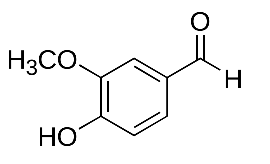
Bromination of Vanillin:
Deducing Directive Effects with Electrophilic Aromatic Substitution

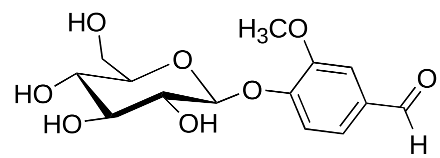
Background

In this lab you will investigate the directive effect of the substituents of vanillin, an aromatic compound that is the major flavor compound in vanilla extract. Pure vanilla extract is made from cured vanilla beans, the seedpods of a tropical orchid native to Central America. Vanillin and other minor flavor compounds are extracted from the cured beans with alcohol to produce vanilla extract. [This is a solid-liquid extraction, rather than the liquid-liquid extractions we perform in class.] Before curing, the beans have no aroma because vanillin is tied up in an odorless glycoside form.

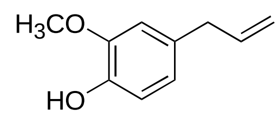
Extracts not labeled as "pure" vanilla extract are made synthetically in a number of ways, typically from wood pulp byproducts, euginol or guaiacol. Synthetic vanilla extract lacks the complexity of natural vanilla because it contains only vanillin and none of the many minor flavor molecules found in vanilla beans.



vanillin

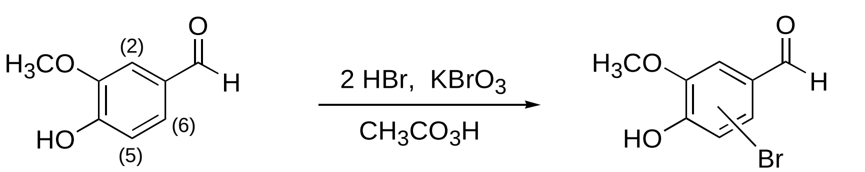


glycoside form



eugenol

The regiochemistry of electrophilic aromatic substitution is heavily influenced by the substituents that are already on the ring. A substituent will cause the substitution to occur either *ortho-para* (called an o/p director) or *meta* (meta director) depending on its resonance and inductive effects. When more than one substituent is present, they can either reinforce each other or compete for the directing effect. Strong electron donors have the greatest influence on the regiochemistry of the substitution product.



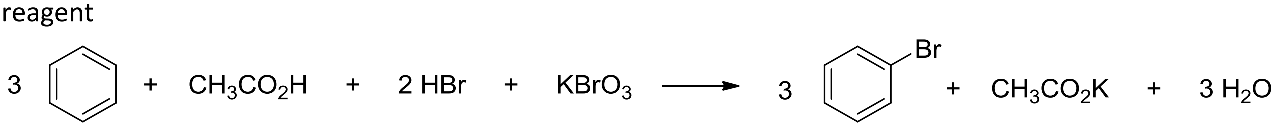
Compound	mp (^oC)
2-bromovanillin	154-155
5-bromovanillin	164-166
6-bromovanillin	177-178

Rather than using elemental bromine, bromine will be formed *in situ* (meaning inside the reaction mixture) with potassium bromate and acid according to the reactions below. Bromonium ion (Br^+), the electrophile in this reaction, is then formed by reaction with one of the protic acids, rather than with a Lewis acid (such as $FeBr_3$) as in textbook reactions.

$$5\ HBr + KBrO_3 + CH_3CO_2H \rightarrow 3\ Br_2 + 3H_2O + CH_3CO_2^- + K^+$$

$$CH_3CO_2H + Br_2 \rightarrow HBr + Br^+ + CH_3CO_2^-$$

The overall reaction stoichiometry for bromination of benzene is follows; Use this stoichiometry to calculate limiting reagent



Procedure

Reaction Setup

Place 0.50 g of vanillin, 0.20g of potassium bromate and 5.0 mL of glacial acetic acid in a 125 mL Erlenmeyer flask. Stir with a magnetic stirbar then add 1.0 mL 48% HBr drop by drop and observe what happens. Continue to stir at room temperature for 45 minutes.

Isolation and Purification

Pour 50 mL of ice-cold water into the Erlenmeyer flask and continue to stir for another 10 minutes. Add 10 drops of sodium thiosulfate solution to destroy any remaining bromine in the reaction mixture. Filter the reaction by vacuum filtration and wash the solid with a few milliliters of cold water. Add the crude solid to hot 50% ethanol/water to remove impurities (the solid will not all dissolve), let the solution to cool and refilter. Allow the product to dry in your lab drawer for a few days.

Characterization

Take the melting point of the product and compare it to the melting points of the possible products. Determine which regioisomer was made and discuss whether this confirms your original hypothesis. Obtain the mass and calculate the percent yield.

Chemicals: vanillin, potassium bromate, 48% hydrobromic acid, acetic acid (glacial), 10% Sodiumthiosulfate, 50% ethanol