

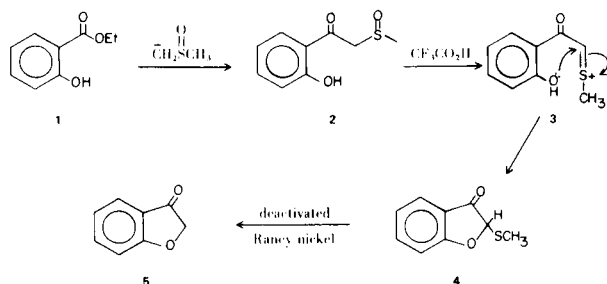
Synthesis of 3-Coumaranone

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It has been shown (2) that the Pummerer rearrangement intermediate, **3**, is formed and cyclizes *via* an intramolecular nucleophilic substitution to give **4**, when the β -ketosulfoxide **2** is heated with trifluoroacetic acid. In principle, this transformation could be utilized to convert salicylic acid derivatives to 3-coumaranones (**5**) in a direct three-step sequence. What is needed is a way to reductively cleave the thiomethyl group of **4**. This paper describes a method for achieving this reduction.



Reaction of ethyl salicylate (**1**) with 3.2 equivalents of the methylsulfinyl carbanion (**4**) afforded 2-hydroxy-1-[(methylsulfinyl)acetyl]benzene (**2**) in 92% yield. Cyclization of the β -ketosulfoxide **2** to 2-methylthio-3-coumaranone (**4**) in 91% yield was effected by refluxing for 30 minutes in benzene in the presence of two equivalents of trifluoroacetic acid. The final step, reductive cleavage of the thiomethyl group of **4** using *deactivated* W-2 Raney-nickel, afforded the desired 3-coumaranone (**5**) in 75% yield.

Deactivation of the catalyst was accomplished by stirring it in 25% acetone-methylene chloride at reflux for 30 minutes prior to the addition of **4**. Failure to deactivate the catalyst in this manner gave reduction of **4** to at least six products (by tlc). The high yield for the conversion of **2** to **4** is a definite improvement over the yield of 45% obtained previously (2). Also, this method provides a means for converting the salicylate **1** to the parent 3-coumaranone.

EXPERIMENTAL

2-Hydroxy-1-[(methylsulfinyl)acetyl]benzene (**2**).

To a solution of 0.16 mole of the methylsulfinyl carbanion (**4**) in 75 ml. of dry dimethyl sulfoxide (under nitrogen) was added 75 ml. of dry tetrahydrofuran, and the temperature was lowered to 5°. A solution of 8.30 g. (0.05 mole) of ethyl salicylate in 20 ml. of dry tetrahydrofuran was added over a 5-minute period, and the cooling bath was removed. After 30 minutes the reaction mixture was poured into 600 ml. of cold water. The solution was acidified with aqueous hydrochloric acid, and then extracted with chloroform (4 X 250 ml.). The organic layers were combined, dried over anhydrous magnesium sulfate, filtered, and concentrated to give a white solid which was triturated with 250 ml. of ether to afford 9.05 g. (45.7 mmoles, 91.5%) of the desired **2**, m.p. 151-152°. Recrystallization from absolute ethanol raised the melting point to 153° (lit. (5), m.p. 152-154°).

2-Methylthio-3-coumaranone (**4**).

A solution of 2.38 g. (12.0 mmoles) of **2**, 2.74 g. (24.0 mmoles) of trifluoroacetic acid, and 180 ml. of benzene was refluxed for 30 minutes, cooled quickly to room temperature, and extracted with saturated sodium bicarbonate solution (2 X 300 ml.). The organic layer was dried over anhydrous magnesium sulfate, filtered, and concentrated to give 1.97 g. (10.92 mmoles, 91%) of **4**, m.p. 76-80° (essentially pure by nmr). Recrystallization from 5% ether-hexane raised the melting point to 81-82°. The spectral data and melting point agree with those in the literature (2,5).

3-Coumaranone (**5**) from **4**.

Two teaspoonsful (approximately 6 g.) of W-2 Raney-nickel was deactivated by refluxing with 50 ml. of 20% acetone-methylene chloride for 45 minutes. Pure 2-methylthio-3-coumaranone (**4**) (0.61 g., 3.38 mmoles) in 5 ml. of methylene chloride was added in one portion. After 90 minutes of stirring at reflux, the reaction was cooled to room temperature and the solution was decanted from the catalyst. The catalyst was then washed successively with 50 ml. of methanol and two 50-ml. portions of methylene chloride. The combined organic layers were filtered through a celite pad and the filtrate was concentrated. The residue was taken up in 100 ml. of methylene chloride, dried over anhydrous magnesium sulfate, filtered, and concentrated to give 0.46 g. of crude 3-coumaranone. Column purification (70 g. of 60-200 mesh silica gel, using 40% methylene chloride-hexane as eluent) afforded 0.340 g. (2.53 mmoles, 75% yield) of pure 3-coumaranone, m.p. 100° (lit. (3-11b), m.p. 100°); ir (potassium bromide): 5.87, 6.29, 6.85, 7.70, 8.42, 8.70, 9.08, 10.13, 11.96, and 13.19 μ ; nmr (deuteriochloroform): τ 2.20-3.10 (4H, m, arom), and 5.38 (2H, s, CH₂).

3-Coumaranone (**5**) directly from **2**.

If **2** is converted to **5** in two steps (*vide supra*) without the isolation of **4**, the overall yield of 3-coumaranone is 64%, based on **2**.

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