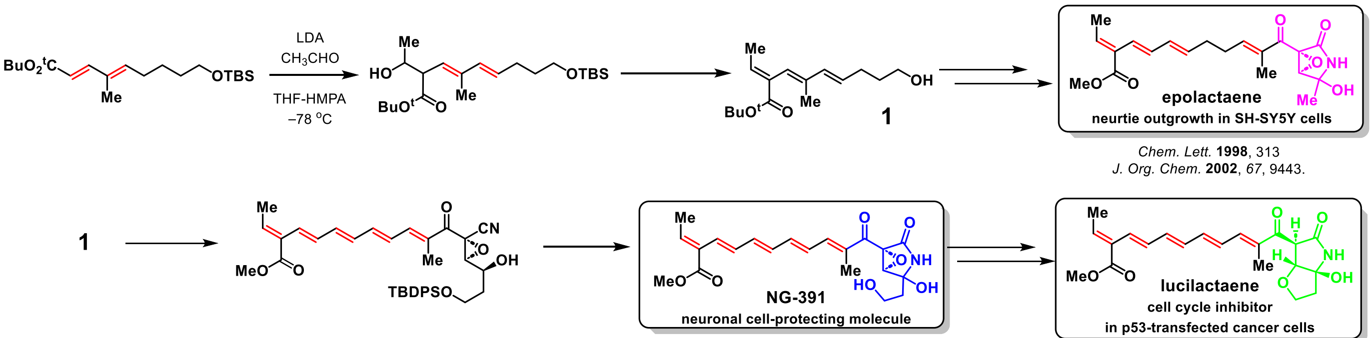
epolactaene, NG-391, lucilactaene

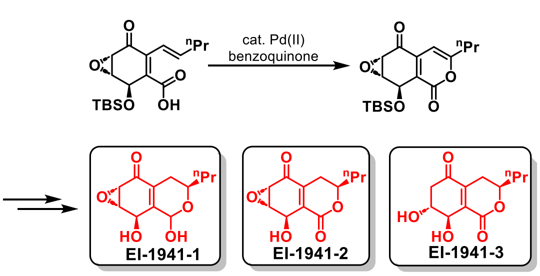


Chem. Lett. **1998**, 313
J. Org. Chem. **2002**, *67*, 9443.

Tetrahedron, **2002**, *58*, 9839.

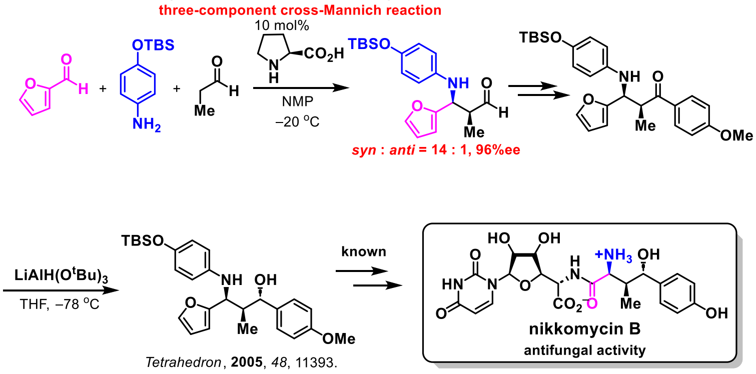
Angew. Chem. Int. Ed. **2005**, *44*, 3110.

EI-1941-1, EI-1941-2, EI-1941-3



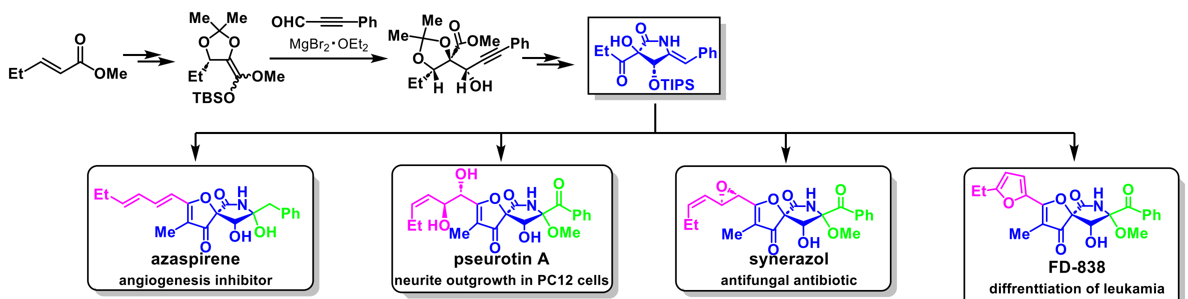
ICE (interleukin 1-β converting enzyme) inhibitor
Org. Lett. **2004**, *6*, 4535.
J. Org. Chem. **2005**, *70*, 9905.

formal total synthesis of nikkomycin B



Tetrahedron, **2005**, *48*, 11393.

azaspirene, pseurotin A, synerazol, FD-838



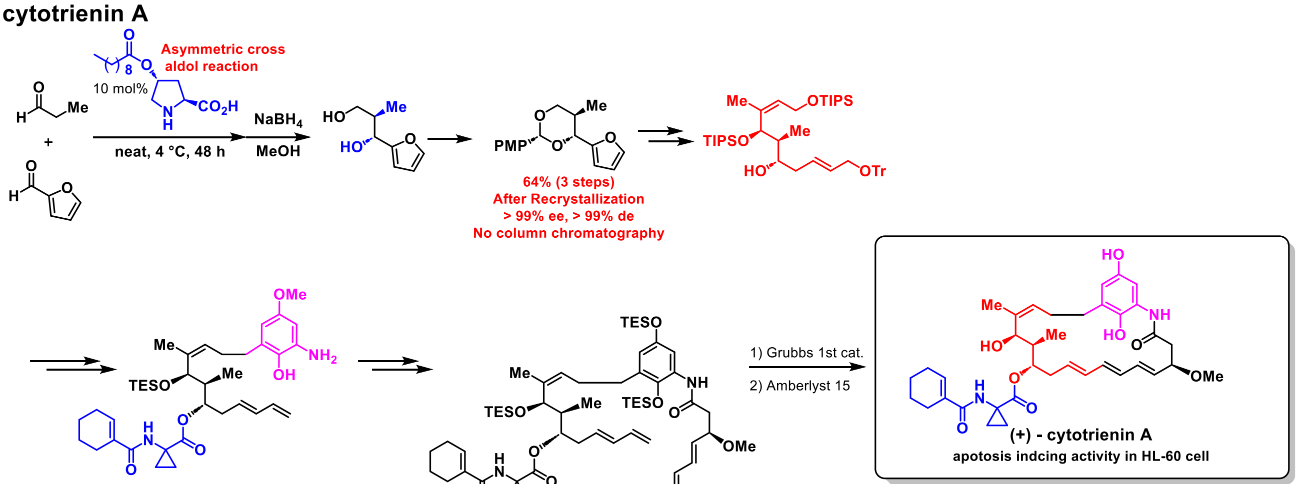
J. Am. Chem. Soc. **2002**, *124*, 12078.

Org. Lett. **2003**, 5, 2287.

J. Org. Chem. **2005**, *70*, 5643.

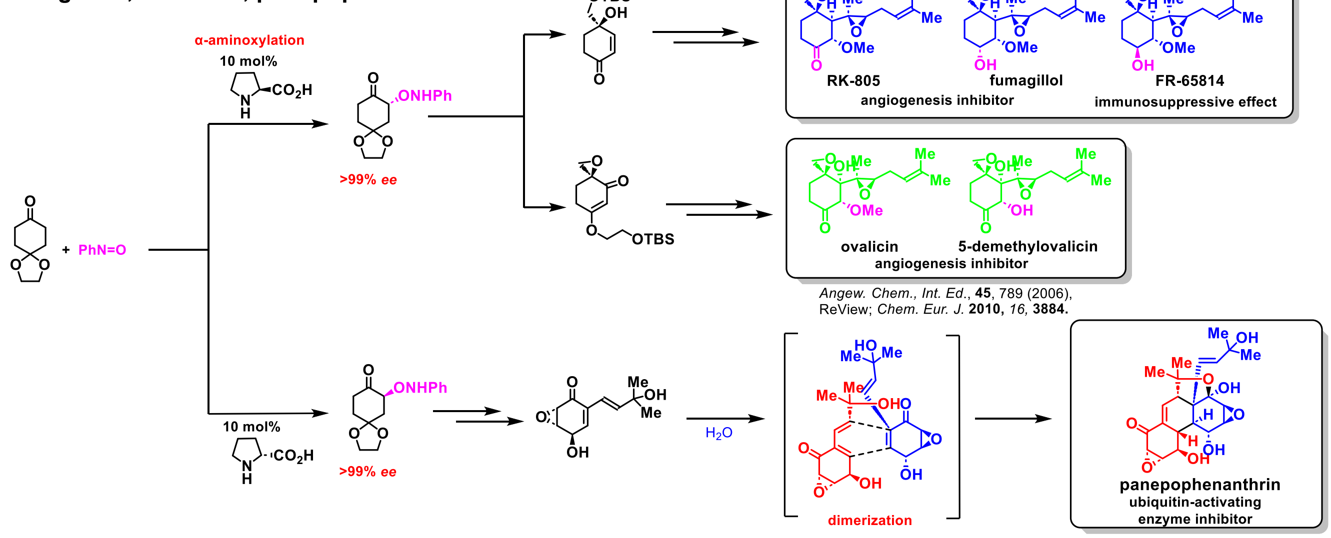
Bioorg. Med. Chem. Lett. **2009**, *19*, 3863.

(+) - cytotrienin A



Angew. Chem. Int. Ed. **2008**, *47*, 6657.

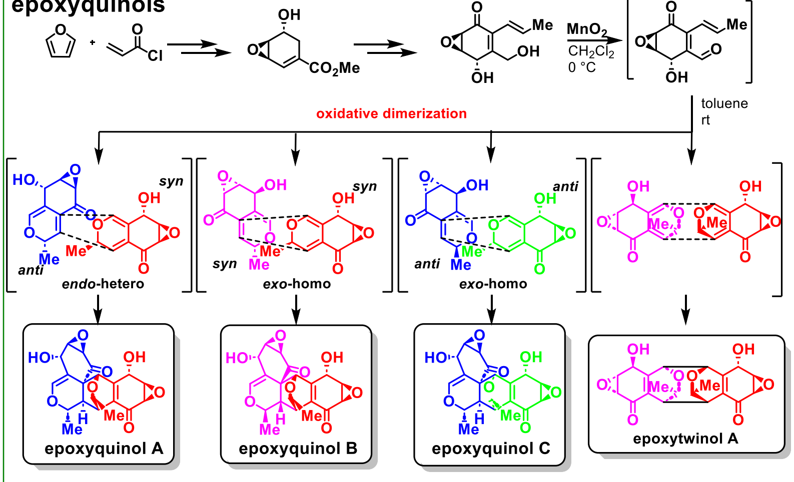
fumagillins, ovalicins, panepophenanthrin



Angew. Chem., Int. Ed., **45**, 789 (2006),
ReView; *Chem. Eur. J.* **2010**, *16*, **3884.**

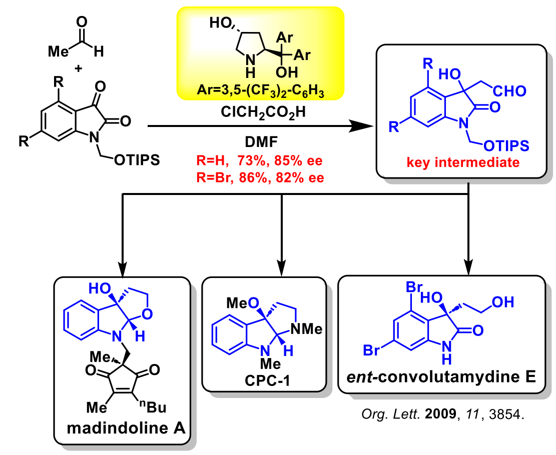
Chem. Asian J., **1**, 845 (2006).

epoxyquinols



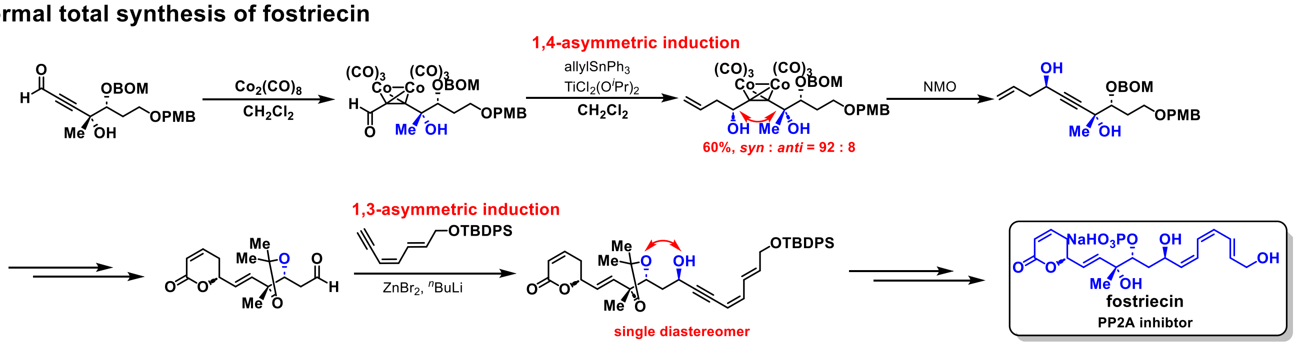
angiogenesis inhibitor
Angew. Chem., Int. Ed., **41**, 3192 (2002); *Tetrahedron Lett.*, **43**, 9155 (2002);
Tetrahedron Lett., **44**, 7205 (2003);*J. Org. Chem.*, **69**, 1548 (2004);
J. Org. Chem., **70**, 79 (2005) ; *Org. Lett.*, **8**, 1041 (2006).
Review*; Eur. J. Org. Chem.*, **23**, 3783 (2007).

CPC-1, *ent*-convolutamydine E, and half segment of madindoline A



Org. Lett. **2009**, *11*, 3854.

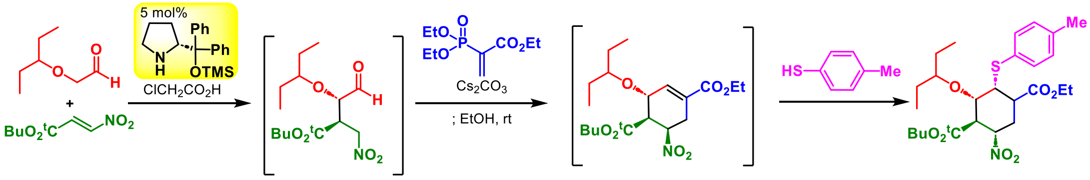
formal total synthesis of fostriecin



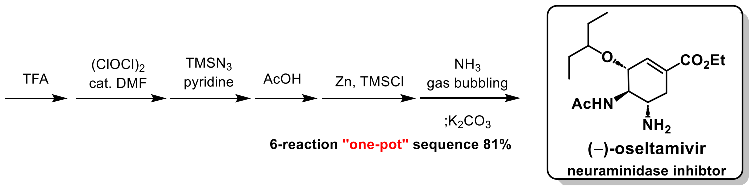
Org. Lett. **2008**, *10*, 1405.
Chem. Eur. J. **2010**, *16*, 10150.

(–)- oseltamivir (Tamiflu®)

1st and 2nd generation



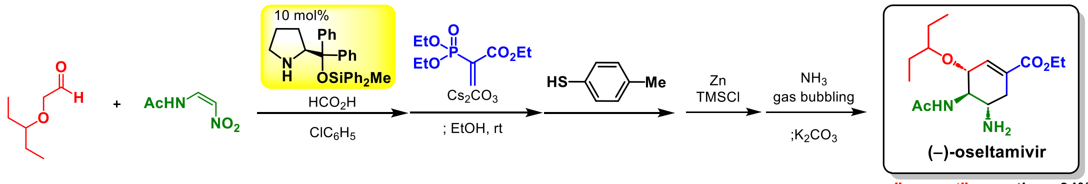
5-reaction "one-pot" sequence : 74%



Angew. Chem. Int. Ed. **2009**, *48*, 1304.
Chem. Eur. J. **2010**, *16*, 12616.
Eur. J. Org. Chem. **2011**, 6020.

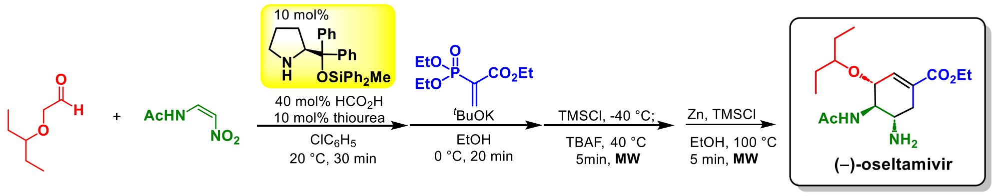
Total yield : 60%

3rd generation



"one-pot" operation : 34%
Chem. Eur. J. **2013**, *19*, 17789.

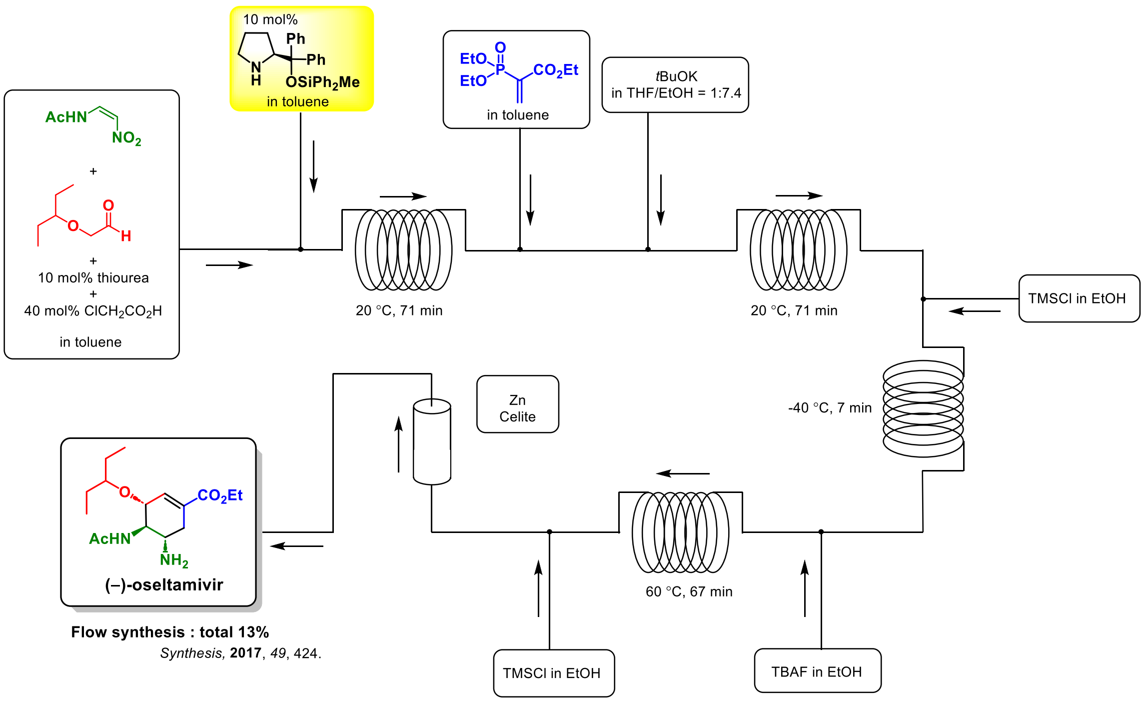
4th generation : Time economical synthesis



Total time 60 min

"one-pot" operation : 15%
Org. Lett. **2016**, *18*, 3426.

5th generation : Flow synthesis

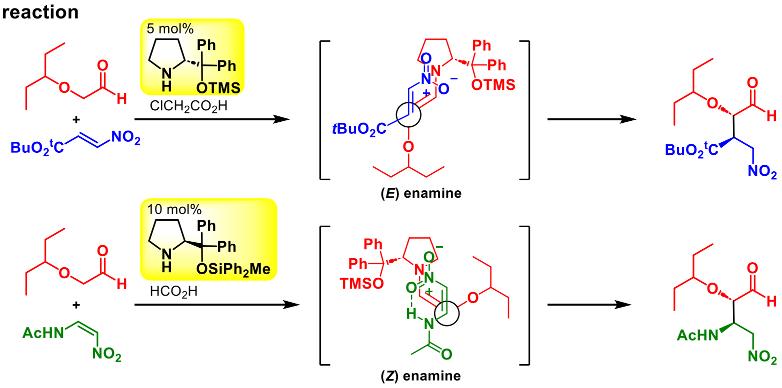


Flow synthesis : total 13%
Synthesis, **2017**, *49*, 424.

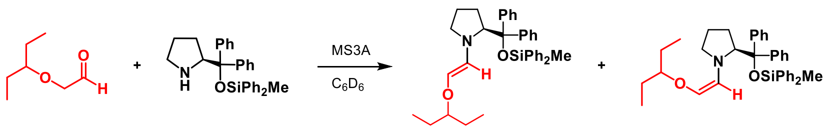
Computational study on *E*/*Z*-alkoxyenamines

Bull. Chem. Soc. Jpn. **2016**, *89*, 455.

Stereoselectivity in Michael reaction



experimental study on generation of *E*- and *Z*- alkoxyenamine

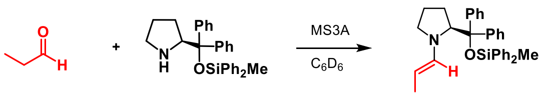


1.0 : 1.7

A mechanistic study identified the origin of streoselectivity in the Michael reaction.

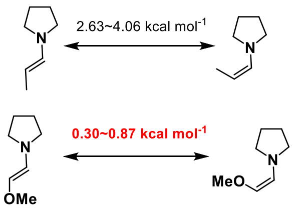
It revealed that *E*-enamine selectively reacts with trans-nitroalkene while *Z*-enamine reacts with cis-nitroalkene.

In this case, an equilibrium exists between *E*- and *Z*- alkoxyenamine under acidic condition.



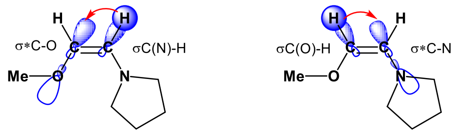
DFT calculation with NBO analysis

Calculated enthalpy differences between the E- and Z- isomers



Total electronic energy difference between *E*- and *Z*- isomers was calculated to be relatively small.

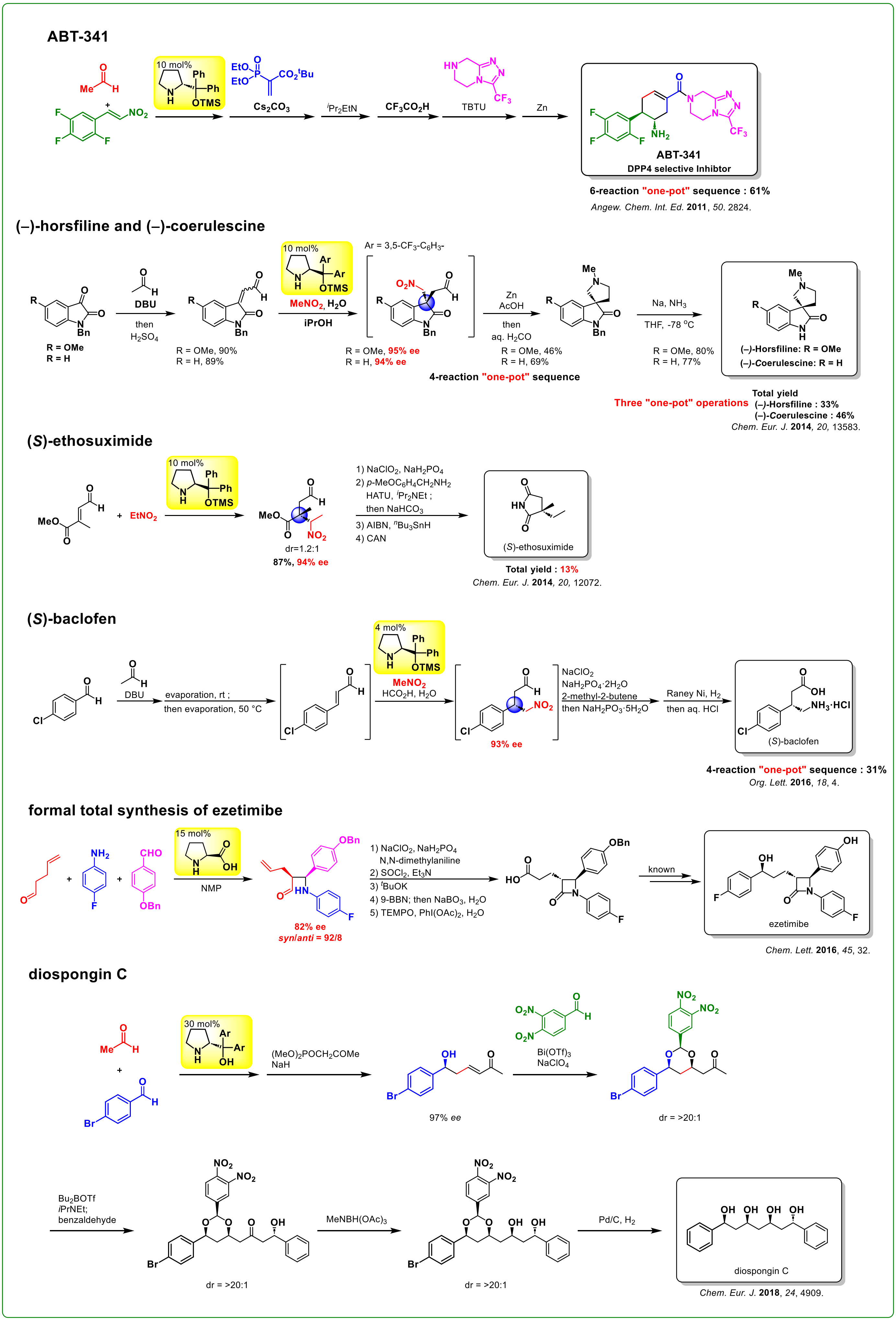
The orbital interactions in (Z)-alkoxyamine : antiperiplanar stabilization



σC(N)-H → σ*C-O : 7.80 kcal mol^{-1}

σC(O)-H → σ*C-N : 7.40 kcal mol^{-1}

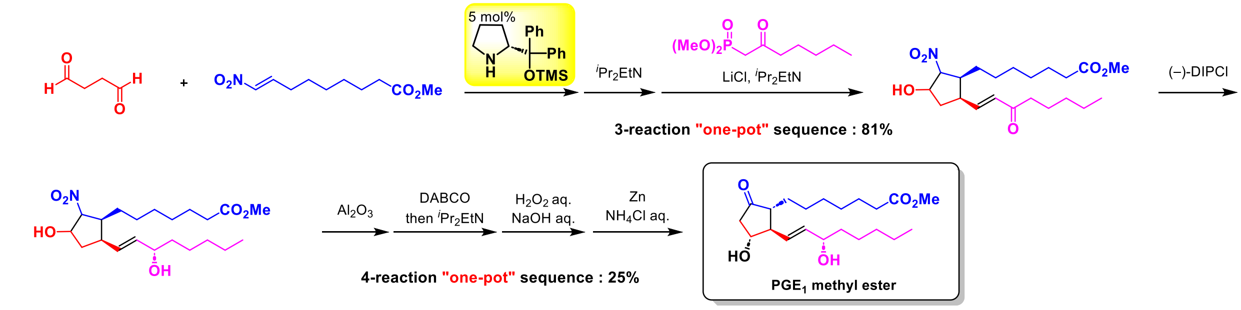
The antiperiplannar interactions are likely to be most contributing for stabilizing the Z-alkoxyenamine.



ABT-341
10 mol%
Cs2CO3
iPr2EtN
CF3CO2H
TBTU
Zn
ABT-341
DPP4 selective Inhibtor
6-reaction "one-pot" sequence : 61%
Angew. Chem. Int. Ed. 2011, 50. 2824.
(–)-horsfiline and (–)-coerulescine
DBU
then H2SO4
R = OMe
R = H
R = OMe, 90%
R = H, 89%
Ar = 3,5-CF3-C6H3-
10 mol%
MeNO2, H2O
iPrOH
R = OMe, 95% ee
R = H, 94% ee
Zn
AcOH
then
aq. H2CO
R = OMe, 46%
R = H, 69%
Na, NH3
THF, -78 °C
R = OMe, 80%
R = H, 77%
(–)-Horsfiline: R = OMe
(–)-Coerulescine: R = H
4-reaction "one-pot" sequence
Three "one-pot" operations
Total yield
(–)-Horsfiline : 33%
(–)-Coerulescine : 46%
Chem. Eur. J. 2014, 20, 13583.
(S)-ethosuximide
10 mol%
EtNO2
dr=1.2:1
87%, 94% ee
1) NaClO2, NaH2PO4
2) p-MeOC6H4CH2NH2
HATU, iPr2NEt ;
then NaHCO3
3) AIBN, nBu3SnH
4) CAN
(S)-ethosuximide
Total yield : 13%
Chem. Eur. J. 2014, 20, 12072.
(S)-baclofen
DBU
evaporation, rt ;
then evaporation, 50 °C
4 mol%
MeNO2
HCO2H, H2O
93% ee
NaClO2
NaH2PO4·2H2O
2-methyl-2-butene
then NaH2PO3·5H2O
Raney Ni, H2
then aq. HCl
(S)-baclofen
4-reaction "one-pot" sequence : 31%
Org. Lett. 2016, 18, 4.
formal total synthesis of ezetimibe
15 mol%
NMP
82% ee
syn/anti = 92/8
1) NaClO2, NaH2PO4
N,N-dimethylaniline
2) SOCl2, Et3N
3) tBuOK
4) 9-BBN; then NaBO3, H2O
5) TEMPO, PhI(OAc)2, H2O
known
ezetimibe
Chem. Lett. 2016, 45, 32.
diospongin C
30 mol%
(MeO)2POCH2COMe
NaH
97% ee
Bi(OTf)3
NaClO4
dr = >20:1
Bu2BOTf
iPrNEt;
benzaldehyde
dr = >20:1
MeNBH(OAc)3
dr = >20:1
Pd/C, H2
diospongin C
Chem. Eur. J. 2018, 24, 4909.

Prostaglandin derivatives

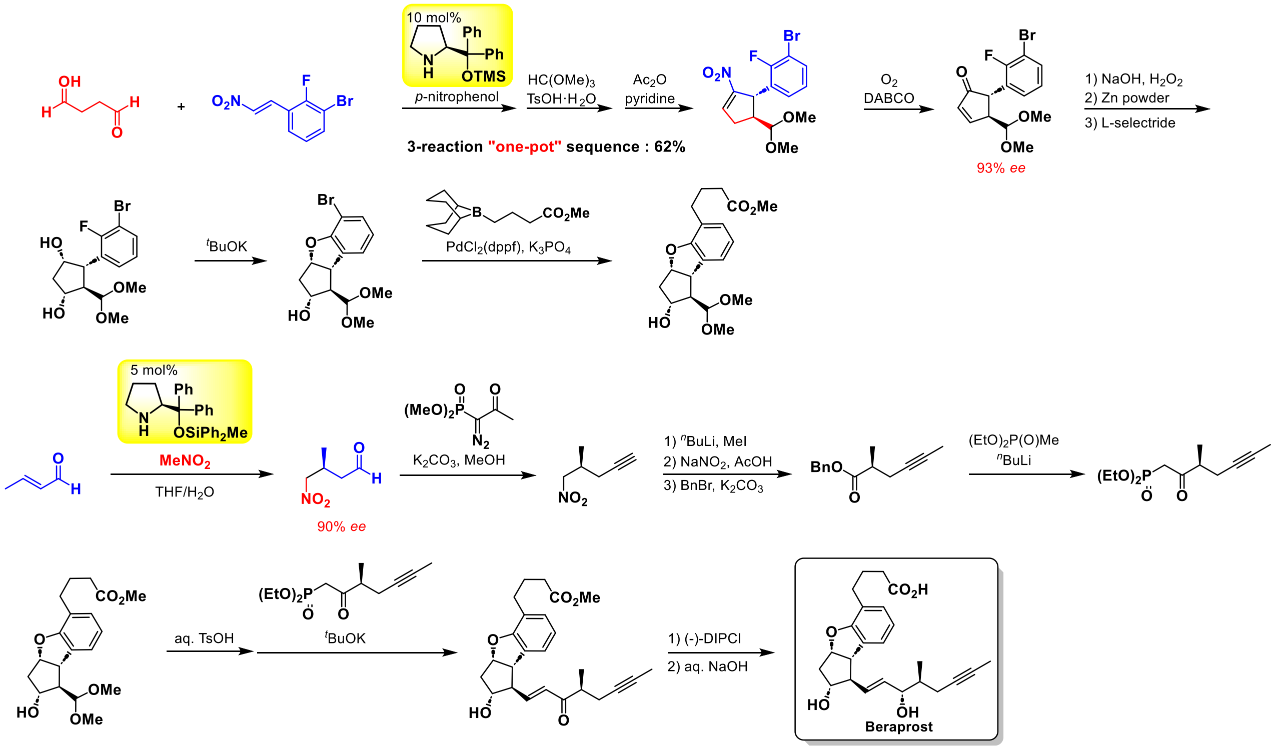
prostaglandin E_1 methyl ester



Total yield : 14%, 3 pot

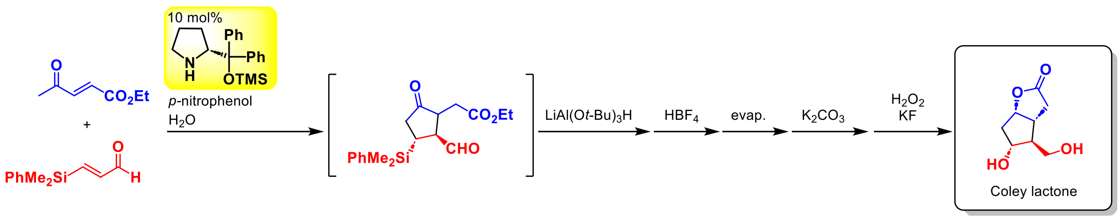
Angew. Chem. Int. Ed. **2013**, *52*, 3450.

beraprost



Org. Lett. **2017**, *19*, 1112.

Corey lactone



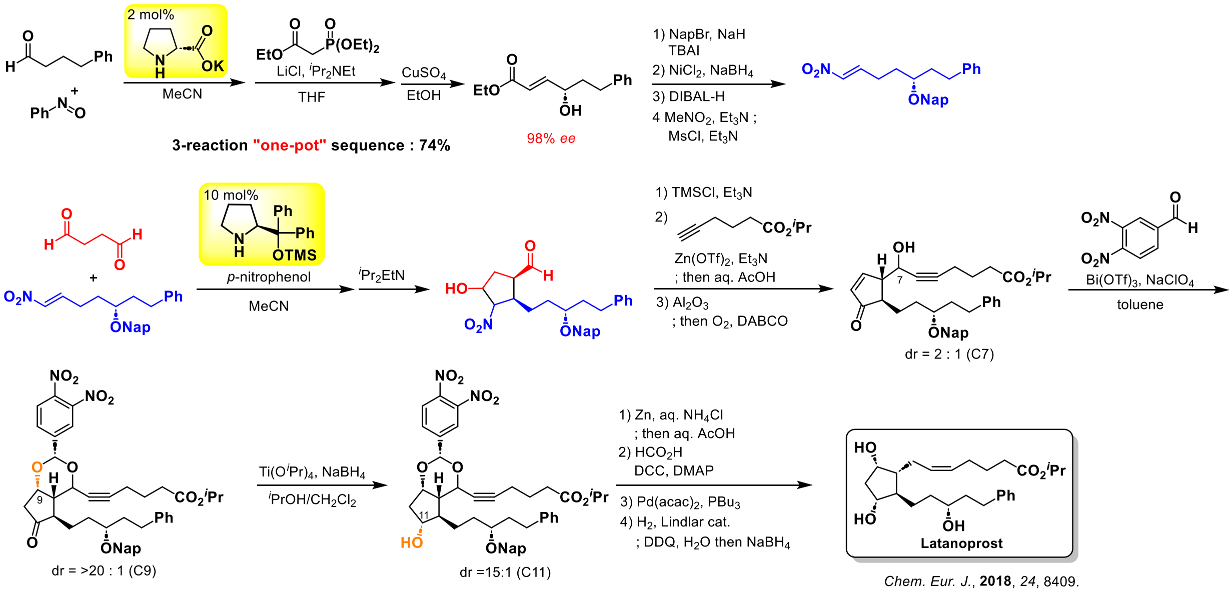
7-reactions "one-pot" sequence
Total yield: 50%
Total reaction time: 152 min
One purification

Chem. Sci., **2020**, *11*, 1205.

Prostaglandin derivatives

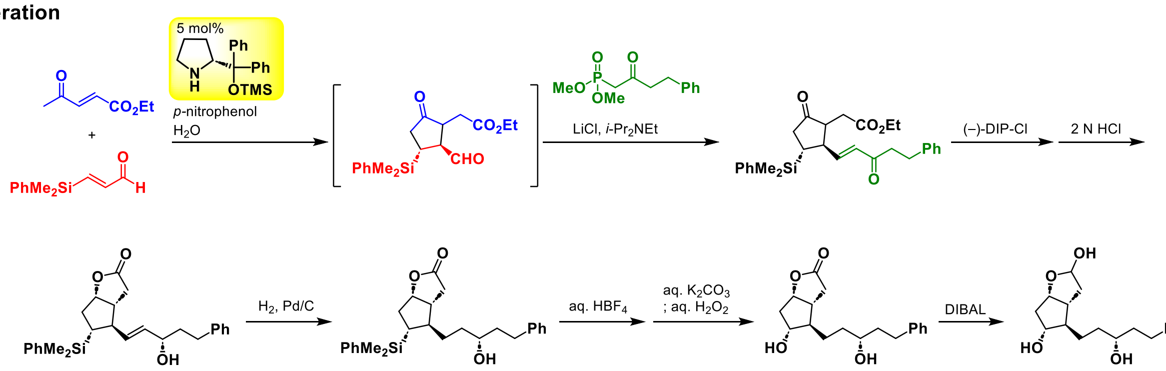
latanoprost

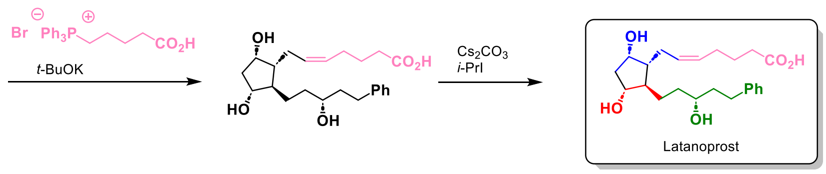
1st generation



Chem. Eur. J., **2018**, *24*, 8409.

2nd generation

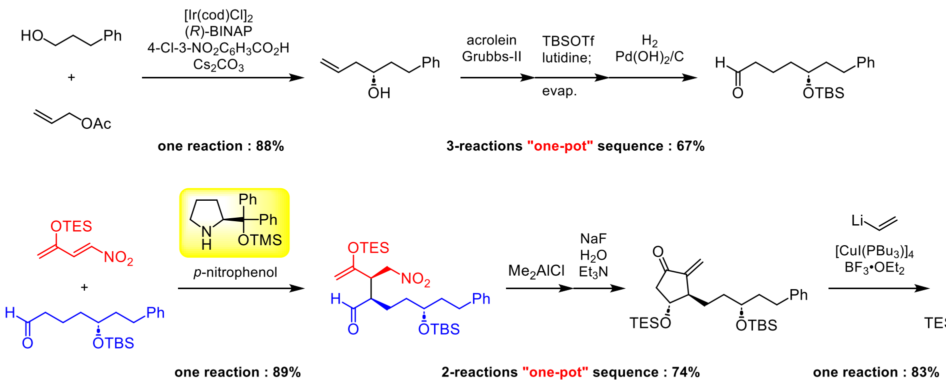


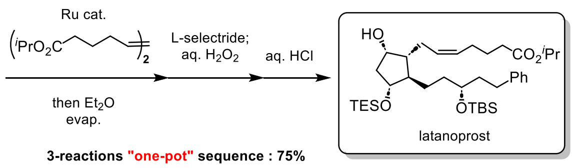


Total yield: 50%
10-reaction steps, 7-pot reaction
One purification

Eur. J. Org. Chem., **2020**, 6221.

3rd generation



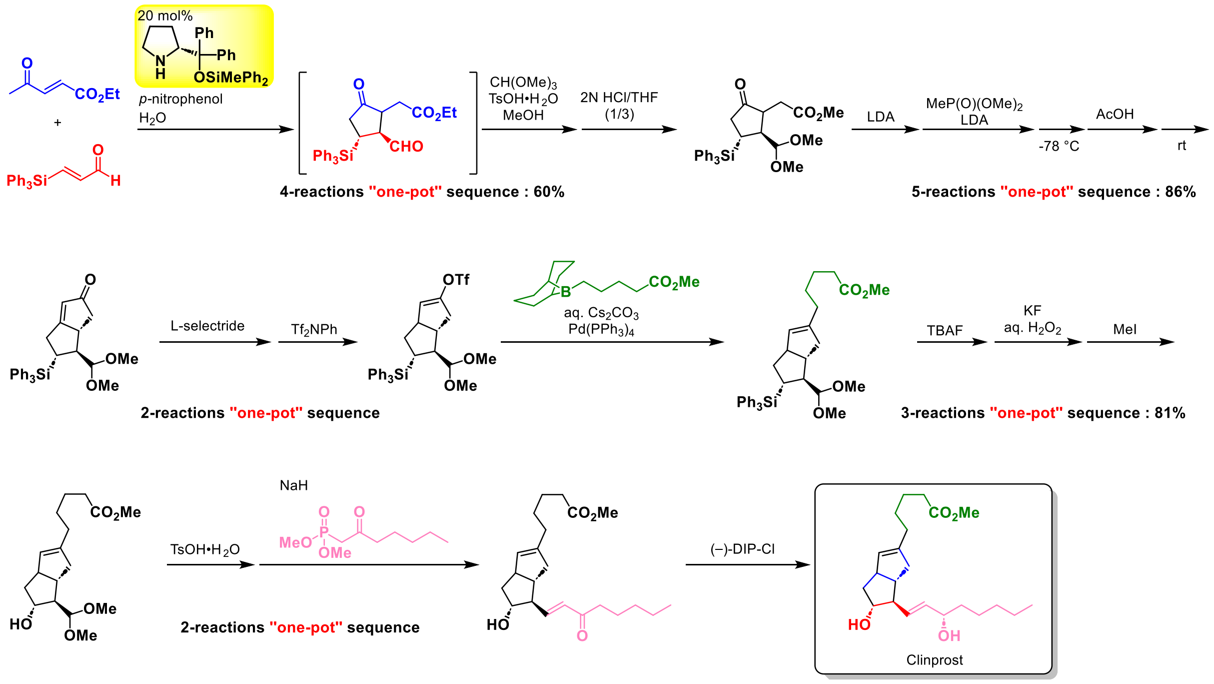


Total yield: 24%
11-reaction steps
6-pot reaction

Chem. Sci., **2023**, ASAP

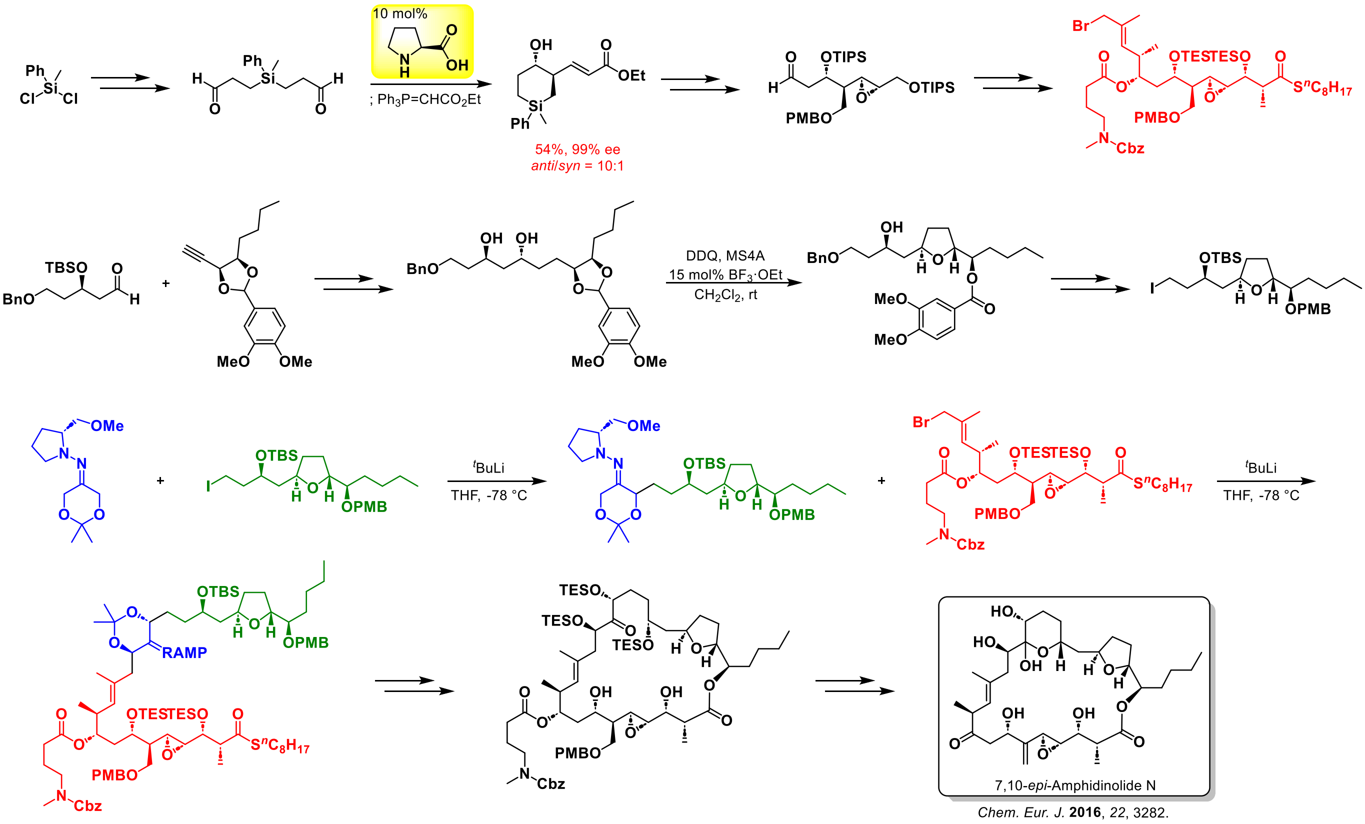
Prostaglandin derivatives

clinprost



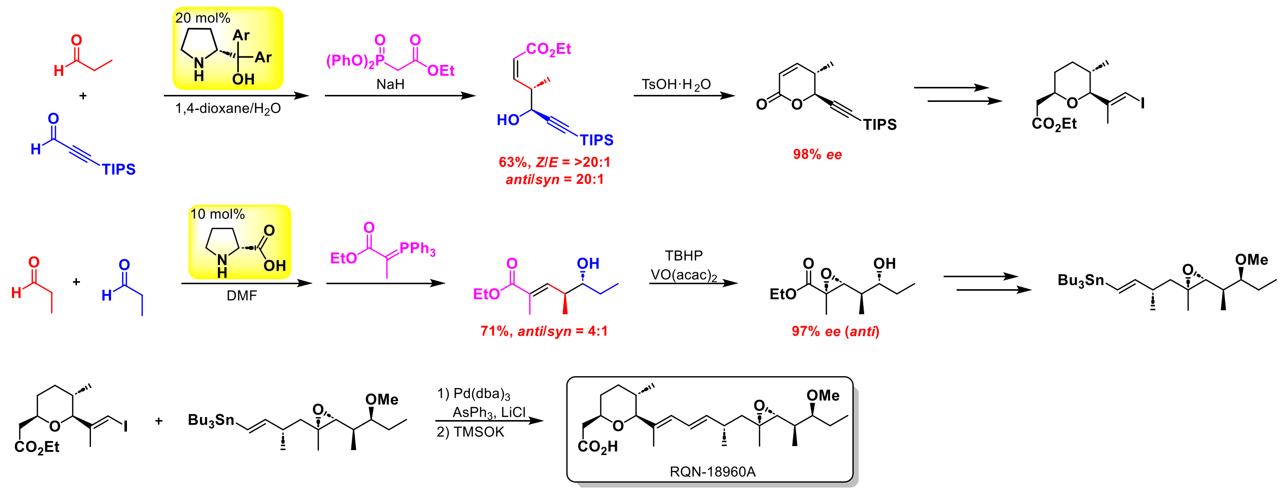
Org. Lett., **2020**, *22*, 9365.

7,10-*epi*-amphidinolide N



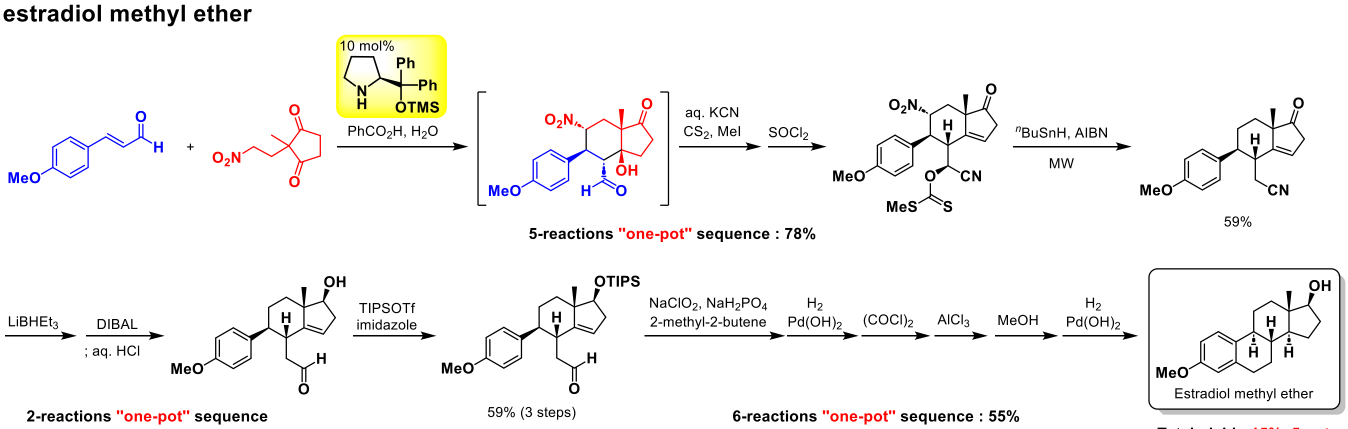
Chem. Eur. J. **2016**, *22*, 3282.
Chem. Eur. J. **2016**, *22*, 3287.

RQN-18690A



Org. Lett. **2016**, *18*, 3382.

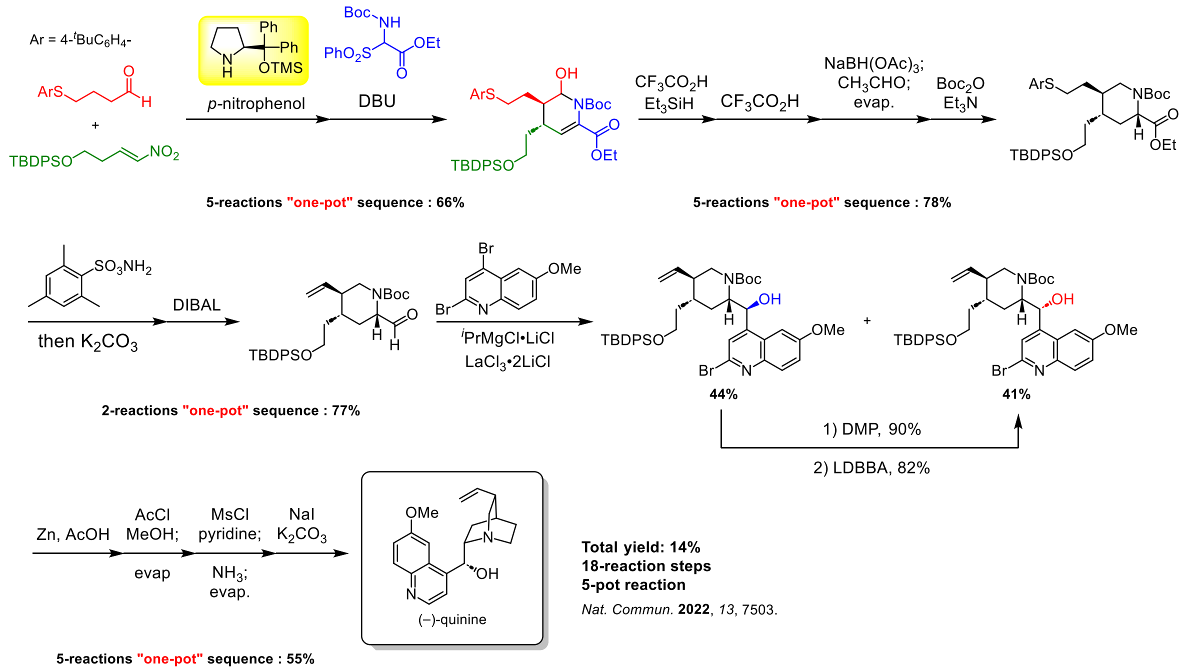
estradiol methyl ether



Total yield : 15%, 5 pot

Angew. Chem. Int. Ed. **2017**, *56*, 11812.
Eur. J. Org. Chem. **2018**, *41*, 5629.

(–)-quinine



Total yield: 14%
18-reaction steps
5-pot reaction

Nat. Commun. **2022**, *13*, 7503.