

## Heterocyclic Systems. Part 14.<sup>1</sup> Condensation Reactions of 2-(4-Oxo-4*H*-1-benzopyran-3-yl)-1,3-dioxolane

Chandra Kanta Ghosh \* and Chandrakanta Bandyopadhyay

Organic Chemistry Laboratory, Department of Biochemistry, Calcutta University, Calcutta 700 019, India

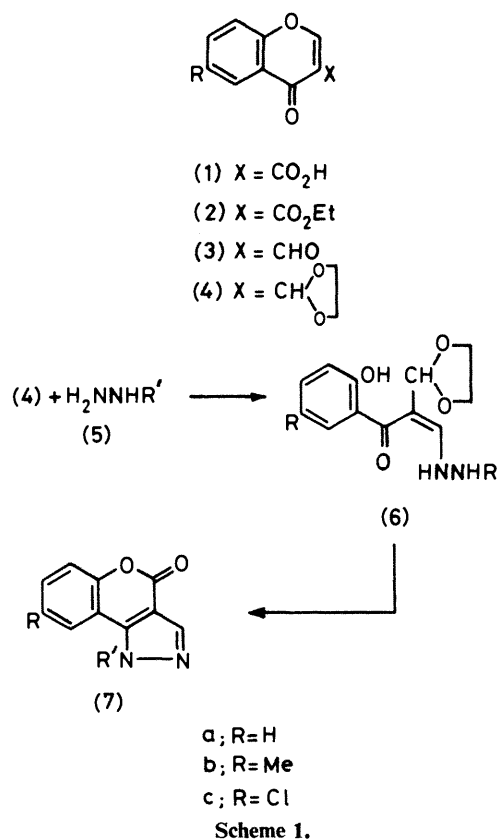
Christophe Morin

Chimie Appliquee Aux Corps Organises, Museum National D'Histoire Naturelle, 75005 Paris, France

Nitrogen nucleophiles under 1,4-addition with the title acetal (4; R = H, Me, and Cl) to give an intermediate that ultimately produces in most cases the same product as is obtained from the corresponding aldehyde (3) under similar conditions. Thus, compound (4) condenses with piperidine and morpholine to give the enamino ketone (14; R<sup>1</sup>R<sup>2</sup> = -[CH<sub>2</sub>]<sub>5</sub>-, -[CH<sub>2</sub>]<sub>2</sub>O[CH<sub>2</sub>]<sub>2</sub>-), with aniline to give the chromanone (15; Z = H, Me, and OMe), and with *o*-phenylenediamine to give the dihydrodiazepine (16), the latter being dehydrogenated to the unsaturated compound (17) by boiling in acetic acid. On being refluxed with hydrazine (5) in pyridine, the acetal (4; R = H) affords smoothly the benzoylpyrazole (20; R' = H, Ph), whereas (4; R = Me or Cl) even with equimolar proportions of hydrazine in refluxing ethanol gives predominantly, if not exclusively, the pyrazole (25; R' = H, Ph). Guanidine and urea with (4) give the fused aminopyrimidine (33) and the hydroxy analogue, respectively.

In an attempt to prepare the coumarinopyrazole (7)<sup>2</sup> from an easily accessible 4-oxo-4*H*-1-benzopyran (chromenone), neither the acid (1)<sup>3</sup> nor the ester (2)<sup>4</sup> was found to be the substrate of choice. The acetal (4),<sup>5</sup> from the aldehyde (3) appeared to be a good synthon for (7) on the basis that, like 2,3-alkyl substituted or unsubstituted chromenones,<sup>6</sup> attack is expected to occur at its 2-position with nucleophiles such as (5) and the pyrone ring-cleaved intermediate (6) thus formed (Scheme 1) could then be converted into (7) by a sequence of simple reactions (cyclisation, deacetalisation, oxidation). Moreover, the acetal (4) has so far been little studied,<sup>7</sup> though its precursor (3) has received much attention.<sup>7-9</sup> We report here an investigation of the reactions of (4) with some nitrogen nucleophiles, including hydrazine (5).

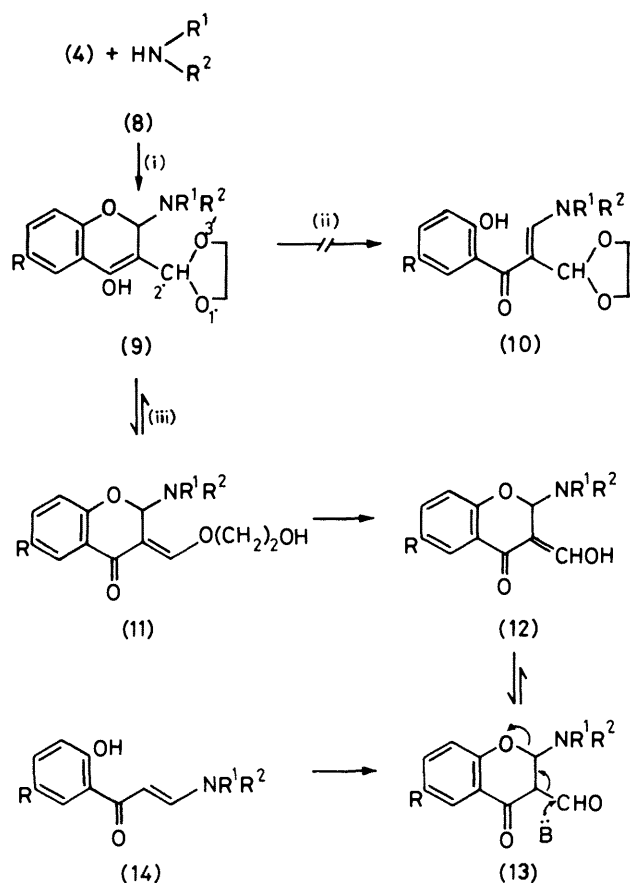
The acetal (4) was refluxed with a secondary amine (8) in ethanol to give the same *trans*-enaminoketone (14) (Table 1) as that obtained<sup>9</sup> from the aldehyde (3) under similar conditions; no reaction occurred in benzene. The reaction can be explained in terms of an initial 1,4-addition of the nucleophile to the  $\gamma$ -pyrone system (4) to afford the chromenol (9) as an intermediate (Scheme 2). The latter is structurally related both to a vinylogue of a hemi-orthoester<sup>10</sup> and to a hemi-orthoamide. In the collapse of a tetrahedral hemi-orthoamide intermediate, the cleavage of the C-N bond is kinetically controlled.<sup>11</sup> So expulsion of the amine (8) from compound (9), *i.e.* the reversal of step (i), under the present reaction conditions is apparently out of the question. Hence two other possible routes for the breakdown of (9), (ii) and (iii), must be considered. Deacetalisation of compound (9) under basic condition as shown in step (iii) is a general reaction for systems in which a carbanion can be generated at the  $\alpha$ -position of the acetal function.<sup>12,13</sup> The benzopyran ring of (9) is not perfectly planar. Its conformers in which the bulky amino group is in an equatorial position and the OH group is oriented so that a lone pair orbital of this hydroxylic oxygen overlaps the p-orbitals of C-2 and C-3 are fairly stable. Rotation around the single bond linking the two heterocyclic moieties (pyran and dioxolane) results in two particular rotamers for the intermediate (9) in which the plane of the benzopyran ring bisects symmetrically the dioxolane ring (through C-2' and the midpoint of the C-C bond). If the Deslongchamps' stereoelectronic theory<sup>14</sup> for the breakdown of a tetrahedral hemi-orthoester is extended to these rotamers (vinylogues of a hemi-orthoester), we see that the p-orbital at C-3 (and hence that of the hydroxylic oxygen) is anti-



periplanar to the O-alkyl bond [O(1')-C(2') or O(3')-C(2')] of the dioxolane moiety. Consequently, cleavage of the acetal, *i.e.* step (iii), leading to the intermediate (11) is an orbital assisted, and hence energetically favoured process, and it predominates over the other pathway [step (ii)] for pyran ring cleavage [→ (10)]. Compound (11) then undergoes base-catalysed hydrolysis<sup>12</sup> to give the hydroxymethylene compound (12), the amine (8) or (11) itself functioning as a base. Anchimeric assistance by the dialkylamino group in the hydrolysis of (11) is ruled out as the process would require a lot of energy for the transient formation of the azetinium ion

involved. The enol tautomerises to the aldehyde (13) which undergoes base-induced Grob fragmentation to afford the *trans*-enaminoketone (14).<sup>9</sup>

Intermediates of type (11) are also involved in the reactions of the acetal (4) with a primary aromatic amine and hydrazine.



Scheme 2.

**Table 1.** 1-(2-Hydroxybenzoyl)-2-(*N,N*-disubstituted amino)-ethylenes (14)

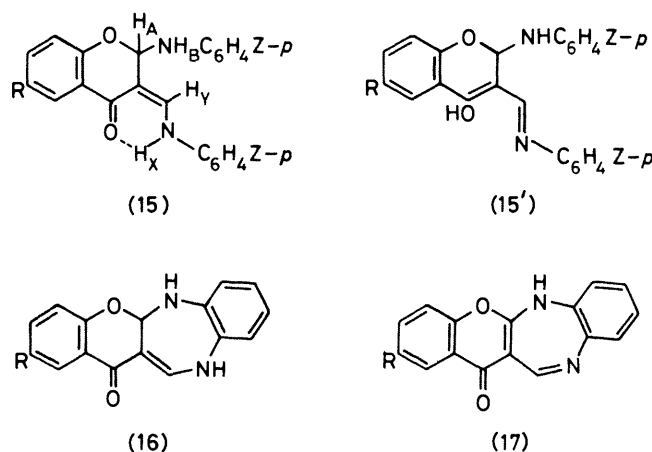
R	R <sup>1</sup> R <sup>2</sup>	Yield (%)	M.p. <sup>a</sup> (°C)
H	-[CH <sub>2</sub> ] <sub>5</sub> -	47 <sup>b</sup>	128 <sup>c</sup>
Me	-[CH <sub>2</sub> ] <sub>5</sub> -	45	145 <sup>c</sup>
Cl	-[CH <sub>2</sub> ] <sub>5</sub> -	43	156 <sup>c</sup>
H	-[CH <sub>2</sub> ] <sub>2</sub> O[CH <sub>2</sub> ] <sub>2</sub> -	27	108
Me	-[CH <sub>2</sub> ] <sub>2</sub> O[CH <sub>2</sub> ] <sub>2</sub> -	37	141
Cl	-[CH <sub>2</sub> ] <sub>2</sub> O[CH <sub>2</sub> ] <sub>2</sub> -	36	134

<sup>a</sup> M.p. of the compound when admixed with an authentic sample<sup>9</sup> was not depressed. <sup>b</sup> Yield from (42) was 44%. <sup>c</sup> <sup>1</sup>H N.m.r. data given in ref. 9.

The chromanone (15) (Table 2) was obtained by refluxing an alcoholic solution of (4) with an aromatic primary amine, optimum yields being obtained with a 1 : 2 molar proportion of the reagents. In this case the second molecule of the amine undergoes a 1,4-addition to the β-alkoxy-α,β-unsaturated ketone function of (11; R<sup>1</sup> = H, R<sup>2</sup> = Ar) with subsequent elimination of the alkoxy group. The chromanone (15) also arises from the reaction of the aldehyde (3) with a primary aromatic amine by another mechanism.<sup>15</sup> A sample prepared by treating the aldehyde (3a) with aniline<sup>15</sup> was found to be identical with the product obtained from the acetal (4a) and aniline, thus confirming the structure of the latter condensation product as (15; R = Z = H). As revealed from the <sup>1</sup>H n.m.r. spectrum, the condensation product of the acetal (4) and aniline exists in chloroform solution predominantly, but not exclusively, as the (*Z*)-ketoamine (15),<sup>16</sup> in tautomeric equilibrium with the imino enol form (15'). In the mass spectra of compound (15), the molecular ions were rarely observed, the highest *m/z* value corresponding to a fragment produced after splitting of an aniline molecule from the parent molecule.

When an equimolar mixture of the acetal (4) and *o*-phenylenediamine was refluxed in ethanol, the diazepine derivative (16)<sup>17</sup> resulted obviously by an intramolecular 1,4-addition-elimination sequence from the initially formed intermediate (11; R<sup>1</sup> = H, R<sup>2</sup> = C<sub>6</sub>H<sub>4</sub>NH<sub>2</sub>-*o*). On digestion in acetic acid (16) was dehydrogenated to give (17).<sup>17,18</sup>

The products obtained from the acetal (4) and hydrazine (5) were dependent on both the reaction conditions and the nature of the R group in (4), but in no case did the reaction go as expected (outlined in Scheme 1), and hence the preparation of the target compound (7) from (4) could not be achieved. Refluxing an equimolar mixture of compounds (4) and (5) in pyridine afforded, irrespective of the nature of R group, the benzoylpyrazole (20) (Table 3) identical with an authentic sample<sup>19</sup> prepared by treating the appropriate aldehyde (3) with hydrazine (5). Uniform results were not obtained when

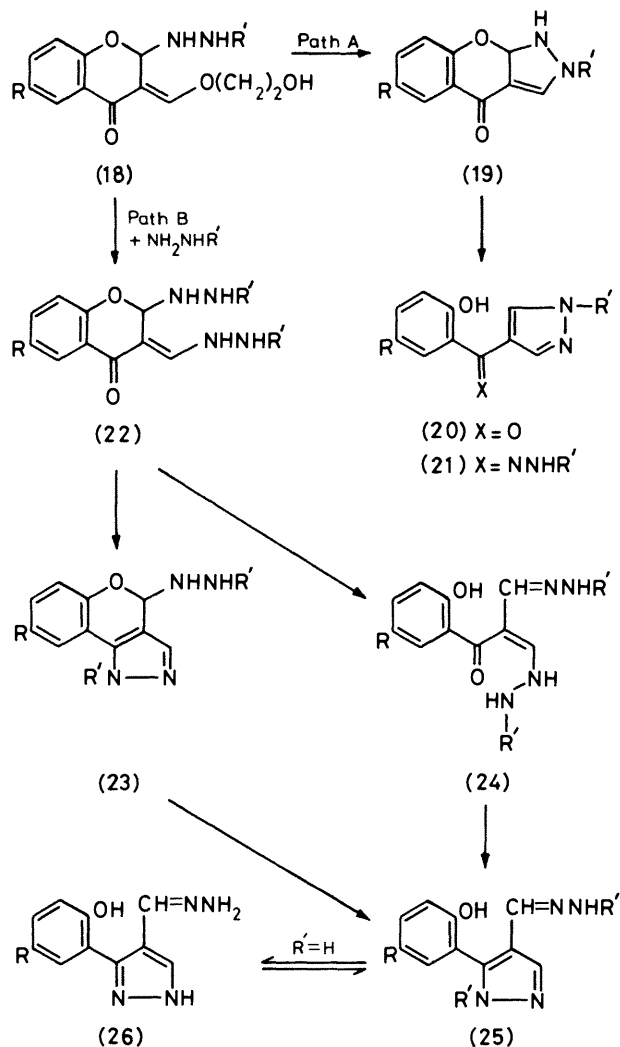


**Table 2.** 2-Arylamino-3-(arylaminoethylene)chromanones (15) from the acetal (4) (1 mol) and aromatic primary amine (2 mol)

R	Z	Yield (%)	M.p. (°C)	Found (%)			Molecular formula	Required (%)		
				C	H	N		C	H	N
H	H	62	158	77.5	4.9	8.4	C <sub>22</sub> H <sub>18</sub> N <sub>2</sub> O <sub>2</sub>	77.2	5.3	8.2
H	Me	70	155	77.6	6.3	7.7	C <sub>24</sub> H <sub>22</sub> N <sub>2</sub> O <sub>2</sub>	77.8	6.0	7.6
H	OMe	65	151	71.2	5.2	7.3	C <sub>24</sub> H <sub>22</sub> N <sub>2</sub> O <sub>4</sub>	71.6	5.5	7.0
Me	H	67	138	77.6	5.4	8.1	C <sub>23</sub> H <sub>20</sub> N <sub>2</sub> O <sub>2</sub>	77.5	5.7	7.9
Me	Me	83	141	78.2	6.1	7.5	C <sub>25</sub> H <sub>24</sub> N <sub>2</sub> O <sub>2</sub>	78.1	6.3	7.3

**Table 3.** 4-(2-Hydroxybenzoyl)pyrazoles (20) from the reaction of the acetal (4) with the hydrazine (5) in pyridine

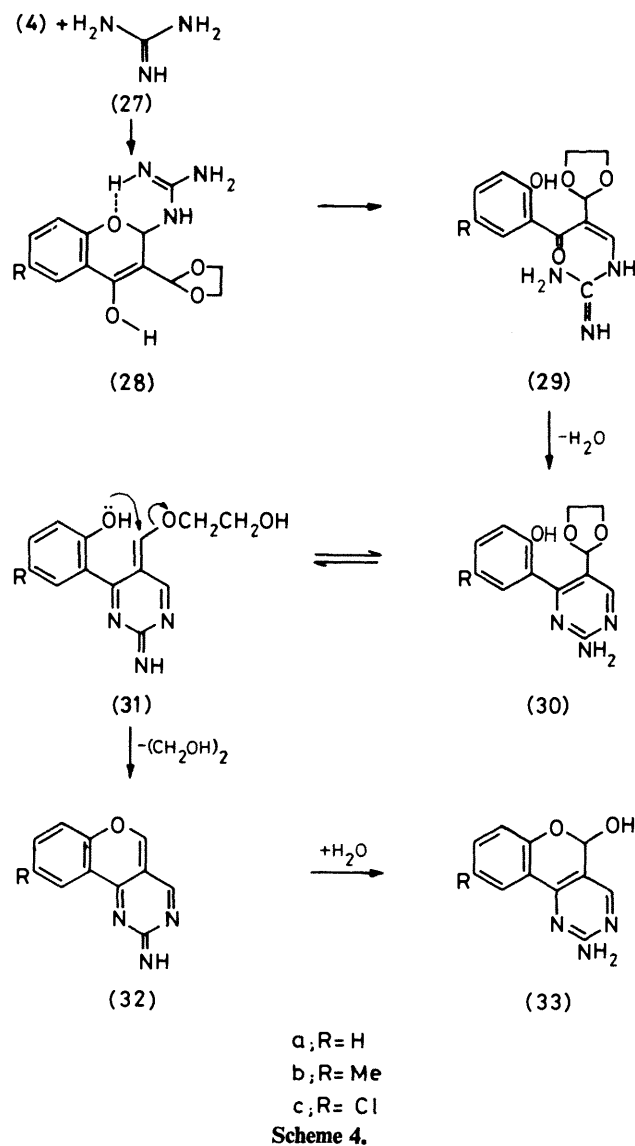
R	R'	Yield (%)	M.p. and mixed m.p. <sup>a</sup>
H	H	62	124
H	Ph	67	113
Me	Ph	72	120
Cl	H	58	180
Cl	Ph	75	145

<sup>a</sup> Ref. 19.

a; R = H  
 b; R = Me  
 c; R = Cl

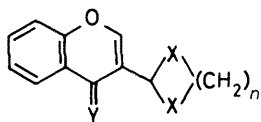
**Scheme 3.**

the above reaction was carried out in ethanol; although (4a) produced the pyrazole (20) in 40–50% yield, the reactions of (4b) and (4c) with (5) took a different course and a new product was formed together with little or no pyrazole (20). Why and how the methyl and chlorine substituents in (4b) and (4c) respectively alter the reaction course cannot be ascertained. As revealed from the elemental analysis and mass spectrum, this

**Scheme 4.**

new product results from the condensation of one molecule of the acetal (4) with two molecules of the hydrazine (5); the yield of the product could be improved by using the reagents in a 1 : 2 molar proportion. This product, being different from but isomeric with the hydrazone (21), prepared by treating compound (20) with (5), was assigned structure (25) on mechanistic grounds (*vide infra*) as well as on the basis of the spectral data. The appearance of the pyrazole proton in the n.m.r. spectrum of a (CD<sub>3</sub>)<sub>2</sub>SO solution of (25; R' = H) at  $\delta$  ca. 8, but not as a sharp singlet,<sup>20</sup> indicates that it is in tautomeric equilibrium with (26). The general rule that 3-arylpyrazole predominates over its tautomeric 5-arylpyrazole<sup>20,21</sup> cannot be applied to the present equilibrium (25; R' = H)  $\rightleftharpoons$  (26) as the effect or otherwise of the CH=NNH<sub>2</sub> group at the 4-position of the pyrazole moiety is not known precisely.

The formation of the pyrazole (20) may be rationalised by cyclisation of the initially formed intermediate (18) [analogous to (11)] to the fused system (19) (intramolecular 1,4-addition followed by elimination), and then isomerisation of the latter *via* pyrone ring cleavage to give (20) (Scheme 3, path A). The cyclisation of (18) to give (19) may not be a facile process, as suggested by the readiness of (18) to react with a second



(34) X = S, Y = O,  $n = 2$

(35) X = S, Y = NNH<sub>2</sub>,  $n = 2$

(36) X = Y = O,  $n = 3$

cule of (5) (Scheme 3, path B) giving (22) which ultimately leads to compound (25) *via* the intermediate (23) (ring closure followed by ring opening) and/or (24) (ring opening preceding ring closure). It is possible that pyridine brings about hydrolysis<sup>12</sup> of the keto enol ether (18) in the presence of water and consequently the cyclisation of the resultant intermediate involving its hydrazino and aldehyde groups becomes a facile process leading exclusively to the benzoylpyrazole (20) *via* (19) (or its  $\Delta^2$ -isomer when R' = H).

Reaction of the acetal (4) with guanidine (27) formed exclusively the pyrimidine (3).<sup>4,7,22,23</sup> This process has been reported previously but not commented on.<sup>7</sup> Here the 1,4-addition product (28) of (4) and (27) assumes a chelated structure involving the imino nitrogen and pyran oxygen (Scheme 4), and the latter thus carries partial positive charge. Consequently, the nucleofugality of the phenoxy group is enhanced, and the pyran ring cleavage [ $\rightarrow$  (29)] predominates over the deacetalisation process. Compound (29) cyclises to give (30) which, owing to the mesomeric effect of its amino group, undergoes deacetalisation to the ether (31); this is converted into the tricyclic compound (32) *via* an intramolecular 1,6-addition-elimination sequence. 2-Iminopyrimidines generally tend to remain in the amino form,<sup>24</sup> and thus compound (32) can only be converted into the amino form (33) by accepting a water molecule (1,6-addition). Like guanidine, urea also reacted with the acetal (4) to give 2,5-dihydroxy-5H-[1]benzopyrano[4,3-*d*]pyrimidine which in CF<sub>3</sub>CO<sub>2</sub>D solution probably assumes by loss of the 5-hydroxy group a pyrylium acetate structure; this is supported by the fact that its 5-H peak appears in the aromatic region of the n.m.r. spectrum.<sup>25</sup>

Finally, a brief comparison of the acetal (4) with its thioanalogue (34) and the dioxane (36) was also made. A secondary amine such as piperidine or morpholine failed to bring about any change in the dithiolane (34), but it reacted with hydrazine to give the hydrazone (35). When treated with piperidine, the dioxane (36), like its lower homologue (4), yielded the enaminketone (14; R = H, R<sup>1</sup>R<sup>2</sup> = -(CH<sub>2</sub>)<sub>5</sub>-). Thus it may be concluded that the protection of the formyl group of compound (3) particularly by acetalisation with a 1,2- or 1,3-diol is of little synthetic advantage.

## Experimental

M.p.s are uncorrected; microanalyses of those products which were not compared with authentic samples are given.

*Preparation of 2-(4-Oxo-4H-1-benzopyran-3-yl)-1,3-dioxolanes (4), -1,3-dithiolane (34), and -1,3-dioxane (36). General Procedure.*—3-Formylchromen-4-one (3) (20 mmol), with ethane-1,2-diol, ethane-1,2-dithiol, or propane-1,3-diol (22 mmol), and toluene-*p*-sulphonic acid (50–100 mg) were heated under reflux in dry benzene (100 ml) in a Dean-Stark water separator for 8 h. The reaction mixture was then cooled, washed thoroughly with water, dried (MgCO<sub>3</sub>) and concentrated. The deposited crystals were filtered off and once again crystallised from benzene–light petroleum. The following

compounds were obtained: unsubstituted acetal (4a) (85%) had m.p. 127 °C,  $\delta$ (CDCl<sub>3</sub>) 8.27 (1 H, dd,  $J$  8, 2 Hz, 5-H), 8.13 (1 H, s, 2-H), 7.78–7.28 (3 H, m, PhH), 6.04 (1 H, s, OCHO), and 4.07 (4 H, s, CH<sub>2</sub>CH<sub>2</sub>); the methyl derivative (4b) (90%), m.p. 143 °C,  $\delta$ (CCl<sub>4</sub>) 7.88 (2 H, br s, 5-, 2-H), 7.25 (2 H, m, 7-, 8-H), 5.78 (1 H, s, OCHO), 3.95 (4 H, m, CH<sub>2</sub>CH<sub>2</sub>), and 2.43 (3 H, s, Me); the chloro derivative (4c), m.p. 120 °C (78%); the dithiolane (34) (82%), m.p. 135 °C,  $\delta$ (CDCl<sub>3</sub>) 8.43 (1 H, s, 2-H), 8.28–7.40 (4 H, m, PhH), 5.86 (1 H, s, SCHS), and 3.40 (4 H, s, CH<sub>2</sub>CH<sub>2</sub>); the dioxane (36) (69%), m.p. 112 °C,  $\delta$ (CDCl<sub>3</sub>) 8.20 (1 H, s, 2-H), 8.00–7.43 (4 H, m, PhH), 5.80 (1 H, s, OCHO), 4.20 (4 H, m, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>O), 2.20 (1 H, m), and 1.44 (1 H, m, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>O).

*trans-1-(2-Hydroxybenzoyl)-2-(N,N-disubstituted amino)ethylenes (14) from Compounds (4) or (36). General Procedure.*—A mixture of compound (4) or (36) (5 mmol) and the secondary amine (8) (10 mmol) was refluxed in ethanol (50 ml) for 6 h. The reaction mixture was then concentrated and diluted with water. The precipitated solid was filtered, dried and further crystallised from chloroform–light petroleum to afford the ketone (14) (Table 1). Compound (14; R = H, R<sup>1</sup>R<sup>2</sup> = -(CH<sub>2</sub>)<sub>2</sub>O(CH<sub>2</sub>)<sub>2</sub>-) had  $\delta$ (CDCl<sub>3</sub>) 13.90 (1 H, s, exchangeable, OH), 7.90 (1 H, d,  $J$  12 Hz, HC=CHCO), 7.90–6.73 (4 H, m, PhH), 6.03 (1 H, d,  $J$  12 Hz, HC=CHC=O), and 3.66 (8 H, m, morpholine H).

*Preparation of the Chromanones (15) from the Acetals (4). Typical Procedure.*—A solution of the dioxolane (4a) (1.09 g, 5 mmol) and aniline (0.93 g, 10 mmol) in ethanol (60 ml) was refluxed for 6 h, then concentrated and diluted with water. The deposited solid was filtered, dried, and crystallised from benzene–light petroleum to afford the chromanone (15; R = Z = H) (1.23 g), m.p. and mixed<sup>15</sup> m.p. 158 °C (lit.,<sup>15</sup> m.p. 142–144 °C);  $m/z$  249 ( $M$  - PhNH<sub>2</sub>), 221 (249 - CO), 172 (249 - Ph), 146 (249 - PhNC). The other chromanones (15), similarly prepared from the appropriate acetal (4) and aniline or *p*-substituted aniline, are listed in Table 2. The i.r. and n.m.r. data of a representative member 6-methyl-2-*p*-tolylamino-3-*p*-tolylaminomethylenechroman-4-one (15; R = Z = Me) are as follows:  $\nu_{\max}$  (Nujol) 3 310, 1 650, 1 575, and 1 450 cm<sup>-1</sup>;  $\delta$ (CDCl<sub>3</sub>) 12.20 (1 H, d,  $J$  12 Hz, exchangeable H<sub>z</sub>), 8.88–6.56 (12 H, m, H<sub>y</sub> + PhH), 6.28 (1 H, d,  $J$  8 Hz, H<sub>A</sub>), 5.00 (1 H, d,  $J$  8 Hz, exchangeable, H<sub>B</sub>), and 2.48 (9 H, three partially overlapping singlets, 3Me).

*6,11-Dihydro[1]benzopyrano[2,3-*b*][1,5]benzodiazepin-13-ones (5aH)-ones (16). General Procedure.*—*o*-Phenylenediamine (0.50 g, 5 mmol) and the acetal (4) (5 mmol) were refluxed together in ethanol (50 ml) for 2 h. The precipitated dihydrodiazepine (16) was filtered off and washed with ethanol. The products (16a) (72%), m.p. 208 °C, (16b) (89%), m.p. 216 °C, and (16c) (82%), m.p. 222 °C, were found to be identical (superimposable i.r.) with the condensation products of *o*-phenylenediamine with the aldehydes (3a–c), respectively.<sup>17</sup> Each of these compounds (16) was converted into the [1]-benzopyrano[2,3-*b*][1,5]benzodiazepin-13(5aH)-ones (17)<sup>18</sup> in 60–65% yield on boiling in acetic acid. Compounds (17a–c) had m.p. 265, 258, and 262 °C respectively.

*Treatment of the Acetals (4) with the Hydrazines (5) in Pyridine.*—Dioxolane (4) (5 mmol) was refluxed with hydrazine hydrate (0.25 g, 5 mmol) or phenylhydrazine (0.54 g, 5 mmol) in pyridine (30 ml) for 5 h. Most of the solvent was distilled out, and the reaction mixture diluted with water to precipitate a solid which on filtration and crystallisation from ethanol–water afforded the 4-(2-hydroxybenzoyl)pyrazoles (20) (Table 3). The identity of each pyrazole (20) was estab-

lished by comparison with an authentic sample<sup>19</sup> prepared from the appropriate aldehyde (3).

**Treatment of the Acetals (4) with the Hydrazines (5; R' = H) in Ethanol.**—The chromenone (4a) (0.44 g, 2 mmol) and hydrazine hydrate (0.10 g, 2 mmol) were refluxed together in ethanol (30 ml) for 4 h. On cooling and dilution of the reaction mixture with water, a solid was obtained that on crystallisation from ethanol–water afforded 4-(2-hydroxybenzoyl)pyrazole (20a; R' = H) (53%), m.p. and mixed<sup>19</sup> m.p. 124 °C. Under similar conditions (4b) (0.46 g, 2 mmol) gave 4-hydrazonomethyl-5-(2-hydroxy-5-methylphenyl)pyrazole (25b; R' = H) (0.09 g, 46%), m.p. 192 °C;  $\nu_{\max}$ . (Nujol) 1 600 (CH=N), 1 435, and 1 315  $\text{cm}^{-1}$ ;  $\delta[(\text{CD}_3)_2\text{SO}]$  13.16 (1 H, br s, OH), 9.73 (1 H, br s, NH), 8.40 (1 H, s, CH=NN), 7.96 [1 H, br s, pyrazole 3-H and pyrazole 5-H of (26b)], 6.72–7.32 (5 H, m, PhH + NH<sub>2</sub>), and 2.24 (3 H, s, Me);  $m/z$  216 ( $M^+$ , 4%), 199 ( $M - \text{NH}_3$ , 2), and 185 ( $M - \text{NHNH}_2$ , 100) (Found: C, 61.2; H, 5.4; N, 26.2. C<sub>11</sub>H<sub>12</sub>N<sub>4</sub>O requires C, 61.1; H, 5.6; N, 25.9%). Likewise (4c) gave 4-hydrazonomethyl-5-(5-chloro-2-hydroxyphenyl)pyrazole (25c; R' = H) (45%), m.p. 190 °C (decomp.);  $\delta[(\text{CD}_3)_2\text{SO}]$  13.46 (1 H, br s, OH), 10.36 (1 H, br s, NH), 8.50 (1 H, s, CH=NN), 8.20 [1 H, br s, pyrazole 3-H and pyrazole 5-H of (26c)], and 7.50–7.00 (5 H, m, PhH + NH<sub>2</sub>) (Found: C, 51.1; H, 3.5; N, 23.6. C<sub>10</sub>H<sub>9</sub>ClN<sub>4</sub>O requires C, 50.8; H, 3.8; N, 23.7%). In neither of the latter two cases could any pyrazole in the form of (20) be isolated. The yields of (25b) and (25c) were 80 and 83% respectively when two moles of hydrazine hydrate per mole of the acetal (4b) and (4c) were used.

**Treatment of the Acetals (4) with Phenylhydrazine in Ethanol.**—A warm solution of phenylhydrazine hydrochloride (0.72 g, 5 mmol) and sodium acetate (1.0 g) in water (3 ml) was added in one portion to a solution of the acetal (4) (5 mmol) in ethanol (30 ml). After being refluxed for 1 h, the mixture was cooled and the precipitated solid crystallised from ethanol–water to give the products. The pyrazole (20a; R' = Ph) (49%) m.p. and mixed<sup>19</sup> m.p. 113 °C was the exclusive product from (4a). The solid precipitated out from the reaction of (4b) with (5; R' = Ph) and, on fractional crystallisation from ethanol–water, afforded compounds (25b; R' = Ph) (31%) and (20b) (5%), the former crystallising out first. Compound (25b; R' = Ph) had m.p. 193 °C,  $\nu_{\max}$ . (Nujol) 1 565 (C=N)  $\text{cm}^{-1}$ ;  $\delta[(\text{CD}_3)_2\text{SO} + \text{D}_2\text{O}]$  8.38 (1 H, s, CH=NN), 7.83 (1 H, s, pyrazole 3-H), 7.66–6.93 (13 H, m, PhH), and 2.50 (3 H, s, Me);  $m/z$  261 ( $M - \text{NHNHPh}$ ) (Found: C, 75.0; H, 5.2; N, 15.1. C<sub>23</sub>H<sub>20</sub>N<sub>4</sub>O requires C, 75.0; H, 5.5; N, 15.2%). By the same procedure, from the reaction of (4c) with (5; R' = Ph) were isolated compounds (20c) (13%) and (25c; R' = Ph) (26%), m.p. 218 °C;  $\delta[(\text{CD}_3)_2\text{SO}]$  10.16 (1 H, br s, exchangeable, OH), 8.23 (1 H, s, CH=NN), 7.70 (1 H, s, pyrazole 3-H), and 7.56–6.73 (14 H, m, PhH + NH) (Found: C, 68.3; H, 4.3; N, 14.4. C<sub>22</sub>H<sub>17</sub>ClN<sub>4</sub>O requires C, 67.9; H, 4.4; N, 14.4%). By carrying out the reactions with a 1 : 2 molar proportion of the acetal (4) and phenylhydrazine hydrochloride, the yields of (25b) and (25c; R' = Ph) were 65 and 71%, respectively.

**2-Amino-5-hydroxy-5H-[1]benzopyrano[4,3-d]pyrimidines (33).**—A mixture of the acetal (4) (2 mmol) and guanidine carbonate (0.18 g, 1 mmol) was refluxed in ethanol (80%; 50 ml) for 3 h. A portion of the solvent was distilled off. The solid which precipitated when the reaction mixture cooled was filtered off and crystallised from ethanol to give the pyrimidine (33), identical (superimposable i.r.) with the authentic sample<sup>4</sup> prepared from the aldehyde (3) under identical conditions. 2-Amino-5-hydroxy-5H-[1]benzopyrano[4,3-d]pyrimi-

dine (33a) (70%), m.p. 250 °C,  $\nu_{\max}$ . (KBr) 3 480, 3 300, 3 125, 1 640, 1 600, and 1 580  $\text{cm}^{-1}$ ;  $\delta[(\text{CD}_3)_2\text{SO}]$  8.28 (1 H, s, 4-H), 8.10 (1 H, dd,  $J$  8, 2 Hz, 10-H), 7.63–6.90 (4 H, m, 1 H exchangeable, PhH and OH), 6.77 (2 H, br s, exchangeable, NH<sub>2</sub>), and 6.38 (1 H, s, 5-H);  $m/z$  215 ( $M^+$ , 67%), 198 ( $M - \text{OH}$ , 28), 187 ( $M - \text{CO}$ , 100). 2-Amino-5-hydroxy-9-methyl-5H-[1]benzopyrano[4,3-d]pyrimidine (33b) (66%), m.p. 315 °C,  $\delta[(\text{CD}_3)_2\text{SO} + \text{D}_2\text{O}]$ , 8.15 (1 H, s, 4-H), 7.80 (1 H, d,  $J$  2 Hz, 10-H), 7.13 (1 H, dd,  $J$  8, 2 Hz, 8-H), 6.81 (1 H, d,  $J$  8 Hz, 7-H), 6.27 (1 H, s, 5-H), and 2.50 (3 H, s, Me);  $m/z$  229 ( $M^+$ ), 212 ( $M - \text{OH}$ ), and 201 ( $M - \text{CO}$ ). 2-Amino-5-hydroxy-9-methyl-5H-benzopyrano[4,3-d]pyrimidine (33c) (62%) had m.p. 340 °C.

**2,5-Dihydroxy-9-methyl-5H-[1]benzopyrano[4,3-d]pyrimidine.**—Acetal (4b) (0.46 g, 2 mmol) together with urea (0.12 g, 2 mmol) was refluxed in rectified spirit (50 ml) for 4 h. Usual work-up of the reaction mixture afforded the title pyrimidine (0.25 g, 55%), m.p. 252 °C,  $\delta[(\text{CF}_3\text{CO}_2\text{D})]$  8.57 (1 H, s, 4-H), 7.80–7.28 (4 H, m, PhH + 5-H), and 2.10 (3 H, s, Me);  $m/z$  230 ( $M^+$ , 23%), 213 ( $M - \text{OH}$ , 3), 187 ( $M - \text{HNCO}$ , 38), and 160 ( $M - \text{HNCO} - \text{HCN}$ , 100) (Found: C, 62.4; H, 4.4; N, 12.0. C<sub>12</sub>H<sub>10</sub>N<sub>2</sub>O<sub>3</sub> requires C, 62.6; H, 4.4; N, 12.2%).

**Reaction of the Thioacetal (34) with Hydrazine.**—Compound (34) (0.50 g, 2 mmol) when treated with hydrazine hydrate (0.10 g, 2 mmol) as described for the reaction of (4) with (5; R' = H) yielded white crystals of the dithiolane (35) (0.44 g, 83%), m.p. 120 °C (ethanol–water);  $\delta[(\text{CF}_3\text{CO}_2\text{D})]$  11.67 (2 H, s, NH<sub>2</sub>), 8.33 (1 H, s, 2-H), 7.77–6.90 (4 H, m, PhH), 5.75 (1 H, s, SCHS), and 3.45 (4 H, s, CH<sub>2</sub>CH<sub>2</sub>) (Found: C, 54.3; H, 4.3; N, 10.6. C<sub>12</sub>H<sub>12</sub>N<sub>2</sub>S<sub>2</sub>O requires C, 54.5; H, 4.6; N, 10.6%).

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### References

- 1 Part 13: C. K. Ghosh, N. Tewari, and C. Bandyopadhyay, *Indian J. Chem.*, in the press.
- 2 S. R. Moorthy, V. Sundaramurthy, and N. V. Subba Rao, *Indian J. Chem.*, 1973, **11**, 854; N. S. Vul'fson and R. B. Jhurin, *Zh. Obshch. Khim.*, 1961, **31**, 3381 (*Chem. Abstr.*, 1962, **57**, 4631).
- 3 C. K. Ghosh and K. K. Mukhopadhyay, *Synthesis*, 1978, 779.
- 4 C. K. Ghosh and S. Khan, *Indian J. Chem., Sect. B*, 1979, **18**, 128.
- 5 F. Eiden and H. Haverland, *Arch. Pharm. (Weinheim, Ger.)*, 1967, **300**, 806.
- 6 W. Baker, J. B. Horborne, and W. D. Ollis, *J. Chem. Soc.*, 1952, 1305; A. Schoenberg and M. M. Sidky, *J. Am. Chem. Soc.*, 1953, **75**, 5128; C. Morin and R. Beugelmans, *Tetrahedron*, 1977, **33**, 3183; G. P. Ellis, *Chem. Heterocycl. Compd.*, 1977, **35**, 566, and references therein.
- 7 C. Pene and M. Hubert-Habart, *J. Heterocycl. Chem.*, 1980, **17**, 329.
- 8 G. P. Ellis, *Chem. Heterocycl. Compd.*, 1977, **35**, 921; C. K. Ghosh and S. Khan, *Synthesis*, 1981, **903**, and references therein.
- 9 C. K. Ghosh and S. Khan, *Synthesis*, 1981, 719.
- 10 P. Deslongchamps, C. Moreau, D. Frehel, and P. Atlani, *Can. J. Chem.*, 1972, **50**, 3402; P. Deslongchamps, P. Atlani, D. Frehel, A. Malval, and C. Moreau, *ibid.*, 1974, **52**, 3651.
- 11 P. Deslongchamps, S. Dube, C. Lebreux, D. R. Patterson, and R. J. Taillefer, *Can. J. Chem.*, 1975, **53**, 2791; M. K. Kaloustian

- and R. B. Nader, *J. Org. Chem.*, 1981, **46**, 5052, and references therein.
- 12 S. Antus, F. Boross, and M. Nogradi, *J. Chem. Soc., Chem. Commun.*, 1977, 333.
- 13 Y. Kikuchi, Y. Hasegawa, and M. Matsumoto, *Tetrahedron Lett.*, 1982, **23**, 2199.
- 14 P. Deslongchamps, *Tetrahedron*, 1975, **31**, 2463; J. F. King and A. D. Allbut, *Can. J. Chem.*, 1970, **48**, 1754.
- 15 A. O. Fitton, J. R. Frost, and H. Suschitzky, *Tetrahedron Lett.*, 1975, 2099; A. O. Fitton, J. R. Frost, P. G. Houghton, and H. Suschitzky, *J. Chem. Soc., Perkin Trans. 1*, 1979, 1691.
- 16 G. O. Dudek and R. H. Holm, *J. Am. Chem. Soc.*, 1962, **84**, 2691; G. O. Dudek, *ibid.*, 1963, **85**, 694.
- 17 A. O. Fitton, P. G. Houghton, and H. Suschitzky, *Synthesis*, 1979, 337.
- 18 C. K. Ghosh and S. Khan, *Synthesis*, 1980, 701.
- 19 C. K. Ghosh and K. K. Mukhopadhyay, *J. Indian Chem. Soc.*, 1978, **55**, 52 and 386.
- 20 J. A. Moore and C. L. Habraken, *J. Am. Chem. Soc.*, 1964, **86**, 1456; C. L. Habraken and J. A. Moore, *J. Org. Chem.*, 1965, **30**, 1892.
- 21 K. von Auwers, *Liebigs Ann. Chem.*, 1937, **527**, 29.
- 22 W. Loewe, *Synthesis*, 1976, 274; G. Hass, J. L. Stanton, A. von Sprecher, and P. Wenk, *J. Heterocycl. Chem.*, 1981, **18**, 607.
- 23 U. Petersen and H. Heitzer, *Liebigs Ann. Chem.*, 1976, 1663.
- 24 L. F. Cavalieri and A. Bendich, *J. Am. Chem. Soc.*, 1950, **72**, 2587.
- 25 I. Degani, L. Lunazzi, and F. Taddei, *Boll. Sci. Fac. Chim. Ind. Bologna*, 1965, **23**, 131 as cited by R. F. M. White and H. Williams, 'Physical Methods in Heterocyclic Chemistry,' ed. A. R. Katritzky, Academic Press, 1971, **4**, 232.

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