# *Experiment 21*

# ELECTROPHILIC AROMATIC SUBSTITUTION

*Fig. 21-1*

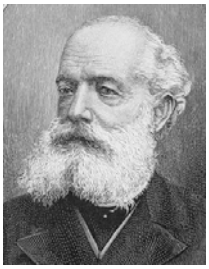
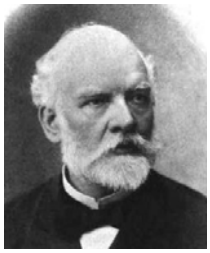


*Fig. 21-2,left*
*Fig. 21-3, right*

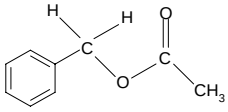


Friedrich A.Kekulé (1829 - 1896) developed first reasonable structure for benzene. http://www.rod.beavon.clara.net/kekule.htm Charles Friedel (1832 - 1899) and James M. Crafts (1839-1917) discovered the extremely

## Text Topics

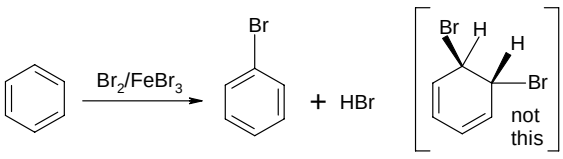
Electrophilic aromatic substitution, inductive, resonance and steric effects. ***Experiment 30*** contains another example of electrophilic aromatic substitution.

## Discussion




Is the molecule aromatic? Originally, the word aromatic was applied to organic chemicals that were fragrant and had a low hydrogen to carbon ratio. Compounds with a benzene ring often satisfy these criteria and were therefore classed as aromatic. The compound above, benzyl acetate, is present in jasmine and is commonly used in perfumes because of its pleasant aromatic properties. Today, organic chemists would call benzyl acetate aromatic not because of its odor but because of other properties that are now used to characterize aromaticity.

Friedrich August Kekulé (1829 - 1896) is recognized as being the first person to attribute the unusual properties of benzene to a cyclic conjugated six membered ring in equilibrium with its equivalent valence isomer. The idea of the ring supposedly came to Kekulé while dreaming and this legend has been the subject of considerable debate ever since. Whatever the consciousness of Kekulé was when he conceived his enlightening idea, Kekulé's ideas significantly contributed to the development of organic chemistry. Technically Kekulé was incorrect about an equilibrium as benzene is a hybrid of two resonance structures and does not go back and forth.




Before Kekulé's concepts about the structure of benzene were developed, organic chemists were puzzled by the reactivity of benzene. While bromine adds readily to ethylene, bromine under similar conditions does not add to benzene despite the presence of its "double bonds". If a Lewis acid catalyst is present, bromine does substitute on the benzene ring. Substitution reactions are typical of the reactions of aromatics and are consistent with our current theory of aromaticity. Aromatics under extreme conditions do hydrogenate. However, the heat of hydrogenation is considerably less than the value calculated for the hydrogenation of "normal" $\pi$ bonds.

Thus aromatics are much more stable than expected due to a sizeable resonance energy. This accounts for the observation that aromatics undergo substitution rather than addition as substitution maintains aromaticity while the aromaticity and most of the resonance energy must be sacrificed for addition to occur.

Nuclear magnetic resonance studies of the aromatic hydrogens reveals that the hydrogens are deshielded due to a ring current. This ring current is consistent with the presence of molecular orbitals that encompass the entire molecule and provide extra stability to the ring.

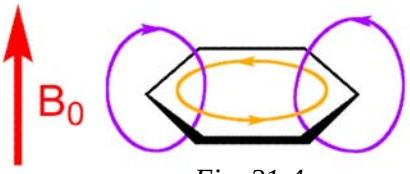
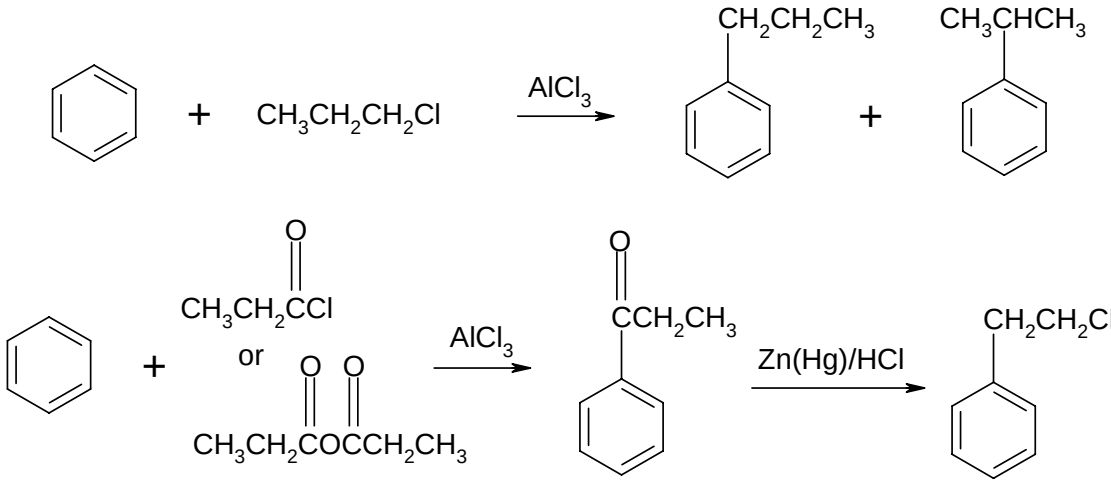



*Fig. 21-4*

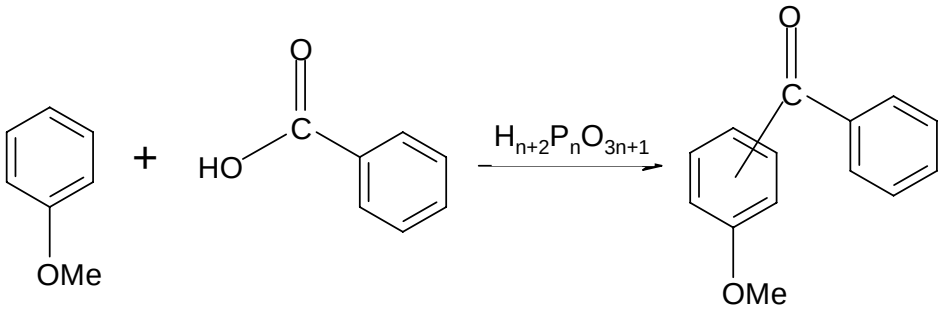
For the purposes here, we will consider aromaticity to be present in compounds that contain a cyclic conjugated ring with $4n + 2$ π electrons. These rings undergo electrophilic substitution reactions and their $^1$H-nmr spectra exhibit evidence of a ring current. As a result of electron delocalization, an aromatic compound has a substantial amount of resonance energy.

When a monosubstituted benzene undergoes an electrophilic aromatic substitution reaction, there are three possible products: ortho (1,2), meta (1,3) and para (1,4) orientation. Electrophilic aromatic substitutions provide an excellent model for the testing of the concepts you have been learning in your organic chemistry course. By applying reasoning based upon inductive, resonance, hyperconjugative and steric effects, it should be possible to make predictions concerning the orientation of the reaction. The application of that reasoning to make predictions for today's experiment will be your responsibility.

It was mentioned in an earlier experiment that reactions such as Grignard's that form carbon to carbon bonds deserve a special place in lists of organic reactions. Friedel-Crafts reactions are electrophilic substitutions on a benzene ring that form a carbon to carbon bond. The two general types of Friedel-Crafts reactions are alkylations and acylations. The former are complicated by the possibility of rearrangement and multiple substitution. To avoid rearrangement, alkyl benzenes are often synthesized by the running of a Friedel-Crafts acylation followed by a reduction (e.g., Clemmenson or Wolf-Kishner).




While reactions of this type are conveniently run in a research laboratory, some problems often accompany these reactions when performed in an instructional laboratory. It is difficult to keep the aluminum chloride dry in an environment where the bottle is continually being opened and closed. Acid chlorides and anhydrides are smelly and hazardous and alkyl halides also should be avoided when reasonable alternatives exist. Other options for electrophilic aromatic substitution for the instructional laboratory include the use of very hazardous bromine. Fortunately, a laboratory textbook by Linstromberg contains a Friedel-Crafts like reaction that does not require the use of aluminium chloride, acid chloride or an alkyl halide. A modified version of this reaction of benzoic acid and anisole with a polyphosphoric acid catalyst will be presented here.




The reaction could potentially yield 2-methoxybenzophenone, 3-methoxybenzophenone, 4-methoxybenzophenone or a mixture of two or three of these products. You should write the mechanism of the reaction, consider the effects of inductive, resonance and steric influences on the stability of the intermediate and predict which products should predominate. You will then run the reaction You should be able to determine which products are formed by determining the physical and spectroscopic properties of the product(s). Finally, you will compare the experimental results to the predicted results.

## Procedure

> Caution: Polyphosporic acid is extremely hazardous to tissue and inhalation. Rubber gloves should be worn when transferring the polyphosphoric acid and the experiment should be performed in a hood.

Equip a 50 mL Erlenmeyer flask with a magnetic stirring bar and add to it, 0.40 g of anisole and 0.60 g of benzoic acid. A bottle of very warm polyphosphoric acid should be available in a warm water bath. Carefully pour about 5 mL of the very viscous acid into the Erlenmeyer flask. Support the flask in a water bath on a magnetic stirring unit. Heat the water until it boils. Magnetically stir the contents at the boiling point of water for about an hour. While the solution is still hot, slowly add 10 mL of water to the flask. After the flask has cooled to room temperature, add 10 mL of ether and stir until any visible solid dissolves. Pour the contents into a separatory funnel. Rinse the flask with two small portions of ether and add them to the separatory funnel and shake. Separate the aqueous layer from the ether layer and extract the aqueous layer with ether an additional time. Combine the ether layers and properly dispose of all the aqueous layers. Wash the ether layer with 10% sodium hydroxide and then with water. Dry the ether layer over sodium sulfate and evaporate the ether. A viscous liquid should remain which might crystallize with cooling or scratching. **If appropriate, recrystallize from hexane.** Identify the product using physical and spectroscopic techniques.

## Extension

It might be interesting and enlightening to compare the rates of electrophilic substitution of anisole and 4-deuteroanisole (***Experiment 20***) and other substituted aromatic compounds. For qualitative rate studies of bromination reactions, see for example:

http://www.chemistry.sfu.ca/assets/uploads/file/Course%20Materials%2009-2/chem286/EAS.pdf
http://www.xula.edu/chemistry/department/organic/Labbook/EASprocedure.pdf
Mohrig, J. R.; Morrill, T. C.; Hammond, C. N.; Neckers, D. C. *Experimental Organic Chemistry*, Freeman, **1998**, pp. 214-217.
Schoffstall, A. M.; Gaddis, B. A.; Druelinger, M. L. *Microscale and Miniscale Organic Chemistry Laboratory Experiments*, McGraw-Hill, **2000**, pp. 292-294.

### References

Linstromberg, W. W.; Baumgarten, H. E. *Organic Experiments*, Heath, 4th ed., **1978**, 247-250.

The following contain some information on the possible products:
http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp
http://www.alfa.com/alf/laboratory_chemical_suppliers.htm
http://www.sigmaaldrich.com/
http://riodb01.ibase.aist.go.jp/sdbs/cgi-bin/cre_index.cgi?lang=eng
http://www.lookchem.com/

The following contain some information on polyphosphoric acid:
http://www.alfa.com/content/msds/USA/L14856.pdf
http://www.sciencelab.com/xMSDS-Polyphosphoric_Acid-9927700
http://progdata.umflint.edu/EHS/MSDS/101551.pdf

### Alternative Electrophilic Aromatic Substitution Experiment

Cardinal, P.; Greer, B.; Luong, H.; Tyagunova, T. *J. Chem. Educ.*, **2012**, *89*, pp. 1061-1063

## Prelaboratory Preparation - *Experiment 21*

First, be sure to list all the goals of the experiment. Prepare a table for insertion of useful and observed data such as molecular mass, mass, moles, melting points and percent yields and recoveries. Determine the limiting reagent and explain the mol ratios of reactants used. Write a complete mechanism for the reaction and based on inductive, resonance and steric considerations, predict which product should predominate. Give a procedure you will use to determine which product is formed. Find an MSDS on the Internet for polyphosphoric acid and list the hazards and precautions that should accompany its use. Locate this type of reaction on the *Reaction-Map of Organic Chemistry* in ***Appendix C*** and include the reaction number in your report.

## Observations

Report all relevant observations including, masses, physical and spectroscopic properties.

## Conclusions

This section should include the following:

1. Were the goals of the experiment achieved? Explain your answer.
2. What was the identity of your product and did it agree with your prediction? Explain your answer.
3. How confident are you in your product identification? Explain your answer.
4. How could the percent yield and recoveries have been improved?
5. Are the concepts of inductive, resonance and steric effects useful for the prediction of orientation in electrophilic aromatic substitution? Explain your answer.
6. Do you think this reaction should be called a Friedel-Crafts reaction? Explain your answer