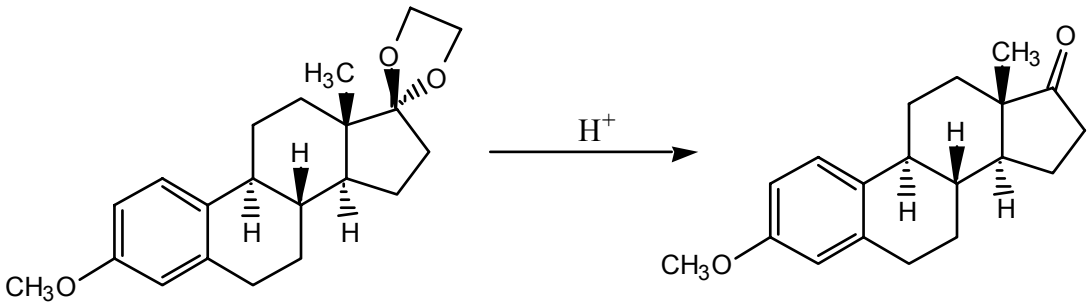
STEP 6:

ESTRONE METHYL ETHER



1. Procedure

Prepare a solution of the starting material, estrone-3-methyl ether-17-ethylene ketal in THF (~ 0.05 M) in a 100-mL round-bottomed flask equipped with a stirbar. Add 10% aqueous HCl solution (same volume as THF). Fit the flask with a reflux condenser topped with a septum and a nitrogen balloon, as shown in Figure 6. Heat the reaction solution to reflux using a heating mantle or an oil bath as a heat source (note 1). Monitor the reaction by TLC. When the reaction is complete (<1 hour), discontinue heating and allow the reaction solution to cool to room temperature.

Dilute the reaction solution with an equal amount of ether and separate the layers. Extract the aqueous layer with ether (3x). Combine the ether layers in a 250-mL Erlenmeyer flask. Slowly pour in saturated aqueous sodium bicarbonate solution and swirl until gas evolution stops (note 2), then pour into the separatory funnel to wash as normal. Wash the ether layer further with distilled water (2x). Dry the organic layer over sodium sulfate, filter, and evaporate the solvent on the rotary evaporator. The crude product may be used purified by column chromatography. (Special note: A simple recyrstallizatiton of the crude product from 95:5 hexane/ethyl acetate may be sufficient to remove all impurities.)

2. Notes

1. **Do not plug a heating mantle or oil bath into the wall.** They must be connected to a **Variac** to regulate the voltage. Never heat an empty heating mantle. Always inspect the bottom of an oil bath for water droplets. Water in an oil bath may explosively vaporize and spray hot oil when the bath is heated near or above 100 ˚C.

2. **Caution**: Acid in the ether layer will cause vigorous gas evolution upon addition of the bicarbonate solution. These solutions are first mixed in an Erlenmeyer flask rather than in a separatory funnel to prevent a "fire-extinguisher" effect. Be certain that no more gas will be generated before shaking them together in the separatory funnel.

3. Characterization and Report

Determine the yield of product.

Characterize the product by IR, ^{1}H and ^{13}C NMR, and melting point.

Tabulate and assign the spectral data.

List the TLC conditions used and the R_f values of starting material and product.

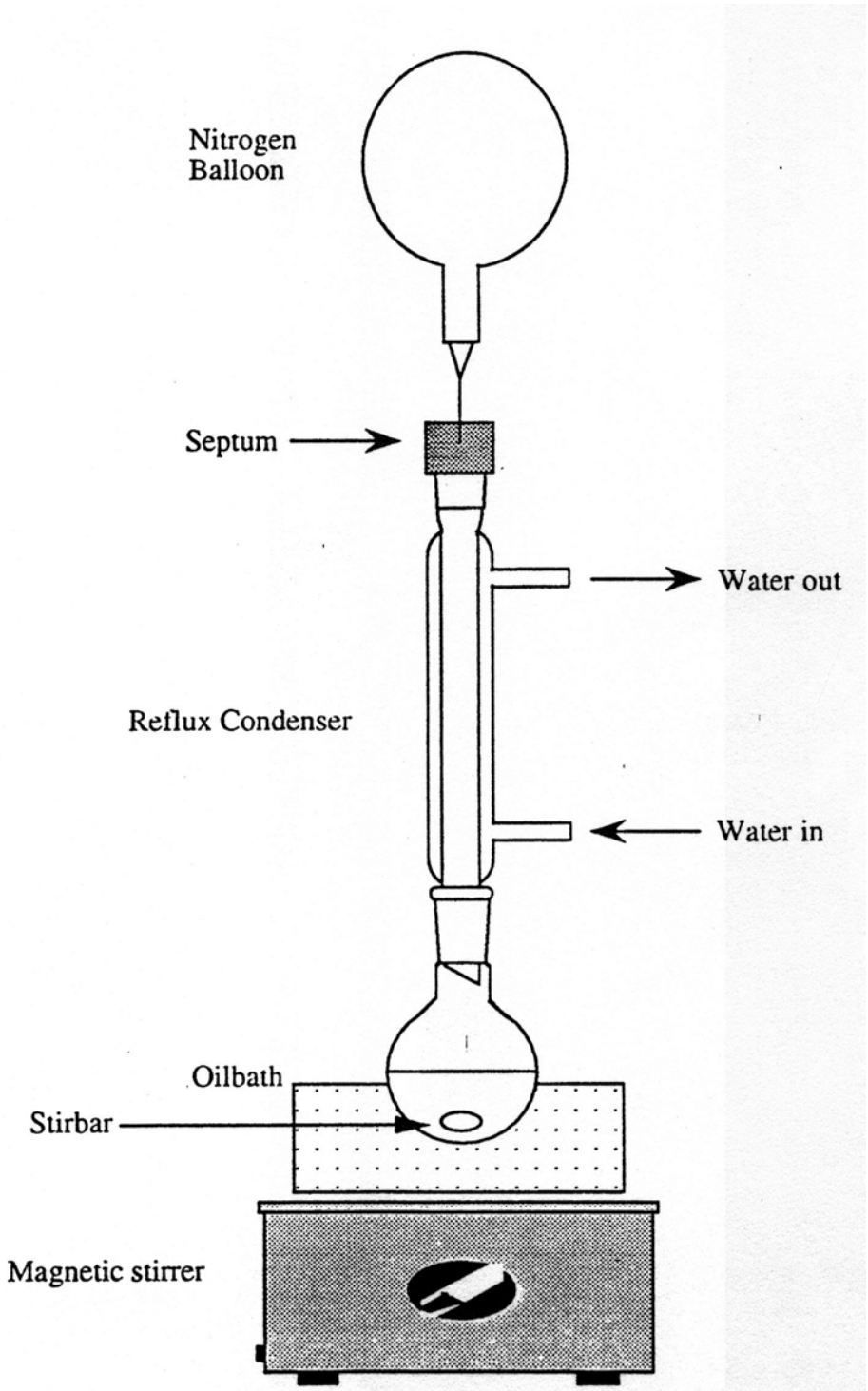


Figure 6. Refluxing Apparatus.