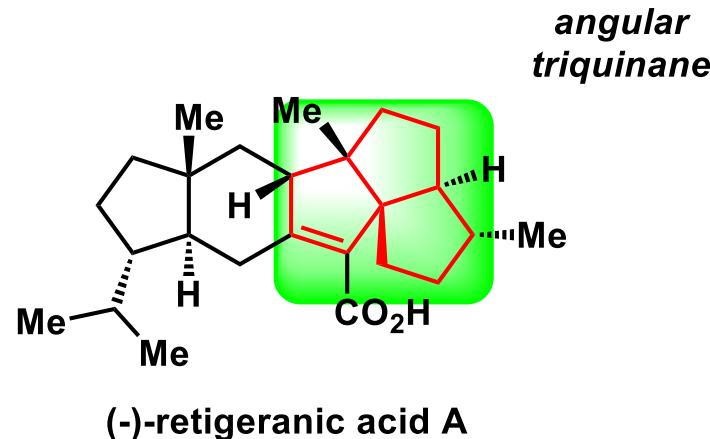
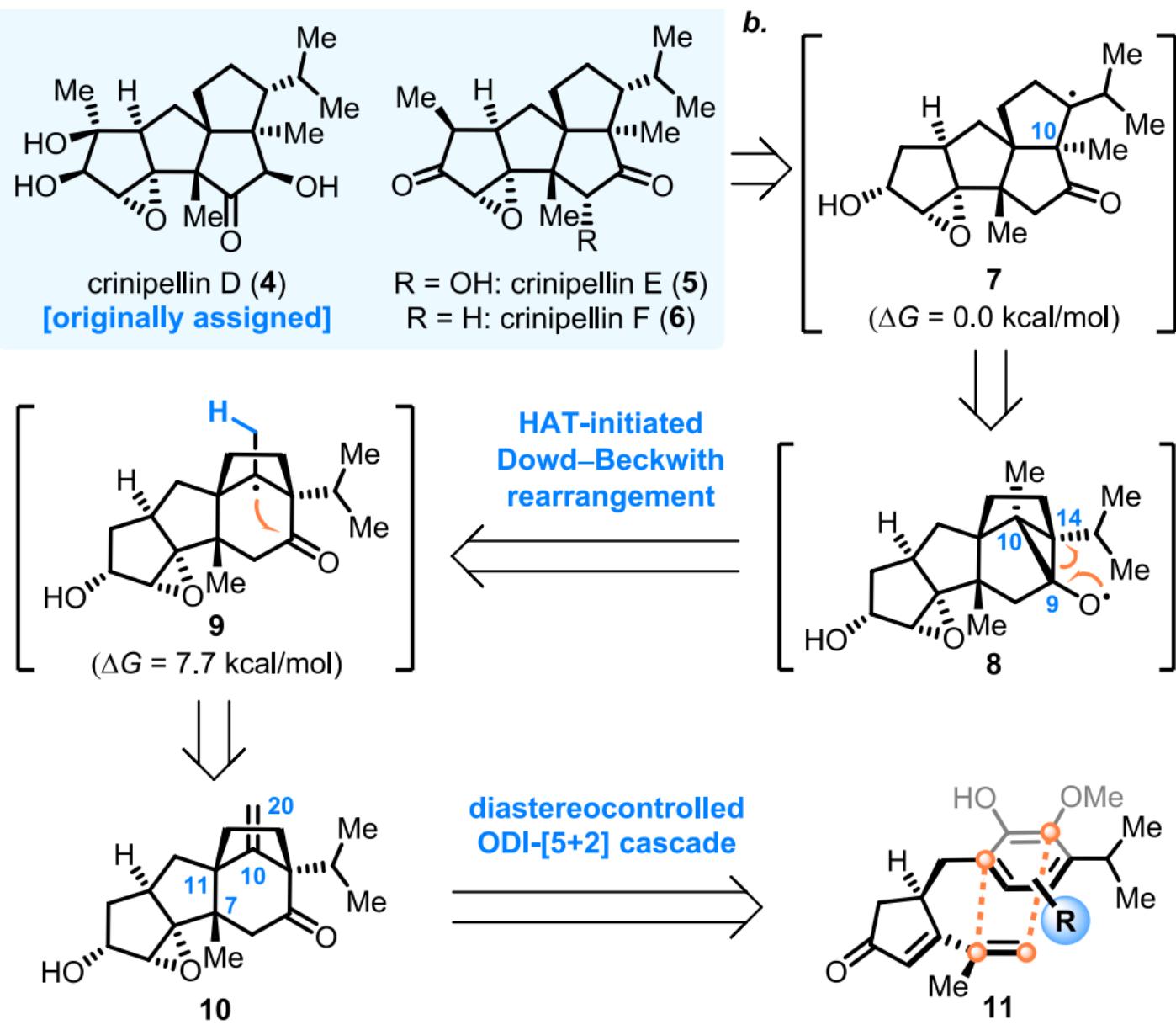


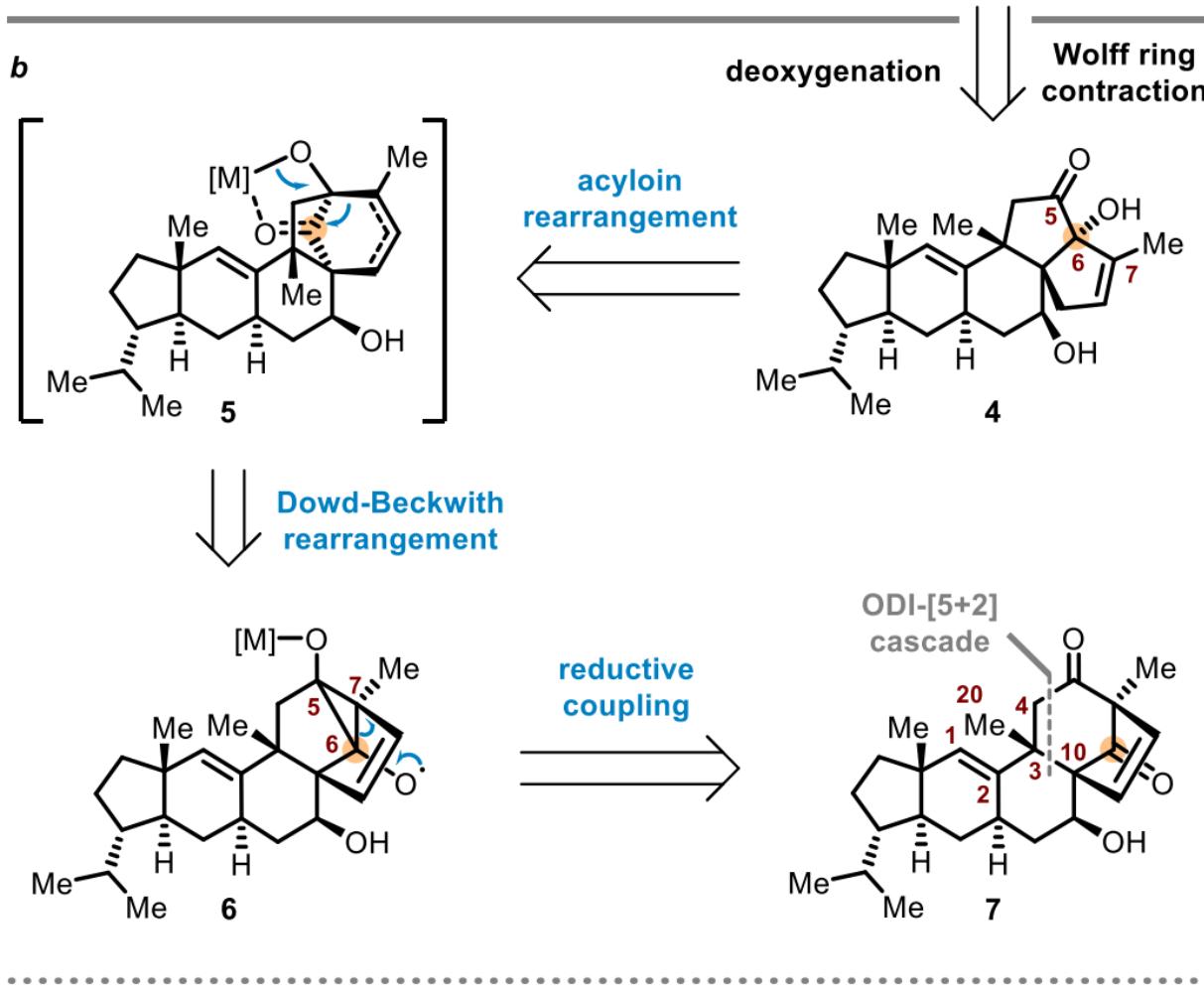
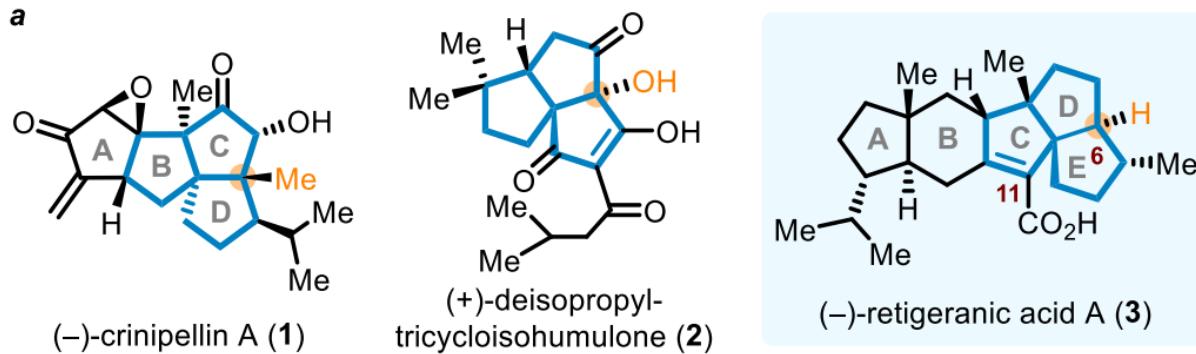
Total Synthesis of (–)-Retigeranic Acid A: A Reductive Skeletal Rearrangement Strategy

Dongyu Sun,[†] Ruyi Chen,[†] Dongmin Tang,[†] Qidong Xia, Yifan Zhao, Chun-Hui Liu, and Hanfeng Ding^{*}

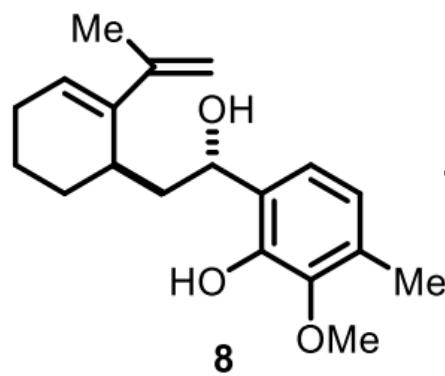


*angular
triquinane*

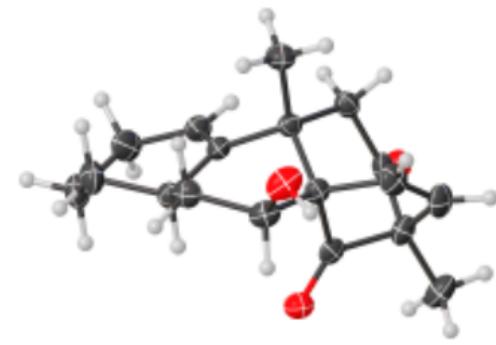


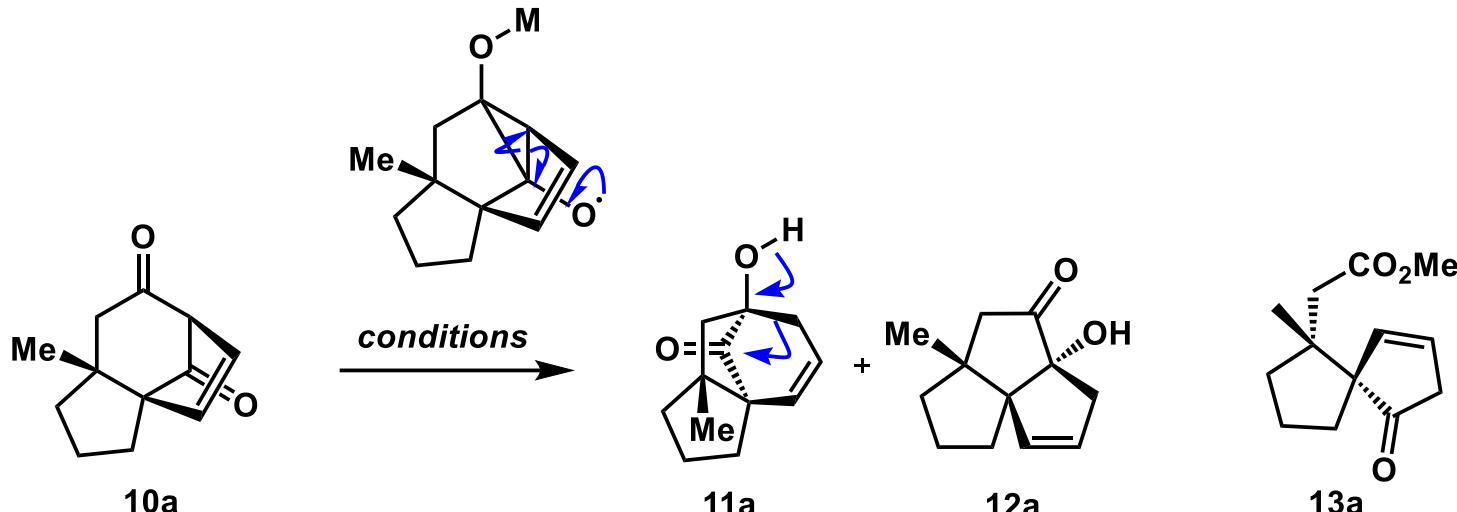


c



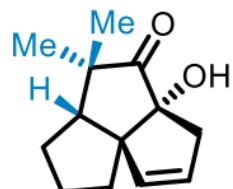
PIFA, K_2CO_3
60%



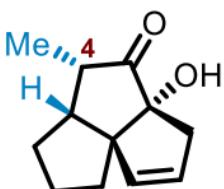


entry	conditions	yield (%) ^b	
		11a	12a
1 ^{c,d}	<i>n</i> -Bu ₃ SnH, AIBN, toluene, 90 °C	0	0
2 ^d	TiCl ₄ , Zn, THF, 0 °C	0	0
3 ^d	VCl ₃ (THF) ₃ , Zn, CH ₂ Cl ₂ , 25 °C	0	0
4	SmI ₂ , THF, 0 to 25 °C	<5	0
5 ^e	SmI ₂ , THF/MeOH, 0 °C	<5	0
6	SmI ₂ , THF/ <i>t</i> -BuOH, 0 °C	73	0
7	SmI ₂ , THF/ <i>t</i> -AmOH, 0 °C	70	0
8	SmI ₂ , THF/ <i>t</i> -BuOH, 0 °C; then KOH ^f	<5	65

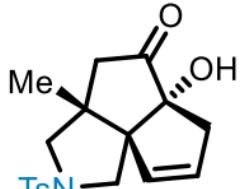
^aReaction conditions: **10a** (0.2 mmol) and low-valent metal (2.2 equiv) in solvent/cosolvent (4.5 mL/0.5 mL) at indicated temperature. ^bIsolated yields. ^c*n*-Bu₃SnH (2.0 equiv), AIBN (0.5 equiv). ^dNo reaction. ^e**13a** (80% yield). ^fKOH (2.0 equiv).



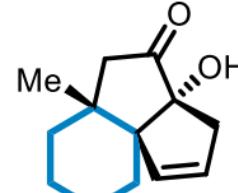
12b, 62%



12c, 56%
(1.8:1 dr at C4)



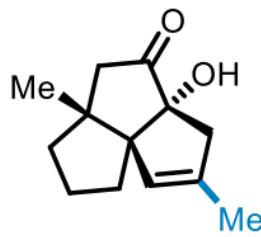
12d, 45%



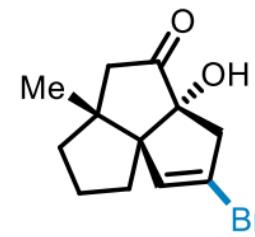
12e, 60%



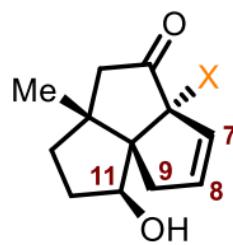
R = Me: **12f**, 62%
R = Br: **12g**, 60%
R = Ph: **12h**, 65%



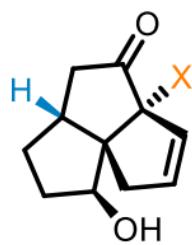
12i, 55%



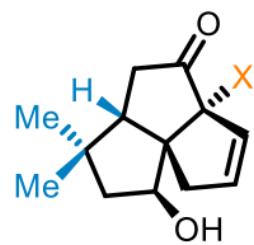
12j, 57%



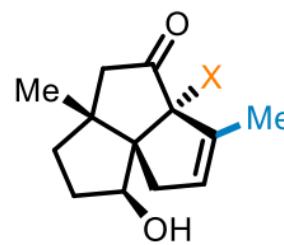
X = OH: **12k**, 65%^a
X = H: **12k'**, 60%^{a,b}



X = OH: **12l**, 56%^a
X = H: **12l'**, 52%^{a,b}

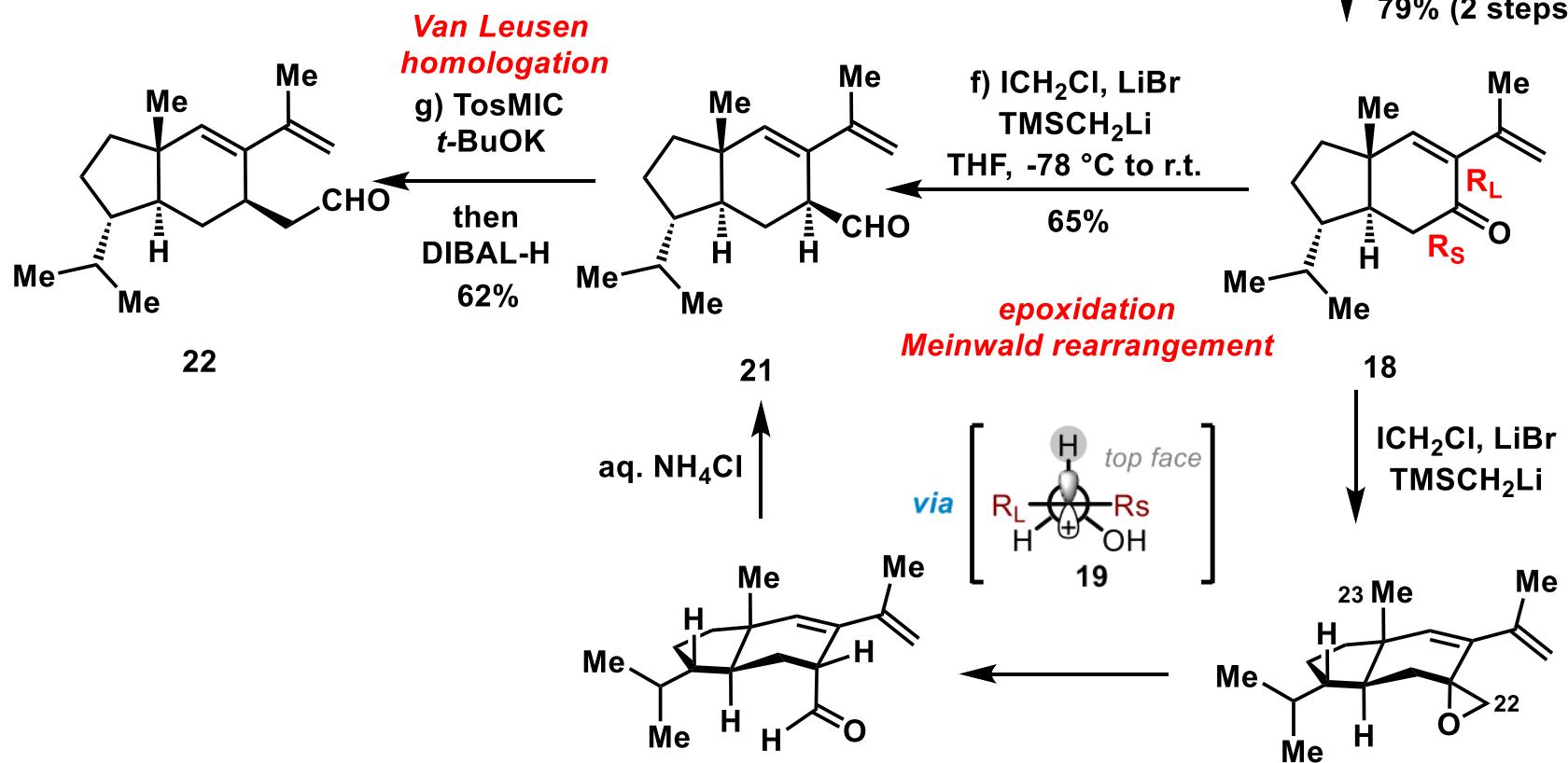
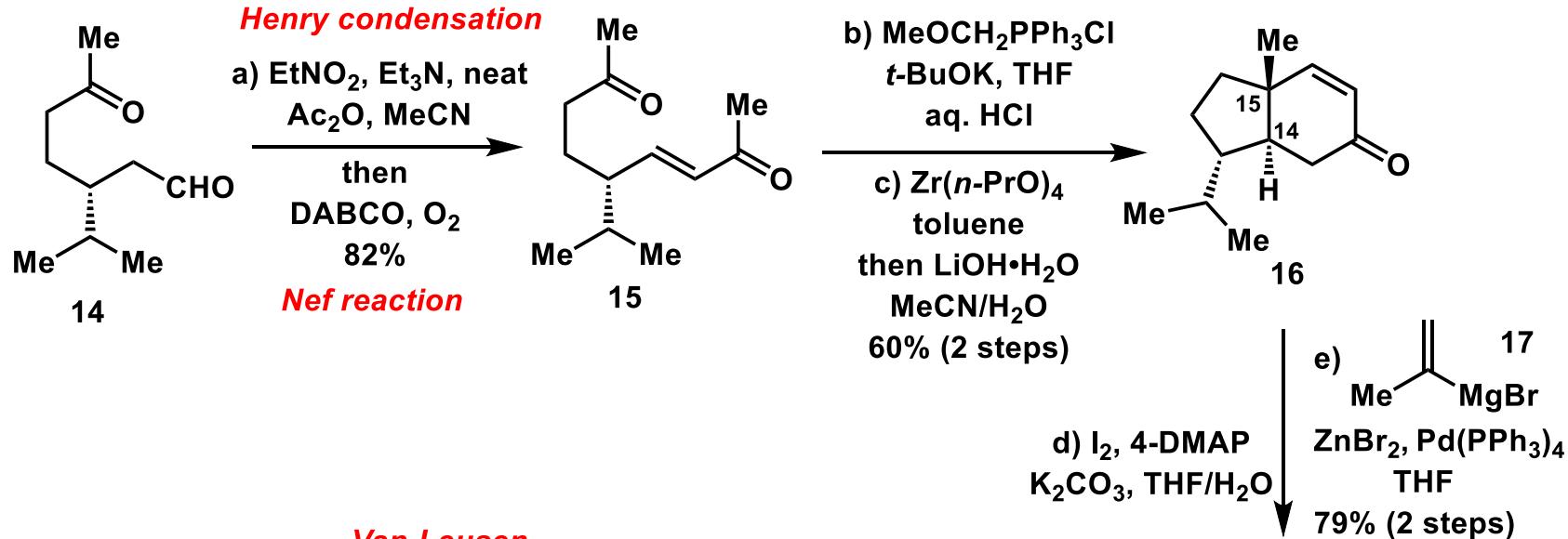


X = OH: **12m**, 55%^a
X = H: **12m'**, 50%^{a,b}

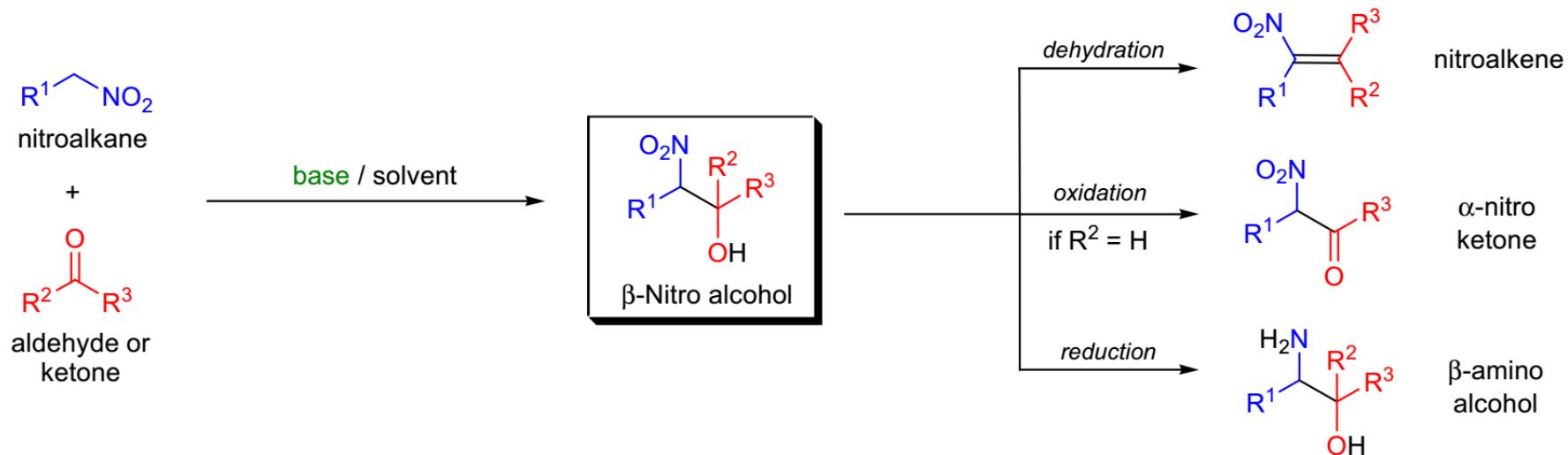


X = OH: **12n**, 70%^a
X = H: **12n'**, 64%^{a,b}

Figure 1. Scope of the reductive skeletal rearrangement. Reaction conditions: entry 8, Table 1. ^aPerformed at 0–60 °C without addition of KOH. ^bSmI₂ (4.4 equiv).

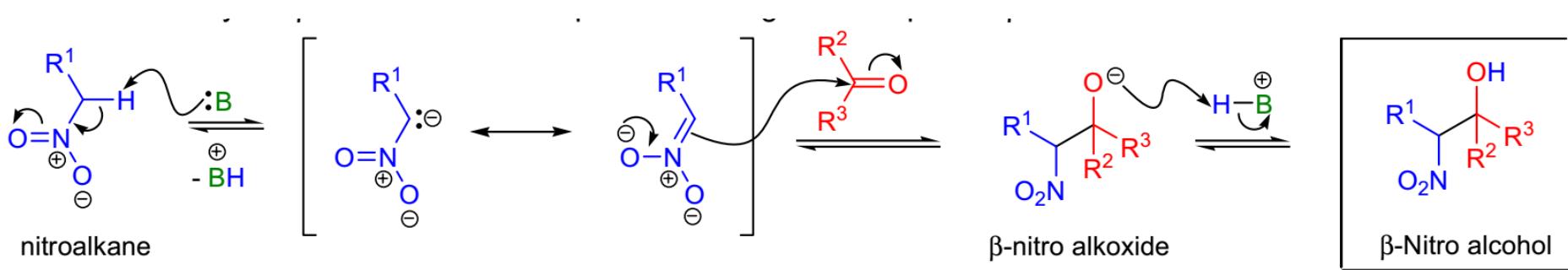


HENRY REACTION



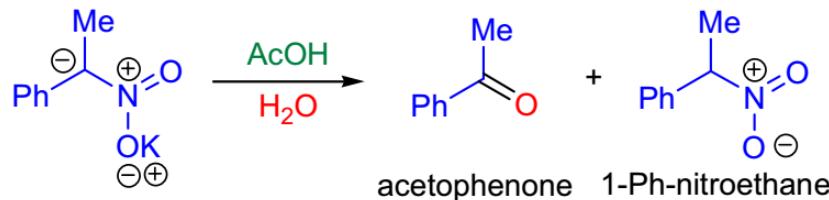
R^1 = alkyl, aryl, CO_2R , alkenyl; R^2, R^3 = alkyl, aryl, H; base = NR_3 , DBU, DBN, PAP, TMG, KF, TBAF, Al_2O_3 , $La_3(OR)_9$, $NaOH$, $NaOR$, amberlyst A-21, etc.

Mechanism:

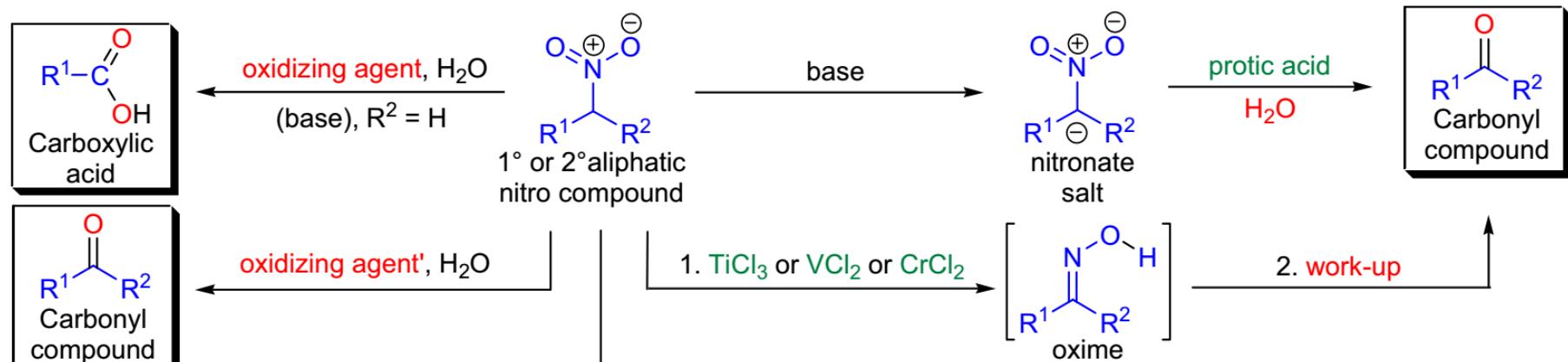
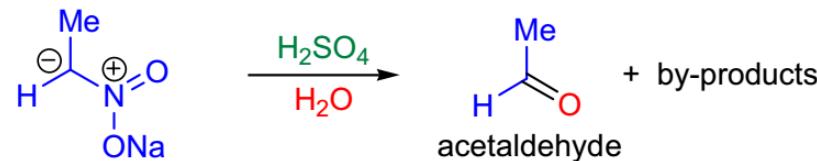


NEF REACTION

Konovalov (1893):

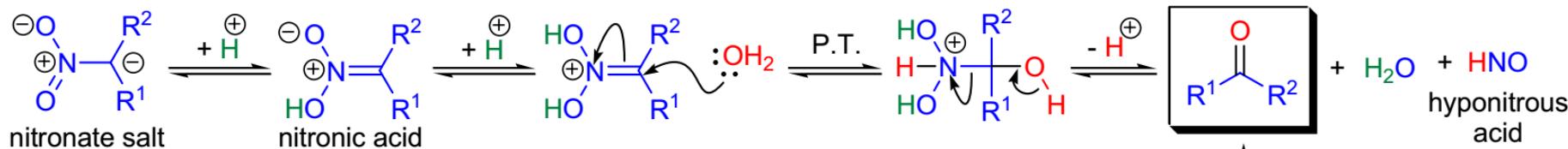


Nef (1894):

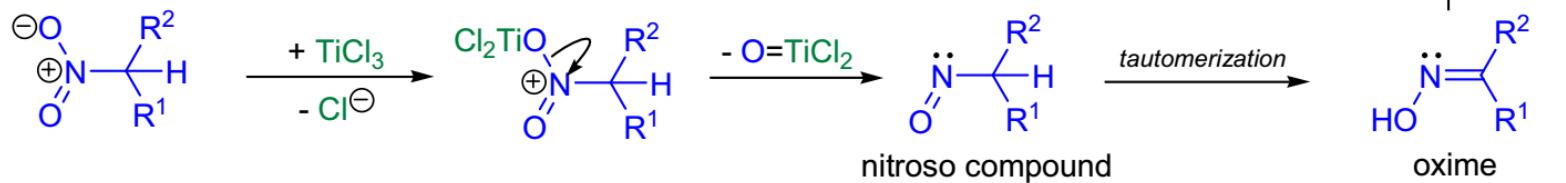


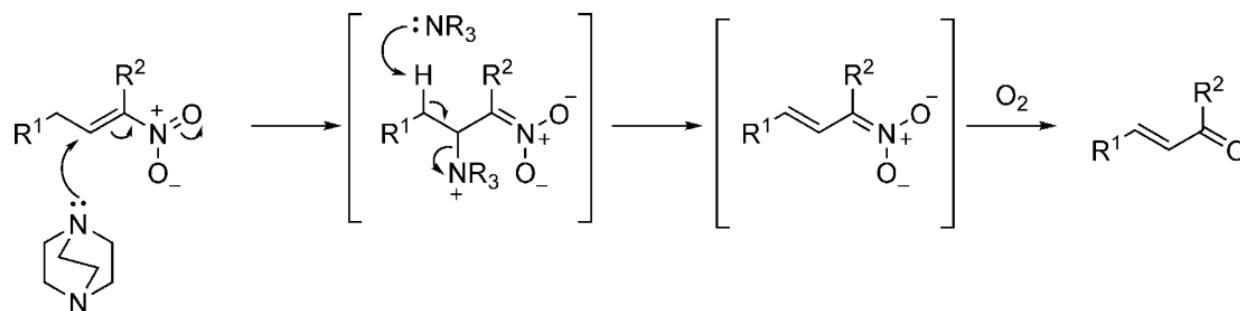
Mechanism:

Nef reaction under acidic conditions:

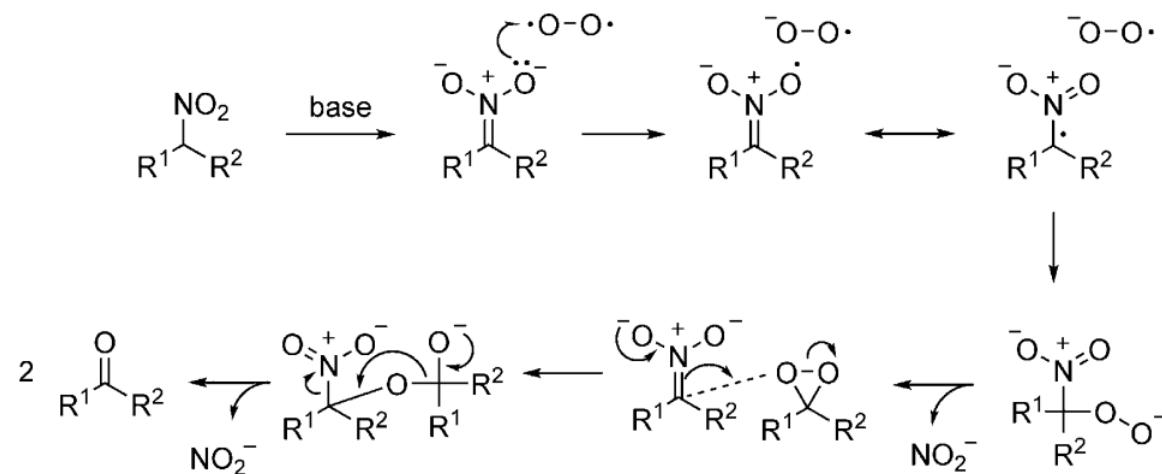


Nef reaction under reductive conditions:

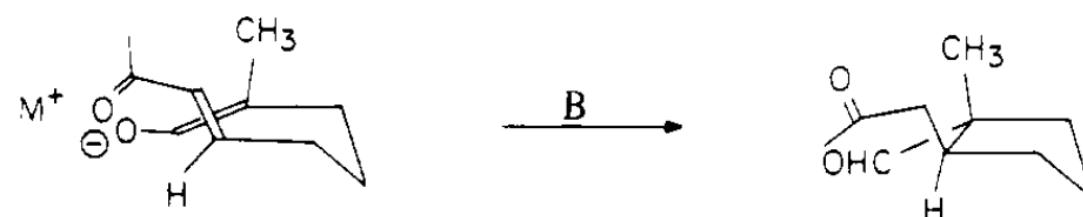
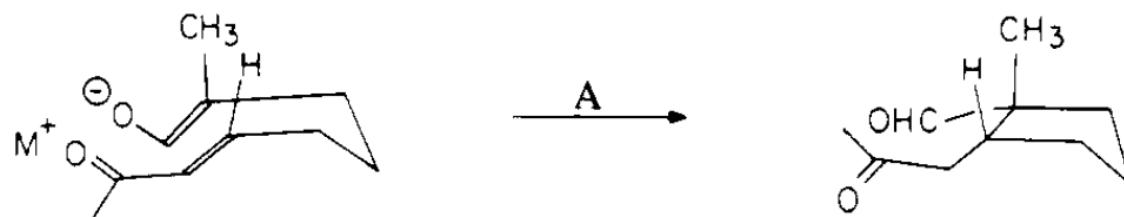




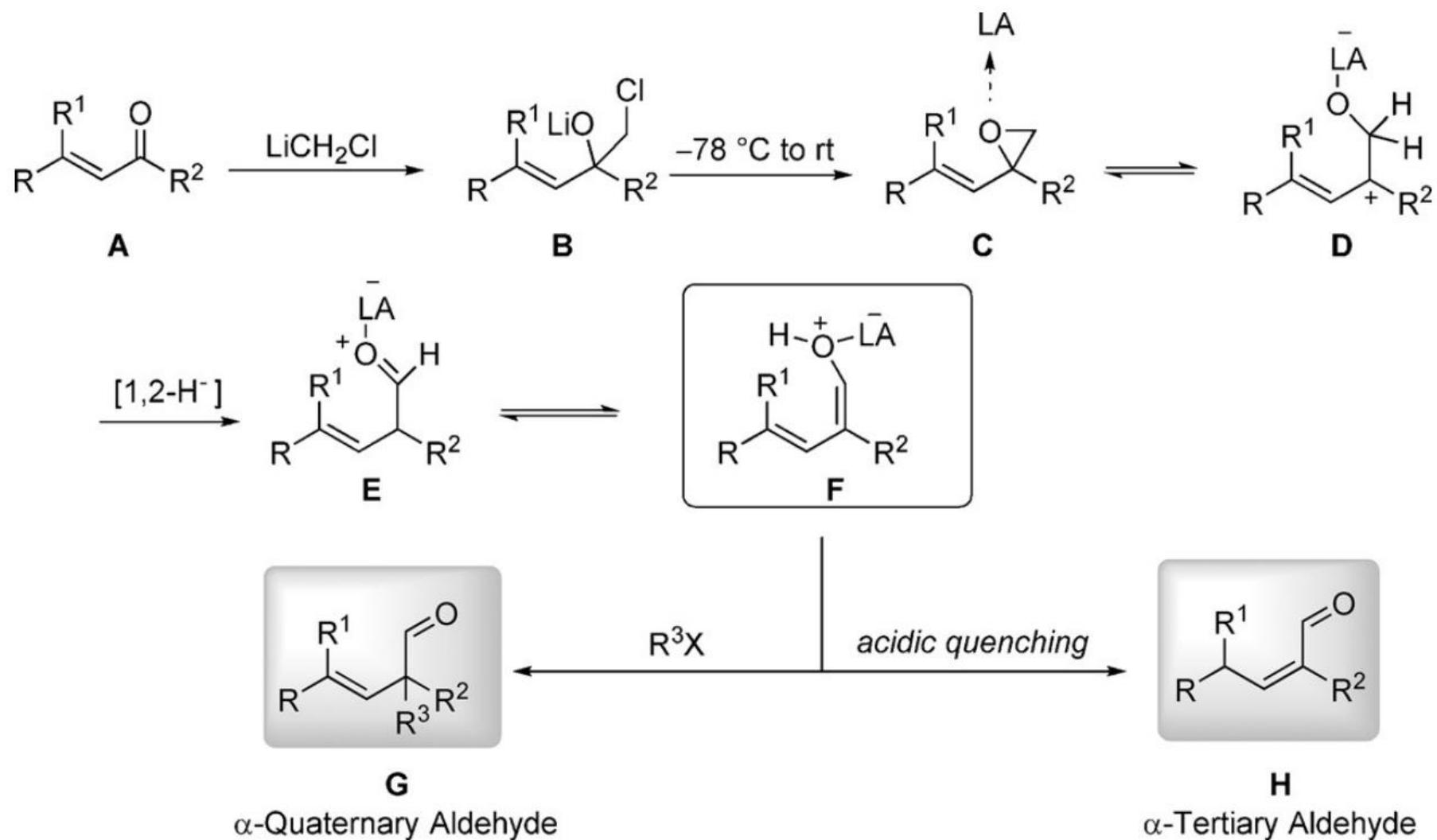
Scheme 2. DABCO-promoted conversion of nitroalkene into α,β -unsaturated ketone.



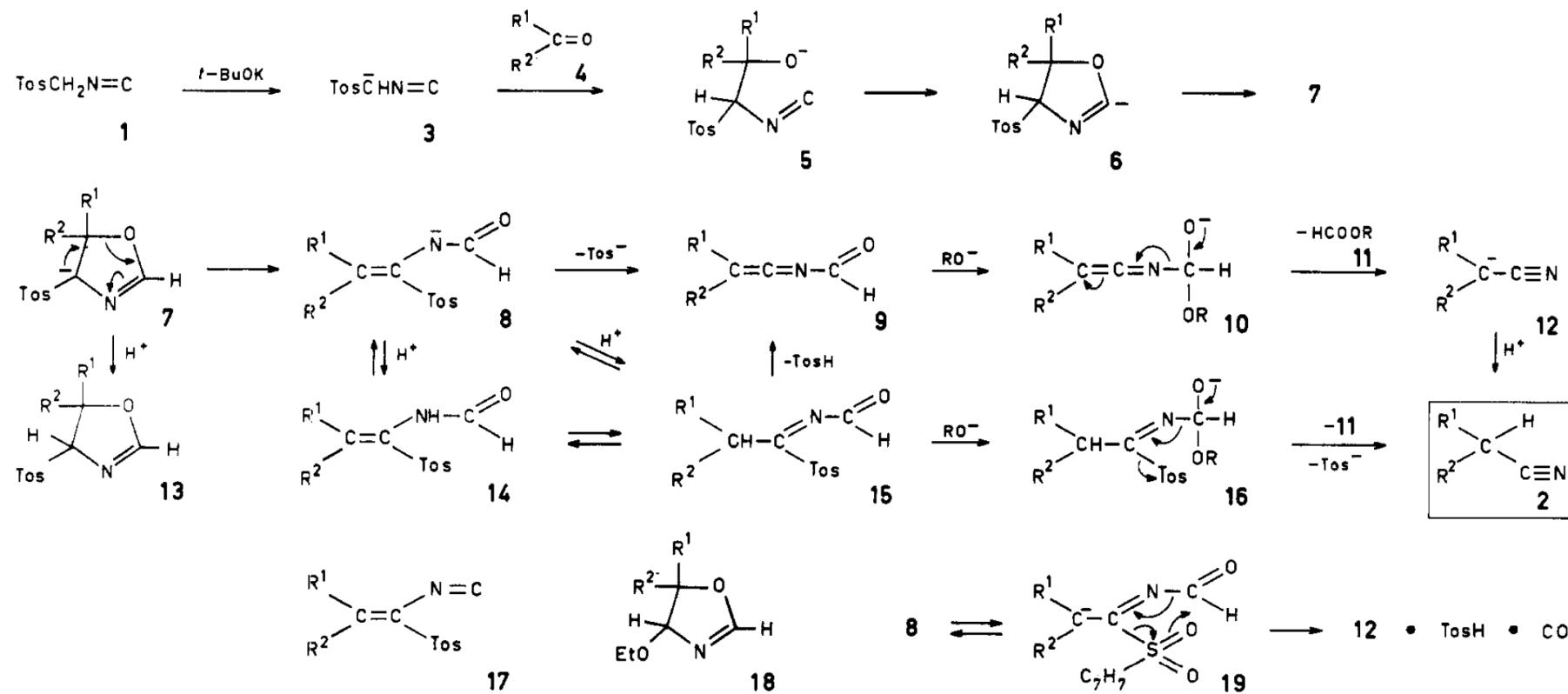
Scheme 3. Proposed mechanism of base-promoted Nef reaction.

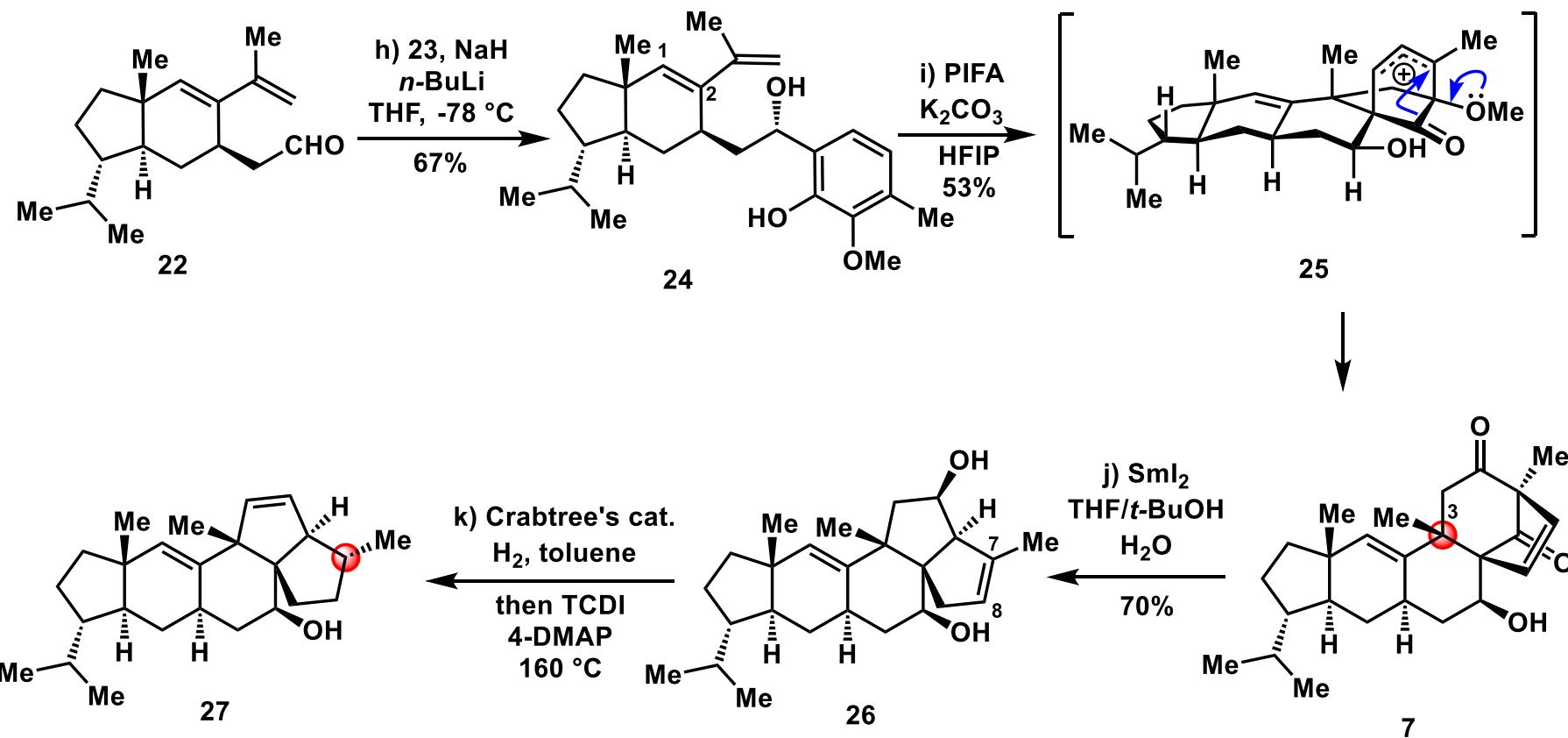
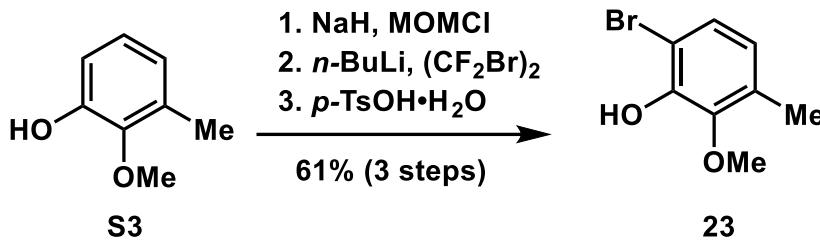


premise that *trans*-hydrindane systems could be made by intramolecular Michael addition had thus been demonstrated. It now remained to test the assumption that the relatively unimpressive stereoselectivity could be improved by suitable variation of the reaction conditions, especially the nature of the base. Indeed, the latter markedly affected the stereochemical outcome of the reaction (trans/cis ratios: KOH/CH₃OH = 2/1; NaOCH₃/CH₃OH = 3/1; LiOH/CH₃OH = 4/1).

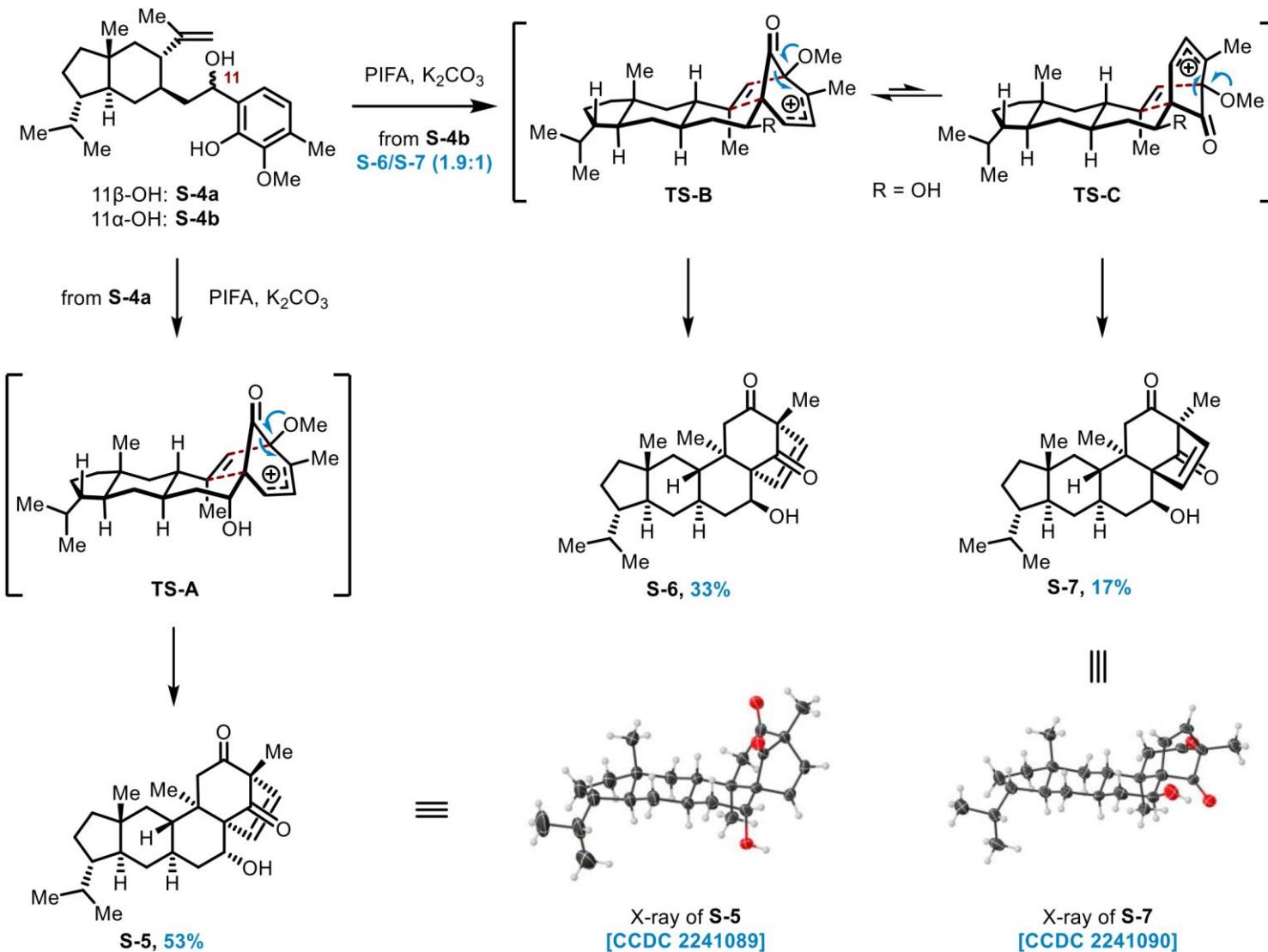


Scheme 4. Plausible mechanism.

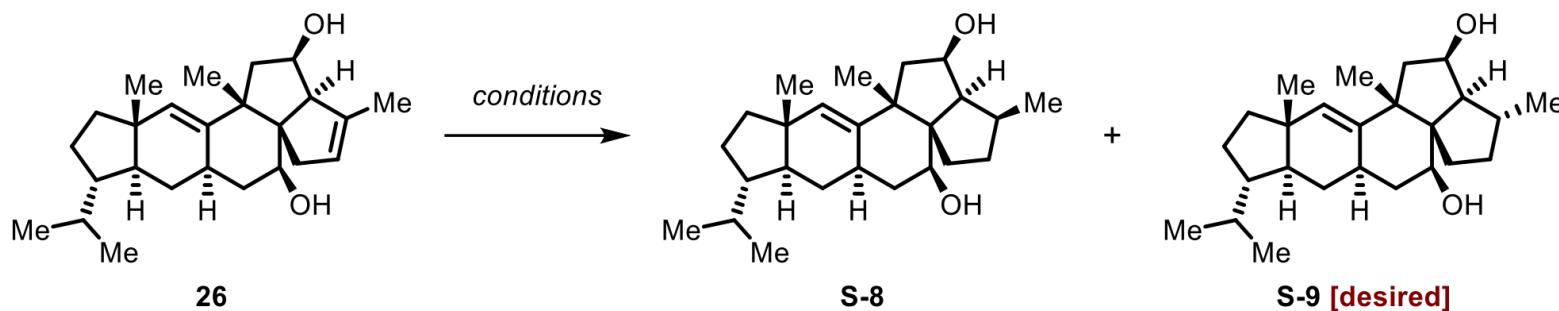




ODI-[5+2] cascade reactions of vinylphenols S-4a and S-4b



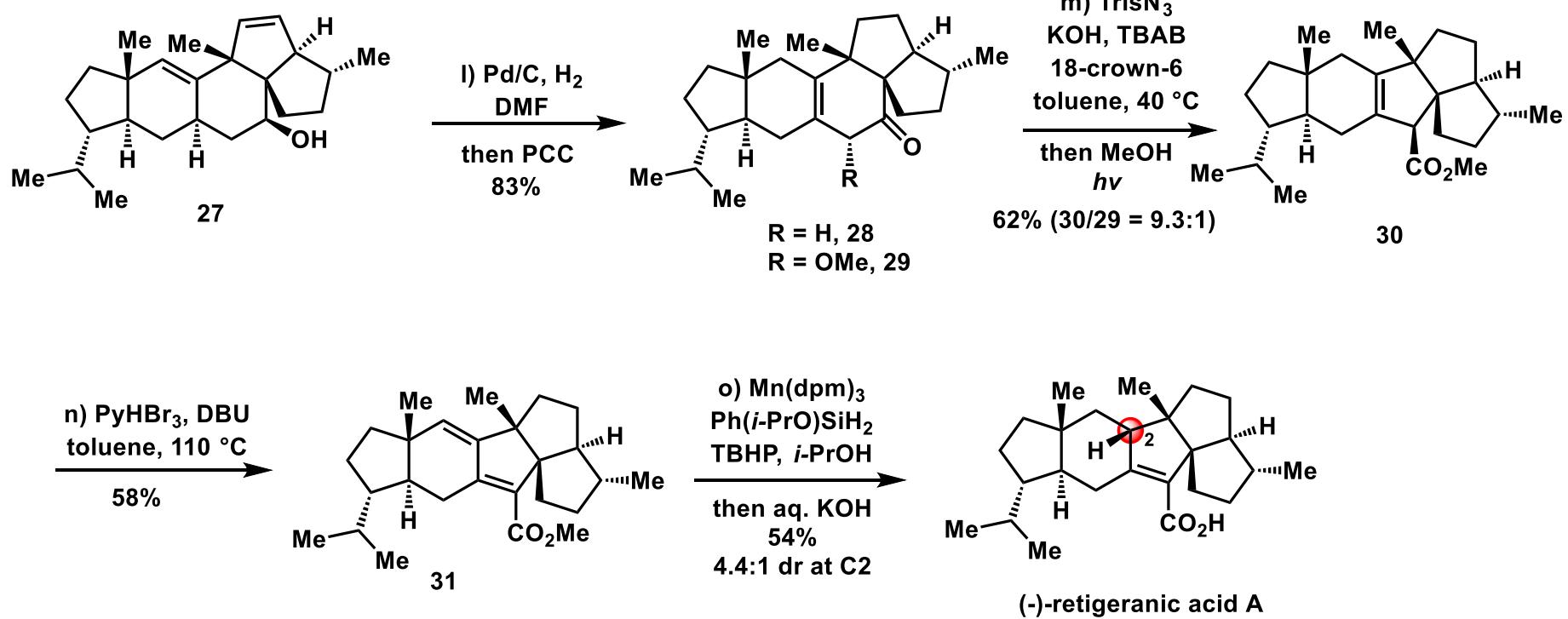
Scheme S2. ODI-[5+2] Cascade Reactions of Vinylphenols **S-4a** and **S-4b**

Table S2. Conditional Screening for the Reduction of Diol **26^a**

entry	reagents	solvent	products (yield) ^b
1	Pd/C (0.05 equiv), H ₂ (14.7 psi)	MeOH	S-8 (83%)
2	Pd(OH) ₂ /C (0.05 equiv), H ₂ (14.7 psi)	MeOH	S-8 (78%)
3	PtO ₂ (0.05 equiv), H ₂ (14.7 psi)	MeOH	S-8 (81%)
4	Rh(PPh ₃) ₃ Cl (0.05 equiv), H ₂ (500 psi)	CH ₂ Cl ₂	— ^c
5	Crabtree's cat. (0.05 equiv), H ₂ (14.7 psi)	toluene	S-9 (95%)
6	Mn(dpm) ₃ (0.1 equiv), PhSiH ₃ (1.0 equiv) TBHP (1.5 equiv)	<i>i</i> -PrOH	— ^d
7	Fe(acac) ₃ (0.1 equiv), PhSiH ₃ (2.0 equiv) PhSH (0.1 equiv)	EtOH	— ^d

^aReactions were performed on 81 µmol scale in solvent (2 mL) at room temperature. ^bIsolated yields. ^cNo reaction.

^dDecomposition.



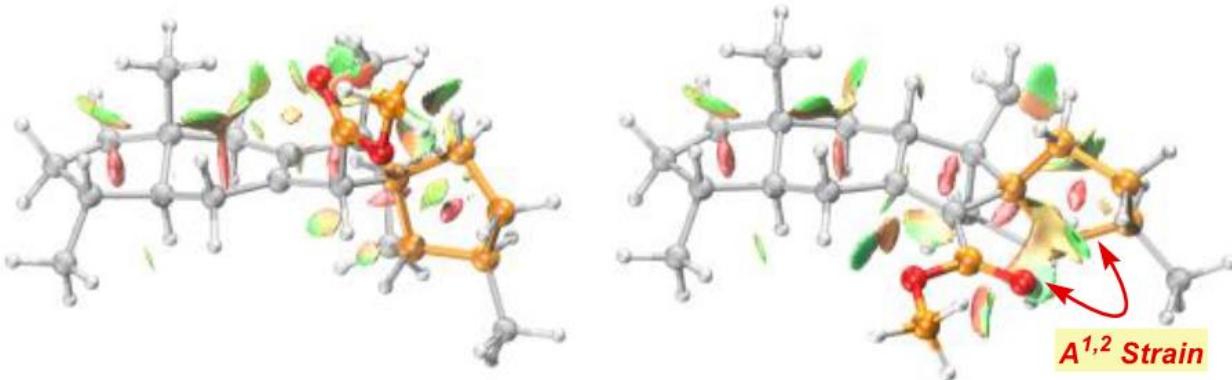
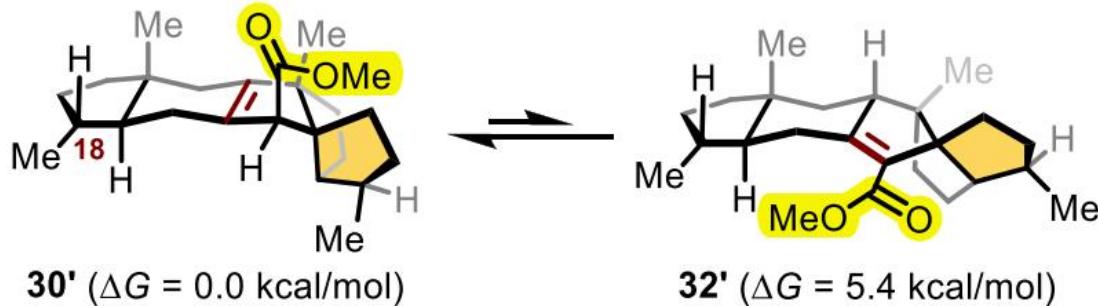
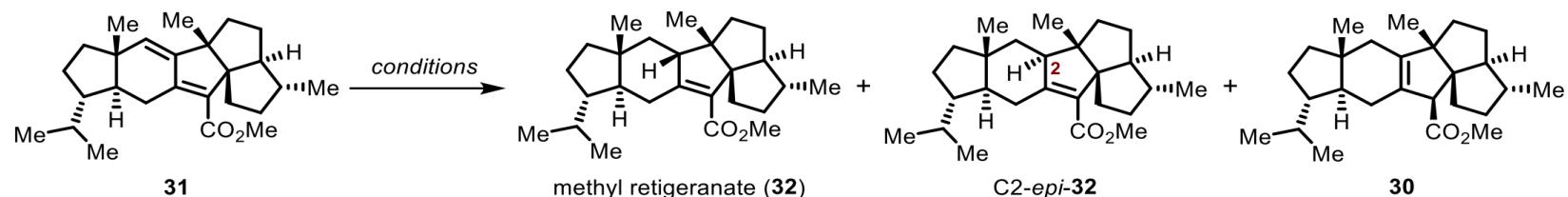


Figure 2. Calculated Gibbs free energy difference between the lowest-energy conformers of **30'** and **32'** at the PWPB95-D3(BJ)/def2-TZVPP/J/C//B3LYP-D3(BJ)/def2-SVP/J level of theory and non-covalent interaction (NCI) analysis (isovalue = 0.5).



entry	reagents	solvent	yield (%) ^b		
			32	C2-epi-32	30
1 ^c	Pd/C, H ₂ (400 psi)	benzene	<5	<5	52
2 ^c	PtO ₂ , H ₂ (400 psi)	MeOH	<5	<5	50
3 ^c	Ir-black, H ₂ (400 psi)	MeOH	<5	<5	47
11 ^g	Mn(dpm) ₃ , PhSiH ₃ , TBHP	i-PrOH	<5	<5	59
12 ^g	Mn(dpm) ₃ , PhSiH ₃ , TBHP	hexane	<5	<5	56
13 ^g	Fe(acac) ₃ , PhSiH ₃ , PhSH ⁱ	EtOH	<5	<5	48
14 ^g	Mn(dpm) ₃ , Ph(i-PrO)SiH ₂ , TBHP	hexane	43	9	<5
15 ^g	Mn(dpm) ₃ , Ph(i-PrO)SiH ₂ , TBHP	i-PrOH	46	11	<5

^aReaction conditions: **31** (25 µmol), metal catalyst (0.1 equiv) w/o [Si-H] (5.0 equiv) and TBHP (1.5 equiv) in solvent (2.5 mL) at room temperature. ^bIsolated yields. ^cStirred for 14 days. ^dStirred for 7 days. ^eNo reaction. ^fFe₂(C₂O₄)₃•6H₂O (20 equiv), NaBH₄ (30 equiv), 0 °C. ^gStirred for 5 h. ^hDecomposition. ⁱPhSH (0.1 equiv).