Synthesis of some Furochromonesulfonamide Derivatives with Potential Pharmacological Activity

M. Hani A. Elgamal* and Nagwa M. M. Shalaby

National Research Centre, Laboratory of Natural Products,
Sh. El-Tahrir, Dokki - Cairo, Egypt

Helmut Duddeck* and Doris Rosenbaum

Ruhr-Universität Bochum, Fakultät für Chemie,
Postfach 102148, D-4630 Bochum 1, West Germany

Received September 23, 1986

A number of visnagin-9-sulfonamides **1-3** have been prepared. In two instances side-products have been isolated in which the γ-pyrone ring is opened. All compounds were characterized by high-field ^1H and ^{13}C nmr and mass spectra.

J. Heterocyclic Chem., **24**, 721 (1987).

Visnagin (**1a**) is an important adjunct in the furochromone constituents [1] of *Ammi visnaga* L. fruits grown locally. It has been reported that visnagin possesses selective spasmolytic [2], antihistaminic [3] and coronary vasodialator activities [4]. So, it was deemed desirable to synthesize some sulfonamide derivatives from visnagin which may have activities.

Visnagin-9-sulfonyl chloride (**1b**) was obtained by chlorosulfonation [5] of the naturally occurring furochromone visnagin (**1a**). Its mass spectrum shows an M^+ peak at m/e 328/330 (intensities 3:1), its ir spectrum bands at 1655, 1625 and 1590 (γ-pyrone), 1372 and 1185 cm^{-1} (SO_2Cl) and its uv spectrum three characteristic maxima for the furochromone skeleton at 240, 290 and 330 nm. The position of the sulfonyl group at C-9 in **1b** was confirmed by the disappearance of the H-9 signal (δ = 7.14 in **1a**) in its ^1H nmr spectrum and the presence of the H-6 signal at δ = 6.13. The doublets at δ = 7.77 and 7.18 (J = 2.7 Hz) are due to H-2 and H-3, respectively, and the signals of CH_3 and OCH_3 groups are at δ = 2.43 and δ =

Scheme

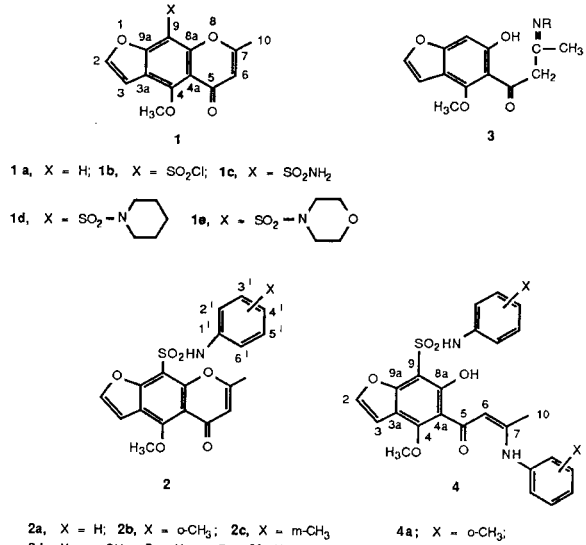

Table 1

^1H Chemical Shifts of the Sulfonamide Compounds **1-4** [a]

	1a [b]	**1b**	**1c**	**2a**	**2b**	**2c**	**2d**	**2e**	**2f**	**2g**	**2i**	**2j**	**3a**	**3b**	**4a** [c]	**4b** [c]
H-2	7.52	7.77	8.15	8.19	8.10	8.21	8.18	8.18	8.20	8.18	8.18	8.14	8.13	8.16	7.52	7.46
H-3	6.96	7.18	7.38	7.43	7.41	7.43	7.43	7.44	7.44	7.44	7.42	7.40	7.43	7.45	6.85	6.79
H-6	5.97	6.13	6.11	6.08	6.07	6.08	6.08	6.09	6.08	6.09	6.08	6.09	6.14	6.14	6.30	6.24
H-10	2.25	2.43	2.41	2.33	2.02	2.34	2.34	2.33	2.33	2.34	2.36	2.35	2.33	2.33	2.04	2.04
OCH_3	4.11	4.34	4.12	4.15	4.16	4.14	4.15	4.16	4.16	4.16	4.15	4.16	4.17	4.18	4.12	4.08
H-2′	– –	– –	– –	7.06	– –	6.91	6.95	7.03	7.14	7.08	6.66	6.96	3.14	3.14	– –	[d]
H-3′	– –	– –	– –	7.16	7.05	– –	6.95	7.36	– –	7.22	– –	6.74	1.50	3.62	[e]	[d]
H-4′	– –	– –	– –	6.94	7.05	6.73	– –	– –	6.98	– –	6.49	– –	1.39	– –	[e]	– –
H-5′	– –	– –	– –	7.16	7.05	7.02	6.95	7.36	7.17	7.22	7.04	6.74	1.50	3.62	[e]	[d]
H-6′	– –	– –	– –	7.06	7.10	6.85	6.95	7.03	7.01	7.08	6.62	6.96	3.14	3.13	[e]	[d]
NH	[f]	[f]	7.7	10.5	9.9	10.8	10.6	11.0	11.0	10.8	10.6	10.2	[f]	[f]	[f]	[f]
Others	7.14 H-9					2.10 Me-Ph	2.11 Me-Ph				3.55 MeO-Ph	3.60 MeO-Ph				

[a] In ppm, 400.12 MHz, relative to internal TMS, solvent, deuteriochloroform for **1a**, **1b**, **4a** and **4b**; DMSO-d_6 for the rest of the compounds. [b] Taken from ref [6]. [c] For better comparison the numbering in **4a** and **4b** is consistent with that of the furochromones **1**, **2** and **3**. [d] Further signals at δ = 7.30, 7.23, 7.14, 7.08, 6.96 corresponding to eight protons in the two benzene rings (two ABCD spin systems). [e] Futher signals at δ = 7.14, 7.13, 7.12, 7.10, 6.93, 6.91, 6.70 and 6.67 corresponding to eight protons in the two benzene rings (two AA′XX′ systems). [f] Not observed.

4.34, respectively. The nmr resonances of C-4, C-5 and C-8a of **1b** are shifted upfield and those of C-4a and C-6 downfield compared to visnagin (**1a**) [6]. Treatment of **1a** with two equimolar amounts of ammonia dissolved in dioxane led to the formation of 4-methoxy-7-methyl-5-oxo-5*H*-furo[3,2-*g*][1]benzopyran-9-sulfonamide (**1c**). The ir bands, the ^1H and ^{13}C nmr signals and the M^+ peak at m/e 309 fit well to its structure. There is a marked downfield shift of the C-9 signal which appears at $\delta = 111.4$ relative to **1a** ($\delta = 95.0$) [6] indicating a pronounced difference in the inductive and/or mesomeric influence between the SO_2NH_2 and the SO_2Cl group.

It has been reported [7] that visnagin (**1a**) reacts with aliphatic primary but not with secondary amines opening the γ-pyrone ring and forming an enamine derivative **3** of 4-methoxy-6-hydroxycoumarone (Scheme). In our study, however, we found that treatment of visnagin-9-sulfonyl chloride (**1b**) with two moles of the appropriate aromatic primary amines and aliphatic secondary amines in dioxane at room temperature gives rise to the corresponding sulfonamide derivatives **2a-j**, **1d** and **1e** without affecting the γ-pyrone ring. The ir and uv spectra of compounds **2a-j**, **3a** and **3b** show the expected bands and maxima. In addition, the structures were confirmed by their ^1H and ^{13}C nmr signals along with the M^+ ions in their mass spectral analysis. It is interesting to note that the signal associated to H-10 in **2b** ($\delta = 2.02$) is shifted upfield relative to $\delta = 2.33$ in **2a**. This may be due to the different orientations of the phenyl rings by steric interference of the CH_3 and the visnagin moiety.

The reaction of **1b** with *ortho*-toluidine and *para*-anisidine afforded the by-products **4a** and **4b**, respectively, if the reaction mixtures are left to stand at room temperature for two weeks. Then the amine reacts not only with the SO_2Cl group but also attacks the γ-pyrone ring. Inspection of the uv spectra of **4a** and **4b** reveals the presence of two maxima at 370 and 242 nm and the absence of the characteristic maxima in furochromone molecule indicating the opening of the γ-pyrone ring. The structures **4a** and **4b** (Scheme) were confirmed by the ^1H and ^{13}C nmr spectra and are supported by homo- (^1H-^1H) and heteronuclear (^1H-^{13}C) correlated two-dimensional nmr spectra [8]. The C-10 chemical shifts (20.9/20.8) are approximately the same as in **1**, **2** and **3** so that we conclude that in **4a** and **4b** the configuration of the C-6-C-7 double bond is *Z* as well; otherwise one would expect a value of $\delta = 14$-15 because of the γ effect of C-5 on C-10. The fast-ion-bombardment (FIB) mass spectra of **4a** showed the $M^+ + 1$ peak at m/z 507; the peaks at 360 and 400 are produced by the cleavage of the C-5-C-6 and the C-7-N bond in the molecular ion, respectively, proving the γ-pyrone ring opening. The corresponding peaks in the FIB ms of **4b** are at m/z 539, 376 and 416.

Table 2

^{13}C Chemical Shifts of the Sulfonamide Compounds **1**-**4** [a]

	1a [b]	**1b**	**1c**	**2a**	**2b**	**2c**	**2d**	**2e**	**2f**	**2g**	**2i**	**2j**	**3a**	**3b**	**4a** [c]	**4b** [c]
C-2	145.0	146.2	146.9	146.9	146.8	146.9	146.9	146.9	146.9	146.9	146.9	146.8	146.9	146.8	144.0	143.9
C-3	105.1	106.1	105.7	106.0	105.9	106.0	105.9	106.1	106.2	106.1	106.1	105.9	106.0	106.0	105.0	104.8
C-3a	116.9	[d]	116.2	115.5	115.8	115.5	115.5	115.5	115.4	115.4	115.6	115.6	116.0	115.9	111.6 [e]	112.0 [e]
C-4	157.6	153.8	155.7	156.9	156.7	157.0	157.0	157.2	157.4	157.8	157.2	156.8	156.9	157.3	166.1 [e]	165.8 [e]
C-4a	112.3	115.3	111.6	111.0	111.2	111.0	111.0	111.0	111.0	111.0	111.1	111.0	111.6	111.6	109.7 [e]	110.0 [e]
C-5	178.0	176.1	176.0	175.4	175.6	175.4	175.4	175.5	175.5	175.4	175.5	175.6	176.0	175.8	188.1	188.0
C-6	110.6	112.0	110.7	110.6	110.8	110.9	110.8	111.0	111.0	111.0	110.9	110.9	111.0	110.9	98.2	98.4
C-7	163.7	164.0	164.6	164.1	164.1	164.1	164.1	164.2	164.1	164.1	164.2	164.2	164.0	163.8	130.6	130.7
C-8a	155.8	153.8	153.0	154.8	154.2	154.9	154.8	154.8	154.9	154.8	151.1	154.8	154.8	154.9	160.5 [e]	160.1 [e]
C-9	95.0	[d]	111.4	106.4	108.3	106.4	106.4	106.0	105.8	106.0	106.2	106.5	105.3	103.9	[d]	[d]
C-9a	153.4	153.8	152.1	152.6	152.7	152.6	152.5	152.7	152.8	152.7	152.7	152.6	153.1	153.2	155.5	155.1
C10	19.8	19.6	19.4	19.2	18.8	19.2	19.2	19.2	19.2	19.2	19.3	19.2	19.3	19.2	20.9	20.8
C-1′	– –	– –	– –	137.5	134.8	137.6	134.8	137.0	139.3	136.5	138.9	129.9	– –	– –		
C-2′	– –	– –	– –	119.0	134.0	119.4	119.5	120.9	118.0	120.6	104.3	122.7	46.4	45.7		
C-3′	– –	– –	– –	129.1	130.7	138.4	129.5	132.1	133.4	129.0	159.8	114.3	25.1	65.7	[f]	[g]
C-4′	– –	– –	– –	123.8	126.4	124.4	133.1	115.9	123.4	127.8	110.8	156.4	23.0	– –		
C-5′	– –	– –	– –	129.1	126.5	128.9	129.5	132.1	130.9	129.0	130.0	114.3	25.1	63.2		
C-6′	– –	– –	– –	119.0	126.5	116.0	119.5	120.9	117.0	120.6	109.0	122.7	46.4	42.7		
OCH_3	61.6	61.7	61.5	61.3	61.4	61.3	61.3	61.3	61.3	61.3	61.3	61.3	61.5	61.4	60.9	60.9
Others					17.4 Me-Ph	21.0 Me-Ph	20.2 Me-Ph				54.9 MeO-Ph	55.1 MeO-Ph			18.0 17.9 MeO-Ph	55.6 55.4 MeO-PH

[a] In ppm, 100.6 MHz, relative to internal TMS, solvent, deuteriochloroform for **1a**, **1b**, **4a** and **4b**, DMSO-d_6 for the rest of the compounds. [b] Taken from ref [6]. [c] For better comparison the numbering in **4a** and **4b** is consistent with that of the furochromones **1**, **2** and **3**. [d] Not observed. [e] May be interchanged. [f] Resonances of the toluidine residues: 136.6, 135.6, 133.8 (C), 131.1, 130.7, 130.6, 127.6, 126.7, 125.0, 121.3 (CH). [g] Resonances of the anisidine residues: 158.7, 157.7, 130.0 (C), 126.7, 124.7, 114.7, 114.4 (2 CH each).

A similar ring cleavage in the khellin (9-methoxyvisnagin) molecules by primary aliphatic amines has been reported by Musante *et al.* [9].

The biological activity of the prepared sulfonamide compounds are currently under investigation.

EXPERIMENTAL

Melting points are not corrected. The ir spectra were recorded in nujol or potassium bromide on a Carl Zeiss spectrophotometer 1 MR 16. The uv spectra were measured in methanol on a Shimadzu UV-240. The ^1H and ^{13}C nmr spectra on Bruker AM-400 using DMSO-d_6 as solvent expect for **1a**, **1b**, **4a** and **4b** which were recorded in deuteriochloroform. The chemical shifts are referred to internal TMS. The two-dimensional nmr spectra were recorded using Bruker standard software. The mass spectra were obtained on Varian MAT CH-5 and CH-7 at 70 eV; for measuring the mass spectra of **4a** and **4b** the fast-ion-bombardment technique (FIB; matrix: dimethylsulfoxide/glycerol) was applied to identify the M^+ peak. Silica gel G 60 was used for thin-layer chromatography (tlc) with benzene-ethyl acetate (1:1) as eluating system and iodine-potassium iodide as spraying reagent.

Visnagin-9-sulfonyl Chloride (**1b**).

This compound was prepared by a procedure based on a method published before [5] but it was impoved so that the yield increased from 31 to 63%. The improvement relies on the dropwise addition of chlorosulfonic acid (10 ml) to visnagin (5 g) under stirring at room temperature followed by stirring the resulting solution for 30 minutes more. The product was separated as yellow material by pouring the reaction mixture onto ice. It was dried in a dissicator, then purified by recrystallization from acetone and gave a white crystalline material, mp 189-190° (reported [5] 190-192°); R_f 0.42; ir (Nujol): cm^{-1} 1655, 1625, 1590 (γ-pyrone), 1372, 1185, (SO_2), 750; uv: nm (log ε) 330 (1.021), 290 (0.993), 240 (1.580); ^1H nmr (deuteriochloroform): δ 7.77 (H-2), 7.18 (H-3), 6.13 (H-6), 2.43 (H-10), 4.34 (OMe); ^{13}C nmr (deuteriochloroform): δ 146.2 (C-2), 106.1 (C-3), 153.8 (C-4), 115.3 (C-4a), 176.1 (C-5), 112.0 (C-6), 164.0 (C-7), 153.8 (C-8a), 153.8 (C-9a), 19.6 (C-10), 61.7 (OMe); ms: m/e (relative intensity) 328/330 (M^+, 100/33), 301 (M^+-CO + H, 12), 299 (M^+-CHO, 28), 282 (M^+-OCH_3-CH_3, 10), 245 (10), 230 (M^+-SO_2Cl + H, 57), 229 (M^+-SO_2Cl, 22), 201 (M^+-SO_2Cl-CO, 89), 200 (M^+-SO_2Cl-CHO, 30), 184 (36), 160 (34), 159 (21), 147 (23), 133 (16), 132 (16).

Anal. Calcd. for $C_{13}H_9ClO_6S$ (328): C, 47.6; H, 2.76. Found: C, 47.55; H, 2.69.

General Procedure for Preparing the Sulfonamide Compounds.

Visnagin-9-sulfonyl chloride (**1b**, 1 mmole) was treated with the appropriate amine (2 mmoles) in dioxane solution (20 ml). The reaction mixture was left to stand at room temperature for 3-5 days and the rate of the reaction was checked by tlc until complete disappearence of the starting material. The precipitated product was filtered off and recrystallized from chloroform-methanol.

4-Methoxy-7-methyl-5-oxo-5*H*-furo[3,2-*g*][1]benzopyran-9-sulfonamide (**1c**).

Compound **1c** was obtained in 95% yield, mp 263-265°; R_f 0.095; ir (potassium bromide): cm^{-1} 3350, 1555 (NH), 1650, 1618, 1590 (γ-pyrone), 1350, 1150 (SO_2), 765; ^1H nmr (DMSO-d_6): δ 8.15 (H-2), 7.38 (H-3), 6.11 (H-6), 2.41 (H-10), 4.12 (OMe); ^{13}C nmr (DMSO-d_6): δ 146.9 (C-2), 105.7 (C-3), 116.2 (C-3a), 155.7 (C-4), 111.6 (C-4a), 176.0 (C-5), 110.7 (C-6), 164.6 (C-7), 153.0 (C-8a), 111.4 (C-9), 152.1 (C-9a), 19.4 (C-10), 61.5 (OMe); ms: m/e (relative intensity) 309 (M^+, 100), 281 (M^+-CO, 8), 280 (M^+-CHO, 58), 263 (M^+-OCH_3-NH, 33), 215 (M^+-CH_3-SO_2NH, 8), 201 (M^+-CHO-SO_2NH, 16), 199 (M^+-OCH_3-SO_2NH, 14), 159 (12), 147 (7).

Anal. Calcd. for $C_{13}H_{11}NO_6S$ (309): C, 50.48; H, 3.56; N, 4.53. Found: C, 50.18; H, 3.41; N, 4.36.

1-[(4-Methoxy-7-methyl-5-oxo-5*H*-furo[3,2-*g*][1]benzopyran-9-yl)sulfonyl]-piperidine (**1d**) [10].

Compound **1d** was obtained in 25% yield, mp 238-239°; R_f 0.44; ir (potassium bromide): cm^{-1} 3120, 1548 (NH), 1665, 1640, 1605 (γ-pyrone), 1380, 1165 (SO_2), 770; ms: m/e (relative intensity) 377 (M^+, 100), 363 (3), 349 (M^+-CO, 6), 348 (M^+-CHO, 30), 331 (4), 245 (12), 230 (23), 216 (12), 201 (48), 184 (12), 159 (10).

Anal. Calcd. for $C_{18}H_{19}NO_6S$ (377): C, 57.29; H, 5.04; N, 3.71. Found: C, 57.11; H, 4.89; N, 3.35.

4-[(4-Methoxy-7-methyl-5-oxo-5*H*-furo[3,2-*g*][1]benzofuran-9-yl)sulfonyl]-morpholine (**1e**) [10].

Compound **1e** was obtained in 80% yield, mp 245-247°; R_f 0.18; ir (Nujol): cm^{-1} 3120, 1555 (NH), 1665, 1642, 1595 (γ-pyrone), 1375, 1168 (SO_2), 760; ms: m/e (relative intensity) 379 M^+, 100), 351 (M^+-CO, 4), 350 (M^+-CHO, 23), 333 (2.5), 245 (13.5), 230 (20), 201 (32), 200 (6), 173 (6), 158 (8), 133 (5).

Anal. Calcd. for $C_{17}H_{17}NO_7S$ (379): C, 53.82; H, 4.48; N, 3.69. Found: C, 53.58; H, 4.80; N, 4.01.

4-Methoxy-7-methyl-5-oxo-*N*-phenyl-5*H*-furo[3,2-*g*][1]benzopyran-9-sulfonamide (**2a**).

Compound **2a** was obtained in 70% yield, mp 264-265°; R_f 0.39; ir (potassium bromide): cm^{-1} 3150, 1552 (NH), 1655, 1620, 1590 (γ-pyrone), 1380, 1175 (SO_2), 755; uv: nm (log ε) 325 (1.1169), 280 (1.2289), 225 (1.7785); ^1H nmr (DMSO-d_6): δ 8.19 (H-2), 7.43 (H-3), 6.08 (H-6), 2.33 (H-10), 4.15 (OMe), 7.06 (H-2'/6'), 7.16 (H-3'/5'), 6.94 (H-4'), 10.5 (NH); ^{13}C nmr (DMSO-d_6): δ 146.9 (C-2), 106.0 (C-3), 115.5 (C-3a), 156.9 (C-4), 111.0 (C-4a), 175.4 (C-5), 110.6 (C-6), 164.1 (C-7), 154.8 (C-8a), 106.4 (C-9), 152.6 (C-9a), 19.2 (C-10), 137.5 (C-1'), 119.0 (C-2'/6'), 129.1 (C-3'/5'), 123.8 (C-4'), 61.3 (OMe); ms: m/e (relative intensity) 385 (M^+, 100), 356 (M^+-CHO, 10), 321 (6), 306 (7), 303 (5), 292 (4), 245 (34), 230 (5), 229 (M^+-$C_6H_5NHSO_2$, 26), 228 (66), 216 (12), 201 (44), 173 (15), 159 (17), 133 (9), 131 (7).

Anal. Calcd. for $C_{19}H_{15}NO_6S$ (385): C, 59.22; H, 3.90; N, 3.63. Found: C, 59.50; H, 3.78; N, 3.34.

4-Methoxy-7-methyl-*N*-(2-methylphenyl)-5-oxo-5*H*-furo[3,2-*g*][1]benzopyran-9-sulfonamide (**2b**) [10].

Compound **2b** was obtained in 50% yield, mp 245-247°; R_f 0.44; ir (potassium bromide): cm^{-1} 3300, 1550 (NH), 1660, 1595 (γ-pyrone), 1380, 1185 (SO_2), 760; ms: m/e (relative intensity) 399 (M^+, 100), 370 (M^+-CHO, 6), 335 (8), 320 (12), 317 (4), 304 (8), 245 (40), 230 (10), 229 (30), 228 (68), 216 (10), 201 (46), 200 (8), 173 (12), 159 (11), 133 (8).

Anal. Calcd. for $C_{20}H_{17}NO_6S$ (399): C, 60.15; H, 4.26; N, 3.51. Found: C, 60.07; H, 4.50; N, 3.58.

4-Methoxy-7-methyl-*N*-(3-methylphenyl)-5-oxo-5*H*-furo[3,2-*g*][1]benzopyran-9-sulfonamide (**2c**) [10].

Compound **2c** was obtained in 45% yield, mp 223-225°C; R_f 0.44; ir (potassium bromide): cm^{-1} 3430, 1535 (NH), 1635, 1590 (γ-pyrone), 1380, 1150 (SO_2), 790; ms: m/e (relative intensity) 399 (M^+, 100), 370 (M^+-CHO, 9), 335 (18), 320 (20), 306 (10), 304 (18), 245 (38), 230 (10), 229 (30), 228 (77), 216 (9), 201 (54), 200 (13), 173 (17), 159 (20), 133 (12).

Anal. Calcd. for $C_{20}H_{17}NO_6S$ (399): C, 60.15; H, 4.26; N, 3.51. Found: C, 59.99; H, 4.38; N, 3.39.

4-Methoxy-7-methyl-*N*-(4-methylphenyl)-5-oxo-5*H*-furo[3,2-*g*][1]-benzopyran-9-sulfonamide (**2d**) [10].

Compound **2d** was obtained in 45% yield, mp 264-266°; R_f 0.44; ir (potassium bromide): cm^{-1} 3175, 1555 (NH), 1660, 1630, 1600 (γ-pyrone), 1380, 1175 (SO_2), 770; ms: m/e (relative intensity) 399 (M^+, 100), 370 (M^+-CHO, 7), 335 (9), 320 (14), 317 (5), 304 (5), 245 (30), 230 (11), 229 (28), 228 (68), 216 (15), 201 (40), 200 (9), 173 (11), 159 (13).

Anal. Calcd. for $C_{20}H_{17}NO_6S$ (399): C, 60.15; H, 4.26; N, 3.51. Found: C, 59.85; H, 4.14; N, 3.60.

N-(4-Bromophenyl)-4-methoxy-7-methyl-5-oxo-5*H*-furo[3,2-*g*][1]benzopyran-9-sulfonamide (**2e**) [10].

Compound **2e** was obtained in 60% yield, mp 160-161°; R_f 0.29; ir

(potassium bromide): cm^{-1} 3430, 1575 (NH), 1670, 1615 (γ-pyrone), 1385, 1210 (SO_2), 800; ms: m/e (relative intensity) 463/465 (M^+, 70/72), 434 (M^+-CHO, 5), 399 (3.5), 245 (59), 230 (9), 229 (44), 228 (100), 216 (16), 201 (72), 200 (15), 173 (25), 159 (21).

Anal. Calcd. for $C_{19}H_{14}BrNO_6S$ (463): C, 49.24; H, 3.02; N, 3.02. Found: C, 49.45; H, 3.33; N, 3.35.

N-(3-Chlorophenyl)-4-methoxy-7-methyl-5-oxo-5*H*-furo[3,2-*g*][1]benzopyran-9-sulfonamide (**2f**) [10].

Compound **2f** was obtained in 65% yield, mp 245-247°; R_f 0.18; ir (potassium bromide): cm^{-1} 3160, 1555 (NH), 1660, 1620, 1595 (γ-pyrone), 1385, 1175 (SO_2), 765; ms: m/e (relative intensity) 419/421 (M^+, 100/30), 390 (M^+-CHO, 8), 355 (16), 340 (6), 245 (52), 229 (36), 228 (82), 216 (24), 201 (68), 200 (18), 173 (22), 159 (25), 133 (14).

Anal. Calcd. for $C_{19}H_{14}ClNO_6S$ (419.5): C, 54.35; H, 3.34; N, 3.34. Found: C, 54.36; H, 3.20; N, 3.43.

N-(4-Chlorophenyl)-4-methoxy-7-methyl-5-oxo-5*H*-furo[3,2-*g*][1]benzopyran-9-sulfonamide (**2g**) [10].

Compound **2g** was obtained in 80% yield, mp 251-252°; R_f 0.44; ir (potassium bromide): cm^{-1} 3150, 1550 (NH), 1655, 1625, 1590 (γ-pyrone), 1380, 1190 (SO_2), 770; ms: m/e (relative intensity) 419/421 (M^+, 100/30), 390 (M^+-CHO, 7), 355 (6), 340 (5), 245 (64), 229 (45), 228 (90), 216 (18), 201 (74), 200 (14), 173 (20), 159 (19).

Anal. Calcd. for $C_{19}H_{14}ClNO_6S$ (419.5): C, 54.35; H, 3.34; N, 3.34. Found: C, 53.98; H, 3.60; N, 3.51.

4-Methoxy-*N*-(2-methoxyphenyl)-7-methyl-5-oxo-5*H*-furo[3,2-*g*][1]benzopyran-9-sulfonamide (**2h**) [10].

Compound **2h** was obtained in 30% yield, mp 213-215°; R_f 0.34; ir (potassium bromide): cm^{-1} 3150, 1552 (NH), 1655, 1620, 1590 (γ-pyrone), 1380, 1175 (SO_2), 755; ms: m/e (relative intensity) 415 (M^+, 100), 386 (M^+-CHO, 5), 351 (4), 336 (4), 320 (4), 245 (14), 230 (5), 229 (21), 228 (47), 216 (6), 201 (19), 200 (5), 173 (6), 159 (7).

Anal. Calcd. for $C_{20}H_{17}NO_7S$ (415): C, 57.83; H, 4.10; N, 3.37. Found: C, 57.58; H, 4.02; N, 3.05.

4-Methoxy-*N*-(3-methoxyphenyl)-7-methyl-5-oxo-5*H*-furo[3,2-*g*][1]benzopyran-9-sulfonamide (**2i**) [10].

Compound **2i** was obtained in 70% yield, mp 226°; R_f 0.39; ir (potassium bromide): cm^{-1} 3160, 1550 (NH), 1655, 1590 (γ-pyrone), 1380, 1180 (SO_2), 770; ms: m/e (relative intensity) 415 (M^+, 34), 351 (38), 336 (70), 320 (100), 308 (20), 290 (14), 245 (38), 216 (24), 201 (53), 173 (19), 159 (22).

Anal. Calcd. for $C_{20}H_{17}NO_7S$ (415) C, 57.83; H, 4.10; N, 3.37. Found: C, 57.50; H, 4.01; N, 3.21.

4-Methoxy-*N*-(4-methoxyphenyl)-7-methyl-5-oxo-5*H*-furo[3,2-*g*][1]benzopyran-9-sulfonamide (**2j**) [10].

Compound **2j** was obtained in 60% yield, mp 241-242°; R_f 0.32; ir (potassium bromide): cm^{-1} 3150, 1550 (NH), 1655, 1620, 1590 (γ-pyrone), 1378, 1150 (SO_2), 760; uv: nm (log ε) 325 (1.24), 280 (1.40), 235 (1.9); ms: m/e (relative intensity) 415 (M^+, 27), 336 (3), 201 (5), 184 (1.5), 173 (1), 122 (100).

Anal. Calcd. for $C_{20}H_{17}NO_7S$ (415): C, 57.82; H, 4.10; N, 3.37. Found: C, 58.04; H, 3.94; N, 3.51.

6-Hydroxy-4-methoxy-*N*-(2-methylphenyl)-5-[3-[(2-methylphenyl)amino]-1-oxo-2-butenyl]-7-benzofuransulfonamide (**4a**).

The total mother liquor remaining after the separation of compound **2b** was left to stand at room temperature for two weeks to deposit a yellow substance which was crystallized from chloroform-methanol giving **4a** as yellow needles, yield 30%, mp 165°; R_f 0.84; ir (potassium bromide): cm^{-1} 3295, 1560 (NH), 1660, 1620, 1590 (C=O), 1380, 1155 (SO_2), 760; ^{1} nmr (deuteriochloroform): δ 7.52 (H-2), 6.85 (H-3), 6.30 (H-6), 2.04 (H-10), 4.12 (OMe), 7.14, 7.13, 7.12, 7.10, 6.93, 6.91, 6.70 and 6.67 (8H; 2 AA'XX' system); ^{13}C nmr (deuteriochloroform): δ 144.0 (C-2), 105.0 (C-3), 111.6/109.7 (C-3a/4a), 166.1/160.5 (C-4/8a), 188.1 (C-5), 98.2 (C-6), 130.6 (C-7), 155.5 (C-9a), 20.9 (C-10), 60.9 (OMe), 18.0/17.9 (2 Me-Ph), 136.6, 135.6, 133.8, 131.1, 130.7, 130.6, 127.6, 126.7, 125.0, 121.3 (2 toluidine residues); ms: m/e (relative intensity) 506 (M^+, 0.3), 400 (3), 384 (0.6), 361 (0.5), 360 (1.7), 320 (0.8), 306 (0.7), 277 (0.8), 263 (1.7), 235 (3.5), 216 (1), 157 (100).

Anal. Calcd. for $C_{27}H_{26}N_2O_6S$ (506): C, 64.03; H, 5.14; N, 5.53. Found: C, 63.81; H, 5.02; N, 5.37.

6-Hydroxy-4-methoxy-*N*-(4-methoxyphenyl)-5-[3-[(4-methoxyphenyl)-amino]-1-oxo-2-butenyl]-7-benzofuransulfonamide (**4b**).

The total mother liquor remaining after the separation of compound **2j** was left to stand at room temperature for two weeks to deposit a yellow substance which was crystallized from chloroform-methanol giving **4b** as yellow needles, yield 30%, mp 192-193°; R_f 0.77; ir (potassium bromide): cm^{-1} 3310, 1500 (NH), 1590, 1565, 1547 (C=O), 1380, 1157 (SO_2), 760; ^{1}H nmr (deuteriochloroform): δ 7.46 (H-2), 6.79 (H-3), 6.24 (H-6), 2.04 (H-10), 4.08 (OMe), 7.30, 7.23, 7.14, 7.08, 6.96 (8H, 2 ABCD systems); ^{13}C nmr (deuteriochloroform): δ 143.9 (C-2), 104.8 (C-3), 112.0/110.0 (C-3a/4a), 165.8/160.1 (C-4/8a), 188.0 (C-5), 98.4 (C-6), 130.7 (C-7), 155.1 (C-9a), 20.8 (C-10), 60.9 (OMe), 55.6/55.4 (MeO-Ph), 158.7, 157.7, 130.0, 126.7, 124.7, 114.7, 114.4 (2 anisidine residues); ms: m/e (relative intensity) 538 (M^+, 0.5), 417 (0.8), 416 (2.6), 376 (2), 368 (0.9), 253 (1.8), 235 (5.5), 225 (1.5), 157 (100).

Anal. Calcd. for $C_{27}H_{26}N_2O_8S$ (538): C, 60.22; H, 4.83; N, 5.20. Found: C, 59.95; H, 4.99; N, 5.15.

Acknowledgement.

M. H. A. E. thanks the Humboldt foundation for a fellowship. This work was supported by the Fonds der Chemischen Industrie.

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[10] Since the ^{1}H and ^{13}C nmr signals of the visnagin part within the series **1** and **2** are very close, they are reported only for **1b**, **1c** and **2a**. The side ring chemical shifts can easily be predicted by well-documented increment rules. Complete tables with the ^{1}H and ^{13}C signals may be obtained from the authors.