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PAPER

A strategy for the synthesis of the fargenone/fargenin family of natural products: synthesis of the tricyclic core†

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A synthesis of the core ring structure of the fargenin/fargenone family of natural products is presented. The general strategy is based upon biosynthetic speculation and exploits a cascade reaction, which transforms a spirocyclic dienone into the core ring system *via* a deprotonation–oxy-Michael–Wittig olefination sequence. This study represents the first synthesis work towards this family of natural products.

Introduction

The genus *Illicium* is characterized by a large number of biologically active and structurally interesting natural products[1] and, in particular, a range of oligomeric phenol-derived compounds, which are linked through the aromatic ring (Fig. 1). Isolated in 2007 from the methanol extract of the pericarps (fruit wall) of *Illicium fargesii* are three such sesqui neolignans (fargenones A-(**2**), B-(**1**) and fargenin-(**3**), Fig. 1).[2] These structures, in common with the un-named natural product **4**,[3] can be traced back to the naturally occurring phenol chavicol-(**10**) (Fig. 1), itself isolated numerous times from biologically active plant extracts.[4] While the isolation study of Fukuyama revealed that structures **1** to **3** were not particularly effective in promoting neurite outgrowth at the micromolar level *in vitro*, a number of structurally related phenolic natural products, particularly those isolated from *Magnolia*, have exhibited this type of biological activity and have been the subject of recent total syntheses. For example, we recently reported concise syntheses of honokiol-(**7**),[5] 4′-*O*-methyl honokiol-(**8**)[6] and dunnianol-(**9**).[7] The synthesis of honokiol-(**7**) and 4′-*O*-methyl honokiol-(**8**) has also been accomplished by a number of other research groups[8] as has the synthesis of a variety of analogues[9] and related natural products.[10]

The relationship between structures **1** to **4** and chavicol-(**10**), which has also been noted by Fukuyama,[2] is depicted in Scheme 1. This analysis reveals that the skeletally distinct trimeric natural products **1–4** are all very likely derived from dienone **11**, which is itself the product of an *ortho*/*para*-oxidative phenolic coupling between simple phenols magnolol-(**6**) and chavicol-(**10**).[11] A series of divergent cyclisation reactions of common intermediate **11** then affords the natural products **1–4**.

There are two possible oxy-Michael cyclisations of **11**, both of which establish the characteristic [4.3.0] ring system found in the fargenone/fargenin family. The first cyclisation, involving the more substituted olefin of the bis enone, results in intermediate **12**, from which either fargenin-(**3**) or the cage-like natural product fargenone B-(**1**) are expected to arise *via* the indicated transformations. The second possible oxy-Michael cyclisation of **11** gives rise to **4**, an unnamed natural product which, after a final oxy-Michael cyclisation and benzylic oxidation, is converted into fargenone A-(**2**). This biogenetic speculation, which implicates chavicol-(**10**) as the precursor to this family of sesqui neolignans (and also to the simpler bi-aryls honokiol-(**7**) and magnolol-(**6**)), has been corroborated *in vitro* by Brown and Sy who have demonstrated that a variety of natural products including dunnianol-(**9**), magnolol-(**6**) and compound **5**, can be obtained in low yield by treatment of chavicol-(**10**) with iron trichloride.[12]

Our synthesis plan for this structurally interesting family of natural products is based on the above analysis and, specifically, on the use of intermediate **11** (or a protected equivalent thereof) as a precursor from which the fargenones and fargenin should be available *via* the pathways indicated in Scheme 1. Given that no previous synthesis work has been reported on this group of natural products we began our studies by targeting compound **5**, which represents the tricyclic core ring system of this family of natural products. Specifically, we wished to ascertain the feasibility of an approach in which the spirocyclic dienone **14** could be transformed into the characteristic [4.3.0] ring system *via* a cascade sequence[13] involving deprotonation, oxy-Michael cyclisation and Wittig olefination (*vide infra*). This approach is depicted in retrosynthetic form in Scheme 2.

Recent work by Magnus *et al.*,[14] indicated that the desired spirocyclisation of **15** to obtain intermediate **14** was likely to be

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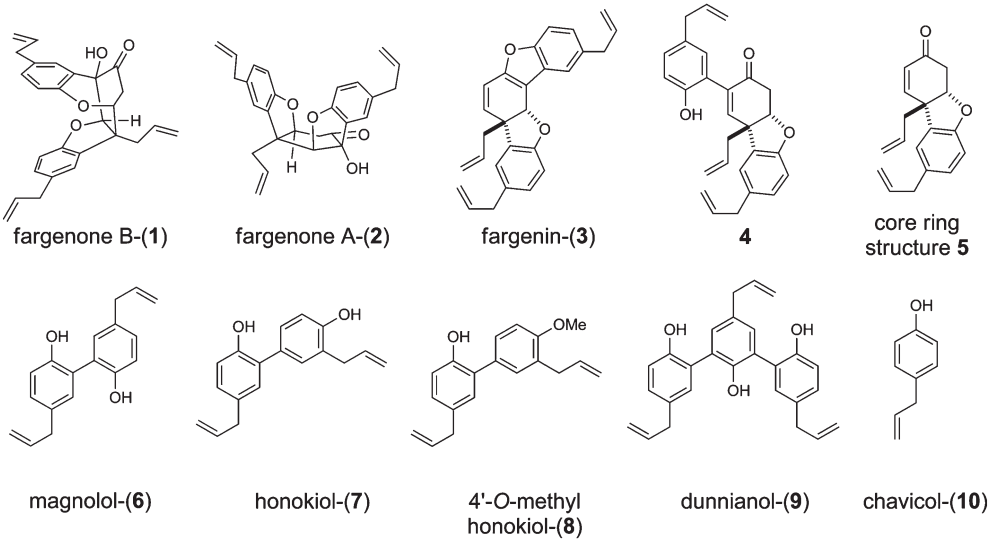
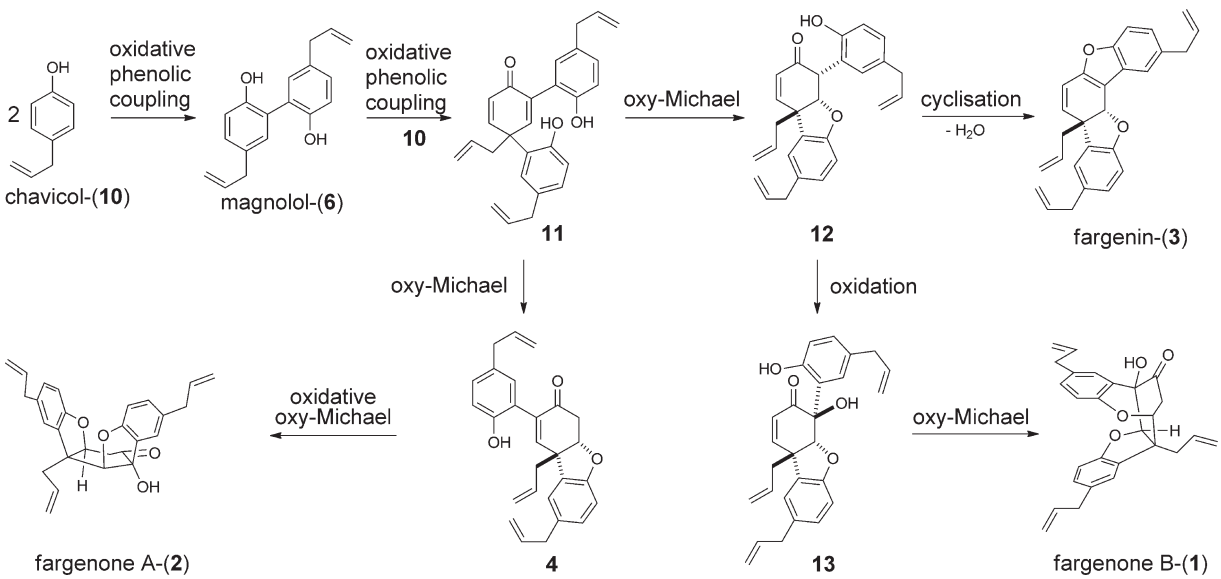


Fig. 1 Neolignan natural products isolated from *Illicium* and *Magnolia* plants and their likely biosynthetic precursor, chavicol-(**10**).



Scheme 1 Biogenetic speculation on the origin of the fargenin/fargenone natural products from chavicol-(**10**).

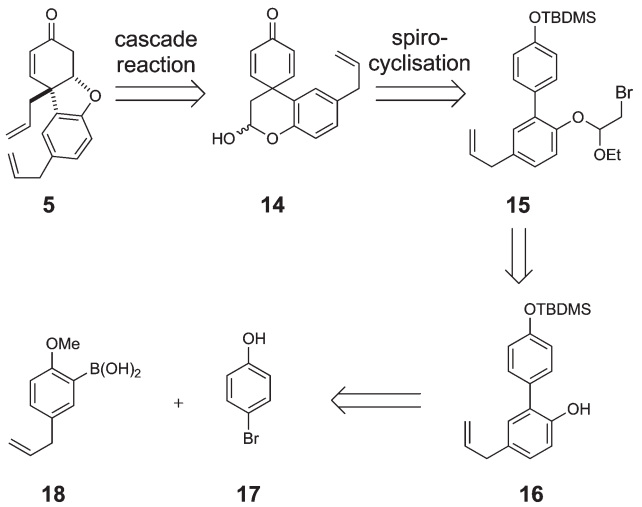
viable following bromo-acetalisation of **16**. This biaryl was expected to arise, after protecting group manipulation, from the Suzuki-Miyaura cross-coupling of **17** and **18**. We were aware of the potential difficulties in carrying the allyl group within **18** through a sequence of reactions in which isomerisation may occur. However, this was deemed preferable to alternatives that would involve progressing, for example, a protected alcohol, that would have to be unmasked, oxidized and methylenated at a later stage adding several steps to the sequence.

Results and discussion

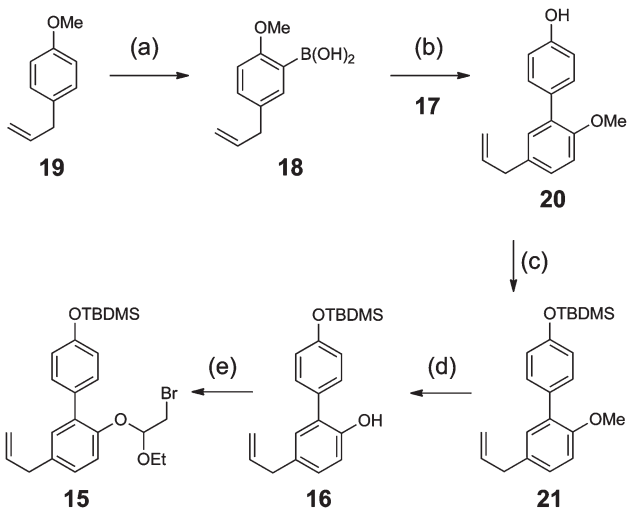
Our studies (Scheme 3) began with the preparation of the boronic acid coupling partner **18**, which was available from our previous syntheses of dunnianol-(**9**)[7] and honokiol-(**7**).[5] Thus, directed *ortho* lithiation of commercial 4-allyl anisole followed by quenching with freshly distilled trimethylborate afforded **18** in 75% isolated yield after hydrolysis of the derived arylboronate ester with aqueous hydrochloric acid.

Suzuki-Miyaura cross-coupling of the latter compound with bromophenol **17** afforded biaryl **20** in an excellent 94% yield without isomerisation of the sensitive allyl group. Protection of the hydroxyl group as a TBDMS ether was then carried out under standard conditions. Subsequent demethylation with $BCl_3{\cdot}SMe_2$ then afforded **16** in excellent yield leaving the silyl group intact. Conversion of this intermediate compound to mixed acetal **15** was next achieved using bromine and ethyl vinyl ether.[14]

With acetal **15** in hand the first of the key steps in the sequence towards model compound **5** could be attempted (Scheme 4). Using conditions developed by Magnus *et al.*[14] we

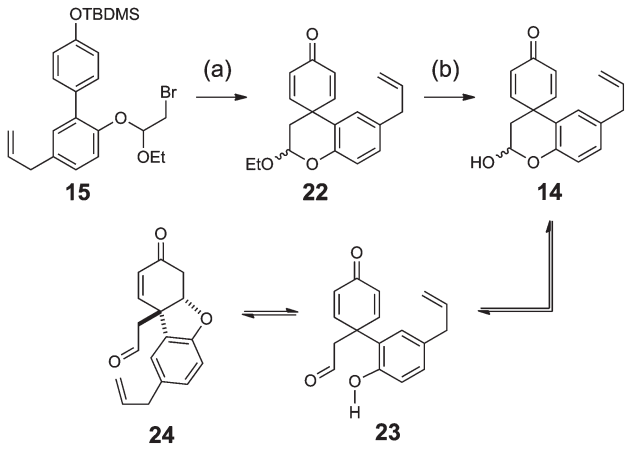


Scheme 2 Retrosynthetic analysis of tricyclic core structure **5**.



Scheme 3 *Reagents and conditions*. (a) (i) *s*-BuLi, TMEDA, THF, −78 °C to rt, 1 h, (ii) $B(OMe)_3$, 24 h, (iii) aq. HCl, 1 h, 75%; (b) $Pd_2(dba)_3$ 10 mol%, S-Phos (30 mol%), KF, THF–H_2O (10 : 1), reflux, 15 h, 94%; (c) TBDMSCl, imidazole, DMF, 1 h, 99%; (d) $BCl_3{\cdot}SMe_2$, 1,2-DCE, reflux, 18 h, 89%; (e) Br_2, CH_2CHOEt, *i*-Pr_2NEt, CH_2Cl_2, 0 °C, 12 h, 92%.

heated **15** to 130 °C in DMF in the presence of CsF and we were pleased to observe, firstly, cleavage of the silyl ether followed by a dearomatising spirocyclization, that afforded dienone **22** in excellent yield; hydrolysis of the acetal within **22** was then examined. This was best achieved by refluxing with aqueous HCl, which afforded a 94% yield of crude material. Inspection of ^1H and ^{13}C NMR spectra revealed that the crude product was a mixture in which lactol **14** was a major constituent. We believe that small amounts of aldehyde **24** were also present as a minor component in the complex mixture. This is supported by the presence of a triplet at δ 9.90, J = 1.0 Hz. Also present in the ^1H NMR were peaks at δ 4.72, 2.98 and 2.72, indicative of protons located at positions 3′, 2′a and 2′b respectively, in **5** as characterised by Brown and Sy.[12] Purification of this mixture by flash chromatography using normal phase silica gel proved to be



Scheme 4 *Reagents and conditions*. (a) CsF, Na_2SO_4, DMF, 130 °C, 1.5 h, 99%; (b) 2 M HCl, dioxane, reflux, 2 h, 94%.

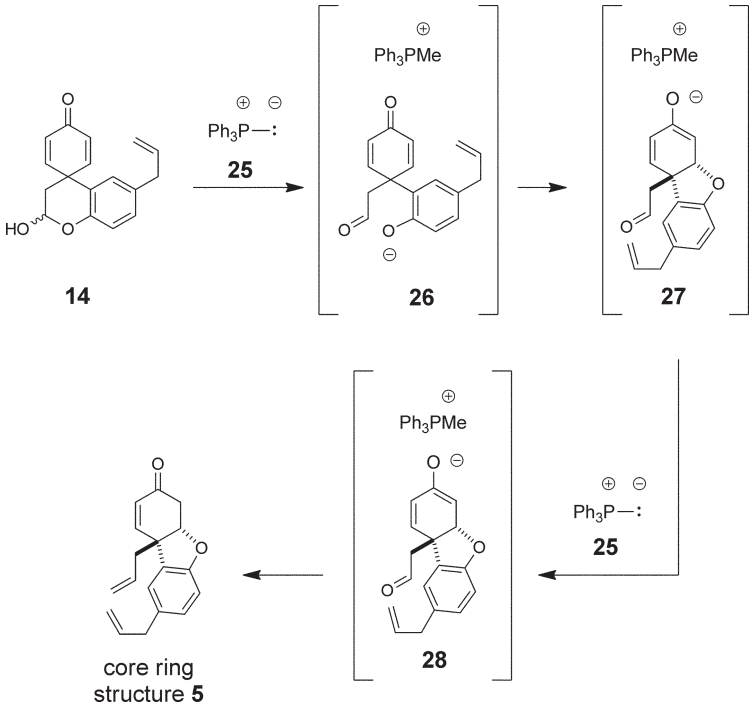
problematic and, therefore, the crude material was progressed directly to the pivotal cascade reaction. We hoped that this process would deliver **5**, the characteristic tricyclic ring system of the fargenin/fargenone family of natural products from spirocycle **14** (Scheme 5). Specifically, we reasoned that, upon treatment with excess ylide **25**, the spirocyclic lactol would undergo a sequence of reactions beginning with deprotonation and ring opening to afford **26**. This represents a truncated and activated version of key intermediate **11** (Scheme 1), which is expected to undergo rapid oxy-Michael cyclisation[15] to afford tricyclic enolate **27**. Finally, methylenation of the aldehyde within **27** should afford the target model compound **5** upon acidic work up.

Unfortunately, despite numerous attempts, we were unable to control the cascade sequence to deliver compound **5** cleanly in an acceptable yield. We summarise below (Table 1) the results of some of our experiments (Scheme 6).

An initial reaction (entry 1) involving exposure of **14** to 3 equivalents of ylide **25** at room temperature afforded a complex mixture of products. Inspection of ^1H and ^{13}C NMR spectra and comparison with the NMR data reported for **5** by Brown and Sy indicated that the desired compound was present in small amounts since peaks at δ 6.51, 4.70, 3.00 and 2.75, corresponding to protons 2′a, 2′b, 3′ and 5′ respectively, were visible.

Based on this we made several attempts to improve upon this reaction and, given that we observed a substantial amount of starting material, we conducted further experiments at 50 °C. At this temperature (entry 2) we obtained a much simpler reaction mixture from which we were able to isolate a tricyclic compound whose ^1H NMR data was similar to that of the desired product **5** in 55% yield. Closer inspection revealed that the material contained an additional alkene and the spectroscopic data were consistent with structure **29**. The stereochemistry of the ring junction was confirmed *via* a NOESY experiment (see Fig. 2) in which the expected interactions between protons on the convex face of the molecule were observed.

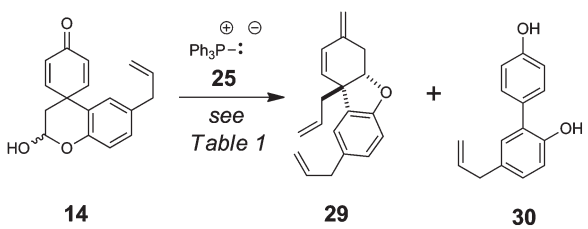
Having obtained compound **29**, which contains the desired [4.3.0] ring system, in reasonable yield we sought to adjust the reaction conditions to prevent the unwanted second Wittig methylenation from occurring. To this end we adjusted the ratio



Scheme 5 Proposed cascade reaction to access the tricyclic core model system from lactol **14**.

Table 1 Conditions screened to construct the tricyclic core

Entry	Ylide source	Base	Solvent	Temp.	Time	Product (yield)
1	Ph_3PMeBr (3.0 eq.)	KHMDS (2.5 eq.)	THF	r.t.	1.5 h	n/a
2	Ph_3PMeBr (3.5 eq.)	KHMDS (3.0 eq.)	THF	50 °C	1.5 h	**29** (55%)
3	Ph_3PMeBr (1.1 eq.)	KHMDS (2.7 eq.)	THF	50 °C	1.5 h	**30** (48%)
4	—	*t*-BuOK (2.5 eq.)	THF	50 °C	1 h	**30** (37%)



Scheme 6 Result of the cascade reaction on lactol **14**.

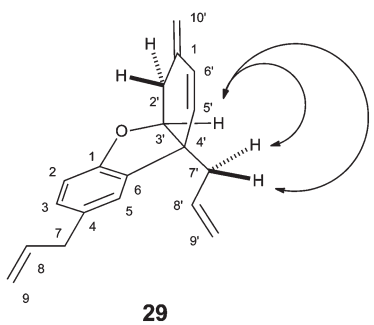


Fig. 2 Key NOESY interactions for compound **29**.

of phosphonium salt to base (entry 3). Frustratingly, this resulted in the formation of yet another unwanted product, this time a simple biaryl **30**, which we had also isolated and characterised before as a by-product during our synthesis of honokiol.[5] This by-product was also obtained when the starting material was heated with other bases including potassium *tert*-butoxide (entry 4). Additional experiments in which the ratio of phosphonium salt to base were further varied resulted in very complex mixtures of products in which varying amounts of products **29** and **30** were visible, however, none were as clean as entry 2.

Conclusion

Model compound **29**, which contains the characteristic [4.3.0] ring system of the fargenin/fargenone family of natural products, was prepared from **14** using a cascade sequence in which activated dienone **26** was an intermediate. This provides the first entry to this class of natural products, validates our synthesis strategy and corroborates the oxy-Michael cyclisation proposed for intermediate **11** in Scheme 1. A modified version of this

strategy that avoids the Wittig problem is now underway in our laboratory.

Experimental

NMR spectra were recorded on a Bruker DPX400 instrument as dilute solutions in the indicated deuterated solvent. All chemical shifts (δ) are reported in parts per million (ppm) relative to residual solvent peaks. All chemical shifts are reported relative to $CHCl_3$ (δ_H = 7.27 ppm and δ_C = 77.0 ppm). Mass spectra were recorded on either VG Micromass 70E, VG Autospec or Micromass LCTOF instruments. Infrared spectra were recorded on a Pelkin-Elmer 1600 FTIR instrument as a dilute solution in the indicated solvent. Reactions were monitored using TLC on Polygram® SIL G/UV_{254} 0.25 mm silica gel pre-coated glass sheets with fluorescent indicator. Flash chromatography was performed using Fluorochem silica gel 60, 35–70 micron. The solvents used were purified according to standard literature techniques and stored under argon.

6-Allyl-2-hydroxyspiro[chroman-4,1′-cyclohexa[2,5]dien]-4′-one (14)

To a solution of HCl (2.00 mL of a 2.00 M aqueous solution) and dioxane (2.00 mL) was added **22** (50.0 mg, 0.170 mmol) and the solution was stirred at rt for 1 h before being heated to reflux for 2 h. The solution was cooled to rt, diluted with H_2O (10.0 mL), extracted with EtOAc (3 × 10.0 mL), washed with brine (3 × 10.0 mL), dried over $MgSO_4$ and concentrated under reduced pressure to give **14** (43.0 mg, 94%) as a colourless oil, R_f 0.34 (petroleum ether–EtOAc, 2 : 1).

^{1}H NMR: (400 MHz, $CDCl_3$) δ 9.90 (t, J = 1.0 Hz, 1H), 7.45–7.39 (m, 2H), 7.18 (d, J = 1.3 Hz, 1H), 7.07–6.99 (m, 4H), 6.91 (d, J = 8.0 Hz, 1H), 6.87 (d, J = 9.9 and 3.5 Hz, 2H), 6.76 (d, J = 2.0 Hz, 1H), 6.37 (dd, J = 10.0 and 1.9 Hz, 1H), 6.39 (dd, J = 10.0 and 1.9 Hz, 1H), 6.01–5.83 (m, 3H), 5.78–5.73 (m, 2H), 5.12–5.00 (m, 5H), 4.73–4.71 (m, 1H), 4.43–4.42 (m, 1H), 3.36 (t, J = 5.4 Hz, 3H), 3.25 (d, J = 6.1 Hz, 2H), 2.98–2.92 (m, 2H), 2.77–2.65 (m, 3H), 2.42–2.14 (m, 5H), 1.88 (dd, J = 6.5 and 1.4 Hz, 1H), 1.83 (dd, J = 6.5 and 1.4 Hz, dd), 1.79 (s, 1H); ^{13}C NMR (100 MHz, CD3CN): δ 207.0, 199.6, 196.3, 158.7, 158.6, 155.4, 155.12, 154.8, 152.7, 151.3, 148.0, 139.3, 138.9, 134.5, 134.0, 133.8, 132.9, 131.5, 131.4, 131.2, 130.5, 130.2, 130.0, 129.5, 129.3, 129.1, 129.0, 128.8, 128.1, 127.3, 125.7, 124.5, 120.5, 119.4, 119.2, 117.2, 116.9, 115.9, 115.8, 115.6, 115.4, 115.3, 115.2, 110.5, 110.3, 101.3, 98.7, 98.2, 91.6, 91.4, 88.8, 88.6, 88.5, 84.2, 81.6, 73.7, 71.1, 46.9, 46.4, 45.7, 45.2, 43.9, 42.2, 40.8, 40.6, 40.2, 39.9, 39.8, 39.6, 38.0, 36.6; IR ($CHCl_3$) 3674, 3584, 3081, 3011, 2980, 2932, 1721, 1666, 1638, 1626, 1611, 1515, 1493, 1434, 1402, 1244, 1179, 1131, 1043, 982 cm^{-1}. HRMS (ESI^+) cald. for $C_{17}H_{16}O_3Na$ $(M + Na)^+$ requires 291.0992; found 291.0992.

(5′-Allyl-2′-(2-bromo-1-ethoxyethoxy)biphenyl-4-yloxy)-(*tert*-butyl)dimethylsilane (15)

To a solution of Br_2 (30.1 μL, 0.587 mmol) in CH_2Cl_2 (10.0 mL) at 0 °C was added ethyl vinyl ether (70.4 μL, 0.735 mmol) dropwise and the solution was stirred for 15 min before i-Pr_2NEt (0.205 mL, 1.18 mmol) was added. A solution of **16** (100 mg, 0.294 mmol) in CH_2Cl_2 (10.0 mL) was added dropwise and the solution was stirred for 12 h. The solution was warmed to rt, diluted with CH_2Cl_2 (10.0 mL), washed with sat. aq. $NaHCO_3$ (2 × 10.0 mL), washed with brine (2 × 10.0 mL), dried over Na_2SO_4 and concentrated under reduced pressure. Purification by flash chromatography (petroleum ether–EtOAc, 9 : 1) gave **15** (133 mg, 92%) as a colourless oil, R_f 0.68 (petroleum ether–EtOAc, 9 : 1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, J = 8.7 Hz, 2H), 7.16 (s, 1H), 7.10–7.08 (m, 2H), 6.88 (d, J = 8.7 Hz, 2H), 5.99 (ddt, J = 16.9, 10.0 and 6.8 Hz, 1H), 5.14–5.06 (m, 3H), 3.62 (dq, J = 7.0 and 7.0 Hz, 1H), 3.46 (dq, J = 7.0 and 7.0 Hz, 1H), 3.39 (dd, J = 6.8 Hz, 2H), 3.37–3.31 (m, 2H), 1.12 (t, J = 7.0 Hz, 3H), 1.01 (s, 9H), 0.23 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.0, 151.8, 137.5, 135.1, 133.1, 131.3, 131.2, 130.8, 128.2, 119.7, 118.8, 116.0, 102.6, 63.0, 39.6, 31.7, 25.8, 18.3, 15.1, −4.2; IR ($CHCl_3$) 3082, 3011, 2980, 2958, 2932, 2898, 2859, 1639, 1607, 1514, 1488, 1472, 1256, 1102, 993, 909 cm^{-1}. HRMS (ESI^+) cald. for $C_{25}H_{39}O_3NBrSi$ $(M + NH_4)^+$ requires 508.1877; found 508.1875.

5-Allyl-4′-(*tert*-butyldimethylsilyloxy)biphenyl-2-ol (16)

To a solution of **21** (310 mg, 0.874 mmol) in 1,2-DCE (5.00 mL) was added $BCl_3{\cdot}SMe_2$ (0.437 mL, 1.75 mmol of a 2.00 M solution in CH_2Cl_2) and the solution was heated to reflux for 18 h. The solution was cooled to rt, H_2O (5.00 mL) was added and the solution was stirred for 15 min. The solution was diluted with CH_2Cl_2 (20.0 mL), washed with brine (3 × 20.0 mL), dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (petroleum ether–EtOAc, 9 : 1) gave **16** (265 mg, 89%) as a colourless oil, R_f 0.49 (petroleum ether–EtOAc, 9 : 1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (d, J = 8.7 Hz, 2H), 7.06 (dd, J = 8.0 and 1.7 Hz, 1H), 7.04 (d, J = 1.7 Hz, 1H), 6.95 (d, J = 8.7 Hz, 2H), 6.91 (d, J = 8.0 Hz, 1H), 5.98 (ddt, J = 16.8, 10.1 and 6.5 Hz, 1H), 5.10 (dd, J = 16.8 and 1.6 Hz, 1H), 5.08 (s, 1H), 5.06 (dd, J = 10.1 and 1.6 Hz, 1H), 3.36 (d, J = 6.5 Hz, 2H), 1.02 (s, 9H), 0.25 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.6, 150.9, 137.9, 132.3, 130.3, 130.3, 129.9, 128.9, 127.8, 120.9, 115.6, 115.6, 39.5, 25.8, 18.3, −4.3; IR ($CHCl_3$) 3553, 3011, 2958, 2932, 2898, 2859, 1606, 1514, 1491, 1264, 1170, 910 cm^{-1}. HRMS: (ESI^-) cald. for $C_{21}H_{27}O_2Si$ $(M - H)^-$ requires 339.1786; found 339.1782.

5-Allyl-2-methoxyphenylboronic acid (18)

To a solution of **19** (2.08 mL, 13.5 mmol) in THF (50 mL) at −78 °C was added TMEDA (2.02 mL, 13.5 mmol) and s-BuLi (14.6 mL, 20.2 mmol of a 1.39 M solution in hexanes) dropwise over 15 min and the solution was stirred for 1 h. The reaction mixture was then warmed to room temperature and stirred for 1 h before $B(OMe)_3$ (1.39 mL, 13.5 mmol) was added and the reaction was stirred for a further 24 h. The reaction was acidified (1 M HCl to pH 3) and stirred for an additional 1 h. The reaction was diluted with EtOAc (50 mL), washed with brine (3 ×

50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (petrol–Et_2O, 3 : 1) gave **18** (1.94 g, 75%) as a colourless solid, mp = 77–79 °C, R_f = 0.13 (petrol–Et_2O, 3 : 1).

^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.67 (d, J = 2.4 Hz, 1H), 7.27 (dd, J = 8.5 and 2.4 Hz, 1H), 6.87 (d, J = 8.5 Hz, 1H), 6.05 (br s, 2H), 5.97 (ddt, J = 16.8, 10.1 and 6.7, 1H), 5.07 (dd, J = 16.8 and 1.5 Hz, 1H), 5.09 (dd, J = 10.1 and 1.5 Hz, 1H), 3.91 (s, 3H), 3.37 (d, J = 6.7 Hz, 2H); ^{13}C NMR: (100 MHz, $CDCl_3$) δ 163.1, 137.7, 136.9, 132.9, 132.6, 132.6, 115.6, 110.1, 55.6, 39.3; IR: (neat) 3422, 3196, 2958, 1633, 1606, 1511, 1410, 1339, 1098, 966, 816 cm^{-1}. HRMS (EI$^+$) cald. for $C_{10}H_{13}O_3B$ (M)$^+$ requires 192.0958, found 192.0960.

5′-Allyl-2′-methoxybiphenol-4-ol (20)

To a solution of **17** (199 mg, 1.15 mmol) in THF (10 mL) and H_2O (1 mL) was added **18** (330 mg, 1.72 mmol), KF (300 mg, 5.75 mmol), 2-dicyclohexylphosphino-2′,6′-dimethoxybiphenyl (142 mg, 0.345 mmol) and $Pd_2(dba)_3$ (66.1 mg, 0.115 mmol) and the solution was heated to reflux and stirred for 15 h. The reaction was cooled to room temperature, diluted with EtOAc (25 mL) and washed with 1 M HCl (2 × 25 mL) and brine (2 × 25 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (petrol–EtOAc, 3 : 1) gave **20** (259 mg, 94%) as a yellow oil, R_f 0.48 (petrol–EtOAc, 3 : 1).

^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.43 (d, J = 8.8 Hz, 2H), 7.13 (s, 1H), 7.12 (d, J = 7.4 Hz, 1H), 6.92 (d, J = 7.4 Hz, 1H), 6.88 (d, J = 8.8 Hz, 2H), 5.99 (ddt, J = 17.0, 11.5 and 6.7 Hz, 1H), 5.11 (dd, J = 17.0 and 1.9 Hz, 1H), 5.07 (dd, J = 11.5 and 1.9 Hz, 1H), 4.80 (br s, 1H), 3.80 (s, 3H), 3.38 (d, J = 6.7 Hz, 2H); ^{13}C NMR: (100 MHz, $CDCl_3$) δ 154.9, 154.5, 137.8, 132.3, 131.2, 131.0, 130.8, 130.2, 128.1, 115.6, 114.9, 111.3, 55.7, 39.4; IR: ($CHCl_3$) 3596, 3082, 3009, 2935, 2837, 1731, 1639, 1613, 1591, 1518, 1496, 1256, 1174, 1044, 1029, 835 cm^{-1}. HRMS: (ESI$^+$) cald. for $C_{16}H_{16}O_2Na$ (M + N)$^+$ requires 263.1039, found 263.1043.

(5′-Allyl-2′-methoxybiphenyl-4-yloxy)(*tert*-butyl) dimethylsilane (21)

To a solution of **20** (363 mg, 1.78 mmol) in DMF (10.0 mL) was added imidazole (424 mg, 6.23 mmol) and TBDMSCl (402 mg, 2.65 mmol) and the solution was stirred for 1 h. The solution was diluted with Et_2O (20.0 mL), washed with H_2O (3 × 20.0 mL), dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (petroleum ether–EtOAc, 9 : 1) gave **21** (630 mg, 99%) as a colourless oil, R_f 0.71 (petroleum ether–EtOAc, 9 : 1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, J = 8.6 Hz, 2H), 7.15 (d, J = 2.0 Hz, 1H), 7.12 (dd, J = 8.4 and 2.0 Hz, 1H), 6.92 (d, J = 8.4 Hz, 1H), 6.88 (d, J = 8.6 Hz, 2H), 6.01 (ddt, J = 17.0, 10.2, and 6.4 Hz, 1H), 5.11 (dd, J = 17.0 and 1.6 Hz, 1H), 5.07 (dd, J = 10.2 and 1.6 Hz, 1H), 3.80 (s, 3H), 3.39 (d, J = 6.4 Hz, 2H), 1.03 (s, 9H), 0.26 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.0, 154.8, 137.9, 132.3, 131.4, 131.1, 130.6, 130.4, 128.0, 119.5, 115.6, 111.5, 55.8, 39.5, 25.8, 18.3, −4.3; IR ($CHCl_3$) 3080, 3011, 2958, 2932, 2899, 2859, 1638, 1607, 1586, 1515, 1494, 1472, 1464, 1363, 1173, 1146, 1070, 1044, 913 cm^{-1}. HRMS (ESI$^+$) cald. for $C_{22}H_{30}O_2Si$ (M + H)$^+$ requires 377.1902; found 377.1907.

6-Allyl-2-ethoxyspiro[chroman-4,1′-cyclohexa[2,5]dien]-4′-one (22)

To a flame dried mixture of CsF (46.5 mg, 0.306 mmol) and Na_2SO_4 (145 mg, 1.02 mmol) was added **15** (50.0 mg, 0.102 mmol) in DMF (10.0 mL) and the solution was heated to 130 °C for 1.5 h. The solution was cooled to rt, diluted with Et_2O (20.0 mL), washed with H_2O (3 × 20.0 mL), dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (petroleum ether–EtOAc, 7 : 3) gave **22** (30.1 mg, 99%) as a colourless oil, R_f 0.37 (petroleum ether–EtOAc, 7 : 3).

^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.46 (dd, J = 10.0 and 3.2 Hz, 1H), 7.04 (dd, J = 8.4 and 2.4 Hz, 1H), 6.88 (d, J = 8.4 Hz, 1H), 6.81 (dd, J = 10.0 and 3.2 Hz, 1H), 6.70 (d, J = 2.4 Hz, 1H), 6.37 (dd, J = 10.0 and 1.8 Hz, 1H), 6.23 (dd, J = 10.0 and 1.8 Hz, 1H), 5.93–5.83 (m, 1H), 5.38 (dd, J = 3.0 and 3.0 Hz, 1H), 5.05–5.00 (m, 2H), 3.93 (dq, J = 7.2 and 3.0 Hz, 1H), 3.65 (dq, J = 7.2 and 3.0 Hz, 1H), 3.25 (d, J = 6.4 Hz, 2H), 2.27 (dd, J = 14.0 and 3.0 Hz, 1H), 2.13 (dd, J = 14.0 and 3.0 Hz, 1H, 1.23 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 186.1, 154.9, 154.2, 148.4, 137.3, 133.5, 129.7, 128.6, 128.4, 126.1, 119.3, 118.5, 115.9, 95.6, 64.4, 40.7, 39.3, 36.4, 15.2; IR ($CHCl_3$) 3081, 3011, 2981, 2933, 1731, 1665, 1625, 1515, 1495, 1434, 1402, 1374, 1345, 1259, 1178, 1131, 1119, 1066, 1043, 990 cm^{-1}. HRMS (ESI$^+$) cald. for $C_{19}H_{20}O_3Na$ (M + Na)$^+$ requires 319.1305; found 319.1294.

8,8b-Diallyl-3-methylene-3,4,4a,9b-tetrahydrodibenzo[*b*,*d*]furan (29)

To a solution of Ph_3PMeBr (91.8 mg, 0.258 mmol) in THF (2.50 mL) was added KHMDS (0.448 mL, 0.224 mmol of a 0.500 M solution in toluene) dropwise over 15 min and the solution was stirred for 30 min before a solution of **14** (20.0 mg, 74.6 μmol) in THF (2.50 mL) was added dropwise over 15 min and the solution was heated to 50 °C for 1.5 h. The solution was cooled to rt, diluted with EtOAc (20.0 mL), washed with brine (3 × 20.0 mL), dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography gave **29** (10.9 mg, 55%) as a colourless oil, R_f 0.76 (petroleum ether–EtOAc, 3 : 1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.95 (s, 1H), 6.93 (d, J = 8.5 Hz, 1H), 6.71 (d, J = 8.5 Hz, 1H), 6.22 (d, J = 9.9 Hz, 1H), 5.95 (ddt, J = 16.8, 10.0 and 6.8 Hz, 1H), 5.83–5.73 (m, 1H), 5.52 (d, J = 9.9 Hz, 1H), 5.15–5.04 (m, 4H), 4.97 (d, J = 11.8 Hz, 2H), 4.70 (t, J = 3.7 and 3.7 Hz, 1H), 3.33, (d, J = 6.8 Hz, 2H), 2.87 (dd, J = 15.9 and 3.8 Hz, 1H), 2.70–2.63 (m, 2H), 2.23 (dd, J = 14.1 and 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.0, 138.1, 137.6, 133.8, 133.7, 132.6, 131.5, 128.6, 128.1, 123.1, 118.4, 115.5, 114.4, 110.0, 85.3, 48.2, 42.4, 39.9, 39.1; IR ($CHCl_3$) 2960, 2929, 2872, 1731, 1593, 1463, 1438, 1379, 1296, 1265, 1177, 1122, 1071, 909 cm^{-1}. HRMS (ESI$^+$) cald. for $C_{19}H_{20}ONa$ (M + Na)$^+$ requires 287.1406; found 287.1407.

5-Allylbiphenyl-2,4′-diol (30)

To a solution of **14** (10.0 mg, 37.3 μmol) in THF (1.00 mL) was added *t*-BuOK (37.3 μL, 37.3 μmol of a 1.00 M solution in THF) and the solution was heated to 50 °C for 1 h. The solution was cooled to rt, diluted with EtOAc (10.0 mL), washed with brine (3 × 10.0 mL), dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (petrol–EtOAc, 3 : 1) also gave **30** (3.70 mg, 37%) as a white solid, mp 104–106 °C, R_f 0.22 (petrol–EtOAc, 3 : 1).

^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.36 (d, J = 8.4 Hz, 2H), 7.07 (dd, J = 8.0 and 2.0 Hz, 1H), 7.04 (d, J = 2.0 Hz, 1H), 6.95 (d, J = 8.4 Hz, 2H), 6.92 (d, J = 8.0 Hz, 1H), 5.99 (ddt, J = 16.8, 10.0 and 6.8 Hz, 1H), 5.21 (br s, 1H), 5.10 (dd, J = 16.8 and 1.6 Hz, 1H), 5.07 (dd, J = 10.0 and 1.6 Hz, 1H), 3.36 (d, J = 6.8 Hz, 2H); ^{13}C NMR: (100 MHz, $CDCl_3$) δ 155.3, 150.8, 137.8, 132.4, 130.5, 130.3, 129.5, 128.9, 127.7, 116.1, 115.7, 115.6, 39.4; IR: ($CHCl_3$) 3594, 3556, 3082, 3060, 2979, 2905, 1639, 1611, 1516, 1493, 1331, 1260, 1171, 911, 839 cm^{-1}. HRMS: (ESI$^+$) cald. for $C_{15}H_{14}O_2Na$ $(M + Na)^+$ requires 249.0891, found 249.0907.

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