

(8 M urea for gel chromatography and sodium dodecyl sulfate for electrophoresis).

The focus of this lab does place some restrictions on the kinds of activities performed. Preparation of the proteins requires significant time, but once prepared they can be used for many years if stored frozen. The main limitation is that students cannot follow the activity of any protein, because none are enzymes. This dilemma could be overcome by including a fifth protein that shows no visible absorbance and that could be followed by an appropriate enzyme assay. For example, carbonic anhydrase ($MW. = 29,000$) elutes in fractions 19–22 (Fig. 2) and could be followed by measuring both the absorbance at 280 nm and enzymatic activity using p-nitrophenylacetate as substrate, although detection of product from this substrate could be hampered by the presence of the other chromogenic proteins. Students also do not practice homogenization, extraction, and differential precipitation techniques, as they would do in more typical protein purification labs.

We feel, however, that the learning potential available from this exercise is significantly greater than in traditional experiments in protein purification, when students rotely follow a defined protocol. For example, it is our experience that students learn little when they spend three hours doing a series of ammonium sulfate fractionations. Asking students to purify a protein from a tissue or cell homogenate is still an excellent learning experience if given to students as an investigative experiment in which they develop their own methods.

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Iron(III) Chloride as a Lewis Acid in the Friedel–Crafts Acylation Reaction

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As one of the most important reactions in aromatic substitution chemistry, the Friedel–Crafts reaction (1) receives extensive coverage in sophomore organic chemistry. The most widely employed Lewis acid for the Friedel–Crafts reaction is aluminum chloride, although several other reagents also have appreciable reactivity (1). The safety and handling problems of aluminum chloride in the sophomore organic laboratory are not easily addressed and prompted us to examine iron(III) chloride as an alternative Lewis acid for the Friedel–Crafts acylation reaction. Previous studies have demonstrated that anhydrous iron(III) chloride is an effective catalyst for the Friedel–Crafts alkylation of biphenyl (2) and benzene (3) with *tert*-butyl chloride. We have found that iron(III) chloride serves admirably in the place of aluminum chloride for several Friedel–Crafts acylation reactions currently described in the literature (4). For example, the Friedel–Crafts acylation of anisole, toluene, *p*-xylene, and biphenyl with acetyl chloride employing $FeCl_3$ gave the corresponding ketones in slightly lower yields (by 10–15%) than the reactions employing $AlCl_3$ under identical conditions. Despite the hygroscopic and mildly corrosive nature of anhydrous iron(III) chloride, the handling and work-up procedures were simpler and readily adaptable to our sophomore organic laboratory (5).

Our students are required to acylate anisole with propionyl chloride using anhydrous $FeCl_3$ as the first step in the synthesis of anethole. The students typically obtained the aromatic ketone in 65–80% yield in greater than 97% purity.

Experimental Procedure

- **Caution:** Anhydrous iron(III) chloride and propionyl chloride are corrosive

Anhydrous iron(III) chloride (3.3 g, 20 mmol) was rapidly weighed and transferred into a 50 mL round bottom flask equipped with a magnetic stirring bar. Methylene chloride (25 mL) and propionyl chloride (2.0 mL, 23 mmol) were added with stirring. A Claisen adapter fitted with a separatory funnel for the addition of the anisole solution and a condenser with a take-off connected to an inverted liquid funnel over a beaker of water for scrubbing the HCl fumes (4a) was placed on the round bottom flask. Anisole

(2.16 g, 20 mmol) in methylene chloride (5 mL) was added dropwise to the reaction mixture over a 2–4 min period with stirring

- **Caution:** This step produces vigorous evolution of HCl and is exothermic.

The deep burgundy red solution was stirred for an additional 20 min. The reaction mixture was quenched by the dropwise addition of water (5 mL) and stirred for 5 min. The reaction mixture was transferred to a separatory funnel with water (50 mL) and methylene chloride (10 mL). The organic phase was separated and the aqueous phase was extracted with additional methylene chloride (10 mL). The combined organic phases were washed with 0.5 M NaOH (50 mL), dried over Na_2SO_4 , decolorized with 0.25 g of activated charcoal, and filtered through a bed of Celite. The organic phase was allowed to evaporate in the back of the hood until the following lab period (high field 1H NMR confirmed that methylene chloride and unreacted anisole completely evaporated over the one-week period). The pale yellow solid or oil (crystallization of the oil can be induced by the addition of a seed crystal) was identified as 1-(4-methoxyphenyl)-1-propanone by 1H NMR and IR.

The use of iron(III) chloride avoids many of the problems commonly associated with aluminum chloride without a substantial loss in yield. We feel that iron(III) chloride deserves wider recognition as a useful Lewis acid in Friedel–Crafts acylation reaction for sophomore organic chemistry. We would like to thank the students of CHEM 222 for their efforts and comments during the development of this experimental procedure.

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