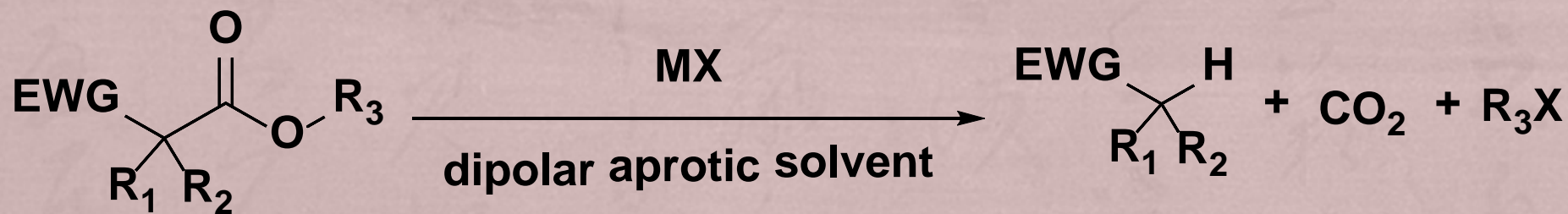


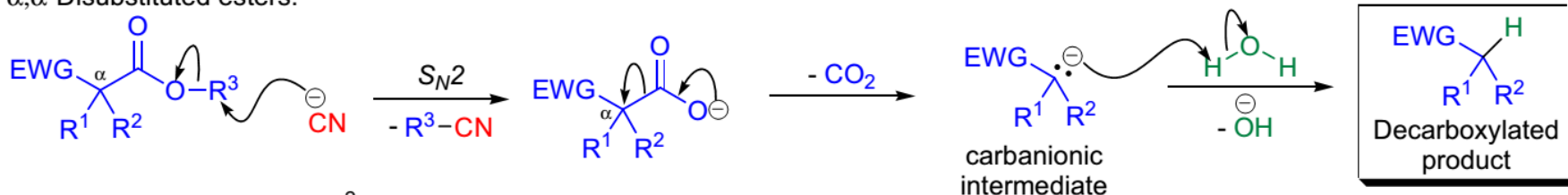
Krapcho dealkoxycarbonylation



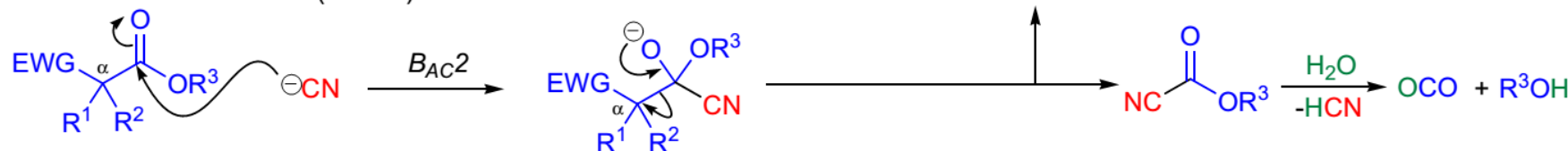
mechanism:

- α,α -disubstituted diesters (especially the methyl esters), the anion from the salt (cyanide ion in the scheme) attacks the alkyl group of the ester in an S_N2 fashion and the decarboxylation results in the formation of a carbanionic intermediate that is quenched by the water;
- α -monosubstituted diesters the cyanide attacks the carbonyl group to form a tetrahedral intermediate, which breaks down to give the same carbanionic intermediate and a cyanoformate, which is hydrolyzed to give carbon dioxide and an alcohol.

α,α -Disubstituted esters:

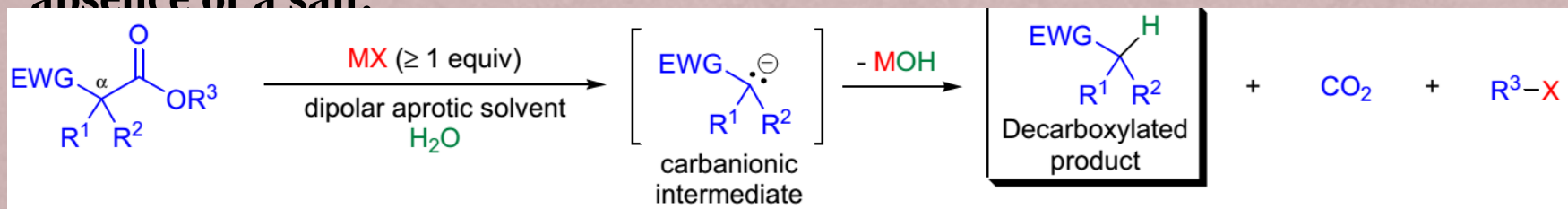


α -Monosubstituted esters ($\text{R}^2 = \text{H}$):



The general features of this reaction :

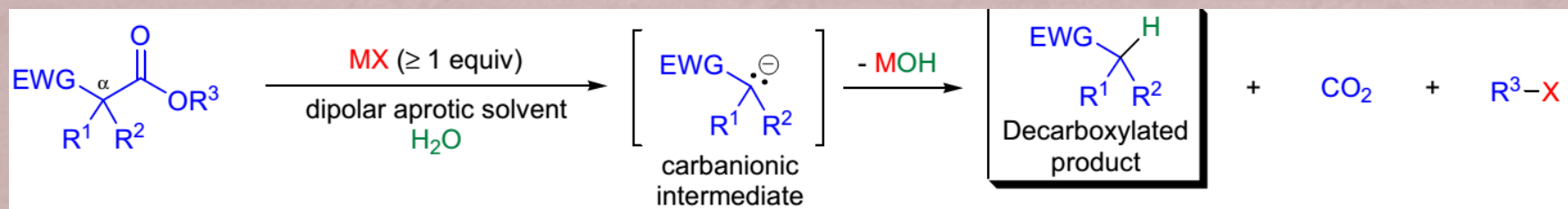
- This nucleophilic dealkoxycarbonylation process is general for methyl- or ethyl esters of carboxylic acids, which have an electron-withdrawing group (CO₂-alkyl, CN, CO-alkyl, SO₂-alkyl, etc.) at their α -position;
- The reaction conditions are essentially neutral, so both acid- and base-sensitive substrates can be used and the otherwise frequent acid-catalyzed rearrange- -ments are avoided.
- Chemoselectivity and the functional group tolerance of the method is very high.
- As a rule of thumb when the substrate has at least one proton at the α -position, the dealkoxycarbonylation can be achieved with wet DMSO at reflux in the absence of a salt.



EWG = CO₂-alkyl, CO₂-aryl, CN, CO-alkyl, SO₂-alkyl, SO₂-aryl; R^{1-2} = H, alkyl, aryl; R^3 = Me, Et; MX = NaCN, KCN, LiCl, NaCl, NaBr, NaI, LiI·H₂O, Na₂CO₃·H₂O, Na₃PO₄·12H₂O, Me₄NOAc; solvent: DMSO, DMF, DMA, HMPT

The general features of this reaction :

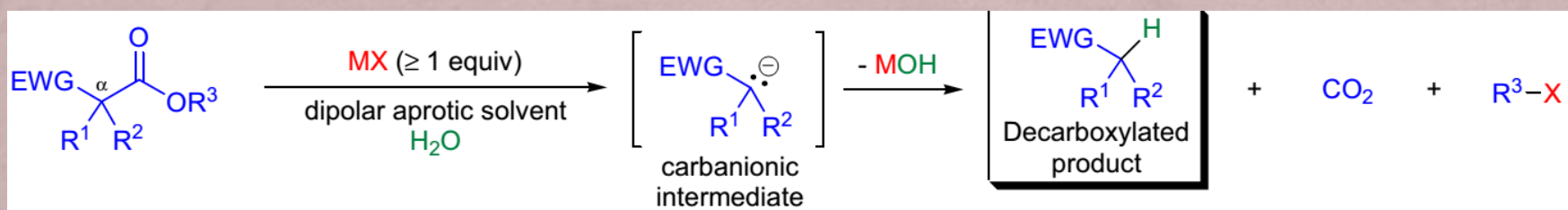
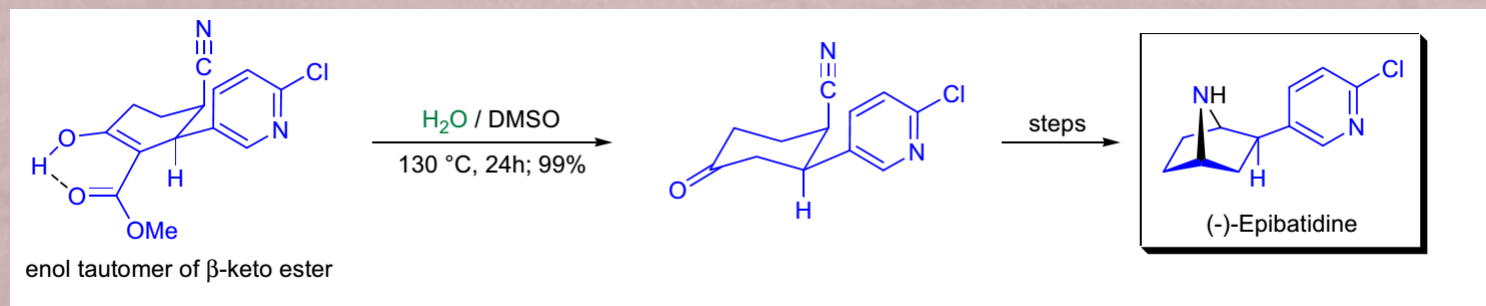
- Double bonds are not isomerized and in the overwhelming majority of cases labile stereocenters are not racemized;
- Monosubstituted malonic esters are dealkoxycarbonylated in hot dipolar aprotic solvent containing at least one equivalent of water;
- Disubstituted malonic esters, however, are dealkoxycarbonylated only in the presence of at least one equivalent of a salt (e.g., KCN, LiCl, etc.) in wet DMSO at reflux;
- The presence of a salt tends to accelerate the rate of the dealkoxycarbonylation of many (but not all) substrates;



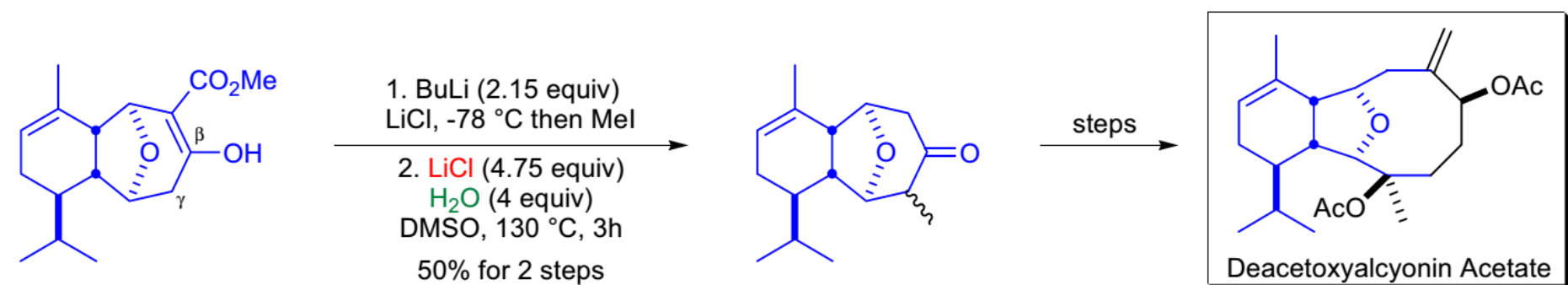
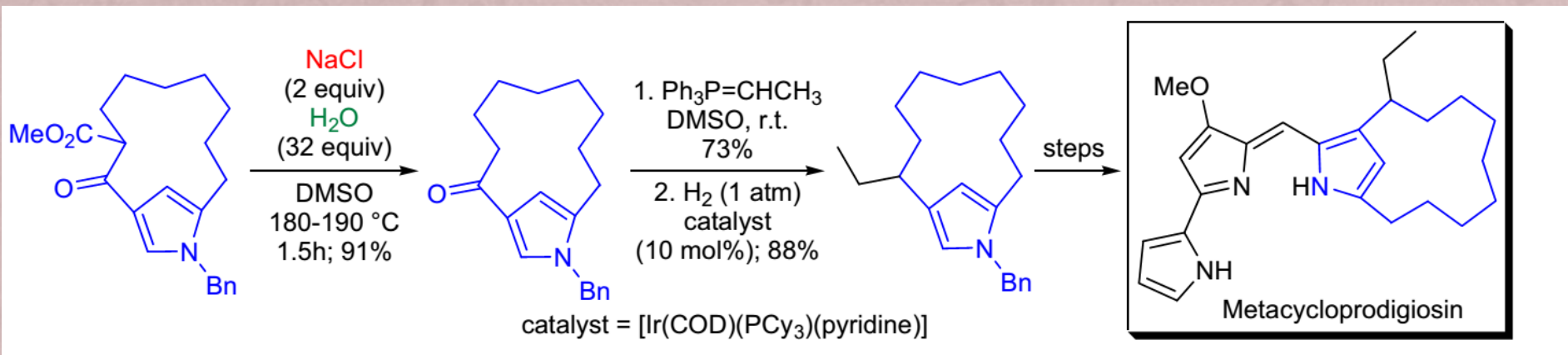
EWG = CO₂-alkyl, CO₂-aryl, CN, CO-alkyl, SO₂-alkyl, SO₂-aryl; R¹⁻² = H, alkyl, aryl; R³ = Me, Et; MX = NaCN, KCN, LiCl, NaCl, NaBr, NaI, LiI·H₂O, Na₂CO₃·H₂O, Na₃PO₄·12H₂O, Me₄NOAc; solvent: DMSO, DMF, DMA, HMPT

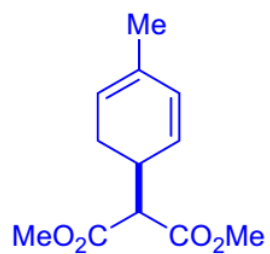
The general features of this reaction :

- Dipolar aprotic solvents :DMSO, DMF, DMA, HMPA;
- Methyl esters are dealkoxycarbonylated faster than ethyl esters;
- vinylogous β -keto esters are also dealkoxycarbonylated in high yield.



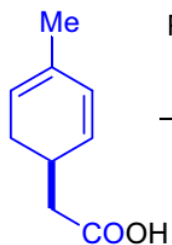
EWG = CO_2 -alkyl, CO_2 -aryl, CN, CO-alkyl, SO_2 -alkyl, SO_2 -aryl; R^{1-2} = H, alkyl, aryl; R^3 = Me, Et; MX = NaCN, KCN, LiCl, NaCl, NaBr, NaI, $\text{LiI}\cdot\text{H}_2\text{O}$, $\text{Na}_2\text{CO}_3\cdot\text{H}_2\text{O}$, $\text{Na}_3\text{PO}_4\cdot 12\text{H}_2\text{O}$, Me_4NOAc ; solvent: DMSO, DMF, DMA, HMPT





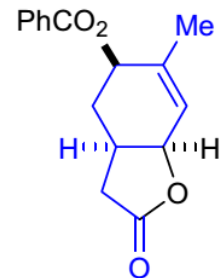
1. NaCN (5 equiv)
H₂O (5 equiv)
DMSO, 60 °C; 48h

2. KOH (3 equiv)
MeOH:H₂O (5:1)
r.t., 4h;
76% for 2 steps

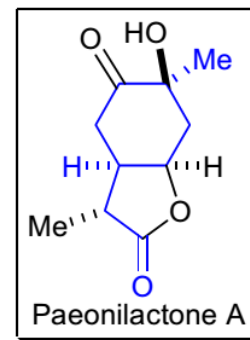


Pd(OAc)₂ (7 mol%)
benzoquinone
(2.2 equiv)

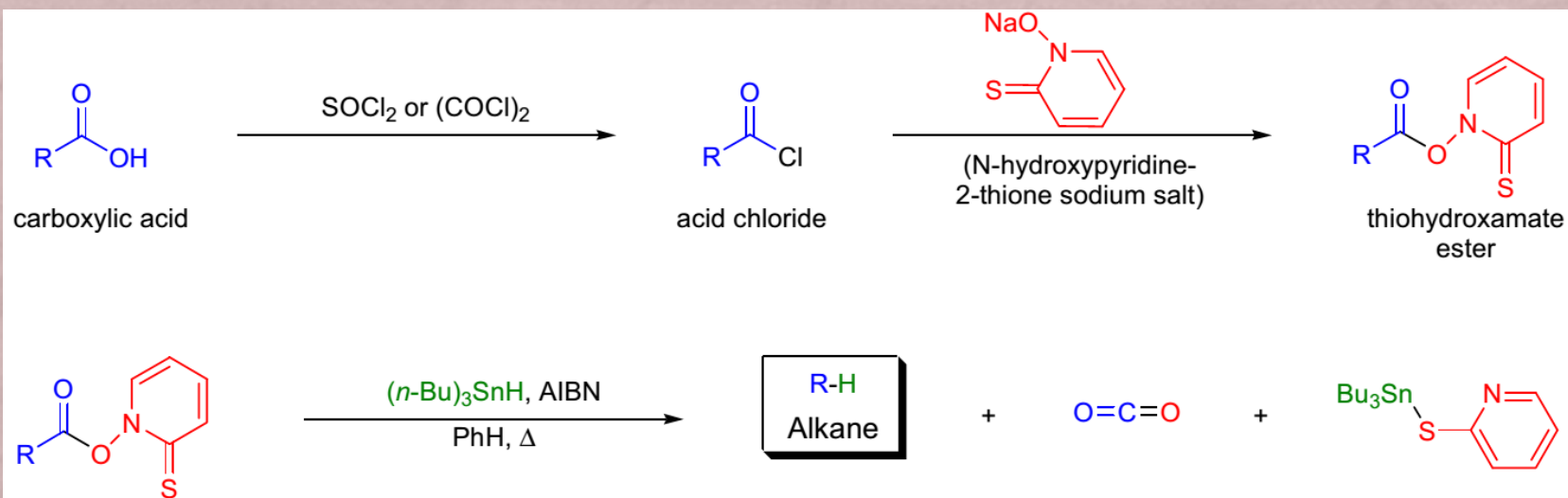
PhCOOH (8 equiv)
acetone, r.t. 40h
70%



steps

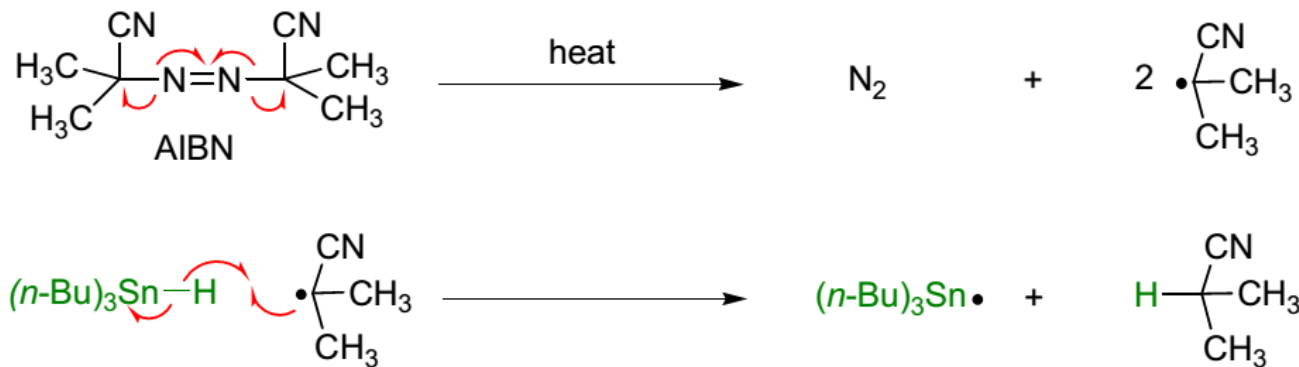


Barton decarboxylation reaction

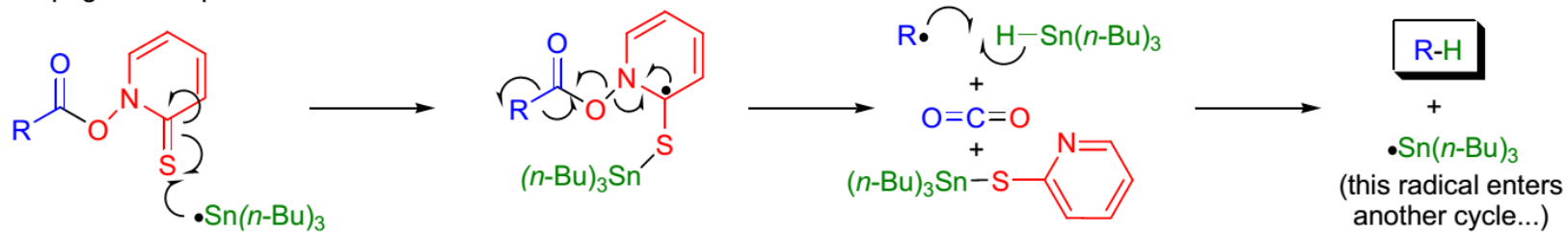


Mechanism:

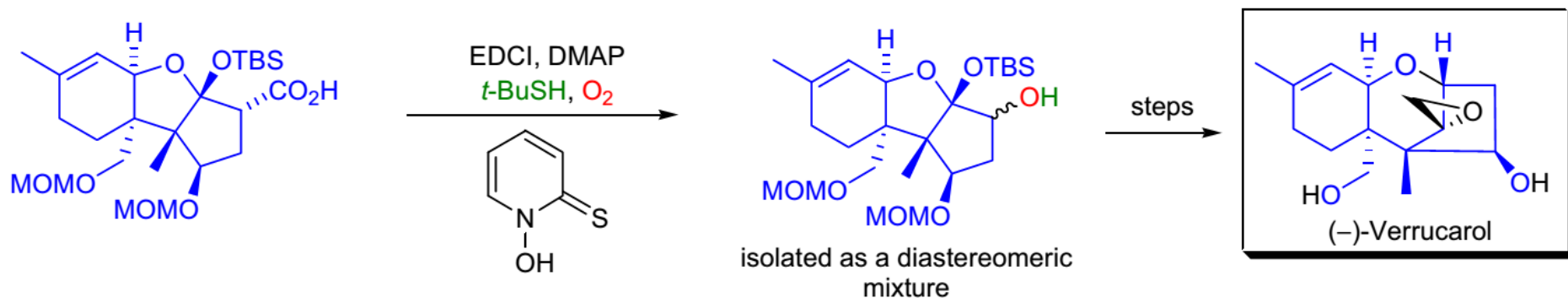
Initiation step:



Propagation step:



1. The initially formed thiohydroxamic ester was decarboxylated to leave a methylene radical on the cyclopentyl ring
2. Trapped by molecular oxygen.
3. Reductive work-up in the presence of t-BuSH finally provided the hydroxylated product.



1. The bis-thiohydroxamic ester was irradiated in the presence of citraconic anhydride
2. the resulting product was stirred for two days at room temperature to ensure complete elimination.

