# UV-induced isomerisation and ring transformation of (E)-3-arylidene-1-thiochromanones and -1-thioflavanones

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Depending on the substituent of the arylidene moiety, photoisomerisation of (E)-3-arylidene-1thiochroman-4-ones 1 and 3 afforded either the expected (Z)-1 and (Z)-3 isomers or the products (2d,e and 4c,d) of an unprecedented phototransformation.

We have developed a simple and convenient method for synthesising (E)-3-arylidene-1-thiochroman-4-ones (E)-1 and (E)-3-arylidene-2-phenyl-1-thiochroman-4-ones (E)-3 [(E)-3arylidene-1-thioflavan-4-ones] by the piperidine-catalysed reaction of 1-thiochroman-4-one or 1-thioflavan-4-one with aromatic aldehydes.<sup>1-3</sup> Since we planned a comparative investigation of the reactivities of the E and Z isomers of these compounds, it was necessary to develop an efficient method for the preparation of the Z isomers as well. Except for the (Z)-3-benzylidene-6-methyl-1-thioflavan-4-one<sup>4</sup> no substituted derivative of such Z compounds has hitherto been reported in the literature.

Previously we have reported that the UV-irradiation of (E)-3-benzylidene-chromanone and -flavanone and their 1-thio analogues resulted in the formation of their Z isomers.<sup>5,6</sup> Now we aim to prepare derivatives of these compounds substituted in the arylidene moiety. <sup>1</sup>H NMR data of the E and Z isomers show a characteristic downfield shift (ca. 0.3 ppm) of the  $\delta_{2-H_2}$ chemical shift of the E isomers compared with those of the Zisomers as a result of the spatial proximity of the aryl group, while a paramagnetic shift was observed for the  $\delta_{9-H}$  signal due to the anisotropy of the C-4=O moiety.<sup>5,7</sup> <sup>13</sup>C NMR investigations revealed a y-steric interaction on the C-2 signal of the E isomers which resulted in a 5-8 ppm upfield shift in comparison with the Z isomers. In the E isomers there is conjugation between the C-4=O and C-9 aryl group, while in the Z isomers, because of steric reasons, the C-9 aryl moiety is nearly perpendicular to the plane of the carbonyl group, which is reflected in a  $\Delta\delta$  ca. 1 ppm C-4 downfield shift in these isomers.<sup>6</sup> These observations make possible an unambiguous differentiation of the Z and E isomers.<sup>6</sup>

#### **Results and discussion**

(E)-3-Arylidene-1-thiochroman-4-ones  $[(E)-1\mathbf{a}-\mathbf{e}]$  in anhydrous benzene dried on sodium was irradiated with a mercury arc lamp (Scheme 1). The careful drying of the solvent with sodium is essential to eliminate the acid traces which may help the reconversion of the Z isomers formed into the starting E isomers. For the same reason, acid-free  $C_6D_6$  and  $CDCl_3$  were used for the 250 and 62.5 MHz NMR studies. Photoisomerisation of (E)-1 $\mathbf{a}-\mathbf{c}$  afforded (Z)-1 $\mathbf{a}-\mathbf{c}$  as sole isolable products in moderate yields (35–46%). A longer irradiation time resulted in an increase in decomposition instead of a higher yield. However, the same reaction of compounds (E)-1 $\mathbf{d}$ , gave 3-methylidene-1-thioflavan-4-ones (2 $\mathbf{d},\mathbf{e}$ ) and no Z isomers could be detected in the reaction mixtures.



Scheme 1

**Table 1** <sup>1</sup>H Chemical shifts of (Z)-1 and 2  $(C_6D_6)$ 

	(Z)-1aª	(Z)-1b	(Z)-1c	2đ	2e
2-Н	3.91	3.37	3.35	4.89	4.81
5-H	8.28	8.49	8.38	8.46	8.30
6-H	7.25	6.90	6.91	6.87	6.78
7 <b>-</b> H	7.40	6.96	6.99	6.93	6.85
8-H	7.31	7.11	7.10	7.09	6.98
9-H <sub>F</sub>	6.93	6.57	6.34	5.09	5.00
$9-H_z$	_			6.48	6.35
2′,6′-H	7.48	7.68	7.32	7.29	7.18
3',5'-H	7.17	7.11	7.13	6.73	6.65
Others	Me	Pr <sup>i</sup>		OMe	OEt
	2.39	2.75		3.32	3.50
		1.18			1.07

" Measured in acid free CDCl<sub>3</sub>.

On the basis of <sup>1</sup>H and <sup>13</sup>C NMR measurements it can be concluded that instead of the S–C-2H<sub>2</sub>–C-3=C-9–Ar moiety of the 3-arylidene-1-thiochromanones an S–C-2H–C-3=C-9H<sub>2</sub> structural element has been introduced (Tables 1 and 2). In the <sup>1</sup>H NMR spectrum the 2-H signal is broad and non-resolved at 4.89 and 4.81 ppm, respectively, while the 9-H<sub>z</sub> 6.48/6.35 and 9-H<sub>E</sub> 5.09/5.00 signals of the terminal methylidene group are triplets with a 1.5 Hz coupling constant [<sup>2</sup>J(9-H<sub>E</sub>, 9-H<sub>z</sub>)  $\approx$  <sup>4</sup>J(2-H, 9-H)  $\approx$  1.5 Hz]. The assignment was corroborated by the 9-H<sub>z</sub> (33.6%), 2-H (2.2%) and 2',6'-H (1.5%) NOE values measured on the irradiation of the 9-H<sub>E</sub>. A *ca.* 1.4 ppm difference in the chemical shifts of the terminal methylidene protons is a consequence of the anisotropic effect of the C-4=O

	(Z)-1aª	(Z)-1b	(Z)-1c	2d	2e
C-2	36.8	37.1	36.8	50.2	50.3
C-3	130.8	131.6	133.0	145.5	145.6
C-4	186.6	186.4	186.0	185.1	185.0
C-4a	131.9	133.2	133.9	132.3	132.3
C-5	129.7	130.2	130.2	130.3	130.3
C-6	124.9	125.3	125.4	125.9	125.9
C-7	132.7	132.9	133.2	133.3	133.3
C-8	127.2	127.5	127.6	127.9	127.9
C-8a	141.3	141.9	141.9	140.7	140.8
C-9	137.4	137.6	135.9	123.6	123.6
C-1'	132.0	133.1	132.7	129.4	129.2
C-2′,6′	129.4	130.6	131.5	129.8	129.8
C-3',5'	128.6	126.4	128.4	114.3	114.8
C-4'	138.6	149.8	134.6	159.8	159.2
Others	Me	Pr <sup>i</sup>		OMe	OEt
	21.1	34.2		54.7	63.2
		23.8			14.8

" Measured in acid free CDCl<sub>3</sub>.

**Table 3** Results of semi-selective 1D INEPT [J(C,H) = 7 Hz] measurements

	Proton	Carbon
(Z)-1a	2-H,	C-3; C-4; C-8a; C-9
	9-H	C-2; C-3; C-4; C-1'; C-2',6'
(Z)-1b	2-H <sub>2</sub>	C-3; C-4; C-8a
	9-H	C-4; C-2',6'
	9-H "	C-2; C-3; C-4; C-1'
(Z)-1c	2-H <sub>2</sub>	C-3; C-4; C-8a; C-9
. ,	9-H <sup>~</sup>	C-2; C-3; C-4; C-2',6'
	9-H <sup>a</sup>	C-2; C-3; C-4; C-1'; C-2',6'
2d	2-H	C-3; C-4; C-8a; C-9; C-1'; C-2'.6'
	5-H	C-4; C-7; C-8a
	8-H	C-4a; C-6

**U**(C,II) 51

group on the neighbouring proton. The presence of the S-C-2H-C-3=C-9H<sub>2</sub> structural unit has been proven by <sup>13</sup>C DEPT measurements. The C-9 signal showed a ca. 14 ppm diamagnetic shift and the C-2 signal a ca. 13 ppm paramagnetic shift in the rearranged products 2 compared with the (Z)-3-arylidene-1thiochroman-4-ones 1, which is in accordance with the presence of the aryl substituent on C-2 instead of C-9. A further proof of this fact is the semi-selective 1D INEPT<sup>8</sup> measurement starting from 2-H, optimised for the J(C,H) = 7 Hz long-range coupling, which reveals the carbon atoms at two or three bond distances (C-1', C-2',6', C-3, C-4, C-8a and C-9) (Table 3). Semi-selective 1D INEPT measurements starting from 5-H and 8-H allowed the unambiguous assignment of the <sup>13</sup>C signals of the condensed aromatic ring. The significant paramagnetic shift of C-3 signals (ca. 14 ppm) in the case of the ring-transformed products 2 is in accordance with the fact that a phenyl group in the  $\beta$ -position of the C-3=C-9 double bond results in a diamagnetic shift, while a phenyl group at the  $\beta$ -position of the C-3-C-2 single bond results in a paramagnetic shift.

#### **Conformational effects**

In the course of the conformational analysis of the (E)- and (Z)-3-arylideneflavanones and their thio analogues we have found that the condensed six-membered ring may adopt two, energetically slightly different envelope conformers (A and B) where the C-2 phenyl group is axial in A and equatorial in B.<sup>6</sup> In flavanone and 1-thioflavanone the equatorial arrangement of the C-2 phenyl group is more favourable than the axial one. In the *E* and *Z* isomers, as a result of the presence of the C-3 *exo* double bond the axial position is more favourable owing to the

1,3-allylic strain,<sup>9</sup> and the ratio of the envelope A is enhanced in the conformational equilibrium. In the E isomer as a result of a steric interaction between the C-2 phenyl group and the *peri*positioned  $\beta$ -substituent of the *exo* double bond, the  $A \implies B$ conformational equilibrium is shifted in the direction of A (*ca.* 90%). It has also been concluded that the <sup>3</sup>J(C-8a, 2-H) coupling constants make possible a nearly quantitative description of the  $A \implies B$  conformational equilibrium. Investigation of model compounds show that the expected coupling constant values are  $J(C-8a, 2-H_{eq})$  *ca.* 8 Hz and  $J(C-8a, 2-H_{ax})$  *ca.* 1 Hz. In compound 2d J(C-8a, 2-H) is 3.6 Hz which reveals an A:B conformer ratio of *ca.* 37:63.

In the case of compound 2d AM1 (Mopac-6, version 1990)<sup>10</sup> calculations have also been performed and the results are in accordance with the NMR data (the energies of the two conformers are very similar with  $\Delta E \ ca.$  1.3 kcal mol<sup>-1</sup>† in favour of the B conformer). Conformation of the C-2 aryl group can be evaluated from the  ${}^{3}J(C-2',6',2-H)$  coupling constants. If the C-2-H bond and the connecting C-2-aromatic ring are coplanar, the coupling constant should be 5-6 Hz which gradually decreases with the ratio of this conformer.<sup>5,6,11</sup> Conformational analysis is made difficult by the fact that an  $\Rightarrow$  **B** conformational equilibrium should be considered in  $\mathbf{A} =$ the case of compound 2d. In conformer B the exo double bond is in spatial proximity to the aromatic ring which adopts a perpendicular position to this and, therefore, the C-2'-C-1'-C-2-2-H moiety is almost coplanar. In the case of compound 2d the AM1 calculations gave the dominant conformer of the aryl group for both conformers (see Scheme 2). The C-2'-C-1'-C-2-



Scheme 2 Preferred conformations of compound 2d obtained by AM1

2-H dihedral angle is 11° for conformer **B** and  $-56^{\circ}$  for conformer **A**.  ${}^{3}J(\text{C-2'},6',2\text{-H}) = 4.2$  Hz coupling constant, an average value determined by semi-selective 2D INEPT<sup>12</sup> measurement is in accord with the results of the semi-empirical calculations, since 5–6 and 2–3 Hz coupling constants belong to dihedral angles 11 and 56°, respectively, and the observed value belongs to a fast equilibrium.

#### Mechanism for ring transformation

The unprecedented ring transformation of compounds (E)-1d,e may probably take place as shown in Scheme 3. Homolytic splitting of the S–C-2 bond maybe promoted by the stabilisation of the radical centre on the arylidene group with alkoxy substituent.

(E)-3-Arylidene-1-thioflavan-4-ones 3 have also been included in our study. Since beside the  $E \rightarrow Z$  isomerisation a ring transformation may take place as well, formation of four products, viz. (E)-3, (Z)-3, (E)-4 and (Z)-4 (Scheme 4) should be considered. Irradiation of the (E)-3a, b resulted in the formation of (Z)-3a, b which is reflected in the characteristic changes of the 2-H; 9-H and C-2 chemical shift values (Table 4). In the case of (E)-3c a mixture was obtained and in the <sup>1</sup>H spectrum two major components (55 and 28%) and two minor components

 $\dagger 1 \text{ cal} = 4.184 \text{ J}.$ 



Scheme 3



Table 4 Characteristic <sup>1</sup>H and <sup>13</sup>C chemical shifts of 3 and 4  $(C_6D_6)^a$ 

	$\delta_{2-H}$	$\delta_{9-H}$	$\delta_{C-2}$	$\delta_{C-4}$	$\delta_{C-9}$	$\delta_{ ext{C-1}^{\prime\prime}}$
(Z)-3b	4.98	6.73	53.9	187.2	137.7	
(E)- <b>3b</b>	5.77	8.32	46.4	185.6	138.7	
(Z)-3c	4.93	6.48	53.2	186.9	136.1	
(Z)-4c	4.76	6.62				
(E)-3c	5.53	8.04	46.0	185.4	137.0	
(E)- <b>4</b> c	5.55	8.20				
(Z)- <b>3d</b>	4.99	6.72	54.0	187.2	137.1	138.1
(Z)- <b>4d</b>	5.01	6.70	53.2	187.4	137.9	129.1
( <i>E</i> )-3d	5.79	8.30	46.4	185.5	138.8	140.7
(E) <b>-4d</b>	5.71	8.24				

<sup>a</sup> The chemical shifts of compounds **3-4c,d** were obtained from the spectra of the isomeric mixtures.

(7 and 10%) have been detected, but in the <sup>13</sup>C NMR spectra assignment of only the two major components could be made. On the basis of the 2-H, 9-H and C-2 signals, the component which is present in 55% is (*Z*)-3c and that present in 28% is the starting compound (*E*)-3c.

Irradiation of (*E*)-**3d** resulted in the formation of four products as well. The two *Z* isomers [(*Z*)-**3d** and (*Z*)-**4d**] have been differentiated by the C-1" chemical shift since it is known that a *p*-OMe group results in a *ca.* 8 ppm diamagnetic shift. Semi-selective 1D INEPT measurements starting from the 2-H of the *Z* compound and optimised for J(C,H) = 7 Hz longrange coupling revealed the C-3, C-4, C-8a, C-9, C-1" and C-2",6" signals. In (*Z*)-**3d**  $\delta_{C-1"}$  is 138.1 ppm and 129.1 ppm in (*Z*)-**4d** which prove that in the latter isomer a *p*-OMe-phenyl group is connected to the C-2 atom, *viz.* a ring transformation

Table 5 Physical constants of the isolated products

Compound	Formula <sup>a</sup>	Yield (%)	Mp/°C
(Z)-1a	C <sub>17</sub> H <sub>14</sub> OS	35	53-55
(Z)-1b	$C_{19}H_{18}OS$	41	Yellow oil
(Z)-1c	C <sub>16</sub> H <sub>14</sub> ClOS	46	Yellow oil
2d	$C_{17}H_{14}O_{2}S$	42	94-95
2e	$C_{18}H_{16}O_{2}S$	36	77-78
(Z)- <b>3a</b>	$C_{23}H_{18}OS$	55	Yellow oil
(Z)-3b	$C_{25}H_{22}OS$	39	Yellow oil
(Z)-3c	$C_{22}H_{15}ClOS$	42	Yellow oil

<sup>a</sup> Elemental analyses (C,H) were in good agreement with the calculated values.

took place due to the irradiation, similar to 3-arylidene-1thiochroman-4-ones. Prolongation of the irradiation time resulted in a pronounced decomposition of 3 and 4 and after 12 h irradiation they could not be detected in the reaction mixture by NMR spectroscopy. Irradiation for 3 h resulted in *ca.* 50% decomposition and the formation of a four component mixture (Z)-3d:(Z)-4d:(E)-3d:(E)-4d = 1:2:1:1. We failed to isolate the rearranged products (Z)-3d and 4c,d from the reaction mixture.

In summary, we have observed an unprecedented phototransformation of alkoxy substituted 3-arylidene-1-thiochroman-4ones leading to 3-methylene-1-thioflavan-4-ones. This reaction may serve as a synthetic procedure for the preparation of 3-methyldiene-1-thioflavan-4-ones. A similar phototransformation with the analogous 3-arylidene-1-chroman-4-ones and 3arylidene-1-flavan-4-ones was not observed.<sup>7,13-15</sup> The only example of such compounds is the 3-methylidene-1-thioflavan-4-one itself obtained by the reaction of 1-thioflavan-4-one with bis(dimethylamino)methane.<sup>16</sup>

#### Experimental

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. NMR spectra were recorded on a Bruker AC-250 spectrometer at room temperature in  $CDCl_3$  or in  $C_6D_6$ . Chemical shifts are given on the  $\delta$  scale and referenced to internal TMS. In the 1D measurements 32 K data points were used for the FID. A delay time of 5 s was applied for homonuclear NOE experiments. The 1D semiselective INEPT measurements were optimised for J(C,H) =7 Hz coupling and 25 Hz selectivity. In the 2D semi-selective INEPT measurement the data matrices were 8 K × 64 data points and the spectral width in the F1 (proton) dimension was 10 Hz.

## General procedure for the photoisomerisation of (E)-1a-e and (E)-3a-d

Compounds (E)-1a-e and (E)-3a-d (10 mmol) were dissolved in anhydrous benzene (300 cm<sup>3</sup>) and irradiated with a 400 W mercury arc lamp at ambient temperature for 3 h. The solvent was evaporated under reduced pressure (*ca.* 20 Torr) and the residue was purified on a silica gel (Merck) column using dichloromethane:hexane (3:2 v/v) as eluent to afford substances (Z)-1a-c, 2d,e, (Z)-3a-c (Schemes 1 and 4, Table 5).

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