New Approach for the Construction of the Coumarin Frame and Application in the Total Synthesis of Natural Products

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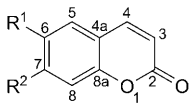
A new synthetic approach is described for building the coumarin scaffold through the *Lewis* acid-promoted cyclization of novel aryl 3-(dimethylamino)prop-2-enoates **2a**–**2f**. The latter precursors were prepared *via* aminomethylenation of the corresponding aryl acetates **4a**–**4f** with the *Bredereck* reagent. This approach was used for the synthesis of biologically active natural compounds **1a**–**1f**, through a three-step procedure starting from the corresponding phenols.

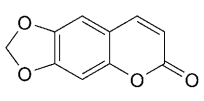
1. Introduction. – Coumarins (=2*H*-1-benzopyran-2-ones) are some of the most abundant metabolites found in extracts of many plant families, such as *Orchidaceae*, *Rutaceae*, *Euphorbiaceae*, and *Asteraceae*, among others, and occur in several parts of the plant [1]. The biogenetic route of coumarins follows the shikimate biosynthesis [2]. They have attracted widespread interest in view of their biological activity and potential as pharmacological agents [3], since they have exhibited inhibitory properties in platelet aggregation [4], as well as antibacterial action [5], and antifungal [6], antitumor [7], and antiviral activities [8]. Accordingly, diverse synthetic strategies have been reported to build their benzo-heterocyclic scaffold [9]. Among them, *Pechmann* reaction is a common and useful method, starting from phenols and β-dicarbonyl compounds, or the latter can be replaced by a propiolate or a 5-alkylidene *Meldrum*'s acid [10]. Both methods involve a C(4)–C(4a) bond-formation through the cyclization step. Moreover, the coupling reactions, catalyzed by transition-metal complexes, the *Wittig* reaction, and the ring-closing metathesis, among others, have resulted in very efficient strategies to prepare functionalized coumarins [11].

Recently, we designed a new method for the preparation of benzofurans [12], which was successfully extended to the synthesis of indoles [13]. This method was based on the formation of the heterocycle by a *Lewis* acid-promoted cyclization of the properly functionalized enaminones. With the aim of evaluating the versatility of this strategy in the construction of the benzo-six-membered heterocyclic framework, we investigated the preparation of coumarins, and their application in the total synthesis of naturally occuring metabolites. Among these targets, we chose the biologically active coumarin

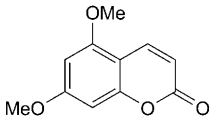
scopoletin (**1a**), which has been isolated from different plants and fruits, such as the leaves and root of *Nicotiana tabacum* [14] and *Sapium sebiferum* [15]. The latter is called *Wu-Jiu* and used in the Chinese traditional medicine for the treatment of squithosomiasis, or as a diuretic or cathartic [16]. Compound **1a** is also isolated from *Morinda citrifolia* [17], whose fruit is commonly known as *Noni*, which exhibits a wide spectrum of folk medicine treatments, such as for arthritis, diabetes, hypertension, menstrual disorders, AIDS, cancer, gastric ulcers, atherosclerosis, among others [18]. Compound **1a** exhibits anticonvulsant [19] and hypotensive [20] activities, and it has also been isolated from Mexican tarragon (*Tagetes lucida* Cv.), along with coumarins such as *isoscopoletin* (**1b**), *scoparone* (**1c**), and *herniarin* (**1d**), which showed antibacterial and fungicide activities [6][21]. Coumarins **1a**–**1c** were also extracted from many plants [22], or from the fruit of *Solanum dasyphyllum* [23], exhibiting anticonvulsant action in a murine model [24]. *Ayapin* (**1e**) and *citropten* (**1f**) are two coumarins isolated from diverse natural sources, with potential antileukemia activity [25].



	R^1	R^2
1a	MeO	OH
1b	OH	MeO
1c	MeO	MeO
1d	H	MeO



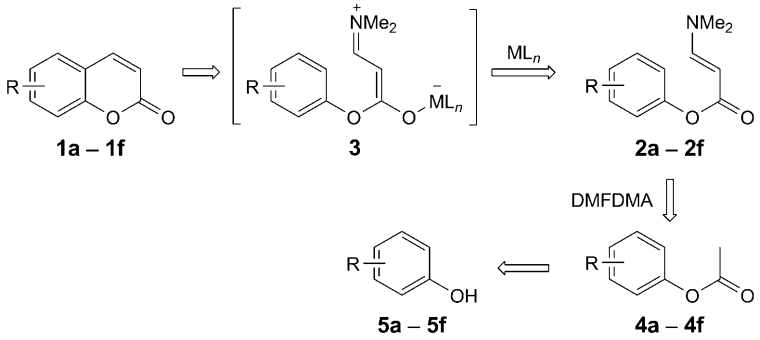
1e



1f

2. Results and Discussion. – 2.1. *Synthesis of Coumarins* **1a**–**1f**. 2.1.1. *Synthetic Design*. A retrosynthetic analysis of the preparation of coumarins **1a**–**1f** is depicted in *Scheme 1*. The last step of the route involves the cyclization of the key enaminone precursors **2a**–**2f**. Considering that the complex species **3** undergoes such a cyclization, in accordance with *Baldwin*'s rules, this step would correspond to a favored 6-*exo-trig* ring closure [26]. Actually, an additional challenge in this strategy is the formation of enaminones **2**, since the Ac group in their precursors, **4a**–**4f**, is probably not stable

Scheme 1. *Proposed Synthetic Route*



enough under the reaction conditions of the condensation with dimethylformamide dimethyl acetal (DMFDMA) [12][13]. Finally, acetates **4a**–**4f** would be prepared from their properly functionalized phenols **5a**–**5f**.

2.1.2. *Preparation of Enaminones* **2a**–**2e**. Suitable phenolic substrates **5a** and **5b**, to provide coumarins **1a** and **1b**, were prepared by conversion of the Bn-protected aldehydes **7a** and **7b** in a three-step procedure in good yields (*Scheme 2*). The latter were obtained by benzylation of isovanilline (**6a**) and vanilline (**6b**), respectively, followed by *Baeyer–Villiger* rearrangement with *m*-chloroperbenzoic acid (MCPBA) to yield formates **8a** and **8b**, which were hydrolyzed with K_2CO_3 in MeOH to give the desired phenols **5a** and **5b**, respectively (*Table 1*). The latter were treated with Ac_2O under 4-(dimethylamino)pyridine (DMAP) catalysis (5.0 mol%) to provide the respective acetates **4a** and **4b** in high yields (> 95%). A similar reaction sequence was followed to obtain acetate **4c**, starting from the methyl ether of vanilline, **7c**, *via* intermediates **8c** and **5c** (*Scheme 2*).

Scheme 2. *Preparation of Enaminones* **2a**–**2e**

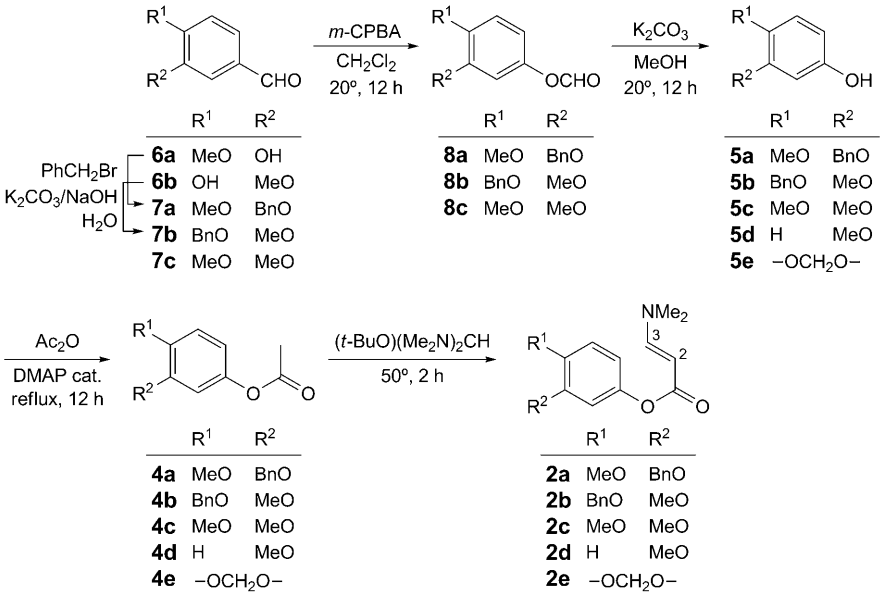
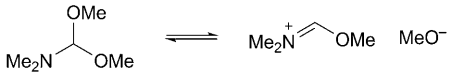


Table 1. *Reagents and Yields in the Preparation of Products* **8a**–**8c**, **5a**–**5c**, **4a**–**4f**, *and* **2a**–**2e**

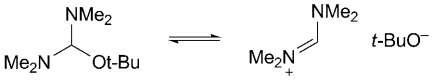
Sub-strate	Reagents	Product ([%])	Sub-strate	Reagents	Product ([%])	Sub-strate	Reagents	Product ([%])
7a	*m*-CPBA	**8a** (97)	**5a**	Ac_2O/DMAP	**4a** (99)	**4a**	(*t*-BuO)(Me_2N)$_2$CH	**2a** (75)
7b	*m*-CPBA	**8b** (98)	**5b**	Ac_2O/DMAP	**4b** (99)	**4b**	(*t*-BuO)(Me_2N)$_2$CH	**2b** (72)
7c	*m*-CPBA	**8c** (97)	**5c**	Ac_2O/DMAP	**4c** (98)	**4c**	(*t*-BuO)(Me_2N)$_2$CH	**2c** (78)
8a	K_2CO_3	**5a** (99)	**5d**	Ac_2O/DMAP	**4d** (98)	**4d**	(*t*-BuO)(Me_2N)$_2$CH	**2d** (76)
8b	K_2CO_3	**5b** (95)	**5e**	Ac_2O/DMAP	**4e** (97)	**4e**	(*t*-BuO)(Me_2N)$_2$CH	**2e** (74)
8c	K_2CO_3	**5c** (99)	**5f**	Ac_2O/DMAP	**4f** (95)			

Once acetates **4a**–**4c** were prepared, they were reacted with DMFDMA under the known reaction conditions (90° for 24 h) [12]. However, instead of the expected aryl 3-(dimethylamino)prop-2-enoates, **2a**–**2c**, phenols **5a**–**5c** were isolated as the main products. This reversal of reaction originated from the hydrolysis of the acetate group in the presence of the MeO^-, which is produced by decomposition of DMFDMA in the middle of the reaction, when the reactive species ((dimethylamino)(methoxy)methane carbocation) is generated (*Scheme 3*). To avoid this undesired reaction, we investigated the use of the *Bredereck* reagent {(*tert*-butoxy)[bis(dimethylamino)]methane} [27], since the sterically hindered *t*-BuO^- ion should be a less nucleophilic species (*Scheme 4*). Indeed, when acetates **4a**–**4c** were reacted with this reagent at 50° for 2 h under solvent-free conditions, aryl 3-(dimethylamino)propenoates **2a**–**2c** were obtained in fairly good yields (*Table 1*).

Scheme 3



Scheme 4



Compounds **2d** and **2e** were also prepared in similar yields by reacting acetate **4d** and **4e** with the *Bredereck* reagent (*Table 1*). These latter compounds were prepared in almost quantitative yield by acetylation of 3-methoxyphenol (**5d**) and sesamol (**5e**), respectively (*Scheme 2*).

In all cases, the propenoates **2a**–**2e** were obtained as a single stereoisomer, as shown by NMR analysis of the crude mixture. The (*E*)-configuration of the C=C bond was indicated by the large coupling constant ($J = 12.9$ Hz) between H–C(2) and H–C(3) and confirmed by the NOE experiments. Thus, an enhancement of both *doublet*s of the vinylic H-atoms was observed, when the signal attributed to the Me_2N group was irradiated. The preference for the configuration of the (*E*)-stereoisomer parallels with that observed in the preparation of analogous compounds [28]. This is probably due to the higher stability achieved by the planar π-conjugated acrylate system, when the bulky Me_2N group is located at the opposite side of the C=C bond. The (*E*)-configuration of **2c** was established by the X-ray crysrallography (*Fig.*). In the crystal, this acrylate system adopts a planar s-*cis* conformation about the C(1)–O(6) bond, keeping the group distant from the PhO enamine moiety and in a non-planar conformation with respect to the C=O group.

2.1.3. *Preparation of Coumarins* **1a**–**1e**. Submitting aryl 3-(dimethylamino)propenoates **2a**–**2e** to *Lewis*-acid catalysis to carry out the cyclization to the corresponding coumarins **1a**–**1e** was a more difficult process than that leading to the benzo-fused five-membered heterocycles, *i.e.*, benzofurans and indoles (*Scheme 5*). The formation of a larger size heterocycle must have a more disfavorable entropic balance of the reaction, retarding the conversion.

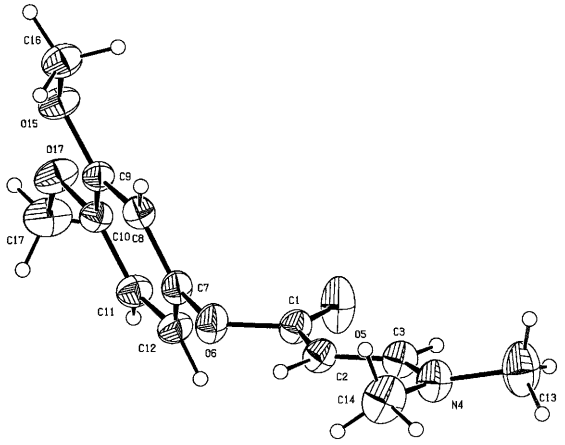
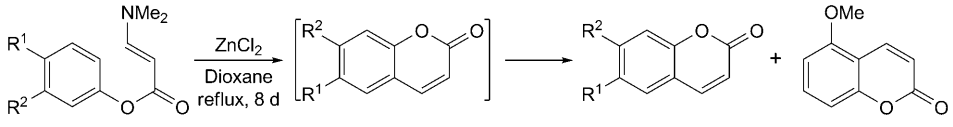


Figure. *X-Ray structure of* **2c** (ellipsoids with 30% probability level)

Scheme 5. *Preparation of Coumarins* **1a** – **1e**



	R^1	R^2
2a	MeO	BnO
2b	BnO	MeO
2c	MeO	MeO
2d	H	MeO
2e	$-OCH_2O-$	

	R^1	R^2
9a	MeO	BnO
9b	BnO	MeO

	R^1	R^2
1a	MeO	OH
1b	OH	MeO
1c	MeO	MeO
1d	H	MeO
1e	$-OCH_2O-$	

1g

Although many *Lewis* acids such as CuCl, $TiCl_4$, $BF_3 \cdot Et_2O$, $AlCl_3$, and $ZnCl_2$ were tested, only the latter was able to catalyze the desired cyclization. The reaction conditions had to be largely improved to enhance the yields (*Table 2*). For instance, a variety of solvents (CH_2Cl_2, $Cl_2CHCHCl_2$, toluene, dioxane, DMF, and MeCN), different temperatures, and reaction times, were tested, establishing the optimal and reproducible conditions as follows: a stirring mixture of the enaminone **2** and activated

Table 2. *Reagents and Yields in the Preparation of Coumarins* **1a** – **1g**

Entry	Substrate	Reagents	Product ([%])
1	**2a**	$ZnCl_2$	**1a** (71)
2	**2b**	$ZnCl_2$	**1b** (60)
3	**2c**	$ZnCl_2$	**1c** (44)
4	**2d**	$ZnCl_2$	**1d**/**1g** (9 : 1) (35)
5	**2e**	$ZnCl_2$	**1e** (43)
6	**4f**	*i*) (*t*-BuO)$(Me_2N)_2CH$ *ii*) $ZnCl_2$	**1f** (35)

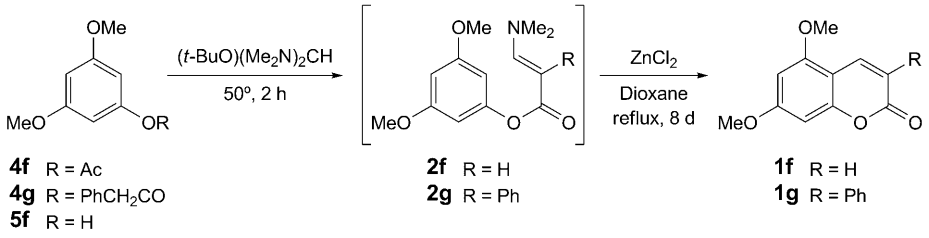
$ZnCl_2$ (3.0 mol-equiv.) in dry dioxane was heated to 100° for 8 days. It is worth noting that, at the workup stage, the acid treatement (8% aq. soln. of HCl) of the residue was necessary to obtain the best yields [11c][29]. The crude was recrystallized from MeOH or purified by column chromatography to give the corresponding coumarins **1**.

Interestingly, under these conditions, aryl 3-(dimethylamino)prop-2-enoates **2a**–**2b** were directly converted into the natural coumarins **1a** and **1b** through a one-pot two-step procedure, since the Bn-protected coumarin derivatives **9a** and **9b** were not observed, and the yields were the best in the whole series (*Table 2*).

Unlike coumarins **1a**–**1c** and **1e**, which were obtained as single regioisomers, the cyclization of **2d** led to the formation of the two possible regioisomers **1d**/**1g** in a 9:1 ratio (*Table 2*). This is in contrast with the highly regioselective cyclization for the analoguous 3-methoxyphenyl enaminones to give the corresponding benzofuran and indole [12][13]. It is likely that the drastic and long reaction time to give coumarins decreases such selectivity, mainly when the aryl ring is substituted with only one activating group.

2.2. *Synthesis of Coumarins* **1f** *and* **1g**. In the case of the synthesis of citroptene (**1f**), we found that the aryl 3-(dimethylamino)prop-2-enoate **2f** was very unstable upon isolation and purification of the crude mixture after the reaction between acetate **4f** and the *Bredereck* reagent. Therefore, a better option was to carry out the transformation without purification of **2f** (*Scheme 6*). A mixture of **4f**, which was prepared by acetylation of **5f** in the presence of Ac_2O and DMAP, the *Bredereck* reagent in dry dioxane, and the *Lewis* acid, was heated to reflux for 8 days, to give **1f** in 35% yield as a pale yellow powder.

Scheme 6. *Preparation of Coumarins* **1f** *and* **1g**



4f R = Ac
4g R = $PhCH_2CO$
5f R = H

2f R = H
2g R = Ph

1f R = H
1g R = Ph

We also assessed the efficacy of this approach in the preparation of 3-substituted coumarins. For this purpose, 5,7-dimethoxy-3-phenylcoumarin (**1g**) was prepared following a similar synthetic route as shown for citroptene (**1f**; *Scheme 6*). Thus, phenol **5f** was treated with 2-phenylacetic acid in the presence of dicyclohexylcarbodiimide (DCC) to afford **4g** in 80% yield. The latter was reacted with the *Bredereck* reagent under analogous conditions as **4f**, to obtain enaminone **2g**, which was used without purification as the substrate to carry out the cyclization in the presence of the *Lewis* acid to furnish coumarin **1g** in low yield (20%). All efforts to enhance the yield by purification of the enaminone **2g** or by modifying the reaction conditions or the catalyst were unsuccessful.

3. Conclusions. – We have described a new synthesis of naturally occurring coumarins **1a**–**1e** in three steps, starting from the corresponding phenols, in moderate-to-good overall yields. The approach included an intramolecular cyclization of enaminones **2a**–**2e** as the final key step. For most of the cases, this reaction was highly regioselective providing the desired heterocycles. Enaminones **2a**–**2e** were successfully prepared by using the *Bredereck* reagent, avoiding hydrolysis of the acetate precursors **4a**–**4e**. This pathway was also efficient for the preparation of citroptene (**1f**) and the 3-substituted coumarin **1g**, starting from the acetates **4f** and **4g**, respectively, in a one-pot two-step reaction.

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Experimental Part

General. All air-moisture-sensitive reactions were carried out under N_2 using oven-dried glassware. Dioxane and THF were freshly distilled on Na, and CH_2Cl_2 on CaH_2, prior to use. $ZnCl_2$ (5.0 g, 0.0366 mol) was activated in the presence of Zn (0.500 g, 0.076 mol) by refluxing in dry dioxane (40 ml) at 150° for 24 h; the Zn was removed by filtration, and the $ZnCl_2$ was precipitated at r.t., filtered, and dried in vacuum before being used [30]. All other reagents were used without further purification. Anal TLC: *E. Merck* silica gel *60* F_{254}-coated 0.25 plates were visualized by long- and short-wavelength UV lamps. Column chromatography (CC): silica gel (SiO_2; 230–400 mesh; *Natland International Co.*). M.p.: *Electrothermal* cap. melting-point apparatus, uncorrected. IR Spectra: *Perkin-Elmer* (*Spectrum 2000*) FT-IR spectrometer. ^{1}H- (300 or 500 MHz) and ^{13}C-NMR (75 or 125 MHz) spectra: *Varian Mercury-300* or *VNMR-500* instruments, with Me_4Si as internal standard. EI-MS (70 eV): *Thermo-Finnigan Polaris Q*. High-resolution mass spectra (HR-MS: in electron impact (EI; 70 eV) and FAB (*m*NBA) modes, on a *Jeol JSM-GCMateII* and *Jeol JMS-AX 505 HA* spectrometers, resp. X-Ray crystal-structure determination: *Oxford XcaliburS* diffractometer.

3-(Benzyloxy)-4-methoxybenzaldehyde (**7a**). At r.t. and under N_2, **6a** (0.803 g, 5.28 mmol) was added to a mixture of K_2CO_3 (0.728 g, 5.28 mmol) and NaOH (0.211 g, 5.28 mmol) in 50 ml of H_2O. The suspension was heated to reflux until the soln. became transparent, then BnBr (1.303 g, 7.62 mmol) was slowly added, and the mixture was stirred at the same temp. for 1 h. The org. layer was separated, and the aq. layer was washed with CH_2Cl_2 (2 × 45 ml). The combined org. layers were washed with brine until neutral, dried (Na_2SO_4), and the solvent was removed under vacuum. The residue was purified by CC (SiO_2 (60 g); hexane/AcOEt 9 :1): to give **7a** (1.25 g, 98%) as colorless crystals. R_f (hexane/AcOEt 9 :1) 0.27. M.p. 63–65° ([31]: 65–66°).

4-(Benzyloxy)-3-methoxybenzaldehyde (**7b**). As described for **7a**, **6b** (4.56 g, 0.03 mmol), K_2CO_3 (4.14 g, 0.03 mmol), and BnBr (7.36 g, 0.043 mol) gave **7b** (6.9 g, 95%). Pale yellow crystals. R_f (hexane/AcOEt 9 :1) 0.26. M.p. 62–64° ([12b][32]: 62–64°).

3,4-Dimethoxybenzaldehyde (**7c**). At r.t. and under N_2, a mixture of **6b** (2.0 g, 13.16 mmol) and K_2CO_3 (2.72 g, 19.7 mmol) in 20 ml of dry THF was stirred and heated to reflux for 1 h. At 40°, MeI (3.74 g, 26.3 mmol) was slowly added, and the mixture was heated to reflux overnight. The mixture was filtered, and the filtrate was washed with $NaHCO_3$ until neutral. The org. layer was dried (Na_2SO_4), and the solvent was removed under vacuum. The residue was purified by CC ((SiO_2 (20 g); hexane/AcOEt 95 :5) to give **7c** (1.77 g, 81%). White powder. R_f (hexane/AcOEt 9 :1) 0.16. M.p. 44–45° ([33][34]: 41–43°).

3-(Benzyloxy)-4-methoxyphenyl Formate (**8a**). A mixture of **7a** (0.50 g, 2.07 mmol) and *m*-CPBA (1.39 g, 6.20 mmol) in 25 ml of CH_2Cl_2 was stirred at 20° overnight. The mixture was filtered, and the

filtrate was washed with $NaHCO_3$ until neutral. The org. layer was dried (Na_2SO_4), and the solvent was removed under vacuum. The residue was purified by CC (SiO_2 (10 g); hexane/AcOEt 95:5): to give **8a** (0.518 g, 97%). White powder. R_f (hexane/AcOEt 9:1) 0.37. M.p. 68–70° ([12b]: 69–71°).

4-(Benzyloxy)-3-methoxyphenyl Formate (**8b**). As described for **8a**, a mixture of **7b** (1.0 g, 4.12 mmol) and *m*-CPBA (5.56 g, 12.36 mmol) in 35 ml of CH_2Cl_2 was stirred at 20° overnight to give **8b** (1.04 g, 98%). White solid. R_f (hexane/AcOEt, 9:1) 0.37. M.p. 70–72° ([8b]: 69–71°).

3,4-Dimethoxyphenyl Formate (**8c**) [35]. As described for **8a**, a mixture of **7c** (0.50 g, 3.01 mmol) and *m*-CPBA (1.39 g, 6.9 mmol) in 25 ml of CH_2Cl_2 was stirred at 20° overnight to give **8c** (0.53 g, 97%). White solid. R_f (hexane/AcOEt 9:1) 0.40. M.p. 48–50°.

Preparation of Phenols **5a**–**5c**. *3-(Benzyloxy)-4-methoxyphenol* (**5a**) [36]. A mixture of **8a** (0.50 g, 1.94 mmol) in MeOH (10 ml) and a 10% aq. soln. of K_2CO_3 (10 ml), at r.t. and under N_2, was stirred for 30 min. The solvent was removed under vacuum. The residue was extracted with CH_2Cl_2 (2 × 20 ml), and the soln. was washed with a 2% aq. soln. of HCl until neutral. The org. layer was washed with brine (2 × 25 ml), dried (Na_2SO_4), and the solvent was removed under vacuum. The residue was purified by CC (SiO_2 (10 g); hexane/AcOEt 9:1): to give **5a** (0.44 g, 99%). White powder. R_f (hexane/AcOEt 8:2) 0.20. M.p. 83–85°. IR (KBr): 3504, 1599, 1511, 1450, 1385, 1275, 1218, 1186, 1160, 1123, 1008, 967, 831, 758. ^{1}H-NMR (300 MHz, $CDCl_3$): 3.79 (*s*, MeO); 5.03 (*s*, PhCH_2O); 5.34 (br. *s*, OH); 6.32 (*dd*, *J* = 8.4, 3.0, H–C(6)); 6.44 (*d*, *J* = 3.0, H–C(2)); 6.72 (*d*, *J* = 8.4, H–C(5)); 7.23–7.40 (*m*, 5 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 56.8 (MeO); 70.8 (Ph*C*H_2O); 102.8 (C(2)); 106.5 (C(6)); 113.1 (C(5)); 127.2 (2 arom. C); 127.9 (arom. C); 128.6 (2 arom. C); 136.8 (arom. C); 143.8 (C(4)); 149.0 (C(3)), 149.8 (C(1)). HR-EI-MS: 230.0939 (M^+, $C_{14}H_{14}O_3^+$; calc. 230.0943).

4-(Benzyloxy)-3-methoxyphenol (**5b**). As described for **5a**, **8b** (0.50 g, 1.94 mmol) gave **5b** (0.42 g, 95%). White powder. R_f (hexane/AcOEt 8:2) 0.20. M.p. 85–86° ([12b]: 85–86°).

3,4-Dimethoxyphenol (**5c**). As described for **8a**, **8c** (0.50 g, 2.75 mmol) gave **5c** (0.42 g, 99%). White powder. R_f (hexane/AcOEt 8:2) 0.26. M.p. 80–82° ([37a]: 78–80°; [37b]: 80–82°).

Preparation of Acetates **4a**–**4e**. *3-(Benzyloxy)-4-methoxyphenyl Acetate* (**4a**). A mixture of **5a** (0.095 g, 0.413 mmol), Ac_2O (0.541 g, 5.30 mmol), and DMAP (0.005 g, 0.041 mmol), under N_2, was stirred at 70° for 12 h. The mixture was extracted with CH_2Cl_2 (2 × 10 ml), and the soln. was washed with a 10% aq. soln. of $NaHCO_3$ until neutral. The org. layer was washed with brine (2 × 20 ml), dried (Na_2SO_4), and the solvent was removed under vacuum. The residue was purified by CC (SiO_2, (10 g); hexane/AcOEt 85:15): **4a** (0.111 g, 99%). White powder. R_f (hexane/AcOEt 8:2) 0.25. M.p. 76–77°. IR (KBr): 1761, 1595, 1510, 1390, 1368, 1259, 1203, 1177, 1150, 1121, 1009. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.26 (*s*, $MeCO_2$); 3.87 (*s*, MeO); 5.11 (*s*, PhCH_2O); 6.62–6.68 (*m*, 2 H–C(2); H–C(6)); 6.86 (*d*, *J* = 8.7 H–C(5)); 7.28–7.48 (*m*, 5 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 21.0 (*Me*CO_2); 56.3 (MeO); 71.1 (Ph*C*H_2O); 108.0 (C(2)); 111.8 (C(5)); 113.5 (C(6)); 127.3 (2 arom. C); 127.9 (arom. C); 128.6 (2 arom. C); 136.6 (arom. C); 144.1 (C(1)); 147.5 (C(4)); 148.6 (C(3)); 169.8 (Me*C*O_2). EI-MS (70 eV): 272 (14, M^+), 230 (70), 91 (100), 65 (16).

4-(Benzyloxy)-3-methoxyphenyl Acetate (**4b**). As described for **4a**, a mixture of **5b** (0.95 g, 4.13 mmol), Ac_2O (5.41 g, 0.053 mol), and DMAP (0.051 g, 0.413 mmol) was stirred at 70° for 12 h to give **4b** (1.112 g, 99%). White powder. R_f (hexane/AcOEt 7:3) 0.40. M.p. 77–79°. IR (KBr): 1763, 1600, 1510, 1454, 1386, 1366, 1269, 1203, 1182, 1128, 998, 751. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.27 (*s*, $MeCO_2$); 3.86 (*s*, MeO); 5.13 (*s*, PhCH_2O); 6.56 (*dd*, *J* = 8.8, 3.0, H–C(6)); 6.65 (*d*, *J* = 3.0, H–C(2)); 6.85 (*d*, *J* = 8.8, H–C(5)), 7.26–7.45 (*m*, 5 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 20.9 (*Me*CO_2); 55.8 (MeO); 71.2 (Ph*C*H_2O); 105.9 (C(2)); 112.7 (C(5)); 113.9 (C(6)); 127.2 (2 arom. C); 127.7 (arom. C); 128.4 (2 arom. C); 136.8 (arom. C); 144.6 (C(1)); 145.8 (C(4)); 149.9 (C(3)); 169.7 (Me*C*O_2). EI-MS (70 eV): 272 (35, M^+), 230 (100), 139 (76), 92 (60), 65 (30). HR-EI-MS: 272.1046 (M^+, $C_{16}H_{16}O_4^+$; calc. 272.1049).

3,4-Dimethoxyphenyl Acetate (**4c**) [38]. As described for **4a**, a mixture of **5c** (0.90 g, 5.84 mmol), Ac_2O (7.15 g, 0.07 mol), and DMAP (0.072 g, 0.584 mmol) was stirred at 70° for 12 h to give **4c** (1.12 g, 98%). White powder. R_f (hexane/AcOEt 8:2) 0.30. M.p. 43–44°. IR (KBr): 2960, 2834, 1760, 1603, 1510, 1461, 1264, 1236, 1206, 1186, 1146, 1126, 1025, 955, 894, 766. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.29 (*s*, $MeCO_2$); 3.86 (*s*, MeO); 3.87 (*s*, MeO); 6.62–6.67 (*m*, 2 H–C(2), H–C(6)); 6.84 (*d*, *J* = 8.3, H–C(5)). ^{13}C-NMR (75 MHz, $CDCl_3$): 21.0 (*Me*CO_2); 55.9 (MeO); 56.1 (MeO); 105.6 (C(2)); 111.0 (C(5)); 112.7 (C(6)); 144.2 (C(1)); 146.7 (C(4)); 149.2 (C(3)); 169.9 (Me*C*O_2). EI-MS (70 eV): 197 (45, $[M+1]^+$), 196

(50, M^+), 154 (100), 139 (40), 111 (25), 93 (18), 65 (20). HR-EI-MS: 196.0739 (M^+, $C_{10}H_{12}O_4^+$; calc. 196.0736).

3-Methoxyphenyl Acetate (**4d**) [39]. As described for **4a**, a mixture of **5d** (1.5 g, 12.1 mmol), Ac_2O (14.80 g, 0.145 mol), and DMAP (0.149 g, 1.21 mmol) was stirred at 70° for 12 h to give **4d** (1.97 g, 98%). Pale yellow oil. R_f (hexane/AcOEt 7:3) 0.52. IR (film): 1764, 1607, 1592, 1489, 1370, 1285, 1264, 1209, 1137, 1041, 951, 777. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.27 (*s*, $MeCO_2$); 3.78 (*s*, MeO); 6.64 (*t*, $J = 2.1$, H–C(2)); 6.68 (*ddd*, $J = 8.1, 2.1, 1.2$, H–C(4) or H–C(6)); 6.77 (*ddd*, $J = 8.1, 2.1, 1.2$, H–C(6) or H–C(4)); 7.26 (*t*, $J = 8.1$, H–C(5)). ^{13}C-NMR (75 MHz, $CDCl_3$): 20.8 ($MeCO_2$); 55.1 (MeO); 107.4 (C(2)); 111.4 (C(5)); 113.6 (C(6)); 129.6 (C(4)); 151.5 (C(1)); 160.3 (C(3)); 169.1 (Me*C*O_2). EI-MS (70 eV): 167 (45, $[M+1]^+$), 166 (100, M^+), 125 (28), 124 (70), 95 (10).

1,3-Benzodioxol-5-yl Acetate (**4e**). As described for **4a**, a mixture of **5e** (0.51 g, 3.70 mmol), Ac_2O (4.53 g, 0.044 mol), and DMAP (0.046 g, 0.37 mmol) was stirred at 70° for 12 h to give **4e** (0.65 g, 97%). Colorless oil. R_f (hexane/AcOEt 9:1) 0.28. IR (film): 1761, 1614, 1503, 1484, 1444, 1370, 1248, 1212, 1171, 1120, 1037, 947, 895, 817. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.22 (*s*, $MeCO_2$); 5.92 (*s*, OCH_2O); 6.49 (*dd*, $J =$ 8.7, 2.4, H–C(6)); 6.59 (*d*, $J = 2.4$, H–C(4)); 6.74 (*d*, $J = 8.7$, H–C(7)). ^{13}C-NMR (75 MHz, $CDCl_3$): 20.6 (*Me*CO_2); 101.5 (C(2)); 103.5 (C(4)); 107.7 (C(7)); 113.7 (C(6)); 144.7 (C(5)); 145.1 (C(7a)); 147.7 (C(3a)); 169.5 (Me*C*O_2). EI-MS (70 eV): 180 (20, M^+), 139 (10), 138 (100), 137 (84), 79 (8).

3,5-Dimethoxyphenyl Acetate (**4f**) [40]. As described for **4a**, a mixture of **5f** (1.19 g, 12.4 mmol), Ac_2O (15.01 g, 0.147 mol), and DMAP (0.153 g, 1.24 mmol) was stirred at 70° for 12 h to give **4f** (2.30 g, 95%). Colorless oil. R_f 0.37 (hexane/AcOEt 9:1). IR (film): 1766, 1613, 1477, 1430, 1369, 1207, 1155, 1130, 1052, 890, 829. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.18 (*s*, $MeCO_2$); 3.67 (*s*, 2 MeO); 6.18 (*d*, $J = 2.1$, 2 H–C(2), H–C(6)); 6.25 (*t*, $J = 2.1$, H–C(4)). ^{13}C-NMR (75 MHz, $CDCl_3$): 21.0 (*Me*CO_2); 55.3 (MeO); 98.1 (C(4)); 100.1 (C(2), C(6)); 152.1 (C(1)); 161.0 (C(3), C(5)); 169.2 (Me*C*O_2). EI-MS (70 eV): 197 (50, $[M+1]^+$), 196 (100, M^+), 155 (8), 125 (20). HR-EI-MS: 196.0735 (M^+, $C_{10}H_{13}O_4^+$; calc. 196.0736).

3,5-Dimethoxyphenyl 2-Phenylacetate (**4g**). A mixture of **10** (0.44 g, 3.25 mmol) and DCC (0.742 g, 3.60 mmol) in dry AcOEt (10 ml), under N_2, was stirred at 20° for 10 min. Then, **5f** (0.50 g, 3.25 mmol) was added dropwise at the same temp., and the mixture was stirred overnight. The mixture was filtered, and the filtrate washed with brine (2×15 ml). The org. layer was dried (Na_2SO_4), and the solvent was removed under vacuum. The residue was purified by CC (SiO_2 (20 g); hexane/AcOEt 95:5): to give **4g** (0.706 g, 80%). Colorless oil. R_f (hexane/AcOEt 9:1) 0.21. IR (film): 1757, 1614, 1477, 1455, 1429, 1346, 1327, 1234, 1205, 1129, 1061, 989, 832, 727. ^{1}H-NMR (300 MHz, $CDCl_3$): 3.71 (*s*, 2 MeO); 3.82 (*s*, H–C(2)); 6.23 (*d*, $J = 2.4$, 2 H–C(2″), H–C(6″)); 6.31 (*t*, $J = 2.4$, H–C(4″)); 7.24–7.38 (*m*, 5 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 41.0 (C(2)); 55.1 (MeO); 97.9 (C(4″)); 99.8 (C(2″), C(6″)); 127.1 (C(4′)); 128.5 (C(3′)); 129.1 (C(2′)); 133.2 (C(1′)); 152.0 (C(1″)); 160.8 (C(3″), C(5″)); 169.6 (CO). HR-FAB-MS: 272.1046 (M^+, $C_{16}H_{16}O_4^+$; calc. 272.1049).

Preparation of Enaminones **2a**–**2e**. *3-(Benzyloxy)-4-methoxyphenyl (2*E*)-3-(Dimethylamino)prop-2-enoate* (**2a**). Under N_2, a mixture of **4a** (0.047 g, 0.173 mmol) and the *Bredereck* reagent (0.036 g, 0.207 mmol), in a threaded ACE glass pressure tube with a sealed *Teflon* screw cap, was heated to 50° for 1 h. The mixture was diluted with CH_2Cl_2 (5 ml), and 5 ml of cold H_2O were added. The org. layer was washed with brine (2×5 ml), dried (Na_2SO_4), and the solvent was removed under vacuum. The residue was purified by CC (SiO_2 (5 g); hexane/AcOEt 75:25) to give **2a** (0.042 g, 75%). White powder. R_f (hexane/AcOEt 6:4) 0.21. M.p. 121–122°. IR (KBr): 1698, 1638, 1509, 1347, 1264, 1213, 1187, 1151, 1123, 1009, 968. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.88 (br., Me_2N); 3.86 (*s*, MeO); 4.65 (*d*, $J = 12.9$, H–C(2)); 5.10 (*s*, Ph*C*H_2O); 6.67 (*dd*, $J = 8.6, 2.7$, H–C(6′)); 6.72 (*d*, $J = 2.7$, H–C(2′)); 6.86 (*d*, $J = 8.6$, H–C(5′)); 7.27–7.46 (*m*, 5 arom. H); 7.57 (*d*, $J = 12.9$, H–C(3)). ^{13}C-NMR (75 MHz, $CDCl_3$): 45.5 (Me_2N); 56.2 (MeO); 70.8 (Ph*C*H_2O); 82.9 (C(2)); 108.4 (C(2′)); 111.8 (C(5′)); 113.8 (C(6′)); 127.3 (2 arom. C); 127.7 (arom. C); 128.4 (2 arom. C); 136.7 (arom. C); 145.0 (C(1′)); 146.6 (C(4′)); 148.3 (C(3′)); 154.1 (C(3)); 168.2 (CO). EI-MS (70 eV): 327 (4, M^+), 279 (8), 207 (12), 167 (50), 149 (100). HR-EI-MS: 327.1478 (M^+, $C_{19}H_{21}NO_4^+$; calc. 327.1471).

*4-(Benzyloxy)-3-methoxyphenyl (2*E*)-3-(Dimethylamino)prop-2-enoate* (**2b**). As described for **2a**, a mixture of **4b** (0.052 g, 0.191 mmol) and the *Bredereck* reagent (0.040 g, 0.229 mmol) was heated to 50° for 1 h to give **2b** (0.045 g, 72%). White powder. R_f (hexane/AcOEt 6:4) 0.18. M.p. 114–116°. IR (KBr): 1697, 1639, 1616, 1509, 1346, 1264, 1213, 1188, 1124, 1091, 988, 969. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.95

(br., Me_2N); 3.86 (*s*, MeO); 4.67 (*d*, *J* = 12.9, H–C(2)); 5.12 (*s*, PhCH_2O); 6.57 (*dd*, *J* = 8.5, 2.4, H–C(6′)); 6.69 (*d*, *J* = 2.4, H–C(2′)); 6.84 (*d*, *J* = 8.5, H–C(5′)); 6.95–7.46 (*m*, 5 arom. H); 7.58 (*d*, *J* = 12.9, H–C(3)). ^{13}C-NMR (75 MHz, $CDCl_3$): 45.5 (Me_2N); 55.9 (MeO); 71.5 (Ph*C*H_2O); 83.0 (C(2)); 106.6 (C(2′)); 113.2 (C(6′)); 114.2 (C(5′)); 127.3 (2 arom. C); 127.7 (arom. C); 128.5 (2 arom. C); 137.2 (arom. C); 145.2 (C(4′)); 145.7 (C(1′)); 149.9 (C(3′)); 154.2 (C(3)); 168.2 (CO). EI-MS (70 eV): 327 (3, M^+), 143 (10), 98 (100), 92 (8). HR-EI-MS: 327.1471 (M^+, $C_{19}H_{21}NO_4^+$; calc. 327.1471).

*3,4-Dimethoxyphenyl (2*E*)-3-(Dimethylamino)prop-2-enoate* (**2c**). As described for **2a**, a mixture of **4c** (0.50 g, 2.55 mmol) and the *Bredereck* reagent (0.533 g, 3.06 mmol) was heated to 50° for 1 h to give **2c** (0.499 g, 78%). Pale yellow crystals (hexane/AcOEt 1:9). R_f (hexane/AcOEt 6:4) 0.12. M.p. 96–98°. IR (KBr): 1700, 1608, 1511, 1436, 1348, 1265, 1234, 1195, 1137, 1088, 1026, 984, 865, 786. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.88 (br., Me_2N); 3.86 (*s*, MeO); 3.87 (*s*, MeO); 4.68 (*d*, *J* = 12.9, H–C(2)); 6.63–6.70 (*m*, 2 H–C(2′), H–C(6′)); 6.84 (*d*, *J* = 8.4, H–C(5′)); 7.59 (*d*, *J* = 12.9, H–C(3)). ^{13}C-NMR (75 MHz, $CDCl_3$): 44.4 (Me_2N); 55.7 (MeO); 56.0 (MeO); 82.9 (C(2)); 106.1 (C(2′)); 111.0 (C(5′)); 113.1 (C(6′)); 145.1 (C(1′)); 146.0 (C(4′)); 149.0 (C(3′)); 154.1 (C(3)); 168.2 (CO). EI-MS (70 eV): 251 (5, M^+), 154 (10), 99 (14), 98 (100), 83 (20). HR-FAB-MS: 252.1234 ($[M+H]^+$, $C_{13}H_{18}NO_4^+$; calc. 252.1236).

*3-Methoxyphenyl (2*E*)-3-(Dimethylamino)prop-2-enoate* (**2d**). As described for **2a**, a mixture of **4d** (0.50 g, 3.01 mmol) and the *Bredereck* reagent (0.63 g, 3.61 mmol) was heated to 50° for 1 h to give **2d** (0.506 g, 76%). Pale red oil. R_f (hexane/AcOEt 6:4) 0.33. IR (film): 1705, 1615, 1489, 1436, 1347, 1225, 1136, 1090, 979. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.90 (br., Me_2N); 3.77 (*s*, MeO); 4.66 (*d*, *J* = 12.9, H–C(2)); 6.65–6.75 (*m*, 3 H–C(2′), H–C(4′), H–C(6′)); 7.24 (*t*, *J* = 8.1, H–C(5′); 7.58 (*d*, *J* = 12.9, H–C(3)). ^{13}C-NMR (75 MHz, $CDCl_3$): 36.6 (MeN); 44.4 (MeN); 55.1 (MeO); 82.7 (C(2)); 107.7 (C(2′)); 110.6 (C(4′) or C(6′)); 114.1 (C(6′) or C(4′)); 129.3 (C(5′)); 152.4 (C(1′)); 154.2 (C(3)); 160.1 (C(3′)); 167.8 (CO). EI-MS (70 eV): 222 (4, $[M+1]^+$), 124 (14), 99 (6), 98 (100), 70 (9), 55 (8). HR-EI-MS: 221.1050 (M^+, $C_{12}H_{15}NO_3^+$; calc. 221.1052).

*1,3-Benzodioxol-5-yl (2*E*)-3-(Dimethylamino)prop-2-enoate* (**2e**). As described for **2a**, a mixture of **4e** (0.50 g, 2.78 mmol) and the *Bredereck* reagent (0.58 g, 3.33 mmol) was heated to 50° for 1 h to give **2e** (0.483 g, 74%). White powder. R_f (hexane/AcOEt 7:3) 0.17. M.p. 112–113°. IR (KBr): 1705, 1613, 1473, 1434, 1349, 1225, 1204, 1153, 1131, 1091, 1052, 988. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.90 (br., Me_2N); 4.65 (*d*, *J* = 12.9, H–C(2)); 5.95 (*s*, OCH_2O); 6.53 (*dd*, *J* = 8.2, 2.1, H–C(6′)); 6.63 (*d*, *J* = 2.1, H–C(4′)); 6.75 (*d*, *J* = 8.2, H–C(7′)); 7.57 (*d*, *J* = 12.9, H–C(3)). ^{13}C-NMR (75 MHz, $CDCl_3$): 36.9 (MeN); 44.6 (MeN); 82.8 (C(2)); 101.3 (C(2′)); 104.3 (C(4′)); 107.7 (C(7′)); 114.2 (C(6′)); 144.5 (C(7a′)); 145.8 (C(5′)); 147.7 (C(3a′)); 154.2 (C(3)); 168.2 (CO). EI-MS (70 eV): 235 (4, $[M+1]^+$), 137 (4), 98 (100), 70 (10), 55 (8). HR-EI-MS: 235.0844 (M^+, $C_{12}H_{13}NO_4^+$; calc. 235.0845).

Preparation of Coumarins **1a**–**1g**. *7-Hydroxy-6-methoxy-2*H*-1-benzopyran-2-one* (= *Scopoletin*; **1a**). Under N_2, a mixture of **2a** (0.120 g, 0.37 mmol) and activated $ZnCl_2$ (0.151 g, 1.11 mmol) in dry dioxane (10 ml) was stirred at 100° for 8 days. The solvent was removed under vacuum, and an 8% aq. soln. of HCl (20 ml) was added. Then, it was extracted with CH_2Cl_2 (2 × 20 ml), and the org. layer was washed with brine (2 × 10 ml), dried (Na_2SO_4), and the solvent was removed under vacuum. The residue was purified by recrystallization from MeOH to give **1a** (0.05 g, 71%). Pale brown solid. R_f (hexane/AcOEt 1:1) 0.26. M.p. 200–202° ([41a]: 205–206°; [41b]: 201–202°). IR (KBr): 3341, 1703, 1608, 1562, 1510, 1436, 1290, 1139, 922. ^{1}H-NMR (500 MHz, $CDCl_3$/(D_6)DMSO 99:1): 3.92 (*s*, MeO), 6.21 (*d*, *J* = 9.5, H–C(3)); 6.86 (*s*, H–C(5)); 6.90 (*s*, H–C(8)); 7.62 (*d*, *J* = 9.5, H–C(4)); 8.80 (br. *s*, OH). ^{13}C-NMR (125 MHz, $CDCl_3$/(D_6)DMSO 99:1): 59.1 (MeO); 103.2 (C(8)); 108.0 (C(5)); 110.8 (C(4a)); 112.2 (C(3)); 143.5 (C(4)); 145.0 (C(6)); 149.9 (C(8a)); 150.7 (C(7)); 161.5 (C(2)). EI-MS (70 eV): 192 (4, M^+), 150 (6), 108 (100), 107 (74), 79 (28), 77 (34). HR-EI-MS: 192.0422 (M^+, $C_{10}H_8O_4^+$; calc. 192.0423).

*6-Hydroxy-7-methoxy-2*H*-1-benzopyran-2-one* (= *Isoscopoletin*; **1b**). As described for **1a**, a mixture of **2b** (0.12 g, 0.37 mmol) and activated $ZnCl_2$ (0.151 g, 1.11 mmol) was stirred at 100° for 8 d; then, the residue was purified by CC (SiO_2 (15 g); CH_2Cl_2/MeOH 99.5:0.5): to give **1b** (0.039 g, 60%). White powder. R_f (hexane/AcOEt 1:1) 0.26. M.p. 138–140° ([42]: 147°). IR (KBr): 3339, 1704, 1608, 1564, 1510, 1435, 1291, 1263, 1219, 1190, 1140, 1019, 922, 861. ^{1}H-NMR (500 MHz, $CDCl_3$): 3.96 (*s*, MeO); 6.15 (br. *s*, OH); 6.27 (*d*, *J* = 9.5, H–C(3)); 6.85 (*s*, H–C(5)); 6.92 (*s*, H–C(8)); 7.59 (*d*, *J* = 9.5, H–C(4)). ^{13}C-NMR (125 MHz, $CDCl_3$): 56.4 (MeO); 103.2 (C(8)); 107.5 (C(5)); 111.5 (C(4a)); 113.4 (C(3)); 143.3

(C(4)); 144.0 (C(7)); 149.7 (C(6)); 150.3 (C(8a)); 161.4 (C(2)). MS (70 eV): 192 (100, M^+), 177 (60), 164 (58), 149 (92), 121 (68), 79 (15), 69 (23). HR-EI-MS: 192.0425 (M^+, $C_{10}H_8O_4^+$; calc. 192.0423).

*6,7-Dimethoxy-2*H*-1-benzopyran-2-one* (= *Scoparone*; **1c**). As described for **1a**, a mixture of **2c** (0.20 g, 0.80 mmol) and activated $ZnCl_2$ (0.33 g, 2.43 mmol) was stirred at 100° for 8 d; then, the residue was purified by recrystallization (EtOH) to give **1c** (0.072 g, 44%). Pale brown powder. R_f (hexane/AcOEt 1:1) 0.34. M.p. 138–140° ([10 h]: 144–146°). IR (film): 1727, 1616, 1514, 1452, 1424, 1384, 1279, 1248, 1206, 1171, 1141, 1006. ^{1}H-NMR (500 MHz, $CDCl_3$): 3.92 (*s*, MeO); 3.95 (*s*, MeO); 6.28 (*d*, *J* = 9.5, H–C(3)); 6.84 (*s*, H–C(8)); 6.87 (*s*, H–C(5)); 7.63 (*d*, *J* = 9.5, H–C(4)). ^{13}C-NMR (125 MHz, $CDCl_3$): 56.3 (MeO); 56.4 (MeO); 99.9 (C(8)); 108.0 (C(5)); 111.4 (C(4a)); 113.5 (C(3)); 143.3 (C(4)); 146.3 (C(6)); 150.0 (C(8a)); 152.8 (C(7)); 161.4 (C(2)). EI-MS (70 eV): 206 (100, M^+), 191 (42), 178 (49), 163 (55), 135 (50), 107 (50), 79 (30), 77 (32). HR-EI-MS: 206.0577 (M^+, $C_{11}H_{10}O_4^+$; calc. 206.0579).

*7-Methoxy-2*H*-1-benzopyran-2-one* (= *Herniarin*; **1d**). *5-Methoxy-2*H*-1-benzopyran-2-one* (**1g**) [43]. As described for **1a**, a mixture of **2d** (0.10 g, 0.45 mmol) and activated $ZnCl_2$ (0.185 g, 1.36 mmol) was stirred at 100° for 8 d; then, the residue was purified by CC (SiO_2 (15 g); hexane/AcOEt 9:1): **1d**/**1g** 9:1 (0.028 g, 35%). Pale yellow powder.

Data of **1d**. R_f (hexane/AcOEt 1:1) 0.60. M.p. 110–112° ([11c]: 117–118°; [43]: 119–120°; [44]: 117–119°). IR (film): 1706, 1611, 1507, 1464, 1399, 1351, 1282, 1232, 1205, 1123, 1024, 980, 829. ^{1}H-NMR (500 MHz, $CDCl_3$): 3.88 (*s*, MeO); 6.25 (*d*, *J* = 9.5, H–C(3)); 6.81 (*d*, *J* = 2.7, H–C(8)); 6.84 (*dd*, *J* = 8.4, 2.7, H–C(6)); 7.38 (*d*, *J* = 8.4, H–C(5)); 7.65 (*d*, *J* = 9.5, H–C(4)); signals attributed to the minor isomer: 3.94 (*s*, MeO); 6.34 (*d*, *J* = 9.6, H–C(3)); 6.72 (br. *d*, *J* = 8.5, H–C(6)); 6.92 (br. *d*, *J* = 8.5, H–C(8)); 7.44 (*t*, *J* = 8.5, H–C(7)); 8.10 (*d*, *J* = 9.6, H–C(4)). ^{13}C-NMR (125 MHz, $CDCl_3$): 55.7 (MeO); 100.8 (C(8)); 112.5 (C(4a)); 112.5 (C(6)); 113.0 (C(3)); 128.7 (C(5)); 143.4 (C(4)); 155.9 (C(8a)); 161.2 (C(2)); 162.8 (C(7)); signals attributed to the minor isomer: 56.0 (MeO); 105.1 (C(8)); 109.1 (C(6)); 109.6 (C(4a)), 114.5 (C(3)); 132.3 (C(7)); 138.5 (C(4)); 155.1 (C(8a)); 156.1 (C(5)); 160.9 (C(2)). MS (70 eV): 176 (62, M^+), 148 (98), 133 (100), 105 (20), 77 (26). HR-EI-MS: 176.0473 (M^+, $C_{10}H_8O_3^+$; calc. 176.0474).

*6*H*-[1,3]Dioxolo[4,5-g]-1-benzopyran-6-one* (= *Ayapin*; **1e**). As described for **1a**, a mixture of **2e** (0.10 g, 0.43 mmol) and activated $ZnCl_2$ (0.174 g, 1.28 mmol) was stirred at 100° for 8 d; then, the residue was purified by recrystallization (PrOH) to give **1e** (0.034 g, 43%). Pale brown powder. R_f (hexane/AcOEt 1:1) 0.54. M.p. 220–222° ([10h]: 222–223°; [11a][11c]: 225–227°; [43]: 225–226°; [11f][11g]: 229–230°). IR (KBr): 1707, 1628, 1579, 1491, 1452, 1256, 1120, 1040, 940, 833. ^{1}H-NMR (500 MHz, $CDCl_3$): 6.07 (*s*, 2 H–C(2)); 6.28 (*d*, *J* = 9.5, H–C(7)); 6.82 (*s*, H–C(4)); 6.83 (*s*, H–C(9)); 7.58 (*d*, *J* = 9.5, H–C(8)). ^{13}C-NMR (125 MHz, $CDCl_3$): 98.4 (C(4)); 102.3 (OCH_2O); 105.0 (C(9)); 112.7 (C(8a)); 113.4 (C(7)); 143.5 (C(8)); 144.9 (C(9a)); 151.2 (C(3a)); 151.3 (C(4a)); 161.2 (C(6)). MS (70 eV): 190 (77, M^+), 163 (11), 162 (95), 161 (100), 76 (14). HR-EI-MS: 190.0264 (M^+, $C_{10}H_6O_4^+$; calc. 190.0266).

*5,7-Dimethoxy-2*H*-1-benzopyran-2-one* (= *Citropten*; **1f**). As described for **2a**, a mixture of **4f** (0.28 g, 1.43 mmol) and the *Bredereck* reagent (0.373 g, 2.14 mmol) was heated to 50° for 1 h to give **2f** (0.25 g) as a crude material, which was used without purification in the next reaction. Thus, as described for **1a**, the crude **2f** and activated $ZnCl_2$ (0.572 g, 4.21 mmol) were reacted, and the residue obtained was purified by recrystallization from EtOH to give **1f** (0.103 g, 35%). Pale yellow powder: R_f (hexane/AcOEt 1:1) 0.58. M.p. 146–147° ([10h]: 143–144°; [11c]: 147.5–149°; [43]: 143–144°). IR (KBr): 1711, 1611, 1468, 1456, 1363, 1222, 1206, 1153, 1117, 817. ^{1}H-NMR (500 MHz, $CDCl_3$): 3.85 (*s*, MeO), 3.88 (*s*, MeO), 6.14 (*d*, *J* = 10.0, H–C(3)); 6.29 (*d*, *J* = 2.4, H–C(6)); 6.42 (br. *d*, *J* = 2.4, H–C(8)); 7.95 (*dd*, *J* = 10.0, 0.5, H–C(4)). ^{13}C-NMR (125 MHz, $CDCl_3$): 55.8 (MeO); 55.9 (MeO); 92.8 (C(8)); 94.8 (C(6)); 104.0 (C(4a)); 110.9 (C(3)); 138.7 (C(4)); 156.8 (C(8a)); 157.0 (C(5)); 161.5 (C(2)); 163.7 (C(7)). EI-MS (70 eV): 206 (72, M^+), 178 (100), 163 (59), 149 (19), 135 (51), 77 (18). HR-EI-MS: 206.0580 (M^+, $C_{11}H_{10}O_4^+$; calc. 206.0579).

*5,7-Dimethoxy-3-phenyl-2*H*-chromen-2-one* (**1g**). As described for **1f**, a mixture of **4g** (0.25 g, 0.92 mmol) and the *Bredereck* reagent (0.24 g, 1.38 mmol) was heated to 50° for 1 h to give **2g** (0.20 g) as a crude material, which was used without purification in the next reaction. Thus, the crude **2g** and activated $ZnCl_2$ (0.816 g, 6.00 mmol) were reacted, and the residue obtained was purified by recrystallization from EtOH to give **1g** (0.051 g, 20%) as a pale yellow powder. R_f (hexane/AcOEt 1:1) 0.70. M.p. 168–170° ([45]: 178°). IR (KBr): 1715, 1619, 1501, 1477, 1453, 1432, 1350, 1318, 1291, 1217, 1153, 1108, 1041, 821, 782. ^{1}H-NMR (500 MHz, $CDCl_3$): 3.87 (*s*, MeO); 3.91 (*s*, MeO); 6.30 (*d*, *J* = 2.5,

H–C(6)); 6.46 (*dd*, *J* = 2.5, 0.5, H–C(8)); 7.33 – 7.38 (*m*, H–C(4′)); 7.40 – 7.45 (*m*, 2 H–C(3′)); 7.70 – 7.72 (*m*, 2 H–C(2′)); 8.12 (*d*, *J* = 0.5, H–C(4)). ^{13}C-NMR (125 MHz, $CDCl_3$): 55.8 (MeO); 56.0 (MeO); 92.4 (C(8)); 94.9 (C(6)); 104.8 (C(4a)); 122.7 (C(3)); 128.1 (C(4′)); 128.3 (C(3′)); 128.4 (C(2′)); 135.3 (C(1′)); 135.4 (C(4)); 156.1 (C(8a)); 157.1 (C(5)); 161.1 (C(2)); 163.4 (C(7)). EI-MS (70 eV): 282 (74, M^+), 255 (36), 254 (43), 239 (80), 199 (93), 155 (55), 153 (54), 127 (45), 125 (94), 101 (52), 99 (80), 85 (84), 45 (100), 41 (53). HR-EI-MS: 282.0893 (M^+, $C_{17}H_{14}O_4^+$; calc. 282.0892).

Single-Crystal X-Ray Crystallography. Single-crystals of **2c** were obtained by recrystallization from AcOEt/hexane 9 : 1 as pale yellow crystals. These were mounted in glass fibers. Crystallographic measurements were performed using MoK_α radiation (graphite crystal monochromator, $\lambda = 71073$ Å), at r.t. Intensities were corrected for *Lorentz* and polarization effects. No absorption correction was applied. Anisotropic temp. factors were introduced for all non-H-atoms. The H-atoms were placed in idealized positions, and their atomic coordinates were refined. Unit weights were used in the refinement. The structure was solved using the SIR92 [46] program as implemented in the WinGX suite [47], and refined using SHELX97 within WinGX, on a personal computer. ORTEP Diagrams were made with PLATON [48].

Data for **2c**. Formula $C_{13}H_{17}NO_4$; M_r, 251.28; crystal size, $0.42 \times 0.39 \times 0.29$ mm; crystal system, monoclinic; space group, *P*1 21/*c*1; unit cell parameters, $a = 14.9384$ (3), $b = 8.55750$ (10), $c = 10.6619$ (3) Å, $\alpha = 90$, $\beta = 104.044$ (2)°, $\gamma = 90°$, $V = 1322.23$ (5) Å^3; temp., 294(2) K; $Z = 4$; $D_x = 1.262$ Mg/m^3; absorption coefficient, 0.094 mm^{-1}; θ scan range, 2.76 – 32.47°; reflections collected, 13849; independent reflections, 4323; reflections observed, 2775; $R = 0.0504$; $wR = 0.1324$; goodness-of-fit 1.054.

CCDC-770542 contains the supplementary crystallographic data for the structure of **2c**. These data can be obtained, free of charge, *via* www.ccdc.cam.ac.uk/data_request/cif.

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