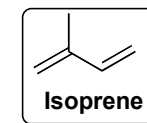
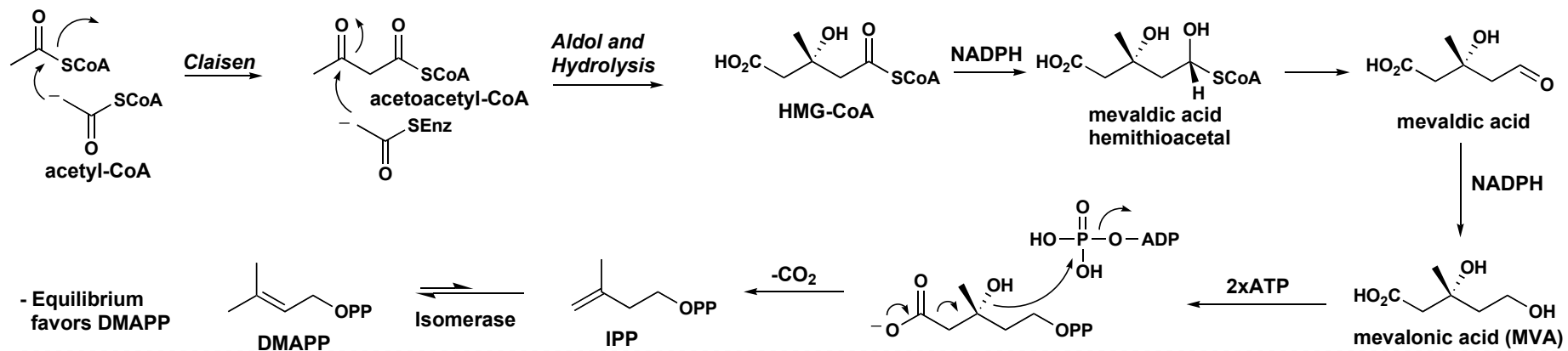


I. An Introduction to Terpenes

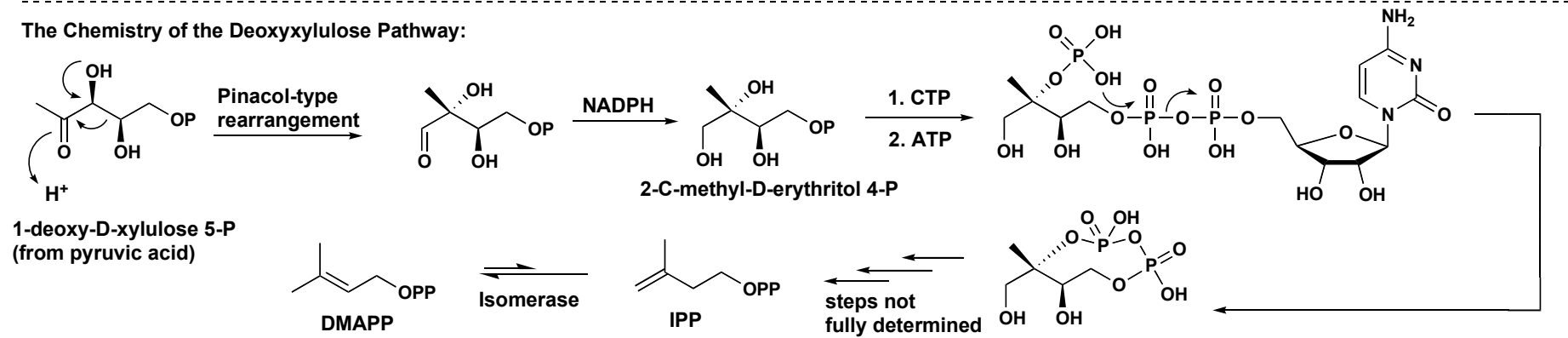
- Terpenes are an enormous class of natural products spanning well over 30,000 members
- They have been used throughout history for a broad variety of purposes including perfume, medicine, and flavoring
- Recognized early on as being composed of isoprene fragments
- Isopentyl diphosphate (IPP) and dimethyl allyl diphosphate (DMAPP) later found to be the actual building blocks
- There are 2 biosynthetic pathways for the production of IPP and DMAPP, the mevalonate pathway and the more recently discovered deoxyxylulose pathway



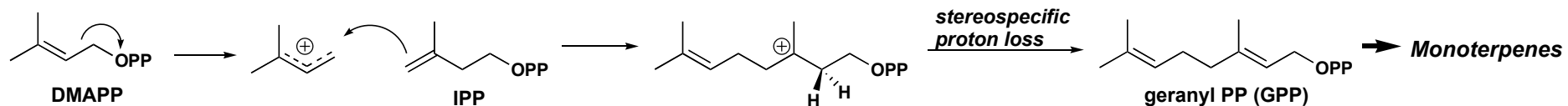
The Chemistry of the Mevalonate Pathway:



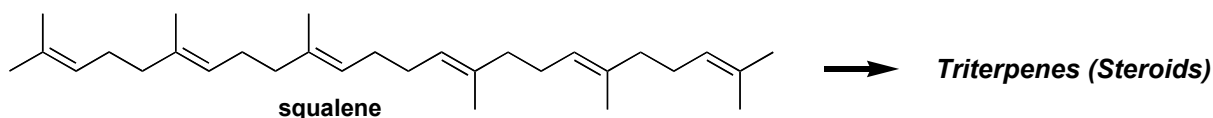
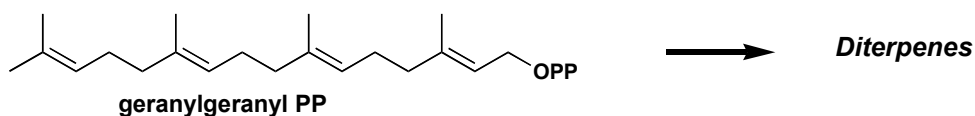
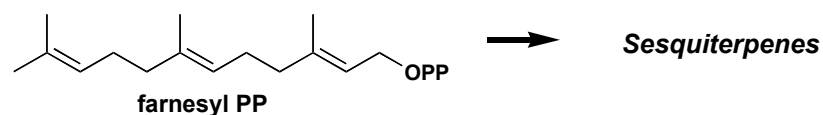
The Chemistry of the Deoxyxylulose Pathway:



- All terpenes are formed through the reactions of IPP and DMAPP:

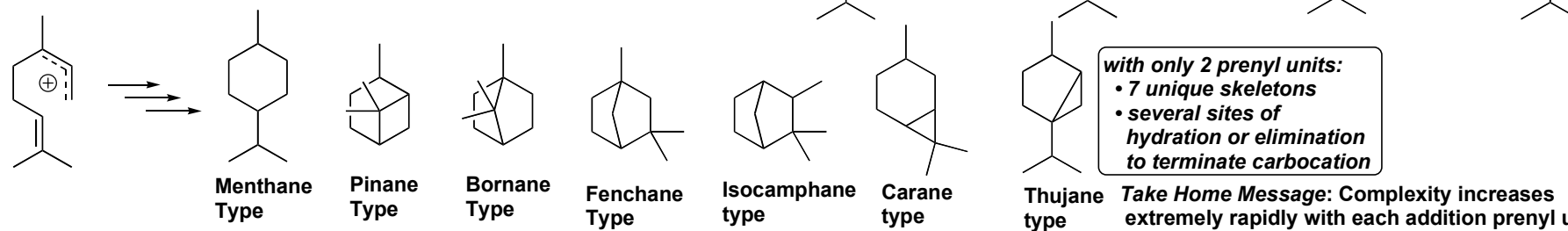


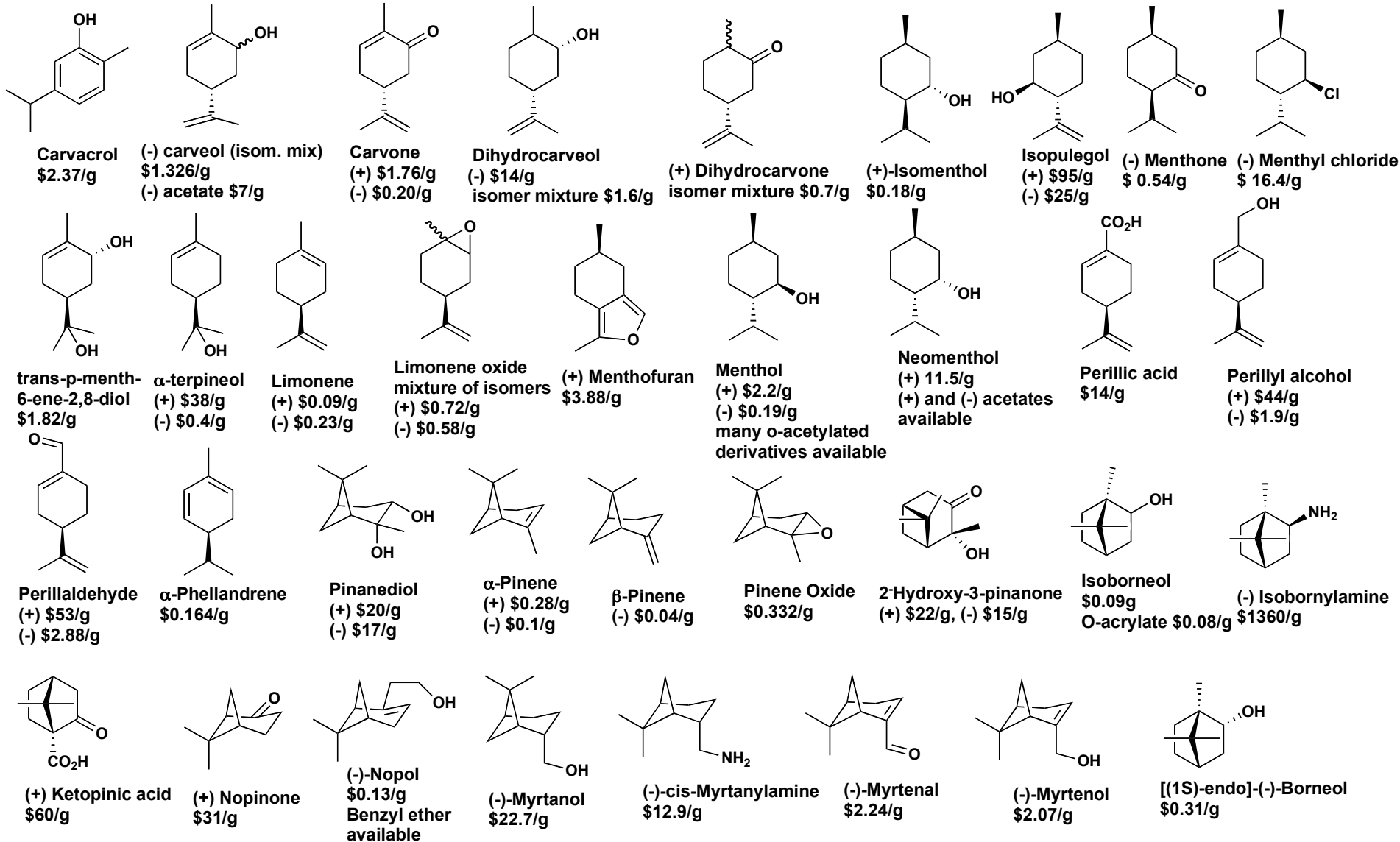
- repeat several times:



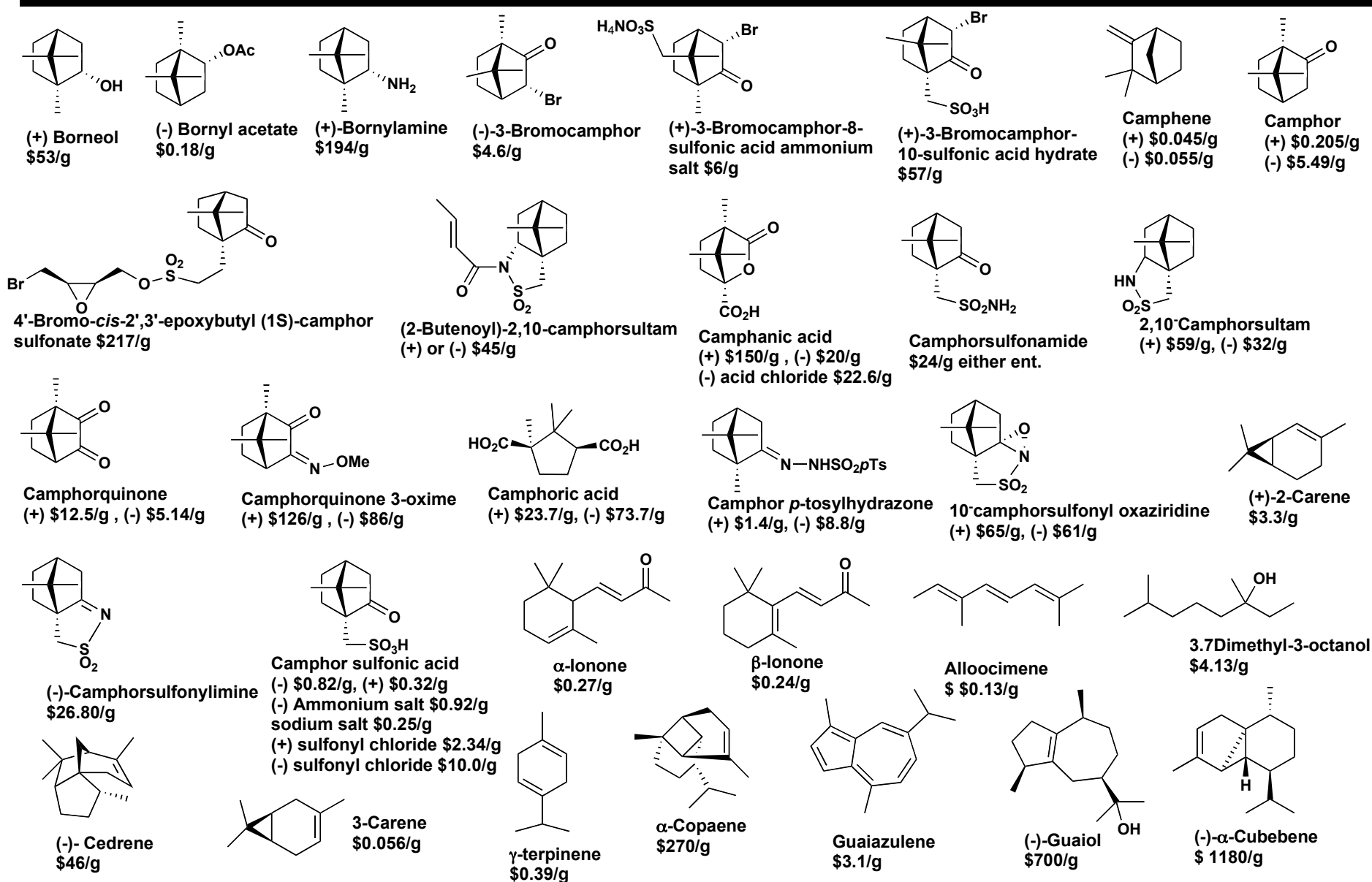
Hemiterpenes (C ₅)
Monoterpenes (C ₁₀)
Sesquiterpenes (C ₁₅)
Diterpenes (C ₂₀)
Sesterterpenes (C ₂₅)
Triterpenes (C ₃₀)
Tetraterpenes (C ₄₀)

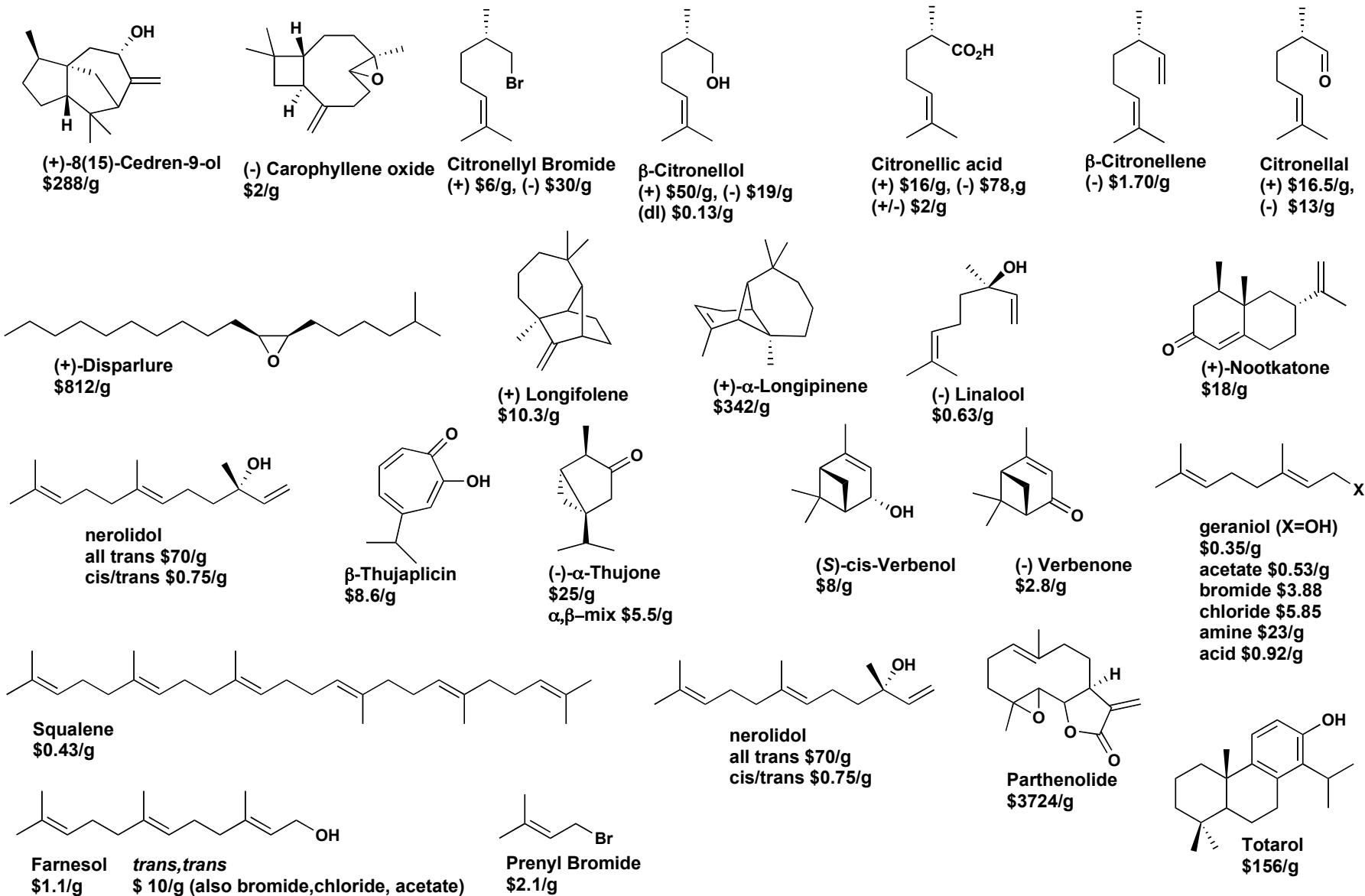
- The interesting Chemistry involves the fate of the open-chain terpenes. A seemingly endless number of (enzyme-mediated) carbocation cyclizations leads to many different carbocyclic skeletons, which are often further oxidized and rearranged.

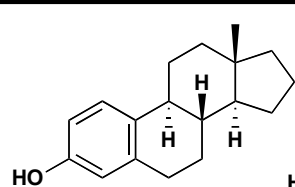


II. Commercially available Terpene Building Blocks*

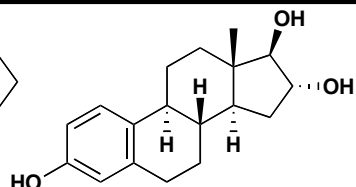
*Aldrich Prices (some prices are significantly lower from other suppliers)



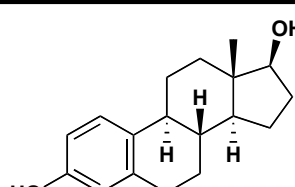




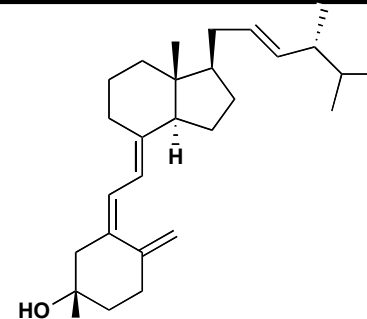
Estrone
\$14.2/g



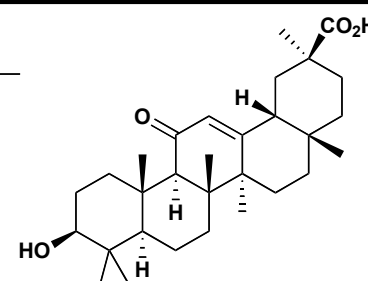
Estriol
\$72/g



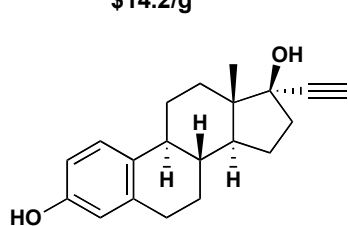
Estradiol
\$24.6/g



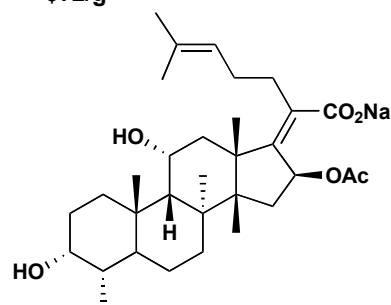
Ergocalciferol (D2)
\$15.7/g



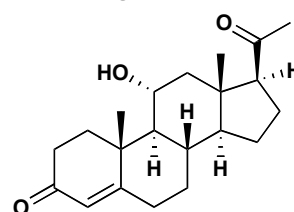
Glycyrrhetic acid
\$5.4/g



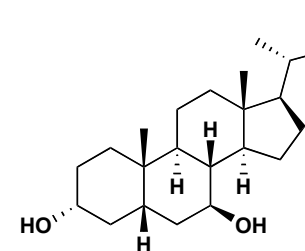
17α-Ethynylestradiol
\$28.6/g



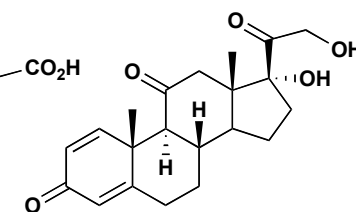
Fusidic acid
\$108/g



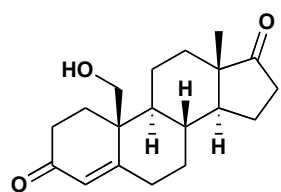
11α-Hydroxyprogesterone
\$8.3/g



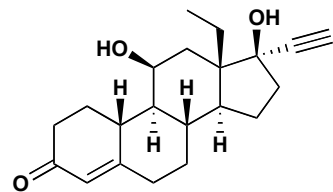
Ursodeoxycholic acid
\$12.3/g



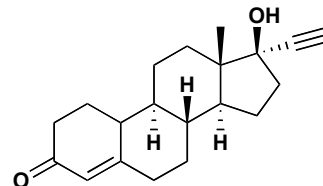
Prednisone
\$13.4/g
several related
derivates available



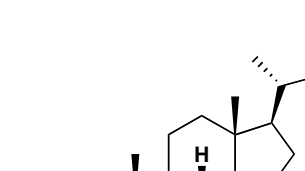
19-Hydroxy-4-androstene-3,17-dione
\$916/g



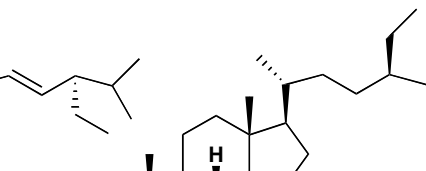
Norgestrel
\$290/g



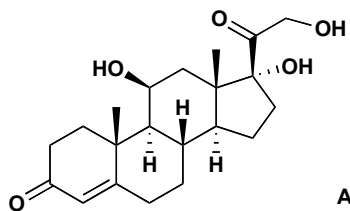
Ethisterone
\$3.4/g



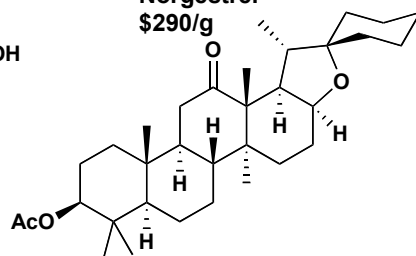
Stigmasterol
\$12.5/g



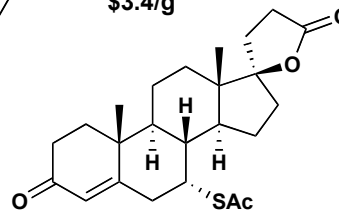
β-Sitosterol
\$0.26/g



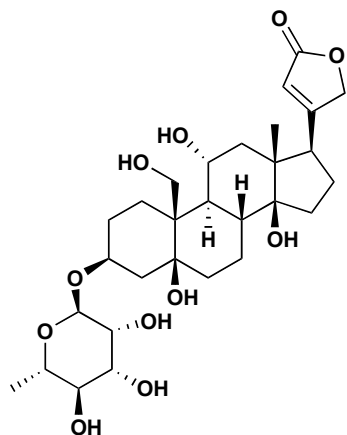
Hydrocortisone
\$10/g



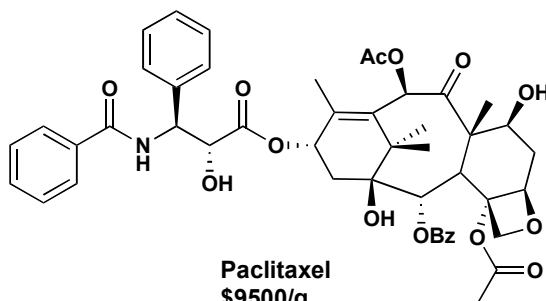
Hecogenin Acetate
\$11.2/g



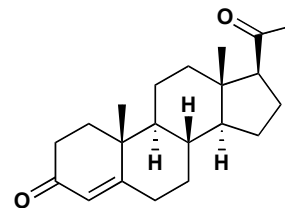
Spirolactone
\$26/g



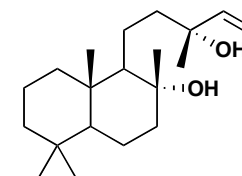
(-)-Oubain Hydrate
\$75/g



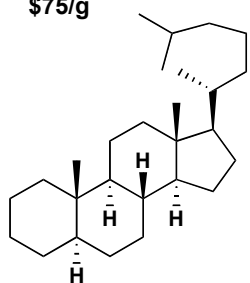
Paclitaxel
\$9500/g



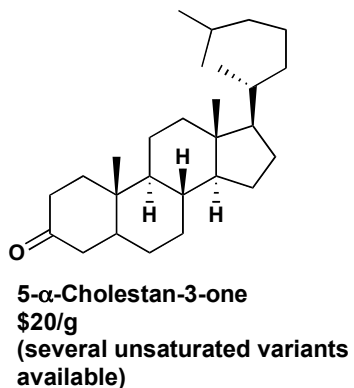
Progesterone
\$2.24/g



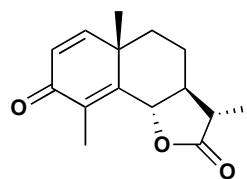
Sclareol
\$32/g



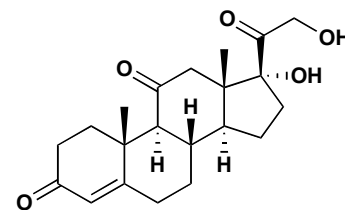
5-α-Cholestan-3-one
\$20/g
(several unsaturated variants available)



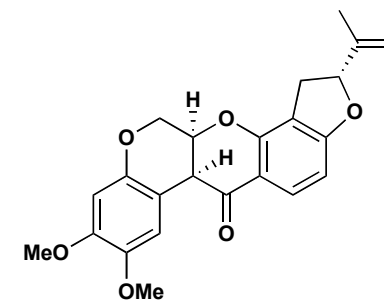
5-α-Cholestane
\$60/g



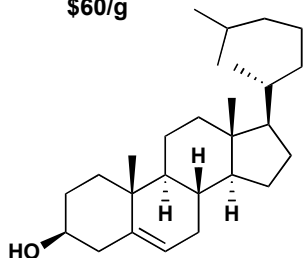
(-)-α-Santonin
\$2.64/g



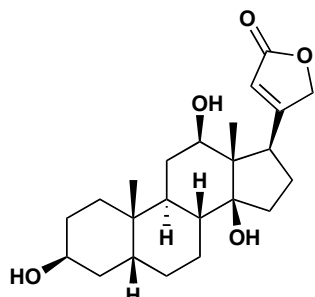
Cortisone
\$22/g (several derivatives available)



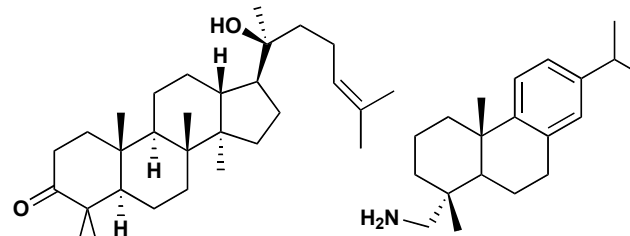
Rotenone
\$4.16/g



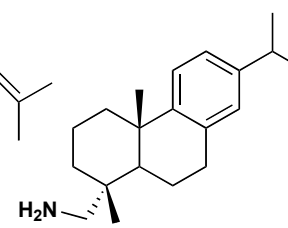
Cholesterol
\$0.30/g
(many derivatives available)



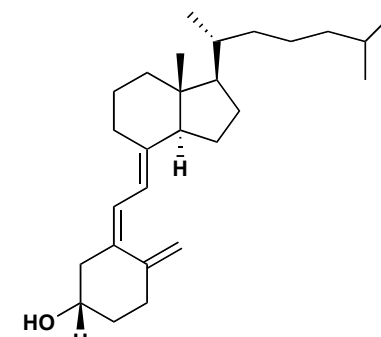
Digoxigenin
\$586/g
(several derivatives available)



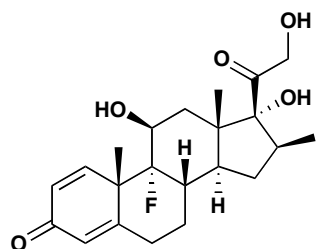
Dipterocarpol
\$138/g



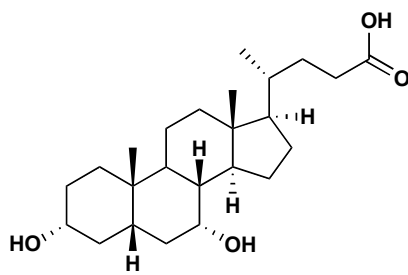
Dehydroabietylamine
(+) \$0.27/g



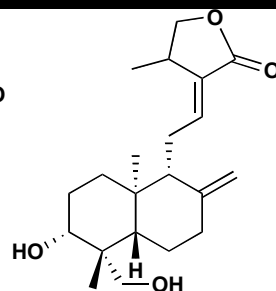
Cholecalciferol
\$19.5/g



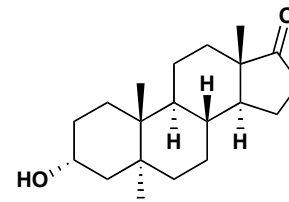
Betamethasone
\$ 696/g



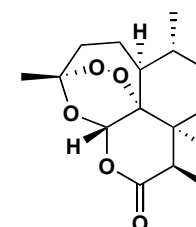
Chenodeoxycholic acid
\$7.94/g



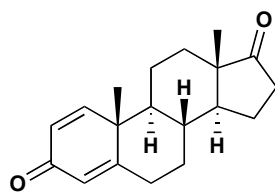
Andrographolide
\$175.4/g



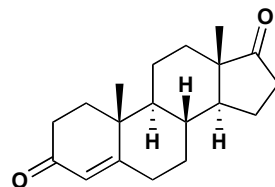
Androsterone
\$45/g



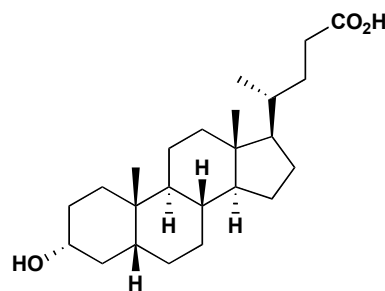
Artemisinin
\$416/g



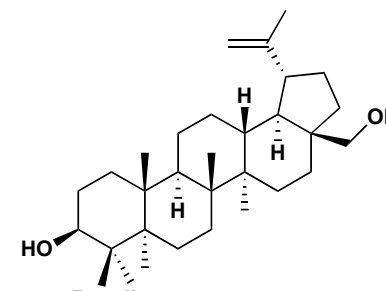
1,4-androstadiene-3,17-dione
\$70/g



4-Androstene-3,17-dione
\$7.44/g



Lithocholic acid
\$1.24/g

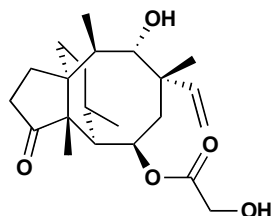


Betulin
\$58.6/g

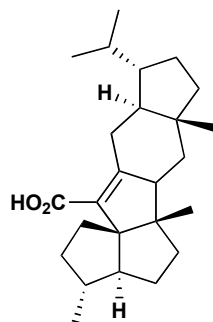
III. Synthesis Discussed**Disclaimer:**

Natural Products arising from mixed biosynthetic pathways (terpene/alkaloid, terpene/polyketide) were not considered.

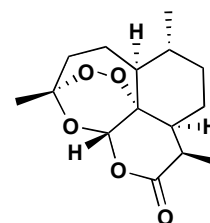
Molecules were chosen that are not typically covered in the synthetic organic chemistry classes at TSRI. The interested reader can find many more classic syntheses in the following locations.*



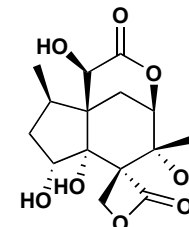
Pleuromutilin
Boeckman



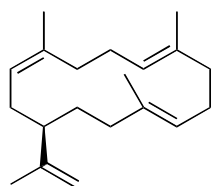
Retigeranic acid
Corey



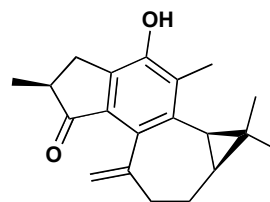
Qinghaosu
Hofheinz



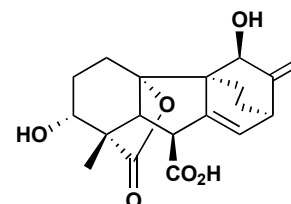
Anisatin
Kende



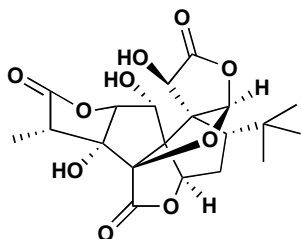
Cembrene
wender



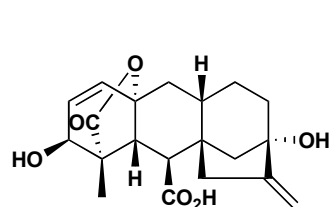
Jatropholones
A.B. Smith



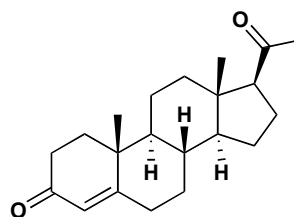
Antheridium-Inducing Factor (A_{An})
Corey

Some Classics not discussed:

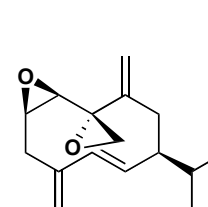
Ginkgolide B
Corey



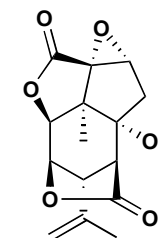
Gibberellic Acid
Corey



Progesterone
Johnson

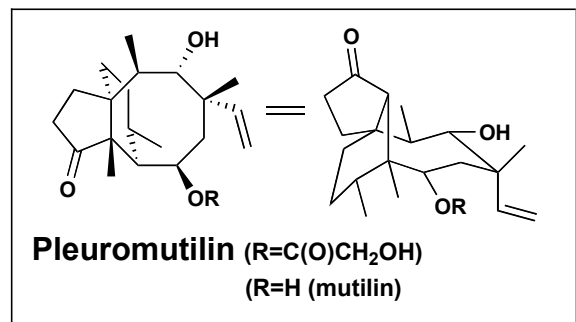


Periplanone
Still

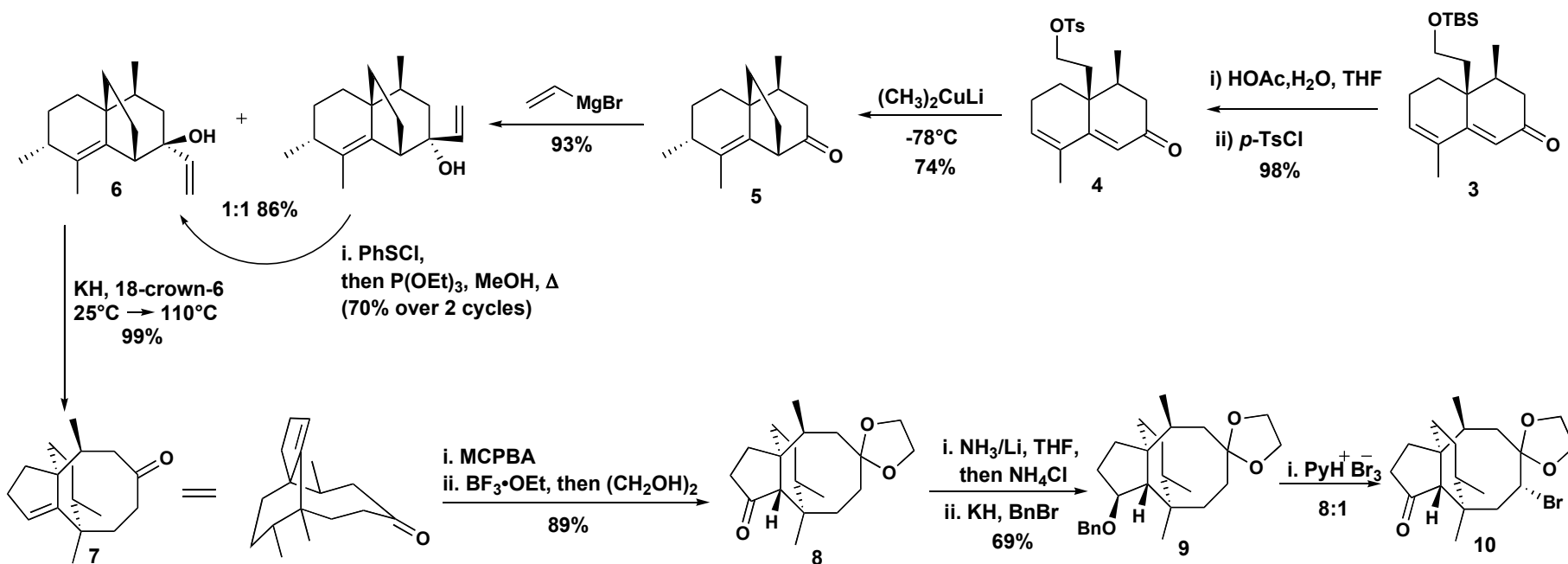
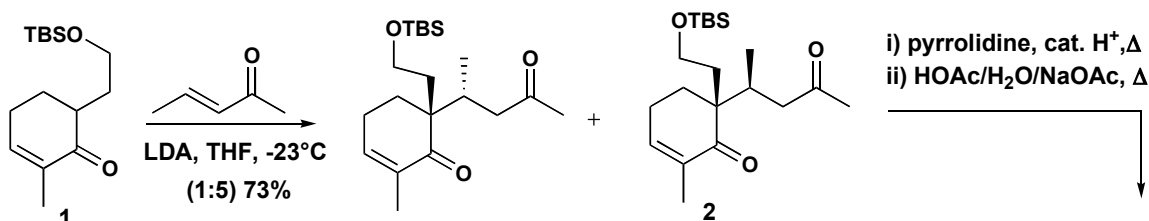


Picrotoxinin
Corey

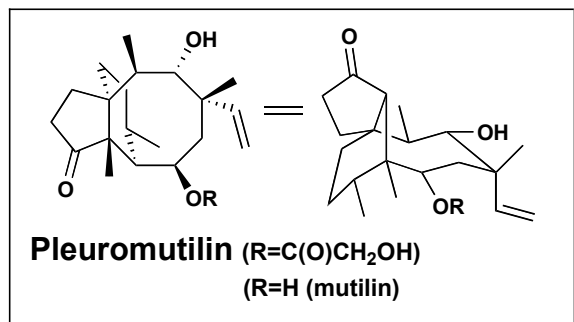
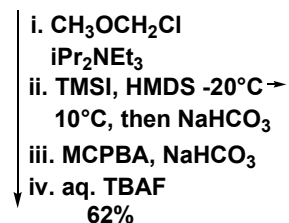
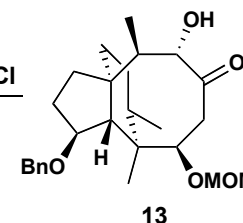
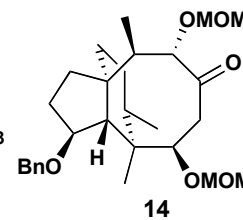
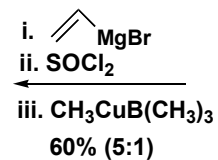
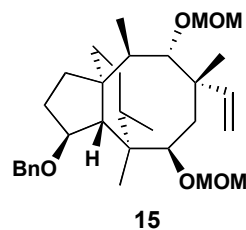
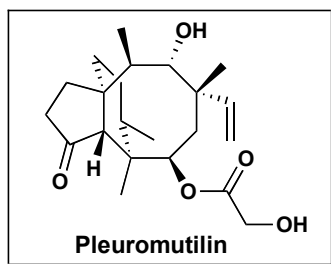
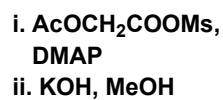
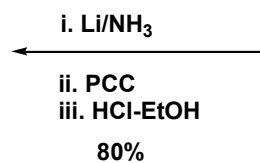
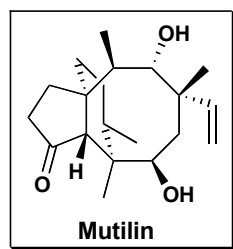
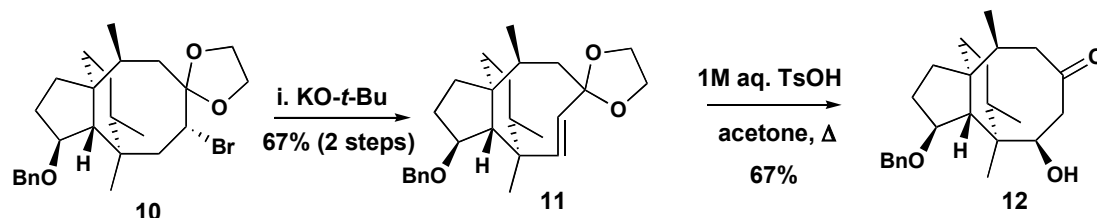
* Nicolaou, K.C.; Sorensen, E.J. *Classics in Total Synthesis*. VCH, Weinheim, **1996**. Nicolaou, K.C.; Snider, S.A. *Classics in Total Synthesis II*. VCH, Weinheim, **2003**.
Corey, E.J.; Chen, X. *The Logic of Chemical Synthesis*. Wiley, **1995**.
Ho, T.L. *Enantioselective Synthesis: Natural Products from Chiral Terpenes*. Wiley, **1992**.

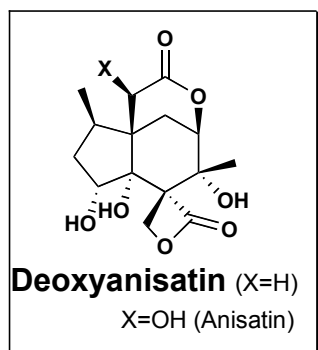
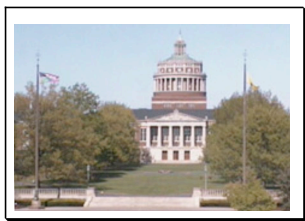
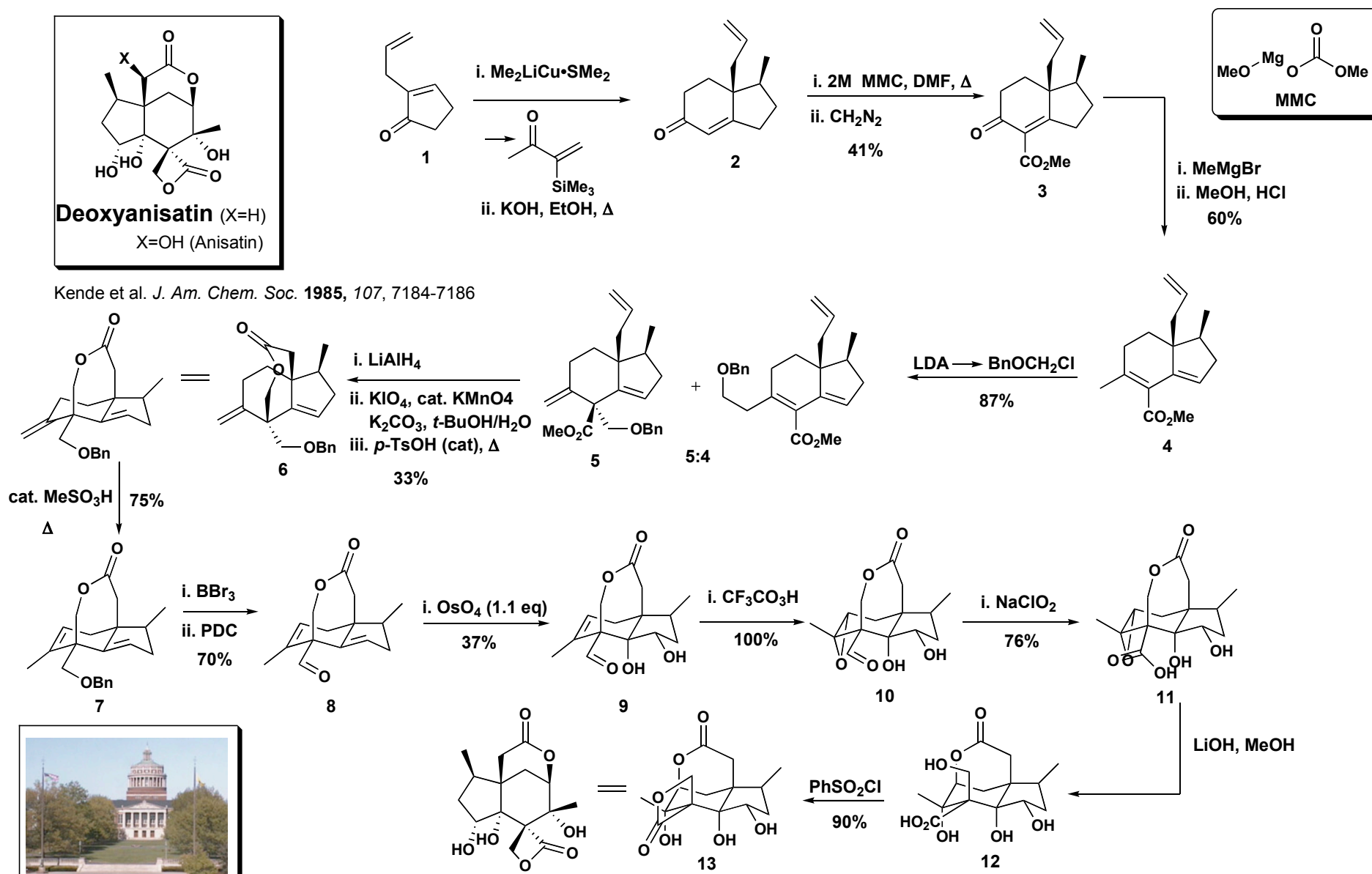


Boeckman et al. *J. Am. Chem. Soc.* **1989**, *111*, 8284-8286

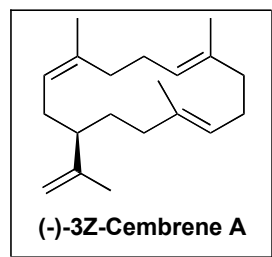


" The relative facility of the rearrangement in the present case may be due in part to the absence of side reactions such as retro ene processes owing to the presence of the allyl unit in a rigid framework"

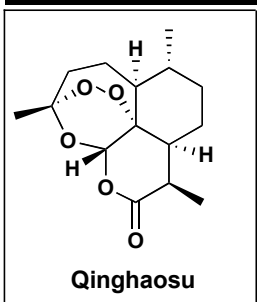
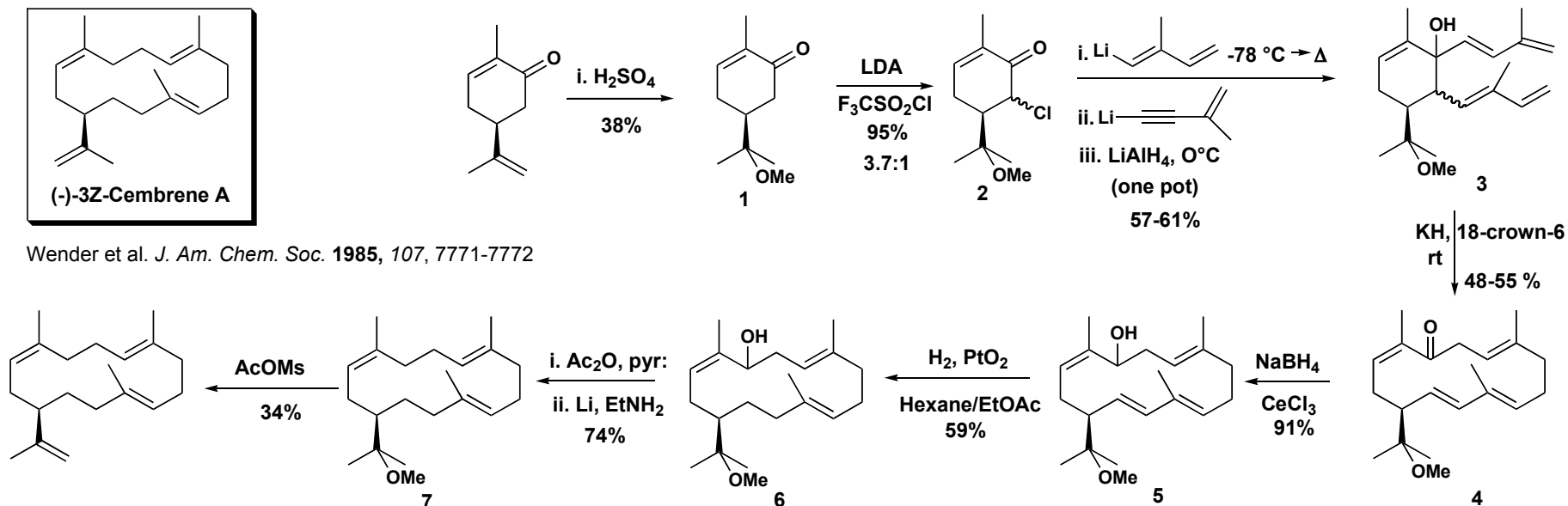
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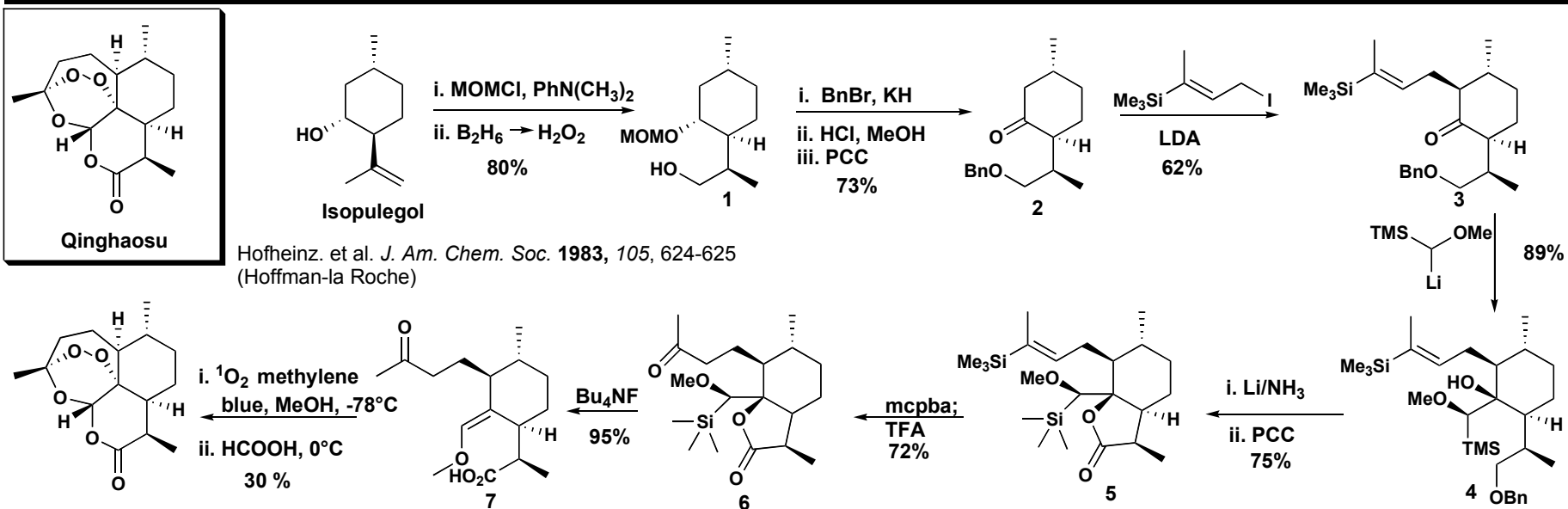
Classic Terpene Syntheses

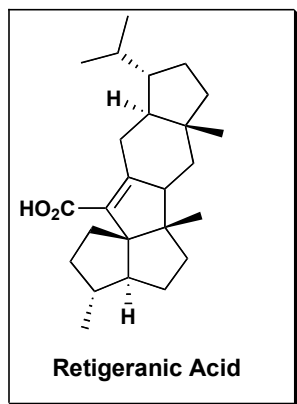


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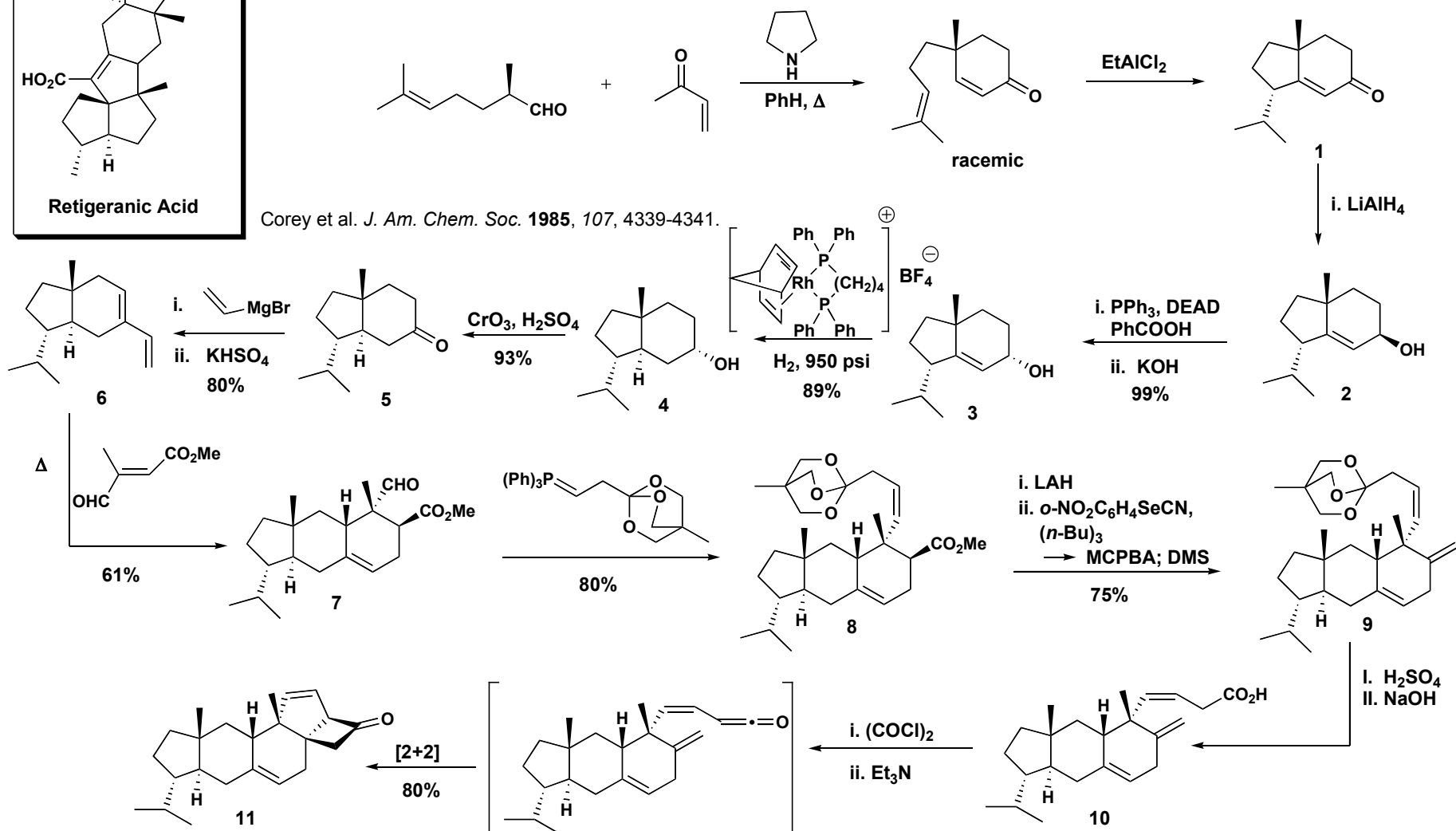


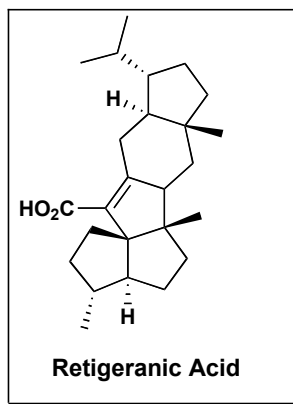
Hofheinz. et al. *J. Am. Chem. Soc.* **1983**, *105*, 624-625
(Hoffman-la Roche)



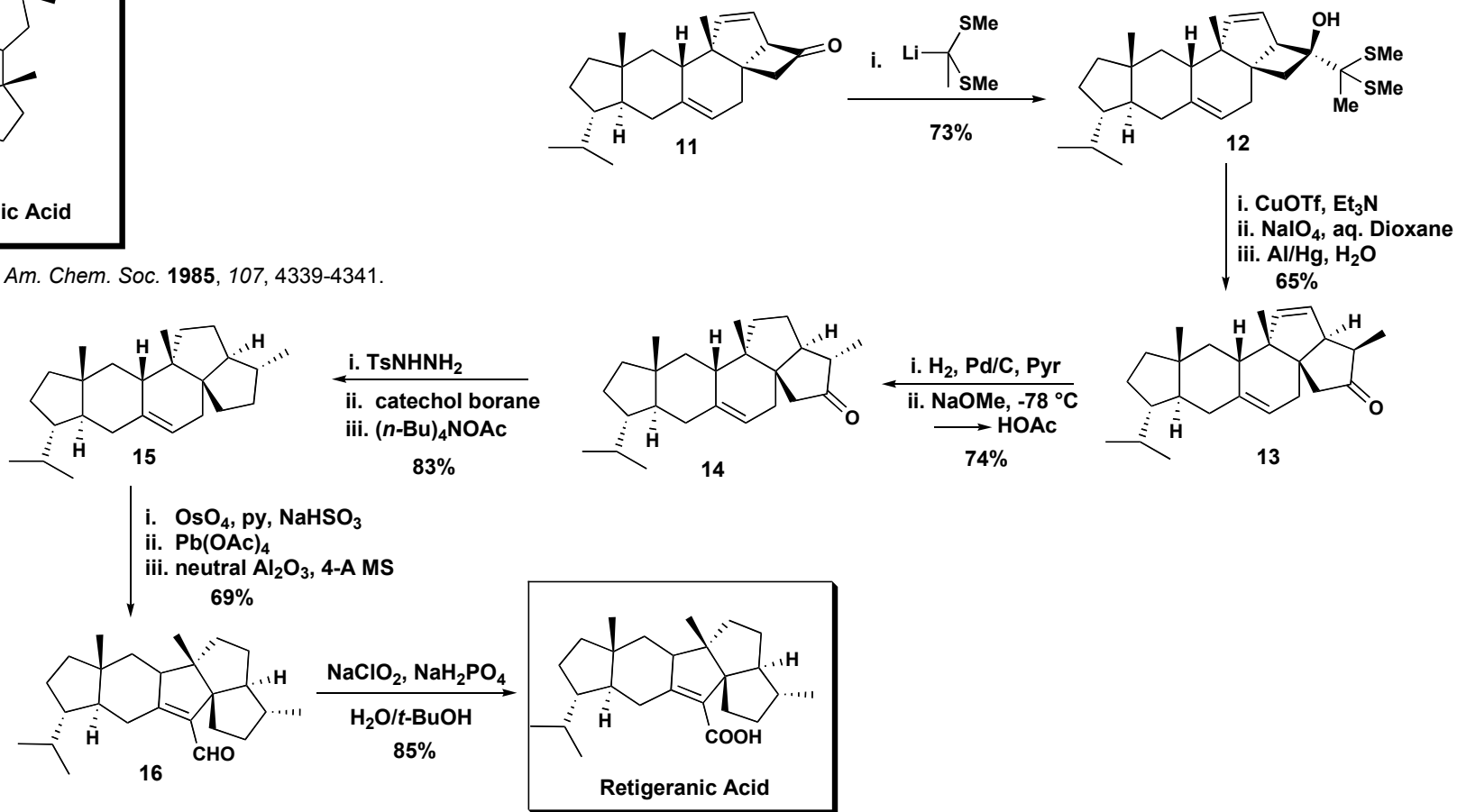


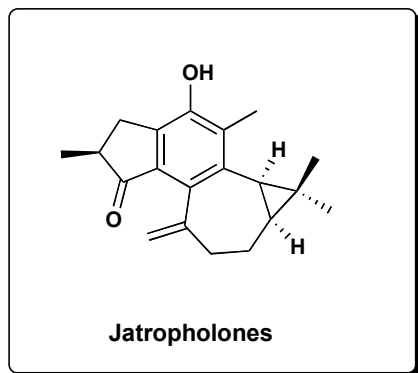
Corey et al. *J. Am. Chem. Soc.* **1985**, *107*, 4339-4341.



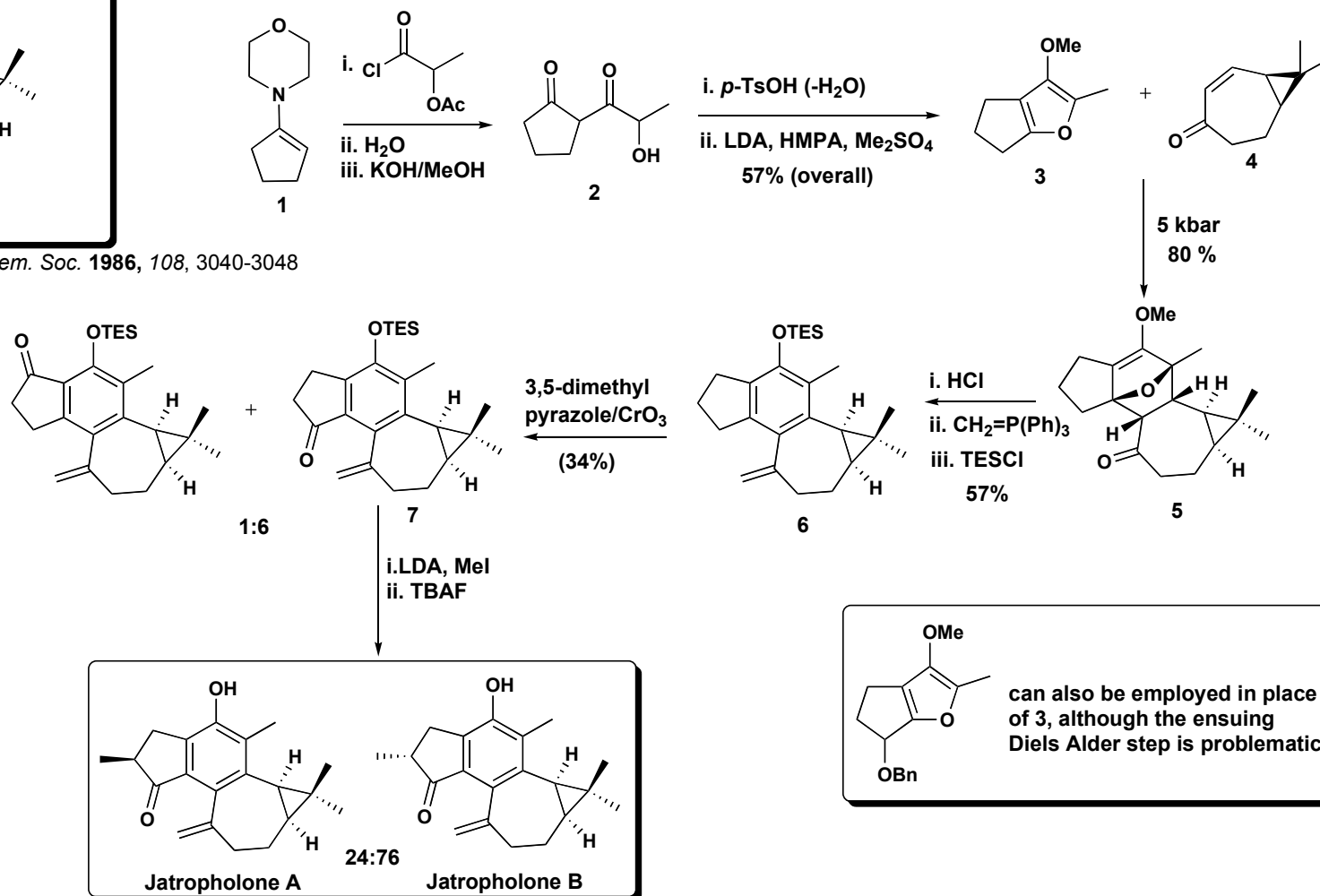


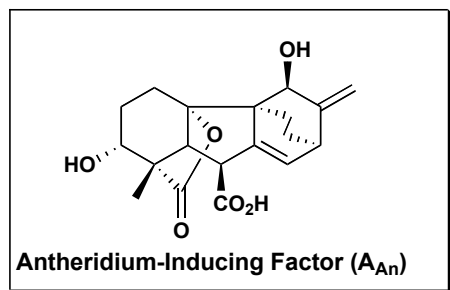
Corey et al. *J. Am. Chem. Soc.* 1985, 107, 4339-4341.



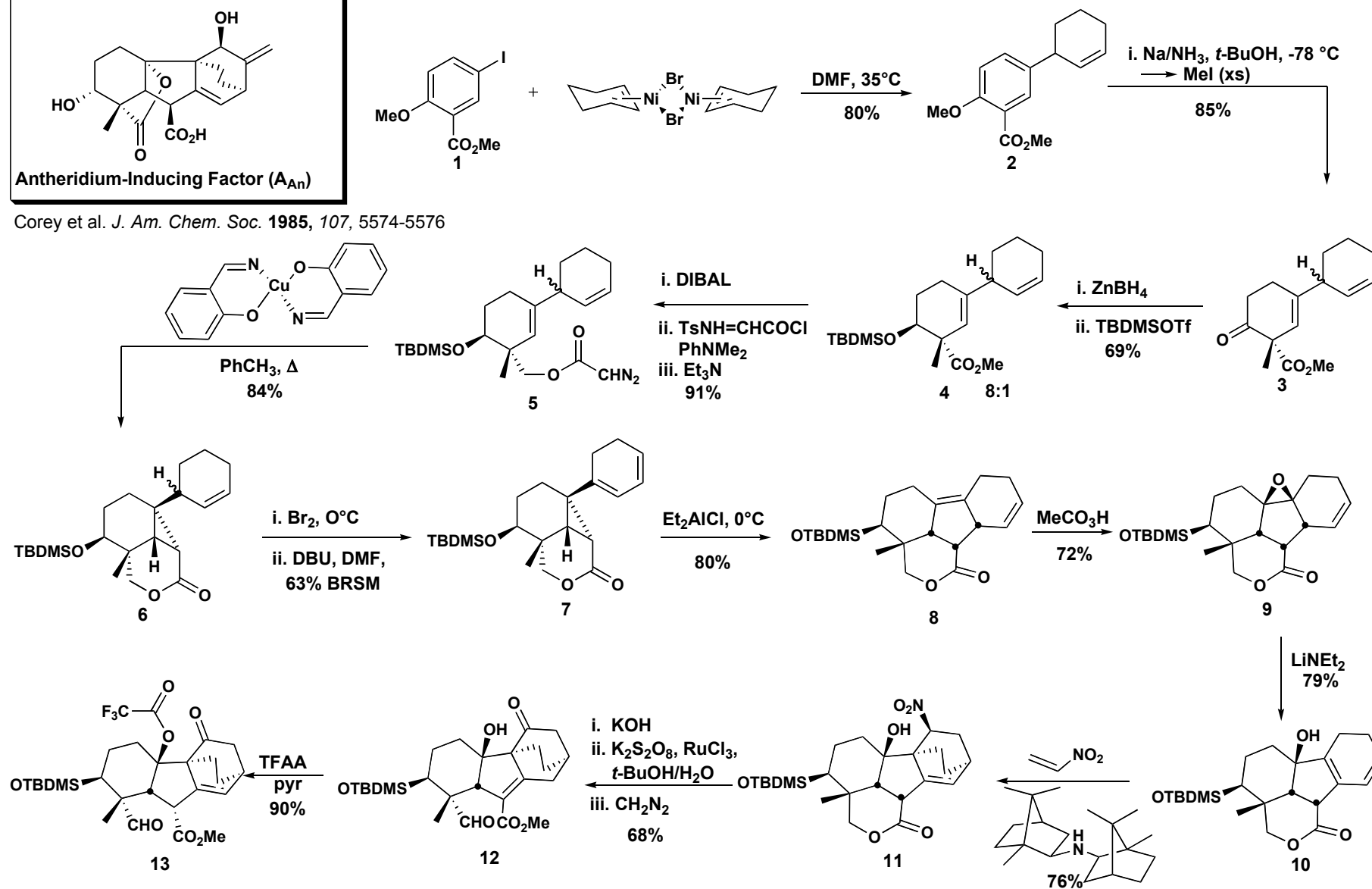


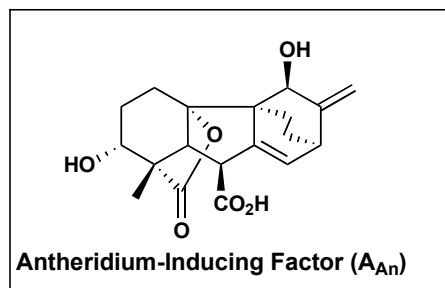
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