Heterocyclic Systems; 9[1]. Reaction of 4-Oxo-4*H*-1-benzopyran-3-carboxaldehydes (3-Formylchromones) with 1,2-Diamines

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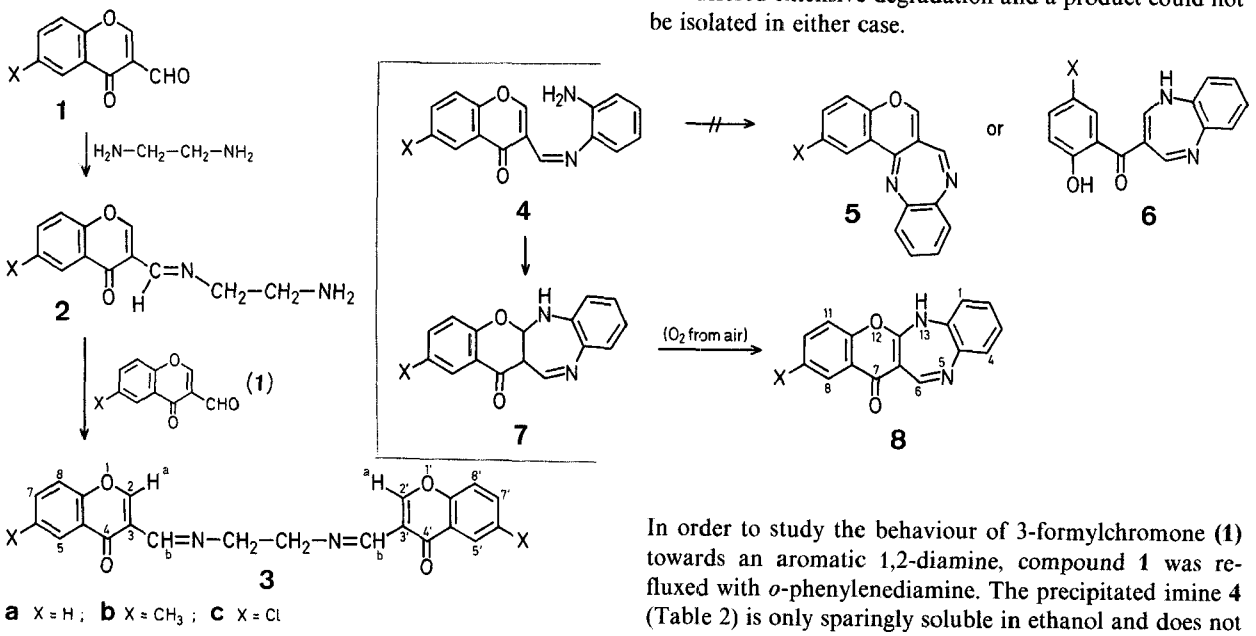
A variety of reactions of 4-oxo-4*H*-1-benzopyran-3-carboxaldehydes (3-formylchromones) has been compiled in a review by Ellis[2]. Conversion of 3-formylchromones into pyrrole and thiophene derivatives has been achieved by Fitton et al.[3]. 3-Formylchromones condense with formamidine[4] or other amidines[5] to give pyrimidines, with enamines[6] to give pyridines, with hydrazine or mono-substituted hydrazines[7,8] to give 4-(2-hydroxybenzoyl)-pyrazoles, and with diphenylketene[9] to give 3-(2,2-diphenylvinyl)-chromone and a fused 2-pyrone. We now report the condensation of 3-formylchromones with 1,2-ethanediamine and *o*-phenylenediamine.

The first step in the reaction of 3-formylchromone (**1**) with 1,2-ethanediamine is evidently the formation of the aldimine **2**, probably via a 1,4-addition-elimination-cyclisation sequence[10]. This aldimine may exist in two isomeric forms.



a X = H; **b** X = CH_3; **c** X = Cl

The (*E*)-isomer can undergo no further intramolecular transformation because the end amino group is too far away to react with either of the two reactive functionalities, namely the ketone function and the potential formyl group (C-2 of the chromone moiety). It can, however, condense with a second molecule of **1** to afford the bis-imine **3**.

On the other hand, the (*Z*)-isomer may either cyclise to a fused diazepine or rearrange via an intramolecular 1,4-addition-elimination sequence[2] to give 6-(2-hydroxybenzoyl)-2,3-dihydro-1*H*-1,4-diazepine.

Upon refluxing of an equimolar mixture of 3-formylchromones (**1**) and 1,2-ethanediamine in benzene, the bis-aldimines **3** precipitate out in more than 85% yield (based on **1**) (Table 1). Neither the intermediate aldimines **2** nor any diazepines could be detected even in trace amounts. The stereochemistry around the two C—N double bonds of the bis-imines **3** could not be assigned precisely. The ^{1}H-N.M.R. spectra of all compounds **3** show that the signals of protons of one half of the molecule overlap with those of the corresponding protons of the other half. Thus, it is certain that the identical groups around both the C—N double bonds are in the same geometric arrangement, i.e., the stereochemistry is either (*E*, *E*) or (*Z*, *Z*). The aldehyde **1** or the bis-imine **3** when refluxed with excess 1,2-ethanediamine suffered extensive degradation and a product could not be isolated in either case.

In order to study the behaviour of 3-formylchromone (**1**) towards an aromatic 1,2-diamine, compound **1** was refluxed with *o*-phenylenediamine. The precipitated imine **4** (Table 2) is only sparingly soluble in ethanol and does not

Table 1. 1,2-Bis[4-oxo-4*H*-1-benzopyran-3-ylmethylenamino]-ethanes (**3**)

3	Yield[a] [%]	m.p.[b] [°C]	Molecular Formula[c]	^{1}H-N.M.R. (DMSO-d_6/TMS) δ [ppm]						
				Ha + Hb (bs, 4H)	5-H, 5′-H (2H)	6-H, 6′-H (2H)	7-H, 7′-H (2H)	8-H, 8′-H (2H)	CH_2—CH_2 (bs, 4H)	2 CH_3 (s, 6H)
a[d]	92	200°	$C_{22}H_{16}N_2O_4$ (372.4)	8.05	7.25 (dd, J = 9, 2 Hz)	[7.15 —	6.95 (m)]	6.50 (m)	3.62	—
b	86	200°	$C_{24}H_{20}N_2O_4$ (400.4)	8.05	7.25 (d, J = 2 Hz)	—	6.85 (dd, J = 9, 2 Hz)	6.50 (d, J = 9 Hz)	3.90	2.10
c	88	198°	$C_{22}H_{14}Cl_2N_2O_4$ (441.3)	8.17	7.32 (d, J = 2 Hz)	—	7.17 (dd, J = 9, 2 Hz)	6.90 (d, J = 9 Hz)	3.43	—

[a] Based on **1**.

[b] m.p. of pure recrystallized (dimethylformamide) product.

[c] The microanalyses were in satisfactory agreement with the calculated values: C, ±0.32; H, ±0.21; N, ±0.18.

[d] M.S. (70 eV): m/e = 372 (M^+, 15%); 252 ($M - C_7H_4O_2$, 3): 187 (Ar—CH=N—CH_3, 100).
I.R. (KCl): ν = 1640 (C=O), 1600 (C=N or C=C) cm^{-1}.

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Table 2. 3-(2-Aminophenyliminomethyl)-chromones[a] (**4**)

4	Yield [%]	m.p.[b] [°C]	Molecular Formula[c]	
a[d]	86	205	$C_{16}H_{12}N_2O_2$	(264.3)
b	90	216	$C_{17}H_{14}N_2O_2$	(278.3)
c	92	228	$C_{16}H_{11}ClN_2O_2$	(298.7)

[a] The N.M.R. spectra could not be recorded because of insufficient solubility of compounds **4** even in DMSO.
[b] m.p. of pure recrystallized (ethanol) product.
[c] The microanalyses were in satisfactory agreement with the calculated values: C, ±0.39; H, ±0.32; N, ±0.28.
[d] I.R. (KCl): ν = 3480, 3400 (NH_2); 1630 (C=O) cm^{-1}.

Table 3. 7-Oxo-7,13-dihydro-[1]benzopyrano[2,3-*b*]-1,5-benzodiazepines (**8**)

8	Yield [%]	m.p.[a] [°C]	Molecular formula[b]	^{1}H-N.M.R. ($CDCl_3$/TMS) δ [ppm]				
				—NH— (bs, exchangeable)	6-H (s)	8-H	Other H_{arom} (m)	CH_3 (s)
a[c]	60	268	$C_{16}H_{10}N_2O_2$ (262.3)	11.87	9.40	8.46 (dd, J = 9, 2 Hz)	8.00–7.26	—
b	53	256	$C_{17}H_{12}N_2O_2$ (276.3)	11.83	9.33	8.17 (Not well split)	7.28–7.23	2.50
c	47	262	$C_{16}H_9ClN_2O_2$ (296.7)	11.81	9.30	8.30 (d, J = 2 Hz)	7.68–7.58	—

[a] m.p. of pure recrystallized (chloroform) compound.
[b] The microanalyses were in satisfactory agreement with the calculated values: C, ±0.28; H, ±0.31; N, ±0.21.
[c] M.S. (70 eV): m/e = 262 (M^+, 100%); 234 (M − CO, 7); 205 (M − CO − HCN, 43); 159 (M − C_6H_5NC, 9); 142 (M − $C_7H_4O_2$ and/or 234 − C_6H_4O, 89); 131 (M − C_6H_5NC − CO, 36).
I.R. (KCl): ν = 3310 (—NH—); 1660 (C=O); 1620 (C=N—) cm^{-1}.

survive further refluxing in glacial acetic acid; this indicates that the imine **4** is not the (*E*)-isomer. The (*Z*)-form of **4** fails to cyclise to the benzodiazepine derivative **5** due to the weak nucleophilicity of the aromatic amino group and the poor electrophilicity of the benzylic carbonyl C-atom. The other possibility would be the rearrangement to the benzoyldiazepine **6**. However, refluxing of imines **4** in acetic acid affords the fused benzodiazepines **8** (Table 3). Here, the diazepine derivative **8** is perhaps formed by air oxidation of **7**, the 7-*endo*-Trig cyclisation[11] product of the imine **4**.

That nucleophiles undergo 1,4-addition to imines of the type **4** without subsequent ring opening as envisaged in the formation of **7** from **4** is well documented[12,13,14].

1,2-Bis[4-oxo-4*H*-1-benzopyran-3-ylmethylenamino]-ethanes (3); General Procedure:
A mixture of the 3-formylchromone **1** (2.5 mmol), 1,2-ethanediamine (151 mg, 2.5 mmol), and benzene (25 ml) is refluxed for 2 h. The precipitated solid **3** is isolated by suction and washed with benzene and light petroleum. The product may be further purified by recrystallisation from dimethylformamide.

3-(2-Aminophenyliminomethyl)-chromones (4); General Procedure:
A mixture of the 3-formylchromone **1** (5 mmol), *o*-phenylenediamine (541 mg, 5 mmol), and ethanol (50 ml) is refluxed for 1 h. The imine **4** separates as a red precipitate. It is isolated by suction, washed with ethanol, and dried in a vacuum desiccator. The product may be further purified by recrystallisation from ethanol.

7-Oxo-7,13-dihydro-[1]benzopyrano[2,3-*b*]-1,5-benzodiazepines (8); General Procedure:
The 3-(2-aminophenyliminomethyl)-chromone **4** (4 mmol) is refluxed in glacial acetic acid (20 ml) for 4 h whereupon part of the solvent is distilled off. The mixture is then cooled and diluted with water (40 ml). The precipitated product **8** is isolated by suction, washed with water, dried, and recrystallised from chloroform.

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