

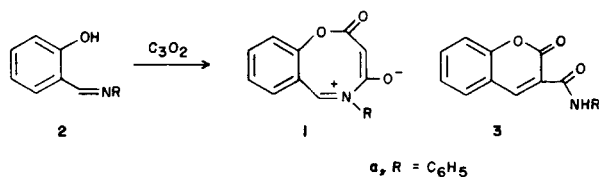
Howard Sard*, Peter C. Meltzer and Raj K. Razdan

SISA Pharmaceutical Laboratories, Inc., 763D Concord Avenue,
Cambridge, MA, 02138 USA

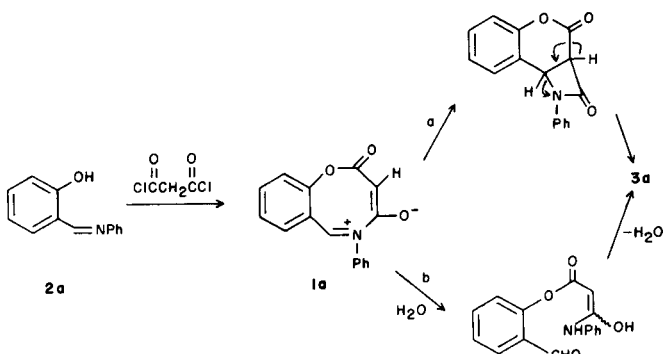
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The reaction of *o*-hydroxybenzylideneamine and malonyl dichloride produces coumarin-3-carboxanilide.*J. Heterocyclic Chem.*, **22**, 257 (1985).

As part of our program to prepare potential chemotherapeutic agents [1], we needed to synthesize the 1,5-benzoxazocine **1a**. In 1982, Bonsignore, *et al.*, had reported [2] the synthesis of compounds **1** from imines **2** and carbon suboxide. Since we required large quantities of **1a**, we chose to repeat their synthesis using commercially available malonyl dichloride rather than the relatively inaccessible carbon suboxide. Malonyl dichloride has been substituted for carbon suboxide previously in the synthesis of similar compounds [3,4]. On the basis of known infrared [5] and melting point data, Boulton [6] had proposed structures **3** for the product obtained by the earlier researchers with carbon suboxide. We now report that reaction of **2a** and malonyl dichloride also produces coumarin **3a**, rather than the desired **1a**, supporting the revised structural assignment.



A reasonable mechanism for this transformation involves **1a** as intermediate, which can either undergo intramolecular rearrangement (route a), or, more likely, hydrolysis followed by dehydration (route b) [7].



EXPERIMENTAL

Melting points were determined on a Thomas-Hoover capillary or Fisher-Johns melting point apparatus and are uncorrected. The nmr spectra were recorded on a Varian T-60 spectrometer. Spectra are expressed in parts per million from TMS as internal standard. Infrared spectra were obtained on a Perkin-Elmer 700 spectrometer. Microanalyses were performed by Atlantic Microlab, Inc.

Coumarin-3-carboxanilide (**3a**).

A solution of the imine **2a** (11.4 g, 58 mmoles) [8] in xylene (150 ml) was added to a solution of malonyl dichloride (8.1 g, 58 mmoles) in xylene (60 ml) dropwise at 25°. A yellow precipitate formed instantly, which soon turned orange. After 10 minutes, an aqueous solution of sodium bicarbonate was added, followed by ethyl acetate, and the reaction mixture was stirred for 1 hour. The organic layer was separated, the aqueous layer was extracted with ethyl acetate, and the combined organic layers were dried (magnesium sulfate), filtered, and concentrated. The residue was washed with hexane and dried to give 5.6 g of **3a** as a yellow solid (37%). Recrystallization from chloroform-ethanol gave a pure sample of **3a** as yellow needles, mp 253.5-255.0°, (lit [2] for **1a** 245°, lit [10] for **3a** 247°); ir (potassium bromide): 1700, 1595, 1545, 1440 and 1200 cm⁻¹; ¹H-nmr (deuteriochloroform and trifluoroacetic acid): δ 10.88 (s, 1H, exchanges with deuterium oxide, NH), 9.05 (s, 1H, =C-H), 6.75-7.85 (m, 9H, Ar-H); ms: m/e (relative intensity) 265 (M⁺, 47), and 173 (M⁺ -NHC₆H₅, 100).

Anal. Calcd. for C₁₆H₁₁NO₃: C, 72.45; H, 4.18; N, 5.28. Found: C, 72.26; H, 4.20; N, 5.23.

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REFERENCES AND NOTES

- [1] Carried out under Master Contract NO1-CM-37637 awarded by the National Cancer Institute.
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- [7] We thank Sir Derek H. R. Barton for this suggestion.
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