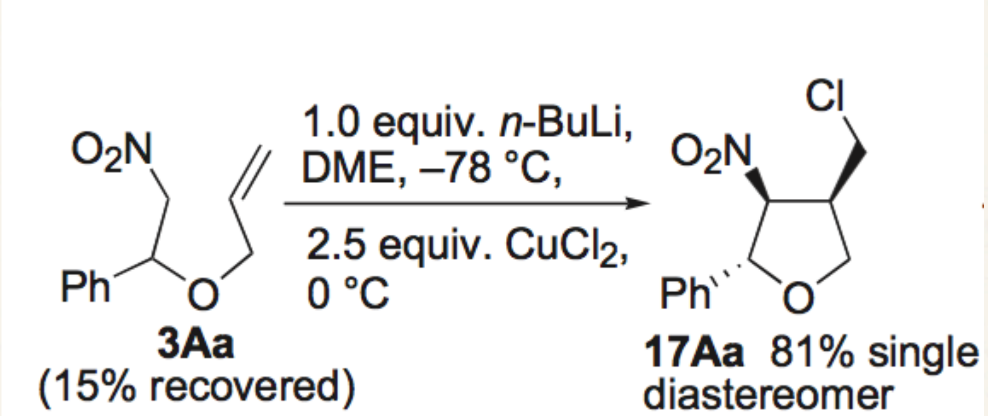
- Total Synthesis of 15-F_{2t}-Isoprostane
- 39% desired isomer



1. *Chem. Eur. J.* **2009,** *15*, 58-62

Trapping Reagents

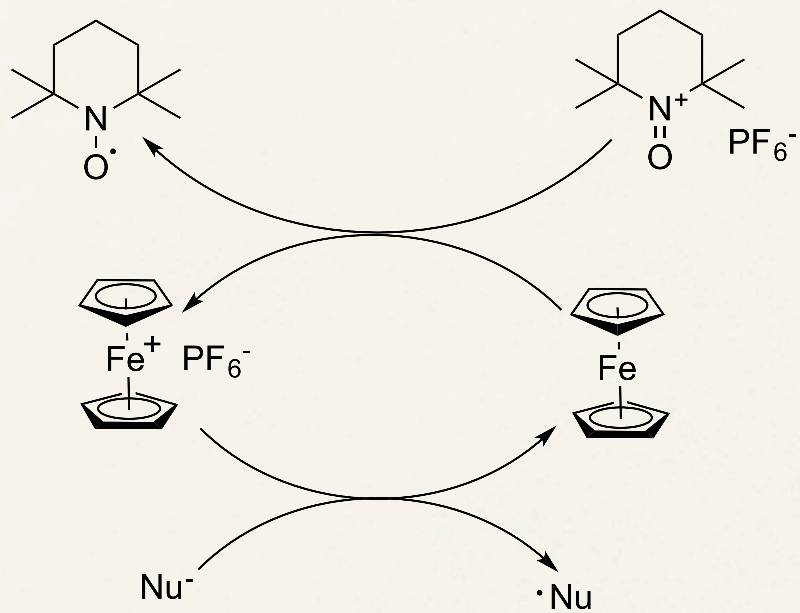
- $CuCl_2$ and $CuBr_2$ as oxidizing/trapping reagent

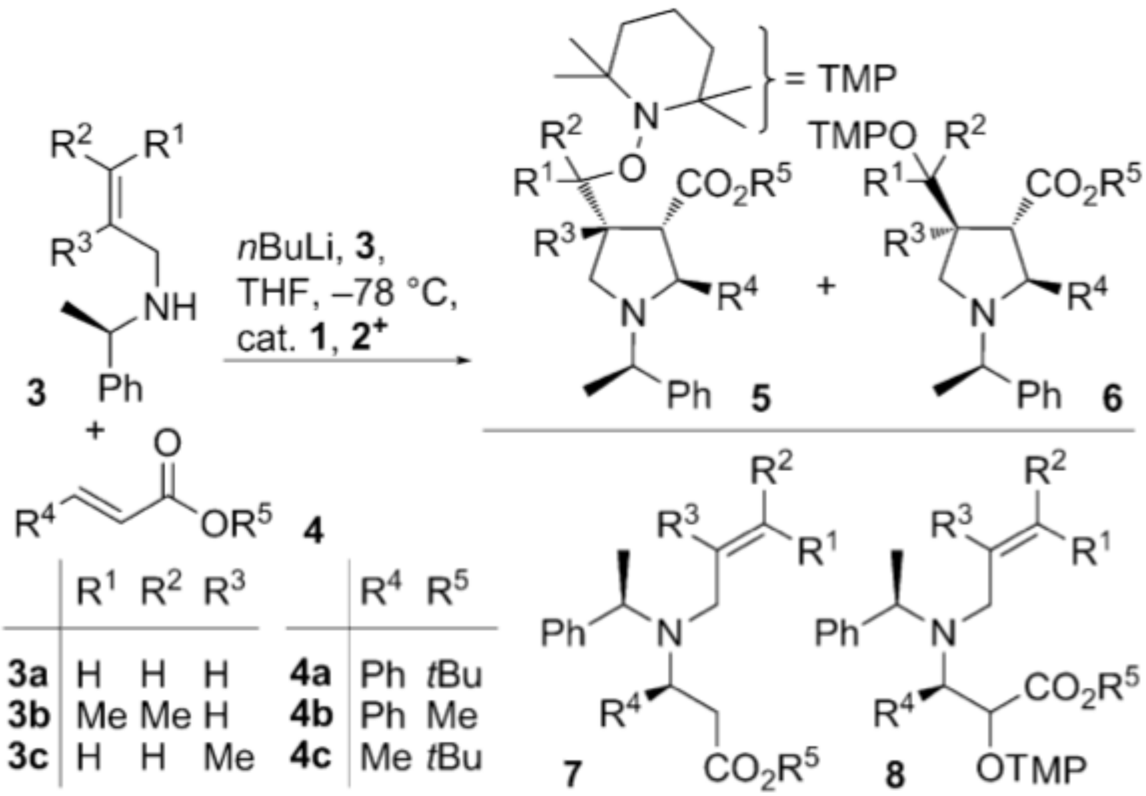


CuBr2 gave pdt with low stereoselectivity

1. *Tetrahedron 68* (**2012**) 1521-1539

Ferrocene/TEMPO Redox Pair





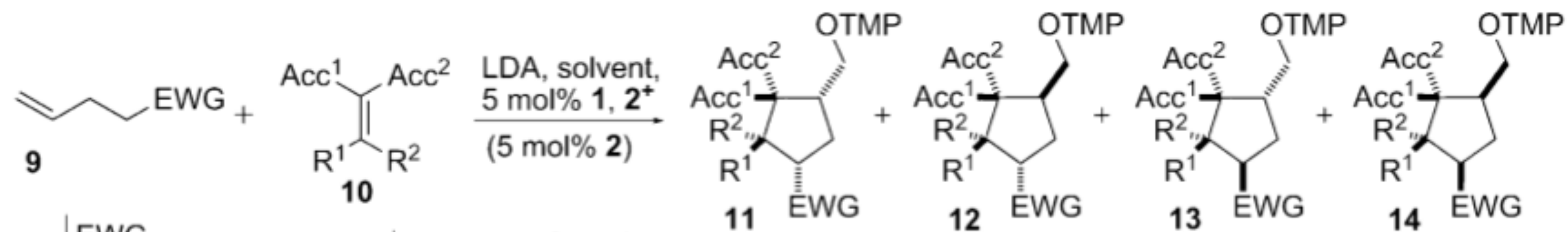
	R^1	R^2	R^3
3a	H	H	H
3b	Me	Me	H
3c	H	H	Me

	R^4	R^5
4a	Ph	*t*Bu
4b	Ph	Me
4c	Me	*t*Bu

all 2 3 trans
34 cis
Ferrocene 1-10%

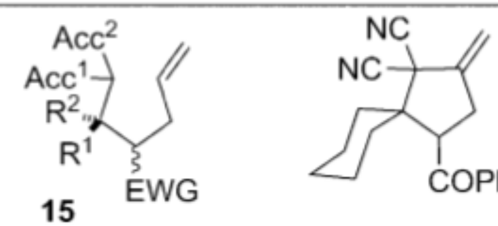
ntry	3	4	1 [mol %]	5+6, yield [%]	d.r. 5:6	Other products, yield [%]
	3a	4a	10	5a+6a, 75	6:1	7a, 16
	3a	4a	1	5a+6a, 71	5:1	7a, 16
	3a	4b	1	5b+6b, 71	3.8:1	7b+8b,[b] <5
	3b	4a	5	5c+6c, 72[c]	1.3:1	7c, 22
5	3a	4c	2	5d+6d, 49	3:1	7d, 9; 8d, 27
6	3a	4c	5	5d+6d, 56	2.3:1	7d, 12
7	3b	4c	10	5e+6e, 56	2.3:1	8e, 19
8	3c	4c	5	5f+6f, 25	3.3:1	8f, 33
9[d]	3c	4c	5	5f+6f, 52	2.4:1	8f, 17

Tandem Michael Addition/Radical Cyclization/Oxygenation Reactions



	EWG
9a	CO_2tBu
9b	CO_2-8-Phmenthyl
9c	$CONBn_2$
9d	COPh
9e	CN

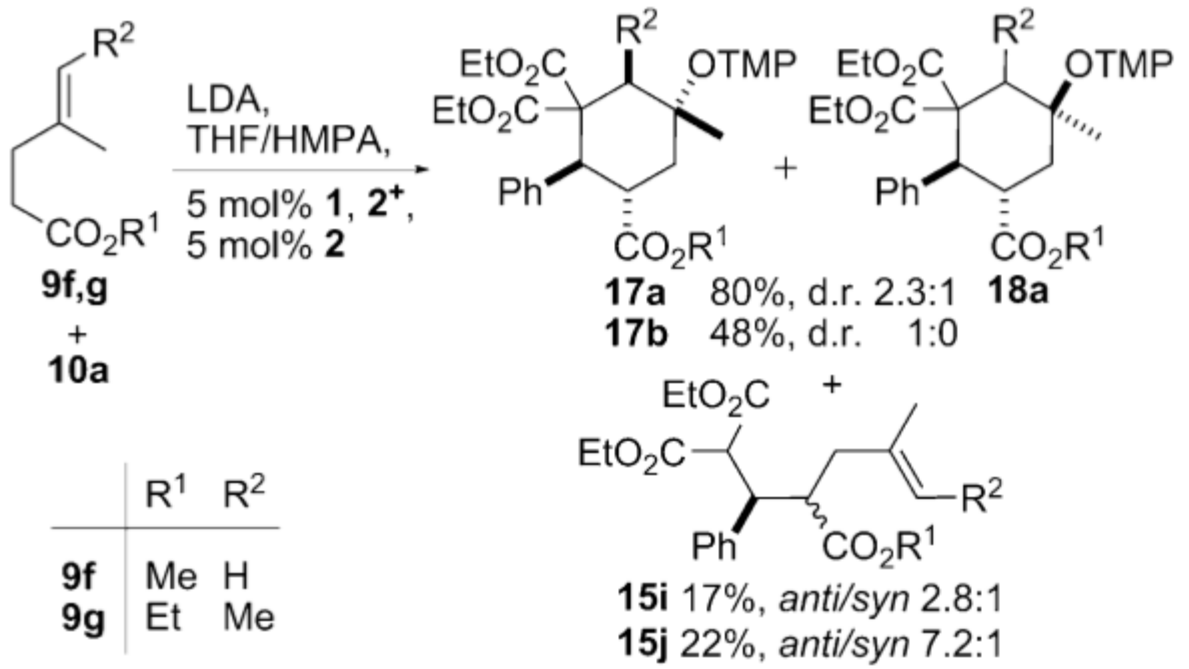
	Acc¹	Acc²	R¹	R²
10a	CO_2Et	CO_2Et	Ph	H
10b	CN	CO_2Et	Ph	H
10c	CN	CN	-$(CH_2)_5$-	
10d	CO_2Et	CO_2Et	CH_3	H



5 mol% 2 add TEMPO in the system to start with 10a sele EWG size trans ewg and R1 major

Entry	9	10	Solvent	2 [mol%]	11–14, yield [%]	d.r. 11:12:13:14	15,
1	9a	10a	THF/HMPA	–	a, 58[b]	40:1:1:1	15a, 27 (5:1)
2	9b	10a	THF/HMPA	–	b, 66[b]	1:0:0:0[c]	15b, 29 (1:0)
3	9c	10a	THF	5	c, 95	1:0:0:0	–
4	9d	10a	THF/HMPA	5	d, 50[b]	20:1:0:0[d]	15d, 11 (1:0)
5	9e	10a	THF	–	e, 82	5:1:1:0[c]	–
6	9c	10b	THF	5	f, 62[b]	8:1:2:1	–
7	9d	10c	THF	5	g, 64	2.4:1:0:0	–
8	9e	10d	THF	5	h, 55[b]	3:1:1.7:1	15h, 8 (0:1)

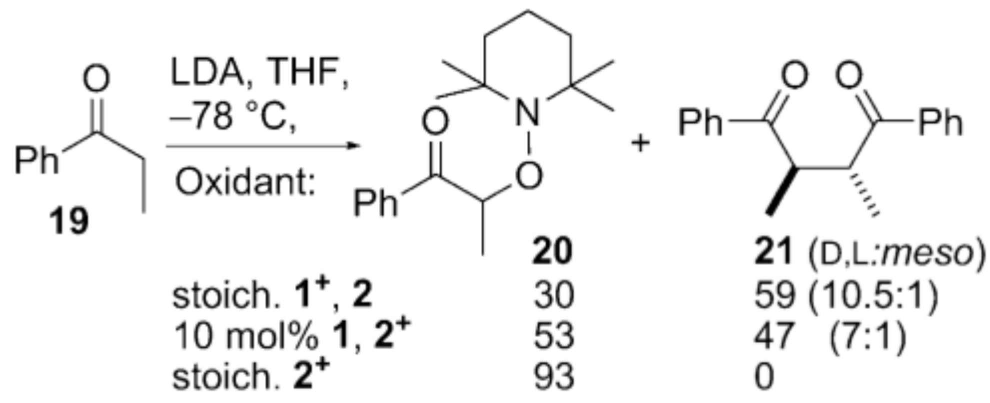
Tandem Michael Addition/Radical Cyclization/Oxygenation Reactions



	R^1	R^2
9f	Me	H
9g	Et	Me

5 exo to 6 endo

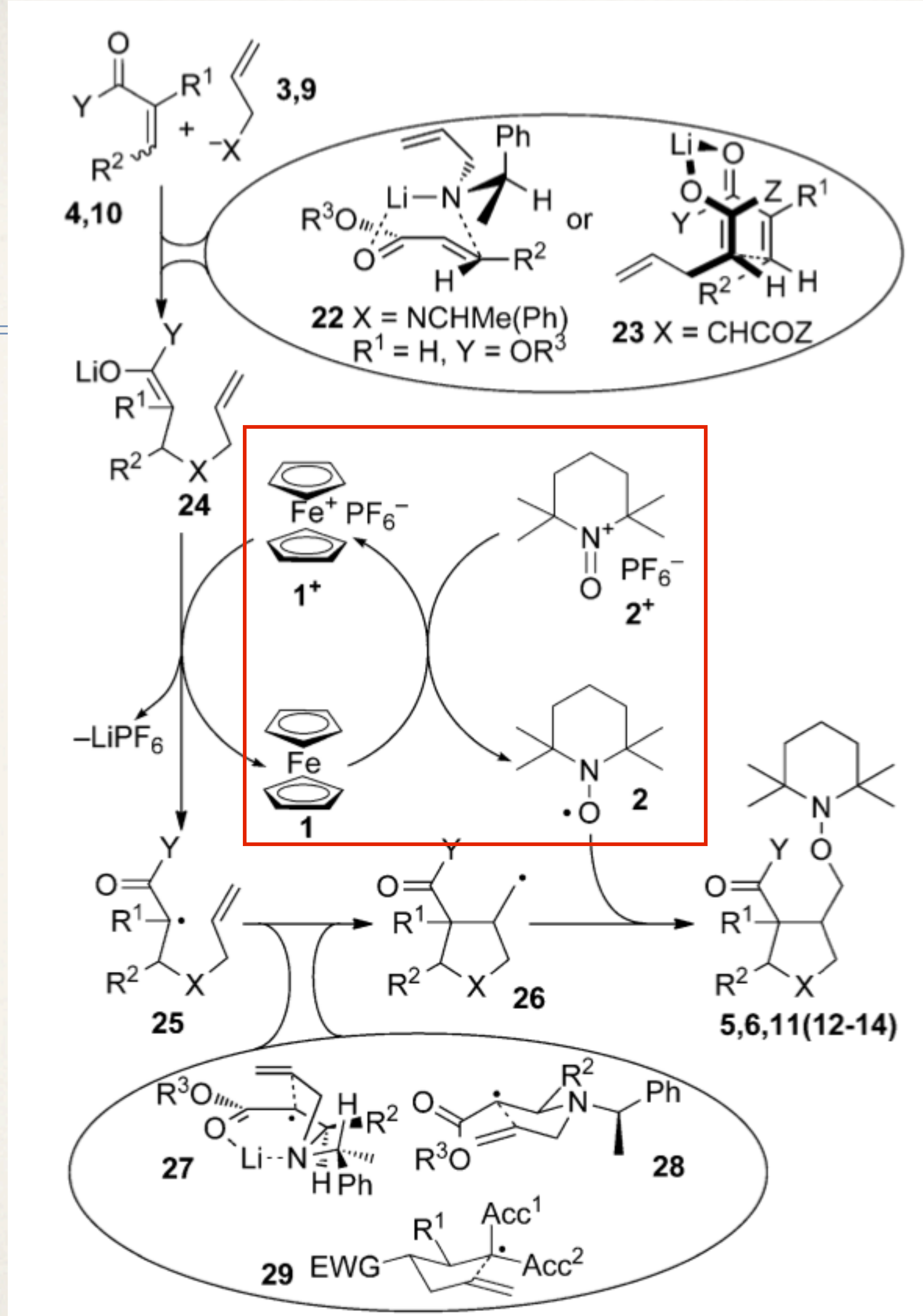
Ferrocene/TEMPO Redox Pair



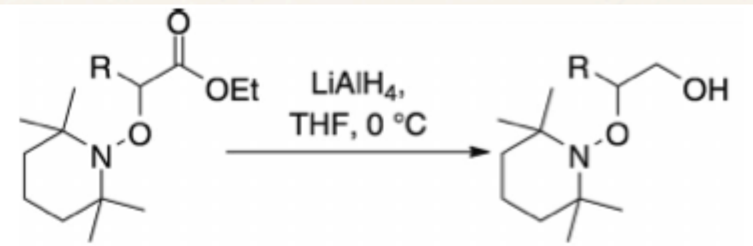
- Comparing with 52% and 47% (6:1)[1]

same distribution
catalytic worked!

1. *Eur. J. Org. Chem. 2012, 4461–4482*

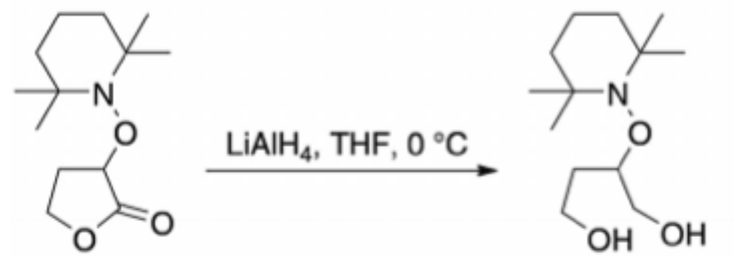

3,9
4,10
22 X = NCHMe(Ph)
R1 = H, Y = OR3
23 X = CHCOZ
24
1+
2+
1
2
–LiPF6
25
26
5,6,11(12-14)
27
28
29 EWG

TMP As Alcohol Protecting Group



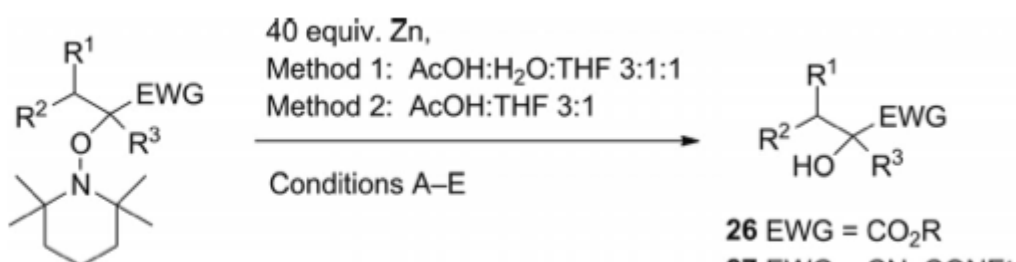
4c R = Pr
4g R = Ph

29c 90%
29g 83%



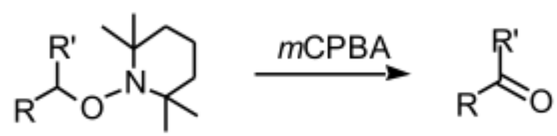
4e

29e 86%



4,9,15

26 EWG = CO_2R
27 EWG = CN, $CONEt_2$
28 EWG = COR^4



2 **3**

Tolerance with reduction
Zn cleavage
mcpba directly oxidize it back

1. *Eur. J. Org. Chem. 2012, 4461–4482*

Conclusion

- High stereoselectivity on several examples.
- TEMPO as a alcohol protecting group saving a protection step/ excessive oxidant usage.
- Potentials in total synthesis
- SET oxidation by Ferroceium and combination with TEMPO

inseparable materials
ONLY TEMPO?