Studies on Novel Heterocyclic Ring Systems. Reaction of 4-Hydroxylcoumarin with o-Aminobenzaldehyde and 2-Mercaptoaniline

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Reactions of 4-hydroxycoumarin (1) with o-aminobenzaldehyde (2) and 2-mercaptoaniline (5) have been investigated. The yet unreported 6,12-dihydro-1-benzopyrano[3,4-b][1,4]benzothiazin-6-one (6) system has been synthesized and characterized on the basis of spectral and analytical data. A novel synthetic route to 6H-1-benzopyrano[4,3-b]quinolin-6-one (4) is reported. HMO calculations predict the most reactive sites on the molecules.

In continuation of our work (2) on the chemistry of derivatives of coumarin (1), the novel heterocyclic ring system 6,12-dihydro-1-benzopyrano[3,4-b][1,4]benzothiazin-6-one (6) has been prepared. In addition, a novel synthetic route to the already known 6H-1-benzopyrano[4,3-b]-quinolin-6-one (4) is established. Compound 4 was first prepared by Buu-Hoi, et al. (3), while several derivatives of this ring system has been studied by Mohanty, et al. (4). The novel synthesis of the compound 4 was carried out in

4   6
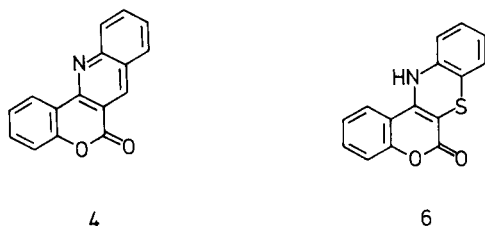
the following way. An ethanolic solution of 4-hydroxy-coumarin (1) and o-aminobenzaldehyde (2) in a 1:1 molar ratio was refluxed for 4 hours producing the compound 3 as a white precipitate. Compound 3 was converted to 4 (after refluxing six hours) by losing a molecule of water *via* intramolecular Schiff base formation (see Scheme 1).

Scheme 1
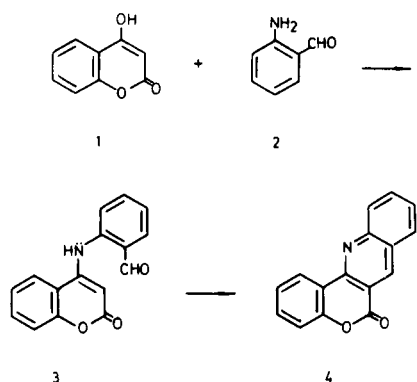
The ir spectrum of 3 shows an NH absorption at 3150 cm⁻¹, CH (aldehyde) absorption at 2850 cm⁻¹, the absorp-

tion due to the carbonyl group of the pyrone ring 1730 cm⁻¹, while the absorption due to the aldehyde carbonyl group was observed at 1665 cm⁻¹, and (C=C) aromatic absorption at 1605 cm⁻¹. Additional confirmation of the structural assignment was obtained by the identification of a mass peak corresponding to m/e 265 (M·⁺). The ir spectrum of 4 shows a carbonyl absorption due to the pyrone ring at 1735 cm⁻¹ and a (C=C) aromatic absorption at 1600 cm⁻¹. The pmr data are consistent with structure 4. Only aromatic protons appear as a multiplet between δ 8.40 and 7.20. The mass spectrum shows a peak at m/e 247 (M·⁺). The same mass spectrum peak was observed by Buu-Hoi (3).

The ring system 6 was obtained *via* oxidative cyclization (5,6) by merely heating a mixture of 1 and 5 in dimethyl sulfoxide at 140-145° for 35 minutes. Since the compound 5 is readily oxidized to *bis*(o-aminophenyl)disulfide (5b) under these reaction conditions, the reaction is considered to proceed *via* the intermediate 5a, which is readily cyclized by the scission of the sulfur-sulfur bond (7,8) upon the attack by the nucleophilic enaminone system (see Scheme 2). The red crystals, which separated on cooling from reaction mixture, are insoluble in most solvents and are of high purity with m.p. 337-340°.

The ir spectrum of 6 shows an NH absorption at 3315 cm⁻¹, carbonyl absorption at 1665 cm⁻¹ and (C=C) aromatic absorption at 1600 cm⁻¹. The pmr spectrum of 6 exhibits a broad signal at δ 7.00 due to NH proton, while aromatic protons appear as a multiplet between δ 7.80 and 6.78. The mass spectrum shows a peak corresponding to m/e 267 (M·⁺).

In order to predict the most reactive sites, towards the electrophilic substitution within the isolated-molecule model (9), on molecules 4 and 6, the HMO calculations with the Hess-Schaad parameters (10) have been performed. The charge density distribution diagrams are given in Figure 1. The position denoted by a on both structures is expected to be the most attractive site for the electrophilic attack (2e,11). It is interesting to compare the charge density distributions in coumarin (Figure 2) and the coumarin
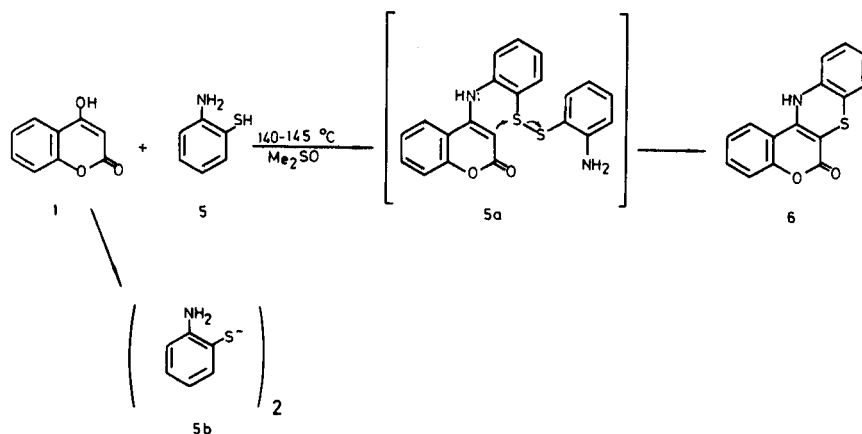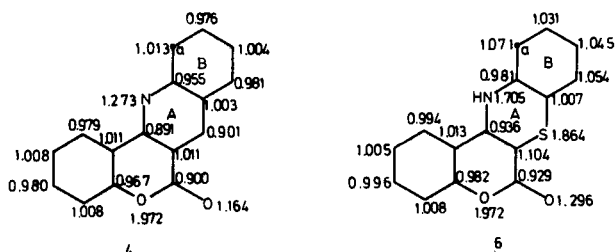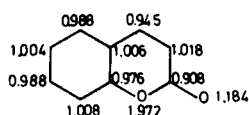
Scheme 2

Figure 1

Figure 2

moieties in **4** and **6**. In one case (molecule **4**) the coumarin fragment is (slightly) π-electron donating and in the other case (molecule **6**) is it π-electron accepting. Similarly, the benzene ring, denoted by B in the former case plays the role of donor whereas in the latter case it is an acceptor. In **4** the heterocyclic ring A is an acceptor, and in **6** it is a donor of π electrons to coumarin in the benzene parts of the system. However, this opposite donor-acceptor behaviour of rings in **4** and **6** does not effect the site a, which remains the most active position for the electrophilic substitution in both cases.

The relative stabilities of **4** and **6** are predicted using the algebraic structure count, ASC, model of Wilcox (12), which was shown to correlate well with the thermodynamic stabilities of conjugated molecules (13,14). We will use here the normalized form of the ASC index:

$$ASC_N = \frac{K}{N}$$

where K is the total number of Kekulé structures and N is

the number of π electrons in the conjugated system. These considerations lead to the prediction that **6** (ASC_N = 0.18) should be more stable than **4** (ASC_N = 0.10).

EXPERIMENTAL

All melting points are uncorrected. The ir spectra (pellets) were recorded on a Perkin-Elmer M-377 spectrophotometer, the pmr spectra were recorded on a Varian-A-60 spectrograph using tetramethylsilane as an internal standard, and the mass spectra were recorded on a Hitachi Perkin-Elmer RMV-6L mass spectrometer.

4-(2-Formylanilino)benzopyran-2-one (**3**).

To a hot solution of 1.138 g. (7.0 mmoles) of **1** in 180 ml. of absolute alcohol, three drops of piperidine and then an ethanolic solution of 0.847 (7.0 mmoles) of **2** were added. After 4 hours refluxing the white precipitate was collected and washed with ethanol to yield 1.21 g. (64.2%) of analytically pure **3**, m.p. 299-300°; ir (potassium bromide pellet): 3150 cm⁻¹ (NH), 2850 (CH, aldehyde), 1730 (pyrone C=O), 1665 (aldehyde C=O), 1650 (C=C aromatic), 1560, 1485, 1160, 760; ms: M⁺ m/e 265.

Anal. Calcd. for $C_{16}H_{11}NO_3$: C, 72.45; H, 4.15; N, 5.28. Found: C, 72.25; H, 4.28; N, 5.19.

6H-1-Benzopyrano[4,3-b]quinolin-6-one (**4**).

To a hot solution of 1.138 g. (7.0 mmoles) of **1** in 180 ml. of absolute alcohol, three drops of piperidine and then an ethanolic solution of 0.847 g. (7.0 mmoles) of **2** were added. After 10 hours of refluxing, the reaction mixture was cooled. The white precipitate was collected to yield 0.98 g. (56.7%) of **4**, recrystallized from ethanol, m.p. 227-228°; ir (potassium bromide pellet): 3060 cm⁻¹ (CH aromatic), 1735 (pyrone C=O), 1600 (C=C aromatic), 1580, 1500, 1180, 1110, 760; pmr (DMSO-d₆): δ 7.2-8.4 (m, 9H, aromatic); ms: M⁺ m/e 247.

Anal. Calcd. for $C_{16}H_9NO_2$: C, 77.73; H, 3.64; N, 5.66. Found: C, 77.76; H, 3.52; N, 5.45. (Analysis by Buu-Hoi and co-workers: C, 77.3; H, 3.7; N, 5.5) (3).

6,12-Dihydro-1-benzoyrano[3,4-b][1,4]benzothiazin-6-one (**6**).

4-Hydroxycoumarin (**1**), 1.62 g. (0.01 mole), 2-mercaptoaniline (**2**), 1.25 ml. (0.01 mole) and dimethyl sulfoxide (8 ml.) were stirred and heated together at 140-145° for 35 minutes. The product crystallized on cooling; it was filtered and recrystallized from methanol. Compound **6** was obtained as red crystals (2.38 g., 89.26%) m.p. 337-340°; (potassium bromide pellet): 3315 cm⁻¹ (NH), 3070 (CH aromatic), 1665 (pyrone C=O), 1615 (C=C aromatic), 1520, 1475, 1215, 1115, 760, 740; pmr (DMSO-d₆): δ 9.0

(br, NH), 6.78-7.80 (m, 8H, aromatic); ms: M⁺ m/e 267.

Anal. Calcd. for $C_{15}H_9NO_2S$: C, 67.40; H, 3.38; N, 5.24. Found: C, 67.40; H, 3.50; N, 4.95.

Acknowledgement.

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(11) Presently we are investigating the substitution reactions on **4** and **6**.

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