A Novel Oxidative Cyclization of 2′-Hydroxychalcones to 4,5-Dialkoxyaurones by Thallium(III) Nitrate†

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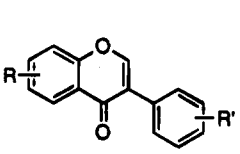
Scope and mechanism studies are reported on a novel oxidative transformation of certain 2′-hydroxy-5′-methoxychalcones to aurones by thallium(III) nitrate (TTN) in alcoholic solvents. A key feature of the reaction is the incorporation of a solvent-derived alkoxy group at C-4 of the aurone. The thermodynamically more stable *Z* isomers of the aurones are obtained in all cases. Aurones are formed regardless of whether electron donating or electron attracting groups are present at the para position of the B ring of the starting chalcone.

Introduction

The use of thallium(III) reagents has recently evolved as a versatile methodology in organic synthesis.[1] The oxidation products obtained on treatment of olefins with thallium(III) salts depend on the structure of the olefin, the solvent, and the thallium salt employed.[2] Due to our current interest in the synthesis of isoflavones **1** as potential protein-tyrosine kinase inhibitors,[3–5] the oxidative rearrangement and cyclization of 2′-hydroxychalcones **2** to the corresponding isoflavones **1**[1,6,7] was investigated. Utilization of thallium(III) trinitrate (TTN) in the oxidative rearrangement of 2′-hydroxychalcones **2** to isoflavone **1** via 1,2-diaryl-3,3-dimethoxypropan-1-ones has been carried out successfully.[6,8,9] However, a major drawback of this method of isoflavone synthesis is that the reaction pathway followed is very sensitive to the nature of the substituents present, often resulting in other types of reaction products.[10–12] For example, TTN oxidation of a 2′-hydroxy-4′,5′,6′-trioxygenated chalcones in methanol gives the corresponding quinone acetals by A-ring oxidation instead of isoflavones.[10,13] Certain 2′-hydroxy chalcones **2** with a chloro or nitro group are also known to react with TTN in an alternative mode to give aurones **3** through the corresponding (α-methoxybenzyl)-coumaranones **4**.[12,14] In the reaction of the chalcones without a free hydroxy group, the A ring migrates to give



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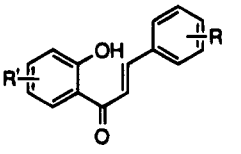

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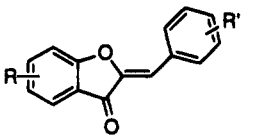

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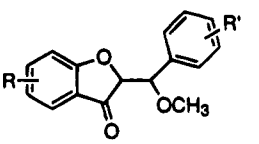

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methyl 2,3-diaryl-3-methoxypropanoates when the chalcone has a B ring with low migrating ability.[11,15] These substituent effects have not been completely defined in spite of numerous studies.[1] Earlier, we investigated an unusual oxidative cyclization of 2′-hydroxychalcones to 4-methoxyaurones by TTN in methanol.[16] The present report details the results of more recent investigations of the scope and mechanism of this reaction.

Results and Discussion

Previous investigations have shown that the treatment of chalcones with thallium(III) trinitrate (TTN) results in oxidative rearrangement to the corresponding acetals or methyl propanoates (Scheme 1).[1] Which of the two reaction pathways is followed depends on the relative migratory aptitudes of the two aromatic rings, which is determined by the electronic effects of the substituents present on each of them.[1,7,17] If the B ring of the chalcone is much more electron rich than the ring A, the oxidative 1,2 aryl migration of ring B occurs to give the corresponding acetal. On the other hand, if the A ring of the chalcone is more electron rich than the B ring, the oxidative 1,2 aryl migration of ring A takes place to yield the corresponding methyl propanoate.

In contrast to these reactions, oxidative cyclization of 2′-hydroxychalcones **2a–f** by thallium(III) trinitrate

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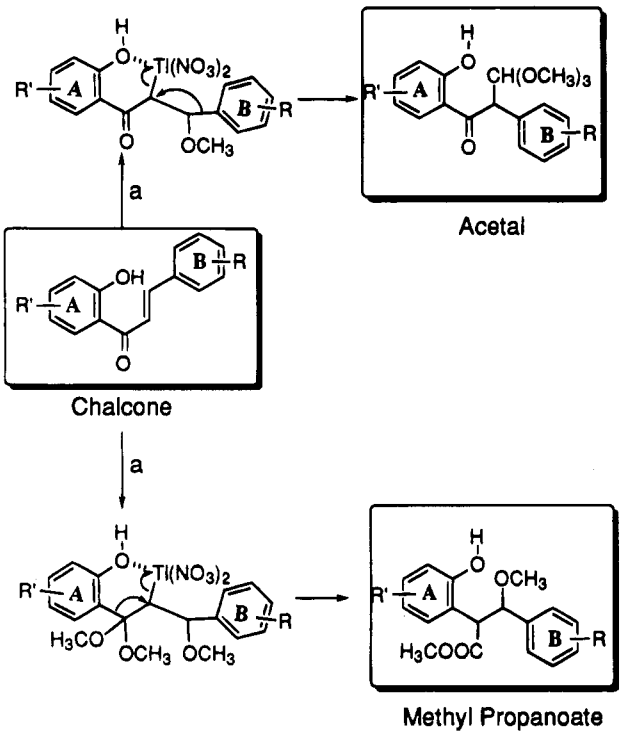
Scheme 1



Reagents and conditions: (a) (i) TTN, MeOH, 23 °C (ii) HCl, 65 °C (10-15 h).

(TTN) in methanol affords 4-methoxyaurones **3a–f** without any noticeable rearrangement of either ring A or ring B (Scheme 2).[16] This has provided important insights into the behavior of TTN in the oxidative cyclization of 2′-hydroxychalcones **2** as well as the oxidative rearrangement of chalcones without hydroxy groups at the 2′ position.

Two synthetic methodologies were utilized for the synthesis of the 2′-hydroxychalcones **2a–m** (Scheme 2). In the first method, the classical aldol condensation was utilized effectively for the synthesis of 2′-hydroxychalcones **2b–m** (yield 58–80%). In the alternative method, 2′-hydroxy-5′-methoxy-4-nitrochalcone **2a** was synthesized by a modified Mukaiyama crossed aldol condensation route.[18] In this method, 2′-hydroxy-5′-methoxyacetophenone (**5a**) was converted to the corresponding silane derivative **6** in 95% yield, which under the modified Mukaiyama aldol condensation with *p*-nitrobenzaldehyde (**7a**) proceeded smoothly to give the corresponding 2′-hydroxychalcone **2a** in 78% yield (Scheme 2).[19,20]

In an attempt to synthesize isoflavones **1** by oxidative rearrangement of 2′-hydroxychalcones **2**, an unusual oxidative cyclization to 4,5-dimethoxyaurones **3** was observed (Scheme 2). The 2′-hydroxychalcones **2a–f** were synthesized to examine the electronic effects of substituents in the para position of ring B on the 4,5-dimethoxyaurone **3a–f** formation. Oxidation of these chalcones **2a–f** with 2.5–3.0 equiv of TTN in methanol proceeded smoothly to afford the corresponding 4,5-dimethoxyaurones **3a–f** in 43–79% yield. The structures of the 3,4-dimethoxyaurones **3a–f** have been determined by X-ray crystallography (Figure 1), elemental analysis,

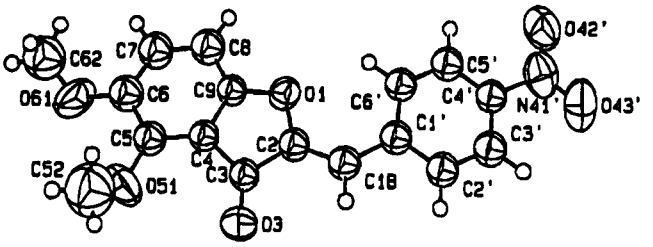


Figure 1. ORTEP-II plot of the X-ray structure of **3a**.

mass spectrometry, and ^{1}H NMR as well as ^{13}C NMR analysis. The key features of this reaction are (1) the addition of a methoxy group at the 4-position in the aurone skeleton, (2) exclusive formation of the *Z*-configuration of the olefinic double bond of the aurones **3a–f**, and (3) the presence of electron donating vs electron withdrawing groups at the para position of the B ring of the chalcones has no effect on the formation of 4,5-dimethoxyaurones **3a–f**.

A plausible mechanism which would account for the observed incorporation of the 4-methoxy group into the aurone skeleton is outlined in Scheme 3. The initial steps in the proposed mechanism may involve ipso thallation or *O*-thallation. Both of these routes do eventually end up giving common quinone monoacetal intermediates **12a–f** through which 3,4-dimethoxyaurones **3a–f** can be obtained as outlined (Scheme 3).

Initially, through the *O*-thallation route, TTN would react with the 2′-hydroxychalcones **2a–f** in methanol to afford the corresponding cyclic *O*-thallated complexes **11a–f**. This is based on studies of the oxidation of several 2′-hydroxyacetophenones reported by Horie *et al.*[13] The nucleophilic attack of methanol leading to elimination of the thallium moiety in **11a–f** would afford the corresponding quinone monoacetal intermediates **12a–f**.

Alternatively, **12a–f** might rise through ipso thallated adducts **9a–f**. Homolytic cleavage of the C–Tl bond followed by nucleophilic attack of methanol would give the quinone monoacetal intermediates **12a–f** through the dethallated intermediates **10a–f** (Scheme 3). This is based on studies of the oxidation of several 4-substituted phenols conducted by McKillop *et al.*[10]

Conformers **13a–f** can then form from **12a–f** by rotation of the bond between the quinone monoacetal ring and the ketone. Michael addition of methanol to **13a–f** and methoxythallation of the olefinic double bond by TTN would give the thallium adducts **14a–f** by antarafacial methoxy-thallation of the trans double bond.[21] The observed regiochemistry of Michael addition of methanol to the six-membered ring is facilitated by two carbonyl groups in conjugation with the reactive double bond as opposed to one carbonyl group in the alternative mode. Cyclization of the thallated intermediates **14a–f** would give the dethallated α-methoxycoumaranones **15a–f**. Under the acidic conditions, the α-methoxycoumaranones **15a–f** could eliminate 2 equiv of methanol and rearomatize to give the corresponding 4,5-dimethoxyaurones **3a–f** with the olefinic double bond in the *Z*-configuration only, resulting from antiperiplanar elimination of methanol. Although the proposed mechanism is logical and would account for the observed *Z*-alkene stereochemistry of the product, the structure of the product is not

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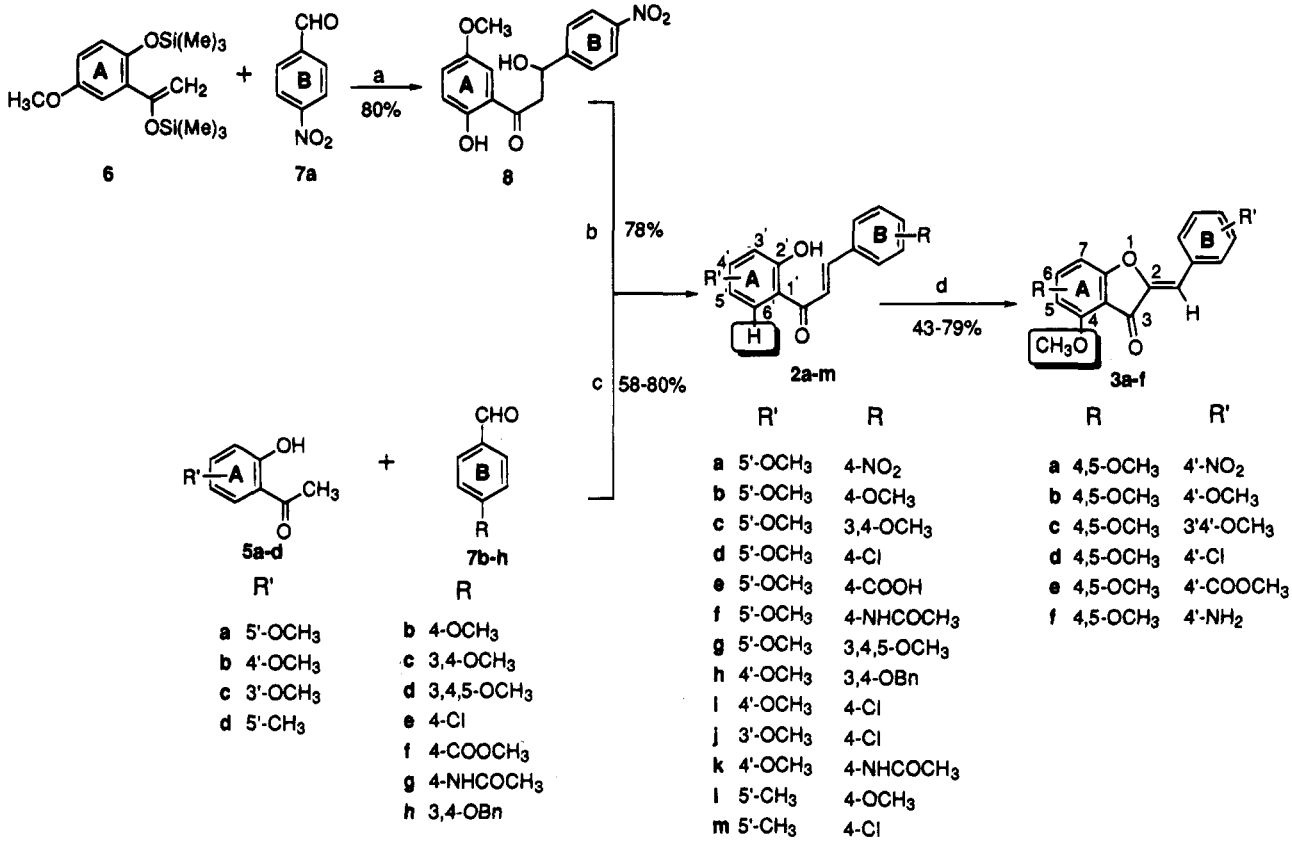
Scheme 2



Reagents and conditions: (a) $TiCl_4$, CH_2Cl_2, 0 °C (0.5 h); (b) $(CF_3CO)_2O$, Et_3N, 0-23 °C (18-20 h); (c) KOH, ethanol, 0-23 °C (12-15 h); (d) (i) TTN, MeOH, 23 °C (ii) HCl, 65 °C (10-15 h).

conclusive with regard to the stereochemistry of the methoxythallation of **13a–f** and subsequent elimination of methanol, since the *Z*-alkene is the thermodynamically more stable isomer and could therefore result from equilibration of the *E*-isomer under the acidic conditions of the reaction.[22]

Several unfruitful attempts were made to isolate the proposed quinone monoacetal intermediate **12d** after treatment of **2d** with 1 equiv of TTN in methanol. Attention was therefore focused on the recent report that phenyliodonium diacetate (PIDA, $PhI(OAc)_2$) in methanol is an excellent oxidizing reagent for the conversion of polysubstituted phenols to the corresponding 4,4-dialkoxycyclohexa-2,5-dienones or 4-alkyl-4-alkoxycyclohexa-2,5-dienones, depending upon the constitution of the phenolic substrates.[23] We attempted to utilize PIDA as an oxidizing agent on the 2′-hydroxychalcone **2d**, but were unsuccessful in obtaining the desired quinone monoacetal intermediate **12d**. Alternatively, the very similar oxidizing agent phenyliodonium bis(trifluoroacetate) (PIFA) in methanol has been reported to be a simple and efficient reagent for preparation of *p*-quinols from the corresponding phenols.[24] Oxidation of **2d** with PIFA led to the novel Michael adduct **16a** (67% yield) as shown in Scheme 4. Recrystallization of the reaction product from ethanol afforded the related product **16b**, which presumably forms by elimination of methanol from

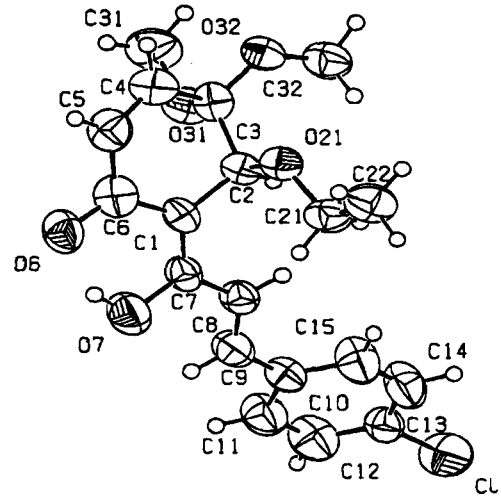


Figure 2. ORTEP-II plot of the X-ray structure of **16b**.

16a to form **12d**, followed by Michael addition of ethanol. The structure of **16b** was confirmed by X-ray crystallography (Figure 2).[29] The solution ^1H NMR spectra of both **16a** and **16b** are rather complex due to the presence of several rotamers and tautomers. These rotamers (**18ab** and **20ab**) and tautomers (**19ab** and **21ab**) can be formed as depicted in Scheme 6. A plausible mechanism for obtaining both these Michael adducts **16a** and **16b** is outlined in Scheme 5. The results indicate that quinone monoacetals such as **12d** (Scheme 3) may be too unstable to isolate under the present reaction conditions, since they rapidly undergo Michael addition under mild acidic conditions.

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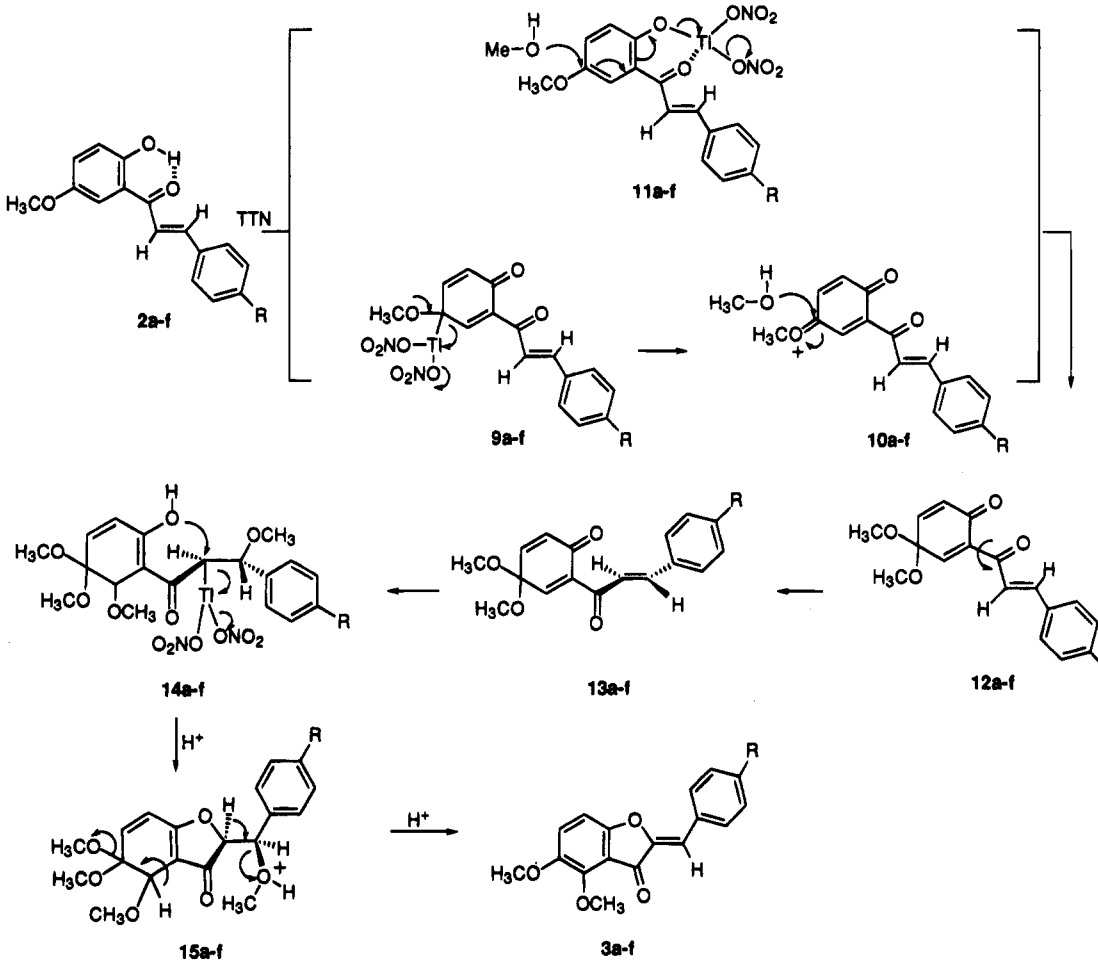
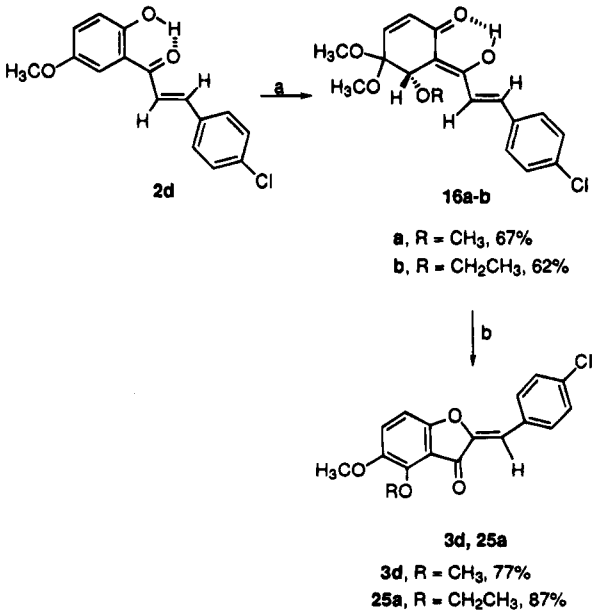
Scheme 3



Scheme 4



Reagents and conditions: (a) PIFA, MeOH, (0-23 °C), 5-10 min. (b) (i) TTN, MeOH, 23 °C (ii) HCl, 65 °C (10-15 h).

The isolated Michael adducts **16ab** were subjected to 1.2 equiv of TTN in methanol, yielding the corresponding aurones **3d** and **25a** in 77% and 87% yields, respectively (Scheme 4). The Michael adducts of type **16** therefore represent likely intermediates between **13** and **14** in the mechanism proposed in Scheme 3.

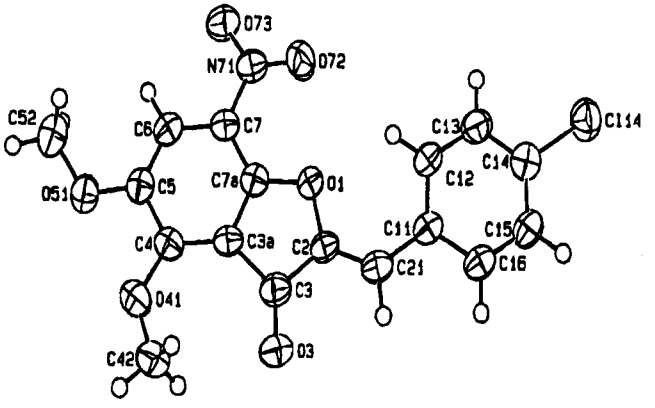
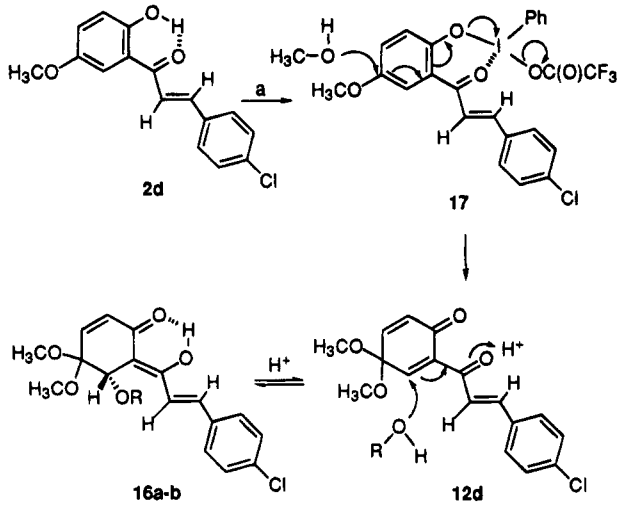


Figure 3. ORTEP-II plot of the X-ray structure of **32**.

In order to gain further insight into the reaction mechanism, the question of whether the observed *Z*-aurone isomers are kinetic or thermodynamic products was investigated. Photoisomerization of the aurone **3e** was therefore carried out.[25] A 1:1 mixture of *E*-aurone **22** and *Z*-aurone **3e** was obtained, which represents the photostationary state (Scheme 7). The ratio of these two isomeric aurones **3e** and **22** could be assigned on the basis of the chemical integrations of the ^{1}H NMR olefinic proton signals of the *E* and *Z* isomers at δ 7.01 and 6.78, respectively.[26,27] Several TLC systems and other chromatographic techniques were tried in order to separate

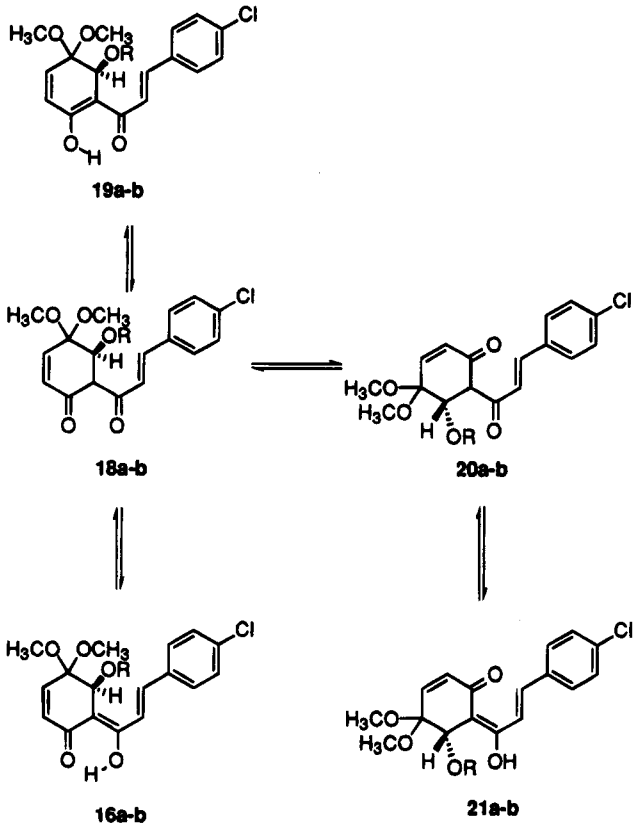
(25) Hastings, J. S.; Heller, H. G. *J. Chem. Soc., Perkin Trans. 1* **1972**, 2128–2132.

Scheme 5



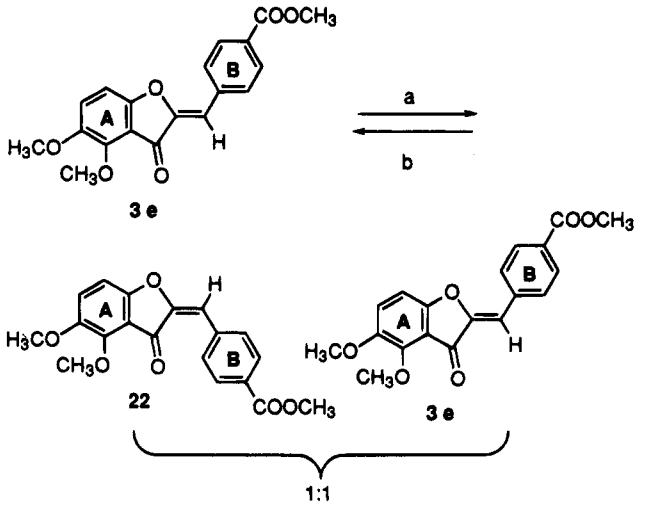
Reagents and conditions: (a) PIFA, ROH, (0 °C), 5-10 minutes

Scheme 6



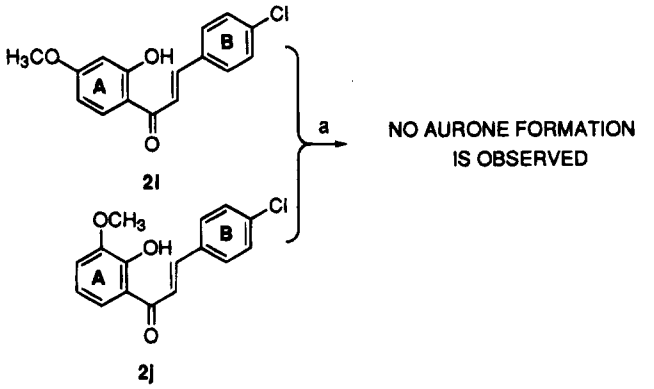
these isomers, but no success was achieved. This inseparable mixture of aurones **3e** and **22** was then treated with 1.2 equivalent of TTN in methanol yielding the *Z*-isomer **3e** in quantitative yield. These experiments have demonstrated that the formation of the *Z*-configuration of the olefinic double bond of the aurones **3a–f** might be due to the thermodynamic equilibration under the acidic conditions of the reaction. The stereochemistry of the products therefore does not necessarily indicate the stereochemistry of the reactions involved in the conversion of **13a–f** to **3a–f** in Scheme 3.

Scheme 7



Reagents and conditions: (a) hυ (366 nm), benzene. (b) (i) TTN, MeOH, 23 °C (ii) HCl, 65 °C (10 h).

Scheme 8



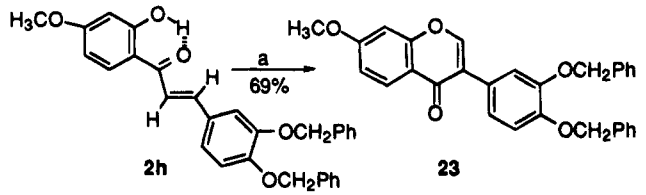
Reagents and conditions: (a) (i) TTN, MeOH, 23 °C (ii) HCl, 65 °C (10-15 h).

To further explore the possible effects of A ring substituents on the cyclization to aurones, 4-chloro-2′-hydroxy-4′-methoxychalcone (**2i**) and 4-chloro-2′-hydroxy-3′-methoxychalcone (**2j**) were synthesized. Prior work with **2d** had established that a 4-chloro substituent in ring B is compatible with aurone formation. Upon oxidative treatment of **2i** and **2j** with TTN in methanol, intractable reaction mixtures were obtained and no corresponding aurone formation was detected (Scheme 8). The substitution pattern of the A ring evidently plays an important role in the oxidative cyclization of chalcones to the corresponding aurones. The reaction seems to depend on the presence of a methoxy group para to the phenol in ring A.

In another comparative study, we synthesized 3,4-bis-(benzyloxy)-2′-hydroxy-4′-methoxychalcone (**2h**) and 2′-hydroxy-3,4,5′-trimethoxychalcone (**2c**). When chalcones **2c** and **2h** were subjected to TTN in methanol, 3′,4,4′,5-tetramethoxyaurone (**3c**, Scheme 2) and 3-methoxy-3′,4′-bis(benzyloxy)isoflavone **23** (Scheme 9) were obtained in 40% and 69% yield, respectively. This result is also consistent with the hypothesis that aurone formation is facilitated by the presence of a methoxy group para to the phenol in ring A.

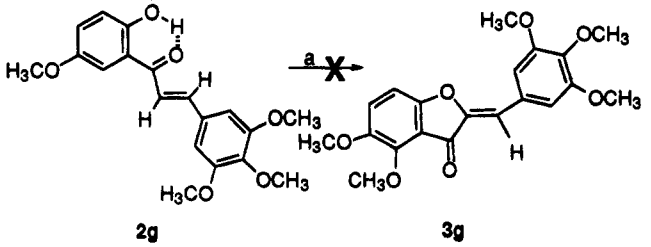
(26) Pelter, A.; Ward, R. S.; Heller, H. G. *J. Chem. Soc., Perkin Trans. 1* **1979**, 328–329.
(27) Brady, B. A.; Healy, M. M.; O'Sullivan, W. I.; Philbin, E. M. *J. Chem. Soc., Chem. Commun.* **1970**, 1434–1435.

Scheme 9



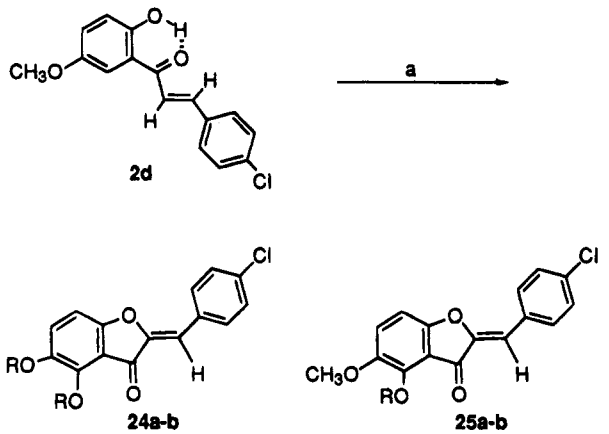
Reagents and conditions: (a) (i) TTN, MeOH, 23 °C (ii) HCl, 65 °C (12 h).

Scheme 10



Reagents and conditions: (a) (i) TTN, MeOH, 23 °C (ii) HCl, 65 °C (12 h).

Scheme 11



a, R = CH_2CH_3, 62%
b, R = $CH_2CH_2CH_3$, 47%

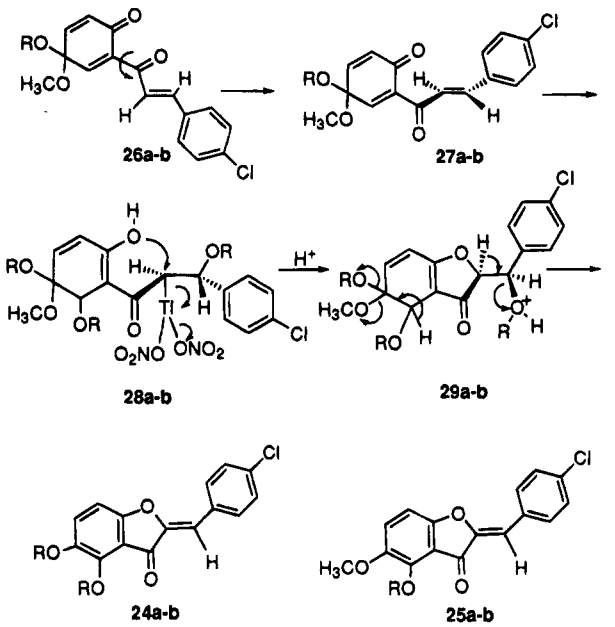
a, R = CH_2CH_3, 17%
b, R = $CH_2CH_2CH_3$, 10%

Reagents and conditions: (a) (i) TTN, ROH, 23 °C (ii) HCl, > 65 °C (12-15 h).

The effect of having additional electron-donating groups on ring B was further explored. Intractable reaction mixtures were obtained when chalcone **2g** was treated with TTN in methanol, and no aurone formation was detected (Scheme 10). The substitution of the B ring in **2g** with multiple electron donating groups may be responsible for the lack of aurone formation.

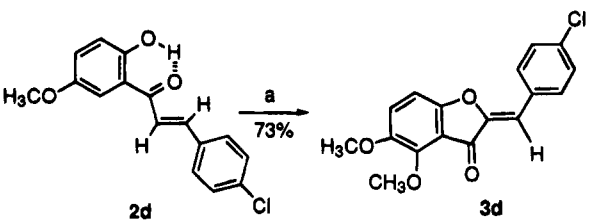
In order to further investigate the scope of this reaction, several alcoholic solvents have been studied. Several 4,5-dialkoxyaurones as major products **24a,b** (yield 62–47%) and 4-alkoxy-5-methoxy aurones **25a,b** as minor products (yield 17–10%) were isolated when ethanol or 1-propanol were used as the solvent (Scheme 11). A mechanism for formation of these products is proposed in Scheme 12. Under the acidic conditions, the α-methoxycoumaranone intermediates **29a,b**, formed from thallated adduct **28a,b**, could eliminate 2 equiv of methanol to rearomatize and form the corresponding 4,5 dialkoxyaurones **24a,b** as the major product. On the other hand, elimination of 1 equiv of methanol and 1 equiv of the respective alcohol would yield the corresponding 4-alkoxy-5-methoxyaurones **25a,b** as the minor product. These results are also consistent with the mechanism proposed in Scheme 3.

Scheme 12



R = C_2H_5 and C_3H_7.

Scheme 13



Reagents and conditions: (a) (i) TTN, trimethyl orthoformate (TMOF), 23 °C (ii) HCl, 65 °C (12 h).

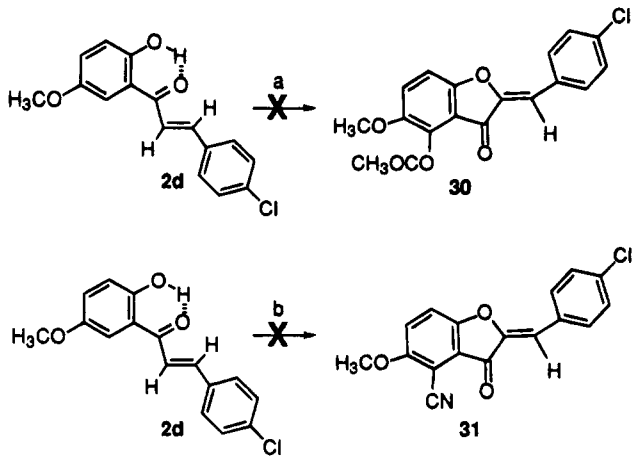
Taylor and his co-workers have reported the remarkable effectiveness of methanol/trimethyl orthoformate (MeOH/TMOF) (1:1) or of TMOF alone as solvents for certain TTN-mediated oxidations.[28] It is believed that TMOF lowers the dielectric constant of the reaction mixture, thus favoring S_N2-type as opposed to S_N1-type reactions of the methoxythallated intermediates. We have attempted to utilize TMOF as solvent alone. Treatment of 4-chloro-2′-hydroxy-5′-methoxychalcone (**2d**) with TTN in TMOF rather than methanol as solvent resulted in a higher yield and a cleaner reaction product during the formation of aurone **3d** (Scheme 13). Addition of the methoxy group at the 4-position of aurone **3d** most likely results from traces of methanol present in the TMOF.

Several other nonalcoholic solvents or nucleophiles have also been examined in these oxidative cyclizations (Scheme 14). McKillop and his co-workers have shown that the treatment of 3,4,5-trimethoxyphenol with TTN and sodium acetate in a mixture of acetic acid and ethyl

(28) Taylor, E. C.; Robey, R. L.; Liu, K.-T.; Favre, B.; Bozimo, H. T.; Conley, R. A.; Chiang, C.-S.; McKillop, A.; Ford, M. E. *J. Am. Chem. Soc.* **1976**, *98*, 3037–3038.

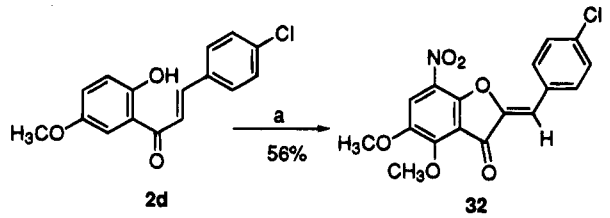
(29) The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

Scheme 14



Reagents and conditions: (a) (i) TTN, $Na^+ {}^-OC(O)CH_3$, ethyl acetate, 23 °C (ii) HCl, 75 °C (12-15 h). (b) (i) TTN, KCN, CCl_4, 23 °C (ii) HCl, 85 °C (12-15 h).

Scheme 15



Reagents and conditions: (a) (i) TTN, MeOH 23 °C (ii) HCl, 75 °C (10 h).

acetate gave 3,4,5-trimethoxy-4-acetoxycyclohexa-2,5-dienone in poor yield (19%).[10] We used similar reaction conditions on 4-chloro-2′-hydroxy-5′-methoxychalcone (**2d**) and observed no formation of the corresponding aurone **30**. Similarly, treatment of **2d** with TTN and potassium cyanide in carbon tetrachloride also did not give any of the corresponding aurone **31**. Due to few nucleophiles other than carboxylate anions and nitriles that are compatible with TTN, no further effort was expended on these transformations. Nucleophiles such as amines and thiols easily oxidize on treatment of TTN and hence could not be used to expand the scope of the reaction. To date, only substituents derived from alcohols have been incorporated at the 4-position during aurone formation.

Oxythallation reactions are carried out in fairly strongly acidic solvents. This is also true of solutions of TTN in methanol, as the salt is obtainable only as the trihydrate, $Tl(ONO_2)_3{\cdot}3H_2O$, and nitric acid is generated during the reaction. On several occasions variable amounts of the nitrated aurone **32** were isolated from reactions involving **2d** (Scheme 15). The structure of **32** was confirmed by X-ray crystallography (Figure 3).[29] The sporadic formation of **32** seems to result from the presence of variable amounts of nitric acid present in the TTN reagent.

The thallium(III)-mediated introduction of an alkoxy group in the A ring of chalcones followed by cyclization to aurones is a novel reaction pathway. The present study may aid in the prediction of the thallium(III)-mediated behavior of chalcones, which are known to give several different types of reaction products.

Experimental Section

Melting points were determined in capillary tubes and are uncorrected. Infrared spectra were obtained using CCl_4 as the solvent unless otherwise specified. Peaks are reported in cm^{-1} with the following intensities: s (strong, 67–100%), m (medium, 34–66%), w (weak, 0–33%). ^1H NMR spectra were obtained using $CDCl_3$ or $(CD_3)_2CO$ as solvents and TMS as internal standard. ^1H NMR spectra were determined at 500 or 200 MHz as noted, and ^{13}C NMR spectra were recorded at 125 MHz. Low resolution chemical ionization mass spectra (CIMS) were determined using isobutane as the reagent gas. Microanalyses were performed at the Purdue University Microanalysis Laboratory. THF was distilled from sodium metal and benzophenone under argon to remove moisture and oxygen. DMF was vacuum distilled from calcium hydride under anhydrous argon atmosphere. Methylene chloride and acetonitrile were distilled from calcium hydride. Triethylamine is dried over potassium hydroxide pellets for at least 24 h before using it in any reactions. Analytical thin-layer chromatography was carried out on Whatman silica 60 K6F and Merck silica 60 F_{254} glass coated plates (1000 and 2000 μm). Silica gel column chromatography was performed using Sigma 70–230 mesh silica gel and flash column chromatography was carried out with 230–400 mesh silica gel.

1-[2′-[(Trimethylsilyl)oxy]-5′-methoxyphenyl]-1-[(trimethylsilyl)oxy]ethylene (6). 2′-Hydroxy-5′-methoxyacetophenone (**5a**, 1.66 g, 10 mmol) and triethylamine (3.30 g 30 mmol) were added to a 100 mL three-necked flask equipped with the mechanical stirrer, reflux condenser with nitrogen inlet, thermometer, and pressure equalizing dropping funnel under argon atmosphere. Chlorotrimethylsilane (3.80 g, 35 mmol) was added dropwise to the stirred mixture at room temperature over a period of 3 min. The flasked was immersed in a water bath, and the contents were warmed to 35 °C. The water bath was removed and the dropping funnel was charged with a solution of sodium iodide (1.49 g, 10 mmol) in acetonitrile (35 mL). The solution was added to the stirred mixture in the flask at such a rate that the temperature was maintained at 35–40 °C without external heating or cooling. The additions required approximately 20 min. When addition was complete, the reaction mixture was stirred for a further 2 h at room temperature. The contents of the flask were then poured into ice-cold water (100 mL), and the aqueous mixture was extracted with hexane (2 × 100 mL). The combined hexane extracts were dried over anhydrous potassium carbonate. Evaporation of solvent from the filtered extract provided the desired product **6** as a pale white oil (2.94 g, 95%): ^1H NMR ($CDCl_3$, 500 MHz) δ 0.25 (s, 18 H), 3.76 (s, 3 H), 4.64 (d, J = 0.5 Hz, 1 H), 5.19 (d, J = 0.5 Hz, 1 H), 6.69 (dd, J = 9.0 Hz, 3.0 Hz, 1 H), 6.73 (d, J = 9.0 Hz, 1 H), 7.10 (d, J = 3.0 Hz, 1 H); IR (CCl_4) 3000 (w), 1647 (w), 1489 (s), 1415 (w), 1322 (w), 1285 (s), 1218 (m), 1042 (m), 1017 (w), 848 (s).

(±)-3-Hydroxy-3-(4-nitrophenyl)-1-(2′-hydroxy-5′-methoxyphenyl)propan-1-one (8). A 100 mL, three-necked flask was fitted with a stirring bar, rubber stopper, 100 mL pressure equalizing dropping funnel, and a three-way stopcock attached to a balloon of argon gas. The flask was charged with freshly distilled methylene chloride (20 mL) and then cooled in an ice bath. Titanium tetrachloride (13 mL, 1 M solution in methylene chloride) was added by a syringe, and a solution of *p*-nitrobenzaldehyde (1.511 g, 10 mmol) in methylene chloride (15 mL) was added dropwise over 2 min. A solution of **6** (2.94 g, 9.5 mmol) was added dropwise to the stirred mixture over a period of 10 min. After 35 min, the reaction mixture was poured into ice-cold water (50 mL) with vigorous stirring. The mixture was extracted with ethyl acetate (7 × 45 mL). The combined organic layers were washed with saturated aqueous sodium carbonate (2 × 60 mL) and saturated NaCl solution (25 mL). The washed organic layers were combined and dried over Na_2SO_4. Evaporation of ethyl acetate *in vacuo* provided the crude product as a pale-yellow solid. The purification of the crude product was done by flash column chromatography (ethyl acetate in hexane, gradient elution 15–80%, silica gel 230–400 mesh) which provided **8** as a pale-yellow solid (2.40 g, 7.6 mmol, 80%): ^1H NMR ($CDCl_3$, 500 MHz) δ 3.34 (s, 1 H), 3.37 (d, J = 6.0 Hz, 1 H), 3.53 (bs, OH, exchangeable with D_2O), 3.73 (s, 3 H), 5.47 (d, J = 6.0 Hz, 1 H), 6.95 (d, J = 9.0 Hz, 1 H), 7.03 (d, J = 3.0 Hz, 1 H), 7.14 (dd, J = 9.0 Hz, 3 Hz, 1 H), 7.59 (d, J = 8.9 Hz, 2 H), 8.23 (d, J = 8.9 Hz, 2 H). CIMS m/z (relative intensity) 318 (MH^+, 100).

2′-Hydroxy-5′-methoxy-4-nitrochalcone (2a). A 100 mL, three-necked flask was fitted with a stirring bar, rubber stopper, 100 mL pressure equalizing dropping funnel and a three-way stop-cock which was attached to a balloon of argon gas. A solution of **8** (2.41 g, 7.6 mmol) in dry methylene chloride (30 mL) was added. The flask was cooled in an ice bath and triethylamine (1.10 g, 10 mmol), a catalytic amount of 4-(*N*,*N*-dimethyamino)pyridine, and methylene chloride (20 mL) were added. A solution of freshly distilled trifluoroacetic anhydride (2.10 g, 10 mmol) was added dropwise, and the mixture was stirred for an additional 3 h. The ice bath was then removed and the reaction mixture was stirred for another 20 h at room temperature. Saturated aqueous sodium carbonate (10 mL), water (10 mL), and ethyl ether (15 mL) were added to the vigorously stirred mixture. The organic layer was separated, and the water layer was extracted with ether (10 mL). The combined ether extracts were washed with brine and dried over Na_2SO_4. The ether layer was condensed using a rotary evaporator, and the residue was distilled under reduced pressure to give the crude reddish-brown product. Recrystallization of this crude product from ethyl acetate and hexane gave dark reddish-brown needles of **2a** (1.76 g, 78%): mp 195–196 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.84 (s, 3 H), 7.02 (d, J = 9.0 Hz, 1 H), 7.20 (dd, J = 9.0 Hz, 2.9 Hz, 1 H), 7.34 (d, J = 9.0 Hz, 1 H), 7.70 (d, J = 15.5 Hz, 1 H), 7.82 (d, J = 9.0 Hz, 2 H), 7.92 (d, J = 15.5 Hz, 1 H), 8.31 (d, J = 9.0 Hz, 2 H), 12.34 (bs, OH, exchangeable with D_2O); ^{13}C NMR [$(CD_3)_2SO$, 125 MHz] δ 55.87, 113.45, 118.60, 120.92, 123.84, 123.92, 126.45, 129.96, 140.83, 141.31, 148.06, 151.70, 155.55, 192.47; IR (thin film) 3745 (w), 3394 (broad w), 1643 (m), 1577 (s), 1517 (s), 1483 (s), 1342 (s), 1264 (m), 1184 (m), 1033 (m), 981 (s), 847 (m); CIMS m/z (relative intensity) 300 (MH^+, 100). Anal. Calcd for $C_{16}H_{13}NO_5$: C, 64.21; H, 4.38; N, 4.68. Found: C, 64.56; H, 4.24; N, 4.70.

2′-Hydroxy-4,5′-dimethoxychalcone (2b). *p*-Anisaldehyde (**7b**, 1.36 g, 10 mmol) and 2′-hydroxy-5′-methoxyacetophenone (**5a**, 1.66 g, 10 mmol) were dissolved in ethanol (15 mL). An aqueous solution of potassium hydroxide (1.12 g, 20 mmol) in water (5 mL) was added to the mixture under ice-cooling and stirring to yield a clear reddish-brown solution. The reaction mixture was kept at room temperature for 18 h and was then poured into ice–water and acidified with 3 N hydrochloric acid (11 mL). The acidic solution was extracted with ethyl acetate (4 × 80 mL). The combined organic layers were washed with saturated sodium chloride solution (50 mL), dried over $MgSO_4$, and filtered. Evaporation of ethyl acetate *in vacuo* gave the crude product as a pale-orange solid. Flash column chromatography (ethyl acetate in hexane, gradient elution 15–80%, silica gel 230–400 mesh) provided the desired chalcone **2b** as a bright-orange solid. Recrystallization of this crude product from ethanol gave bright-orange-red cubic crystals of **2b** (2.25 g, 79%): mp 87–89 °C; ^{1}H NMR [$(CD_3)_2$-CO, 500 MHz] δ 3.84 (s, 3 H), 3.87 (s, 3 H), 6.91 (d, J = 9.0 Hz, 1 H), 7.02 (d, J = 8.9 Hz, 2 H), 7.20 (dd, J = 9.0 Hz, 2.5 Hz, 1 H), 7.69 (d, J = 2.5 Hz, 1 H), 7.85 (d, J = 8.9 Hz, 2 H), 7.91 (d, J = 16.0 Hz, 1 H), 7.93 (d, J = 16.0 Hz, 1 H), 12.61 (bs, OH, exchangeable with D_2O); IR (thin film) 3745 (w), 3394 (broad w), 2938 (w), 2835 (w), 1641 (s), 1603 (s), 1566 (s), 1511 (s), 1486 (s), 1422 (m), 1358 (m), 1255 (s), 1169 (s), 1184 (m), 1020 (m), 981 (w), 827 (m); CIMS m/z (relative intensity) 285 (MH^+, 100). Anal. Calcd for $C_{17}H_{16}O_4$: C, 71.82; H, 5.67. Found: C, 71.50; H, 5.57.

2′-Hydroxy-3,4,5′-trimethoxychalcone (2c). Chalcone **2c** was synthesized from **5a** (0.830 g, 5 mmol) and **7c** (0.830 g, 5 mmol) using the procedure described above for **2b**. The product **2c** was obtained as a bright-red solid (1.14 g, 73%) after the purification of the crude product by flash column chromatography (ethyl acetate in hexane, gradient elution 15–60%, silica gel 230–400 mesh). The analytical sample was recrystallized from ethanol to afford bright-reddish needles of **2c**: mp 108–110 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.83 (s, 3 H), 3.88 (s, 3 H), 3.89 (s, 3 H), 6.91 (d, J = 8.9 Hz, 1 H), 7.04 (d, J = 8.5 Hz, 1 H), 7.21 (dd, J = 8.9 Hz, 3.0 Hz, 1 H), 7.43 (dd, J = 8.5, 2.5 Hz, 1 H), 7.55 (d, J = 2.5 Hz, 1 H), 7.66 (d, J = 3.0 Hz, 1 H), 7.89 (d, J = 15.5 Hz, 1 H), 7.91 (d, J = 15.5 Hz, 1 H), 12.59 (bs, OH, exchangeable with D_2O); IR (thin film) 3691 (w), 3384 (broad w), 2939 (w), 1641 (s), 1565 (s), 1510 (s), 1484 (s), 1420 (m), 1312 (m), 1265 (s), 1159 (s), 1140 (s), 1022 (s), 981 (w), 809 (m); CIMS m/z 315 (MH^+, 100). Anal. Calcd for $C_{18}H_{18}O_5$: C, 68.78; H, 5.77. Found: C, 68.88; H, 5.86.

4-Chloro-2′-hydroxy-5′-methoxychalcone (2d). Chalcone **2d** was synthesized from **5a** (1.66 g, 10 mmol) and **7e** (1.40 g, 10 mmol) using the procedure described above for **2b**. Chalcone **2d** was obtained as a bright-orange solid (2.10 g, 73%) after purification of the crude product by flash column chromatography (ethyl acetate in hexane, gradient elution 10–70%, silica gel 230–400 mesh). The analytical sample was recrystallized from ethanol to afford **2d** as dark-reddish-orange needles: mp 110–112 °C; ^{1}H NMR [$(CD_3)_2CO$, 500 MHz] δ 3.84 (s, 3 H), 6.93 (d, J = 9.0 Hz, 1 H), 7.22 (dd, J = 9.0 Hz, 3.0 Hz, 1 H), 7.50 (d, J = 8.9 Hz, 2 H), 7.70 (d, J = 3.0 Hz, 1 H), 7.90 (d, J = 15.5 Hz, 1 H), 8.01 (d, J = 8.9 Hz, 2 H), 8.10 (d, J = 15.5 Hz, 1 H), 12.65 (bs, OH, exchangeable with D_2O); IR (thin film) 3745 (w), 3278 (broad w), 2940 (w), 2835 (w), 1647 (s), 1578 (s), 1566 (s), 1486 (s), 1405 (w), 1262 (s), 1178 (s), 1089 (m), 1036 (m), 1017 (m), 981 (w), 822 (s); CIMS m/z 289 (MH^+, 100). Anal. Calcd for $C_{16}H_{13}ClO_3$: C, 66.56; H, 4.54; Cl, 12.28. Found: C, 66.20; H, 4.30; Cl, 12.39.

4-Carboxy-2′-hydroxy-5′-methoxychalcone (2e). Chalcone **2e** was synthesized from **5a** (1.66 g, 10 mmol) and **7f** (1.64 g, 10 mmol) using the procedure described above for **2b**. The purification of the crude product was done by flash column chromatography (ethyl acetate–hexane, gradient elution 40–80%, silica gel 230–400 mesh), which provided **2e** as a bright-orange solid (1.75 g, 59%). The analytical sample was recrystallized from ethanol and water to afford **2e** as bright-reddish-orange needles: mp 246–248 °C; ^{1}H NMR [$(CD_3)_2SO$, 500 MHz] δ 3.80 (s, 3 H), 6.95 (d, J = 9.0 Hz, 1 H), 7.21 (dd, J = 9.0 Hz, 3 Hz, 1 H), 7.62 (d, J = 3.0 Hz, 1 H), 7.84 (d, J = 15.5 Hz, 1 H), 7.98 (d, J = 8.9 Hz, 2 H), 8.02 (d, J = 8.9 Hz, 2 H), 8.10 (d, J = 15.5 Hz, 1 H), 12.65 (bs, OH, exchangeable with D_2O); IR (thin film) 3785 (w), 3278 (broad m), 2874 (w), 2835 (w), 1679 (s), 1676 (s), 1581 (s), 1484 (s), 1425 (m), 1266 (s), 1184 (s), 1079 (m), 1036 (w), 1017 (w), 981 (w), 833 (w); CIMS m/z 299 (MH^+, 100). Anal. Calcd for $C_{17}H_{14}O_5$: C, 68.45; H, 4.73. Found: C, 68.12; H, 4.60.

4-Acetamido-2′-hydroxy-5′-methoxychalcone (2f). Starting materials **5a** (0.830 g, 5 mmol) and **7g** (0.815 g, 5 mmol) were dissolved in ethanol (15 mL). An aqueous solution of potassium hydroxide (1.12 g, 20 mmol) in water (5 mL) was added to the mixture under ice cooling with stirring to yield a clear reddish brown solution. The reaction mixture was kept at room temperature for 18 h and was then poured into ice–water and acidified with 3 N hydrochloric acid until the pH was 7. The solution was extracted with ethyl acetate (5 × 35 mL). The combined organic layer was washed with brine (50 mL), dried over $MgSO_4$, and filtered. Evaporation of ethyl acetate *in vacuo* provided the crude product **2f** as a pale-orange solid. The purification of the crude product was done by flash column chromatography (ethyl acetate in toluene, gradient elution 0–40%, silica gel 230–400 mesh) which gave **2f** as bright-orange solid (0.89 g, 58%): mp 164–166 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.10 (s, 3 H), 3.84 (s, 3 H), 6.92 (d, J = 9.0 Hz, 1 H), 7.20 (dd, J = 9.0 Hz, 2.9 Hz, 1 H), 7.69 (d, J = 3.0 Hz, 1 H), 7.75 (d, J = 9.0 Hz, 2 H), 7.82 (d, J = 9.0 Hz, 2 H), 7.84 (bs, NHC(O), exchangeable with D_2O), 7.88 (d, J = 15.5 Hz, 1 H), 7.95 (d, J = 15.5 Hz, 1 H), 11.80 (bs, OH, exchangeable with D_2O); IR (thin film) 3682 (w), 3316 (broad w), 2943 (w), 2868 (w), 1675 (m), 1640 (m), 1572 (s), 1529 (s), 1487 (s), 1411 (m), 1365 (m), 1318 (s), 1267 (s), 1142 (s), 1019 (m), 829 (m); CIMS m/z 312 (MH^+, 100). Anal. Calcd for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.35; H, 5.43; N, 4.78.

2′-Hydroxy-3,4,5,5′-tetramethoxychalcone (2g). Chalcone **2g** was synthesized from **5a** (0.830 g, 5 mmol) and **7d** (0.98 g, 5 mmol) using the procedure described above for **2b**. Chalcone **2g** was obtained as a dark-red solid, (1.18 g, 69%) after the purification of the crude product by flash column chromatography (ethyl acetate–hexane, gradient elution 20–70%, silica gel 230–400 mesh). The analytical sample was recrystallized from ethanol to afford small dark-brick-red

needles: mp 128–129 °C; ^{1}H NMR [$(CD_3)_2CO$, 500 MHz] δ 3.80 (s, 3 H), 3.84 (s, 3 H), 3.92 (s, 6 H), 6.94 (d, J = 8.9 Hz, 1 H), 7.23 (dd, J = 8.9 Hz, 3 Hz, 1 H), 7.25 (s, 2 H), 7.65 (d, J = 3.0 Hz, 1 H), 7.89 (d, J = 15.5 Hz, 1 H), 7.98 (d, J = 15.5 Hz, 1 H), 12.49 (bs, OH, exchangeable with D_2O); IR (thin film) 3278 (broad w), 2940 (w), 2837 (w), 1642 (s), 1580 (s), 1503 (s), 1488 (s), 1419 (m), 1326 (m), 1262 (s), 1178 (s), 1153 (m), 1127 (s), 1044 (m), 1020 (m), 929 (w), 828 (s); CIMS m/z 345 (MH^+, 100). Anal. Calcd for $C_{19}H_{20}O_6$: C, 66.27; H, 5.85. Found: C, 68.38; H, 6.03.

3,4-Bis(benzyloxy)-2′-hydroxy-4′-methoxychalcone (2h). Chalcone **2h** was synthesized from **5b** (0.830 g, 5 mmol) and **7h** (1.59 g, 5 mmol) using the procedure described above for **2b**. The resulting chalcone **2g** was obtained as a pale yellow solid (1.60 g, 69%) after purification of the crude product by flash column chromatography (ethyl acetate–hexane, gradient elution 10–45%, silica gel 230–400 mesh). The analytical sample was recrystallized from ethanol to afford **2h** as yellow needles: mp 124–126 °C; ^{1}H NMR [$(CD_3)_2CO$, 500 MHz] δ 3.88 (s, 3 H), 5.25 (s, 4 H), 6.46 (m, 1 H), 6.52 (dt, J = 9.0 Hz, 3.0 Hz, 1 H), 7.16 (d, J = 8.9 Hz, 1 H), 7.35 (m, 8 H), 7.52 (dd, J = 9.0 Hz, 2.0 Hz, 2 H), 7.55 (dd, J = 9.0 Hz, 2.0 Hz, 2 H), 7.67 (d, J = 2.0 Hz, 1 H), 7.82 (d, J = 2.0 Hz, 1 H), 8.12 (dd, J = 9.0 Hz, 2 Hz, 1 H), 13.36 (bs, OH, exchangeable with D_2O); IR (thin film) 2935 (w), 2862 (w), 1637 (s), 1575 (s), 1508 (s), 1435 (w), 1371 (m), 1261 (s), 1213 (s), 1129 (m), 1036 (m), 1020 (m), 959 (w), 848 (w); CIMS m/z 467 (MH^+, 100). Anal. Calcd for $C_{30}H_{26}O_5$: C, 77.24; H, 5.62. Found: C, 77.18; H, 5.63.

4-Chloro-2′-hydroxy-4′-methoxychalcone (2i). Chalcone **2i** was synthesized from **5b** (1.66 g, 10 mmol) and **7e** (1.40 g, 10 mmol) using the procedure described above for **2b**. The resulting chalcone **2i** was obtained as a bright-yellow solid (2.27 g, 80%) after the purification of the crude product by flash column chromatography (ethyl acetate in hexane, gradient elution 10-80%, silica gel 230–400 mesh). The analytical sample was recrystallized from ethanol to afford **2i** as yellow needles: mp 122–124 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.84 (s, OCH_3, 3 H), 6.46 (dd, J = 10.0 Hz, 2.5 Hz, 1 H), 6.48 (d, J = 2.5 Hz, 1 H), 7.38 (d, J = 8.9 Hz, 2 H), 7.52 (d, J = 15.5 Hz, 1 H), 7.56 (d, J = 8.9 Hz, 2 H), 7.78 (d, J = 10.0 Hz, 1 H), 7.81 (d, J = 15.5 Hz, 1 H), 13.36 (bs, OH, exchangeable with D_2O); IR (thin film) 3424 (broad w), 3031 (w), 2937 (w), 1633 (s), 1570 (s), 1508 (s), 1453 (m), 1441 (w), 1370 (m), 1260 (s), 1212 (s), 1128 (m), 1020 (m), 1017 (m), 960 (w), 844 (s); CIMS m/z 289 (MH^+, 100). Anal. Calcd for $C_{16}H_{13}ClO_3$: C, 66.56; H, 4.54; Cl, 12.28. Found: C, 66.34; H, 4.22; Cl, 12.45.

4-Chloro-2′-hydroxy-3′-methoxychalcone (2j). Chalcone **2j** was synthesized from **5c** (1.66 g, 10 mmol) and **7e** (1.40 g, 10 mmol) using the procedure described above for **2b**. Chalcone **2j** was obtained as a light-yellow solid (1.97 g, 69%) after purification of the crude product by flash column chromatography (ethyl acetate in hexane, gradient elution 10–70%, silica gel 230–400 mesh). The analytical sample was recrystallized from ethanol to afford as **2j** small light-yellow cubic crystals: mp 150–152 °C; ^{1}H NMR [$(CD_3)_2CO$, 500 MHz] δ 3.93 (s, 3 H), 6.95 (dd, J = 8.5 Hz, 1.5 Hz, 1 H), 7.48 (d, J = 8.9 Hz, 2 H), 7.69 (d, J = 1.5 Hz, 1 H), 7.72 (d, J = 15.5 Hz, 1 H), 7.81 (dd, J = 8.5 Hz, 1.5 Hz, 1 H), 7.84 (d, J = 8.9 Hz, 2 H), 7.91 (d, J = 15.5 Hz, 1 H), 13.36 (bs, OH, exchangeable with D_2O); IR (thin film) 3645 (w), 3333 (broad w), 3004 (w), 2935 (w), 1650 (s), 1587 (s), 1514 (m), 1489 (s), 1426 (s), 1328 (s), 1279 (s), 1188 (s), 1089 (m), 1034 (m), 1017 (m), 978 (m), 888 (w), 811 (s), 764 (s); CIMS m/z 289 (MH^+, 100). Anal. Calcd for $C_{16}H_{13}ClO_3$: C, 66.56; H, 4.54; Cl, 12.28. Found: C, 66.29; H, 4.24; Cl, 12.39.

4-Acetamido-2′-hydroxy-4′-methoxychalcone (2k). Compounds **5b** (0.830 g, 5 mmol) and **7g** (0.815 g, 5 mmol) were dissolved in ethanol (15 mL). An aqueous solution of potassium hydroxide (1.12 g, 20 mmol) in water (5 mL) was added to the mixture under ice cooling and stirring to yield a clear reddish-brown solution. The reaction mixture was allowed to react at room temperature for 18 h and was then poured into ice–water and acidified with 3 N hydrochloric acid until the pH was maintained at 7. The acidic solution was extracted with ethyl acetate (5 × 35 mL). The combined organic layers were washed with saturated sodium chloride solution (50 mL). The washed organic layers were combined, dried over $MgSO_4$, and filtered. Evaporation of ethyl acetate *in vacuo* gave the crude product **2k** as an orange solid. Flash column chromatography (ethyl acetate–toluene, gradient elution 0–40%, silica gel 230–400 mesh) gave the desired chalcone **2k** as an orange solid (0.78 g, 56%): mp 200–202 °C; ^{1}H NMR [$(CD_3)_2CO$, 500 MHz] δ 2.10 (s, 3 H), 3.88 (s, 3 H), 6.46 (t, J = 2.0 Hz, 1 H), 6.52 (dt, J = 9.0 Hz, 2.0 Hz, 1 H), 7.75 (d, J = 15.5 Hz, 1 H), 7.81 (d, J = 15.5 Hz, 1 H), 7.84 (d, J = 9.0 Hz, 1 H), 7.87 (d, J = 8.9 Hz, 2 H), 7.86 (d, J = 8.9 Hz, 2 H), 9.40 (bs, NHC(O), exchangeable with D_2O), 13.62 (bs, OH, exchangeable with D_2O); low resolution CIMS m/z 312 (MH^+, 100). Anal. Calcd for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.04; H, 5.58; N, 4.58.

2′-Hydroxy-4-methoxy-5′-methylchalcone (2l). Chalcone **2l** was synthesized from **5d** (1.50 g, 10 mmol) and **7b** (1.36 g, 10 mmol) using the procedure described above for 2′-hydroxychalcone **2b**. Chalcone **2l** was obtained as a very pale orange solid (1.55 g, 59%) after purification of the crude product by flash column chromatography (ethyl acetate in hexane, gradient elution 10–65%, silica gel 230–400 mesh). The analytical sample was recrystallized from ethanol and hexane to yield **2l** as fine light-orange needles: mp 92–94 °C; ^{1}H NMR [$(CD_3)_2CO$, 500 MHz] δ 2.33 (s, 3 H), 3.88 (s, 3 H), 6.88 (d, J = 8.0 Hz, 1 H), 7.03 (d, J = 8.9 Hz, 2 H), 7.38 (dd, J = 8.0 Hz, 2 Hz, 1 H), 7.84 (d, J = 8.9 Hz, 2 H), 7.90 (d, J = 15.5 Hz, 1 H), 7.95 (d, J = 15.5 Hz, 1 H), 8.10 (d, J = 2.0 Hz, 1 H), 12.85 (bs, OH, exchangeable with D_2O); IR (thin film) 3755 (w), 3178 (broad w), 2935 (w), 2838 (w), 1640 (s), 1604 (s), 1564 (s), 1512 (s), 1487 (s), 1423 (m), 1408 (w), 1345 (m), 1257 (s), 1169 (s), 1028 (m), 1017 (m), 982 (w), 825 (s), 805 (s); CIMS m/z 269 (MH^+, 100). Anal. Calcd for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01. Found: C, 76.39; H, 5.96.

4-Chloro-2′-hydroxy-5′-methylchalcone (2m). Chalcone **2m** was synthesized from **5d** (1.50 g, 10 mmol) and **7e** (1.40 g, 10 mmol) using the procedure described above for **2b**. Chalcone **2m** was obtained as a bright-yellow solid (2.00 g, 7.37 mmol, 74%) after purification of the crude product by flash column chromatography (ethyl acetate in hexane, gradient elution 10–70%, silica gel 230–400 mesh). The analytical sample was recrystallized from ethanol and hexane to yield **2m** as yellow needles: mp 154–156 °C; ^{1}H NMR [$(CD_3)_2CO$, 500 MHz] δ 2.33 (s, 3 H), 6.90 (d, J = 8.5 Hz, 1 H), 7.41 (dd, J = 8.5 Hz, 2.5 Hz, 1 H), 7.52 (d, J = 8.9 Hz, 2 H), 7.90 (d, J = 15.5 Hz, 1 H), 7.92 (d, J = 8.9 Hz, 2 H), 8.11 (d, J = 2.5 Hz, 1 H), 8.12 (d, J = 15.5 Hz, 1 H), 12.65 (bs, OH, exchangeable with D_2O); IR (thin film) 3354 (broad w), 2995 (w), 2873 (w), 1645 (s), 1577 (s), 1564 (s), 1489 (s), 1404 (w), 1364 (w), 1262 (m), 1178 (s), 1089 (m), 1024 (m), 1009 (m), 981 (w), 817 (s); CIMS m/z 273 (MH^+, 100). Anal. Calcd for $C_{16}H_{13}ClO_2$: C, 70.46; H, 4.80. Found: C, 70.84; H, 5.02.

(*Z*)-4,5-Dimethoxy-(4′-nitrobenzylidene)benzofuran-3(2*H*)-one (3a). The chalcone **2a** (0.093 g, 0.301 mmol) was dissolved in methanol (50 mL) and TTN (thallium nitrate trihydrate, 0.399 g, 0.900 mmol) was added at room temperature. The reaction mixture was stirred for an additional 15 min, and then 3 N hydrochloric acid (3 mL) was added to yield a small amount of yellow precipitate. The reaction mixture heated at reflux for 10 h. The solvent was distilled off and the orange-brown residue was redissolved in a mixture of ethyl acetate and brine. The mixture was extracted with ethyl acetate (3 × 45 mL). The combined ethyl acetate extracts were washed with saturated aqueous sodium carbonate (2 × 60 mL) and brine (25 mL). The washed organic layers were combined, dried over Na_2SO_4, and filtered. Evaporation of ethyl acetate *in vacuo* gave the crude product as a pale yellow solid. Preparative thin layer chromatography (double elution, ethyl acetate:hexane 2:5 by volume, silica gel uniplate, 1000 μm) gave the desired product **3a** (0.095 g, 60%). Recrystallization of this crude product from ethanol gave bright orange-red needles which were subsequently used for X-ray crystallography determination:[29] mp 193–196 °C; ^{1}H NMR [$(CD_3)_2CO$, 500 MHz] δ 3.87 (s, 3 H), 4.14 (s, 3 H), 6.85 (s, 1 H), 7.08 (d, J = 8.5 Hz, 1 H), 7.47 (d, J = 8.5 Hz, 1 H), 8.23 (d, J = 8.9 Hz, 2 H), 8.33 (d, J = 8.9 Hz, 2 H); ^{13}C NMR [$(CD_3)_2SO$, 125

MHz] δ 57.14, 61.78, 105.99, 107.79, 112.88, 123.19, 123.87, 131.66, 138.69, 146.91, 147.38, 148.46, 159.05, 181.33; IR (thin film) 2979 (w), 2838 (w), 1706 (s), 1654 (m), 1616 (s), 1517 (s), 1498 (s), 1350 (w), 1258 (s), 1162 (m), 1053 (s), 1027 (m), 827 (m), 798 (w); CIMS *m/z* 328 (MH^+, 100).

(*Z*)-(4′-Methoxybenzylidene)-4,5-dimethoxybenzofuran-3(2*H*)-one (3b). Aurone **3b** was synthesized from **2b** (0.142 g, 0.5 mmol) using the procedure described above for **3a** and was obtained as a very bright-yellow solid (0.0842 g, 54%) after purification of the crude product by preparative thin layer chromatography (double elution, ethyl acetate:hexane, 2:5 by volume, silica gel uniplate, 1000 μm): mp 153–155 °C; ^1H NMR [$(CD_3)_2CO$, 500 MHz] δ 3.85 (s, 3 H), 3.87 (s, 3 H), 4.12 (s, 3 H), 6.74 (s, 1 H), 7.04 (d, *J* = 8.5 Hz, 1 H), 7.06 (d, *J* = 8.9 Hz, 2 H), 7.42 (d, *J* = 8.5 Hz, 1 H), 7.93 (d, *J* = 8.9 Hz, 2 H); IR (thin film) 2930 (w), 2848 (w), 1697 (s), 1648 (m), 1601 (s), 1513 (s), 1498 (s), 1350 (w), 1258 (s), 1082 (m), 1053 (s), 1027 (w), 827 (w), 798 (w); CIMS *m/z* 313 (MH^+, 100). Anal. Calcd for $C_{18}H_{16}O_5$: C, 69.22; H, 5.16. Found: C, 68.86; H, 5.23.

(*Z*)-(3′,4′-Dimethoxybenzylidene)-4,5-dimethoxybenzofuran-3(2*H*)-one (3c). Aurone **3c** was synthesized from **2c** (0.102 g, 0.299 mmol) using the procedure described above for aurone **3a**. The resulting **3c** was obtained as a yellow solid (0.068 g, 40%) after preparative thin layer chromatography (double elution, ethyl acetate:hexane, 2:5 by volume, silica gel uniplate, 1000 μm). The analytical sample was recrystallized from ethanol and hexane to afford **3c** as small light-yellow needles: mp 148–149 °C; ^1H NMR [$(CD_3)_2CO$, 500 MHz] δ 3.87 (s, 3 H), 3.90 (s, 3 H), 3.92 (s, 3 H), 4.14 (s, 3 H), 6.75 (s, 1 H), 7.07 (d, *J* = 9.0 Hz, 1 H), 7.09 (d, *J* = 9.0 Hz, 1 H), 7.44 (d, *J* = 9.0 Hz, 1 H), 7.57 (dd, *J* = 8.9 Hz, 2 Hz, 1 H), 7.64 (d, *J* = 2.0 Hz, 1 H); CIMS *m/z* 343 (MH^+, 100); high resolution EIMS (isobutane) calcd for $C_{19}H_{18}O_6$: *m/z* 342.1103; found: 342.1092. Anal. Calcd for $C_{19}H_{18}O_6$: C, 66.66; H, 5.30. Found: C, 66.57; H, 5.53.

(*Z*)-(4′-Chlorobenzylidene)-4,5-dimethoxybenzofuran-3(2*H*)-one (3d). A. From **2d**. Aurone **3d** was synthesized from **2d** (0.200 g, 0.694 mmol) using the procedure described above for **3a**. Aurone **3d** was obtained as a very dark-orange solid (0.157 g, 72%) after purification of the crude product by preparative thin layer chromatography (double elution, ethyl acetate:hexane, 1:4 by volume, silica gel uniplate, 1000 μm). The analytical sample was recrystallized from ethanol to afford **3d** as dark-orange needles: mp 113–115 °C; ^1H NMR[$(CD_3)_2CO$, 500 MHz] δ 3.80 (s, 3 H), 4.04 (s, 3 H), 6.83 (s, 1 H), 7.12 (d, *J* = 9.0 Hz, 1 H), 7.47 (d, *J* = 9.0 Hz, 1 H), 7.55 (d, *J* = 8.9 Hz, 2 H), 7.96 (d, *J* = 8.9 Hz, 2 H); CIMS *m/z* 317 (MH^+, 100). Anal. Calcd for $C_{17}H_{13}ClO_4$: C, 64.47; H, 4.14; Cl, 11.14. Found: C, 64.35; H, 4.04; Cl, 11.20.

B. From **16a**. Compound **16a** (0.080 g, 0.228 mmol) was dissolved in methanol (50 mL), and TTN (0.121 g, 0.273 mmol) was added at room temperature. The reaction mixture was stirred for an additional 15 min, and then 3 N hydrochloric acid (3 mL) was added to yield a small amount of yellow precipitate. The reaction mixture was heated at reflux for 10 h. The solvent was distilled off, and the orange residue was redissolved in a mixture of ethyl acetate and brine. The resultant mixture was extracted with ethyl acetate (3 × 20 mL). The combined ethyl acetate extracts were washed with saturated aqueous sodium carbonate (2 × 20 mL) and brine (15 mL). The washed organic layers were combined, dried over Na_2SO_4, and filtered. Evaporation of ethyl acetate *in vacuo* gave the crude product as a pale-orange solid. Pure (*Z*)-(4′-chlorobenzylidene)-4,5-dimethoxybenzofuran-3(2*H*)-one (**3d**) was obtained as very dark-orange solid (0.055 g, 77%) after the purification of the crude product by preparative thin layer chromatography (double elution, ethyl acetate:hexane, 1:4 by volume, silica gel uniplate, 1000 μm). Satisfactory mp and spectral data were obtained.

(*Z*)-[4′-(Methoxycarbonyl)benzylidene]-4,5-dimethoxybenzofuran-3(2*H*)-one (3e). A. From **2e**. Aurone **3e** was synthesized from **2e** (0.089 g, 0.299 mmol) using the procedure described above for **3a**. Aurone **3e** was obtained as a bright-orange solid (0.065 g, 64%) after purification of the crude product by preparative thin layer chromatography (double elution, ethyl acetate:hexane 1:4 by volume, silica gel uniplate, 1000 μm). The analytical sample was recrystallized from ethanol to give orange needles: mp 190–191 °C; ^1H NMR [$(CD_3)_2CO$, 500 MHz] δ 3.88 (s, 3 H), 3.90 (s, 3 H), 4.13 (s, 3 H), 6.79 (s, 1 H), 7.08 (d, *J* = 8.0 Hz, 1 H), 7.46 (d, *J* = 8.0 Hz, 1 H), 8.08 (s, 4 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 52.25, 57.65, 62.59, 105.33, 110.05, 122.38, 129.38, 130.27, 130.89, 136.84, 147.36, 148.34, 160.12, 166.54, 182.33; IR (thin film) 2930 (w), 2848 (w), 1721 (s), 1702 (s), 1652 (m), 1604 (s), 1503 (s), 1439 (m), 1286 (m), 1263 (s), 1129 (m), 1054 (s), 1027 (w), 965 (w), 797 (w); CIMS *m/z* 341 (MH^+, 100). Anal. Calcd for $C_{19}H_{16}O_6$: C, 67.05; H, 4.73. Found: C, 66.70; H, 4.70.

B. From **3e** and **22**. The mixture of *E* and *Z* isomers of [4′-(methoxycarbonyl)benzylidene]-4,5-dimethoxybenzofuran-3(2*H*)-one (**3e** and **22**) (0.090 g, 0.284 mmol) was dissolved in methanol (50 mL) and TTN (0.151 g, 0.341 mmol) was added at room temperature. The reaction mixture was stirred for an additional 15 min, and then 3 N hydrochloric acid (3 mL) was added to yield a small amount of yellow precipitate. The reaction mixture was heated at reflux for 10 h. The solvent was distilled off, and the orange residue was redissolved in a mixture of ethyl acetate and brine. The resultant mixture was extracted with ethyl acetate (3 × 30 mL). The combined ethyl acetate extracts were washed with saturated aqueous sodium carbonate (2 × 60 mL) and brine (25 mL). The washed organic layers were combined, dried over Na_2SO_4, and filtered. Evaporation of ethyl acetate *in vacuo* gave the crude product as a pale-yellow solid. Purification of the crude product by preparative thin layer chromatography (double elution, ethyl acetate:hexane, 2:5 by volume, silica gel uniplate, 1000 μm) gave exclusively [4′-(methoxycarbonyl)benzylidene]-4,5-dimethoxybenzofuran-3(2*H*)-one (**3e**, 0.087 g, 98%). Satisfactory mp and spectral data were obtained.

(*Z*)-(4′-Aminobenzylidene)-4,5-dimethoxybenzofuran-3(2*H*)-one (3f). Aurone **3f** was synthesized from **2f** (0.093 g, 0.299 mmol) using the procedure described above for **3a**. The resulting aurone **3f** was obtained as a light-yellow solid (0.048 g, 56%) after purification of the crude product by preparative thin layer chromatography (double elution, ethyl acetate:hexane:triethylamine 1:4:0.1 by volume, silica gel uniplate, 1000 μm). The analytical sample was recrystallized from ethanol to afford **3f** as small light-yellow needles: ^1H NMR [$(CD_3)_2CO$, 500 MHz] δ 2.50 (bs, exchangeable with D_2O), 3.84 (s, 3 H), 4.10 (s, 3 H), 6.68 (s, 1 H), 6.76 (d, *J* = 8.9 Hz, 2 H), 7.02 (d, *J* = 8.0 Hz, 1 H), 7.38 (d, *J* = 8.0 Hz, 1 H), 7.73 (d, *J* = 8.9 Hz, 2 H); ^{13}C NMR [$(CD_3)_2SO$, 125 MHz] δ 57.24, 61.76, 106.18, 113.93, 114.10, 114.41, 119.14, 122.46, 133.67, 144.24, 146.64, 146.92, 151.52, 158.78, 180.50; IR (KBr) 3360, 2924, 2360, 1685, 1581, 1517, 1437, 1362, 1251, 1156, 1051, 966, 805 cm^{-1}; CIMS *m/z* 298 (MH^+, 100); high resolution CIMS calcd for $C_{17}H_{15}NO_4$: *m/z* 298.1079 (MH^+); found *m/z* 298.1064 (MH^+).

(±)-6-[3′-(4-Chlorophenyl)-1′-hydroxy-2′(*E*)-propenylene]-4,4,5-trimethoxycyclohex-2-enone (16a). A dry argon-flushed 100 mL round-bottomed flask fitted with a magnetic stirrer and a septum cap was charged with chalcone **2d** (0.100 g, 0.347 mmol) and dry methanol (15 mL). The mixture was stirred and cooled at −3 °C for 20 min, and a solution of phenyliodonium bis(trifluoroacetate) (PIFA, 0.223 g, 0.520 mmol) in dry acetonitrile (10 mL) was added by syringe over 5 min under argon. The solution turned reddish-yellow and then yellow in color upon addition of PIFA. The reaction mixture was stirred for 20 min. Evaporation of solvents (methanol and acetonitrile) gave a dark-yellow oil which was purified by preparative thin layer chromatography (double elution, ethyl acetate:hexane, 1:4 by volume, silica gel uniplate, 1000 μm) to give a yellow solid (0.080 g, 67%). The analytical sample was recrystallized from ethyl acetate/hexane to afford **16a** as an orange solid: ^1H NMR [$(CD_3)_2CO$, 500 MHz] δ 3.19 (s, 3 H), 3.24 (s, 1.5 H), 3.25 (s, 1.5 H), 3.36 (s, 1.5 H), 3.363 (s, 3 H), 4.80 (d, *J* = 1.0 Hz, 2 H), 6.15 (d, *J* = 8.0 Hz, 0.5 H), 6.17 (d, *J* = 8.0 Hz, 0.5 H), 6.28 (d, *J* = 8.0 Hz, 0.25 H), 6.65 (d, *J* = 8.0 Hz, 0.5 H), 6.67 (d, *J* = 8.0 Hz, 0.5 H), 7.01 (dd, *J* = 8.0 Hz, 3.5 Hz, 0.25 H), 7.24 (d, *J* = 16.0 Hz, 0.25 H), 7.31 (d, *J* = 3.5 Hz, 0.5 H), 6.65 (d, *J* = 8.0 Hz, 0.5 H), 7.42 (d, *J* = 8.9 Hz, 2 H), 7.48 (d, *J* = 16.0 Hz, 0.25 H), 7.51 (d, *J* = 16.0

Hz, 0.25 H), 7.58 (d, J = 16.0 Hz, 0.25 H), 7.70 (d, J = 16.0 Hz, 0.5 H), 7.73 (d, J = 16.0 Hz, 0.25 H), 7.76 (d, J = 16.0 Hz, 0.25 H), 7.79 (d, J = 8.9 Hz, 2 H), 15.86 (s, exchangeable with D_2O), 15.87 (s, exchangeable with D_2O). The fractional ^1H NMR proton integrals are due to the presence of a mixture of tautomers (Scheme 6). CIMS m/z 351 (MH^+, 100).

(±)-6-[3'-(4-Chlorophenyl)-1'-hydroxy-2'(*E*)-propenylene]-5-ethoxy-4,4-dimethoxycyclohex-2-enone (16b). A dry argon-flushed 100 mL round-bottomed flask fitted with a magnetic stirrer and a septum cap was charged with chalcone **2d** (0.100 g, 0.347 mmol) and dry methanol (15 mL). The mixture was stirred and cooled at −5 °C for 20 min, and a solution of phenyliodonium bis(trifluoroacetate) (PIFA, 0.223 g, 0.520 mmol) in dry acetonitrile (10 mL) was added by syringe over 5 min under argon. The solution turned reddish-yellow and then yellow in color. The reaction mixture was stirred for 20 min. Evaporation of solvents (methanol and acetonitrile) gave a dark-yellow oil. Thin layer chromatography (triple elution, ethyl acetate:hexane , 2:10 by volume, silica gel uniplate, 1000 μm) gave a yellow solid (0.078 g, 62%). The solid was recrystallized from ethanol to afford **16b** as light-yellow needles which were subsequently used for X-ray crystallographic analysis:[29] ^1H NMR [$(CD_3)_2CO$, 500 MHz] δ 1.08 (t, J = 7.0 Hz, 1 H), 1.09 (t, J = 7.0 Hz, 1 H), 3.19 (s, 3 H), 3.37 (s, 3 H), 3.46 (m, 2 H), 4.86 (m, 1 H), 6.15 (d, J = 8.0 Hz, 0.5 H), 6.16 (d, J = 8.0 Hz, 0.5 H), 6.64 (d, J = 8.0 Hz, 0.5 H), 6.66 (d, J = 8.0 Hz, 0.5 H), 7.42 (d, J = 8.9 Hz, 2 H), 7.45 (d, J = 16 Hz, 0.5 H), 7.49 (d, J = 16.0 Hz, 0.5 H), 7.67 (d, J = 16.0 Hz, 0.5 H), 7.74 (d, J = 16.0 Hz, 0.5 H), 7.78 (d, J = 8.9 Hz, 2 H), 15.86 (s, exchangeable with D_2O), 15.87 (s, exchangeable with D_2O). The fractional ^1H NMR proton integrals are due to the presence of a mixture of tautomers (Scheme 6). IR (thin film) 3424 (broad w), 2973 (w), 2939 (w), 1630 (s), 1574 (s), 1491 (w), 1406 (m), 1283 (m), 1137 (m), 1089 (s), 1055 (w), 1012 (w), 971 (w), 797 (w); CIMS m/z 365 (MH^+, 100). Anal. Calcd for $C_{19}H_{21}ClO_5$: C, 62.55; H, 5.80. Found: C, 62.25; H, 5.69.

General Procedure for Photoisomerization. Preparative photoisomerizations were carried out in a photoreactor using a medium pressure Canrad-Hanovia 450-W Hg lamp (Model 679A-36) encased with a uranium yellow filter transmitting wavelengths greater than 330 nm. Samples were irradiated 6 cm from the light source in a cylindrical tube maintained at 20−23 °C with a Neslab Endocal refrigerated circulating bath. The solvent was benzene deoxygenated by passing nitrogen gas through it for 20 min. The solution was stirred during irradiation by bubbling nitrogen gas through it.

Photoisomerization of (*Z*)-[4'-(Methoxycarbonyl)benzylidene]-4,5-dimethoxybenzofuran-3(2*H*)-one (3e) into the Mixture of *E* and *Z* Isomers of [4'-(Methoxycarbonyl)benzylidene]-4,5-dimethoxybenzofuran-3(2*H*)-one (22 and 3e). Aurone **3e** (100 mg, 0.316 mmol) was dissolved in deoxygenated anhydrous benzene (150 mL) and irradiated for 10 h under the conditions mentioned above. Evaporation of the solvent *in vacuo* gave the inseparable mixture of isomers **22** and **3e** in 1:1 ratio: ^1H NMR [$(CD_3)_2CO$, 500 MHz] δ 3.85 (s, 3 H, *E*-isomer), 3.86 (s, 3 H, *Z*-isomer), 3.89 (s, 3 H, *E*-isomer), 3.90 (s, 3 H, *Z*-isomer), 4.08 (s, 3 H, *E*-isomer), 4.13 (s, 3 H, *Z*-isomer), 6.78 (s, 1 H, *Z*-isomer), 6.91 (d, J = 8 Hz, 1 H, *E*-isomer), 7.01 (s, 1 H, *E*-isomer), 7.07 (d, J = 8 Hz, 1 H, *Z*-isomer), 7.43 (d, J = 8 Hz, 1 H, *E*-isomer), 7.46 (d, J = 8 Hz, 1 H, *Z*-isomer), 8.02 (d, J = 8.9 Hz, 2 H, *E*-isomer), 8.08 (s, 4 H, *Z*-isomer), 8.25 (d, J = 8.9 Hz, 2 H, *E*-isomer).

7-Methoxy-3',4'-bis(benzyloxy)isoflavone (23). Chalcone **2h** (0.233 g, 0.500 mmol) was dissolved in methanol (60 mL) and TTN (thallium nitrate trihydrate, 0.333 g, 0.750 mmol) was added at room temperature. The reaction mixture was stirred for 15 min, and then 3 N hydrochloric acid (3 mL) was added to yield a small amount of yellow precipitate. The reaction mixture was heated at reflux for 12 h. The solvent is distilled off and the orange-brown residue was redissolved in a mixture of ethyl acetate and brine. The mixture was extracted with ethyl acetate (3 × 45 mL). The combined organic layers were washed with saturated aqueous sodium carbonate (2 × 60 mL) and brine (25 mL). The organic layers were combined and dried over Na_2SO_4. Evaporation of ethyl acetate gave the crude product as a pale-yellow solid. The purification of the resulting crude product was done by preparative thin layer chromatography (double elution, ethyl acetate:hexane 2:3 by volume, silica gel uniplate, 1000 μm) which gave the desired isoflavone **23** (0.157 g, 69%). Recrystallization of this crude product from ethanol gave dark-yellow needles of **23**: mp 146−148 °C; ^1H NMR [$(CD_3)_2CO$, 500 MHz] δ 3.96 (s, 3 H), 5.20 (s, 2 H), 5.21 (s, OCH_2Ph, 2 H), 7.06 (dd, J = 8.5 Hz, 2.5 Hz, 2 H), 7.11 (d, J = 8.5 Hz, 1 H), 7.19 (dd, J = 8.5 Hz, 2.5 Hz, 1 H), 7.34 (m, 6 H), 7.43 (d, J = 2.5 Hz, 1 H), 7.53 (m, 4 H), 8.10 (dd, J = 8.0 Hz, 3 Hz, 1 H) 8.24 (s, 1 H); IR (thin film) 2930 (w), 2848 (w), 1642 (s), 1625 (s), 1605 (m), 1567 (w), 1513 (s), 1453 (m), 1440 (s), 1380 (w), 1263 (s), 1203 (m), 1139 (m), 1024 (m), 940 (w), 856 (w), 737 (w); CIMS m/z 465 (MH^+, 100). Anal. Calcd for $C_{30}H_{24}O_5$: C, 77.57; H, 5.21. Found: C, 77.34; H, 5.28.

(*Z*)-(4'-Chlorobenzylidene)-4,5-diethoxybenzofuran-3(2*H*)-one (24a). Aurone **24a** was synthesized from **2d** (0.100 g, 0.347 mmol) using the procedure described above for **3a**, except that the solvent was ethanol and not methanol. The aurone **24a** was obtained as the major product. The yellow solid (0.079 g, 63%) was purified by preparative thin layer chromatography (double elution, ethyl acetate:hexane, 1:4 by volume, silica gel uniplate, 1000 μm): mp 154−156 °C; ^1H NMR [$(CD_3)_2CO$, 500 MHz] δ 1.36 (t, J = 7.0 Hz, 3 H), 1.37 (t, J = 7.0 Hz, 3 H), 4.09 (q, J = 7.0 Hz, 2 H), 4.41 (q, J = 7.0 Hz, 2 H), 6.73 (s, 1 H), 7.04 (d, J = 9.0 Hz, 1 H), 7.44 (d, J = 9.0 Hz, 1 H), 7.51 (d, J = 8.9 Hz, 2 H), 7.98 (d, J = 8.9 Hz, 2 H); IR (thin film) 2979 (w), 2868 (w), 1707 (s), 1654 (m), 1607 (s), 1497 (s), 1406 (m), 1296 (m), 1262 (s), 1156 (m), 1071 (m), 1017 (w), 874 (w), 820 (w); CIMS m/z 345 (MH^+, 100). Anal. Calcd for $C_{19}H_{17}ClO_4$: C, 66.19; H, 4.97. Found: C, 65.90; H, 5.03.

(*Z*)-(4'-Chlorobenzylidene)-4,5-dipropoxybenzofuran-3(2*H*)-one (24b). Aurone **24b** was synthesized from **2d** (0.100 g, 0.347 mmol) using the procedure described above for **3a**, except that the solvent was propanol and not methanol. The resulting yellow solid **24b** (0.061 g, 47%) was obtained as the major product after the purification of the crude product by preparative thin layer chromatography (double elution, ethyl acetate:hexane , 1:5 by volume, silica gel uniplate, 1000 μm): mp 108−110 °C; ^1H NMR [$(CD_3)_2CO$, 500 MHz] δ 1.03 (t, J = 7.0 Hz, 3 H), 1.05 (t, J = 7.0 Hz, 3 H), 1.77 (m, 2 H), 1.79 (m, 2 H), 3.97 (t, J = 7.0 Hz, 2 H), 4.32 (t, J = 7.0 Hz, 2 H), 6.70 (s, 1 H), 6.99 (d, J = 9.0 Hz, 1 H), 7.40 (d, J = 9.0 Hz, 1 H), 7.50 (d, J = 8.9 Hz, 2 H), 7.96 (d, J = 8.9 Hz, 2 H); IR (thin film) 2971 (w), 2937 (w), 2880 (w), 1703 (s), 1655 (m), 1609 (s), 1586 (m), 1488 (m), 1468 (m), 1285 (s), 1253 (s), 1162 (w), 1058 (m), 1031 (w), 958 (w), 872 (w), 801 (w); CIMS m/z 373 (MH^+, 100). Anal. Calcd for $C_{21}H_{21}ClO_4$: C, 67.65; H, 5.68; Cl, 9.51. Found: C, 67.41; H, 5.65; Cl, 9.80.

(*Z*)-(4'-Chlorobenzylidene)-4-ethoxy-5-methoxybenzofuran-3(2*H*)-one (25a). A. From **2d**. Aurone **25a** was synthesized from **2d** (0.100 g, 0.347 mmol) using the procedure described above for **3a**, except that the solvent was ethanol and not methanol. The resulting aurone **25a** was obtained as the minor product (0.021 g, 17%) after purification of the crude product by preparative thin layer chromatography (double elution, ethyl acetate:hexane, 2:10 by volume, silica gel uniplate, 1000 μm): mp 118−121 °C; ^1H NMR[$(CD_3)_2CO$, 500 MHz] δ 1.35 (t, J = 7.0 Hz, 3 H), 3.86 (s, 3 H), 4.41 (q, J = 7.0 Hz, 2 H), 6.73 (s, 1 H), 7.05 (d, J = 9.0 Hz, 1 H), 7.44 (d, J = 9.0 Hz, 1 H), 7.52 (d, J = 8.9 Hz, 2 H), 7.98 (d, J = 8.9 Hz, 2 H); IR (thin film) 2929 (w), 2848 (w), 1702 (s), 1654 (m), 1611 (s), 1493 (s), 1295 (m), 1257 (s), 1078 (m), 1049 (s), 1031 (w), 965 (w), 797 (w); CIMS m/z 331 (MH^+, 100). Anal. Calcd for $C_{18}H_{15}ClO_4$: C, 65.36; H, 4.57. Found: C, 65.42; H, 4.82.

B. From **16b**. Compound **16b** (0.060 g, 0.164 mmol) was dissolved in methanol (50 mL), and TTN (0.088 g, 0.196 mmol) was added at room temperature. The reaction mixture was stirred for an additional 15 min, and then 3 N hydrochloric acid (3 mL) was added to yield a small amount of yellow precipitate. The reaction mixture was heated at reflux for 10 h. The solvent was distilled off, and the orange residue was redissolved in a mixture of ethyl acetate and brine. The resultant mixture was extracted with ethyl acetate (3 × 15

mL). The combined ethyl acetate extracts were washed with saturated aqueous sodium carbonate (2 × 20 mL) and brine (15 mL). The washed organic layers were combined, dried over Na_2SO_4, and filtered. Evaporation of ethyl acetate *in vacuo* gave the crude product as yellow solid. Purification of the crude product by preparative thin layer chromatography (double elution, ethyl acetate:hexane, 2:5 by volume, silica gel uniplate, 1000 μm) gave (*Z*)-(4′-chloro benzylidene)-4-ethoxy-5-methoxybenzofuran-3(2*H*)-one (**25a**, 0.046 g, 87%). Satisfactory mp and spectral data were obtained.

(*Z*)-(4′-Chlorobenzylidene)-5-methoxy-4-(propyloxy)-benzofuran-3(2*H*)-one (25b). Aurone **25b** was synthesized from **2d** (0.100 g, 0.347 mmol) using the procedure described above for **3a**, except that the solvent was propanol and not methanol. The resulting aurone **25b** was obtained as the minor product (0.015 g, 10%) after purification of the crude product by preparative thin layer chromatography (double elution, ethyl acetate:hexane, 2:10 by volume, silica gel uniplate, 1000 μm): mp 102–103 °C; ^{1}H NMR [$(CD_3)_2CO$, 500 MHz] δ 1.03 (t, *J* = 7.0 Hz, 2 H), 1.75 (m, 3 H), 3.86 (s, 3 H), 4.32 (q, *J* = 7.0 Hz, 2 H), 6.72 (s, 1 H), 7.05 (d, *J* = 9.0 Hz, 1 H), 7.44 (d, *J* = 9.0 Hz, 1 H), 7.52 (d, *J* = 8.9 Hz, 2 H), 7.98 (d, *J* = 8.9 Hz, 2 H); CIMS *m*/*z* 345 (MH^+, 100). Anal. Calcd for $C_{19}H_{17}ClO_4$: C, 66.19; H, 4.97. Found: C, 65.90; H, 5.03.

(*Z*)-(4′-Chlorobenzylidene)-4,5-dimethoxy-7-nitrobenzofuran-3(2*H*)-one (32). Aurone **32** was synthesized from **2d** (0.100 g, 0.347 mmol) using the procedure described above for **3a**. The TTN utilized was from a new bottle purchased from Aldrich, and the highest yield of the product is reported. Aurone **32** was obtained as a dark-yellow solid (0.073 g, 57%) after purification of the crude product by preparative thin layer chromatography (double elution, ethyl acetate:hexane, 2:5 by volume, silica gel uniplate, 1000 μm). The analytical sample was recrystallized from ethanol to afford **32** as dark-yellow needles which were subsequently used for X-ray crystallography:[29] mp 242–244 °C; ^{1}H NMR [$(CD_3)_2CO$, 500 MHz] δ 3.91 (s, 3 H), 4.28 (s, 3 H), 7.07 (s, 1 H), 7.63 (d, *J* = 8.9 Hz, 2 H), 8.00 (s, 1 H) 8.11 (d, *J* = 8.9 Hz, 2 H); IR (thin film) 2948 (w), 2868 (w), 1703 (s), 1654 (m), 1605 (s), 1501 (s), 1428 (s), 1289 (m), 1263 (s), 1157 (m), 1064 (s), 1027 (w), 923 (w), 827 (w), 781 (w); CIMS *m*/*z* 362 (MH^+, 100). Anal. Calcd for $C_{17}H_{12}ClNO_6$: C, 56.45; H, 3.34; N, 3.87; Cl, 9.80. Found: C, 56.11; H, 3.13; N, 3.67; Cl, 9.92.

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Supporting Information Available: ^{1}H NMR spectra of compounds **3f**, **6**, **16b**, **8**, and a mixture of **22** and **3e** (22 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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