

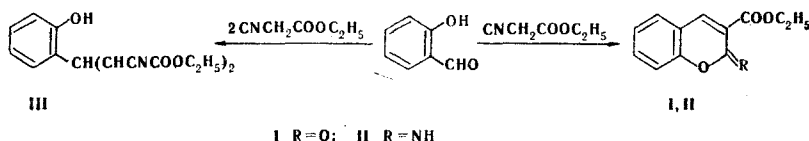
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## SYNTHESIS OF FUNCTIONALLY SUBSTITUTED COUMARINS\*

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We have found that the interaction of salicylaldehyde with ethyl cyanoacetate in the presence of sodium ethoxide or potassium carbonate at room temperature for 40-48 h forms a mixture of 3-ethoxycarbonylcoumarin (I) and 2-imino-3-ethoxycarbonylcoumarin (II) in 5 and 35% yield (with sodium ethoxide) or 4 and 32% yield (with potassium carbonate), respectively.



Increase in the amount of ethyl cyanoacetate caused the yield of (II) to rise. When a twofold excess of ethyl cyanoacetate was used, we obtained only (II) in almost quantitative yield (~93%).

Treatment of the reaction mixture with dilute hydrochloric acid (1:1) (25°C, 18 h) gave a single reaction product, 3-ethoxycarbonylcoumarin in 80% yield.

\*Communication 42; for Communication 41 see [1].

2-Imino-3-ethoxycarbonylcoumarin when refluxed in the presence of acids and bases for 6-8 h formed 3-carboxycoumarin (IV) in good yield.

Several workers have described the interaction of salicylaldehyde with cyanoacetic ester in the presence of piperidine [2, 3] and Amberlite [4]. The major product was a crystalline substance corresponding in melting point to 2-imino-3-ethoxycarbonylcoumarin. However they identified this compound as diethyl salicylidene-biscyanoacetate (III). The IR spectrum of (II) contains absorption bands at 1730, 1620, and 1570  $\text{cm}^{-1}$ , characteristic of ester C=O stretching, C=C stretching, and benzene ring vibrations, 1630 and 1680  $\text{cm}^{-1}$  (C=N), and 3300-3430  $\text{cm}^{-1}$  (NH group). We determined the molecular weights of products (I) and (II) by mass spectrometry.

Passage of gaseous hydrogen chloride through a solution of (II) in absolute benzene formed the hydrochloride of (II) in quantitative yield.

## EXPERIMENTAL

Interaction of Salicylaldehyde with Ethyl Cyanoacetate in the Presence of Sodium Ethoxide or Potassium Carbonate. A. To a solution of sodium ethoxide (from 0.23 g, 0.01 mole Na) (or potassium carbonate) in absolute ethanol (25 ml) were added salicylaldehyde (6.10 g, 0.05 mole) and ethyl cyanoacetate (6.78 g, 0.06 mole). The mixture was left at room temperature for two days. The alcohol was then stripped off. The residue was acidified with dilute hydrochloric acid (1:1) and extracted with ethyl acetate. The extract was dried over anhydrous magnesium sulfate. After removal of the solvent, the mixture was treated with ether and filtered. The precipitate was recrystallized from benzene to give (II) (3.8 g, 35% with sodium ethoxide and 3.5 g, 32.2% with potassium carbonate), mp 136-137°C (from alcohol). Found: C 66.1; H 5.2; N 6.6%.  $\text{C}_{12}\text{H}_{11}\text{NO}_3$ . After removal of the ether the residue was recrystallized from ethanol to give (I) (0.55 g, 5% with sodium ethoxide and 0.44 g, 4% with potassium carbonate). Literature [3]: mp 94°C (from alcohol). Found: C 65.8; H 4.8%.  $\text{C}_{12}\text{H}_{10}\text{O}_4$ . Calculated: C 66.1; H 4.6%.

B. The reaction was carried out as described above but with ethyl cyanoacetate (11.3 g, 0.1 mole), giving (II) (10 g, 92.6% with sodium ethoxide and 9.8 g, 90% with potassium carbonate).

C. The reaction was carried out as described in b) but after removal of the alcohol the residue was acidified with dilute hydrochloric acid and left overnight. The reaction mixture was then extracted with benzene and dried over anhydrous magnesium sulfate. Removal of benzene gave (I) (8.7 g, 80% with sodium ethoxide and 7.95 g, 73% with potassium hydroxide), mp 93-94°C (from alcohol).

2-Imino-3-ethoxycarbonylcoumarin Hydrochloride, mp 114-116°C. Found: C 56.5; H 4.6; N 6.1%.  $\text{C}_{12}\text{H}_2\text{ClNO}_3$ . Calculated: C 56.8; H 4.7; N 5.7%.

Acid and Base Hydrolysis of 2-Imino-3-ethoxycarbonylcoumarin. A. Compound (II) (1.08 g, 5 mmole) was heated in 20% hydrochloric acid (5 ml) with stirring for 1 h 30 min. Filtration and recrystallization from xylene gave 3-carboxycoumarin (IV) (0.8 g, 82%) with mp 187-188°C. Literature [5]: mp 187-188°C (from xylene).

B. Compound (II) (1.08 g, 5 mmole) was heated with NaOH (0.6 g) in alcohol (6 ml) at 90-95°C for 8 h. The alcohol was stripped off. The residue was dissolved in water and acidified (to pH 3-4) with hydrochloric acid. The precipitated crystals were filtered off and recrystallized from xylene to give (IV) (0.48 g, 50%).

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