7-OXO-3,7-DIHYDRO- AND 1,2,7-TRIOXO-1,2,3,7-TETRAHYDROPYRANO[3,2-*e*]INDOLES

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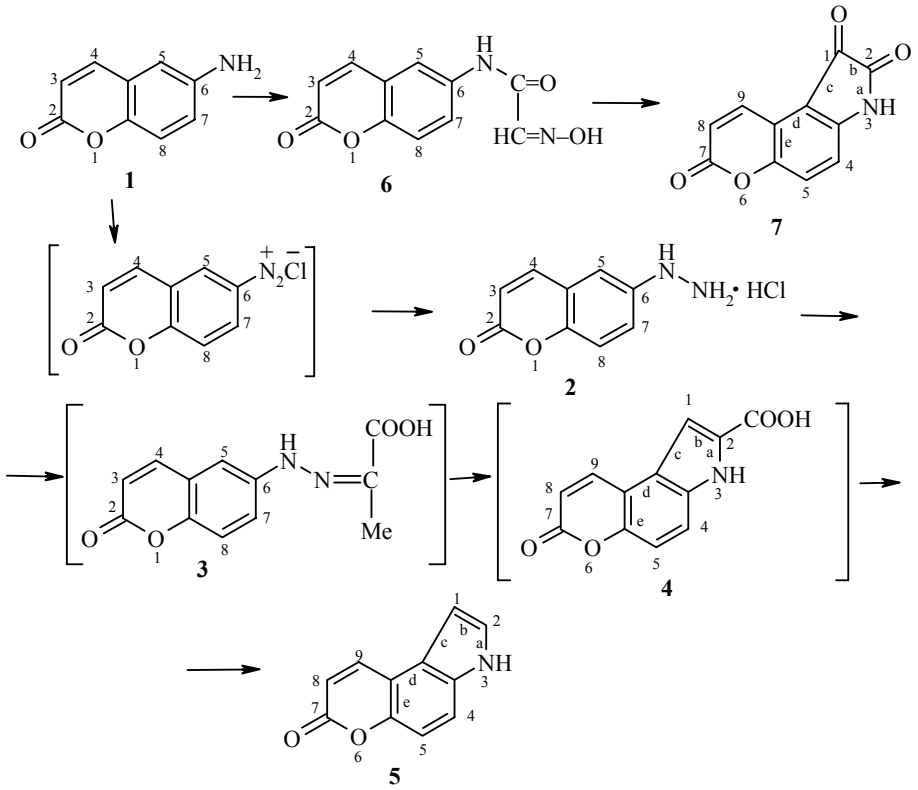
Various coumarin compounds are found in plants and have high biological activity, including anticoagulating, spasmolytic, antitumor, and other properties [1-3]. The importance of the bicyclic indole system is well known; many of its derivatives have valuable therapeutic properties (indomethacin, mexamine, methisazone, etc.) [4].

We have synthesized tricyclic condensed systems in which indole (or isatin) and coumarin moieties are combined. We used the E. Fischer and Sandmeyer reaction to "add" the pyrrole ring onto the bicyclic coumarin system. From 6-aminocoumarin **1** [5], we obtained the hydrazine **2** [5], converted by reaction with pyruvic acid to hydrazone **3**, the indolization of which followed by decarboxylation of the unpurified acid **4** lead to the target product **5** in acceptable yield.



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The same starting amine **1** was converted, via the isonitroso acetamide of coumarin **6**, to 1,2,7-trioxo-1,2,3,7-tetrahydropyrano[3,2-*e*]indole (**7**).

This is the first time that a coumarin-based synthesis of a tricyclic condensed system with an indole moiety in the molecule has been carried out. No analogs of the compounds we obtained have yet been observed in nature. It is certainly of interest to study the pharmacological properties of such condensed heterocycles because of the many diverse types of physiological activity they exhibit, which is typical for the derivatives of each of them individually [6, 7].

7-Oxo-3,7-dihydropyrano[3,2-*e*]indole (5). 6-Coumarinyl hydrazine hydrochloride **2**, obtained by diazotization of 6-aminocoumarin **1** followed by reduction of the diazo solution by $SnCl_2 \cdot 2H_2O$ in hydrochloric acid by the method in [5], was converted by reaction with pyruvic acid to hydrazone **3**, which when heated up to 90°C in the ethyl ester of polyphosphoric acid yields 7-oxo-3,7-dihydropyrano[3,2-*e*]indolyl-2-carboxylic acid (**4**). With no additional purification, 1 g (4 mmol) of the unpurified acid **4** was held at a temperature of 150-160°C under a stream of inert gas until evolution of CO_2 stopped (~2-3 min). The residue was purified on a column with aluminum oxide (eluent ether–hexane 3:1). Yield of compound **5**: 0.4 g (50%); mp 146-147°C. IR spectrum, ν, cm^{-1}: 3410 (NH). UV spectrum, λ_{max}, nm (log ε): 249 (4.33), 255 (4.66), 263 (4.88), 279 (4.91), 295 (4.95), 315 (4.55), 320 (4.35). ^{1}H NMR spectrum (250 MHz, DMSO-d_6), δ, ppm: 11.52 (NH); 6.90 (1H); 7.54 (2H); 7.65 (4H); 7.11 (5H); 6.45 (8H); 8.45 (9H), $J_{4,5}$ = 9.0; $J_{8,9}$ = 9.8; $J_{1,2}$ = 3.0; $J_{1,3}$ = 2.2; $J_{2,3}$ = 2.6 Hz. Found, %: C 71.2; H 4.0; N 7.4. $C_{11}H_7NO_2$. Calculated, %: C 71.4; H 3.8; N 7.6.

6-Isonitrosoacetamidocoumarin (6). Crystalline sodium sulfate (180 g), 6-aminocoumarin **1** (100 mmol) in water (100 ml) with addition of hydrochloric acid (10 ml) and hydroxylamine hydrochloride (330 mmol) in water (50 ml) were added successively to a solution of chloral hydrate (100 mmol) in water (50 ml). The mixture was heated to boiling and held for 3 h. The hot solution was filtered, the precipitate was washed with cold water and dried. Yield 76%; mp 175-177°C. IR spectrum, ν, cm^{-1}: 1680 (C=O); 3290 (NH). UV spectrum, λ_{max}, nm (log ε): 244 (4.49), 288 (4.10), 295 (4.15), 333 (4.25), 350 (4.00). ^{1}H NMR spectrum (250 MHz, DMSO-d_6), δ, ppm: 10.4 (NH); 7.67 (CH); 12.2 (OH); 7.79 (7H); 7.40 (8H); 8.09 (3H); 6.49 (4H), $J_{3,4}$ = 9.0; $J_{7,8}$ = 9.0; $J_{6,8}$ = 2.3 Hz. Found, %: C 57.1; H 3.3; N 12.4. $C_{11}H_8N_2O_4$. Calculated, %: C 56.9; H 3.4; N 12.1.

1,2,7-Trioxo-1,2,3,7-tetrahydropyrano[3,2-*e*]indole (7). Compound **6** (100 mmol) was added in small portions with stirring to 95% sulfuric acid heated up to 50°C. When addition was complete, the temperature was brought up to 90°C and held there for another 2 h. The reaction mixture was cooled down, transferred to a beaker with crushed ice (200 g), and allowed to stand overnight. The precipitated crystals were filtered out, carefully washed with water, and dried. Yield 70%; mp 255-257°C. IR spectrum, ν, cm^{-1}: 3415 (NH); 3250 (NH···O=C); 1700 (C=O). ^{1}H NMR spectrum (250 MHz, acetone-d_6), δ, ppm: 11.29 (NH); 7.29 (4H); 7.59 (5H); 6.69 (8H); 8.48 (9H); $J_{4,5}$ = 9.0; $J_{8,9}$ = 9.8; $J_{9,5}$ = 0.4 Hz. Found, %: C 61.3; H 2.2; N 6.2. $C_{11}H_5NO_4$. Calculated, %: C 61.4; H 2.3; N 6.5.

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