JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

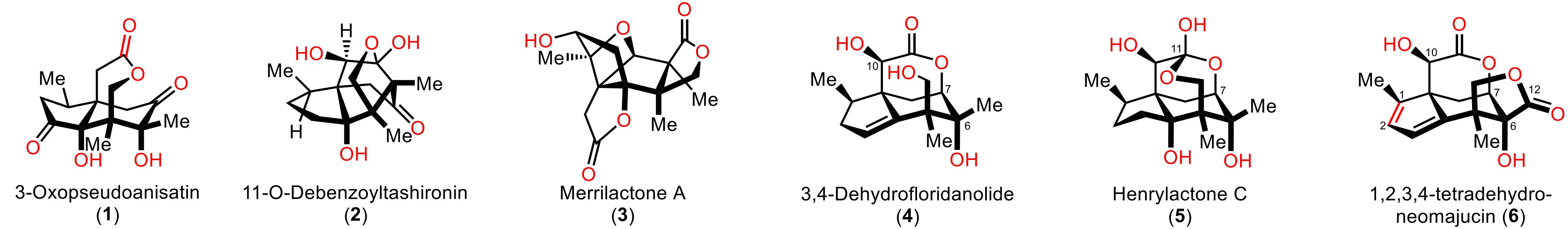
pubs.acs.org/JACS

Article

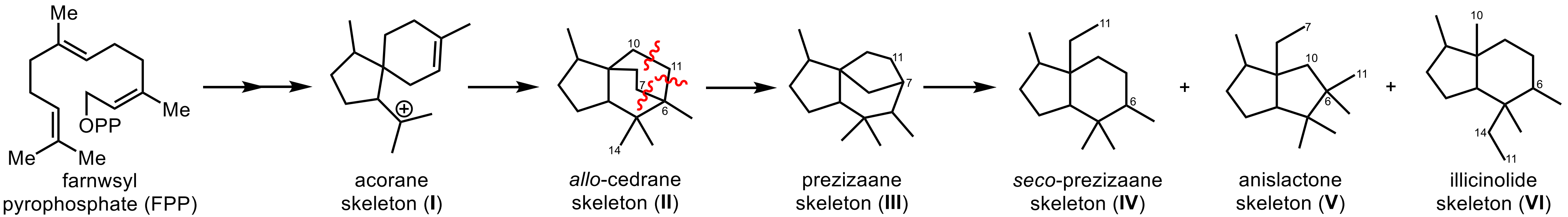
Divergent Total Syntheses of *Illicium* Sesquiterpenes through Late-Stage Skeletal Reorganization

Pengfei Fu,† Tao Liu,† Yang Shen,† Xin Lei, Tianjie Xiao, Peng Chen, Dongsheng Qiu, Zhen Wang, and Yandong Zhang*

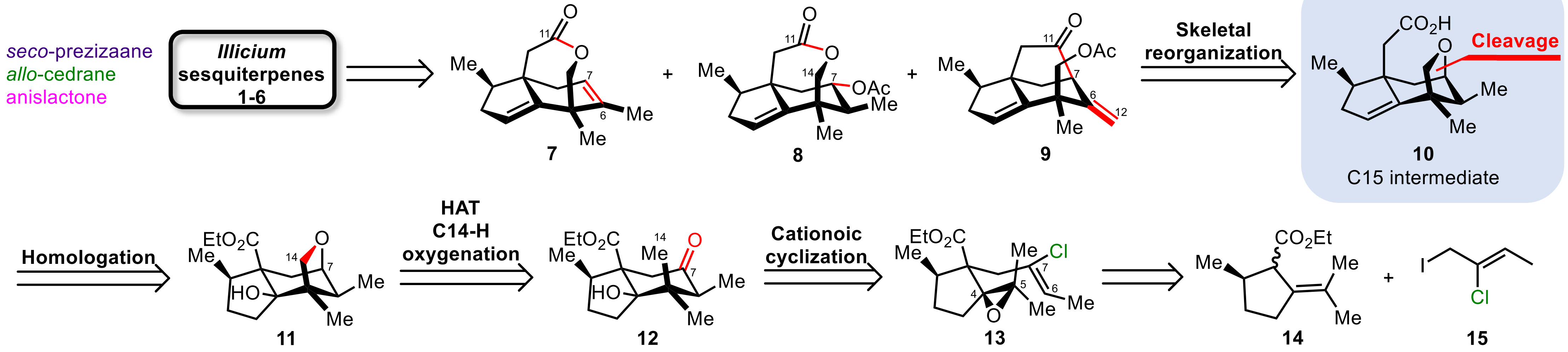
A. Selected examples of *Illicium* sesquiterpenes



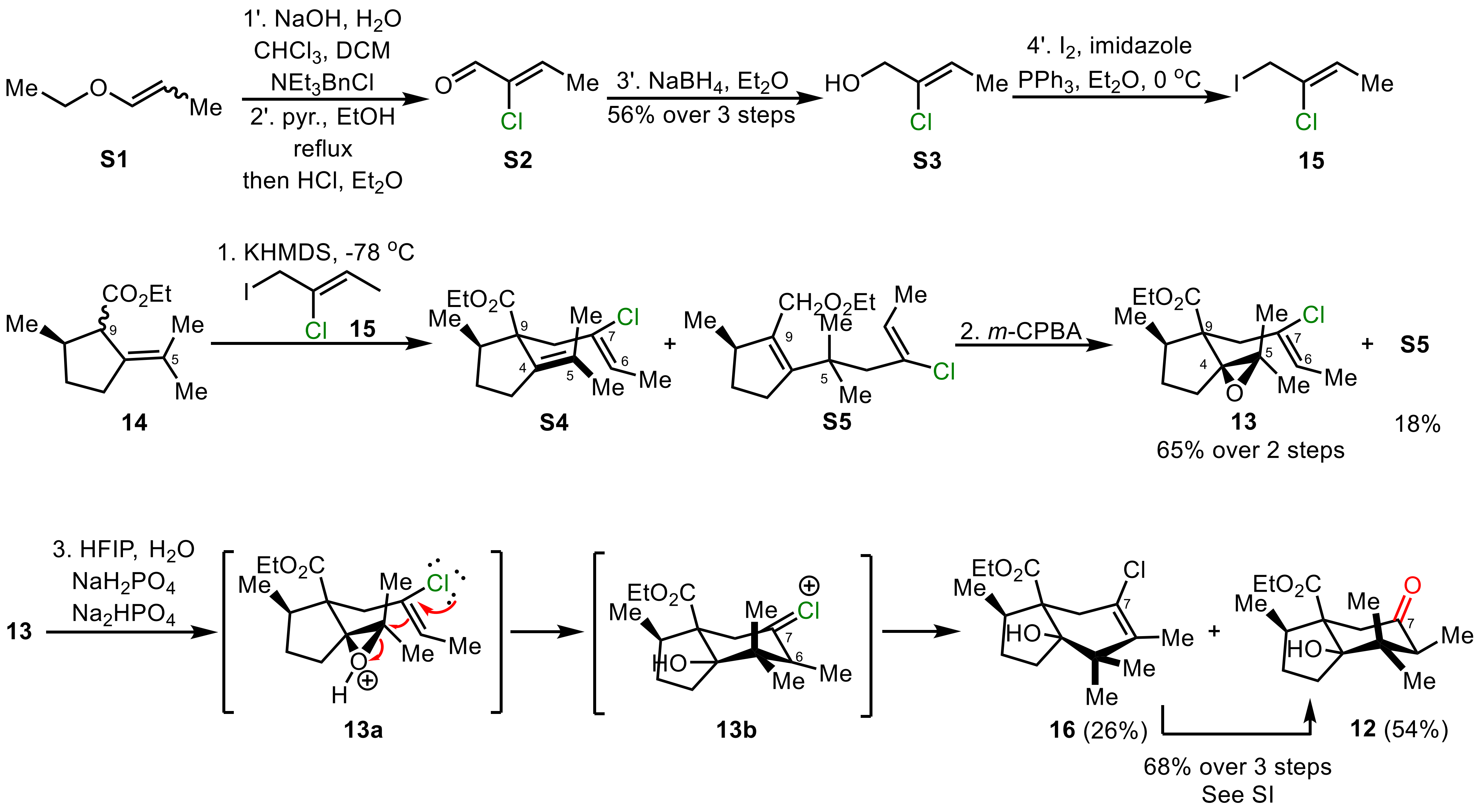
B. Proposed skeletal reorganization in biosynthesis of *Illicium* sesquiterpenes by Fukuyama and Huang



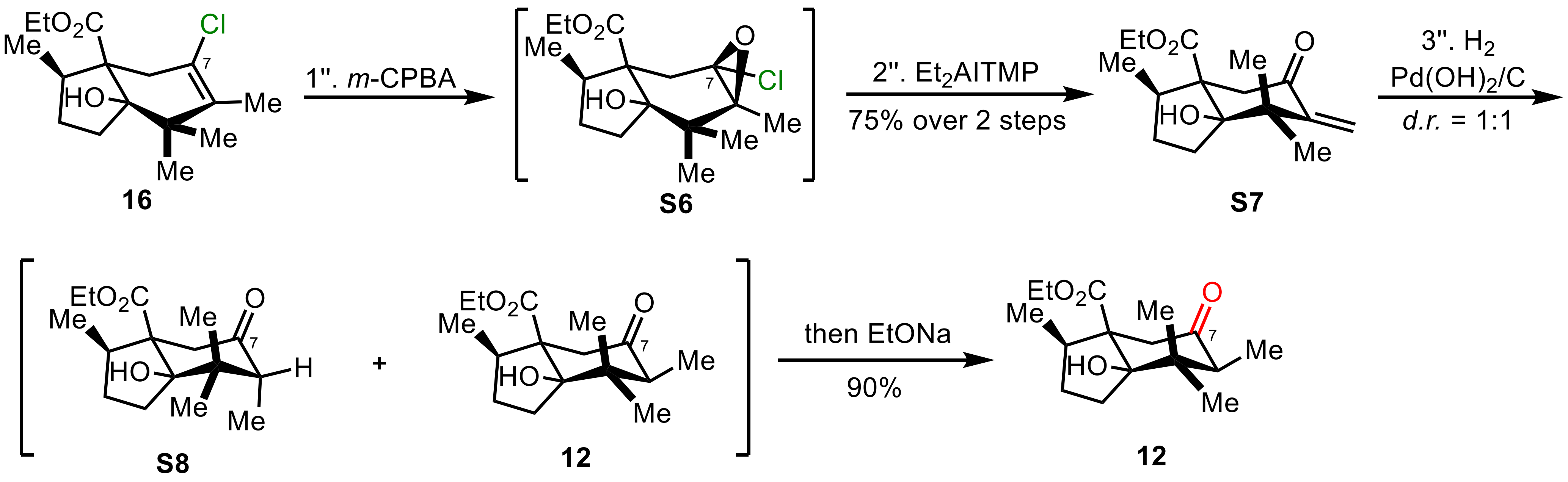
C. Divergent synthetic strategy based on late-stage skeletal reorganization (this work)

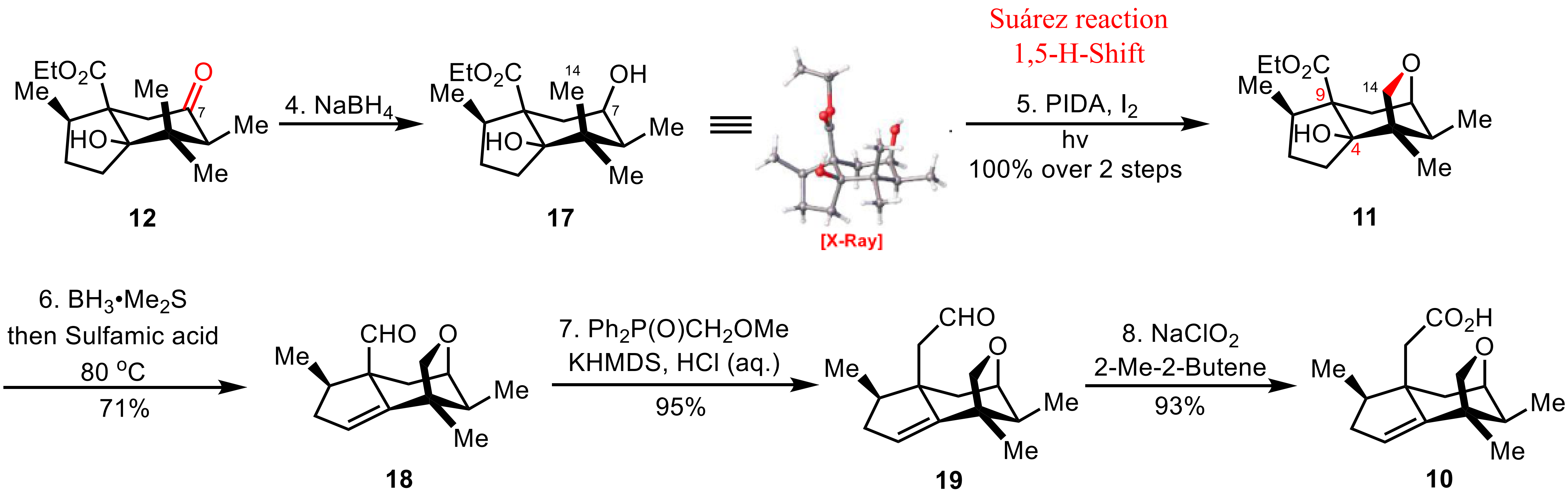


Scheme 1. Synthesis of C15 Intermediate 10

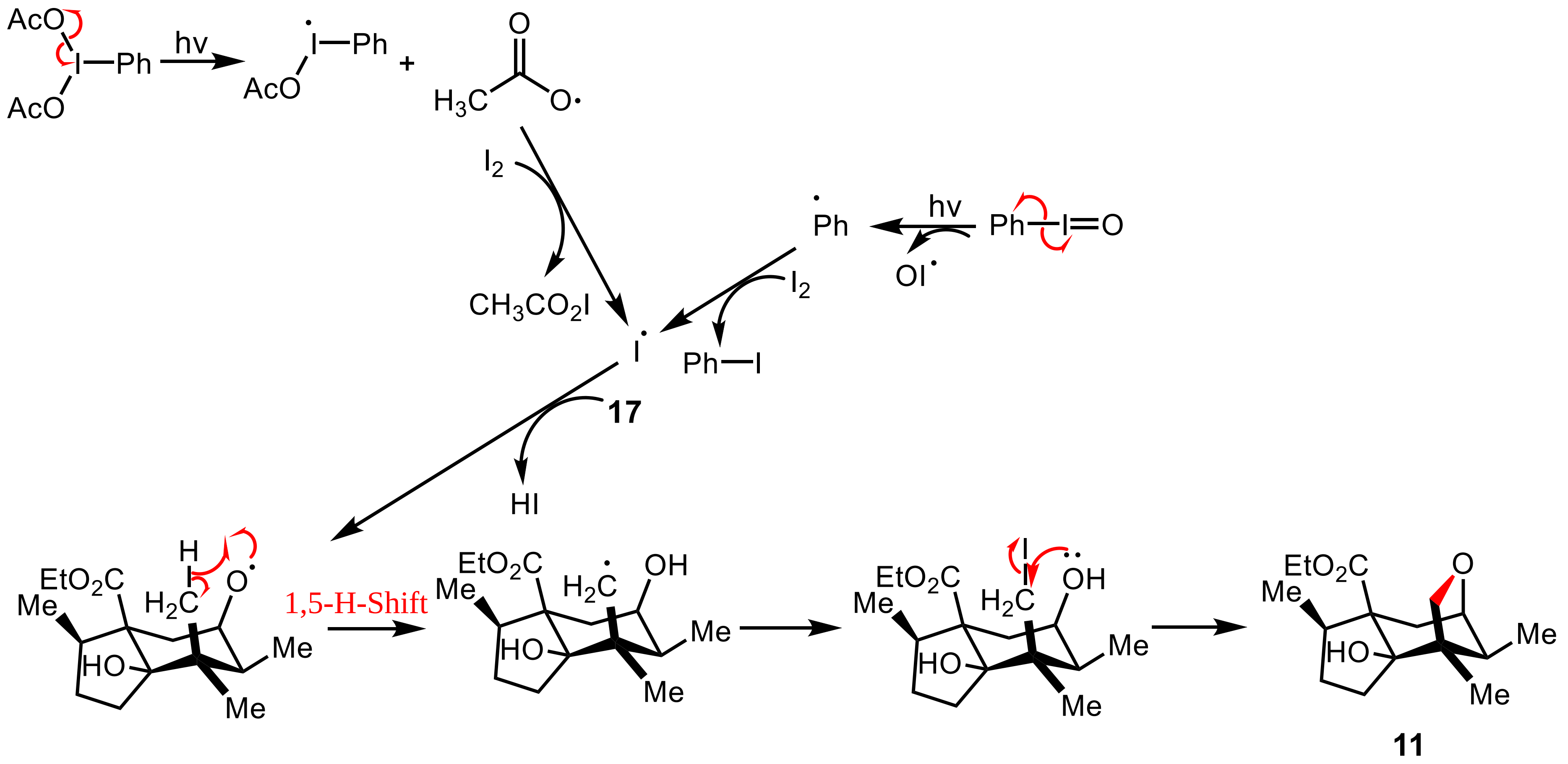


16→12


EtO2C
Me
Cl
7
HO
Me
Me
Me
16
1''. m-CPBA
S6
O
Cl
2''. Et2AlTMP
75% over 2 steps
S7
O
3''. H2
Pd(OH)2/C
d.r. = 1:1
S8
H
+
12
then EtONa
90%
12

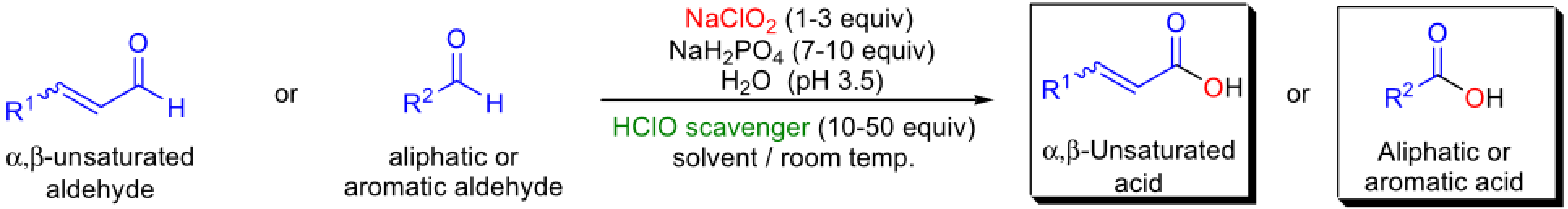

EtO2C
Me
HO
Me
O
7
Me
Me
12
4. NaBH4
EtO2C
Me
HO
14
Me
OH
7
Me
Me
17
[X-Ray]
Suárez reaction
1,5-H-Shift
5. PIDA, I2
hv
100% over 2 steps
EtO2C
Me
9
14
O
HO
4
Me
Me
11
6. BH3•Me2S
then Sulfamic acid
80 oC
71%
CHO
O
Me
Me
Me
18
7. Ph2P(O)CH2OMe
KHMDS, HCl (aq.)
95%
CHO
O
Me
Me
Me
19
8. NaClO2
2-Me-2-Butene
93%
CO2H
O
Me
Me
Me
10

17→11



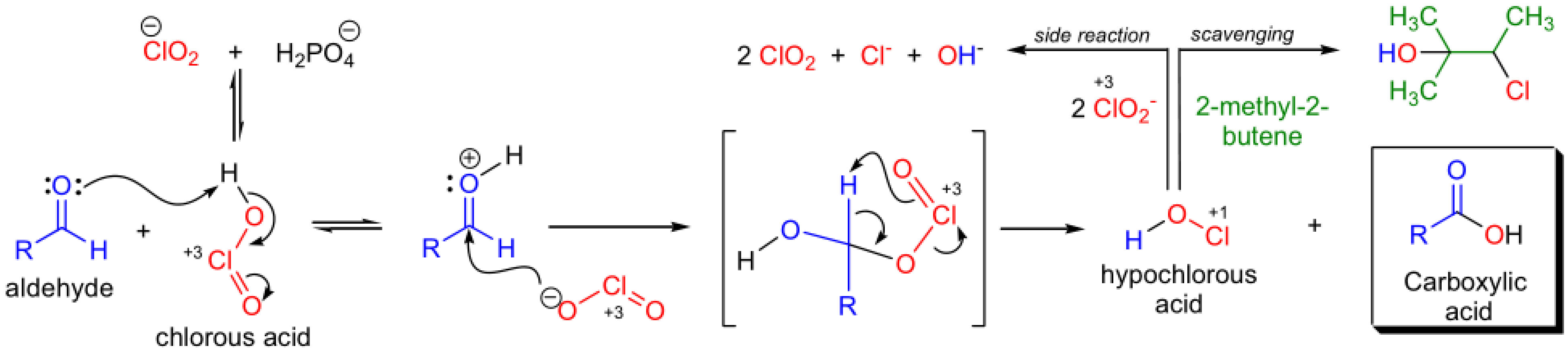
Tetrahedron Lett., **1984**, *25*, 1953.
John Wiley & Sons. Inc., **2010**, 2718.

PINNICK OXIDATION



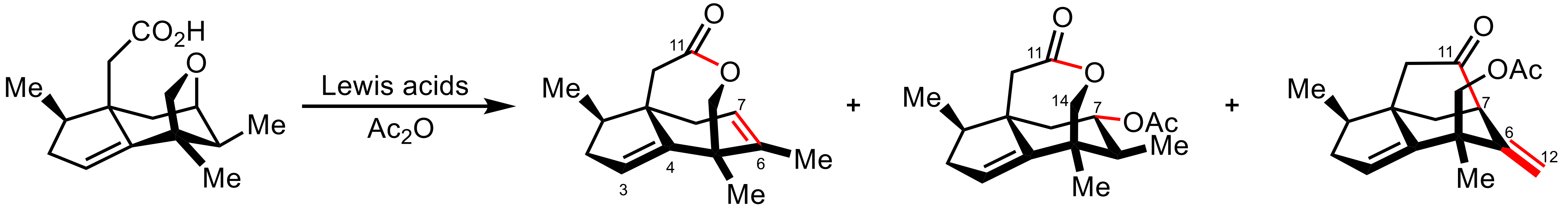
R^1 = H, alkyl, aryl, alkenyl, allyl; R^2 = alkyl, aryl, allyl, homoallyl; <u>scavenger</u> = 2-methyl-2-butene, H_2O_2, H_2NSO_3H, *m*-$C_6H_4(OH)_2$, DMSO; <u>solvent</u> = *t*-BuOH, *t*-BuOH/THF

<u>Mechanism:</u> [10,6]

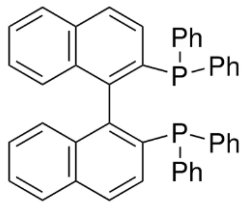


Scheme 2. Development of Divergent Skeletal Reorganization Strategy

A. Conditions Screening



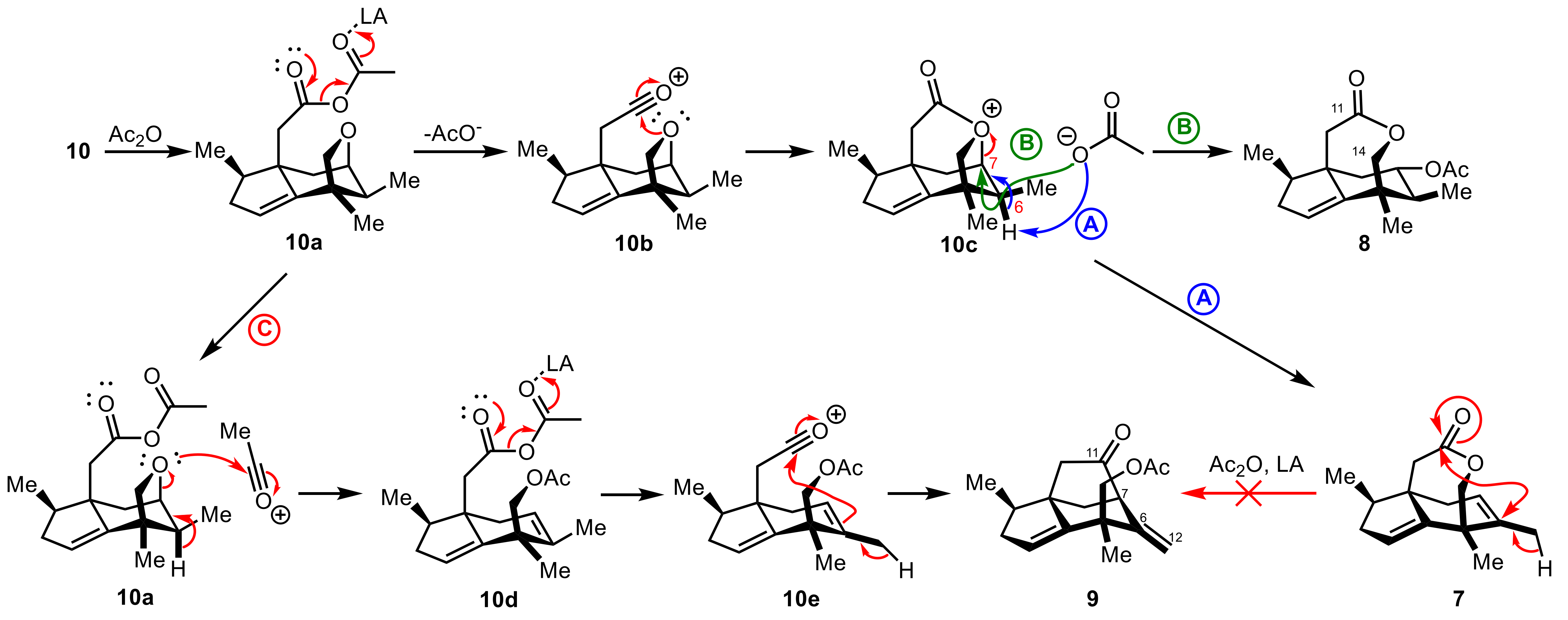
10 7 8 9



BINAP

entry	Lewis acid	additive & solvent & T	Time (h)	yields (%)		
				7	**8**	**9**
1	BCl_3	Ac_2O (8.0 equiv), CH_2Cl_2, 0 °C	1.0	45	0	0
2	$BF_3 \cdot OEt_2$	Ac_2O (8.0 equiv), CH_2Cl_2, 0 °C	1.0	90	7	0
3	TMSOTf	Ac_2O (8.0 equiv), CH_2Cl_2, 0 °C	1.0	75	12	0
4	$Sc(OTf)_3$	Ac_2O (8.0 equiv), CH_2Cl_2, 0 °C	0.5	74	21	1
5	$Bi(OTf)_3$	Ac_2O/CH_2Cl_2 (1:1), 0 °C	0.5	72	25	0
6	$Bi(OTf)_3$	Ac_2O/AcOH (1:1), 0 °C	0.5	47	50	2
7	$Bi(OTf)_3$	Ac_2O, 0 °C	0.5	80	10	2
8	TMSOTf	Ac_2O, −78 °C to 23 °C	8.0	19	6	30
9	TMSOTf	Ac_2O, (±)-BINAP, −78 °C to 23 °C	8.0	3	4	61

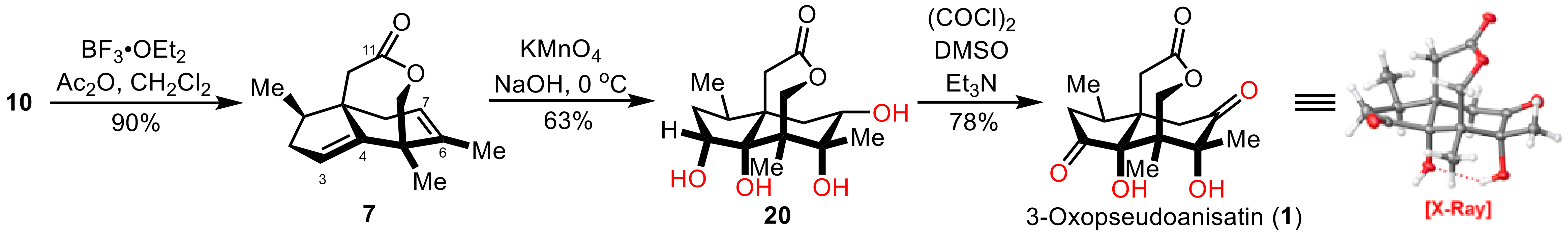
B. Mechanistic Proposal



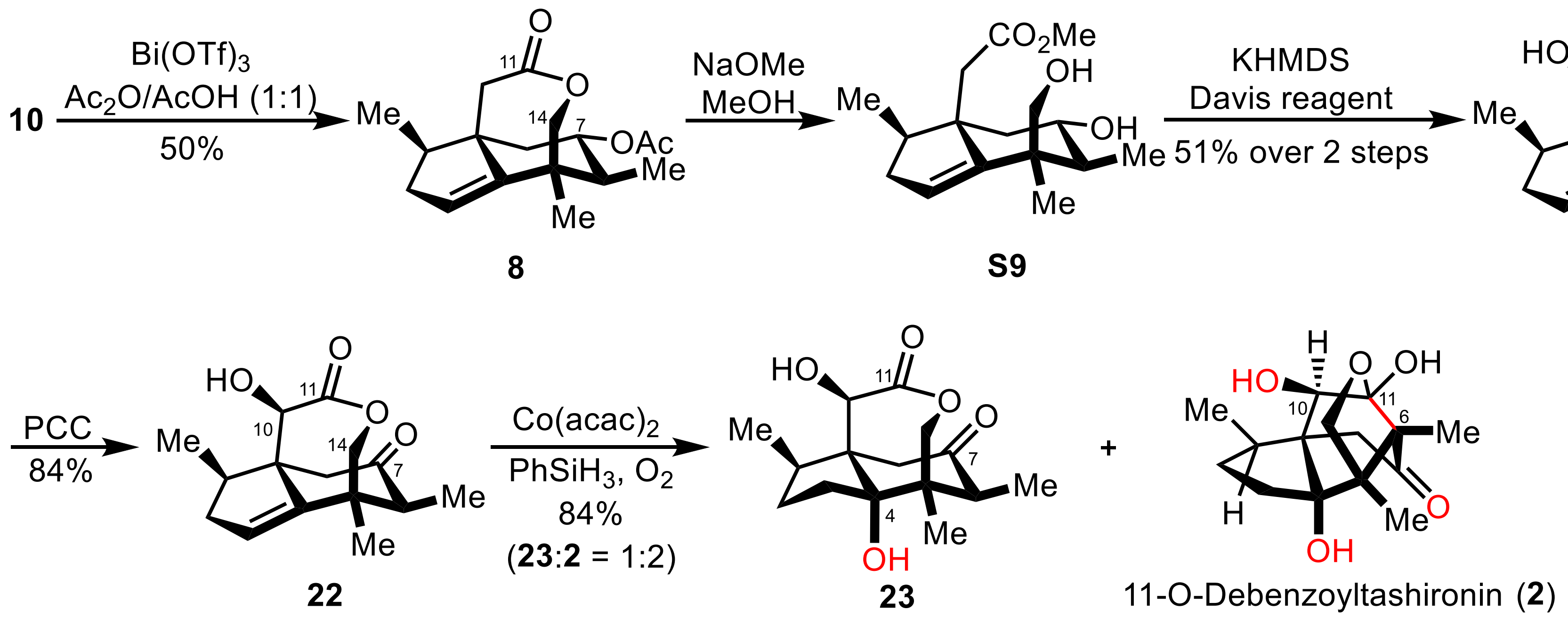
BINAP有利于乙酰
基阳离子的形成

Scheme 3. Divergent Total Synthesis of 13 Illicium Sesquiterpenes

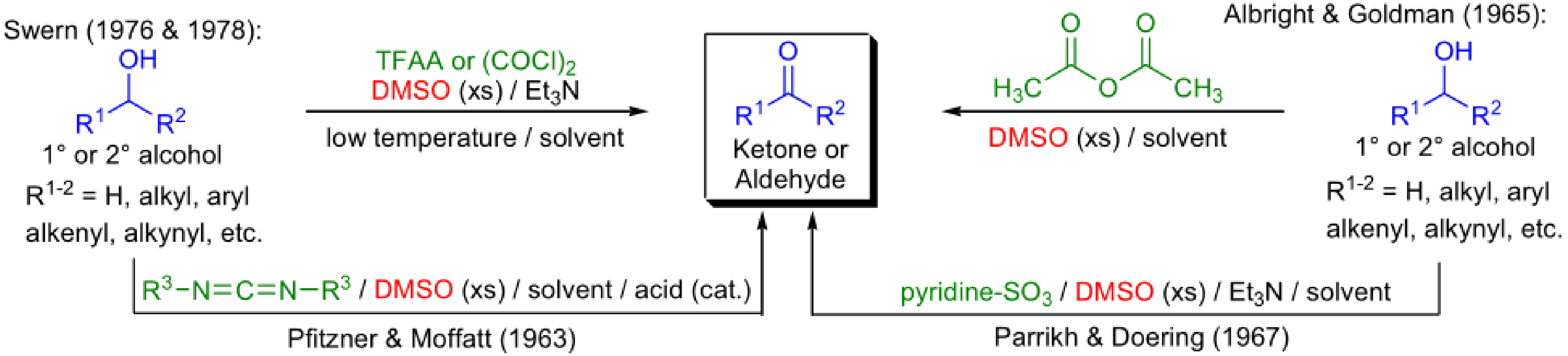
A. Entry to 3-oxopseudoanisatin

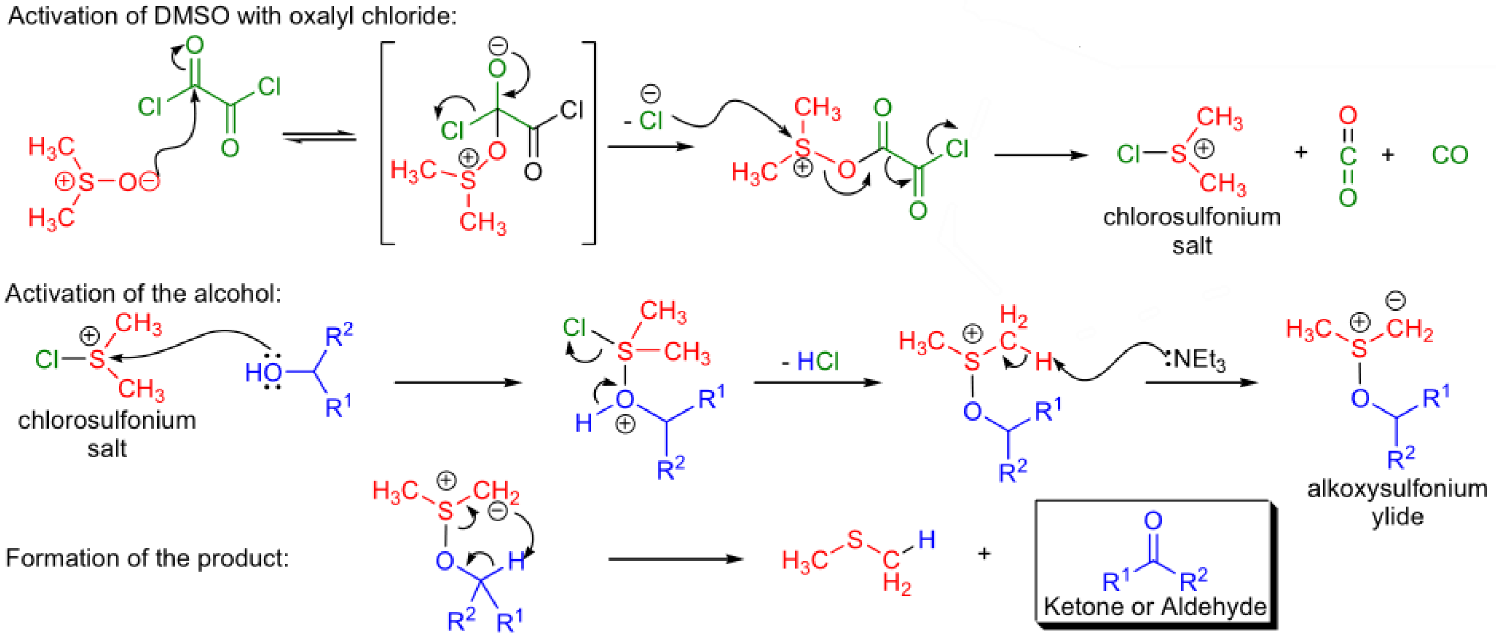


B. Entry to 11-O-debenzoyltashironin and formal syntheses of five anislactone sesquiterpenes

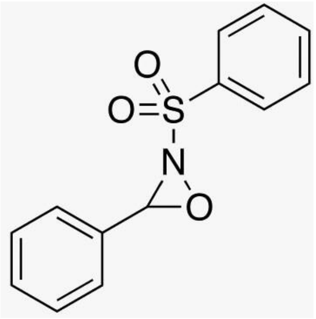


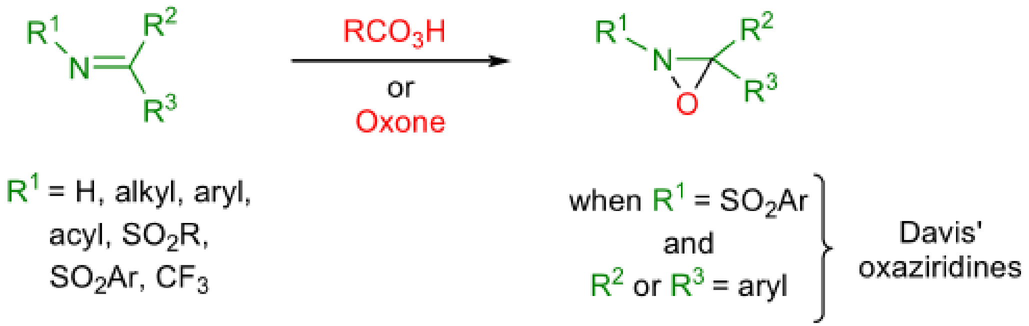
SWERN OXIDATION

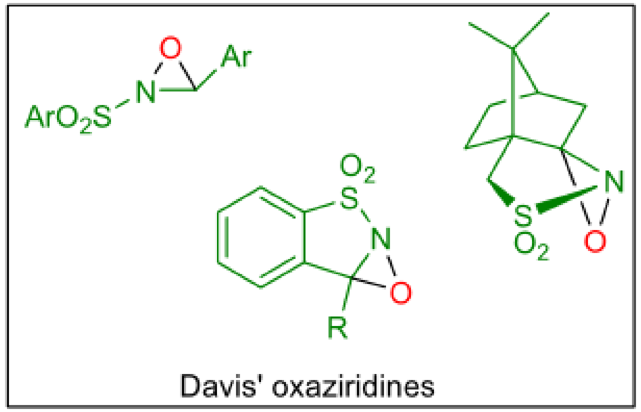


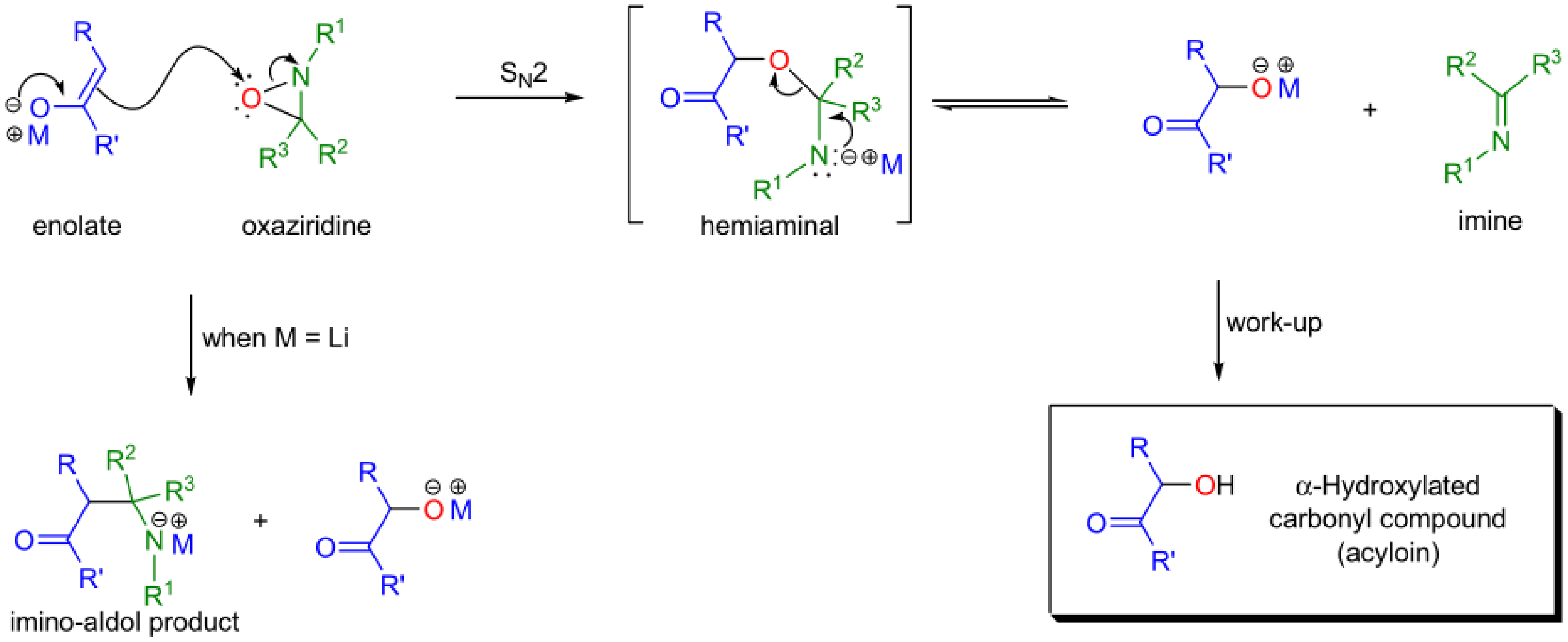


DAVIS' OXAZIRIDINE OXIDATIONS

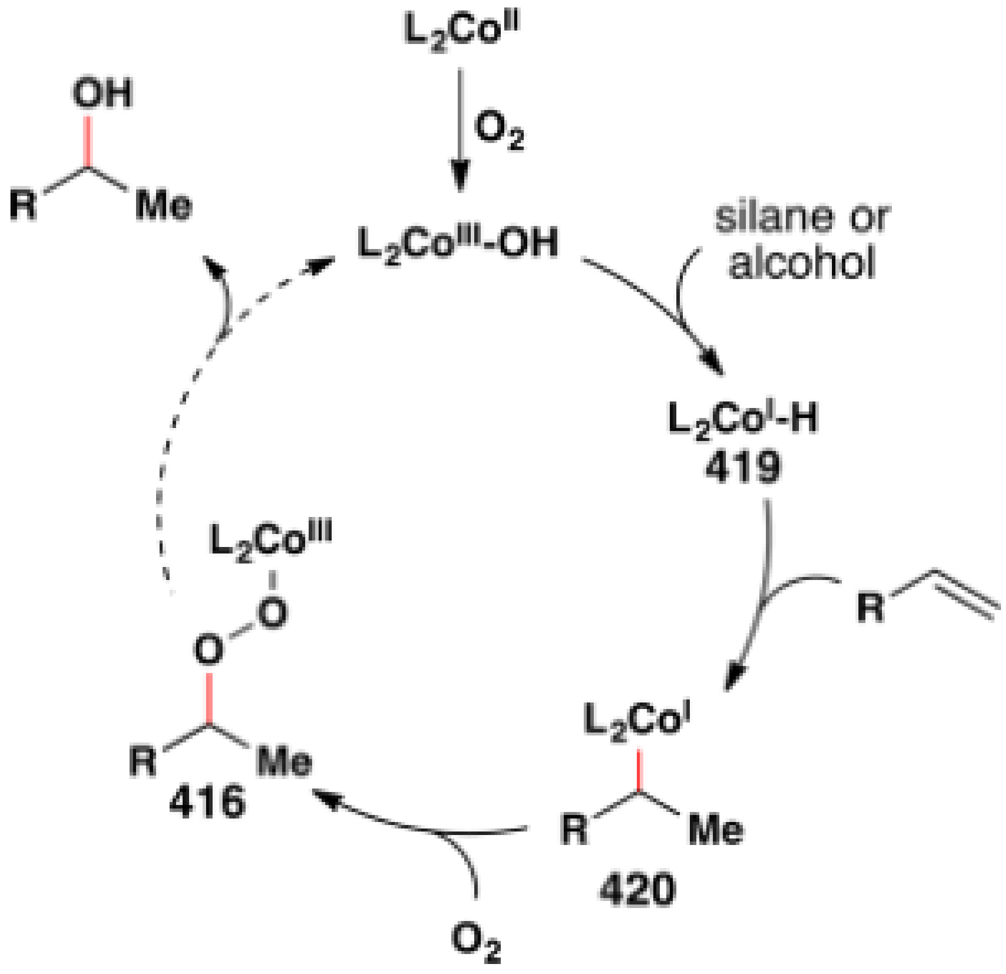




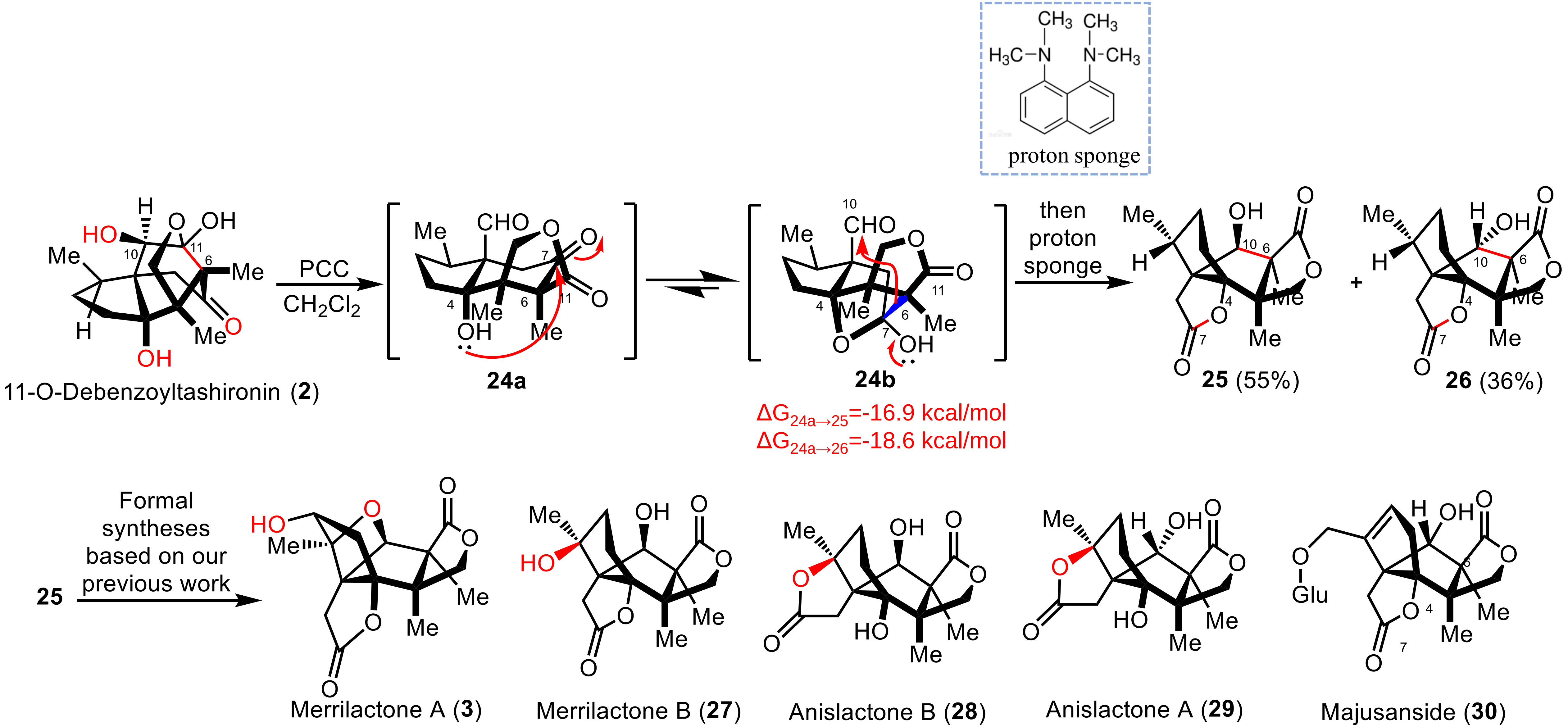




Mukaiyama Hydration

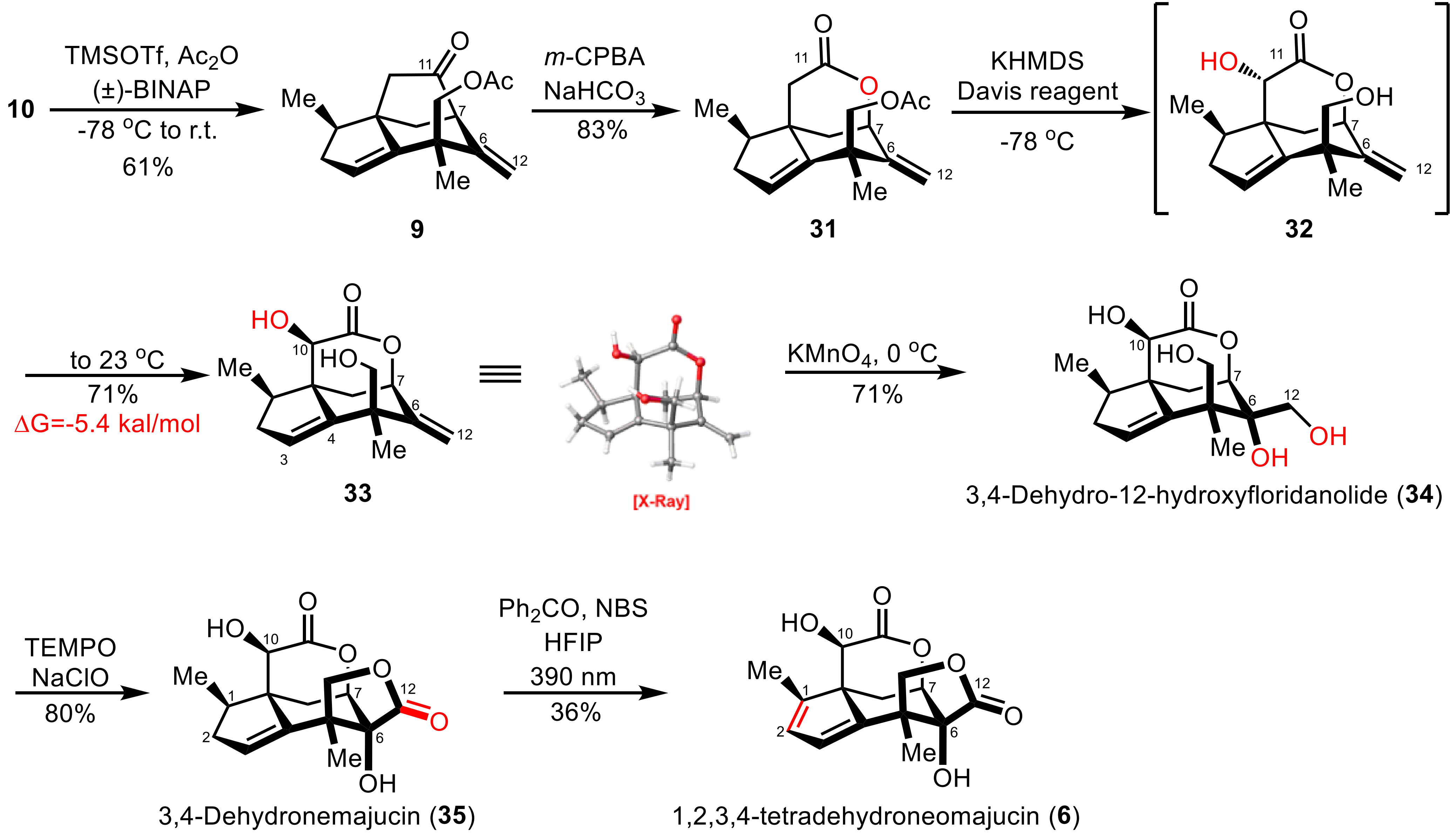


Chem. Rev., **2016**, *116*, 8912.

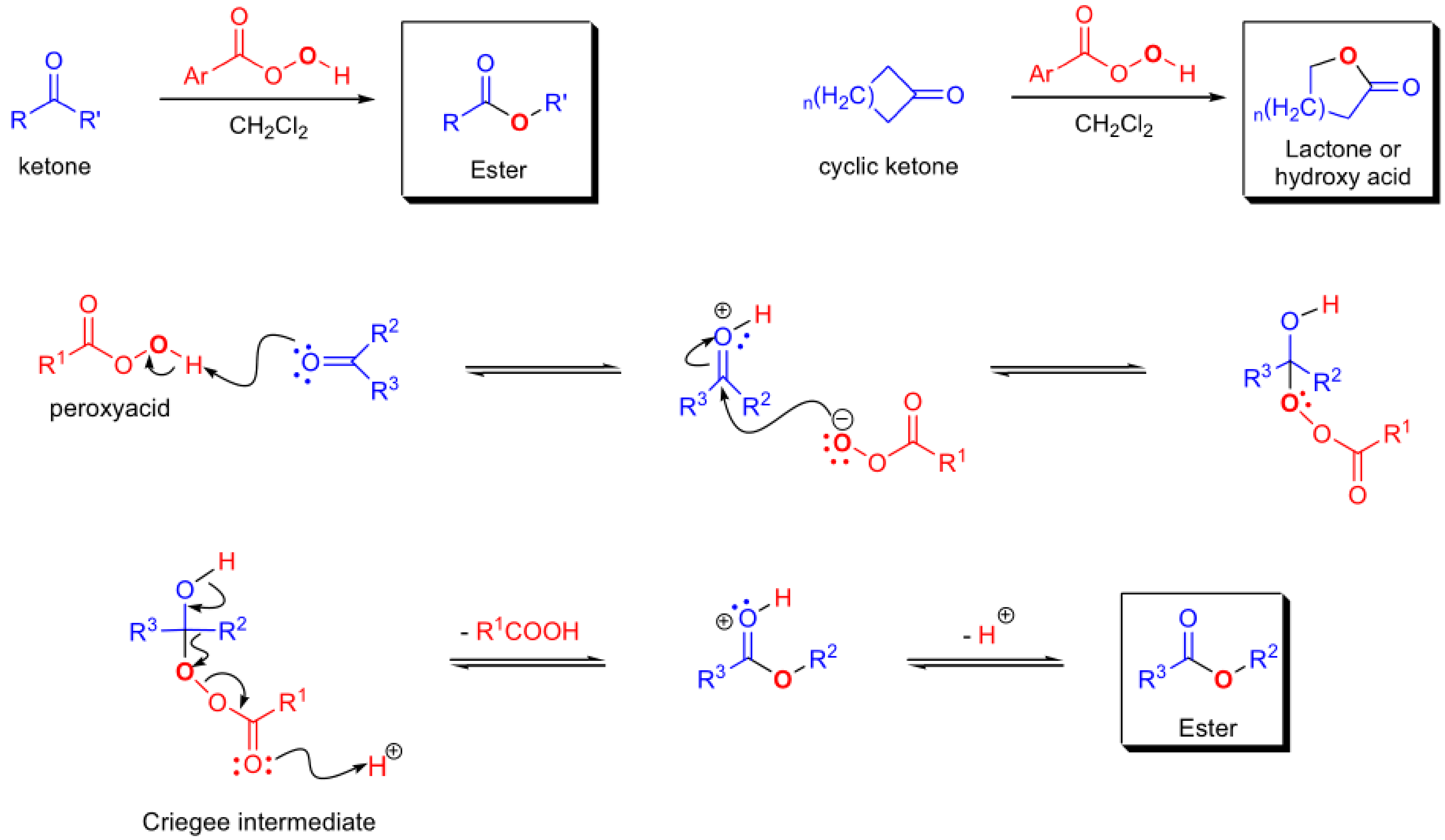


proton sponge
11-O-Debenzoyltashironin (2)
PCC
CH2Cl2
24a
24b
then
proton
sponge
25 (55%)
26 (36%)
ΔG24a→25=-16.9 kcal/mol
ΔG24a→26=-18.6 kcal/mol
25
Formal
syntheses
based on our
previous work
Merrilactone A (3)
Merrilactone B (27)
Anislactone B (28)
Anislactone A (29)
Majusanside (30)

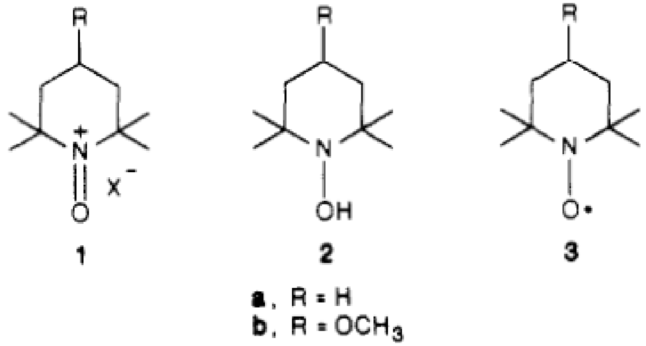
C. Entry to seco-prezizaane sesquiterpenes



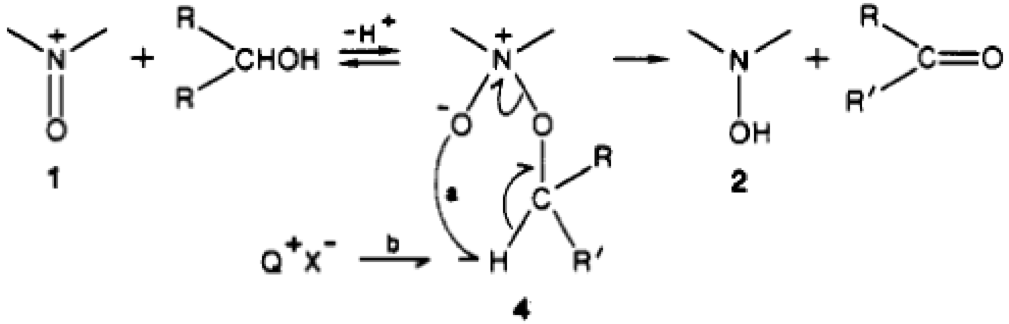
BAEYER-VILLIGER OXIDATION/REARRANGEMENT

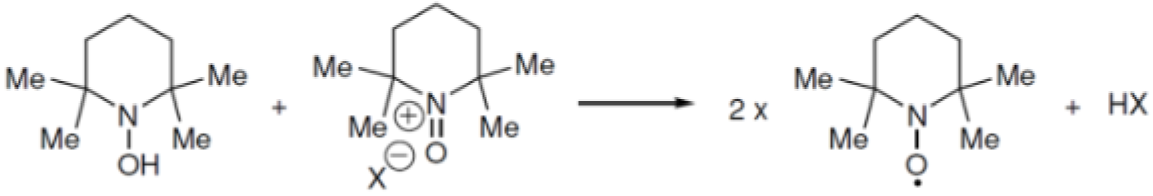


$$RCH_2OH + NaOCl \xrightarrow[\textbf{3b}\ (0.01\ \text{mol equiv}),\ 0\ ^\circ C]{CH_2Cl_2\text{–}H_2O,\ NaHCO_3,\ KBr\ (0.1\ \text{mol equiv})} RCHO \quad (1)$$

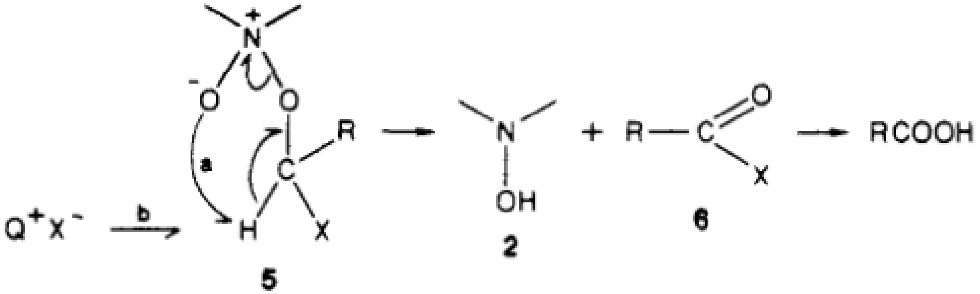


Scheme I

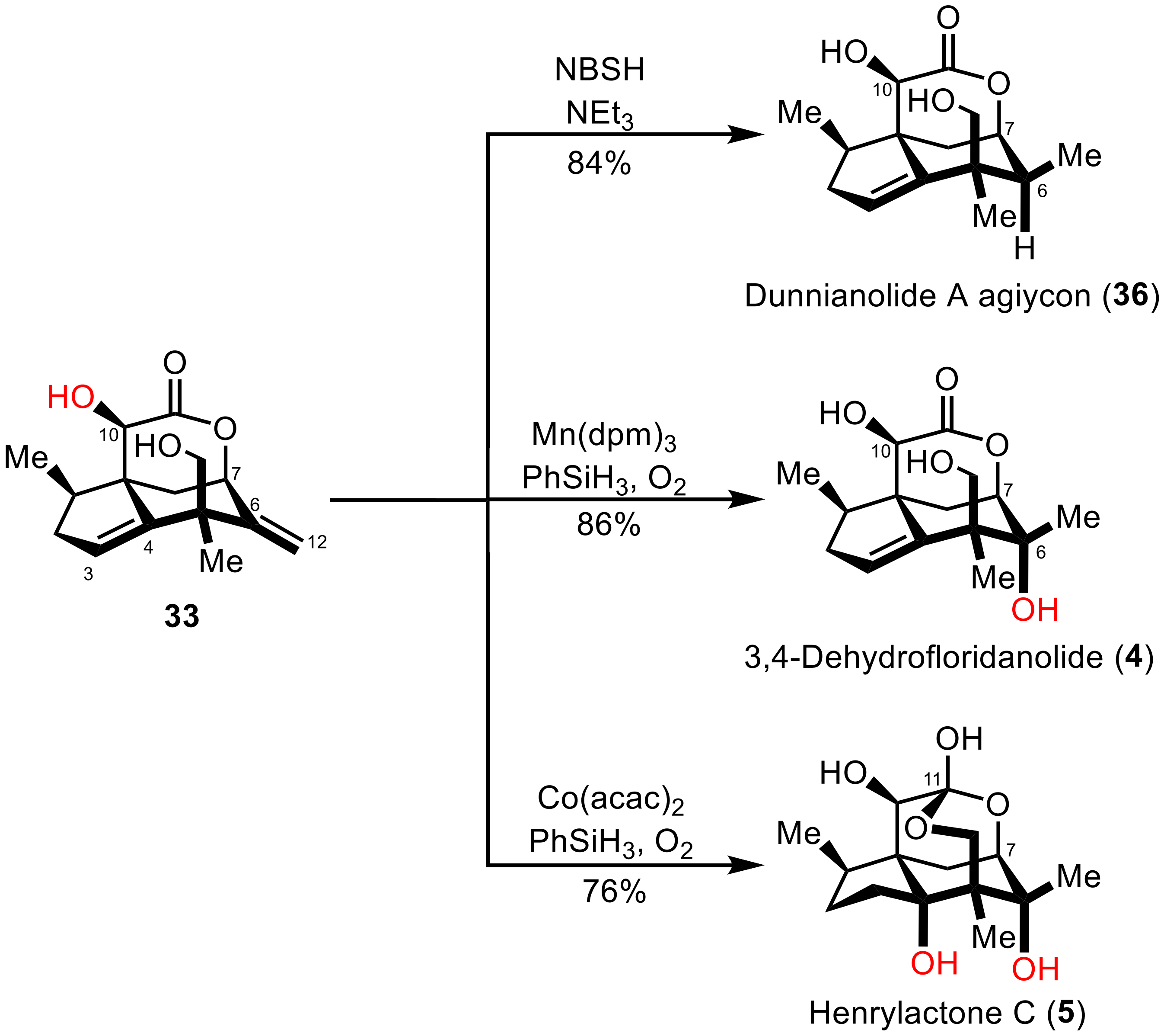


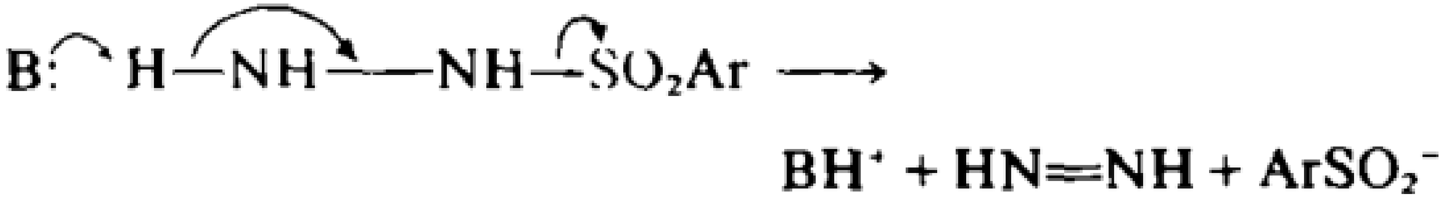


Scheme II



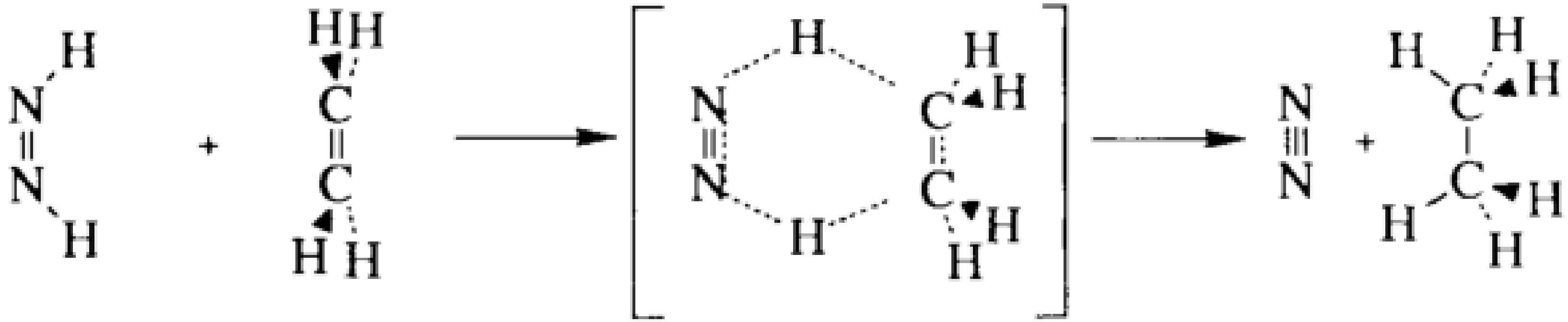
J. Org. Chem., **1987**, *52*, 12.


HO
O
O
10
HO
Me
7
6
12
4
3
Me
33
NBSH
NEt3
84%
Dunnianolide A agiycon (36)
Mn(dpm)3
PhSiH3, O2
86%
OH
3,4-Dehydrofloridanolide (4)
Co(acac)2
PhSiH3, O2
76%
11
OH
Henrylactone C (5)



Scheme 1.

Tetrahedron., **1976**, *32*, 2157.



John Wiley & Sons, Inc., **1991**, *91*, 156.