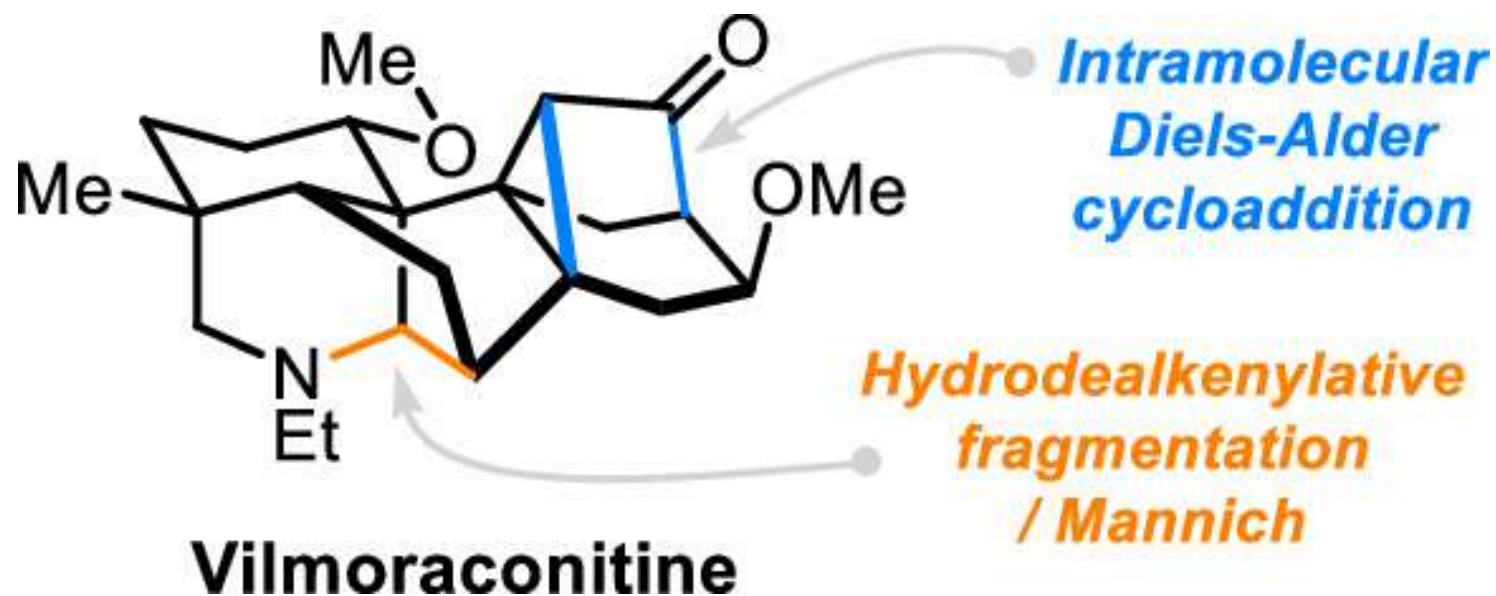


# Total Synthesis of Vilmoraconitine





**Yong Qin**

**Education :**

1985-1989 B.S., Yunnan University

1989-1992 Ms., Chengdu Institute of Organic Chemistry, CAS, ( Prof. Jiqui Yang)

1992-1995 PhD., Institute of Chemistry, CAS, ( Prof. Zhitang Huang and Yaozhong Jiang)

**Work Experience :**

1995-1996 Assistant Professor,

Associate Professor of Chengdu Institute of Organic Chemistry, CAS

1996-2000 Postdoc Associate, the University of Vermont, (Prof. Martin E. Kuehne)

2000-2003 Research scientist, Triad Therapeutics Inc., San Diego

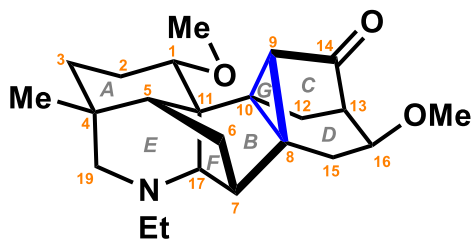
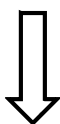
2003-present Prof. West china school of Pharmacy, Sichuan university

**Research Interests**

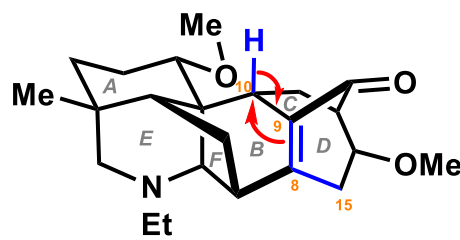
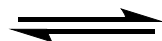
Total synthesis of structurally and biologically interesting natural products



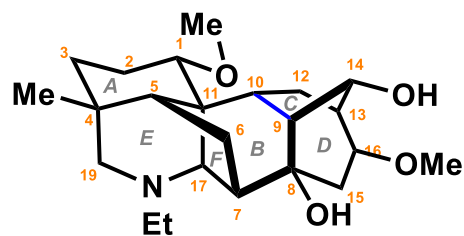
roots of *Aconitum vilmorinianum*



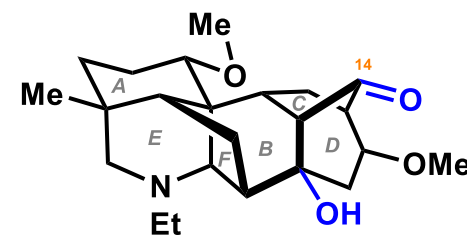
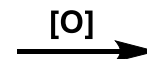
**vilmoraconitine (1)**  
 rearranged-type II C<sub>19</sub>-DTAs



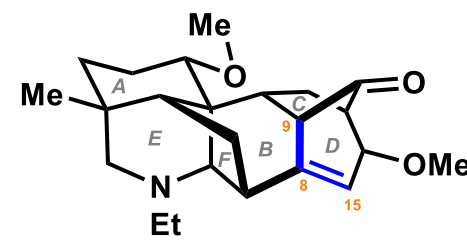
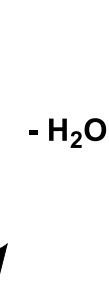
5



**vilmorrianine D (2)**  
 aconitine type C<sub>19</sub>-DTAs

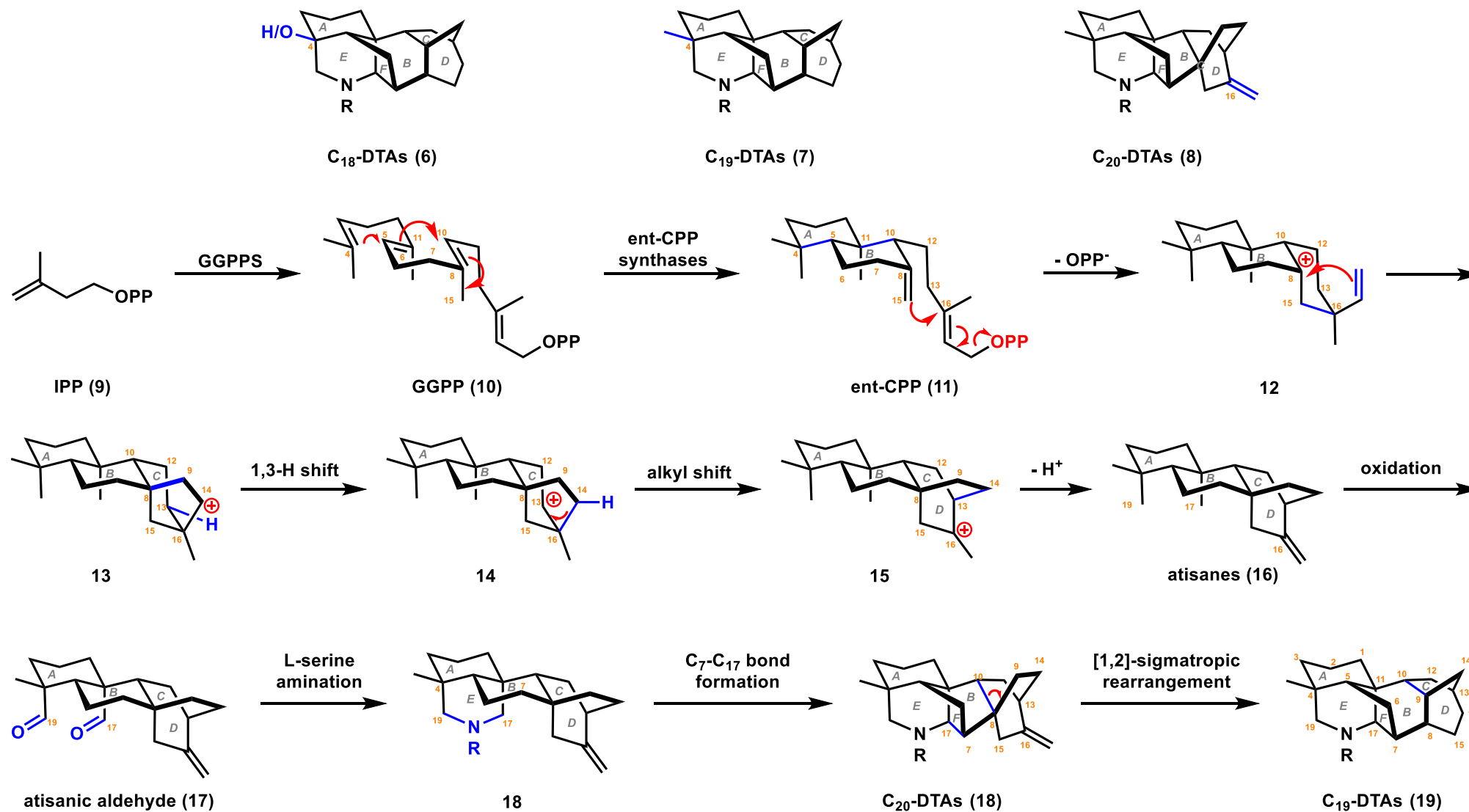


3

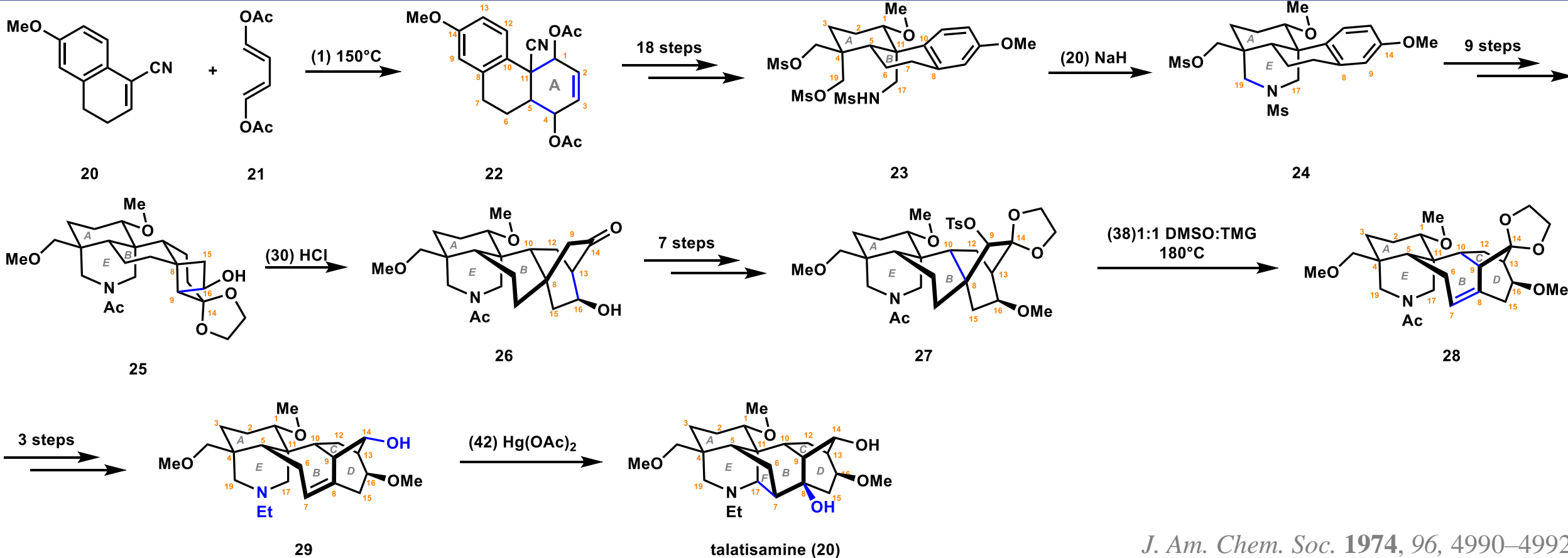
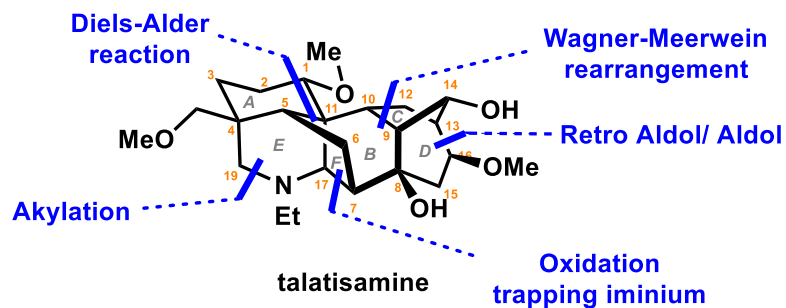


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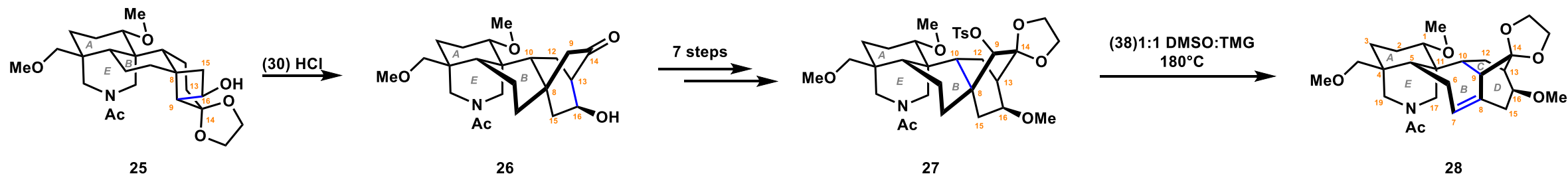




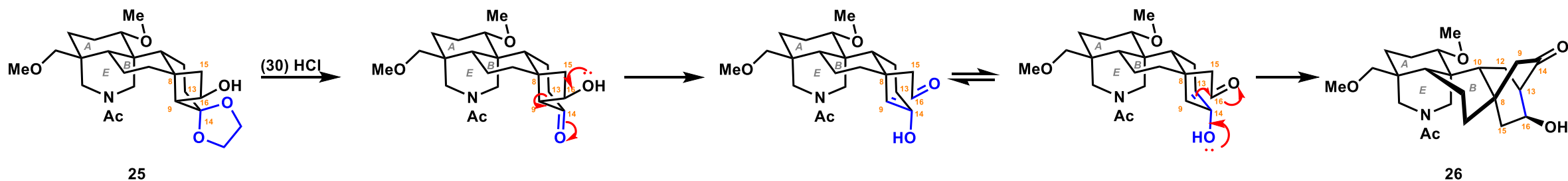
● 1974 Wiesner's work



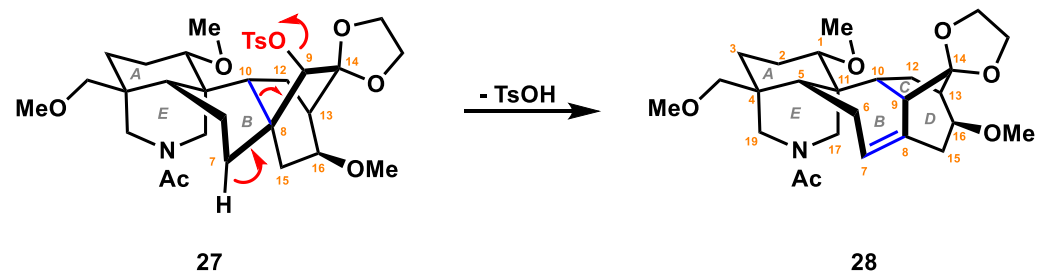
● 1974 Wiesner's work



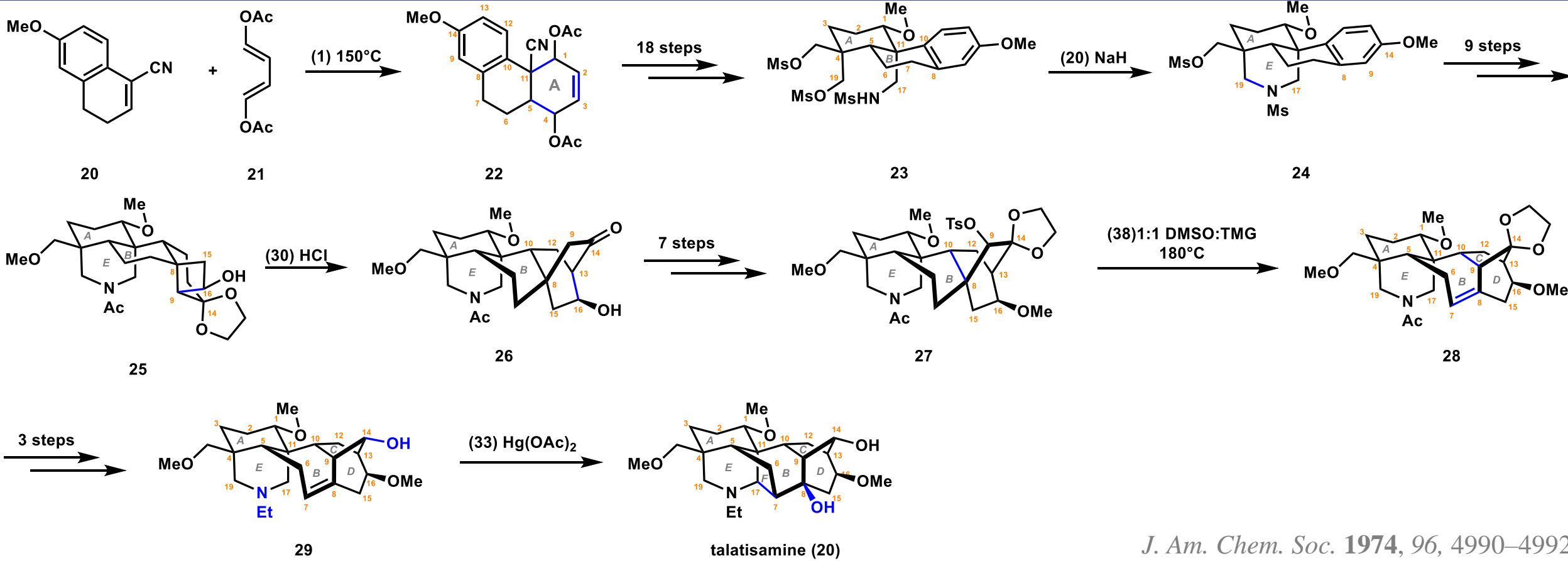
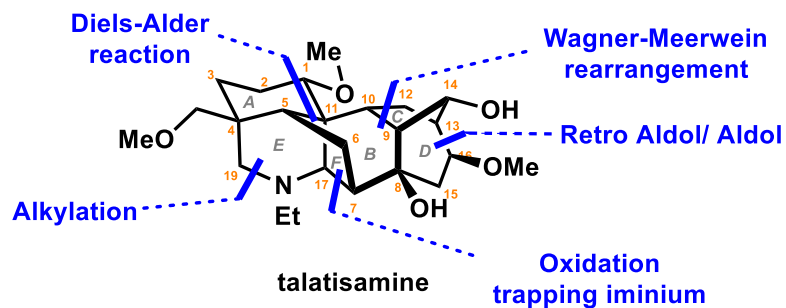
Retro-aldol-Aldol



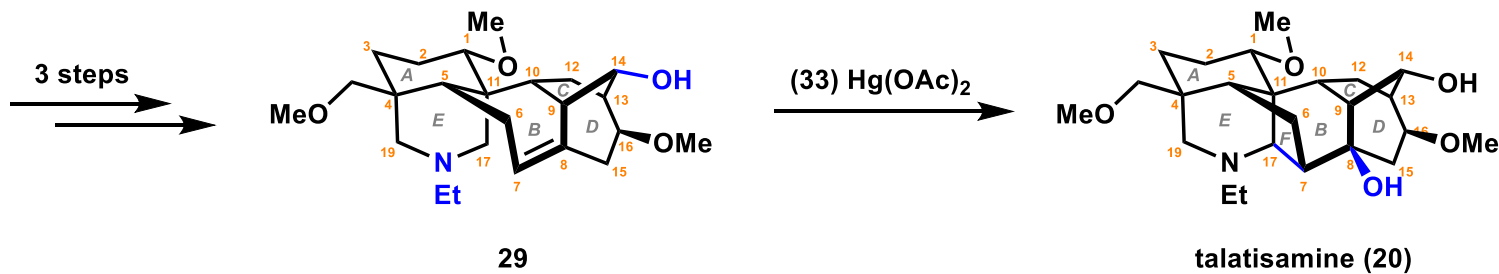
Wagner-Meerwein rearrangement



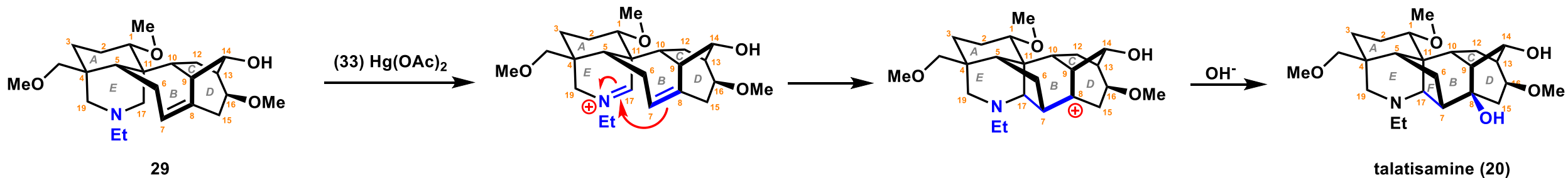
● 1974 Wiesner's work



● 1974 Wiesner's work

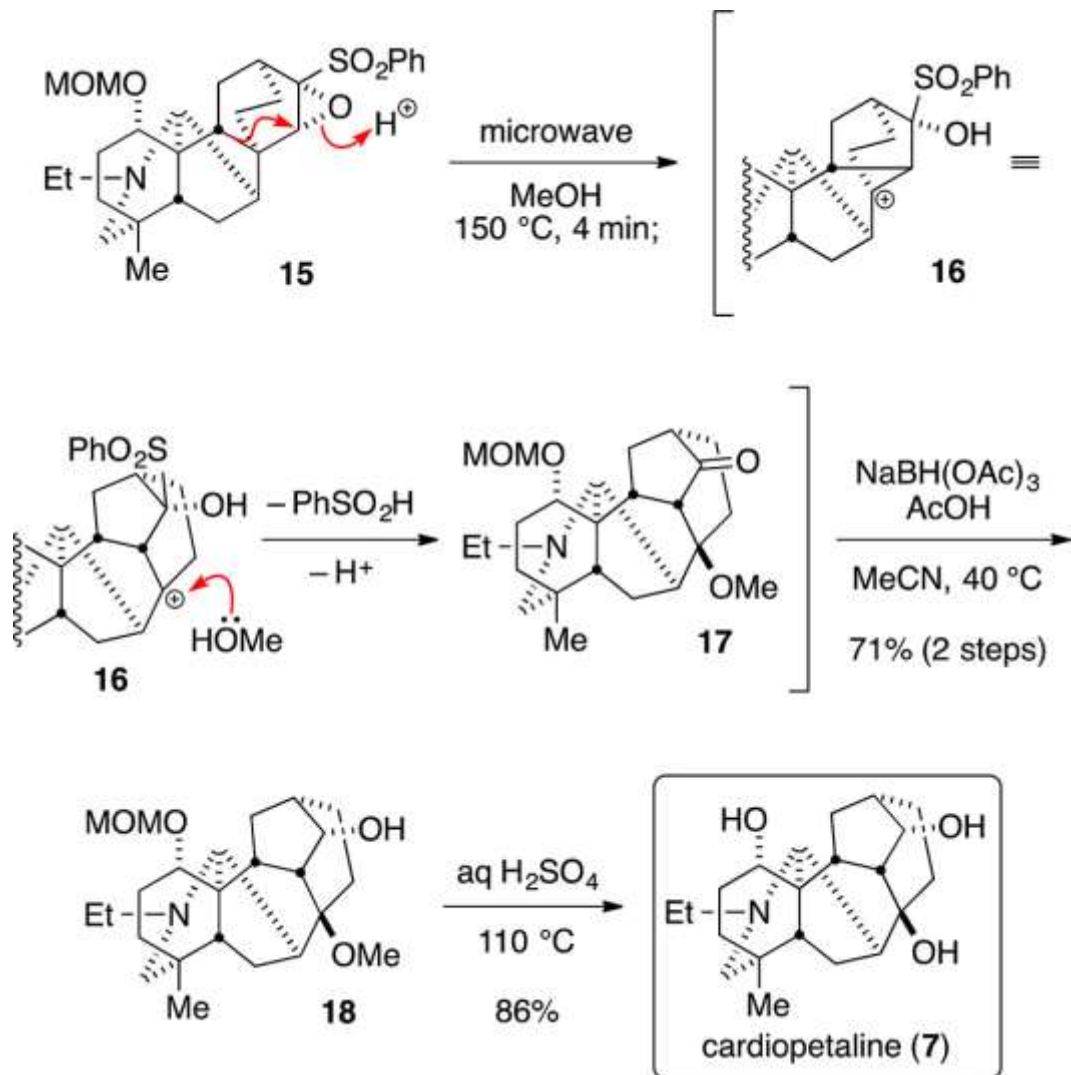


Oxidation-trapping iminium

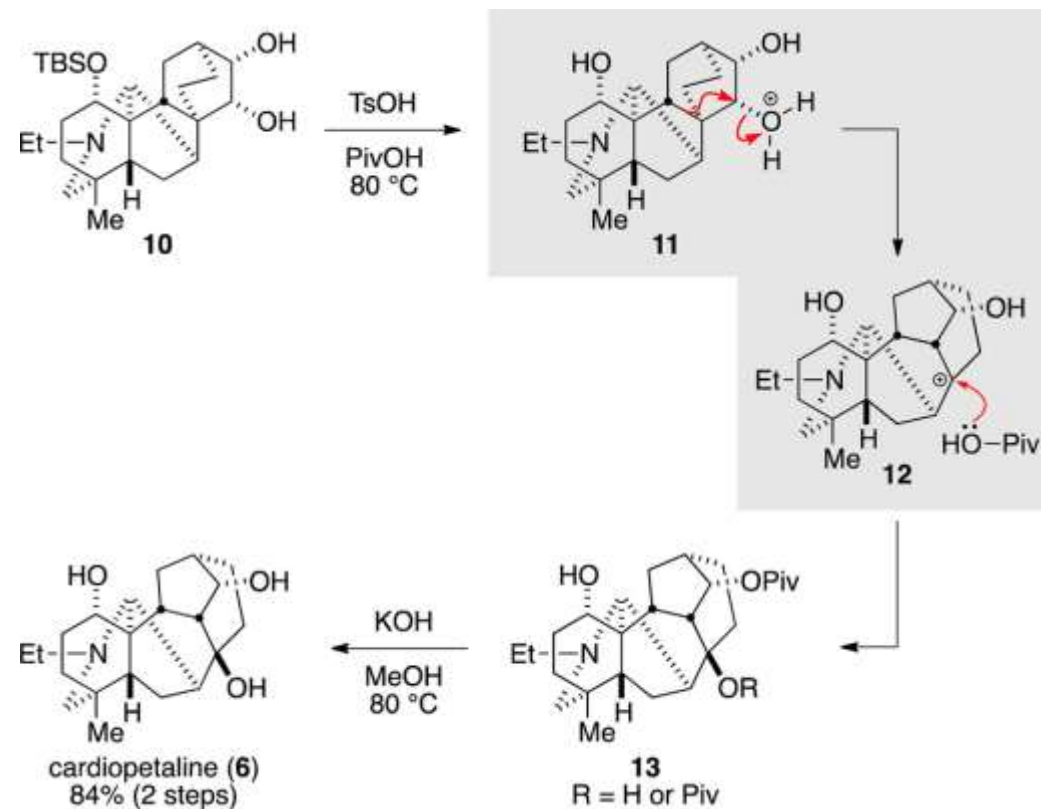




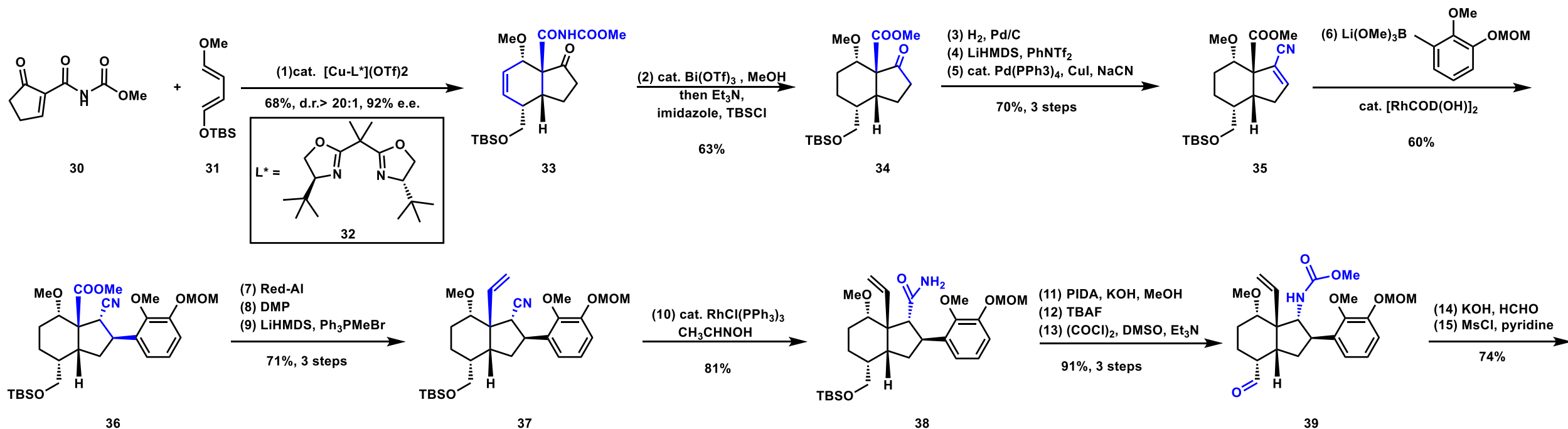
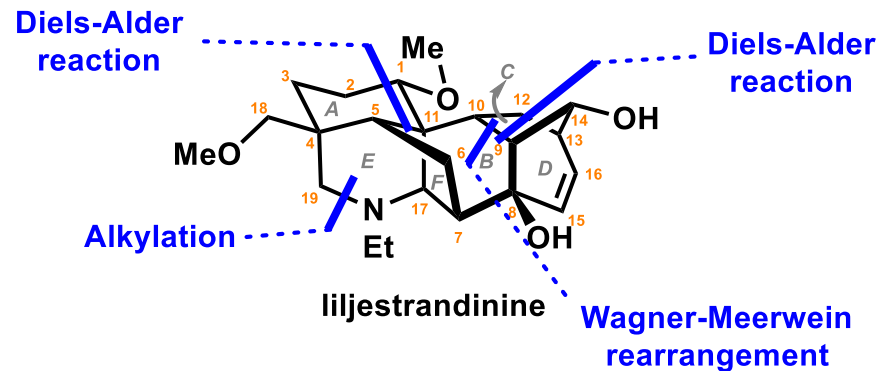
## ● 2016 Tohru Fukuyama



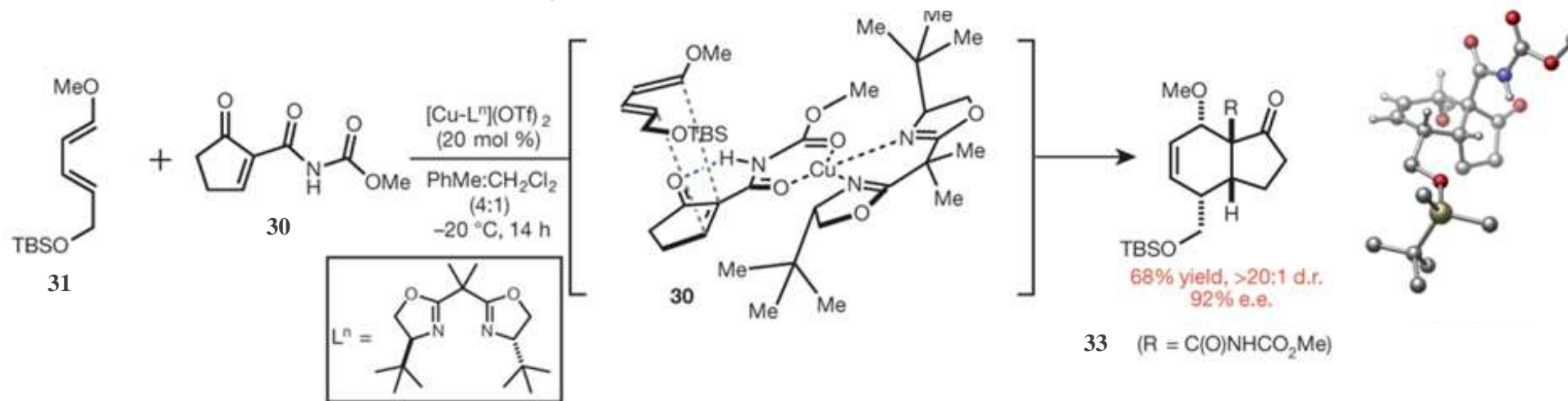
## ● 2017 Tohru Fukuyama



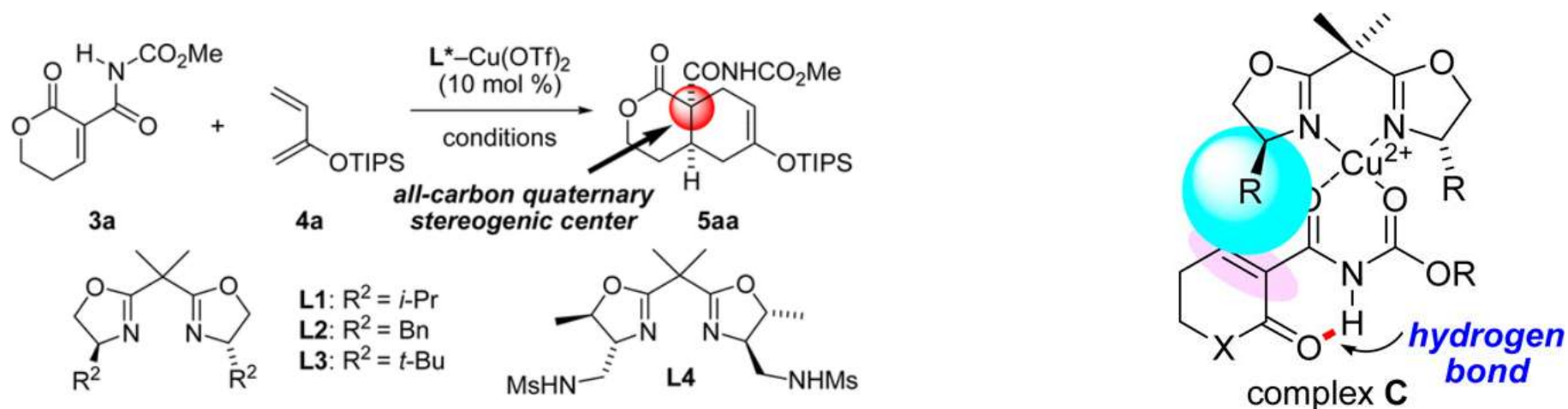
● 2017 Sarpong's work



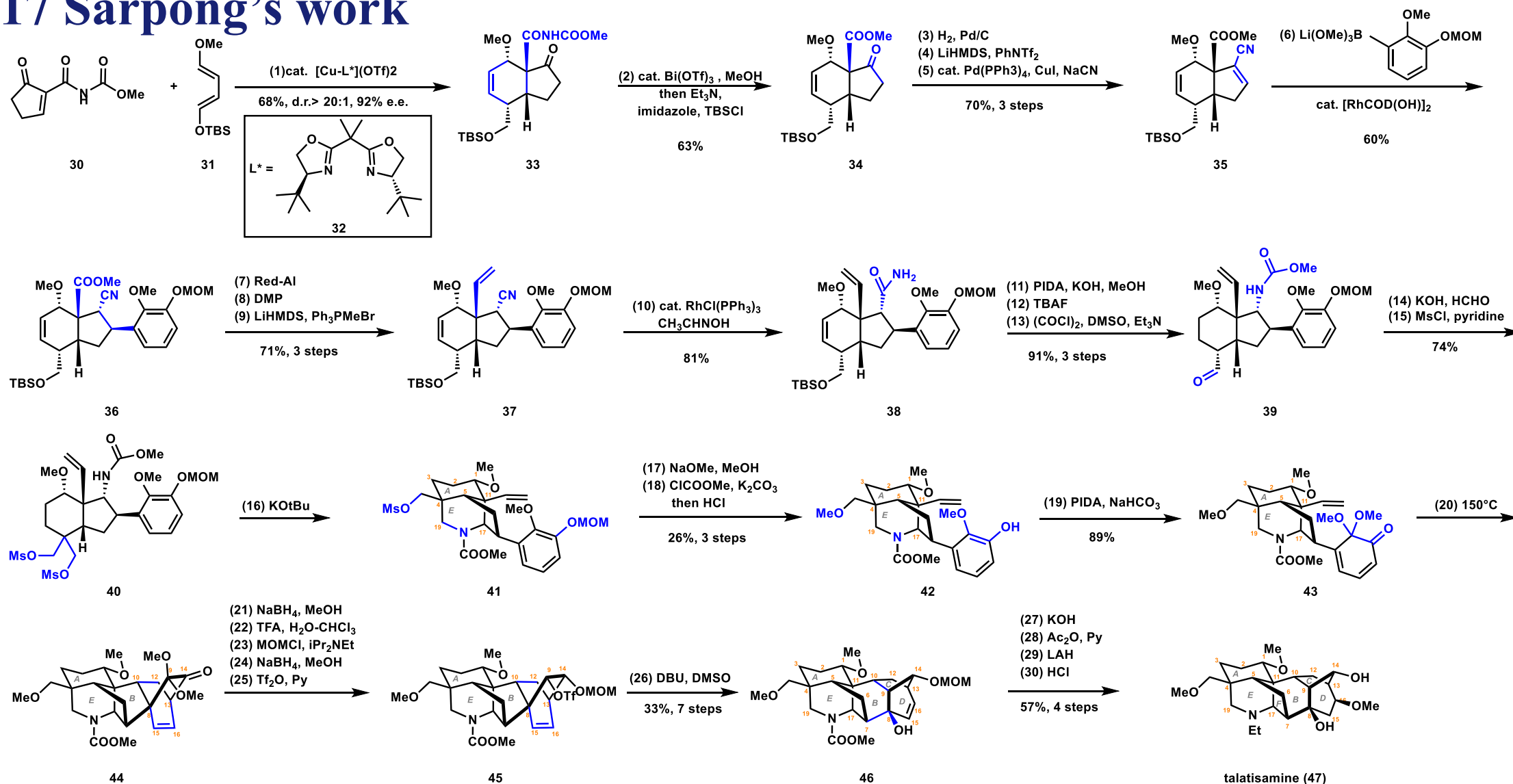
## ● Enantioselective Diels–Alder cycloaddition



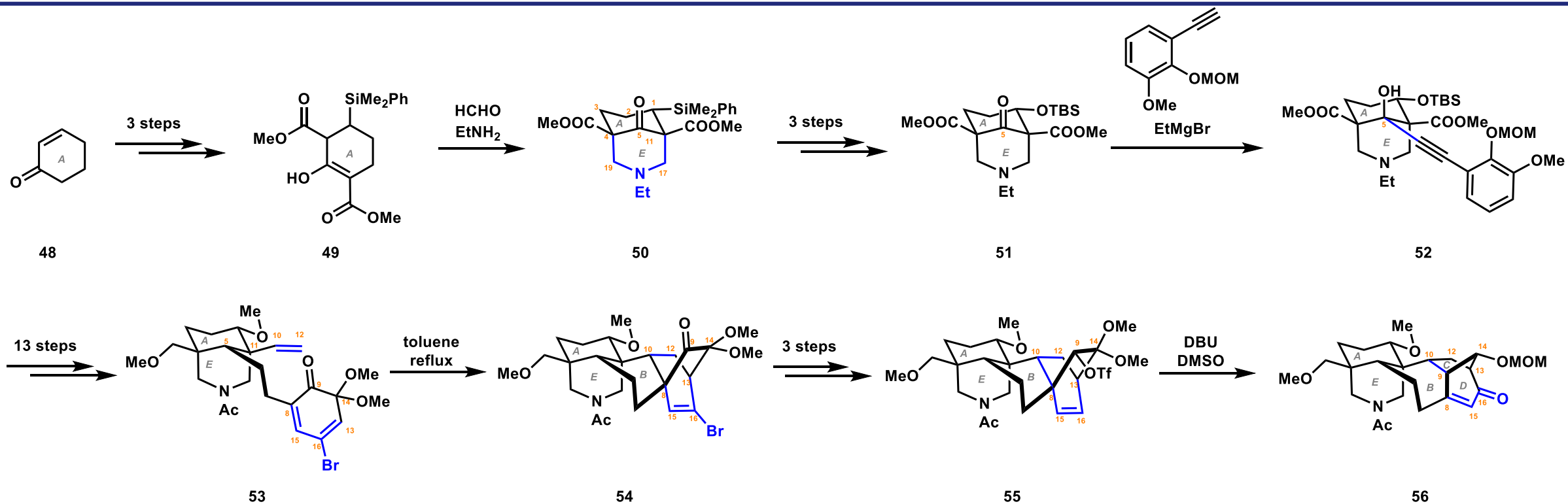
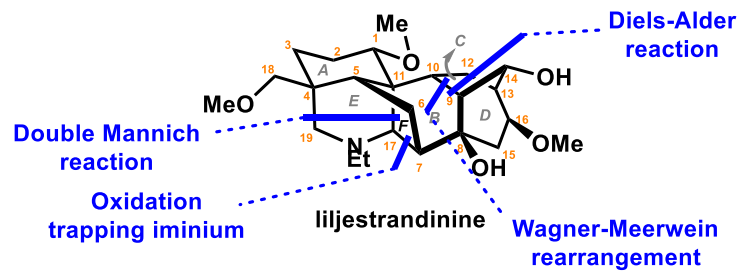
## 2013 Masahisa Nakada



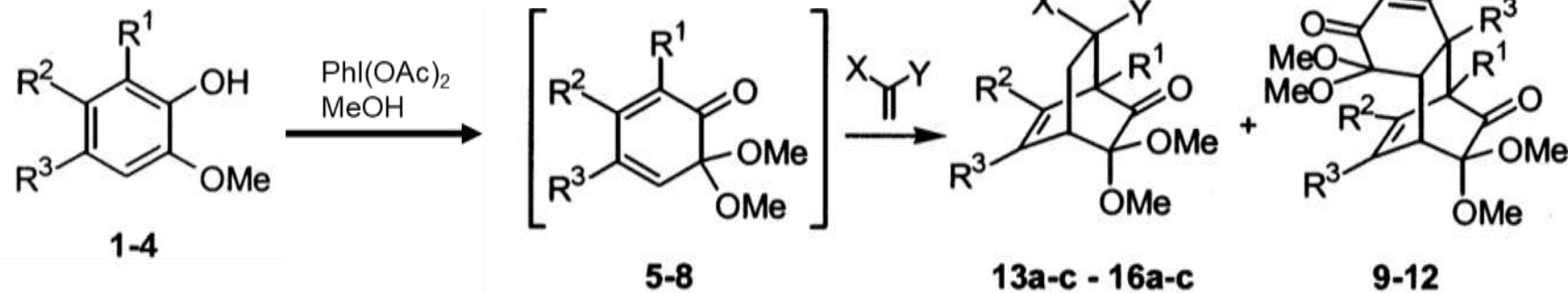
# ● 2017 Sarpong's work



● 2020 Masayuki Inoue



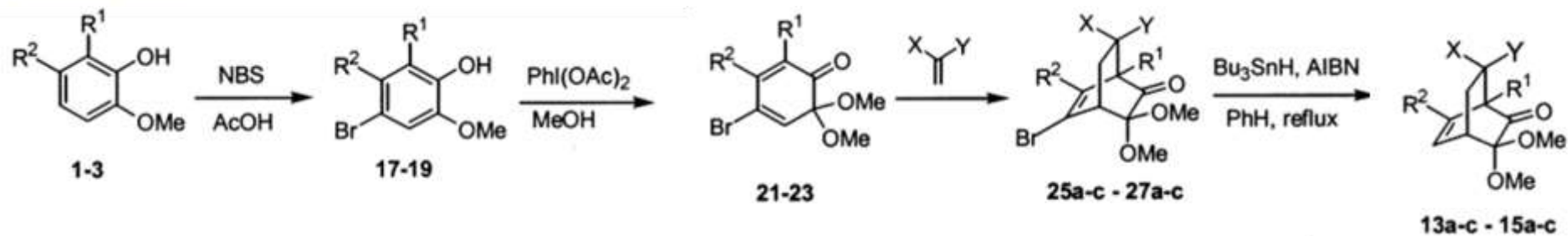
# ● Oxidation-IMDA



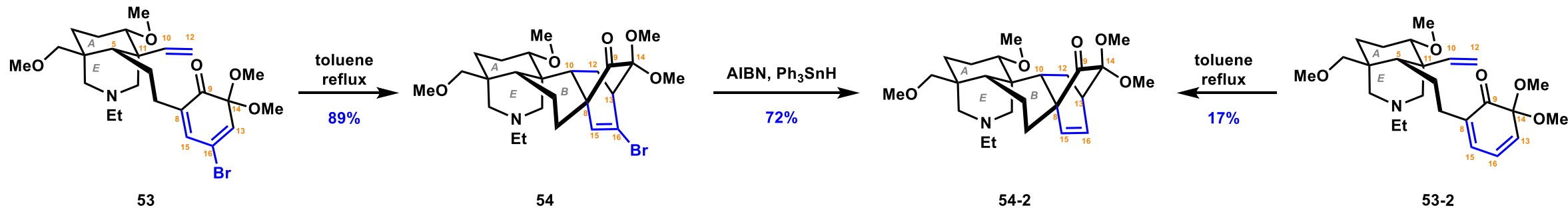
For **1,5,9,13a-c**:  $\text{R}^1 = \text{R}^2 = \text{H}$ ,  $\text{R}^3 = \text{H}$   
**2,6,10,14a-c**:  $\text{R}^1 = \text{Me}$ ,  $\text{R}^2 = \text{R}^3 = \text{H}$   
**3,7,11,15a-c**:  $\text{R}^1 = \text{R}^3 = \text{H}$ ,  $\text{R}^2 = \text{Me}$   
**4,8,12,16a-c**:  $\text{R}^1 = \text{R}^2 = \text{H}$ ,  $\text{R}^3 = \text{O}^{\ominus}$

a:  $\text{X} = \text{CO}_2\text{Me}$ ,  $\text{Y} = \text{H}$   
b:  $\text{X} = \text{CO}_2\text{Me}$ ,  $\text{Y} = \text{Me}$   
c:  $\text{X} = \text{COMe}$ ,  $\text{Y} = \text{H}$

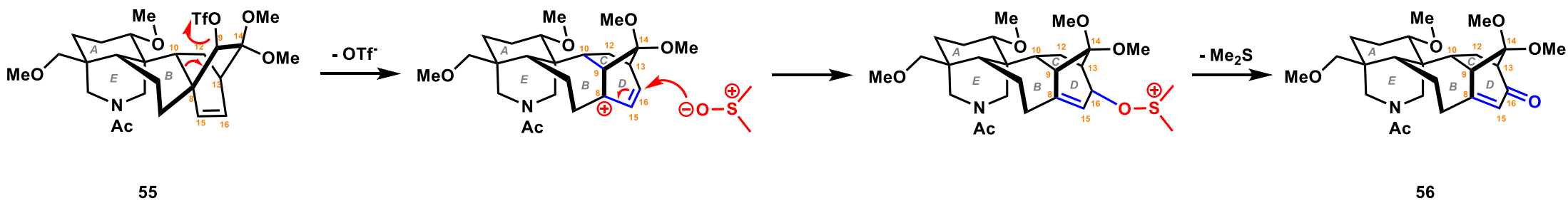
entry	phenol	MOB	dienophile <sup>b</sup>	reaction conditions		adduct/Y (%)	dimer/Y (%)
				addition time <sup>c</sup> /temp	after addition <sup>d</sup>		
1	<b>1</b>	<b>5</b>	MA	10 h/rt	rt/1 h	<b>13a/29</b>	<b>9/70</b>
2			MA	10 h/reflux	reflux/1 h	<b>13a/40</b>	<b>9/60</b>
3			MMA	10 h/rt	rt/1 h	<b>13b/9</b>	<b>9/90</b>
4			MMA	48 h/reflux	reflux/1 h	<b>13b/28</b>	<b>9/65</b>
5			MVK	5 h/rt	rt/1 h	<b>13c/54</b>	<b>9/24</b>
6			MVK	10 h/rt	reflux/1 h	<b>13c/62</b>	<b>9/10</b>
7	<b>2</b>	<b>6</b>	MA	8 h/reflux	reflux/1 h	<b>14a/86</b>	<b>10/13</b>
8			MMA	8 h/reflux	reflux/1 h	<b>14b/43</b>	<b>10/38</b>
9			MVK	8 h/reflux	reflux/1 h	<b>14c/22</b>	<b>10/42</b>
10	<b>3</b>	<b>7</b>	MA	8 h/reflux	reflux/1 h	<b>15a/35</b>	<b>11/34</b>
11			MMA	8 h/reflux	reflux/1 h	<b>15b/19</b>	<b>11/45</b>
12			MVK	8 h/reflux	reflux/1 h	<b>15c/25</b>	<b>11/48</b>
13 <sup>e</sup>	<b>4</b>	<b>8</b>	MA	rt <sup>f</sup>	rt/60 h	<b>16a/86</b>	<b>12/0</b>
14 <sup>e</sup>			MMA	rt <sup>f</sup>	rt/72 h	<b>16b/84</b>	<b>12/0</b>
15 <sup>e</sup>			MVK	rt <sup>f</sup>	rt/20 h	<b>16c/88</b>	<b>12/0</b>



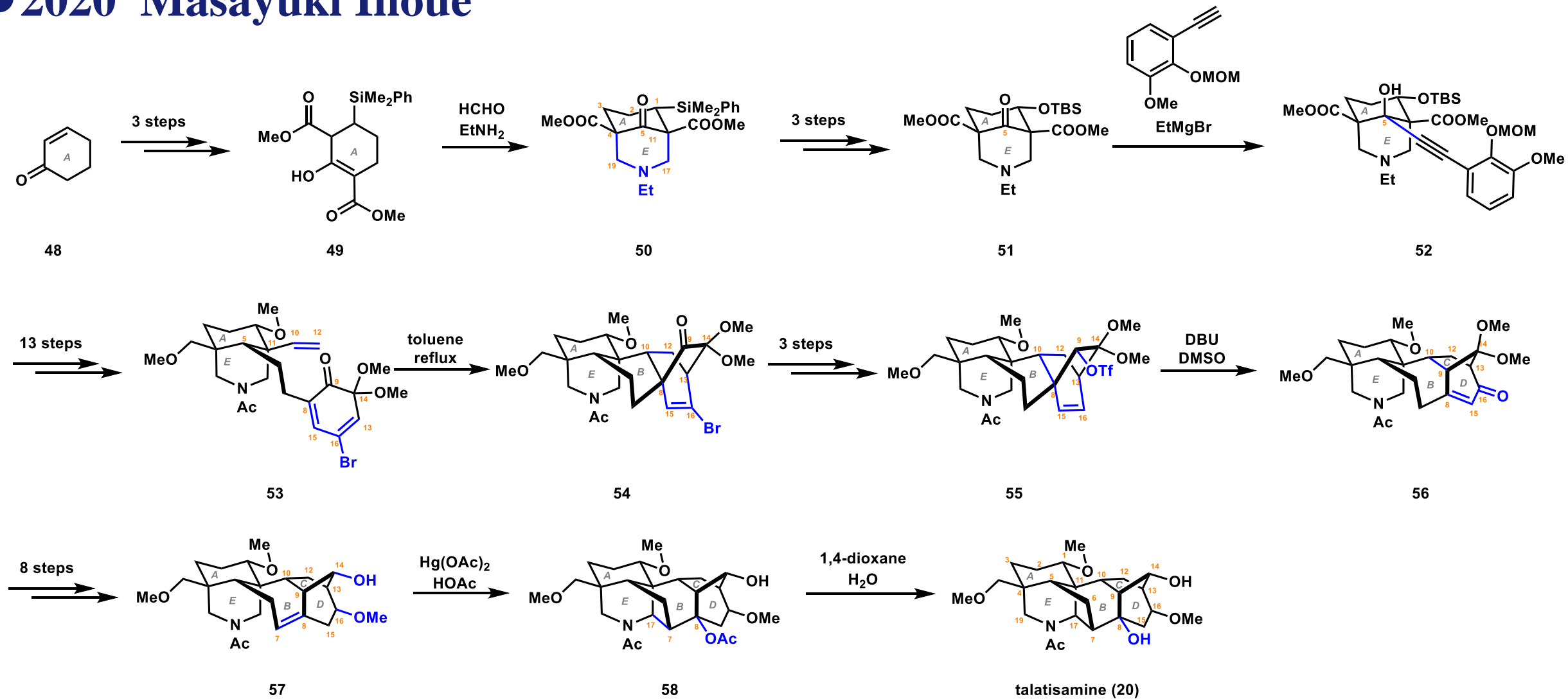
For 1, 13a-c, 17, 21, 25a-c:  $R^1 = R^2 = \text{H}$   
 2, 14a-c, 18, 22, 26a-c:  $R^1 = \text{Me}, R^2 = \text{H}$   
 3, 15a-c, 19, 23, 27a-c:  $R^1 = \text{H}, R^2 = \text{Me}$   
 a:  $\text{X} = \text{CO}_2\text{Me}, \text{Y} = \text{H}$   
 b:  $\text{X} = \text{CO}_2\text{Me}, \text{Y} = \text{Me}$   
 c:  $\text{X} = \text{COMe}, \text{Y} = \text{H}$



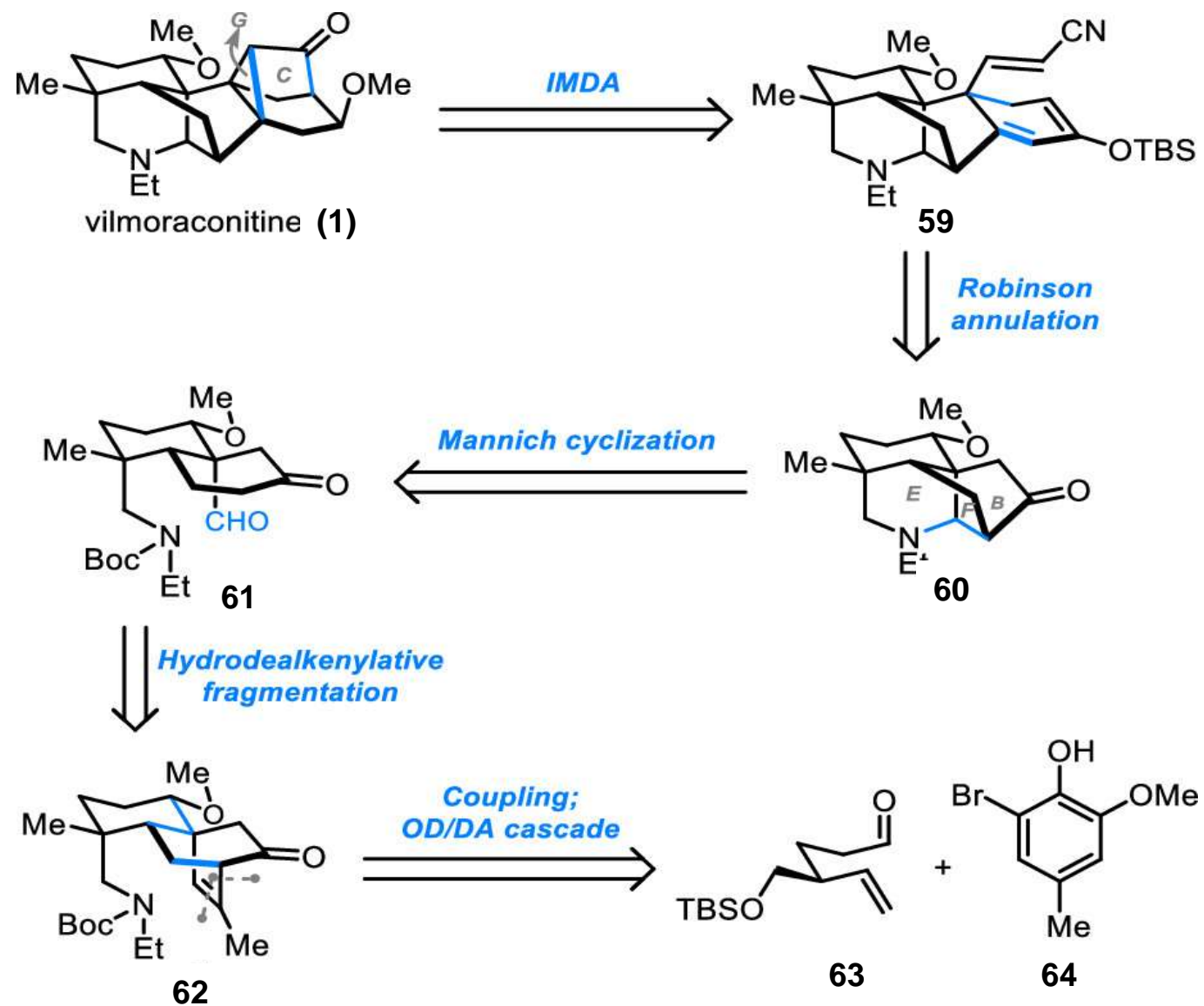
## Wagner-Meerwein rearrangement

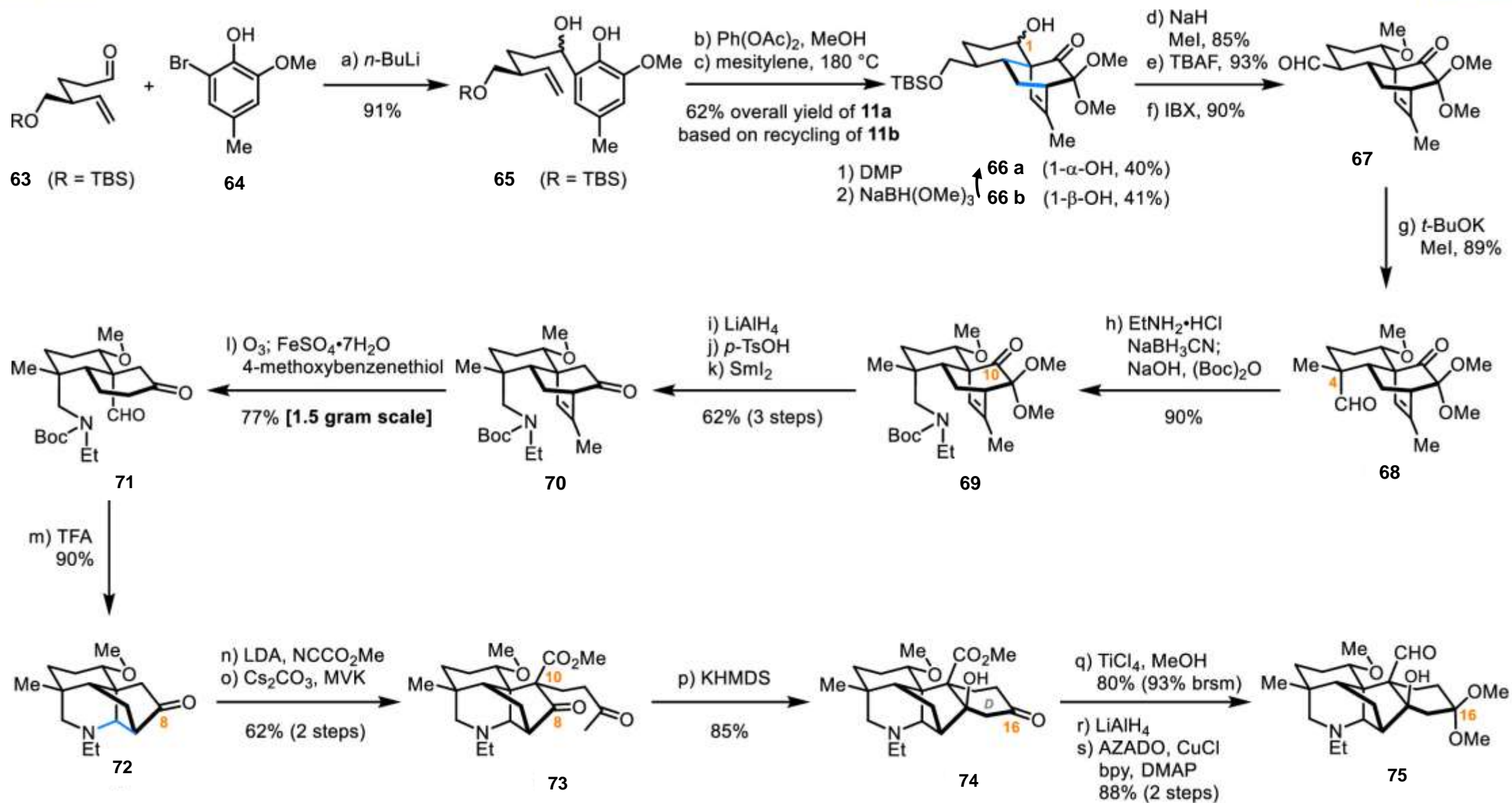


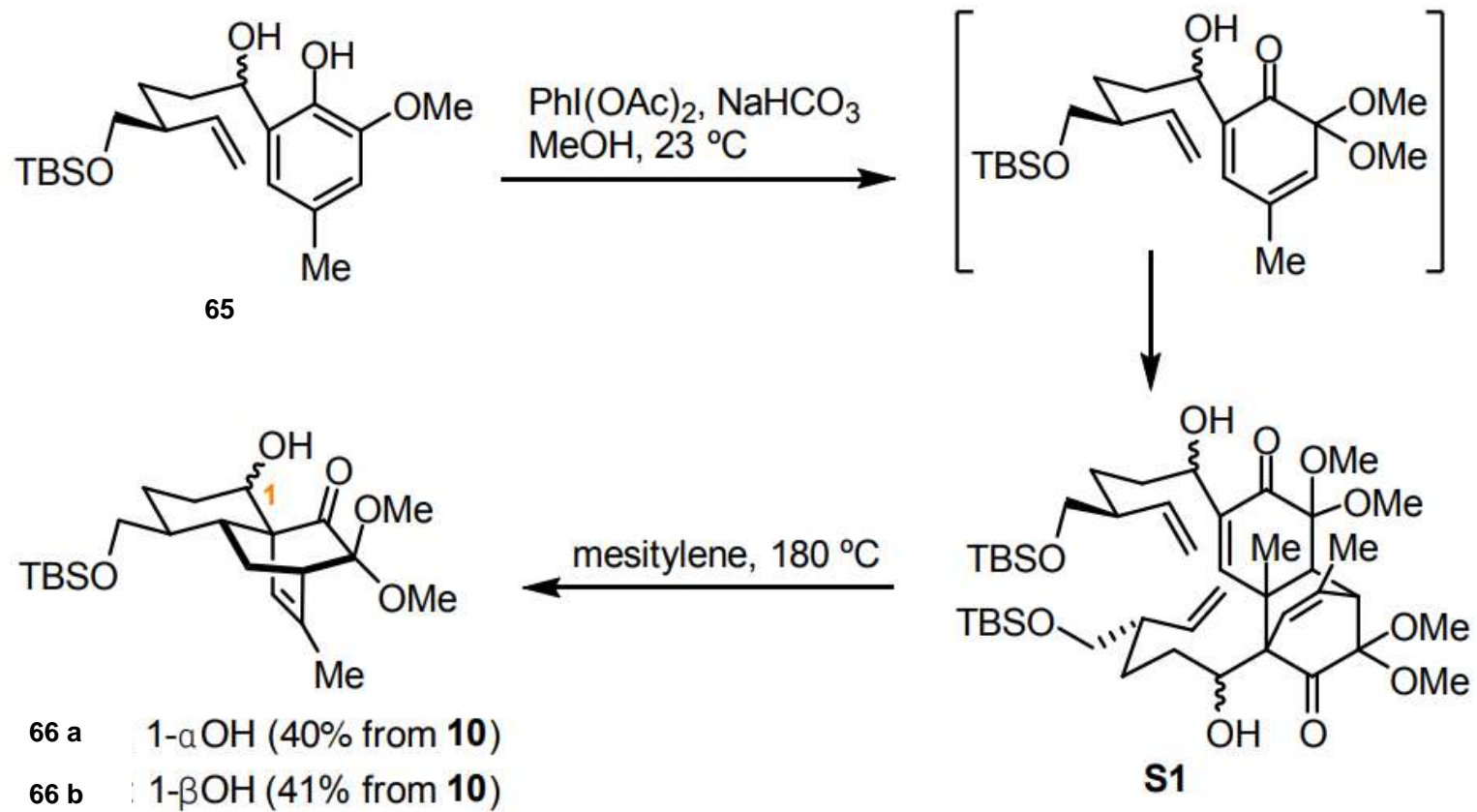
● 2020 Masayuki Inoue

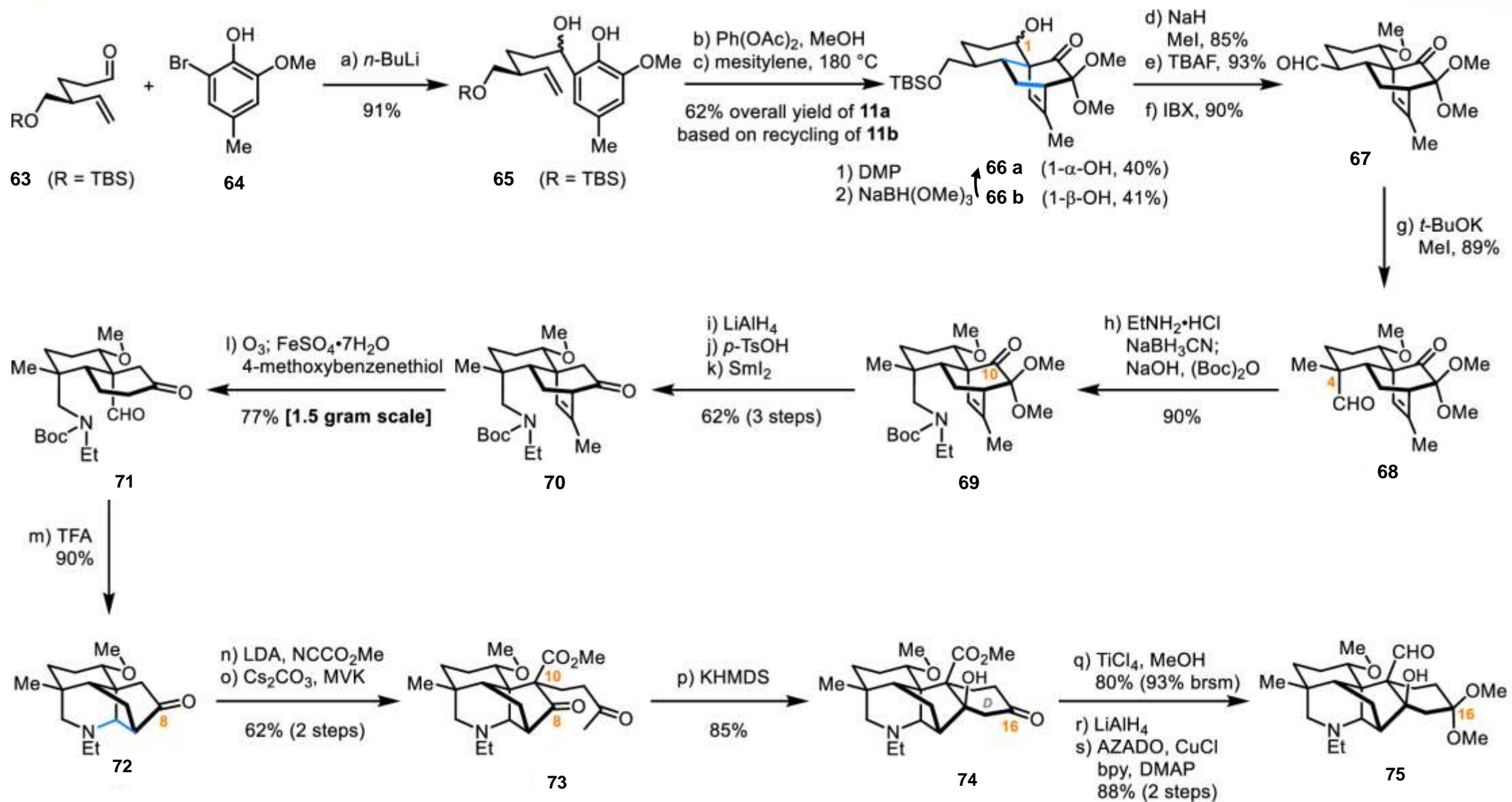




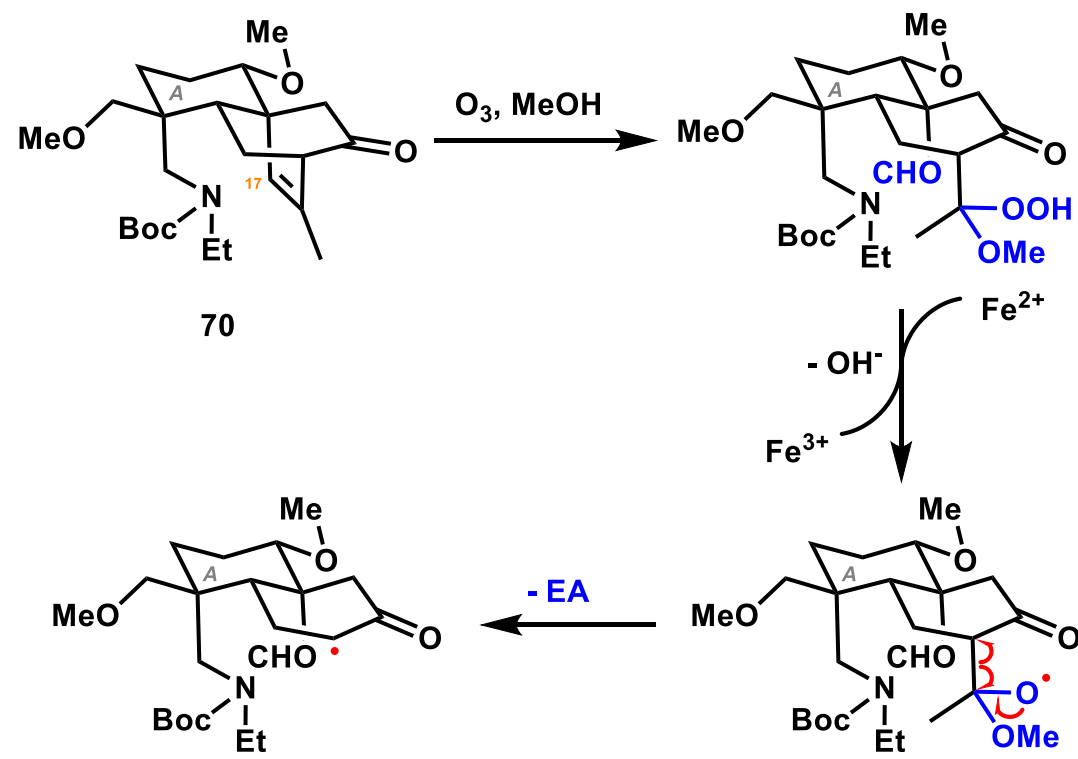
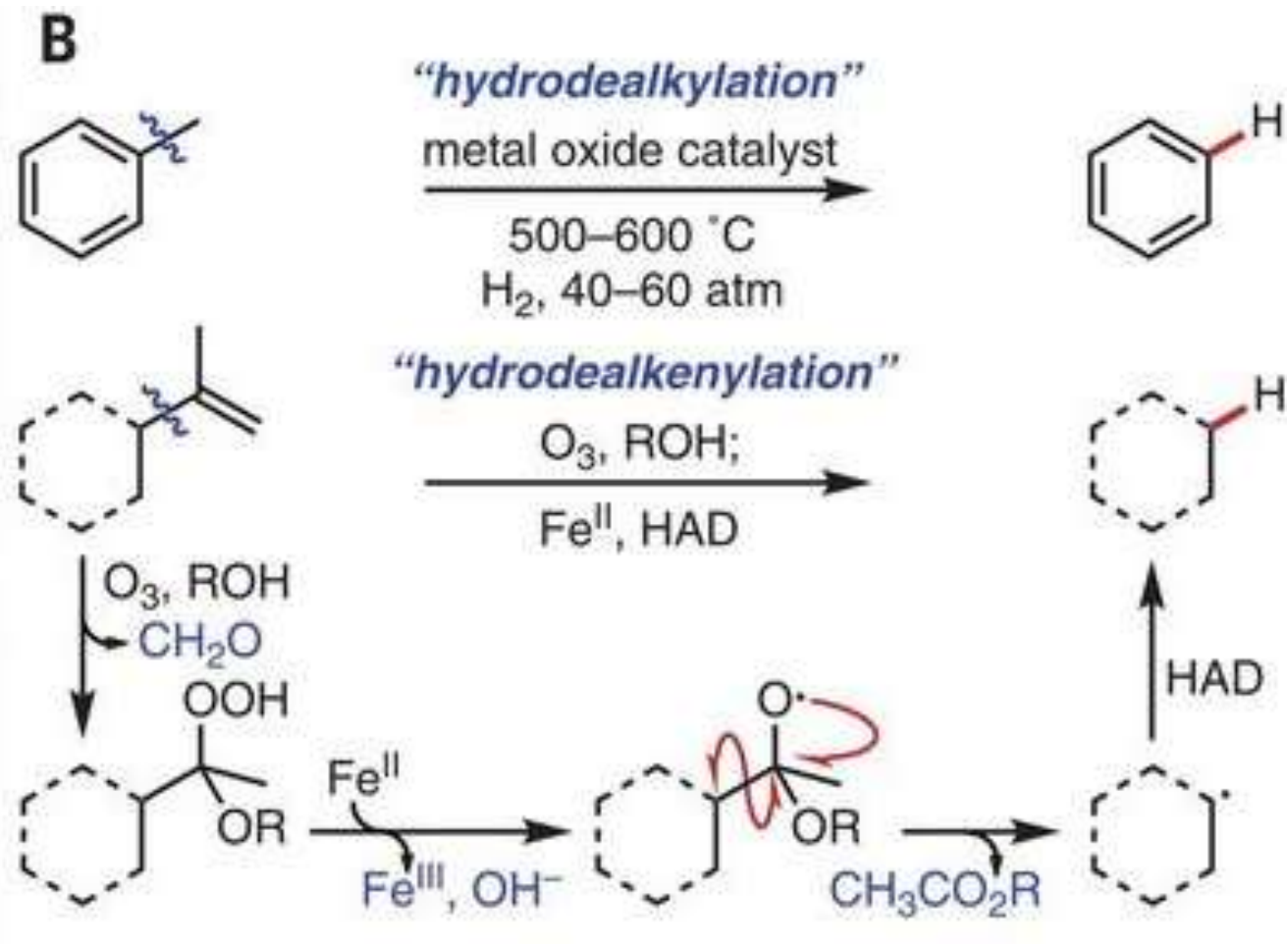


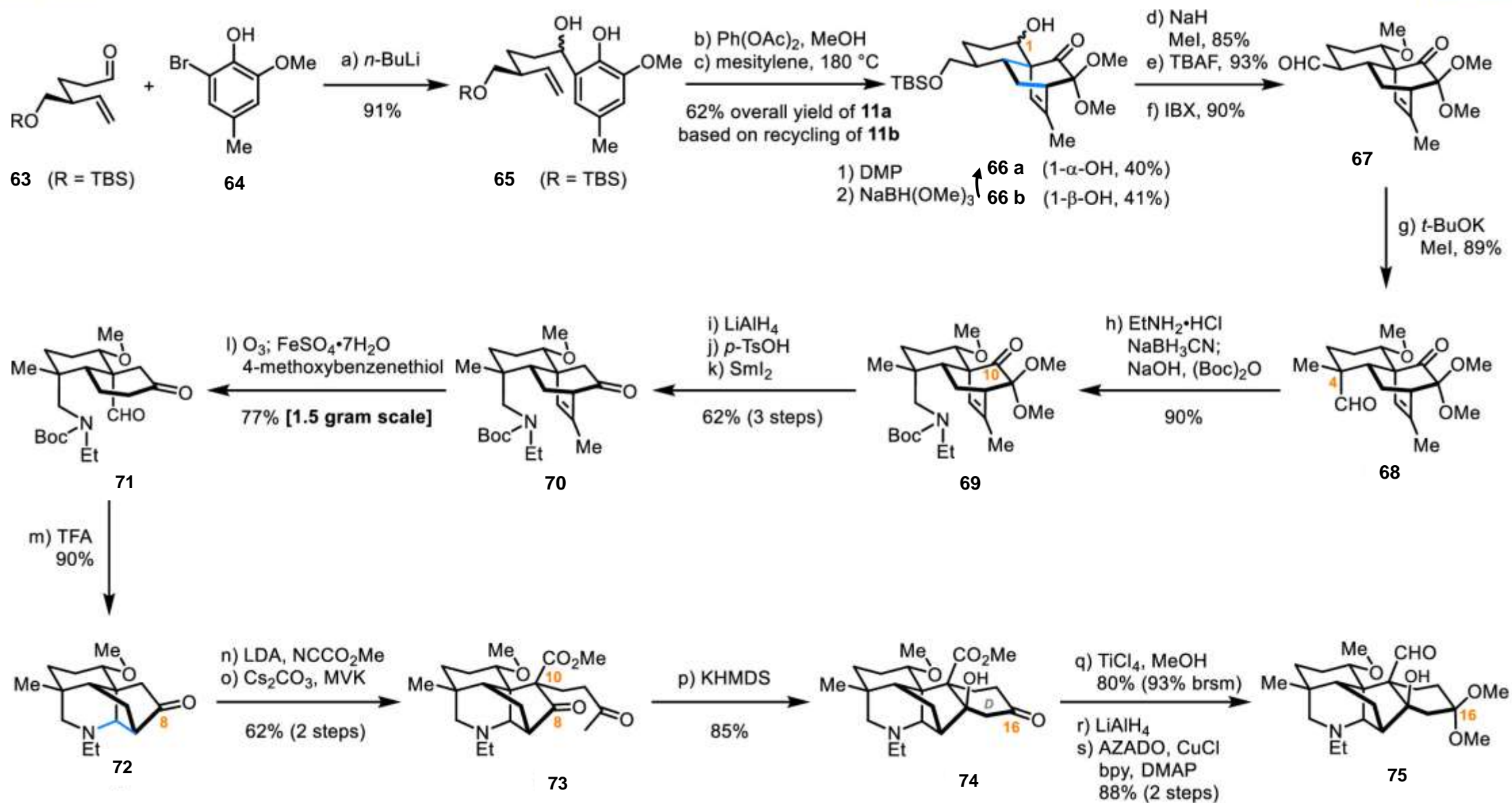


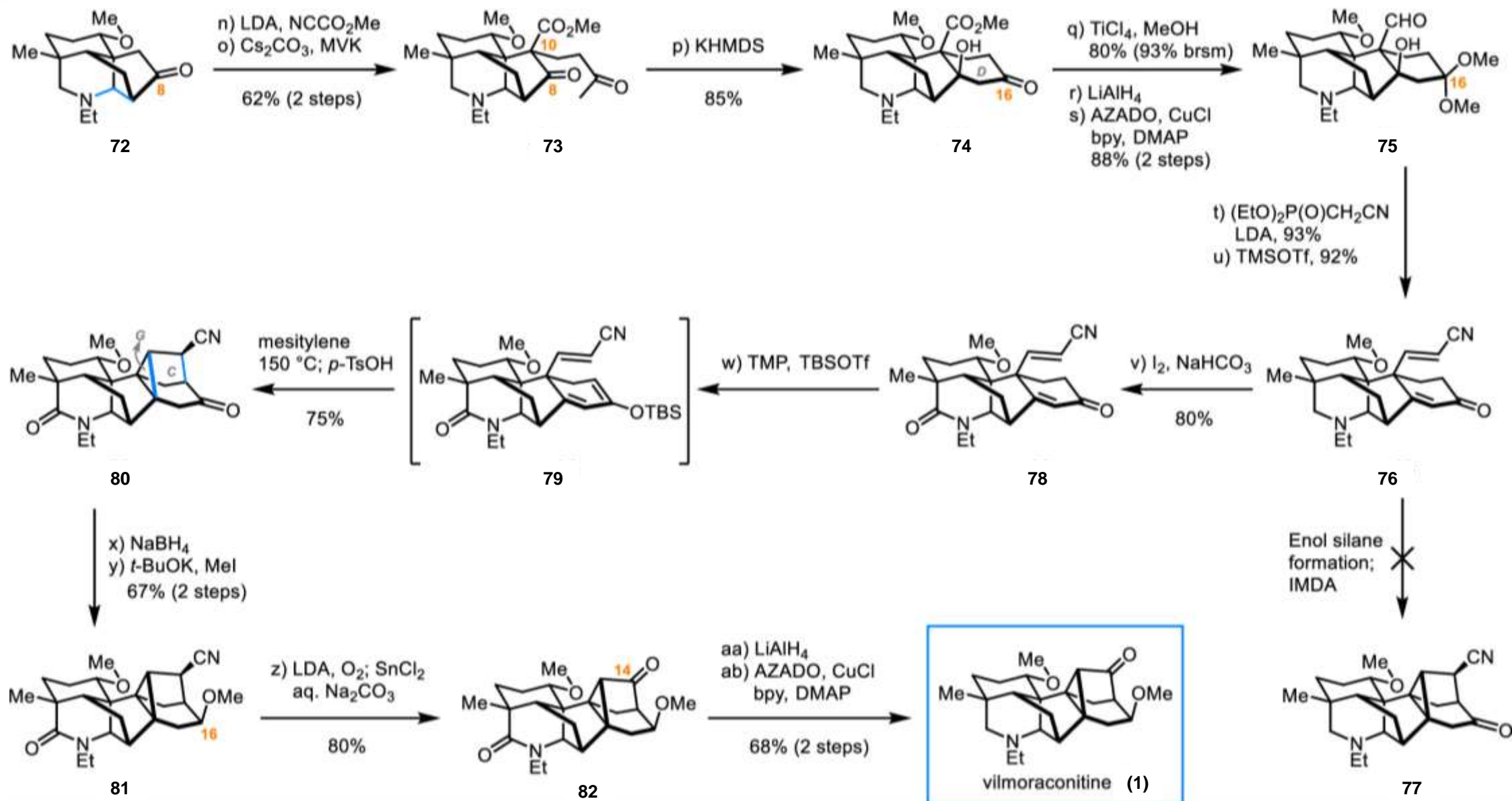




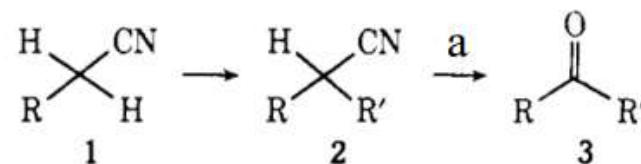
# Hydrodealkenylative fragmentation



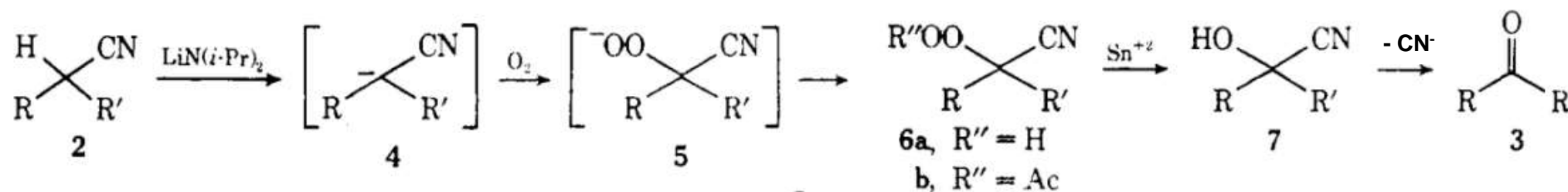




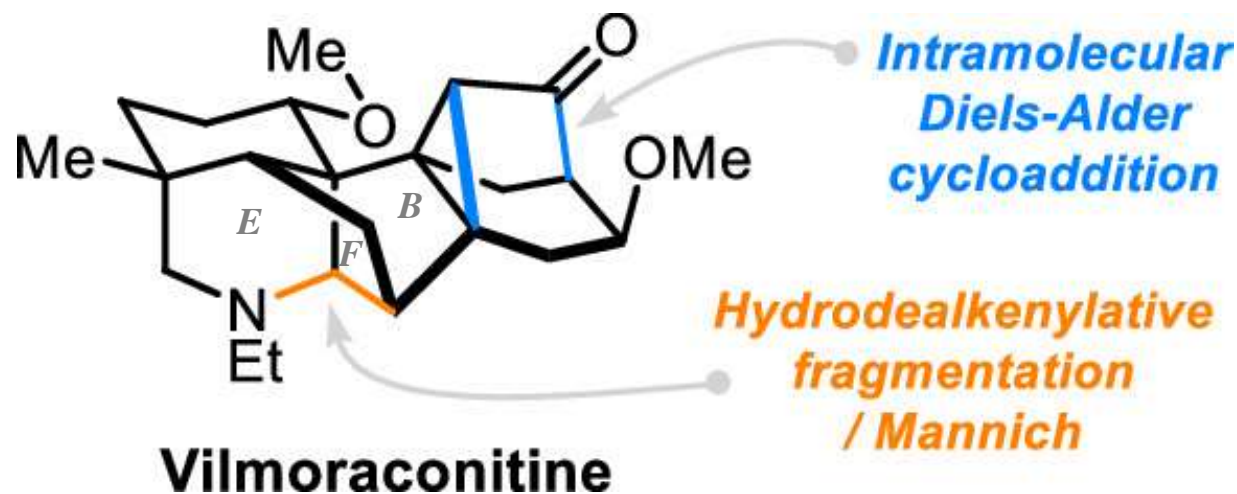
● Oxidative decyanation  
1975 David S. Watt



a: LDA, O<sub>2</sub>, THF, -78°C; then SnCl<sub>2</sub>, *aq.* HCl







- First total synthesis of vilmoraconitine (28 steps, 0.96%)
- Hydrodealkenylative fragmentation/ Mannich sequence was utilized to assemble the B/E/F rings
- IMDA reaction allowed for construction of the C/G rings bearing a highly substituted cyclopropane moiety

**Thanks for Your Attention!**