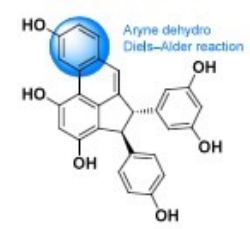
Traversing the Regioselectivity of Intermolecular Pericyclic Aryne Reactions: Total Syntheses of Laetevirenol A and Isoampelopsin D

Long Huu Nguyen, Seoyeong Kim, Jiah Kim, EunHyeon Kim, Sugyeong Ha, Myeonggyo Jeong, Ki Wung Chung, Yeonjoon Kim, Seokwoo Lee, Hwayoung Yun

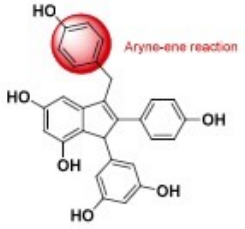
Journal American Chemical Society 2026, 148 (40): 42876–42882.

unique phenanthrene moiety



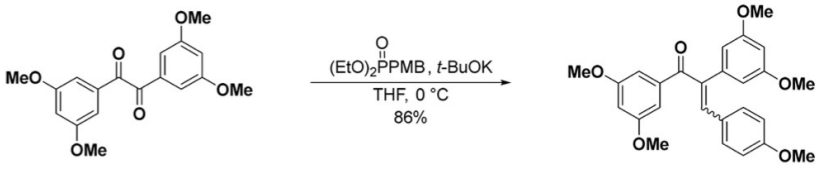
Laetevirenol A

- Unusual regioselectivity
- DFT calculations



Isoampelopsin D

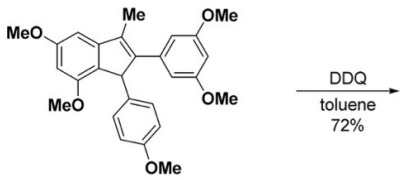
- Late-stage diversification
- Antioxidant activity evaluation



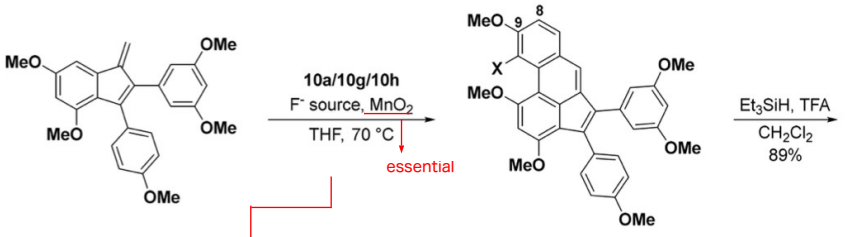
Conditions	Yield%
MeMgI	<30%
MeLi	27%
MeMgI, $CeCl_3$	26%
MeLi, $CeCl_3$	86%

then $BF_3{\cdot}OEt_2$, CH_2Cl_2

organometallic addition/ Nazarov-type cyclization



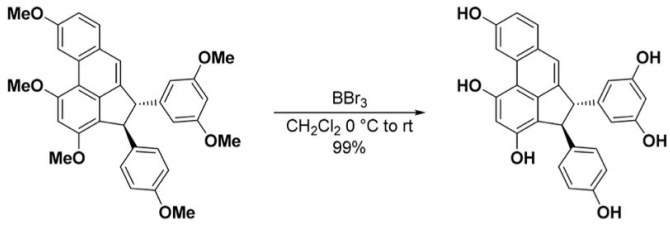
aryne dehydro Diels–Alder reaction

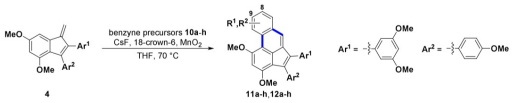


HCO_2Na, $Pd(OAc)_2$, SPhos
MeOH/THF, 70 °C, 64%

11g (X = Cl)
11h (X = Br)
11a (X = H)

HCO_2H, $Pd(PPh_3)_4$, Et_3N
dioxane, 100 °C, 89%



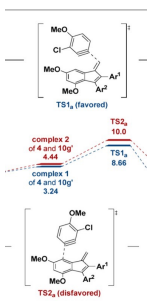


Entry	Benzyne Precusor	Cycloadducts	Entry	Benzyne Precusor	Cycloadducts
1	10a	11a:12a = 1.3:1, 42%	5	10e	11e, not observed; 12e, 16%
2	10b	11b:12b > 20:1, 46%	6	10f	11f, not observed; 12f, 23%
3[b]	10c	11c, not observed; 12c, 28%	7[b]	10g	11g:12g = 6:1, 42%
4	10d	11d, not observed; 12d, 31%	8[b]	10h	11h:12h = 5.5:1, 39%

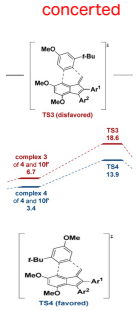
[a]General condition: benzyne precursor (2 equiv), CsF (5 equiv), 18-crown-6 (3 equiv), MnO_2 (10 equiv), 70 °C, 5 h. [b]Benzyne precursor (9 equiv), CsF (15 equiv) were used without 18-crown-6, 20 h. Ratios were calculated based on isolated yields.

the concerted and stepwise pathways depending on substituents

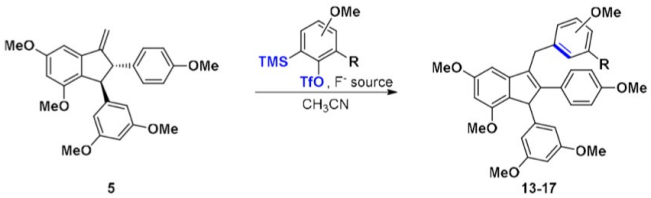
stepwise

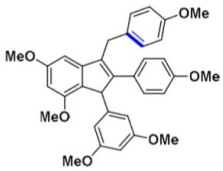


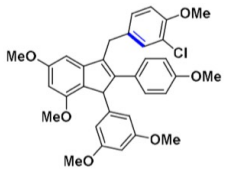
concerted

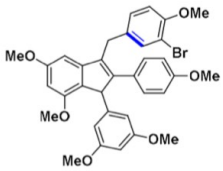


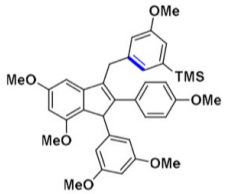
aryne-ene reaction.

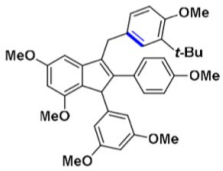






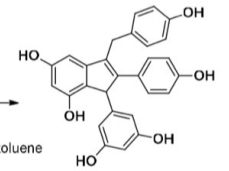






1. BBr_3, CH_2Cl_2 0 °C to rt, 72%
2. $AlCl_3$, $MeNO_2$/toluene 60°C, 54%

retro-Friedel–Crafts



[a]TBAT was used. [b]CsF was used.