Ten-Step Total Synthesis of (±)-Phaeocaulisin A Enabled by Cyclopropanol Ring-Opening Carbonylation

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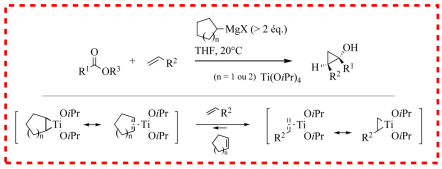
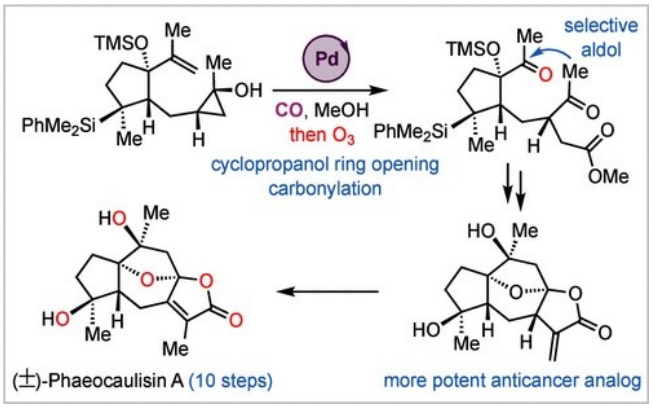
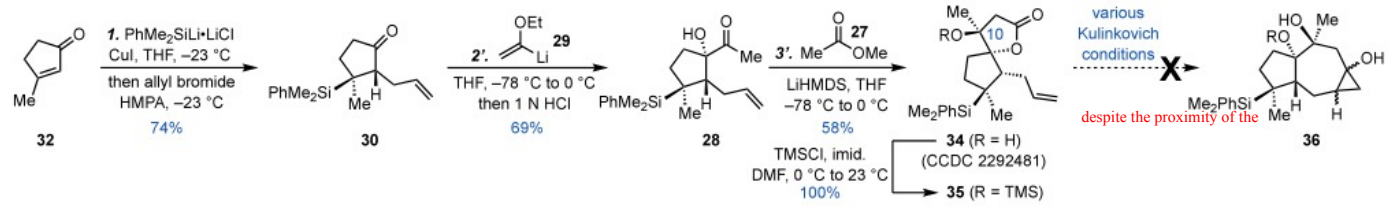
palladiumcatalyzed hydroxycyclopropanol ring-opening carbonylative

Kulinkovich Reaction active spiecies

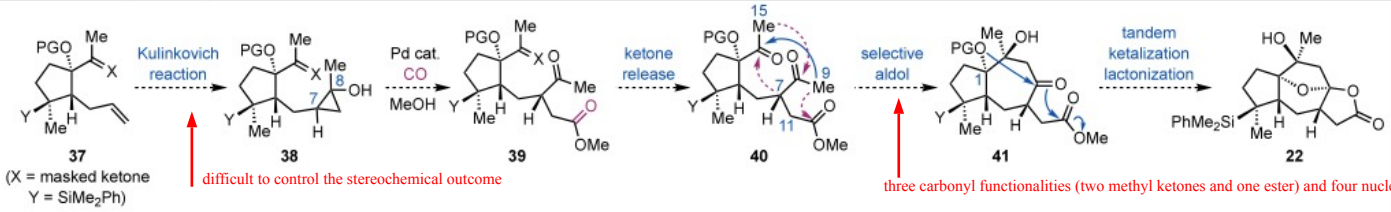




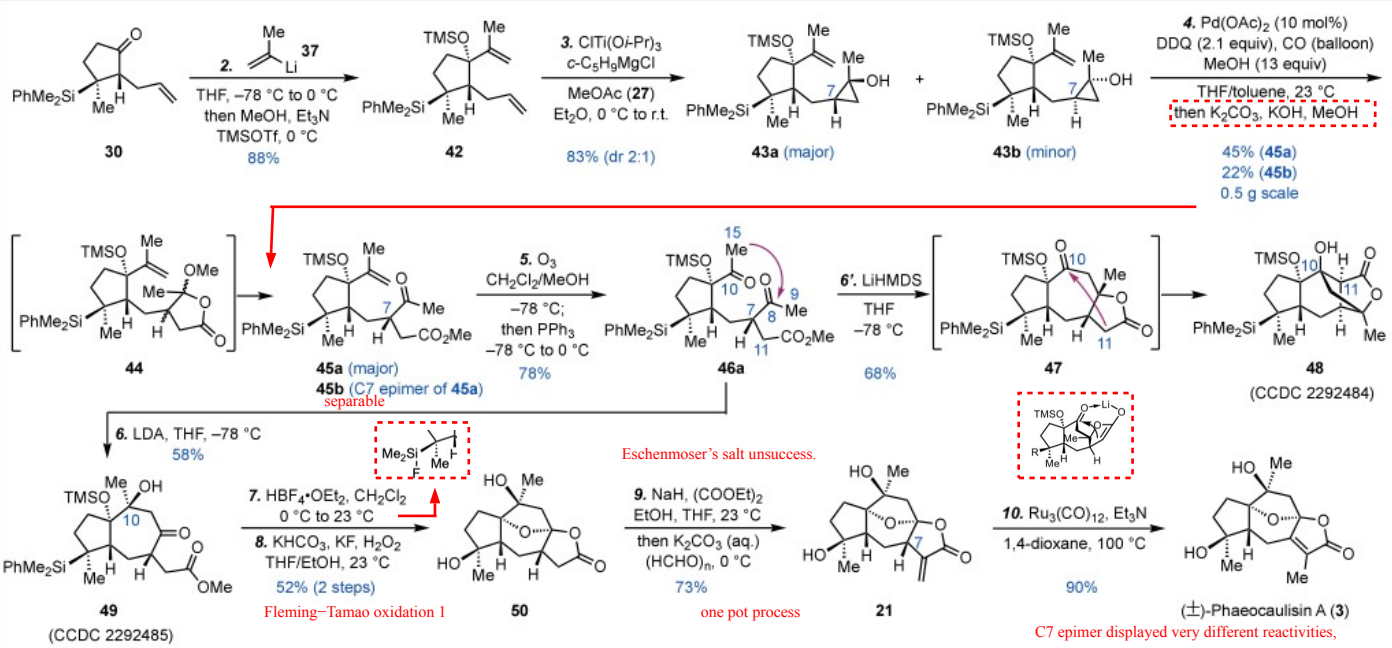
A. Unsuccessful attempt of the intramolecular Kulinkovich reaction



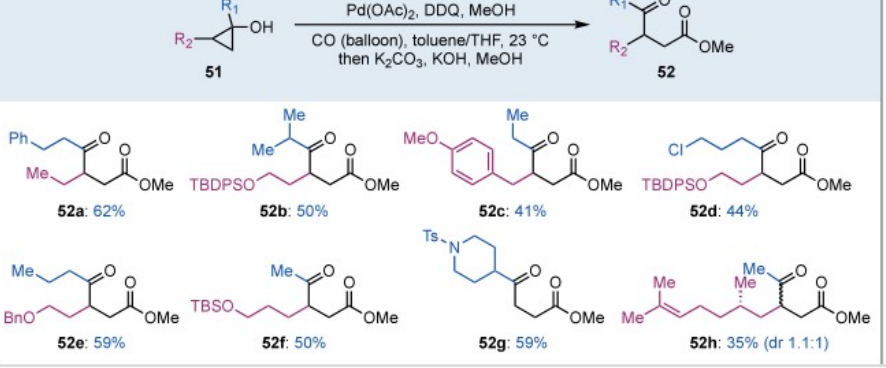
B. Revised synthetic plan



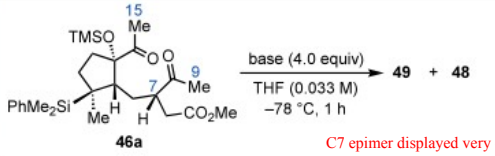
C. Total synthesis of of (±)-phaeocaulisin A



D. Palladium-catalyzed cyclopropanol ring opening carbonylation to β-ketoesters



E. Evaluation of the aldol reaction



C7 epimer displayed very different reactivities,

entry	base	yield (49)[a]	yield (48)[a]	ratio (49/48)
1	LiHMDS	8%	69%	1/8.6
2	NaHMDS	19%	43%	1/2.3
3	KHMDS	22%	n.d.	n.d.
4	LDA	54%	23%	2.3/1
5	LiTMP	63%	13%	4.8/1
6	$LiNCy_2$	6%	n.d.	n.d.
7	LiCyan	6%	52%	1/8.7

[a]NMR yield with $BrCH_2CH_2Br$ as internal standard.

pKa of amine in THF		
LDA	LiHMDS	LiTMP
35.7	29.5	37.3