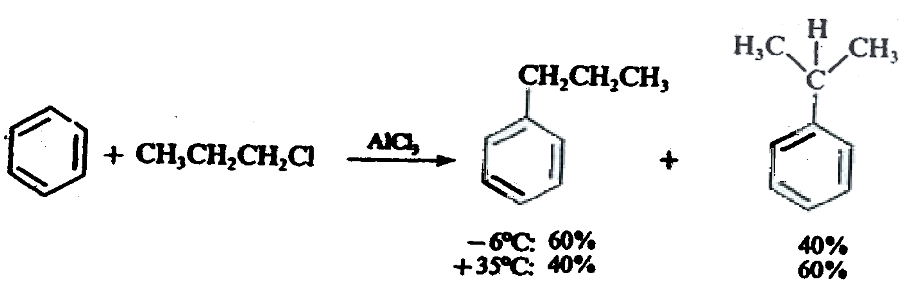
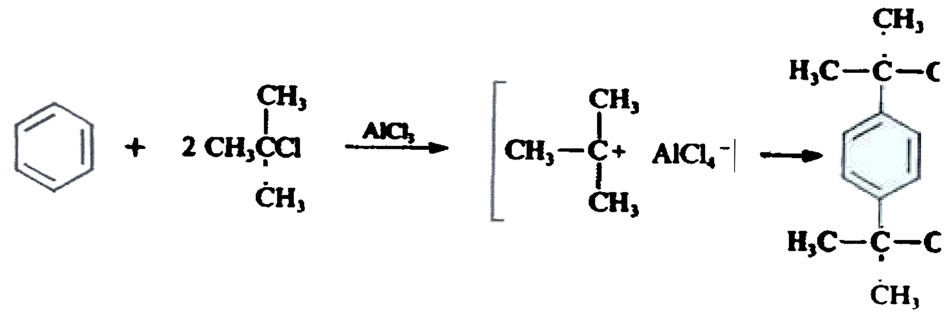
Laboratory #6 (Lab handout #4)
Microscale preparation of 1,4-ditertbutylbenzene
Example of Friedel-Crafts substitution

Friedel-Crafts alkylation of aromatic rings most often employs an alkyl halide and a strong Lewis acid catalyst. Some of the catalysts that can be used, in order of decreasing activity, are the halides of Al, Sb, Fe, Ti, Sn, Bi, and Zn. Although useful, the reaction has several limitations. The aromatic ring must be unsubstituted or bear activating groups and because the product, an alkylated aromatic molecule, is more reactive than the starting material, multiple substitution usually occurs. Furthermore, primary halides will rearrange under the reaction conditions:



In the present reaction a tertiary halide and the most powerful Friedel-Crafts catalyst, $AlCl_3$, are allowed to react with benzene. The initially formed *t*-butylbenzene is a liquid while the product, 1,4-di-*t*-butylbenzene, which has a symmetrical structure, is a beautifully crystalline solid. The alkylation reaction probably proceeds through the carbocation under the conditions of the present experiment:



Benzene
MW 78.11, den 0.88
bp 80°C

2-Chloro-2-methylpropane (*t*-Butyl chloride)
MW 92.57, den 0.85
bp 51°C

1,4-Di-*t*-butylbenzen
MW 190.32, mp 77–7
bp 167°C

The reaction is reversible. If 1,4-di-*t*-butylbenzene is allowed to re with *t*-butyl chloride and aluminum chloride (1.3 moles) at 0–5°C, 1,3-di butylbenzene, 1,3,5-tri-*t*-butylbenzene, and unchanged starting m are found in the reaction mixture. Thus, the mother liquor from cry zation of 1,4-di-*t*-butylbenzene in the present experiment probably contai *t*-butylbenzene, the desired 1,4-di-product, the 1,3-di-isomer, and 1,3,5-tri butylbenzene.

Host-guest chemistry

Although the mother liquor probably contains a mixture of seve components, the 1,4-di-*t*-butylbenzene can be isolated easily as an inclusi complex. Inclusion complexes are examples of host-guest chemistry. T molecule thiourea, NH_2CSNH_2, the host, has the interesting property crystallizing in a helical crystal lattice that has a cylindrical hole in it. T guest molecule can reside in this hole if it is the correct size. It is not bou to the host, and there are often a nonintegral number (on the average) of hc molecules per guest. The inclusion complex of thiourea and 1,4-di-*t*-but benzene crystallizes very nicely from a mixture of the other hydrocarbons a thus more of the product can be obtained. Because thiourea is very solub in water the product is recovered from the complex by shaking it with mixture of ether and water. The complex immediately decomposes and tl product dissolves in the ether layer, from which it can be recovered.

Compare the length of the 1,4-di-*t*-butylbenzene molecule with tl length of various *n*-alkanes and predict the host/guest ratio for a give alkane. You can then check your prediction experimentally.

Experiments

MICROSCALE

1. 1,4-Di-*t*-Butylbenzene

Measure, using a 0.5-mL plastic syringe, 0.40 mL of dry 2-chloro-2-methy propane (*t*-butyl chloride) and 0.20 mL of dry benzene into a dry 10 × 10

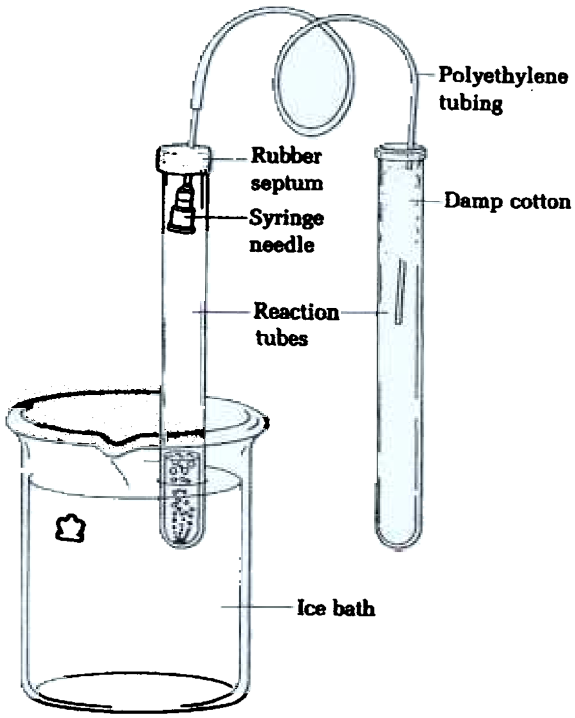


FIG. 37.1 Hydrogen chloride gas trap for Friedel-Crafts reaction.

mm reaction tube equipped with a septum, inverted needle, and polyethylene tubing as seen in Fig. 37.1. The benzene and the alkyl chloride will be found ir ~~ptum-stoppered containers. Cool the tube in ice and then add to it 20 mg (uminum chloride. Weighing and transferring this small quantity is ult because aluminum chloride reacts with great rapidity with moist air. Keep the reagent bottle closed as much of the time as possible while weighing the reagent into a very small dry, capped vial. Since the aluminum chloride is a catalyst, the amount need not be exactly 20 mg.

Caution! Benzene is a mild carcinogen. Handle in the hood, do not breathe vapors or allow liquid to come in contact with the skin.

Aluminum chloride dust is extremely hygroscopic and irritating. It hydrolyzes to hydrogen chloride on contact with moisture. Clean up spilled material immediately.

Mix the contents of the reaction tube by flicking the tube with the finger. After an induction period of about 2 min, a vigorous reaction sets in, with bubbling and liberation of hydrogen chloride. The hydrogen chloride is trapped using the apparatus depicted in Fig. 37.1. The wet cotton in the empty reaction tube will dissolve the hydrogen chloride. Near the end of the reaction the product separates as a white solid. When this occurs, remove the tube from the ice and let it stand at room temperature for 5 min.

Add about 1.0 mL of ice water to the reaction mixture, mix the contents thoroughly, and extract the product with three 0.8-mL portions of ether. Wash the combined ether extracts with about 1.5 mL of saturated sodium chloride solution and dry the ether over anhydrous sodium sulfate. Add sufficient drying agent so that it does not clump together. After 5 min transfer the ether solution to a dry, tared reaction tube using more ether to wash the drying agent and evaporate the ether under a stream of air in the hood.

Add powdered anhydrous sodium sulfate until it no longer clumps together

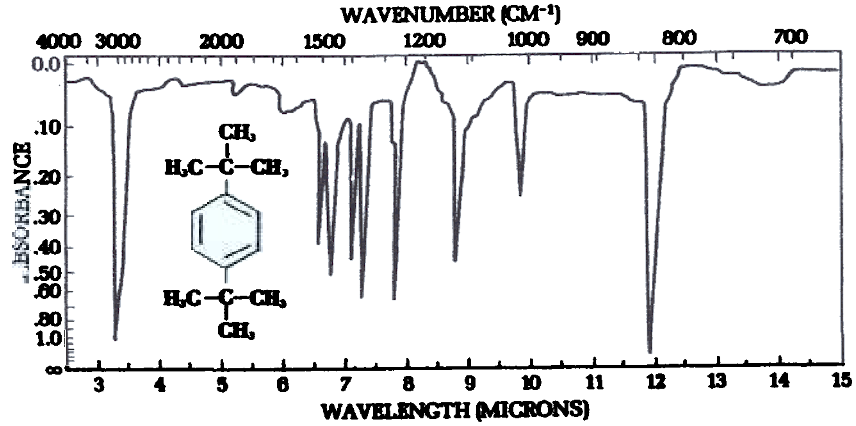


FIG. 37.2 Infrared spectrum of 1,4-di-*t*-butylbenzene.

Remove the last traces of ether under water aspirator vacuum. The oily product should solidify on cooling and weigh about 300 mg.

Spontaneous crystallization gives beautiful needles or plates

For crystallization, dissolve the product in 0.40 mL of methanol and let the solution come to room temperature without disturbance. After thorough cooling at 0°C, remove the methanol with a Pasteur pipette and rinse the crystals with a drop of ice-cold methanol while keeping the reaction tube in ice. Save this methanol solution for analysis by thin-layer chromatography. The yield of recrystallized material after drying under aspirator vacuum should be about 160 mg. Remove a sample of crystals for analysis by infrared spectroscopy, thin-layer chromatography, and melting point determination.

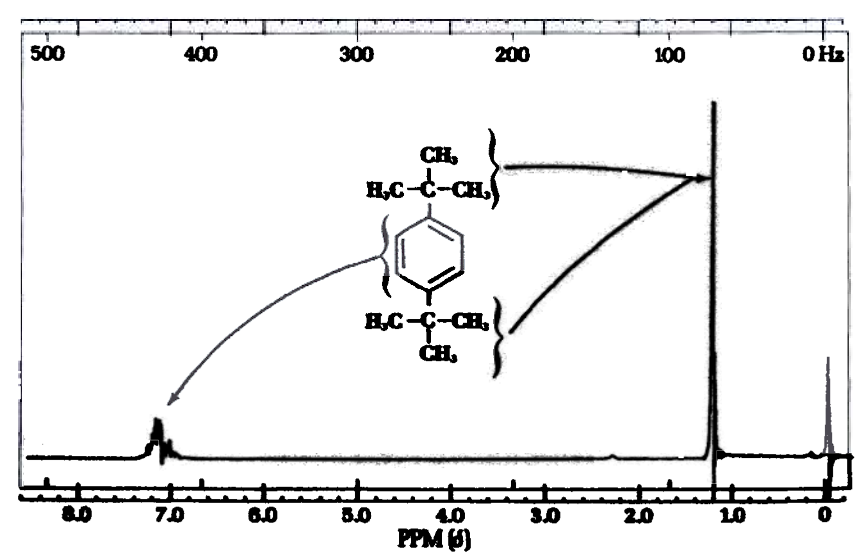


FIG. 37.3 ^{1}H nmr spectrum of 1,4-di-*t*-butylbenzene.

Using thin-layer chromatography compare the pure crystalline product with the residue left after evaporation of the methanol.

Cleaning Up Place any unused *t*-butyl chloride in the halogenated organic waste container, any unused benzene in the hazardous waste container for benzene. Any unused aluminum chloride should be mixed thoroughly with a large excess of sodium carbonate and the solid mixture added to a large volume of water before being flushed down the drain. The combined aqueous layers from the reaction should be neutralized with sodium carbonate and then flushed down the drain. Methanol from the crystallization is to be placed in the organic solvents container.

2. Preparation of Thiourea Inclusion Complex

MICROSCALE

In a tared reaction tube dissolve 200 mg of thiourea (*Caution! See margin note.*) and 120 mg of 1,4-di-*t*-butylbenzene in 2.0 mL of methanol at room temperature; then cool the mixture in ice, at which time the inclusion complex will crystallize. Using a Pasteur pipette remove the solvent and wash the product twice with just enough methanol to cover the crystals while keeping the tube on ice. Connect the reaction tube to a water aspirator and using the heat of the hand evaporate the remaining methanol under reduced pressure until the weight of the tube is constant. The yield should be about 200 mg.

Caution! Thiourea is a mild carcinogen. Handle the solid in a hood. Do not breathe dust.

Thiourea
MW 76.12

Remove a small sample, determine carefully the weight of the remaining complex, and then add about 1.2 mL of water and 1.2 mL of ether to the tube. ake the mixture until the crystals disappear. This causes the breakup of the nplex with the thiourea remaining in the aqueous layer and the 1,4-di-*t*-butylbenzene passing into the ether layer. Draw off the aqueous layer and dry the ether layer with anhydrous sodium sulfate. Add sufficient drying agent so that it does not clump together. More ether can be added if necessary. Transfer the ether to a tared reaction tube and wash the drying agent twice with fresh portions of ether. The object is to make a quantitative transfer of the butylbenzene. Evaporate the ether and remove the last traces under aspirator vacuum as before. After the weight of the tube is constant, record the weight of the hydrocarbon. Calculate the number of molecules of thiourea per molecule of hydrocarbon (probably *not* an integral number).

Inclusion complex starts to crystallize in 10 min

Cleaning Up Place any unused thiourea and the 1.2 mL of the aqueous solution containing thiourea in the hazardous waste container for thiourea. Alternatively treat the thiourea with excess aqueous 5.25% sodium hypochlorite solution (household bleach), dilute the mixture with a large amount of water, and flush it down the drain. Allow the ether to evaporate from the sodium sulfate and then place it in the nonhazardous solid waste container.