

## Experiment 40

# ALKYL PARABENS: SYNTHESIS AND DETECTION IN COSMETICS

Fig. 40-1



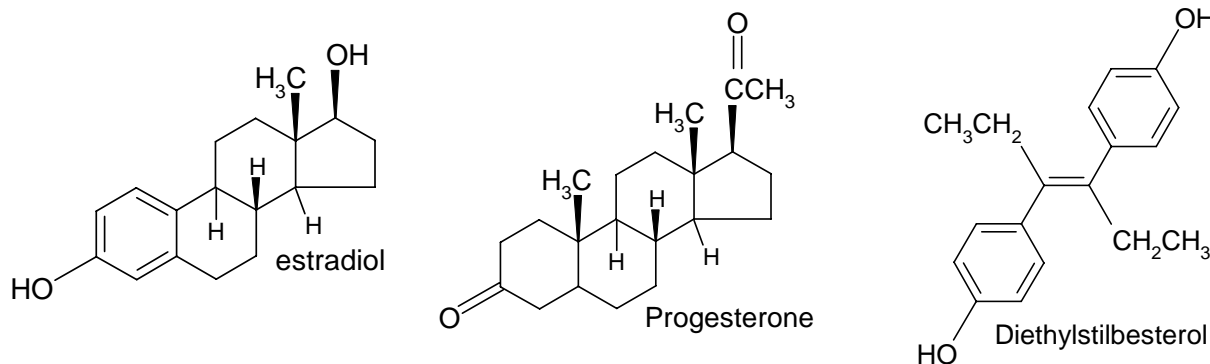
Elizabeth of Poland, Queen of Hungary is credited with introducing perfume to the Western world in 1340.  
[http://en.wikipedia.org/wiki/History\\_of\\_perfume](http://en.wikipedia.org/wiki/History_of_perfume)  
[http://en.wikipedia.org/wiki/Elisabeth\\_of\\_Poland](http://en.wikipedia.org/wiki/Elisabeth_of_Poland)

### Text Topics and Comments

Esterification, estrogens, thin layer chromatography. This experiment should be considered a research project as it has not been tested for student use. While the synthesis should work, the thin layer chromatography methods needed for the analysis will have to be developed. There are references included that suggest methods for the chromatography but these methods will undoubtedly have to be modified to achieve useful results.

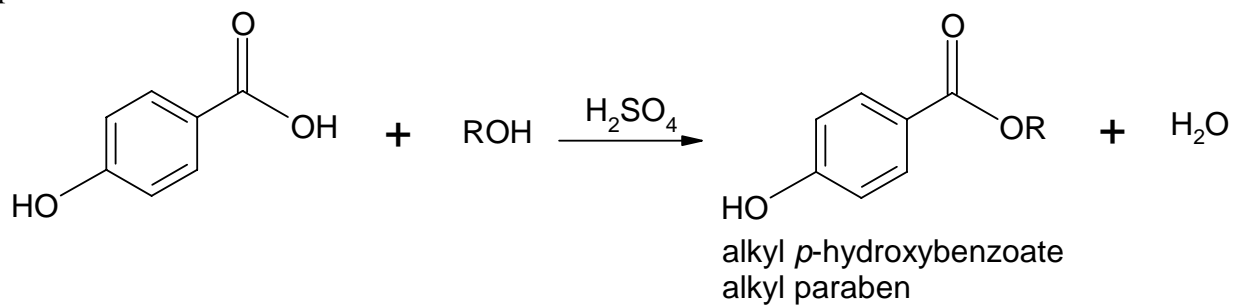
### Discussion

Estrogens are steroids that are important in the estrous cycle and function as the primary female hormones. Estrogens have been used medically including extensive use as birth control pills (combined with a synthetic progesterone analog) and in estrogen replacement therapy of postmenopausal women.



Diethylstilbesterol (DES) was first synthesized in 1938 and although not a steroid, was found to behave as an estrogen when administered to women. Because DES was relatively inexpensive and discovered to be very effective for some therapies such as treatment of prostate cancer, prevention of miscarriage, and treatment of advanced breast cancer, DES found wide usage in the mid-20th century. However, in 1971, DES was found to be a teratogen and its use was gradually phased out. In addition to the estrogen mimicker, DES, it has been found that many other compounds, both natural and synthetic, have estrogenic properties in the body. Since some of these properties cause increased risks such as the tendency to develop breast cancer, the presence of estrogens in our environment is a significant concern. Methods to decrease the use of synthetic estrogens deserves our attention.

For decades, cosmetic formulators have been using esters of *p*-hydroxybenzoic acid as preservatives. Commonly called parabens, these compounds are widely used because they are effective preservatives, reliable and cost effective. However, it has recently been discovered that parabens are weak estrogen mimickers and in addition might play a role in accelerating the rate of skin aging. Parabens are often found in low concentrations in breast cancers. Although the evidence that parabens could have negative health effects is still weak, some cosmetic formulators have replaced parabens with alternatives. The goal of this experiment will be to synthesize different alkyl parabens and to detect the presence of parabens in commercial products.



<u>alcohol</u>	<u>paraben</u>	<u>melting point (°C)</u>
methanol	methyl	127
ethanol (anhydrous)	ethyl	116
1-propanol	1-propyl	97
1-butanol	1-butyl	69

## Procedure

**Synthesis.** Assemble an apparatus with a 50 mL round bottom flask and a reflux condenser on a heating mantle preferably on a magnetic stirring unit. Transfer 0.020 moles of *p*-hydroxybenzoic acid and 10 mL of a selected alcohol (methanol, anhydrous ethanol, 1-propanol, 1-butanol) and a stirring bar or boiling chips into the round bottom flask. Stir to dissolve and carefully add 0.60 mL of concentrated sulfuric acid to the flask and reflux for about 2 hours. After cooling, transfer the contents of the flask to a separatory funnel that contains 5 mL of water and 5 mL of dichloromethane. Rinse the flask with a couple of mL of dichloromethane and add it to the separatory funnel. Shake the separatory funnel. Draw off the bottom organic phase and save it. Wash the aqueous layer with another 5 mL of dichloromethane and add the dichloromethane layer to the previously saved organic liquid. Appropriately dispose of the aqueous acidic layer that contains sulfuric acid and methanol. Wash the organic layer with a few mL of water followed carefully by 5 mL of 5% sodium bicarbonate twice (it will foam). Dry the organic layer over anhydrous magnesium sulfate. Remove the dichloromethane either by distillation or rotary evaporation. Purify as necessary using recrystallization or vacuum distillation. Determine the melting range of the product as well as appropriate spectra.

**Analysis.** The references below contain various method of analyzing parabens using thin layer chromatography. Select a method and try it with the product of your synthesis as well as some over the counter products that list parabens in their contents list. For the commercial product, it might be necessary to perform an extraction and a concentrating procedure.

## References

### synthesis

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### chromatography

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### uses, health effects, environmental issues

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<http://en.wikipedia.org/wiki/Paraben>  
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<http://www.mindfully.org/Pesticide/2004/Parabens-Breast-Significance1jan04.htm>  
<http://www.organicconsumers.org/bodycare/breastcancer090604.cfm>  
[http://ntp-server.niehs.nih.gov/ntp/htdocs/Chem\\_Background/ExSumPdf/Butylparaben.pdf](http://ntp-server.niehs.nih.gov/ntp/htdocs/Chem_Background/ExSumPdf/Butylparaben.pdf)

## Prelaboratory Preparation - *Experiment 40*

First, be sure to list all the goals of the experiment. Prepare a table for insertion of useful and observed data such as molecular mass, mass, moles, melting points and percent yields and recoveries. Decide which of the four possible parabens you would like to synthesize. Compare the structures of estradiol with DES. Can you find any structural features that could help understand why DES is an estrogen mimicker? Browse a cosmetics shelf in a store and list at least three products that have parabens on their content labels. Locate the synthesis on the *Reaction-Map of Organic Chemistry* in **Appendix C** and include the reaction number for the synthesis in this experiment in your report.

## Procedure and Observations

Report all relevant observations including, masses, melting ranges and all chromatography methods and results.

## Conclusions

This section should include the following:

1. Were the goals of the experiment achieved? Explain your answer.
2. What was the identity of your product and did it agree with your prediction? Explain your answer.
3. How pure was your product? Explain your answer.
4. What was the product yield and how could it have been improved?
5. Did your chromatographic procedure enable you to analyze for and distinguish between different parabens? Discuss the sensitivity of the procedure.
6. Were your results consistent with the product label? Explain your answer.
7. Comment on the use of parabens in cosmetics.