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Synthesis and Spectroscopic Investigation of Some Dimeric Coumarin and Furanocoumarin Models

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Summary. The synthesis of some dimeric coumarin and furanocoumarin models and their structure elucidation by ^{1}H NMR, ^{13}C NMR, and mass spectroscopy is presented. In the presence of moisture some aldehydes are accompanied by their hydrates. Methoxy signal doubling in the presence of a chiral lanthanide shift reagent proves the dimeric nature of compound **8**. In the mass spectra, heterolytic cleavage of the O-C linkage was noticed which is a rare fragmentation in the case of aromatic ethers.

Keywords. *bis*-Coumarins; *bis*-Furanocoumarins; Chirality; Aldehyde hydrates; ^{1}H NMR; ^{13}C NMR; Mass spectrometry; Fragmentation.

Synthese und spektroskopische Untersuchung einiger dimerer Cumarin- und Furanocumarinmodelle

Zusammenfassung. Die Synthese einiger dimerer Cumarin- und Furanocumarin-Modellverbindungen und ihre Strukturaufklärung mit ^{1}H- und ^{13}C-NMR- sowie Massenspektrometrie werden beschrieben. In Gegenwart von Feuchtigkeit werden einige der Aldehyde von ihren Hydraten begleitet. Verdoppelungen der Methoxy-^{1}H-Signale von **8** in Anwesenheit eines chiralen Lanthanoid-Verschiebungsreagenzes beweisen, daß **8** ein Dimer ist. In den Massenspektren finden sich Hinweise für heterolytische Spaltungen der O-C-Bindungen. Solche Fragmentierungen sind bei aromatischen Ethern ungewöhnlich.

Introduction

The potential anticoagulant activity of naturally occurring coumarin dimers as dicoumarol [1] and daphnoretin [2, 3] prompted some investigators to synthesize many of their derivatives [4]. Recently, syntheses of bicoumarin derivatives with possible antifertility activity have been reported [5]. The two coumarin moieties in the dimers are either linked at C-3/C-7′ by an ether linkage [2,3] or by a methylene

group fixed at C-3/C-3′ [1] as well as a C-4/C-4′-methylene dioxy group [6]. Recently, other linkages at different sites in the dimer have also been described [7]. The only reported dimers in the furanocoumarin series are 6,6-methylene substituted *bis*-5 hydroxy furanocoumarins in which two molecules are linked either by a methylene [8] or a phenylated methine group [9, 10]. *Matsukaze*'s lactone represents another type of a bicoumarin in which two coumarin molecules are linked by a C-8/C-8′ carbon-carbon bond [11, 12].

The dimers introduced here are synthesized by formylation of 4-hydroxy coumarin (**1**) and/or the 4-hydroxy furanocoumarins **2** and **3**, respectively, in *DMF*-$POCl_3$. *Arora et al.* found that the reaction may lead to the formation of a tricoumarol derivative [13].

Inspite of the synthesis of various coumarin dimers, literature reports on only two furanocoumarin analogues, and no decisive information about their NMR properties as well as their mass spectral fragmentation is known. Therefore it seemed desirable to synthesize some more new models of furanocoumarin dimers which incorporate ether linkages.

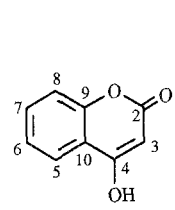
Results and Discussion

Syntheses and structure determinations

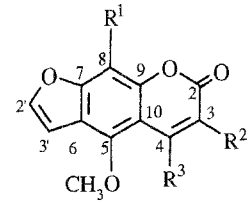
All molecular structures are collected in Scheme 1. Their structure elucidation is based mainly on high-field ^1H and ^{13}C NMR spectroscopy and on comparison with data of other related molecules [7, 14]. The assignment of the NMR signals was achieved by gradient-selected ^1H, ^1H COSY, HMQC, and HMBC measurements [15], the latter optimized for $J(^{13}C, ^1H) = 7$ Hz long-range couplings. The ^{13}C chemical shifts are listed in Table 1, whereas the ^1H chemical shifts can be found in the experimental section. ^{13}C, ^1H long-range connectivities are compiled in Table 2.

The assigning procedure proceeded *via* the following general route: in furanocoumarins the unambiguous differentiation between C-7 and C-9 as well as C-6 and C-10 signals, respectively, was achieved by long-range responses to H-2′ and H-3′. The HMBC correlations of the methoxy protons provided a straightforward assignment of the C-5 signals and, moreover allowed the differentiation of the 5-OCH_3 and 8-OCH_3 proton and carbon signals in **8** and **12**. It is worth to mention that C-4 is strongly deshielded ($\delta \approx 179$ ppm) in the aldehydes, whereas its chemical shift is about 20 ppm lower in the hydrates. Owing to the wide-spread π-electron delocalization, a ^{13}C chemical shift alteration of nearly 2 ppm can be observed for C-7 when the HC=O group is formally replaced by $HC(OH)_2$.

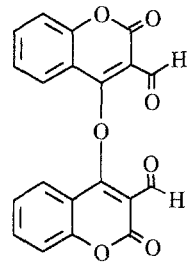
Although the dimeric nature of compounds **6–12** was unequivocally shown by mass spectrometry (see Experimental), we searched for an independent proof. Rotation around the central C–O–C bonds connecting the two identical subunits in **6–8** is severely hindered due to sterical interference. Thus, the molecules are chiral, and the compound is a racemate. Therefore, at least some of their ^1H signals should be doubled in the presence of a chiral lanthanide shift reagent. Figure 2 demonstrates the result of such an experiment with **8** and *tris*[3-(heptafluoropropyl-



1



2 $R^1 = H$ $R^2 = H$ $R^3 = OH$
3 $R^1 = OCH_3$ $R^2 = H$ $R^3 = OH$
4 $R^1 = H$ $R^2 = CHO$ $R^3 = Cl$
5 $R^1 = OCH_3$ $R^2 = CHO$ $R^3 = Cl$



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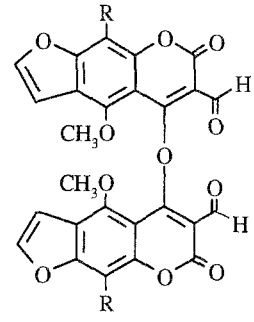
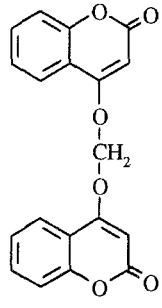


7 R = H
8 $R = OCH_3$



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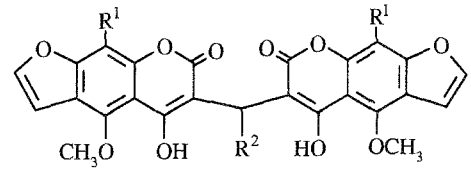


10 $R^1 = H$ $R^2 = H$
11 $R^1 = OCH_3$ $R^2 = H$
12 $R^1 = OCH_3$ $R^2 = C_6H_5$

Scheme 1. Structures **1–12**; the numbering is analogous for coumarins and furocoumarins for the sake of comparability

hydroxy-methylene)-(+)camphorato]europium(III) (Eu(*hfc*)$_3$, Aldrich) where both methoxy signals are split into 1:1 doublets. The structure assignments were further assisted and confirmed by microanalysis, mass spectrometry, and IR and UV spectroscopy.

When **1** is treated with *DMF*/$POCl_3$ at 20°C (*Vilsmeier* reaction), it affords **6** which, in the presence of moisture, may exist as its hydrate as revealed from the

Table 1. ^{13}C chemical shifts of **4** and **6–12** (ppm relative to internal *TMS*)

	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-2′	C-3′	5-OCH_3	8-OCH_3	CHO or $CH(OH)_2$	Solvent
4	161.0	100.2	178.9	155.3	115.4	160.5	95.4	154.4	102.2	145.5	105.6	61.2		194.1	$CDCl_3/CD_3OD$ (9:1)
6 hydrate	158.6	98.7	159.2	123.0	124.9	134.3	117.0	153.2	113.3					87.9	*DMSO*-d_6
9[a]	163.3	88.8	167.7	122.7	123.7	130.4	115.3	152.4	119.4						$CDCl_3$
7	160.9	100.2	179.1	155.3	115.4	160.5	95.5	154.5	102.5	145.4	105.6	61.3		194.1	$CDCl_3$
7 hydrate	161.8	96.0	159.4	152.3	117.8	158.3	95.9	152.3	102.6	145.5	104.8	62.5		88.4	$CDCl_3$
8	163.4	102.1	178.8	147.8	118.1	148.4	128.5	145.1	105.0	145.7	105.0	61.9	60.3	188.1	*DMSO*-d_6
8 hydrate	161.7	96.4	158.9	146.2	120.0	149.7	128.8	143.2	103.9	146.2	103.9	63.2	61.6	88.4	$CDCl_3$
10[b]	169.6	100.1	162.8	145.3	116.7	155.5	94.1	152.1	104.7	151.1	108.6	61.9			*DMSO*-d_6
11[c]	169.6	100.2	162.5	143.4	118.3	146.9	128.2	145.4	109.9	146.0	104.8	62.3	60.9		*DMSO*-d_6
12[d]	162.6	100.2	165.4	144.8	116.3	148.0	128.0	142.5	102.3	146.3	105.4	62.0	61.2		*DMSO*-D_6

[a] CH_2: $\delta = 19.5$ ppm; [b] CH_2: $\delta = 16.4$ ppm; [c] CH_2: $\delta = 20.0$ ppm; [d] 3-CH-Ph: $\delta = 36.4$, 141.0 (*ipso*), 127.1 (*ortho*), 127.8 (*meta*), 115.3 (*para*) ppm

Table 2. Characteristic ^{13}C, ^{1}H long-range connectivities of **4**, **6–8**, and **12**

Compound	Proton	Carbon
4	H-8	C-6, C-7, C-9, C-10
	H-2′	C-6, C-7, C-3′
	H-3′	C-6, C-7, C-2′
	5-OCH_3	C-5
	H–C=O	C-3, C-4, C-10
6	H-5	C-4, C-7, C-9
	H-6	C-5, C-7, C-8, C-10
	H-7	C-5, C-9
	H-8	C-4, C-6, C-9, C-10
7[a]	H-8	C-6, C-7, C-9, C-10
	H-2′	C-6, C-7, C-3′
	H-3′	C-6, C-7, C-2′
	5-OCH_3	C-5
	H–C=O	C-3, C-4, C-10
	$HC(OH)_2$	C-2, C-3
8[a]	H-2′	C-6, C-7, C-3′
	H-3′	C-6, C-7, C-2′
	5-OCH_3	C-5
	8-OCH_3	C-8
	H–C=O	C-2, C-3, C-4
	$HC(OH)_2$	C-2, C-3, C-4
12	H-2′	C-6, C-7, C-3′
	H-3′	C-6, C-7, C-2
	5-OCH_3	C-5
	8-OCH_3	C-8
	3-CH	C-2, C-3, C-4, C-10, *ipso*-Ph, *ortho*-Ph

[a] The correlation are identical for the aldehyde and its corresponding hydrate; the only difference concerns the H-C=O and $HC(OH)_2$ signals

signals at $\delta(^1H)= 7.02$ ppm for $CH(OH)_2$ and $\delta(^{13}C)=87.8$ ppm for $CH(OH)_2$. It should be noted that *Arora et al.* [13] reported that the same reaction of **1** yielded tricoumarol, whereas *Moorty* [16] had announced the formation of 4-chloro-3-formylcoumarin.

Reaction of an equimolar amount of the 4-hydroxyfuranocoumarin derivatives **2** and **3** and $POCl_3$ in dry *DMF* afforded **7** and **8**, respectively, the two furanocoumarins beeing linked by an ether bridge between the 4- and 4′-carbon atoms. Again, the NMR spectra of **7** and **8** showed the presence of the dihydrates when moisture was present. On the other hand, using an excess of $POCl_3$ led to the formation of the 4-chloro-3-formylfuranocoumarin derivatives **4** and **5**.

The methylenation of 4-hydroxycoumarin was carried out by refluxing **1** with anhydrous potassium carbonate, dry acetone, and methylene iodide for 35 hours to afford the dimeric compound **9** where two coumarin subunits are linked by a

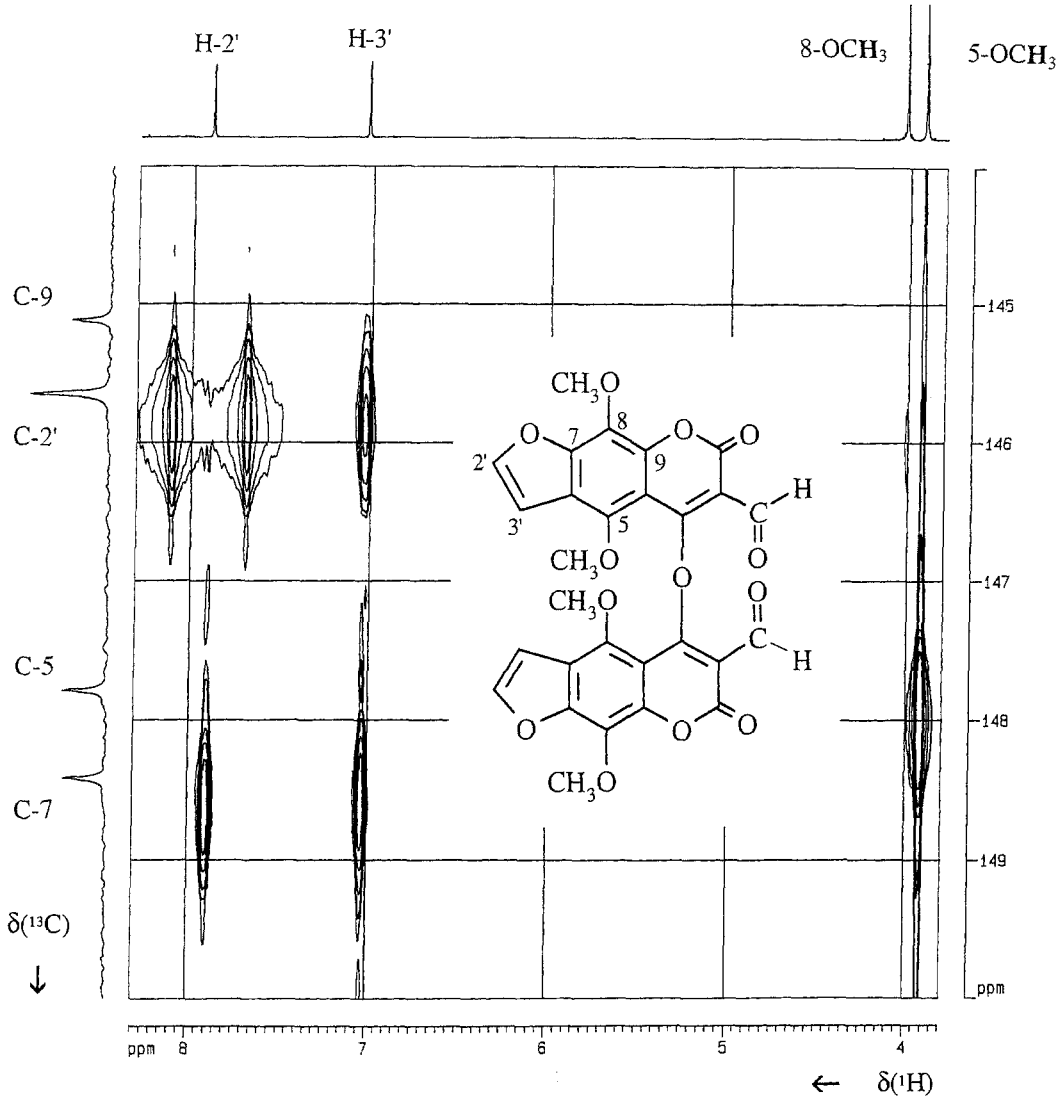
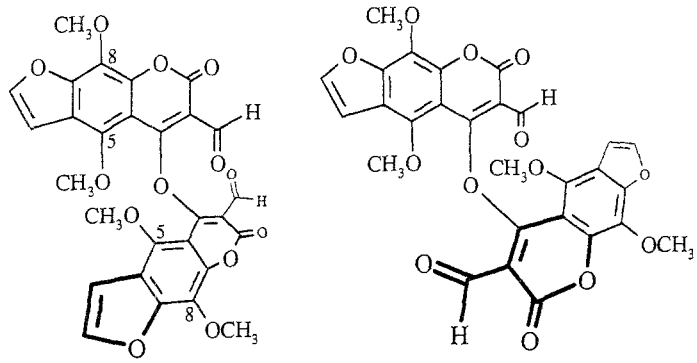


Fig. 1. Expanded region of the HMBC spectrum of **8**; for explanation, see text

methylenedioxy group in their 4-positions. This compound has been described previously by *Parekh et al.* [6].

In contrast to the reaction **1**→**9**, the 4-hydroxyfuranocoumarins **2** and **3** gave the methylene-*bis*-furanocoumarins **10** and **11**, respectively, under the same conditions. These two compounds have previously been prepared by *Schönberg et al.* [8] *via* formylation of their parent 4-hydroxyfuranocoumarins.

Finally, the reaction of **3** with benzaldehyde in absolute ethanol afforded compound **12** which has recently been reported by *Mahran et al.* [9].



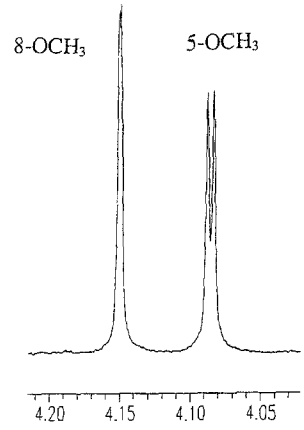
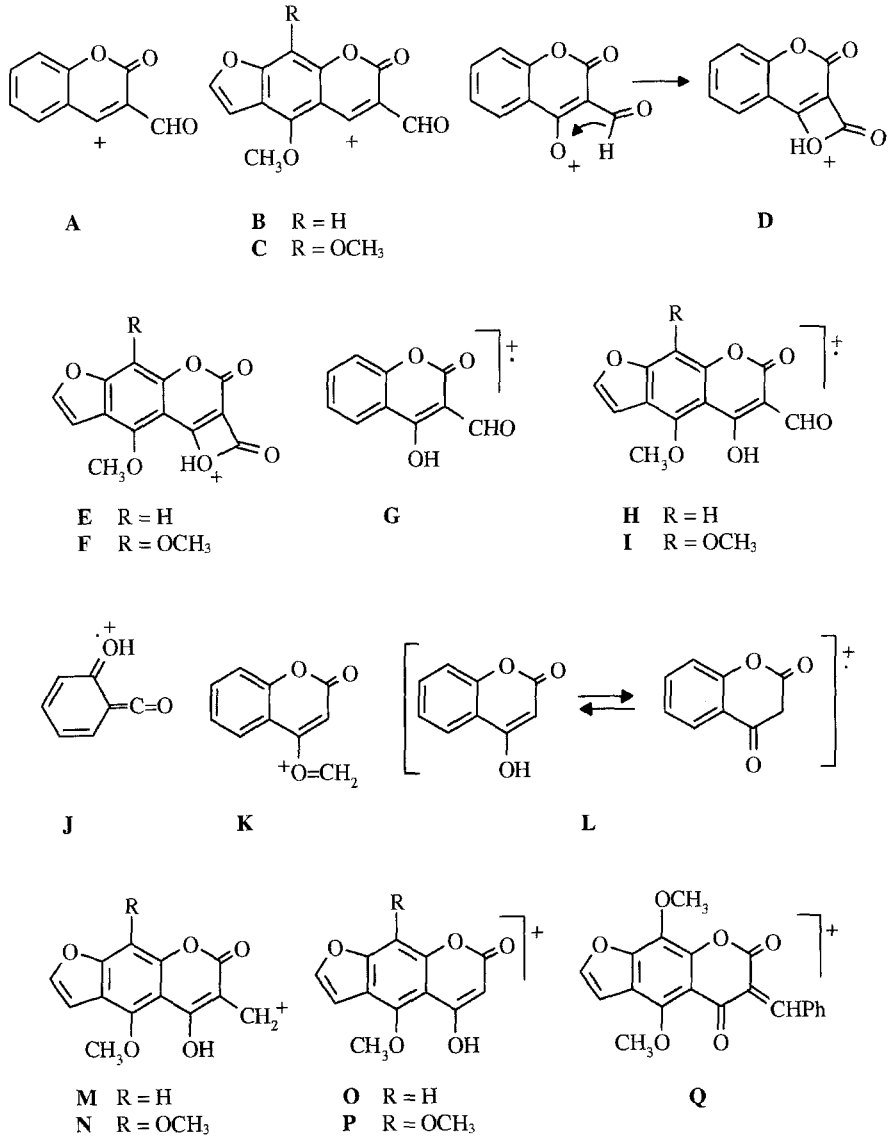


Fig. 2. Methoxy region of the ^{1}H NMR spectrum of **8** in the presence of Eu(*hfc*)$_3$

Mass spectrometry

An inspection of the electron impact mass spectra (EI MS) of the dimeric compounds shows the expected extrusion of CO, CHO, and methyl radicals from their molecular ions beside other more uncommon fragmentation patterns; the most prominent ionic species are collected in Scheme 2. A characteristic heterolytic fragmentation of the diaryl C-O-C linkage occurs in the *bis*-coumarin dimer **6** and the *bis*-furanocoumarins **7** and **8**. Simple O-C cleavage of compounds **6** and **8** with charge retention on the formed coumarin and furanocoumarin cations occurs to give ion species **A** from **6** (m/z = 173 (81%)), **C** from **8** (m/z = 273 (100%)), and **B** from **7** (m/z = 243 (6%)). Apparently, the ions **B** and **C** do not show any further fragmentation, a behaviour which reflects their remarkable stability. Surprisingly, however, the other part of the molecule incorporating the ethereal hetero atom can form an intermediate ion species with a relatively unfavourable electron sextet which is expected to rearrange to ion species **D** (from **6**), **E**, (from **7**), and **F** (from **8**). Such behaviour is known from dialkyl ethers and ethylene ketal derivatives and



Scheme 2. Ion species observed in the mass spectra of **6–12**

was confirmed by deuterium labelling experiments [17]. The ion species **E** from compound **7** represents even the base peak with $m/z = 259$ (100%), whereas **D** and **F** appear with lower intensity ($m/z = 189$ (44%) and $m/z = 289$ (31%), respectively). Due to the instability of these intermediate ions derived from compounds **6–8**, they can also accept another hydrogen atom to give ions **G**, **H**, and **I** with $m/z = 190$, 260, and 290. Ions **G** – **I** afford the expected fragmentation patterns resulting from the loss of CO, CHO, CH_3, and/or a methylene group. The most characteristic fragment from compound **6** is the ion species **J** with $m/z = 121$ (100%) which presumably results from fragment **G**.

The cleavage of the methylenedioxy group in **9** gave the ions **K** (m/z = 175(50%)) and **L** (m/z = 162 (9%)); **L** is formed by hydrogen ion transfer to the external oxygen. Since **L** can tautomerize to an oxochromone form, it is subjected to a *retro-Diels-Alder* fragmentation (loss of CH_2=C=O) to afford ion species **J** with m/z = 121 (100%).

Different ion species were found in the spectra of compounds **10–12** resulting from a cleavage at the methylene or methine moiety, respectively, to give the corresponding ion species **M** (from **10**); m/z = 245 (12%)), **N** (from **11**); m/z = 275 (13%), **O** (from **10**; m/z = 232 (29%)); **P** (from **11** m/z = 262 (50%)), and **Q** (from **12**; m/z = 350 (100%)). Probably, the ions **M**, **N**, and **Q** form seven-membered ring species to escape the unstable exocyclic carbenium ion form.

Experimental

Spectroscopy

NMR spectra were recorded at Bruker (DRX-500, AM-400) and Jeol (FX-200) spectrometers. Standard Bruker software was used for the 1D and 2D experiments. For all experiments, 1k data points in t_2, 256 experiments in t_1, linear prediction to 512 and zero filling up to 1k were applied. IR spectra were taken on a Shimadzu CVT-04 as KBr pellets and UV/Vis spectra on a Graphicord UV-240 spectrophotometer. Mass spectra (EI and FAB) were obtained on Varian MAT 711 a VG Autospec spectrometers.

Starting materials

Compound **1** is commercially available (Merck). 4-Hydroxybergapten (**2**) and -isopimpinellin (**3**) were prepared by *Claisen* condensation of khellinone and visnaginone, respectively, with diethyl carbonate in the presence of powdered sodium metal [8]. Khellinone and visnaginone were obtained by alkali hydrolysis of visnagin and khellin [8].

General synthetic formylation procedure

The hydroxy coumarin derivatives **1–3** (0.01 mol) were dissolved in 30 ml of dry dimethylformamide, followed by dropwise addition of a freshly distilled solution of phosphoroxychloride (0.01 mol) over 30 min at 20°C. The mixture was left overnight under stirring at 40°C. Then it was poured slowly onto ice-water under vigorous stirring to give a pale yellow precipitate. The precipitate was washed carefully with water and three times with 2% aqueous sodium carbonate solution, dried, and recrystallized from aqueous acetone to give compounds **6–8**. Using an excess of phosphoroxychloride (0.05 mol) in the reaction with **2** and **3** led to the formyl derivatives **4** and **5**.

4-Chloro-3-formyl-5-methoxyfuranocoumarin (**4**)

Yield: 78%; m.p.: 185°C (aqueous acetone); IR (KBr): ν = 2900 (CH-aldehyde), 1745, 1715 (C=O), 1605, 1580 (C=C), 1270 (C–O)cm^{-1}; UV (MeOH): λ_{max} = 205, 210, 265, 305 nm; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.29 (s, 3H, 5-OCH_3), 7.08 (d, 1H, J = 2.3 Hz, H-3′), 7.16 (s, 1H, H-8), 7.65 (d, 1H, J = 2.3 Hz, H-2′), 10.40 (s, 1H, CHO) ppm; MS (70 eV): m/z (%) = 278/280 (34/12) [M^+], 250/252 (100/33) [M^+–CO], 235/237 (30/11) [M^+–CH_3–CO], 222/224 (23/10) [M^+–2CO], 207/209 (71/23) [M^+–CH_3–2CO], 179/181 (16/5) [M^+–CH_3–3CO], 171 (14) [M^+–CH_3–2CO–HCl]; $C_{13}H_7ClO_5$ (278); calc.: C 56.11, H 2.52, Cl 12.59; found: C 56.00, H 2.87, Cl 12.50.

4-Chloro-3-formyl-5,8-dimethoxyfuranocoumarin (**5**)

Yield: 75%; m.p.: 175°C (aqueous acetone); IR (KBr): $\nu = 2900$ (CH-aldehyde), 1725 (C=O), 1620, 1600 (C=C), 1280 (C–O) cm^{-1}; UV (MeOH): $\lambda_{max} = 205, 245, 255, 305$ nm; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 4.12$ (s, 3H, 8-OCH_3), 4.20 (s, 3H, 5-OCH_3), 7.02 (d, 1H, $J = 2.3$ Hz, H-3'), 7.70 (d, 1H, $J = 2.3$ Hz, H-2'), 10.42 (s, 1H, CHO) ppm; MS (70 eV): m/z (%) = 308/310 (38/13) [M^+], 293/295 (8/3) [M^+–CH_3], 280/282 (36/13) [M^+–CO], 265/267 (100/37) [M^+–CH_3–CO–], 229 (38) [M^+–CH_3–CO–HCl], 201 (47) [M^+–CH_3–2CO–HCl], 173 (12) [M^+–CH_3–3CO–HCl]; $C_{14}H_9ClO_6$ (308); calc.: C 54.54, H 2.92, Cl 11.36; found: C 54.62, H 3.00, Cl 11.54.

Bis(3-formylcoumarin-4-yl)ether hydrate (**6**)

Yield: 66%; m.p.: > 300°C (aqueous acetone); IR (KBr): $\nu = 2950$ (CH-aldehyde), 1715, 1690 (C=O), 1660, 1600 (C=C), 1305 (C–O) cm^{-1} ^1H NMR (500 MHz, *DMSO*-d_6): $\delta - 7.02$ (s, 1H, $CH(OH)_2$), 7.50 (m, 2H, H-5 and H-6), 7.78 (ddd, 1H, $J = 8.6, 1.7$ Hz, H-7), 7.88 (dd, 1H, $J = 8.2$, 1.7 Hz, H-8) ppm; MS (70 eV): m/z (%) = 362 (70) [M^+], 334 (60) [M^+–CO], 333 (88) [M^+–CHO], 306 (18) [M^+–2CO], 305 (44) [M^+–CO–CHO], 189 (44) [**D**, see Scheme 2], 190 (17) [**G**, see Scheme 2], 173 (81) [**A**, see Scheme 2], 174 (45) [**A** + H], 145 (43) [**A**–CO], 121 (100) [**J**], 105 (34) [**G**–2CO–CHO], 92 (78) [**J**–CHO]; $C_{20}H_{10}O_7$ (362); calc.: C 66.29, H 2.76; found: C 65.97, H 2.97.

Bis(3-formyl-5-methoxyfuranocoumarin-4-yl)ether (**7**) *and its hydrate*

Yield: 60%; m.p.: > 300°C (aqueous acetone); IR (KBr): $\nu = 2900$ (CH-aldehyde), 1720 (C=O), 1610, 1560 (C=C), 1280 (C–O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): *aldehyde*: $\delta = 4.28$ (s, 3H, 5-OCH_3), 7.05 (d, 1H, $J = 2.4$ Hz, H-3'), 7.15 (s, 1H, H-8), 7.63 (d, 1H, $J = 2.4$ Hz. H-2'), 9.94 (s, 1H, CHO) ppm; *hydrate*: $\delta = 4.15$ (s, 3H, 5-OCH_3), 6.98 (d, 1H, $J = 2.4$ Hz, H-3'), 7.20 (s, 1H, H-8), 7.60 (d, 1H, $J = 2.4$ Hz, H-2'), 6.74 (s, 1H, $CH(OH)_2$) ppm; MS (70 eV): m/z (%) = 502 (5) [M^+], 431 (2) [M^+–CH_3-2CO], 259 (100) [**E**, see Scheme 2], 260 (68) [**H**, see Scheme 2], 243 (6) [**B**, see Scheme 2], 231 (3) [**H**, see Scheme 2], 216 (9) [**H**–CH_3–CHO], 215 (9) [**H**–CH_3–CH_2O], 188 (2) [**H**–CH_3–CO–CHO]; $C_{26}H_{14}O_{11}$ (502); calc.: C 62.15, H 2.78; found: C 61.70 H, 2.97.

Bis(3-formyl-5,8-dimethoxyfuranocoumarin-4-yl)ether (**8**) *and its hydrate*

Yield: 55%; m.p.: > 300°C (aqueous acetone); IR (KBr): $\nu = 2900$ (CH-aldehyde), 1715 (C=O) 1650, 1600 (C=C), 1280 (C–O) cm^{-1} ^1H NMR (500 MHz, *DMSO*-d_6): *aldehyde*: $\delta = 3.92$ (s, 3H, 5-OCH_3), 4.02 (s, 3H, 8-OCH_3), 7.03 (d, 1H, $J = 2.4$ Hz, H-3'), 7.90 (d, 1H, $J = 2.4$ Hz, H-2'), 9.90 (s, 1H, CHO) ppm; *hydrate*: $\delta = 4.05$ (s, 3H, 5-OCH_3), 4.14 (s, 3H, 8-OCH_3), 6.96 (d, 1H, $J = 2.4$ Hz, H-3'), 7.63 (d, 1H, $J = 2.4$ Hz, H-2'), 6.76 (s, 1H, $CH(OH)_2$) ppm; MS (70 eV): m/z(%) = 562 (50) [M^+], 533 (5) [M^+–CHO], 518 (2) [M^+–CH_3–CHO], 503 (1.5) [M^+–2CH_3–CHO], 475 (1.95) [M^+–2CH_3–CO–CHO], 289 (31) [**F**, see Scheme 2], 290 (13) [**I**, see Scheme 2], 273 (100) [**C**, see Scheme 2], 274 (53) [**C**+H], 262 (5) [**I**–CO], 247 (3.5) [**I**–CO–CH_3], 220 (26) [**I**–2CO–CH_2], 205 (33) [**I**–2CO–CH_2–CH_3], 177 (12) [**I**–3CO–CH_2–CH_3]; $C_{28}H_{18}O_{13}$ (562); calc.: C 59.78, H 3.20; found: C 59.35, H 3.21.

General methylenation procedure

The hydroxy coumarins **1–3** (0.02 mol) were refluxed with methylene iodide (0.01 mol) and anhydrous potassium carbonate (0.04 mol) in dry acetone for 35 h. Acetone was filtered while hot, and the residue evaporated till dryness. The resulting yellow residue was recrystallized from acetic acid to give pale yellow needles.

Bis(Coumarin-4-oxy)methane (**9**)

Yield: 42%; m.p.: 254–256°C (acetic acid); IR (KBr): $\nu = 1710$ (C=O), 1595 (C=C), 1366, 1270 (C–O) cm^{-1}; UV (MeOH): $\lambda_{max} = 205, 265, 277, 305$ nm; MS (70 eV): *m/z* (%) = 336 (13) [M^+], 175 (50) [**K**, see Scheme 2], 162 (9) [**L**, see Scheme 2], 147 (5) [**K**–CO], 121 (100) [**J**, see Scheme 2], 92 (14) [**J**–CHO]; $C_{19}H_{12}O_6$ (336); calc.: C 67.85, H 3.57; found: C 67.42, H 3.61.

Bis(4-hydroxy-5-methoxyfuranocoumarin-3-yl)methane (**10**)

Yield: 50%; m.p.: > 300°C (acetic acid); IR (KBr): $\nu = 3250$ (OH) 1680 (C=O), 1615 (C=C), 1295 (C–O) cm^{-1}; UV (MeOH): $\lambda_{max} = 205, 230, 265$ sh, 295, 325 sh nm; ^{1}H NMR (400 MHz, *DMSO*-d_6): $\delta = 3.60$ (s, 2H, CH_2), 4.00 (s, 3H, 5-OCH_3), 7.10 (d, 1H, H-3′), 7.23 (s, 1H, H-8), 7.93 (d, 1H, H-2′) ppm; MS (70 eV): *m/z* (%) = 476 (3) [M^+], 447 (2.5) [M^+–CHO], 433 (1) [M^+–CH_3-CO], 405 (2) [M^+–CH_3–2CO], 376 (1.5) [M^+–CH_3–2CO–CHO], 245 (12) [**M**, see Scheme 2], 232 (29) [**O**, see Scheme 2], 203 (7) [**O**–CHO], 190 (100) [**O**–CO–CH_2], 175 (23) [O–CO–CHO], 147 (31) [**O**–2CO–CHO]; $C_{25}H_{16}O_{10}$ (476); calc.: C 63.02, H 3.36; found: C 63.12, H 3.29.

Bis(4-hydroxy-5,8-dimethoxyfuranocoumarin-3-yl)methane (**11**)

Yield: 48%; m.p.: > 300°C (acetic acid); IR (KBr): $\nu = 3350$ (OH), 1660 (C=O), 1575 (C=C), 1295 (C–O) cm^{-1} UV (MeOH): $\lambda_{max} = 205, 230, 268$ sh, 295, 328 sh nm; ^{1}H NMR (400 MHz, *DMSO*-d_6): $\delta = 3.60$ (s, 2H, CH_2), 3.91 (s, 3H, 8-OCH_3), 4.00 (s, 3H, 5-OCH_3), 7.08 (d, 1H, H-3′), 7.96 (d, 1H, H-2′) ppm; MS (70 eV): *m/z* (%) = 536 (9) [M^+], 537 (9) [M^+–H], 507 (2) [M^+–CHO], 506 (2) [M^+–CH_2O], 488 (2.5) [M^+–CH_2O–H_2O], 276 (44) [**N**+H, see Scheme 2], 275 (13) [**N**], 262 (50) [**P**, see Scheme 2], 245 (13) [**P**–OH], 220 (100) [**P**–CO–CH_2], 205 (97) [**P**–CO–CH_2–CH_3], 191 (17) [**P**–2CO–CH_3], 177 (57) [**P**–2CO–CH_2–CH_3]; $C_{27}H_{20}O_{12}$ (536); calc.: C 60.44, H 3.73; found: C 60.57, H 3.62.

Bis(4-hydroxy-5,8-dimethoxyfuranocoumarin-3-yl)phenylmethane (**12**)

A mixture of 4-hydroxy-5,8-dimethoxyfuranocoumarin (**3**, 0.02 mol) and benzaldehyde (0.01 mol) was refluxed for 5 h in absolute ethanol (20 ml). The solvent was evaporated till dryness, and the residual material was recrystallized from ethanol to give **12**.

Yield: 55%; m.p.: 230–231°C (ethanol); IR (KBr): $\nu = 3250$ (OH), 1695, 1680 (C=O), 1620, 1580 (C=C), 1290 (C–O) cm^{-1}; UV (MeOH): $\lambda_{max} = 205, 235, 260, 270, 300$ nm; ^{1}H NMR (500 MHz, *DMSO*-d_6): $\delta = 4.10$ (s, 3H, 8-OCH_3), 4.12 (s, 3H, 5-OCH_3) 6.20 (s, 1H, C*H*Ph), 7.19 (t, 1H, *para*-H), 7.24 (t, 2H, *ortho*-H), 7.28 (t, 2H; *meta*-H), 7.33 (d, 1H, $J = 2.4$ Hz, H-3′), 8.11 (d, 1H, $J = 2.4$ Hz, H-2′) ppm; MS (70 eV): *m/z* (%) = 612 (0.2) [M^+], 597 (0.2) [M^+–CH_3], 569 (0.1) [M^+–CH_3–CO], 351 (25) [**Q**+H], 350 (100) [**Q**, see Scheme 2], 262 (52) [**P**, see Scheme 2], 220 (87) [**P**–CO–CH_2], 205 (75) [**P**–CO–CHO], 206 (11) [**P**–2CO], 177 (24) [**P**–2CO-CHO]; $C_{33}H_{24}O_{12}$ (612); calc.: C 64.70, H 3.92; found: C 64.22, H 4.10.

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