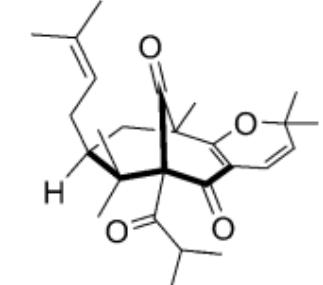
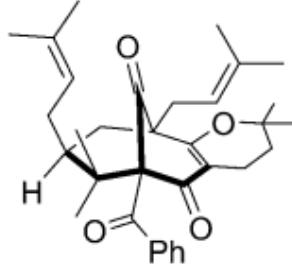
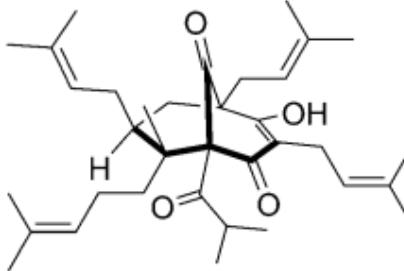
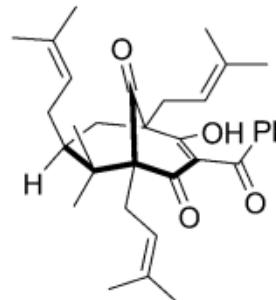
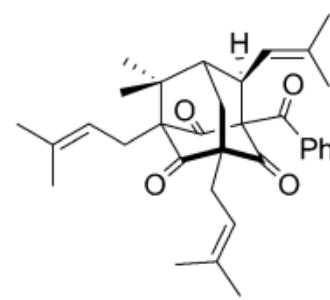
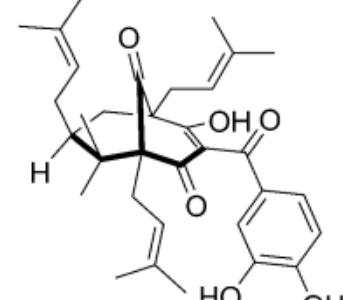
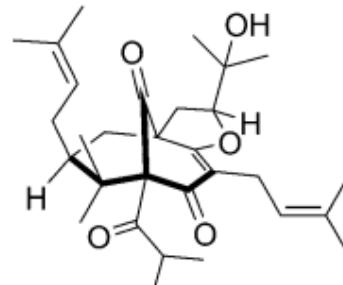
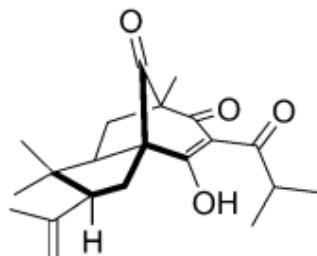
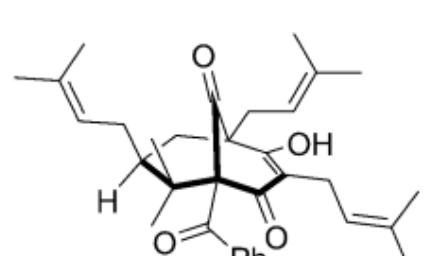
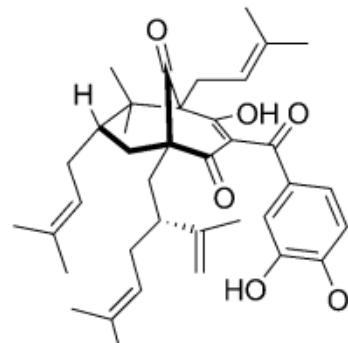
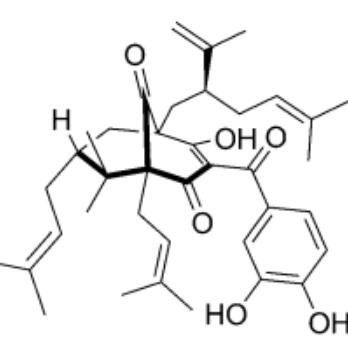
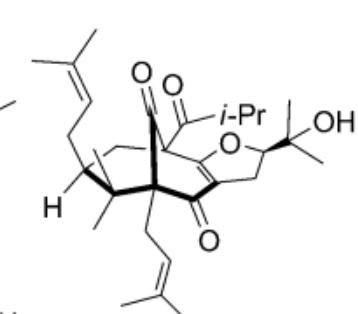
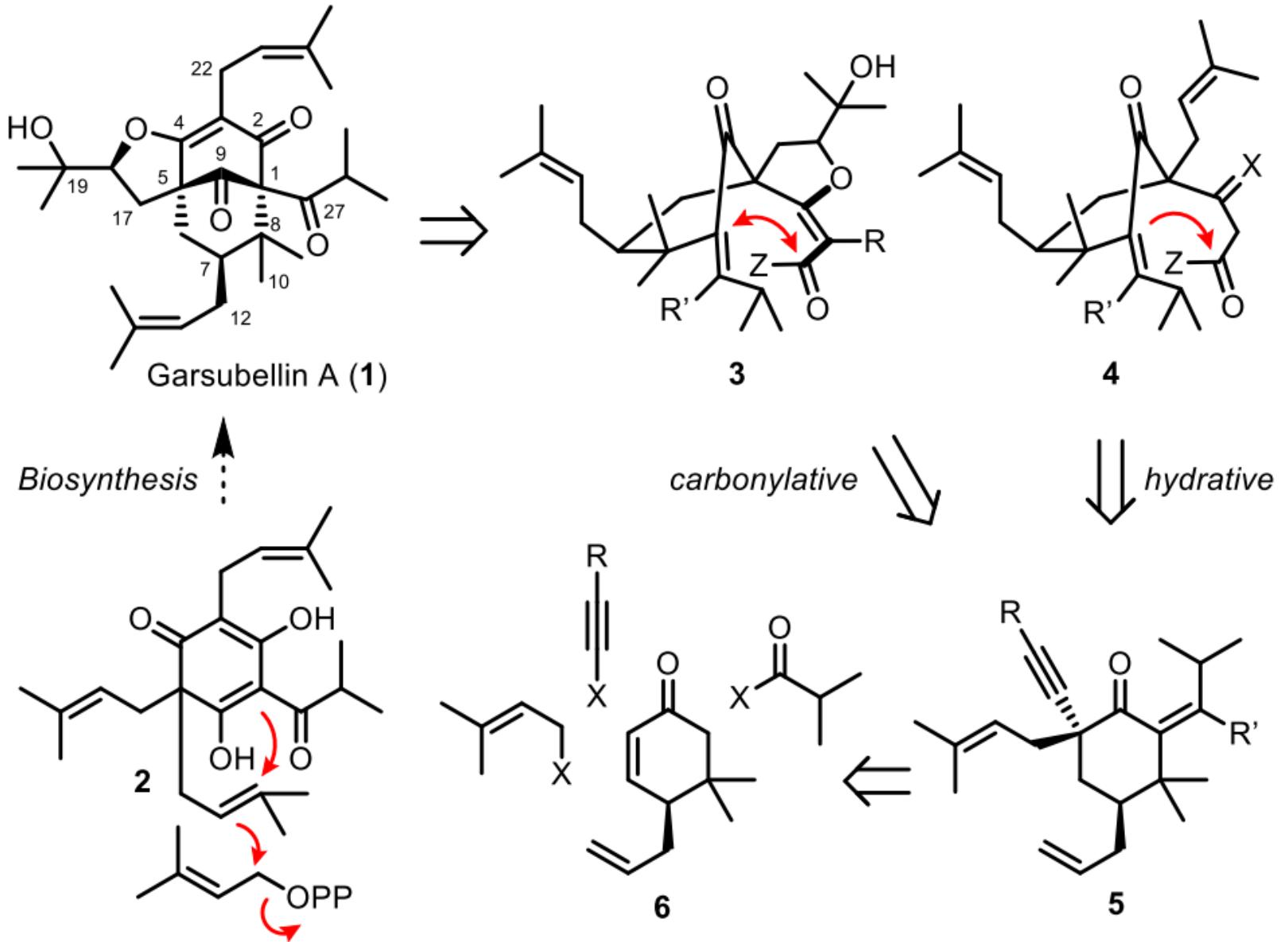


Enantioselective Total Synthesis of (+)-Garsubellin A

Dongseok Jang, Minchul Choi, Jinglong Chen, and Chulbom Lee*

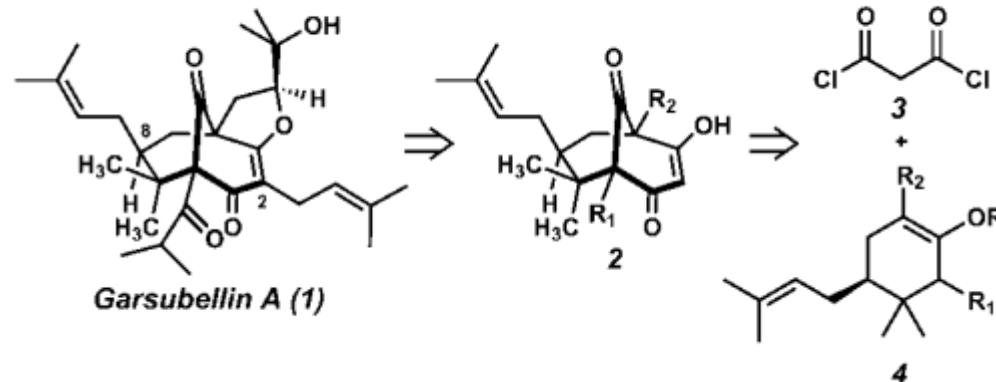
DOI: 10.1002/anie.202109193.

This paper is dedicated to Professor Eun Lee on the occasion of his 75th birthday.papuaforin A (**1**)
Anticancer/antibacterialpropolone A (**2**)
Anti-HIVhyperforin (**3**)
Antidepressant/antibacterial
antimalarialclusianone (**7**)
Anticancer/anti-HIVhyperibone K (**8**)
Anticanceraristophenone A (**9**)
Anticancer/antioxidantgarsubellin A (**4**)
Antineurodegenerativeialibinone A (**5**)
Antibacterialnemorosone (**6**)
Antibacterial/antioxidant
cytotoxicguttiferone E (**10**)
Anti-HIV/anticancergarcinol (camboginol) (**11**)
Antibacterial/antiulcer
anticancergarcinielliptone L (**12**)
Anti-inflammatory

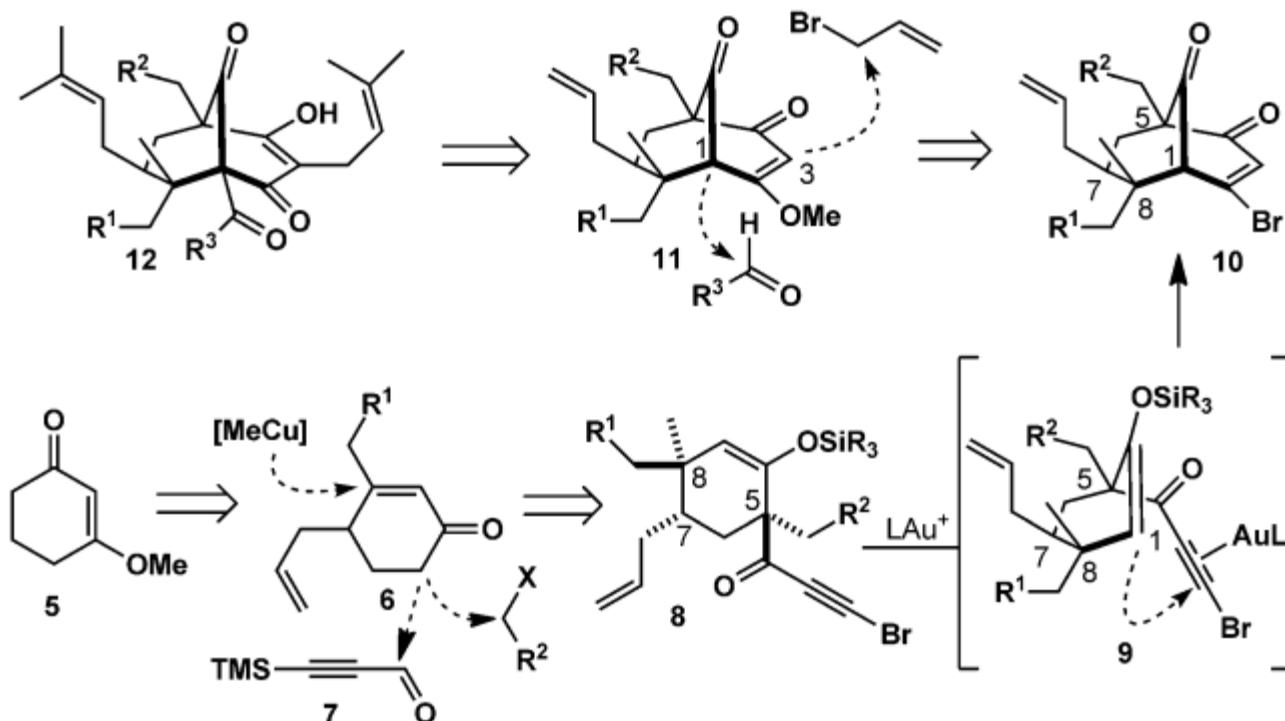


Scheme 1. Structure and Retrosynthesis of Garsubellin A.

Scheme 1

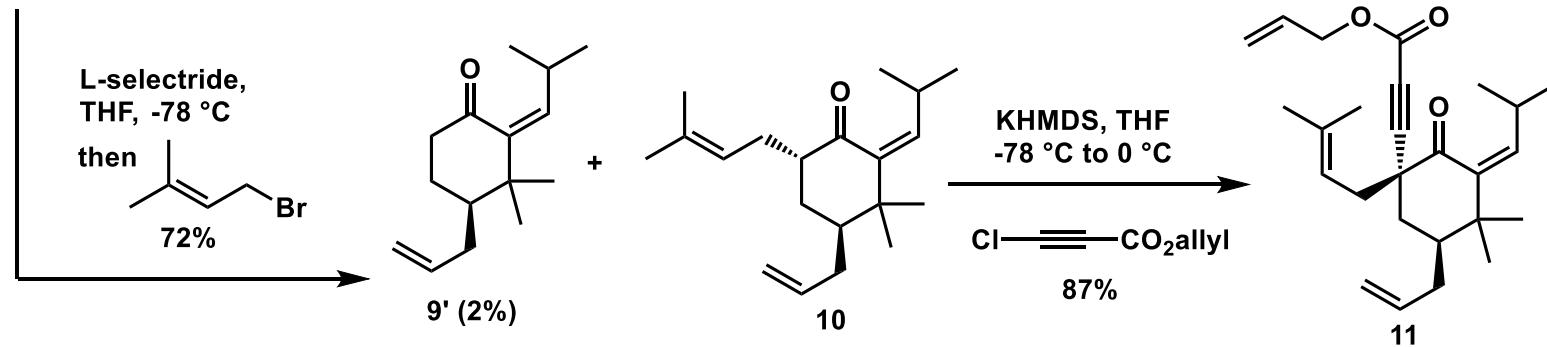
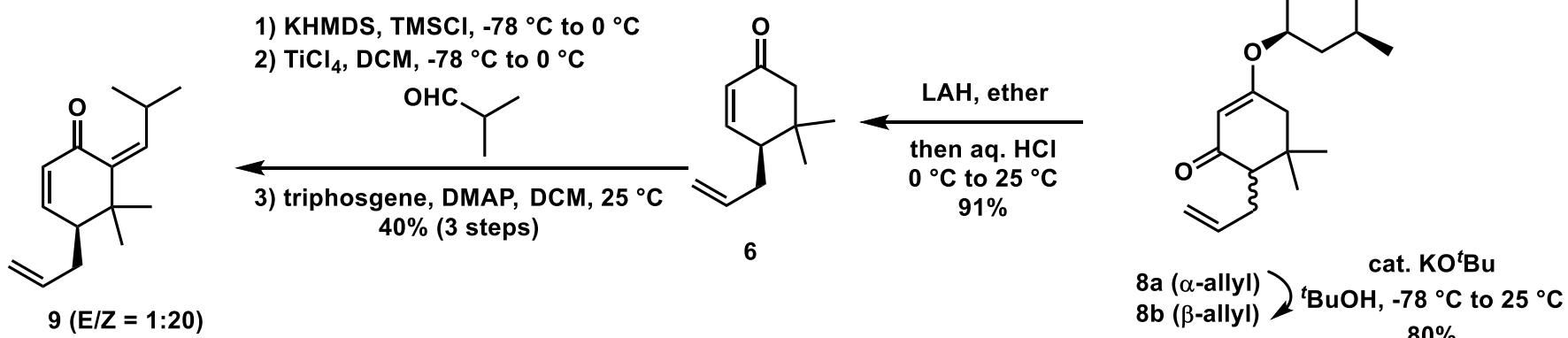
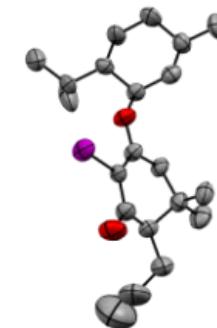
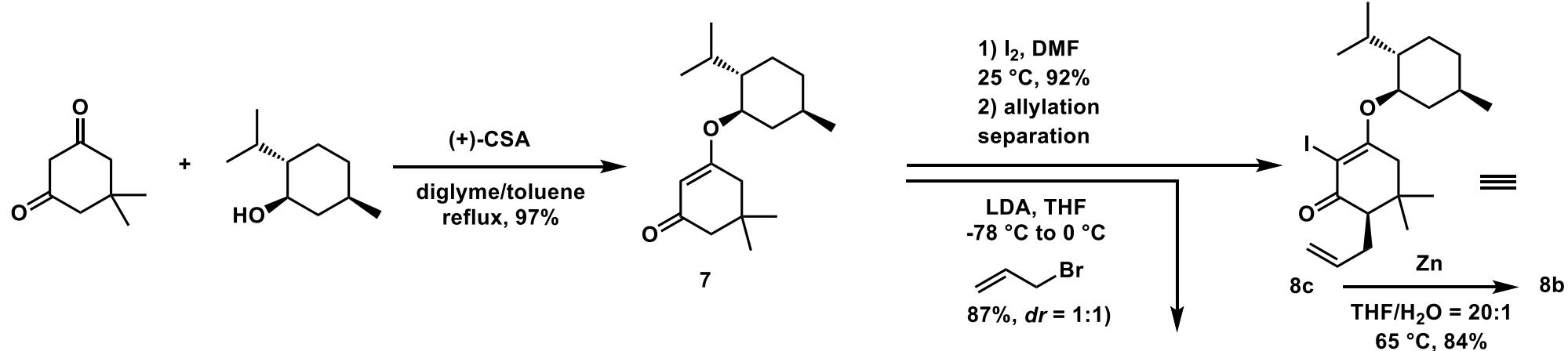


Org. Lett. **2002**, *4*, 1943-1946

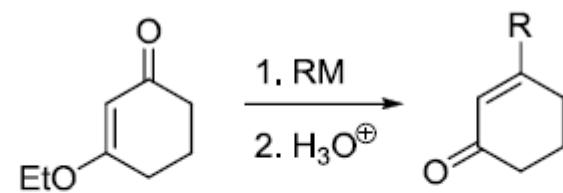


Scheme 1. Retrosynthetic analysis.

Angew. Chem. Int. Ed. **2014**, *53*, 6701.



Stork–Danheiser反应



β -烷氧基烯酮和有机金属化合物（格氏试剂或有机锂）反应接着进行酸处理得到另一种烯酮的反应，新生成的烯酮的羧基的位置是原料中烯醇醚的烯碳的位置。

反应机理

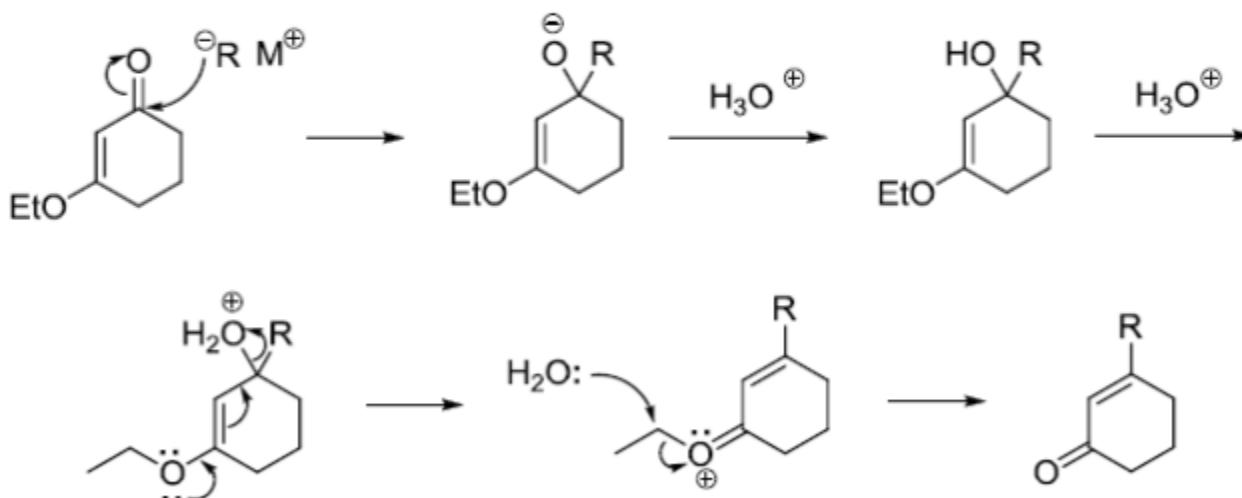
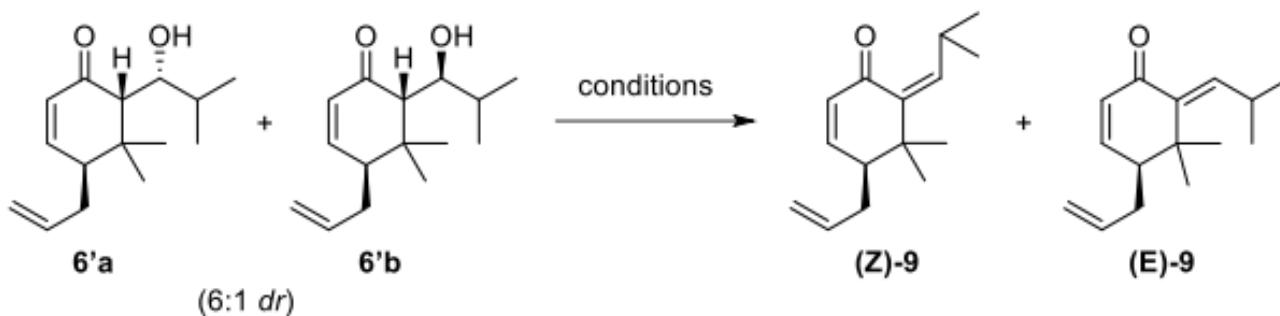


Table S1. Dehydration of alcohol **6'**



entry	conditions ^a	results ^{b,c}
1	5 mol% <i>p</i> -TsOH, toluene, 65 °C, 30 min	(Z) (51%) + (E) (10%)
2	5 mol% <i>p</i> -TsOH, benzene, 25 °C, 24 h	(Z) (57%) + (E) (11%)
3	3 equiv MsCl, 6 equiv TEA, DCM, 25 °C, then basic alumina	complex mixture
4	2.0 equiv Burgess reagent, benzene, 65 °C, 3 h	(Z) (52%) + (E) (16%)
5	0.5 equiv Triphosgene, 2.0 equiv DMAP, DCM, 25 °C, 12 h	(Z) (78%) + (E) (4%)

^aAll entry reactions were carried out using a 6:1 diastereomeric mixture of the aldol adducts. ^bIsolated yield. ^cThe E/Z information was determined by NOESY experiments.

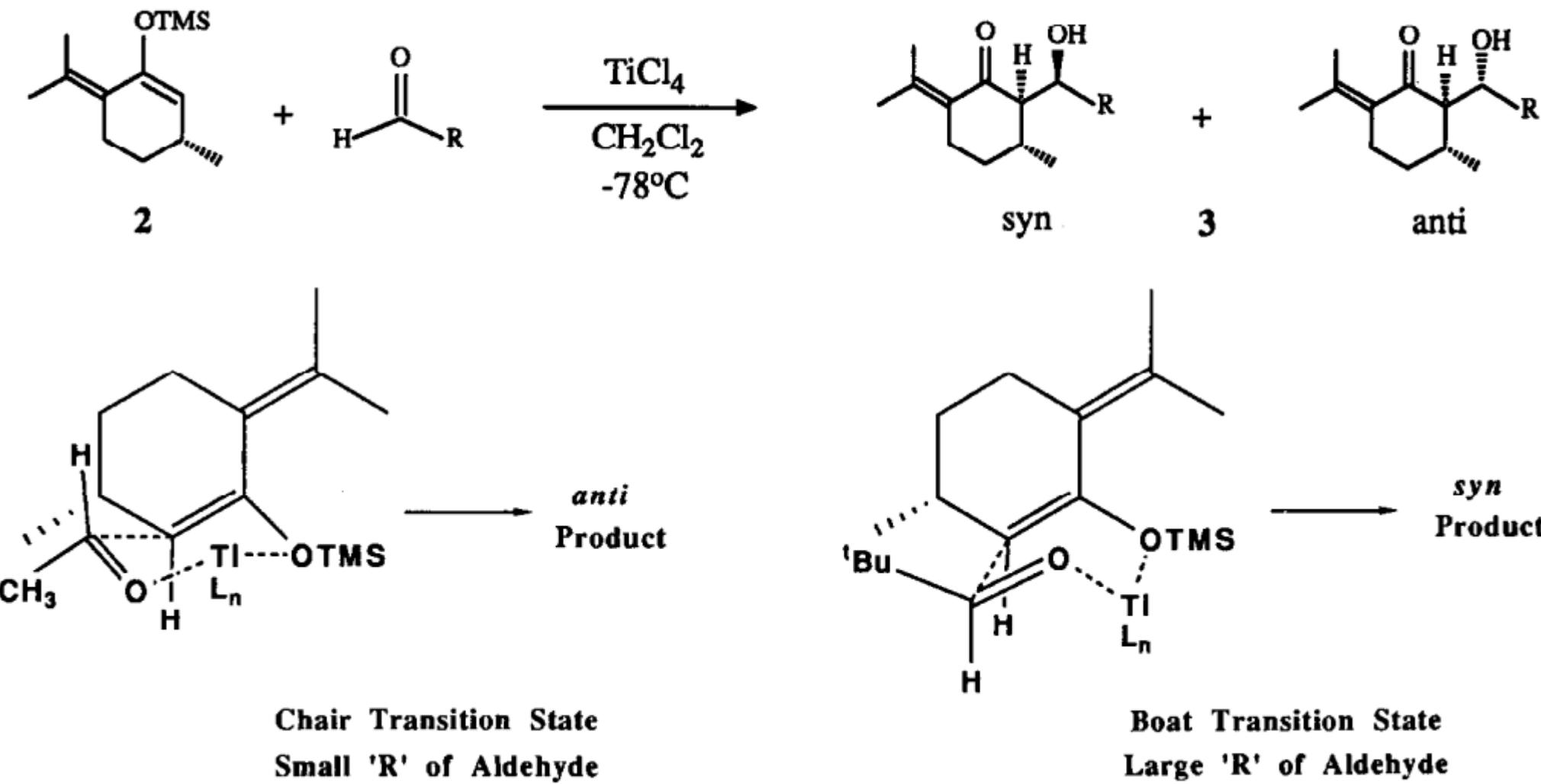
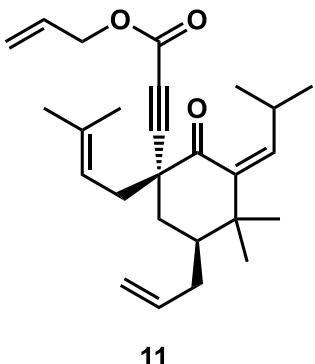
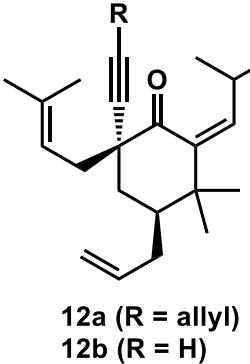


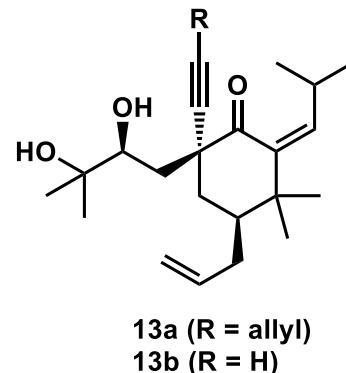
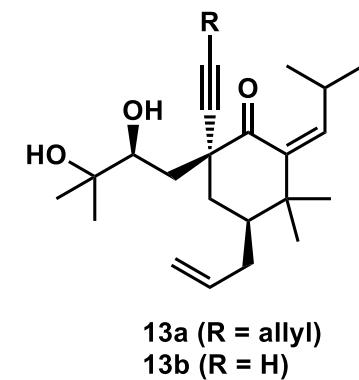
Figure 3



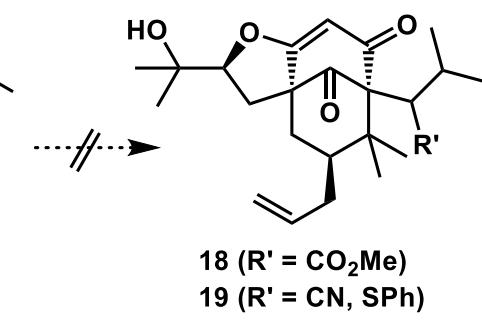
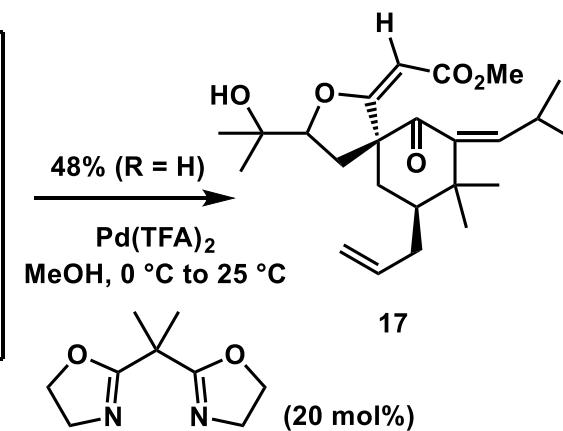
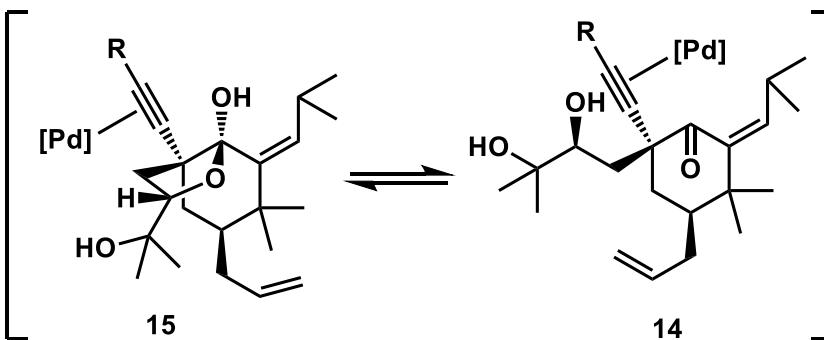
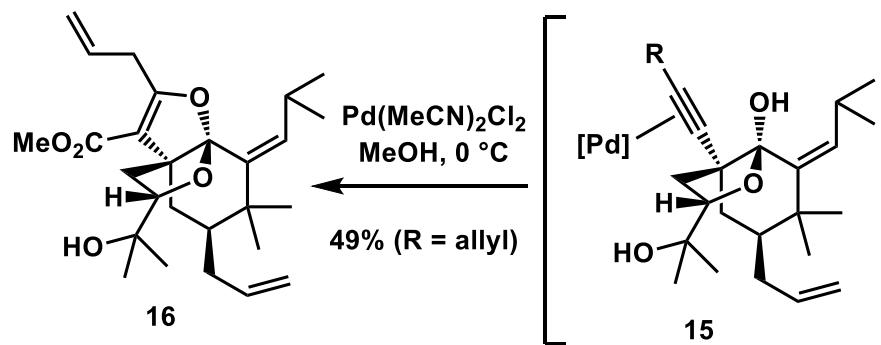
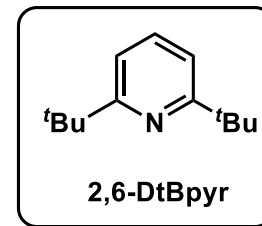
10 mol% Pd(PPh_3)₄
toluene, 90 °C
12a (69%)
with morpholine
12b (88%)

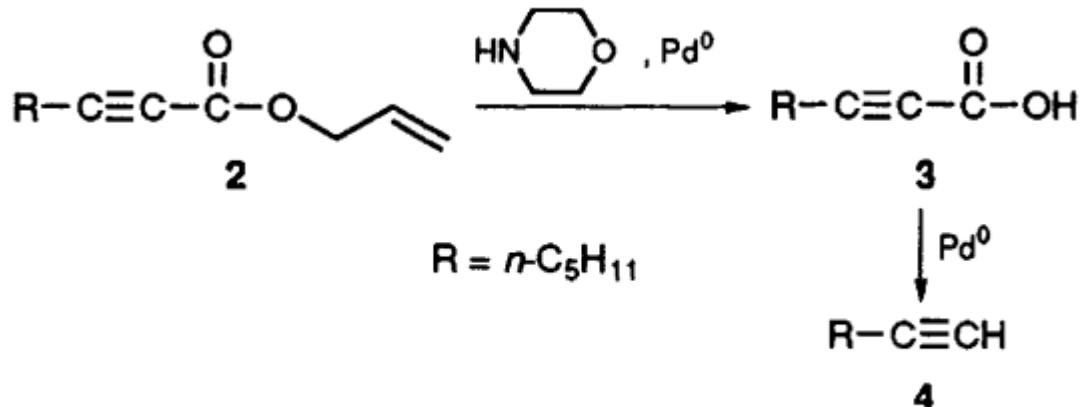


1) *m*-CPBA, DCM
2) THA, H₂O-THF
13a (78%, *dr* = 2.3:1)
13b (71%, *dr* = 1.2:1)

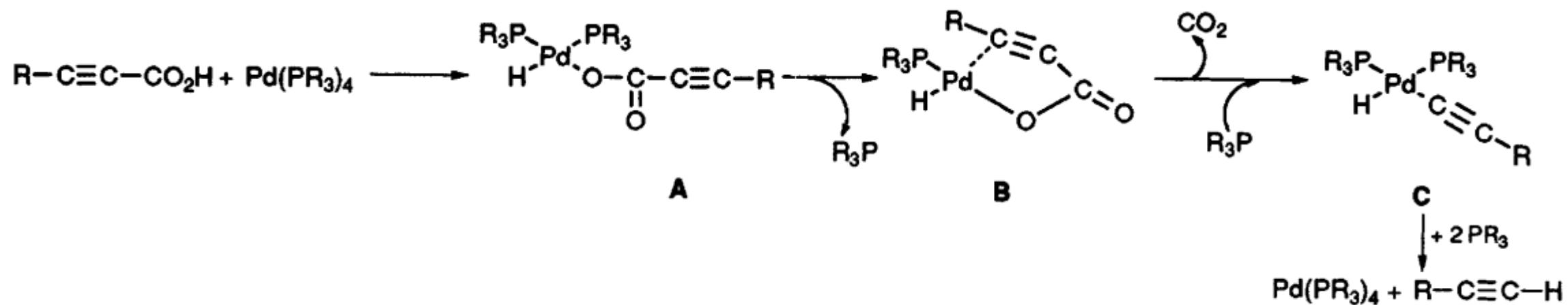


CO, MeOH, 0 °C
benzoquinone
↓
10 mol% Pd catalyst
20 mol% 2,6-DtBpyr

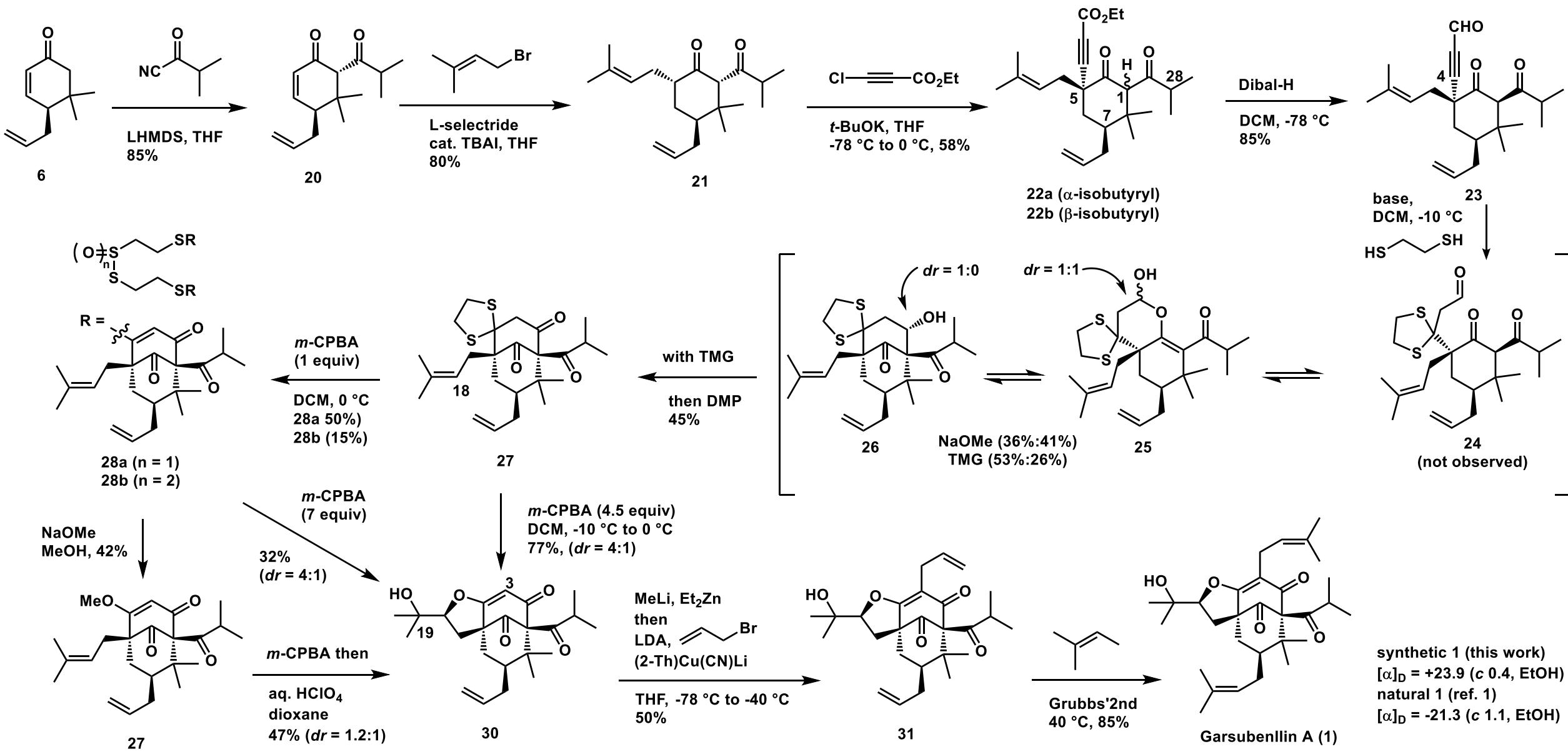


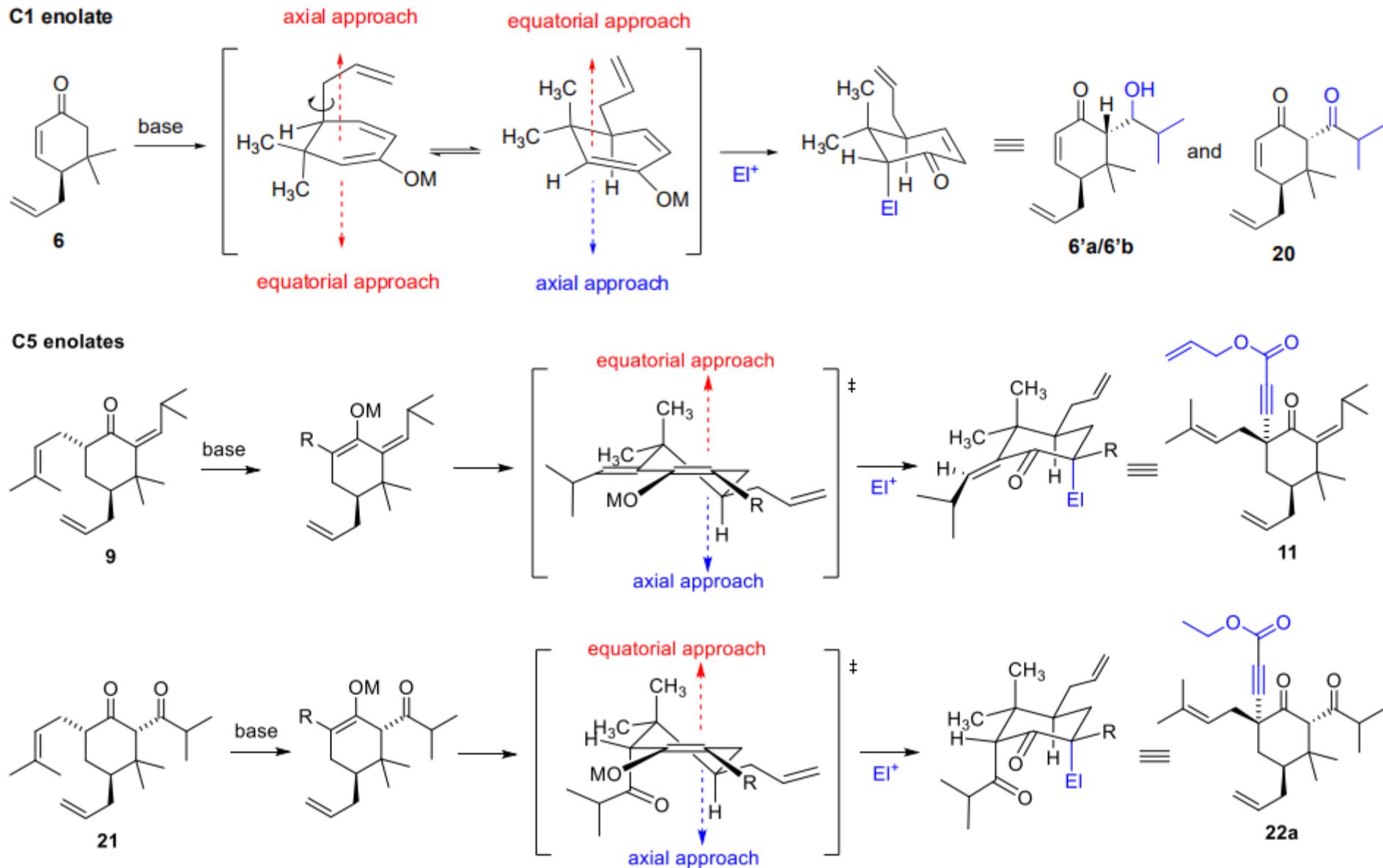


Scheme 1



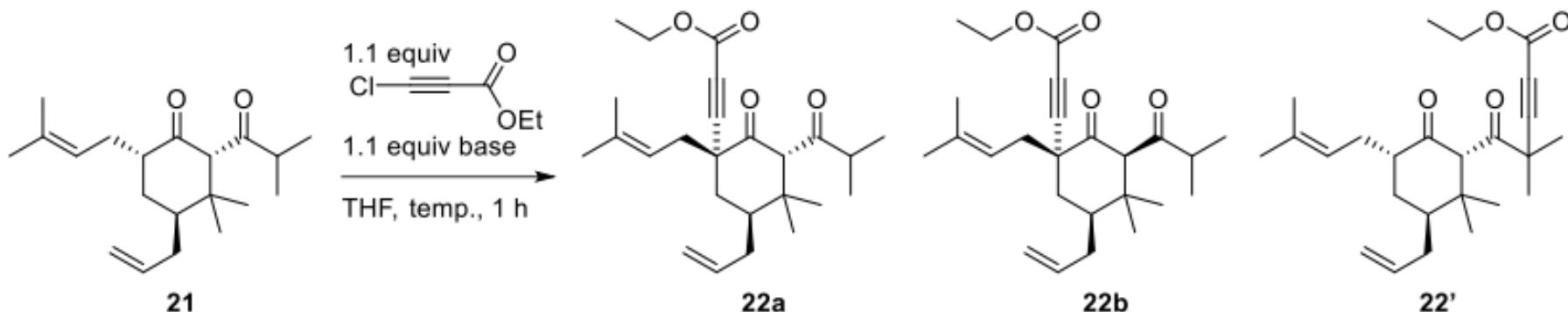
Scheme 2





Scheme S4. Rationale for the diastereoselectivity in the reactions of the enolate

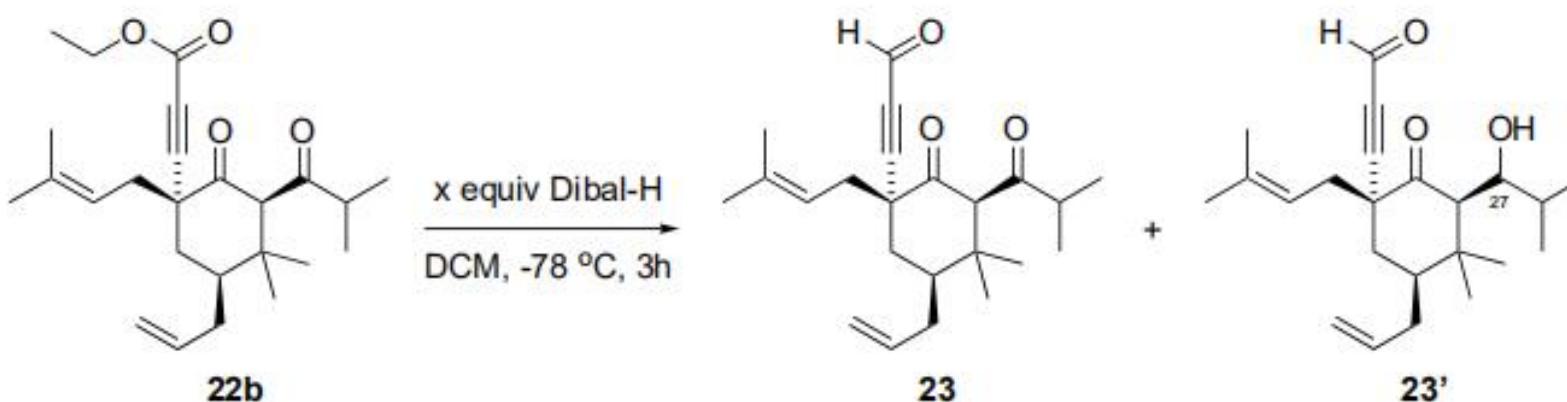
Table S4. Alkynylation of diketone **21**



entry	base	reaction temp. (°C)	results ^{a,b}
1	LDA	-78	22' (31%) + 21 recovered (21%) ^c
2	LiTMP	-78	22' (63%)
3	KHMDS	-78	22a (38%) + 21 recovered (19%) ^b
4	KOtBu	-78	22a (59%) ^d
5 ^e	KOtBu	-78 → 0	22b (58%)

^aEthyl 3-chloropropionate was synthesized using the known method by Jørgensen (ref 5). ^bThe structural determination of isomers **22a**, **22b** and **22'** was carried out based on 1D NOESY and HMBC experiments. ^cThe starting material (**21**) was recovered as a 1:1 diastereomeric mixture. ^dThe α -isomer **22a** was converted to the β -isomer **22b** under basic conditions ($K_2CO_3/EtOH$). ^eThe reaction was performed at -78 °C for 1 h and at 0 °C for additional 6 h.

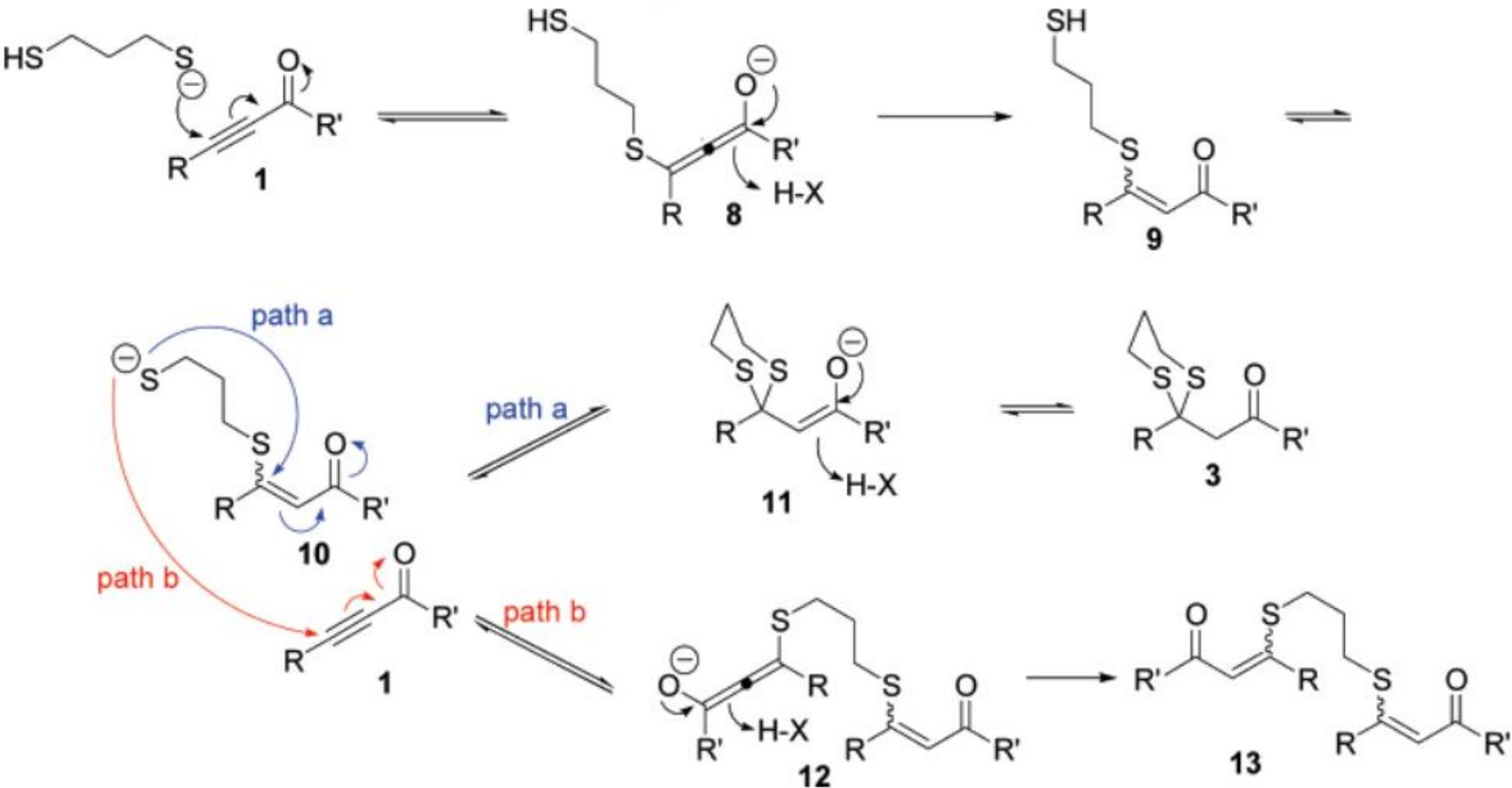
Table S5. Reduction of diketone alkyne **22b**

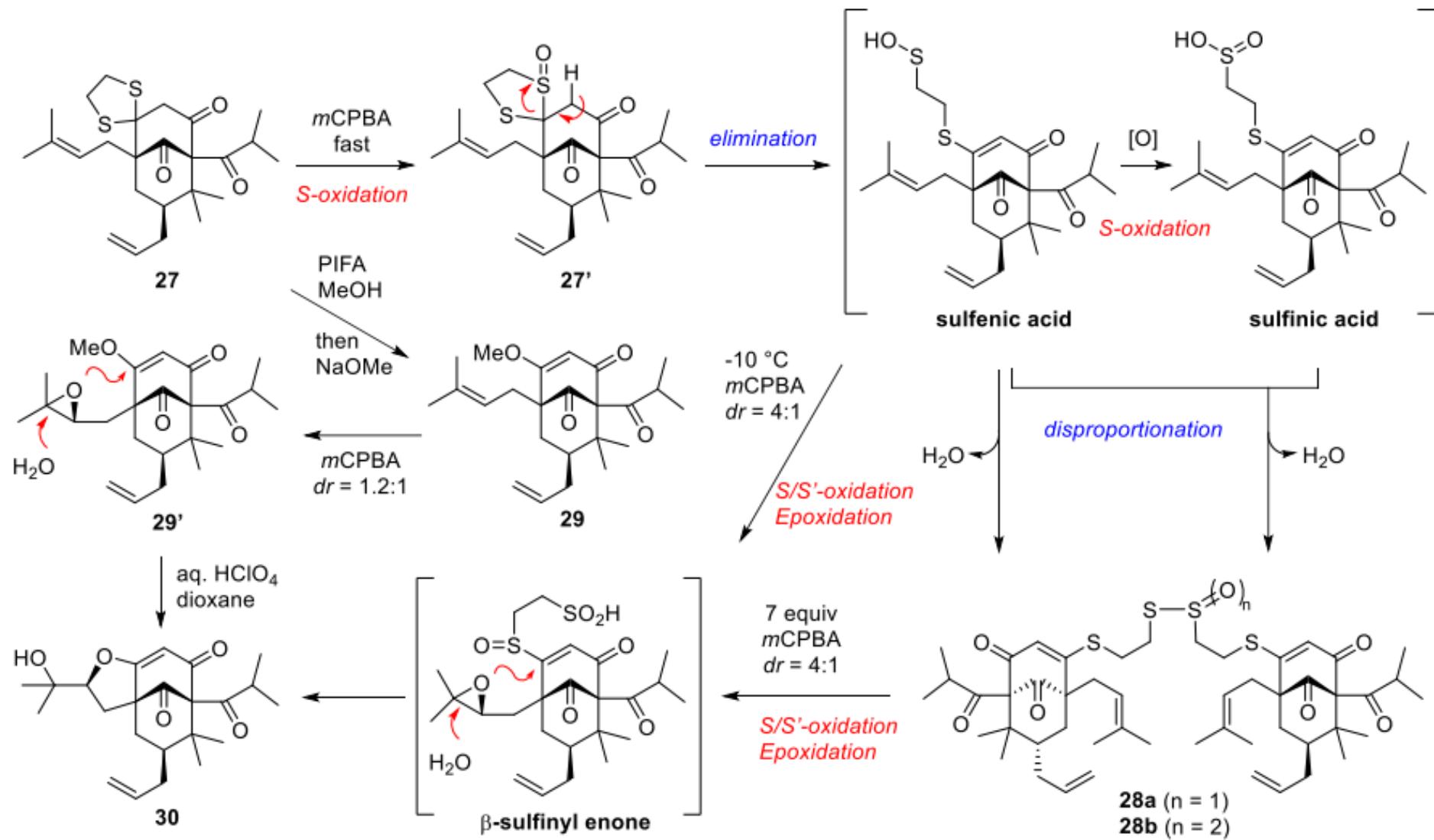


entry	<i>x</i> (equivalent)	results ^{a,b}
1	1.1	23 (21%) + 22b recovered (59%)
2	2.1	23 (85%) + 23' (5%)
3	2.5	23 (33%) + 23' (48%)

^aThe C27 alcohol **23'** was obtained as a single isomer with undetermined stereochemistry and was recycled to aldehyde **23** through oxidation (DMP, DCM). ^bUnder the conditions examined, a propargylic alcohol from over-reduction of the aldehyde was not detected.

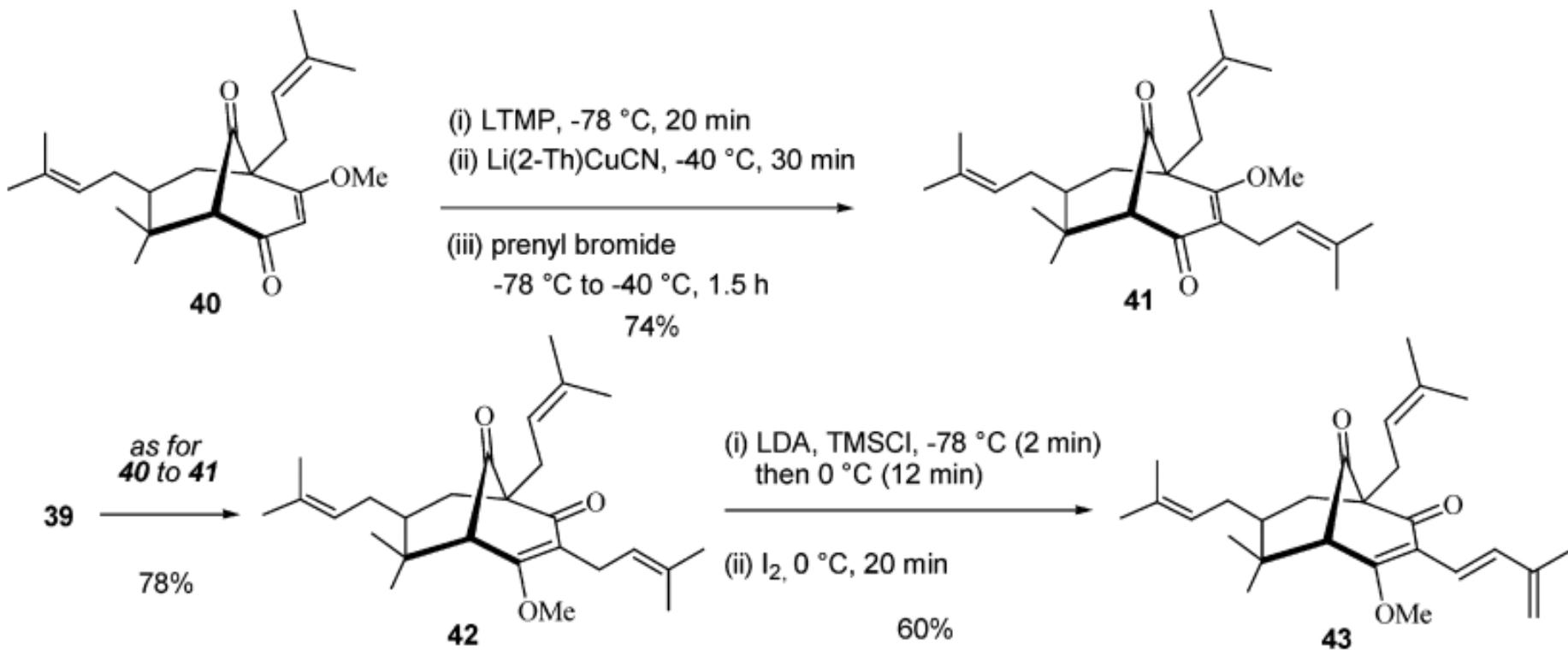
SCHEME 3. Proposed Mechanism for the Formation of β -Keto-1,3-dithianes

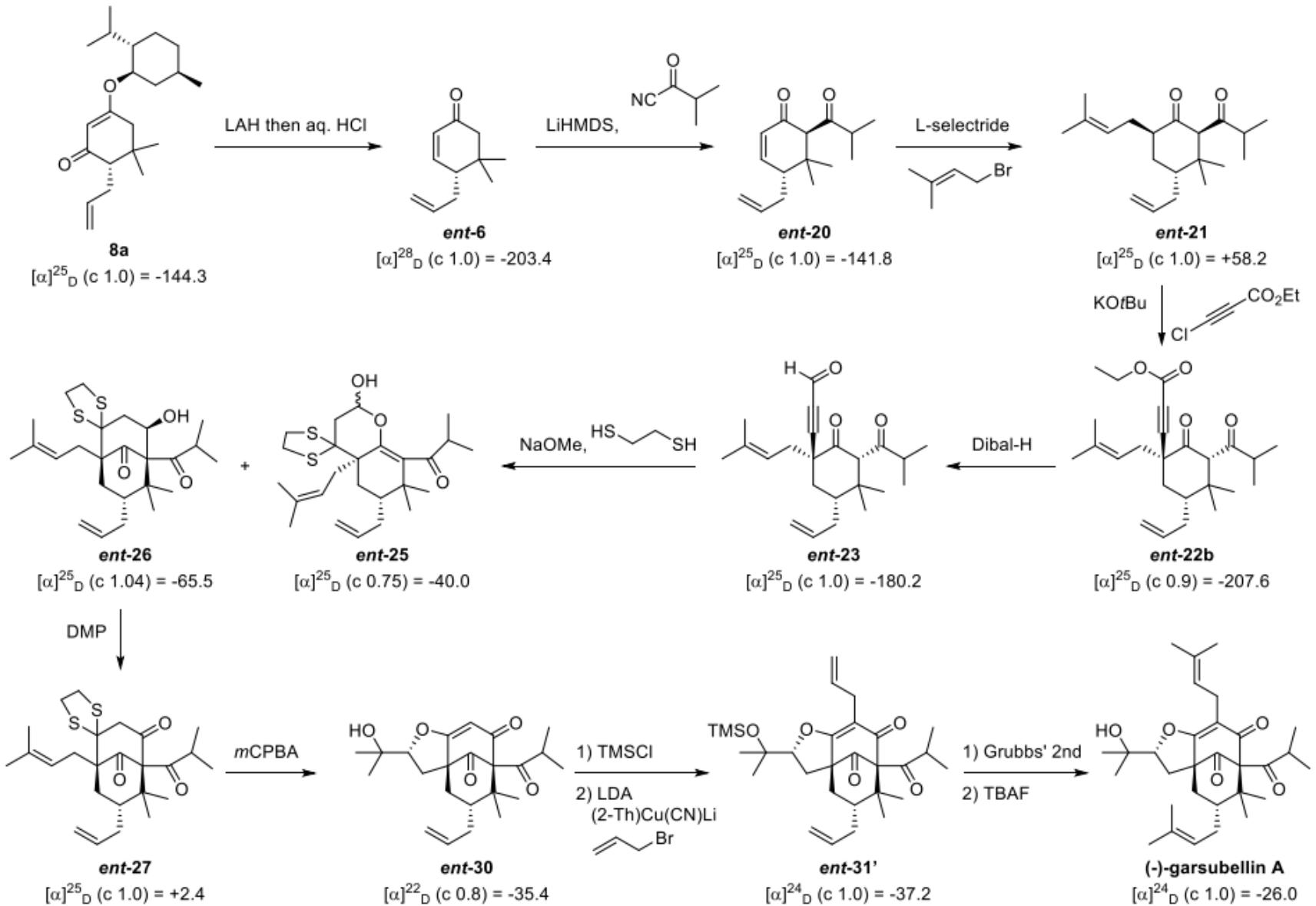




Scheme S5. Possible reaction pathways in the dithiolane oxidative removal step

SCHEME 10. Copper-Mediated Vinylic Alkylation and Attempted Bridgehead Substitution





- All optical rotation data were measured in EtOH solvent

Scheme S7. Total synthesis of **(-)-garsubellin A** from isomer **8a**