

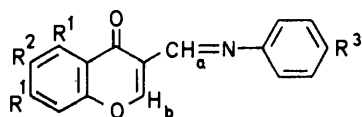
## Reactions of Formylchromone Derivatives. Part 1. Cycloadditions to 2- and 3-(Aryliminomethyl)chromones

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The reactions of several 2- and 3-(aryliminomethyl)chromones with various chloroketens have been investigated. Whereas the 2-substituted chromones gave 2-(4-oxoazetidin-2-yl)chromones, the 3-substituted chromones yielded fused pyridone derivatives.

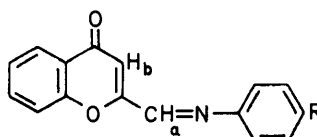
CHROMONES substituted in the 2- or 3-position by groups which conjugate with the 2,3-double bond are capable of undergoing [4 + 2] cycloaddition reactions with various dienophiles. Thus, 2-styrylchromones react with maleic

iminomethyl)chromones [(1) and (2)] with various mono- and di-chloroketens, generated in the presence of these anils by dehydrohalogenation of the corresponding acid chlorides.



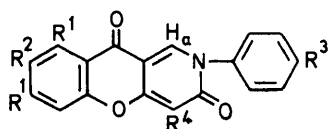
(1)

- a; R<sup>1</sup>=R<sup>2</sup>=H, R<sup>3</sup>=OMe  
 b; R<sup>1</sup>=Me, R<sup>2</sup>=H, R<sup>3</sup>=OMe  
 c; R<sup>1</sup>=R<sup>2</sup>=H, R<sup>3</sup>=Cl  
 d; R<sup>1</sup>=H, R<sup>2</sup>=Me, R<sup>3</sup>=OMe



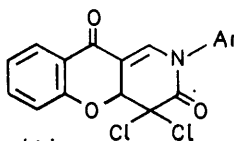
(2)

- a; R=OMe e; R=Br  
 b; R=Cl f; R=OPh  
 c; R=H g; R=NEt<sub>2</sub>  
 d; R=Me

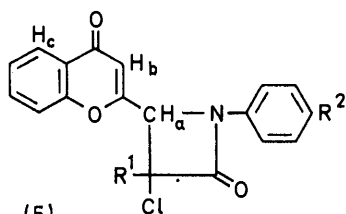


(3)

- a; R<sup>1</sup>=R<sup>2</sup>=H, R<sup>3</sup>=OMe, R<sup>4</sup>=Cl  
 b; R<sup>1</sup>=R<sup>2</sup>=H, R<sup>3</sup>=R<sup>4</sup>=Cl  
 c; R<sup>1</sup>=Me, R<sup>2</sup>=H, R<sup>3</sup>=OMe, R<sup>4</sup>=Cl  
 d; R<sup>1</sup>=H, R<sup>2</sup>=Me, R<sup>3</sup>=OMe, R<sup>4</sup>=Cl  
 e; R<sup>1</sup>=R<sup>2</sup>=H, R<sup>3</sup>=Me, R<sup>4</sup>=Ph

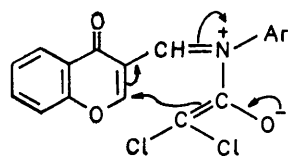


(4)

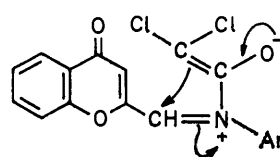


(5)

- a; R<sup>1</sup>=H, R<sup>2</sup>=OMe (*trans*) h; R<sup>1</sup>=Cl, R<sup>2</sup>=Me  
 b; R<sup>1</sup>=H, R<sup>2</sup>=OMe (*cis*) i; R<sup>1</sup>=Cl, R<sup>2</sup>=Br  
 c; R<sup>1</sup>=H, R<sup>2</sup>=Cl (*trans*) j; R<sup>1</sup>=Cl, R<sup>2</sup>=NEt<sub>2</sub>  
 d; R<sup>1</sup>=H, R<sup>2</sup>=Cl (*cis*)  
 e; R<sup>1</sup>=Cl, R<sup>2</sup>=OMe  
 f; R<sup>1</sup>=R<sup>2</sup>=Cl  
 g; R<sup>1</sup>=Cl, R<sup>2</sup>=H



(6)



(7)

anhydride<sup>1</sup> and maleimide,<sup>2</sup> and 3-benzoylchromone yields a  $\delta$ -lactone with diphenylketen.<sup>3</sup>

The present paper describes the preparation of novel systems derived from the interaction of 3- and 2-(aryl-

The 3-(aryliminomethyl)chromones (1) (see Table 1) were readily obtained from 3-formylchromones by interaction with the appropriate aromatic amines, and in the presence of dichloroketen or chloro(phenyl)keten they

<sup>1</sup> A. Schönberg, A. Mustafa, and G. Aziz, *J. Amer. Chem. Soc.*, 1954, **76**, 4576.

<sup>2</sup> A. Mustafa and M. I. Ali, *J. Org. Chem.*, 1956, **21**, 849.

<sup>3</sup> F. Eiden and M. Peglow, *Arch. Pharm.*, 1970, **303**, 825.

gave the 2-aryl[1]benzopyrano[3,2-*c*]pyridine-3,10(2*H*)-diones (3) (see Table 2). These products presumably arise from the [4 + 2] adducts (4) by dehydrohalogenation, but these intermediates were not isolated.

visualized to occur from the intermediate (6), by the well known nucleophilic attack at the chromone 2-position. On the other hand, formation of a pyridone from (7) would require nucleophilic attack at the chromone 3-

TABLE 1

Compound *	Cryst. solvent	M.p. (°C)	Yield (%)	Found (%)			Formula	Required (%)			τ (CDCl <sub>3</sub> )		
				C	H	N		C	H	N	H <sub>a</sub> (s)	H <sub>b</sub> (s)	ArH (m)
(1a)	PhH-LP †	153—155	60	72.9	5.1	5.0	C <sub>17</sub> H <sub>13</sub> NO <sub>3</sub>	73.1	4.7	5.0	1.23	1.33	3.24—2.18
(1b)	PhH	160—162	47	74.0	5.1	4.2	C <sub>19</sub> H <sub>17</sub> NO <sub>3</sub>	74.25	5.6	4.6	1.50	1.32	3.25—2.71
(1c)	PhH-LP	131—133	Quant.	67.45	3.3	5.0	C <sub>16</sub> H <sub>16</sub> ClNO <sub>2</sub>	67.7	3.55	4.9	1.30	1.30	3.30—2.11
(1d)	PhH-LP	119—120	80	73.7	5.2	4.75	C <sub>18</sub> H <sub>16</sub> NO <sub>3</sub>	73.7	5.15	4.77	1.20	1.31	3.20—2.50
(2a)	EtOH	147	78	72.6	4.8	4.9	C <sub>17</sub> H <sub>13</sub> NO <sub>3</sub>	73.1	4.7	5.0	1.65	3.11	3.10—2.16
(2b)	PhH	204	83	67.6	3.4	4.8	C <sub>16</sub> H <sub>16</sub> ClNO <sub>2</sub>	67.7	3.55	4.9	1.58	3.01	2.70—2.13
(2c)	EtOH	169—170	80	77.3	4.9	5.5	C <sub>16</sub> H <sub>11</sub> NO <sub>2</sub>	77.1	4.45	5.6	1.61	3.05	2.69—1.66
(2d)	EtOH	169	74	77.4	5.15	5.55	C <sub>17</sub> H <sub>13</sub> NO <sub>3</sub>	77.55	5.6	5.3	1.65	3.10	2.66—1.71
(2e)	PhH	193	72	58.7	3.0	4.0	C <sub>16</sub> H <sub>10</sub> BrNO <sub>2</sub>	58.55	3.0	4.25	1.75	3.14	2.89—2.26
(2f)	PhH	177	59	77.5	4.6	4.1	C <sub>22</sub> H <sub>15</sub> NO <sub>3</sub>	77.4	4.4	4.1	1.71	3.12	3.01—2.29
(2g)	PhH	155—156	58	75.3	6.4	8.4	C <sub>20</sub> H <sub>20</sub> N <sub>2</sub> O <sub>2</sub>	75.0	6.3	8.75	1.72	3.36	3.25—2.37

\* ν<sub>max</sub>. 1 645—1 660 cm<sup>-1</sup> (C=O).

† Light petroleum (b.p. 80—100 °C).

Maximum yields of the products (3) were obtained when sufficient base was present to generate the keten and accommodate the dehydrogenation of the intermediate.

Surprisingly, monochloroketen did not react with the 3-(aryliminomethyl)chromones. This is reminiscent of its failure to react with cinnamylideneaniline,<sup>4</sup> with which dichloroketen reacts 'normally.'

In contrast to the 3-(aryliminomethyl)chromones, the 2-substituted analogues (2) gave with both mono- and di-chloroketen [2 + 2] adducts, namely the azetidiones (5) (Table 3). The reaction of monochloroketen with 2-

position, which is unfavourable<sup>9</sup> in comparison with azetidione formation.

#### EXPERIMENTAL

N.m.r. spectra were determined at 90 MHz with tetramethylsilane as internal reference. Mass spectra were recorded with an A.E.I. MS12 spectrometer, and i.r. spectra were determined for Nujol mulls.

3-(Aryliminomethyl)chromones (1a—d).—A solution of equimolar quantities (0.005 mol) of 3-formylchromone and the appropriate aniline and one crystal of toluene-*p*-sulphonic acid in dry benzene (100 ml) was heated under reflux (Dean-Stark water trap) for ca. 30 min. The solvent

TABLE 2

Compound *	M.p. (°C)	Yield (%)	Found (%)			Formula	Required (%)			τ †		
			C	H	N		C	H	N	H <sub>a</sub> (s)	R <sup>b</sup>	ArH (m)
(3a)	310	74	64.3	3.4	3.8	C <sub>17</sub> H <sub>12</sub> ClNO <sub>4</sub>	64.5	3.4	4.0	0.93	5.92	2.76—1.84
(3b)	330—332	54	60.0	2.6	4.35	C <sub>18</sub> H <sub>7</sub> Cl <sub>2</sub> NO <sub>3</sub>	60.5	2.5	3.9	0.95		2.40—1.84
(3c)	279—280	85	66.1	4.4	3.7	C <sub>21</sub> H <sub>16</sub> ClNO <sub>4</sub>	66.1	4.2	3.7	1.63	5.92	2.75—2.30
(3d)	318	72	65.7	3.5	3.75	C <sub>20</sub> H <sub>14</sub> ClNO <sub>4</sub>	65.3	3.8	3.8	1.15	6.03	2.93—2.0
(3e)	250—252	21	78.7	4.5	3.5	C <sub>25</sub> H <sub>17</sub> NO <sub>3</sub>	79.1	4.5	3.7	1.25	7.56	2.80—2.06

\* ν<sub>max</sub>. ca. 1 690 and 1 660 cm<sup>-1</sup> (2 C=O). † (3a—d) in CF<sub>3</sub>CO<sub>2</sub>D; (3e) in CDCl<sub>3</sub>.

(*p*-methoxyphenyliminomethyl)chromone (2a) yielded a 1 : 1 mixture of *trans*- and *cis*-azetidiones, separable by fractional crystallisation. Similarly, 2-(*p*-chlorophenyliminomethyl)chromone (2b) reacted with monochloroketen to give the corresponding *trans*- and *cis*-azetidiones in the ratio 2 : 1, respectively. Duran and Ghosez<sup>5</sup> found that benzylideneaniline and monochloroketen gave solely the *trans*-azetidione.

The formation of pyridones (3) or azetidiones (5) is explained on the basis that zwitterionic intermediates [*e.g.* (6) and (7)] are involved in the cyclisation, in accord with earlier proposals<sup>5-8</sup> of an ionic rather than a concerted pathway for the reaction of chloroketens with anils. Thus, formation of the pyridones (3) is readily

was evaporated off and the products were purified by crystallisation; see Table 1.

2-(Aryliminomethyl)chromones (2a—g).—A solution of equimolar quantities of 2-formylchromone and the aniline derivative in dry toluene was heated at 100 °C for 30 min then cooled. The product was filtered off and crystallised (see Table 1).

2-Aryl[1]benzopyrano[3,2-*c*]pyridine-3,10(2*H*)-diones (3a—e).—To a refluxing solution of the 3-(aryliminomethyl)chromone (0.003 mol) and triethylamine (0.009 mol) in dry benzene (200 ml) was added the appropriate acid chloride (0.006 mol) in dry benzene, dropwise during the time specified in Table 2. The mixture was cooled and filtered, and the filtrate was retained. The residue was freed from triethylamine hydrochloride by slurring with water, and

<sup>4</sup> D. Johnson, Ph.D. Thesis, University of Salford, 1974.

<sup>5</sup> F. Duran and L. Ghosez, *Tetrahedron Letters*, 1970, 245.

<sup>6</sup> H. B. Kagan and J. K. Luche, *Tetrahedron Letters*, 1968, 3093.

<sup>7</sup> R. Huisgen, B. A. Davis, and M. Morikawa, *Angew. Chem. Internat. Edn.*, 1968, 7, 826.

<sup>8</sup> A. Gomes and M. M. Joville, *Chem. Comm.*, 1967, 935.

<sup>9</sup> G. Wurm, *Arch. Pharm.*, 1975, 308, 67.

the resulting crude product was dried and combined with the product obtained by evaporation of the filtrate. Crystallisation from anisole gave the 2-aryl[1]benzopyrano[3,2-c]-pyridine-3,10(2H)-diones (see Table 2).

1-Aryl-3-chloro-4-(4-oxochromen-2-yl)azetid-2-ones (5a—

1-Aryl-3,3-dichloro-4-(4-oxochromen-2-yl)azetid-2-ones (5e—j).—To a refluxing solution of the 2-(aryliminomethyl)-chromone (0.005 mol) and triethylamine (0.01 mol) in dry benzene (100 ml) was added dichloroacetyl chloride (0.01 mol) in dry benzene (25 ml) dropwise over 45 min. The

TABLE 3

1-Aryl-3-chloro- and 3,3-dichloro-4-(4-oxochromen-2-yl)azetid-2-ones (5)

Compound *	M.p. (°C)	Yield (%)	Found (%)			Formula	Required (%)			$\tau$ (CDCl <sub>3</sub> )				
			C	H	N		C	H	N	R <sup>2</sup>	H <sub>a</sub>	H <sub>b</sub> (s)	H <sub>c</sub> (dd)	ArH (m)
(5a) ( <i>trans</i> )	185—187	37	64.6	4.1	3.9	C <sub>19</sub> H <sub>14</sub> ClNO <sub>4</sub>	64.1	4.0	3.9	6.22 (OMe)	4.72 (q, J, 2 Hz)	3.33	1.79	3.15—2.16
(5b) ( <i>cis</i> )	176—177	35	63.9	3.9	3.9	C <sub>19</sub> H <sub>14</sub> ClNO <sub>4</sub>	64.4	4.0	3.9	6.22 (OMe)	4.66 (q, J 5 Hz)	3.56	1.73	3.18—2.25
(5c) ( <i>trans</i> )	203—204	30	60.4	3.2	3.6	C <sub>18</sub> H <sub>10</sub> Cl <sub>2</sub> NO <sub>3</sub>	60.0	3.1	3.9		4.41 (dd)	3.27	1.95	2.69—2.24
(5d) ( <i>cis</i> )	188—189	28	59.8	3.0	3.8	C <sub>18</sub> H <sub>11</sub> Cl <sub>2</sub> NO <sub>3</sub>	60.0	3.1	3.9		4.07 (q, J 5 Hz)	3.43	1.99	2.59—2.15
(5e)	176—177	93	58.9	3.7	3.3	C <sub>19</sub> H <sub>13</sub> Cl <sub>2</sub> NO <sub>4</sub>	58.5	3.4	3.6	6.18 (s, OMe)	4.66 (s)	3.56	1.73	3.16—2.26
(5f)	166—167	76	54.5	2.4	3.55	C <sub>18</sub> H <sub>10</sub> Cl <sub>2</sub> NO <sub>3</sub>	54.8	2.55	3.55		4.50 (s)	3.48	1.69	2.61—2.00
(5g)	134	55	60.4	3.3	3.9	C <sub>18</sub> H <sub>11</sub> Cl <sub>2</sub> NO <sub>3</sub>	60.0	3.1	3.9		4.58 (s)	3.59	1.85	2.86—2.20
(5h)	159—160	82	61.1	3.8	3.5	C <sub>19</sub> H <sub>13</sub> Cl <sub>2</sub> NO <sub>3</sub>	61.0	3.5	3.7	7.72 (s, Me)	4.55 (s)	3.60	1.88	2.94—2.24
(5i)	169	60	49.6	2.4	2.9	C <sub>18</sub> H <sub>10</sub> BrCl <sub>2</sub> NO <sub>3</sub>	49.2	2.3	3.2		4.60 (s)	3.59	1.81	2.78—2.27
(5j)	148—149	67	61.2	4.8	6.2	C <sub>22</sub> H <sub>20</sub> Cl <sub>2</sub> N <sub>2</sub> O <sub>3</sub>	61.2	4.7	6.5	8.85 (t), 6.69 (q), (NEt <sub>2</sub> )	4.66 (s)	3.58	1.83	3.44—2.20

\*  $\nu_{\max}$ . ca. 1 800 and 1 650 cm<sup>-1</sup> (C=O).

d).—To a refluxing solution of the 2-(aryliminomethyl)-chromone (2) (0.006 mol) and triethylamine (0.012 mol) in dry benzene (100 ml) was added chloroacetyl chloride (0.012 mol) in dry benzene (25 ml) dropwise over 30 min. The mixture was cooled and filtered and the filtrate was evaporated. The residue\* was triturated with ethanol, and the resulting solid was crystallised to give the *trans*-1-aryl-3-chloro-4-(4-oxochromen-2-yl)azetid-2-one (5a or c). When the mother liquor from crystallisation was appropriately concentrated the *cis*-isomer (5b or d) was obtained (see Table 3).

mixture was cooled and filtered and the filtrate was evaporated. The residue was triturated with ethanol and the resulting solid was crystallised to give the 1-aryl-3,3-dichloro-4-(4-oxochromen-2-yl)azetid-2-ones (see Table 3).

We thank Fisons (Loughborough) and the S.R.C. for studentships (for J. R. F. and P. G. H., respectively).

[6/2189 Received, 29th November, 1976]

\* N.m.r. spectra of the residue showed that the *trans-cis* ratios (c : d and a : b) were 2 : 1 and 1 : 1, respectively.