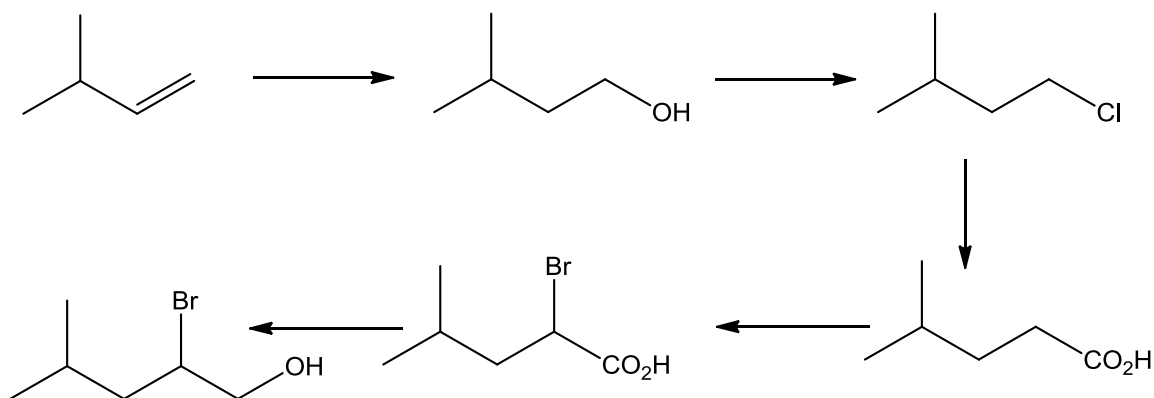


Problem Set 9 – Reactions of carboxylic acid and their derivatives

- Propose a sequence of reactions to effect the following conversions:
 - 3,5-dinitrobenzoyl chloride from benzene
 - phenylethanoic acid from toluene
 - butanoic acid from ethanol
 - 4-phenyl-4-heptanol from methyl benzoate
- Propose a synthesis of $\text{CH}_3^{13}\text{CH}_2\text{CO}_2\text{H}$ using $^{13}\text{CO}_2$ as source of ^{13}C .
- Tropic acid is isolated from atropine, an alkaloid found in *Atropa belladonna* (deadly nightshade). Its molecular formula is $\text{C}_9\text{H}_{10}\text{O}_3$. Tropic acid forms benzoic acid on oxidation with hot KMnO_4 . Tropic acid also reacts with HBr to form compound "A", $\text{C}_9\text{H}_9\text{O}_2\text{Br}$. Compound "A" reacts with alcoholic KOH to give atropic acid, $\text{C}_9\text{H}_8\text{O}_2$. On catalytic hydrogenation, atropic acid forms hydratropic acid, $\text{C}_9\text{H}_{10}\text{O}_2$. Hydratropic acid may be synthesized by treating the Grignard reagent formed from 1-chloro-1-phenylethane with dry ice followed by acid workup. Oxidation of tropic acid gives a dicarboxylic acid, $\text{C}_9\text{H}_8\text{O}_4$.
 - What is the structure of hydratropic acid?
 - What is the structure of atropic acid?
 - What is the structure of the dicarboxylic acid?
 - What is the structure of tropic acid?
- Give a structure of compound "X", $\text{C}_3\text{H}_5\text{ClO}_2$, consistent with the following ^1H NMR data:

$\delta = 1.73$ (3H, doublet), $\delta = 4.47$ (1H, quartet), $\delta = 11.22$ (1H, singlet).
- Identify the reagents in the following scheme:

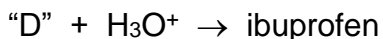
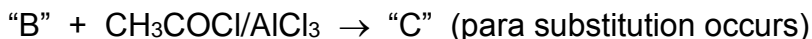
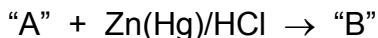


6. Write the structure(s) of the organic product(s) of the following reactions:

- propyl benzoate + i) LiAlH_4 ii) H_3O^+
- 5-hydroxypentanoic acid + Δ
- acetic anhydride + 1-propanol
- butanoyl chloride + lithium diphenylcuprate

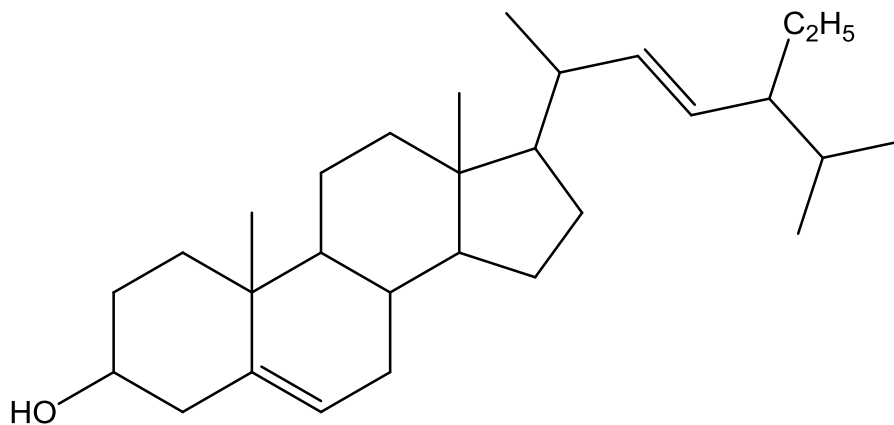
7. Compound "A", $\text{C}_6\text{H}_{13}\text{NO}$, produces a gas on heating with aqueous NaOH . When the resulting solution is acidified and extracted with ether, compound "B" is isolated. "C" is formed when "B" is heated with acidic methanol. Reduction of "C" with LiAlH_4 yields methanol and 4-methyl-1-pentanol. What are the structures of "A", "B" and "C"?

8. (S)-Ibuprofen is an antiinflammatory drug. Racemic ibuprofen can be synthesized from benzene:

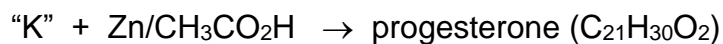
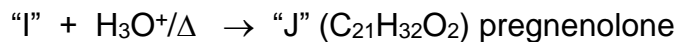
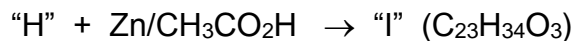
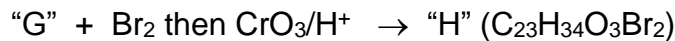
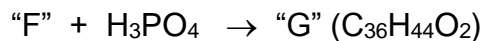
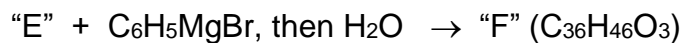
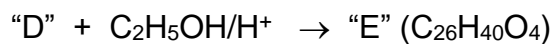
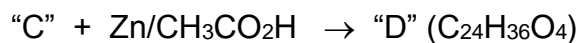
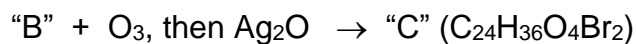
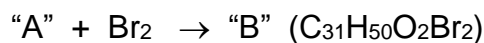


Give the structures of "A", "B", "C", "D" and ibuprofen.

9. Progesterone is a hormone, secreted by the corpus luteum. It is involved in the control of pregnancy. It can be synthesized from stigmasterol, obtained from soybean.

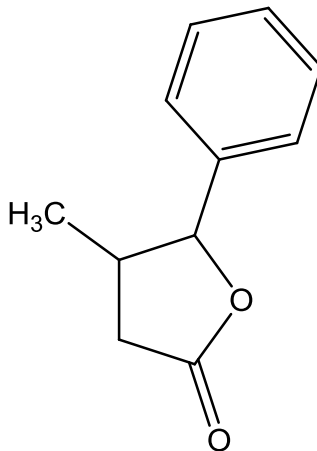


stigmasterol



What are the structures of pregnenolone and of progesterone?

10. In clinical studies with atherosclerotic patients it was found that one of the metabolites of the hyperlipidemia drug (Z)-3-methyl-4-phenyl-3-butenamide is compound "A" which has the formula $C_{11}H_{15}NO_2$. When heated with aqueous acid, the following lactone is formed along with NH_4^+ :



- What is the structure of metabolite "A"?
- Write a mechanism for its transformation into the lactone.