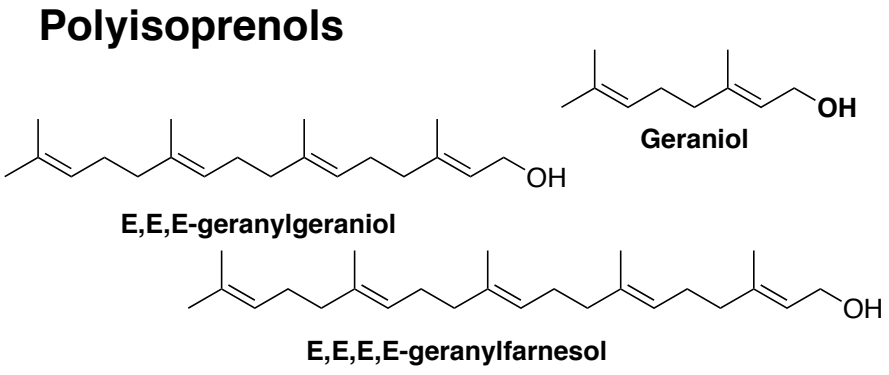
Polyisoprenols



Isolated from bacteria, plants and animals. Short chain polyisoprenols are far more prevalent in nature than their longer counterparts

Uses

Various polyisoprenols are used in perfume and pharmacology.

Although synthetic routes have been shown to produce decent yields, metabolic engineering is the preferred route to these compounds.

- **Antioxidant activities**
- **Lowers the propensity for humans to develop prostate cancers**

Ji, M., H. Choi, et al. (2001). Angew. **40**(19): 3627-3629.

- **Precursers of pharmaceutials for stomach ulcers and vitamins**

Muramatsu, M., C. Ohto, et al. (2008). Journal of Bioscience and Bioengineering **106**(3): 263-267.

Geraniol (150 mg/kg) caused a 26% reduction in tumor size

Carnesecchi, S., R. Bras-GonÁalves, et al. (2004). Cancer Letters **215**(1): 53-59.

- **phytoalexins**
- **pet detterents and toxins**
- **pollinator attractants**

After 24-h treatment apoptosis and caspase activation could be prevented

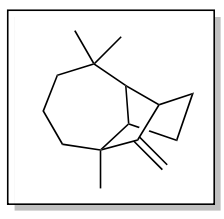
Farnesol cyclizes to produce a number of sesquiterpenes: thujopsene, longifolene, cedrol, germacrene, globulol

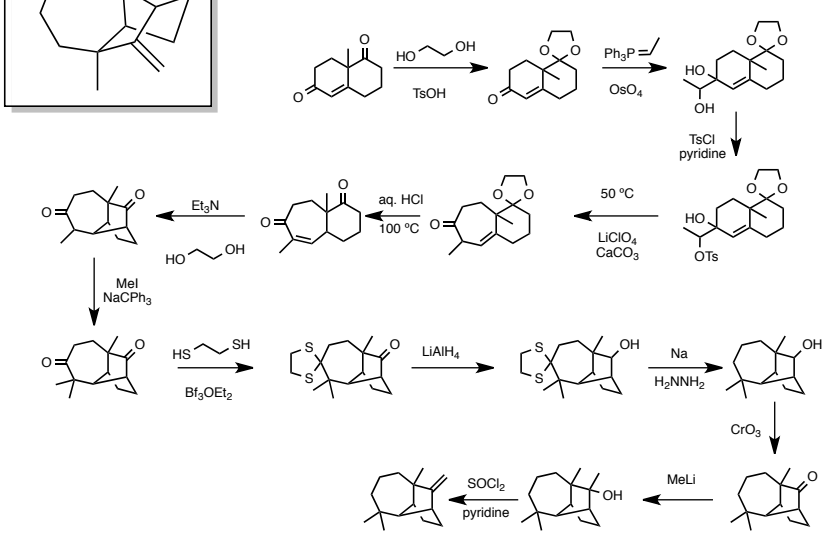
Benford HL, Frith JC, Auriola S, Mönkkönen J and Rogers MJ: Mol Pharmacol *56*: 131-140, 1999

Yu, J. S., T. S. Kleckley, et al. (2005). Organic Letters **7**(22): 4803-4806.

August 16th, 2010

d,l-Longifolene Synthesis, Corey et al.

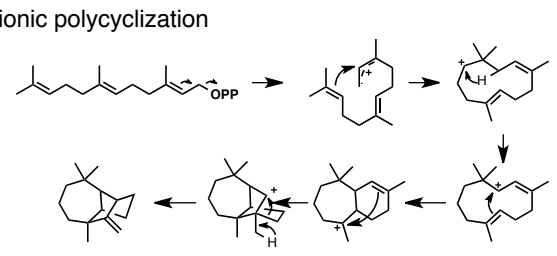




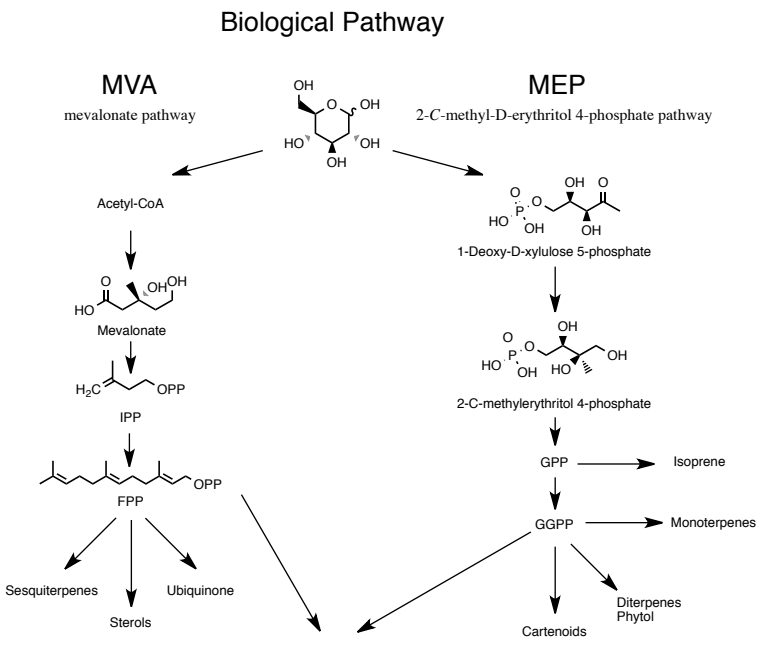
Corey, E. J., M. Ohno, et al. (1961). "TOTAL SYNTHESIS OF d,l-LONGIFOLENE." J. Am. Chem. Soc. **83**(5): 1251-1253.

Nature's Pathway

Cationic polycyclization



Industrial Production and Expenses



Polyisoprenoid Alcohols

Industrially, most polyisoprenols are isolated from metabolic engineering. Cells have upregulated production of a certain polyisoprenyl diphosphate and are then converted to the target alcohol.

Microorganisms, preferably a yeast cell culture, are genetically modified to increase production of necessary pyrophosphates and decrease production of other products.

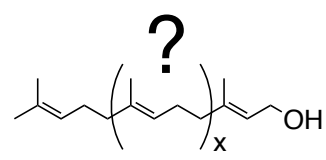
Isolation can be done through a number of methods: chromatography, extraction, solvent extraction, crystallization, etc.

Cost of production are high for longer chain because of the low occurance in nature and the difficulties of generating long chains with high stereoselectivity.

Overproduction can be deleterious!

Pichersky et al. April, 2010-770416

Synthetic Methods

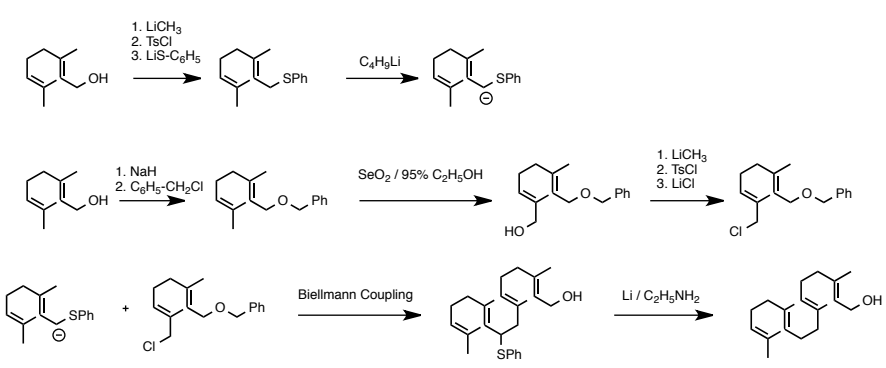


Solanesol x = 7

6000g of dried potatoe leaves yields 90g (1.5%) of solanesol

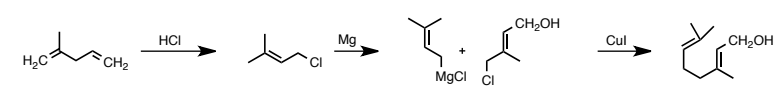
Previous Syntheses

Altman synthesis



L. J. Altman, et. al., J. Am. Chem. Soc., 1972, **94,** 3257

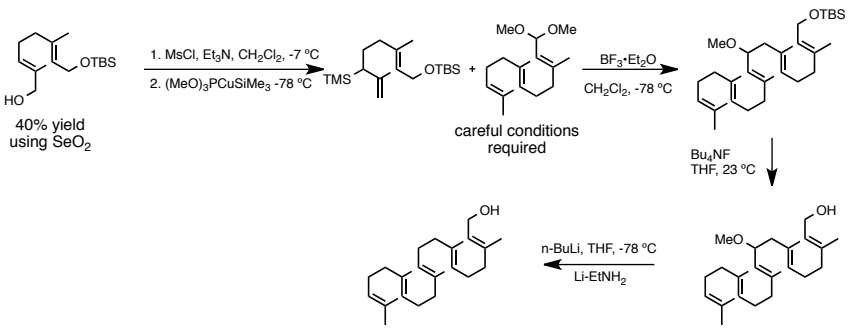
trans-geranylgeraniol



Derguini-Boumechal, F., R. Lorne, et al. (1977). Tet. Lett. **18**(13): 1181-1184.

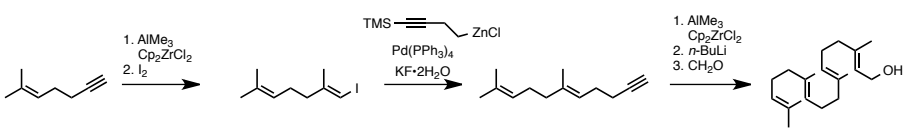
Kwart, H.; R. K. Miller (1954). J. Am. Chem. Soc **76**(21): 5403-5405.

Corey Synthesis

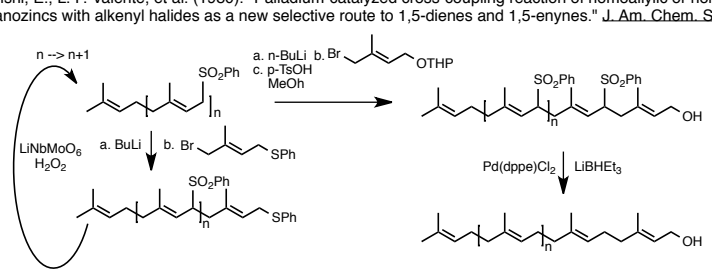


Radetich, B. and E. J. Corey (2002). "A General Stereocontrolled, Convergent Synthesis of Oligoprenols That Parallels the Biosynthetic Pathway." J. Am. Chem. Soc. **124**(11): 2430-2431.

Iterative Methods

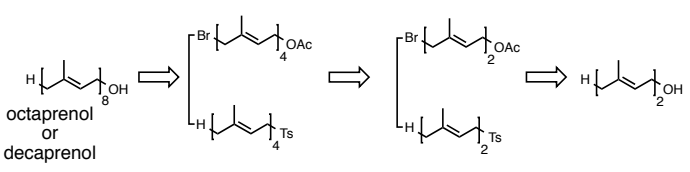


Negishi, E., L. F. Valente, et al. (1980). "Palladium-catalyzed cross-coupling reaction of homoallylic or homopropargylic organozincs with alkenyl halides as a new selective route to 1,5-dienes and 1,5-enynes." J. Am. Chem. Soc. **102**(9): 3298-3299.



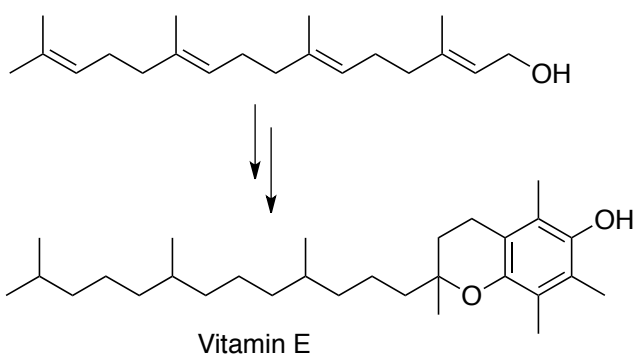
Kuk, J., B. S. Kim, et al. (2008). "General Preparation and Controlled Cyclization of Acyclic Terpenoids." J. Org. Chem. **73**(5): 1991-1994.

Ji, M., H. Choi, et al. (2001). "A Highly Efficient Chain-Extension Process in the Systematic Syntheses of Carotenoid Natural Products." *Angew. Chem., Int. Ed* **40**(19): 3627-3629.



Yu, X. J., H. Zhang, et al. (2008). "An Improved Convergent Strategy for the Synthesis of Oligoprenols." Helvetica Chimica Acta **91**(10): 1967-1974.

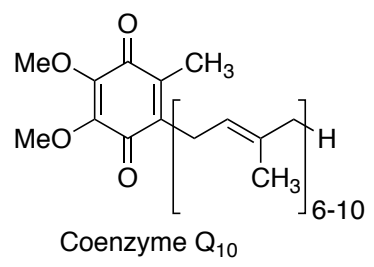
Ultimate Utility



Vitamin E

Hyatt, J. A., G. S. Kottas, et al. (2002). Organic Process Research & Development **6**(6): 782-787.

solanesol



Coenzyme Q_{10}