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Synthesis of Pulvinic Acid and Norbadione A Analogues by Suzuki–Miyaura Cross-Coupling of Benzylated Intermediates

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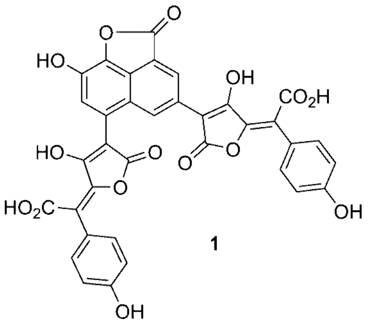
Pulvinic acid and norbadione A analogues can be prepared by Suzuki–Miyaura cross-coupling of functionalized arylboronic esters with appropriate vinyl triflates, in which the hydroxy functions are protected either with methyl or benzyl groups, the latter being cleaved in a more reliable fashion at the end of the synthetic sequence.

We have recently become interested in developing a convenient synthetic approach towards the mushroom pigment norbadione A (**1**) and analogues.[1] This compound was first isolated by Steglich et al.[2] from the edible mushroom bay boletus [*Xerocomus badius* (Fr.) Kühn. ex Gilb.] and by Gill et al.[3] from *Pisolithus tinctorius* (Pers.) Coker et Couch. Norbadione A has been shown to have interesting properties. For example, it can form a complex with caesium cation, which may account for the high levels of radioactive caesium found in bay boletus following the Chernobyl accident.[1,4,5] It was also recently shown to have antioxidant properties.[6] Norbadione A is structurally related to the larger pigment family of pulvinic acids **2**.[7]



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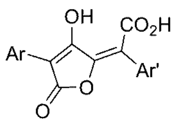

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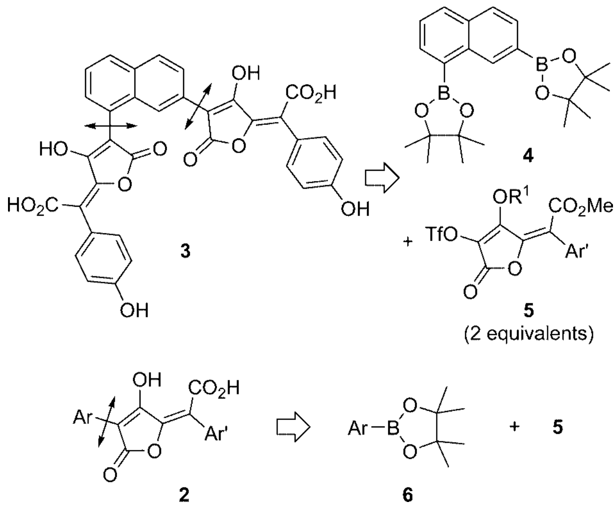
Our synthetic approach towards **1** was mainly based on the use of a double Suzuki–Miyaura cross-coupling to connect the two identical enolic lactone moieties simultaneously to the naphthalene part of the molecule. Hence, diacid **3**, an analogue of norbadione A, would be obtained from the product of such a reaction involving a bis(boronate) **4** and two equivalents of a vinyl triflate **5** (Scheme 1). The method can also be applied to the synthesis of pulvinic acids by using triflate **5** and an aryl boronate **6** as the reaction partners in the cross-coupling step (Scheme 1).[1] Interestingly, this approach would be suitable for the synthesis of unsymmetrical pulvinic acids in which the two aryl groups Ar and Ar′ are different, which are less easily prepared than the symmetrical ones.[7,8] The method chosen for the preparation of the triflate **5** relies essentially on the cyclocondensation of a bis(silylated) diene with oxalyl chloride reported by Langer et al.[9] Following the publication by this group of the synthesis of pulvinic acids, which is based on a similar strategy,[10] we now report our own results on the preparation of pulvinic acids and norbadione A-related products.



Scheme 1.

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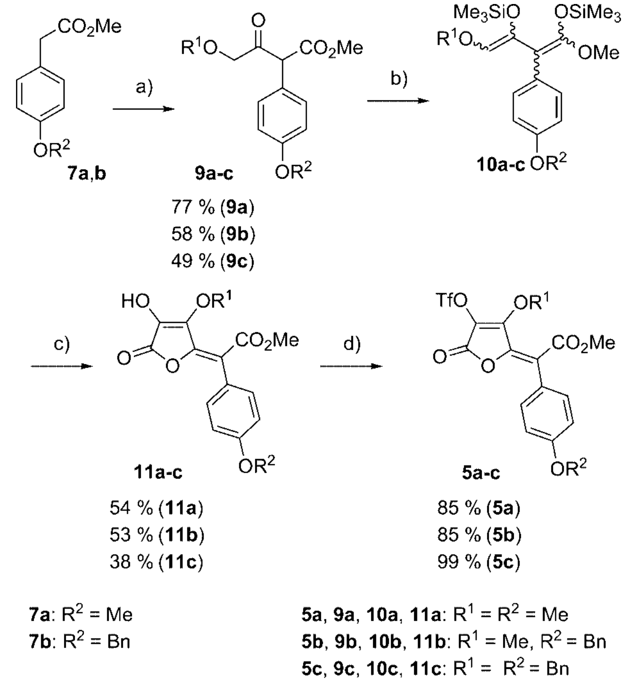
Preparation of Triflates 5a–c

Triflates **5a**–**c** were prepared as described in Scheme 2. They differ in the groups (methyl or benzyl) employed for the protection of the hydroxy functions. Benzyl ethers were expected to be cleavable under milder conditions than methyl ethers. Such protecting groups have been previously employed in the context of pulvinic acids' synthesis.[11] The β-keto esters **9a**–**c** were obtained by Claisen condensation[12] of aryl acetates **7a** or **7b** with the appropriate alkoxy acetate **8a** or **8b**. The anion of aryl acetate **7a** was generated at –78 °C in THF by treatment with lithium diisopropylamide. The less soluble anion of **7b** was generated in a THF/HMPA mixture. It was necessary to use a twofold excess of the aryl acetate vs. the alkoxy acetate.



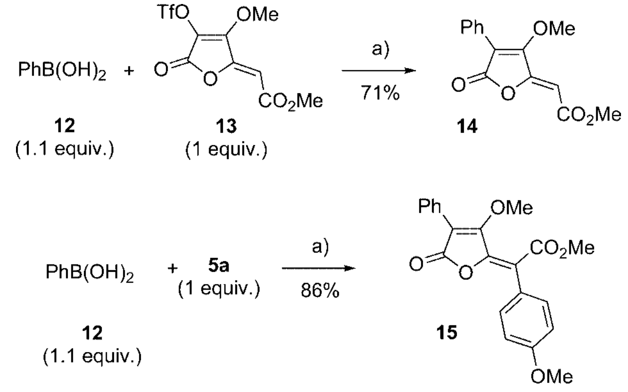
Scheme 2. Reagents and conditions: a) *i*Pr$_2$NLi, THF or THF/HMPA, –78 °C, then methyl methoxyacetate (**8a**) or methyl (benzyloxy)acetate (**8b**); b) *i.* Et$_3$N, ClSiMe$_3$, THF, room temperature, 12 h, *ii. i*Pr$_2$NLi, ClSiMe$_3$, THF, –78 °C to room temperature, 3 h; c); oxalyl chloride (1 equiv.), TfOSiMe$_3$ (0.3 equiv.), CH$_2$Cl$_2$, –78 °C to room temperature, overnight d) Tf$_2$O (1.2 equiv.), pyridine (2.5 equiv.), CH$_2$Cl$_2$, –78 °C to room temperature, 4 h.

Compounds **9a**–**c** were then converted in two steps into the corresponding bis(trimethylsilyloxy)dienes **10a**–**c**. The first silylation was carried out using chlorotrimethylsilane in the presence of triethylamine. The second one employed lithium diisopropylamide as the base and chlorotrimethylsilane. The products were dried thoroughly and were not purified further. Compounds **10a** and **10b** are fairly stable and can be stored for several months at –18 °C, while compound **10c** is unstable and was thus used rapidly in the next reaction. Two stereoisomers were usually observed in the ^{1}H NMR spectra of these compounds, in varying proportions.

The cyclocondensation of the silylated compounds **10a**–**c** with oxalyl chloride was performed in the presence of 0.3 equivalents of trimethylsilyl triflate as catalyst, in dichloromethane at –78 °C.[9] Lactones **11a** and **11b** were obtained in fair yields. The yield of adduct **11c** was significantly lower, probably due to the unfavorable steric interactions with the benzyl protecting group R^1. In each case, only the (*E*)-configured stereoisomer was obtained. The corresponding triflates **5a**–**c** were then obtained efficiently by treatment with triflic anhydride in the presence of pyridine. With these synthetic intermediates in hand, the preparation of pulvinic acid derivatives could be envisioned.

Synthesis of Pulvinic Acid Derivatives

Cross-coupling conditions were first tested with phenylboronic acid (**12**). The reaction of the model triflate **13**[9c] under the usual conditions {K$_3$PO$_4$, [Pd(PPh$_3$)$_4$], dioxane, reflux} worked well, leading to compound **14** in 71% yield (Scheme 3). Analogous conditions applied to triflate **5a** therefore allowed the preparation of the pulvinic acid derivative **15** in 86% yield. Comparison of the physical and spectroscopic data of compound **15** with the values reported for both stereoisomers, which had been previously synthesized,[13] allowed the unambiguous assignment of the (*E*) configuration for this compound.

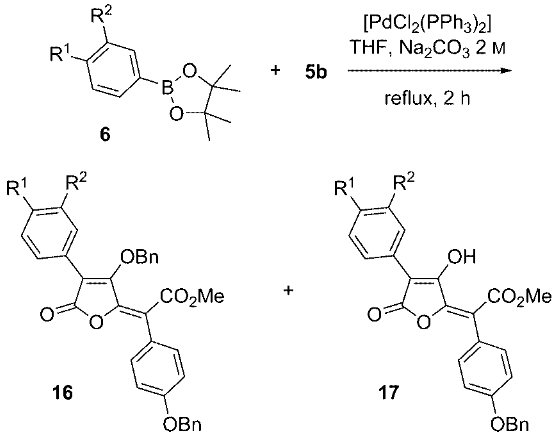


Scheme 3. Reagents and conditions: a) K$_3$PO$_4$ (1.5 equiv.), [Pd(PPh$_3$)$_4$] (3 mol-%), dioxane, reflux, 4 h.

The cleavage of the methyl protecting groups of pulvinic acid derivative **15** with iodotrimethylsilane has been described previously.[13] Under analogous conditions, we obtained mixtures of partially and fully deprotected pulvinic compounds. We thus preferred to carry out the syntheses of other pulvinic compounds from triflate **5b**, in which the enol and phenol functions are protected as benzyl ethers.

In order to access norbadione A analogues containing two pulvinic moieties, we first envisaged using a naphthalenic compound substituted by two boronic acids, which would be obtained from the bis(boronate) **4**, in the cross-coupling step. However, cleavage of the boronic ester moieties was found to be difficult. Hence, the cross-coupling had to be carried out using boronate esters. Various unsuccessful conditions employing either [PdCl$_2$(dppf)] or [Pd(PPh$_3$)$_4$] as catalyst were tried at first. However, the procedure developed by Occhiato et al.[14] for the cross-coupling of vinyl triflates with pinacol boronate esters, which employs [$PdCl_2(PPh_3)_2$] as catalyst in 4:1 2 M aqueous Na_2CO_3/THF at 80 °C, proved to be very satisfactory. Several arylboronates **6a–e** were reacted with **5b** under the above-mentioned conditions (Table 1).

Table 1. Preparation of pulvinic acid derivatives by cross-coupling of boronates **6** with triflates **5**.



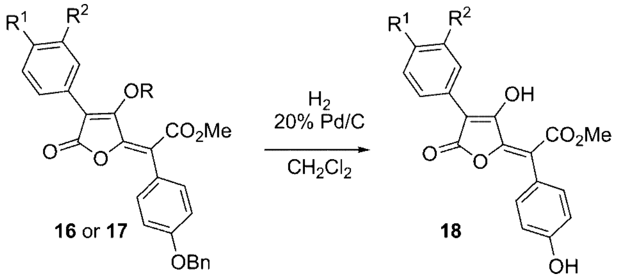
Entry	Boronate	R¹	R²	Yield of **16** [%]	Yield of **17** [%]
1	**6a**	H	H	97	
2	**6b**	OH	H	67	
3	**6c**	OMe	H	85	
4	**6d**	H	OH		99
5	**6e**	OBn	OBn	99	

The reactions proceeded with good to excellent yields, thus showing that the presence of the enol benzyl protecting group is not detrimental to the cross-coupling. However, adduct **17**, resulting from the cleavage of this protecting group, was obtained as a by-product in some experiments, and the reaction of triflate **5b** with boronate **6d**, in which the phenyl group is substituted by a hydroxy function in the *meta* position, led exclusively to compound **17d**.

The hydrogenolysis of the benzyl ethers of the cross-coupling adducts was then carried out using 20% palladium on carbon (Table 2). The reactions were conducted at first in methanol or ethanol, but this led to complex mixtures. In dichloromethane, the reactions were more satisfactory, although some reduction of the exocyclic double bond of the compounds occurred after long reaction times.

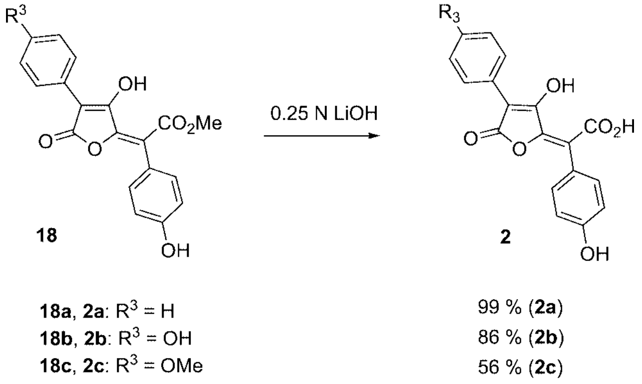
Compounds **18a–c** were obtained in very good yields (entries 1–3). These compounds have been described previously (**18a**,[15] **18b**,[15] **18c**[16]) and the spectroscopic and physical data agree well with the reported values. Compounds **18d** and **18e** were obtained in much lower yields. The deprotection of **16e**, which contains four benzyl groups, required the use of a larger amount of palladium. Besides the expected methyl ester **18e**, a by-product, which could not be isolated in a pure form and which may correspond to the (*Z*)-isomer of **18e**, was formed.

Table 2. Hydrogenolysis of pulvinic acid derivatives **16** and **17**.



Entry	Starting material	R	R¹	R²	Product	R¹	R²	**18** [% yield]
1	**16a**	Bn	H	H	**18a**	H	H	98
2	**16b**	Bn	OH	H	**18b**	OH	H	99
3	**16c**	Bn	OMe	H	**18c**	OMe	H	87
4	**17d**	H	H	OH	**18d**	H	OH	47
5	**16e**	Bn	OBn	OBn	**18e**	OH	OH	35

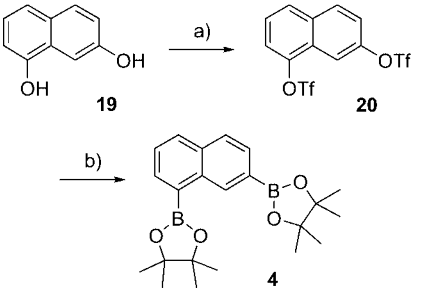
Saponification of esters **18a–c** using 0.25 N LiOH (reflux, 2 hours) proceeded efficiently, leading to the expected acids **19a–c** (Scheme 4). The spectroscopic and physical data observed for 4′-hydroxypulvinic acid (**2a**)[17] and for the natural product atromentic acid (**2b**)[15,17] were in good agreement with the reported values. To the best of our knowledge, 4-*O*-methylatromentic acid (**2c**) has not been synthesized previously. Attempted saponifications of esters **18d** and **18e** in the presence of LiOH were not successful, leading to the degradation of these compounds.



Scheme 4.

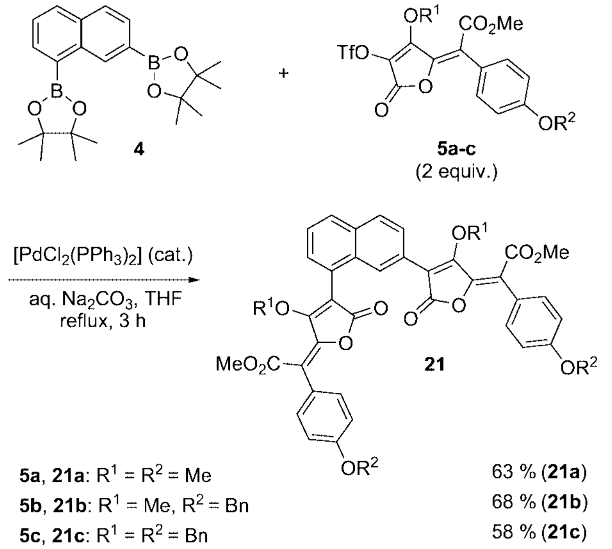
Preparation of a Naphthalene-Derived Compound Containing Two Pulvinic Moieties

The possibility to carry out a double cross-coupling using triflate **5a–c** and the bis(boronate) **4** derived from 1,7-dihydroxynaphthalene (**19**) was then examined. Compound **4** was prepared from the known bis(triflate) **20**,[18] obtained by reaction of **19** with triflic anhydride in pyridine (Scheme 5). The palladium-catalyzed borylation of aryl triflates using pinacolborane, according to the method developed by Masuda et al.,[19] enabled the preparation of bis(boronate) **4** in 45% yield.



Scheme 5. Reagents and conditions: a) Tf_2O, pyridine, 95%; b) pinacolborane (6 equiv.), [$PdCl_2$(dppf)] (0.06 equiv.), Et_3N (12 equiv.), dioxane, 80 °C, 13 h, 45%.

Several attempts to cleave the boronate groups of **4**, with the aim of obtaining 1,7-naphthalenediboronic acid, were unsuccessful. We thus employed **4** directly in the cross-coupling reactions with the three triflates **5a–c** (two equivalents), again under the conditions described above, which allowed the formation of the corresponding bis(pulvinic) acid adducts **21a–c** (Scheme 6).



5a, **21a**: $R^1 = R^2 = Me$ 63 % (**21a**)
5b, **21b**: $R^1 = Me$, $R^2 = Bn$ 68 % (**21b**)
5c, **21c**: $R^1 = R^2 = Bn$ 58 % (**21c**)

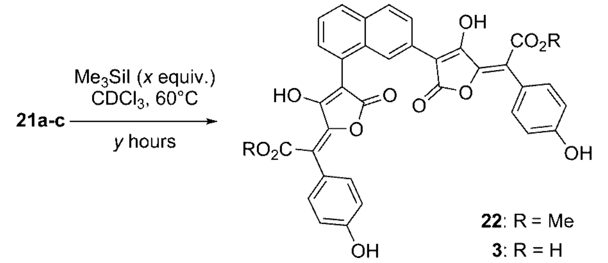
Scheme 6.

Although it was suspected that the boron environment in the compounds arising from the first cross-coupling would be significantly sterically crowded, thus threatening the occurrence of the second cross-coupling, fair yields of adducts **21a–c** were nevertheless obtained. These compounds were characterized by ^1H and ^{13}C NMR spectroscopy and by HRMS.

Cleavage of the protecting groups of compounds **21a–c** was then attempted, first by treatment with iodotrimethylsilane in $CDCl_3$ at 60 °C (Table 3).

We observed that, when applied to the permethylated derivative **21a**, the deprotection of all the hydroxy groups required 48 hours, even in the presence of 15 equivalents of iodotrimethylsilane (entry 1); however, this actually led to a mixture of compounds, probably formed by isomerization of the double bonds as well as shift of the lactone moieties (i.e. to compounds where a lactone moiety is bonded to the aryl group rather than to the naphthalene). Treatment of compound **21b** with 15 equivalents of iodotrimethylsilane for 18 h led to a mixture of compounds from which the expected deprotected diacid **3** was isolated in 37% yield (entry 2). Increasing the quantity of iodotrimethylsilane to 20 equivalent allowed us to reduce the reaction time to 8.5 hours and to improve the yield of **3** to 65% (entry 3). As benzyl groups are cleaved much more easily than the methyl groups, it was possible to prepare diester **22** in 60% yield by treatment of **21c** with iodotrimethylsilane (15 equivalents) for 2 h (entry 4).

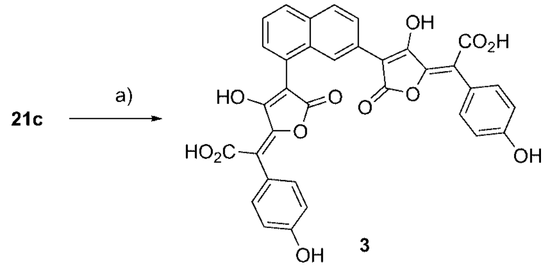
Table 3. Treatment of compounds **21a–c** with iodotrimethylsilane.



Entry	Starting material	R^1	R^2	x	y [h]	Yield of diacid **3** [%]	Yield of diester **22** [%]
1	**21a**	Me	Me	15	48	–[a]	–[a]
2	**21b**	Me	Bn	15	18	37[b]	–[b]
3	**21b**	Me	Bn	20	8.5	65	–
4	**21c**	Bn	Bn	15	2	–	60

[a] A mixture of deprotected products was obtained. [b] A mixture of deprotected products was also obtained as by-products.

Eventually, the preparation of bis(pulvinic acid) **3** was performed under the conditions previously described for the preparation of pulvinic acid derivatives **2a–c**. Thus, hydrogenolysis of compound **21c** proceeded efficiently, leading to diester **22** in 90% yield. Hydrolysis of the two methyl ester functions in the presence of 2.5 N NaOH then afforded diacid **3** in 90% yield. (Scheme 7).



Scheme 7. Reagents and conditions: a) *i.* H_2, Pd/C, CH_2Cl_2, room temp., 40 h, 90%; *ii.* 2.5 N aq. Na_2CO_3, reflux, 2 h, 90%.

In conclusion, the synthesis of several pulvinic acid derivatives has been described. The general procedure makes use of the cyclocondensation developed by Langer and of Suzuki–Miyaura coupling of vinyl triflates and arylboronic esters. Benzyl protecting groups have been shown to be cleaved more reliably than methyl groups in this context. A route to norbadione A analogues has been developed, which should be useful in view of the chemical synthesis of this unusual mushroom pigment.

Experimental Section

General: THF was freshly distilled from sodium benzophenone ketyl. Dichloromethane was freshly distilled from over P_2O_5. Moisture-sensitive reactions were performed in a flame-dried flask, under argon. TLC: silica gel 60F_{254} plates, with detection by UV light and with an ethanol solution of phosphomolybdic acid. Column chromatography: 40–63-µm silica gel. Melting points are uncorrected. NMR: 300.13 MHz for ^{1}H, 75.47 MHz MHz for ^{13}C. Chemical shifts (δ) are in ppm; coupling constants (J) are in Hz.

Methyl (4-Hydroxyphenyl)acetate:[20] A solution of (4-hydroxyphenyl)acetic acid (8.9 g, 59 mmol, 1 equiv.) and $BF_3{\cdot}Et_2O$ (0.9 mL) in methanol (100 mL) was stirred under argon at room temperature for 11 h. Saturated aqueous $NaHCO_3$ solution (100 mL) was then added. The aqueous phase was extracted with ethyl acetate (3×40 mL) and the combined organic phases were dried with $MgSO_4$, filtered, and concentrated under vacuum to afford methyl (4-hydroxyphenyl)acetate (9.6 g, 98%) as a colorless oil, which was used in the next reaction without further purification. TLC: R_f = 0.30 (8:2 pentane/AcOEt). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.11 (d, J = 8.5 Hz, 2 H, Ar-*H*), 6.77 (d, J = 8.5 Hz, 2 H, Ar-*H*), 3.72 (s, 3 H, CH_3O), 3.58 (s, 2 H, CH_2) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 173.3, 155.1, 130.2, 125.0, 115.4, 52.0, 40.1 ppm.

Methyl [4-(Benzyloxy)phenyl]acetate (7b):[21] Benzyl bromide (17.85 mL, 150 mmol) was added to a suspension of methyl (4-hydroxyphenyl)acetate (25 g, 150 mmol) and potassium carbonate (20.73 g, 150 mmol) in acetone (300 mL). The reaction mixture was then refluxed for 18 h. After cooling to room temperature, the suspension was filtered and the filtrate was concentrated under vacuum. Chloroform (200 mL) was added to the residue. The organic phase was washed successively with water (2×50 mL) and brine (50 mL), dried with $MgSO_4$, filtered, and concentrated under vacuum. Hexane was added and after overnight storage, precipitation occurred. After filtration, methyl [4-(benzyloxy)phenyl]acetate (**7b**) was obtained as colorless needles (34.94 g, 91%). M.p. 59–60 °C (ref.[21] 61–62 °C). TLC: R_f = 0.70 (8:2 pentane/AcOEt). IR (KBr pellet): $\tilde{\nu}$ = 2957, 2923, 1726, 1509, 1267, 1233, 1170, 1010 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.39–7.45 (m, 5 H, Ph-*H*), 7.23 (d, J = 8.6 Hz, 2 H, Ar-*H*), 6.97 (d, J = 8.6 Hz, 2 H, Ar-*H*), 5.08 (s, 2 H, CH_2Ph), 3.72 (s, 3 H, CH_3O), 3.60 (s, 2 H, CH_2CO_2Me) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 172.1, 157.8, 136.8, 130.1, 128.4, 127.8, 127.3, 126.1, 114.7, 69.8, 51.8, 40.1 ppm. $C_{16}H_{16}O_3$ (256.30): calcd. C 74.98, H 6.29; found C 74.66, H 6.29. MS (CI/NH_3): m/z = 274 $[M + NH_4]^+$.

Methyl (Benzyloxy)acetate (8b):[22] Thionyl chloride (2.6 mL, 35.6 mmol) was added dropwise with a syringe to methanol (21 mL) at 0 °C and the resulting solution was stirred for 20 min. A solution of (benzyloxy)acetic acid (5 g, 30 mmol) in methanol (9 mL) was then added dropwise from a dropping funnel. After stirring for 4 h at room temperature, the solution was concentrated under vacuum. Methylene chloride (200 mL) was added to the residue. The organic phase was washed successively with a saturated aqueous $NaHCO_3$ solution (2×50 mL) and water (2×50 mL), dried with $MgSO_4$, filtered, and concentrated under vacuum to afford methyl ester **8b** (5.2 g, 97%) as a colorless oil, which was used in the next reaction without further purification. TLC: R_f = 0.55 (CH_2Cl_2). IR (NaCl, film): $\tilde{\nu}$ = 3031, 2952, 1755, 1439, 1211, 1128, 743, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.30–7.39 (m, 5 H, Ph-*H*), 4.64 (s, 2 H, OCH_2CO), 4.12 (s, 2 H, CH_2Ph), 3.76 (s, 2 H, CH_3O) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 170.5, 135.5, 128.2, 128.1, 127.9, 73.1, 66.9, 51.6 ppm.

General Procedure for the Preparation of β-Keto Esters. Synthesis of Methyl 4-Methoxy-2-(4-methoxyphenyl)-3-oxobutanoate (9a): A solution of lithium diisopropylamide (2 M in THF; 42 mL, 83.8 mmol) was added over 20 min, from a dropping funnel, to a solution of methyl (4-methoxyphenyl)acetate (**7a**; 13.3 mL, 83.8 mmol) and HMPA (3.0 mL, 16.8 mmol) in THF (50 mL) cooled to –78 °C. After stirring for 1 h at –78 °C, methyl methoxyacetate (**8a**; 4.2 mL, 41.9 mmol) was added dropwise with a syringe. The reaction mixture was warmed to room temperature overnight whilst stirring. A saturated aqueous NH_4Cl solution was added and the aqueous phase was extracted with CH_2Cl_2. The combined organic phases were washed with saturated aqueous NH_4Cl solution, dried with $MgSO_4$, filtered, and concentrated under vacuum. Silica gel chromatography (9:1 pentane/AcOEt) afforded keto ester **9a** as a white solid (8.1 g, 77%). M.p. 44 °C. TLC: R_f = 0.45 (CH_2Cl_2). IR (KBr pellet): $\tilde{\nu}$ = 3434, 3013, 2960, 2836, 1741, 1612, 1515, 1449, 1212, 1025, 825, 741 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.22 (d, J = 9.1 Hz, 2 H, Ar-*H*), 6.86 (d, J = 9.1 Hz, 2 H, Ar-*H*), 4.87 (s, 1 H, $CHCO_2Me$), 4.04 (d, J = 13.1 Hz, 1 H, $CHHOMe$), 4.03 (d, J = 13.1 Hz, 1 H, $CHHOMe$), 3.74 (s, 3 H, CO_2Me), 3.68 (s, 3 H, CH_3OAr), 3.30 (s, 3 H, CH_3OCH_2) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 202.0, 169.0, 159.5, 132.0, 130.6, 123.7, 114.2, 113.6, 69.6, 59.8, 59.3, 55.2, 52.5 ppm. $C_{16}H_{16}O_5$ (252.26): calcd. C 61.90, H 6.39; found C 61.96, H 6.39.

Methyl 2-[4-(Benzyloxy)phenyl]-4-methoxy-3-oxobutanoate (9b): Following the general procedure, keto ester **9b** was prepared from methyl [4-(benzyloxy)phenyl]acetate (**7b**; 11.7 g, 45.6 mmol) and methyl methoxyacetate (**8a**; 2.3 mL, 22.8 mmol). After chromatographic purification, keto ester **9b** was obtained as a white solid (4.3 g, 58%). M.p. 55 °C. TLC: R_f = 0.35 (9:1 pentane/AcOEt). IR (KBr pellet): $\tilde{\nu}$ = 2948, 1741, 1512, 1308, 1246, 1217, 1183, 1105, 1008, 750, 698 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.28–7.47 (m, 7 H, Ar-*H* and Ph-*H*), 7.01 (d, J = 8.6 Hz, 2 H, Ar-*H*), 5.08 (s, 2 H, CH_2Ph), 4.95 (s, 1 H, $CHCO_2Me$), 4.09 (d, J = 13.2 Hz, 1 H, $CHHOMe$), 4.07 (d, J = 13.2 Hz, 1 H, $CHHOMe$), 3.74 (s, 3 H, CO_2Me), 3.37 (s, 3 H, CH_3OCH_2) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 201.9, 168.9, 158.7, 136.7, 132.1, 130.6, 128.4, 127.3, 123.9, 115.4, 69.8, 59.7, 59.1, 52.4 ppm. $C_{19}H_{20}O_5$ (328.36): calcd. C 69.49, H 6.14; found C 69.49, H 6.17.

Methyl 4-(Benzyloxy)-2-[4-(benzyloxy)phenyl]-3-oxobutanoate (9c): Following the general procedure, keto ester **9c** was prepared from methyl [4-(benzyloxy)phenyl]acetate (**7b**; 29.7 g, 115.8 mmol) and methyl (benzyloxy)acetate (**8b**; 10.4 g, 57.9 mmol). After chromatographic purification, keto ester **9c** was obtained as a white solid (11.5 g, 49%). M.p. 56 °C. TLC: R_f = 0.05 (8:2 pentane/AcOEt). IR (KBr pellet): $\tilde{\nu}$ = 2964, 1747, 1721, 1511, 1160, 823, 693 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.24–7.43 (m, 12 H, Ar-*H* and Ph-*H*), 6.98 (d, J = 8.5 Hz, 2 H, Ar-*H*), 5.08 (s, 2 H, OCH_2Ph), 4.97 (s, 1 H, $CHCO_2Me$), 4.56 (d, J = 12.2 Hz, 1 H, $OCHHPh$), 4.51 (d, J = 12.2 Hz, 1 H, $OCHHPh$), 4.19 (d, J = 16.5 Hz, 1 H, $CHHOBn$), 4.13 (d, J = 16.5 Hz, 1 H, $CHHOBn$), 3.73 (s, 3 H, CO_2Me) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 201.9, 168.9, 158.7, 136.8, 136.7, 130.6, 128.7, 128.5, 128.3, 127.9, 127.7, 127.3, 123.9, 115.0, 73.3, 69.9, 66.9, 59.9, 52.4 ppm. $C_{25}H_{24}O_5$ (404.46): calcd. C 74.20, H 5.98; found C 74.07, H 5.98.

General Procedure for the Preparation of Bis(silylated) Compounds 10a–c. Synthesis of 4-Methoxy-6-(methoxymethylene)-5-(4-methoxyphenyl)-2,2,8,8-tetramethyl-3,7-dioxa-2,8-disilanon-4-ene (10a):

Et_3N (3.8 mL, 26.8 mmol) and Me_3SiCl (3.7 mL, 29.1 mmol) were added to a solution of keto ester **9a** (2.8 g, 11.1 mmol) in 20 mL of THF and the reaction mixture was allowed to stir at room temperature overnight. The solvents were evaporated and pentane (20 mL) was added. The resulting suspension was filtered through millipore to yield the monosilylated derivative. A solution of this monosilylated derivative (3.9 g, 12.0 mmol) in 15 mL of THF was cooled to –78 °C and lithium diisopropylamide (12 mL, 24 mmol) was added. The reaction mixture was stirred at –78 °C for 1 h before Me_3SiCl (3.6 mL, 28.6 mmol) was added. Further agitation at –78 °C was continued for 1 h, after which the reaction mixture was warmed to room temperature over 4 h. The solvents were evaporated and pentane (20 mL) was added. The resulting suspension was filtered through millipore to yield the bis(silylated) derivative **10a** as an orange oil (4.7 g, quantitative). ^1H NMR ($CDCl_3$, 300 MHz): major isomer δ = 7.24–7.31 (m, 2 H, Ar-*H*), 6.84 (d, *J* = 8.5 Hz, 2 H, Ar-*H*), 5.62 (s, 1 H, =C*H*OMe), 3.80 (s, 3 H, CO_2Me), 3.56 (s, 3 H, CH_3OAr), 3.46 (s, 3 H, -CHOCH_3), 0.30 [s, 9 H, $OSi(CH_3)_3$], 0.04 [s, 9 H, $OSi(CH_3)_3$] ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 157.2, 153.1, 134.2, 131.5, 130.4, 128.7, 112.8, 97.5, 58.9, 56.1, 54.9, 0.3, 0.1 ppm.

5-(4-Benzyloxyphenyl)-4-methoxy-6-(methoxymethylene)-2,2,8,8-tetramethyl-3,7-dioxa-2,8-disilanon-4-ene (10b): Following the general procedure, bis(silylated) derivative **10b** was prepared from keto ester **9b** (1.4 g, 4.4 mmol). Compound **10b** was obtained as an orange oil (2.1 g, quantitative). ^1H NMR ($CDCl_3$, 300 MHz): major isomer δ = 7.10–7.52 (m, 7 H, Ar-*H* and Ph-*H*), 6.95 (d, *J* = 9.2 Hz, 2 H, Ar-*H*), 5.68 (s, 1 H, =C*H*OMe), 5.09 (s, 2 H, $PhCH_2O$-), 3.61 (s, 3 H, CH_3O), 3.51 (s, 3 H, CH_3O), 0.36 [s, 9 H, $OSi(CH_3)_3$], 0.09 [s, 9 H, $OSi(CH_3)_3$] ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 156.5, 153.1, 137.2, 134.4, 131.4, 127.3–129.9, 125.4, 114.5, 97.6, 69.7, 58.8, 56.1, 0.3, 0.1 ppm.

4-(Benzyloxy)-6-(benzyloxymethylene)-5-(4-benzyloxyphenyl)-2,2,8,8-tetramethyl-3,7-dioxa-2,8-disilanon-4-ene (10c): Following the general procedure, bis(silylated) derivative **10c** was prepared from keto ester **9c** (7.2 g, 17.8 mmol). Compound **10c** was obtained as a yellow oil (9.8 g, quantitative). ^1H NMR ($CDCl_3$, 300 MHz): major isomer δ = 7.20–7.49 (m, 12 H, Ar-*H* and Ph-*H*), 6.92 (d, *J* = 8.6 Hz, 2 H, Ar-*H*), 5.83 (s, 1 H, =C*H*OBn), 5.08 (s, 2 H, ArOCH_2Ph), 4.79 (s, 2 H, CH–OCH_2Ph), 3.47 (s, 3 H, CO_2Me), 0.28 [s, 9 H, $OSi(CH_3)_3$], 0.06 [s, 9 H, $OSi(CH_3)_3$] ppm.

General Procedure for the Cyclization. Synthesis of Methyl [4-Hydroxy-3-methoxy-5-oxofuran-2(5*H*)-ylidene](4-methoxyphenyl)acetate (11a): A solution of bis(silylated) derivative **10a** (4.7 g, 11.8 mmol) in 220 mL of degassed CH_2Cl_2 was placed in a three-necked, round-bottomed flask fitted with an addition funnel. The solution was cooled to –78 °C before oxalyl chloride (1.4 mL, 15.3 mmol) was added dropwise with a syringe. A solution of TMSOTf (0.6 mL, 3.5 mmol) in 40 mL of degassed CH_2Cl_2 was placed in the addition funnel and slowly added to the reaction mixture over 45 min. The reaction mixture was warmed to room temperature whilst stirring overnight. A saturated aqueous NaCl solution was added and the aqueous phase was extracted with CH_2Cl_2. The combined organic phases were dried with $MgSO_4$, filtered, and concentrated under vacuum. Silica gel chromatography (9:1 pentane/AcOEt) afforded compound **11a** as a pale-yellow solid (1.9 g, 54%). M.p. 160 °C. TLC: R_f = 0.35 (6:4 pentane/AcOEt). IR (KBr pellet): $\tilde{\nu}$ = 3309, 2954, 1737, 1669, 1513, 1378, 1113, 828 cm^{-1}. ^1H NMR ([D_6]acetone, 300 MHz): δ = 8.90 (s, 1 H, OH), 7.52 (d, *J* = 9.2 Hz, 2 H, Ar-*H*), 7.01 (d, *J* = 9.2 Hz, 2 H, Ar-*H*), 4.19 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3) ppm. ^{13}C NMR ([D_6]acetone, 75 MHz): δ = 167.3, 164.7, 160.6, 140.0, 130.9, 124.8, 124.7, 114.7, 59.9, 55.4, 52.5 ppm. $C_{15}H_{14}O_7$ (306.27): calcd. C 58.82, H 4.61; found C 59.07, H 4.92.

Methyl (4-Benzyloxyphenyl)[4-hydroxy-3-methoxy-5-oxofuran-2(5*H*)-ylidene]acetate (11b): Following the general procedure, enol **11b** was prepared from bis(silylated) derivative **10b** (5.4 g, 11.5 mmol). After chromatographic purification, compound **11b** was obtained as a pale-yellow solid (2.3 g, 53%). M.p. 144 °C. TLC: R_f = 0.15 (8:2 pentane/AcOEt). IR (KBr pellet): $\tilde{\nu}$ = 3259, 2925, 1772, 1731, 1677, 1603, 1510, 1373, 1231, 1042, 831, 741 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 7.54 (d, *J* = 9.2 Hz, 2 H, Ar-*H*), 7.40–7.45 (m, 5 H, Ph-*H*), 6.99 (d, *J* = 9.2 Hz, 2 H, Ar-*H*), 5.09 (s, 2 H, OCH_2Ar), 4.20 (s, 3 H, =$COCH_3$), 3.87 (s, 3 H, CO_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 166.8, 165.6, 159.7, 159.0, 142.7, 138.5, 130.3, 128.4, 127.8, 127.2, 123.5, 114.0, 113.9, 69.8, 59.8, 52.5 ppm. HRMS: calcd. for $C_{21}H_{18}NaO_7$ [M + Na]$^+$ 405.0950; found 405.0939.

Methyl [3-(Benzyloxy)-4-hydroxy-5-oxofuran-2(5*H*)-ylidene](4-benzyloxyphenyl)acetate (11c): Following the general procedure, enol **11c** was prepared from bis(silylated) derivative **10c** (1.8 g, 3.5 mmol). After chromatographic purification, compound **11c** was obtained as a white solid (0.6 g, 38%). M.p. 119 °C. TLC: R_f = 0.40 (7:3 pentane/AcOEt). IR (KBr pellet): $\tilde{\nu}$ = 3411, 1754, 1675, 1356, 1255, 1143, 1116, 1045 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 7.51 (d, *J* = 9.2 Hz, 2 H, Ar-*H*), 7.40–7.45 (m, 10 H, Ph-*H*), 6.98 (d, *J* = 9.2 Hz, 2 H, Ar-*H*), 5.49 (s, 2 H, OCH_2Ph), 5.09 (s, 2 H, $ArOCH_2Ph$), 3.45 (s, 3 H, OCH_3) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 165.2, 159.7, 142.5, 130.3, 128.5–127.0, 114.8, 113.5, 73.9, 69.8, 52.2 ppm. HRMS: calcd. for $C_{27}H_{22}NaO_7$ [M + Na]$^+$ 481.1263; found 481.1243.

General Procedure for the Preparation of Triflates. Synthesis of Methyl {3-Methoxy-5-oxo-4-[(trifluoromethylsulfonyl)oxy]furan-2(5*H*)-ylidene}(4-methoxyphenyl)acetate (5a): Pyridine (1.2 mL, 14.8 mmol) and triflic anhydride (1.2 mL, 7.1 mmol) were added to a solution of enol **11a** (1.8 g, 5.9 mmol) in CH_2Cl_2 (60 mL) cooled to –78 °C. The reaction mixture was warmed to room temperature whilst stirring over 4 h. Water was added and the organic layer was washed with water, dried with $MgSO_4$, filtered, and concentrated under vacuum. Silica gel chromatography (8:2 pentane/AcOEt) afforded triflate **5a** as a yellow solid (2.3 g, 89%). M.p. 93 °C. TLC: R_f = 0.30 (8:2 pentane/AcOEt). IR (KBr pellet): $\tilde{\nu}$ = 2961, 1802, 1783, 1744, 1733, 1667, 1643, 1604 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 7.57 (d, *J* = 9.2 Hz, 2 H, Ar-*H*), 6.91 (d, *J* = 9.2 Hz, 2 H, Ar-*H*), 4.26 (s, 3 H, CH_3O–C=), 3.87 (s, 3 H, $ArOCH_3$), 3.80 (s, 3 H, CO_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 165.7, 160.9, 159.9, 155.5, 131.0, 122.2, 120.5, 114.2, 60.8, 55.1, 52.7 ppm.

Methyl (4-Benzyloxyphenyl){3-methoxy-5-oxo-4-[(trifluoromethylsulfonyl)oxy]furan-2(5*H*)-ylidene}acetate (5b): Following the general procedure, triflate **5b** was prepared from alcohol **11b** (1.7 g, 4.4 mmol). After chromatographic purification, compound **5b** was obtained as a pale-yellow solid (1.9 g, 85%). M.p. 85 °C. TLC: R_f = 0.40 (8:2 pentane/AcOEt). ^1H NMR ($CDCl_3$, 300 MHz): δ = 7.60 (d, *J* = 5.7 Hz, 2 H, Ar-*H*), 7.37–7.43 (m, 5 H, Ph-*H*), 7.02 (d, *J* = 5.7 Hz, 2 H, Ar-*H*), 5.12 (s, 2 H, OCH_2Ph), 4.30 (s, 3 H, CH_3O–C=), 3.91 (s, 3 H, CO_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 168.2, 166.8, 159.7, 159.1, 131.1, 128.5, 128.1, 127.2, 121.3, 115.1, 69.9, 60.2, 52.8. MS (CI/NH_3): *m/z* 532 [M + NH_4]$^+$.

Methyl {3-(Benzyloxy)-5-oxo-4-[(trifluoromethylsulfonyl)oxy]furan-2(5*H*)-ylidene}(4-benzyloxyphenyl)acetate (5c): Following the general procedure, triflate **5c** was prepared from alcohol **11c** (206 mg, 0.5 mmol). After chromatographic purification, compound **5c** was obtained as a white solid (263 mg, 99%). M.p. 61 °C. TLC: R_f = 0.75 (7:3 pentane/AcOEt). IR (KBr pellet): $\tilde{\nu}$ = 3037, 2951, 1791, 1735, 1652, 1600, 1510, 1422, 1236, 1087, 1045, 609 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.57 (d, J = 9.2 Hz, 2 H, Ar-H), 7.27–7.42 (m, 10 H, Ph-H), 7.00 (d, J = 9.2 Hz, 2 H, Ar-H), 5.50 (s, 2 H, OCH_2Ph), 5.11 (s, 2 H, $ArOCH_2Ph$), 3.27 (s, 3 H, OCH_3) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 160.0, 132.8, 131.0, 130.7, 129.7, 129.1, 128.9, 128.8, 128.5, 127.2, 115.1, 75.6, 69.9, 52.2 ppm. $C_{28}H_{21}F_3O_9S$ (590.52): calcd. C 56.94, H 3.58, F 9.65; found C 56.93, H 3.73, F 9.80.

Methyl [3-Methoxy-5-oxo-4-phenylfuran-2(5*H*)-ylidene](4-methoxyphenyl)acetate (15):[13,23] Triflate **5a** (130 mg, 0.30 mmol), phenylboronic acid (40 mg, 0.34 mmol), K_3PO_4 (95 mg, 0.45 mmol), [$Pd(PPh_3)_4$] (10 mg, 3 mol-%), and 1.5 mL of degassed dioxane were placed in a round-bottomed flask fitted with a reflux condenser. The reaction mixture was heated to reflux for 4 h and then saturated aqueous NaCl was added. The aqueous layer was extracted thrice with diethyl ether and the combined organic layers were washed with water, dried with $MgSO_4$, filtered, and concentrated under vacuum. Silica gel chromatography (7:3 pentane/AcOEt) afforded **15** as a yellow solid (96 mg, 86%). M.p. 168 °C (ref.[13] 172–173°C; ref.[23] 171–172 °C). TLC: R_f = 0.55 (CH_2Cl_2). IR (KBr pellet): $\tilde{\nu}$ = 3428, 2934, 1768, 1725, 1622, 1597 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.67 (d, J = 9.2 Hz, 2 H, Ar-H), 7.53 (dd, J = 2.1 and 7.1 Hz, 2 H, Ph-H), 7.47 (dd, J = 2.1 and 7.1 Hz, 2 H, Ph-H), 7.43 (t, J = 2.1 Hz, 1 H, Ph-H), 6.95 (d, J = 9.2 Hz, 2 H, Ar-H), 3.92 (s, 3 H, CO_2Me), 3.86 (s, 3 H, $ArOCH_3$), 3.79 (s, 3 H, OCH_3) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 168.0, 167.4, 162.9, 160.7, 140.2, 130.9, 130.1, 129.0, 128.7, 128.6, 123.6, 116.5, 114.5, 107.9, 61.4, 55.5, 52.9 ppm. MS (CI/NH_3): m/z = 384 [M + NH_4]$^+$.

2-[3,4-Bis(benzyloxy)phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (6e): A 1.6 M solution of butyllithium in hexanes (0.910 µL, 1.45 mmol) was added dropwise to a solution of 1,2-bis(benzyloxy)-4-bromobenzene[24] (413 mg, 1.12 mmol) in anhydrous THF (10 mL) cooled to –78 °C under argon. After 1 h stirring at –78 °C, trimethyl borate (0.256 mL, 1.34 mmol) was added dropwise. The reaction mixture was stirred for 1 h at –78 °C, and then warmed to room temperature. A 1 N HCl aqueous solution (5 mL) was added and the aqueous phase was extracted with diethyl ether (3 × 10 mL). The combined organic phases were dried with $MgSO_4$, filtered, and concentrated under vacuum. Pinacol (160 mg, 1.34 mmol) and $MgSO_4$ (10.9 g) were added to a solution of the residue obtained in CH_2Cl_2 (8 mL). After stirring for 2 h at room temperature, the suspension was filtered and the filtrate was concentrated under vacuum. Silica gel chromatography (99:1 to 95:5 pentane/AcOEt) afforded compound **6e** as a colorless oil (308 mg, 66%). TLC: R_f = 0.70 (CH_2Cl_2). IR (KBr pellet): $\tilde{\nu}$ = 2973, 1600, 1524, 1420, 1354, 1265, 1135, 1018, 965, 856, 734, 682 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.37–7.52 (m, 12 H, Ar-H, Ph-H), 6.99 (d, J = 7.9 Hz, 1 H, Ar-H), 5.22 and 5.21 (2 s, 2 H each, 2 CH_2Ph), 1.38 (s, 12 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 151.6, 148.4, 137.3, 129.1, 128.9, 128.3, 128.2, 128.1, 127.6, 127.3, 127.2, 127.0, 126.4, 126.0, 120.6, 113.8, 83.5, 71.2, 70.6, 24.7 ppm. MS (ESI-TOF): m/z = 439 [M + Na]$^+$.

General Procedure for the Suzuki–Miyaura Coupling. Synthesis of Methyl [3-(Benzyloxy)-5-oxo-4-phenylfuran-2(5*H*)-ylidene](4-benzyloxyphenyl)acetate (16a): [$PdCl_2(PPh_3)_2$] (42 mg, 0.06 mmol) as a suspension in degassed THF (5 mL), phenylboronic acid pinacol ester (363 mg, 1.79 mmol) dissolved in degassed THF (25 mL), and an aqueous solution of Na_2CO_3 (2 M, 26 mL) were added to a solution of triflate **5c** (700 mg, 1.18 mmol) in degassed THF (75 mL). The reaction mixture was refluxed for 2 h and water (50 mL) was added. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layers were dried with $MgSO_4$, filtered, and concentrated under vacuum. Silica gel chromatography (8:2 pentane/AcOEt) afforded **16a** as a yellow solid (599 mg, 97%). M.p. 142 °C. TLC: R_f = 0.65 (CH_2Cl_2). IR (KBr pellet): $\tilde{\nu}$ = 3411, 1757, 1728, 1593, 1511, 1350, 1305, 1280, 1255, 1230, 1188, 1152 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.66 (d, J = 8.6 Hz, 2 H, Ar-H), 7.54 (dd, J = 1.2 and 7.6 Hz, 2 H, Ph-H), 7.50 (t, J = 3.2 Hz, 1 H, Ph-H), 7.36–7.45 (m, 10 H, Ph-H), 7.26 (m, 2 H, Ph-H), 7.02 (d, J = 8.6 Hz, 2 H, Ar-H), 5.12 (s, 2 H, $ArOCH_2Ph$), 4.96 (s, 2 H, OCH_2Ph), 3.38 (s, 3 H, CO_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 171.0, 166.8, 161.3, 159.4, 139.9, 136.3, 134.1, 130.6, 129.9, 128.8, 128.7, 128.6, 128.4, 128.3, 127.9, 127.1, 123.6, 116.3, 114.9, 75.2, 69.9, 52.1 ppm. HRMS: calcd. for $C_{33}H_{26}NaO_6$ [M + Na]$^+$ 541.1627; found 541.1646.

Methyl [3-Benzyloxy-4-(4-hydroxyphenyl)-5-oxofuran-2(5*H*)-ylidene](4-benzyloxyphenyl)acetate (16b): Following the general procedure, pulvinic derivative **16b** was prepared from (4-hydroxyphenyl)boronic acid pinacol ester (31 mg, 0.14 mmol) and triflate **5c** (50 mg, 0.08 mmol). After chromatographic purification, compound **16b** was obtained as a yellow-orange solid (19 mg, 42%). M.p. 108 °C. TLC: R_f = 0.70 (1:1 pentane/AcOEt). IR (KBr pellet): $\tilde{\nu}$ = 3400, 2921, 2852, 1728, 1601, 1510 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.63 (d, J = 9.2 Hz, 2 H, Ar-H), 7.26–7.44 (m, 12 H, Ar-H and Ph-H), 7.00 (d, J = 8.6 Hz, 2 H, Ar-H), 6.91 (d, J = 8.6 Hz, 2 H, Ar-H), 5.11 (s, 2 H, $ArOCH_2Ph$), 4.96 (s, 2 H, OCH_2Ar), 3.39 (s, 3 H, CO_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 168.5, 167.1, 160.2, 159.3, 140.1, 131.3, 130.6, 128.9, 128.8, 128.5, 128.4, 128.3, 127.9, 127.2, 123.6, 115.9, 115.3, 114.9, 74.9, 69.8, 52.2 ppm. HRMS: calcd. for $C_{33}H_{26}NaO_7$ [M + Na]$^+$ 557.1576; found 557.1591.

Methyl [3-Benzyloxy-4-(4-methoxyphenyl)-5-oxofuran-2(5*H*)-ylidene](4-benzyloxyphenyl)acetate (16c): Following the general procedure, pulvinic derivative **16c** was prepared from (4-methoxyphenyl)boronic acid pinacol ester (77 mg, 0.33 mmol) and triflate **5c** (130 mg, 0.22 mmol). After chromatographic purification, compound **16c** was obtained as a yellow solid (103 mg, 85%). M.p. 113 °C. TLC: R_f = 0. 45 (7:3 pentane/AcOEt). IR (KBr pellet): $\tilde{\nu}$ = 3035, 2932, 1756, 1729, 1508, 1252, 1156, 1041, 941, 834, 698 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.65 (d, J = 9.2 Hz, 2 H, Ar-H), 7.51 (d, J = 8.5 Hz, 2 H, Ar-H), 7.37–7.44 (m, 8 H, Ph-H), 7.29 (m, 2 H, Ph-H), 6.99–7.03 (m, 4 H, Ar-H), 5.11 (s, 2 H, $ArOCH_2Ph$), 4.97 (s, 2 H, OCH_2Ph), 3.87 (s, 3 H, OCH_3), 3.39 (s, 3 H, CO_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 168.0, 166.9, 160.7, 159.9, 140.1, 136.3, 134.2, 131.08, 130.6, 128.8, 128.7, 128.6, 128.4, 128.3, 127.9, 127.2, 120.7, 115.9, 114.9, 107.9, 74.8, 69.8, 55.2, 52.2 ppm. HRMS: calcd. for $C_{34}H_{28}NaO_7$ [M + Na]$^+$ 571.1733; found 571.1749.

Methyl (4-Benzyloxyphenyl)[3-hydroxy-4-(3-hydroxyphenyl)-5-oxofuran-2(5*H*)-ylidene]acetate (17d): Following the general procedure, pulvinic derivative **17d** was prepared from (3-hydroxyphenyl)boronic acid pinacol ester (87 mg, 0.40 mmol) and triflate **5c** (156 mg, 0.26 mmol). After chromatographic purification, compound **17d** was obtained as a yellow solid (122 mg, 86%). M.p. 134 °C. TLC: R_f = 0.45 (AcOEt). IR (KBr pellet): $\tilde{\nu}$ = 3483, 2925, 2856, 1713, 1570, 1508, 1444, 1256, 1177, 1044, 961, 851, 789, 743, 693, 639 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.17 (br. s, 1 H, OH), 7.81 (s, 1 H, Ar-H), 7.76 (d, J = 7.9 Hz, 1 H, Ar-H), 7.32–7.55 (m, 7 H, Ar-H and Ph-H), 7.13 (dd, J = 7.9 and 7.3 Hz, 1 H, Ar-H), 7.07 (d, J = 8.5 Hz, 2 H, Ar-H), 6.66 (d, J = 7.3 Hz, 1 H, Ar-H), 5.11 (s, 2 H, OCH_2Ph), 3.89 (s, 3 H, CO_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 172.8, 172.1, 169.2, 159.2, 157.6, 134.6, 132.5, 131.2, 130.4, 129.3, 129.2, 129.0, 128.3, 128.1, 126.3, 118.2, 115.0, 113.4, 113.2, 70.2, 53.6 ppm. HRMS: calcd. for $C_{26}H_{20}NaO_7$ [M + Na]$^+$ 467.1107; found 467.1111.

Methyl {3-Benzyloxy-4-[3,4-bis(benzyloxy)phenyl]-5-oxofuran-2(5*H*)-ylidene}(4-benzyloxyphenyl)acetate (16e): Following the general procedure, pulvinic derivative **16e** was prepared from [3,4-bis(benzyloxy)phenyl]boronic acid pinacol ester (237 mg, 0.57 mmol) and triflate **5c** (224 mg, 0.38 mmol). After chromatographic purification, compound **16e** was obtained as a yellow solid (282 mg, 99%). M.p. 136–138 °C. TLC: R_f = 0.30 (8:2 pentane/AcOEt). IR (KBr pellet): $\tilde{\nu}$ = 1762, 1597, 1510, 1255, 1132, 1042, 736, 694 cm^{-1}. ^{1}H NMR (CDCl$_3$, 300 MHz): δ = 7.63 (d, J = 9.2 Hz, 2 H, Ar-*H*), 7.30–7.47 (m, 20 H, Ph-*H*), 7.10 (d, J = 1.8 Hz, 1 H, Ar-*H*), 6.98–7.05 (m, 4 H, Ar-*H*), 5.24 (s, 2 H, OCH$_2$Ph), 5.15 (s, 2 H, OCH$_2$Ph), 5.12 (s, 2 H, OCH$_2$Ph), 4.89 (s, 2 H, OCH$_2$Ph), 3.46 (s, 3 H, CO$_2$CH$_3$) ppm. ^{13}C NMR (CDCl$_3$, 75 MHz): δ = 167.9, 166.9, 160.7, 159.3, 140.0, 136.7, 136.3, 134.3, 130.6, 128.9, 128.7, 128.4, 128.3, 128.2, 127.9, 127.7, 127.6, 127.3, 127.0, 126.1, 123.6, 121.3, 116.2, 114.9, 107.8, 70.9, 69.9, 69.8, 52.2 ppm. HRMS: calcd. for $C_{47}H_{38}NaO_8$ [M + Na]$^+$ 753.2464; found 753.2455.

General Procedure for the Hydrogenolysis. Synthesis of Methyl [3-Hydroxy-5-oxo-4-phenylfuran-2(5*H*)-ylidene](4-hydroxyphenyl)-acetate (Methyl 4′-Hydroxypulvinate, 18a): Protected pulvinic acid derivative **16a** (22 mg, 0.04 mmol), Pd/C (9 mg, 0.01 mmol) and CH$_2$Cl$_2$ (2 mL) were placed in a round-bottomed flask. The reaction mixture was stirred under hydrogen atmosphere for 28 h before being filtered through celite (elution with AcOEt). The filtrate was then concentrated under vacuum. Silica gel chromatography (7:3 pentane/AcOEt then pure AcOEt) afforded **18a** as a yellow solid (14 mg, 98%). M.p. 226 °C (ref.[15] 235–236 °C). TLC: R_f = 0.30 (1:1 pentane/AcOEt). IR (KBr pellet): $\tilde{\nu}$ = 3404, 1767, 1710, 1605, 1561, 1280, 1063 cm^{-1}. ^{1}H NMR ([D$_6$]acetone, 300 MHz): δ = 8.66 (br. s, 1 H, OH), 8.25 (dd, J = 8.6 and 1.2 Hz, 2 H, Ph-*H*), 7.41 (d, J = 8.6 Hz, 2 H, Ar-*H*), 7.34 (t, J = 7.3 Hz, 2 H, Ph-*H*), 7.16 (t, J = 7.3 Hz, 1 H, Ph-*H*), 6.89 (d, J = 9.2 Hz, 2 H, Ar-*H*), 3.90 (s, 3 H, CO$_2$CH$_3$) ppm. ^{13}C NMR ([D$_6$]acetone, 75 MHz): δ = 172.1, 169.2, 168.6, 158.1, 150.9, 132.7, 131.6, 131.4, 128.4, 126.9, 126.3, 124.6, 115.6, 113.7, 98.2, 53.7 ppm. HRMS: calcd. for $C_{19}H_{14}NaO_6$ [M + Na]$^+$ 361.0688; found 361.0689.

Methyl [3-Hydroxy-4-(4-hydroxyphenyl)-5-oxofuran-2(5*H*)-ylidene](4-hydroxyphenyl)acetate (Methyl 4,4′-Dihydroxypulvinate, 18b): Following the general procedure, pulvinic derivative **18b** was prepared from protected pulvinic acid derivative **16b** (38 mg, 0.57 mmol). After chromatographic purification, compound **18b** was obtained as a yellow solid (24 mg, quantitative). M.p. > 300 °C (ref.[15] 330–332 °C). TLC: R_f = 0.15 (1:1 pentane/AcOEt). IR (KBr pellet): $\tilde{\nu}$ = 3331, 1734, 1605, 1513, 1435, 1312, 1275, 1068, 970, 835 cm^{-1}. ^{1}H NMR ([D$_6$]acetone, 300 MHz): δ = 8.58 (br. s, 1 H, OH), 8.09 (d, J = 9.2 Hz, 2 H, Ar-*H*), 7.44 (d, J = 9.2 Hz, 2 H, Ar-*H*), 6.88 (d, J = 6.7 Hz, 2 H, Ar-*H*), 6.83 (d, J = 8.6 Hz, 2 H, Ar-*H*), 3.87 (s, 3 H, CO$_2$CH$_3$) ppm. ^{13}C NMR ([D$_6$]acetone, 75 MHz): δ = 172.1, 168.1, 157.7, 156.9, 134.0, 131.9, 128.4, 128.2, 124.7, 123.0, 116.2, 115.8, 115.6, 53.8 ppm.

Methyl [3-Hydroxy-4-(4-methoxyphenyl)-5-oxofuran-2(5*H*)-ylidene](4-hydroxyphenyl)acetate (Methyl 4-Methoxy-4′-hydroxypulvinate, 18c): Following the general procedure, pulvinic derivative **18c** was prepared from protected pulvinic acid derivative **16c** (56 mg, 0.10 mmol). After chromatographic purification, compound **18c** was obtained as a yellow solid (33 mg, quantitative). TLC: R_f = 0.65 (AcOEt). IR (KBr pellet): $\tilde{\nu}$ = 3244, 2927, 1737, 1599, 1276, 1064, 838 cm^{-1}. ^{1}H NMR ([D$_6$]acetone, 300 MHz): δ = 13.74 (br. s, 1 H, OH), 8.62 (br. s, 1 H, OH), 8.12 (d, J = 8.6 Hz, 2 H, Ar-*H*), 7.28 (d, J = 7.3 Hz, 2 H, Ar-*H*), 7.04 (d, J = 7.3 Hz, 2 H, Ar-*H*), 6.91 (d, J = 9.2 Hz, 2 H, Ar-*H*), 3.93 (s, 3 H, OCH$_3$), 3.86 (s, 3 H, -CO$_2$CH$_3$) ppm. ^{13}C NMR ([D$_6$]acetone, 75 MHz): δ = 171.9, 162.6, 157.8, 141.5, 134.3, 131.5, 127.8, 122.3, 117.7, 116.0, 113.7, 55.1, 53.9 ppm. HRMS: calcd. for $C_{20}H_{16}NaO_7$ [M + Na]$^+$ 391.0794; found 391.0765.

Methyl [3-Hydroxy-4-(3-hydroxyphenyl)-5-oxofuran-2(5*H*)-ylidene](4-hydroxyphenyl)acetate (Methyl 3,4′-Dihydroxypulvinate, 18d): Following the general procedure, pulvinic derivative **18d** was prepared from protected pulvinic acid derivative **17d** (48 mg, 0.11 mmol). After chromatographic purification, compound **18d** was obtained as a yellow solid (18 mg, 47%). M.p. > 300 °C. TLC: R_f = 0.35 (AcOEt). IR (KBr pellet): $\tilde{\nu}$ = 3238, 1706, 1555, 1509, 1436, 1233, 1045, 974, 839, 789, 689, 626 cm^{-1}. ^{1}H NMR ([D$_6$]-acetone, 300 MHz): δ = 8.73 (br. s, 1 H, OH), 7.93 (s, 1 H, Ar-*H*), 7.82 (d, J = 7.9 Hz, 1 H, Ar-*H*), 7.52 (d, J = 8.5 Hz, 2 H, Ar-*H*), 7.04 (t, J = 7.9 Hz, 1 H, Ar-*H*), 6.89 (d, J = 9.2 Hz, 2 H, Ar-*H*), 6.49 (d, J = 6.7 Hz, 1 H, Ar-*H*), 3.85 (s, 3 H, CO$_2$CH$_3$) ppm. ^{13}C NMR ([D$_6$]acetone, 75 MHz): δ = 171.6, 170.9, 157.3, 157.2, 132.3, 130.5, 128.8, 128.7, 125.4, 116.9, 115.5, 111.9, 52.3 ppm.

Methyl [4-(3,4-Dihydroxyphenyl)-3-hydroxy-5-oxofuran-2(5*H*)-ylidene](4-hydroxyphenyl)acetate (Methyl 3,4,4′-Trihydroxypulvinate, 18e): Following the general procedure, pulvinic derivative **18e** was prepared from protected pulvinic acid derivative **16e** (189 mg, 0.26 mmol). After chromatographic purification, compound **18e** was obtained as a deep-red solid (33 mg, 35%). M.p. 259 °C (ref.[16] 258–259 °C). TLC: R_f = 0.20 (AcOEt). IR (KBr pellet): $\tilde{\nu}$ = 3287, 2927, 2360, 1752, 1677, 1602, 1276, 1062, 962, 869, 819 cm^{-1}. ^{1}H NMR ([D$_6$]acetone, 300 MHz): δ = 8.65 (br. s, 1 H, OH), 8.17 (br. s, 1 H, OH), 7.74 (d, J = 1.8 Hz, 1 H, Ar-*H*), 7.60 (dd, J = 8.5 and 1.8 Hz, 1 H, Ar-*H*), 7.27 (d, J = 8.5 Hz, 2 H, Ar-*H*), 6.90 (m, 3 H, Ar-*H*), 3.91 (s, 3 H, CO$_2$CH$_3$) ppm. ^{13}C NMR ([D$_6$]acetone, 75 MHz): δ = 172.6, 169.3, 166.8, 158.1, 153.9, 145.3, 132.2, 124.4, 122.2, 120.8, 115.8, 115.3, 115.2, 113.1, 54.4 ppm. HRMS: calcd. for $C_{19}H_{14}NaO_8$ [M + Na]$^+$ 393.0586; found 393.0605.

General Procedure for the Saponification. Synthesis of [3-Hydroxy-5-oxo-4-phenylfuran-2(5*H*)-ylidene](4-hydroxyphenyl)acetic Acid (4′-Hydroxypulvinic Acid, 2a): Pulvinic ester **18a** (6 mg, 0.018 mmol) and an aqueous solution of LiOH (205 µL, 0.5 N) were placed in a round-bottomed flask fitted with a reflux condenser. The reaction mixture was heated to reflux for 2 h. The reaction mixture was acidified to pH 1 with a solution of HCl 1 N. The aqueous layer was extracted with AcOEt and the combined organic layers were dried with MgSO$_4$, filtered, and concentrated under vacuum. Reverse phase chromatography (8:2 water/MeOH) afforded acid **2a** as a yellow solid (5 mg, quantitative). M.p. 162 °C (ref.[17] 160–163 °C). TLC: R_f = 0.35 (9:1 AcOEt/MeOH). IR (KBr pellet): $\tilde{\nu}$ = 3451, 2925, 1742, 1581, 1510, 1464, 1392, 1175, 964, 836, 782, 692 cm^{-1}. ^{1}H NMR ([D$_6$]acetone, 300 MHz): δ = 8.27 (d, J = 8.6 Hz, 2 H, Ar-*H*), 7.34 (t, J = 7.3 Hz, 2 H, Ar-*H*), 7.18 (d, J = 7.3 Hz, 2 H, Ar-*H*), 7.17 (t, J = 7.3 Hz, 1 H, Ar-*H*), 6.82 (d, J = 7.3 Hz, 2 H, Ar-*H*) ppm. ^{13}C NMR ([D$_6$]acetone, 75 MHz): δ = 169.7, 168.9, 157.1, 151.2, 132.4, 131.0, 128.3, 128.2, 126.6, 126.1, 115.3, 114.5, 97.9 ppm. MS (EI/TOF): m/z = 325 [M + H]$^+$.

[3-Hydroxy-4-(4-hydroxyphenyl)-5-oxofuran-2(5*H*)-ylidene](4-hydroxyphenyl)acetic Acid (Atromentic Acid, 2b): Following the general procedure, pulvinic derivative **2b** was prepared from pulvinic ester **18b** (11 mg, 0.03 mmol). After chromatographic purification, compound **2b** was obtained as a yellow solid (9 mg, 85%). M.p. > 300 °C (ref.[15] 360–362 °C; ref.[17] 287–289 °C). TLC: R_f = 0.30 (9:1 AcOEt /MeOH). IR (KBr pellet): $\tilde{\nu}$ = 3800–3000, 2360, 1730, 1601, 1571, 1513, 1391, 1231, 1173, 968, 836 cm^{-1}. ^{1}H NMR ([D$_6$]acetone, 300 MHz): δ = 13.77 (br. s, 1 H, OH), 8.18 (d, J = 8.6 Hz, 2 H, Ar-H), 7.16 (d, J = 8.6 Hz, 2 H, Ar-H), 6.79–6.84 (m, 4 H, Ar-H) ppm. ^{13}C NMR ([D$_6$]acetone, 75 MHz): δ = 172.1, 169.2, 168.6, 158.1, 150.9, 132.7, 131.6, 131.4, 126.3, 124.6, 115.6, 113.7, 98.2, 53.7 ppm.

[3-Hydroxy-4-(4-methoxyphenyl)-5-oxofuran-2(5*H*)-ylidene](4-hydroxyphenyl)acetic Acid (4′-Hydroxy-4-methoxypulvinic Acid, 2c): Following the general procedure, pulvinic derivative **2c** was prepared from pulvinic ester **18c** (6 mg, 0.015 mmol). After chromatographic purification, compound **2c** was obtained as a yellow solid (3 mg, 56%). TLC: R_f = 0.45 (9:1 AcOEt /MeOH). IR (KBr pellet): $\tilde{\nu}$ = 3424, 1727, 1601, 1570, 1513, 1391, 1245, 1174, 968, 835 cm^{-1}. ^{1}H NMR ([D$_6$]acetone, 300 MHz): δ = 8.27 (d, J = 8.6 Hz, 2 H, Ar-H), 7.16 (d, J = 8.6 Hz, 2 H, Ar-H), 6.90 (d, J = 8.6 Hz, 2 H, Ar-H), 6.80 (d, J = 8.6 Hz, 2 H, Ar-H), 3.79 (s, 3 H, -OCH$_3$) ppm. ^{13}C NMR ([D$_6$]acetone, 75 MHz): δ = 146.9, 132.5, 130.9, 127.5, 125.8, 123.1, 114.3, 113.6, 112.9, 54.9 ppm. MS (EI/TOF): m/z = 355 [M + H]$^+$.

2,2′-Naphthalene-1,7-diyl(4,4,5,5-tetramethyl-1,3,2-dioxoborolane) (4): A solution of bis(triflate) **20**[18] (2.44 g, 5.75 mmol) in 10 mL of dioxane, triethylamine (9.6 mL, 69 mmol), 4,4,5,5-tetramethyl-[1,3,2]-dioxaborolane (5 mL, 34 mmol), and dioxane (20 mL) were added successively, with a syringe, to a suspension of [PdCl$_2$(dppf)] (280 mg, 0.35 mmol) in degassed dioxane (10 mL). The reaction mixture was heated to reflux for 10 h and hexane was added. The layers were separated and the organic layer was washed with brine, dried with MgSO$_4$, filtered, and concentrated under vacuum. After chromatographic purification (99:1 pentane/AcOEt), compound **4** was obtained as a translucent oil (979 mg, 45%). TLC: R_f = 0.60 (9:1 pentane/AcOEt). IR (KBr pellet): $\tilde{\nu}$ = 2978, 1454, 1357, 1138 cm^{-1}. ^{1}H NMR (CDCl$_3$, 300 MHz): δ = 9.32 (s, 1 H, H-8), 8.08 (d, J = 8.3 Hz, 1 H, H-4), 7.95 (d, J = 7.8 Hz, 1 H, H-2), 7.87 (d, J = 8.3 Hz, 1 H, H-5 or H-6), 7.83 (d, J = 8.3 Hz, 1 H, H-5 or H-6), 7.54 (dd, J = 8.2 and 9.5 Hz, 1 H, H-3), 1.49 (s, 12 H, CH$_3$), 1.43 (s, 12 H, CH$_3$) ppm. ^{13}C NMR (CDCl$_3$, 75 MHz): δ = 136.6, 136.0, 134.8, 134.6, 131.0, 129.8, 127.2, 125.7, 83.6, 24.8 ppm. MS (CI/NH$_3$): m/z = 398 [M+ NH$_4$]$^+$.

General Procedure for the Suzuki Coupling. Synthesis of Dimethyl 2,2′-[Naphthalene-1,7-diylbis(3-methoxy-5-oxofuran-4-yl-2-ylidene)]bis[(4-methoxyphenyl)acetate] (21a): A suspension of [PdCl$_2$(PPh$_3$)$_2$] (19 mg, 1 mol-%) in THF (5 mL), a solution of bis(boronate) **4** (89 mg, 0.43 mmol) in THF (5 mL), and 5 mL of an aqueous Na$_2$CO$_3$ solution (2 M) were added to a solution of triflate **5a** (214 mg, 0.488 mmol) in degassed THF (10 mL). The reaction mixture was heated to reflux for 3 h and water was added. The aqueous layer was extracted with CH$_2$Cl$_2$ and the combined organic layers were dried with MgSO$_4$, filtered, and concentrated under vacuum. After chromatographic purification (8:2 pentane/AcOEt), compound **21a** was obtained as a green-yellow solid (104 mg, 63%). TLC: R_f = 0.10 (6:4 hexane/AcOEt). IR (KBr pellet): $\tilde{\nu}$ = 3447, 3007, 2950, 1769, 1732, 1626, 1603, 1512, 1285, 1256, 1158, 1042, 975, 917, 836, 757 cm^{-1}. ^{1}H NMR (CDCl$_3$, 300 MHz): δ = 7.96–7.99 (m, 2 H, naphthyl-H), 7.90 (s, 1 H, naphthyl-H), 7.66–7.74 (m, 5 H, naphthyl-H and Ar-H), 7.57–7.59 (m, 2 H, naphthyl-H), 6.94–6.99 (m, 4 H, Ar-H), 3.92 (s, 3 H, CO$_2$CH$_3$), 3.90 (s, 3 H, CO$_2$CH$_3$), 3.87 (s, 3 H, CH$_3$O), 3.86 (s, 3 H, CH$_3$O), 3.80 (s, 3 H, CH$_3$O), 3.63 (s, 3 H, CH$_3$O) ppm. ^{13}C NMR (CDCl$_3$, 75 MHz): δ = 168.4, 168.0, 166.9, 166.8, 164.0, 163.0, 160.4, 160.3, 139.5, 139.4, 130.7, 130.6, 133.1, 131.3, 130.1, 129.8, 129.3, 128.7, 127.5, 127.3, 126.5, 125.9, 123.2, 116.9, 114.1, 106.5, 103.4, 61.5, 60.6, 55.2, 52.6 ppm. C$_{40}$H$_{32}$O$_{12}$ (704.68): calcd. C 68.18, H 4.58; found C 68.03, H 4.83.

Dimethyl 2,2′-[Naphthalene-1,7-diylbis(3-methoxy-5-oxofuran-4-yl-2-ylidene)]bis[(4-benzyloxyphenyl)acetate] (21b): Following the general procedure, bis(pulvinic) derivative **21b** was prepared from bis(boronate) **4** (164 mg, 0.43 mmol) and triflate **5b** (466 mg, 0.91 mmol). After chromatographic purification, compound **21b** was obtained as a brown solid (250 mg, 68%). M.p. 140 °C. TLC: R_f = 0.20 (8:2 pentane/AcOEt). IR (KBr pellet): $\tilde{\nu}$ = 2360, 1769, 1732, 1601, 1509, 1229, 1182, 1043, 977, 911, 834, 744, 694 cm^{-1}. ^{1}H NMR (CDCl$_3$, 300 MHz): δ = 7.97 (m, 2 H, naphthyl-H), 7.90 (s, 1 H, naphthyl-H), 7.66–7.73 (m, 5 H, naphthyl-H and Ar-H), 7.59 (m, 1 H, naphthyl-H), 7.57 (m, 1 H, naphthyl-H), 7.35–7.44 (m, 10 H, Ph-H), 7.00–7.06 (m, 4 H, Ar-H), 5.13 (s, 2 H, CH$_2$), 5.12 (s, 2 H, CH$_2$), 3.92 (s, 3 H, CO$_2$CH$_3$), 3.90 (s, 3 H, CO$_2$CH$_3$), 3.79 (s, 3 H, CH$_3$O), 3.62 (s, 3 H, CH$_3$O) ppm. ^{13}C NMR (CDCl$_3$, 75 MHz): δ = 165.3, 163.3, 159.9, 151.3, 147.5, 136.2, 131.3, 130.8, 130.2, 129.9, 129.5, 129.3, 128.7, 128.6, 128.5, 128.2, 127.9, 127.7, 127.3, 126.9, 126.4, 126.2, 125.9, 124.2, 115.0, 114.7, 105.4, 102.3, 69.8, 60.7, 61.6, 52.6 ppm. HRMS: calcd. for C$_{52}$H$_{40}$O$_{12}$ [M]$^+$ 856.2520; found 856.2519.

Dimethyl 2,2′-[Naphthalene-1,7-diylbis(3-benzyloxy-5-oxofuran-4-yl-2-ylidene)]bis[(4-benzyloxyphenyl)acetate] (21c): Following the general procedure, bis(pulvinic) derivative **21c** was prepared from bis(boronate) **4** (81 mg, 0.21 mmol) and triflate **5c** (266 mg, 0.45 mmol). After chromatographic purification, compound **21c** was obtained as a brown solid (123 mg, 58%). M.p. 175–176 °C. TLC: R_f = 0.20 (8:2 pentane/AcOEt). IR (KBr pellet): $\tilde{\nu}$ = 3034, 2925, 1767, 1731, 1603, 1509, 1310, 1284, 1230, 1182, 1042, 970, 912, 835, 739, 696 cm^{-1}. ^{1}H NMR (CDCl$_3$, 300 MHz): δ = 7.95–8.06 (m, 3 H, naphthyl-H), 7.86 (s, 1 H, naphthyl-H), 7.73 (d, J = 9.2 Hz, 2 H), 7.69 (d, J = 9.2 Hz, 2 H), 7.59–7.63 (m, 5 H, Ph-H), 7.42–7.45 (m, 10 H, Ph-H), 7.27–7.29 (m, 2 H, naphthyl-H), 7.21–7.24 (m, 5 H, Ph-H), 7.04 (d, J = 9.2 Hz, 2 H), 7.02 (d, J = 9.2 Hz, 2 H, Ar-H), 5.14 (s, 2 H, OCH$_2$Ph), 5.12 (s, 2 H, OCH$_2$Ph), 5.09 (s, 2 H, OCH$_2$Ph), 4.93 (d, J = 10.9 Hz, 1 H, benzylic H), 4.89 (d, J = 10.9 Hz, 1 H, benzylic H), 3.35 (s, 3 H, CO$_2$CH$_3$), 3.30 (s, 3 H, CO$_2$CH$_3$) ppm. ^{13}C NMR (CDCl$_3$, 75 MHz): δ = 168,1, 167.9, 166.7, 166.6, 163.0, 159.4, 125.9–132.3, 123.7, 123.6, 116.5, 114.9, 114.0, 77.3, 76.9, 69.9, 52.1, 51.9 ppm. HRMS: calcd. for [M]$^+$ 1008.3146; found 1008.3200.

Synthesis of Dimethyl 2,2′-[Naphthalene-1,7-diylbis(3-hydroxy-5-oxofuran-4-yl-2-ylidene)]bis[(4-hydroxyphenyl)acetate] (22) by Hydrogenolysis of Compound 21c (Method A): A suspension of compound **21c** (20 mg, 0.019 mmol) and 10% Pd/C (16 mg) in dichloromethane (5 mL) was stirred under a hydrogen atmosphere for 26 h. The suspension was filtered through a pad of celite, which was washed with ethyl acetate. The solution was concentrated under vacuum. After chromatographic purification on a C-18 column (gradient from 9:1 H$_2$O/MeOH to pure MeOH), compound **22** was obtained as a yellow solid (11 mg, 90%).

Synthesis of 22 by Treatment of Compound 21c with Iodotrimethylsilane (Method B): Iodotrimethylsilane (22 µL, 0.15 mmol) was added with a syringe to a solution of compound **21c** (10 mg, 0.01 mmol) in CDCl$_3$ (1 mL), placed in an NMR tube, under argon. The tube was sealed and then heated in an oil bath at 60 °C for 2 h. After cooling to room temperature, the tube was opened and water (1 mL) was added. The mixture was stirred for 1 h then concentrated under vacuum. After chromatographic purification on a C-18 column (4:1 H$_2$O/MeOH), compound **22** was obtained as a yellow solid (4 mg, 60%). M.p. > 300 °C. TLC: R_f = 0.25 (AcOEt). IR (KBr pellet): $\tilde{\nu}$ = 3428, 3245, 2961, 1716, 1559, 1510, 1266, 1039, 803 cm^{-1}. ^{1}H NMR (CD$_3$OD, 300 MHz): δ = 8.53 (s, 1 H, naphthyl-H), 8.17 (d, J = 8.6 Hz, 2 H, naphthyl-H), 7.69 (d, *J* = 8.6 Hz, 2 H, naphthyl-*H*), 7.60 (d, *J* = 9.2 Hz, 2 H, naphthyl-*H*), 7.44–7.50 (m, 2 H, naphthyl-*H*), 7.36 (d, *J* = 7.3 Hz, 2 H, Ar-*H*), 7.27 (d, *J* = 7.3 Hz, 2 H, Ar-*H*), 6.78(d, *J* = 8.6 Hz, 2 H, Ar-*H*), 6.74 (d, *J* = 8.6 Hz, 2 H, Ar-*H*), 3.85 (s, 3 H, CO_2CH_3), 3.81 (s, 3 H, CO_2CH_3) ppm. ^{13}C NMR ([D$_6$]acetone, 75 MHz): δ = 177.4, 177.3, 171.7, 169.5, 168.2, 161.9, 159.6, 157.1, 152.9, 152.3, 142.3, 132.2, 131.9, 130.2, 128.9, 127.4, 127.1, 126.9, 126.2, 125.8, 121.3, 120.3, 115.8, 100.3, 56.4 ppm. HRMS: calcd. for [M + Na]$^+$ 671.1165; found 671.1192.

2,2′-[Naphthalene-1,7-diylbis(3-hydroxy-5-oxofuran-4-yl-2-ylidene)]-bis[(4-hydroxyphenyl)acetic Acid] (3): A 0.5-N NaOH aqueous solution (300 µL) was added to compound **22** (10 mg, 0.015 mmol) and the mixture was heated at 100 °C for 1 h. After cooling to room temperature, 1 N aqueous HCl was added until pH 1. The aqueous phase was extracted with AcOEt (2 × 5 mL). The combined organic phases were dried with $MgSO_4$, filtered, and then concentrated under vacuum. After chromatographic purification on a C-18 column (9:1 H_2O/MeOH), diacid **3** was obtained as a yellow solid (9 mg, 90%). M.p. 175–176 °C. TLC: R_f = 0.15 (AcOEt). IR (KBr pellet): $\tilde{\nu}$ = 3449, 1743, 1563, 1511, 1389, 1147, 1062, 974, 837, 767 cm^{-1}. ^1H NMR ([D$_6$]acetone, 300 MHz): δ = 8.64 (s, 1 H, naphthyl-*H*), 8.30 (d, *J* = 8.6 Hz, 2 H, naphthyl-*H*), 7.78 (d, *J* = 8.6 Hz, 2 H, naphthyl-*H*), 7.73 (dd, *J* = 7.2, 2.5 Hz, 2 H, naphthyl-*H*), 7.39–7.42 (m, 2 H, naphthyl-*H*), 7.19 (d, *J* = 8.6 Hz, 2 H, Ar-*H*), 7.12 (d, *J* = 8.6 Hz, 2 H, Ar-*H*), 6.77 (d, *J* = 8.6 Hz, 2 H, Ar-*H*), 6.73 (d, *J* = 8.6 Hz, 2 H, Ar-*H*) ppm. ^{13}C NMR ([D$_6$]acetone, 75 MHz): δ = 172.2, 157.9, 133.8, 133.7, 133.1, 132.8, 132.7, 130.4, 129.5, 128.5, 128.1, 125.8, 124.9, 121.6, 115.3 ppm.

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