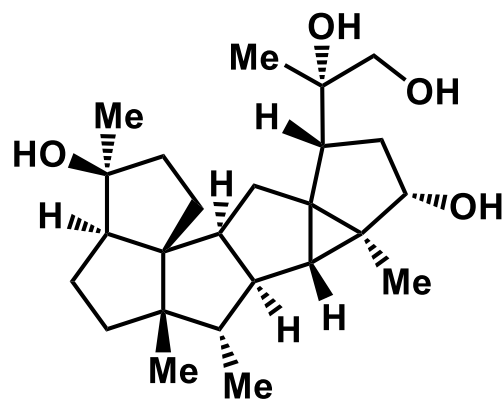
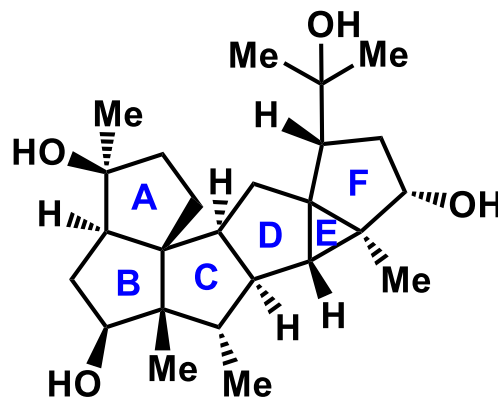


# Total Synthesis of the Hexacyclic Sesterterpenoid Niduterpenoid B via Structural Reorganization Strategy

Yuan Xue, Si-Hua Hou,\* Xiang Zhang, Fu-Min Zhang, Xiao-Ming Zhang, and Yong-Qiang Tu\*



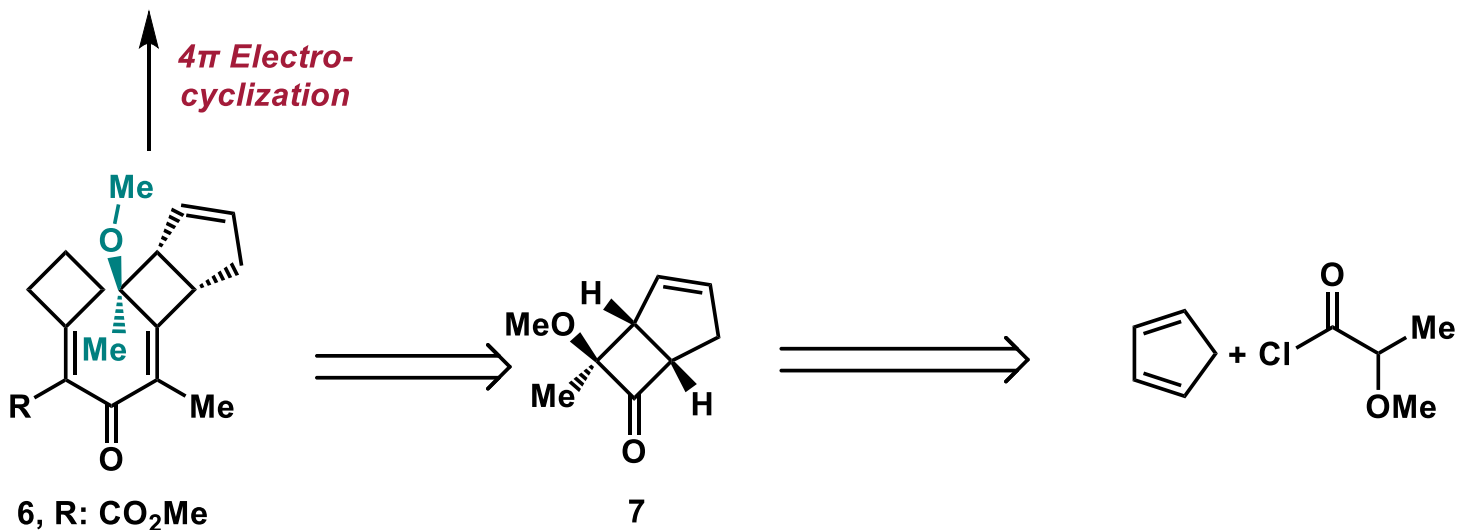
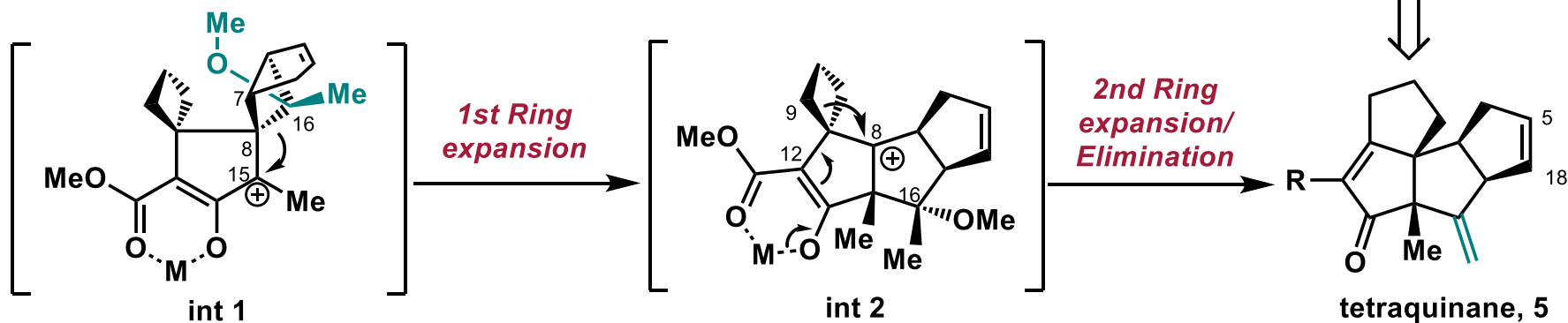
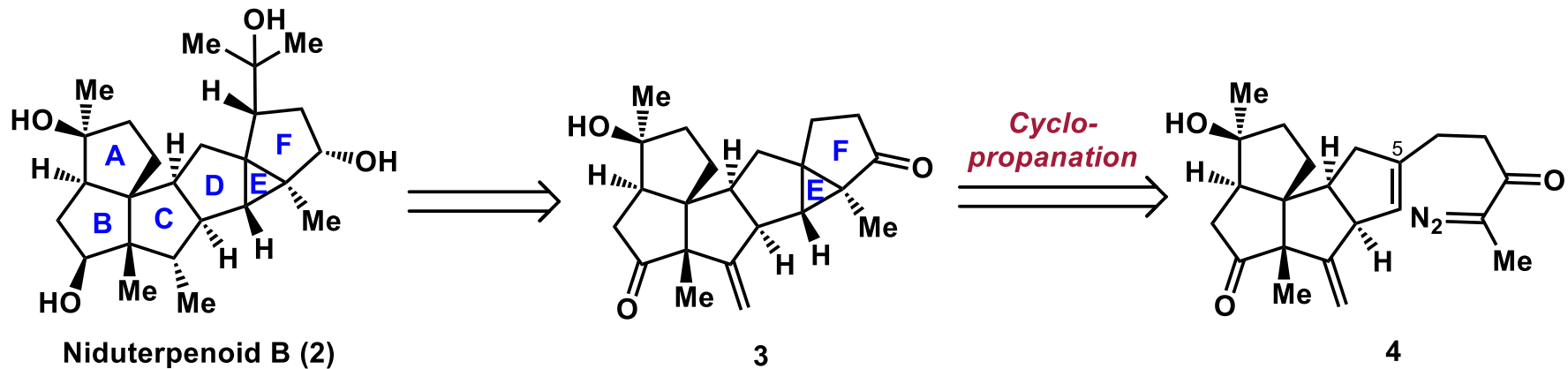
Niduterpenoid A (1)

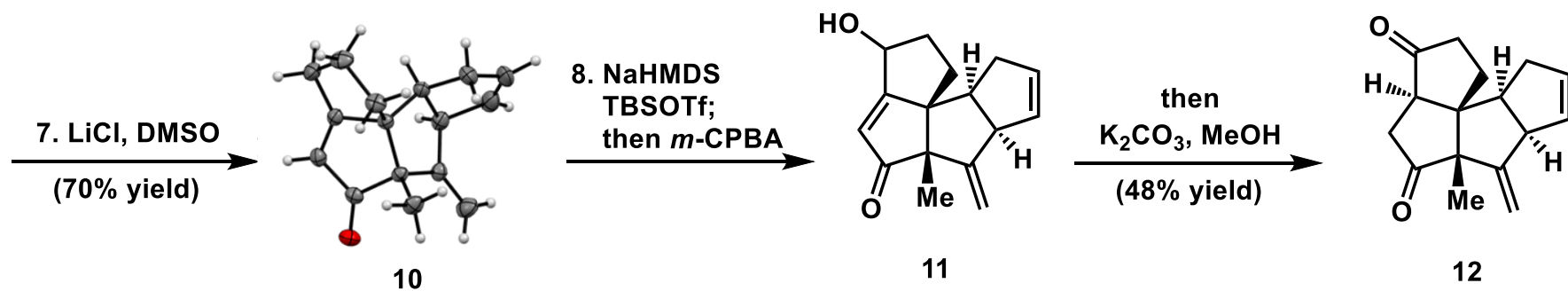
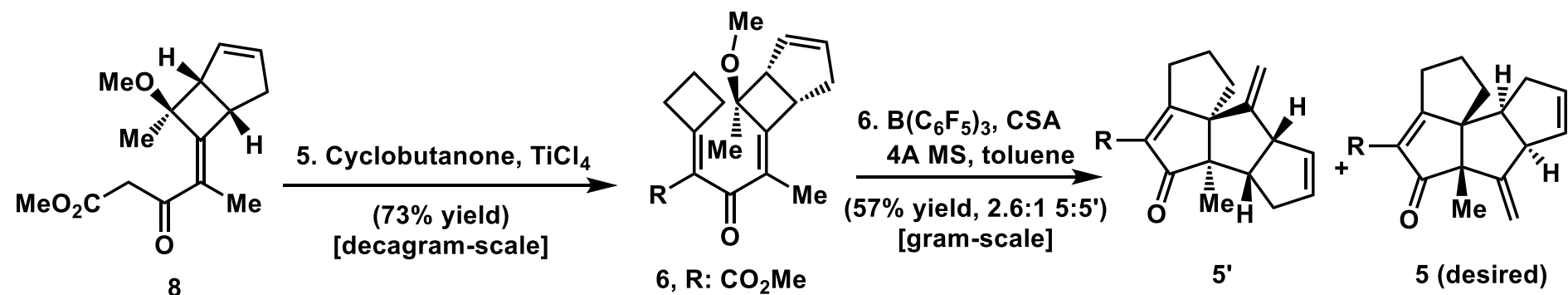
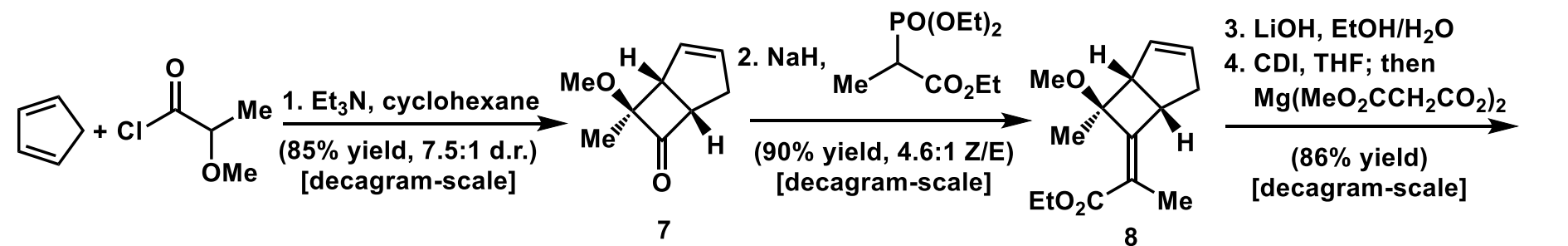


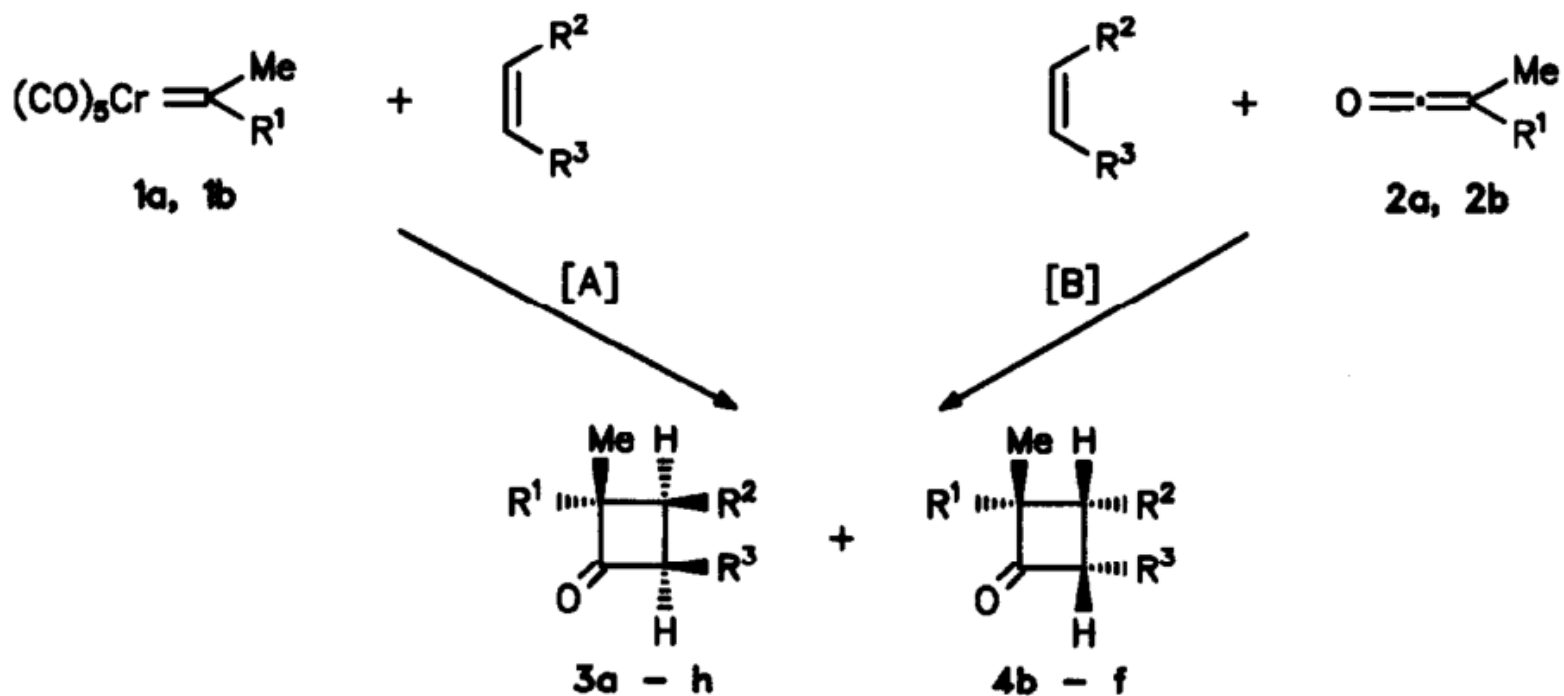
Niduterpenoid B (2)

Structure features of 1-2:

- 5/5/5/5/3/5-fused (A-F) rings
- 13 contiguous stereocenters
- 4 quaternary carbons



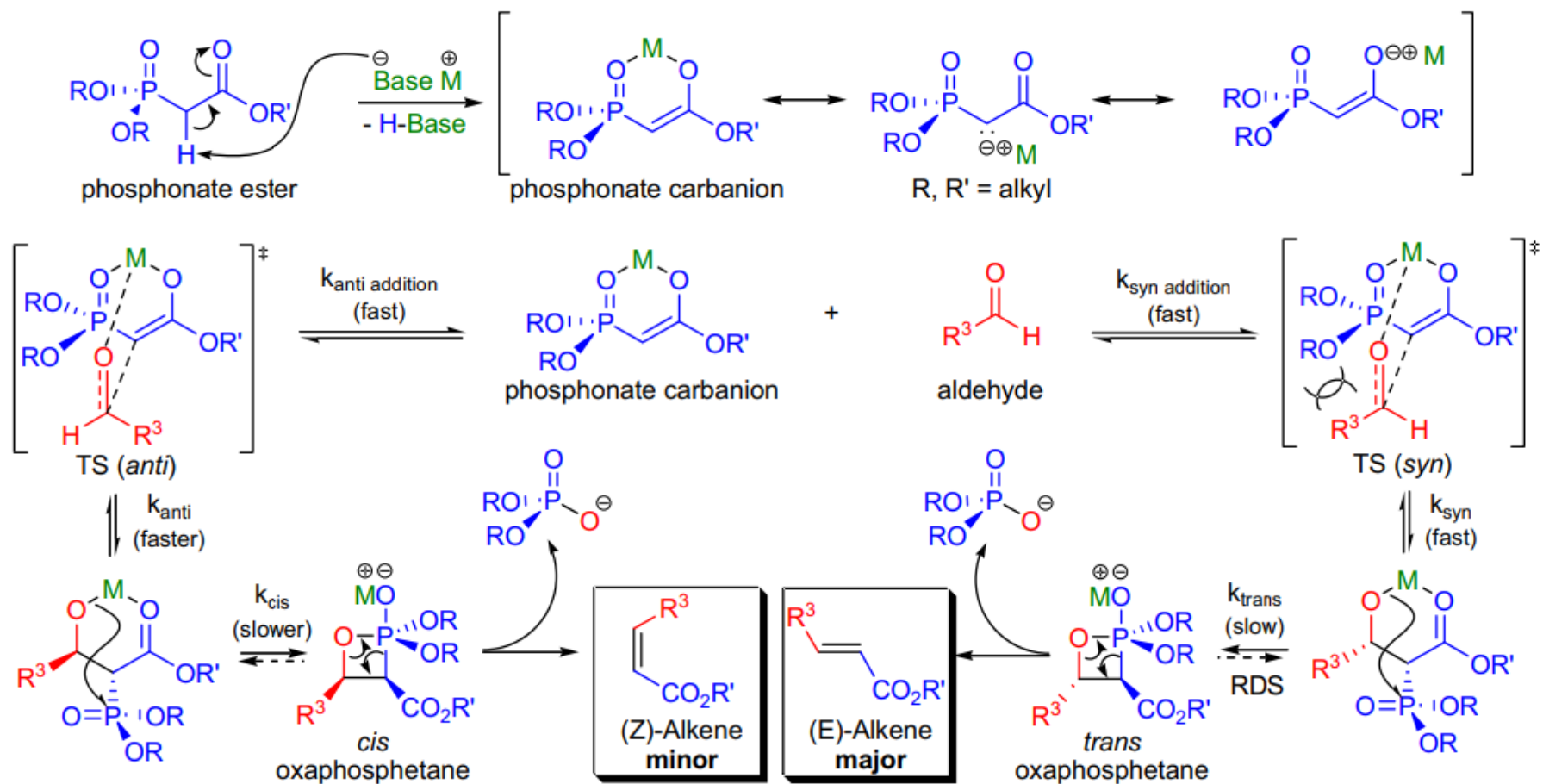


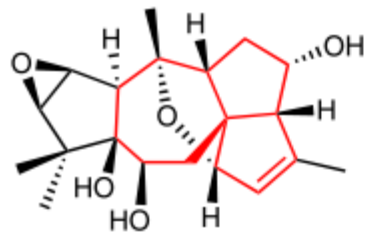


**Scheme 1:** 1a, 2a, 3a - f, 4b - f  $\text{R}^1 = \text{OMe}$ ; 1b, 2b, 3g - h  $\text{R}^1 = \text{SPh}$ ;  $\text{R}^2, \text{R}^3$  see table 1 and 2; conditions: [A]  $h\nu$  (Philips HPK 125 W) / 15 - 20 h / 5 bar CO / 1 mmol complex and 5 mmol olefin in 20 ml ether /  $\lambda > 400$  nm for  $\text{R}^1 = \text{SPh}$ ; [B]  $\text{Et}_3\text{N}$  / cyclohexane / 5 equiv. of olefin /  $80^\circ\text{C}$  for 4 h then room temperature for 12 h / for  $\text{R}^1 = \text{SPh}$  see ref. 8.

# HORNER-WADSWORTH-EMMONS OLEFINATION

**Mechanism:** 47,9,48,11

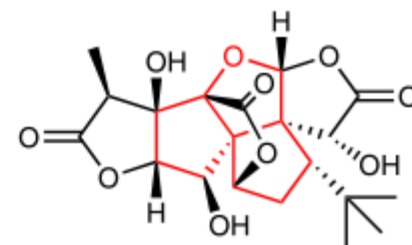




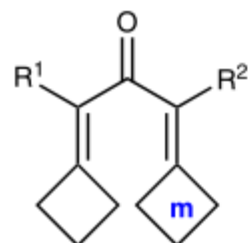
Rhodomollanol A



Angular triquinanes  
1 / 3

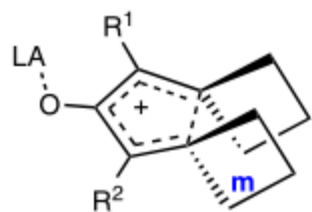


Ginkgolide B



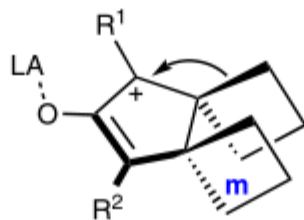
Divinyl ketones  
2 / 4

Lewis acid  
(LA)



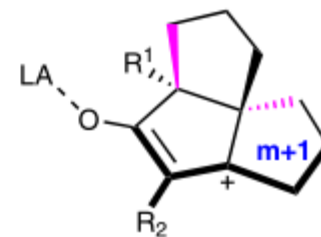
5

Challenging  
4 $\pi$ -Electron  
Cyclization



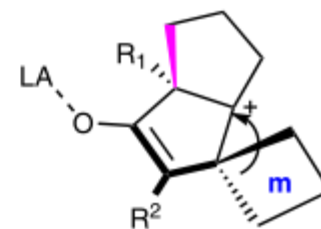
6

1st Cyclo-  
Expansion



8

2nd Cyclo-  
Expansion

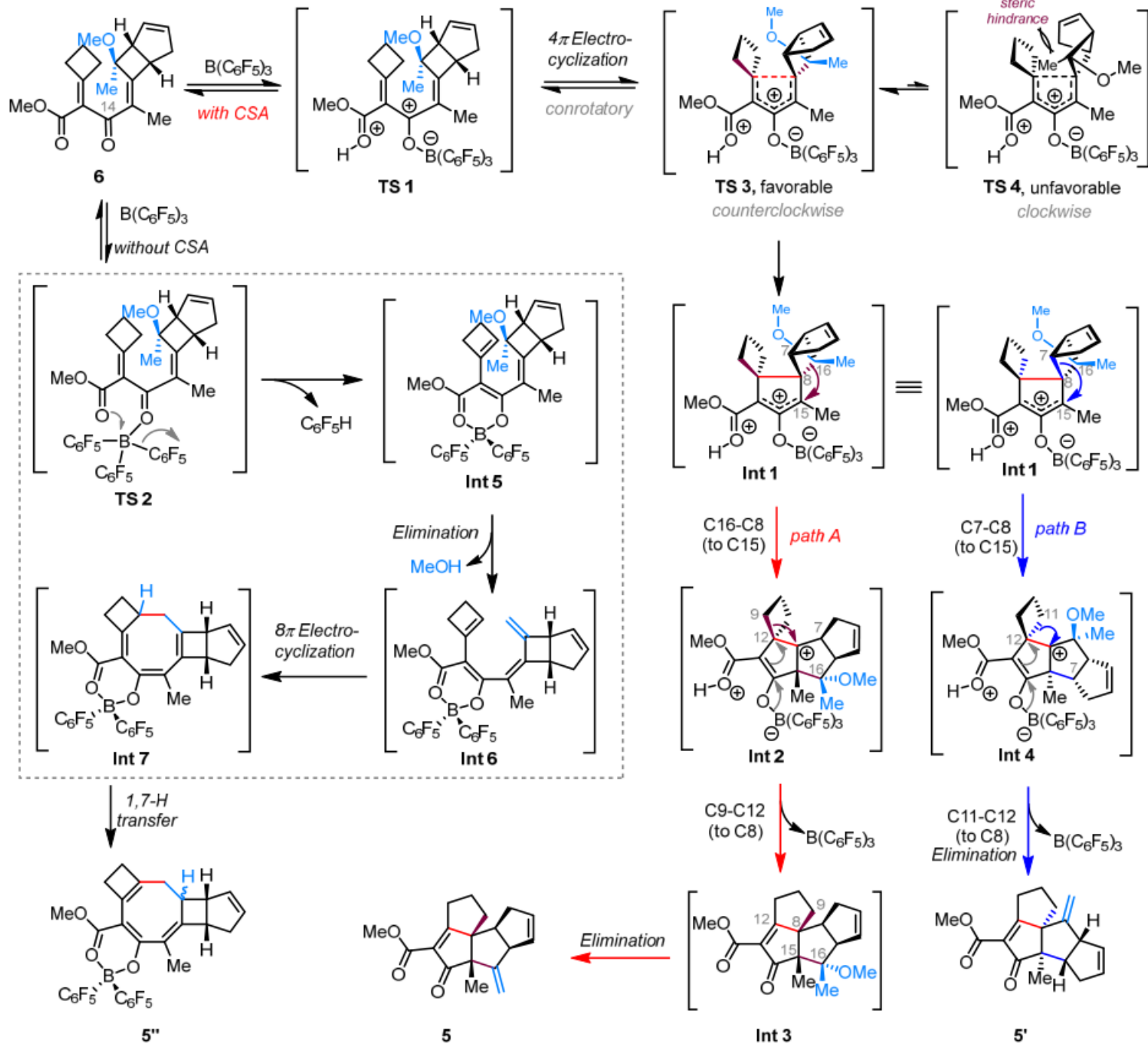


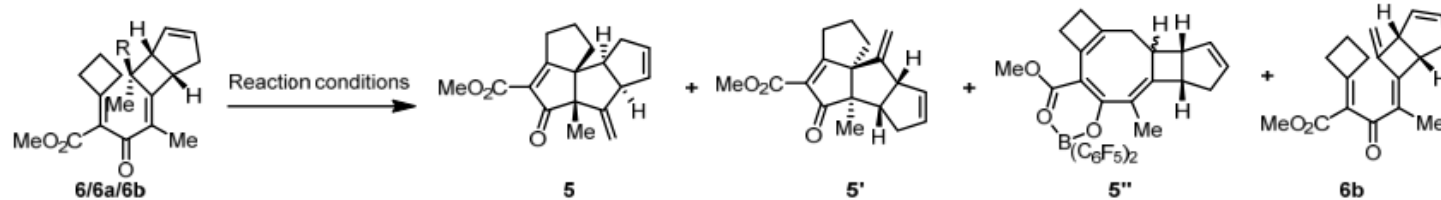
7

One step

- LA

Our  
design

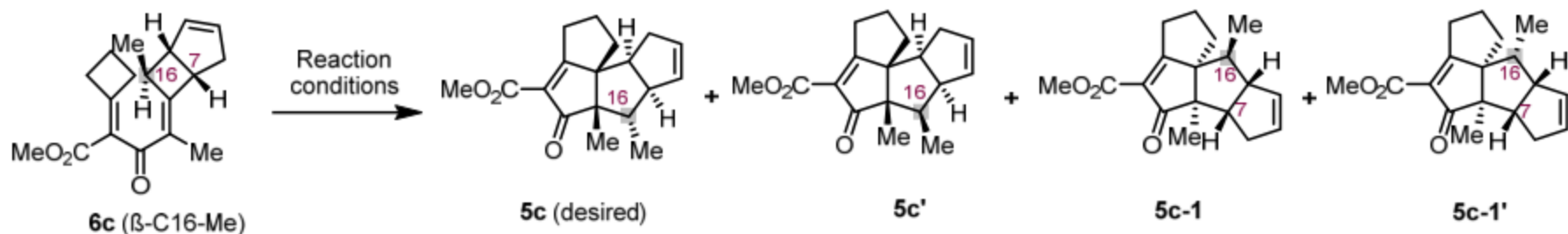


**Table S1.** Optimization of the 4 $\pi$  Electrocyclization/Double Ring Expansions/Elimination Cascade.<sup>a</sup>

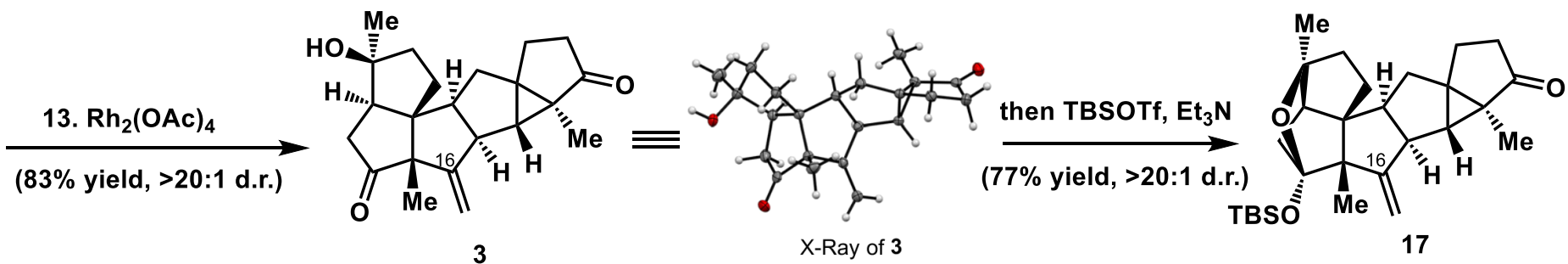
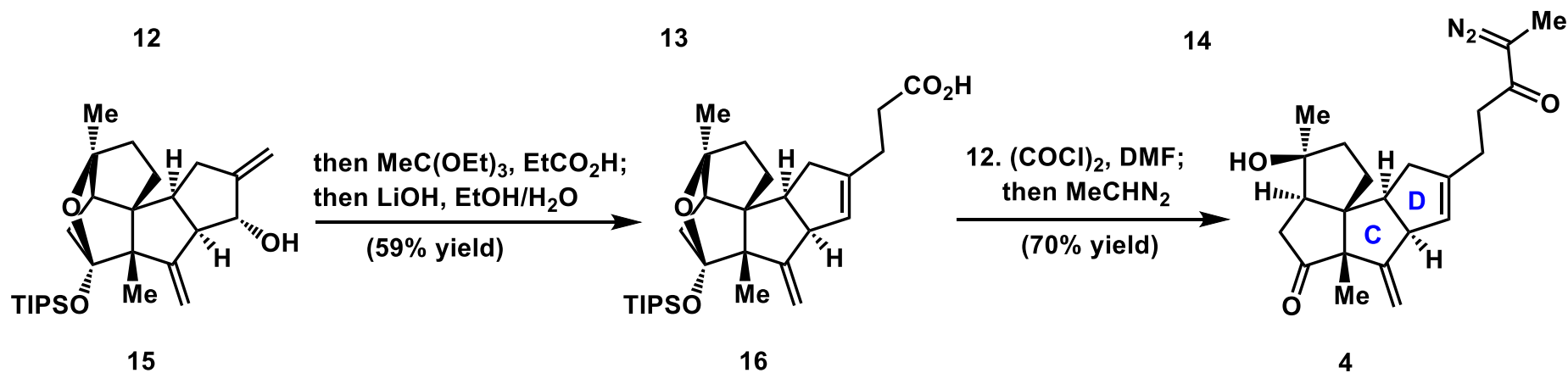
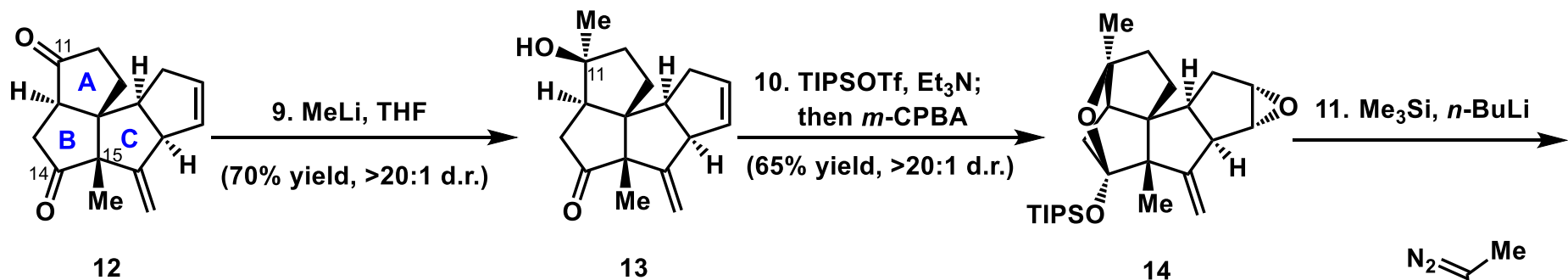
Entry	Substrate	Reaction conditions <sup>a</sup>	Conversion/%	Yield/%			
				5	5'	5''	6b
1 <sup>b</sup>	6, R = OMe	InCl <sub>3</sub> (0.1 equiv.), AgSbF <sub>6</sub> (0.3 equiv.), CHCl <sub>3</sub> , r.t. to 80°C, 12 h	100	0	0	-	0
2 <sup>b</sup>	6, R = OMe	InCl <sub>3</sub> (0.1 equiv.), DCM, 80°C, 12 h	100	0	0	-	0
3	6, R = OMe	B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> (1.0 equiv.), CCl <sub>4</sub> , 100°C, 12 h	100	8	trace	63	12
4	6, R = OMe	B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> (1.0 equiv.), toluene, 120°C, 12 h	100	8	trace	65 <sup>e</sup>	9
5	6, R = OMe	B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> (1.0 equiv.), 4 Å MS, toluene, 120°C, 12 h	100	11	<5	14	8
6	6, R = OMe	B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> (1.0 equiv.), 3 Å MS, toluene, 120°C, 12 h	100	10	trace	ND	ND
7	6, R = OMe	B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> (1.0 equiv.), 5 Å MS, toluene, 120°C, 12 h	100	trace	trace	ND	ND
8	6, R = OMe	B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> (1.0 equiv.), AgNTf <sub>2</sub> (0.5 equiv.), 4 Å MS, toluene, 100°C, 5 h	100	5	trace	65	0
9	6, R = OMe	B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> (0.5 equiv.), AgNTf <sub>2</sub> (0.5 equiv.), 4 Å MS, toluene, 100°C, 5 h	74	trace	0	0	24
10	6, R = OMe	B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> (0.5 equiv.), PTSA (0.5 equiv.), 4 Å MS, toluene, 120°C, 12 h	100	23	9	ND	ND
11	6, R = OMe	B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> (0.5 equiv.), PTSA (0.5 equiv.), 4 Å MS, toluene, 100°C, 5 h	100	30	12	ND	ND
12	6, R = OMe	B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> (0.5 equiv.), MsOH (0.5 equiv.), 4 Å MS, toluene, 100°C, 5 h	100	32	13	ND	ND
13	6, R = OMe	B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> (0.5 equiv.), CSA (0.5 equiv.), 4 Å MS, toluene, 100°C, 5 h	100	36	14	12	10
14	6, R = OMe	B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> (0.5 equiv.), CSA (0.5 equiv.), 4 Å MS, CCl <sub>4</sub> , 100°C, 5 h	100	33	5	ND	ND
15	6, R = OMe	B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> (0.5 equiv.), CSA (0.5 equiv.), 4 Å MS, CCl <sub>4</sub> /toluene (1:1), 100°C, 5 h	100	37	11	ND	ND
16 <sup>c</sup>	6, R = OMe	B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> (0.5 equiv.), CSA (0.5 equiv.), 4 Å MS, CCl <sub>4</sub> /toluene (1:1), 100°C, 5 h	100	31	10	ND	ND
17 <sup>d</sup>	6, R = OMe	B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> (0.6 equiv.), CSA (0.7 equiv.), 4 Å MS, toluene, 100°C, 5 h	100	41	16	16	15


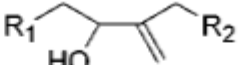
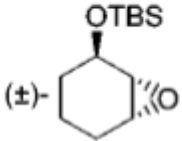
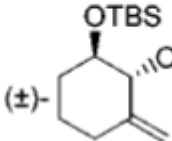


**Table S2.** Selected Attempts for the Cascade of Compound **6c**.<sup>a</sup>

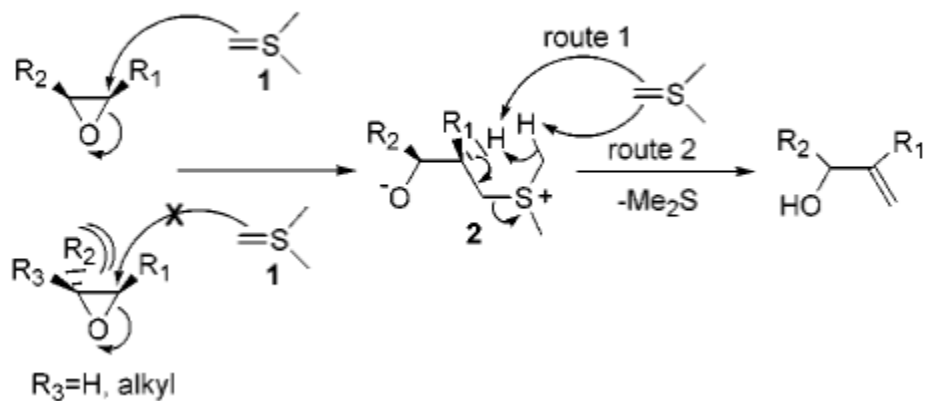


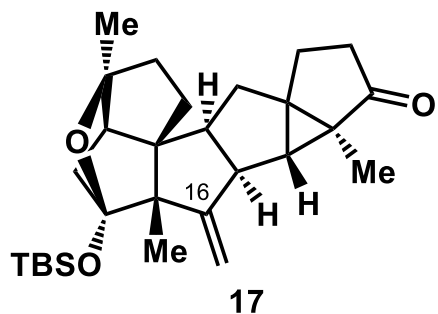
Entry	Substrate	Reaction conditions <sup>a</sup>	Conversion	Yield & Ratio <b>5c: 5c': 5c-1: 5c-1'</b>
1	<b>6c</b> , 1:8 d.r.	B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> (0.5 equiv.), CSA (0.5 equiv.), 4 Å MS, toluene, 100°C, 5 h	38%	18%, 0: 1: <0.1: 1.5
2	<b>6c</b> , 1:8 d.r.	B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> (0.5 equiv.), CSA (0.5 equiv.), 4 Å MS, CCl <sub>4</sub> /toluene (1:1), 100°C, 5 h	31%	14%, 0: 1: <0.1: 1.7
3	<b>6c</b> , 1:8 d.r.	B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> (0.5 equiv.), CSA (0.5 equiv.), 4 Å MS, CCl <sub>4</sub> , 100°C, 5 h	24%	12%, 0: 1: <0.1: 2
4	<b>6c</b> , 1:8 d.r.	B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> (3 equiv.), toluene, 100°C, 5 h	100%	41%, 0: 1: 0.1: 2.1
5	<b>6c</b> , 1:8 d.r.	B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub> (3 equiv.), CH <sub>2</sub> Cl <sub>2</sub> , r.t., 5 h	100%	62%, 0: 1: 0.2: 4.5
6	<b>6c</b> , 1:8 d.r.	BF <sub>3</sub> ·Et <sub>2</sub> O (3 equiv.), CH <sub>2</sub> Cl <sub>2</sub> , 40°C, 12 h	100%	89%, 0: 1: 0.1: 3.2
7	<b>6c</b> , 1:10 d.r.	BF <sub>3</sub> ·Et <sub>2</sub> O (3 equiv.), CH <sub>2</sub> Cl <sub>2</sub> , 40°C, 12 h	100%	92%, 0: 1: 0.1: 3.3
8	<b>6c</b> , 3:1 d.r.	BF <sub>3</sub> ·Et <sub>2</sub> O (3 equiv.), CH <sub>2</sub> Cl <sub>2</sub> , 40°C, 12 h	100%	85%, 0: 1: 4.1: 3.2



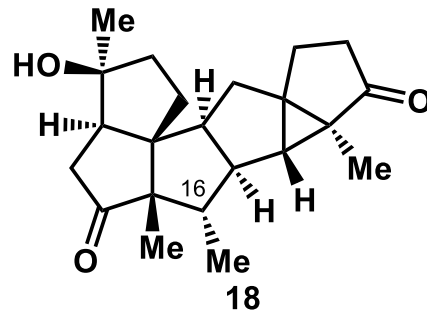
entry	substrate	products (Ratio) <sup>a</sup>	yield (%) <sup>b</sup>
4		 R <sub>1</sub> =Me; R <sub>2</sub> =OTr: 1 R <sub>1</sub> =OTr; R <sub>2</sub> =Me: 3	72%
5			80%

Scheme 3



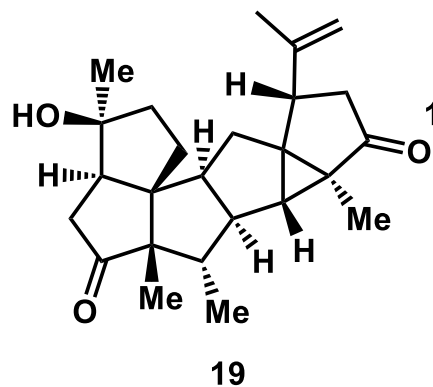


14.  $\text{Mn}(\text{dpm})_3$ , TBHP  
 $\text{Ph}(i\text{-PrO})\text{SiH}_2$ ,  $i\text{-PrOH}$ ;  
then  $\text{HF}\cdot\text{pyridine}$   
(62% yield, 5.9:1 d.r.)

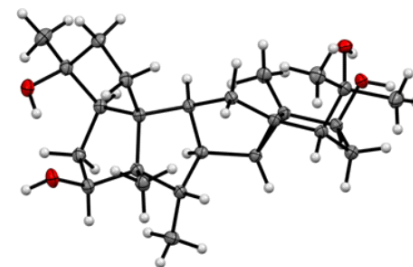
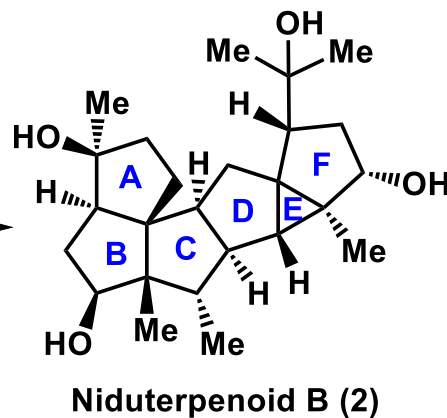


15. TBSOTf; then  $\text{PhSeCl}$ ;  
then  $\text{H}_2\text{O}_2$ ; (45% yield)

16. *iso*-propenyl  $\text{MgBr}$ ,  $\text{CuBr}$   
(76% yield, >20:1 d.r.)

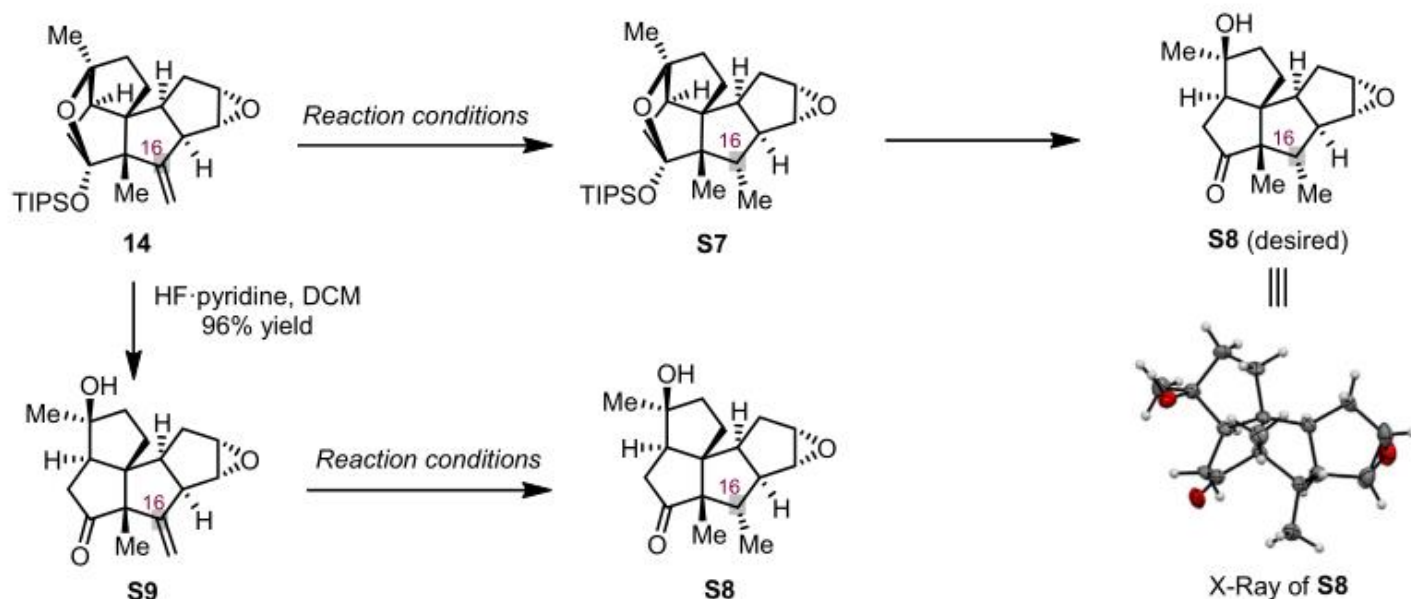


17.  $\text{Mn}(\text{dpm})_3$ ,  $\text{PhSiH}_3$   
 $\text{O}_2$ ,  $\text{EtOH}$ ; then  $\text{NaBH}_4$   
(79% yield)



X-Ray of 2

**Figure S4.** Optimization of the Hydrogenation with Compounds **14** and **S9**.<sup>a</sup>



Entry	Substrate	Reaction conditions <sup>a</sup>	Conversion	Yield & ratio <b>S7</b>	Yield & ratio <b>S8</b>
1	<b>14</b>	Pd/C (10 mol%), H <sub>2</sub> (1.0 atm), MeOH	<5%	0	
2	<b>14</b>	PtO <sub>2</sub> (10 mol%), H <sub>2</sub> (1.0 atm), DCM	<5%	0	
3	<b>14</b>	Wilkinson's catalyst (10 mol%), H <sub>2</sub> (1.0 atm), MeOH	<5%	0	
4	<b>14</b>	Crabtree's catalyst (10 mol%), H <sub>2</sub> (1.0 atm), DCM	<5%	0	
5	<b>14</b>	Mn(dpm) <sub>3</sub> , PhSiH <sub>3</sub> , TBHP, <i>i</i> -PrOH then HF·pyridine	100%		72%, > 20: 1
6	<b>S9</b>	Mn(dpm) <sub>3</sub> , PhSiH <sub>3</sub> , TBHP, <i>i</i> -PrOH	95%		49%, 1: 3.5

<sup>a</sup> The reaction was run on a 0.1 mmol scale of substrate in solvent (1.0 mL) at r.t. for 3 hours. All yields were isolated yields. The d.r. ratio of product (at C16 position) was **S8** ( $\alpha$ -C16-Me) and **S8'** ( $\beta$ -C16-Me).

