The Condensation Products of 6-Methoxy-2,3-dihydro-4*H*-Benzopyran-4-one and 6-Nitroveratraldehyde. Part I.

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The condensation of 2,3-dihydro-6-methoxy-4*H*-benzopyran-4-one (**1**) and 6-nitroveratraldehyde (**2**) gave the expected 2,3-dihydro-6-methoxy-3-(6-nitroveratrylidene)-4*H*-benzopyran-4-one (**3**) plus an unexpected product identified as 2,3-dihydro-3-(α-ethoxy-4,5-dimethoxy-2-nitrobenzyl)-6-methoxy-4*H*-benzopyran-4-one (**4**).

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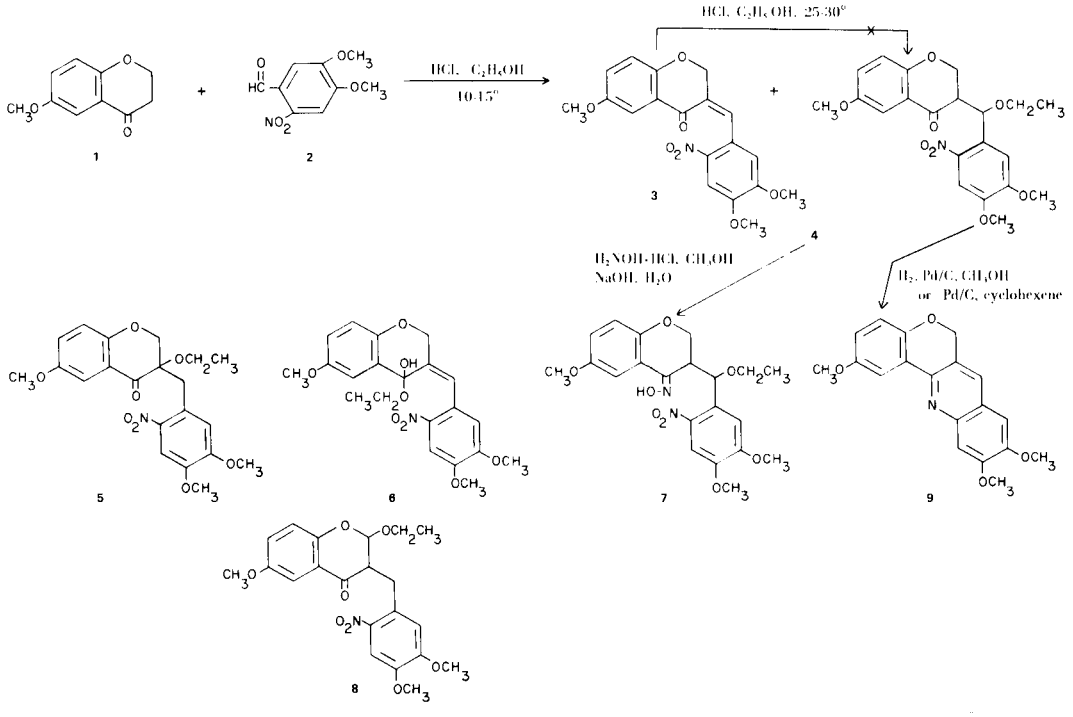
Discussion

During the preparation of 2,3-dihydro-6-methoxy-3-(6-nitroveratrylidene)-4*H*-benzopyran-4-one (**3**), an unexpected secondary product was obtained. The present paper covers the isolation and identification of this secondary product.

The primary product of the low temperature condensation of 2,3-dihydro-6-methoxy-4*H*-benzopyran-4-one (**1**) (3) and 6-nitroveratraldehyde (**2**) (2) was 2,3-dihydro-6-methoxy-3-(6-nitroveratrylidene)-4*H*-benzopyran-4-one (**3**) (53% yield). A secondary product (18% yield) was also isolated.

Three possible structures (**4**, **5**, and **6**, Scheme 1) were considered for the secondary product of the above reaction. The infrared spectrum of the compound exhibited strong carbonyl absorption at 5.92 μ, significantly lower than that observed at 6.02 μ for **3**, an α,β-unsaturated ketone, and the compound formed an oxime

Scheme 1



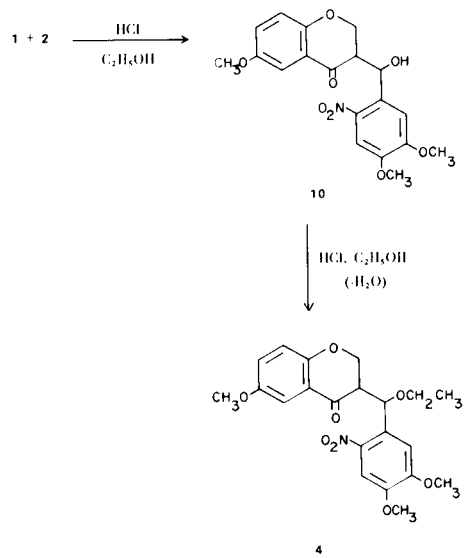
derivative which retained the ethoxy function. Thus structure **6**, with no carbonyl and no potential for oxime formation short of elimination of the ethoxy moiety, was eliminated. Furthermore, the observed nmr spectrum of the compound is consistent with that expected for structure **4** but not consistant for structure **5**. The observed downfield doublet centered at δ = 5.81 (integral = 1) meets the requirements for the benzylic proton of **4**, bonded to the same carbon as the ethoxy group and split by the adjacent 3-dihydrobenzopyran ring proton. On the other hand, the benzylic protons of **5** would be expected further up-field as a singlet. Also, the observed nmr spectrum of the oxime derivative is consistent with that expected for structure **7** (see Experimental). Therefore, it is concluded that the secondary product of the above reaction is **4**.

Still another structure (**8**) is theoretically possible for the secondary product, and although the physical properties of **8** would be expected to be very similar to those of **4**, mechanistically **8** would not be expected to form.

The reductive ring closure of **4** with palladium/carbon gave 2,9,10-trimethoxy-6*H*-[1]benzopyrano[4,3-*b*]quinoline (**9**) (3), illustrative of the facile loss of ethanol to give the fully aromatic species **9**.

An attempt to convert **3** directly to **4** with ethanolic hydrogen chloride resulted in the recovery (94%) of **3**. Thus, the formation of **4** does not appear to occur via direct addition of ethanol to the double bond of **3**. It appears that the formation of **4** may be best rationalized through the reaction of the intermediate condensation product of **1** and **2** (namely **10**) and ethanol (Scheme 2).

Scheme 2



EXPERIMENTAL

Infrared spectra were obtained with a Perkin-Elmer Infracord 137 and nmr spectra were determined in DMSO-d_6 using tetramethylsilane as an internal standard on a Varian A-60A spectrometer. Melting point data were obtained on a Fisher-Johns hot stage and are uncorrected.

2,3-Dihydro-6-methoxy-3-(6-nitroveratrylidene)-4*H*-benzopyran-4-one (**3**).

To a solution of 6-methoxy-4*H*-benzopyran-4-one (**1**) (2) (36 g., 0.20 mole) in absolute ethanol (250 ml.) was added 6-nitroveratraldehyde (**2**) (42 g., 0.20 mole) (3) at 30°, using mechanical stirring. The mixture was cooled in an ice-salt bath and treated with dry hydrogen chloride at 0-7° over 3 hours until saturated. The resultant yellow, crystalline product was washed well with cold 2-propanol and ether, yield, 53 g. (71%). Recrystallization twice from nitromethane gave analytically pure **3**, m.p. 159-162°; ir (Nujol) μ: 6.02 (C=O); nmr (δ): 3.83 (s, 1, CH_3O); 3.97 (s, 2, CH_3O); 5.25 (d, J = 2 Hz, 2, CH_2); 6.94, 7.38, and 7.86 (3s, 3, aromatic); 7.10-7.23 (m, 2, aromatic); 8.00 (t, J = 2 Hz, 1, =CH-).

Anal. Calcd. for $C_{19}H_{17}NO_7$: C, 61.45; H, 4.61; N, 3.77. Found: C, 61.67; H, 4.58; N, 3.79.

3-(α-Ethoxy-4,5-dimethoxy-2-nitrobenzyl)-2,3-dihydro-6-methoxy-4*H*-benzopyran-4-one (**4**).

The nitromethane filtrate (from the isolation of **3**) in a 1.99 molar run was concentrated to one-fifth volume under reduced pressure and cooled. The resultant yellow, crystalline solid was collected by filtration and washed well with 2-propanol and ether, m.p. 140-150°, yield, 147 g. (18%). The product (63 g.) was recrystallized from acetone (450 ml.) (charcoal) m.p. 147-150°, yield, 51 g. (14%); ir (Nujol) μ: 5.92 (C=O); ir (chloroform) μ: 5.97 (C=O); nmr (δ): 1.00 and 3.39 (t and q, 5, CH_3CH_2); 3.28 (d, J = 4.5 Hz, 1, =CH-); 4.53 (m, 2, $-CH_2-O-$); 3.78, 3.90 and 3.96 (3s, 9, CH_3O); 5.81 (d, J = 4.8 Hz, 1, =CH-O-); 7.05 and 7.70 (singlets, 2 aromatic); 7.11-7.30 (multiplets, 3 aromatic); no D_2O-exchangeable protons present.

Anal. Calcd. for $C_{21}H_{23}NO_8$: C, 60.43; H, 5.55; N, 3.36. Found: C, 60.41; H, 5.43; N, 3.36.

3-(α-Ethoxy-4,5-dimethoxy-2-nitrobenzyl)-2,3-dihydro-6-methoxy-4*H*-benzopyran-4-one Oxime (**7**).

A mixture of **4** (160 g., 0.38 mole) and methanol (3000 ml.) was treated with a solution of hydroxylamine hydrochloride (192 g., 2.76 moles) in a cooled solution of sodium hydroxide (74 g., 1.8 mole) in water (320 ml.). The reaction mixture was refluxed on the steam bath for 17 hours, cooled to 5-10°, and filtered to remove insoluble yellow solid (unreacted **4**). The filtrate was concentrated under reduced pressure to a volume of approximately 1500 ml. and stored at room temperature overnight. The resultant product was collected by filtration and recrystallized from nitromethane (430 ml.). A second recrystallization of the product (38 g.) from acetonitrile gave **7**, m.p. 203-205°, yield, 7.5 g. (4.6%); ir (Nujol) μ: 3.08 (HON=); nmr (δ): 0.99 and 3.38 (t and q, 5, CH_3CH_2); 3.37 (d, J = 6 Hz, 1, =CH-); 3.75, 3.84, and 3.90 (3s, 9, CH_3O); 4.05-4.55 (m, 2, $-CH_2-O-$); 5.45, J = 6 Hz, 1, >CH-O-); 6.74-7.25 (m, 3, aromatic); 7.25 and 7.45 (2s, 2, aromatic); 11.1 (s, <1, HON, exchanged with deuterium oxide).

Anal. Calcd. for $C_{21}H_{24}N_2O_8$: C, 58.33; H, 5.59; N, 6.48. Found: C, 58.04; H, 5.58; N, 6.95.

Reductive Ring Closure of **4** to **9**.

A mixture of **4** (100 g., 0.24 mole), methanol (800 ml.), and 5% palladium/carbon (50% water) (7.0 g.) was subjected to hydrogenation at 41 psig over 30 hours; the hydrogen uptake was 93% of theory. The reaction mixture was cooled and the product (plus catalyst) was collected and washed well with cold 2-propanol and ether, yield, 85 g. Recrystallization from DMF (300 ml.) gave **9**; m.p. 170-173°, yield, 19 g. (24%); the ir (Nujol) abosrption spectrum was identical with that of authentic **9** (3). Additional product (53 g., 68%) was recovered from the filtrate, m.p. 123-124°; the ir (Nujol) absorption spectrum was nearly identical to that of authentic **9**.

Acknowledgements

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REFERENCES AND NOTES

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