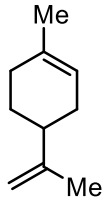
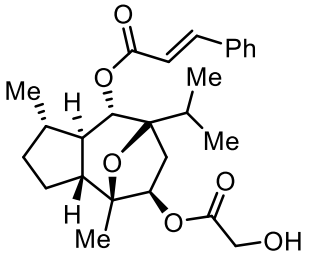
Limonene: cheap chiral starting material found in the oil of citrus peels

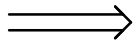


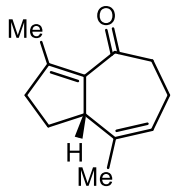


(-)-4-*epi*-EnglerinA

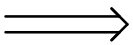
suggest disconnections
and strategy

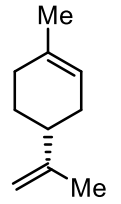
a few steps



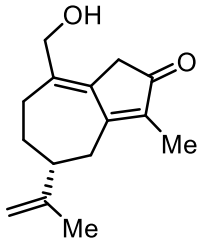


5 steps



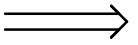


(*R*)-(+)-limonene

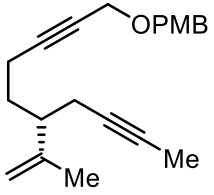


(+)-indicanone

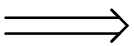
6 steps



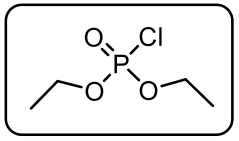
what type of cyclisation is it?
(name)

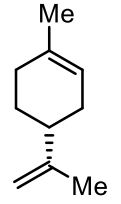


7 steps

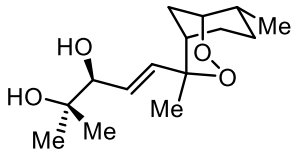


using:





(*R*)-(+)-limonene



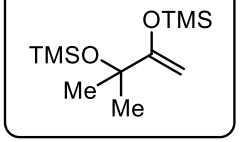
(+)-Yingzhaosu

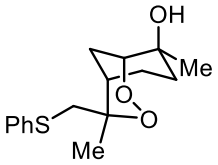
a few steps

using:

Pummerer rearrangement

and

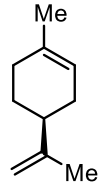




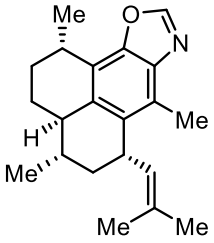
1 step

using:

AIBN



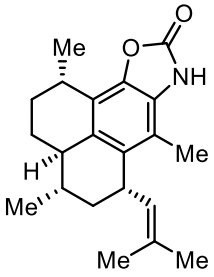
(*S*)-(-)-limonene



(+)-pseudopteroxazole

2-3 steps

Boc_2O



a few steps

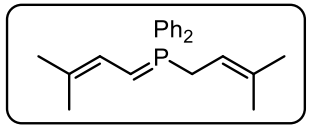
using:

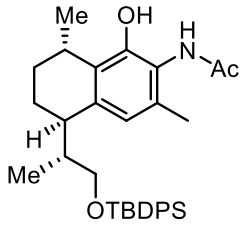
CDI

and

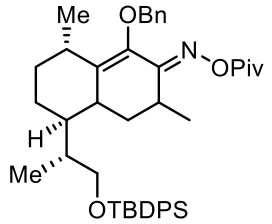
Ley oxidation

and

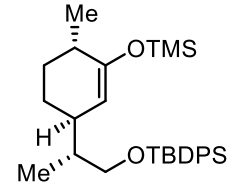




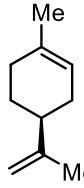
2 steps



5 steps



5 steps



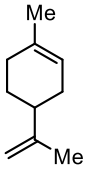
(*S*)-(-)-limonene

using:

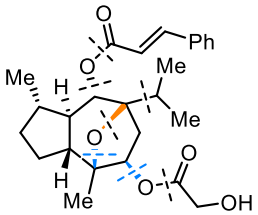
enzymatic kinetic resolution

Solutions

Limonene: cheap chiral starting material found in the oil of citrus peels

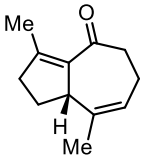


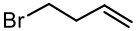
epoxide opening



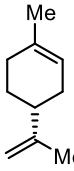
suggest disconnections and strategy

a few steps



1) O_3/O_2,
CH_2Cl_2–MeOH (5:1), -70 °C;
Me_2S, rt, 5 h;
2) piperidine, AcOH,
C_6H_6, reflux, 1 h;
3) Li, 
4) IBX, DMSO
5) $Ti(OiPr)_4$,
Grubbs' catalyst (II)

5 steps



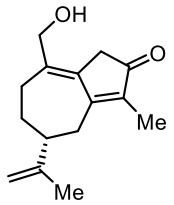
(*R*)-(+)-limonene

Sharpless dihydoxilation

(-)-4-*epi*-EnglerinA

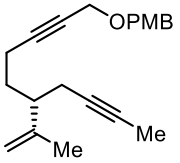
Eur. J. Org. Chem.
2021, *22*, 3190–3196

1) DDQ, DCM/H_2O, rt
2) $ClCO_2Me$
pyridine, DCM, rt
3) 5 mol% $Pd(OAc)_2$
25 mol% PPh_3, MeOH,
10 atm CO, 40 °C
4) DIBAL-H
toluene, -78 °C
5) TBSCl, DMAP, Et_3N, DCM
0 °C to rt
6) 5 mol% $[RhCl(CO)dppp]_2$
toluene, 1 atm CO, reflux
then 10% HCl aq., MeOH, rt



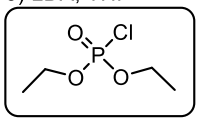
(+)-indicanone

Org. Biomol. Chem.
2012, *10*, 4747-4751

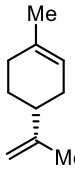


what type of cyclisation is it?
(Pauson-Khand)

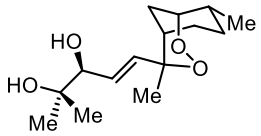
1) O_3, MeOH
then $(H_2N)_2CS$/ MeOH
2) $HC(OCH_3)_3$,
$CeCl_3.6H_2O$/MeOH
3) LDA, THF



4) *s*BuLi
$(HCHO)_n$
THF, -78 °C to rt
5) NaH, PMBCl, DMF
0 °C to rt
then 35% HCl aq. acetone
6) Ohira-Bestmann
reagent, K_2CO_3
MeOH, rt
7) LHMDS, MeI, -78 °C



(*R*)-(+)-limonene

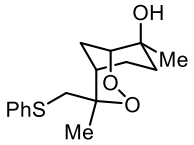


(+)-Yingzhaosu

J. Org. Chem.
2005, *70*,
3618−3632

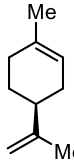
1) $SOCl_2$, pyr, DCM, 0 °C
2) *m*CPBA, EtOAc, - 40 °C
3) $(CF_3CO)_2O$
2,6-lutidine, DCM, -35 °C
4) morpholine, MeOH, -10 to 0 °C
then diastereomer separation

Pummerer rearrangement



AIBN
PhSH,
hv, O_2
CH_3CN

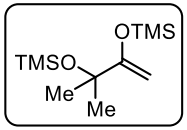
then PPh_3



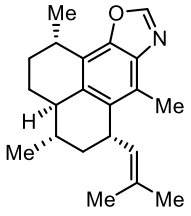
(*S*)-(-)-limonene

2 steps

5) PtO_2, H_2
6) $TiCl_4$



then pyr.
7) *R*-CBS cat.
BH_3.THF, THF, -55 °C
8) HF

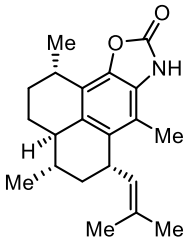


(+)-pseudopteroxazole

J. Am. Chem. Soc.
2003, *125*, 13486−13489

1) Boc_2O
DMAP

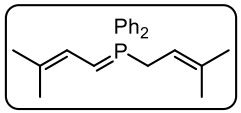
2) MeMgBr
-78 to 23 °C
then TFA,
$HC(OEt)_3$



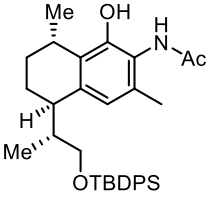
1) CDI, Et_3N
then aq. $NaHCO_3$
2) HF.pyr
3) TPAP, NMO

Ley oxidation

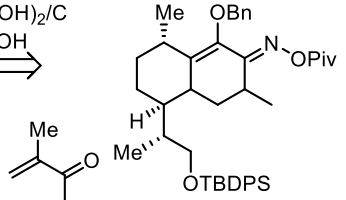
4)



5) MsOH, AcOH, 18 °C

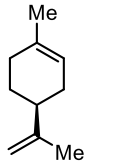


1) AcCl,
toluene, 80 °C
2) $Pd(OH)_2/C$
H_2, EtOH



1) OBn , $SnCl_4$
DCM, -78 °C
2) KOH, EtOH, -10 °C
3) $SOCl_2$, pyr
4) $NH_2OH.HCl$
5) PivCl, pyr

5 steps



(*S*)-(-)-limonene

1) thexylborane
then H_2O_2, NaOH
2) NaOCl
3)

Amano
PS lipase

4) TBDPSCl
imidazole, DMF
5) LDA then TMSCl