Tandem Claisen Condensation/Transesterification between Arylacetate Enolates and Arylmethylene-Substituted 2,2-Dimethyl-1,3-dioxolan-4-ones: An Improved Synthesis of *Z*-Configured Pulvinones

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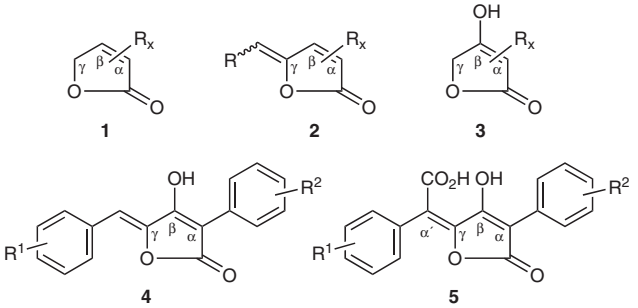
Abstract: Horner–Wadsworth–Emmons (HWE) alkenations of aromatic aldehydes with the novel phosphonate **24b** led to *E*-configured arylmethylene-substituted 2,2-dimethyl-1,3-dioxolan-4-ones **25a–f** (79–88% yield). The latter condensed with the lithium enolates of methyl arylacetates lithio-**20b–d** to give, after acid treatment and crystallization, isomerically pure (*Z*)-pulvinones **8d–s** in 75–91% yield. We also showed that Horner–Wadsworth–Emmons reactions between phosphonate **24b** and aliphatic aldehydes lead to *E*-configured alkylmethylene-substituted 2,2-dimethyl-1,3-dioxolan-4-ones **25g–i** (82–96% yield).

Key words: crossed Claisen condensation, Horner–Wadsworth–Emmons alkenation, O-protected α-hydroxyacrylates, α-oxocarboxylates, stereoselective synthesis

α,β-Unsaturated γ-lactones (Δ^3-butenolides, **1**, Scheme 1) are encountered in many natural products.[1] A subclass of these compounds contains an alkylidene substituent at Cγ (γ-alkylidene-Δ^3-butenolides,[2] **2**) and in another subclass, a hydroxy group at Cβ (tetronic acids,[3] **3**). Several dyes from fungi combine the aforementioned structural features and are arylated at Cα, namely the pulvinones **4**;[4] accordingly, they constitute γ-(arylmethylene)butenolides with α-aryl and β-hydroxy groups, or tetronic acids with α-aryl and γ-(arylmethylene) substituents. Pulvinones with an additional carboxy group at Cα′ of the (arylmethylene) substituent are classified separately as pulvinic acids **5**.[5]



Scheme 1 Structural survey of Δ^3-butenolides **1**: γ-alkylidene-Δ^3-butenolides **2**, tetronic acids **3**, pulvinones **4**, and pulvinic acids **5**.

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The most straightforward published access to pulvinones proceeds via the enol[6] **6** of a triketone; such triketones are accessible by condensing[7] 1,3-diarylacetones[8] with diethyl oxalate (Scheme 2). The key step of this synthesis is the thermal [1,3]-sigmatropic rearrangement of enol **6**, as described by Campbell et al.;[9] it provided pulvinone **8b** in 77% yield. However, the symmetry of the triketone tautomer of enol **6** limits this approach to the synthesis of pulvinones with two identical aryl groups.

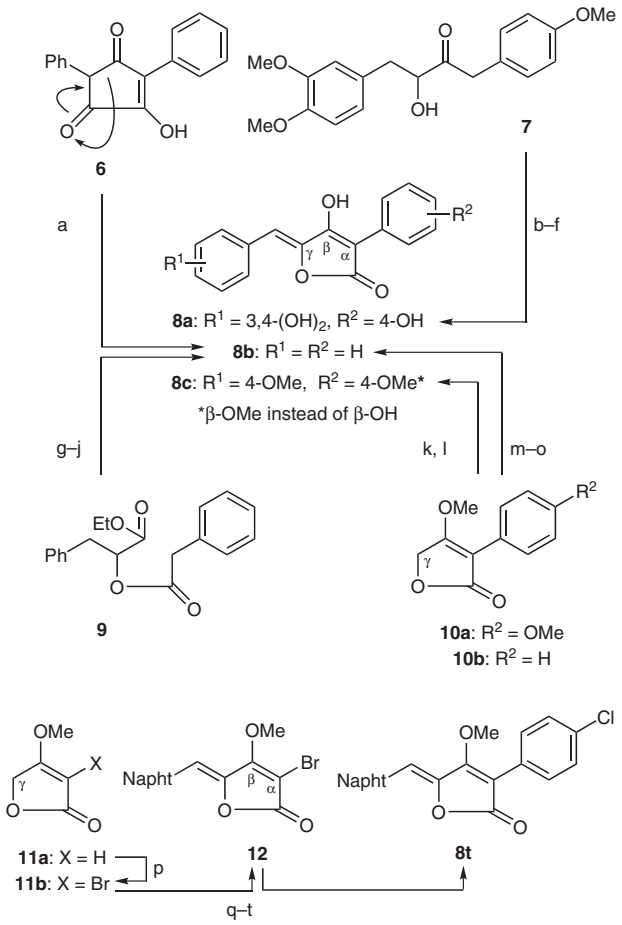
Gill et al. synthesized pulvinones from unsymmetrical acyloins like compound **7**[10] (Scheme 2).[11] Deprotonation generated an oxy-substituted enolate, which was cyclized by double acylation with 1,1′-carbonyldiimidazole. Adjustment of the oxidation state including temporary protection of the hydroxy group gave pulvinones (e.g., **8a**) in a further three steps.[12]

Campbell's second route to pulvinones[9] is based on the Dieckmann condensation of diesters like **9**[13] (Scheme 2). They provided tetronic acids that were dehydrogenated to give pulvinone **8b** by the three-step sequence already mentioned for the conversion of **7** to **8a**.

Pattenden and Knight prepared pulvinone **8c** with a methyl group at Oβ *Z*-selectively by a two-step aldol condensation between the enolate of tetronic ester **10a**[14] and 4-methoxybenzaldehyde (Scheme 2).[15] This approach was modified by the Campbell group who established the $C\gamma{=}C_{exocyclic}$ bond between a phosphorus ylide, derived from tetronic ester **10b**[16] by functionalizing Cγ, and benzaldehyde during their synthesis of pulvinone **8b**.[9] The latter was a *Z*/*E* mixture whose constituents were separated by recrystallization.

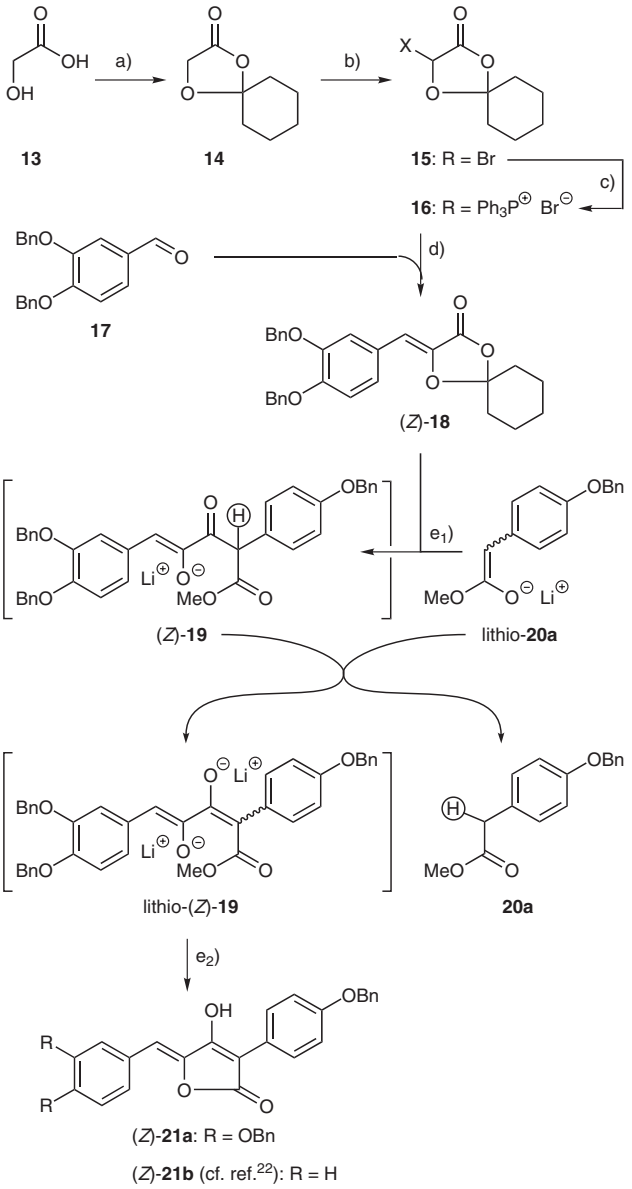
Very recently, a group from Wyeth Research synthesized a large number of pulvinones as exemplified by their five-step access to pulvinone **8t** (Scheme 2).[17] The known brominated derivative **11b**[18] of commercially available tetronic ester **11a** was condensed with an aldehyde at Cγ to give **12** and then coupled at Cα with a boronic acid. Cleavage of the β-OMe bond furnished the target structure (seemingly[19] isomerically pure).

Considering the availability of starting materials, overall number of steps, and convergency, the most efficient route to pulvinones was developed by Ramage et al. in 1984.[20,21] It began with a three-step preparation of phosphonium bromide **16**[20] (Scheme 3). The latter allowed the synthesis of pulvinones (*Z*)-**21a**, (*Z*)-**21b**, and (*Z*)-**8b** after



Scheme 2 Published syntheses of pulvinones, part 1. *Reagents and conditions*: Ref.[9]: (a) **6**, no solvent, 230 °C; 77% (*Z*)-**8b**. Ref.[11]: (b) **7**, LDA (2 equiv), THF, –78 °C; 1,1′-carbonyldiimidazole, –78 °C to 15 °C; (c) Me_2SO_4, K_2CO_3, acetone, heat; (d) NBS, CCl_4, heat, then hν; DBU, benzene, r.t.; (e) BBr_3, CH_2Cl_2, heat; (f) LiBr, $CaCO_3$, DMF, heat; 23% (*Z*)-**8a** over five steps. Ref.[9]: (g) **9**, KO-*t*-Bu, *t*-BuOH, heat; (h) Me_2SO_4, K_2CO_3, acetone, heat; (i) NBS, AIBN (cat.), 1,2-dichloroethane, heat; (j) LiBr, $CaCO_3$, DMF, heat; >26% (*Z*)-**8b** over four steps. Ref.[15]: (k) **10a**, LiN(*i*-Pr)Cy, THF, –78 °C; 4-$MeOC_6H_4CHO$, –50 °C; (l) benzene, TsOH (cat.), r.t.; 70% (*Z*)-**8c**. Ref.[9]: (m) **10b**, NBS, AIBN (cat.), 1,2-dichloroethane, heat; (n) Ph_3P, benzene, heat (includes cleavage of methyl tetronate); (o) benzaldehyde, NaOEt, EtOH, r.t.; 41% (*Z*)-**8b** and 16% (*E*)-**8b** over three steps (plus recrystallization). Ref.[17]: (p) **11a**, NBS, CCl_4, heat (following ref.[18]); (q) **11b**, LiN(*i*-Pr)Cy, THF, –78 °C; 1-naphthaldehyde; (r) **12**, MsCl, Et_3N, CH_2Cl_2, 0 °C; (s) 4-$ClC_6H_4B(OH)_2$, K_3PO_4, $Pd(PPh_3)_4$, dioxane, microwaves; (t) LiBr, DMF, microwaves; 11% over five steps (step p, ref.[18]; steps q–t, ref.[19]).

steps 4 and 5.[21,22] In step 4, phosphonium salt **16** and 1,4-diazabicyclo[2.2.2]octane generated an ylide,[20] which condensed[21] with aldehyde **17** to provide the cyclohexylidene acetal **18** of a β-arylated *Z*-configured pyruvic acid enol. Being an enol ester, acetal (*Z*)-**16** acts as an acylating agent in step 5, namely a Claisen condensation with ester enolate lithio-**20a**. Since closely related Claisen condensations of **25a–f** with lithio-**20b–c**, shown in Table 5, are a key step of the present study, too, it is important to understand why each condensation gave the best yield if 2.5 equivalents of the ester enolate were used. The primary products must be the enolate-containing β-oxo ester (*Z*)-**19** and cyclohexanone. Being an active methylene compound, (*Z*)-**19** is expected to quench one equivalent of enolate lithio-**20a**, thereby delivering bis(enolate) lithio-(*Z*)-**19**. Hence, two equivalents of lithio-**20a** are required for such Claisen condensations to proceed to completion. At the end[22] of Ramage's sequence, protonation is required, whether before or after lactone formation remains indeterminate. All in all one pulvinone (*Z*)-**21a** was obtained with complete retention of the (*Z*)-configuration of enol ester (*Z*)-**18**.



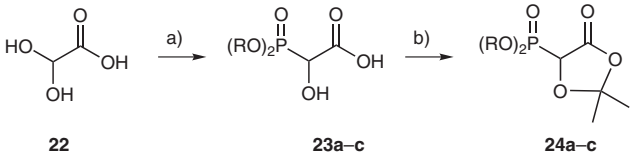
Scheme 3 Published syntheses of pulvinones, part 2: Ramage's synthesis of tribenzyl ether (*Z*)-**21a** of pulvinone (*Z*)-**8a**. *Reagents and conditions*: Ref.[20]: a) cyclohexanone, TsOH (1 mol%), toluene, heat, 5 h; 73%; b) NBS (1.06 equiv), AIBN (0.2 mol%), CCl_4, hν, heat, reaction time not disclosed; c) Ph_3P (1.0 equiv), toluene, r.t., overnight; 79% over two steps; d) **16** (1.33 equiv), DABCO (1.0 equiv), toluene, r.t., 4 min; yield not given. – Ref.[21]: Addition of **17**, 70 °C, 4 h; 80% over two steps; e_1) lithio-**20a** (2.5 equiv), THF, –78 °C to r.t., overnight; e_2) evaporation of THF; addition of Et_2O–H_2O (1:1); recrystallization of the resulting solid (H_2O or AcOH–H_2O); 78% (*Z*)-**21a**.

The present study improves and extends Ramage's ylide methodology by introducing the dioxolanone-substituted phosphonate **24b** (Table 1). This is a superior reagent for the preparation of arylmethylene-substituted dioxolanones **25a–f** (Tables 2 and 3) because of the inherent advantage of Horner–Wadsworth–Emmons versus the analogous Wittig alkenations: the byproduct of the former, a phosphonate anion, is easily extracted into water, while the byproduct of the latter, triphenylphosphine oxide, must be removed by chromatography or crystallization. Also, the synthesis of phosphonate **24b** is one step shorter than the synthesis of Ramage's phosphonium salt **16**. Quite like Ramage's congener (*Z*)-**18** (Scheme 3), our dioxolanones **25** can be transformed into pulvinones **8** efficiently and stereoselectively (Table 5). We consider this a significantly improved access.

Dioxolanone-substituted dialkyl phosphonates **24a–c** were obtained from the corresponding 2-(dialkoxyphosphoryl)-2-hydroxyacetic acids **23a–c** (Table 1). These, in turn, were prepared as published for the 2-(diethoxyphosphoryl)-2-hydroxyacetic acid[23] by the addition of dimethyl, dibutyl, and diisopropyl phosphite, respectively, to glyoxylic acid (commercially available as the hydrate **22**). The crude dimethyl, dibutyl, and diisopropyl phosphonates **23a–c** were ≥92% pure according to ^{1}H NMR analysis ($CDCl_3$). Therefore, they were subjected to acetonide formation to give **24a–c** by treatment with acetone and excess boron trifluoride–diethyl ether complex[24] without prior purification. Workup comprised hydrolysis of the Lewis acid (by the addition of aqueous hydrogen carbonate solution) and extraction with diethyl ether. This procedure was inefficient in the case of the dioxolanone-substituted dimethyl phosphonate **24a** due to its high solubility in the aqueous phase. Accordingly, the isolated yield of **24a** (after purification by flash chromatography[25]) was only 25%. On the other hand, the dioxolanone-substituted dibutyl and diisopropyl phosphonates **24b** and **24c**, respectively, were only sparingly water soluble. They could be readily extracted from the aqueous phase with diethyl ether and purified by filtration through a pad of silica gel to give **24b** and **24c**, both in 80% yield and on a 20 g and 3.5 g scale, respectively.

The Horner–Wadsworth–Emmons alkenation reactions involving dibutyl phosphonate **24b** and diisopropyl phosphonate **24c** were studied with 4-methoxybenzaldehyde as the prototype aldehyde (Table 2). The selected reaction conditions were gleaned from Horner–Wadsworth–Emmons reactions of other phosphonates.[26–30] In the presence of both sodium iodide and 1,8-diazabicyclo[5.4.0]undec-7-ene, an activator/base combination described by Masamune and Roush,[26] dibutyl phosphonate **24b** delivered the 4-methoxybenzylidene-substituted dioxolanone **25c** in 66% yield as a 76:24 *E*/*Z* mixture (Table 2, entry 1). In the presence of sodium iodide, 1,8-diazabicyclo[5.4.0]undec-7-ene, and 1,3-dimethyl-3,4,5,6-tetrahydropyrimidin-2(1*H*)-one[31] the yield of **25c** was higher (75%) and the *E*/*Z* ratio increased to 96:4 (Table 2, entry 2). Potassium hexamethyldisilazanide and 18-crown-6 in tetrahydrofuran[28] furnished dioxolanone **25c** in 55% yield after 12 hours at –78 °C (Table 2, entry 3) but the *E*/*Z* ratio sank to 77:23. Sodium hydride as a base[29] gave the Horner–Wadsworth–Emmons product **25c** in only 47% yield but with very good *E*/*Z* selectivity 96:4 (Table 2, entry 4). Lithium diisopropylamide[30] in tetrahydrofuran/1,3-dimethyl-3,4,5,6-tetrahydropyrimidin-2(1*H*)-one (4:1) was the best base for making compound **25c** both efficiently (81% yield) and *E*-selectively (*E*/*Z* 95:5; Table 2, entry 5). When treated with lithium diisopropylamide/tetrahydrofuran/1,3-dimethyl-3,4,5,6-tetrahydropyrimidin-2(1*H*)-one, diisopropyl phosphonate **24c** condensed with 4-methoxybenzaldehyde to give **25c** in similar yield (78%) but with a drop in stereoselectivity (*E*/*Z* 79:21; Table 2, entry 6).[31]

Table 1 Synthesis of dioxolanone-substituted phosphonates **24a–c**[a]



22 **23a–c** **24a–c**

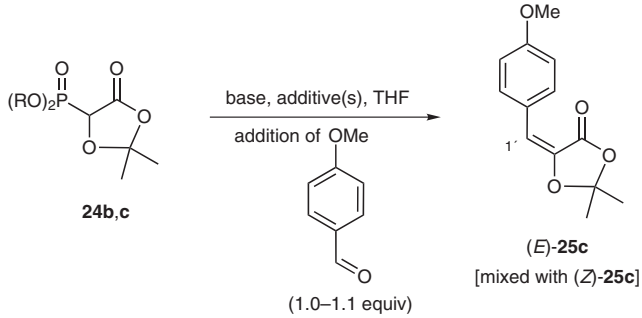
23, **24**	R	Yield (%)	
		23[b]	**24**
a	Me	92	25
b	Bu	95	80
c	*i*-Pr	95	80

[a] Reagents and conditions: (a) dialkyl phosphite (1.0 equiv), 50 °C, 5 h; (b) acetone (1.0 equiv), $BF_3{\cdot}OEt_2$ (1.75 equiv), Et_2O, r.t., 12 h.
[b] Products not purified.

As a result of these optimizations, dibutyl phosphonate **24b** became the reagent of choice for the remaining Horner–Wadsworth–Emmons alkenations. As documented in Table 3, we used only aromatic aldehydes in these reactions. Most of them bear one or several oxygenated moieties corresponding to the many naturally occurring pulvinones, which contain several hydroxy groups.[4] We obtained the alkenation products **25a–f** in consistently good yields (79–88%). The *E*/*Z* selectivity, with which we had made compound **25c** (95:5), was not surpassed by the other *E*/*Z* ratios, which spanned the range from 95:5 to 87:13. Fortunately, this lack of stereointegrity has no consequence in the context of pulvinone synthesis, because the double bond geometries of the final pulvinone **8** did not reflect the double bond geometries of their dioxolanone precursors **25**.

The *E*- vs. *Z*-configuration of dioxolanones **25a–f** could not be deduced from their ^{1}H NMR spectra: The two last columns of Table 3 reveal that the chemical shift of the alkene-bound nucleus H1′ is only marginally affected by a change of the alkene geometry: $\Delta\delta$ = 0.02–0.04. This

Table 2 Optimization of the Horner–Wadsworth–Emmons Alkenation of 4-Methoxybenzaldehyde with Deprotonated Phosphonates **24b**,**c**

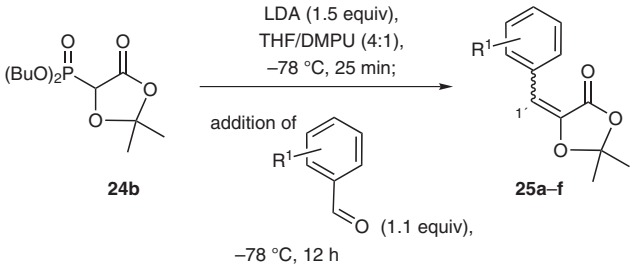


Entry	Phosphonate[a]	Base, additive(s)	Deprotonation; condensation	Yield (%)	Ratio *E*/*Z*
1	**24b**	DBU (1.0 equiv), NaI (1.2 equiv)	0 °C, 30 min; –78 °C to r.t., 12 h[26]	66	76:24
2	**24b**	DBU (1.0 equiv), NaI (1.2 equiv), DMPU (2.5 equiv)	0 °C, 1 h; –78 °C to r. t., 12 h[27]	75	96:4
3	**24b**	KHMDS (1.0 equiv), 18-crown-6 (5.0 equiv)	–78 °C, 30 min; –78 °C, 12 h[28]	55	77:23
4	**24b**	NaH (1.0 equiv)	0 °C, 1 h; 0 °C, 12 h[29]	47	96:4
5	**24b**	LDA[27] (1.5 equiv), DMPU[30] (20% in THF)	–78 °C, 30 min; –78 °C, 12 h	81	95:5
6[31]	**24c**	LDA (1.5 equiv), DMPU (20% in THF)	–78 °C, 30 min; –78 °C, 12 h	78	79:21

[a] **24b** R = Bu, **24c** R = *i*-Pr.

phenomenon is reminiscent of the virtual independence of the chemical shift of the analogous proton in pulvinones from the double bond geometry.[9] The C1′=C geometry of dioxolanones **25a–f** was therefore established by a different criterion, the magnitude of the three-bond coupling ^3J(C=O,H1′) between ^{13}C=O and ^{1}H1′. For the major and minor isomers of dioxolanes **25b**,**c**,**f** this was observed by gated-decoupled one-dimensional ^{13}C NMR spectroscopy. Such couplings are larger when the bonds between the nuclei under scrutiny have a zigzag rather than a U-shaped array.[32] The zigzag ^{13}C=O/^{1}H1′ coupling in the major isomers **25b**,**c**,**f** is 10.1 Hz, which gives proof for their *E*-configuration, while the U-shaped ^{13}C=O/^{1}H1′ coupling in the minor isomers **25b**,**c**,**f** is 3.7 Hz and this gives proof for their *Z*-configuration. The *E*-configuration for the major isomers of dioxolanes **25a**,**d**,**e** was assigned by analogy with these results.

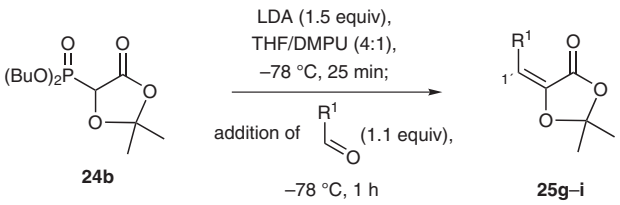
Table 3 Horner–Wadsworth–Emmons Alkenations Rendering Arylmethylene-Substituted Dioxolanones **25a–f**



25	R^1	Yield (%)	Ratio *E*/*Z*	^{1}H NMR δ (H1′)	
				E	*Z*
a	H	80	95:5	6.51	6.47
b	4-OH	79	87:13	6.44	6.42
c	4-OMe	88	95:5	6.46	6.43
d	3,4-$(OMe)_2$	80	87:13	6.45	6.43
e	3,4-(OCH_2O)	80	89:11	6.41	6.39
f	3,4,5-$(OMe)_3$	84	90:10	6.42	6.39

The *E*-selectivity of the Horner–Wadsworth–Emmons reactions which allowed us to transform aromatic aldehydes into dioxolanones **25a–f** (Table 3) is in complete contrast with the *Z*-selective Wittig alkenation by which Ramage et al.[20,21] obtained dioxolanone (*Z*)-**18** and its benzyloxy-

Table 4 Horner–Wadsworth–Emmons Reactions Leading to Alkylmethylene-Substituted Dioxolanones **25g–i**



25	R^1	Yield (%)	Ratio *E*/*Z*	^{1}H NMR δ (H1′)	
				E	*Z*
g	*i*-Pr	96	95:5	5.36	5.51
h	Cy	82	100:0	5.38	–
i	*n*-C_9H_{19}	92	96:4	5.52	5.61

free analogue. For this reason we also examined some Horner–Wadsworth–Emmons reactions between phosphonate **24b** and aliphatic aldehydes (Table 4). Under the previously established conditions (Table 2, entry 5) and within one hour at –78 °C, this provided the alkylidene-substituted dioxolanones **25g–i** in 82–96% yield and with *E*/*Z* selectivities between 95:5 and 100:0. The *E*-configuration of dioxolanone **25h** was determined from ^3J(C=O, H1′) = 10.5 Hz. The *E*-configuration of the other dioxolanones **25g** and **25i** was assigned by analogy.

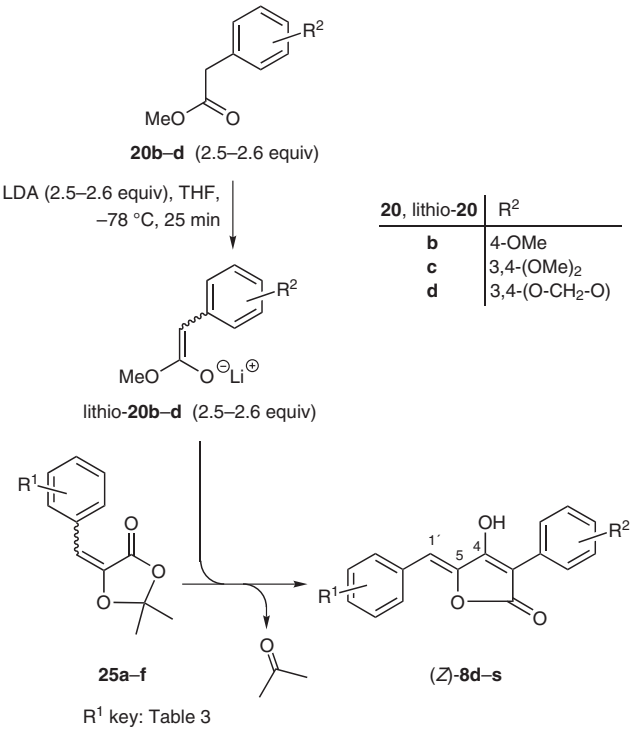
The last step of our modified pulvinone synthesis consists of the Claisen condensation between dioxolanones **25a–f** (acetonide esters) and ester enolates lithio-**20b–d** (Table 5). The latter were produced by treatment of methyl arylacetates **20b–d** with equimolar amounts of lithium diisopropylamide. For the reason previously discussed (*vide supra*), enolates lithio-**20b–d** were combined with the acetonide esters **25a–f** in a 2.5:1 (**8d–g**) or 2.6:1 (**8h–s**) ratio.[33] Assuming a strictly analogous course as for Ramage et al.'s reaction between (*Z*)-**19** and lithio-**20a** (cf. Scheme 3) and like compounds, we relied on the same temperature profile (–78 °C to room temperature) and a related workup procedure.[22] In accordance with the mechanism given in Scheme 3 [lithio-(*Z*)-**19** to (*Z*)-**21a**], lactone formation became visible when a yellow precipitate formed. Recrystallization from methanol (**8d–m**) or methanol–water (10:1; **8n–s**) afforded pulvinones **8d–s** in uniformly good yields (75–91%).

Pulvinones **8d–s** were obtained as single isomers, as judged by their 300, 400 or 500 MHz ^{1}H NMR spectra. This was confirmed by single sets of ^{1}H and ^{13}C NMR resonances in freshly prepared acetone-d_6 solution. Small ^{1}H NMR signals assignable to a single new compound, the respective *E*-isomer, were observed when ^{1}H NMR spectra of the initial sample solutions were recorded after prolonged standing. It is noteworthy that the underlying dioxolanones **25a–f**, irrespective of their *E*/*Z* ratio (96:4–77:23), gave the resulting pulvinones **8d–s** as pure *Z*-isomers (*vide infra*). This indicates that pulvinone formation by way of Scheme 3 or Table 5 is stereoconvergent, not stereospecific.

The *Z*-configuration of the exocyclic C1′=C5 bond in pulvinone **8r** was established by measuring the three-bond coupling between H1′ and C4. The magnitude of this coupling constant (3.7 Hz; measured by gated-decoupled ^{13}C NMR spectroscopy) means that the underlying structure H1′–C1′=C5–C4 is U-shaped.[32] Plausibly, pulvinones **8d–q**,**s** are also *Z*-configured.

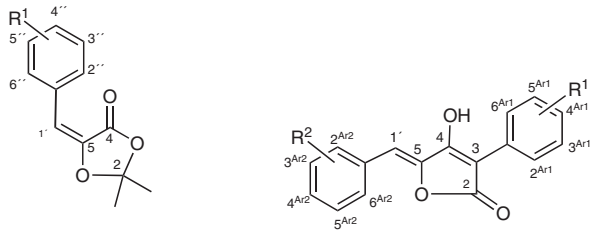
In summary, a reliable route has been established, which gave pulvinones **8d–s** as *Z*-isomers in two steps from aromatic aldehydes, phosphonate **24b**, and aryl acetates lithio-**20b–d**.[36]

Table 5 Claisen Condensation/Transesterification Route from Alkylidenedioxolanones **25a–f** to Pulvinones (*Z*)-**8d–s**



(*Z*)-**8**	R^1	R^2	Yield (%)	^{1}H NMR δ (H1′)
d	H	4-OMe	90	6.58
e	4-OH	4-OMe	90	6.61
f[34]	4-OMe	4-OMe	90	6.52
g	3,4,5-$(OMe)_3$	4-OMe	91	6.49
h	H	3,4-$(OMe)_2$	79	6.59
i	4-OH	3,4-$(OMe)_2$	78	6.52
j[35]	4-OMe	3,4-$(OMe)_2$	80	6.56
k	3,4-$(OMe)_2$	3,4-$(OMe)_2$	80	6.53
l	3,4-(OCH_2O)	3,4-$(OMe)_2$	79	6.76
m	3,4,5-$(OMe)_3$	3,4-$(OMe)_2$	81	6.55
n	H	3,4-(OCH_2O)	75	6.77
o	4-OH	3,4-(OCH_2O)	78	6.53
p	4-OMe	3,4-(OCH_2O)	80	6.74
q	3,4-$(OMe)_2$	3,4-(OCH_2O)	80	6.72
r	3,4-(OCH_2O)	3,4-(OCH_2O)	79	6.70
s	3,4,5-$(OMe)_3$	3,4-(OCH_2O)	82	6.70

Products were purified by flash chromatography[25] on Macherey-Nagel silica gel 60 (details given in parentheses). ^{1}H NMR [TMS (0.00 ppm) as internal standard in $CDCl_3$ or acetone-d_5 (2.05 ppm) as internal standard in acetone-d_6] and ^{13}C NMR [$CDCl_3$ (77.10 ppm) as internal standard in $CDCl_3$ or acetone-d_6 (29.80 ppm) as internal standard in acetone-d_6]: Varian Mercury VX 300 or Bruker AM 400 or DRX 500. Integrals in accordance with assignments. The assignments of ^{1}H and ^{13}C NMR resonances refer to the IUPAC nomenclature (see Figure 1) with primed and multiply primed numbers belonging to side chains. NMR: Dr. M. Keller, Institut für Organische Chemie and Biochemie, Universität Freiburg. Combustion analyses: E. Hickl, Institut für Organische Chemie and Biochemie, Universität Freiburg. HRMS (EI, 70 eV): Dr. J. Wörth, Institut für Organische Chemie and Biochemie, Universität Freiburg. IR spectra: FTIR Perkin-Elmer Spectrum 1000. Melting points: Dr. Tottoli apparatus (Büchi), uncorrected.



(*E*)-**25a–f** (*Z*)-**8d–s**

Figure 1

(*Z*)-5-(Benzylidene)-4-hydroxy-3-(4-methoxyphenyl)furan-2(5*H*)-one [(*Z*)-8d]

Prepared analogously as described for pulvinone (*Z*)-**8g** from *i*-Pr_2NH (0.49 mL, 0.35 g, 3.5 mmol, 2.6 equiv), THF (4 mL), 1.5 M BuLi in hexane (2.26 mL, 3.39 mmol, 2.5 equiv), ester **20b** (0.55 mL, 0.61 g, 3.4 mmol, 2.5 equiv) in THF (4 mL), and dioxolanone **25a** (0.277 g, 1.36 mmol) in THF (2 mL). Yellow crystals (MeOH); yield: 0.359 g (90%); mp 219–222 °C.

IR (KBr): 3425, 3055, 3000, 2940, 2835, 1705, 1630, 1610, 1515, 1450, 1425, 1400, 1310, 1290, 1255, 1185, 1155, 1130, 1100, 1035, 1000, 830 cm^{-1}.

^{1}H NMR (300 MHz, acetone-d_6): δ = 3.84 (s, 4^{Ar1}-OCH_3), 6.58 (s, H1′), AA′BB′ signal centered at 7.01 ($H3^{Ar1}$, $H5^{Ar1}$) and 7.92 ($H2^{Ar1}$, $H6^{Ar1}$), 7.33–7.39 (m, $H4^{Ar2}$), 7.43–7.48 (m, $H3^{Ar2}$, $H5^{Ar2}$), 7.79–7.82 (m, $H2^{Ar2}$, $H6^{Ar2}$); 4-OH was not detected.

^{13}C NMR (126 MHz, acetone-d_6): δ = 55.6 (4^{Ar1}-OCH_3)^I, 102.9 (C3)^{II}, 107.3 (C1′)^I, 114.6 ($C3^{Ar1}$, $C5^{Ar1}$)^I, 122.9 ($C1^{Ar1}$)^{III}, 129.5 ($C4^{Ar2}$)^I, 129.7 ($C3^{Ar2}$, $C5^{Ar2}$)^I, 130.1 ($C2^{Ar1}$, $C6^{Ar1}$)^I, 131.1 ($C2^{Ar2}$, $C6^{Ar2}$)^I, 134.1 ($C1^{Ar2}$)^{III}, 143.6 (C5)^{II}, 160.1 and 161.9 ($C4^{Ar1}$, C4), 168.6 (C2)^I.

Anal. Calcd for $C_{18}H_{14}O_4$ (294.2): C, 72.96; H, 5.44. Found: C, 73.01; H, 5.28.

(*Z*)-4-Hydroxy-5-(4-hydroxybenzylidene)-3-(4-methoxyphenyl)furan-2(5*H*)-one [(*Z*)-8e]

Prepared analogously as described for pulvinone (*Z*)-**8g** from *i*-Pr_2NH (0.62 mL, 0.44 g, 4.4 mmol, 2.6 equiv), THF (4 mL), 1.5 M BuLi in hexane (2.8 mL, 4.2 mmol, 2.5 equiv), ester **20b** (0.68 mL, 0.76 g, 4.2 mmol, 2.5 equiv) in THF (4 mL), and dioxolanone **25b** (0.369 g, 1.68 mmol) in THF (2 mL). Yellow crystals (MeOH); yield: 0.468 g (90%); mp 239–241 °C.

IR ($CDCl_3$ soln): 3620, 3525, 3395, 3095, 2330, 2265, 2115, 1790, 1760, 1730, 1680, 1610, 1515, 1420, 1290, 1260, 1235, 1170, 1115, 1070, 1030, 1010, 985 cm^{-1}.

^{1}H NMR (300 MHz, acetone-d_6): δ = 3.31 (s, 4^{Ar2}-OH), 3.82 (s, 4^{Ar1}-OCH_3), 6.61 (s, H1′), AA′BB′ signal centered at 6.90 ($H3^{Ar2}$, $H5^{Ar2}$) and 7.67 ($H2^{Ar2}$, $H6^{Ar2}$), AA′BB′ signal centered at 6.97 ($H3^{Ar1}$, $H5^{Ar1}$) and 8.05 ($H2^{Ar1}$, $H2^{Ar1}$); 4-OH was not detected.

^{13}C NMR (101 MHz, acetone-d_6): δ = 55.6 (4^{Ar1}-OCH_3), 107.8 (C1′), 114.6, and 116.7 ($C3^{Ar1}$, $C5^{Ar1}$, $C3^{Ar2}$, $C5^{Ar2}$), 125.8 and 129.4 ($C1^{Ar1}$, $C1^{Ar2}$), 123.0 and 133.9 ($C2^{Ar1}$, $C6^{Ar1}$, $C2^{Ar2}$, $C6^{Ar2}$), 141.5 (C5), 168.7 (C2); $C4^{Ar2}$, C3, C4, $C4^{Ar1}$, and $C4^{Ar2}$ were not detected due to low signal/noise ratio.

Anal. Calcd for $C_{18}H_{14}O_5$ (310.3): C, 69.22; H, 5.16. Found: C, 68.19; H, 4.92 (no better analysis could be obtained).

(*Z*)-4-Hydroxy-5-(4-methoxybenzylidene)-3-(4-methoxyphenyl)furan-2(5*H*)-one [(*Z*)-8f][34]

Prepared analogously as described for pulvinone (*Z*)-**8g** from *i*-Pr_2NH (0.12 mL, 0.086 g, 0.85 mmol, 2.6 equiv), THF (1.0 mL), 1.5 M BuLi in hexane (0.54 mL, 0.81 mmol, 2.5 equiv), ester **20b** (0.13 mL, 0.15 g, 0.81 mmol, 2.5 equiv) in THF (1.0 mL), and dioxolanone **25c** (0.076 g, 0.33 mmol) in THF (2 mL). Yellow crystals (MeOH); yield: 0.095 g (90%); mp 245–250 °C (Lit.[9] 250–253 °C).

^{1}H NMR (300 MHz, acetone-d_6): δ = 3.81 and 3.84 (2 s, 4^{Ar1}-OCH_3, 4^{Ar2}-OCH_3), 6.52 (s, H1′), AA′BB′ signal centered at 6.96 ($H3^{Ar2}$, $H5^{Ar2}$)* and 7.74 ($H2^{Ar2}$, $H6^{Ar2}$), AA′BB′ signal centered at 6.99 ($H3^{Ar1}$, $H5^{Ar1}$)* and 7.98 ($H2^{Ar1}$, $H6^{Ar1}$); *assignment interchangeable.

(*Z*)-4-Hydroxy-3-(4-methoxyphenyl)-5-(3,4,5-trimethoxybenzylidene)furan-2(5*H*)-one [(*Z*)-8g]

A soln of *i*-Pr_2NH (0.17 mL, 0.12 g, 1.2 mmol, 2.6 equiv) in THF (2 mL) and 1.5 M BuLi in hexane (0.73 mL, 1.1 mmol, 2.5 equiv) were combined at –78 °C for 25 min while stirring. Ester **20b** (0.18 mL, 0.20 g, 1.1 mmol, 2.5 equiv) in THF (2 mL) was added dropwise. After 25 min, dioxolanone **25f** (0.133 g, 0.452 mmol) in THF (2 mL) was added dropwise. The mixture was gradually (3 h) warmed to r.t. and stirred overnight. Et_2O–H_2O (1:1, 20 mL) was added and the organic phase was separated. The aqueous phase was acidified until with 1 M HCl until pH 1 and then extracted with Et_2O (3 × 15 mL). The combined ethereal phases were dried ($MgSO_4$). Removal of the solvent in vacuo gave a solid which, after recrystallization (MeOH) provided the title compound as yellow crystals (MeOH); yield: 0.158 g (91%); mp 180–185 °C.

IR ($CDCl_3$ soln): 3615, 3155, 2985, 2360, 2335, 2255, 1815, 1795, 1650, 1560, 1540, 1470, 1385, 1170, 1095, 985 cm^{-1}.

^{1}H NMR (300 MHz, acetone-d_6): δ = 3.78 and 3.84 (2 s, 4^{Ar1}-OCH_3, 4^{Ar2}-OCH_3), 3.88 (s, twofold intensity; 3^{Ar2}-OCH_3, 5^{Ar2}-OCH_3), 6.49 (s, H1′), AA′BB′ signal centered at 7.00 ($H3^{Ar1}$, $H5^{Ar1}$) and 7.88 ($H2^{Ar1}$, $H6^{Ar1}$), 7.13 (s, $H2^{Ar2}$, $H6^{Ar2}$); 4-OH was not detected.

^{13}C NMR (126 MHz, acetone-d_6): δ = 55.6 and 60.7 (4^{Ar1}-OCH_3, 4^{Ar2}-OCH_3), 56.5 (twofold intensity; 3^{Ar2}-OCH_3, 5^{Ar2}-OCH_3), 102.8 (C3), 107.7 (C1′), 108.9 ($C2^{Ar2}$, $C6^{Ar2}$), 114.6 ($C3^{Ar1}$, $C5^{Ar1}$), 122.8 and 129.4 ($C1^{Ar1}$, $C1^{Ar2}$), 130.2 ($C2^{Ar1}$, $C6^{Ar1}$), 142.9 (C5), 154.5 ($C3^{Ar2}$, $C5^{Ar2}$), 160.1 ($C4^{Ar1}$), 161.8 (C4), 168.5 (C2); $C4^{Ar2}$ was not detected.

Anal. Calcd for $C_{21}H_{20}O_7$ (384.4): C, 65.63; H, 5.21. Found: C, 65.43; H, 5.36.

(*Z*)-5-(Benzylidene)-3-(3,4-dimethoxyphenyl)-4-hydroxyfuran-2(5*H*)-one [(*Z*)-8h]

Prepared analogously as described for pulvinone (*Z*)-**8g** from *i*-Pr_2NH (0.13 mL, 0.094 g, 0.93 mmol, 2.5 equiv), THF (1.0 mL), 2.5 M BuLi in hexane (0.37 mL, 0.93 mmol, 2.5 equiv), ester **20d** (0.19 g, 0.93 mmol, 2.5 equiv) in THF (1.0 mL), and dioxolanone **25a** (0.075 g, 0.37 mmol) in THF (2 mL). Yellow crystals (MeOH); yield: 0.094 g (79%); mp 190–194 °C.

IR ($CDCl_3$ soln): 3515, 3395, 2260, 2225, 1765, 1750, 1720, 1700, 1635, 1515, 1455, 1385, 1300, 1180, 1135, 1095, 1065, 1015, 970 cm^{-1}.

^1H NMR (300 MHz, acetone-d_6): δ = 3.840 and 3.844 (2 s, 3^{Ar1}-OCH_3, 4^{Ar1}-OCH_3), 6.59 (s, H1′), 7.01 (d, $J(H5^{Ar1},H6^{Ar1})$ = 8.4 Hz, $H5^{Ar1}$), 7.33–7.38 (m, $H4^{Ar2}$), 7.43–7.48 (m, $H3^{Ar2}$, $H5^{Ar2}$), 7.57 (dd, $J(H6^{Ar1},H5^{Ar1})$ = 8.5 Hz, $^4J(H6^{Ar1},H2^{Ar1})$ = 2.1 Hz, $H6^{Ar1}$), 7.62 (d, $^4J(H2^{Ar1},H6^{Ar1})$ = 1.9 Hz, $H2^{Ar1}$), 7.79–7.82 (m, $H2^{Ar2}$, $H6^{Ar2}$); 4-OH was not detected.

^{13}C NMR (75 MHz, acetone-d_6): δ = 56.1 (3^{Ar1}-OCH_3, 4^{Ar1}-OCH_3), 103.0 (C3), 107.4 (C1′), 112.6 and 112.6 ($C2^{Ar1}$, $C5^{Ar1}$), 121.8 ($C6^{Ar1}$), 123.1 ($C1^{Ar1}$), 129.5 ($C4^{Ar2}$), 129.6 (twice as intense as preceding peak, $C3^{Ar2}$, $C5^{Ar2}$), 131.0 (twice as intense as preceding peak, $C2^{Ar2}$, $C6^{Ar2}$), 134.1 ($C1^{Ar2}$), 143.5 (C5), 150.0 and 150.1 ($C3^{Ar1}$, $C4^{Ar1}$), 161.3 (C4), 168.5 (C2).

HRMS: *m/z* [M^+] calcd for $C_{19}H_{16}O_5$: 324.0998; found: 324.0991.

(*Z*)-3-(3,4-Dimethoxyphenyl)-4-hydroxy-5-(4-hydroxybenzylidene)furan-2(5*H*)-one [(*Z*)-8i]

Prepared analogously as described for pulvinone (*Z*)-**8g** from *i*-Pr_2NH (0.16 mL, 0.12 g, 1.1 mmol, 2.5 equiv), THF (1.0 mL), 2.5 M BuLi in hexane (0.45 mL, 1.1 mmol, 2.5 equiv), ester **20c** (0.238 g, 1.14 mmol, 2.5 equiv) in THF (1.0 mL), and dioxolanone **25b** (0.100 g, 0.455 mmol) in THF (2 mL). Yellow crystals (MeOH); yield: 0.120 g (78%); mp 198 °C.

IR (KBr): 3420, 2360, 2340, 1710, 1605, 1515, 1410, 1275, 1225, 1175, 1125, 1025, 995 cm^{-1}.

^1H NMR (400 MHz, acetone-d_6): δ = 3.83 (s, 3^{Ar1}-OCH_3, 4^{Ar1}-OCH_3), 6.52 (s, H1′), AA′BB′ signal centered at 6.92 ($H3^{Ar2}$, $H5^{Ar2}$) and 7.68 ($H2^{Ar2}$, $H6^{Ar2}$), 7.00 (d, $J(H5^{Ar1},H6^{Ar1})$ = 8.5 Hz, $H5^{Ar1}$), 7.57 (dd, $J(H6^{Ar1},H5^{Ar1})$ = 8.4 Hz, $^4J(H6^{Ar1},H2^{Ar1})$ = 2.0 Hz, $H6^{Ar1}$), 7.64 (d, $^4J(H2^{Ar1},H6^{Ar1})$ = 1.9 Hz, $H2^{Ar1}$); 4-OH was not detected.

^{13}C NMR (101 MHz, acetone-d_6): δ = 56.10 (3^{Ar1}-OCH_3, 4^{Ar1}-OCH_3), 107.6 (C1′), 112.6 and 112.7 ($C2^{Ar1}$, $C5^{Ar1}$), 116.6 ($C3^{Ar2}$, $C5^{Ar2}$), 121.5 ($C6^{Ar1}$), 124.1 and 125.9 ($C1^{Ar1}$, $C1^{Ar2}$), 132.9 ($C2^{Ar2}$, $C6^{Ar2}$), 141.8 (C5), 149.7 and 150.0 ($C3^{Ar1}$, $C4^{Ar1}$), 158.9 ($C4^{Ar2}$ or C4); C2, C3, and either C4 or $C4^{Ar2}$ were not observed due to the low signal/noise ratio.

HRMS: *m/z* [M^+] calcd for $C_{19}H_{16}O_6$: 340.0947; found: 340.0942.

(*Z*)-3-(3,4-Dimethoxyphenyl)-4-hydroxy-5-(4-methoxybenzylidene)furan-2(5*H*)-one [(*Z*)-8j][35]

Prepared analogously as described for pulvinone (*Z*)-**8g** from *i*-Pr_2NH (0.16 mL, 0.12 g, 1.1 mmol, 2.5 equiv), THF (1.0 mL), 2.5 M BuLi in hexane (0.45 mL, 1.1 mmol, 2.5 equiv), ester **20c** (0.238 g, 1.14 mmol, 2.5 equiv) in THF (1.0 mL), and dioxolanone **25c** (0.106 g, 0.455 mmol) in THF (2 mL). Yellow crystals (MeOH); yield: 0.128 g (80%); mp 190–195 °C.

IR ($CDCl_3$ soln): 3395, 3005, 2965, 2930, 2360, 2330, 2260, 2115, 1785, 1735, 1695, 1665, 1605, 1515, 1455, 1390, 1345, 1300, 1270, 1220, 980, 955, 890 cm^{-1}.

^1H NMR (300 MHz, acetone-d_6): δ = 3.84 (twice as intensive as the following peak) and 3.86 (2 s, 3^{Ar1}-OCH_3, 4^{Ar1}-OCH_3, 4^{Ar2}-OCH_3), 6.56 (s, H1′), 7.01 (d, $J(H5^{Ar1},H6^{Ar1})$ = 8.5 Hz, $H5^{Ar1}$), overlapped by high-field part of AA′BB′ signal centered at 7.02 ($H3^{Ar2}$, $H5^{Ar2}$) and 7.76 ($H2^{Ar2}$, $H6^{Ar2}$), 7.55 (dd, $J(H6^{Ar1},H5^{Ar1})$ = 8.4 Hz, $^4J(H6^{Ar1},H2^{Ar1})$ = 2.1 Hz, $H6^{Ar1}$), 7.61 (d, $^4J(H2^{Ar1},H6^{Ar1})$ = 1.9 Hz, $H2^{Ar1}$); 4-OH was not detected.

^{13}C NMR (101 MHz, acetone-d_6): δ = 55.71 and 56.1 (twice as intense as preceding peak; 3^{Ar1}-OCH_3, 4^{Ar1}-OCH_3, 4^{Ar2}-OCH_3), 102.47 (C3), 107.53 (C1′), 112.7 and 112.8 ($C2^{Ar1}$, $C5^{Ar1}$), 115.3 (twice as intense as preceding peak, $C3^{Ar2}$, $C5^{Ar2}$), 121.8 ($C6^{Ar1}$), 123.5 and 126.7 ($C1^{Ar1}$, $C1^{Ar2}$), 132.8 ($C2^{Ar2}$, $C6^{Ar2}$), 141.9 (C5), 150.0 (presumably $C3^{Ar1}$ and $C4^{Ar1}$), 161.2 and 162.0 (C4, $C4^{Ar2}$), 168.6 (C2).

HRMS: *m/z* [M^+] calcd for $C_{20}H_{18}O_6$: 354.1103; found: 354.1096.

(*Z*)-5-(3,4-Dimethoxybenzylidene)-3-(3,4-dimethoxyphenyl)-4-hydroxyfuran-2(5*H*)-one [(*Z*)-8k]

Prepared analogously as described for pulvinone (*Z*)-**8g** from *i*-Pr_2NH (0.16 mL, 0.12 g, 1.1 mmol, 2.5 equiv), THF (1.0 mL), 2.5 M BuLi in hexane (0.45 mL, 1.1 mmol, 2.5 equiv), ester **20c** (0.238 g, 1.14 mmol, 2.5 equiv) in THF (1.0 mL), and dioxolanone **25d** (0.120 g, 0.455 mmol) in THF (2 mL). Yellow crystals (MeOH); yield: 0.138 g (80%); mp 191–193 °C.

IR (KBr): 3430, 2995, 2940, 2840, 1700, 1630, 1600, 1515, 1465, 1430, 1325, 1260, 1140, 1025 cm^{-1}.

^1H NMR (300 MHz, acetone-d_6): δ = 3.841, 3.844, and 3.869 (3 s, the low-field signal being twice as intense as each of the high-field signals, 3^{Ar1}-OCH_3, 3^{Ar2}-OCH_3, 4^{Ar1}-OCH_3, 4^{Ar2}-OCH_3), 6.53 (s, H1′), 7.01 (d, $J(H5^{Ar1},H6^{Ar1})$ = 8.6 Hz, $H5^{Ar1}$), superimposes in part 7.03 (d, $J(H5^{Ar2},H6^{Ar2})$ = 8.6 Hz, $H5^{Ar2}$), 7.36 (dd, $J(H6^{Ar2},H5^{Ar2})$ = 8.4 Hz, $^4J(H6^{Ar2},H2^{Ar2})$ = 1.9 Hz, $H6^{Ar2}$), 7.46 (d, $^4J(H2^{Ar2},H6^{Ar2})$ = 1.7 Hz, $H2^{Ar2}$), 7.54 (dd, $J(H6^{Ar1},H5^{Ar1})$ = 8.6 Hz, $^4J(H6^{Ar1},H2^{Ar1})$ = 2.1 Hz, $H6^{Ar1}$), 7.61 (d, $^4J(H2^{Ar1},H6^{Ar1})$ = 2.1 Hz, $H2^{Ar1}$).

^{13}C NMR (101 MHz, acetone-d_6): δ = 56.1 (3^{Ar1}-OCH_3, 3^{Ar2}-OCH_3, 4^{Ar1}-OCH_3, 4^{Ar2}-OCH_3), 102.4 (C3), 107.8 (C1′), 112.7, 112.8, 112.8, and 114.5 ($C2^{Ar1}$, $C5^{Ar1}$, $C2^{Ar2}$, $C5^{Ar2}$), 121.8 ($C6^{Ar1}$), 123.5 and 127.0 ($C1^{Ar1}$, $C1^{Ar2}$), 125.0 ($C6^{Ar2}$), 142.0 (C5), 150.0, 150.1, 150.4 and 151.4 ($C3^{Ar1}$, $C4^{Ar1}$, $C3^{Ar2}$, $C4^{Ar2}$), 162.2 (C4), 168.6 (C2).

HRMS: *m/z* [M^+] calcd for $C_{21}H_{20}O_7$: 384.1209; found: 384.1212.

(*Z*)-3-(3,4-Dimethoxyphenyl)-4-hydroxy-5-[3,4-(methylenedioxy)benzylidene]furan-2(5*H*)-one [(*Z*)-8l[

Prepared analogously as described for pulvinone (*Z*)-**8g** from *i*-Pr_2NH (0.16 mL, 0.12 g, 1.1 mmol, 2.5 equiv), THF (1.0 mL), 2.5 M BuLi in hexane (0.45 mL, 1.14 mmol, 2.5 equiv), ester **20c** (0.238 g, 1.14 mmol, 2.5 equiv) in THF (1.0 mL), and dioxolanone **25e** (0.113 g, 0.455 mmol) in THF (2 mL). Yellow crystals (MeOH); yield: 0.132 g (79%); mp 240–245 °C.

IR (KBr): 3435, 1700, 1615, 1600, 1515, 1505, 1270, 1245, 1165, 1145, 1095, 1040, 1000 cm^{-1}.

^1H NMR (300 MHz, acetone-d_6): δ = 3.836 and 3.840 (2 s, 3^{Ar1}-OCH_3, 4^{Ar1}-OCH_3), 6.08 (s, OCH_2O), 6.76 (s, H1′), 6.93 (d, $J(H5^{Ar2},H6^{Ar2})$ = 8.2 Hz, $H5^{Ar2}$), 7.00 (d, $J(H5^{Ar1},H6^{Ar1})$ = 8.5 Hz, $H5^{Ar1}$), 7.24 (dd, $J(H6^{Ar2},H5^{Ar2})$ = 8.1 Hz, $^4J(H6^{Ar2},H2^{Ar2})$ = 1.6 Hz, $H6^{Ar2}$), 7.42 (d, $^4J(H2^{Ar2},H6^{Ar2})$ = 1.5 Hz, $H2^{Ar2}$), 7.64 (dd, $J(H6^{Ar1},H5^{Ar1})$ = 8.5 Hz, $^4J(H6^{Ar1},H2^{Ar1})$ = 2.1 Hz, $H6^{Ar1}$), 7.71 (d, $^4J(H2^{Ar1},H6^{Ar1})$ = 1.9 Hz, $H2^{Ar1}$); 4-OH was not detected.

^{13}C NMR (101 MHz, acetone-d_6): δ = 56.1 (3^{Ar1}-OCH_3, 4^{Ar1}-OCH_3), 101.4 (C3), 102.5 (OCH_2O), 108.1 (C1′), 109.3, 110.1, 112.5 and 112.6 ($C2^{Ar1}$, $C5^{Ar1}$, $C2^{Ar2}$, $C5^{Ar2}$), 121.4 ($C6^{Ar1}$), 124.0 and 128.5 ($C1^{Ar1}$, $C1^{Ar2}$), 126.3 ($C6^{Ar2}$), 142.2 (C5), 149.0, 149.1, 149.6, and 149.9 ($C3^{Ar1}$, $C4^{Ar1}$, $C3^{Ar2}$, $C4^{Ar2}$), 162.9 (C4), 168.7 (C2).

HRMS: *m/z* [M^+] calcd for $C_{20}H_{16}O_7$: 368.0896; found: 368.0892.

(*Z*)-3-(3,4-Dimethoxyphenyl)-4-hydroxy-5-(3,4,5-trimethoxybenzylidene)furan-2(5*H*)-one [(*Z*)-8m]

Prepared analogously as described for pulvinone (*Z*)-**8g** from *i*-Pr_2NH (0.16 mL, 0.12 g, 1.1 mmol, 2.5 equiv), THF (1.0 mL), 2.5 M BuLi in hexane (0.45 mL, 1.1 mmol, 2.5 equiv), ester **20c** (0.238 g, 1.14 mmol, 2.5 equiv) in THF (1.0 mL), and dioxolanone **25f** (0.134 g, 0.455 mmol) in THF (2 mL). Yellow crystals (MeOH); yield: 0.153 g (81%); mp 210–212 °C.

IR (KBr): 3425, 2940, 1755, 1635, 1580, 1520, 1510, 1465, 1425, 1325, 1260, 1235, 1125, 1030, 975 cm^{-1}.

^1H NMR (500 MHz, acetone-d_6): δ = 3.78, 3.841, 3.844, and 3.88 (last signal twice as intense as preceding 3 signals; 4 s, 3^{Ar1}-OCH_3, 3^{Ar2}-OCH_3, 4^{Ar1}-OCH_3, 4^{Ar2}-OCH_3, 5^{Ar2}-OCH_3), 6.55 (s, H1′), 7.01 (d, J(H5^{Ar1},H6^{Ar1}) = 8.5 Hz, H5^{Ar1}), 7.13 (s, H2^{Ar2}, H6^{Ar2}), 7.52 (dd, J(H6^{Ar1},H5^{Ar1}) = 8.5 Hz, ^4J(H6^{Ar1},H2^{Ar1}) = 2.0 Hz, H6^{Ar1}), 7.57 (d, ^4J(H2^{Ar1},H6^{Ar1}) = 2.0 Hz, H2^{Ar1}); 4-OH was not detected.

^{13}C NMR (126 MHz, acetone-d_6): δ = 56.1 (twice as intense as δ = 60.7), 56.5 (twice as intense as δ = 60.7), and 60.7 (3^{Ar1}-OCH_3, 3^{Ar2}-OCH_3, 4^{Ar1}-OCH_3, 4^{Ar2}-OCH_3, 5^{Ar2}-OCH_3), 102.8 (C3), 107.8 (C1′), 108.9 (C2^{Ar2}, C6^{Ar2}), 112.6 and 112.7 (C2^{Ar1}, C5^{Ar1}), 121.9 (C6^{Ar1}), 123.1 and 129.5 (C1^{Ar1}, C1^{Ar2}), 140.3 and 142.8 (C4^{Ar2}, C5), 150.0 and 150.1 (C3^{Ar1}, C4^{Ar1}), 154.5 (twice as intense as preceding signal, C3^{Ar2}, C5^{Ar2}), 162.9 (C4), 168.4 (C2).

HRMS: m/z [M$^+$] calcd $C_{22}H_{22}O_8$: 414.1315; found: 414.1310.

(*Z*)-5-(Benzylidene)-4-hydroxy-3-[3,4-(methylenedioxy)phenyl]furan-2(5*H*)-one [(*Z*)-8n]

Prepared analogously as described for pulvinone (*Z*)-**8g** from *i*-Pr_2NH (0.16 mL, 0.12 g, 1.1 mmol, 2.5 equiv), THF (1.0 mL), 2.5 M BuLi in hexane (0.45 mL, 1.14 mmol, 2.5 equiv), ester **20d** (0.221 g, 1.14 mmol, 2.5 equiv) in THF (1.0 mL), and dioxolanone **25a** (0.093 g, 0.46 mmol) in THF (2 mL). Yellow crystals (MeOH–H_2O, 10:1); yield: 0.105 g (75%); mp 235–238 °C.

IR (KBr): 3430, 3085, 3015, 2900, 1700, 1625, 1500, 1450, 1400, 1240, 1095, 1040, 1005 cm^{-1}.

^1H NMR (400 MHz, acetone-d_6): δ = 6.03 (s, OCH_2O), 6.77 (s, H1′), 6.93 (d, J(H5^{Ar1},H6^{Ar1}) = 8.2 Hz, H5^{Ar1}), 7.35 (incompletely resolved tt, J_{ortho} = 7.7 Hz, $^4J_{meta}$ = 1.9 Hz, H4^{Ar2}), 7.45 (m_c, approximately interpretable as dd, J_{ortho} = J_{ortho} = 7.5 Hz, H3^{Ar2}, H5^{Ar2}), 7.61 (d, ^4J(H2^{Ar1},H6^{Ar1}) = 1.3 Hz, H2^{Ar1}), 7.63 (dd, J(H6^{Ar1},H5^{Ar1}) = 8.2 Hz, ^4J(H6^{Ar1},H2^{Ar1}) = 1.7 Hz, H6^{Ar1}), 7.80 (m_c, approximately interpretable as br d, J_{ortho} = 7.3 Hz, H2^{Ar2}, H6^{Ar2}); 4-OH was not detected.

^{13}C NMR (101 MHz, acetone-d_6): δ = 101.6 (C3), 101.9 (OCH_2O), 108.1, 108.5, and 108.9 (C1′, C2^{Ar1}, C5^{Ar1}), 122.4 (C6^{Ar1}), 125.0 (C1^{Ar1}), 129.3 (half as intense as the next 2 peaks, C4^{Ar2}), 129.6 (C3^{Ar2}, C5^{Ar2}), 131.0 (C2^{Ar2}, C6^{Ar2}), 134.2 (C1^{Ar2}), 143.5 (C5), 147.5 and 148.3 (C3^{Ar1}, C4^{Ar1}), 163.1 (C4), 168.7 (C2).

HRMS: m/z [M$^+$] calcd for $C_{18}H_{12}O_5$: 308.0685; found 308.0678.

(*Z*)-4-Hydroxy-5-(4-hydroxybenzylidene)-3-[3,4-(methylenedioxy)phenyl]furan-2(5*H*)-one [(*Z*)-8o]

Prepared analogously as described for pulvinone (*Z*)-**8g** from *i*-Pr_2NH (0.16 mL, 0.12 g, 1.1 mmol, 2.5 equiv), THF (1.0 mL), 2.5 M BuLi in hexane (0.45 mL, 1.1 mmol, 2.5 equiv), ester **20d** (0.221 g, 1.14 mmol, 2.5 equiv) in THF (1.0 mL), and dioxolanone **25b** (0.100 g, 0.455 mmol) in THF (2 mL). Yellow crystals (MeOH–H_2O, 10:1); yield: 0.120 g (78%), mp 201 °C.

IR (KBr): 3410, 3305, 1710, 1605, 1500, 1440, 1400, 1265, 1240, 1170, 1095, 1040, 1020, 995 cm^{-1}.

^1H NMR (300 MHz, acetone-d_6): δ = 6.03 (s, OCH_2O), 6.53 (s, H1′), 6.92 (d, J(H5^{Ar1},H6^{Ar1}) = 7.8 Hz, H5^{Ar1}), overlaps with high-field portion of AA′BB′ signal centered at 6.93 (H3^{Ar2}, H5^{Ar2}) and 7.69 (H2^{Ar2}, H6^{Ar2}), 7.52 (d, ^4J(H2^{Ar1},H6^{Ar1}) = 1.2 Hz, H2^{Ar1}), flanked by 7.54 (dd, J(H6^{Ar1},H5^{Ar1}) = 8.1 Hz, ^4J(H6^{Ar1},H2^{Ar1}) = 1.6 Hz, H6^{Ar1}); 4-OH was not detected.

^{13}C NMR (101 MHz, acetone-d_6): δ = 100.9 (C3), 101.9 (OCH_2O), 108.4, 108.8, and 108.9 (C1′, C2^{Ar1}, C5^{Ar1}), 116.7 (C3^{Ar2}, C5^{Ar2}), 122.2 (C6^{Ar1}), 125.4 (C1^{Ar1}, C1^{Ar2}), 132.9 (C2^{Ar2}, C6^{Ar2}), 141.1 (C5), 147.3 and 148.3 (C3^{Ar1}, C4^{Ar1}), 159.6 (C4^{Ar2}), 163.2 (C4), 168.8 (C2).

HRMS: m/z [M$^+$] calcd for $C_{18}H_{12}O_6$: 324.0634; found: 324.0627.

(*Z*)-4-Hydroxy-5-(4-methoxybenzylidene)-3-[3,4-(methylenedioxy)phenyl]furan-2(5*H*)-one [(*Z*)-8p]

Prepared analogously as described for pulvinone (*Z*)-**8g** from *i*-Pr_2NH (0.16 mL, 0.12 g, 1.1 mmol, 2.5 equiv), THF (1.0 mL), 2.5 M BuLi in hexane (0.45 mL, 1.1 mmol, 2.5 equiv), ester **20d** (0.221 g, 1.14 mmol, 2.5 equiv) in THF (1.0 mL), and dioxolanone **25c** (0.106 g, 0.455 mmol) in THF (2 mL). Yellow crystals (MeOH–H_2O, 10:1); yield: 0.123 g (80%); mp 235–238 °C.

IR ($CDCl_3$ soln): ca. 3560, 3385, 3280, 2615, 2270, 2110, 1780, 1760, 1735, 1700, 1675, 1660, 1650, 1515, 1490, 1445, 1295, 1280, 1200, 1130, 980 cm^{-1}.

^1H NMR (500 MHz, acetone-d_6): δ = 3.85 (s, 4^{Ar2}-OCH_3), 6.02 (s, OCH_2O), 6.74 (s, H1′), 6.92 (d, J(H5^{Ar1},H6^{Ar1}) = 8.2 Hz, H5^{Ar1}), AA′BB′ signal centered at 7.02 (H3^{Ar2}, H5^{Ar2}) and 7.75 (H2^{Ar2}, H6^{Ar2}), 7.61 (d, ^4J(H2^{Ar1},H6^{Ar1}) = 1.7 Hz, H2^{Ar1}), 7.63 (dd, J(H6^{Ar1},H5^{Ar1}) = 8.2 Hz, ^4J(H6^{Ar1},H2^{Ar1}) = 1.7 Hz, H6^{Ar1}); 4-OH was not detected.

^{13}C NMR (126 MHz, acetone-d_6): δ = 55.67 (4^{Ar2}-OCH_3), 101.0 (C3), 101.9 (OCH_2O), 108.3, 108.4, and 108.8 (C1′, C2^{Ar1}, C5^{Ar1}), 115.2 (C3^{Ar2}, C5^{Ar2}), 122.2 (C6^{Ar1}), 125.2 and 126.8 (C1^{Ar1}, C1^{Ar2}), 132.7 (C2^{Ar2}, C6^{Ar2}), 141.7 (C5), 147.3 and 148.3 (C3^{Ar1}, C4^{Ar1}), 161.0 (C4^{Ar2}), 163.2 (C4), 168.7 (C2).

HRMS: m/z [M$^+$] calcd for $C_{19}H_{14}O_6$: 338.0790; found: 338.0792.

(*Z*)-5-(3,4-Dimethoxybenzylidene)-4-hydroxy-3-[3,4-(methylenedioxy)phenyl]furan-2(5*H*)-one [(*Z*)-8q]

Prepared analogously as described for pulvinone (*Z*)-**8g** from *i*-Pr_2NH (0.16 mL, 0.12 g, 1.1 mmol, 2.5 equiv), THF (1.0 mL), 2.5 M BuLi in hexane (0.45 mL, 1.14 mmol, 2.5 equiv), ester **20d** (0.221 g, 1.14 mmol, 2.5 equiv) in THF (1.0 mL), and dioxolanone **25d** (0.120 g, 0.455 mmol) in THF (2 mL). Yellow crystals (MeOH–H_2O, 10:1); yield: 0.134 g (80%); mp 245–250 °C.

IR (KBr): 3435, 1700, 1615, 1600, 1515, 1505, 1460, 1405, 1270, 1245, 1165, 1145, 1095, 1040, 1000 cm^{-1}.

^1H NMR (400 MHz, acetone-d_6): δ = 3.86 and 3.87 (2 s, 3^{Ar2}-OCH_3, 4^{Ar2}-OCH_3), 6.03 (s, OCH_2O), 6.72 (s, H1′), 6.92 (d, J(H5^{Ar1},H6^{Ar1}) = 8.2 Hz, H5^{Ar1}), 7.04 (d, J(H5^{Ar2},H6^{Ar2}) = 8.3 Hz, H5^{Ar2}), 7.34 (dd, J(H6^{Ar2},H5^{Ar2}) = 8.4 Hz, ^4J(H6^{Ar2},H2^{Ar2}) = 1.9 Hz, H6^{Ar2}), 7.43 (d, ^4J(H2^{Ar2},H6^{Ar2}) = 2.0 Hz, H2^{Ar2}), 7.60 (d, ^4J(H2^{Ar1},H6^{Ar1}) = 1.4 Hz, H2^{Ar1}), 7.62 (dd, J(H6^{Ar1},H5^{Ar1}) = 8.2 Hz, ^4J(H6^{Ar1},H2^{Ar1}) = 1.7 Hz, H6^{Ar1}); 4-OH was not detected.

^{13}C NMR (101 MHz, acetone-d_6): δ = 56.0 (3^{Ar2}-OCH_3, 4^{Ar2}-OCH_3), 101.1 (C3), 102.4 (OCH_2O), 107.9 (C1′), 109.3, 110.0, 112.2, and 112.5 (C2^{Ar1}, C5^{Ar1}, C2^{Ar2}, C5^{Ar2}), 121.2 (C6^{Ar1}), 123.91 and 128.3 (C1^{Ar1}, C1^{Ar2}), 126.1 (C6^{Ar2}), 142.2 (C5), 148.8, 148.9, 149.4 and 149.7 (C3^{Ar1}, C4^{Ar1}, C3^{Ar2}, C4^{Ar2}), 163.1 (C4), 168.7 (C2).

HRMS: m/z [M$^+$] calcd for $C_{20}H_{16}O_7$: 368.0896; found: 368.0889.

(*Z*)-4-Hydroxy-5-[3,4-(methylenedioxy)benzylidene]-3-[3,4-(methylenedioxy)phenyl]furan-2(5*H*)-one [(*Z*)-8r]

Prepared analogously as described for pulvinone (*Z*)-**8g** from *i*-Pr_2NH (0.16 mL, 0.12 g, 1.1 mmol, 2.5 equiv), THF (1.0 mL), 2.5 M BuLi in hexane (0.45 mL, 1.14 mmol, 2.5 equiv), ester **20d** (0.221 g, 1.14 mmol, 2.5 equiv) in THF (1.0 mL), and dioxolanone **25e** (0.113 g, 0.455 mmol) in THF (2 mL). Yellow crystals (MeOH–H_2O, 10:1); yield: 0.126 g (79%); mp 250–255 °C.

IR (KBr): 3425, 3085, 3015, 2905, 1695, 1620, 1500, 1490, 1445, 1415, 1315, 1260, 1245, 1110, 1095, 1040 cm^{-1}.

^1H NMR (400 MHz, acetone-d_6): δ = 6.03 and 6.08 (2 s, OCH_2O^{Ar1}, OCH_2O^{Ar2}), 6.70 (s, H1′), 6.92 (d, J(H5^{Ar1},H6^{Ar1}) = 7.7 Hz, H5^{Ar1})*,

in part overlapped by 6.94 (d, $J(H5^{Ar2},H6^{Ar2})$ = 7.7 Hz, $H5^{Ar2}$)*, 7.23 (dd, $J(H6^{Ar2},H5^{Ar2})$ = 8.2 Hz, $^4J(H6^{Ar2},H2^{Ar2})$ = 1.7 Hz, $H6^{Ar2}$), 7.41 (d, $^4J(H2^{Ar2},H6^{Ar2})$ = 1.7 Hz, $H2^{Ar2}$), 7.59 (d, $^4J(H2^{Ar1},H6^{Ar1})$ = 1.7 Hz, $H2^{Ar1}$), 7.61 (dd, $J(H6^{Ar1},H5^{Ar1})$ = 7.7 Hz, $^4J(H6^{Ar1},H2^{Ar1})$ = 1.7 Hz, $H6^{Ar1}$); 4-OH was not detected; *assignments interchangeable.

^{13}C NMR (101 MHz, acetone-d_6): δ = 100.9 (C3), 101.8 and 102.4 (OCH_2O^{Ar1}, OCH_2O^{Ar2}), 108.2, 108.3, 108.8, 109.3, and 110.0 (C1′, $C2^{Ar1}$, $C5^{Ar1}$, $C2^{Ar2}$, $C5^{Ar2}$), 122.1 ($C6^{Ar1}$), 125.0 and 128.2 ($C1^{Ar1}$, $C1^{Ar1}$), 126.2 ($C6^{Ar2}$), 142.0 (C5), 147.2, 148.2, 148.9, and 148.9 ($C3^{Ar1}$, $C4^{Ar1}$, $C3^{Ar2}$, $C4^{Ar2}$), 163.2 (C4), 168.5 (C2).

Selected signal from gated-decoupled (126 MHz, acetone-d_6): δ = 163.23 (d, $^3J_{C4,H1'}$ = 3.7 Hz, C4; proof of origin of this doublet splitting: selective irradiation of $\delta_{H1'}$ = 6.70 makes resonance at δ_{C4} = 163.2 collapse into s).

Anal. Calcd for $C_{19}H_{12}O_7$ (352.1): C, 64.78; H, 3.43. Found: C, 64.51; H, 3.52.

(*Z*)-4-Hydroxy-3-[3,4-(methylenedioxy)phenyl]-5-(3,4,5-trimethoxybenzylidene)furan-2(5*H*)-one [(*Z*)-8s]

Prepared analogously as described for pulvinone (*Z*)-**8g** from *i*-Pr_2NH (0.16 mL, 0.12 g, 1.1 mmol, 2.5 equiv), THF (1.0 mL), 2.5 M BuLi in hexane (0.45 mL, 1.14 mmol, 2.5 equiv), ester **20d** (0.221 g, 1.14 mmol, 2.5 equiv) in THF (1.0 mL), and dioxolanone **25f** (0.134 g, 0.455 mmol) in THF (2 mL). Yellow crystals (MeOH–H_2O, 10:1); yield: 0.148 g (82%); mp 210–212 °C.

IR (KBr): 3435, 3005, 2945, 1710, 1635, 1620, 1580, 1505, 1455, 1425, 1400, 1335, 1295, 1250, 1235, 1155, 1135, 1040, 995 cm^{-1}.

^{1}H NMR (400 MHz, acetone-d_6): δ = 3.78 (s, 4^{Ar2}-OCH_3), 3.88 (s, twofold intensity, 3^{Ar2}-OCH_3, 5^{Ar2}-OCH_3), 6.03 (s, OCH_2O), 6.70 (s, H1′), 6.93 (d, $J(H5^{Ar1},H6^{Ar1})$ = 8.2 Hz, $H5^{Ar1}$), 7.11 (s, $H2^{Ar2}$, $H6^{Ar2}$), 7.59 (d, $^4J(H2^{Ar1},H6^{Ar1})$ = 1.7 Hz, $H2^{Ar1}$), 7.61 (dd, $J(H6^{Ar1},H5^{Ar1})$ = 8.2 Hz, $^4J(H6^{Ar1},H2^{Ar1})$ = 1.7 Hz, $H6^{Ar1}$); 4-OH was not detected.

^{13}C NMR[5] (101 MHz, acetone-d_6): δ = 56.48 (twofold intensity, 3^{Ar2}-OCH_3, 5^{Ar2}-OCH_3), 60.6 (4^{Ar2}-OCH_3), 101.3 (C3), 101.9 (OCH_2O), 108.4, 108.5, and 108.8 (C1′, $C2^{Ar1}$, $C5^{Ar1}$, $C2^{Ar2}$, $C6^{Ar2}$), 122.3 ($C6^{Ar1}$), 124.9 and 129.5 ($C1^{Ar1}$, $C1^{Ar2}$), 140.1 ($C4^{Ar2}$), 142.7 (C5), 147.4 and 148.3 ($C3^{Ar1}$, $C4^{Ar1}$), 154.3 ($C3^{Ar2}$, $C5^{Ar2}$), 163.1 (C4), 168.5 (C2).

2-(Dibutoxyphosphoryl)-2-hydroxyacetic Acid (23b)

A mixture of dihydroxyacetic acid **22** (10.6 g, 113 mmol) and dibutyl phosphite (22.1 mL, 20.9 g, 113 mmol, 1.0 equiv) was stirred at 50 °C for 5 h. The resulting product (**23b**, 28.9 g, 95%) was not purified but directly converted into dioxolanone **24b**.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.94 (t, J(H4′,H3′) = 7.4 Hz, 2 × 3 H4′), 1.42 (qt, J(H3′,H2′) = J(H3′,H4′) = 7.6 Hz, 2 × 2 H3′), 1.68 (br tt, J(H2′,H1′) = J(H2′,H3′) = 6.6 Hz, 2 × 2 H2′), 4.20 (m_c, 2 × 2 H1′), 4.58 (d, ^2J(H2,P) = 16.3 Hz, H2), 5.50 (br s, 1-OH, 2-OH).

4-(Dibutoxyphosphoryl)-2,2-dimethyl-1,3-dioxolan-5-one (24b)

Method A: A soln of crude hydroxy acid **23b** (3.77 g, 14.1 mmol) and 2,2-dimethoxypropane (2.64 mL, 2.19 g, 21.1 mmol, 1.5 equiv) in toluene (60 mL) was heated in an inverse H_2O-separator at reflux for 12 h. The solvent was removed under reduced pressure and the residue purified by flash chromatography (silica gel, column diameter 6 cm, cyclohexane–EtOAc, 3:1). This provided **24b** (3.46 g, 80%) as a colorless oil.

Method B: At r.t., BF_3·OEt_2 (34.6 mL, 38.9 g, 274 mmol, 1.75 equiv) was added dropwise to a soln of crude hydroxy acid **23b** (42.0 g, 157 mmol) in Et_2O (70 mL) and acetone (11.8 mL, 9.11 g, 157 mmol, 1.0 equiv) and stirring continued overnight. Sat. aq $NaHCO_3$ (50 mL) was added. The aqueous phase was discarded and the organic phase first extracted with H_2O (3 × 50 mL) and then dried (Na_2SO_4). Evaporation of the solvent in vacuo and purification of the non-volatile residue by flash chromatography (silica gel, column diameter 12 cm, cyclohexane–EtOAc, 3:1) yielded **24b** (38.6 g, 80%).

IR ($CDCl_3$ soln): 2965, 2940, 2910, 2875, 1805, 1465, 1435, 1390, 1260, 1125, 1030, 960 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.94 (t, J(H4′,H3′) = 7.4 Hz, 2 × 3 H4′), 1.42 (qt, J(H3′,H2′) = J(H3′,H4′) = 7.3 Hz, 2 × 2 H3′), 1.58 and 1.72 [2 s, 2-$(CH_3)_2$], the last signal superimposes in part 1.70 (br tt, J(H2′,H1′) = J(H2′,H3′) = 7.0 Hz, 2 × 2 H2′), 4.19 (m_c, 2 × 2 H1′), 4.69 (d, ^2J(H4,P) = 11.0 Hz, H4).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 13.6 (2 × C4′), 18.6 (2 × C3′), 26.5 and 26.9 [2-$(CH_3)_2$], 32.5 and 32.5 (2 d, ^3J(C2′,P) = 5.4 Hz, 2 × C2′), 67.7 and 67.9 (2 d, ^2J(C1′,P) = 7.0 Hz, 2 × C1′), 71.3 (d, ^1J(C4,P) = 169.5 Hz, C4), 113.2 (d, ^3J(C2,P) = 5.4 Hz, C2), 167.2 (C5).

Anal. Calcd for $C_{13}H_{25}O_6P$ (308.3): C, 50.65; H, 8.12. Found: C, 50.75; H, 8.11.

2-(Diisopropoxyphosphoryl)-2-hydroxyacetic Acid (23c)

A mixture of dihydroxyacetic acid **22** (1.25 g, 13.6 mmol) and diisopropyl phosphite (2.26 mL, 2.26 g, 13.6 mmol, 1.0 equiv) was stirred at 60 °C for 5 h. The resulting product (**23c**, 3.1 g, 95%) was not purified but directly converted into dioxolanone **24c**.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.37 (d, J(H2′,H1′) = 6.0 Hz, 4 × 3 H2′), 4.51 (d, ^2J(H2,P) = 16.3 Hz, H2), 4.83 (sept, J(H1′,H2′) = 6.4 Hz, 2 × H1′), 5.50 (br s, 1-OH, 2-OH).

4-(Diisopropoxyphosphoryl)-2,2-dimethyl-1,3-dioxolan-5-one (24c)

A soln of crude hydroxy acid **23c** (3.50 g, 14.7 mmol) and 2,2-dimethoxypropane (2.74 mL, 2.28 g, 21.9 mmol, 1.5 equiv) in toluene (60 mL) was treated as described for the conversion **23b** into **24b** until the title compound was obtained (3.3 g, 80%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.37 and 1.39 (2 d, J(H2′,H1′) = 6.0 Hz, 4 × 3 H2′), 1.57 and 1.72 [2 s, 2-$(CH_3)_2$], 4.62 (d, ^2J(H4,P) = 11.0 Hz, H4), 4.79–4.91 (m_C, 2 × H1′).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 23.8 (d, ^3J(C2′,P) = 2.4 Hz, C2′), 23.9 (d, ^3J(C2′,P) = 3.0 Hz, C2′), 24.2 (d, ^3J(C2′,P) = 2.1 Hz, C2′), 24.2 (d, ^3J(C2′,P) = 2.7 Hz, C2′), 26.6 [d, ^4J(2-CH_3,P) = 1.5 Hz, 2-$(CH_3)^1$], 26.9 [2-$(CH_3)^2$], 71.7 (d, ^1J(C4,P) = 170.5 Hz, C4), 73.1 and 73.2 (2 d, ^2J(C1′,P) = 7.0 Hz, 2 × C1′), 112.9 (d, ^3J(C2,P) = 5.4 Hz, C2), 167.3 (C5).

(*E*)-5-Benzylidene-2,2-dimethyl-1,3-dioxolan-4-one [(*E*)-25a]

Prepared analogously as described for benzylidenedioxolanone (*Z*)-**25c** from *i*-Pr_2NH (0.35 mL, 0.26 g, 2.5 mmol, 1.5 equiv), 2.5 M BuLi in hexane (1.0 mL, 2.5 mmol, 1.5 equiv), phosphoryldioxolanone **24b** (0.511 g, 1.66 mmol), and benzaldehyde (0.19 mL, 0.20 g, 1.8 mmol, 1.1 equiv). Flash chromatography (4 cm, cyclohexane–EtOAc, 5:1) provided the title compound as an oil; yield: 0.27 g (80%); ratio *E*/*Z* 95:5.

IR ($CDCl_3$ soln): 3000, 2940, 1780, 1650, 1495, 1455, 1390, 1365, 1225, 1180, 1045, 995, 935, 920, 905, 880 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$):

(*E*)-**25a**: δ = 1.67 [s, 2-$(CH_3)_2$], 6.51 (s, H1′), 7.28–7.38 (m, H3″, H4″, H5″), 7.71–7.74 (m, H2″, H6″).

(*Z*)-**25a**: δ = 1.73 [s, 2-$(CH_3)_2$], 6.47 (s, H1′), 7.66–7.69 (m, H2″, H6″); the remaining Ar-H were not identified unequivocally.

^{13}C NMR (126 MHz, $CDCl_3$):

(*E*)-**25a**: δ = 26.9 [2-(CH_3)$_2$], 110.4 (C2), 115.1 (C1′), 128.3 (C3″, C5″), 128.4 (C4″), 129.9 (C2″, C6″), 132.0 (C1″), 138.0 (C5), 161.5 (C4).

(*Z*)-**25a**: δ = 27.0 [2-(CH_3)$_2$], 108.4 (C1′), 128.6 (C4″), 128.7 (C3″, C5″), 129.6 (C2″, C6″); the resonances of C2, C4, C5, and C1″ were not detected.

Anal. Calcd for $C_{12}H_{12}O_3$ (204.2): C, 70.59; H, 5.88. Found: C, 70.34; H, 6.07.

(*E*)-5-(4-Hydroxybenzylidene)-2,2-dimethyl-1,3-dioxolan-4-one [(*E*)-25b]

Prepared analogously as described for benzylidenedioxolanone (*Z*)-**25c** from *i*-Pr_2NH (0.35 mL, 0.26 g, 2.5 mmol, 1.5 equiv), 2.5 M BuLi in hexane (1.0 mL, 2.5 mmol, 1.5 equiv), phosphoryldioxolanone **24b** (0.511 g, 1.66 mmol), and 4-hydroxybenzaldehyde (0.223 g, 1.83 mmol, 1.1 equiv). Flash chromatography (4 cm, cyclohexane–EtOAc 5:1) provided the title compound as a solid; yield: 0.288 g (79%); ratio *E*/*Z* 87:13.

IR (film): 3400, 3000, 2940, 1760, 1610, 1540, 1515, 1440, 1390, 1380, 1365, ca. 1280, 1180, 1055, 1000, 920, 880, 830, 765 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$):

(*E*)-**25b**: δ = 1.65 [s, 2-(CH_3)$_2$], 4.79 (s, OH), 6.44 (s, H1′), AA′BB′ signal centered at 6.81 (H3″, H5″) and 7.69 (H2″, H6″).

(*Z*)-**25b**: δ = 1.72 [s, 2-(CH_3)$_2$], 4.82 (s, OH), 6.42 (s, H1′), AA′BB′ signal centered at ca. 6.85 (partly superimposed by *E*-isomer; H3″, H5″) and 7.58 (H2″, H6″).

^{13}C NMR (126 MHz, $CDCl_3$):

(*E*)-**25b**: δ = 26.8 [2-(CH_3)$_2$], 110.5 (C2), 115.4 (C3″, C5″), 115.7 (C1′)*, 124.6 (C1″), 131.8 (C2″, C6″), 136.6 (C5), 156.2 (C4″), 162.3 (C4); *interchangeable with C3″/C5″ of (*Z*)-**25b**.

(*Z*)-**25b**: δ = 27.0 [2-(CH_3)$_2$], 108.7 (C1′), 111.9 (C2), 115.8 (C3″, C5″)*, 125.8 (C1″), 131.5 (C2″, C6″), 135.6 (C5); signals of C4 and C4″ not detected; *interchangeable with C1′ of (*E*)-**25b**.

Selected signals from gated-decoupled ^{13}C NMR (126 MHz, $CDCl_3$): δ = 162.4 (d, ^3J(C4,H1′) = 10.1 Hz, $C4_{(E)\text{-}\mathbf{25b}}$), 164.6 (d, ^3J(C4,H1′) = 3.7 Hz, $C4_{(Z)\text{-}\mathbf{25b}}$).

Anal. Calcd for $C_{12}H_{12}O_4$ (220.2): C, 65.45; H, 5.45. Found: C, 65.39; H, 6.08.

(*E*)-5-(4-Methoxybenzylidene)-2,2-dimethyl-1,3-dioxolan-4-one [(*E*)-25c]

At –78 °C 2.5 M BuLi in hexane (1.0 mL, 2.5 mmol, 1.5 equiv) was added dropwise to a soln of *i*-Pr_2NH (0.35 mL, 0.26 g, 2.5 mmol, 1.5 equiv) in THF (1.0 mL) and DMPU (0.2 mL). Stirring at that temperature was continued for 1 h. A soln of dioxolanone **24b** (0.512 g, 1.66 mmol) in THF (1.0 mL) and DMPU (0.2 mL) was added, followed 25 min later by 4-methoxybenzaldehyde (0.24 mL, 0.24 g, 1.8 mmol, 1.1 equiv) in THF (1.0 mL). After stirring at –78 °C overnight, sat. aq. NH_4Cl (5 mL) was added. The phases were separated. The aqueous phase was extracted with EtOAc (3 × 5 mL). The combined organic phases were dried (Na_2SO_4) and then evaporated in vacuo. Purification of the residue by flash chromatography (column diameter 3 cm, cyclohexane–EtOAc, 5:1) furnished the title compound as an oil; yield: 0.341g (88%); ratio *E*/*Z* 95:5.

IR (film): 2995, 2940, 2840, 1780, 1605, 1515, 1460, 1305, 1220, 1175, 1035, 995, 920, 905, 830, 765 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$):

(*E*)-**25c**: δ = 1.65 [s, 2-(CH_3)$_2$], 3.82 (s, 4″-OCH_3), 6.46 (s, H1′), AA′BB′ signal centered at 6.88 (H3″, H5″) and 7.73 (H2″, H6″).

(*Z*)-**25c**: δ = 1.71 [s, 2-(CH_3)$_2$], 3.83 (s, 4″-OCH_3), 6.43 (s, H1′), AA′BB′ signal centered at ca. 6.91 (H3″, H5″) and 7.62 (H2″, H6″).

^{13}C NMR (101 MHz, $CDCl_3$):

(*E*)-**25c**: δ = 26.8 [2-(CH_3)$_2$], 55.4 (4″-OCH_3), 110.2 (C2), 113.8 (C3″, C5″), 115.4 (C1′), 124.7 (C1″), 131.6 (C2″, C6″), 136.7 (C5), 159.8 (C4″), 161.9 (C4).

(*Z*)-**25c**: δ = 27.1 [2-(CH_3)$_2$], 114.3 (C3″, C5″), 131.2 (C2″, C6″); the other ^{13}C nuclei were not detected.

Selected signals from gated-decoupled ^{13}C NMR (126 MHz, $CDCl_3$): δ = 161.9 (d, ^3J(C4,H1′) = 10.1 Hz, $C4_{(E)\text{-}\mathbf{25c}}$), 164.2 (d, ^3J(C4,H1′) = 3.7 Hz, $C4_{(Z)\text{-}\mathbf{25c}}$).

Anal. Calcd for $C_{13}H_{14}O_4$ (234.3): C, 66.67; H, 5.98. Found: C, 66.59; H, 5.75.

(*E*)-5-(3,4-Dimethoxybenzylidene)-2,2-dimethyl-1,3-dioxolan-4-one [(*E*)-25d]

Prepared analogously as described for benzylidenedioxolanone (*Z*)-**25c** from *i*-Pr_2NH (0.35 mL, 0.26 g, 2.5 mmol, 1.5 equiv), 2.5 M BuLi in hexane (1.0 mL, 2.5 mmol, 1.5 equiv), phosphoryldioxolanone **24b** (0.512 g, 1.66 mmol), and 3,4-dimethoxybenzaldehyde (0.304 g, 1.83 mmol, 1.1 equiv). Flash chromatography (4 cm, cyclohexane–EtOAc, 5:1) provided the title compound as an oil; yield: 0.35 g (80%); ratio *E*/*Z* 87:13.

IR (film): 3095, 3005, 2940, 2840, 1770, 1595, 1515, 1465, 1390, 1375, 1330, 1270, 1215, 1180, 1140, 1025, 910, 900, 800 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$):

(*E*)-**25d**: δ = 1.66 [s, 2-(CH_3)$_2$], 3.90 and 3.93 (2 s, 3″-OCH_3, 4″-OCH_3), 6.45 (s, H1′), 6.83 (d, J(H5″,H6″) = 8.4 Hz, H5″), 7.13 (dd, J(H6″,H5″) = 8.4 Hz, ^4J(H6″,H2″) = 2.0 Hz, H6″), 7.83 (d, ^4J(H2″,H6″) = 2.0 Hz, H2″).

(*Z*)-**25d**: δ = 1.72 [s, 2-(CH_3)$_2$], 3.908 and 3.913 (2 s, 3″-OCH_3, 4″-OCH_3), 6.43 (s, H1′), 6.89 (d, J(H5″,H6″) = 8.4 Hz, H5″), 7.23 (d, ^4J(H2″,H6″) = 2.0 Hz, H2″), ca. 7.27 (dd, J(H6″,H5″) = 9.3 Hz, ^4J(H6″,H2″) = 2.7 Hz, H6″).

^{13}C NMR (126 MHz, $CDCl_3$, slightly contaminated):

(*E*)-**25d**: δ = 26.8 [2-(CH_3)$_2$], 55.9 and 56.0 (3″-OCH_3, 4″-OCH_3), 110.4 (C2), 110.7 (C5″), 112.6 (C2″), 116.0 (C1′), 123.8 (C6″), 125.2 (C1″), 136.7 (C5), 148.6 and 149.5 (C3″, C4″), 162.0 (C4).

(*Z*)-**25d**: δ = 27.1 [2-(CH_3)$_2$], 108.8 (C1′), 111.3 (C5″), 112.5 (C2″), 123.3 (C6″), 126.0 (C1″), 135.8 (C5), 149.0 and 149.7 (C3″, C4″); the resonances of C2 and C4 were not identified.

HRMS: *m*/*z* [M$^+$] calcd for $C_{14}H_{16}O_5$: 264.0998; found: 264.0991.

(*E*)-2,2-Dimethyl-5-[3,4-(methylenedioxy)benzylidene]-1,3-dioxolan-4-one [(*E*)-25e]

Prepared analogously as described for benzylidenedioxolanone (*Z*)-**25c** from *i*-Pr_2NH (0.35 mL, 0.26 g, 2.5 mmol, 1.5 equiv), 2.5 M BuLi in hexane (1.0 mL, 2.5 mmol, 1.5 equiv), phosphoryldioxolanone **24b** (0.511 g, 1.66 mmol), and 3,4-(methylenedioxy)benzaldehyde (0.274 g, 1.83 mmol, 1.1 equiv). Flash chromatography (4 cm, cyclohexane–EtOAc, 5:1) provided the title compound as a solid; yield: 0.33 g (80%); ratio *E*/*Z* 89:11.

IR (film): 3000, 2945, 2900, 1770, 1690, 1605, 1495, 1450, 1385, 1340, ca. 1255, 1180, 1110, 1040, 1000, 930, 810, 760 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$):

(*E*)-**25e**: δ = 1.65 [s, 2-(CH_3)$_2$], 5.97 (s, OCH_2O), 6.41 (s, H1′), 6.77 (d, J(H5″,H6″) = 8.2 Hz, H5″), 7.10 (dd, J(H6″,H5″) = 8.2 Hz, ^4J(H6″,H2″) = 1.3 Hz, H6″), 7.55 (d, ^4J(H2″,H6″) = 1.8 Hz, H2″).

(*Z*)-**25e**: δ = 1.71 [s, 2-(CH_3)$_2$], 5.99 (s, OCH_2O), 6.39 (s, H1′), 6.82 (d, J(H5″,H6″) = 8.1 Hz, H5″), ca. 7.11 (dd, not entirely separated from the H6″ signal of (*E*)-**25e** ⇒ J(H6″,H5″) invisible, ^4J(H2″,H6″) = 1.9 Hz, H6″), 7.29 (d, ^4J(H2″,H6″) = 1.6 Hz, H2″).

^{13}C NMR (75 MHz, $CDCl_3$):

(*E*)-**25e**: δ = 26.8 [2-(CH_3)$_2$], 101.3 (OCH_2O), 108.2 and 109.9 (C2″, C5″), 110.4 (C2), 115.6 (C1′), 125.0 (C6″), 126.2 (C1″), 136.9 (C5), 147.7 and 147.9 (C3″, C4″), 161.7 (C4).

(*Z*)-**25e**: δ = 27.0 [2-(CH_3)$_2$], 101.4 (OCH_2O), 108.6, 108.7 and 109.2 (C1′, C2″, C5″), 111.8 (C2), 124.8 (C6″), 127.3 (C1″); signals of C4, C5, C3″, and C4″ not detected.

HRMS: *m*/*z* [M$^+$] calcd for $C_{13}H_{12}O_5$: 248.0685; found: 248.0679.

(*E*)-2,2-Dimethyl-5-(3,4,5-trimethoxybenzylidene)-1,3-dioxolan-4-one [(*E*)-25f]

Prepared analogously as described for benzylidenedioxolanone (*Z*)-**25c** from *i*-Pr_2NH (0.35 mL, 0.26 g, 2.6 mmol, 1.5 equiv), 2.5 M BuLi in hexane (1.0 mL, 2.5 mmol, 1.5 equiv), phosphoryldioxolanone **24b** (0.511 g, 1.66 mmol), and 3,4,5-trimethoxybenzaldehyde (0.359 g, 1.83 mmol, 1.1 equiv). Flash chromatography (4 cm, cyclohexane–EtOAc, 3:1) provided the title compound as a solid; yield: 0.41g (84%); ratio *E*/*Z* 90:10.

IR (film): 3060, 3000, 2965, 1775, 1585, 1460, 1330, 1265, 1225, 1200, 1135, 1000, 740, 705 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$):

(*E*)-**25f**: δ = 1.67 [s, 2-(CH_3)$_2$], 3.87 (s, 4″-OCH_3), 3.88 (s, twofold intensity; 3″-OCH_3, 5″-OCH_3), 6.42 (s, H1′), 7.14 (s, H2″, H6″).

(*Z*)-**25f**: δ = 1.73 [s, 2-(CH_3)$_2$], 6.39 (s, H1′), 6.93 (s, H2″, H6″).

^{13}C NMR (101 MHz, $CDCl_3$):

(*E*)-**25f**: δ = 26.8 [2-(CH_3)$_2$], 56.3 (twice as intense as the following peak, 3″-OCH_3, 5″-OCH_3), 61.0 (half as intense as the preceding peak, 4″-OCH_3), 107.6 (C2″, C6″), 110.5 (C2), 115.8 (C1′), 127.5 (C1″), 137.7 (C4″), 138.6 (C5), 152.9 (C3″, C5″), 161.8 (C4).

(*Z*)-**25f**: δ = 27.1 [2-(CH_3)$_2$], 107.3 (C2″, C6″), 108.7 (C1′), 128.5 (C1″), 153.4 (C3″, C5″); the other ^{13}C nuclei were not detected.

Selected signals from gated-decoupled ^{13}C NM (126 MHz, $CDCl_3$): δ = 161.8 (d, ^3J(C4,H1′) = 10.1 Hz, $C4_{(E)\text{-}\mathbf{25f}}$), 163.8 (d, ^3J(C4,H1′) = 3.7 Hz, $C4_{(Z)\text{-}\mathbf{25f}}$).

Anal. Calcd for $C_{15}H_{18}O_6$ (294.3): C, 61.22; H, 6.12. Found: C, 61.02; H, 6.11.

(*E*)-5-(2-Methylpropylidene)-2,2-dimethyl-1,3-dioxolan-4-one [(*E*)-25g]

Prepared analogously as described for benzylidenedioxolanone (*Z*)-**25c** from *i*-Pr_2NH (0.35 mL, 0.26 g, 2.5 mmol, 1.5 equiv), 2.5 M BuLi in hexane (1.0 mL, 2.5 mmol, 1.5 equiv), phosphoryldioxolanone **24b** (0.511 g, 1.66 mmol), and isobutyraldehyde (0.17 mL, 0.135 g, 1.8 mmol, 1.1 equiv). Flash chromatography (4 cm, petroleum ether–acetone, 4:1) provided the title compound as an oil; yield: 0.27 g (96%); ratio *E*/*Z* 95:5.

^{1}H NMR (400 MHz, $CDCl_3$):

(*E*)-**25g**: δ = 1.03 (d, *J*(H3′,H2′) or *J*(2′-CH_3,H2′) = 6.6 Hz, 2′-CH_3, 3 H3′), 1.59 [s, 2-(CH_3)$_2$], 3.48–3.53 (m_C, H2′), 5.36 (d, *J*(H1′,H2′) = 10.4 Hz, H1′).

(*Z*)-**25g**: δ = 1.07 (d, *J*(H3′,H2′) or *J*(2′-CH_3,H2′) = 6.6 Hz, 2′-CH_3, 3 H3′), 1.62 [s, 2-(CH_3)$_2$], 5.51 (d, *J*(H1′,H2′) = 9.1 Hz, H1′).

^{13}C NMR (101 MHz, $CDCl_3$):

(*E*)-**25g**: δ = 23.4 (twice as intense as the following peak, 2′-CH_3, 3 H3′), 24.1 (C2′), 26.7 [2-(CH_3)$_2$], 110.0 (C2), 122.4 (C1′), 136.2 (C5), 162.6 (C4).

(*Z*)-**25g**: δ = 26.8 [2-(CH_3)$_2$]; the other ^{13}C nuclei were not detected.

HRMS: *m*/*z* [M$^+$] calcd for $C_9H_{14}O_3$: 170.0943; found: 170.09441.

(*E*)-5-(Cyclohexylmethylene)-2,2-dimethyl-1,3-dioxolan-4-one [(*E*)-25h]

Prepared analogously as described for benzylidenedioxolanone (*Z*)-**25c** from *i*-Pr_2NH (0.35 mL, 0.26 g, 2.5 mmol, 1.5 equiv), 2.5 M BuLi in hexane (1.0 mL, 2.5 mmol, 1.5 equiv), phosphoryldioxolanone **24b** (0.511 g, 1.66 mmol), and cyclohexanecarbaldehyde (0.22 mL, 0.21 g, 1.8 mmol, 1.1 equiv). Flash chromatography (4 cm, petroleum ether–acetone, 4:1) provided the title compound as a solid; yield: 0.29 g (82%); pure (*E*) isomer.

IR (KBr): 2935, 2850, 2360, 2330, 1785, 1735, 1720, 1680, 1445, 1380, 1345, 1300, 1230, 1185, 1145, 995, 915 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.03–1.45 (m, H2 × 2 H2″, H2 × 2 H3″), 1.59 [s, 2-(CH_3)$_2$], 1.68–1.95 (m, 2 H4″), 3.16 (tdt, *J*(H1″,H2″$_{ax}$) = 11.0 Hz, *J*(H1″,H1′) = 10.9 Hz, *J*(H1″,H2″$_{eq}$) = 3.3 Hz, H1″), 5.38 (d, *J*(H1′,H1″) = 10.5 Hz, H1′).

^{13}C NMR (101 MHz, $CDCl_3$; contaminated with cyclohexanecarbaldehyde): δ = 25.6 (twice as intense as the following peak, 2 × C3″), 25.9 (C4″), 26.7 [2-(CH_3)$_2$], 33.3 (C1″), 33.6 (twice as intense as the preceding peak, 2 × C2″), 110.0 (C2), 121.1 (C1′), 136.4 (C5), 162.5 (C4).

Selected signal from gated-decoupled ^{13}C NMR (126 MHz, $CDCl_3$): δ = 162.6 (d, ^3J(C4,H1′) = 10.5 Hz, $C4_{(E)\text{-}\mathbf{25h}}$).

HRMS: *m*/*z* [M$^+$] calcd for $C_{12}H_{18}O_3$: 210.1256; found: 210.1255.

(*E*)-2,2-Dimethyl-5-nonylidene-1,3-dioxolan-4-one [(*E*)-25i]

Prepared analogously as described for benzylidenedioxolanone (*Z*)-**25c** from *i*-Pr_2NH (0.35 mL, 0.26 g, 2.5 mmol, 1.5 equiv), 2.5 M BuLi in hexane (1.0 mL, 2.5 mmol, 1.5 equiv), phosphoryldioxolanone **24b** (0.511 g, 1.66 mmol), and nonanal (0.31 mL, 0.26 g, 1.8 mmol, 1.1 equiv). Flash chromatography (4 cm, petroleum ether–acetone, 4:1) provided the title compound as a solid; yield: 0.37 g (92%); ratio *E*/*Z* 96:4.

IR (film): 2925, 2855, 2360, 2335, 1790, 1735, 1695, 1680, 1650, 1460, 1385, 1355, 1320, 1225, 1130, 1025, 995 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$):

(*E*)-**25i**: δ = 0.88 (t, *J*(H9′,H8′) = 7.0 Hz, 3 H9′), 1.27–1.43 (m, 2 H3′, 2 H4′, 2 H5′, 2 H6′, 2 H7′, 2 H8′), 1.59 [s, 2-(CH_3)$_2$], 2.55 (dt, *J*(H2′,H1′) = 7.8 Hz*, *J*(H2′,H3′) = 7.7 Hz*, 2 H2′), 5.52 (t, *J*(H1′,H2′) = 8.4 Hz, H1′); *interchangeable.

(*Z*)-**25i**: δ = 1.62 [s, 2-(CH_3)$_2$], 5.61 (t, $J_{H1',H2'}$ = 7.8 Hz, H1′).

^{13}C NMR (101 MHz, $CDCl_3$; contaminated with nonanal):

(*E*)-**25i**: δ = 14.2 (C9′), 22.7 and 24.4 (C7′, C8′), 26.7 [2-(CH_3)$_2$], 29.2, 29.3, 29.5, and 29.9 (C3′, C4′, C5′, C6′), 31.9 (C2′), 109.9 (C2), 115.6 (C1′), 137.5 (C5), 162.6 (C4).

HRMS: *m*/*z* [M$^+$] calcd for $C_{14}H_{24}O_3$: 240.1725; found: 240.1724.

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References

(1) Reviews: (a) Rao, Y. S. *Chem. Rev.* **1976**, *76*, 625. (b) Pattenden, G. *Prog. Chem. Nat. Prod.* **1978**, *35*, 133.
(2) Reviews: (a) Knight, D. W. *Contemp. Org. Synth.* **1994**, *1*, 287. (b) Negishi, E.-I.; Kotora, M. *Tetrahedron* **1997**, *53*, 6707. (c) Brückner, R. *Chem. Commun.* **2001**, 141. (d) Brückner, R. *Curr. Org. Chem.* **2001**, *5*, 679. (e) Rossi, R.; Bellina, F. In *Targets in Heterocyclic Systems: Chemistry and Properties*, Vol. 5; Attanasi, O. A.; Spinelli, D., Eds.; Società Chimica Italiana: Rome, **2002**, 169–198.

(3) Review: (a) Tejedor, C.; Garcia-Tellado, F. *Org. Prep. Proced. Int.* **2004**, *36*, 33. For recent syntheses of tetronic acids using Dieckmann condensations, see: (b) Sodeoka, M.; Sampe, R.; Kojima, S.; Baba, Y.; Usui, T.; Ueda, K.; Osada, H. *J. Med. Chem.* **2001**, *44*, 3216. (c) Mitsos, C. A.; Zografos, A. L.; Igglessi-Markopoulou, O. *J. Org. Chem.* **2000**, *65*, 5852. For a recent synthesis of tetronic acids by cyclization of γ-bromo-β-oxocarboxylic acids, see: (d) Tabake, K.; Mase, N.; Nomoto, M.; Daicho, M.; Tauchi, T.; Yoda, H. *J. Chem. Soc., Perkin Trans. 1* **2002**, 500. For a recent synthesis of tetronic acids by acid-treatment of the 2:1-adducts formed from aldehydes and methyl propiolate, see: (e) Aragón, D. T.; López, G. V.; Garcia-Tellado, F.; Marrero-Tellado, J. J.; de Armas, P.; Terrero, D. *J. Org. Chem.* **2003**, *68*, 3363. For a recent synthesis of tetronic acids by lactonization of γ-hydroxy-β-oxo esters resulting from the [2,3]-Wittig rearrangement of γ-(allyloxy)-β-oxo esters, see: (f) Pévet, I.; Meyer, C.; Cossy, J. *Tetrahedron Lett.* **2001**, *42*, 5215. For a recent synthesis of tetronic acids by the oxidation of β-hydroxy-γ-butyrolactones, see: (g) Kapferer, T.; Brückner, R.; Herzig, A.; König, W. A. *Chem. Eur. J.* **2005**, *11*, 2154.

(4) Review: (a) Brückner, R. *Curr. Org. Chem.* **2001**, *5*, 679, Section 7. Recent synthesis of pulvinones using methodology from ref. 9: (b) Klostermeyer, D.; Knops, L.; Sindlinger, T.; Polborn, K.; Steglich, W. *Eur. J. Org. Chem.* **2000**, *4*, 603.

(5) Reviews: (a) Brückner, R. *Curr. Org. Chem.* **2001**, *5*, 679, Sections 8–9. (b) Pattenden, G. *Prog. Chem. Nat. Prod.* **1978**, *35*, 133, Sections III.1, III.3, and IV.2. (c) Gill, M.; Steglich, W. *Prog. Chem. Nat. Prod.* **1987**, *51*, 1, Section 2.1.3. Syntheses of pulvinic acids by Suzuki couplings with tetronic esters containing a triflate substituent at Cβ: (d) Ahmed, Z.; Langer, P. *Tetrahedron* **2005**, *61*, 2055. (e) Ahmed, Z.; Langer, P. *J. Org. Chem.* **2004**, *64*, 3753; and literature cited therein. For more applications of Langer's methodology, see: (f) Heurtaux, B.; Lion, C.; Le Gall, T.; Mioskowski, C. *J. Org. Chem.* **2005**, *70*, 1474. (g) Desage-El Mur, M.; Nowaczyk, S.; Le Gall, T.; Mioskowski, C.; Amekraz, B.; Moulin, C. *Angew. Chem. Int. Ed.* **2003**, *42*, 1289; *Angew. Chem.*, **2003**, *115*, 1327.

(6) Sheley, C. F.; Shechter, H. *J. Org. Chem.* **1970**, *35*, 2367.

(7) Claisen, L.; Ewan, T. *Justus Liebigs Ann. Chem.* **1895**, *284*, 245.

(8) Huang, R. L. *J. Chem. Soc.* **1957**, 4089.

(9) Campbell, A. C.; Maidment, M. S.; Pick, J. H.; Stevenson, D. F. M. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1567.

(10) Type **7** compounds were obtained by the addition of substituted benzylmagnesium chlorides to the C≡N bond of the O-trimethylsilylated cyanohydrin of arylacetaldehydes, followed by hydrolysis.[11]

(11) Gill, M.; Kiefel, M. J.; Lally, D. A.; Ten, A. *Aust. J. Chem.* **1990**, *43*, 1497.

(12) Method is given in ref. 9.

(13) Ester **9** was prepared by the alkylation of potassium phenylacetate with ethyl 2-bromo-3-phenylpropionate.[9]

(14) Tetronic ester **10a** was obtained by the base-mediated condensation of (4-methoxyphenyl)acetonitrile with diethyl oxalate followed by O-methylation of the enol and anhydride formation: Knight, D. W.; Pattenden, G. *J. Chem. Soc., Perkin Trans. 1* **1979**, 62. Hydride reduction provided a separable mixture of **10a** and hydroxy-**10a** which was once more reduced giving more **10a**.

(15) Knight, D. W.; Pattenden, G. *J. Chem. Soc., Perkin Trans. 1* **1979**, 70.

(16) Tetronic ester **10b** was obtained differently than tetronic ester **10a**, namely by the Dieckmann condensation of (ethoxycarbonyl)methyl phenylacetate followed by O-methylation.[9]

(17) Antane, S.; Caufield, C. E.; Hu, W.; Keeney, D.; Labthavikul, P.; Morris, K.; Naughton, S. M.; Petersen, P. J.; Rasmussen, B. A.; Singh, G.; Yang, Y. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 176.

(18) Reffstrup, J.; Boll, P. M. *Phytochemistry* **1979**, *18*, 325.

(19) Caufield, C. E.; Antane, S. A.; Morris, K. M.; Naughton, S. M.; Quagliato, D. A.; Andrae, P. M.; Enos, A.; Chiarello, J. F. WO 2005/019196, **2005**.

(20) Ramage, R.; Griffiths, G. J.; Shutt, F. E.; Sweeney, J. N. A. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1531.

(21) Ramage, R.; Griffiths, G. J.; Shutt, F. E.; Sweeney, J. N. A. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1539.

(22) Each of Ramage et al.'s three pulvinones emerged from a slightly different protocol:[21] (*Z*)-**21a**: Scheme 3, steps (e_1) and (e_2) (there appeared to be no addition of acid other than in one of the two recrystallization procedures); (*Z*)-**21b** was obtained from PhCHO and lithio-**20a** in 71% yield analogously as described in (e_1); step (e_2) was replaced by no evaporation of THF, adding H_2O, refluxing (30 min), evaporating the solvents, adding Et_2O–H_2O (1:1), keeping the aqueous phase, adding HCl (to pH 1), isolating the resulting solid; (*Z*)-**8b** was obtained from PhCHO and the lithium enolate of methyl phenylacetate in 94% yield analogously as described in (e_1); step (e_2) was replaced by evaporating THF, adding Et_2O–H_2O (1:1), keeping the aqueous phase, adding HCl (to pH 1), isolating the resulting solid. We followed a blend of the three procedures, replacing Ramage's step (e_2) by no evaporation of THF (i.e., like towards (*Z*)-**21b**), no refluxing with H_2O (i.e., unlike towards (*Z*)-**21b**), adding Et_2O–H_2O (1:1), etc.

(23) (a) Burk, M. J.; Kalberg, C. S.; Pizzano, A. *J. Am. Chem. Soc.* **1998**, *120*, 4345. Analogous addition of dialkyl phosphites/dialkyl *H*-phosphonates to butyl glyoxylate: (b) Pudovik, A. N.; Gur'yanova, I. V. *J. Gen. Chem. USSR (Engl. Transl.)* **1967**, *37*, 1566; *Zh. Obshch. Khim.*, **1967**, *37*, 1649. Analogous addition of diethyl phosphite/diethyl *H*-phosphonate to ethyl glyoxylate, liberated from its hemi(ethyl acetal): (c) Schmidt, U.; Langner, J.; Kirschbaum, B.; Braun, C. *Synthesis* **1994**, 1138.

(24) Method is given in: Gerlach, U.; Hünig, S. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 1283; *Angew. Chem.* **1987**, *99*, 1323.

(25) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(26) Blanchette, M. A.; Choy, W.; Davis, J. T.; Essenfeld, A. P.; Masamune, S.; Roush, W. R. *Tetrahedron Lett.* **1984**, *25*, 2183.

(27) Diaryl phosphonates $(ArO)_2P(=O)CH_2CO_2Et$ undergoing *Z*-selective Horner–Wadsworth–Emmons reactions with α-chiral aldehydes in the presence of NaI, DBU, and HMPA: Ando, K.; Oishi, T.; Hirama, M.; Hiroali, O.; Ibuka, T. *J. Org. Chem.* **2000**, *65*, 4745; in order to minimize health hazards, we replaced HMPA by DMPU.

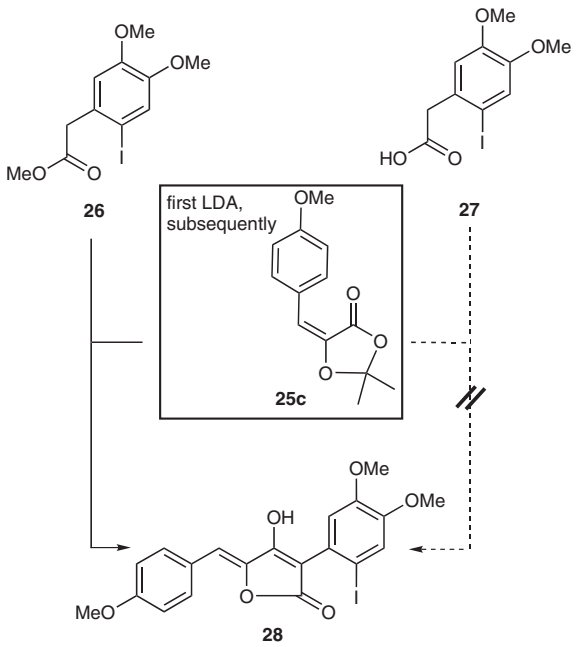
(28) Still, W. C.; Gennari, C. *Tetrahedron Lett.* **1983**, *24*, 4405.

(29) Kokin, K.; Iitake, K.-I.; Takaguchi, Y.; Aoyama, H.; Hayashi, S.; Motoyoshiya, J. *Phosphorus, Sulfur Silicon Relat. Elem.* **1998**, *133*, 21.

(30) Methyl 2-(*tert*-butyldimethylsiloxy)-2-(dimethoxyphosphoryl)acetate, upon deprotonation with LDA in pure THF, and 4-methoxy-2-(methoxymethoxy)benzaldehyde condense with seemingly perfect *Z*/*E* selectivity: Boehlow, T. R.; Harburn, J. J.; Spilling, C. D. *J. Org. Chem.* **2001**, *66*, 3111.

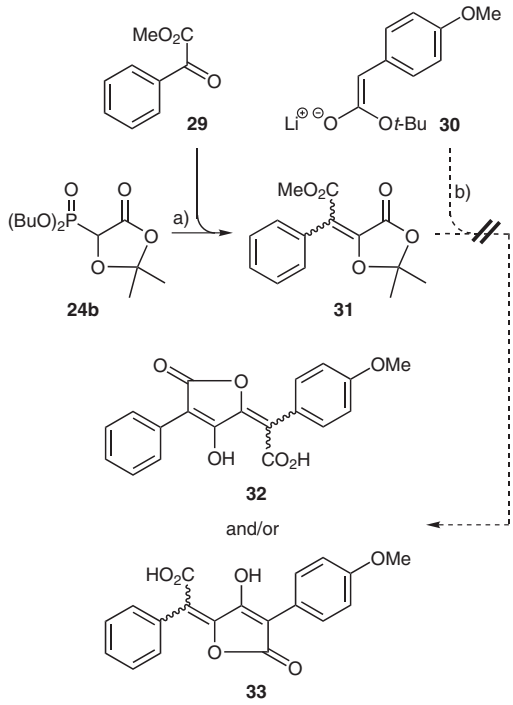
(31) (a) Nagaoka, H.; Kishi, Y. *Tetrahedron* **1981**, *37*, 3873. (b) Related finding: Boschelli, D.; Takemasa, T.; Nishitani, Y.; Masamune, S. *Tetrahedron Lett.* **1985**, *26*, 5239.

(32) Vogeli, U.; von Philipsborn, W. *Org. Magn. Reson.* **1975**, *7*, 617.
(33) In a related condensation using lithium diisopropylamide/ester **26**/dioxolanone **25c**, we ascertained that the yield of pulvinone **28** decreased from 60% to 40% upon changing the reactant ratio from 2.5:2.5:1 to 2.5:1.25:1 (Scheme 4). The analogous condensation using lithium diisopropylamide/carboxylic acid **27**/dioxolanone **25c** (2.2:1.1:1 ratio of the reactants) did not give pulvinone **28** under the conditions otherwise identical to those of Table 5 (Kaczybura, N. *Dissertation;* Universität Freiburg: Germany, **2005**).



Scheme 4

(34) Earlier description of pulvinone (*Z*)-**8f**: Ojima, N.; Takenaka, S.; Seto, S. *Phytochemistry* **1973**, *12*, 2527.
(35) Pulvinone (*Z*)-**8j** was synthesized in a mixture which also contained the isomeric pulvinone (*Z*)-5-(3,4-dimethoxybenzylidene)-4-hydroxy-3-(4-methoxyphenyl)furan-2(5*H*)-one: Edwards, R. L.; Gill, M. *J. Chem. Soc., Perkin Trans. 1* **1973**, 1921.
(36) We could not extend our approach to a synthesis of pulvinic acids **32** and **33**. While dioxolanone **31** was accessible by a Horner–Wadsworth–Emmons reaction between phosphonate **24b** and α-oxo ester **29** (79% yield), it did not react with the ester enolate **30** by Claisen condensation/transesterification (Scheme 5).



Scheme 5 *Reagents and conditions*: a) **24b** (1.0 equiv), LDA (1.7 equiv), THF, –78 °C, 30 min; **29**, 2.5 h; 79% (60:40 mixture of unassigned isomers); (b_1) **30** (2.5 equiv), THF, –78 °C, 2 h, to r.t., 0–2 h; (b_2) evaporation of THF; addition of Et_2O–H_2O (1:1), 60 °C, 1 h.