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The diazotization of 3-aminocoumarin followed by its reduction gave the coumarin-3-yl-hydrazine which, without isolation, reacted with various carbonyl compounds in a Fisher's indolization reaction to give derivatives (Ib-Ih) of the yet unreported system 3*H*,4*H*[1]benzopyrano[3,4-*b*]pyrrol-4-one.

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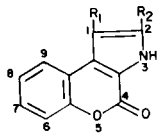
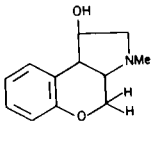
The ring system 3*H*,4*H*[1]benzopyrano[3,4-*b*]pyrrol-4-one (Ia) which arises from the fusion of a pyrrole ring to the 3,4 bond of coumarin is not described in the literature. The only example of a related compound (II) has recently been reported (2) where both rings, the pyran as well as the pyrrole ring, are reduced. Since the system I is composed of two moieties one of which is base sensitive (the coumarin ring) while the other being sensitive to acids (the pyrrole ring), a combination of these may present a ring system with interesting properties, and as such we would like to report here the synthesis of this system.

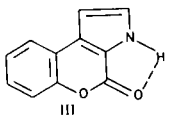


I

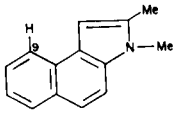
Ia, $R_1 = R_2 = H$
Ib, $R_1 = R_2 = Me$
Ic, $R_1 = R_2 = -(CH_2)_4-$
Id, $R_1 = Me$; $R_2 = H$
Ie, $R_1 = Me$; $R_2 = Ph$
If, $R_1 = Ph$; $R_2 = Me$
Ig, $R_1 = H$; $R_2 = CO_2H$
Ih, $R_1 = H$; $R_2 = Me$



II



III



IV

For the synthesis of this system we decided at first to test the feasibility of the Fisher's indolization reaction. This would require coumarin-3-ylhydrazine as the starting material, but there is no mention in the literature of this hydrazine. As the 3-aminocoumarin, the precursor of the hydrazine, has previously been thought to have an "enamine" structure (3), we were hesitant to attempt the synthesis of this hydrazine by the usual diazotization and subsequent reduction of the diazonium salt. However, earlier we had observed that 3-aminocoumarin does exist as the amino rather than the "imino" tautomer and that it does take part in the Gould-Jacobs reaction as well as in the Skraup type synthesis (4), and as such we were encouraged to try this route taking usual precautions.

Since 3-aminocoumarin is easily hydrolyzed by acids (3), we diazotized it at a lower temperature (-30°) followed by stannous chloride reduction of the resulting diazonium salt. The hydrazine formed during the reduction of the diazonium salt was, without isolation, heated in acetic acid together with suitable carbonyl compounds to produce Ib-Ih. The replacement of acetic acid by ethanol in some cases lowered the yield of the products. In the reaction of pyruvic acid the corresponding hydrazone was formed in this step. This hydrazone was later cyclized in polyphosphoric acid. Various attempts were made to decarboxylate Ig in order to obtain the basic ring system Ia, but all preliminary attempts were unsuccessful (heating in refluxing Dowtherm, in diphenyl methane, with copper-quinoline system, *etc.*), either Ig was recovered unchanged or extensive decomposition was noted.

The infrared spectra of Ib-Ih show an NH absorption between 3235 and 3230 cm^{-1} while the absorption due to the carbonyl group of the pyrone ring was observed between 1680 and 1695 cm^{-1}. The shift to the shorter wavenumber can be attributed to a strong intramolecular hydrogen bonding between the pyrone carbonyl and the NH of the pyrrole ring as is shown in III. This type of hydrogen bonding was also observed earlier in the case of derivatives of 5*H*[1]benzopyrano[3,4-*b*]pyridin-5-one (4).

The signals in the proton magnetic resonance spectra of various compounds I due to the protons of the benzene ring appear as multiplets between δ 7.15 and 8.00. A complete analysis is not attempted at this stage but it seems reasonable that the signal as a multiplet due to a single proton at the lower field may be ascribed as due to the proton at C-9, since in the 3-methylcoumarins the proton at this position (C-5) is found to be at lower field (5). A similar analogy for this position may be drawn with the C-9 of 2,3-dimethylbenzo[e]indole (IV) where the proton at this position was also found to appear as a doublet at δ 8.12 (6). However, in the pmr spectrum of If the multiplet due to this proton at the 9 position was found to have moved to the higher field and was within the envelope of the signals due to the rest of the benzenic protons between δ 7.20 and 7.60 due to the shielding effect of the phenyl ring at the 1 position.

EXPERIMENTAL

All melting points are uncorrected. Pmr spectra were taken on a 60 MHz Hitachi Perkin-Elmer R-20B using tetramethylsilane as an internal standard. Ir absorption spectra were measured on Perkin-Elmer model 180 and the elemental analysis on Perkin-Elmer 240.

Most of the starting materials and the carbonyl compounds used in this work were commercial products and were used without

further purification.

3-Aminocoumarin.

The following method used for the hydrolysis of 3-*N*-acetylaminocoumarin gave repeatedly good yields of the amine. To a stirred solution of 10 g. (0.049 mole) of 3-*N*-acetylaminocoumarin in 100 ml. of glacial acetic acid there was added dropwise 100 ml. of 50% sulfuric acid. The mixture was heated on a water bath for a period of 1 hour under constant agitation. After cooling, the reaction mixture was inverted into a beaker containing 200 g. of crushed ice and carefully neutralized with sodium bicarbonate and extracted with ether (3 x 150 ml.). The ethereal extract was dried over anhydrous magnesium sulfate, filtered and freed of the solvent leaving behind a yellow solid which was crystallized from ethanol to give 3-aminocoumarin, m.p. 132-133° (3), yield 6.3 g. (80%).

3*H*,4*H*[1]Benzopyrano[3,4-*b*]pyrrol-4-ones.

General Procedure.

A solution of 1.6 g. (0.01 mole) of 3-aminocoumarin in 5 ml. of hydrochloric acid was diazotized at -30° with sodium nitrite solution (0.8 g. dissolved in 3 ml. of water). After keeping at this temperature for 30 minutes, the resulting diazonium salt was reduced by adding into a cold (-10--5°) solution of 5 g. of stannous chloride dissolved in 5 ml. of hydrochloric acid. The mixture was allowed to stand in the refrigerator for a minimum period of two hours. The resulting mixture of coumarin-3-ylhydrazine hydrochloride and stannic chloride in hydrochloric acid (henceforth referred to as "coumarin-3-ylhydrazine") was directly reacted with the appropriate carbonyl compounds according to one of the two methods: Method A. The mixture of the "coumarin-3-ylhydrazine" and 0.01 mole of the carbonyl compound was heated under reflux for an hour in ethanol (20 ml.) or acetic acid (10 ml.). After cooling the reaction mixture was inverted over 100 g. of crushed ice. The product was filtered and purified. Method B. The mixture of "coumarin-3-ylhydrazine" and 0.01 mole of the carbonyl compound was dissolved in 10 ml. of polyphosphoric acid and heated for an hour at 130°. After cooling, the reaction mixture was inverted over 100 g. of crushed ice, filtered and purified. The yields are based on the starting 3-aminocoumarin.

1,2-Dimethyl-3*H*,4*H*[1]benzopyrano[3,4-*b*]pyrrol-4-one (Ib).

This was obtained from the reaction of "coumarin-3-ylhydrazine" with 2-butanone in acetic acid (Method A). The pale yellow solid obtained on filtration was dried and crystallized from acetic acid (activated charcoal) giving colorless crystals of Ib, m.p. 287-289°, yield 36.2%; pmr (DMSO-d_6): δ 2.28 (s, CH_3), 2.31 (s, CH_3), 7.20-7.50 (m, H-6-H-8), 7.90 (m, H-9), 12.20 (br. NH); ir (potassium bromide pellet): 3235 cm^{-1} (br. NH), 1680 (pyrone C=O), 1590, 1500, 1390, 1140, 1130, 1040, 750, 740, 660.

Anal. Calcd. for $C_{13}H_{11}NO_2$: C, 73.22; H, 5.20; N, 6.57. Found: C, 73.51; H, 5.17; N, 6.55.

1,2-Tetramethylene-3*H*,4*H*[1]benzopyrano[3,4-*b*]pyrrol-4-one (Ic).

Compound Ic was obtained from the reaction of "coumarin-3-ylhydrazine" and cyclohexanone in acetic acid (Method A). Crystallization from acetic acid (activated charcoal) gave Ic in 42% yield, m.p. 298°; pmr (DMSO-d_6): δ 1.80 (m, $(CH_2)_2$), 2.75 (m, $(CH_2)_2$), 7.15-7.45 (m, H-6-H-8), 7.75 (m, H-9), 12.15 (br. NH); ir (potassium bromide pellet): 3230 cm^{-1} (br. NH), 2940, 1690 (pyrone C=O), 1610, 1560, 1500, 1455, 1160, 1150, 1120, 1080, 755, 740.

Anal. Calcd. for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85. Found: C, 75.50; H, 5.65; N, 5.68.

1-Methyl-3*H*,4*H*[1]benzopyrano[3,4-*b*]pyrrol-4-one (Id).

The reaction of "coumarin-3-ylhydrazine" and propanal in acetic acid (Method A) gave a pale yellow solid which was filtered, dried and crystallized from benzene (activated charcoal) giving Id as colorless crystals, m.p. 276-277° in 33.5% yield; pmr (DMSO-d_6): δ 2.43 (s, CH_3), 7.20-7.50 (m, H-6-H-8 and H-2), 7.90 (m, H-9), 12.40 (br. NH); ir (potassium bromide pellet): 3230 cm^{-1} (br. NH), 1685 (pyrone C=O), 1610, 1590, 1510, 1460, 1165, 1120, 1080, 750, 740.

Anal. Calcd. for $C_{12}H_9NO_2$: C, 72.35; H, 4.55; N, 7.03. Found: C, 72.09; H, 4.72; N, 7.24.

1-Methyl-2-phenyl-3*H*,4*H*[1]benzopyrano[3,4-*b*]pyrrol-4-one (Ie).

The reaction of propiophenone and "coumarin-3-ylhydrazine" in acetic acid (Method A) gave a yellow precipitate which was filtered off and crystallized from acetic acid (activated charcoal) giving Id as orange color crystals in 47% yield, m.p. 249-251°; pmr (DMSO-d_6): δ 2.50 (s, CH_3), 7.30-7.60 (m, H-6-H-8 and C_6H_5), 8.00 (m, H-9), 12.60 (br. NH); ir (potassium bromide pellet): 3230 cm^{-1} (br. NH), 1690 (pyrone C=O), 1560, 1510, 1500, 1230, 1110, 1080, 760, 740.

Anal. Calcd. for $C_{18}H_{13}NO_2$: C, 78.53; H, 4.76; N, 5.09. Found: C, 78.40; H, 4.78; N, 4.93.

2-Methyl-1-phenyl-3*H*,4*H*[1]benzopyrano[3,4-*b*]pyrrol-4-one (If).

From the reaction of "coumarin-3-ylhydrazine" and phenylacetone in acetic acid (Method A) there was obtained a pale yellow solid which was crystallized from benzene (activated charcoal). Colorless crystals of If, m.p. 280-281°, were isolated in 51% yield; pmr (DMSO-d_6): δ 2.25 (s, CH_3), 7.20-7.60 (m, H-6-H-9 and C_6H_5), 12.70 (br. NH): ir (potassium bromide pellet): 3230 cm^{-1} (br. NH), 1695 (pyrone C=O), 1600, 1510, 1260, 1195, 980, 755, 740.

Anal. Calcd. for $C_{18}H_{13}NO_2$: C, 78.53; H, 4.76; N, 5.09. Found: C, 78.52; H, 4.76; N, 5.24.

4-Oxo-3*H*,4*H*[1]benzopyrano[3,4-*b*]pyrrole-2-carboxylic Acid (Ig).

The reaction of "coumarin-3-ylhydrazine" and pyruvic acid in acetic acid (Method A) gave a yellow solid which was crystallized from a mixture of *N*,*N*-dimethylformamide and water giving 50% yield of pyruvic acid coumarin-3-ylhydrazone, m.p. 274-276°; pmr (CF_3CO_2H): δ 2.25 (s, CH_3), 7.20-7.40 (m, arom.), 8.35 (s, H-4); ir (potassium bromide pellet): 3300 cm^{-1} (br. NH), 1710 (pyrone C=O), 1740 (acid C=O).

Anal. Calcd. for $C_{12}H_{10}N_2O_4$: C, 58.54; H, 4.09; N, 11.38. Found: C, 58.32; H, 4.07; N, 11.58.

The reaction of "coumarin-3-ylhydrazine" and pyruvic acid when carried out in polyphosphoric acid (Method B) gave a 48% yield of Ig as a cream color solid, m.p. 290-296°. It was dissolved in saturated sodium bicarbonate solution (50 ml.), extracted with ether (3 x 10 ml.) and then acidified with hydrochloric acid. The precipitate was filtered and dried. The white solid was sublimed (0.6 mm Hg, 250°) to give Ig as white amorphous solid, m.p. 297-299°.

The hydrazone obtained from Method A above, on heating in polyphosphoric acid at 130° for 15 minutes also gave Ig; pmr (DMSO-d_6): δ 7.30-7.55 (H-6-H-8 and H-1), 8.00 (m, H-9), 13.35 (br. NH); ir (potassium bromide pellet): 3235 cm^{-1} (br. NH), 1690 (pyrone C=O), 1730, (acid C=O), 1620, 1500, 1230, 1180, 1030, 750, 740, 660.

Anal. Calcd. for $C_{12}H_7NO_4$: C, 62.89; H, 3.08; N, 6.11. Found: C, 62.61; H, 3.17; N, 6.02.

2-Methyl-3*H*,4*H*[1]benzopyrano[3,4-*b*]pyrrol-4-one (Ih).

A reaction of "coumarin-3-ylhydrazine" and acetone (Method B) gave a cream color solid which was filtered and twice crystallized from acetic acid (activated charcoal) to furnish Ih as colorless crystals, m.p. 261-263° in 51% yield; pmr (DMSO-d_6): δ 2.40 (s, CH_3), 6.65 (s, H-1), 7.20-7.60 (m, H-6-H-8), 7.80 (m, H-9), 12.35 (br. NH); ir (potassium bromide pellet): 3230 cm^{-1} (br. NH), 1690 (pyrone C=O), 1600, 1590, 1500, 1455, 1130, 1125, 1080, 750, 740.

Anal. Calcd. for $C_{12}H_9NO_2$: C, 72.36; H, 4.55; N, 7.03. Found: C, 72.41; H, 5.22; N, 6.92.

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