Total syntheses of three natural products, vignafuran, 2-(4-hydroxy-2-methoxyphenyl)-6-methoxybenzofuran-3-carboxylic acid methyl ester, and coumestrol from a common starting material

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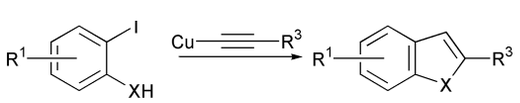
Vignafuran **2**, 2-(4-hydroxy-2-methoxyphenyl)-6-methoxybenzofuran-3-carboxylic acid methyl ester **3**, and coumestrol **4** were efficiently synthesized from the same starting material, 4-bromoresorcinol **14a**, through the common intermediate, diarylacetylene **7**. The key steps of these syntheses were the tetrabutylammonium fluoride (TBAF)-catalyzed benzo[*b*]furan ring formation for **2** and the carbonylative ring closure methodology catalyzed by a Pd complex for **3** and **4**.

Introduction

Heterocyclic compounds, particularly indole[1] and benzo[*b*]-furan[2] derivatives, are of interest because they occur widely in Nature and have unique biological activities.[3] Many synthetic methods for indole and benzo[*b*]furan structures have already been reported.[4,5] Among them, the cyclization reaction of 2-ethynylphenol or 2-ethynylaniline derivatives is a powerful method for constructing such ring systems because of the availability of the starting materials and its efficiency.[4,5] For the last few decades, many efforts toward developing new methods using this strategy have been published, and most studies have been carried out using metal species, *e.g.,* copper(I) species,[6] $NaAuCl_4 \cdot H_2O$,[7] palladium(II) species,[8–10] and metal alkoxides.[11]

Between 1966 and 1969, Castro *et al.*[6a,b] reported pioneering work involving the copper(I) halide-catalyzed sequential coupling and cyclization reactions of 2-iodophenol and 2-iodoaniline with Cu-acetylide derivatives to give benzo[*b*]furans and indoles, respectively (Scheme 1). In spite of its usefulness,



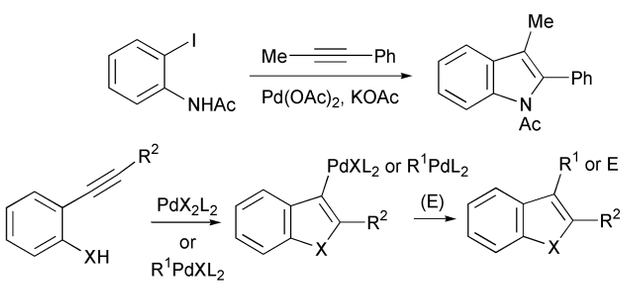
X = O or NR[2]; R^1 = Me, OH, halogen; R^2 = H, Et, Me; R^3 = Ph, Pr, pyridinyl

Scheme 1

Castro's method has not seen wide use, because explosive Cu-acetylides have to be prepared and isolated. Subsequently, Owen[6c] and Nilsson[6d] independently improved this problem by using Cu_2O in pyridine or ^{t}BuOCu in pyridine, respectively, although heating was necessary for the cyclization reaction.

The palladium(II) species-promoted cyclization reaction of 2-ethynylaniline and/or 2-ethynylphenol derivatives, which was first reported in the middle 1980s,[8a,b] was found to have wide applicability because of the milder reaction conditions than the previously reported methods.[8–10] Later on, this methodology was extended for constructing 2,3-disubstituted benzo[*b*]furans and indoles using disubstituted acetylenic compounds as the starting materials.[9] More recently, the trapping methodologies of the resulting 3-substituted Pd species have been well investigated.[10] (Scheme 2).

During the course of our continuous interests in the syntheses of substituted heterocyclic compounds, we have already published efficient synthetic procedures for 2-mono- and 2,3-disubstituted indoles and/or benzo[*b*]furans, which involve (1) the cyclization reaction of 2-ethynylphenylcarbamates to indoles under basic conditions (sodium ethoxide in ethanol or potassium *tert*-butoxide in *tert*-butyl alcohol),[11] (2) the Pd-catalyzed cyclization followed by alkenylation,[10k] (3) the Pd-catalyzed carbonylative cyclization reaction,[10a] and (4) the tetrabutylammonium fluoride (TBAF)-promoted cyclization reaction (Scheme 3).[12]



X = O or NR; E = electrophile

Scheme 2

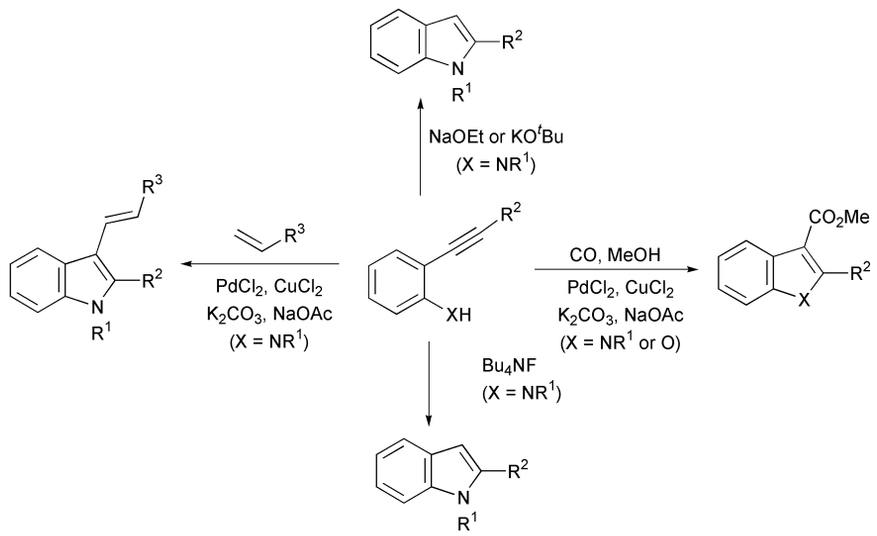
However, other synthetic procedures for the methyl 2-substituted indole-3-carboxylate derivatives have recently been independently reported by Yang[10j] and Scammells.[10h,i] Yang argued about the difficulty in reproducing the reaction conditions reported by Scammells,[10h,i] which are almost the same as those we have already reported.[10a] Consequently, Yang reported an improved procedure for trapping the C-Pd species by carbon monoxide, although their catalytic system seems to be slightly complicated.[10j]

Based on the above background about the heterocyclic ring system syntheses, we report here the synthesis of three different natural products from the same starting materials utilizing our own method.

Results and discussion

(a) Target molecules and synthetic strategy

Vignafuran **2**, isolated from the leaves of cowpea seedlings (*Vigna unguiculata* (L.) Walp.) grown in daylight and infected



Scheme 3

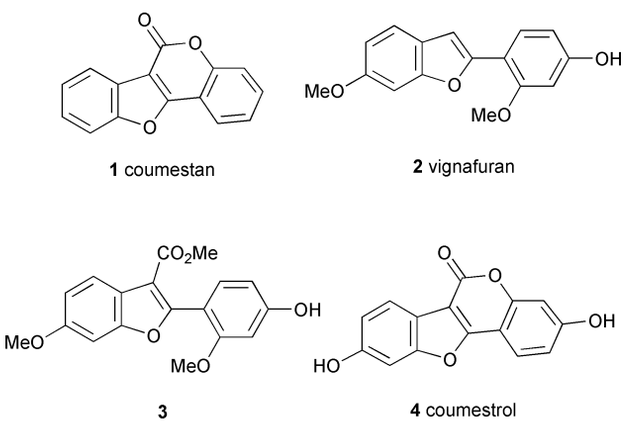


Fig. 1

with *Colletotrichum lindemuthianum*, has been shown to have strong antifungal activity (Fig. 1).[13] The biosynthetic pathway to vignafuran **2** has been elucidated by Martin and Dewick utilizing feeding experiments with labelled amino acids.[14] Kinoshita later showed the chemical mechanism by careful analysis.[15d] The total synthesis of vignafuran **2** was first reported at the same time as its isolation,[13a] after which four different synthetic methods were reported.[15]

In the meantime, 2-(4-hydroxy-2-methoxyphenyl)-6-methoxybenzofuran-3-carboxylic acid methyl ester **3** was isolated from exudates released by the roots of iron-deficient alfalfa (*Medicago sativa*) (Fig. 1).[16] However, not only the biological activities of **3**, but also both the biosynthetic pathway and its relationship to iron deficiency have yet to be determined.

Coumestrol **4** was isolated from alfalfa and ladino clover by Bickoff *et al.* in the 1950s (Fig. 1).[17] As the structure of **4** has some resemblance to the well known (*E*)-4,4′-dihydroxystilbene derivatives, which has potent pharmacological activity, coumestrol **4** shows estrogenic activity.[18] Total syntheses of **4** have been reported by several groups using different approaches;[17d,18,19] however, most of the reported methods required multiple steps and it appears that the overall yield could be improved.

Before the synthesis of the natural products, we planned to apply our carbonylative cyclization strategy[10a] toward constructing the coumestan ring system **1** (Fig 1). Namely, the intramolecular carbonylative cyclization reaction of the diphenylacetylene **5**, which would be prepared from a 2-halogenophenol **6** and acetylene, could produce the coumestan ring system **1** in one step.

For the synthesis of three benzo[*b*]furan natural products, we planned the following strategy. Coumestrol **4** could be synthesized from **3** by successive deprotection and lactonization reactions. Compounds **2** and **3** could be synthesized from diphenylacetylene **7** either by a cyclization reaction to benzo[*b*]-furan or *via* our method involving the carbonylative cyclization reaction[10a] to methyl benzo[*b*]furan-3-carboxylates. Compound **7** could be synthesized by the Sonogashira coupling reaction between **8** and **9**. Both **8** and **9** could be constructed from the same starting material **10** (Fig. 2).

(b) Synthesis of the coumestan ring system

2-Iodophenol **11** was used as the starting material for the synthesis of the coumestan ring system. Pal and Kundu reported that the Pd-catalyzed cross-coupling reaction of aryl iodides under an acetylene atmosphere gave the corresponding diarylacetylene.[20] Thus, by using their conditions, **13** was afforded in one step using the reaction of the acetate **12** under acetylene gas with aryl iodides in the presence of $PdCl_2(PPh_3)_2$, CuI, and Et_3N (75%). Deacetylation of **13** under basic conditions, followed by the intramolecular carbonylative cyclization reaction of **5** as catalyzed by $PdCl_2$ under carbon monoxide atmosphere,[10a] afforded **1** in one step (35%) (Scheme 4). The synthesized product was identified based on a comparison with previously reported data.[18,19c,d,21]

(c) Synthesis of the substituted phenylacetylene derivatives

Commercially available 4-bromoresorcinol **14a** was selectively tosylated and the resulting monohydroxy compound was converted into both the methyl ether **15a** and the methoxymethyl ether **16a** under standard conditions, respectively. The Sonogashira coupling reaction[22] of the bromide **15a** with trimethylsilylacetylene catalyzed by $PdCl_2(PPh_3)_2$ in the presence of CuI and Et_3N in DMF, followed by the detrimethylsilylation reaction, gave **9** in 87% yield (2 steps). On the other hand, the tosyl ester **16a** was converted into the methyl ether **17** by alkaline hydrolysis followed by the standard methylation reaction. The methoxymethyl group of **17** was removed under acidic conditions, then the resulting hydroxy group was acetylated to afford the acetate **8a** (Scheme 5).

The iodides **15b** and **16b** also could be synthesized in exactly the same way as described above from the known 4-iodoresorcinol **14b** which was synthesized from resorcinol and iodine monochloride.[23] However, as the overall yields of both **15b** and **16b** from **14b** were quite low due to the lack of regioselectivity during the monotosylation reaction, we have to improve the synthesis of these compounds.

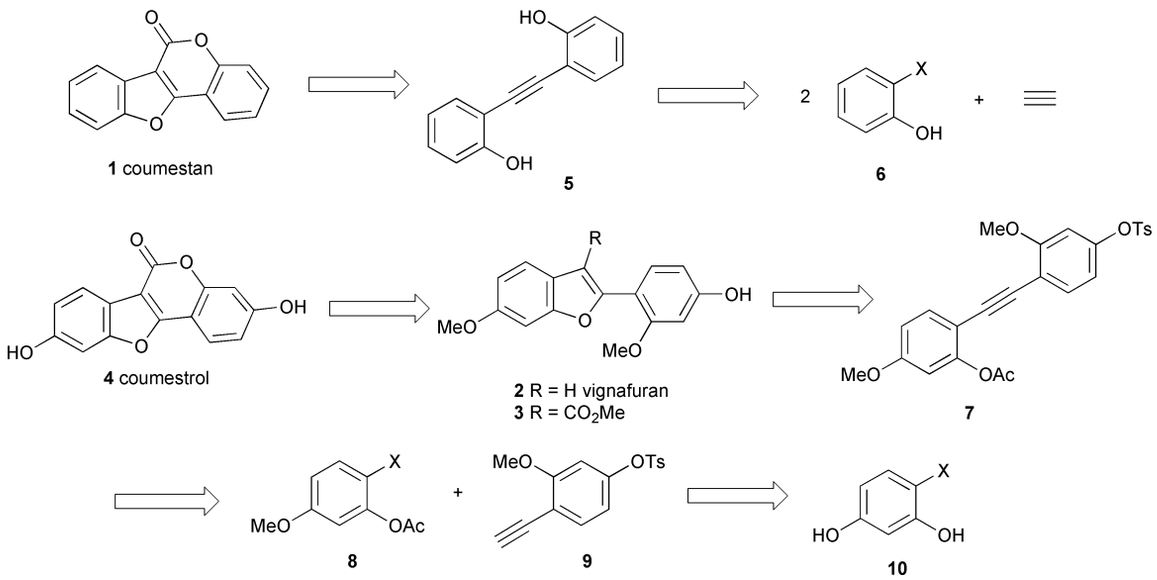
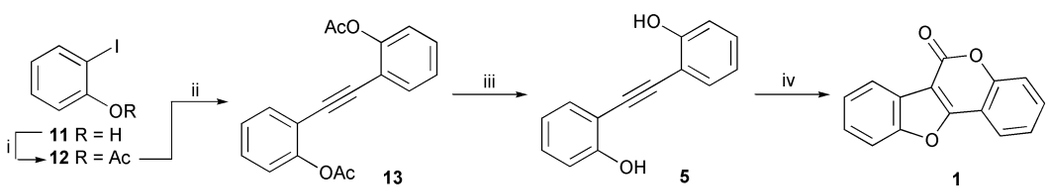
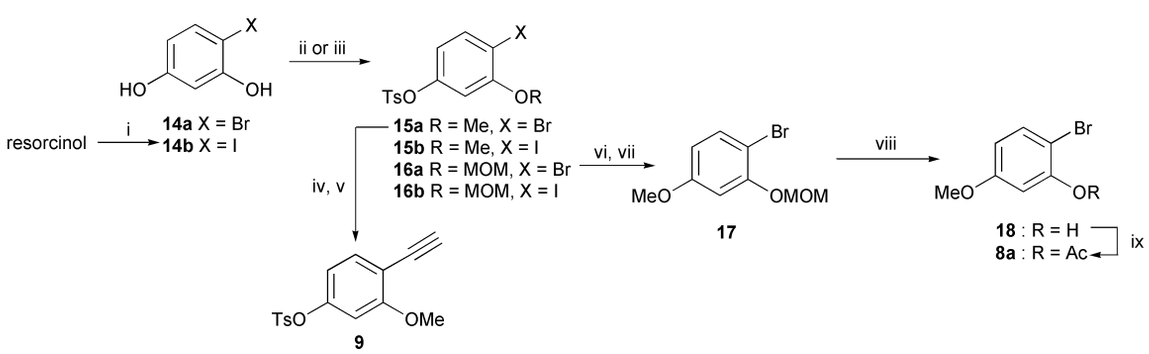


Fig. 2



Scheme 4 *Reagents*, *conditions and yields*: i, Ac_2O, pyridine; ii, acetylene (1 atm), $PdCl_2(PPh_3)_2$, CuI, Et_3N, DMF, 60 °C, 75% from **11**; iii, NaOH, aq. MeOH, RT, 90%; iv, CO (1 atm), $PdCl_2$, $CuCl_2$, AcONa, K_2CO_3, MeCN, 35%.

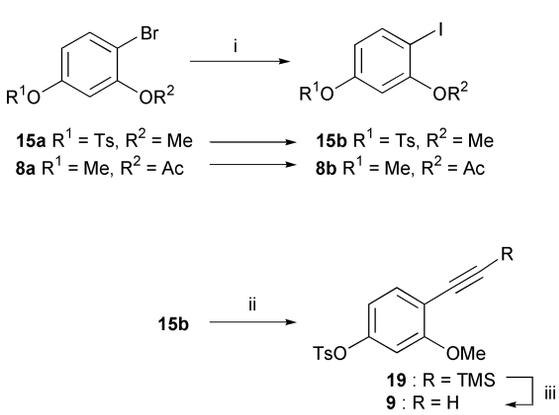


Scheme 5 *Reagents*, *conditions and yields*: i, ICl, Et_2O, RT, 70%; ii, TsCl, K_2CO_3, acetone, reflux; then MeI, reflux, 79% (**14a** ⟶ **15a**), 56% (**14b** ⟶ **15b**); iii, TsCl, K_2CO_3, acetone, reflux; then MOMCl, reflux, 82% (**14a** ⟶ **16a**), 56% (**14b** ⟶ **16b**); iv, trimethylsilylacetylene, $PdCl_2(PPh_3)_2$, CuI, Et_3N, DMF, 100 °C; v, K_2CO_3, MeOH, RT, 87% from **15a**; vi, KOH, aq. EtOH, reflux; vii, K_2CO_3, MeI, acetone, reflux, 74% from **16a**; viii, $(COOH)_2 \cdot 2H_2O$, aq. MeOH, reflux, 96%; ix, AcCl, K_2CO_3, acetone, reflux, 90%.

This problem has been solved by conversion of the bromides into the iodides by employing Suzuki's method.[24] Thus, reaction of the bromides **15a** and **8a** with KI and CuI in warm HMPA gave the iodides **15b** and **8b**, each in 94% yield, respectively. Also, the Sonogashira coupling reaction was carried out using the iodide **15b** as the starting material under milder conditions to give **9** in a much higher overall yield (91% from **15a**) (Scheme 6).

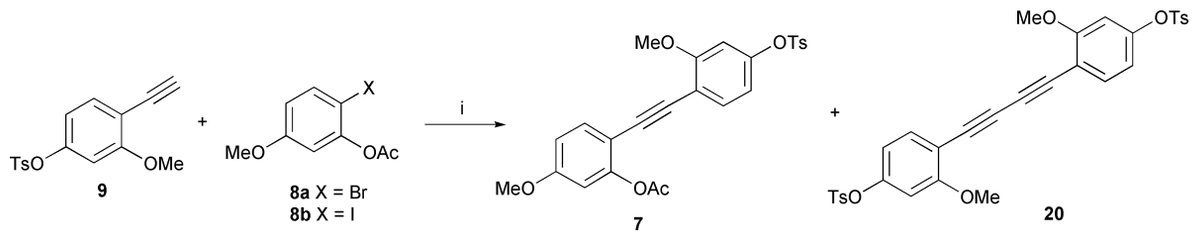
(d) Coupling and cyclization reaction

When the acetylenic compound **9** and the bromide **8a** were heated at 100 °C in the presence of $PdCl_2(PPh_3)_2$, CuI and Et_3N in DMF, only the homocoupled product **20** was isolated (Table 1, entry 1). However, under almost the same reaction conditions but using the more reactive iodide **8b** as the counterpart, the desired heterocoupled product **7** was obtained in 41% yield at room temperature and 68% yield under reflux (Table 1, entries 2 and 3).



Scheme 6 *Reagents*, *conditions and yields*: i, KI, CuI, HMPA, 150 °C, 94% (**15a** ⟶ **15b**), 94% (**8a** ⟶ **8b**); ii, trimethylsilylacetylene, $PdCl_2(PPh_3)_2$, CuI, Et_3N, DMF, RT, 98%; iii, TBAF, THF, RT, 99%.

Table 1 Sonogashira coupling reaction of terminal alkyne **9** and halides **8a** and **8b**



Reagents and solvent: i, $PdCl_2(PPh_3)_2$, CuI, base, DMF.

					Yield (%)	
Entry	X	Base	Temperature	Time (*t*/h)	**7**	**20**
1	Br	Et_3N	100 °C	1	0	39
2	I	Et_3N	RT	1.5	41	0
3	I	Et_3N	Reflux	1.5	68	0
4	I	$^iPr_2NH$	RT	1.5	53	0
5	I	$^iPr_2NH$	Reflux	1.5	Decomposition	0
6	I	$^iPr_2NH$	60 °C	1.5	96	0

In 1997, Miller and Johnson reported the acceleration of the Sonogashira reaction by employing $^iPr_2NH$ as the base.[25] In our case, an improvement in the yield was observed using their reaction conditions (Table 1, entry 2 *vs.* entry 4). However, when the reaction mixture was refluxed, the desired product could not be isolated at all. Presumably the instability of the coupled compound **7** causes a decrease in the yield. Finally, the coupled compound **7** was obtained in 96% yield when the reaction mixture was heated at 60 °C for 1.5 h (Table 1, entry 6).

(e) Synthesis of vignafuran, 2-(4-hydroxy-2-methoxyphenyl)-6-methoxybenzo[*b*]furan-3-carboxylic acid methyl ester, and coumestrol

The availability of **7** described above prompted us to attempt to use it for the syntheses of the three kinds of benzo[*b*]furan natural products.

Thus, the acetyl group of **7** was reductively removed by DIBAL-H to give the phenol **21**, which was cyclized by applying the TBAF-promoted reaction[12] to afford the benzo[*b*]furan **22** in 53% overall yield from **7**. Finally, the detosylation of **22** with sodium methoxide afforded vignafuran **2** in 78% yield (Scheme 7). The ^{1}H NMR and mass spectral data of the synthesized vignafuran **2** were identical with those of the reported natural product.[13]

For the synthesis of **3**, the methoxycarbonyl analogue of vignafuran **2**, the acetate **7** was allowed to react with carbon monoxide in MeOH in the presence of $PdCl_2(PPh_3)_2$, $CuCl_2{\cdot}2H_2O$, AcONa, and K_2CO_3 at room temperature for 2 days. Deacetylation, cyclization, and trapping reactions of the C3-Pd species by carbon monoxide proceeded successively and the desired methyl 2-arylbenzo[*b*]furan-3-carboxylate **23** was obtained in 71% yield (Scheme 7). The structure of **23** was confirmed by the molecular-ion peak (*m*/*z* 482) from EI mass spectrometry, the absorption at 1720 cm^{-1} from IR spectroscopy, and the three methoxy peaks (δ 3.71, 3.80, 3.87) and two typical 1,2,4-trisubstituted benzene ring patterns [δ 6.63 (1H, dd, *J* 8.5, 2.2), 6.71 (1H, d, *J* 2.2), 6.98 (1H, dd, *J* 8.5, 2.2), 7.03 (1H, dd, *J* 8.5, 2.2), 7.44 (1H, d, *J* 8.5), 7.87 (1H, d, *J* 8.5)] in the ^{1}H NMR spectrum. Finally, the tosyl group of **23** was removed by treatment with sodium methoxide in MeOH to afford quantitatively the target benzo[*b*]furan natural product **3** (Scheme 7).

For the coumestrol **4** synthesis, we first tried to cleave the two methoxy group of **3**. However, in our hands, it was not possible to remove the two methyl groups at the same time (BBr_3, CH_2Cl_2, −78 °C or $AlCl_3$, MeCN, 70 °C). The only isolated product was a monodemethylated compound. Therefore, we changed the order of the reactions based on the assumption that the unreactivity of the second demethylation reaction will be due to the higher electron density on the aromatic ring. When the tosyl ester **23** was treated with BBr_3 at from −78 to −40 °C, as we expected, the double demethylation reaction smoothly proceeded to afford the dihydroxy compound **24** in 72% yield. Alkaline hydrolysis of the tosyl compound **24** (3 M KOH, THF, reflux), followed by acid-catalyzed lactonization (cat. TsOH, THF, 60 °C) gave coumestrol **4** in 53% yield from **24**. The spectral data of the synthesized **4** were identified with those of the reported compound (Scheme 7).[16,19d]

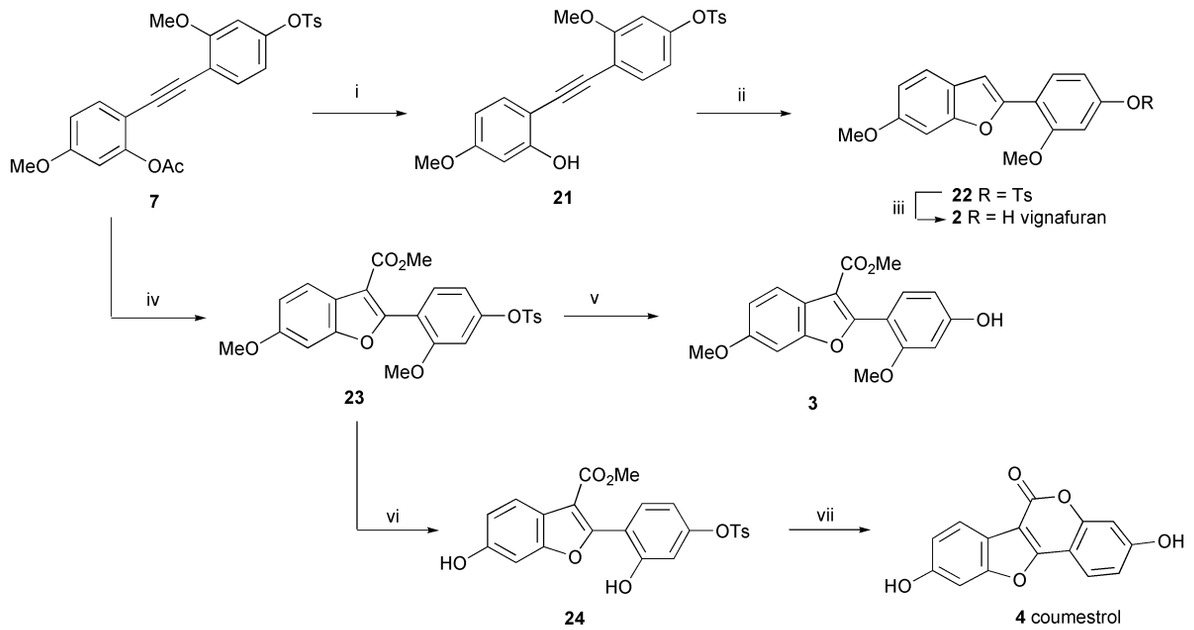
Experimental

Mps were measured on a YAZAWA Micro Melting Point BY-2 apparatus. All mps and bps are uncorrected. IR spectra were measured using a JASCO IR-810 spectrophotometer. ^{1}H NMR spectra were recorded on a Varian Gemini 2000 (300 MHz) and a JEOL GX-500 (500 MHz) with samples in $CDCl_3$ solvent, unless otherwise stated. The chemical shifts are expressed in δ (ppm)-values with tetramethylsilane (TMS) as the internal reference and coupling constants (*J*) are given in Hz. Mass spectra and high-resolution mass spectra were recorded on JEOL JMS-DX303 and JMS-AX500 instruments, respectively.

2,2′-Diacetoxydiphenylacetylene 13

Acetic anhydride (0.89 ml, 10 mmol) was added to a solution of 2-iodophenol **11** (2.2 g, 10 mmol) in pyridine (50 ml) at 0 °C. After the solution had been stirred for 1 h at room temperature, pyridine was evaporated off and 3 M HCl (50 ml) was added to the residue. The aqueous solution was extracted by $CHCl_3$ and the organic solution was washed with water, dried over $MgSO_4$ and evaporated. Crude **12** was used in the next reaction without further purification.

A mixture of **12** (0.52 g, 2 mmol), $PdCl_2(PPh_3)_2$ (50 mg, 0.07 mmol), CuI (40 mg, 0.23 mmol) and Et_3N (0.59 ml, 10 mmol) in DMF (20 ml) was stirred at 60 °C under dried acetylene gas. After the mixture had been stirred for 16 h, the mixture was filtered through a Celite® pad and the filtrate was extracted with Et_2O. The combined organic solution was washed successively with water and saturated aq. NaCl, dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel with hexane–AcOEt (7 : 1) as eluent to give **13** (0.45 g, 75%) as a *white powder*, mp 143–145 °C (Found: C, 73.44; H, 4.84. $C_{18}H_{14}O_4$ requires C, 73.46; H, 4.79%); ν_{max} (KBr)/cm^{-1} 1760, 1220, 1180; δ_H (500 MHz) 2.36 (6H, s), 7.12 (2H, d, *J* 8.0), 7.22–7.26 (2H, m), 7.38 (2H, dt, *J* 8.0, 1.8), 7.54 (2H, dd, *J* 8.0, 1.8);



Scheme 7 *Reagents, conditions and yields*; i, DIBAL-H, PhMe, −78 °C, 81%; ii, TBAF, THF, reflux, 67%; iii, NaOMe, MeOH, reflux, 78 °C; iv, $PdCl_2(PPh_3)_2$, $CuCl_2{\cdot}2H_2O$, AcONa, K_2CO_3, MeOH, CO, RT, 71%; v, NaOMe, MeOH, reflux, 100%; vi, BBr_3, CH_2Cl_2, −78 to 40 °C, 72%; vii, 3 M KOH, THF, reflux; then cat. TsOH, THF, 60 °C, 53%.

m/*z* 294 (M^+, 13.6%) and 210 (100) (Found: M^+, 294.0909. $C_{18}H_{14}O_4$ requires *M*, 294.0892).

2,2′-Dihydroxydiphenylacetylene 5

A mixture of **13** (0.21 g, 0.78 mmol) and 3 M NaOH (0.57 ml, 1.7 mmol) in MeOH (12 ml) was stirred at room temperature. After the mixture had been stirred for 30 min, the mixture was concentrated under reduced pressure and the residue was extracted with $CHCl_3$. The combined organic solution was washed successively with water and saturated aq. NaCl, dried over $MgSO_4$ and evaporated. The residue was purified by column chromatography and elution with hexane–AcOEt (7 : 1) to afford the *bisphenol* **5** (0.15 g, 90%) as a white powder, mp 95–97 °C (Found: C, 80.22; H, 5.06. $C_{14}H_{10}O_2$ requires C, 79.98; H, 4.79%); ν_{max} (KBr)/cm^{-1} 3300; δ_H (300 MHz) 5.87 (2H, s), 6.92–7.00 (4H, m), 7.30 (2H, ddd, *J* 8.8, 7.4, 1.4), 7.44 (2H, dd, *J* 7.7, 1.4); *m*/*z* 210 (M^+, 100%) and 181 (73.3) (Found: M^+, 210.0725. $C_{14}H_{10}O_2$ requires *M*, 210.0681).

6*H*-[1]Benzofuro[3,2-*c*]chromen-6-one (coumestan ring system) 1

A mixture of **5** (0.12 g, 0.56 mmol), $PdCl_2$ (10 mg, 0.06 mmol), $CuCl_2$ (0.16 g, 1.23 mmol), AcONa (0.09 g, 0.56 mmol) and K_2CO_3 (0.15 g, 1.1 mmol) in MeCN (5 ml) was stirred at room temperature for 20 h. The reaction mixture was concentrated under reduced pressure, then the residue was extracted with $CHCl_3$. The combined extracts were washed successively with water and saturated aq. NaCl. The organic solution was dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel with hexane–AcOEt (10 : 1) as eluent to give coumestan **1**[18,19c,d,21] (0.046 g, 35%) as a white powder, mp 178–181 °C (lit.,[19c] mp 182–183 °C, mp 179–180 °C[19d]) (Found: C, 76.09; H, 3.57. Calc. for $C_{15}H_8O_3$: C, 76.27; H, 3.41%); δ_H (300 MHz) 7.40–7.53 (4H, m), 7.60–7.70 (2H, m), 8.05 (1H, d, *J* 7.7), 8.15 (1H, dd, *J* 6.3, 4.1); *m*/*z* 236 (M^+, 100%) (Found: M^+, 236.0457. Calc. for $C_{15}H_8O_3$: *M*, 236.0473).

4-Iodoresorcinol 14b

A solution of resorcinol (2.75 g, 25.0 mmol) and ICl (4.0 g, 25.0 mmol) in dry Et_2O (25 ml) was stirred at room temperature for 1 h. Water (50 ml) and Na_2SO_3 (1.0 g) were added to the mixture, then the aqueous phase was extracted with Et_2O. The combined organic solution was washed successively with water and saturated aq. NaCl, dried over $MgSO_4$ and evaporated. The residue was successively purified with silica gel chromatography [AcOH–$CHCl_3$ (1 : 9)] and alumina chromatography [hexane–AcOEt (2 : 1)] to afford **14b**[23] as a colorless solid (4.13 g, 70%), δ_H (300 MHz) 5.21 (2H, br), 6.27 (1H, dd, *J* 8.6, 2.8), 6.54 (1H, d, *J* 2.8), 7.46 (1H, d, *J* 8.6); *m*/*z* 236 (M^+, 100%) (Found: M^+, 235.9356. Calc. for $C_6H_5IO_2$: *M*, 235.9327).

1-Bromo-2-methoxy-4-(tosyloxy)benzene 15a

A mixture of 4-bromoresorcinol **14a** (10.0 g, 53.0 mmol), K_2CO_3 (22.0 g, 159 mmol) and TsCl (11.1 g, 58.0 mmol) in acetone (150 ml) was refluxed for 21 h. MeI (15.0 g, 106 mmol) was added to the mixture, which was further refluxed for 3 h. The inorganic precipitate was filtered off and the filtrate was concentrated under reduced pressure. The residue was diluted with water and extracted with AcOEt. The combined organic solution was washed successively with water and saturated aq. NaCl, dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel with hexane–AcOEt (3 : 1) as eluent to give **15a** (15.0 g, 79%) as a white powder. An analytical sample was recrystallized from AcOEt–hexane to give *colorless needles*, mp 69–72 °C (Found: C, 47.17; H, 3.76; S, 8.90. $C_{14}H_{13}BrO_4S$ requires C, 47.07; H, 3.67; S, 8.97%); ν_{max} ($CHCl_3$)/cm^{-1} 1380, 1280, 1180, 1030; δ_H (300 MHz) 2.46 (3H, s), 3.79 (3H, s), 6.41 (1H, dd, *J* 8.5, 2.5), 6.60 (1H, d, *J* 2.5), 7.33 (2H, d, *J* 8.5), 7.41 (1H, d, *J* 8.5), 7.72 (2H, d, *J* 8.5).

1-Bromo-2-methoxymethoxy-4-(tosyloxy)benzene 16a

A mixture of 4-bromoresorcinol **14a** (5.00 g, 26.5 mmol), K_2CO_3 (11.0 g, 79.4 mmol) and TsCl (5.56 g, 29.2 mmol) in acetone (100 ml) was refluxed for 21 h. MOMCl (4.27 g, 53.0 mmol) was added to the mixture, which was further refluxed for 3 h. The inorganic precipitate was filtered off and the filtrate was concentrated under reduced pressure. The residue was diluted with water and extracted with AcOEt. The combined organic solution was washed successively with water and saturated aq. NaCl, dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel with hexane–AcOEt (3 : 1) as eluent to give **16a** (8.45 g, 82%) as a white powder. An analytical sample was recrystallized from AcOEt–hexane to give *colorless needles*, mp 70–72 °C (Found: C, 46.54; H,

3.82; S, 8.25. $C_{15}H_{15}BrO_5S$ requires C, 46.52; H, 3.90; S, 8.28%); ν_{max} ($CHCl_3$)/cm^{-1} 1380, 1280, 1180, 1040; δ_H (300 MHz) 2.47 (3H, s), 3.43 (3H, s), 5.10 (2H, s), 6.57 (1H, dd, *J* 8.8, 2.7), 6.77 (1H, d, *J* 8.8), 7.33 (2H, d, *J* 8.2), 7.44 (1H, d, *J* 8.8), 7.72 (2H, d, *J* 8.2).

1-Iodo-2-methoxy-4-(tosyloxy)benzene 15b

(a) Synthesis from 4-iodoresorcinol 14b. A mixture of 4-iodoresorcinol **14b** (1.60 g, 6.78 mmol), K_2CO_3 (2.82 g, 20.4 mmol) and TsCl (1.40 g, 7.40 mmol) in acetone (30 ml) was refluxed for 15 h. MeI (2.89 g, 20.4 mmol) was added to the mixture, which was further refluxed for 3 h. The inorganic precipitate was filtered off and the filtrate was concentrated under reduced pressure. The residue was diluted with water and extracted with AcOEt. The combined organic solution was washed successively with water and saturated aq. NaCl, dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel with hexane–AcOEt (4 : 1) as eluent to give **15b** (1.53 g, 56%) as a *yellow viscous oil*, ν_{max} ($CHCl_3$)/cm^{-1} 1380, 1280, 1180, 1040; δ_H (300 MHz) 2.46 (3H, s), 3.77 (3H, s), 6.30 (1H, dd, *J* 8.3, 2.5), 6.52 (1H, d, *J* 2.5), 7.30 (2H, d, *J* 8.3), 7.63 (1H, d, *J* 8.4), 7.72 (2H, d, *J* 8.4); *m*/*z* 404 (M^+, 76.2%) and 91(100) (Found: M^+, 403.9555. $C_{14}H_{13}IO_4S$ requires *M*, 403.9579).

(b) Synthesis from 15a. A mixture of **15a** (0.36 g, 1.00 mmol), KI (2.46 g, 15.0 mmol) and CuI (0.95 g, 5.00 mmol) in HMPA (3 ml) was stirred under an Ar atmosphere at 150 °C for 3 h. The reaction mixture was acidified by 3 M HCl and extracted with Et_2O. The organic solution was washed successively with aq. Na_2SO_3, water, and saturated aq. NaCl, dried over $MgSO_4$ and evaporated. The residue was purified by silica gel column chromatography with hexane–AcOEt (2 : 1) as eluent to afford **15b** (0.38 g, 94%) as a yellow viscous oil.

1-Iodo-2-methoxymethoxy-4-(tosyloxy)benzene 16b

A mixture of 4-iodoresorcinol **14b** (3.25 g, 13.8 mmol), K_2CO_3 (9.54 g, 67.0 mmol) and TsCl (2.86 g, 15.0 mmol) in acetone (50 ml) was refluxed for 5 h. MOMCl (2.20 g, 27.4 mmol) was added to the mixture, which was further refluxed for 3 h. The inorganic precipitate was filtered off and the filtrate was concentrated under reduced pressure. The residue was diluted with water and extracted with AcOEt. The combined organic solution was washed successively with water and saturated aq. NaCl, dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel with hexane–AcOEt (2 : 1) as eluent to give **16b** (3.67 g, 56%) as a *yellow viscous oil*, δ_H (300 MHz) 2.45 (3H, s), 3.43 (3H, s), 5.10 (2H, s), 6.46 (1H, dd, *J* 8.5, 2.6), 6.69 (1H, d, *J* 2.6), 7.33 (2H, d, *J* 8.5), 7.67 (1H, d, *J* 8.5), 7.72 (2H, d, *J* 8.5); *m*/*z* 434 (M^+, 13.6%) and 45 (100) (Found: M^+, 433.9680. $C_{15}H_{15}IO_5S$ requires *M*, 433.9685).

1-Bromo-4-methoxy-2-(methoxymethoxy)benzene 17

A solution of **16a** (7.51 g, 19.4 mmol) and KOH (5.88 g, 105 mmol) in a mixture of EtOH (315 ml) and water (35 ml) was heated under reflux for 2 h. 3 M HCl was added to the mixture at room temperature until pH 4. The aqueous phase was extracted with Et_2O and the extracts were washed successively with water and saturated aq. NaCl. The organic solution was dried over $MgSO_4$ and evaporated to give the crude phenol, which was used to the next reaction without further purification.

A mixture of the crude phenol, K_2CO_3 (14.0 g, 101 mmol) and MeI (19.0 g, 134 mmol) in acetone (1 l) was refluxed for 2.5 h. The inorganic precipitate was filtered off and the filtrate was concentrated under reduced pressure. The residue was extracted with Et_2O and the combined extract was washed successively with water and saturated aq. NaCl. The organic solution was dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel with hexane–AcOEt (4 : 1) as eluent to give **17** (3.56 g, 74%) as a *colorless oil*, bp 95 °C/3 mmHg (Found: C, 44.02; H, 4.62. $C_9H_{11}BrO_3$ requires C, 43.75; H, 4.49%); ν_{max} ($CHCl_3$)/cm^{-1} 1310, 1280, 1060, 1030; δ_H (300 MHz) 3.52 (3H, s), 3.78 (3H, s), 5.20 (2H, s), 6.48 (1H, dd, *J* 8.8, 2.7), 6.77 (1H, d, *J* 2.7), 7.41 (1H, d, *J* 8.8).

2-Bromo-5-methoxyphenol 18

A solution of **17** (3.56 g, 14.4 mmol) and oxalic acid dihydrate (3.66 g, 29.0 mmol) in MeOH–water (1 : 1; 80 ml) was refluxed for 2.5 h. The reaction mixture was extracted with Et_2O and the combined extract was washed successively with water and saturated aq. NaCl. The organic solution was dried over $MgSO_4$ and evaporated. The residue was purified by silica gel column chromatography and elution with hexane–AcOEt (7 : 1) to give **18**[26] (2.82 g, 96%) as a colorless oil, bp 90 °C/3 mmHg (Found: C, 41.39; H, 3.55. Calc. for $C_7H_7BrO_2$: C, 41.41; H, 3.47%); δ_H (300 MHz) 3.77 (3H, s), 5.53 (1H, br), 6.41 (1H, dd, *J* 8.8, 2.9), 6.60 (1H, d, *J* 2.9), 7.30 (1H, d, *J* 8.8).

2-Acetoxy-1-bromo-4-methoxybenzene 8a

A mixture of **18** (2.30 g, 11.3 mmol), K_2CO_3 (3.10 g, 22.4 mmol) and AcCl (2.21 g, 28.1 mmol) in acetone (60 ml) was refluxed for 2 h. Water (200 ml) was added to the mixture, which was extracted with AcOEt. The combined extract was washed successively with water and saturated aq. NaCl, dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel with hexane–AcOEt (5 : 1) as eluent to give **8a** (2.50 g, 90%) as a colorless oil, bp 110 °C/4 mmHg (Found: C, 44.30; H, 3.79. $C_9H_9BrO_3$ requires C, 44.11; H, 3.70%); ν_{max} ($CHCl_3$)/cm^{-1} 1780, 1290, 1200, 1020; δ_H (300 MHz) 2.30 (3H, s), 3.71 (3H, s), 6.66 (1H, dd, *J* 8.5, 2.7), 6.68 (1H, d, *J* 2.7), 7.43 (1H, d, *J* 8.5).

2-Acetoxy-1-iodo-4-methoxybenzene 8b

A mixture of **8a** (0.38 g, 1.55 mmol), KI (3.86 g, 23.3 mmol) and CuI (1.48 g, 7.75 mmol) in HMPA (3 ml) was stirred under an Ar atmosphere at 150 °C for 3 h. The reaction mixture was acidified by 3 M HCl and extracted with Et_2O. The organic solution was washed successively with aq. Na_2SO_3, water, and saturated aq. NaCl, dried over $MgSO_4$ and evaporated. The residue was purified by silica gel column chromatography and elution with hexane–AcOEt (2 : 1) to afford **8b**[27] (0.43 g, 94%) as a colorless oil; ν_{max} (film)/cm^{-1} 1780, 1240, 1200, 1040; δ_H (300 MHz) 2.36 (3H, s), 3.78 (3H, s), 6.60 (1H, dd, *J* 8.8, 3.0), 6.69 (1H, d, *J* 3.0), 7.66 (1H, d, *J* 8.8); *m*/*z* 292 (M^+, 76.2%) and 250 (100) (Found: M^+, 291.9587. $C_9H_9IO_3$ requires *M*, 291.9595).

2-Methoxy-4-(tosyloxy)phenylacetylene 9

(a) Synthesis from 15a. A mixture of **15a** (0.20 g, 0.56 mmol), trimethylsilylacetylene (0.33 g, 3.36 mmol), CuI (13.0 mg, 0.06 mmol) and $PdCl_2(PPh_3)_2$ (23.0 mg, 0.03 mmol) in a mixture of Et_3N (1.0 ml) and DMF (0.5 ml) was heated at 100 °C for 24 h. The precipitate was filtered off and the filtrate was concentrated under reduced pressure. The residue was extracted with Et_2O and the combined extracts were washed successively with water and saturated aq. NaCl. The organic solution was dried over $MgSO_4$ and evaporated to afford **19** as a colorless solid, which was used to the next reaction without further purification.

A mixture of the crude silyl compound **19** and K_2CO_3 (0.35 g, 2.52 mmol) in MeOH (100 ml) was stirred at room temperature for 1.5 h. The excess of K_2CO_3 was filtered off and the residue was concentrated under reduced pressure. The

residue was extracted with Et_2O and the combined organic solution was washed successively with water and saturated aq. NaCl. The organic solution was dried over $MgSO_4$ and evaporated. The residue was purified by silica gel column chromatography and elution with hexane–AcOEt (3:1) to give **9** (0.44 g, 87%) as a yellow viscous oil, ν_{max} (film)/cm^{-1} 3300, 1380, 1280, 1180, 1040; δ_H (300 MHz) 2.45 (3H, s), 3.30 (1H, s), 3.79 (3H, s), 6.48 (1H, dd, *J* 8.2, 2.2), 6.59 (1H, d, *J* 2.2), 7.32 (2H, d, *J* 8.3), 7.33 (1H, d, *J* 8.5), 7.72 (2H, d, *J* 8.3); *m/z* 302 (M^+, 17.3%) and 91 (100) (Found: M^+, 302.0611. $C_{16}H_{14}O_4S$ requires *M*, 302.0613).

(b) Synthesis from 15b. A mixture of **15b** (1.05 g, 2.60 mmol), trimethylsilylacetylene (1.78 g, 18.2 mmol), CuI (50 mg, 0.26 mmol) and $PdCl_2(PPh_3)_2$ (92 mg, 0.13 mmol) in a mixture of Et_3N (4.0 ml) and DMF (6.0 ml) was stirred at room temperature for 1 h. Water was added to the mixture and extracted with Et_2O. The combined extracts were washed successively with water and saturated aq. NaCl, dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel with hexane–AcOEt (5:1) as eluent to give the *TMS-acetylene* **19** (0.95 g, 98%) as a colorless solid. The analytical sample was further purified by recrystallization from AcOEt–hexane to afford colorless needles, mp 105–107 °C (Found: C, 61.02; H, 5.96; S, 8.46. $C_{19}H_{22}O_4SSi$ requires C, 60.93; H, 5.92; S, 8.56%); ν_{max} ($CHCl_3$)/cm^{-1} 1380, 1280, 1180, 1040; δ_H (300 MHz) 0.24 (9H, s), 2.44 (3H, s), 3.75 (3H, s), 6.45 (1H, dd, *J* 8.4, 2.2), 6.53 (1H, d, *J* 2.2), 7.30 (3H, d, *J* 8.4), 7.69 (2H, d, *J* 8.4).

A solution of **19** (0.56 g, 1.50 mmol) and TBAF (1.0 M solution in THF; 1.50 ml, 1.50 mmol) in THF (30 ml) was stirred at room temperature for 10 min. Water was added to the mixture, which was extracted with Et_2O. The organic solution was washed successively with water and saturated aq. NaCl, dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel with hexane–AcOEt (3:1) as eluent to give **9** (0.45 g, 99%) as a yellow viscous oil.

2-Acetoxy-2′,4-dimethoxy-4′-(tosyloxy)diphenylacetylene 7. Typical procedure (Table 1, entry 6)

A mixture of **8b** (148 mg, 0.51 mmol), **9** (200 mg, 0.66 mmol), CuI (10.0 mg, 0.05 mmol), $PdCl_2(PPh_3)_2$ (18.0 mg, 0.03 mmol) and $^iPr_2NH$ (0.11 ml, 0.77 mmol) in DMF (3.0 ml) was stirred at 60 °C for 1.5 h. Water was added to the mixture, which was extracted with $CHCl_3$. The organic solution was washed successively with water and saturated aq. NaCl, dried over $MgSO_4$ and evaporated. The residue was purified by silica gel column chromatography with hexane–AcOEt (2:1) as eluent to give **7** (230 mg, 96%) as a *yellow viscous oil*, ν_{max} ($CHCl_3$)/cm^{-1} 1770, 1380, 1280, 1180, 1040; δ_H (300 MHz) 2.35 (3H, s), 2.45 (3H, s), 3.78 (3H, s), 3.82 (3H, s), 6.48 (1H, dd, *J* 8.5, 2.2), 6.59 (1H, d, *J* 2.2), 6.66 (1H, d, *J* 2.2), 6.77 (1H, dd, *J* 8.5, 2.2), 7.30 (1H, d, *J* 8.5), 7.32 (2H, d, *J* 8.5), 7.47 (1H, d, *J* 8.5), 7.72 (2H, d, *J* 8.5); *m/z* 466 (29.9%, M^+) and 269 (100) (Found: M^+, 466.1091. $C_{25}H_{22}O_7S$ requires *M*, 466.1087).

2-Hydroxy-2′,4-dimethoxy-4′-(tosyloxy)diphenylacetylene 21

DIBAL-H (1.0 M solution in PhMe; 1.56 ml, 1.56 mmol) was added to a solution of **7** (240 mg, 0.52 mmol) in CH_2Cl_2 (3 ml) at −78 °C. After the solution had been stirred at the same temperature for 3 h, Et_2O and saturated aq. NH_4Cl were successively added to the mixture, which was then extracted with $CHCl_3$. The combined organic solution was washed successively with water and saturated aq. NaCl, dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel and eluted with hexane–AcOEt (6:1) to afford **21** (180 mg, 81%) as a *viscous yellow oil*, ν_{max} ($CHCl_3$)/cm^{-1} 3400, 1380, 1280, 1180, 1040; δ_H (300 MHz) 2.45 (3H, s), 3.80 (3H, s), 3.85 (3H, s), 6.46 (1H, dd, *J* 8.5, 2.2), 6.53 (1H, dd, *J* 8.5, 2.2), 6.55 (1H, d, *J* 2.2), 6.63 (1H, d, *J* 2.2), 6.74 (1H, s), 7.27 (1H, d, *J* 8.5), 7.30 (1H, d, *J* 8.5), 7.33 (2H, d, *J* 8.0), 7.73 (2H, d, *J* 8.0); *m/z* 424 (39.3%, M^+) and 269 (100) (Found: M^+, 424.0932. $C_{23}H_{20}O_6S$ requires *M*, 424.0981).

6-Methoxy-2-[2-methoxy-4-(tosyloxy)phenyl]benzo[*b*]furan 22

A solution of **21** (120 mg, 0.28 mmol) and TBAF (1.0 M solution in THF; 0.56 ml, 0.56 mmol) in THF (7 ml) was refluxed for 3 h. The reaction mixture was diluted with water and the precipitate was filtered off. The filtrate was concentrated *in vacuo*, then the residue was extracted with $CHCl_3$. The combined organic solution was washed successively with water and saturated aq. NaCl, dried over $MgSO_4$ and evaporated. The residue was purified by silica gel column chromatography and eluted with hexane–AcOEt (6:1) to afford **22** (80 mg, 67%) as a *colorless solid*, mp 89–91 °C; ν_{max} ($CHCl_3$)/cm^{-1} 3400, 1270, 1040; δ_H (300 MHz) 2.45 (3H, s), 3.87 (3H, s), 3.89 (3H, s), 6.58 (1H, dd, *J* 8.5, 2.2), 6.71 (1H, d, *J* 2.2), 6.86 (1H, dd, *J* 8.5, 2.2), 7.02 (1H, d, *J* 2.2), 7.25 (1H, s), 7.33 (2H, d, *J* 8.0), 7.44 (1H, d, *J* 8.5), 7.75 (2H, d, *J* 8.0), 7.87 (1H, d, *J* 8.5); *m/z* 424 (33.6%, M^+) and 269 (100) (Found: M^+, 424.1011. $C_{23}H_{20}O_6S$ requires *M*, 424.0981).

Vignafuran 2

A solution of **22** (80 mg, 0.19 mmol) and NaOMe (21 mg, 0.38 mmol) in MeOH (20 ml) was refluxed for 20 h. MeOH was evaporated off and the residue was extracted with $CHCl_3$. The combined organic solution was washed successively with water and saturated aq. NaCl, dried over $MgSO_4$ and concentrated. The residue was chromatographed on silica gel and eluted with hexane–AcOEt (6:1) to afford **2**[13–15] (40 mg, 78%) as a viscous oil; ν_{max} ($CHCl_3$)/cm^{-1} 3400, 1270, 1040; δ_H (500 MHz) 3.86 (3H, s), 3.91 (3H, s), 5.36 (1H, br), 6.49–6.51 (2H, m), 6.84 (1H, dd, *J* 8.5, 2.4), 7.04 (1H, d, *J* 2.4), 7.10 (1H, s), 7.84 (1H, d, *J* 8.5); *m/z* 270 (100%, M^+) and 255 (64.8) (Found: M^+, 270.0845. Calc. for $C_{16}H_{14}O_4$: *M*, 270.0891).

Methyl 6-methoxy-2-[2-methoxy-4-(tosyloxy)phenyl]benzo[*b*]-furan-3-carboxylate 23

A mixture of **7** (440 mg, 0.94 mmol), K_2CO_3 (260 mg, 1.88 mmol), $PdCl_2(PPh_3)_2$ (33.0 mg, 0.19 mmol), $CuCl_2{\cdot}2H_2O$ (480 mg, 2.82 mmol) and AcONa (154 mg, 1.88 mmol) in MeOH (20 ml) was stirred under CO at room temperature. After 2 days, the inorganic precipitate was filtered off and the filtrate was extracted with $CHCl_3$. The organic solution was washed successively with water and saturated aq. NaCl, dried over $MgSO_4$ and evaporated. The residue was purified by silica gel column chromatography with hexane–AcOEt (5:1) as eluent to afford **23** (370 mg, 71%) as a *colorless solid*, mp 124–126 °C (Found: C, 62.31; H, 4.41; S, 6.87. $C_{25}H_{22}O_8S$ requires C, 62.23; H, 4.60; S, 6.65%); ν_{max} ($CHCl_3$)/cm^{-1} 1720, 1380, 1280, 1180, 1040; δ_H (300 MHz) 2.46 (3H, s), 3.71 (3H, s), 3.80 (3H, s), 3.87 (3H, s), 6.63 (1H, dd, *J* 8.5, 2.2), 6.71 (1H, d, *J* 2.2), 6.98 (1H, dd, *J* 8.5, 2.2), 7.03 (1H, dd, *J* 8.5, 2.2), 7.35 (2H, d, *J* 8.5), 7.44 (1H, d, *J* 8.5), 7.79 (2H, d, *J* 8.5), 7.87 (1H, d, *J* 8.5); *m/z* 482 (58.6%, M^+) and 327 (100) (Found: M^+, 482.1021. $C_{25}H_{22}O_8S$ requires *M*, 482.1034).

Methyl 2-(4-hydroxy-2-methoxyphenyl)-6-methoxybenzo[*b*]-furan-3-carboxylate 3

A solution of **23** (60 mg, 0.12 mmol) and NaOMe (9.60 mg, 0.24 mmol) in MeOH (15 ml) was heated under reflux for 4 h. The mixture was acidified by 3 M HCl and extracted with $CHCl_3$. The organic solution was washed successively with water and saturated aq. NaCl, dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel

and eluted with hexane–AcOEt (4:1) to give **3**[16] (40 mg, 100%) as a colorless solid; mp 153–155 °C (Found: C, 65.95; H, 4.95. Calc. for $C_{18}H_{16}O_6$: C, 65.85; H, 4.91%); ν_{max} ($CHCl_3$)/cm^{-1} 3400, 1720, 1280, 1040; δ_H (500 MHz; CD_3OD) 3.75 (3H, s), 3.78 (3H, s), 3.84 (3H, s), 6.48 (1H, dd, *J* 8.6, 1.8), 6.52 (1H, d, *J* 1.8), 6.94 (1H, dd, *J* 8.6, 1.8), 7.08 (1H, d, *J* 1.8), 7.32 (1H, d, *J* 8.6), 7.77 (1H, d, *J* 8.6); *m*/*z* 328 (100%, M^+) (Found: M^+, 328.0941. Calc. for $C_{18}H_{16}O_6$: *M*, 328.0947).

Methyl 6-hydroxy-2-[2-hydroxy-4-(tosyloxy)phenyl]benzo[*b*]-furan-3-carboxylate 24

A solution of BBr_3 (1 M solution in CH_2Cl_2; 0.64 ml, 0.64 mmol) was added to a solution of **23** (40 mg, 0.08 mmol) in CH_2Cl_2 (5 ml) at −78 °C. After the mixture had been stirred at the same temperature for 30 min, the mixture was allowed to warm at −40 °C and was further stirred for 30 h. The mixture was acidified by 3 M HCl and extracted with $CHCl_3$. The organic solution was washed successively with water and saturated aq. NaCl, dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel and eluted with hexane–AcOEt (6:1) to give **24** (26 mg, 72%) as a *colorless solid*; mp 95–97 °C; ν_{max} ($CHCl_3$)/cm^{-1} 3350, 1700, 1380, 1260, 1180, 1040; δ_H (300 MHz) 2.45 (3H, s), 4.01 (3H, s), 5.88 (1H, br), 6.76 (1H, d, *J* 2.2), 6.81 (1H, dd, *J* 8.5, 2.2), 6.91 (1H, dd, *J* 8.5, 2.2), 6.98 (1H, d, *J* 2.2), 7.34 (1H, d, *J* 8.5), 7.56 (1H, d, *J* 8.5), 7.78 (2H, d, *J* 8.5), 7.80 (1H, d, *J* 8.5), 8.59 (1H, s); *m*/*z* 454 (3.6%, M^+) and 267 (100) (Found: M^+, 454.0675. $C_{23}H_{18}O_8S$ requires *M*, 454.0721).

Coumestrol 4

A mixture of **24** (30 mg, 0.07 mmol) and 3 M KOH (0.14 ml) in THF (20 ml) was refluxed for 2 h. The mixture was acidified by 3 M HCl and extracted with AcOEt. The organic solution was washed successively with water and saturated aq. NaCl, dried over $MgSO_4$ and evaporated. The crude acid was used in the next reaction without further purification.

A solution of the crude acid and $TsOH{\cdot}H_2O$ (10 mg, 0.06 mmol) in THF (20 ml) was stirred at 60 °C for 5 h. The reaction mixture was extracted with AcOEt. The organic solution was washed with saturated aq. NaCl, dried over $MgSO_4$ and evaporated. The residue was purified by silica gel column chromatography and elution with hexane–AcOEt (5:1) to afford **4**[17,19] (10 mg, 53%) as a colorless solid; mp >360 °C (lit.[17a] mp 385 °C); δ_H (500 MHz; DMSO-D_6) 6.90 (1H, d, *J* 1.9), 6.92 (1H, dd, *J* 8.8, 1.9), 6.94 (1H, dd, *J* 8.8, 1.9), 7.16 (1H, d, *J* 1.9), 7.68 (1H, d, *J* 8.8), 7.84 (1H, d, *J* 8.8); δ_H (500 MHz; CD_3OD) 6.84 (1H, d, *J* 2.4), 6.88–6.90 (2H, m), 7.04 (1H, d, *J* 2.4), 7.70 (1H, d, *J* 8.5), 7.81 (1H, d, *J* 8.5); *m*/*z* 268 (100%, M^+) (Found: M^+, 268.0357. Calc. for $C_{15}H_8O_5$: *M*, 268.0371).

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