

## Experiment 1: Friedel-Crafts Acylation

### Background:

Goals: a) work with water-sensitive reagents; b) design experimental procedure and work-up; and c) to assess the procedural design.

Electrophilic aromatic substitution reactions take place between the nucleophilic  $\pi$  electrons of an aromatic ring and a strong electrophile. The intermediate carbocation rapidly loses  $H^+$  to reform the aromatic system. In the case of Friedel-Crafts acylation, the electrophile is an acylium ion, formed by the reaction of an acid chloride with aluminum chloride. The mechanism is shown in Figure 1.

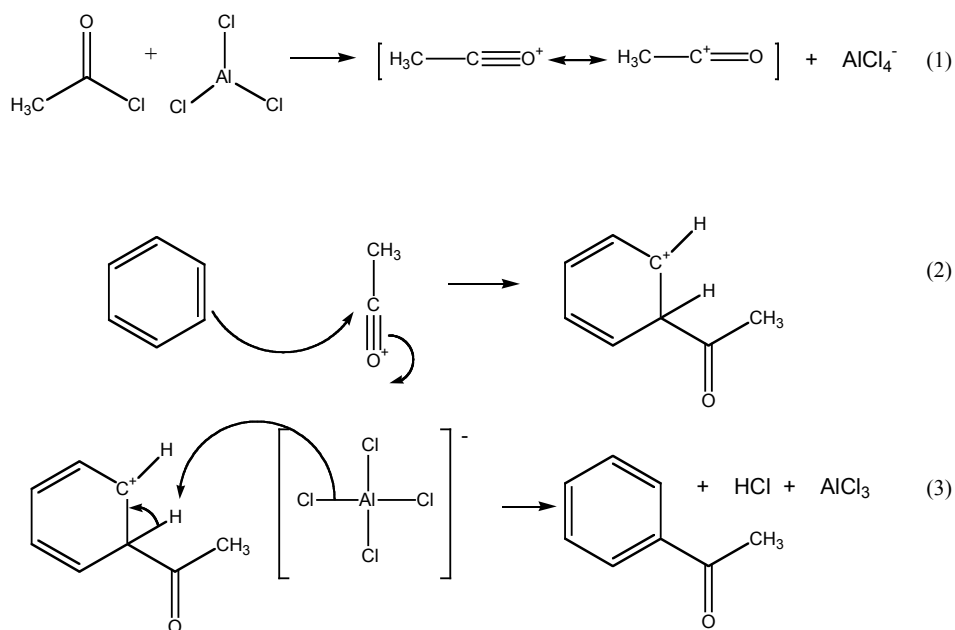


Figure 1: Mechanism for Friedel-Crafts Acylation

You will be assigned either toluene (methylbenzene), ethylbenzene, or anisole (methoxybenzene) to acylate. The reaction is one that comes out of your organic chemistry textbook, so no procedure is available. What variables should you consider when planning your reaction?

The three starting materials that you want to try:

Reactants		Products	
anisole $C_6H_5OCH_3$	Liquid bp 154	4'-methoxyacetophenone $CH_3OC_6H_4C(O)CH_3$	Liquid bp 154/26 mm Hg
ethylbenzene $CH_3CH_2C_6H_5$	Liquid bp 136	4'-ethylacetophenone $CH_3CH_2C_6H_4C(O)CH_3$	Liquid bp 125/20 mm Hg
toluene $CH_3C_6H_5$	Liquid bp 110	4'-methylacetophenone $CH_3C_6H_4C(O)CH_3$	bp 226

Scale 0.050 moles reactant anhydrous (anisole, ethylbenzene, or toluene)

Group 1: *Reaction set up including glassware and stoichiometry.* Two things will affect your reaction design: 1) air sensitive reagents anhydrous aluminum chloride and acyl chloride. The reaction between aluminum chloride and acyl chloride is highly exothermic so the rate of reaction should be controlled so that the solutions do not boil. Consider also, the order that you add the reactants.

Group 2: *Safety; determine when reaction is complete.* MSDS sheets in folder. Hint: TLC... which of the starting material or product has lower Rf; what solvents will you use?

Group 3: *Isolate the product.* What is present at end of reaction? How do you separate the product from the HCl and  $AlCl_3$  remaining at the end of the reaction? How would you test for left over starting material or multiple products? How would you separate out product from starting material if this is an issue? Hint: Do the things left in the reaction differ in solubility or boiling point?

Group 4: *Characterization of product and waste.* What are the best method mp, UV-Vis, IR and/or NMR or TLC to characterize your product? (You will have the proposed products available in the lab for reference.) What are other possible products you could see? Your main solvent is  $CH_2Cl_2$ . How will you label the waste containers generically (halogenated organics, vs organics, vs. aqueous) and specifically?

*A version of the procedure:*

Aluminum chloride is water sensitive, an irritant, and corrosive. It will react with the moisture on your skin to liberate HCl. Handle it with care, weigh out only what is necessary, and work quickly but safely. Acetyl chloride is also corrosive. Keep it in a hood. Keep all reagent bottles tightly capped.

Anhydrous aluminum chloride (0.055 mol, 1.1 equiv) and 15 mL\* of methylene chloride were placed in a 100-mL, round-bottomed (RB) flask with an addition funnel (grease the joints) capped with a septum, reflux condenser capped with septum, and a septum. The system was flushed with nitrogen, venting first through the top of the reflux condenser and then through the addition funnel. Nitrogen was bubbled through the solution venting through the condenser. The mixture was cooled to 0°C in an ice/water bath. Acetyl chloride (0.055 mol, 1.1 equiv) as a solution in 10 mL\* of methylene chloride was added to the addition funnel using a syringe and then to the aluminum chloride dropwise over 10 min. After the addition was complete, the aromatic compound (0.050 mol) as a solution in 10 mL\* of methylene chloride was added in the same manner. The addition rate was adjusted so the solution did not boil excessively. After addition was complete, the ice bath was removed and the reaction was allowed to come to room temperature. After stirring for an additional 15 minutes at room temperature, the reaction mixture was poured carefully and slowly, with stirring, into about 25 g of ice and 15 mL of concentrated HCl in a beaker. The mixture was transferred to a separatory funnel and the organic layer collected. The aqueous layer was extracted with 20 mL of methylene chloride. The combined organic layers were extracted with two portions of saturated sodium bicarbonate and dried over anhydrous MgSO<sub>4</sub>. The drying agent was removed by gravity filtration into an appropriately sized round-bottomed flask. The methylene chloride was removed by rotary evaporation. TLC was used to quickly assess presence of starting material. If necessary, a flask was set up for simple distillation and insulated with aluminum foil or glass wool. The mixture was distilled, raising the setting on the variac as necessary. If residual starting material was present, it distilled around 150°C, while each of the products has a boiling point greater than 200°C. The product was weighed and analyzed by IR and NMR spectroscopy and TLC (ethyl acetate : hexanes = 1 : 4) in comparison with the proposed starting material.

\*These volumes are designed for the use of a 100-mL, round-bottomed (RB) flask. If using a 250-mL RB flask, double and if using a 500-mL, RB flask, multiply by four.

Notes:

Do not wash your glassware just before doing this experiment. Your glassware must be clean and dry. Do not wash your addition funnel between adding the acetyl chloride and the aromatic compound.

## Write-up (Experiment 1)

Write up a journal style experimental including characterization. (10 points)

### Experimental

- (10) Experimental are written correctly in content and style; publishable Journal-style experimental text
- (8) Experimental complete, but style in need of improvement OR procedure complete in journal style but missing a set of details such as NMR/IR, etc. data that is reported elsewhere.
- (6) Experimental complete in journal style but missing minor information OR procedure needs style improvement AND information such as IR/NMR missing but reported elsewhere
- (4) Experimental incomplete in a way that is misleading or information missing
- (2) Procedures are poorly and incorrectly written

Score: \_\_\_\_\_

Include a results section with properly labeled spectrum (10 points)

### Spectroscopic Interpretations

- (10) Spectroscopic interpretations follow assigned format, complete and accurate, with appropriate assignments
- (8) Follows assigned format but missing some peak assignments OR good assignments but wrong format.
- (6) Follows assigned format; critical data missing in one or more spectrum OR incorrect assignments
- (3) Spectroscopic interpretations are poorly done and unjustified

Score: \_\_\_\_\_

Write one paragraph critiquing the procedure addressing its effectiveness for making high purity, high yield of the desired product. What would you change if anything? (5 points)

- (5) Succinct, scientific critique addressing both purity and yield
- (3) Needs improvement in length, organization, or addressing purity or yield
- (1) Lacking in two or more areas

Score: \_\_\_\_\_