



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

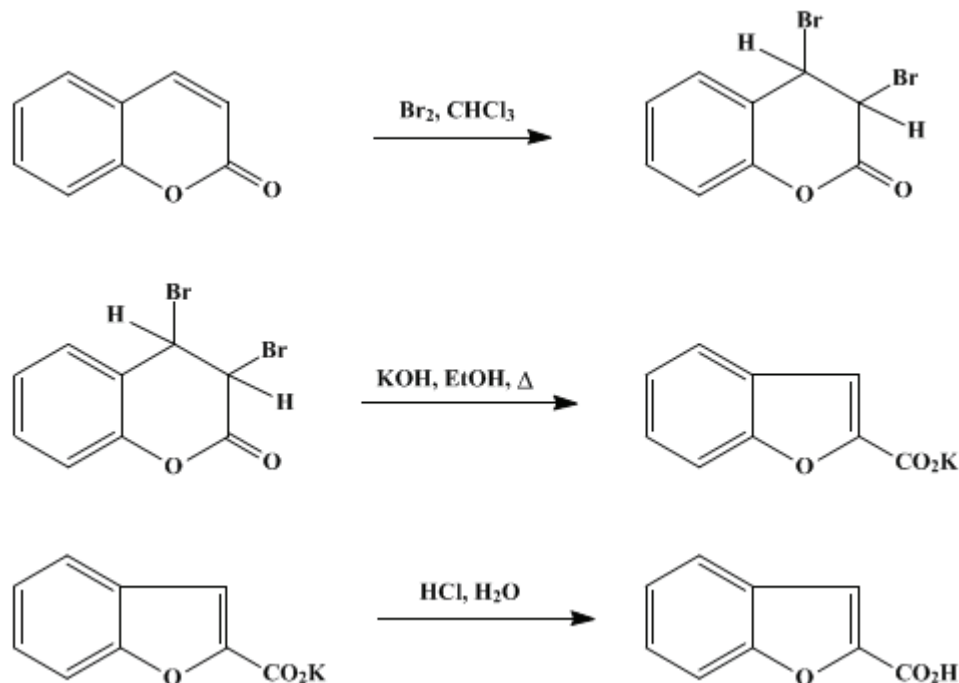
In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 3, p.209 (1955); Vol. 24, p.33 (1944).

COUMARILIC ACID



Submitted by R. C. Fuson, J. Wayne Kneisley, and E. W. Kaiser.
Checked by W. E. Bachmann and G. Dana Johnson.

1. Procedure

A. *Coumarin dibromide*. In a 1-l. three-necked flask, equipped with a mechanical stirrer, a dropping funnel, and a condenser fitted with a trap for hydrogen bromide, are placed 146 g. (1 mole) of coumarin and 200 ml. of chloroform. A solution of 160 g. (1 mole) of bromine in 85 ml. of chloroform is added dropwise to the well-stirred solution of coumarin at room temperature over a period of 3 hours (Note 1). Excess bromine is removed by adding approximately 200 ml. of a 20% solution of sodium sulfite through the dropping funnel. The colorless chloroform layer is separated, washed with two 200-ml. portions of water, and dried over magnesium sulfate (Note 2). After the mixture has stood for only a few minutes (Note 3), the magnesium sulfate is removed by filtration and the solution of the dibromide is evaporated to 100 ml. in a rapid stream of dry air (Note 4). The coumarin dibromide is collected on a filter, and the mother liquor is evaporated nearly to dryness by an air blast. This mixture is filtered, and the slightly yellow mother liquor is evaporated to dryness. The product of the third evaporation is slightly discolored, and it is washed with two 15-ml. portions of ether (Note 5). The combined precipitates weigh 215 g. (70%) and melt at 102–105° (Note 6).

B. *Coumarilic acid*. In a 5-l. three-necked flask fitted with a mechanical stirrer and reflux condenser, 450 g. (8 moles) of solid potassium hydroxide is dissolved in 700 ml. of absolute ethanol. The solution is cooled to 15° by immersing the flask in an ice bath, and 215 g. (0.7 mole) of finely divided coumarin dibromide is added in 10- to 15-g. portions to the well-stirred basic solution. The rate of addition is controlled so that the temperature never rises above 20°; the addition requires about 30 minutes. After all the dibromide has been added, the reaction mixture is refluxed, with stirring, for 30 minutes (Note 7). One and a half liters of water is added, and the resulting solution is steam-distilled until 2.5 l. of distillate has been collected (Note 8). The residue is cooled to room temperature by the addition of 1 kg. of cracked ice (Note 9) and is then acidified by the addition of 1.2 l. of 6 *N* hydrochloric acid. The crude coumarilic acid is collected on a filter and stirred with 600 ml. of cold water. The acid is separated from the water by filtration, sucked as dry as possible on the filter, and then

crystallized from a mixture of 250 ml. of ethanol and 250 ml. of water (Note 10). The recrystallized coumarilic acid is colorless, weighs 93–100 g. (82–88%) (Note 11), and melts at 190–193°.

2. Notes

1. Occasional use of an ice bath is necessary to keep the temperature from rising.
2. If any coumarin dibromide separates before the magnesium sulfate is removed, enough chloroform should be added to dissolve the dibromide.
3. The mixture should be worked up immediately in order to avoid decomposition of the dibromide.
4. The checkers found that considerable decomposition occurred when this procedure was employed, perhaps because it happened to be carried out on a warm, humid day; they found it preferable to remove the chloroform by distillation under reduced pressure from a water bath at this step and the succeeding ones. Because of the instability of the dibromide, it is advisable to convert it to coumarilic acid on the day it is made.
5. The first evaporation produces 136 g. of colorless crystals; the second, 63 g.; and the third, 16 g. of ether-washed product.
6. The first crop of crystals melts at 102–105°. The succeeding products melt somewhat lower but are sufficiently pure for the next reaction.
7. The suspension of potassium bromide must be stirred vigorously to avoid bumping.
8. The steam distillation is carried out conveniently by fitting the reaction vessel with a steam inlet tube and a condenser set for downward distillation. The flask should be heated so that the final volume of the distilland is not more than 3 l.
9. A heavy precipitate composed of potassium coumarilate and potassium bromide may appear if the steam distillation has been very efficient. The precipitate dissolves during the addition of hydrochloric acid.
10. The crude acid is dissolved in 250 ml. of boiling absolute ethanol to which has been added 3 g. of Norit; 250 ml. of water, previously heated to 85°, is then added to the filtered solution.
11. The over-all yield, based on the amount of coumarin, is 57–62%.

3. Discussion

Coumarilic acid has been prepared by treating coumarin dibromide with alcoholic potassium hydroxide and acidifying with hydrochloric acid, a method due essentially to Perkin.¹ Coumarilic acid has also been prepared by Perkin from 3-chlorocoumarin and from 3-bromocoumarin by the action of alcoholic potassium hydroxide.²

Coumarilic acid has also been prepared from 2-bromobenzofuran by reaction with *n*-butyllithium and subsequent carbonation³ and by the oxidation (NaOCl) of 2-acetylbenzofuran.⁴

Coumarin dibromide has been prepared by the addition of bromine to coumarin in chloroform solution.^{1,2}

References and Notes

1. Perkin, *J. Chem. Soc.*, **23**, 368 (1870).
2. Perkin, *J. Chem. Soc.*, **24**, 37 (1871).
3. Gilman and Melstrom, *J. Am. Chem. Soc.*, **70**, 1655 (1948).
4. Farrar and Levine, *J. Am. Chem. Soc.*, **72**, 4433 (1950).

ethanol (64-17-5)
hydrochloric acid (7647-01-0)
ether (60-29-7)
sodium sulfite (7757-83-7)
chloroform (67-66-3)
hydrogen bromide (10035-10-6)
bromine (7726-95-6)
potassium hydroxide (1310-58-3)
potassium bromide (7758-02-3)
NaOCl (7681-52-9)
magnesium sulfate (7487-88-9)
n-butyllithium (109-72-8)
coumarin
Coumarin dibromide (55077-11-7)
3-chlorocoumarin
3-bromocoumarin
2-bromobenzofuran
2-acetylbenzofuran (1646-26-0)
Coumarilic acid (496-41-3)
potassium coumarilate