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Synthesis of pulvinones via tandem Dieckmann condensation–alkoxide β-elimination

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ABSTRACT

A series of pulvinones were prepared in three steps from a common precursor, methyl 3-phenylglycidate. This compound was readily converted to several diesters containing an ether function. Then, treatment of these compounds with lithium hexamethyldisilazide afforded the corresponding pulvinones, via tandem Dieckmann condensation–alkoxide β-elimination. The use of a 2,2,2-trifluoroethyl ether instead of a methyl ether facilitated the β-elimination and led to better yields of product.

1. Introduction

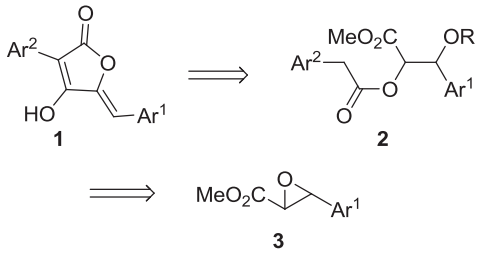
Pulvinones are benzylidene-4-hydroxy-3-phenyl-5-furan-2(5*H*)-one pigments isolated from several fungi, including boletus *Suillus grevillei*[1] and mold *Aspergillus terreus*.[2] Natural or synthetic compounds of this class display interesting biological activities, such as anticoagulant[3] or anti-inflammatory[4] properties. Inhibitors of bacterial cell wall biosynthesis have been recently reported.[5]

In connection with previous studies concerning the antioxidant activity of the related pigments pulvinic acids,[6,7] we became interested in an efficient synthetic access to pulvinones.[8] Pulvinone was first obtained as a by-product in the synthesis of pulvinic acid by Volhard[9] and its structure was ascertained by a synthesis by Claisen and Ewan.[10] Several syntheses were then reported.[11–15] The various synthetic strategies toward pulvinones have been discussed in a recent report by Brückner's group.[15b]

As for us, we focused on an adaptation of our previously described synthesis of pulvinic acids derivatives from dimethyl tartrate,[7] which relied on the use of a Lacey–Dieckmann condensation for the formation of the tetronic acid moiety,[16] the exocyclic double bond being created by dehydration of an alcohol precursor. According to this strategy, a pulvinone would then be accessible from the diol derived from an alkyl cinnamate, or more conveniently, from the corresponding epoxide.

The retrosynthetic analysis is summarized in the Scheme 1.

Herein we wish to present the implementation of this scheme, which led to the synthesis of several pulvinones having various Ar^2 groups.



Scheme 1. Planned synthesis of pulvinones.

2. Results and discussion

The starting material, methyl 3-phenylglycidate (**3**), was easily prepared as previously reported by Darzens reaction of methyl chloroacetate and benzaldehyde.[17]

The opening of methyl 3-phenylglycidate was realized using two alcohols, methyl alcohol and 2,2,2-trifluoroethyl alcohol, under boron trifluoride diethyl etherate catalysis.[18]

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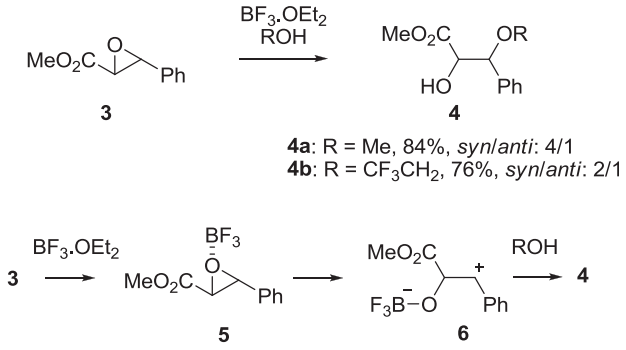
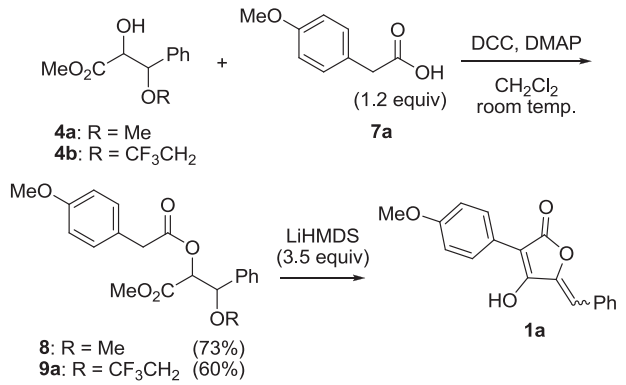
The corresponding alcohols **4a**,**b** were obtained as mixture of diastereoisomers, due to the intermediacy of a carbocation (Scheme 2).



Scheme 2. Synthesis of alcohols **4a**,**b**.

At first, the mixture of *syn*- and *anti*-alcohols **4a** was converted to diester **8** by treatment with 4-methoxyphenylacetic acid (**7a**), in the presence of dicyclohexylcarbodiimide (DCC) and 4-(dimethylamino)pyridine (DMAP) in dichloromethane, at room temperature (Scheme 3).



Scheme 3.

The direct conversion of diester **8** to the corresponding pulvinone necessitated that both the Dieckmann condensation and the β-elimination of the alkoxide would occur successively. Several conditions were tested, that led to pulvinone **1a**, having a 4-methoxyphenyl group at the 3-position of the tetronic acid ring (Scheme 3, Table 1).

Table 1
Optimization for the preparation of **1a**

Entry	R	Ether	Conditions	*Z*/*E* ratio[a]	Yield[b] (%)
1	Me	**8**	−78 °C, 1 h, then rt, 1 h	10/3	16
2	Me	**8**	−78 °C, 4 h, then rt, overnight	10/2	14
3	Me	**8**	−78 °C, 1 h, then rt, overnight	10/3	19
4	CF_3CH_2	**9a**	−78 °C, 1 h, then rt,1 h	10/1	61
5	CF_3CH_2	**9a**	−78 °C, 1 h, then rt, overnight	10/3	78

[a] Ratio according to ^{1}H NMR integrations.
[b] Yield in *Z*/*E* isomers mixture.

Ether **8** was thus treated at −78 °C with 3.5 equiv lithium hexamethyldisilazide (LiHMDS), according to the conditions previously reported to perform the Dieckmann condensation from a dimethyl tartrate-derived ester.[7]

Despite several attempts in which the reaction time and the reaction temperature were modified, it was not possible to obtain a good yield in pulvinone **1a** starting from methyl ether **8** (entries 1–3). It is noteworthy that tetronic acids intermediates, which had not undergone the β-elimination step, were present in the crude product, aside from the pulvinone and other unidentified by-products. Using more equivalents of base did not improve the yield either.

The reaction was then carried out using as starting material the 2,2,2-trifluoroethyl ether **9a** (a mixture of *syn*- and *anti*-isomers), prepared from alcohol **4b** and 4-methoxyphenylacetic acid **7a** (Scheme 3). Much better results were obtained from this precursor (Table 1, entries 4 and 5). The conditions leading to the best yield in pulvinone **1a** (78%) involved a treatment with the base at −78 °C for 1 h, followed by stirring at room temperature overnight.

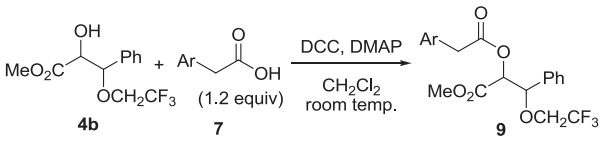
The leaving ability of 2,2,2-trifluoroethoxide was expected to be higher than that of methoxide on the basis of the pK_a values of the conjugate alcohols (15.07 for methanol, 12.32 for 2,2,2-trifluoroethanol).[19] It is also noteworthy that Brückner et al. showed that a 2,2,2-trifluoroethyl ester was an electrophile superior to a methyl or an ethyl ester in a Dieckmann reaction.[15b]

In every case, pulvinone **1a** was isolated as a mixture of isomers, the *Z*-isomer being always predominant. Their spectral characteristics were in agreement with those reported in the literature.[15c] The ethylenic protons of the *E*-isomer and the *Z*-isomer appear at δ=6.59 ppm and δ=6.82 ppm, respectively, in acetone-d_6.

Following these first results, we embarked in the preparation of several pulvinones starting from esters **9**. The two isomeric 2,2,2-trifluoroethyl ethers *syn*-**4b** or *anti*-**4b** were first separated by chromatography. Esters **9** were then prepared, in yields varying from 50 to 100%, from diverse arylacetic acids **7** and either *syn*-**4b** or *anti*-**4b** (Table 2).

The attribution of the *syn*/*anti* configurations was based on the X-ray structure of *anti*-**9i**, the 4-fluorophenylacetate obtained from *anti*-**4b** (Fig. 1).[20]

Table 2
Synthesis of diesters **8**



Entry	**4b**	**7**	Ar	**9**	Yield (%)
1	*syn*-**4b**	**7b**	C_6H_5	*syn*-**9b**	85
2	*anti*-**4b**	**7b**	C_6H_5	*anti*-**9b**	64
3	*anti*-**4b**	**7c**	4-MeC_6H_4	*anti*-**9c**	67
4	*syn*-**4b**	**7d**	2-(MeO)C_6H_4	*syn*-**9d**	81
5	*syn*-**4b**	**7e**	3-(MeO)C_6H_4	*syn*-**9e**	80
6	*anti*-**4b**	**7e**	3-(MeO)C_6H_4	*anti*-**9e**	88
7	*syn*-**4b**	**7f**	3,4-$(MeO)_2C_6H_3$	*syn*-**9f**	84
8	*anti*-**4b**	**7f**	3,4-$(MeO)_2C_6H_3$	*anti*-**9f**	100
9	*anti*-**4b**	**7g**	4-ClC_6H_4	*anti*-**9g**	60
10	*syn*-**4b**	**7h**	4-BrC_6H_4	*syn*-**9h**	50
11	*syn*-**4b**	**7i**	4-FC_6H_4	*syn*-**9i**	61
12	*anti*-**4b**	**7i**	4-FC_6H_4	*anti*-**9i**	61

Conditions similar to those described for the preparation of **1a** were then applied to the synthesis of several pulvinones **1b**–**i** derived from diesters **9**. Both *syn*- and *anti*-isomers have been used and in some cases the reaction was performed from a mixture of isomers. The results are summarized in Table 3.

The corresponding pulvinones were purified either by precipitation of the crude product in diethyl ether or *tert*-butyl methyl ether or by silica gel chromatography, and then isolated in 54–77% yield. Usually, a given pulvinone was obtained in similar yields from both *anti*- and *syn*-isomers of the corresponding diester **9**, as well as from a mixture of isomers (see entries 7–9, for the synthesis of pulvinone **1f**).

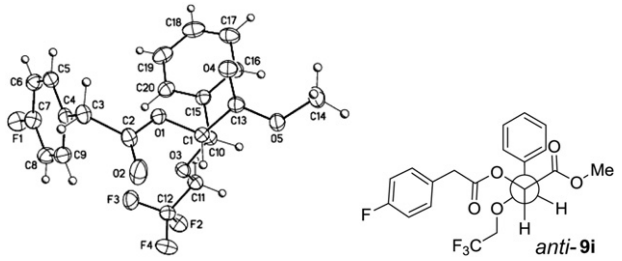
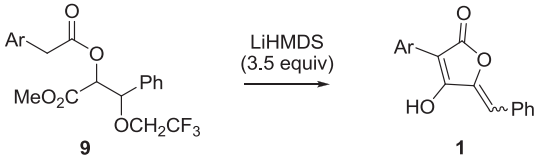


Fig. 1. Molecular structure of diester *anti*-**9i**.

Table 3
Synthesis of pulvinones **1**



9 **1**

Entry	**9**	Ar	**1**	*Z*/*E* ratio[a]	Yield (%)
1	*syn*-**9b**	C_6H_5	**1b**	92/8	74
2	*syn*/*anti*-**9b**	C_6H_5	**1b**	>98/2[b]	71
3	*anti*-**9c**	4-MeC_6H_4	**1c**	97/3	74
4	*syn*-**9d**	2-$(MeO)C_6H_4$	**1d**	96/4	54
5	*syn*-**9e**	3-$(MeO)C_6H_4$	**1e**	96/4	55
6	*anti*-**9e**	3-$(MeO)C_6H_4$	**1e**	97/3	70
7	*syn*-**9f**	3,4-$(MeO)_2C_6H_3$	**1f**	97/3	68
8	*anti*-**9f**	3,4-$(MeO)_2C_6H_3$	**1f**	97/3	63
9	*syn*/*anti*-**9f**	3,4-$(MeO)_2C_6H_3$	**1f**	>98/2[b]	76
10	*anti*-**9g**	4-ClC_6H_4	**1g**	97/3	65
11	*syn*-**9h**	4-BrC_6H_4	**1h**	>98/2[b]	71
12	*anti*-**9i**	4-FC_6H_4	**1i**	>98/2[b]	77

[a] Ratio according to ^{1}H NMR integrations.
[b] Only one isomer was observed in the ^{1}H NMR spectrum.

All the reactions led to the predominant formation of the pulvinone as the *Z*-isomer. Since anti-elimination is likely to occur under the reaction conditions, one could have expected that *anti*-**9** would have produce a *E*-pulvinone and that *syn*-**9** would have led to a *Z*-pulvinone. The outcome might be explained either by an epimerization of the stereogenic center on the tetronic acid prior to the elimination of the alkoxide, or by a conversion of the *E*-pulvinone to the more thermodynamically stable *Z*-isomer under the basic conditions. It has been reported by Campbell et al.[4] that the alkaline hydrolysis of the acetate of a *E*-pulvinone usually led to the *Z*-pulvinone, which implies that an isomerization had occurred under these conditions.

The X-ray structure of the *Z*-configurated fluorinated pulvinone **1i**, was determined, revealing the planarity of this compound (Fig. 2)[20]

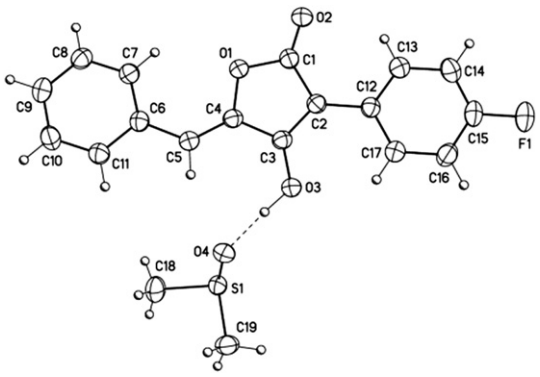


Fig. 2. Molecular structure of pulvinone **1i** (co-crystallized with DMSO).

3. Conclusion

In summary, a novel, straightforward three-step synthetic access to a series of pulvinones, obtained from methyl 3-phenylglycidate and various arylacetic acids was developed. The approach relied on a tandem Dieckmann condensation–β-elimination.

4. Experimental section

4.1. General

THF was freshly distilled from sodium benzophenone ketyl. Dichloromethane was freshly distilled over P_2O_5. Reactions were performed under an argon atmosphere. TLC: Silica Gel 60 F_{254} plates with detection by UV light and by an ethanol solution of phosphomolybdic acid. Column chromatography: 40–63 μm silica gel. Melting points were uncorrected. NMR: 400.133 and 100.624 MHz for ^{1}H and ^{13}C, respectively. Chemical shifts (δ) are in parts per million (s=singlet, d=doublet, t=triplet, m=multiplet, br=broad), coupling constants (J) are in hertz. In the descriptions of ^{1}H NMR spectra, the term Ar corresponds to the aryl group that originates from the arylacetic acid; the notations *o*-Ar–*H*, *m*-Ar–*H*, *p*-Ar–*H* indicate the proton positions on the aryl group, which are *ortho*, *meta*, *para* to the tetronic acid ring.

4.2. General procedure for the reaction of methyl phenylglycidate with an alcohol

Boron trifluoride diethyl etherate (350 μL, 2.8 mmol, 0.2 equiv) was added dropwise to a solution of methyl 3-phenylglycidate (2.5 g, 14.0 mmol, 1 equiv) in 2,2,2-trifluoroethanol (15 mL) at 0 °C under argon. The mixture was stirred at 0 °C for 30 min and at room temperature for 2 h. The mixture was then diluted with Et_2O, washed with a saturated $NaHCO_3$ solution. The aqueous layers were extracted with Et_2O, the organic layers were combined and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude oil was purified by flash chromatography (5–30% AcOEt/cyclohexane) to afford the alcohols *syn*-**4b** (1.99 g, 51%) as a colorless oil and *anti*-**4b** (1.0 g, 25%) as a white solid.

*4.2.1. syn-Methyl 2-hydroxy-3-phenyl-3-(2,2,2-trifluoroethoxy)propanoate (syn-**4b**).* IR (NaCl film) ν_{max}=3507, 3033, 2957, 2901, 2850, 1747, 1453, 1440, 1280, 1164, 1112, 1021, 966 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.38–7.32 (5H, m, Ph–*H*), 4.88 (1H, d, *J*=2.8 Hz, *CH*Ph), 4.26 (1H, d, *J*=2.8 Hz, *CH*CO_2Me), 3.85–3.75 (1H, m, *CH*CF_3), 3.77 (3H, s, CO_2CH_3), 3.64–3.54 (m, 1H, *CH*CF_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=172.2, 135.6, 128.9, 128.7 (2C), 127.6 (2C), 123.9 (q, *J*=279.6 Hz), 83.5, 74.6, 66.1 (q, 33.7 Hz), 52.7; MS, $[M+Na]^+$: (ESI$^+$) *m*/*z* 301.1 $[M+Na]^+$; HRMS (ESI$^+$) *m*/*z* calcd for $C_{12}H_{13}O_4F_3Na$, $[M+Na]^+$: 301.0664, found: 301.0671.

*4.2.2. anti-Methyl 2-hydroxy-3-phenyl-3-(2,2,2-trifluoroethoxy) propanoate (anti-**4b**).* Mp 61–62 °C; IR (NaCl film) ν_{max}=3479, 3035, 2956, 2901, 1744, 1453, 1440, 1280, 1165, 1131, 1003, 967 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.38–7.27 (5H, m, Ph–*H*), 4.75 (1H, d, *J*=4.5 Hz, *CH*Ph), 4.49 (1H, d, *J*=4.5 Hz, *CH*CO_2Me), 3.88–3.74 (1H, m, *CH*CF_3), 3.70 (3H, s, CO_2CH_3), 3.72–3.62 (m, 1H, *CH*CF_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=172.1, 135.0, 129.1, 128.7 (2C), 127.7 (2C), 123.9 (q, *J*=279.1 Hz), 84.1, 74.3, 66.5 (q, 34.5 Hz), 52.6; MS (ESI$^+$) *m*/*z* 301.1 $[M+Na]^+$; HRMS (ESI$^+$) *m*/*z* calcd for $C_{12}H_{13}F_3NaO_4$, $[M+Na]^+$: 301.0664, found: 301.0652.

4.3. General procedure for the esterification of alcohols *syn*-4b and *anti*-4b

Alcohol *syn*-**4b** (500 mg, 1.797 mmol, 1 equiv), DCC (445 mg, 2.16 mmol, 1.2 equiv), and DMAP (110 mg, 0.898 mmol, 0.5 equiv)

were added to phenylacetic acid (294 mg, 2.16 mmol, 1.2 equiv) in CH_2Cl_2 (5 mL) at room temperature, under nitrogen. The mixture was stirred at room temperature for 12 h and the solvent was removed under reduced pressure. Et_2O was added and the mixture was filtered. The filtrate was washed with sodium acetate buffer (pH=5) and the aqueous layer was extracted with Et_2O. The organic layers were combined, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by flash chromatography (0–5% AcOEt/cyclohexane) to afford compound *syn*-**9b** (605 mg, 85%) as a colorless oil.

*4.3.1. (2S,3R)-Methyl 3-phenyl-2-(2-phenylacetoxy)-3-(2,2,2-trifluoroethoxy)propanoate (syn-**9b**).* IR (NaCl film) ν_{max}=3066, 3033, 2955, 2850, 1748, 1496, 1454, 1437, 1280, 1243, 1216, 1158, 1133, 1069, 1030, 968 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=7.39–7.27 (8H, m, 5Ph–*H*+3 Ar–*H*), 6.20 (2H, m, Ar–*H*), 5.35 (1H, d, *J*=3.9 Hz, C*H*CO_2Me), 5.14 (1H, d, *J*=3.9 Hz, C*H*Ph), 3.94–3.82 (1H, m, C*H*CF_3), 3.77 (3H, s, OCH_3), 3.76 (1H, d, *J*=15.3 Hz, CH_2CO), 3.71 (1H, d, *J*=15.3 Hz, CH_2CO), 3.71–3.61 (1H, m, C*H*CF_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=170.6, 167.6, 134.5, 133.3, 129.4 (2C), 129.2, 128.8 (2C), 128.6 (2C), 127.5, 127.2, 123.8 (q, *J*=279.9 Hz), 81.9, 75.3, 66.4 (q, *J*=34.5 Hz), 52.6, 40.7; MS (ESI$^+$) *m*/*z* 419.1 [M+Na]$^+$; HRMS (ESI$^+$) *m*/*z* calcd for $C_{20}H_{19}O_5F_3Na$, [M+Na]$^+$: 419.1082, found: 419.1095.

*4.3.2. Methyl 2-(2-(4-methoxyphenyl)acetoxy)-3-phenyl-3-(2,2,2-trifluoroethoxy)propanoate (**9a**).* A mixture of alcohols *anti*- and *syn*-**4b** (781 mg, 2.8 mmol, 1 equiv), DCC (695 mg, 3.37 mmol, 1.2 equiv), DMAP (171 mg, 1.40 mmol, 0.5 equiv), and 4–methoxyphenylacetic acid (562 mg, 3.37 mmol, 1.2 equiv) were used following the general procedure to afford compound **9a** as a yellow oil (3/2 mixture of *syn*/*anti* isomers, 882 mg, 61%). TLC R_f=0.60 (30% AcOEt/cyclohexane); IR (NaCl film) ν_{max}=3325, 3035, 2934, 2848, 1748, 1615, 1584, 1514, 1455, 1279, 1249, 1161, 1133, 1033, 967 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=7.38–7.26 (5H, m, Ph–*H*), 7.09–7.02 (2H, m, *o*-Ar–*H*), 6.87–6.78 (2H, m, *p*-Ar–*H*), 5.29 (1H, d, *J*=6.5 Hz, C*H*CO_2Me minor diast.), 5.28 (1H, d, *J*=3.8 Hz, C*H*CO_2Me major diast.), 5.08 (1H, d, *J*=3.8 Hz, C*H*Ph major diast.), 4.82 (1H, d, *J*=6.5 Hz, C*H*Ph minor diast.), 3.90–3.66 (2H, m, CH_2CF_3), 3.79 (3H, s, OCH_3), 3.75–3.60 (2H, m, CH_2CO), 3.71 (3H, s, ArOCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=171.0, 170.6, 168.0, 167.7, 158.8, 135.0, 134.5, 130.1 (2C), 129.3, 129.2, 128.8 (2C), 128.7 (2C), 127.8 (2C), 127.5 (2C), 125.4, 125.3, 123.7(q, *J*=280.7 Hz), 123.6 (q, *J*=280.7 Hz), 114.1 (2C), 82.0, 81.7, 75.3, 74.7, 66.4 (q, *J*=34.6 Hz), 66.3 (q, *J*=34.6 Hz), 55.4, 52.7, 52.5; MS (ESI$^+$) *m*/*z* 449 [M+Na]$^+$; HRMS (ESI$^+$) *m*/*z* calcd for $C_{21}H_{21}F_3NaO_6$ [M+Na]$^+$: 449.1188, found: 449.1183.

*4.3.3. (2R,3R)-Methyl 3-phenyl-2-(2-phenylacetoxy)-3-(2,2,2-trifluoroethoxy)propanoate (anti-**9b**).* Alcohol *anti*-**4b** (301 mg, 1.08 mmol, 1 equiv), DCC (268 mg, 1.3 mmol, 1.2 equiv), DMAP (66 mg, 0.541 mmol, 0.5 equiv), and phenylacetic acid (177 mg, 1.3 mmol, 1.2 equiv) were used following the general procedure to afford compound *anti*-**9b** as a yellow oil (406 mg, 95%). TLC R_f=0.60 (30% AcOEt/cyclohexane); ^1H NMR (400 MHz, $CDCl_3$): δ=7.39–7.10 (10H, m, Ar–*H*), 5.33 (1H, d, *J*=6.2 Hz, C*H*CO_2Me), 4.83 (1H, d, *J*=6.2 Hz, C*H*Ph), 3.90–3.60 (2H, m, C*H*CF_3), 3.70 (3H, s, OCH_3), 3.62 (2H, s, CH_2CO); ^{13}C NMR (100 MHz, $CDCl_3$): δ=170.3, 168.2, 135.0, 133.2, 129.4 (2C), 129.2, 128.7 (2C), 128.6 (2C), 127.7 (2C), 127.2, 123.8 (q, *J*=278.3 Hz), 81.7, 74.8, 66.2 (q, *J*=34.6 Hz), 52.4, 40.8; HRMS (ESI$^+$) *m*/*z* calcd for $C_{20}H_{19}F_3NaO_5$ [M+Na]$^+$: 419.1082, found: 419.1081.

*4.3.4. (2R,3R)-Methyl 3-phenyl-2-(2-(p-tolyl)acetoxy)-3-(2,2,2-trifluoroethoxy)propanoate (anti-**9c**).* Alcohol *anti*-**4b** (538 mg, 1.93 mmol, 1 equiv), DCC (479 mg, 2.32 mmol, 1.2 equiv), DMAP (118 mg, 0.965 mmol, 0.5 equiv), and *p*-tolylacetic acid (348 mg, 2.32 mmol, 1.2 equiv) were used following the general procedure to afford compound *anti*-**9c** as a colorless solid (528 mg, 67%). TLC R_f=0.40 (25% AcOEt/cyclohexane); mp 68–69 °C; IR (NaCl film) ν_{max}=3032, 2955, 1748, 1517, 1492, 1454, 1437, 1415, 1363, 1280, 1209, 1160, 1133, 1010, 967; ^1H NMR (400 MHz, $CDCl_3$): δ=7.38–7.29 (3H, m, *m*–Ph–*H*+*p*–Ph–*H*), 7.24–7.22 (2H, m, *o*–Ph–*H*), 7.08 (2H, d, *J*=8.1 Hz, *o*–Ar–*H*), 7.02 (2H, d, *J*=8.1 Hz, *m*–Ar–*H*), 5.29 (1H, d, *J*=6.3 Hz, C*H*CO_2Me), 4.81 (1H, d, *J*=6.3 Hz, C*H*Ph), 3.78–3.61 (2H, m, C*H*CF_3), 3.71 (3H, s, OCH_3), 3.57 (2H, s, CH_2CO), 2.32 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=170.1, 168.0, 137.0, 135.1, 130.3, 129.4 (2C), 129.3 (2C), 129.2, 128.7 (2C), 127.8 (2C), 123.8 (q, *J*=279.1 Hz), 74.8, 66.6 (q, *J*=34.5 Hz), 52.6, 40.5, 21.2; MS (ESI$^+$) *m*/*z* 433.1 [M+Na]$^+$; HRMS (ESI$^+$) *m*/*z* calcd for $C_{21}H_{21}F_3NaO_5$ [M+Na]$^+$: 433.1239, found: 433.1255.

*4.3.5. (2S,3R)-Methyl 2-(2-(2-methoxyphenyl)acetoxy)-3-phenyl-3-(2,2,2-trifluoroethoxy)propanoate (syn-**9d**).* Alcohol *syn*-**4b** (500 mg, 1.797 mmol, 1 equiv), DCC (445 mg, 2.16 mmol, 1.2 equiv), DMAP (110 mg, 0.898 mmol, 0.5 equiv), and 2-methoxyphenylacetic acid (358 mg, 2.16 mmol, 1.2 equiv) were used following the general procedure to afford compound *syn*-**9d** as a colorless oil (618 mg, 81%). IR (NaCl film) ν_{max}=3066, 3033, 3008, 2941, 2842, 1749, 1603, 1497, 1457, 1439, 1281, 1250, 1153, 1099, 1030, 968 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=7.34 (3H, m, Ph–*H*), 7.28 (2H, m, Ph–*H*), 7.25 (1H, ddd, *J*=1.8, 7.5, 8.1 Hz, *p*-Ar–*H*), 7.11 (1H, dd, *J*=1.8, 7.5 Hz, *o*-Ar–*H*), 6.89 (1H, dt, *J*=1.0, 7.5 Hz, *m*–Ar–*H*), 6.82 (1H, dd, *J*=1.0, 8.1 Hz, *m*–Ar–*H*), 5.29 (1H, d, *J*=3.8 Hz, C*H*CO_2Me), 5.08 (1H, d, *J*=3.8 Hz, C*H*Ph), 3.84–3.75 (1H, m, C*H*CF_3), 3.72 (3H, s, CO_2CH_3), 3.71 (2H, m, CH_2CO), 3.67–3.57 (1H, m, C*H*CF_3), 3.64 (3H, s, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=171.1, 167.9, 157.7, 134.8, 131.1, 129.1, 128.9 (2C), 128.8, 127.7 (2C), 123.8 (q, *J*=280.6 Hz), 122.5, 120.6, 110.6, 82.1, 75.3, 66.4 (q, *J*=34.5 Hz), 55.4, 52.6, 35.6; MS (ESI$^+$) *m*/*z* 449.1 [M+Na]$^+$; HRMS (ESI$^+$) *m*/*z* calcd for $C_{21}H_{21}F_3NaO_6$, [M+Na]$^+$: 449.1188, found: 449.1188.

*4.3.6. (2S,3R)-Methyl 2-(2-(3-methoxyphenyl)acetoxy)-3-phenyl-3-(2,2,2-trifluoroethoxy)propanoate (syn-**9e**).* Alcohol *syn*-**4b** (500 mg, 1.797 mmol, 1 equiv), DCC (445 mg, 2.16 mmol, 1.2 equiv), DMAP (110 mg, 0.898 mmol, 0.5 equiv), and 3-methoxyphenylacetic acid (358 mg, 2.16 mmol, 1.2 equiv) were used following the general procedure to afford compound *syn*-**9e** as a colorless oil (530 mg, 69%). TLC R_f=0.60 (30% AcOEt/cyclohexane); IR (NaCl film) ν_{max}=3065, 3033, 3008, 2956, 2840, 1747, 1602, 1587, 1493, 1455, 1438, 1414, 1360, 1279, 1216, 1163, 1099, 1042, 1001, 967 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=7.32–7.25 (5H, m, Ph–*H*), 7.22–7.16 (1H, m, *m*–Ar–*H*), 6.81–6.78 (1H, m, *p*–Ar–*H*), 6.75–6.72 (2H, m, *o*–Ar–*H*), 5.28 (1H, d, *J*=3.8 Hz, C*H*CO_2Me), 5.07 (1H, d, *J*=3.8 Hz, C*H*Ph), 3.86–3.75 (1H, m, C*H*CF_3), 3.77 (3H, s, CO_2CH_3), 3.71 (3H, s, OCH_3), 3.70 (1H, d, *J*=15.4 Hz, CH_2CO), 3.64 (1H, d, *J*=15.4 Hz, CH_2CO), 3.65–3.58 (1H, s, C*H*CF_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ=170.5, 167.6, 159.8, 134.6, 134.5, 129.6, 129.2, 128.8 (2C), 127.5 (2C), 123.8 (q, *J*=279.4 Hz), 121.8, 114.9, 81.9, 75.3, 66.6 (q, *J*=35.4 Hz), 55.2, 52.8, 40.7; MS (ESI$^+$) *m*/*z* 449 [M+Na]$^+$; HRMS (ESI$^+$) *m*/*z* calcd for $C_{21}H_{21}F_3NaO_6$, [M+Na]$^+$: 449.1188, found: 449.1197.

*4.3.7. (2R,3R)-Methyl 2-(2-(3-methoxyphenyl)acetoxy)-3-phenyl-3-(2,2,2-trifluoroethoxy)propanoate (anti-**9e**).* Alcohol *anti*-**4b** (500 mg, 1.797 mmol, 1 equiv), DCC (445 mg, 2.16 mmol, 1.2 equiv), DMAP (110 mg, 0.898 mmol, 0.5 equiv), and 3-methoxyphenylacetic acid (358 mg, 2.16 mmol, 1.2 equiv) were used following the general procedure to afford compound *anti*-**9e** as a white solid (677 mg, 88%). Mp 48–50 °C; IR (NaCl film) ν_{max}=3034, 3007, 2955, 2839, 1748, 1602, 1586, 1493, 1456, 1438, 1278, 1209, 1164, 1049, 1009, 967 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=7.33 (3H, m, Ph–*H*), 7.25 (2H, m, Ph–*H*), 7.19 (1H, dd, *J*=6.8, 8.3 Hz, *m*-Ar–*H*), 6.81 (1H, m, Ar–*H*), 6.74 (2H, m, Ar–*H*), 5.35 (1H, d, *J*=6.1 Hz, C*H*CO_2Me), 4.86 (1H, d, *J*=6.1 Hz, C*H*Ph), 3.74 (4H, m, C*H*CF_3+OCH_3), 3.70 (3H, s, OCH_3), 3.69–3.62 (1H, m, C*H*CF_3), 3.62 (1H, d, *J*=15.3 Hz, CH_2CO),

3.58 (1H, d, J=15.3 Hz, CH_2CO); ^{13}C NMR (100 MHz, $CDCl_3$): δ=170.1, 168.1, 159.7, 134.9, 134.5, 129.5, 129.1, 128.6 (2C), 127.9 (2C), 123.6 (q, J=279.1 Hz), 121.6, 114.8, 112.9, 81.6, 74.7, 66.2 (q, J=34.5 Hz), 55.0, 52.4, 40.8; MS (ESI$^+$) m/z 449.4 [M+Na]$^+$, 327.1 [M−CF_3CH_2OH+H]$^+$; HRMS (ESI$^+$) m/z calcd for $C_{21}H_{21}F_3NaO_6$, [M+Na]$^+$: 449.1188, found: 449.1190.

*4.3.8. (2S,3R)-Methyl 2-(2-(3,4-dimethoxyphenyl)acetoxy)-3-phenyl-3-(2,2,2-trifluoroethoxy)propanoate (syn-**9f**).* Alcohol *syn*-**4b** (500 mg, 1.797 mmol, 1 equiv), DCC (445 mg, 2.16 mmol, 1.2 equiv), DMAP (110 mg, 0.898 mmol, 0.5 equiv), and 3,4-dimethoxyphenylacetic acid (423 mg, 2.16 mmol, 1.2 equiv) were used following the general procedure to afford compound *syn*-**9f** as a colorless oil (691 mg, 84%). IR (NaCl film) ν_{max}=3006, 2956, 2838, 1747, 1593, 1516, 1454, 1440, 1266, 1238, 1158, 1097, 1029, 969 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.26 (5H, m, Ph−*H*), 6.74 (1H, m, Ar−*H*), 6.68 (1H, br s, *o*−Ar−*H*), 6.67 (1H, m, Ar−*H*), 5.27 (1H, d, J=3.7 Hz, C*H*CO_2Me), 5.05 (1H, d, J=3.7 Hz, C*H*Ph), 3.82 (3H, s, OCH_3), 3.83−3.74 (1H, m, C*H*CF_3), 3.78 (3H, s, OCH_3), 3.68 (3H, s, OCH_3), 3.64−3.54 (1H, m, C*H*CF_3), 3.62 (1H, d, J=15.5 Hz, CH_2CO), 3.56 (1H, d, J=15.5 Hz, CH_2CO); ^{13}C NMR (100 MHz, $CDCl_3$): δ=170.7, 167.5, 148.8, 148.1, 134.4, 129.0, 128.6 (2C), 127.4 (2C), 125.7, 123.7 (q, J=279.9 Hz), 121.5, 112.4, 111.1, 81.8, 75.0, 66.2 (q, J=34.5 Hz), 55.5, 55.7, 52.5, 40.1; MS (ESI$^+$) m/z 479.2 [M+Na]$^+$; HRMS (ESI$^+$) m/z calcd for $C_{22}H_{23}O_7F_3Na$, [M+Na]$^+$: 479.1294, found: 479.1292.

*4.3.9. (2R,3R)-Methyl 2-(2-(3,4-dimethoxyphenyl)acetoxy)-3-phenyl-3-(2,2,2-trifluoroethoxy)propanoate (anti-**9f**).* Alcohol *anti*-**4b** (500 mg, 1.797 mmol, 1 equiv), DCC (445 mg, 2.16 mmol, 1.2 equiv), DMAP (110 mg, 0.898 mmol, 0.5 equiv), and 3,4-dimethoxyphenylacetic acid (423 mg, 2.16 mmol, 1.2 equiv) were used following the general procedure to afford compound *anti*-**9f** as an amorphous colorless solid (820 mg, 99%). IR (NaCl film) ν_{max}=3005, 2955, 2838, 1748, 1593, 1516, 1455, 1440, 1267, 1238, 1159, 1028, 967 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.27 (3H, m, Ph−*H*), 7.19 (2H, m, Ph−*H*), 6.73 (1H, d, J=7.7 Hz, Ar−*H*), 6.66 (1H, m, Ar−*H*), 6.65 (1H, br s, *o*−Ar−*H*), 5.29 (1H, d, J=6.1 Hz, C*H*CO_2Me), 4.80 (1H, d, J=6.1 Hz, C*H*Ph), 3.80 (3H, s, OCH_3), 3.72−3.66 (1H, m, C*H*CF_3), 3.65 (3H, s, OCH_3), 3.64−3.57 (1H, m, C*H*CF_3), 3.55 (1H, d, J=14.7 Hz, CH_2CO), 3.50 (1H, d, J=14.7 Hz, CH_2CO); ^{13}C NMR (100 MHz, $CDCl_3$): δ=170.4, 168.0, 148.8, 148.1, 134.8, 129.0, 128.5 (2C), 127.6 (2C), 125.6, 123.5 (q, J=278.3 Hz), 121.4, 112.3, 111.0, 81.5, 74.5, 66.1 (q, J=34.5 Hz), 55.7, 55.6, 52.3, 40.2; MS (ESI$^+$) m/z 479.1 [M+Na]$^+$; HRMS (ESI$^+$) m/z calcd for $C_{22}H_{23}F_3NaO_7$, [M+Na]$^+$: 479.1294, found: 479.1284.

*4.3.10. (2R,3R)-Methyl 2-(2-(4-chlorophenyl)acetoxy)-3-phenyl-3-(2,2,2-trifluoroethoxy)propanoate (anti-**9g**).* Alcohol *anti*-**4b** (500 mg, 1.797 mmol, 1 equiv), DCC (445 mg, 2.16 mmol, 1.2 equiv), DMAP (110 mg, 0.898 mmol, 0.5 equiv), and 4-chlorophenylacetic acid (368 mg, 2.16 mmol, 1.2 equiv) were used following the general procedure to afford compound *anti*-**9g** as a white powder (462 mg, 60%). Mp 48−50 °C; IR (NaCl film) ν_{max}=3035, 2955, 2907, 2850, 1749, 1493, 1454, 1279, 1212, 1161, 1133, 1095, 1016, 967 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.35−7.28 (3H, m, Ph−*H*), 7.22−7.18 (4H, m, Ph−*H*+*o*-Ar−*H*), 7.03 (2H, d, J=8.5 Hz, *m*-Ar−*H*), 5.30 (1H, d, J=8.5 Hz, C*H*CO_2Me), 4.82 (1H, d, J=8.5 Hz, C*H*Ph), 3.77−3.69 (1H, m, C*H*CF_3), 3.68 (3H, s, OCH_3), 3.67−3.61 (1H, m, C*H*CF_3), 3.56 (2H, s, CH_2CO); ^{13}C NMR (100 MHz, $CDCl_3$): δ=169.8, 168.1, 134.8, 133.1, 131.7, 130.7 (2C), 129.2, 128.6 (4C), 127.6 (2C), 123.6 (q, J=278.3 Hz), 81.5, 74.7, 66.1 (q, J=34.5 Hz), 52.4, 40.0; MS (ESI$^+$) m/z 453.1 [M+Na]$^+$, 331.1 [M−CF_3CH_2OH+H]$^+$; HRMS (ESI$^+$) m/z calcd for $C_{20}H_{18}O_5ClF_3Na$, [M+Na]$^+$: 453.0693, found: 453.0699.

*4.3.11. (2S,3R)-Methyl 2-(2-(4-bromophenyl)acetoxy)-3-phenyl-3-(2,2,2-trifluoroethoxy)propanoate (syn-**9h**).* Alcohol *syn*-**4b** (500 mg, 1.8 mmol, 1 equiv), DCC (445 mg, 2.16 mmol, 1.2 equiv), DMAP (110 mg, 0.894 mmol, 0.5 equiv), and 4-bromophenylacetic acid (464 mg, 2.16 mmol, 1.2 equiv) were used following the general procedure to afford compound *syn*-**9h** as a colorless oil (348 mg, 41%). TLC R_f=0.60 (30% AcOEt/cyclohexane); IR (NaCl film) ν_{max}=3033, 2955, 2850, 1748, 1490, 1453, 1437, 1360, 1280, 1216, 1157, 1097, 1013, 968 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.39 (2H, d, J=8.3 Hz, *m*-Ar−*H*), 7.35−7.24 (5H, m, Ph−*H*), 7.02 (2H, d, J=8.3 Hz, *o*-Ar−*H*), 5.28 (1H, d, J=3.8 Hz, C*H*CO_2Me), 5.09 (1H, d, J=3.8 Hz, C*H*Ph), 3.91−3.79 (1H, m, C*H*CF_3), 3.72 (3H, s, OCH_3), 3.67−3.57 (1H, m, C*H*CF_3), 3.63 (1H, s, CH_2CO), 3.62 (1H, s, CH_2CO); ^{13}C NMR (100 MHz, $CDCl_3$): δ=170.1, 167.5, 134.4, 132.3, 131.7 (2C), 131.2 (2C), 129.2, 128.8 (2C), 127.4 (2C), 123.7 (q, J=279.3 Hz), 121.3, 81.9, 75.3, 66.4 (q, J=34.5 Hz), 52.6, 40.1; MS (ESI$^+$) m/z 499.0, 497.0 [M+Na]$^+$; HRMS (ESI$^+$) m/z calcd for $C_{20}H_{22}{}^{79}BrF_3NO_5$, [M+$NH_4$]$^+$: 492.0633, found: 4492.0618.

*4.3.12. (2R,3R)-Methyl 2-(2-(4-fluorophenyl)acetoxy)-3-phenyl-3-(2,2,2-trifluoroethoxy)propanoate (anti-**9i**).* Alcohol *anti*-**4b** (500 mg, 1.797 mmol, 1 equiv), DCC (445 mg, 2.16 mmol, 1.2 equiv), DMAP (110 mg, 0.898 mmol, 0.5 equiv), and 4-fluorophenylacetic acid (464 mg, 3.01 mmol, 1.7 equiv) were used following the general procedure to afford compound *anti*-**9i** as a white solid (576 mg, 77%). TLC R_f=0.60 (30% AcOEt/cyclohexane); mp: 53−54 C; IR (NaCl film) ν_{max}=3067, 3033, 2957, 2850, 1748, 1606, 1512, 1455, 1363, 1280, 1224, 1163, 1136, 1013, 967 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.38−7.30 (3H, m, *m*-Ph−*H*+*p*-Ph−*H*), 7.23−7.21 (2H, m, *o*−Ph−*H*), 7.11−7.07 (2H, m, *o*−Ar−*H*), 6.97−6.93 (2H, m, *m*-Ar−*H*), 5.36 (1H, d, J=3.9 Hz, C*H*CO_2Me), 4.82 (1H, d, J=3.9 Hz, C*H*Ph), 3.75−3.62 (2H, m, CH_2CF_3), 3.72 (3H, s, OCH_3), 3.59 (2H, s, CH_2CO); ^{13}C NMR (100 MHz, $CDCl_3$): δ=169.9, 168.0, 161.9 (d, J=245.5 Hz), 134.7, 130.8 (2C, d, J=8.2 Hz), 129.2, 128.7 (d, J=3.4 Hz), 128.5 (2C), 127.6 (2C), 123.5 (q, J=278.8 Hz), 115.3 (2C, d, J=21.5 Hz), 81.5, 74.6, 66.1 (q, J=34.7 Hz), 52.4, 39.8; MS (ESI$^+$) m/z 437.2 [M+Na]$^+$; HRMS (ESI$^+$) m/z calcd for $C_{20}H_{18}F_4NaO_5$, [M+Na]$^+$: 437.0988, found: 437.0981.

4.4. General procedure for the synthesis of pulvinones

A 1 M solution of LiHMDS in THF (0.832 mL, 0.832 mmol, 3.5 equiv) was added dropwise at −78 °C to a solution of diester *syn*-**9h** (113 mg, 0.238 mmol, 1 equiv) in THF (5 mL) under nitrogen. The mixture was stirred at −78 °C for 15 min and for 24 h at room temperature. The reaction was quenched with 2 mL of saturated NH_4Cl solution and acidified with 5 mL of 2 N HCl solution. The mixture was extracted with 2×10 mL of CH_2Cl_2 and the solvent was removed under reduced pressure. The crude product was purified by precipitation in *tert*-butyl methyl ether to afford pulvinone **1h** as a yellow solid (58 mg, $Z/E \geq$98/2, 71%).

*4.4.1. (Z)-5-Benzylidene-3-(4-bromophenyl)-4-hydroxyfuran-2(5H)-one (**1h**).* Mp 248−249 °C; IR (KBr pellet) ν_{max}=3073, 3029, 1691, 1656, 1605, 1584, 1490, 1420, 1391, 1251, 1009 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ=7.93 (2H, dm, J=8.6 Hz, *m*-Ar−*H*), 7.74 (2H, d, J=7.4 Hz, *o*-Ph−*H*), 7.62 (2H, d, J=8.6 Hz, *o*-Ar−*H*), 7.46 (2H, t, J=7.4 Hz, *m*-Ph−*H*), 7.37 (1H, t, J=7.4 Hz, *p*-Ph−*H*), 6.76 (1H, s, CH); ^{13}C NMR (100 MHz, DMSO-d_6): δ=167.7, 164.6, 142.3, 132.6, 131.2 (2C), 130.2 (2C), 129.3, 129.0 (2C), 128.9, 128.8 (2C), 119.9, 108.0, 98.7; MS (ESI$^+$) m/z 345.0, 343.0 [M+H]$^+$; MS (ESI$^-$) m/z 340.8, 342.8 [M−H]$^-$; HRMS (ESI$^+$) m/z calcd for $C_{17}H_{12}O_3{}^{79}Br$, [M+H]$^+$: 342.9970, found: 342.9973.

*4.4.2. (Z)-5-Benzylidene-3-(4-methoxyphenyl)-4-hydroxyfuran-2(5H)-one (**1a**).* LiHMDS (1 M in THF, 1.7 mL, 1.7 mmol, 3.5 equiv) and diester **9a** (mixture of *syn*- and *anti*-isomers, 200 mg, 0.48 mmol) were used following the general procedure to afford pulvinone **1a** as a yellow solid (86 mg, Z/E=10/1, 61%). Mp 221−222 °C (lit.[15a] mp 219−222 °C; lit.[15c] mp 223−226 °C); IR (KBr

pellet) ν_{max}=3002, 2937, 2833, 2619, 1893, 1704, 1631, 1607, 1573, 1515, 1494, 1449, 1424, 1402, 1346, 1332, 1310, 1291, 1253, 1182, 1157, 1130, 1101, 1037, 998, 920, 872, 831, 747, 690, 655, 613, 571, 532 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6): δ=10.97 (1H, br s, OH); 7.94 (2H, d, J=8.8 Hz, *o*-Ar−*H*), 7.82 (2H, d, J=7.4 Hz, *o*-Ph−*H*), 7.48−7.32 (3H, m, *m*-Ph−*H*, *p*-Ph−*H*), 7.01 (2H, d, J=8.8 Hz, *m*-Ar−*H*), 6.59 (1H, s, CH), 3.83 (1H, s, OCH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ=168.0, 162.2, 158.3, 142.5, 132.8, 130.0 (2C), 129.0 (2C), 128.7, 128.6 (2C), 122.1, 113.8, 107.2, 100.4, 55.1; MS (ESI$^+$) *m*/*z* 295 $[M+H]^+$.

*4.4.3. (Z)-5-Benzylidene-4-hydroxy-3-phenylfuran-2(5H)-one (**1b**).* LiHMDS (1 M in THF, 1.766 mL, 1.766 mmol, 3.5 equiv) and diester **9b** (200 mg, 0.504 mmol, *syn*/*anti* mixture) were used following the general procedure to afford pulvinone **1b** as a yellow solid (94 mg, *Z*/*E* ≥98/2, 71%). Mp 245−246 °C (lit.[4] mp 250−251 °C); IR (KBr pellet) ν_{max}=3084, 3052, 3004, 1702, 1659, 1624, 1492, 1450, 1410, 1253, 1153, 1123, 1006 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ=7.95 (2H, d, J=7.6 Hz, *m*-Ar−*H*), 7.75 (2H, d, J=7.4 Hz, *o*-Ph−*H*), 7.45 (4H, m, *o*-Ar−*H*+*m*-Ph−*H*), 7.36 (1H, m, *p*-Ph−*H*), 7.30 (1H, m, *p*-Ar−*H*), 6.75 (1H, s, CH); ^{13}C NMR (100 MHz, DMSO-d_6): δ=167.9, 163.8, 142.4, 132.7, 130.1, 129.8, 129.0, 128.8, 128.3, 127.3, 127.2, 107.7, 100.2; MS (ESI$^+$) *m*/*z* 265.1 $[M+H]^+$; MS (ESI$^-$) *m*/*z* 262.9 $[M-H]^-$.

*4.4.4. (Z)-5-Benzylidene-4-hydroxy-3-(p-tolyl)furan-2(5H)-one (**1c**).* LiHMDS (1 M in THF, 0.290 mL, 0.29 mmol, 3.5 equiv) and diester *anti*-**9c** (34 mg, 0.083 mmol) were used following the general procedure to afford pulvinone **1c** as a yellow solid (17 mg, *Z*/*E*=97/3, 74%). Mp 234−235 °C; IR (KBr pellet) ν_{max}=3011, 2913, 1699, 1657, 1625, 1451, 1422, 1399, 1252, 1150, 1003, 916 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ=7.84 (2H, d, J=8.1 Hz, *m*-Ar−*H*), 7.74 (2H, d, J=7.6 Hz, *o*-Ph−*H*), 7.47 (2H, m, *m*-Ph−*H*), 7.37 (1H, m, *p*-Ph−*H*), 7.25 (2H, d, J=8.1 Hz, *o*-Ar−*H*), 6.72 (1H, s, CH), 2.32 (3H, s, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ=167.9, 163.1, 142.4, 136.6, 132.7, 130.1, 129.0, 128.9, 128.8, 127.1, 126.8, 107.4, 100.3, 20.9; MS (ESI$^+$) *m*/*z* 279.1 $[M+H]^+$; HRMS (ESI$^+$) *m*/*z* calcd for $C_{18}H_{15}O_3$, $[M+H]^+$: 279.1021, found: 279.1031.

*4.4.5. (Z)-5-Benzylidene-4-hydroxy-3-(2-methoxyphenyl)furan-2(5H)-one (**1d**).* LiHMDS (1 M in THF, 1.642 mL, 1.642 mmol, 3.5 equiv) and diester *syn*-**9d** (200 mg, 0.469 mmol) were used following the general procedure to afford pulvinone **1d** as a yellow solid (74 mg, *Z*/*E*=96/4, 54%) after a purification by flash chromatography (10−20% AcOEt/cyclohexane containing 0.5% HCO_2H). Mp 120−123 °C; IR (NaCl film) ν_{max}=3061, 2940, 2844, 1752, 1619, 1600, 1494, 1461, 1333, 1246, 1232, 1011, 970 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6): δ=10.0 (1H, s, OH), 7.85 (2H, dm, J=7.2 Hz, *o*-Ph−*H*), 7.63 (1H, dd, J=1.7, 7.6 Hz, *o*-Ar−*H*), 7.46 (2H, m, *m*-Ph−*H*), 7.38 (2H, *p*-Ar−*H*+*p*-Ph−*H*), 7.11 (1H, dd, J=1.1, 8.4 Hz, *m*-Ar−*H*), 7.06 (1H, dt, J=1.1, 7.6 Hz, *m*-Ar−*H*), 6.45 (CH), 3.95 (3H, s, OMe); ^{13}C NMR (100 MHz, acetone-d_6): δ=168.5, 163.5, 157.5, 143.6, 134.1, 131.6 (2C), 131.1, 130.6, 129.7 (2C), 129.5, 121.7, 118.6, 112.2, 107.2, 100.1, 56.5; MS (ESI$^+$) *m*/*z* 295.1 $[M+H]^+$; MS (ESI$^-$) *m*/*z* 292.9 $[M-H]^-$; HRMS (ESI$^+$) *m*/*z* calcd for $C_{18}H_{15}O_4$, $[M+H]^+$: 295.0970, found: 295.0970.

*4.4.6. (Z)-5-Benzylidene-4-hydroxy-3-(3-methoxyphenyl)furan-2(5H)-one (**1e**).* LiHMDS (1 M in THF, 1.642 mL, 1.642 mmol, 3.5 equiv) and diester *anti*-**9e** (200 mg, 0.469 mmol) were used following the general procedure to afford pulvinone **1e** as a yellow solid (96 mg, *Z*/*E*=97/3, 70%). Mp 202−204 °C; IR (KBr pellet) ν_{max}=3067, 3005, 2918, 2833, 1700, 1658, 1626, 1575, 1486, 1415, 1402, 1253, 1232, 1124, 1017, 991 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ=7.75 (2H, d, J=7.5 Hz, *o*-Ph−*H*), 7.56 (2H, m, Ar−*H*), 7.46 (2H, t, J=7.5 Hz, *m*-Ph−*H*), 7.35 (2H, m, *p*-Ph−*H*+Ar−*H*), 6.88 (1H, dm, J=8.8 Hz, Ar−*H*), 6.75 (1H, s, CH), 3.78 (3H, s, OMe); ^{13}C NMR (100 MHz, DMSO-d_6): δ=167.8, 164.1, 159.0, 142.4, 132.7, 131.1, 130.1 (2C), 129.3, 129.0 (2C), 128.9, 119.6, 112.8, 112.6, 107.7, 99.9, 55.0; MS (ESI$^+$) *m*/*z* 295.1 $[M+H]^+$; MS (ESI$^-$) *m*/*z* 292.9 $[M-H]^-$; HRMS (ESI$^+$) *m*/*z* calcd for $C_{18}H_{15}O_4$, $[M+H]^+$: 295.0970, found: 295.0981.

*4.4.7. (Z)-5-Benzylidene-3-(3,4-dimethoxyphenyl)-4-hydroxyfuran-2(5H)-one (**1f**).* LiHMDS (1 M in THF, 1.533 mL, 1.533 mmol, 3.5 equiv) and diester *syn*-**9f** (200 mg, 0.438 mmol) were used following the general procedure to afford pulvinone **1f** as a brown solid (97 mg, *Z*/*E*=97/3, 68%). Mp 190−192 °C (lit.[15a] mp 190−194 °C); IR (KBr pellet) ν_{max}=3061, 3002, 2940, 2835, 1696, 1630, 1602, 1518, 1453, 1392, 1257, 1139, 1027 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6): δ=7.81 (2H, d, J=7.2 Hz, *o*-Ph−*H*), 7.61 (1H, d, J=2.0 Hz, *o*-Ar−*H*), 7.56 (1H, dd, J=8.4, 2.0 Hz, *o*-Ar−*H*), 7.45 (2H, m, *m*-Ph−*H*), 7.36 (1H, m, *p*-Ph−*H*), 7.01 (1H, d, J=8.4 Hz, *m*-Ar−*H*), 6.59 (1H, s, CH), 3.84 (6H, s, 2OMe); ^{13}C NMR (100 MHz, acetone-d_6): δ=168.6, 162.0, 150.1, 150.0, 143.6, 134.1, 131.1 (2C), 129.8 (2C), 129.6, 123.2, 121.9, 112.6, 112.5, 107.5, 103.0, 56.1 (2C); MS (ESI$^+$) *m*/*z* 325.1 $[M+H]^+$; MS (ESI$^-$) *m*/*z* 322.9 $[M-H]^-$.

*4.4.8. (Z)-5-Benzylidene-3-(4-chlorophenyl)-4-hydroxyfuran-2(5H)-one (**1g**).* LiHMDS (1 M in THF, 1.625 mL, 1.625 mmol, 3.5 equiv) and diester *anti*-**9g** (200 mg, 0.464 mmol) were used following the general procedure to afford pulvinone **1g** as a yellow solid (90 mg, *Z*/*E*=97/3, 65%). Mp 247−248 °C; IR (KBr pellet) ν_{max}=3063, 3004, 1698, 1658, 1625, 1591, 1493, 1450, 1420, 1395, 1249, 1155, 1129, 1095, 1002 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ=8.01 (2H, d, J=8.6 Hz, *m*-Ar−*H*), 7.74 (2H, d, J=8.0 Hz, *o*-Ph−*H*), 7.46 (4H, m, *o*-Ar−*H*+*m*-Ph−*H*), 7.36 (1H, m, *p*-Ph−*H*), 6.74 (1H, s, CH); ^{13}C NMR (100 MHz, DMSO-d_6): δ=167.9, 165.0, 142.6, 132.8, 131.2, 130.1 (2C), 129.2, 129.0 (2C), 128.8, 128.4 (2C), 128.3 (2C), 107.7, 98.3; MS (ESI$^+$) *m*/*z* 299.1 $[M+H]^+$; MS (ESI$^-$) *m*/*z* 296.8 $[M-H]^-$; HRMS (ESI$^+$) *m*/*z* calcd for $C_{17}H_{12}O_3Cl$, $[M+H]^+$: 299.0475, found: 299.0489.

*4.4.9. (Z)-5-Benzylidene-3-(4-fluorophenyl)-4-hydroxyfuran-2(5H)-one (**1i**).* Diester *anti*-**9i** (200 mg, 0.48 mmol) was used following the general procedure to afford pulvinone **1i** as a yellow solid (90 mg, *Z*/*E* >98/2, 77%). Mp 260−262 °C (lit.[3] mp 256−260 °C); ^1H NMR (400 MHz, acetone-d_6): δ=8.03 (2H, dd, J=8.8, 5.6 Hz, *o*-Ar−*H*), 7.81 (2H, d, J=7.5 Hz, *o*-Ph−*H*), 7.48−7.44 (2H, m, *m*-Ph−*H*), 7.39−7.31 (1H, m, *p*-Ph−*H*), 7.23−7.17 (2H, m, *m*-Ar−*H*), 6.64 (1H, s, CH); ^{13}C NMR (100 MHz, DMSO-d_6): δ=137.9, 163.7, 160.9 (d, J=244.6 Hz), 142.3, 132.7, 130.1 (2C), 129.2 (2C, d, J=7.7 Hz), 129.0 (2C), 128.9, 126.3, 115.2 (2C, d, J=20.7 Hz), 107.7, 99.2; MS (ESI$^+$) *m*/*z* 283 $[M+H]^+$; HRMS (ESI$^+$) *m*/*z* calcd for $C_{17}H_{12}O_3F$, $[M+H]^+$: 283.0770, found: 283.0780.

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Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2011.02.011.

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