SOME NEW REACTIONS OF COUMARINS

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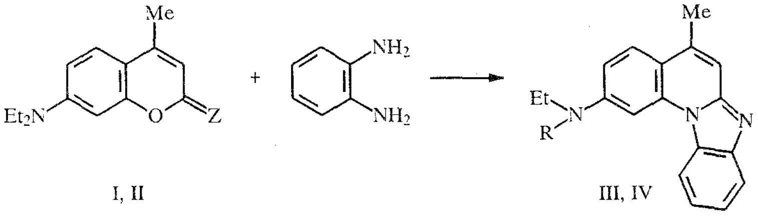
The direction of the reaction of coumarin derivatives with o-phenylenediamine depends on their structure, leading to 2-(2'-hydroxyphenyl)benzimidazole in the case of unsubstituted coumarin and to derivatives of benzimidazo[1,2-a]quinoline in the case of 7-amino-substituted coumarins.

Derivatives of benzimidazo[1,2-*a*]quinolines, which have a number of practically important properties, are obtained by the reaction of o-methoxybenzaldehydes with benzimidazoles containing an activated methylene group at position 2 [1-3]. In order to study the possibility of routes to new derivatives of benzimidazo[1,2-*a*]quinolines, we have investigated the interaction of a series of coumarins and their thio derivatives with o-phenylenediamine. In fact, 2-N-ethylamino-5-methylbenzimidazo[1,2-*a*]quinoline (III) was formed in 18% yield when 7-diethylamino-4-methylcoumarin (I) reacted with o-phenylenediamine in the presence of acid catalysts (polyphosphoric acid, hydrogen chloride).



I Z=O, II Z=S, III R=H, IV R=Et

The mechanism of this reaction evidently includes opening of the pyrone ring of the coumarin, formation of the benzimidazole unit, and subsequent closing of the six-membered heterocycle.

When 7-diethylamino-4-methyl-2-thiocoumarin (II) is used the reaction can occur under milder conditions in the absence of a catalyst thanks to the greater reactivity of the C=S bond. Dealkylation of the diethylamino group does not occur and the yield of 2-diethylamino-5-methyl[1,2-*a*]quinoline (IV) reached 26%.

Unlike the aminocoumarins I and II, when unsubstituted coumarin was melted with o-phenylenediamine at 260°C, 2-(2'-hydroxyphenyl)benzimidazole (IX) was produced in low yield together with tarry products. The structure of IX was confirmed by retrosynthesis [4].

Replacement of the carbonyl oxygen by sulfur permits the reaction to be carried out under milder conditions so that compound IX was isolated in 32% yield.

The direction of the reaction is not changed by introduction of a methyl group at position 4 (compounds VII and VIII).

The long-wavelength absorption bands of the benzimidazo[1,2-*a*]quinolines III and IV are bathochromically shifted somewhat in comparison with the initial coumarin (~20 nm in ethanol). They are luminescent (λ_{lum}^{max} = 435 nm) with a quantum yield of ~0.6 (see below).

Hence the direction of the reaction of substituted coumarins with o-phenylenediamine depends on the presence of substituents in the coumarin molecule. In the case of 7-aminocoumarins, thanks to the greater polarization of the carbonyl group, the reaction produces a poorly-studied class of luminescent dyestuffs, derivatives of benzimidazo[1,2-*a*]quinoline.

EXPERIMENTAL

Absorption spectra were recorded on a Specord UV-VIS spectrophotometer. Fluorescence obtained with an SLM 4800S phase spectrofluorometer, IR spectra of KBr disks with a Zeiss UR-20 spectrometer, and mass spectra were measured on an MX-1320 instrument at an ionizing voltage of 50 eV. Silufol UV-254 plates were used for TLC.

Purity of substances was monitored by TLC. Experimental elemental analyses for C, H, N, and S agreed with calculated values.

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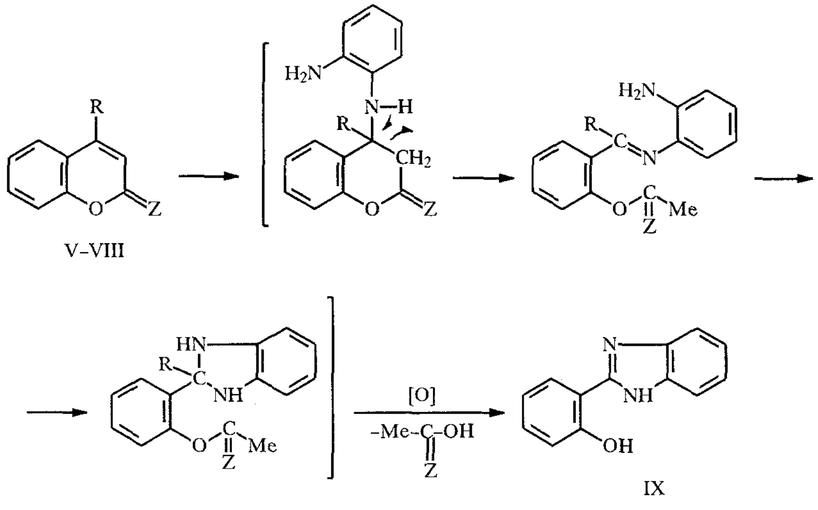

V R=H, Z=O; VI R=H, Z=S; VII R=Me, Z=O; VIII R=Me, Z=S

2-N-Ethylamino-5-methylbenzimidazo[1,2-*a*]quinoline (III, $C_{18}H_{17}N_3$). A. A solution of 7-diethylamino-4-methylcoumarin (I) (4.62 g, 20 mmoles) and o-phenylenediamine (2.38 g, 22 mmoles) in polyphosphoric acid (30 g) was heated to 240°C and stirred at 240-250°C for 3 h. The reaction mass was cooled, poured into water (150 ml), and neutralized with 10% sodium hydroxide solution. The precipitate was filtered off, dried, and extracted with ethyl acetate (4 × 50 ml). The extracts were washed with water, dried over $CaCl_2$, and concentrated. Compound III was isolated by chromatography (silicagel 40/100, ethyl acetate eluent) and recrystallized from toluene (1.01 g, 18%), mp 245-246°C. Mass spectrum: M^+ 275. IR spectrum (cm^{-1}): 3278 (N—H), 1647 and 1620 (C=C, C=N), 1578 cm^{-1} (N—H). Absorption spectrum (ethanol), λ_{max} (log ε): 374 (4.32), 392 nm (4.28). Fluorescence spectrum (ethanol): λ_{max} 432 nm. Quantum yield η = 0.62.

B. A thoroughly blended mixture of coumarin (I) (0.92 g, 4 mmoles) and o-phenylenediamine dihydrochloride (0.80 g, 4.4 mmoles) was heated in a sealed ampul for 2 h at 230-240°C. The cooled reaction mixture was treated with sodium carbonate solution and extracted with ethyl acetate (2 × 30 ml). The extract was filtered and evaporated and the resultant residue was crystallized from a toluene—octane mixture to give compound III (0.12 g, 11%).

7-Diethylamino-4-methyl-2H-1-benzopyran-2-thione (II, $C_{14}H_{17}NOS$). P_2S_5 (8.88 g, 40 mmoles) was added with stirring to a hot solution of coumarin I (8.09 g, 35 mmoles) in toluene (50 ml) and the mixture was boiled for 3 h. The toluene solution was decanted and the residue extracted with ethyl acetate (2 × 30 ml). The solutions were combined and evaporated in vacuum. The product was isolated chromatographically (silicagel 40/100, eluent benzene—ethyl acetate) and recrystallized from heptane to give the thiocoumarin II (4.37 g, 51%), mp 95-96°C. IR spectrum: 1633 cm^{-1} (C=C).

2-Diethylamino-5-methylbenzimidazo[1,2-*a*]quinoline (IV, $C_{20}H_{21}N_3$). A carefully blended mixture of thiocoumarin II (0.50 g, 2 mmoles) and o-phenylenediamine (0.27 g, 2.5 mmoles) was heated in a sealed ampul for 1 h at 180-200°C. After cooling, the reaction mixture was extracted with ethyl acetate (2 × 30 ml), the extract was filtered, the solvent removed in vacuum, and the resultant residue was crystallized from heptane plus activated carbon to give compound IV (0.16 g, 26%), mp 137-138°C. Mass spectrum: M^+ 303. IR spectrum: 1642 and 1620 cm^{-1} (C=C, C=N). Absorption spectrum (ethanol): λ_{max} (log ε): 378 (4.36), 400 nm (4.37). Fluorescence spectrum (ethanol): λ_{max} 440 nm. Quantum yield η = 0.65.

2H-1-Benzopyran-2-thione (VI). P_2S_5 (10 g, 45 mmoles) was added to a solution of coumarin V (10 g, 68.5 mmoles) in toluene (25 ml) and the mixture was boiled for 2 h. The toluene was evaporated in vacuum and the residue recrystallized from ethanol to give the thiocoumarin VI (8.96 g, 81%), mp 98-99°C; the literature [6] gives mp 99°C.

4-Methyl-2H-1-benzopyran-2-thione (VIII). P_2S_5 (4.2 g, 19 mmoles) was added to a solution of 4-methylcoumarin VII (4.2 g, 26 mmoles) in toluene (15 ml) and the mixture was boiled for 2 h. The toluene was evaporated in vacuum and ethanol (120 ml) and activated carbon (2 g) was added to the residue. The mixture was boiled for 10 min, cooled, filtered, and the ethanol evaporated to 30-35 ml. The precipitate which appeared on cooling was filtered off and washed with cold ethanol (10 ml) to give compound (VIII) (2.57 g, 56%), mp 117-118°C. The literature [7] gives mp 118.5°C.

2-(2′-Hydroxyphenyl)benzimidazole (IX). A. A mixture of coumarin V (1.46 g, 10 mmoles) and o-phenylenediamine dihydrochloride (1.99 g, 11 mmoles) was heated to 260°C and kept at 260-265°C for 2.5 h. The melt was cooled, extracted with ethyl acetate (3 × 30 ml), the extract filtered and evaporated. Purification by chromatography (silicagel 40/100, eluent benzene—ethyl acetate), and recrystallization from toluene gave compound IX (0.14 g, 7%), mp 239-240°C; the literature [4] gives 241.6-242.2°C.

B. When coumarin VII (1.60 g, 10 mmoles) and o-phenylenediamine dihydrochloride (1.99 g, 11 mmoles) were melted together under analogous conditions, compound IX was obtained (0.12 g, 6%).

C. A mixture of thiocoumarin VI (1.62 g, 10 mmoles) and o-phenylenediamine dihydrochloride (1.30 g, 12 mmoles) was heated to 200°C, maintained at 200-210°C for 1.5 h, and cooled. The solid dissolved in a mixture of benzene and ethyl acetate and was chromatographed on a column (silicagel 40/100, eluent benzene—ethyl acetate), and recrystallized to give compound IX (0.67 g, 32%).

D. When thiocoumarin VIII (1.76 g, 10 mmoles) and o-phenylenediamine dihydrochloride (1.30 g, 12 mmoles) were melted together under analogous conditions, compound IX was obtained (0.17 g, 8%).

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