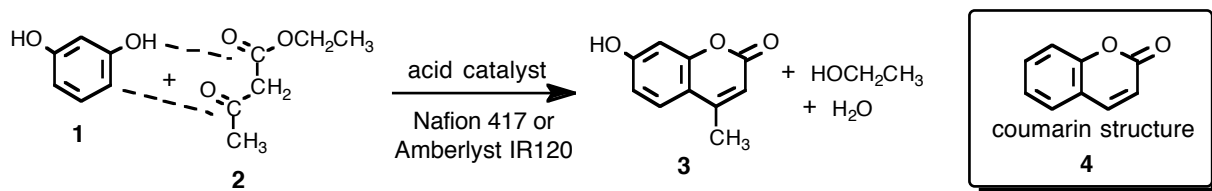


## The Pechmann Reaction

Adapted by M. Thimons, C.A.Chua, and M. Achalabun  
from an experiment by Michael S. Holden and R. David Crouch, (Dickinson College, Carlisle, PA) *J. Chem. Ed.*, 75, 12 (1998)

### Introduction:

In organic synthesis, it is not uncommon to produce a fairly complex structure via multiple reactions in a single step. For example, when the phenol, resorcinol, (**1**), is reacted with the ester, ethyl acetoacetate (**2**) in the presence of an acid catalyst, three reactions, hydroxyalkylation, transesterification, and dehydration occur concomitantly condensing together the two reactants at two sites to form the heterocycle **3**, which is called a coumarin. This is an example of the Pechmann reaction.



Coumarins have the general structure **4**. The most famous coumarin is warfarin which is used in low doses in humans as a blood thinner. In high doses, it is a rat poison that works by causing internal bleeding. The rat becomes very thirsty and goes outside seeking water. Thus, the dead rat carcass does not rot inside a building such as a granary. The coumarin **3**, 7-hydroxy-4-methylcoumarin, is not a blood thinner but rather is used commercially as laser dye<sup>2</sup>. It is also the starting material for the production of the insecticide Hymecromone<sup>3</sup>.

Usually, harsh condensation reagents are required for the reaction, leading to safety concerns. Recently solid acid catalysts have been found effective in the Pechmann reaction, making the reaction less hazardous. There are many commercially available solid acid catalyst, but in this reaction you will be using either Amberlyst IR120 or Nafion 417. Both these have  $\text{H}^+$  attached to the surface of a large polymer.

### Cautions:

Nafion 417 and Amberlyst IR120, although they look like very benign solids, are strongly acidic irritants. Avoid skin contact when handling them. Toluene is flammable and should be kept away from heating sources.

### Synthesis:

In one reaction tube, place a boiling chip and 2 to 3 mL of toluene and start heating gently on a sand bath so that it barely refluxes. In another reaction tube, place 220 mg resorcinol (2.0 mmol), 0.25 mL ethylacetoacetate (260 mg, 2.0 mmol), toluene (1.5ml), a 1-cm stirbar and two 2 x 20 mm pieces of Nafion 417 acid catalyst sheet (or 0.2 g Amberlyst 16 acid catalyst). While stirring, heat this tube for 90 min so that the toluene gently refluxes and toluene vapors barely come out the top of the reaction tube. Remember that you can adjust the rate of reflux by adjusting the depth of the tube in the sand bath. If the toluene level drops a few mm, add some preheated toluene from the supply tube.

### Isolation and Purification:

Let the mixture cool to room temperature and add 2mL of warm methanol to dissolve all of the white solid. Vacuum filter the mixture on a Hirsh funnel to remove the brown acid strips or resin and wash with a little warm methanol. Put the used Nafion 417 pieces into the recycling vial that is attached to the Nafion supply bottle. Allow the toluene and methanol to evaporate from the filter flask until the next lab period. Take a <sup>1</sup>H NMR of the crude product. Recrystallize the light orange solid with a 1:1 mixture of methanol and water. Cool the mixture in an ice-bath for several minutes. Collect the precipitate by vacuum filtration using a Hirsh funnel and wash the off-white solid with some cold 1:1 methanol:water. Let the product air dry, weigh it., take its mp and prepare the samples accordingly for IR, <sup>1</sup>H NMR and <sup>13</sup>C NMR, and GC-MS analyses.

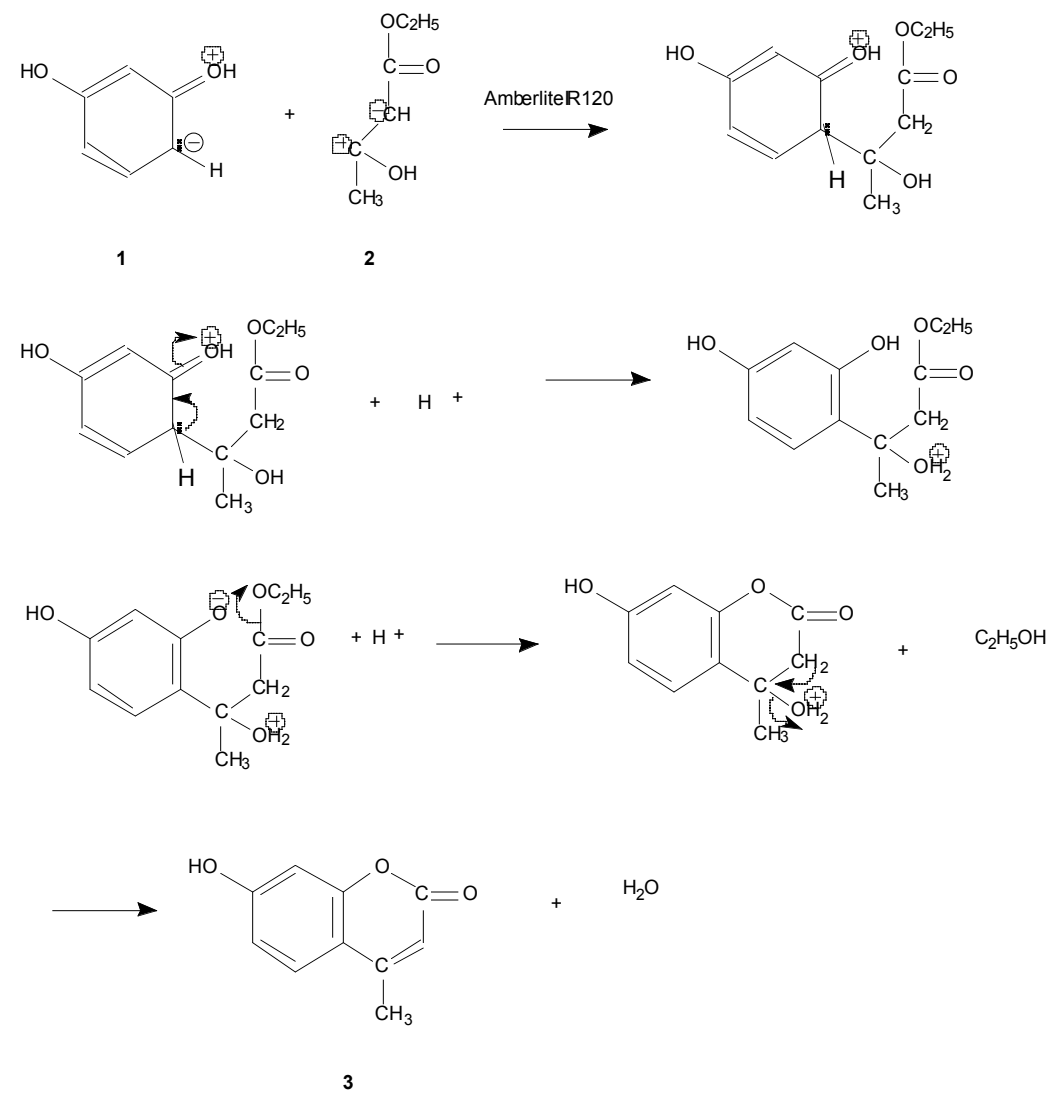
### Cleaning-up:

Any filtrate should be disposed of in the nonhalogenated waste container. If you used Amberlyst IR16, neutralize with sodium bicarbonate before discarding it into the trash can.

**Final Report:**

Calculate the % yield. Typical yields are about 40 to 50%. Draw the structure and interpret the spectral data. Do this exercise and include in the Discussion section of your final report:

Below is the mechanism for the reaction of resorcinol and ethyl acetoacetate. Redraw this mechanism and label which step or steps is/are the hydroxyalkylation (a type of electrophilic aromatic substitution), which step(s) is/are the dehydration and which is/are the transesterification.



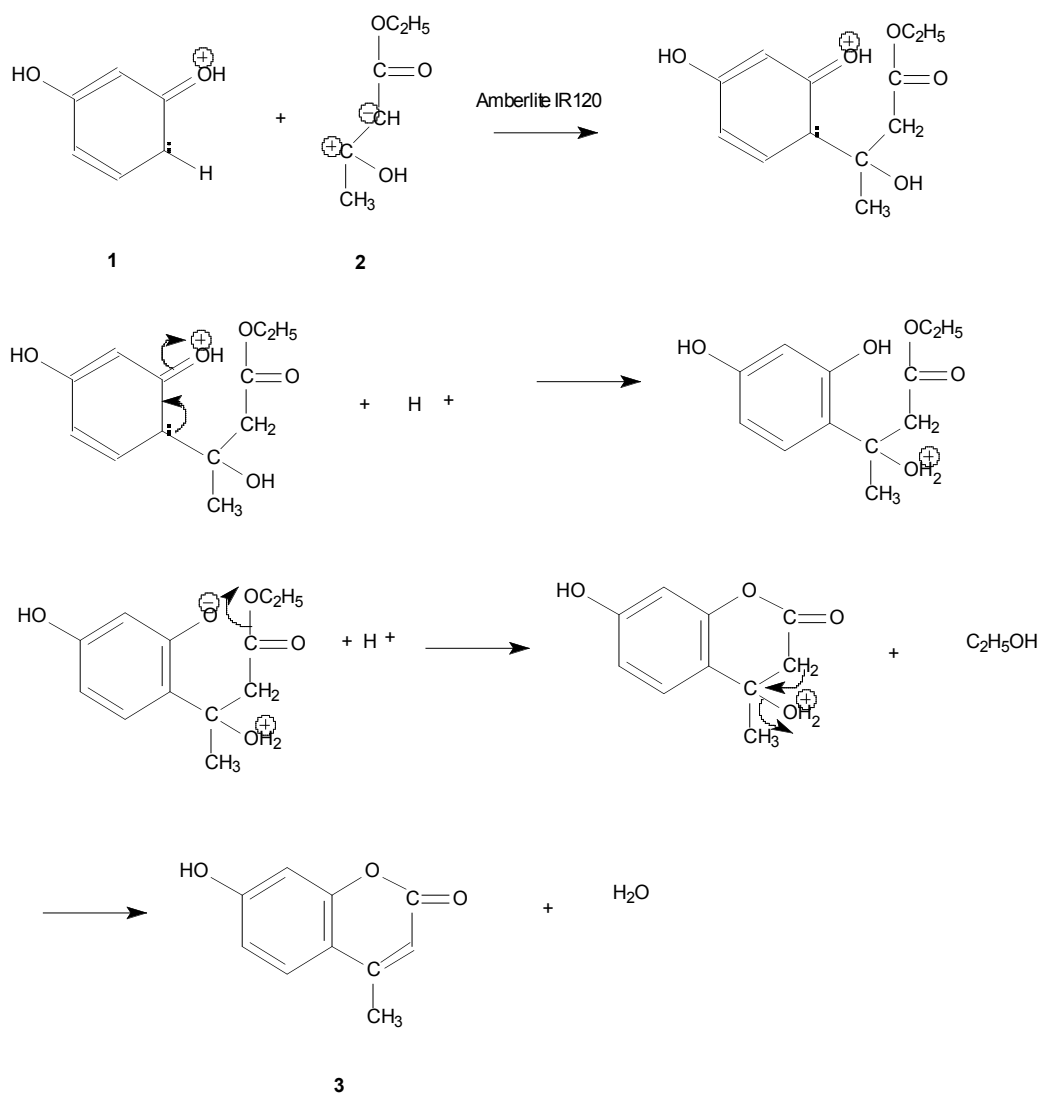
## Results and Discussion

7-hydroxy-4-methylcoumarin was produced in 15% yield by refluxing resorcinol and ethylacetoacetate in toluene for 90 min. Amberlite IR120 was used as condensing agent and water is removed azeotropically. Purified **3** formed as an off-white powder and the mechanism is shown in Scheme 1. As a result of resonance, resorcinol has a center of high electron density at its ortho position to the other OH group<sup>4</sup>. Hence, resorcinol is added to the enolic form of ethylacetoacetate via nucleophilic attack. Ethanol is eliminated during the process of ring closure. Hydrogen ion from the acid resin causes dehydration and produces an olefinic bond.

The IR spectra (spectra A) showed distinctly strong absorptions at  $1070\text{ cm}^{-1}$  for

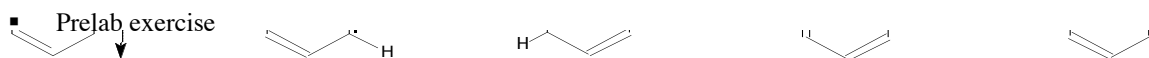
C-O, at  $1500\text{ cm}^{-1}$  for the aromatics, and at  $1700\text{ cm}^{-1}$  for C=O. The absorptions are within the range of comparison spectra B<sup>5</sup> at  $1069, 1602, 1679,$  and  $3163\text{ cm}^{-1}$  respectively. The

H NMR showed the characteristic doublet<sup>6</sup> of methylene at 2.5ppm, vinylic proton at 6.4ppm, and three aromatic protons at 5.1, 5.9, and 7.2 ppm. The uncorrected mp was  $179\text{-}181^\circ\text{C}$  and this closely matches the literature value of  $180\text{-}182^\circ\text{C}$ <sup>1</sup>.



## Scheme 1

### Answers:



### Final report

Please refer to the results and discussion section for complete reaction mechanism of resorcinol and ethylacetoacetate.

Yes. The reaction will still occur but less reactively. The other OH group meta to the hydroxyl group in resorcinol acts as an electron-donating group and hence enhances the effectiveness of its addition to ethylacetoacetate<sup>7</sup>.

### References

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