Synthesis of 2-Aryl(Heteroaryl)-9-oxo-1,9-dihydropyrrolo[3,2-*b*][1]benzopyrans; A Novel Ring System

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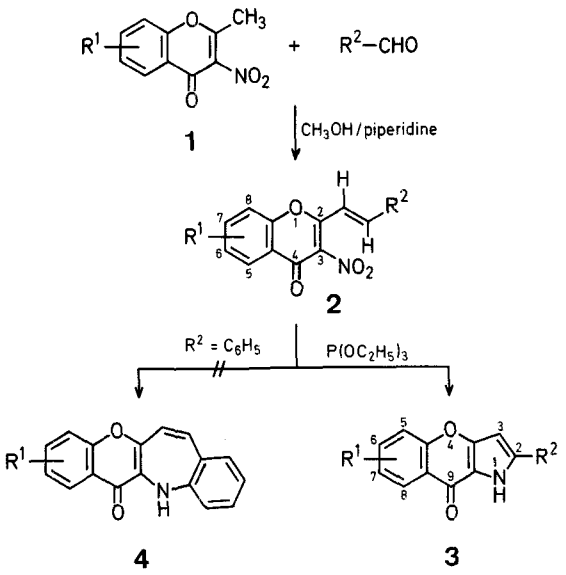
The pharmacological interest of certain chromone derivatives and the paucity of literature on 2,3-fused chromone ring systems led us to work out a general and facile synthesis of 2-aryl- and 2-heteroaryl-9-oxo-1,9-dihydropyrrolo[3,2-*b*][1]benzopyrans **(3)** which contain a new ring system. The method consists of condensation of an aromatic or heterocyclic aldehyde with a 2-methyl-3-nitrochromone **(1)** and reductive cyclisation of the resultant 3-nitro-2-styrylchromones **(2)** using triethyl phosphite at 180 °C.



We have previously reported[1] the synthesis of 2-methyl-3-nitrochromones **(1)** starting from 2-hydroxy-ω-nitroacetophenones. The methyl group in 2-methyl-3-nitrochromones **(1)** is sufficiently activated for condensation with aldehydes by the presence of the vicinal nitro group. Thus, compounds **2** may be obtained in 65–70% yield by condensation of **1** with benzaldehyde, substituted benzaldehydes, or heterocyclic aldehydes. Reductive cyclisation of compounds **2** using the procedure of Cadogan et al.[2] affords the pure pyrrolo[3,2-*b*][1]benzopyran derivatives **3** as pale pink or colourless solids in 45–50% yields. This cyclisation reaction does not proceed, however, with 6-methyl-3-nitro-2-[2-(5-nitro-2-furyl)-vinyl]chromone **(2i)**.

The structure of the styrylchromones **2** is corroborated by the mass spectrum. Compounds **2** are unstable to electron impact as evidenced by the low abundance of molecular ion. In general, *o*-nitro-styryl derivatives undergo rearrangements[5,6] under electron impact due to an *ortho* effect. The I.R. absorption[3] of compounds **2** ($\nu = 960\ cm^{-1}$) and the ^1H-N.M.R. coupling constant ($J = 15$ Hz) indicate *trans* disposition of the olefinic protons.

In analogy to the reductive cyclisation of *o*-nitrostilbenes to indoles and on the basis of their spectral data, the 2-aryl(heteroaryl)-9-oxo-1,9-dihydropyrrolo[3,2-*b*][1]benzopyran structure was assigned to the cyclisation products **3**. Compounds **3** are highly stable to electron impact as evidenced by the appearance of the molecular ion as the base peak in the mass spectrum and by the occurrence of relatively little fragmentation, characteristic of pyrrole-fused heterocycles[7]. The parent molecular ion is accompanied by the doubly charged ion which is characteristic of nitrogen heterocycles[8]. Probably due to the high stability of the pyrrole-fused ring system, the characteristic retro-Diels-Alder fragmentation of chro-

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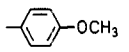
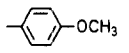
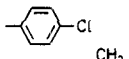
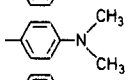
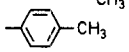
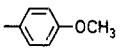
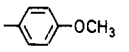
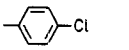
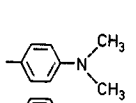
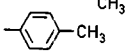
Table 1. 3-Nitro-2-styrylchromones (2)

2	R^1	R^2	Yield [%]	m.p.[a] [°C]	Molecular formula[b]	M.S.[c] *m/e* (M^+)	I.R. (KBr)[d] ν [cm^{-1}] C=O	C=C	NO_{2asym}	NO_{2sym}	U.V. (methanol)[e] λ_{max} [nm]
a	H		75	228°	$C_{18}H_{13}NO_5$[f] (323.3)	323	1650	1610	1520	1375	225, 285, 318
b	6-CH_3		70	232°	$C_{18}H_{12}ClNO_4$ (341.7)	341	1650	1610	1525	1375	243, 338
c	6-CH_3		70	228°	$C_{19}H_{15}NO_5$ (337.3)	337	1650	1600, 1630	1545	1350	248, 350
d	6-CH_3		80	280°	$C_{18}H_{12}ClNO_4$ (341.7)	341	1650	1610, 1630	1540	1350	222, 336
e	6-CH_3		70	217°	$C_{20}H_{18}N_2O_4$ (350.4)	350	1650	1615, 1640	1540	1380	232, 325
f	6-CH_3		75	234°	$C_{19}H_{15}NO_4$ (321.3)	321	1640	1600, 1625	1525	1380	247, 328
g	6-CH_3		72	236°	$C_{18}H_{13}NO_4$ (307.3)	307	1650	1615, 1640	1530	1350	235, 344
h	6-CH_3		72	188°	$C_{16}H_{11}NO_5$ (297.3)	297	1650	1615, 1640	1530	1350	235, 344
i	6-CH_3		65	244°	$C_{16}H_{10}N_2O_7$ (342.3)	342	1640	1610, 1625	1535	1355	240, 290, 350
j	6-CH_3		70	224°	$C_{16}H_{11}NO_4S$ (313.3)	313	1650	1610, 1630	1525	1360	242, 340

[a] Uncorrected.
[b] The microanalysis were in satisfactory agreement with the calculated values: C, ±0.18; H, ±0.06; N, ±0.06.
[c] Recorded on a Perkin-Elmer Hitachi RMU 6L instrument.
[d] Recorded on a Perkin-Elmer I.R. spectrophotometer.
[e] Recorded on a Hilger & Watts instrument.
[f] ^{1}H-N.M.R. (CF_3COOH/TMS): δ = 7.40–7.65 (m, 7H); 8.10 (dd, 1 H_{arom}, J = 2 and 8 Hz); 7.25 (d, 1H, J = 15 Hz); 6.51 (d, 1H, J = 15 Hz); 3.33 ppm (s, 3H, OCH_3). The spectrum was recorded on a Varian A-60 D-spectrometer. The N.M.R. spectra of the other compounds **2** were not recorded because of the poor solubility of these compounds in the usual N.M.R. solvents.

Table 2. 2-Aryl(Heteroaryl)-9-oxo-1,9-dihydropyrrolo[3,2-*b*][1]benzopyrans **(3)**

3	R^1	R^2	Yield [%]	m.p.[a] [°C]	Molecular formula[b]	M.S.[c] *m/e* (M^+, 100%)	I.R. (KBr)[d] ν [cm^{-1}] C=O	NH	U.V. (methanol)[e] λ_{max} [nm]	^{1}H-N.M.R. (CF_3COOH/TMS)[f] δ [ppm]
a	H		55	215°	$C_{18}H_{13}NO_3$ (291.3)	291	1635	3185	235, 250, 350	
b	7-CH_3		50	>300°	$C_{18}H_{12}ClNO_2$ (309.7)		1640	3160	240, 330	
c	7-CH_3		55	302°	$C_{19}H_{15}NO_3$ (305.3)		1635	3175	230, 242, 345	
d	7-CH_3		55	>300°	$C_{18}H_{12}ClNO_2$ (309.7)	309	1630	3185	241, 332	6.85 (s, 1H, 8-H); 8.10 (s, 1H, 3-H); 2.60 (s, 3H, 7-CH_3); 7.35–7.75 (m, 6 H_{arom})
e	7-CH_3		50	>300°	$C_{20}H_{18}N_2O_2$ (318.4)	318	1630	3170	225, 268	
f	7-CH_3		50	>300°	$C_{19}H_{15}NO_2$ (289.3)	289	1630	3180	230, 260	7.65 (s, 1H, 8-H); 8.00 (s, 1H, 3-H); 2.55 (s, 3H, 7-CH_3); 2.83 (s, 3H, 4-CH_3); 7.10–7.66 (m, 6 H_{arom})
g	7-CH_3		55	>300°	$C_{18}H_{13}NO_2$ (275.3)		1630	3180	227, 338	
h	7-CH_3		40	>300°	$C_{16}H_{11}NO_3$ (265.3)		1635	3175	234, 316	
j	7-CH_3		40	>300°	$C_{16}H_{11}NO_2S$ (281.3)	281	1630	3175	230, 314	

[a,c,d,e] As in Table 1.
[b] The microanalyses were in satisfactory agreement with the calculated values: C, ±0.10; H, ±0.08; N, ±0.08.
[f] Recorded on a Varian A-60/A-90 D-spectrometer.

mones was not observed with compounds **3**. The I.R. spectrum of compounds **3** shows no absorption around $\nu = 3300–3500\ cm^{-1}$ but shows a broad band around $\nu = 3150\ cm^{-1}$ assigned to the stretching vibration of the N—H proton which is strongly chelated with the chromone C O group. In the ^{1}H-N.M.R. spectrum in trifluoroacetic acid in which the protonated compounds **3** exist mainly in the C-protonated form **II**,

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the signal of the NH proton is not observed. The alternative structure **4** of the cyclisation product cannot only be ruled out on the basis of spectral data but also by the known fact that in cyclisations of nitrenes the formation of a five-membered ring is preferred to that of a seven-membered ring[2].

3-Nitro-2-styrylchromones (2); General Procedure:
The 2-methyl-3-nitrochromone **1** (2.5 mmol) is dissolved in the minimum quantity of dry methanol (15 ml) and the aromatic or heterocyclic aldehyde (2.5 mmol) and a few drops of piperidine are added. The mixture is heated to reflux on a water bath for ~30 min. The yellow crystalline solid which separates in the hot is isolated by suction and recrystallised from methanol.

2-Aryl(Heteroaryl)-9-oxo-1,9-dihydropyrrolo[3,2-*b*][1]benzopyrans (3); General Procedure:
In an apparatus with a nitrogen inlet placed so that nitrogen is bubbled through the reaction mixture, the 3-nitro-2-styrylchromone **2** (2 mmol) and excess triethyl phosphite (7 ml) are mixed and the mixture is heated to reflux (180 °C) in an oil bath. Compound **2** dissolves and the colour of the solution gradually changes from pale yellow to dark brown. A solid begins to separate after 6 h and the reaction is complete after 9 h of heating. The mixture is then cooled to room temperature and product **3** isolated by suction. It is washed thoroughly with petroleum ether in order to remove triethyl phosphite and triethyl phosphate. Recrystallisation from acetone affords the product as shining pale pink to colorless needles.

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[1] K. V. Rao, V. Sundaramurthy, *Indian J. Chem.* **15B**, 236 (1977).
[2] J. I. G. Cadogan, R. K. Mackie, *Chem. Soc. Rev.* **3**, 87 (1974).
J. I. G. Cadogan, M. Cameron-Wood, R. K. Mackie, R. J. Searle, *J. Chem. Soc.* **1965**, 4831.
R. J. Sundberg, *J. Org. Chem.* **30**, 3604 (1965).
[3] L. J. Bellamy, in: *The Infrared Spectra of Complex Molecules*, John Wiley & Sons, New York, 1958, p. 34.
[4] L. M. Jackman, *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, Pergamon Press, Oxford · New York, 1959, p. 85.
[5] J. Seibl, J. Völlmin, *Org. Mass Spectrom.* **1**, 714 (1968).
[6] D. V. Ramana, M. Vairamani, *Org. Mass Spectrom.* **9**, 1158 (1974).
[7] Q. N. Porter, J. Baldas, *Mass Spectrometry of Heterocyclic Compounds*, Wiley-Interscience, New York, 1971, p. 343.
[8] W. J. Houlihan, *Indoles*, Part I, Wiley-Interscience, New York, 1972, p. 41.