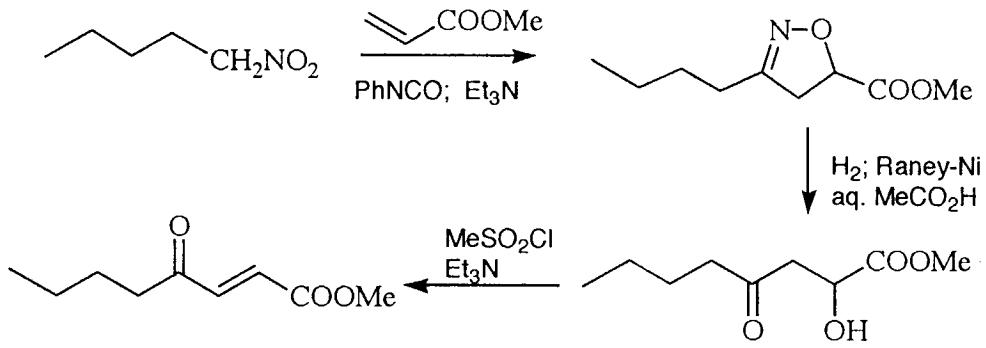
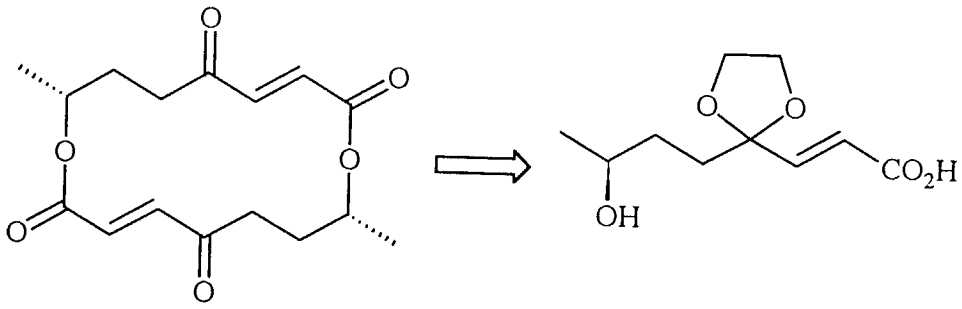
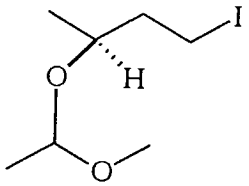
The [3+2]-nitrile oxide cycloaddition approach to γ-Ketoacrylate unit.



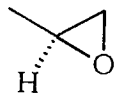


(-)-Pyrenophorin

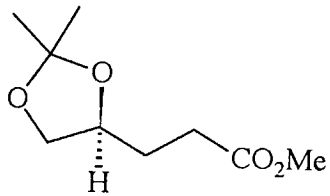


from β-hydroxybutyrate

D. Seebach et al., Angew. Chem Int. Ed. Engl., **1977**, *16*, 264.

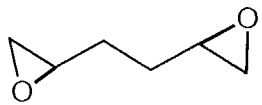


D. Seebach et al. Liebigs Ann. Chem., **1981**, 2272.

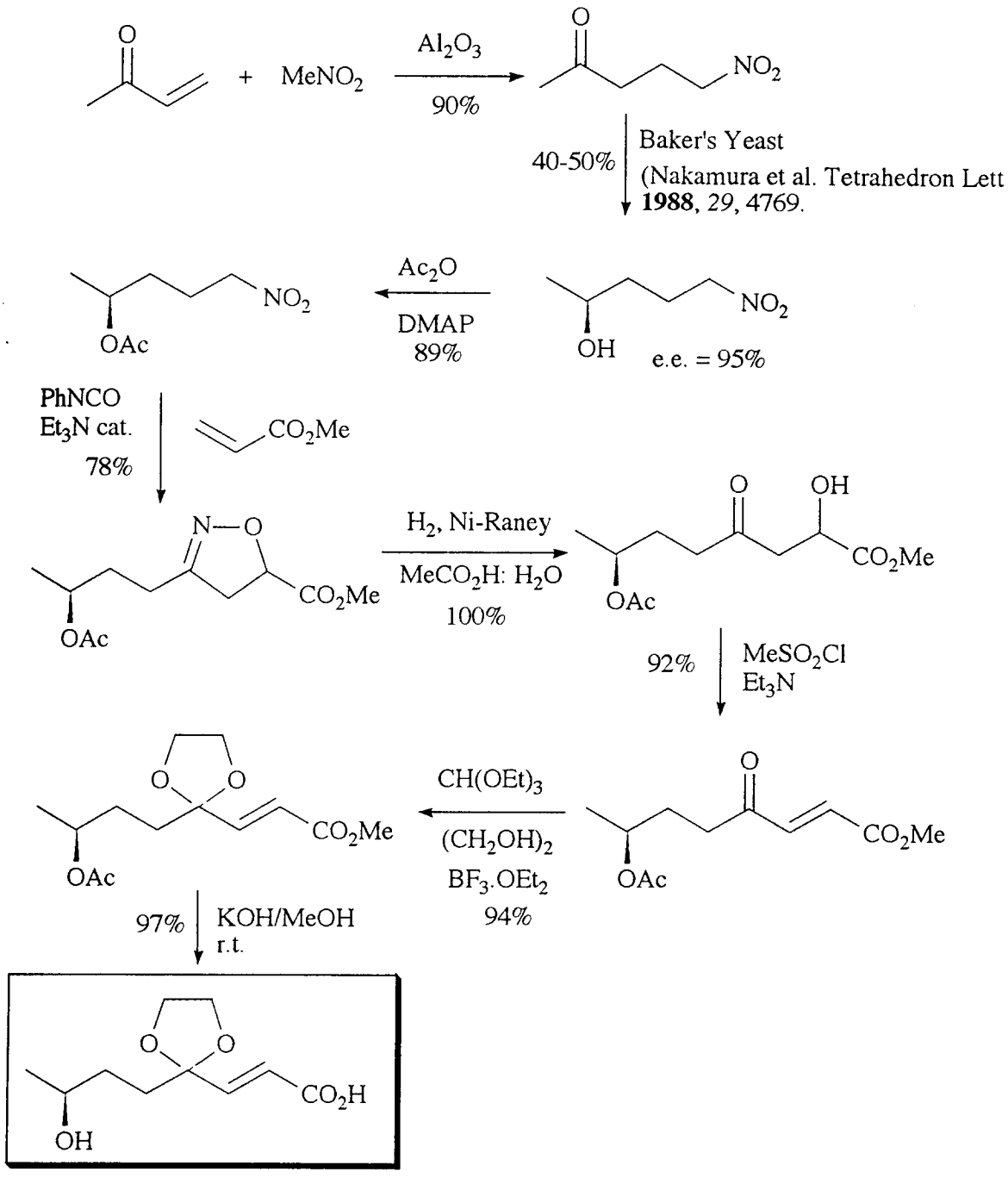


from D-mannitol

Takano et al., Tetrahedron Lett., **1987**, *28*, 2717.

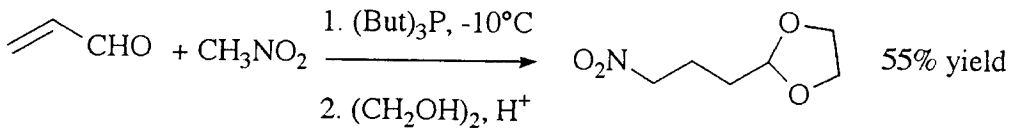


N. Machinaga, C.Kibayashi, Tetrahedron Lett., **1993**, *34*, 841.


+ MeNO2
Al2O3
90%
NO2
40-50%
Baker's Yeast
(Nakamura et al. Tetrahedron Lett
1988, 29, 4769.
Ac2O
DMAP
89%
OAc
OH
e.e. = 95%
PhNCO
Et3N cat.
78%
CO2Me
N—O
H2, Ni-Raney
MeCO2H: H2O
100%
92%
MeSO2Cl
Et3N
CH(OEt)3
(CH2OH)2
BF3.OEt2
94%
97%
KOH/MeOH
r.t.

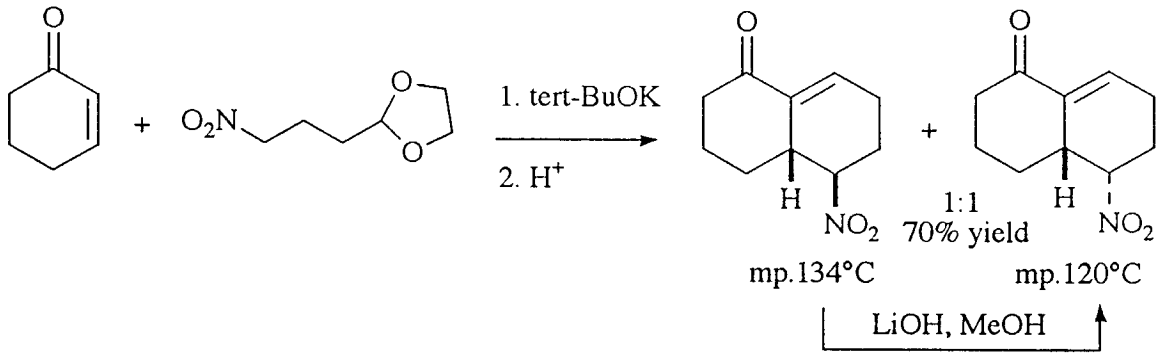
2-(3-Nitropropyl)-1,3-dioxolane as four carbon bifunctional annelating agent.

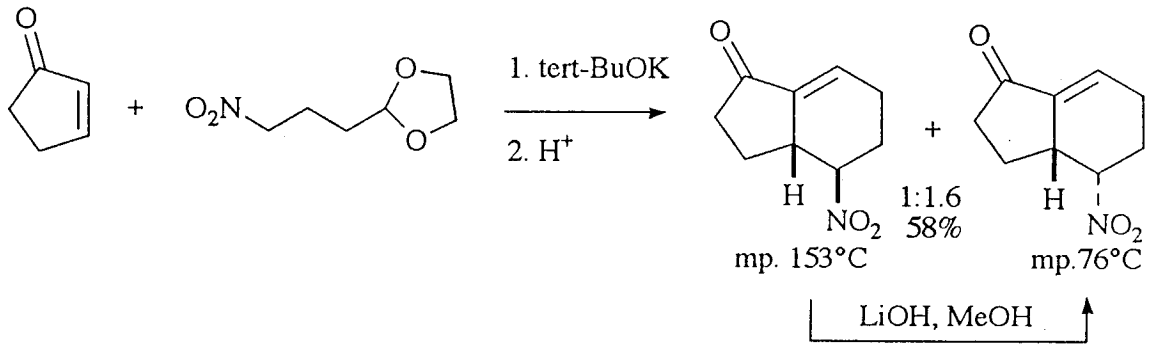
Preparation:

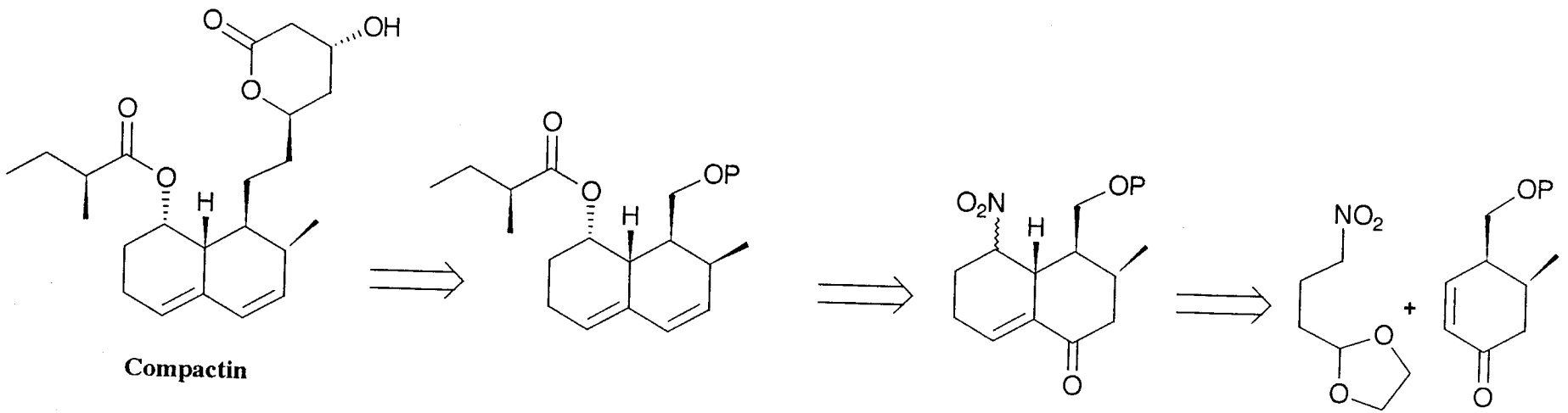


55% yield

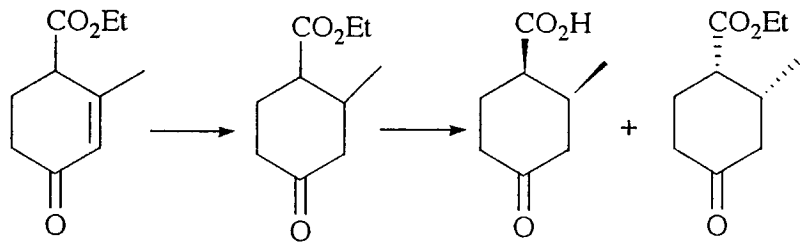
Model studies:



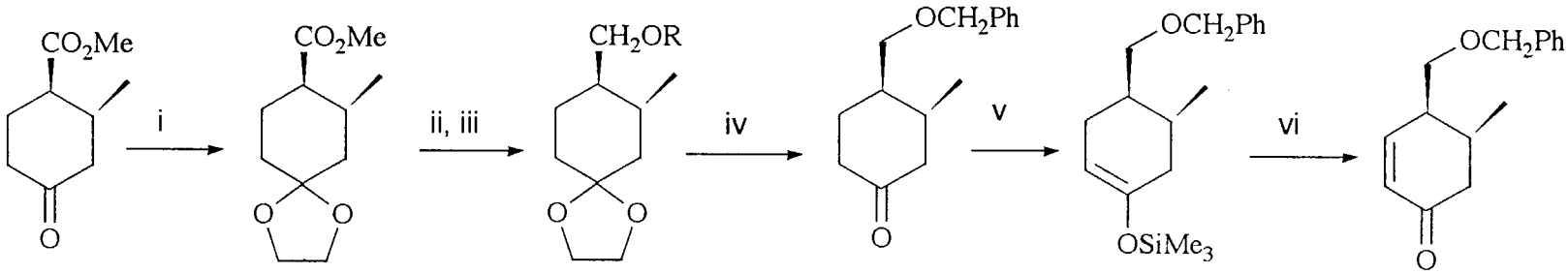




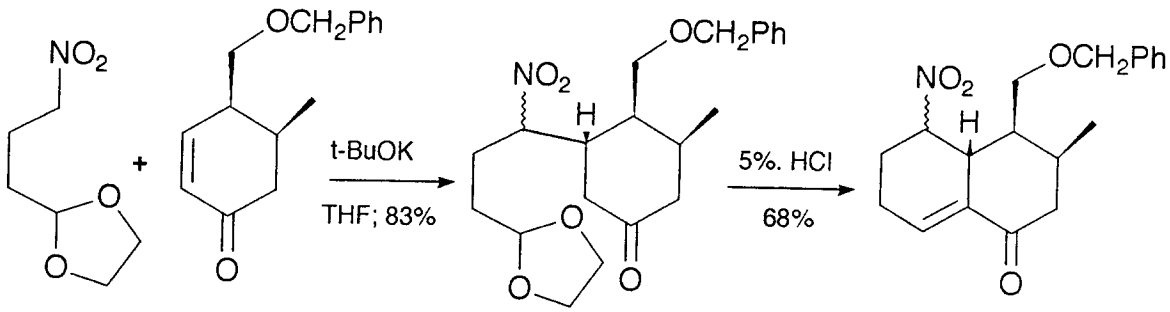
Compactin

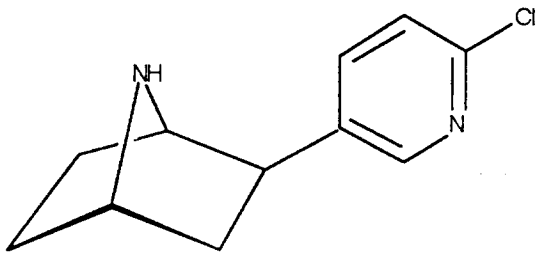


Reagents: i, H_2, 5% Pd/C; ii, PLE.



Reagents: i, $(CH_2OH)_2$, H^+; ii, $LiAlH_4$; iii, $PhCH_2Br$, NaH, $Bu_4N^+I^-$; iv, H^+, H_2O; v, LDA, Me_3SiCl; vi, $Pd^{II}(OAc)_2$.


NO2
OCH2Ph
t-BuOK
THF; 83%
5%. HCl
68%
H
O



EPIBATIDINE:

Isolated from *EPIPEDOBATES TRICOLOR* by Daly et al., J. Am. Chem. Soc., 1992,114, 3475-3478.

A new interesting non-opioid-analgesic.

500 times more potent than morphine in the Straub tail effect, and this effect is not reversed by the opiate antagonist naloxone;

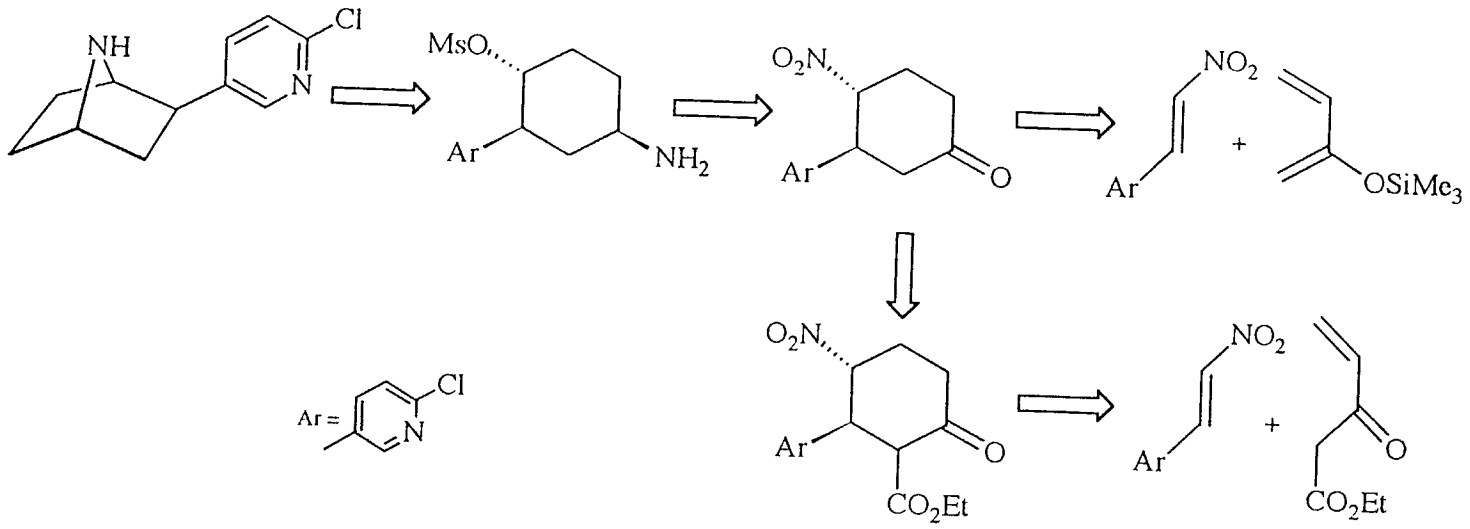
200 times more potent than morphine in hot plate assay.

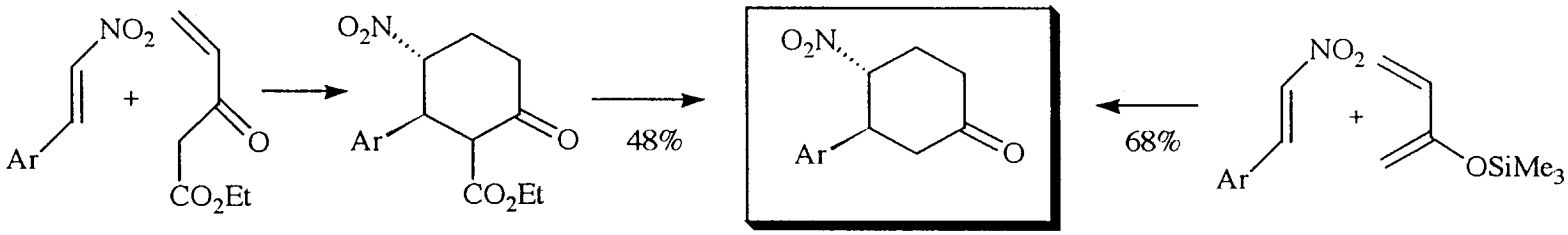
Opiate receptor binding studies indicated negligible (1/8000xmorphine) affinity for this receptor.

Both epibatidine and nicotine are analgesic acting on the receptor N of CNS and are antagonized by Mecamylamine: Epibatidine is 120 times more potent than Nicotine and has longer duration, acting exclusively on this receptor.

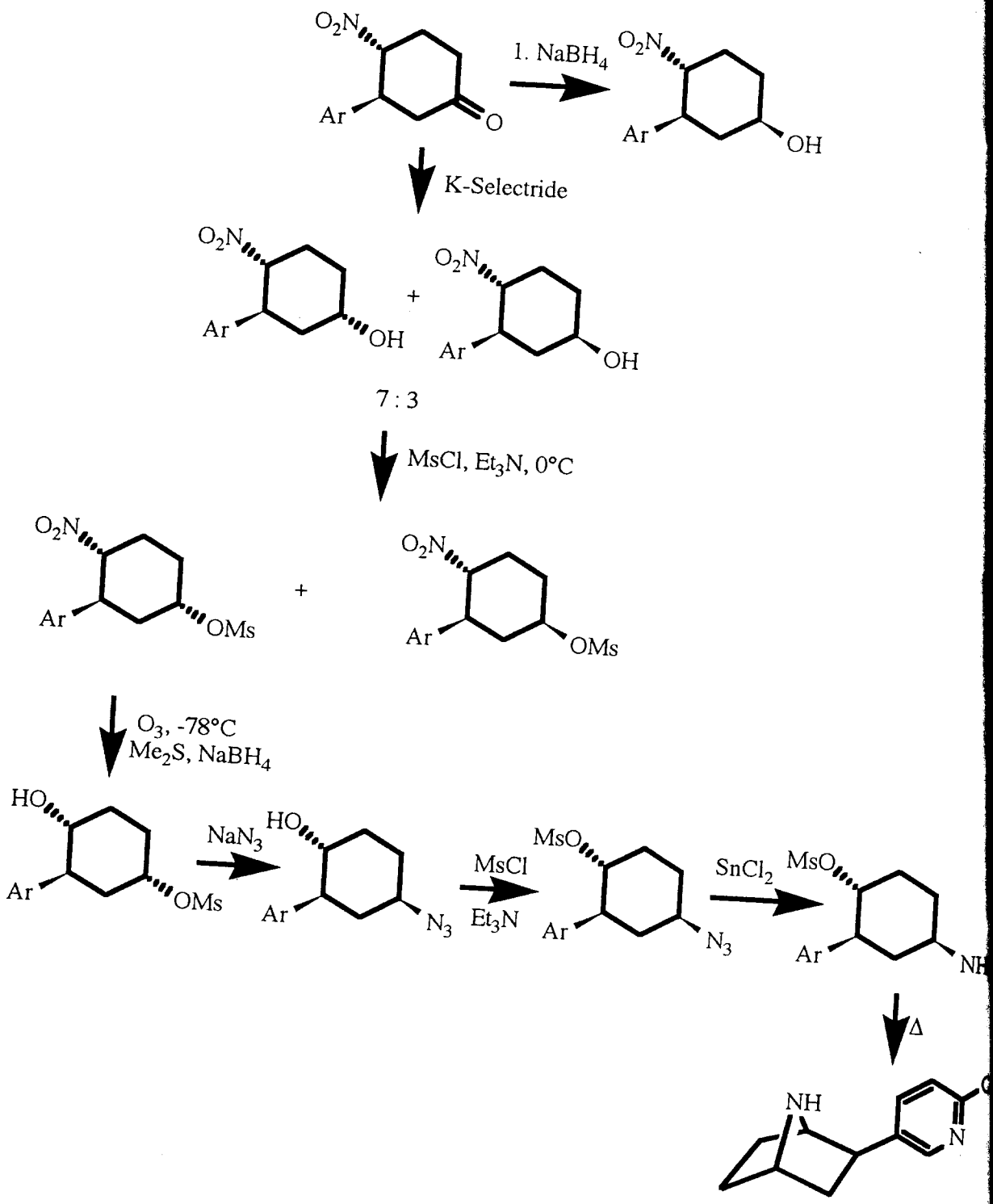
Nicotine acetylcholine receptor has been found to be involved in the mediation of several human diseases, including Parkinson's disease, Alzheimer's disease, tobacco dependence, ulcerative colitis.

Epibatidine, as a selective and extremely potent nicotinic receptor agonist, may be a useful tool for further investigations of the roles of nicotinic acetylcholine receptor in human diseases.

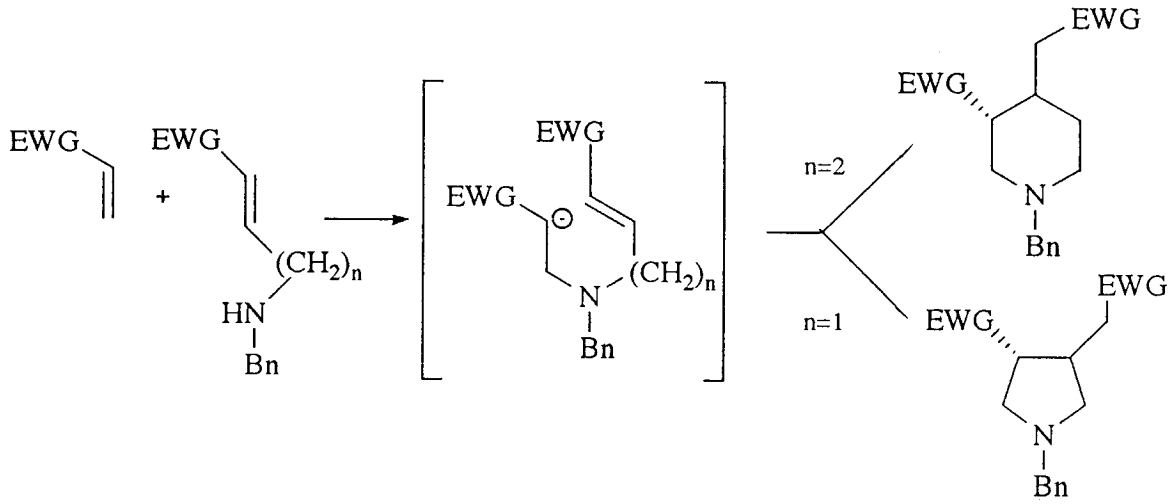

NH
Cl
N
MsO
Ar
NH2
O2N
Ar
O
NO2
Ar
+
OSiMe3
Ar =
Cl
N
O2N
Ar
O
CO2Et
NO2
Ar
+
O
CO2Et

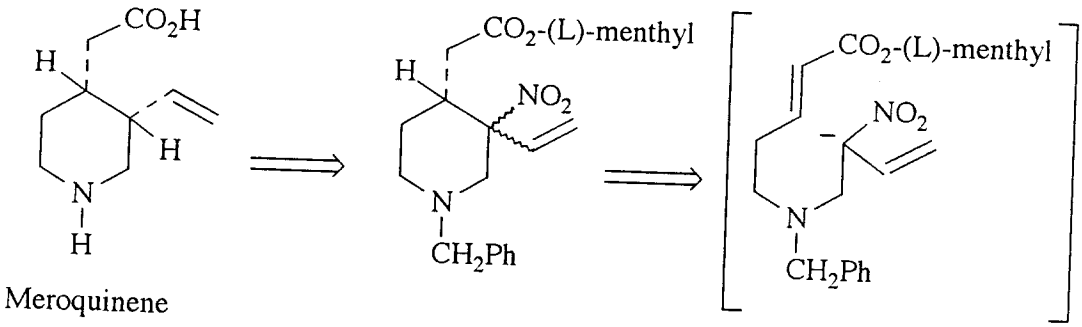


Reagents and conditions: i, $BnMe_3N^+ {}^-OMe$, dioxane, r.t.; ii, LiCl, DMSO; iii, 120°C, 48h

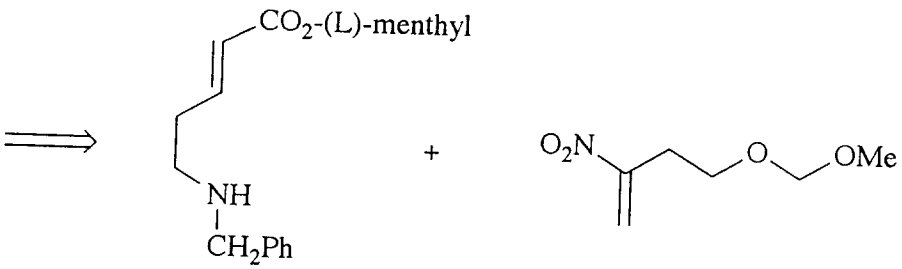

O2N
Ar
O
1. NaBH4
OH
K-Selectride
+
7 : 3
MsCl, Et3N, 0°C
OMs
O3, -78°C
Me2S, NaBH4
HO
NaN3
N3
MsCl
Et3N
MsO
SnCl2
NH
Δ
N

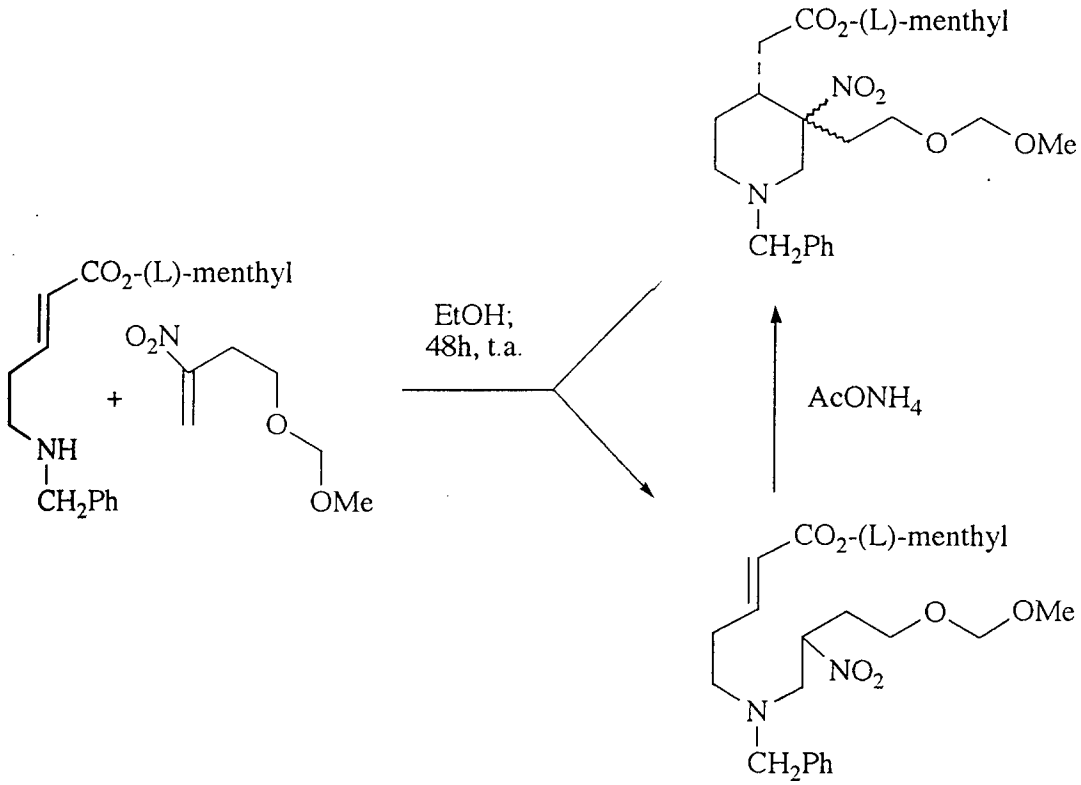
Tandem Michael reaction methodology for pyrrolidine and piperidine ring systems.

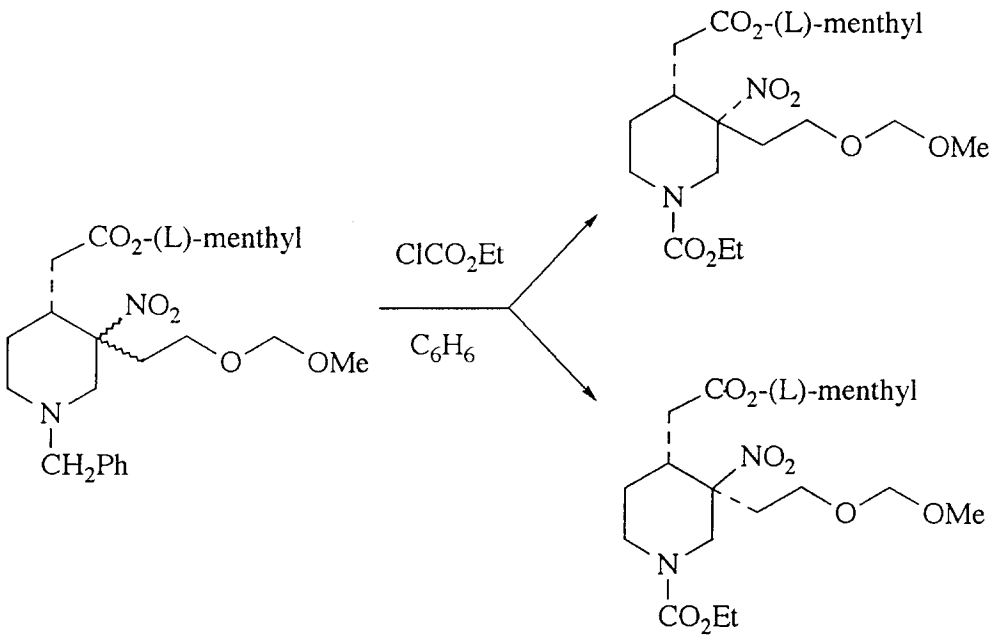


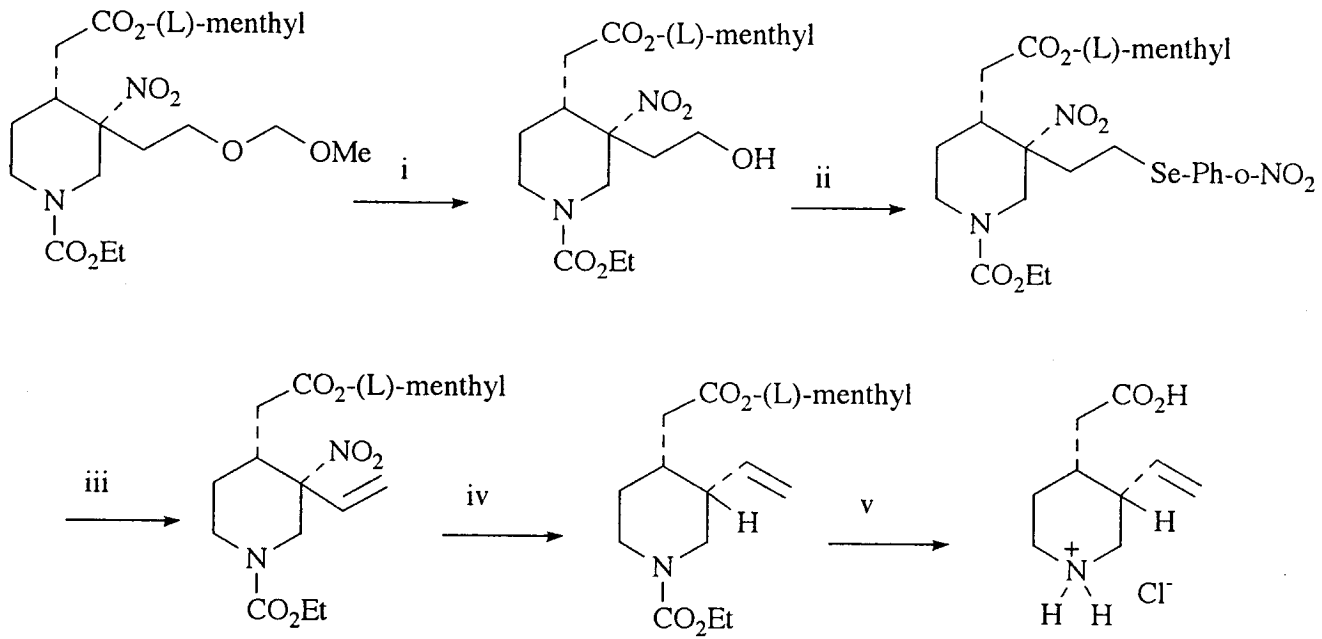


Meroquinene

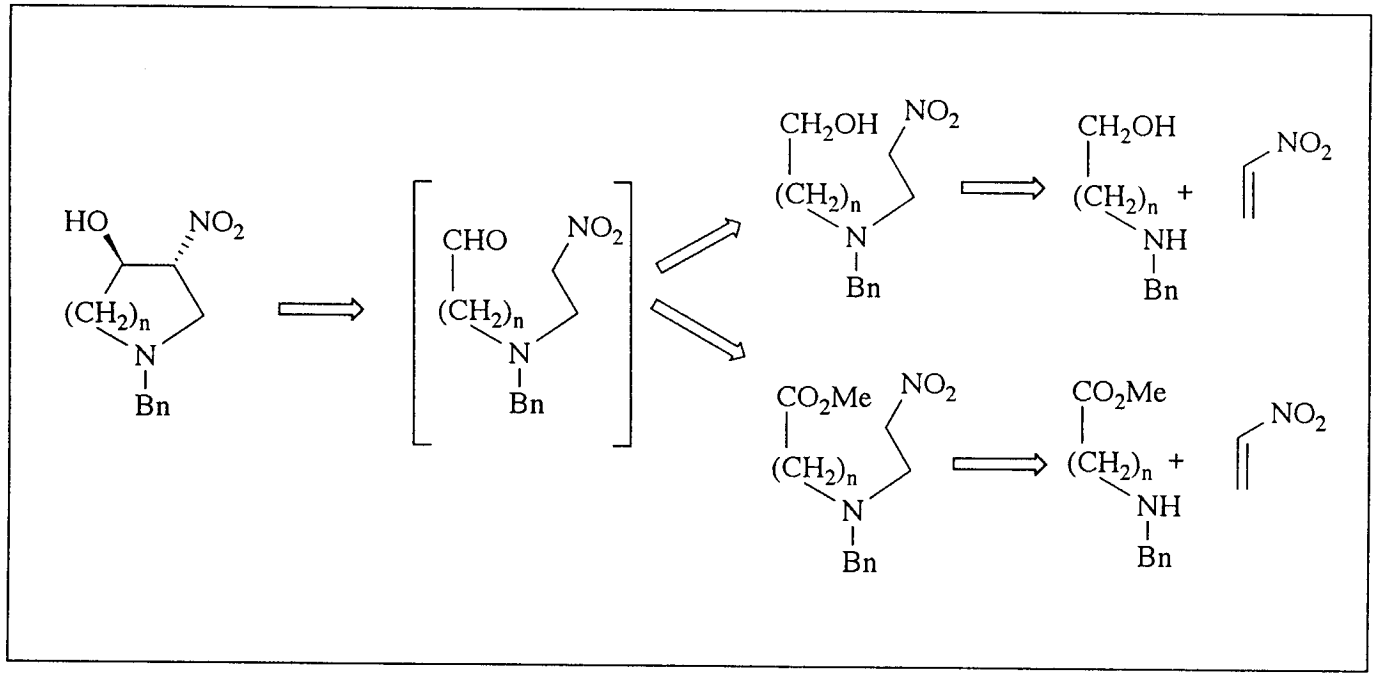



CO2-(L)-menthyl
NO2
O
OMe
N
CH2Ph
CO2-(L)-menthyl
O2N
+
NH
CH2Ph
O
OMe
EtOH;
48h, t.a.
AcONH4
CO2-(L)-menthyl
O
OMe
NO2
N
CH2Ph

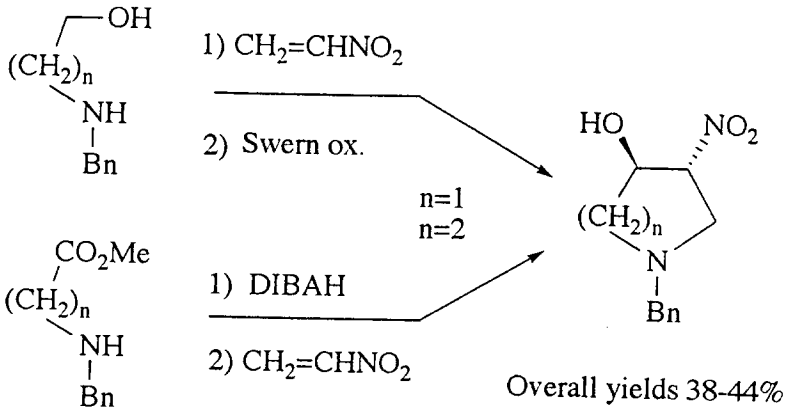

CO2-(L)-menthyl
NO2
O
OMe
N
CH2Ph
ClCO2Et
C6H6
CO2-(L)-menthyl
NO2
O
OMe
N
CO2Et
CO2-(L)-menthyl
NO2
O
OMe
N
CO2Et



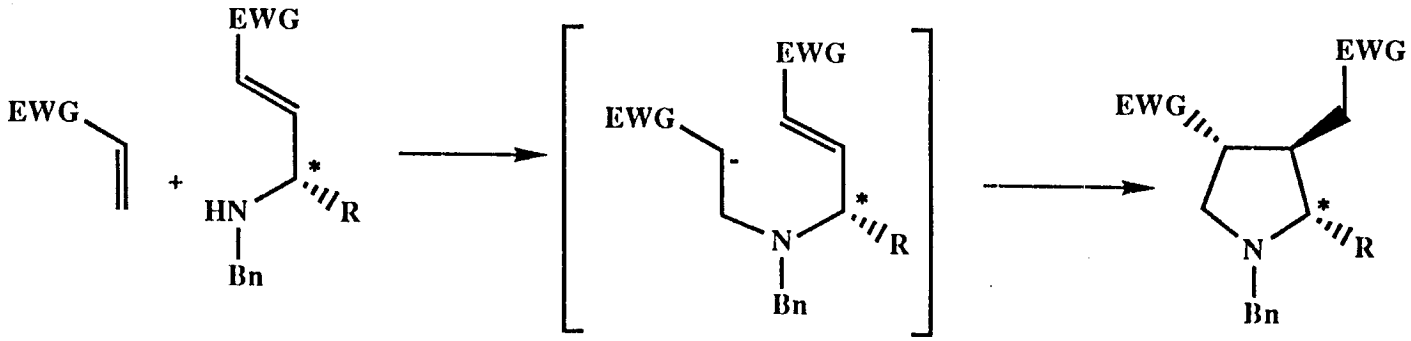
Reagents: i, H^+, $Me_2CO : H_2O$; ii, o-NO_2-Ph-SeCN, $(n\text{-But})_3P$; iii, $NaBO_3.4H_2O$;
iv, $Pd^0(PPh_3)_4$, Ph_3P, HCO_2NH_4, THF, 80°C; v, 10% HCl, reflux, 6h.


HO
NO2
(CH2)n
N
Bn
CHO
NO2
(CH2)n
N
Bn
CH2OH
NO2
(CH2)n
N
Bn
CH2OH
(CH2)n +
NH
Bn
NO2
CO2Me
NO2
(CH2)n
N
Bn
CO2Me
(CH2)n +
NH
Bn
NO2

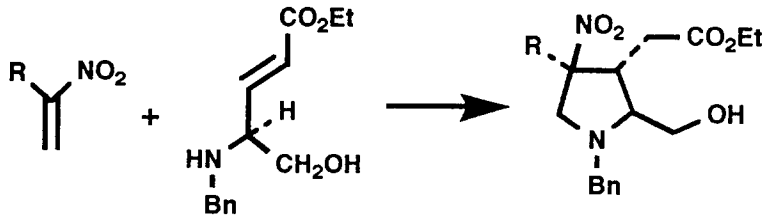
One-pot formation of nitrohydroxypyrrolidine and piperidine ring systems.



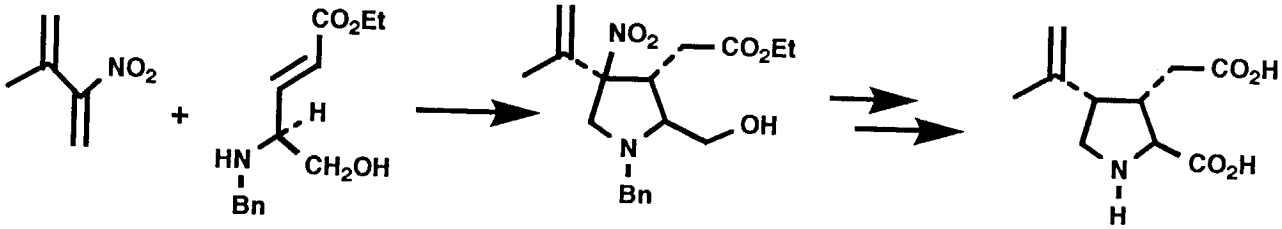
Overall yields 38-44%


EWG
EWG
HN
Bn
R
EWG
EWG
N
Bn
R
EWG
EWG
N
Bn
R

General Strategy for Kainoids

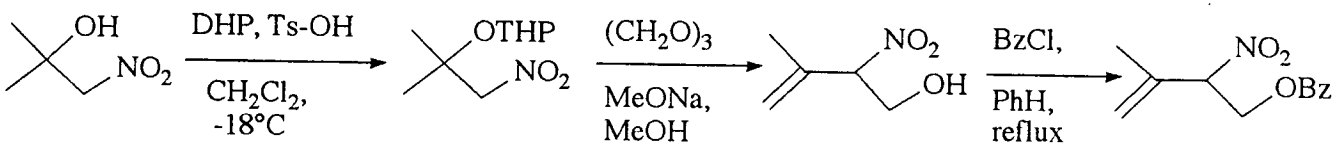


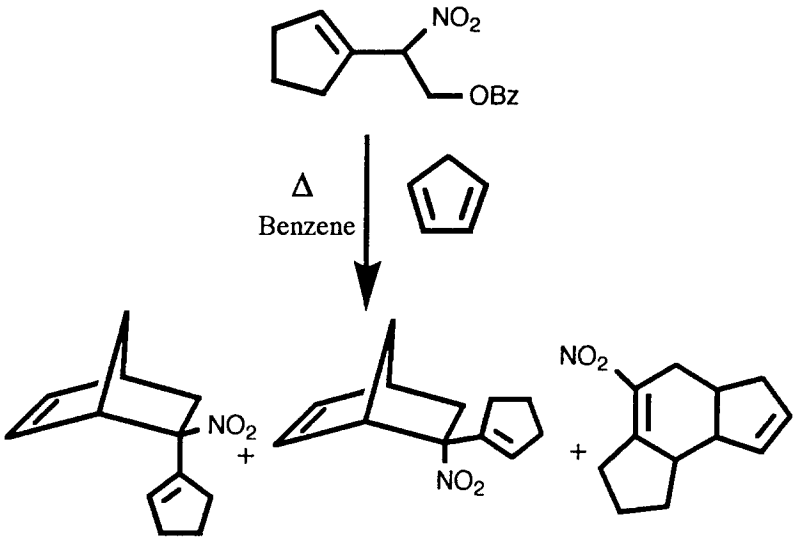
1. The nitro group offers sufficient steric and electronic interactions in the transition state leading to cyclization to obtain the desired product with syn relationship of the C-4 substituent to the C-3 acetic chain.
2. An allylic nitro group can be removed stereoselectively.



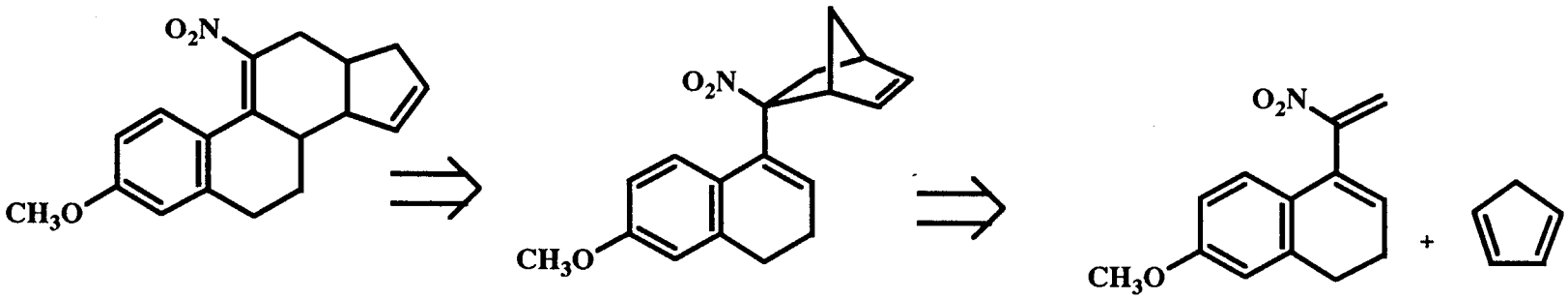
(-)–α-Kainic acid

Preparation of 2-nitro-3-methyl-1,3-butadiene precursor.





12,5 % 40 % 47,5 %


O2N
CH3O
O2N
CH3O
O2N
CH3O
+