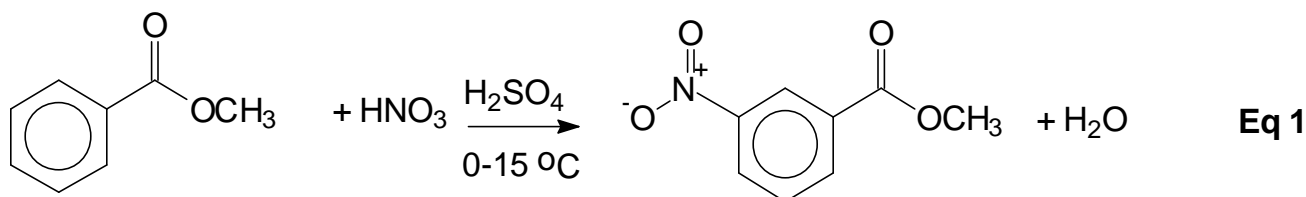


AROMATIC ELECTROPHILIC REACTION.
I. PREPARATION OF METHYL *m*-NITROBENZOATE
II. REACTIVITIES OF BENZENOIDS



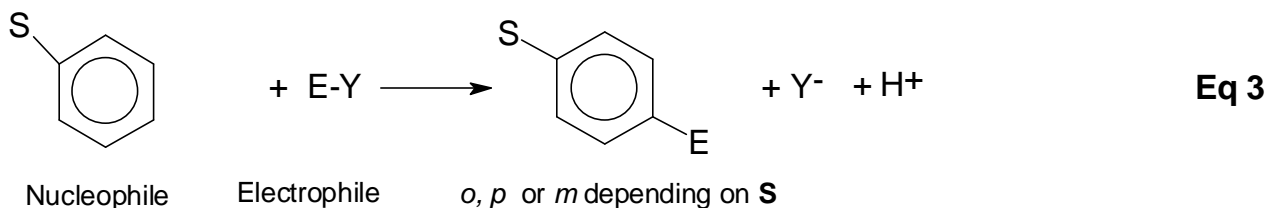
THE PROBLEM TO BE INVESTIGATED: Methyl benzoate will be reacted with concentrated nitric and sulfuric acids to yield a product of substitution. The product and other benzenoids will be examined for their relative rates of reaction with bromine.

BACKGROUND INFORMATION: Nitric acid is a strong acid and in its concentrated form is a good oxidizing



agent. In the environment it is known more for its part in mixtures comprising of sulfur and nitrogen oxides emitted into the air. The consequential increase of acidity (lower *pH*) is a recognized concern in all societies today.

In concentrated H_2SO_4 , a **nitronium cation** (and, hence, a good **electrophile**) is generated from nitric acid (see: Eq. 2). Under the proper conditions (heat), an **electrophilic aromatic substitution** may result. Reactions expressed in Eqs. 1 & 3 are the focus of our attention today. The nitronium ion is generated in concentrated sulfuric acid; but in some cases, glacial acetic acid or other appropriate medium may be used to moderate the concentration and electrophilicity of the intermediate.



THE NATURE OF THIS INVESTIGATION: In the reaction of an **aromatic** compound with an **electrophile** (E-Y), the **nucleophile** (Nu) is the **aromatic** compound (Eq. 3). Both the **rate of reaction** and **substitution** pattern on the aromatic nucleus are governed by the nature of the substituent (**S**) placed on the **aromatic** nucleus. Inductively, the substituent may be either **electron withdrawing** (S_{EW}) or **electron donating** (S_{ED}). For a monosubstituted benzene, for example, an **ED** substituent will direct the **electrophile** into the *ortho*- and *para*- positions with rates of reaction generally *faster* relative to benzene itself. On the other hand, an **EW** moiety will direct the **electrophile** to the *meta*- position with rates of reaction generally *slower* relative to benzene itself. Besides inductive effects, **resonance** is also a factor. The Group VII elements are **EW** elements inductively, but *o, p-directors* under resonance considerations.

Depending upon the nature of the **ED** group, the **aromatic** substrate may be rendered a stronger nucleophile. A catalyst in these cases may not be needed. On the other hand for **EW** substituents, a catalyst is generally required (why?).

In performing this reaction, consider the conditions of the reaction. For example, if phenol is used instead of methyl benzoate, picric acid (2,4,6-trinitrophenol) may be obtained. Though not a carboxylic acid, consider why it is called an "acid".

Caution: Both nitric and sulfuric acids are corrosive. Avoid contact. Clean spillage immediately!

PROCEDURE. Part I. Nitration of Methyl Benzoate

The reaction system is a 50 mL RBF equipped with a Claisen connecting adapter (U-shape) and a 100° C thermometer. The other end of the Claisen adapter is left open into which the nitration mixture will be added. An ice bath is required to maintain the internal reaction medium between 0-15° C throughout the reaction.

Carefully pour 10 mL **concentrated sulfuric acid** through the Claisen adapter attached to the RBF placed in an ice bath. The neck of the RBF is "rested" in the clamp attached to a ring stand. The reaction system should be free to permit swirling of the flask from time to time as the nitration mixture is added.

When the temperature is about 0-5° C, add 5.5 mL **methyl benzoate**. Allow the temperature to drop to ca. 0-5° C again. While cooling, prepare (with cooling) the nitrating mixture consisting of 4 mL each of concentrated sulfuric acid and nitric acid in a 25 mL Erlenmeyer flask.

Nitration of methyl benzoate is moderated by adding the **HNO₃/H₂SO₄** dropwise (use disposable pipet) through the open-end of the adapter. The reaction flask is swirled in the ice bath from time to time, and the temperature carefully maintained between 5-15° C. Hence, the rate of addition is important. Care should be exercised such that the reaction medium is not lower than 5°. Too low a temperature may prompt one to add too much nitrating medium. In this case, an induction period ensues -- followed by a rapid rise of temperature. On the other hand, if the reaction exceeds 15° C, further nitration may occur. (Cautions: Be sure to see the viscous material well) Upon addition of the final drop of the **HNO₃/H₂SO₄** mixture, allow the flask to warm to room temperature by removing the ice bath.

During the warming period (ca. 15-30 minutes), weigh and place ca. 30-50 g ice in a 200 mL beaker. Pour the reaction mixture over the ice and allow the ice to melt. The mixture is stirred, the lumps of ice removed, and the crystals filtered (don't forget to wet the filter paper first) under suction through a Büchner funnel. Compact the crystals with a cork, and, using ca. 25 mL cold water, pour the water over the crystals under suction. Allow the crystals to suction dry for about 10 minutes.

A portion of the crystals, although still moist, may be used in **Part II**. Recrystallization is required, use methanol as a solvent. The melting point of the pure product is 78° C. After recrystallization, the crystals will be left in the drawer to dry for one week. Determine the weight of product, calculate percent yield, and measure the melting point.

Part II. Relative Rates of Reactions of Benzenoids with Bromine.

Caution: Handle reagents with care. After the reactions are completed, dispose of the solutions in the waste container marked "**Halogenated Wastes**".

Bromine will be used as the **electrophile (E-Y)** in these reactions. In small (7 cm) or medium (12 cm) test tubes, dissolve 3 drops of the liquid, or ca. 5 mg (estimate by using tip of spatula) of the solid benzenoid in ca. 1 mL of t-butyl methyl ether. Add the bromine/CCl₄ solution dropwise at room temperature and note the color changes of the bromination solution.

The compounds (**N-S**) shown below are to be tested:

| <u>COMPOUND*</u> | <u>S</u> |
|------------------|----------------------------------|
| Acetanilide | -NHCOCH ₃ |
| Aniline | -NH ₂ |
| Benzene | -H |
| Cyclohexene | ---- |
| Methyl benzoate | -CO ₂ CH ₃ |
| Phenol | -OH |
| Solvent blank | ---- |

* Although cyclohexene is not an aromatic compound, it is used here for comparison purposes.

Your product, methyl *m*-nitrobenzoate (a disubstituted benzenoid), should also be tested. Excluding cyclohexene in your ranking, where should this compound be ranked with respect to the compounds tested above?

Remember to distinguish between a **reaction** and a **dilution** as your bromine solution is dropped into the test solution of your test compound. Hence, number-of-drops and your description of the color changes are necessary to determine whether a reaction has occurred. In your report, rank the substituents (**S**) according to the rates of reactions observed in this experiment; *i.e.* use symbols such as ">", or "~" in your relative ranking. Comment on the relative ranking with what you understand about electron donating and withdrawing groups as "promoters" or "retarders" in aromatic electrophilic substitution.

Helpful Hints - METHYL *m*-NITROBENZOATE

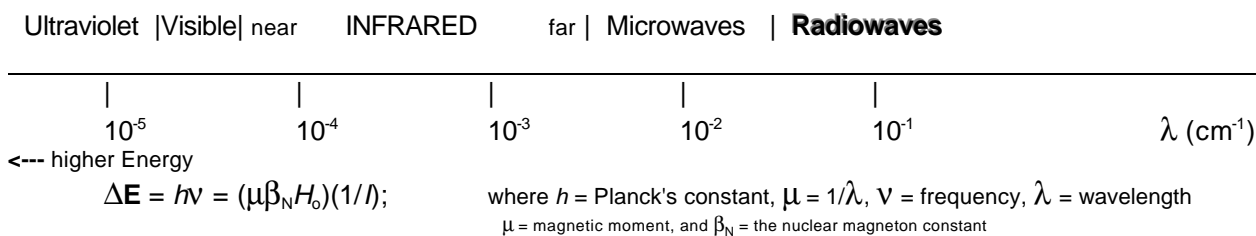
- * Some nitro compounds, such as trinitrotoluene (TNT), are explosive. Although dinitration may occur in our preparation, the risk of explosion is minimal -- *i.e.*, if precautions are taken! Use of an addition funnel without compensation for pressure is to be avoided -- otherwise, a **closed system** may lead to an "unexpected event".
- * **Recrystallization** of the product is necessary if the melting point range is wide (more than 4-5 degrees) and lower than the reported melting point. In this case, byproducts may be present and should be removed by recrystallization. As you may recall from earlier experiments, a **solvent** is chosen such that the impure compound will dissolve at elevated temperature and will crystallize at room temperature (please see detailed instructions on the next page).
- * As a general rule, crystals should not be dried in an oven if the oven temperature is more than 30 degrees above the reported melting point. Solids with low mps often have residual solvent trapped in its lattice and will liquify at temperatures considerably lower than its melting point.
- * In comparing your IR spectra as requested above, note the differences between the two carbonyl functional groups. Consult your text regarding spectroscopic tools employing IR and NMR.

QUESTIONS

1. Instead of methyl benzoate, its isomer, phenyl acetate, is used as the substrate:
 - (a) Show how phenyl acetate is prepared using phenol and acetic anhydride as the starting material.
 - (b) Write a mechanism for this reaction.
 - (c) Specify the conditions (solvent, temperature, catalyst) necessary for this reaction.
 - (d) Phenyl acetate is nitrated in glacial acetic acid. What is (are) the product(s)?
2. Starting from benzene, plan the synthesis of methyl *m*-nitrobenzoate. [**Hint**: What did you do recently -- I mean in the laboratory?]
3. Draw the ¹H NMR spectrum for methyl *m*-nitrobenzoate with the chemical shifts clearly shown. Which proton(s) is (are) at highest field, and which, at lowest field?

INSTRUMENTAL METHODS IN ORGANIC CHEMISTRY. NUCLEAR MAGNETIC RESONANCE

BACKGROUND INFORMATION: Complemented with provisional information gleaned from both spectral and chemical evidence, the use of **radio frequency** in Nuclear Magnetic Resonance (**NMR**) spectroscopy provides a powerful tool in structural determination of organic compounds. The chemical shift, δ , and coupling constant, J , are characteristic for the types of protons or carbons in their own environment as they **couple** or **interact** with other atoms in the molecule. Students should be familiar with the use of the correlation tables. For example, the chemical shifts of the ^1H - and ^{13}C resonances from **Tables 13.2 & 13.4** of the lecture text should be consulted.



The absorption of energy, or **resonance**, by a nucleus depends upon the transitions between nuclear spin states. When placed in a magnetic field, H_0 , the ^1H or ^{13}C nucleus (In our discussion, we will confine our attention to these two.) will experience $(2I + 1)$ spin orientations, where I represents the nuclear spin quantum number. The orientation or spin state is with respect to the direction of the applied magnetic field. The spin states are degenerate in the absence of a magnetic field, but lose their degeneracy in an applied magnetic field. The separation of energy (ΔE) for each nucleus depends on μ and I in the same applied magnetic field.

| NUCLEUS | NATURAL ABUNDANCE | SPECTRAL RANGE, δ |
|---|-------------------|--------------------------|
| Carbon, ^{13}C | ca. 1.1 % | 0 - 250 ppm |
| Proton, ^1H | 99.9+ % | 0 - 11 ppm |

<- Low Field (**deshielded**) Protons

High Field (**shielded**) Protons ->

| | | | | | |
|--|-------------|--------------|--------------------------|---------------------------|-------------|
| Aldehydic Carboxylic | Aromatic | Vinylic | Heteroatom, X,N,O | $\text{sp}^2\text{C H-C}$ | Saturated |
| H-CO-R H-O₂C-R | Ar-H | C=C-H | X-C-H | C=C-C-H | C-H |
| 14-9 ppm | 8.5-6.5 ppm | 7.5-5.5 ppm | 4.5-2.5 ppm | 3.4-2.0 ppm | 1.5 - 0 ppm |

PROCEDURE - Preparation of Sample for NMR Analysis. Samples for analysis are dissolved in a nonprotic solvent such as CDCl_3 , CD_3COCD_3 , CD_3SOCD_3 , C_6D_6 , D_2O or CD_2Cl_2 . The normal hydrogen isotope should not be part of the solvent structure. Your instructor will provide the sample tube and solvents and guide you in preparation of your sample for analysis.