Total Synthesis of Gelsenicine via a Catalyzed Cycloisomerization Strategy

Eric T. Newcomb, Phil C. Knutson, Blaine A. Pedersen, and Eric M. Ferreira

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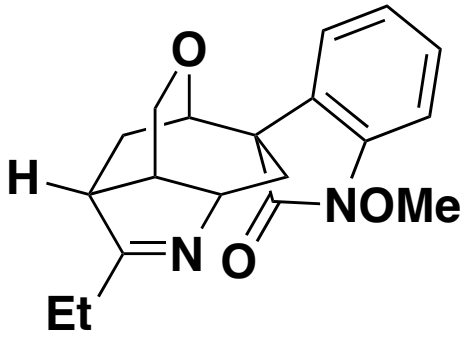

gelsenicine

Ruiting Liu
Wipf Group Current Literature
01/16/2016

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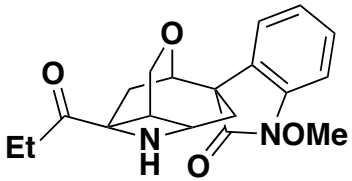
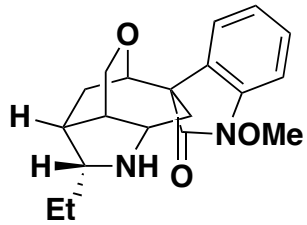
Gelsemium Alkaloid

- Gelsemium alkaloids were isolated from the toxic gelsemium plant which has prominsing antipsoriasis, antitumor, and analgesic characteristics.
- Gelsenicine was isolated in 1982, possesing a polycyclic framework including bridgehead pyrroline and oxane ring, and a spiro-fused N-methoxy oxindole.

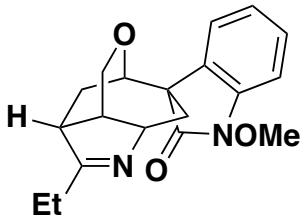
Gelsedine-Type



gelsemoxonine



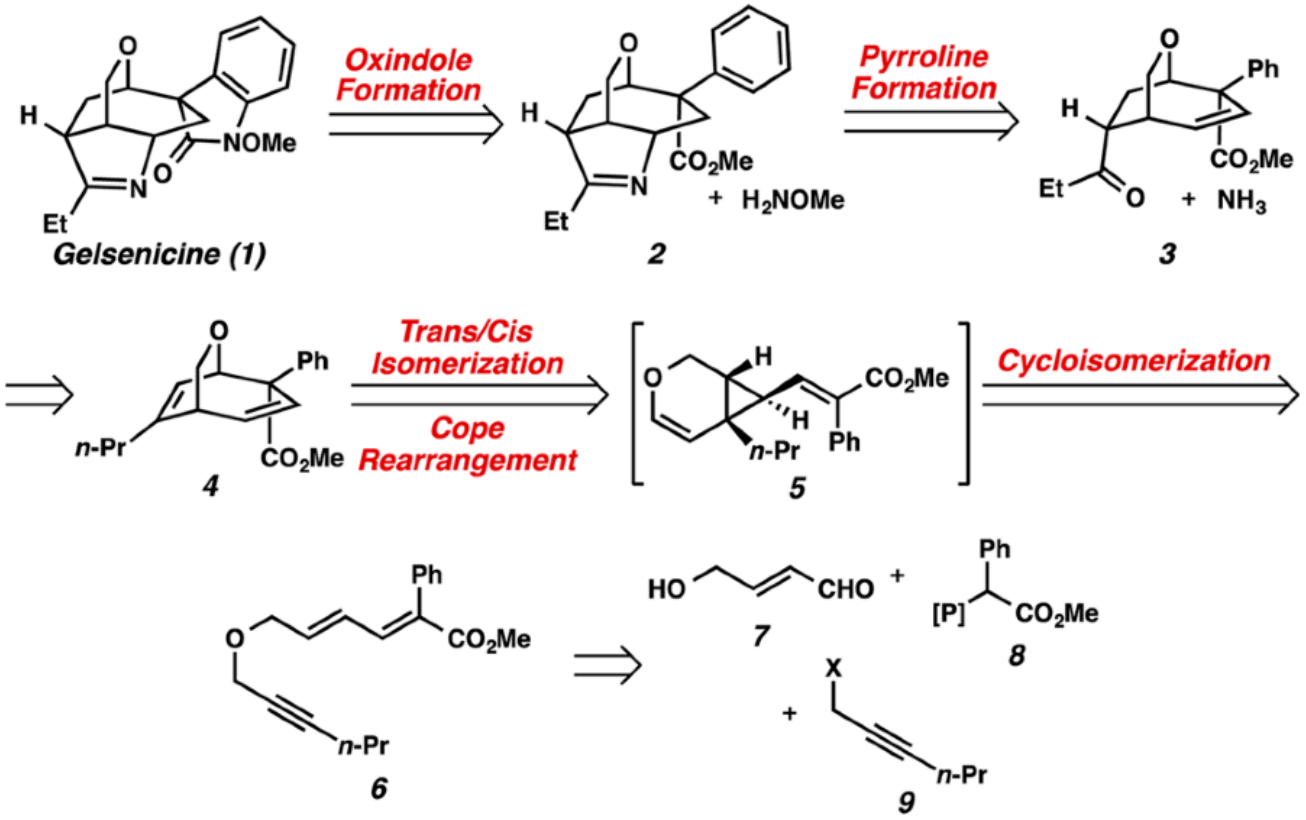
gelsedine



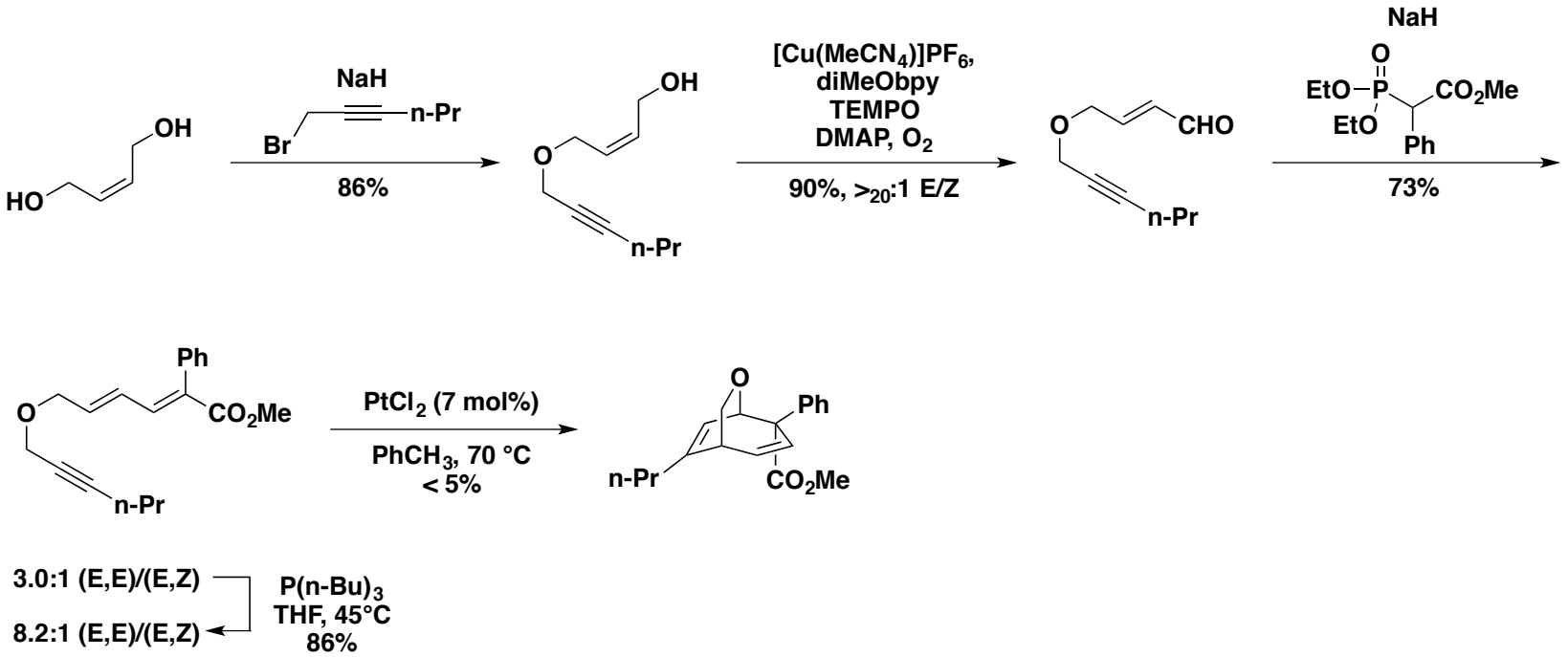
gelsenicine

Huaxue Xuebao, **1982**, 1137

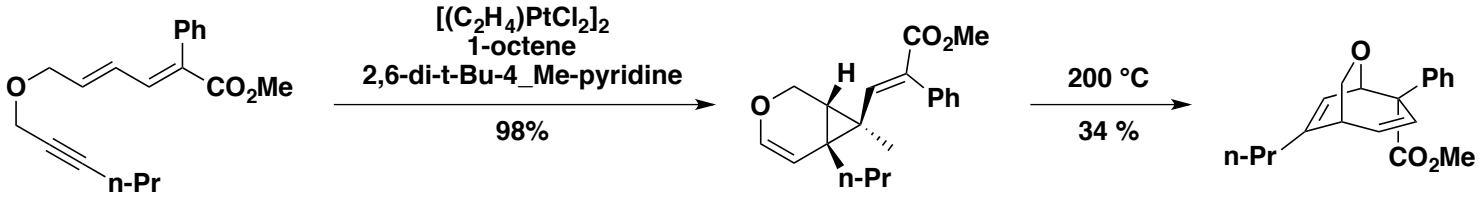
Retrosynthesis



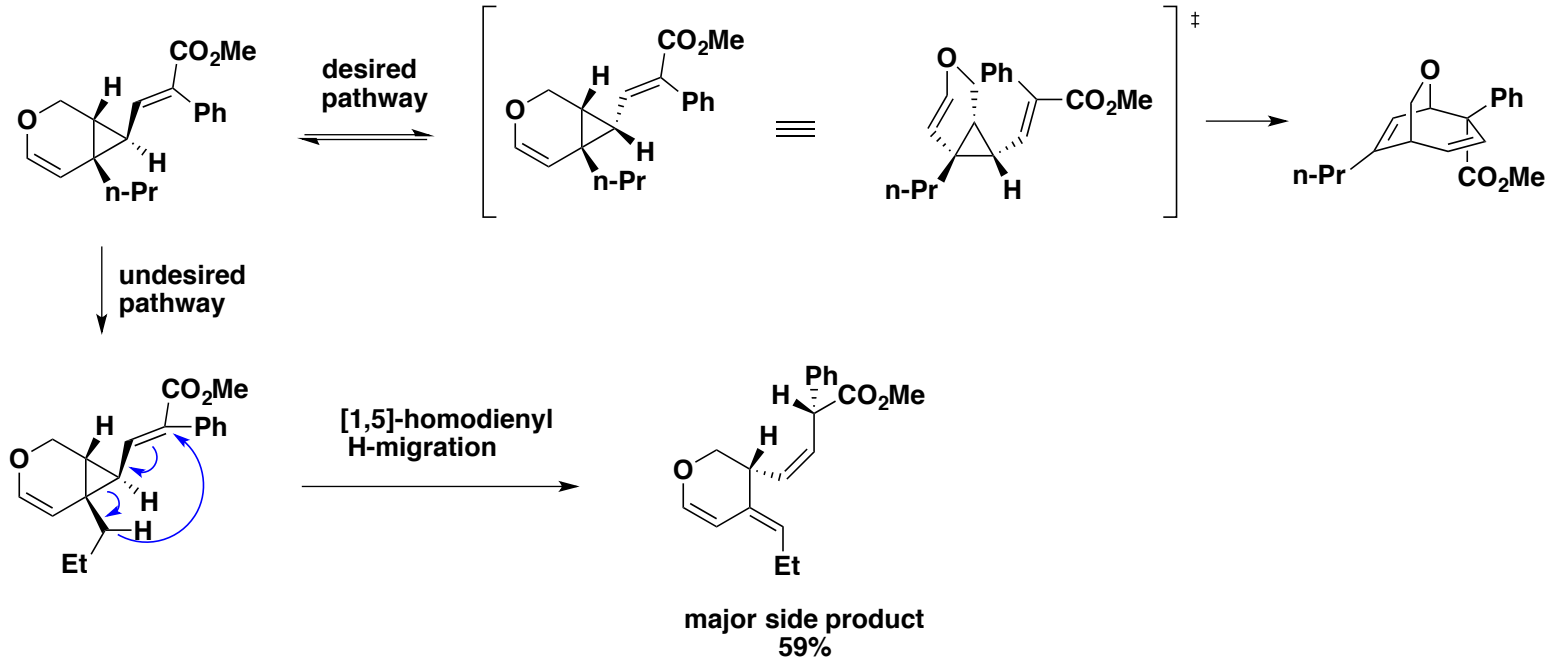
Initial Cascade Attempt



Org. Lett. **2012**, 5258
Org. Lett. **2013**, 1772



Possible mechanism



major side product
59%

Modified Approach

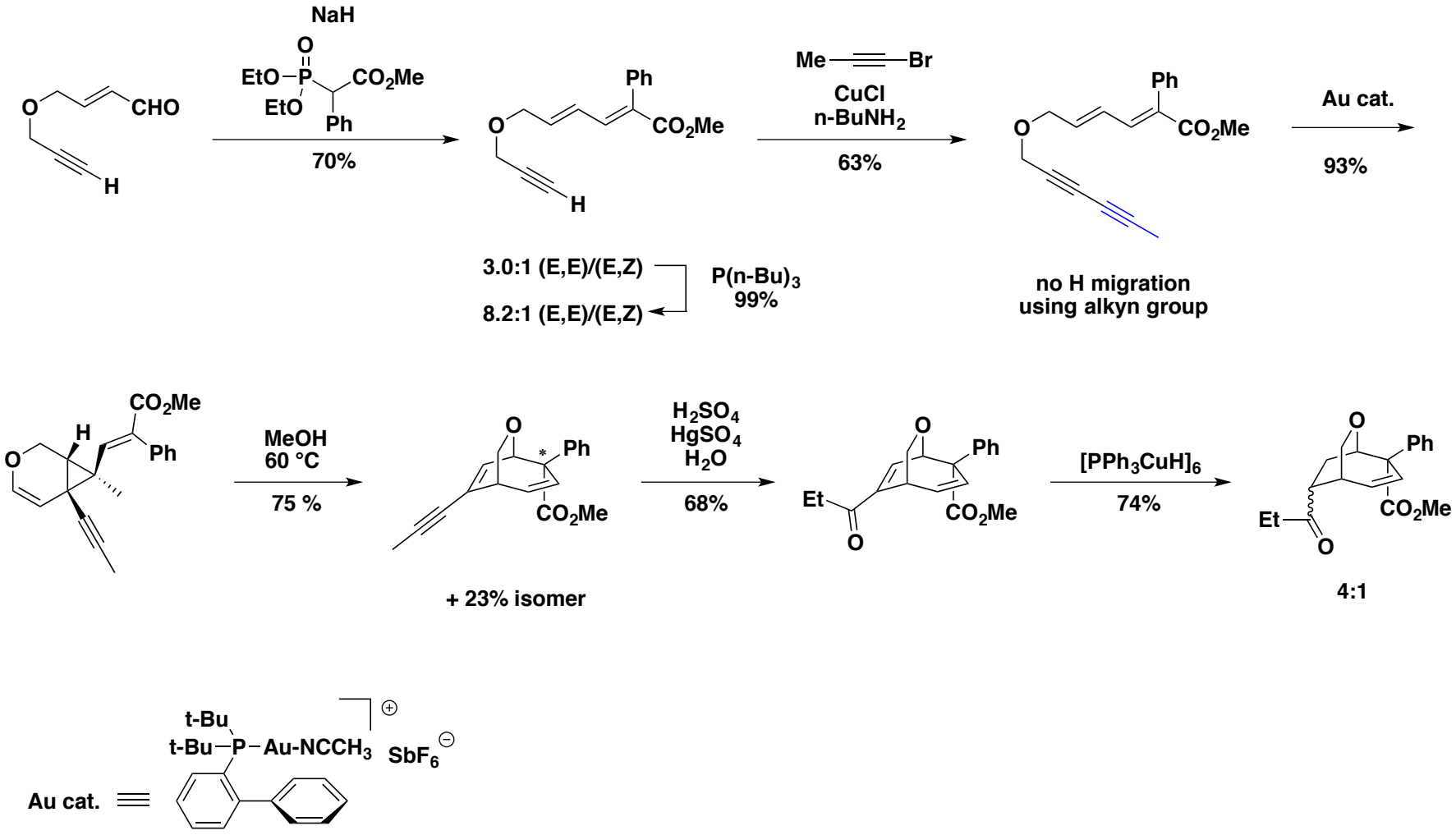
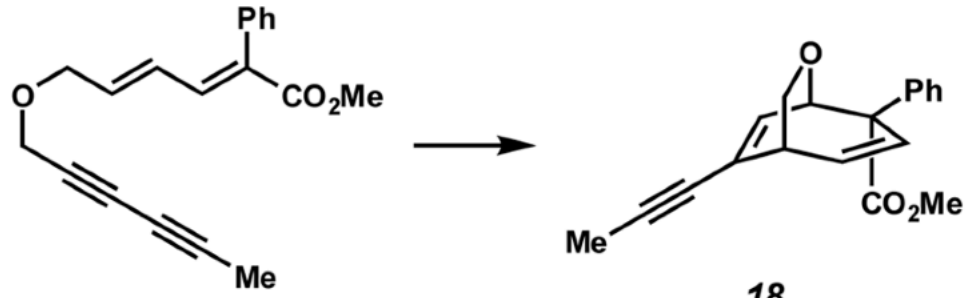


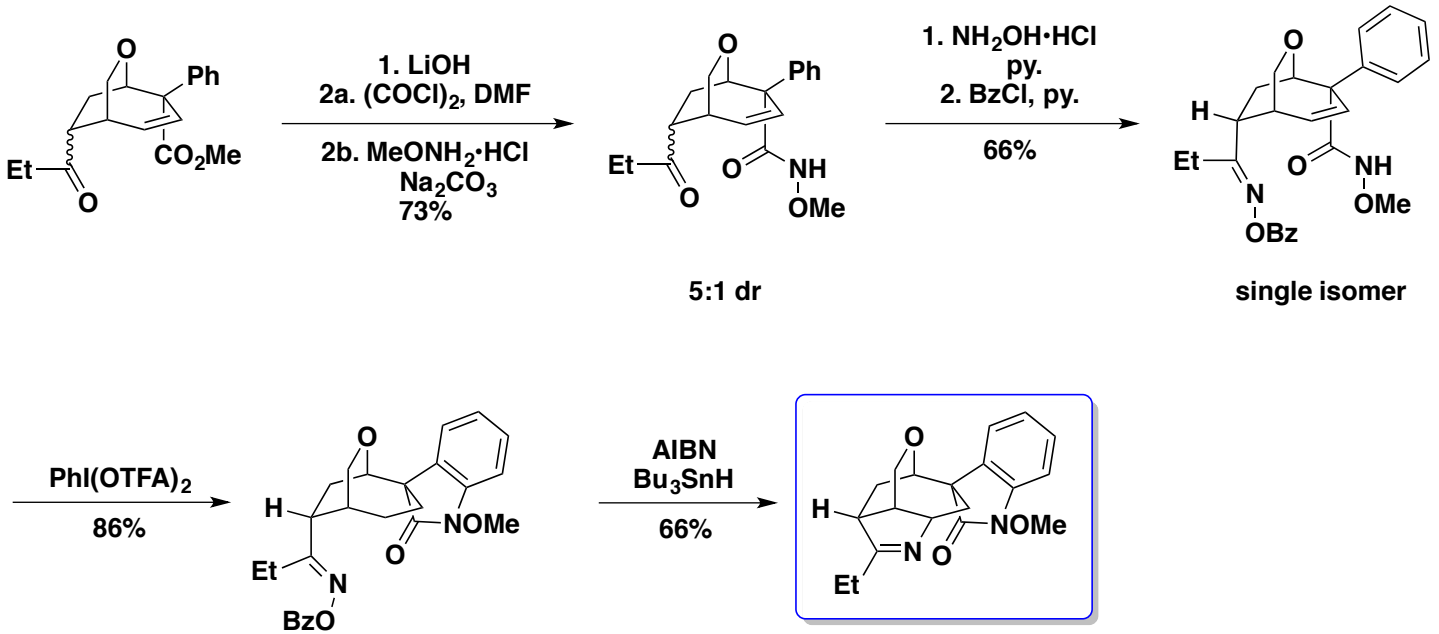
Table 1. Cycloisomerization/Cope Rearrangement of (*E,E*)-16



(*E,E*)-*16* → ***18*** (major diastereomer)

Process	Catalytic Conditons	Yield (%)	***18*** dr
Pt cascade	cat. $[(C_2H_4)PtCl_2]_2$/β-pinene $MgSO_4$, CH_2Cl_2, 60 °C, 24 h	64	2.6 : 1
Au cascade	cat. $LAu(CH_3CN)SbF_6$ CH_2Cl_2, 23 °C, 18 h → 60 °C, 8 h	83	1.9 : 1
Au stepwise	cat. $LAu(CH_3CN)SbF_6$ CH_2Cl_2, 23 °C, 18 h, purify; MeOH, 60 °C, 8 h	***91***	***3.2 : 1***

Selective C-N Bond Cyclization



Conclusion

- The first formal total synthesis of (±)-gelsenicine was reported
- 13 steps, employing a cycloisomerization/ rearrangement sequence, two selective cyclization to form the C-N bond.

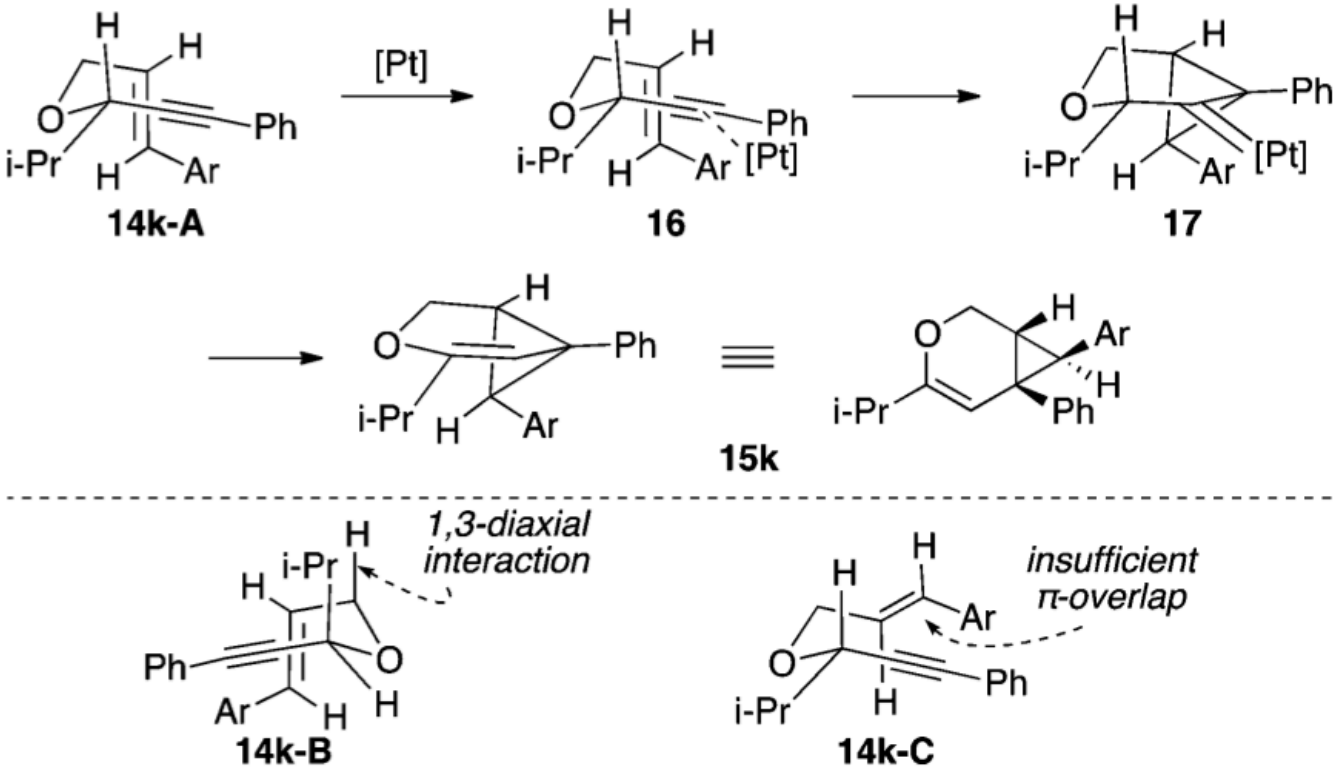


Figure 2. Stereochemical rationalization.

Org. Lett. **2013**, 15, 1772− 1775