170. The Chemistry of Coumarin Derivatives

Part 2[1])

Reaction of 4-Hydroxycoumarin with α,β-Unsaturated Aldehydes

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4-Hydroxycoumarin (= 4-hydroxy-2*H*-1-benzopyran-2-one) reacts with enals to give 1,2- or 1,4-addition products, depending on the nature and relative location of the substituents on the olefinic double bond (*Scheme 2*). The resulting adducts further react intra- or intermolecularly, affording dimeric coumarins or pyranocoumarins in the case of 1,2-addition and acetalic pyranocoumarins in the case of 1,4-addition. With enals bearing alkyl groups at C(β), 2*H*-pyrano[3,2-*c*]coumarins are the only products formed, and the reaction represents an easy and straightforward entry into this class of recently described biologically active natural products.

Introduction. – As part of an investigation on the toxins from *Ferula communis* L., we reported the structure elucidation of the haemorrhagic 2*H*-pyrano[3,2-*c*]coumarin ferprenin (**1**) [1b]. The isolation of **1** was tedious and low-yielding, but its synthesis could be accomplished in a straightforward way *via* the tandem *Knoevenagel*/hetero-*Diels-Alder* condensation[2]) of farnesal (**2**) and 4-hydroxycoumarin (= 4-hydroxy-2*H*-1-benzopyran-2-one) [1b]. The success of this reaction is surprising since under similar experimental conditions (heating in pyridine), citral (**3**) has been reported to give the tetracyclic compounds **4** and **5** [3], derived from a terpenic-type cyclization (*Scheme 1*).

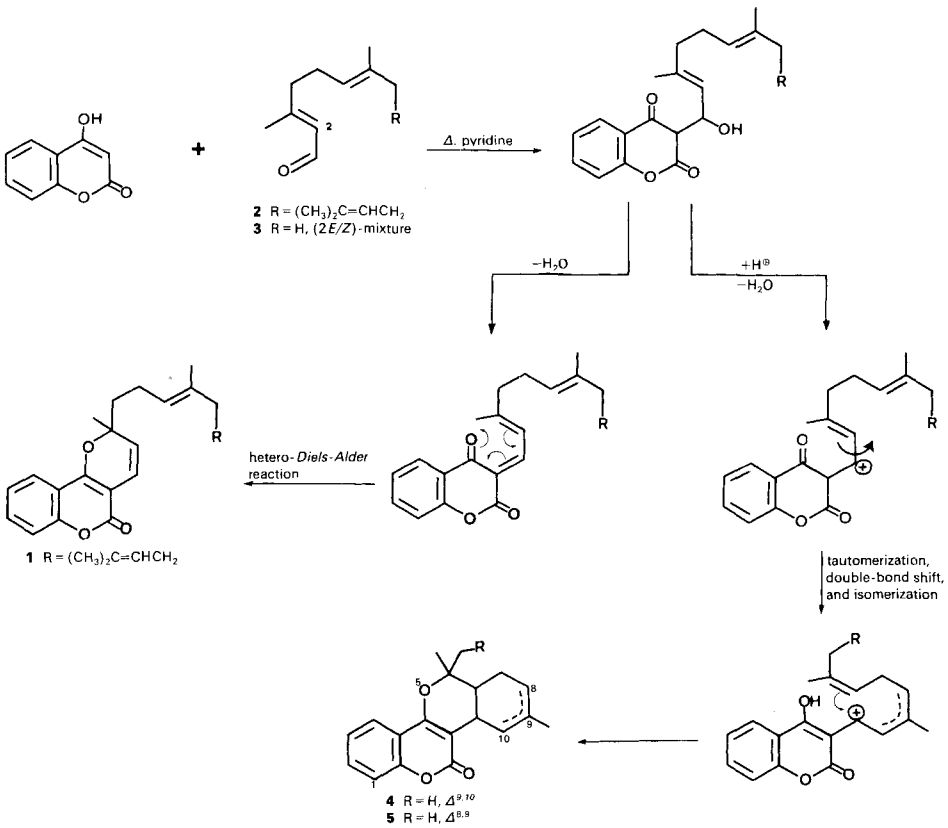
Furthermore, non-acetalic pyranocoumarins like **1** had never been obtained from the reaction of 4-hydroxycoumarin and enals; instead, dicoumarol-type dimers (from acrolein (= prop-2-enal), 3-ethoxy-2-methylacrolein, 3-amino-2-methylacrolein, and cinnamaldehyde (= 3-phenylprop-2-enal) [4–6][3])) or intensely coloured chromandiones (from 4-(dimethylamino)cinnamaldehyde [8]) were formed. In contrast with these data, a recent review claims instead, apparently only by analogy with the reaction of enones, that 1,4-addition followed by hemiacetal formation takes place [9]. These different reaction

[1]) Part 1, see [1a].

[2]) For a recent review on the application of this reaction to the synthesis of natural products, see [2].

[3]) The formation of an acetophenone and an unidentified product from the reaction of cinnamaldehyde and 4-hydroxycoumarin has also been reported [7].

Scheme 1. *Reaction of Farnesal* (**2**) *and Citral* (**3**) *with 4-Hydroxycoumarin*

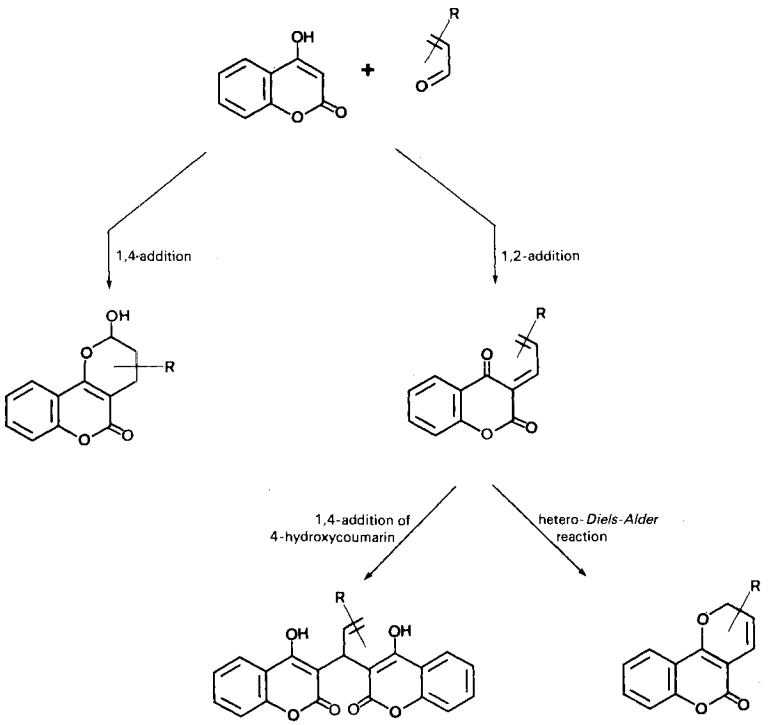


modes are summarized in *Scheme 2*. Their inconsistency prompted us to carry out a systematic investigation on the reaction of 4-hydroxycoumarin and enals. The aim was to assess its utility for the synthesis of 2*H*-pyrano[3,2-*c*]coumarins (=2*H*,5*H*-pyrano[3,2-*c*]-[1]benzopyran-5-ones). These, besides being in some cases natural products [10][4]), had previously been obtained only in multistep syntheses [11] [12] and were needed in gram amounts for structure-activity-relationship studies.

Results and Discussion. – Owing to the thermal unstability and low boiling point of some enals, all reactions were carried out at room temperature. Reaction conditions were optimized using farnesal (**2**); the best results were obtained in MeOH or EtOH as solvent and in the presence of catalytic amounts of ethylenediammonium diacetate [13]. Under these conditions, the reaction was complete in < 3 h, and the yield was 88%. The use of organic bases (pyridine, Et_3N, $(i\text{-}Pr)_2NH$) as solvent resulted in much lower yields and longer reaction times (> 60 h), as did substitution of acetone for MeOH or EtOH, probably on account of the poorer solubility of 4-hydroxycoumarin. The latter is a relatively strong acid (pK_a *ca.* 4) [14], and its alcoholic solutions are red to methylorange

[4]) The review [10a] updates the book [10b].

Scheme 2. *Different Reaction Modes of 4-Hydroxycoumarin and Enals*



(pH of a saturated MeOH solution *ca.* 2.5). The addition of 1 mol-equiv. of organic base (pyridine, Et_2N) suppressed completely in reaction; thus, in alcoholic medium and at room temperature, acidic conditions are required for the reaction to take place. Under these conditions, cationic (terpenic-type) cyclizations of polyolefinic substrates such as the isoprenoid aldehydes **2** and **3**, were not observed.

The course of the reaction was then investigated with the enals $R^2C(R^3)=C(R^1)CHO$ (*Table*). All reactions were carried out using a 1.2:1 molar ratio of 4-hydroxycoumarin and enal. As evident from the *Table*, different types of products could be obtained, depending on location and nature of the substituents at the olefinic double bond. Both 4-hydroxycoumarin and enals are in fact polydent reagents, and several reaction modes are thus possible by a combination of 1,4 *vs.* 1,2 addition and C(3) *vs.* O(2) and O(4) alkylation of the coumarin moiety [15]. In the cases examined, however, 4-hydroxycoumarin reacted regioselectively at C(4), in contrast to what was observed with sp^3-type C electrophiles [15], and the variety of products obtained derived from further reaction of the 1,2- and 1,4-addition products.

Based on the results of the reaction, the enals investigated can be divided into three groups: β-unsubstituted, β-alkyl-substituted, and β-aryl-substituted enals.

Enals without Substituents at C(β) (see *Table, Entries 1–3*). With β-unsubstituted enals, conjugated addition followed by hemiacetal formation between the enolic OH and

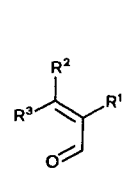
Table. *Reaction of Enals and 4-Hydroxycoumarin*

Entry	Enal	R^1	R^2	R^3	Reaction time [h]	Workup procedure[a])	Products (yield)[b])
1	Propenal	H	H	H	70	*C*	**6a** (28%), **7a** (4%)
2	2-Ethylpropenal	Et	H	H	20	*C*	**6b** (8%), **7b** (3%), **6h** (28%)
3	2-Phenylpropenal	Ph	H	H	24	*B*	**6c** (39%)
4	But-2-enal	H	Me	H	1	*A*	**7c** (54%)
5	2-Methyl-but-2-enal	Me	Me	H	5	*A*	**7d** (39%)
6	5-Methyl-2-phenyl-hex-2-enal	Ph	i-Bu	H	24	*A*	**7e** (74%)
7	3-Methyl-but-2-enal	H	Me	Me	4	*A*	**7f** (84%)
8	Geranial	H	$(CH_3)_2C{=}CH(CH_2)_2$	Me	3	*A*	**7g** (79%)
9	Neral	H	Me	$(CH_3)_2C{=}CH(CH_2)_2$	3	*A*	**7g** (68%)
10	Citral (geranial/neral)[c])			Me	3	*A*	**7g** (70%)
11	(*E,E*)-Farnesal	H	$(CH_3)_2C{=}CH(CH_2)_2C(CH_3){=}CH(CH_2)_2$	Me	3	*A*	**1** (88%)
12	Safranal (**13**)				40	*A*	**14** (51%)
13	3,4-Dihydro-2*H*-pyran-5-carbaldehyde		$CH_2CH_2CH_2O$	H	6	*C*	**7h** (12%), **15** (59%)
14	Cinnamaldehyde	H	Ph	H	3	*C*	**7i** (2.8%), **17b** (54%)
15	4-Nitrocinnamaldehyde	H	$4\text{-}NO_2C_6H_4$	H	18	*B*	**17a** (47%)
16	4-Methoxycinnamaldehyde	H	$4\text{-}MeOC_6H_4$	H	18	*C*	**6i** (36%), **16a** (10%)
17	4-(Dimethylamino)cinnamaldehyde	H	$4\text{-}(Me_2N)C_6H_4$	H	48	*B*	**16b** (38%)
18	5-Phenylpenta-2,4-dienal	H	$PhCH{=}CH_2$	H	24	*B*	**17c** (44%)

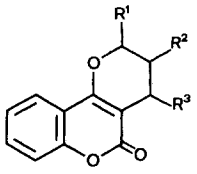
[a]) See *Exper. Part.*

[b]) Yields refer to chromatographically and spectroscopically pure products.

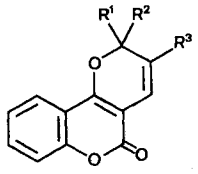
[c]) Geranial/neral 62:38 (GC analysis).



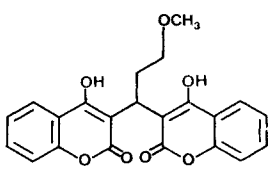
enal (see *Table*)



	R^1	R^2	R^3
6a	OH	H	H
b	OH	Et	H
c	OH	Ph	H
d	MeO	H	H
e	MeO	ξ-Et	H
f	MeO	*cis*-Ph	H
g	MeO	*trans*-Ph	H
h		*trans*-Et	H
i		H	4-$MeOC_6H_4$



	R^1	R^2	R^3
7a	H	H	H
b	H	H	Et
c	Me	H	H
d	Me	H	Me
e	i-Bu	H	Ph
f	Me	Me	H
g	Me	$(CH_3)_2C{=}CHCH_2CH_2$	H
h	H	$OCH_2CH_2CH_2$	
i	Ph	H	H



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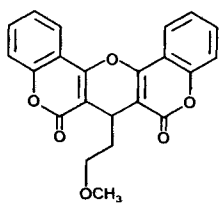

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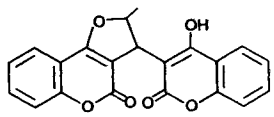

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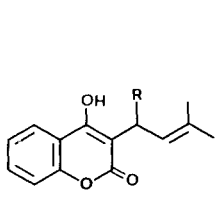
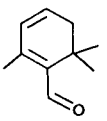
CH=O took place (→ **6a–c**). In the presence of an α-substituent (*Entries 2* and *3*), the resulting hemiacetalic pyranocoumarins **6b** and **6c** were isolated as a mixture of diastereoisomers, that could be separated in the case of **6c** after methylation (MeOH, TsOH, reflux; → **6f**, **6g**). Minor amounts of the non-acetalic pyranocoumarins **7a** and **7b** could also be isolated with acrolein and 2-ethylacrolein. The latter afforded also the asymmetric dimeric compound **6h** (*vide infra* for the mechanism of its formation). With acrolein, conjugated addition of MeOH to give a saturated aldehyde (3-methoxypropanal) was faster than the reaction with 4-hydroxycoumarin, and the symmetric dimer **8** was formed in MeOH [16]. Attempted acetylation of **8** resulted in dehydration to the 4,4′-epoxydicoumarin **9** whose structure was confirmed by X-ray analysis [17]. The 1,4-addition product **6a** could be isolated in non-protic solvents (DMSO) or in i-PrOH. In EtOH, a complex mixture was formed. In no case, the formation of the asymmetric dimer **10**, previously reported as the major reaction product of acrolein and 4-hydroxycoumarin [6], could be observed.

Enals with a β-Alkyl Substituent (see *Table, Entries 4–12*). With β-alkyl-substituted enals, 2*H*-pyrano[3,2-*c*]coumarins **7c–g** were the only reaction products. These compounds derive from a 1,2-addition process, followed by dehydration to an alkylidenechromandione and hetero-*Diels-Alder* cyclization (*Scheme 2*). The intermediate alkylidenechromandiones could be trapped with thiophenol or, more efficiently, with trimethyl phosphite. The *Michael*-addition products (*e.g.* **11** and **12**) were stable and

could be isolated and characterized (see *Exper. Part*). Under these conditions (MeOH, cat. ethylenediammonium diacetate, r.t.), the synthesis of the haemorrhagic pyranocoumarin ferprenin (**1**) proceeded faster and with better yields (*Entry 11*: 88%), than originally reported [1b] (see also *Scheme 1*). In the same way, also the bis- and monodeprenyl analogues **7f** and **7g** of **1** could be efficiently synthesized (prenyl = 3-methylbut-2-enyl). The dienal safranal (**13**) gave the pyranocoumarin **14**, showing that the reaction can also be applied to a γ,δ-unsaturated enal. The β-*O*-substituted enal 3,4-dihydro-2*H*-pyran-5-carbaldehyde gave the pyranocoumarin **7h** and its acid-catalyzed-methanolysis product **15**.



11 R = PhS
12 R = $(MeO)_2P(O)$



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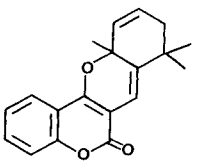

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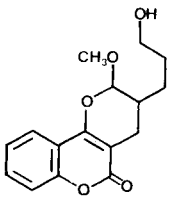

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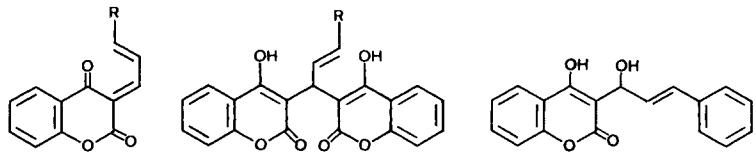
In MeOH and at room temperature, the only product from citral (**3**) and 4-hydroxycoumarin was deprenylferprenin (**7g**); no trace of the tetracyclic compounds 4 and **5** (*Scheme 1*) could be detected by 270-MHz ^{1}H-NMR analysis of the crude mixture. The reaction carried out as reported in [3] (4-hydroxycoumarin/citral/pyridine in a 1:1:1 molar ratio) gave the pyranocoumarin **7g** at 50°, and a complex mixture at 120°. At 120°, a much cleaner reaction took place with 2 mol-equiv. of pyridine, and the tetracyclic compound **4** could, thus, be obtained as a crystalline solid in 18% yield. Although only traces of pyranocoumarins were formed under these conditions, **7g** was the main product when the reaction was carried out with 5–10 mol-equiv. of pyridine and became the only product with a larger excess of pyridine. A similar trend (increased formation of pyran derivatives with respect to cationic cyclizations) had been observed in the condensation of citral and olivetol [18]. This effect is presumably due to the basicity of pyridine that suppresses terpenic-type cyclizations involving carbonium ions, a competitive reaction at high temperature.

Enals with a β-Aryl Substituent (see *Table, Entries 14–18*). With β-aryl-substituted enals, 1,2-addition still took place, but the fate of the resulting alkylidenechromandione was dramatically dependent on the substitution pattern of the aryl ring: 4-methoxy- and 4-(dimethylamino)cinnamaldehyde gave the relatively stable and intensely coloured (red and blue, respectively) alkylidenechromandiones **16a** and **16b**. In contrast, 4-nitrocinnamaldehyde afforded the dimer **17a**, and cinnamaldehyde a 95:5 mixture of the dimer **17b** and the pyranocoumarin **7i**, the latter in equilibrium with its valence tautomer **16c**[5]). Thus, an aryl ring at C(β) of the enal stabilizes the intermediate chromandione, making possible the attack of another 4-hydroxycoumarin molecule or even its isolation. This

[5]) The ratio between the valence tautomers **7i** and **16c** was *ca.* 1.9:1 in $CDCl_3$ and 2.6:1 in (D_6)DMSO. The equilibrium was slow on the NMR time scale at room temperature, allowing detection of both forms. A reversible line-broadening was observed at temperatures > 70°.



16a R = 4-$MeOC_6H_4$
b R = 4-$(Me_2N)C_6H_4$
c R = Ph

17a R = 4-$NO_2C_6H_4$
b R = Ph
c R = PhCH=CH (*E*)

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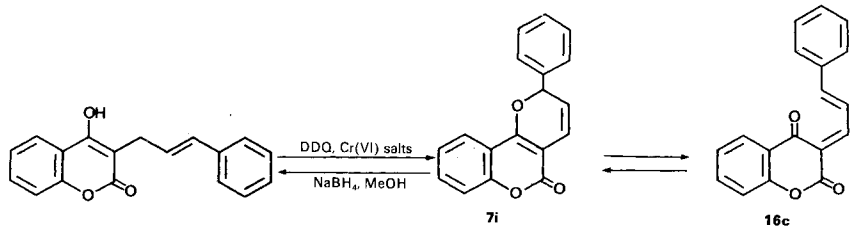
effect is presumably of electronic nature, and with enals bearing a Ph group at C(α), little difference was observed when compared with the corresponding alkyl-substituted enals (*cf.* 2-ethyl- and 2-phenylpropenal (*Table 1, Entries 2* and *3*) and 2-methylbut-2-enal and 2-phenyl-5-methylhex-2-enal (*Table 1, Entries 5* and *6*)). This electronic dependence is in accordance with the formation of the dimeric product **17c** from the reaction of 4-hydroxycoumarin and 5-phenylbuta-2,4-dienal, the vinylogue of cinnamaldehyde.

The orange mixture of the valence tautomers **7i** and **16c** obtained as a minor product besides **17b** from the reaction of cinnamaldehyde, has characteristics (colour, m.p.) similar to the ones reported for **18** [5] which formally can be derived from **16c** by H_2O addition. The structure attribution to our product **7i**/**16c** was based on the reactions depicted in *Scheme 3*: Oxidation of 3-cinnamyl-4-hydroxycoumarin[6]) with 4,5-dichloro-3,6-dioxo-1,4-cyclohexadiene-1,2-dicarbonitrile (DDQ) or Cr(VI)-based reagents [1b] gave a mixture of tautomers identical to the product **7i**/**16c** obtained from the condensation of 4-hydroxycoumarin and cinnamaldehyde. Conversely, reduction of **7i**/**16c** with $NaBH_4$ in MeOH gave 3-cinnamyl-4-hydroxycoumarin as the only product.

Scheme 3. *Chemical Correlation between 3-Cinnamyl-4-hydroxycoumarin and the Valence Tautomers* **7i** *and* **16c**



7i **16c**

The alkylidenechromandiones obtained from the reaction of 4-methoxy- and 4-(dimethylamino)cinnamaldehyde were tautomerically unitary, since their NMR spectra showed only one set of signals. Using $NaBH_4$, **16a** was reduced to 4-hydroxy-3-(4-methoxycinnamyl)coumarin, and **16a** underwent the slow tandem 1,6/1,4-addition of another molecule of 4-hydroxycoumarin, giving the asymmetrical dimer **6i**. Compound **16b** was decoloured by $NaBH_4$, but the reduction product was air oxidized to a mixture of blue products that could not be characterized. The chromandione **16b** was stable towards 4-hydroxycoumarin, and no dimeric product was formed in the condensation reaction.

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[6]) Obtained in quantitative yield from the reductive cleavage of the dimer **17b** with sodium cyanoborohydride in MeOH. The mechanism and applicability of this reaction will be reported as Part 3 in this series.

The pyranocoumarins obtained from the reaction of enals bearing a β-alkyl substituent were tautomerically unitary. The absence of the alkylidenechromandione valence tautomer was in accordance with the spectral analysis of these products, as well as with the results obtained from the treatment of the pyranocoumarin **7f** with various reducing agents: catalytic hydrogenation reduced the disubstituted double bond of the pyran ring, whereas **7f** could be recovered unchanged after treatment with $NaBH_4$ in MeOH or Li in liquid NH_3. The presence of a pyranocoumarin $\leftrightarrows$ alkylidenechromandione valence tautomerism would have led instead to the isolation of 4-hydroxy-3-(3-methylbut-2-enyl)- or 4-hydroxy-3-(3-methylbutyl)coumarin.

Conclusion. – The reaction of 4-hydroxycoumarin with suitably substituted enals represents a straigthforward entry into 2*H*-pyrano[3,2-*c*]coumarins, a recently described novel class of biologically active natural products. The reaction is easily carried out and is in principle extensible to all enals bearing at least one substituent different from a phenyl group at C(β).

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Experimental Part

General. 2-Phenylprop-2-enal (atropaldehyde) [19], 3,4-dihydro-2*H*-pyrane-5-carbaldehyde [20], and 5-phenylpenta-2,4-dienal [21] were prepared according to the referenced literature methods. (*E,E*)-Farnesal was prepared by MnO_2 oxidation of (*E,E*)-farnesol (*Aldrich*). Safranal (=2,6,6-trimethylcyclohexa-1,3-diene-1-carbaldehyde), and 5-methyl-2-phenylhex-2-enal were a gift from *SGA Flavors*, Torino. All other enals as well as 4-hydroxycoumarin were purchased (*Aldrich*, *Fluka*, *Lancaster*, *Merck*) and used as such. Column chromatography (CC): silica gel *60* (*Merck*, 70–230 mesh). TLC: precoated silica gel *60* F_{254} plates (*Merck*); detection with UV light (245 nm) or 5% H_2SO_4 in MeOH and heating. Prep. HPLC: *Waters Microporasil* column (80 × 3 cm), *Waters* differential refractometer *R401*, *Waters* chromatographic pump *6000A*. M.p.: *Büchi-SMP-20* apparatus (uncorrected). UV (λ_{max} in nm): *Beckman-DB-GT* spectrophotometer; in EtOH. IR (in cm^{-1}): *Perkin-Elmer-237* grating spectrometer. ^1H- and ^{13}C-NMR spectra: *Jeol-GX270/89* apparatus (270 and 67.5 MHz, resp.); chemical shifts in ppm downfield from TMS (= 0 ppm). EI-MS: *Varian-Mat-CH7A* spectrometer (70 eV). CI-MS: *VGEQ-70/70* spectrometer. Microanalyses (C and H) agreed with theoretical values (±0.3%).

Reaction of 4-Hydroxycoumarin and Enals (see *Table*). *General:* The enal was treated at r.t. with 1.2 mol-equiv. of 4-hydroxycoumarin and 0.05 mol-equiv. of ethylenediammonium diacetate in MeOH as solvent (i-PrOH in *Entry 1*). The workup depended on the formation or not of a precipitate and on the presence of only one or more products. The following cases are reported as representative.

Workup Procedure A (formation of only one product, soluble in the reaction mixture): To a soln. of 4-hydroxycoumarin (10.96 g, 66.8 mmol, 1.2 mol-equiv.) and ethylenediammonium diacetate (500 mg, 2.8 mmol, 0.05 mol-equiv.) in 150 ml of MeOH, a soln. of farnesal (12.40 g, 55.7 mmol) in MeOH was added dropwise during *ca.* 5 min. After 3 h stirring at r.t., the solvent was evaporated. The pasty residue was mixed with silica gel *40* (35–70 mesh; *ca.* 25 g) and added to a short column of silica gel *60* (70–230 mesh; 100 g) containing *ca.* 5 g of activated carbon at the top. The column was washed with hexane (*ca.* 300 ml) to remove some apolar impurities and then with hexane/AcOEt 9:1 (*ca.* 500 ml): chromatographically and spectroscopically pure *ferprenin* (**1**; 17.86 g, 88%) as yellowish oil.

Workup Procedure B (formation of only one product, insoluble in the reaction mixture): To a soln. of 4-hydroxycoumarin (1.098 g, 6.7 mmol, 1.2 mol-equiv.) and ethylenediammonium diacetate (50.4 mg, 0.28 mmol, 0.05 mol-equiv.) in 15 ml MeOH, 1.00 g of 4-nitrocinnamaldehyde (5.6 mmol) in 30 ml of MeOH was added. Formation of a thick yellowish precipitate started within 1 h. After stirring 18 h at r.t., the precipitate was filtered and washed with cold MeOH: 1.270 g (47%) of **17a**. The mother liquors contained unreacted aldehyde and 4-hydroxycoumarin (TLC (hexane/AcOEt 1:9 + one drop of AcOH)). The ^1H-NMR showed also the presence of

small amounts of the dimethyl acetal of the starting aldehyde. Addition of 1 further equiv. of 4-hydroxycoumarin to the mother liquors gave an additional 1.065-g crop of **17a** (total yield: 86%).

Workup Procedure C (formation of more than one reaction product): To a soln. of 4-hydroxycoumarin (3.086 g, 19.0 mmol, 1.2 mol-equiv.) and ethylenediammonium diacetate (142 mg, 0.79 mmol, 0.05 mol-equiv.) in 35 ml of MeOH, 2.00 ml (2.096 g, 15.9 mmol) of cinnamaldehyde were added. After stirring 3 h at r.t., the orange soln. was separated from the yellowish precipitate of **17b**. The latter was washed with cold MeOH and dried (yield: 3.390 g, 52%). The mother liquors were evaporated and chromatographed (50 g of silica gel) to give pyranocoumarin **7i**/cinnamaldehyde dimethyl acetal (with hexane/AcOEt 8:2) and 120 mg of **17b** (hexane/AcOEt 1:9). Total yield of **17b**, 54%. The crude orange **7i** was purified by prep. HPLC (hexane/AcOEt 7:3): 122 mg (2.8%) of pure **7i** as an orange powder. If the reaction was carried out as described in [5] and [6], **7i** was also formed, albeit in lower yield.

CC was used to separate the mixtures formed in the reactions corresponding to *Entries 1,2, 13*, and *16* (see *Table*). *Entry 1*: hexane/AcOEt 8:2 for the elution of **7a** and hexane/AcOEt 1:9 for the elution of **6a**. *Entry 2*: **6h** was separated by filtration, and the mother liquors containing **6b**/**7b** were separated with hexane/AcOEt 8:2. *Entry 13*: hexane/AcOEt 1:1 for the elution of **7h** and hexane/AcOEt 3:7 for the elution of **15**. *Entry 16*: hexane/AcOEt 8:2 for the elution of **16a** and hexane/AcOEt 1:9 for the elution of **6i**.

*3,4-Dihydro-2-hydroxy-2*H,*5*H-*pyrano[3,2-c][1]benzopyran-5-one* (**6a**). M.p. 163°. UV (EtOH): 312, 282. IR (KBr): 3340, 1680, 1630, 1575, 1410, 1355, 1310, 1165, 1080, 1060, 940, 760. ^{1}H-NMR (270 MHz, (D_6)DMSO): 7.86 (br. *d*, OH); 7.77 (*d*, *J* = 7.2, 1 H); 7.65 (*t*, *J* = 7.8, 1 H); 7.44–7.37 (overlapped signals, 2 H); 5.79 (br. *s*, 1 H); 2.52 (*t*, *J* = 6.7, 2 H); 2.01 (*m*, 2 H). CI-MS (isobutane): 219 (100, $[M + 1]^+$, $[C_{12}H_{10}O_4 + 1]^+$).

Refluxing **6a** in MeOH in the presence of TsOH (*ca.* 0.3 mol-equiv.) gave the *O*-Me derivative **6d**. Oil. IR (film): 1720, 1635, 1500, 1410, 1105, 1055, 950, 915, 755. ^{1}H-NMR (270 MHz, $CDCl_3$): 7.64 (*d*, *J* = 8.2, 1 H); 7.36 (*t*, *J* = 7.8, 1 H); 7.15–7.13 (overlapped signals, 2 H); 5.26 (br. *s*, 1 H): 3.46 (*s*, 3 H); 2.46 (*m*, 2 H); 2.00 (*m*, 1 H); 1.90 (*m*, 1 H). EI-MS: 232 (100, M^+, $C_{13}H_{12}O_4^+$), 217 (67), 200 (38), 189 (75), 121 (85), 92 (60).

*3-Ethyl-3,4-dihydro-2-hydroxy-2*H,*5*H-*pyrano[3,2-c][1]benzopyran-5-one* (**6b**). M.p. 107°. UV (EtOH): 307, 283. IR (KBr): 3350, 1680, 1630, 1575, 1495, 1160, 1090, 1060, 910, 870, 755. ^{1}H-NMR (270 MHz, $CDCl_3$; 2:1 mixture of isomers): 7.65 (br. *d*, *J* = 7.2, 1 H); 7.39 (br. *t*, *J* = 7.8, 1 H); 7.16–7.10 (overlapped signals, 2 H); 5.75, 5.50 (br. *s*, 1 H); 2.81–1.18 (overlapped signals, 5 H); 0.98, 0.94 (2*t*, *J* = 7.2, 3 H). EI-MS: 246 (35M^+, $C_{14}H_{14}O_4^+$), 218 (30), 176 (100), 175 (95), 121 (40), 120 (40).

Methylation as described for **6a** gave **6e** (4:3 mixture of isomeric *O*-Me derivatives). Colourless oil. IR (film): 1720, 1640, 1610, 1580, 1495, 1400, 1090, 1045, 920, 755. ^{1}H-NMR (270 MHz, $CDCl_3$): 7.82 (*d*, *J* = 7.9, 1 H); 7.53 (*t*, *J* = 7.6, 1 H); 7.35–7.27 (overlapped signals, 2 H); 5.27, 5.10 (2*d*, *J* = 2.4 and 3.7, resp., 1 H); 3.61, 3.56 (2*s*, 3 H); 2.75, 2.69 (2 *dd*, each *J* = 16.8, 6.4, 1 H); 2.44, 2.28 (2 *dd*, *J* = 16.8, 3.6 and *J* = 16.8, 12.2, resp., 1 H); 2.03, 1.91 (*m*, 1 H); 1.58, 1.29 (*m*, 2 H); 1.05, 1.02 (*t*, *J* = 7.02, 3 H). ^{13}C-NMR (67.5 MHz, $CDCl_3$; multiplicities from the DEPT spectra): 101.86, 103.49 (2*s*, C(2)); 36.36, 37.21 (2*d*, C(3)); 23.03, 23.86 (2*t*, C(4)); 100.93, 102.29 (2*s*, C(4a)); 162.95, 162.79 (2*s*, C(5)); 152.43 (*s*, C(6a)); 116.47 (*d*, C(7)); 131.27, 131.22 (2*d*, C(8)); 123.79, 122.08 (2*d*, C(9), C(10)); 115.50, 115.69 (*s*, C(10a)); 156.93, 156.87 (2*s*, C(10b)).

*3α-Ethyl-3,4-dihydro-2β-(4′-hydroxy-2′-oxo-2*H*-1′-benzopyran-3′-yl)-2*H,*5*H-*pyrano[3,2-c][1]benzopyran-5-one* (**6h**). M.p. 188°. UV (EtOH): 306, 283, 264. IR (KBr): 3200, 1715, 1675, 1635, 1575, 1500, 1460, 1400, 1275, 1220, 1175, 1115, 1055, 955, 760. ^{1}H-NMR (270 MHz, (D_6)DMSO): 8.07 (*d*, *J* = 7.3, 1 H); 7.70–7.56 (overlapped signals, 3 H); 7.43–7.37 (overlapped signals, 3 H); 7.27 (*t*, *J* = 7.6, 1 H); 5.46 (*d*, *J* = 10.8, 1 H)[7]); 3.46 (br. *s*, exchangeable, 1 H); 2.76 (overlapped signals, 2 H); 2.15 (*m*, 1 H); 1.45 (*m*, 1 H); 1.19 (*m*, 1 H); 0.90 (*t*, *J* = 7.3, 3 H).

Treatment with diazomethane gave a mixture of the 4′-*O*- and 2′-*O*-Me derivatives that were separated by CC (hexane/AcOEt 7:3) to give a 9:1 mixture of the 4′-*O*- and 2′-*O*-Me derivatives.

*3α-Ethyl-3,4-dihydro-2β-(4′-methoxy-2′-oxo-2′*H*-1′-benzopyran-3′-yl)-2*H,*5*H-*pyrano[3,2-c][1]benzopyran-5-one*: M.p. 222°. UV (EtOH): 306, 273. IR (KBr): 1710, 1635, 1610, 1575, 1380, 1350, 1060, 950, 775, 760. ^{1}H-NMR (270 MHz, $CDCl_3$): 7.75 (*d*, *J* = 7.6, 1 H); 7.67 (*d*, *J* = 7.9, 1 H); 7.61 (*t*, *J* = 7.0, 1 H); 7.45 (*t*, *J* = 7.8, 1 H); 7.40–7.26 (overlapped signals, 3 H); 7.17 (*t*, *J* = 7.6, 1 H); 5.29 (*d*, *J* = 10.4, 1 H); 4.06 (*s*, 3 H); 2.95 (*dd*, *J* = 16.8, 4.9, 1 H); 2.78 (*m*, 1 H); 2.20 (*dd*, *J* = 16.8, 11.3, 1 H); 1.49 (*m*, 1 H); 1.19 (*m*, 1 H); 0.97 (*t*, *J* = 7.3, 3 H). EI-MS: 404 (58 M^+, $C_{24}H_{20}O_6^+$), 230 (83), 215 (100), 201 (36), 189 (27), 175 (33), 121 (38).

*3α-Ethyl-3,4-dihydro-2β-(2′-methoxy-4′-oxo-4′*H*-1′-benzopyran-3′-yl)-2*H,*5*H-*pyrano[3,2-c][1]benzopyran-5-one:* IR (KBr): 1725, 1710, 1635, 1620, 1570, 1490, 1460, 1360, 1100, 1060, 755. ^{1}H-NMR (270 MHz, $CDCl_3$):

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[7]) Diagnostic of a *trans*-relationship between the 4-hydroxy-3-coumarinyl and the Et group.

8.25 (*d*, *J* = 8.2, 1 H); 7.70 (overlapped signals, 2 H); 7.49–7.44 (overlapped signals, 3 H); 7.30 (*d*, *J* = 8.5, 1 H); 7.17 (*t*, *J* = 7.5, 1 H); 5.41 (*d*, *J* = 10.7, 1 H); 4.17 (*s*, 3 H); 2.95 (*dd*, *J* = 16.9, 4.8, 1 H); 2.65 (*m*, 1 H); 2.26 (*dd*, *J* = 16.9, 11.26, 1 H); 1.51 (*m*, 1 H); 1.26 (*m*, 1 H); 0.97 (*t*, *J* = 7.4, 3 H).

*3,4-Dihydro-2-hydroxy-3-phenyl-2*H,5H-*pyrano[3,2-c][1]benzopyran-5-one* (**6c**). M.p. 157°. UV: 307, 282, 272. IR (KBr): 3210, 1680, 1630, 1610, 1580, 1405, 1060, 930, 750, 740. ^{1}H-NMR (270 MHz, $CDCl_3$; all signals br.): 7.65 (*d*, *J* = 7.4, 1 H); 7.35–7.07 (overlapped signals, 8 H); 5.86, 5.70 (br. *s* and *d* (*J* = 5.8), 1 H); 3.09–2.74 (overlapped signals, 3 H). FAB-MS: 295 ($[M + 1]^+$, $[C_{18}H_{14}O_4 + 1]^+$).

Methylation as described for **6a** gave a 2:1 mixture of isomeric O-Me derivatives **6f** and **6g** that were separated by prep. HPLC (hexane/AcOEt 8:2).

Data of the major *O*-Me derivative: M.p. 108°. UV (EtOH): 307, 282, 271. IR (KBr): 1710, 1635, 1610, 1580, 1490, 1400, 1075, 1030, 940, 920. ^{1}H-NMR (270 MHz, $CDCl_3$): 7.86 (*d*, *J* = 7.8, 1 H); 7.56 (*t*, *J* = 7.4, 1 H); 7.43–7.28 (overlapped signals, 7 H); 5.42 (*d*, *J* = 2.5, 1 H); 3.50 (*s*, 3 H); 3.29 (*ddd*, *J* = 17.0, 6.0, and 2.5, 1 H); 3.03 (*t*, *J* = 17.0, 1 H); 2.90 (*dd*, *J* = 17.0, 6.0, 1 H). EI-MS: 308 (30, M^+, $C_{19}H_{16}O_4^+$), 276 (24), 134 (100), 91 (38).

Data of the minor 2-Me derivative: M.p. 126°. UV (EtOH): 307, 282, 271. IR (KBr): 1695, 1630, 1610, 1575, 1490, 1410, 930, 740, 700. ^{1}H-NMR (270 MHz, $CDCl_3$): 7.84 (*d*, *J* = 7.8, 1 H); 7.56 (*t*, *J* = 7.4, 1 H); 7.45–7.21 (overlapped signals, 7 H); 5.41 (*d*, *J* = 3.9, 1 H); 3.62 (*s*, 3 H); 3.38 (*m*, 1 H); 3.08 (*dd*, *J* = 18.0, 6.0, 1 H); 2.89 (*dd*, *J* = 18.0, 6.0, 1 H). EI-MS: 308 (30, M^+, $C_{19}H_{16}O_4^+$), 276 (48), 134 (100), 91 (65).

*3,4-Dihydro-2-(4′-hydroxy-2′-oxo-2′*H*-1-benzopyran-3′-yl)-4-(4-methoxyphenyl)-2*H,5H-*pyrano[3,2-c][1]-benzopyran-5-one* (**6i**). M.p. 198°. UV (EtOH): 315, 305, 290, 270. IR (KBr): 1710, 1665, 1620, 1575, 1510, 1500, 1400, 1250, 1210, 1110, 760. ^{1}H-NMR (270 MHz, (D_6)DMSO): 8.03 (*d*, *J* = 7.4, 1 H); 7.79 (*d*, *J* = 7.7, 1 H); 7.69–7.33 (overlapped signals, 6 H); 7.21 (*d*, *J* = 8.4, 2 H); 6.92 (*d*, *J* = 8.4, 2 H); 5.58 (br. *d*, *J* = 10.8, 1 H); 4.19 (br. *d*, *J* = 3.2, 1 H); 3.76 (*s*, 3 H); 3.11 (*ddd*, *J* = 13.5, 10.8, 3.2, 1 H); 2.00 (br. *d*, *J* = 13.5, 1 H). ^{13}C-NMR (67.5 MHz, (D_6)DMSO): 68.25 (*d*, C(2)); 31.55 (*t*, C(3)); 34.08 (*d*, C(4)); 101.14, 101.50 (2*s*, C(4a), C(3′)); 162.98, 160.75 (2*s*, C(5), C(2′)); 152.22, 151.69 (2*s*, C(6a), C(8′a)); 115.97, 115.81 (2*d*, C(7), C(8′)); 132.53, 131.51 (2*d*, C(8), C(7′)); 123.52, 123.38, 122.28 (3*d*, C(9), C(6′), C(10), C(5′)); 115.37, 114.69 (2*s*, C(10a), C(4′a)); 160.33, 157.40 (2*s*, C(10b), C(4′)); anisyl residue: 135.20 (*s*), 113.31 (*d*), 128.36 (*d*), 160.33 (*s*), 54.53 (*q*). EI-MS: no M^+($C_{28}H_{20}O_7^+$), 306 (100), 162 (45), 132 (67), 131 (72), 115 (85), 92 (95).

2H,5H-*Pyrano[3,2-c][1]benzopyran-5-one* (**7a**). M.p. 145°. UV (EtOH): 348, 250. IR (KBr): 1700, 1635, 1610, 1330, 1190, 1115, 1050, 990, 760, 705. ^{1}H-NMR (270 MHz, $CDCl_3$): 7.67 (br. *d*, *J* = 8.2, 1 H); 7.47 (br. *t*, *J* = 7.8, 1 H); 7.27–7.19 (overlapped signals, 2 H); 6.54 (br. *d*, *J* = 10.1, 1 H); 5.60 (*dt*, *J* = 10.1, 3.9, 1 H); 5.08 (br. *d*, *J* = 3.9, 2 H). EI-MS: 200 (100, M^+, $C_{12}H_8O_3^+$), 172 (15), 144 (28), 121 (30), 91 (70).

*3-Ethyl-2*H,5H-*pyrano[3,2-c][1]benzopyran-5-one* (**7b**). M.p. 115°. UV (EtOH): 353, 249. IR (KBr): 1700, 1660, 1620, 1570, 1495, 1420, 1190, 1080, 760, 750. ^{1}H-NMR (270 MHz, $CDCl_3$): 7.69 (*d*, *J* = 7.6, 1 H); 7.47 (*t*, *J* = 7.9, 1 H); 7.27–7.20 (overlapped signals, 2 H); 6.30 (br. *s*, 1 H); 4.95 (br. *s*, 2 H); 2.08 (*q*, *J* = 7.3, 2 H); 1.14 (*t*, *J* = 7.3, 3 H). EI-MS: 228 (38, M^+, $C_{14}H_{12}O_3^+$), 191 (25), 121 (100), 92 (70).

*2-Methyl-2*H,5H-*pyrano[3,2-c][1]benzopyran-5-one* (**7c**). M.p. 129°. UV (EtOH): 348, 252. IR (KBr): 1715, 1630, 1615, 1575, 1500, 1420, 1195, 1040, 765. ^{1}H-NMR (270 MHz, $CDCl_3$): 7.78 (*d*, *J* = 7.8, 1 H); 7.55 (*t*, *J* = 7.5, 1 H); 7.38–7.25 (overlapped signals, 2 H); 6.59 (*dd*, *J* = 10.0, 1.5, 1 H); 5.59 (*dd*, *J* = 10.0, 3.0, 1 H); 5.31 (*m*, 1 H); 1.56 (*d*, *J* = 6.7, 3 H). EI-MS: 214 (25, $M^{+\cdot}$, $C_{13}H_{10}O_3^+$), 199 (62), 191 (27), 121 (88), 92 (100), 84 (53).

*2,3-Dimethyl-2*H,5H-*pyrano[3,2-c][1]benzopyran-5-one* (**7d**). M.p. 65°. UV (EtOH): 340, 250. IR (KBr): 1710, 1620, 1410, 1275, 1200, 1070, 760. ^{1}H-NMR (270 MHz, $CDCl_3$): 7.76 (*d*, *J* = 7.9, 1 H); 7.50 (*t*, *J* = 7.8, 1 H); 7.31–7.24 (overlapped signals, 2 H); 6.33 (*s*, 1 H); 5.11 (*q*, *J* = 6.7, 1 H); 1.86 (*s*, 3 H); 1.48 (*d*, *J* = 6.7, 3 H). EI-MS: 228 (63, M^+, $C_{14}H_{12}O_3^+$), 213 (100), 121 (28), 92 (25), 77 (18).

*2-(2-Methylpropyl)-3-phenyl-2*H,5H-*pyrano[3,2-c][1]benzopyran-5-one* (**7e**). M.p. 97°. UV: 340, 255. IR (KBr): 3060, 2960, 2910, 1715, 1635, 1565, 1415, 1060, 750, 740, 690. ^{1}H-NMR (270 MHz, $CDCl_3$): 8.08 (*d*, *J* = 7.6, 1 H); 7.80 (*t*, *J* = 7.1, 1 H); 7.76–7.51 (overlapped signals, 7 H); 6.05 (*dd*, *J* = 10.3, 2.1, 1 H); 2.34–2.20 (overlapped signals, 2 H); 1.60 (*m*, 1 H); 1.34 (*d*, *J* = 6.7, 3 H); 1.16 (*d*, *J* = 6.7, 3 H). EI-MS: 332 (28, M^+, $C_{22}H_{20}O_3^+$), 275 (100), 121 (18), 114 (18), 105 (15).

*2,2-Dimethyl-2*H,5H-*pyrano[3,2-c][1]benzopyran-5-one* (**7f**). M.p. 92–93°. UV (EtOH): 340, 246. IR (KBr): 1715, 1650, 1610, 1570, 1420, 1360, 1120, 1040, 1000, 760, 730. ^{1}H-NMR (270 MHz, $CDCl_3$): 7.80 (*d*, *J* = 7.9, 1 H); 7.53 (*t*, *J* = 7.6, 1 H); 7.29–7.26 (overlapped signals, 2 H); 6.52 (*d*, *J* = 10.1, 1 H); 5.52 (*d*, *J* = 10.1, 1 H); 1.54 (*s*, 6 H). EI-MS: 228 (39, *M*, $C_{14}H_{12}O_3^+$), 213 (100), 121 (28), 107 (8), 92 (13), 79 (10).

*2-Methyl-2-(4-methylpent-3-enyl)-2*H,*5*H-*pyrano[3,2-c][1]benzopyran-5-one* (**7g**). Colourless oil. UV (EtOH): 3344, 245. IR (film): 2960, 2920, 2850, 1720, 1645, 1610, 1570, 1495, 1415, 1365, 1115, 1040. ^{1}H-NMR (270 MHz, $CDCl_3$): 7.78 (*d*, *J* = 7.9, 1 H); 7.51 (*t*, *J* = 7.6, 1 H); 7.30–7.24 (overlapped signals, 2 H); 6.57 (*d*, *J* = 10.1, 1 H); 5.46 (*d*, *J* = 10.1, 1 H); 5.08 (br. *t*, *J* = 6.5, 1 H); 2.14–1.67 (overlapped signals, 4 H); 1.60 (br. *s*, 3 H); 1.54 (br. *s*, 3 H); 1.51 (*s*, 3 H). ^{13}C-NMR (65.4 MHz, (D_6)DMSO): 83.03 (*s*, C(2)); 125.96 (*d*, C(3)); 116.22 (*d*, C(4)); 99.22 (*s*, C(4a)); 159.44 (*s*, C(5)); 152.56 (*s*, C(6a)); 116.36 (*d*, C(7)); 132.38 (*d*, C(8)); 124.15 (*d*, C(9)); 122.26 (*d*, C(10)); 114.21 (*s*, C(10a)); 158.14 (*s*, C(10b)); 26.70 (*q*, *C*H$_3$–C(2)); homoprenyl residue: 40.87 (*t*), 22.07 (*t*), 123.64 (*d*), 130.98 (*s*), 17.21 (*q*), 25.12 (*q*). EI-MS: 296 (30, M^+, $C_{19}H_{20}O_3^+$), 281 (10), 253 (15), 213 (100), 121 (70), 107 (30), 69 (95).

*9,10-Dihydro-6*H,*8*H,*11a*H-*pyrano[3',2':5,6]pyrano[3,2-c][1]benzopyran-6-one* (**7h**). M.p. 142°. UV (EtOH): 346, 242. IR (KBr): 1725, 1620, 1420, 1335, 1190, 1040, 1010, 950, 755. ^{1}H-NMR (270 MHz, $CDCl_3$): 7.86 (*d*, *J* = 7.9, 1 H); 7.51 (*t*, *J* = 8.5, 1 H); 7.32–7.25 (overlapped signals, 2 H); 6.53 (*s*, 1 H); 6.15 (*s*, 1 H); 4.17 (br. *s*, 1 H); 3.93 (br. *s*, 1 H); 2.61 (br. *s*, 1 H); 2.43 (br. *s*, 1 H); 1.87 (br. *s*, 2 H). EI-MS: 256 (100, $M^+C_{15}H_{12}O_4^+$), 228 (52), 214 (12), 199 (18), 121 (48).

*3-(3-Hydroxypropyl)-2-methoxy-2*H,*5*H-*pyrano[3,2-c][1]benzopyran-5-one* (**15**). M.p. 139°. UV (EtOH): 343, 246. IR (KBr): 3460, 1690, 1660, 1610, 1580, 1415, 1085, 1070, 930, 760. ^{1}H-NMR (270 MHz, $CDCl_3$): 7.90 (br. *d*, *J* = 8.1, 1 H); 7.56 (br. *t*, *J* = 7.3, 1 H); 7.38–7.28 (overlapped signals, 2 H); 6.73 (br. *s*, 1 H); 5.79 (br. *s*, 1 H); 3.76 (br. *t*, *J* = 7.2, 2 H); 3.58 (*s*, 3 H); 2.43 (*t*, *J* = 7.3, 2 H); 1.90 (*m*, 2 H). ^{13}C-NMR (67.5 MHz, (D_6)DMSO): 100.22 (*d*, C(2)); 131.61 (*s*, C(3)); 114.21 (*d*, C(4)); 101.38 (*s*, C(4a)); 159.59 (*s*, C(5)); 152.04 (*s*, C(6)); 116.49 (*d*, C(7)); 132.26 (*d*, C(8)); 124.57 (*d*, C(9)); 122.10 (*d*, C(10)); 114.50 (*s*, C(10a)); 154.90 (*s*, C(10b)); 54.96 (*q*, *C*H$_3$O); 3-hydroxypropyl residue: 29.49 (*t*), 30.20 (*t*), 60.02 (*t*). EI-MS: 288 (15, M^+, $C_{16}H_{16}O_5^+$), 256 (100), 228 (38), 213 (29), 199 (18), 121 (26).

*9,11a-Dihydro-8,8,11a-trimethyl-6*H,*8*H-*[1]benzopyrano[4,3-b][1]benzopyran-6-one* (**14**). M.p. 122°. UV (EtOH): 345, 245. IR (KBr): 1725, 1640, 1605, 1570, 1500, 1390, 1370, 1050, 765. ^{1}H-NMR (270 MHz, $CDCl_3$): 7.79 (*d*, *J* = 7.4, 1 H); 7.51 (*t*, *J* = 7.8, 1 H); 7.32–7.24 (overlapped signals, 2 H); 6.50 (*s*, 1 H); 5.98 (*ddd*, *J* = 11.0, 5.5, 1.6, 1 H); 5.92 (*dd*, *J* = 11.0, 1.6, 1 H); 2.16 (*d*, *J* = 17.4, 1 H); 2.00 (*dd*, *J* = 17.4, 5.5, 1 H); 1.51 (*s*, 3 H); 1.31 (*s*, 3 H); 1.19 (*s*, 3 H). EI-MS: 294 (45, M^+, $C_{19}H_{18}O_3^+$), 279 (100), 149 (22), 131 (42), 115 (20).

*2-Phenyl-2*H,*5*H-*pyrano[3,2-c][1]benzopyran-5-one* (**7i**). Orange solid. M.p. 180° ([5]: 183–185°). UV (EtOH): 380, 310, 295, 250, 240. IR (KBr): 1730, 1660, 1610, 1595, 1550, 1460, 1365, 1320, 1100, 760. ^{1}H-NMR (270 MHz, $CDCl_3$): 7.74–7.20 (overlapped signals, 9 H); 6.97 (*dd*, *J* = 10.0, 1.5, 1 H); 6.18 (*dd*, *J* = 3.3, 1.5, 1 H); 5.74 (*dd*, *J* = 10.0, 3.3, 1 H). EI-MS: 276 (100, M^+, $C_{18}H_{12}O_3^+$), 199 (28), 187 (15), 156 (20), 128 (25), 121 (25).

The minor tautomeric *3-(3-phenylprop-2-enylidene)-2*H-*1-benzopyran-2,4(3*H)*-dione* (**16c**) had typical ^{1}H-NMR signals ($CDCl_3$) at 8.88 (*dd*, *J* = 15.14, 11.7) and 8.50 (overlapped signals, 2 H), and a diagnostic ^{13}C-NMR peak at 182.41 (C(4)=O). Ratio **16c**/**7i** 1:1.9 by integration ($CDCl_3$) at 8.88 (*dd*) and 6.18 (*dd*).

*(*E,E*)-3-[3-(4-Methoxyphenyl)-prop-2-enylidene]-2*H-*1-benzopyran-2,4(3*H)*-dione* (**16a**). Red powder. M.p. 156°. UV (EtOH): 360, 330, 268. IR (KBr): 1725, 1650, 1615, 1590, 1565, 1530, 1465, 1370, 1310, 1260, 1170. ^{1}H-NMR (270 MHz, (D_6)DMSO): 8.47 (*m*, 2 H); 8.13 (*dd*, *J* = 8.6, 1.8, 1 H); 7.75 (*d*, *J* = 8.8, 2 H); 7.60–7.24 (overlapped signals, 4 H); 6.96 (*d*, *J* = 8.8, 2 H); 3.90 (*s*, 3 H). EI-MS: 306 (100, M^+, $C_{19}H_{14}O_4^+$), 291 (32), 186 (42), 185 (41), 158 (34), 121 (42), 115 (59).

*(*E,E*)-3-{3-[4-(Dimethylamino)phenyl]prop-2-enylidene}-2*H-*1-benzopyran-2,4(3*H)*-dione* (**16b**). Blue powder. M.p. 190° (dec.). UV/VIS (EtOH): 585, 390, 280. IR (KBr): 1720, 1645, 1615, 1550, 1375, 1325, 1225, 1190, 1100, 810, 755. ^{1}H-NMR (270 MHz, $CDCl_3$): 8.48 (*d*, *J* = 12.6, 1 H); 8.42 (*m*, 1 H); 8.50–8.40 (overlapped signals, 2 H); 8.11 (*d*, *J* = 7.8, 1 H); 7.66 (*d*, *J* = 9.0, 2 H); 7.59–7.55 (overlapped, 2 H); 7.24 (*m*, 1 H); 6.71 (*d*, *J* = 9.0, 2 H); 3.14 (*s*, 6 H). ^{13}C-NMR (67.4 MHz, $CDCl_3$): 161.46 (*s*, C(2)); 126.87 (*s*, C(3)); 180.10 (*s*, C(4)); 121.97 (*s*, C(4a)); 121.47 (*d*, C(5)); 124.03 (*d*, C(6)); 135.17 (*d*, C(7)); 117.25 (*d*, C(8)); 160.26 (*s*, C(8a)); 159.86 (*d*, C(1')); 127.21 (*d*, C(2')); 160.36 (*d*, C(3')); 4-(dimethylamino)phenyl: 124.16 (*s*), 133.07 (*d*), 153.63 (*s*), 40.14 (*q*). EI-MS: 319 (100, M^+, $C_{20}H_{17}NO_3^+$), 218 (20), 198 (85), 171 (80), 158 (40), 128 (30), 121 (25).

*(*E*)-3,3'-[3-(4-Nitrophenyl)prop-2-enylidene]bis[4-hydroxy-2*H-*1-benzopyran-2-one]* (**17a**). M.p. 187°. UV (EtOH): 315, 280. IR (KBr): 1680, 1600, 1510, 1340, 1120, 1040, 865. ^{1}H-NMR (270 MHz, (D_6)DMSO): 8.12 (*d*, *J* = 7.6, 2 H); 7.93 (*d*, *J* = 8.0, 2 H); 7.62 (*d*, *J* = 7.6, 2 H); 7.57 (*t*, *J* = 7.4, 2 H); 7.34–7.28 (overlapped signals, 4 H); 7.04 (*dd*, *J* = 16.3, 5.3, 1 H); 6.51 (*d*, *J* = 16.3, 1 H); 5.79 (*d*, *J* = 5.3, 1 H). CI-MS (isobutane): no M^+ at 483 ($C_{27}H_{17}NO_8^+$), 322 (100).

Methylation with ethereal diazomethane afforded a *ca.* 8:1 mixture of the 4,4-di-*O*-Me and 2′,4-di-*O*-Me derivative. The 4,4′-di-*O*-Me derivative was purified by CC (hexane/AcOEt 7:3). IR (KBr): 1720, 1610, 1570, 1510, 1340, 1100, 960, 760. ^{1}H-NMR (270 MHz, $CDCl_3$): 8.04 (*d*, *J* = 7.4, 2 H); 7.61 (*d*, *J* = 7.9, 2 H); 7.49 (*d*, *J* = 7.4, 2 H); 7.40 (*t*, *J* = 7.3, 2 H); 7.27–7.19 (overlapped, 5 H); 6.57 (*d*, *J* = 15.9, 1 H); 5.35 (*d*, *J* = 8.9, 1 H); 3.97 (*s*, 6 H).

(E)-3,3′-(3-Phenylprop-2-enylidene)bis[4-hydroxy-2H-1-benzopyran-2-one] (**17b**). M.p. 220–224°. UV (EtOH): 305, 280, 250. IR (KBr): 3450, 1670, 1625, 1610, 1570, 1360, 1310, 1110, 1100, 770. ^{1}H-NMR (270 MHz, (D_6)DMSO): 8.80 (br. *s*, exchangeable, 2 H); 7.97 (*d*, *J* = 7.8, 2 H); 7.58 (*t*, *J* = 7.9, 2 H); 7.36–7.16 (overlapped signals, 9 H); 6.76 (*dd*, *J* = 15.9, 6.2, 1 H); 6.44 (*d*, *J* = 15.9, 1 H); 5.84 (*d*, *J* = 9.2, 1 H). ^{13}C-NMR (67.4 MHz, (D_6)DMSO): 163.74 (*s*, C(2)); 104.96 (*s*, C(3)); 164.48 (*s*, C(4)); 117.17 (*s*, C(4a)); 121.54 (*d*, C(5)); 124.59 (*d*, C(6)); 132.17 (*d*, C(7)); 116.16 (*d*, C(8)); 152.08 (*s*, C(8a)); cinnamyl residue: 34.67 (*d*),129.00 (*d*), 126.12 (*d*), 137.16 (*s*), 127.16 (*d*), 126.12 (*d*), 128.55 (*d*). EI-MS: no M^+ at 438 ($C_{27}H_{18}O_6^+$), 276 (36), 135 (53), 120 (25), 92 (25), 88 (34), 70 (52), 61 (100).

Methylation with ethereal diazomethane afforded a *ca.* 4:1 mixture of Me derivatives that were separated by CC (hexane/AcOEt 7:3). *(E)-3,3′-(3-phenylprop-2-enylidene)bis[4-methoxy-2H-1-benzopyran-2-one]*: major Me derivative. M.p. 200°. UV (EtOH): 310, 276. IR (KBr): 1730, 1615, 1570, 1465, 1350, 1100, 970, 770. ^{1}H-NMR (270 MHz, $CDCl_3$): 7.72 (*d*, *J* = 7.9, 2 H); 7.48 (*t*, *J* = 7.6, 2 H); 7.35–7.22 (overlapped signals, 9 H); 7.12 (*dd*, *J* = 15.9, 9.2, 1 H); 6.61 (*d*, *J* = 15.9, 1 H); 5.39 (*d*, *J* = 9.2, 1 H); 4.06 (*s*, 6 H). EI-MS: 466 (93, M^+, $C_{29}H_{22}O_6^+$), 434 (100), 419 (23), 375 (48), 277 (44), 149 (48), 121 (23).

(E)-4-Methoxy-3-[1-(2-methoxy-4-oxo-4H-1-benzopyran-3-yl)-3-phenylprop-2-enyl]-2H-1-benzopyran-2-one: minor Me derivative. M.p. 187°. UV (EtOH): 328, 290, 258. IR (KBr): 1710, 1625, 1565, 1460, 1380, 1355, 1150, 760. ^{1}H-NMR (270 MHz, $CDCl_3$): 8.15 (*d*, *J* = 7.3, 1 H); 7.74 (*d*, *J* = 7.9, 1 H); 7.58 (*t*, *J* = 7.8, 1 H); 7.50–7.19 (overlapped signals, 10 H); 7.07 (*dd*, *J* = 15.9, 9.1, 1 H); 6.54 (*d*, *J* = 15.9, 1 H); 5.42 (*d*, *J* = 9.1, 1 H); 4.20 (*s*, 3 H); 4.13 (*s*, 3 H). EI-MS: 466 (82, M^+, $C_{29}H_{22}O_6^+$), 451 (36), 434 (42), 375 (100), 331 (38), 277 (44), 121 (22).

(E,E)-3,3′-(5-Phenylpenta-2,4-dienylidene)bis[4-hydroxy-2H-1-benzopyran-2-one] (**17c**). M.p. 120° (dec.). Characterized as its 4,4′-di-*O*-Me derivative. M. p. 93°. UV (EtOH): 316, 288, 250. IR (KBr): 1730, 1615, 1570, 1460, 1350, 1100, 760. ^{1}H-NMR (270 MHz, $CDCl_3$): 7.71 (*d*, *J* = 7.9, 2 H); 7.50 (*t*, *J* = 7.8, 2 H); 7.41–7.21 (overlapped signals, 9 H); 6.89–6.38 (overlapped signals, 4 H); 5.26 (*d*, *J* = 8.4, 1 H); 4.60 (*s*, 6 H). CI-MS (isobutane): 493 (28, $[M + 1]^+$, $C_{31}H_{24}O_6^+$).

3,3′-(3-Methoxypropylidene)bis[4-hydroxy-2H-1-benzopyran-5-one] (**8**) *from 4-Hydroxycoumarin and Acrolein in MeOH.* To a stirred soln. of 4-hydroxycoumarin (3.46 g, 21.4 mmol, 1.2 mol-equiv.) in MeOH (35 ml), 160 mg of ethylenediammonium diacetate (0.89 mmol, 0.05 mol-equiv.) were added, followed by 1.19 ml (1.00 g, 17.8 mmol) of acrolein. After 4 h stirring at r.t., the mixture was filtered and the white precipitate washed with cold MeOH: 310 mg (4.4%) of **8**. M.p. 149° (dec.). UV (EtOH): 310, 279. IR (KBr: 1660, 1610, 1570, 1500, 1450, 1380, 1330, 1280, 1220, 1110, 1060, 1000, 760. ^{1}H-NMR (270 MHz, (D_6)DMSO): 7.98 (*d*, *J* = 7.4, 2 H); 7.53 (*t*, *J* = 7.6, 2 H); 7.35–7.25 (overlapped signals, 4 H); 4.76 (*t*, *J* = 8.0, 2 H); 3.36 (*t*, *J* = 5.8, 2 H); 3.24 (*s*, 3 H); 2.63 (*m*, 2 H). ^{13}C-NMR (67.4 MHz, (D_6)DMSO): 164.27 (*s*, C(2)); 105.25 (*s*, C(3)); 168.04 (*s*, C(4)); C(4a) not detected; 123.86 (*d*, C(5)); 124.46 (*d*, C(6)); 132.25 (*d*, C(7)); 116.24 (*d*, C(8)); 151.94 (*s*, C(8a)); 3-methoxypropylidene: 28.78 (*d*), 28.55 (*t*), 70.17 (*t*), 58.45 (*q*). EI-MS: 394 (3, M^+, $C_{22}H_{18}O_7^+$), 336 (8), 232 (6), 200 (40), 162 (80), 120 (100).

7-(2-Methoxyethyl)-6H,7H,8H-pyrano[3,2-c:5,6-c′]di[1]benzofuran-6,8-dione (**9**). A mixture of 500 mg of **8** and 10 ml of pyridine/Ac_2O 1:1 was stirred 24 h at r. t. and then worked up by the addition of ice and MeOH. After 10 min, CH_2Cl_2 was added and the org. phase washed with sat. $NaHCO_3$ soln., sat. $CuSO_4$ soln., and brine. The residue was chromatographed on a short column of silica gel (5 g, hexane/AcOEt 8:2); 406 mg (79%) of **9** as white powder. Crystallization from cyclohexane afforded long needles that were suitable for X-ray analysis [17]. M.p. 196°. UV (EtOH): 305, 260. IR (KBr): 1725, 1670, 1610, 1395, 1190, 1050, 890, 770. ^{1}H-NMR (270 MHz, $CDCl_3$): 8.00 (*d*, *J* = 7.6, 2 H); 7.64 (br. *t*, *J* = 6.9, 2 H); 7.46–7.40 (overlapped signals, 4 H); 4.26 (*t*, *J* = 4.9, 1 H); 3.44 (*t*, *J* = 5.9, 2 H); 3.06 (*s*, 3 H); 2.27 (*m*, 2 H). EI-MS: 376 (5, M^+, $C_{22}H_{16}O_6^+$), 344 (88), 318 (80), 317 (100), 189 (18), 176 (15), 92 (20), 63 (18).

6a,7,8,10a-Tetrahydro-6,6,9-trimethyl-6H,11H-[2]benzopyrano[4,3-c][1]benzopyran-11-one (**4**) *from Citral, 4-Hydroxycoumarin, and Pyridine*: A mixture of 4-hydroxycoumarin (944 mg, 5.8 mmol) and pyridine (0.943 ml, 922 mg, 11.6 mmol, 2 mol-equiv.) was heated to 140°. Then, 1 ml (888 mg, 5.8 mmol) of citral was added during 10 min. The mixture was heated at 140° for 7 h. After cooling to r.t., CH_2Cl_2 was added, and the mixture washed with HCl, H_2O, and sat. $NaHCO_3$ soln. After drying ($MgSO_4$), the org. phase was chromatographed (15 g of silica gel,

hexane/AcOEt 9:1) to give a mixture of several products. HPLC (hexane/AcOEt 8:2) showed the presence of a major peak from which crystalline colourless **4** was obtained in 18% yield ([3]: viscous oil). M.p. 120°. UV (EtOH): 308, 270. IR (KBr): 1720, 1620, 1520, 1280, 1190, 1030, 990. ^{1}H-NMR (270 MHz, $CDCl_3$): 7.77 (*d*, *J* = 7.2, 1 H); 7.45 (*t*, *J* = 6.8, 1 H); 7.28–7.20 (overlapped signals, 2 H); 6.35 (br. *s*, 1 H); 3.12 (br. *d*, *J* = 7.2, 1 H); 1.69 (*s*, 3 H); 1.57 (*s*, 3 H); 1.22 (*s*, 3 H).

Reaction of 4-Hydroxycoumarin and 3-Methylbut-2-enal in the Presence of Nucleophiles. A) *Trimethyl Phosphite as Nucleophile*: To a soln. of 486 mg (3.0 mmol) of 4-hydroxycoumarin in 10 ml of MeOH, 27 mg (0.15 mmol, 0.05 mol-equiv.) of ethylenediammonium diacetate were added, followed by 0.708 ml (6 mmol, 2 mol-equiv.) of $P(MeO)_3$ and 0.289 ml (3.0 mmol) of 3-methylbut-2-enal. After 24 h, the mixture was evaporated and the residue chromatographed on 25 g of silica gel. Elution with hexane/AcOEt 6:4 gave 400 mg (39.5%) of *dimethyl[1-(4-hydroxy-2-oxo-2*H*-1-benzopyran-3-yl)-3-methylbut-2-enyl]phosphonate* (**12**) as white powder. M.p. 127°. IR (KBr): 1690, 1620, 1570, 1345, 1200, 1025, 765. ^{1}H-NMR (270 MHz, $CDCl_3$): 11.97 (br. *s*, exchangeable, 1 H); 7.93 (*d*, *J* = 8.2, 1 H); 7.49 (*t*, *J* = 7.6, 1 H); 7.28–7.22 (overlapped signals, 2 H); 5.46 (br. *s*, 1 H); 4.81 (*dd*, *J* = 25.3, 10.4, 1 H); 3.81 (*d*, *J* = 10.7, 3 H); 3.70 (*d*, *J* = 11.0, 3 H); 1.77 (*d*, *J* = 3.4, 3 H); 1.73 (*d*, *J* = 4.6, 3 H). EI-MS: 338 (18, M^+, $C_{16}H_{19}O_6P^+$), 306 (36), 251 (44), 229 (100), 213 (72), 121 (58), 69 (65).

B) *Thiophenol as Nucleophile*: As described in *A*, but with 1.6 g of 4-hydroxycoumarin substituting thiophenol for $P(OMe)_3$. After 24 h, the mixture was evaporated and the residue chromatographed on silica gel (20 g, hexane/AcOEt 9:1): 108 mg (3%) of *4-hydroxy-3-[3-methyl-1-(phenylthio)but-2-enyl]-2*H*-1-benzopyran-5-one* (**11**). M.p. 162°. IR (KBr): 1685, 1625, 1575, 1495, 1410, 1190, 1120, 1030, 750, 700. ^{1}H-NMR (270 MHz, $CDCl_3$): 7.81 (br. *d*, *J* = 7.8, 1 H); 7.59–7.53 (overlapped signals, 3 H); 7.35–7.24 (overlapped signals, 5 H); 4.82 (*d* = 7.6, 1 H); 4.26 (*s*, exchangeable, 1 H); 3.41 (*d*, *J* = 7.6, 1 H); 1.73 (*s*, 3 H); 1.54 (*s*, 3 H). EI-MS: no M^+ at 338 ($C_{20}H_{18}O_3S$), 228 (48, $[M - PhSH]^+$), 213 (100), 164 (98), 121 (55), 83 (34).

Oxidation of 3-Cinnamyl-4-hydroxycoumarin (*= 4-Hydroxy-3-(3-phenylprop-2-enyl)-2*H*-1-benzopyran-2-one*): To a stirred soln. of 3-cinnamyl-4-hydroxycoumarin (835 mg, 3.0 mmol) in THF (15 ml), 750 mg (3.3 mmol, 1.1 mol-equiv.) of DDQ were added. After 24 h stirring at r.t. under N_2, the soln. was evaporated and chromatographed (20 g of silica gel, hexane/AcOEt 8:2) to give 600 mg (72%) of **7i**/**16c** as an orange powder, identical (m.p., ^{1}H-NMR, TLC, IR) with the minor compound obtained from the reaction of 4-hydroxycoumarin and cinnamaldehyde.

Reduction of **7i**/**16c**: To a soln. of 360 mg of **7i**/**16c** in 8 ml of EtOH, an excess $NaBH_4$ was added, causing the immediate disappearance of the orange colour. The excess $NaBH_4$ was distroyed with acetone, and sat. aq. NH_4Cl soln. was added. The mixture was extracted with CH_2Cl_2 and the org. phase washed with brine, dried ($MgSO_4$) and evaporated. The residue was filtered through a short pad of *Celite*®, giving 296 mg (79%) of *3-cinnamyl-4-hydroxycoumarin* as the only reaction product. M.p. 164–168°. IR (KBr): 1670, 1630, 1500, 1455, 1395, 1200, 1150, 970, 940, 760. ^{1}H-NMR (270 MHz, (D_6)DMSO): 7.97 (*d*, *J* = 7.8, 1 H); 7.62 (*t*, *J* = 7.1, 1 H); 7.40–7.16 (overlapped signals, 7 H); 6.45 (*d*, *J* = 15.9, 1 H); 6.32 (*dt*, *J* = 15.9, 5.6, 5.6, 1 H); 3.46 (*d*, *J* = 5.6, 2 H). EI-MS: 278 (70, M^+, $C_{18}H_{14}O_3^+$), 249 (8), 231 (18), 187 (100), 176 (28), 121 (25), 91 (50).

Reduction of **16a** *with NaBH*$_4$: To a stirred suspension of **16a** (200 mg) in MeOH, an excess $NaBH_4$ was added, resulting in the instantaneous disappearance of the red colour. The mixture was worked up by the addition of sat. NH_4Cl soln. and extraction with CH_2Cl_2. After drying ($MgSO_4$) and evaporation, the residue was crystallized from AcOEt/acetone: 120 mg (60%) of *(E)-4-hydroxy-3-[(4-methoxyphenyl)prop-2-enyl]-2*H*-1-benzopyran-2-one* as a white powder. M.p. 180°. UV (EtOH): 330, 265, 250. IR (KBr): 1670, 1630, 1510, 1395, 1240, 1180, 1150, 750. ^{1}H-NMR (270 MHz, (D_6)DMSO): 8.03 (*d*, *J* = 8,5, 1 H); 7.59 (*t*, *J* = 7.9, 1 H); 7.36–7.30 (overlapped signals, 2 H); 7.29 (*d*, *J* = 8.5, 2 H); 6.85 (*d*, *J* = 8.5, 2 H); 6.38 (*d*, *J* = 15.9, 1 H); 6.15 (*dt*, *J* = 15.9, 6.4, 1 H); 3.73 (*s*, 3 H); 3.43 (*d*, *J* = 6.4, 2 H). EI-MS: 308 (41, M^+, $C_{19}H_{16}O_4^+$), 187 (27), 147 (25), 134 (87), 121 (55), 81 (47), 69 (100).

Catalytic Hydrogenation of **7f**. To a soln. of **7f** in 20 ml of EtOH, 5% Pd/C (50 mg) was added. After three evacuation cycles, the suspension was stirred under H_2 for 20 min and then filtered on *Celite*®. Removal of the solvent gave 498 mg (99%) of *3,4-dihydro-2,2-dimethyl-2*H*,5*H*-pyrano[3,2-c][1]benzopyran-5-one* as a white powder. M.p. 109–110°. IR (KBr): 1700, 1630, 1610, 1580, 1490, 1400, 1120, 1060, 760. ^{1}H-NMR (270 MHz, $CDCl_3$): 7.77 (*d*, *J* = 6.4, 1 H); 7.45 (*t*, *J* = 7.0, 1 H); 7.30–7.21 (overlapped signals, 2 H); 2.58 (*t*, *J* = 6.7, 2 H); 1.87 (*t*, *J* = 6.7, 2 H); 1.43 (*s*, 6 H).

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