

## Honors Cup Synthetic Proposal

Section: 291

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Title: Preparation of Benzocaine (ethyl-p-aminobenzoate) from p-acetotoluidide

### Introduction:

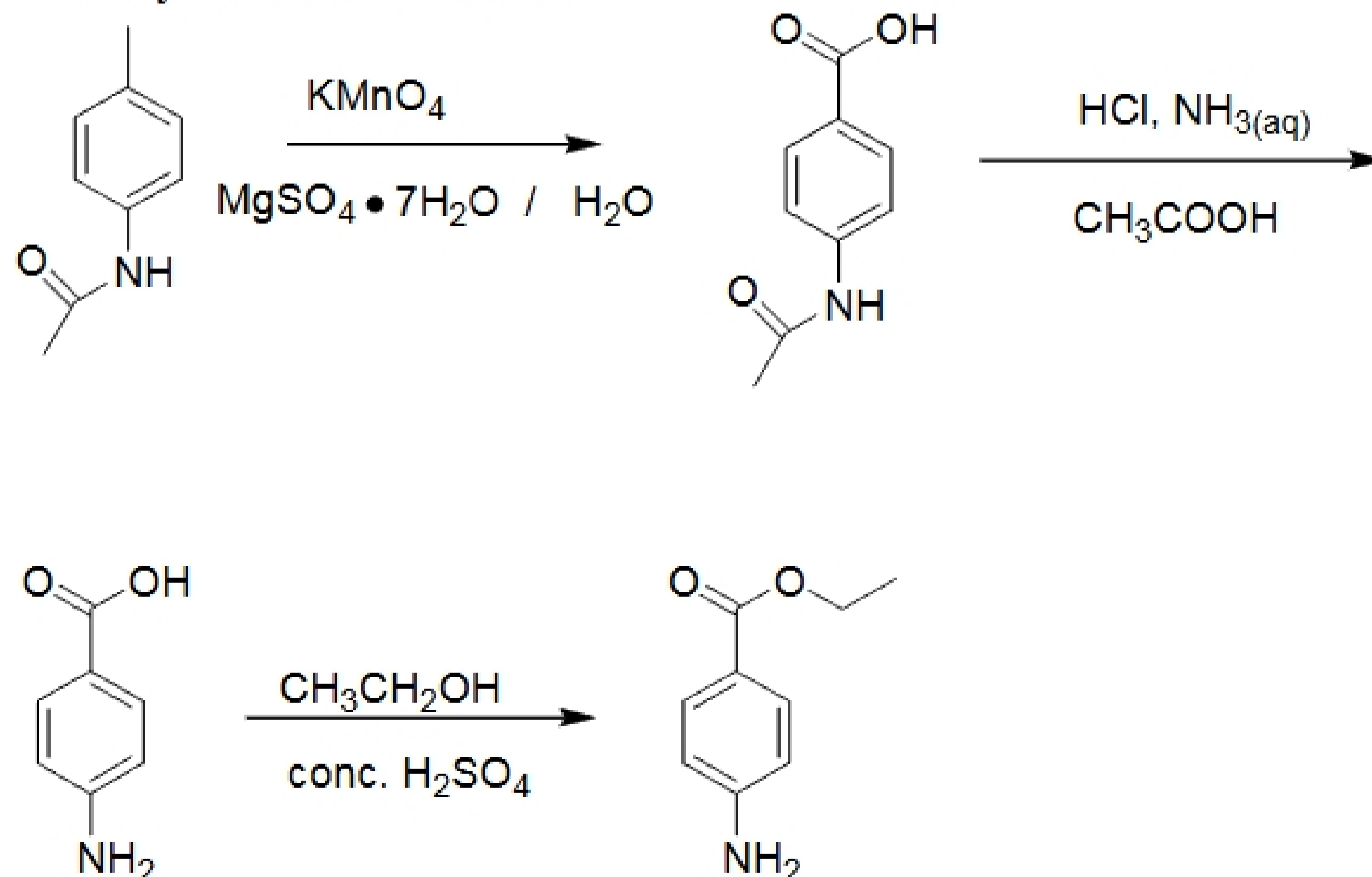
Benzocaine is one of many widely used anesthetics from a family of esters. These esters are synthesized from the organic acid para-aminobenzoic acid (PABA) and ethanol, which are also present in folic acid and vitamin B<sub>10</sub>. This essential drug is found in the liquid, gel, lozenge, lotion, eardrop and aerosol spray forms. It used as a temporary topical anesthetic that numbs the nerve endings near the surface of the skin where applied. Physicians throughout the world prescribe benzocaine for people 4 months and older.

Benzocaine is frequently synthesized from p-nitrotoluene. This pathway involves many reduction steps of the nitro group. However because of our small scale needs we have found a procedure that involves the synthesis from p-acetotoluidide. P-acetotoluidide is oxidized by magnesium sulfate to produce p-aminobenzoic acid, which is then heated with hydrochloric acid to create an amino acid. Ethanol is added in the subsequent step to esterify the amino acid and produce our desired product, benzocaine.

### Reference:

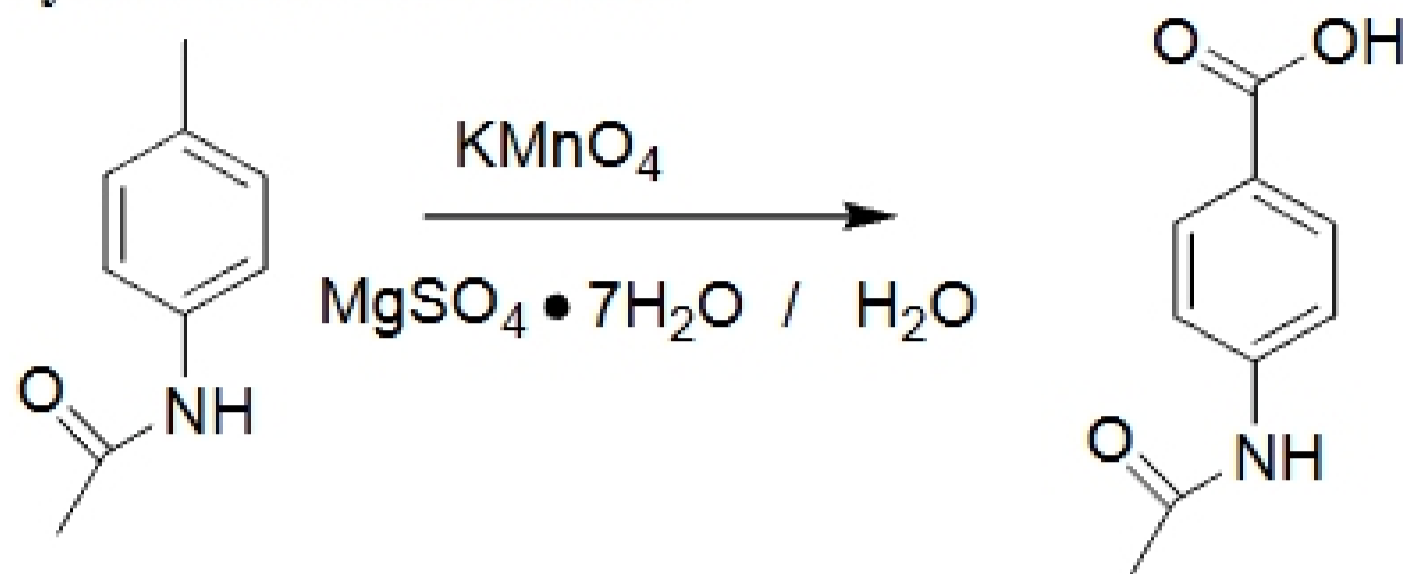
"Benzocaine." [Drugs.com. invisalign](http://www.drugs.com/invisalign). 05 Feb. 2005  
<<http://www.drugs.com/cons/Benzocaine.html>>.

### Overall synthetic reaction scheme:



## Step 1

### Synthetic transformation 1:



**Experimental 1** In a 1 L beaker or flask, add 7.6 g (.052 mol) p-acetotoluidide, 20 g (.08 mol) magnesium sulfate hydrate (MgSO<sub>4</sub> · 7H<sub>2</sub>O) and 500 mL H<sub>2</sub>O. Heat to about 85 degrees C. Prepare a solution of 20.4 g KMnO<sub>4</sub> (.128 mol) in 80 mL of boiling water. While stirring the p-acetotoluidide solution vigorously, add the permanganate solution slowly over 30 minutes. After all the permanganate has been added, swirl vigorously. Filter off the manganese dioxide precipitate from the hot solution using a fluted filter, and wash with water. If the solution is still purple from the permanganate, add 1 mL ethanol, boil until color has been discharged, and filter again. Cool the solution and acidify to pH 3-4 with 20% aqueous sulfuric acid. Filter with suction and dry.

\*we scaled the reaction to 400%.

**Expected yield: 50% 3.50 g**

### Safety, disposal and green issues 1:

#### P-acetotoluidide

**Engineering Controls:** Use adequate ventilation to keep airborne concentrations low.

**Handling:** Wash thoroughly after handling. Remove contaminated clothing and wash before reuse. Use with adequate ventilation. Minimize dust generation and accumulation. Avoid contact with eyes, skin, and clothing. Keep container tightly closed. Avoid ingestion and inhalation.

**Storage:** Store in a tightly closed container. Store in a cool, dry, well-ventilated area away from incompatible substances.

#### Potassium Permanganate

**Handling:** Wash thoroughly after handling. Remove contaminated clothing and wash before reuse. Use only in a well-ventilated area. Minimize dust generation and accumulation. Do not get in eyes, on skin, or on clothing. Keep container tightly closed. Avoid contact with clothing and other combustible materials. Do not ingest or inhale. Do not store near combustible materials. Discard contaminated shoes.

**Storage:** Keep away from sources of ignition. Do not store near combustible materials. Keep

container closed when not in use. Store in a tightly closed container. Store in a cool, dry, well-ventilated area away from incompatible substances.

**Hazardous Decomposition Products:** Irritating and toxic fumes and gases, oxygen, oxides of potassium, oxides of manganese.

**Other:** Harmful to aquatic life in very low concentrations

**P-acetamidobenzoic acid**

**Chemical Stability:** Stable under normal temperatures and pressures.

**Conditions to Avoid:** Incompatible materials, dust generation, excess heat.

**Incompatibilities with Other Materials:** Oxidizing agents.

**Hazardous Decomposition Products:** Carbon monoxide, oxides of nitrogen, irritating and toxic fumes and gases, carbon dioxide.

**Ecotoxicity:** Bacteria: *Phytobacterium phosphoreum*