Towards a Total Synthesis of the New Anticancer Agent Mensacarcin: Synthesis of the Carbocyclic Core

Lutz F. Tietze,* Scott G. Stewart, Marta E. Polomska, Andrea Modi, and Axel Zeeck[a]

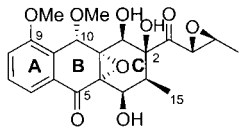
Dedicated to Professor Karsten Krohn on the occasion of his 60th birthday

Abstract: A synthesis of the carbocyclic core associated with the new anticancer agent mensacarcin (**1**) is reported. The strategy involves the synthesis of several novel highly substituted aromatic compounds, such as **12** and **23**. The lithium derivative of **12** readily engages in a nucleophilic addition to benzaldehyde **4** to provide the diphenylcarbinol *rac*-**15**. The analogous benzyl ether *rac*-**16** undergoes an intramolecular Heck reaction to provide the required tetrahydroanthracene *rac*-**17**, which can be transformed into the key tricyclic methyl ether *rac*-**20**. In a second approach, the lithium derivative of **21** is added to the hexasubstituted benzaldehyde **23** to give the diphenylcarbinol *rac*-**35**. Subsequent methylation to *rac*-**36** followed by an intramolecular Heck reaction provides tricycle *rac*-**37**. Similarly, the oxidised compound **40** provides an electronically more suitable intramolecular Heck partner to afford compound **41**. Further transformations of these substrates leads to *rac*-**43**, which incorporates the core structure of mensacarcin (**1**).

Keywords: anthracenes · antibiotics · antitumor agents · carbocycles · Heck reactions

Introduction

Mensacarcin (**1**) is a novel polyfunctionalised hexahydroanthracene isolated from a strain of *Streptomyces* (Gö C4/4) by Zeeck and Arnold.[1] Mensacarcin (**1**) shows cytostatic and cytotoxic activity comparable to doxorubicin (**2**), another anticancer agent currently used in the treatment of malignant lymphomas and leukemias.[2,3] Interestingly, mensacarcin (**1**) has a high level of oxygenation, similar to that found in compound **2**, along with some other structural similarities. At present, the only known natural product with a closely related structure to mensacarcin (**1**) is cavicarcin (**3**), which displays a much lower biological activity.[4] The challenges involved with the highly substituted tricyclic core of mensacarcin (**1**) along with its pronounced bioactivity make it an attractive target for organic synthesis. When the prevalence of anthraquinone-type frameworks in a variety of natural products is considered, it is not surprising that many approaches have been developed for their synthesis.[5] However, only a few methods exist for the formation of the hydroxy- or methoxy-substituted dihydroanthracenone, either by regioselective reduction of anthraquinone or by other synthetic pathways.[6] For this reason, and because of our interest in preparation of natural products by transition-metal-catalysed transformations,[7] we have devised a synthesis of the tricyclic core of **1** by means of an intramolecular Heck reaction.



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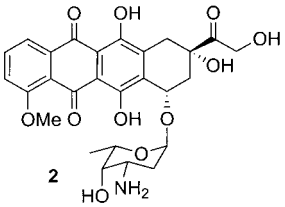

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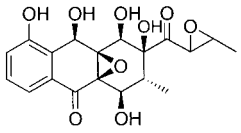

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The strategy for the synthesis of the carbocyclic core of mensacarcin (**1**) is outlined in Scheme 1. In an initial retrosynthesis analysis, it was envisaged that the tricyclic compound **1** could be broken up into the two aromatic fragments, **4** and **5**. Nucleophilic addition of the aryllithium species **5** to the aldehyde **4** should afford the diphenylcarbinol **6**. An intramolecular Heck reaction involving a protected

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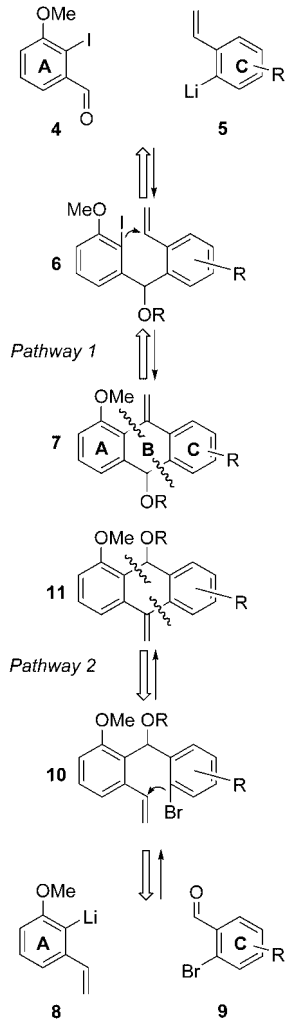
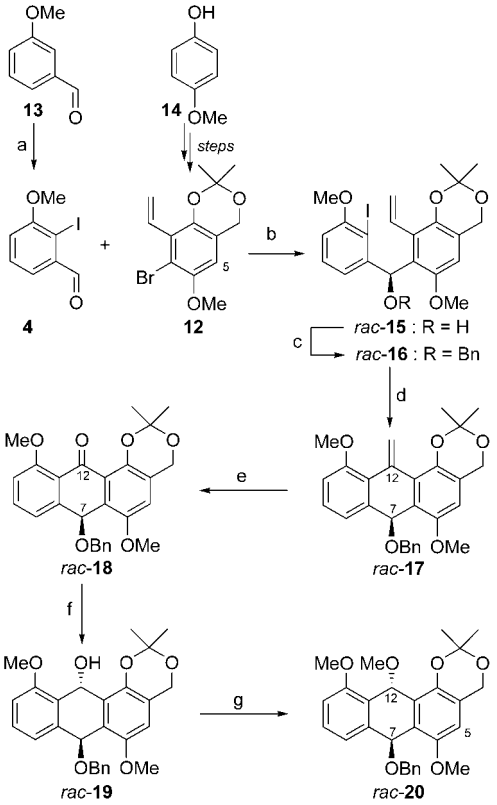


Scheme 1. Retrosynthesis analysis of the carbocyclic core of mensacarcin (**1**).

derivative of diphenylcarbinol **6** would then provide the required tetrahydroanthracene compound **7** (Pathway 1). In a second retrosynthesis approach, the building blocks **8** and **9** were utilised (Pathway 2). Nucleophilic addition of the lithium compound **8** to the aldehyde **9** would provide the diphenylcarbinol **10**, which should then lead to the tetrahydroanthracene **11**, again by way of an intramolecular Heck reaction. However, before such retrosynthesis approaches were realised, the synthesis of the corresponding highly substituted building blocks **4** and **9** had to be performed. Additionally, at this stage it was not clear whether the planned Heck reactions would be at all feasible, due to the high electron density in rings A and C. For the synthesis of mensacarcin (**1**), we initially focussed on the preparation of building block **12**, assuming that the missing methyl group at C-3 could be introduced by addition of a methyl cuprate to an epoxide in ring C; this reaction would also allow the introduction of a hydroxy group at C-2 (mensacarcin numbering). As a second building block, 2-iodo-3-methoxybenzaldehyde (**4**) had to be prepared.

Results and Discussion

The synthesis of 2-iodo-3-methoxybenzaldehyde (**4**) was achieved, in 52% yield, by converting the commercially available benzaldehyde **13** into the corresponding *ortho*-aryllithium compound by using *n*BuLi, TriMEDA and PhLi and then quenching with iodine (Scheme 2).[8] The C-ring

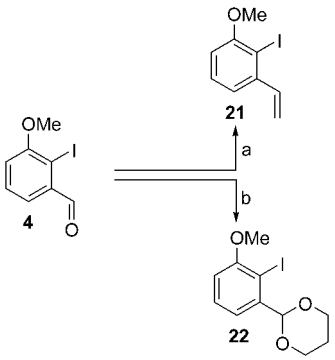


Scheme 2. Synthesis of tricycle *rac*-**20**. a) TriMEDA, C_6H_6, *n*BuLi, 0°C, then **13**, 0°C, PhLi, 7 h, then THF, −78°C, I_2, 12 h, 55%; b) **12**, *t*BuLi, THF, −78°C, 10 min, then **4**, Et_2O, 20°C, 30 min, 80%; c) NaH, THF, BnBr, 40°C, 12 h, 65%; d) $Pd(OAc)_2$, PPh_3, nBu_4NCl, K_2CO_3, DMF, 40°C, then **16**, 80°C, 12 h, 85%; e) $RuCl_3$, $NaIO_4$, CCl_4, MeCN, H_2O, 20°C, 20 min, 81%; f) $LiAlH_4$, THF, 0°C, 30 min, 91%; g) NaH, MeI, THF, 40°C, 12 h, 96%. Bn = benzyl, TriMEDA = *N*′,*N*,*N*-trimethylethylenediamine.

building block **12** was synthesised in 12 steps from *p*-methoxyphenol **14** in 12% overall yield.[9] Treatment of **12** with *t*BuLi at −78°C generated the corresponding aryllithium compound, which was in turn treated with aldehyde **4**. The resulting alcohol from this reaction, *rac*-**15**, was not isolated but was protected under standard conditions with NaH, BnBr and THF at 40°C to provide the benzyl ether **16** as a racemic mixture in 52% yield over two steps. Compound *rac*-**16** was subsequently employed in the key ring-closure step. Thus, intramolecular Heck reaction with $Pd(OAc)_2$, PPh_3, nBu_4NCl and K_2CO_3 in DMF allowed a smooth transformation to form the desired methylene tetrahydroanthracene *rac*-**17** in an excellent yield of 85%. As anticipated, none of the seven-membered *endo* product was detected, due to the highly favoured and less sterically demanding six-*exo*-*trig* cyclisation.[10]

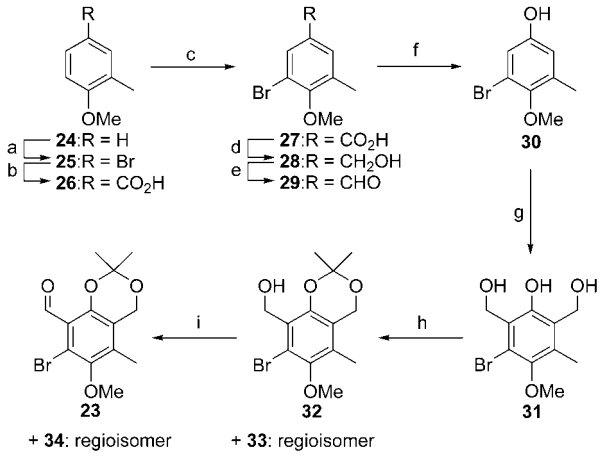
Once we had succeeded in forming the carbocyclic core of mensacarcin (**1**), our attention was then focussed on installing the methoxy substituent at C-12 (mensacarcin numbering: C-10). To this end, the methylene group within the tricyclic *rac*-**17** was initially oxidatively cleaved with a mixture of $RuCl_3$ (5 mol%) and $NaIO_4$ to give the ketone *rac*-**18** in 81% yield.[11] The latter compound was then stereoselectively reduced to afford the alcohol *rac*-**19**. The *anti*-orientated substituents at C-7 and C-12 within *rac*-**19** probably arise from a neighbouring-group effect of the benzyloxy moiety at the C-7 position during reduction. Final methylation of the hydroxy group in *rac*-**19** provided the racemic ether **20**, in 96% yield, which was characterised by standard spectroscopic techniques as well as ^{1}H-NOESY NMR spectroscopy. This compound contains the desired ABC ring system as well as the C-12 functionality as found in mensacarcin (**1**) but is missing the methyl group at C-5 (mensacarcin numbering: C-10 and C-3, respectively).

In addition to compound **12**, we also prepared the C-ring building block **23**, which already contains the necessary methyl group at C-5. The connection of this compound with ring A was envisaged according to retrosynthesis pathway 2 (Scheme 1), for which the building blocks **21** and **22** (Scheme 3) were needed. For the synthesis of the first



Scheme 3. Synthesis of iodobenzenes **21** and **22**. a) Ph_3PCH_3Br, NaHMDS, THF, 20°C, 1 h, then **4**, 1 h, 90%; b) 1,3-propanediol, Amberlyst 15 H^+, C_6H_6, reflux, 5 h, 66%. NaHMDS = sodium hexamethyldisilazanide.

A ring building block, the previously synthesised aldehyde **4** was subjected to a Wittig reaction with PPh_3CH_3Br and NaHMDS to give **21** in 90% yield. Furthermore, the presumably more stable acetal-protected derivative **22** was also prepared in a single step, in 66% yield, by using 1,3-propanediol. Synthesis of the more complex aldehyde **23** started with bromination in the *para* position of the commercially available anisole **24** by using Br_2 and NaOAc in CH_2Cl_2 to give **25** (Scheme 4). This step was followed by preparation of the corresponding magnesium compound, which was CO_2 (dry) quenched to produce the carboxylic acid **26** in 70% yield over 2 steps.[12] Reaction of carboxylic acid **26** with 2.0 equivalents of Br_2 in dioxane furnished compound **27**, in 84% yield, containing a bromine atom in the *ortho* position to the methoxy substituent.[13] As intended, the carboxylic acid at C-1 in **26** was successful in directing the bromination



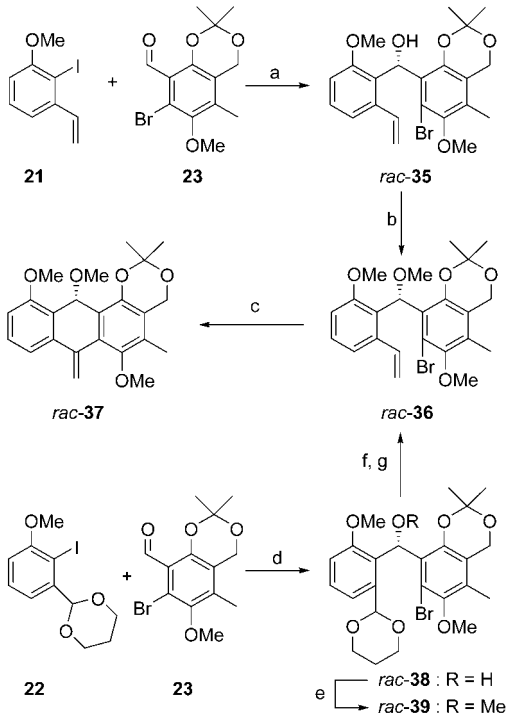
Scheme 4. Synthesis of bromobenzenes **23** and **34**. a) Br_2, CH_2Cl_2, NaOAc, 0°C, 2 h, 85%; b) Mg, THF, Et_2O, reflux, 1 h 30 min, then 20°C, CO_2, 2 h, 82%; c) Br_2, dioxane, 20°C, 7 d, 84%; d) $LiAlH_4$, THF, Et_2O, 0°C, 1 h, 72%; e) MnO_2, CH_2Cl_2, 20°C, 12 h, 87%; f) *m*-CPBA, CH_2Cl_2, 20°C, then K_2CO_3, MeOH, 20°C, 15 min, 68%; g) HCHO, H_2O, CaO, 20°C, 5 d, 69%; h) $(CH_3)_2CO$, *p*-TsOH, 20°C, 18 h, 91%; i) DMSO, ClCOCOCl, CH_2Cl_2, −78°C, 30 min, then **32**/**33**, −78°C, 1.5 h, then NEt_3, 5 min, 20°C, 30 min, 83%. DMSO = dimethylsulfoxide, *m*-CPBA = *meta*-chloroperoxybenzoic acid, *p*-TsOH = *para*-toluenesulfonic acid.

and this functionality subsequently needed to be "unmasked" as the phenol to allow the introduction of two *ortho*-hydroxymethyl units.[14] This transformation first required an acid to aldehyde reduction, which was achieved in 2 steps by initial treatment of **27** with $LiAlH_4$ to give the alcohol **28** in 72% yield and subsequent oxidation with MnO_2 to afford aldehyde **29** in 87% yield. Baeyer–Villiger oxidation of **29** to give the corresponding formate was followed by solvolysis with K_2CO_3 and MeOH to furnish phenol **30** in reasonable yield (68%).[15] The ^{1}H NMR spectrum of **30** shows two *meta*-coupled resonances ($J = 1.2$ Hz), which are characteristic for the aromatic substitution pattern in this compound. In a final transformation, the last two nonsubstituted positions within phenol **30** were hydroxymethylated by exposure to formaldehyde and calcium oxide in water to give the novel hexasubstituted aromatic compound **31** in 69% yield.[16]

Acetonide protection of triol **31** by using acetone and catalytic amounts of *p*-TsOH gave a mixture of regioisomers **32** and **33** in a 1:1.1 ratio,[17] respectively, and in 91% overall yield.[18] Unfortunately, at this stage alcohols **32** and **33** could not be separated by conventional chromatography. Therefore, the mixture was carried through the synthesis sequence and oxidised under Swern conditions to give the corresponding aldehydes **23** and **34** in 83% overall yield. Here, the two aromatic regioisomers could be chromatographically separated and individually characterised by using standard spectroscopic techniques, as well as NOE difference measurements to determine their substitution pattern. Aldehyde **23**, which represented the desired C-ring building block, was used for the anticipated ring coupling, while compound **34** was used for another independent pathway to mensacarcin (**1**).

The crucial connection of the two A and C-ring aromatic fragments was performed as previously anticipated in the

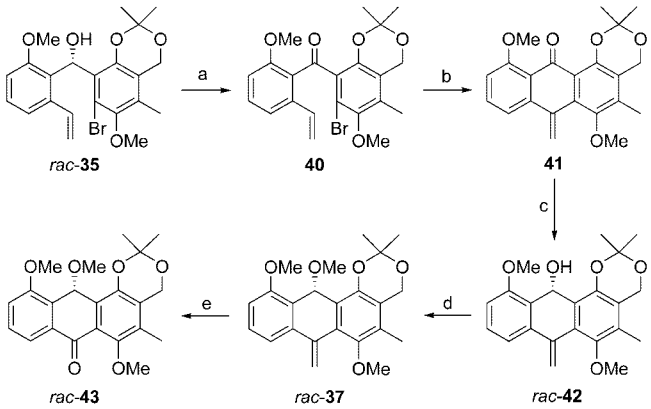
retrosynthesis analysis (Pathway 2, Scheme 2). The aryllithium was prepared in situ from **21** by a lithium–iodine exchange with *n*BuLi (Scheme 5). This was followed by addi-



Scheme 5. Synthesis of tricycle *rac*-**37**. a) **21**, *n*BuLi, THF, −78 °C, 20 min, then **23**, THF, −78 °C, 20 min, 20 °C, 58 %; b) KH, THF, 0 °C, 40 min, then MeI, 20 °C, 1 h, 87 %; c) nBu_4NOAc, DMF/CH_3CN/H_2O, 60 °C, then Herrmann–Beller catalyst, 120 °C, 4 h, 24 %; d) **22**, *n*BuLi, THF, −78 °C, 10 min, then **23**, THF, 20 °C, 35 min, 74 %; e) KH, THF, 0 °C, 40 min, then MeI, 20 °C, 2 h, 91 %; f) PPTS, $(CH_3)_2O$, H_2O, 20 °C→reflux, 3 h, 81 %; g) Ph_3PCH_3Br, NaHMDS, THF, 20 °C, 1 h, then the aldehyde from (f), 20 °C, 1 h, 81 %. PPTS = pyridinium *p*-toluenesulfonate.

tion of the aldehyde **23** which led to formation of the diphenylcarbinol *rac*-**35** in a reasonable yield of 58 %. Initial evidence for the success of this reaction was obtained upon H^1 NMR spectral analysis by observation of a new resonance at $\delta = 6.82$ ppm (d, $J = 8.1$ Hz), which was attributed to the 1-H proton. Subsequent installation of what would become the C-10 methoxy substituent in mensacarcin (**1**) was achieved by subjection of *rac*-**35** to KH and MeI in THF to give *rac*-**36** in 87 % yield. In an effort to improve the aryllithium to aldehyde addition and hence the overall yields, an alternative pathway to compound *rac*-**36**, the intramolecular Heck reaction precursor, was devised. Thus, the aryllithium of acetal **22** was added in the same manner to the aldehyde **23** to give the diphenylcarbinol *rac*-**38** with a superior yield (74 %). The reasons for the protected iodo compound **22** performing better under these conditions than its styrene counterpart **21** are unknown. However, one could assume that the oxygen atoms within the acetal moiety at the *ortho* position facilitate the lithiation and stabilise the formed metal organic compound. Alcohol *rac*-**38** was then methylated by using KH and MeI to give *rac*-**39** (91 %); this was followed by cleavage of the acetal moiety with PPTS in acetone/water (81 %) and olefination with PPh_3CH_3Br and NaHMDS (81 %) to give the desired alkene *rac*-**36**. However, due to the additional steps, the overall yield of this pathway does not exceed the previously mentioned direct and shorter approach to *rac*-**36** by using compound **21** as the substrate.

The intramolecular Heck reaction of olefin *rac*-**36**, with the Herrmann–Beller catalyst,[19] provided the desired methylene tetrahydroanthracene *rac*-**37** in a low yield of 24 % (54 % based on recovery of starting material). After similar poor yields with several other palladium catalysts, the highly electron-donating C-ring within substrate *rac*-**36** was deemed to negatively effect the initial insertion process of the Heck reaction cycle and hence lower the turnover rate of this transformation. With this in mind, a new precursor, benzophenone **40**, was devised to accelerate the Heck transformation. It was thought that such a substrate would lower the C-ring aromatic electron density as well as bring the olefin and the organopalladium intermediate in close proximity to each other through conjugation. Benzophenone **40** was synthesised from *rac*-**35** by using Dess–Martin periodinane in 81 % yield (Scheme 6). As predicted, the intramolecular Heck reaction of this compound proceeded smoothly under the previously described conditions with the Herrmann–Beller catalyst to afford the anthracenone derivative **41** in 74 % yield. This latter tricyclic derivative could be converted into the required compound *rac*-**37**. This conversion was achieved through a reduction with $LiAlH_4$ and a methylation sequence in 37 % overall yield. This poor yield was due to the susceptibility of the intermediate tetrahydroanthracene *rac*-**42** to rearomatise. Finally, an oxidative cleavage of the methylene moiety within anthracene *rac*-**37** by using $RuCl_3$ (5 mol %) and $NaIO_4$ allowed the formation of *rac*-**43**, in 69 % yield, containing the correct ABC tricyclic core and the AB ring functionality as found in mensacarcin (**1**).



Scheme 6. Synthesis of tricycle *rac*-**43**. a) Dess–Martin periodinane, CH_2Cl_2, 20 °C, 15 min, 81 %; b) nBu_4NOAc, DMF/CH_3CN/H_2O, 60 °C, then Herrmann–Beller catalyst, 110 °C, 17 h, 74 %; c) $LiAlH_4$, THF, 0 °C, 10 min; d) NaH, MeI, THF, 0 °C→20 °C, 14 h, 37 % over two steps; e) $RuCl_3$, $NaIO_4$, CCl_4, MeCN, H_2O, 0 °C, 15 min, 69 %.

An essential factor of the described synthesis pathways to provide a viable route to the natural product mensacarcin

(**1**) is the ability to dearomatise the C-ring. Methods for carrying out this transformation include oxidation by using ceric ammonium nitrate (CAN),[16] hypervalent iodine reagents[20] or anodic methods.[21] Initial efforts in this area have been fruitful with the successful CAN oxidation of compound *rac*-**20**.

Conclusion

In summary, we have developed an efficient pathway to the tricyclic carbocycles **17**, **37** and **41**. Furthermore, compounds **37** and **41** could be readily converted into the 12-methoxydihydroanthracenone **43** which contains the desired ABC tricyclic core found in mensacarcin (**1**), the correct AB functionality and the carbon pattern of ring C. It is also expected that, following alternative transformations, compounds **41** and **43** will serve as useful precursors to mensacarcin (**1**). This work demonstrates the value of intramolecular Heck transformations in organic synthesis. The utility of this synthetic pathway for the synthesis of the natural product mensacarcin (**1**) and biologically active analogues is currently being explored within this group.

Experimental Section

General: All reactions were performed in flame-dried glassware under an argon atmosphere. Solvents were dried and purified according to the method defined by Perrin and Armarego.[22] TLC chromatography was performed on precoated aluminium silica gel SIL G/UV254 plates (Macherey, Nagel Co.), and silica gel 32–63 (0.032–0.064 mm; Macherey, Nagel Co.) was used for column chromatography. Apparatus used: melting points: Mettler FP61; IR spectroscopy: Brucker IFS25; UV/Vis spectroscopy: Perkin-Elmer Lambda 9; NMR spectroscopy: Varian VXR-200 (200 MHz, ^{1}H) or Bruker AM-300 (300 MHz, 75 MHz, for ^{1}H and ^{13}C, respectively); MS: Varian MAT 731. For ^{1}H and ^{13}C NMR spectroscopy, $CDCl_3$ and C_6D_6 were used as solvents. HRMS was performed by using a modified peak-matching technique, with an error of ± 2 ppm and a resolution of approximately 10000. Elemental analysis was performed at the Mikroanalytisches Labor des Institutes für Organische und Biomolekulare Chemie der Universität Göttingen.

2-Iodo-3-methoxybenzaldehyde (4): A solution of *N*,*N*′,*N*′-trimethylethylenediamine (3.22 g, 31.5 mmol) in benzene (100 mL) was treated dropwise with *n*BuLi (12.60 mL, 2.5 M in hexane, 31.5 mmol) at 0 °C. The resulting solution was warmed to 20 °C while being continuously stirred for 15 min. The mixture was then cooled again to 0 °C and 3-methoxybenzaldehyde (**13**; 4.00 g, 29.4 mmol) was added in one portion. The resulting yellow solution was stirred for another 15 min at 20 °C before being cooled again to 0 °C and treated with a solution of phenyllithium (44.1 mL, 2.0 M in dibutyl ether, 88.2 mmol). After the mixture was stirred at 20 °C for 7 h, THF (50 mL) was added while the mixture was cooled to −78 °C. This solution was then treated with freshly sublimed iodine (29.9 g, 118 mmol) in THF (50 mL), the cooling bath was removed and the reaction mixture was allowed to warm to 20 °C. After being stirred for a further 12 h, the slurry was diluted with ethyl acetate (100 mL), washed with HCl (1×20 mL, 1 M) and $Na_2S_2O_3$ (3×50 mL, saturated solution), dried ($MgSO_4$), filtered and concentrated under reduced pressure. Subjection of the resulting crude oil to flash chromatography (pentane/EtOAc 19:1) and concentration of the appropriate fractions afforded iodobenzene **4** as a yellow solid (4.23 g, 16.2 mmol, 55 %), recrystallised from EtOAc/hexane. $R_f = 0.5$; m.p. 84 °C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 3.95$ (s, 3H; OCH_3), 7.05 (d, $J = 7.9$ Hz, 1H; 4-H), 7.39 (t, $J = 7.9$ Hz, 1H; 5-H), 7.50 (d, $J = 7.9$ Hz, 1H; 6-H), 10.19 ppm (s, 1H; CHO); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 56.8$, 93.9, 116.0, 122.2, 129.4, 136.7, 158.2, 196.4 ppm; UV/Vis (CH_3CN): λ_{max} ($\log\varepsilon$) = 222.0 (4.4167), 326.5 nm (3.7352); IR (KBr): $\tilde{\nu} = 2849$, 1950, 1562, 1466, 1270, 1013, 787 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 261 (100) $[M]^+$, 133.0 (10), 104.0 (8), 76.0 (12); HRMS: calcd for $C_8H_7IO_2$: 261.9491; confirmed.

(1′*RS*)-7-[1′-Benzyloxy-(2′-iodo-3′-methoxyphenyl)-methyl]-6-methoxy-2,2-dimethyl-8-vinyl-4*H*-benzo[1,3]dioxine (16): A magnetically stirred solution of bromobenzene **12** (500 mg, 1.76 mmol) in Et_2O (20 mL) at −78 °C was treated with *t*BuLi (2.18 mL, 1.7 M in hexane, 3.7 mmol). The resulting mixture was stirred at this temperature for 10 min before being treated with aldehyde **4** (507 mg, 1.94 mmol) in Et_2O (2 mL). Stirring was continued at −78 °C for 30 min and the ensuing solution was warmed to 20 °C. The resulting mixture was diluted with Et_2O (20 mL) and washed with water (2×5 mL), then the organic phases were dried (Na_2SO_4), filtered and concentrated under reduced pressure to afford alcohol **15** as a yellow oil (684 mg, 1.42 mmol, approximately 80 %).[23]

A magnetically stirred solution of alcohol **15** in THF (20 mL) was treated with NaH (141 mg, 60 % in oil, 3.52 mmol) and benzyl bromide (418 μL, 3.52 mmol) at 20 °C. The resulting mixture was warmed to 40 °C and stirring was continued for 12 h. The ensuing cloudy solution was diluted with Et_2O (40 mL), washed with water (2×10 mL), dried (Na_2SO_4), filtered and concentrated under reduced pressure to afford a pale oil. Subjection of this material to flash chromatography (pentane/methyl *tert*-butyl ether 3:1) and concentration of the appropriate fractions afforded benzyl ether **16** as a yellow foam (654 mg, 1.14 mmol, 65 %). $R_f = 0.4$; ^{1}H NMR (300 MHz, C_6D_6): $\delta = 1.42$ (s, 3H; CH_3), 1.44 (s, 3H; CH_3), 3.18 (s, 6H; 2×OCH_3), 4.59 (s, 2H; 4-H), 4.62 (d, $J = 11.0$ Hz, 1H; OCH_2Ph), 4.83 (d, $J = 11.0$ Hz, 1H; OCH_2Ph), 5.43 (dd, $J = 12.0$, 2.6 Hz, 1H; 2″-H), 6.01 (dd, $J = 17.7$, 2.6 Hz, 1H; 2″-H), 6.03 (s, 1H; 7-H), 6.19 (dd, $J = 8.3$, 1.3 Hz, 1H; 4′-H), 6.64 (s, 1H; 5-H), 6.88 (t, $J = 8.0$ Hz, 1H; 5′-H), 7.03–7.20 (m, 3H; Ar-H), 7.30 (dd, $J = 7.8$, 1.4 Hz, 1H; 6′-H), 7.40–7.51 ppm (m, 3H; Ar-H, 1″-H); ^{13}C NMR (50.3 MHz, C_6D_6): $\delta = 24.7$, 25.1, 55.9, 55.9, 61.2, 71.7, 82.1, 94.0, 99.5, 106.6, 110.1, 119.9, 120.8, 126.1, 123.0, 127.8, 128.2, 128.3, 128.9, 132.0, 139.2, 144.2, 145.7, 152.6, 158.7 ppm; IR (KBr): $\tilde{\nu} = 3442$, 3029, 2938, 2838, 1726, 1603, 1584, 1463, 1425, 1340, 1385, 1279, 1202, 1065, 851, 797 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 572.0 (28) $[M]^+$, 513.9 (20) $[M-C_3H_6O]^+$, 422.9 (100), 387.1 (38), 279.0 (24), 165.0 (20), 91.0 (100) $[C_7H_7]^+$; HRMS: calcd for $C_{28}H_{29}IO_5$: 572.1059; confirmed.

(7*RS*)-7-Benzyloxy-6,11-dimethoxy-2,2-dimethyl-12-methylene-7,12-dihydro-4*H*-1,3-dioxabenzo[*a*]anthracene (17): A magnetically stirred solution of $Pd(OAc)_2$ (16 mg, 5 mol %, 77 μmol), PPh_3 (36 mg, 10 mol %, 1.4 mmol), nBu_4NCl (793 mg, 2.86 mmol) and K_2CO_3 (395 mg, 2.86 mmol) in DMF (30 mL) was heated at 40 °C for 30 min. The resulting solution was treated with olefin **16** (818 mg, 1.43 mmol) in one portion and the mixture was immediately degassed and heated to 80 °C. Stirring was continued at this temperature for 12 h, before the solution was cooled to 20 °C. The ensuing mixture was diluted with Et_2O (60 mL), washed with water (1×10 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting crude oil was subjected to flash chromatography (pentane/methyl *tert*-butyl ether 1:1) and concentration of the appropriate fractions afforded anthracene **17** as a yellow foam (540 mg, 1.22 mmol, 85 %). $R_f = 0.6$; ^{1}H NMR (300 MHz, C_6D_6): $\delta = 1.28$ (s, 3H; CH_3), 1.46 (s, 3H; CH_3), 3.21 (s, 3H; OCH_3), 3.33 (s, 3H; OCH_3), 4.56 (d, $J = 15.3$ Hz, 1H; 4-H), 4.62 (d, $J = 15.3$ Hz, 1H; 4-H), 4.62 (d, $J = 12.0$ Hz, 1H; OCH_2Ph), 4.68 (d, $J = 12.0$ Hz, 1H; OCH_2Ph), 6.01 (s, 1H; 5-H), 6.20 (s, 1H; 7-H), 6.54 (dd, $J = 7.3$, 2.5 Hz, 1H; 10-H), 6.78 (s, 2H; 1′-H), 6.97–7.13 (m, 5H; Ar-H), 7.31–7.38 ppm (m, 2H; Ar-H); ^{13}C NMR (150.8 MHz, C_6D_6): $\delta = 24.1$, 25.5, 55.1, 55.6, 61.3, 69.8, 71.4, 99.4, 105.5, 111.5, 120.1, 122.0, 122.2, 127.2, 127.6, 127.9, 128.2, 125.4, 127.7, 129.6, 132.0, 137.9, 140.1, 142.8, 150.9, 157.4 ppm; IR (KBr): $\tilde{\nu} = 3424$, 2937, 1601, 1461, 1434, 1384, 1265, 1139, 858, 799 cm^{-1}; UV/Vis (CH_3CN): λ_{max} ($\log\varepsilon$) = 191.0 (4.8328), 306.0 nm (3.7432); MS (EI, 70 eV): *m*/*z* (%): 444.0 (8) $[M]^+$, 386.0 (5) $[M-C_3H_6O]^+$, 279.0 (100), 249.0 (8), 91.0 (1) $[C_7H_7]^+$; HRMS: calcd for $C_{28}H_{28}O_5$: 444.519; confirmed; elemental analysis calcd (%) for $C_{28}H_{28}O_5$: C 75.65, H 6.35; found: C 75.71, H 6.20.

(7*RS*)-7-Benzyloxy-6,11-dimethoxy-2,2-dimethyl-4,7-dihydro-1,3-dioxabenzo[*a*]anthracen-12-one (18): A magnetically stirred solution of compound **17** (293 mg, 0.66 mmol) in CCl_4/MeCN/H_2O 1:1:1.5 (10.5 mL) at 20 °C was treated in one portion with a mixture of $RuCl_3$ (6.8 mg, 5 mol %, 0.03 mmol) and $NaIO_4$ (705 mg, 3.0 mmol). After being stirred for 20 min, the suspension was diluted with CH_2Cl_2 (10 mL), washed with

water (1×5 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting brown solid was diluted with pentane (10 mL), filtered and washed further with pentane (1×5 mL) to afford crude anthracenone **18** as a brown solid (254 mg, 0.57 mmol, 81%). ^{1}H NMR (300 MHz, C_6D_6): δ=1.37 (s, 3H; CH_3), 1.53 (s, 3H; CH_3), 3.25 (s, 3H; OCH_3), 3.28 (s, 3H; OCH_3), 4.45 (d, J=12.0 Hz, 1H; OCH_2Ph), 4.50 (s, 2H; 4-H), 4.52 (d, J=12.0 Hz, 1H; OCH_2Ph), 5.98 (s, 1H; 7-H), 6.09 (br s, 1H; 5-H), 6.42 (d, J=8.6 Hz, 1H; 10-H), 6.86 (d, J=7.3 Hz, 1H; 8-H), 6.96–7.11 (m, 4H; Ar-H), 7.18–7.24 ppm (m, 2H; Ar-H); ^{13}C NMR (75.5 MHz, C_6D_6): δ=24.7, 24.9, 55.4, 55.8, 61.0, 69.2, 69.6, 100.0, 110.5, 112.7, 121.2, 121.6, 127.3, 127.9, 128.2, 132.2, 125.8, 126.8, 139.3, 141.4, 144.9, 150.1, 159.3, 183.2 ppm; IR (KBr): $\tilde{\nu}$=3424, 3002, 2941, 2841, 1680, 1472, 1431, 1384, 1270, 1196, 1141, 1087, 1020, 865, 742 cm^{-1}; UV/Vis (CH_3CN): λ_{max} ($\log\varepsilon$)=191.0 (4.8334), 287.5 (3.4882), 332.0 (3.6248), 357.0 nm (3.6562); MS (EI, 70 eV): m/z (%): 446.4 (24) $[M]^+$, 388.4 (16) $[M-C_3H_6O]^+$, 282.2 (100), 267.2 (30), 253.2 (20), 239.2 (24), 167.1 (30), 149.1 (50), 108.1 (20), 91.0 (28) $[C_7H_7]^+$; HRMS: calcd for $C_{27}H_{26}O_6$: 446.1729; confirmed.

(7*RS*,12*RS*)-7-Benzyloxy-6,11-dimethoxy-2,2-dimethyl-7,12-dihydro-4*H*-1,3-dioxabenzo[*a*]anthracen-12-ol (19): A magnetically stirred solution of ketone **18** (251 mg, 0.56 mmol) in THF (10 mL) at 0°C was treated dropwise with $LiAlH_4$ (674 μL, 1M in THF, 674 mmol). Stirring was continued for 30 min before the solution was warmed to 20°C. The ensuing suspension was then quenched dropwise with water (2 mL), extracted with Et_2O (3×10 mL), washed with brine (2 mL), dried (Na_2SO_4), filtered and concentrated under reduced pressure to give a yellow oil. Subjection of this material to flash chromatography (pentane/methyl *tert*-butyl ether 1:1) and concentration of the appropriate fractions gave anthracenol **19** as a yellow foam (223 mg, 0.51 mmol, 91%). R_f=0.4; ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.52 (s, 3H; CH_3), 1.60 (s, 3H; CH_3), 3.22 (d, J=10.1 Hz, 1H; OH), 3.75 (s, 3H; OCH_3), 3.89 (s, 3H; OCH_3), 4.46 (d, J=12.2 Hz, 1H; OCH_2Ph), 4.52 (d, J=12.2 Hz, 1H; OCH_2Ph), 4.77 (d, J=15.5 Hz, 1H; 4-H), 4.84 (d, J=15.5 Hz, 1H; 4-H), 5.70 (s, 1H; 7-H), 6.29 (d, J=10.1 Hz, 1H; 12-H), 6.44 (s, 1H; 5-H), 6.88 (d, J=8.5 Hz, 1H; 10-H), 6.97 (d, J=7.2 Hz, 1H; 8-H), 7.19–7.39 ppm (m, 6H; Ar-H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=24.7, 24.8, 55.7, 55.9, 57.2, 61.0, 69.9, 70.3, 99.7, 106.2, 111.0, 120.2, 121.3, 126.3, 128.7, 130.5, 138.2, 139.1, 127.4, 127.9, 128.1, 128.5, 142.7, 150.6, 157.3 ppm; IR (KBr): $\tilde{\nu}$=3430, 2937, 2872, 1588, 1482, 1434, 1375, 1303, 1281, 1248, 1201, 1098, 1024, 994, 954, 851, 799 cm^{-1}; UV/Vis (CH_3CN): λ_{max} ($\log\varepsilon$)=192.5 (4.8358), 307.0 nm (3.7024); MS (EI, 70 eV): m/z (%): 448.1 (20) $[M]^+$, 430.1 (4) $[M-H_2O]^+$, 390.1 (8) $[M-C_3H_6O]^+$, 372.1 (20), 282.0 (100), 266.0 (74), 254.0 (20), 91.0 (20) $[C_7H_7]^+$; HRMS: calcd for $C_{27}H_{28}O_6$: 448.1886; confirmed.

(7*RS*,12*RS*)-7-Benzyloxy-6,11,12-trimethoxy-2,2-dimethyl-7,12-dihydro-4*H*-1,3-dioxabenzo[*a*]anthracene (20): A magnetically stirred solution of alcohol **19** (210 mg, 0.47 mmol) in THF (10 mL) at 20°C was treated with NaH (37 mg, 60% in oil, 0.94 mmol) and methyl iodide (59 μL, 0.94 mmol). The resulting mixture was warmed to 40°C and stirred for a further 12 h. After this time, the reaction was cooled to 20°C, diluted with Et_2O (10 mL) and washed with water (5 mL). The water layer was extracted further with Et_2O (3×10 mL) and the combined organic phases were dried (Na_2SO_4), filtered and concentrated under reduced pressure. Subjection of the resulting crude oil to flash chromatography (pentane/methyl *tert*-butyl ether 2:1) and concentration of the appropriate fractions afforded anthracenol **20** as a yellow oil (208 mg, 0.45 mmol, 96%). R_f=0.2; ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.55 (s, 3H; CH_3), 1.61 (s, 3H; CH_3), 3.54 (s, 3H; OCH_3), 3.76 (s, 3H; OCH_3), 3.91 (s, 3H; OCH_3), 4.53 (d, J=12.5 Hz, 1H; OCH_2Ph), 4.64 (d, J=12.5 Hz, 1H; OCH_2Ph), 4.80 (d, J=14.5 Hz, 1H; 4-H), 4.87 (d, J=14.5 Hz, 1H; 4-H), 5.69 (s, 1H; 12-H), 6.02 (s, 1H; 7-H), 6.47 (s, 1H; 5-H), 6.89 (d, J=8.2 Hz, 1H; 10-H), 6.97 (d, J=7.9 Hz, 1H; 8-H), 7.17–7.31 (m, 4H; Ar-H), 7.33–7.39 ppm (m, 2H; Ar-H); ^{13}C NMR (150.8 MHz, $CDCl_3$): δ=24.7, 25.1, 55.7, 55.9, 55.9, 64.7, 61.1, 69.1, 69.4, 99.5, 111.4, 119.4, 122.3, 126.5, 127.8, 127.0, 127.7, 128.1, 128.7, 138.7, 139.4, 143.2, 151.3, 157.8 ppm; IR (KBr): $\tilde{\nu}$=3449, 2992, 2936, 2838, 1603, 1589, 1464, 1434, 1384, 1279, 1100, 990, 864, 798, 739 cm^{-1}; UV/Vis (CH_3CN): λ_{max} ($\log\varepsilon$)=190.5 (4.8915), 192.0 (4.8935), 94.5 (4.8872), 199.0 (4.8685), 307.0 nm (3.7363); MS (EI, 70 eV): m/z (%): 462.1 (26) $[M]^+$, 430.1 (2) $[M-CH_3OH]^+$, 373.1 (8), 266.1 (100), 223 (8), 91.0 (20) $[C_7H_7]^+$; HRMS: calcd for $C_{28}H_{30}O_6$: 462.2042; confirmed.

2-Iodo-3-vinyl-anisole (21): A solution of Ph_3PCH_3Br (1.38 g, 3.87 mmol) in THF (50 mL) was treated with sodium bis(trimethylsilyl) amide (3.87 mL, 1M in THF, 3.87 mmol) and stirred for 1 h at 20°C. The reaction mixture was then treated with a solution of 2-iodo-3-methoxybenzaldehyde **4** (676 mg, 2.58 mmol) in THF (20 mL) and stirred for 1 h, before silica gel was added and the suspension concentrated under reduced pressure. Subjection of the resulting yellow solid to the flash chromatography (pentane/EtOAc 9:1) and concentration of the appropriate fractions afforded styrene **21** as a white solid (601 mg, 2.31 mmol, 90%) recrystallised from EtOAc/hexane. R_f=0.8; m.p. 64°C; ^{1}H NMR (200 MHz, $CDCl_3$): δ=3.87 (s, 3H; OCH_3), 5.30 (d, J=11.0 Hz, 1H; 2′-H), 5.62 (d, J=17.3 Hz, 1H; 2′-H), 6.71 (d, J=7.5 Hz, 1H; 6-H), 7.00 (dd, J=17.3, 11.0 Hz, 1H; 1′-H), 7.12 (d, J=7.5 Hz, 1H; 4-H), 7.24 ppm (t, J=7.5 Hz, 1H; 5-H); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ=56.5, 92.0, 100.7, 116.9, 122.2, 129.4, 136.7, 158.2, 196.4 ppm; IR (KBr): $\tilde{\nu}$=3081, 2962, 2935, 1616, 1558, 1465, 1057, 786 cm^{-1}; UV/Vis (CH_3CN): λ_{max} ($\log\varepsilon$)=222.0 (4.4427), 296.5 (3.3006), 249.0 nm (3.9419); MS (EI, 70 eV): m/z (%): 260.0 (100) $[M]^+$, 245.0 (8) $[M-CH_3]^+$, 104.0 (8), 133.1 (4) $[M-I]^+$; HRMS: calcd for C_9H_9IO: 259.9698; confirmed.

2-(2′-Iodo-3′-methoxyphenyl)-[1,3]dioxane (22): A magnetically stirred solution of aldehyde **4** (1.73 g, 6.65 mmol) in benzene (60 mL) was treated with 1,3-propanediol (961 μL, 13.30 mmol) and amberlyst 15 (192 mg) at 20°C. The resulting mixture was heated to reflux for 5 h with a Dean–Stark apparatus. After cooling, the mixture was diluted with Et_2O (60 mL), washed with H_2O (4×10 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting white solid was recrystallised (EtOAc/hexane) to afford acetal **22** as white solid (1.40 g, 4.39 mmol, 66%). M.p. 134°C; ^{1}H NMR (200 MHz, C_6H_6): δ=0.58–0.78 (m, 1H; 5-H), 1.70–2.00 (m, 1H; 5-H), 3.15 (s, 3H; OCH_3), 3.51–3.68 (m, 2H; 4-H/6-H), 3.33–3.97 (m, 2H; 4H/6-H), 5.79 (s, 1H; 2-H), 6.19 (d, J=8.3 Hz, 1H; 4′-H), 6.99 (t, J=8.0 Hz, 1H; 5′-H), 7.65 ppm (d, J=7.7 Hz, 1H; 6′-H); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ=25.6, 56.6, 67.5, 90.1, 105.2, 111.4, 120.0, 129.3, 142.0, 157.7 ppm; IR (KBr): $\tilde{\nu}$=2972, 1571, 1433, 1379, 1267, 1105, 1065, 991, 781 cm^{-1}; UV/Vis (CH_3CN): λ_{max} ($\log\varepsilon$)=204.5 (4.5436), 280.0 (3.5111), 287.0 (3.5195), 227.0 nm (0.3184); MS (EI, 70 eV): m/z (%): 320.1 (100) $[M]^+$, 319.2 (76) $[M-H]^+$, 261.1 (17) $[M-C_3H_6O]^+$; HRMS: calcd for $C_{11}H_{13}IO_3$: 320.1240; confirmed.

3-Bromo-4-methoxy-5-methylbenzoic acid (27): A magnetically stirred solution of carboxylic acid **26** (88.0 g, 0.53 mol) in dioxane (850 mL) was treated dropwise with bromine (54.0 mL, 1.06 mol) at 20°C. Stirring was continued in the absence of light for 7 days before the reaction mixture was diluted with diethyl ether (300 mL), transferred to a separating funnel and washed vigorously with an aqueous saturated solution of $Na_2S_2O_3$ until the solution changed from orange to yellow (approximately 2×100 mL). The remaining organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure to give bromobenzene **27** as a pale yellow solid (109.1 g, 0.44 mol, 84%) recrystallised from EtOAc/pentane. M.p. 160°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.35 (s, 3H; CH_3), 3.81 (s, 3H; OCH_3), 7.84 (d, J=1.1 Hz, 1H; Ar-H), 8.11 ppm (d, J=1.1 Hz, 1H; Ar-H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=16.6, 61.5, 64.0, 117.3, 130.2, 132.5, 133.0, 159.9, 170.5 ppm; IR (KBr): $\tilde{\nu}$=2950, 1603, 1416, 1104, 775, 661 cm^{-1}; UV/Vis: λ_{max} ($\log\varepsilon$)=208 (4.4228), 245 nm (3.7995); MS (EI, 70 eV): m/z (%): 246.1 (96), 244.1 (100) $[M]^+$, 229.1 (68), 227.1 (55) $[M-H_2O]^+$, 166.1 (30) $[M-Br]^+$; HRMS: calcd for $C_9H_9BrO_3$: 243.9735; confirmed.

(3-Bromo-4-methoxy-5-methylphenyl)-methanol (28): A magnetically stirred solution of carboxylic acid **27** (60.5 g, 0.25 mol) in THF/Et_2O 1:1 (300 mL) was treated with $LiAlH_4$ (70.0 mL, 2.64M in Et_2O, 0.185 mol) through a cannula over 30 min at 0°C. Stirring was continued for a further 30 min before the reaction mixture was treated with $MgSO_4$ (51 g) and with water (38 mL) dropwise. The resulting suspension was filtered and washed thoroughly with Et_2O (6×50 mL). The combined organic fractions were dried ($MgSO_4$), filtered and concentrated under reduced pressure to give a yellow oil. Subjection of the resulting crude oil to flash chromatography (pentane/EtOAc 9:1) and concentration of the appropriate fractions afforded alcohol **28** as a pale yellow oil (41.6 g, 0.18 mmol, 72%). R_f=0.3; ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.29 (s, 3H; CH_3), 3.80 (s, 3H; OCH_3), 4.55 (s, 2H; 1′-H), 7.07 (d, J=0.8 Hz, 1H; Ar-H), 7.35 ppm (d, J=0.8 Hz, 1H; Ar-H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=16.6, 60.1, 64.2, 117.2, 128.5, 129.4, 133.2, 137.9, 154.6 ppm; IR (KBr): $\tilde{\nu}$=2931, 1736, 1478, 1276, 821 cm^{-1}; UV/Vis: λ_{max} ($\log\varepsilon$)=201.5 (4.6209),

272.5 nm (2.8340); MS (EI, 70 eV): *m/z* (%): 232.1 (98), 230.1 (100) $[M]^+$, 215.1 (25), 213.1 (20) $[M-OH]^+$, 153.2 (33), 151.2 (30) $[M-Br]^+$; HRMS: calcd for $C_9H_{11}BrO_2$: 229.9943; confirmed.

3-Bromo-4-methoxy-5-methylbenzaldehyde (29): A magnetically stirred solution of alcohol **28** (17.8 g, 0.08 mol) in CH_2Cl_2 (400 mL) was treated with MnO_2 (67.0 g, 0.80 mol) in one portion at 20 °C. Stirring was continued for 12 h before the reaction mixture was filtered and washed thoroughly with CH_2Cl_2 (3×100 mL). The organic filtrate was concentrated under reduced pressure to give a yellow oil. Subjection of the resulting crude oil to flash chromatography (pentane/EtOAc 19:1) and concentration of the appropriate fractions afforded the aldehyde **29** as a yellow oil (16.1 g, 0.07 mol, 87%). R_f=0.3; ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.36 (s, 3H; CH_3), 3.84 (s, 3H; OCH_3), 7.61 (d, J=1.8 Hz, 1H; Ar-H), 7.87 (d, J=1.8 Hz, 1H; Ar-H), 9.82 ppm (s, 1H; CHO); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=16.5, 60.2, 118.1, 131.5, 132.6, 133.2, 134.1, 160.4, 189.8 ppm; IR (KBr): $\tilde{\nu}$=1695, 1271, 1110, 740 cm^{-1}; UV/Vis: λ_{max} ($\log\varepsilon$)=217.0 (4.3877), 261 nm (4.0649); MS (EI, 70 eV): *m/z* (%): 230.1 (100), 228.1 (97) $[M]^+$, 213.1 (8), 215.1 (6) $[M-CH_3]^+$, 187.1 (6), 185.0 (8) $[M-C_2H_3O]^+$, 171.0 (5), 77.1 (44) $[C_6H_5]^+$; HRMS: calcd for $C_9H_9{}^{79}BrO_2$: 227.9786; confirmed.

3-Bromo-4-methoxy-5-methylphenol (30): A magnetically stirred solution of aldehyde **29** (2.6 g, 11.4 mmol) in CH_2Cl_2 (100 mL) was treated with *m*-CPBA (4.1 g, 70% in water, 17.0 mmol) in one portion at 20 °C. Stirring was continued for 12 h before the CH_2Cl_2 was removed under reduced pressure. The ensuing white solid was diluted with MeOH (150 mL), treated with K_2CO_3 (2.3 g, 17.0 mmol) and stirred at 20 °C for 15 min. The resulting mixture was treated with silica gel (3.5 g), concentrated under reduced pressure and subjected to flash chromatography (pentane/EtOAc 9:1). Concentration of the appropriate fractions afforded phenol **30** as colourless solid (1.68 g, 7.7 mmol, 68%) recrystallised from EtOAc/pentane. R_f=0.2; m.p. 114 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.25 (s, 3H; CH_3), 3.82 (s, 3H; OCH_3), 7.61 (d, J=1.2 Hz, 1H; Ar-H), 7.87 (d, J=1.2 Hz, 1H; Ar-H), 9.82 ppm (s, 1H; OH); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=16.7, 60.5, 117.1, 117.2, 117.5, 133.6, 148.8, 152.2 ppm; IR (KBr): $\tilde{\nu}$=2951, 1602, 1456, 1418, 1225, 760 cm^{-1}; UV/Vis: λ_{max} ($\log\varepsilon$)=199.5 (4.6526), 289.0 nm (3.5079); MS (EI, 70 eV): *m/z* (%): 218.0 (90), 216.0 (89) $[M]^+$, 203.0 (95), 201.0 (100) $[M-CH_3]^+$; HRMS: calcd for $C_8H_9BrO_2$: 215.9786; confirmed; elemental analysis calcd (%) for $C_8H_9BrO_2$: C 44.27, H 4.18; found: C 44.27, H 3.95.

3-Bromo-2,6-bis(hydroxymethyl)-4-methoxy-5-methylphenol (31): A magnetically stirred solution of phenol **30** (2.0 g, 9.2 mmol), formaldehyde (1.76 mL, 30% in water, 23.4 mmol) in water (7.6 mL) was treated with CaO (258 mg, 4.6 mmol) at 20 °C. The resulting mixture was stirred for 30 min before being left unstirred in the dark for 5 days. The resulting suspension was dissolved in warm $CHCl_3$ (50 mL) and acetic acid (10 mL) and then diluted twofold with $CHCl_3$. The organic phase was washed with a saturated aqueous solution of $NaHCO_3$ until the acetic acid was removed. The mixture was concentrated under reduced pressure to afford a yellow solid. This crude solid was washed with pentane/EtOAc 4:1 to afford triol **31** as a colourless solid (1.67 g, 6.4 mmol, 69%), recrystallised from EtOAc/hexane. R_f=0.4; m.p. 132 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.26 (s, 3H; CH_3), 2.76 (br s, 1H; OH), 2.81 (br s, 1H; OH), 3.68 (s, 3H; OCH_3), 4.77 (s, 2H; CH_2), 4.96 (s, 2H; CH_2), 8.89 ppm (s, 1H; OH); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=12.5, 58.2, 60.5, 62.9, 109.9, 117.7, 124.2, 126.7, 131.5, 153.2 ppm; IR (KBr): $\tilde{\nu}$=3384, 3259, 2959, 1453, 1005, 760 cm^{-1}; UV/Vis: λ_{max} ($\log\varepsilon$)=205.5 nm (4.6195); MS (EI, 70 eV): *m/z* (%): 278.1 (58), 276.1 (60) $[M]^+$, 260.1 (57), 258.1 (59) $[M-H_2O]^+$, 245.1 (100), 243.1 (90) $[M-H_2O-CH_3]^+$, 229.1 (45), 231 (40); HRMS: calcd for $C_{10}H_{13}BrO_4$: 275.9997; confirmed.

(7-Bromo-6-methoxy-2,2,5-trimethyl-4*H*-benzo[1,3]dioxin-8-yl)-methanol (32) and (5-bromo-6-methoxy-2,2,7-trimethyl-4*H*-benzo[1,3]dioxin-8-yl)-methanol (33): A magnetically stirred solution of triol **31** (1.92 g, 7.0 mol) in acetone (100 mL) at 20 °C was treated with a few crystals of *p*-TsOH. The resulting mixture was stirred for 18 h then concentrated under reduced pressure to afford a colourless oil. Subjection of the resulting crude oil to flash chromatography (pentane/EtOAc 4:1) and concentration of the appropriate fractions afforded a mixture of two regioisomeric acetonides **32** and **33** as a colourless oil (2.02 g, 6.37 mmol, 91%); R_f= 0.3.

(7-Bromo-6-methoxy-2,2,5-trimethyl-4*H*-benzo[1,3]dioxin-8-carbaldehyde (23) and (5-bromo-6-methoxy-2,2,7-trimethyl-4*H*-benzo[1,3]dioxin-8-carbaldehyde (34): A solution of oxalyl chloride (436 μL, 5.06 mmol) in CH_2Cl_2 (20 mL) at −78 °C was added through a cannula over 30 min to a magnetically stirred solution of DMSO (719 μL, 0.01 mol) in CH_2Cl_2 (20 mL), also maintained at −78 °C. The resulting clear solution was treated dropwise with a mixture of **32** and **33** (1.0 g, 3.16 mmol in 6 mL of CH_2Cl_2) from the above reaction, stirred at −78 °C for 1.5 h and then treated dropwise with NEt_3 (1.9 mL). The solution was stirred at this temperature for 5 min before being warmed to 20 °C and stirred for a further 30 min. The ensuing solution was quenched with water (20 mL) and extracted with CH_2Cl_2 (3×20 mL). The combined organic fractions were dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a pale oil. Subjection of the crude oil to flash chromatography (pentane/EtOAc 20:1) and concentration of the appropriate fractions afforded aldehydes **23** and **34**.

Compound **23**: A colourless solid (420 mg, 1.33 mmol, 42%), recrystallised from pentane/EtOAc; R_f=0.3; m.p. 122 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.55 (s, 6H; 2×CH_3), 2.17 (s, 3H; CH_3), 3.75 (s, 3H; OCH_3), 4.71 (s, 2H; CH_2), 10.32 ppm (s, 1H; CHO); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=12.1, 24.6, 59.7, 60.7, 100.1, 117.3, 118.9, 121.4, 134.4, 149.1, 150.7, 189.4; IR (KBr): $\tilde{\nu}$=2986, 1697, 1580, 1396, 1005 cm^{-1}; UV/Vis: λ_{max} ($\log\varepsilon$) 195.5 (4.3540), 268.5 (3.8656), 334.0 nm (0.1779); MS (EI, 70 eV): *m/z* (%): 316.1 (45), 314.1 (44) $[M]^+$, 258.0 (98), 256.0 (100) $[M-C_3H_6O]^+$, 243.0 (45), 241.0 (40) $[M-C_3H_6O-CH_3]^+$; HRMS: calcd for $C_{13}H_{15}BrO_4$: 314.0154; found: 314.0154; elemental analysis: calcd (%) for $C_{13}H_{15}BrO_4$: C 49.54, H 4.80; found: C 49.68, H 4.62.

Compound **34**: A colourless solid (410 mg, 1.30 mmol, 41%), recrystallised from pentane/EtOAc; R_f=0.5; m.p. 107 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.56 (s, 6H; 2×CH_3), 2.53 (s, 3H; CH_3), 3.72 (s, 3H; OCH_3), 4.74 (s, 2H; CH_2), 10.49 ppm (s, 1H; CHO); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=13.6, 24.5, 60.6, 61.9, 100.4, 118.2, 121.7, 122.4, 133.7, 148.9, 151.9, 191.1 ppm; IR (KBr): $\tilde{\nu}$=2996, 2938, 1685, 1563, 1451, 839 cm^{-1}; UV/Vis: λ_{max} ($\log\varepsilon$)=220.0 (4.4725), 332.0 nm (4.3181); MS (EI, 70 eV): *m/z* (%): 316.1 (45), 314.1 (44) $[M]^+$, 258.0 (98), 256.0 (100) $[M-C_3H_6O]^+$, 243.0 (45), 241.0 (40) $[M-C_3H_6O-CH_3]^+$; HRMS: calcd for $C_{13}H_{15}BrO_4$: 314.0154; confirmed.

(1′*RS*)-(7-Bromo-6-methoxy-2,2,5-trimethyl-4*H*-benzo[1,3]dioxin-8-yl)-(3′-methoxy-7′-vinylphenyl)-methanol (35): A magnetically stirred solution of iodobenzene **21** (240 mg, 0.92 mmol) in THF (10 mL) at −78 °C was treated dropwise with *n*BuLi (406 μL, 2.5 M in hexane, 1.01 mmol). The resulting mixture was stirred at this temperature for 20 min before being treated with aldehyde **23** (264 mg, 0.84 mmol) in THF (5 mL). Stirring was continued at this temperature for 20 min then the solution was warmed to 20 °C and quenched immediately with a saturated aqueous solution of NH_4Cl (4 mL). The resulting mixture was extracted with diethyl ether (3×10 mL) and washed with brine (1×2 mL), then the combined organic fractions were dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a clear yellow oil. Subjection of the resulting crude oil to flash chromatography (pentane/EtOAc 9:1) and concentration of the appropriate fractions afforded diphenylcarbinol **35** as a colourless solid (220 mg, 0.49 mmol, 58%) recrystallised from EtOAc/hexane. R_f=0.3; m.p. 128 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.95 (s, 3H; Me) 1.33 (s, 3H; CH_3), 2.10 (s, 3H; CH_3), 3.74 (s, 3H; OCH_3), 3.79 (s, 3H; OCH_3), 4.61 (dd, J=22.5, 7.2 Hz, 2H; 4-H), 5.15 (dd, J=10.8, 1.8 Hz, 1H; 2″-H), 5.39 (dd, J=17.1, 1.8 Hz, 1H; 2″-H), 6.48 (d, J=9.0 Hz, 1H; Ar-H), 6.82 (d, J=8.1 Hz, 1H; 1′-H), 6.92 (d, J=17.1, 10.8 Hz, 1H; 1″-H), 7.00 (d, J=7.5 Hz, 1H; Ar-H), 7.18 ppm (t, J=8.4 Hz, 1H; Ar-H); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ=11.3, 22.6, 25.0, 55.9, 60.1, 60.6, 73.0, 98.6, 110.9, 116.2, 118.4, 119.1, 120.0, 126.8, 127.5, 128.2, 129.1, 135.8, 138.4, 146.2, 148.7, 158.1 ppm; IR (KBr): $\tilde{\nu}$=3500, 1569, 1408, 1261, 1044 cm^{-1}; UV/Vis: λ_{max} ($\log\varepsilon$)=207.5 (4.7345), 293.5 nm (3.7238); MS (EI, 70 eV): *m/z* (%): 450.2 (1), 448.2 (1) $[M]^+$, 392.1 (88) $[M-C_3H_6O]^+$, 390.1 (92), 311.2 (100) $[M-C_3H_6O-Br]^+$, 293 (36), 148.1 (47); HRMS: calcd for $C_{22}H_{25}BrO_5$: 448.0885; confirmed.

(1′*RS*)-7-Bromo-6-methoxy-8-[1′-methoxy-(3′-methoxy-7′-vinylphenyl)-methyl]-2,2,5-trimethyl-4*H*-benzo[1,3]dioxine (36): A magnetically stirred solution of diphenylcarbinol **35** (145 mg, 0.32 mmol) in THF (5 mL) was treated with KH (26 mg, 0.65 mmol) in one portion at 0 °C. Stirring was continued for 40 min before the reaction mixture was treated dropwise with MeI (40 μL, 0.64 mmol). The ensuing solution was warmed to

20 °C and stirred for a further 1 h before being treated with water (2 mL) and extracted with diethyl ether (3×5 mL). The combined organic fractions were dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a colourless solid. Subjection of this material to flash chromatography (pentane/EtOAc 19:1) and concentration of the appropriate fractions afforded methyl ether **36** as colourless solid (130 mg, 0.28 mmol, 87 %) recrystallised from EtOAc. R_f=0.4; m.p. 202 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.72 (s, 3H; CH_3), 1.29 (s, 3H; CH_3), 2.06 (s, 3H; CH_3), 3.36 (s, 3H; OCH_3), 3.58 (s, 3H; OCH_3), 3.75 (s, 3H; OCH_3), 4.65 (dd, J=26.5, 15.6 Hz, 2H; 4-H), 5.12 (dd, J=10.8, 1.8 Hz, 1H; 2″-H), 5.43 (dd, J=17.5, 1.8 Hz, 1H; 2″-H), 6.17 (s, 1H; 1′-H), 6.67 (dd, J=8.1, 0.9 Hz, 1H; 4′-H), 7.06 (t, J=8.4 Hz, 1H; Ar-H), 7.14 (t, J=7.8 Hz, 1H; Ar-H), 7.81 ppm (dd, J=17.5, 10.8 Hz, 1H; 1″-H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=11.3, 21.7, 25.4, 55.7, 57.6, 60.0, 60.5, 80.4, 98.5, 109.6, 112.5, 118.6, 120.0, 121.2, 126.7, 127.0, 127.1, 127.2, 139.9, 140.1, 146.2, 148.5, 156.9 ppm; IR (KBr): $\tilde{\nu}$=2937, 1408, 1071 cm^{-1}; UV/Vis: λ_{max} ($\log\varepsilon$)= 294.5 (3.7312), 206.5 nm (4.5609); MS (EI, 70 eV): m/z (%): 464.2 (1), 462.0 (>1) $[M]^+$, 384.2 (12), 374.1 (13), 294.2 (100); HRMS: calcd for $C_{23}H_{27}BrO_5$: 462.1042; confirmed; elemental analysis calcd (%) for $C_{23}H_{27}BrO_5$: C 59.62, H 5.87; found: C 59.38, H 5.71.

(12*RS*)-6,11,12-Trimethoxy-2,2,5-trimethyl-7-methylene-7,12-dihydro-4*H*-1,3-dioxabenzo[*a*]anthracene (37): A magnetically stirred solution of olefin **36** (70 mg, 0.15 mmol) and nBu$_4$NOAc (46 mg, 0.15 mmol) in a previously degassed mixture of DMF/CH_3CN/H_2O 5:5:1 (2 mL) at 60 °C was treated with *trans*-di(μ-acetato)-bis[*ortho*(di-*ortho*-tolylphosphino)-benzyl]-dipalladium(II) catalyst (14 mg, 0.015 mmol) in one portion. The resulting suspension was heated to 120 °C and stirring was continued for 4 h. The ensuing brown mixture was diluted with diethyl ether (20 mL) and washed with water (3×3 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a crude brown solid. Subjection of this material to flash chromatography (pentane/EtOAc19:1) and concentration of the appropriate fractions afforded tetrahydroanthracene **37** as a yellow solid (14 mg, 0.004 mmol, 24 %) and starting material **36** (40 mg, 0.086 mmol).

37: R_f=0.2; ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.57 (s, 3H; CH_3), 1.61 (s, 3H; CH_3), 2.11 (s, 3H; CH_3), 3.30 (s, 3H; OCH_3), 3.57 (s, 3H; OCH_3), 9.92 (s, 3H; OCH_3), 4.77 (s, 2H; 4-H), 5.95 (d, J=1.2 Hz, 1H; 1′-H), 6.16 (s, 1H; 12-H), 6.34 (d, J=1.2 Hz, 1H; 1′-H), 6.85–6.89 (m, 1H; Ar-H), 7.26–7.30 ppm (m, 2H; Ar-H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=10.7, 24.5, 25.0, 55.7, 56.3, 59.7, 60.2, 64.0, 98.9, 109.5, 116.6, 117.2, 117.8, 122.2, 123.4, 127.0, 128.8, 129.2, 137.9, 140.8, 145.1, 148.9, 157.0 ppm; UV/Vis: λ_{max} ($\log\varepsilon$)=201.5 (4.4756), 290.5 (4.5398), 306.0 ppm (3.5456); IR (KBr): $\tilde{\nu}$=2929, 1456, 1269, 1065, 742 cm^{-1}; MS (EI, 70 eV): m/z (%): 382 (32) $[M^+]$, 324 (100) $[M-C_3H_6O]^+$, 293 (86) $[M-C_3H_6O-CH_3O]^+$, 278 (65) $[M-C_3H_6O-CH_3O-CH_3]^+$, 265 (29); HRMS: calcd for $C_{23}H_{26}O_5$: 382.1780; confirmed.

(1′*RS*)-(7-Bromo-6-methoxy-2,2,5-trimethyl-4*H*-benzo[1,3]dioxin-8-yl)-(7′-[1″,3″]dioxan-2″-yl-2′-methoxyphenyl)-methanol (38): A magnetically stirred solution of iodobenzene **22** (448 mg, 1.40 mmol) in THF (20 mL) at −78 °C was treated dropwise with nBuLi (560 μL, 2.5 M in hexane, 1.40 mmol). The resulting mixture was stirred at this temperature for 10 min before being treated dropwise with aldehyde **23** (400 mg, 1.27 mmol) in THF (7 mL). Stirring was continued at this temperature for 35 min then the solution was warmed to 20 °C and immediately quenched with a saturated aqueous solution of NH_4Cl (4 mL). The resulting mixture was extracted with diethyl ether (3×20 mL) and washed with brine (1×5 mL). The combined organic fractions were dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a clear yellow oil. Subjection of the resulting crude oil to flash chromatography (pentane/EtOAc 19:1 → pentane/EtOAc 9:1) and concentration of the appropriate fractions (R_f=0.3 in pentane/EtOAc 9:1) afforded alcohol **38** as a colourless solid (481 mg, 0.945 mmol, 74 %). ^{1}H NMR (200 MHz, $CDCl_3$): δ=0.70 (s, 3H; CH_3), 1.28 (s, 3H; CH_3), 1.40 (m, 1H; 5″-H), 2.07 (s, 3H; CH_3), 2.10–2.32 (m, 1H; 5″-H), 3.64 (s, 3H; OCH_3), 3.75 (s, 3H; OCH_3), 3.80–4.02 (m, 2H; 4″-H/6″-H), 4.02–4.25 (m, 2H; 6″-H/4″-H), 4.58 (d, J= 4.6 Hz, 2H; 4-H), 4.78 (s, 1H; OH), 6.20 (s, 1H; 2″-H), 6.66 (d, J= 4.8 Hz, 1H; Ar-H), 6.76 (d, J=8.2 Hz, 1H; Ar-H), 7.20 ppm (d, J=4.8, 1H; Ar-H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=11.2, 21.4, 25.4, 25.5, 55.9, 60.0, 60.5, 67.2, 67.3, 72.5, 98.5, 99.3, 111.7, 118.4, 118.7, 119.8, 126.9, 127.2, 128.9, 129.3, 137.6, 146.2, 148.6, 157.1 ppm; IR (KBr): $\tilde{\nu}$=3455, 2991, 2960, 1456, 1257, 1046 cm^{-1}; UV/Vis: λ_{max} ($\log\varepsilon$)=285.0 (3.7282), 201.5 nm (4.7676); MS (EI, 70 eV): m/z (%): 510.3 (10) $[M]^+$, 508.0 (9), 452.0 (4) $[M-C_3H_6O]^+$, 450.2 (3), 374.1 (42), 371.3, (67) 312.3 (58), 295.2 (100), 222.2 (50), 163.1 (61); HRMS: calcd for $C_{24}H_{29}BrO_7$: 508.1097; confirmed.

(1′*RS*)-7-Bromo-8-{[7′-(1″,3″)dioxan-2″-yl-3′-methoxyphenyl]-1′-methoxymethyl}-6-methoxy-2,2,5-trimethyl-4*H*-benzo[1,3]dioxine (39): A magnetically stirred solution of alcohol **38** (480 mg, 0.943 mmol) in THF (15 mL) was treated with KH (75 mg, 1.89 mmol) in one portion at 0 °C. Stirring was continued for 40 min before the reaction mixture was treated with MeI (118 μL, 1.89 mmol) and stirred at 20 °C for a further 2 h. The resulting mixture was treated with water (5 mL) and extracted with diethyl ether (3×15 mL). The combined organic fractions were dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a colourless solid. Subjection of this material to flash chromatography (pentane/EtOAc 17:3) and concentration of the appropriate fractions afforded olefin **39** as colourless solid (451 mg, 0.862 mmol, 91 %). R_f=0.3; ^{1}H NMR (200 MHz, $CDCl_3$): δ=1.37 (s, 3H; CH_3), 1.42 (m, 1H; H-5″), 1.55 (s, 3H; CH_3), 2.10–2.40 (m, 1H; H-5″), 2.30 (s, 3H; CH_3), 3.56 (s, 6H; 2×OCH_3), 3.78 (s, 3H; OCH_3), 3.83–4.04 (m, 2H; 4″-H), 4.11–4.27 (m, 2H; 6″-H), 4.57 (d, J=6.0, Hz, 2H; 4-H), 6.26 (s, 1H; 2″-H), 6.59 (s, 1H; 1′-H), 6.68 (d, J=4.8 Hz, 1H; Ar-H), 7.19 (m, 1H; Ar-H), 7.45 ppm (d, J=8.2 Hz, 1H; Ar-H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=11.3, 21.3, 25.2, 26.0, 55.8, 58.5, 59.9, 60.5, 67.1, 67.4, 80.7, 98.9, 99.8, 99.8, 110.8, 118.8, 118.9, 127.0, 127.2, 127.3, 127.4, 139.4, 146.3, 148.5, 156.4 ppm; IR (KBr): $\tilde{\nu}$=2942, 1456, 1255, 1074 cm^{-1}; UV/Vis: λ_{max} ($\log\varepsilon$)=285.5 (3.7228), 199.0 nm (4.7657); MS (EI, 70 eV): m/z (%): 524.3 (24), 522.0 (20) $[M]^+$, 443.0 (14) $[M-Br]^+$, 385.3 (37) $[M-Br-C_3H_6O]^+$, 326.2 (25), 236 (38), 206.1 (100); HRMS: calcd for $C_{25}H_{31}BrO_7$: 464.0835; confirmed.

(1′*RS*)-7-Bromo-6-methoxy-8-[1′-methoxy-(3′-methoxy-7′-vinylphenyl)-methyl]-2,2,5-trimethyl-4*H*-benzo[1,3]dioxine (36): A magnetically stirred solution of acetal **39** (140 mg, 0.269 mmol) in a water/acetone mixture (2.5:5 mL) was treated with a few crystals of pyridinium *p*-toluenesulfonate in one portion at 20 °C. The resulting suspension was heated at reflux for 3 h before being extracted with diethyl ether (3×15 mL). The combined organic fractions were washed with brine (1×2 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a crude solid. Subjection of this material to flash chromatography (pentane/EtOAc 17:3) and concentration of the appropriate fractions afforded the corresponding aldehyde as a colourless solid (101 mg, 0.217 mmol, 81 %) recrystallised from EtOAc/hexane. R_f=0.3; m.p. 140 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.78 (s, 3H; CH_3), 1.30 (s, 3H; CH_3), 2.11 (s, 3H; CH_3), 3.45 (s, 3H; OCH_3), 3.66 (s, 3H; OCH_3), 3.79 (s, 3H; OCH_3), 4.60 (dd, J=28.8, 15.6 Hz, 2H; 4-H), 6.33 (s, 1H; 1′-H), 6.92 (d, J=8.1, 1.2 Hz, 1H; Ar-H), 7.30 (d, J=8.1 Hz, 1-H, Ar-H), 7.42 (dd, J=8.1, 1.2 Hz, 1H; Ar-H), 11.07 ppm (s, 1H; CHO); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=11.4, 22.0, 25.3, 55.8, 57.1, 59.9, 60.6, 80.6, 98.8, 114.2, 118.8, 119.3, 121.5, 125.3, 127.6, 127.9, 131.1, 138.3, 146.4, 148.6, 156.3, 197.4 ppm; IR (KBr): $\tilde{\nu}$=1685, 1578, 1455, 1267, 1047 cm^{-1}; UV/Vis: λ_{max} ($\log\varepsilon$)=206.0 (4.7348), 296.0 nm (3.7415); MS (EI, 70 eV): m/z (%): 466.3 (5), 464.3 (5) $[M]^+$, 408.2 (7), 406.2 (6) $[M-C_3H_6O]^+$, 376.2 (100), 374.2 (97) $[M-C_7H_6]^+$, 295.3 (16) $[M-C_7H_6-Br]^+$, 178.2 (7); HRMS: calcd for $C_{22}H_{25}BrO_6$: 465.0835; confirmed.

A magnetically stirred solution of PPh_3CH_3Br (399 mg, 1.12 mmol) in THF (5 mL) at 20 °C was treated dropwise with sodium bis(trimethylsilyl) amide (1.12 mL, 1 M in THF, 1.12 mmol). The resulting yellow suspension was stirred for 1 h before being treated with above-mentioned aldehyde (260 mg, 0.56 mol) in THF (5 mL). The resulting suspension was stirred for 1 h, treated with silica gel (1 g) and concentrated under reduced pressure. The resulting white solid was subjected to column chromatography (pentane/EtOAc 19:1) and concentration of the appropriate fractions afforded olefin **36** as a colourless solid (210 mg, 0.45 mmol, 81 %). R_f=0.4; m.p. 202 °C. This material was identical in all respects with that obtained previously.

(7-Bromo-6-methoxy-2,2,5-trimethyl-4*H*-benzo[1,3]dioxin-8-yl)-(3′-methoxy-7′-vinylphenyl)methanone (40): A magnetically stirred solution of alcohol **35** (125 mg, 0.278 mmol) in CH_2Cl_2 (10 mL) at 20 °C was treated with Dess–Martin periodinane (177 mg, 0.417 mmol) in one portion. The resulting mixture was stirred for 15 min before being treated with a saturated solution of $NaHCO_3$ (2 mL) and a 1 M solution of $Na_2S_2O_3$ (2 mL). Stirring was continued until the cloudy solution became clear (approximately 1 h). The resulting mixture was transferred to a separating funnel

and extracted with CH_2Cl_2 (3×10 mL). The combined organic fractions were subjected to flash chromatography (pentane/EtOAc 10:1) and concentration of the appropriate fractions afforded benzophenone **40** as a colourless solid (101 mg, 0.225 mmol, 81%). R_f=0.3; m.p. 129°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.14 (br s, 6H; 2×CH_3), 2.13 (s, 3H; CH_3), 3.58 (s, 3H; OCH_3), 3.78 (s, 3H; OCH_3), 4.64 (s, 2H; 4-H), 5.28 (dd, J=10.8, 1.2 Hz, 1H; 2″-H), 5.70 (dd, J=17.4, 1.2 Hz, 1H; 2″-H), 6.75 (d, J=8.1 Hz, 1H; Ar-H), 6.93 (dd, J=17.4, 10.8 Hz, 1H; 1″-H), 7.22 (d, J=7.8 Hz, 1H; Ar-H), 7.31 ppm (t, J=7.8 Hz, 1H; Ar-H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=11.5, 23.6, 24.0, 55.9, 59.8, 60.7, 98.9, 110.4, 114.7, 115.9, 118.0, 118.1, 129.4, 129.9, 130.2, 130.8, 135.1, 138.8, 145.9, 148.9, 157.8, 195.4 ppm; IR (KBr): $\tilde{\nu}$=1680, 1471, 1400, 1271, 1045, 881 cm^{-1}; UV/Vis: λ_{max} (logε)=207.5 (4.6472), 313.0 nm (3.6938); MS (EI, 70 eV): m/z (%): 448.3 (10) 446.3 (9) $[M]^+$, 390.2 (43), 388.2 (40) $[M-C_3H_6O]^+$, 309.3 (100) $[M-Br-C_3H_6O]^+$, 281.2 (20), 255.2 (24); HRMS: calcd for $C_{22}H_{23}BrO_5$: 446.0729; confirmed.

6,11-Dimethoxy-2,2,5-trimethyl-7-methylene-4,7-dihydro-1,3-dioxabenzo[*a*]anthracen-12-one (41): A magnetically stirred solution of benzophenone **40** (215 mg, 0.481 mmol) and nBu$_4$NOAc (290 mg, 0.961 mmol) in a previously degassed mixture of DMF/CH_3CN/H_2O 5:5:1 (10 mL) at 60°C was treated with *trans*-di(μ-acetato)-bis[*ortho*(di-*ortho*-tolylphosphino) benzyl]dipalladium (II) (45 mg, 0.048 mmol) in one portion. The resulting suspension was heated at 110°C for 17 h, cooled to 20°C, diluted with diethyl ether (30 mL) and washed with water (3×3 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a crude brown solid. Subjection of this material to flash chromatography (pentane/EtOAc 9:1) and concentration of the appropriate fractions afforded anthracenone **41** as yellow solid (130 mg, 0.355 mmol, 74%). R_f=0.3; ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.60 (s, 6H; 2×CH_3), 2.14 (s, 3H; CH_3), 3.61 (s, 3H; OCH_3), 3.94 (s, 3H; OCH_3), 4.77 (s, 2H; CH_2), 6.07 (s, 1H; 1′-H), 6.53 (s, 1H; 1′-H), 6.95 (d, J=8.2 Hz, 1H; Ar-H), 7.31–7.44 ppm (m, 2H; Ar-H); ^{13}C NMR (150.8 MHz, $CDCl_3$): δ= 11.3, 24.7, 56.2, 59.8, 60.1, 67.0, 99.2, 111.2, 116.0, 119.3, 120.0, 121.7, 122.4, 129.3, 131.9, 132.5, 136.2, 141.1, 146.6, 147.9, 158.3, 183.5 ppm; IR (KBr): $\tilde{\nu}$=1672, 1456, 1273, 1058, 842 cm^{-1}; UV/Vis: λ_{max} (logε)=194.0 (4.6834), 229.0 nm (4.6089); MS (EI, 70 eV): m/z (%): 366.2 (10) $[M]^+$, 308.1 (23) $[M-C_3H_6O]^+$, 293.1 (100) $[M-C_3H_6O-CH_3]^+$, 265.1 (6), 165.1 (6); HRMS: calcd for $C_{22}H_{22}O_5$: 366.1467; confirmed.

(12*RS*)-6,11,12-Trimethoxy-2,2,5-trimethyl-7-methylene-7,12-dihydro-4*H*-1,3-dioxabenzo[*a*]anthracene (37): A magnetically stirred solution of $LiAlH_4$ (2 mg, 0.05 mmol) in THF (1 mL) at 0°C was treated dropwise with ketone **41** (20 mg, 0.05 mmol) in THF (0.5 mL). The resulting solution was stirred for 10 min before being treated with a saturated aqueous solution of NH_4Cl (1 mL) and extracted with diethyl ether (3 mL). The combined organic fractions were dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a yellow solid. The resulting alcohol **42** was not isolated but was immediately subjected to the next reaction.

The crude solid from the above reaction (approximately 20 mg) in THF (1 mL) at 0°C was treated with KH (4 mg, 0.11 mmol) and then immediately with MeI (6 μL, 0.11 mmol). The resulting solution was stirred at this temperature for 30 min before being warmed to 20°C and stirred for a further 14 h. The resulting mixture was treated with water (1 mL) and extracted with diethyl ether (3×3 mL), then the combined organic fractions were dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a colourless solid. Subjection of this material to flash chromatography (pentane/EtOAc 19:1) and concentration of the appropriate fractions afforded **37** as a yellow solid (7.7 mg, 0.02 mmol, 37%). R_f=0.2. This material was identical in all respects to that obtained previously.

(12*RS*)-6,11,12-Trimethoxy-2,2,5-trimethyl-11a,12-dihydro-4*H*,7a*H*-1,3-dioxabenzo[*a*]anthracen-7-one (43): A magnetically stirred solution of compound **37** (10 mg, 0.026 mmol) in CCl_4/MeCN/H_2O 1:1:1.5 (350 μL) at 20°C was treated with a mixture of $RuCl_3$ (0.2 mg, 5 mol%, 1.3×10^{-3} mmol) and $NaIO_4$ (28 mg, 0.139 mmol). The ensuing solution was stirred for 15 min and the suspension was diluted with CH_2Cl_2 (10 mL). The organic layer was washed with water (2×1 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. Subjection of the resulting brown solid to flash chromatography through a small plug of silica (pentane/EtOAc 9:1) afforded crude anthracenone **43** as a yellow foam (7 mg, 0.018 mmol, 69%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.60 (s, 3H; CH_3), 1.63 (s, 3H; CH_3), 2.14 (s, 3H; CH_3), 3.25 (s, 3H; OCH_3), 3.87 (s, 3H; OCH_3), 3.97 (s, 3H; OCH_3), 4.81 (s, 2H; CH_2), 6.15 (s, 1H; 12-H), 7.10 (dd, J=8.4, 0.9 Hz, 1H; Ar-H), 7.43 (t, J=8.1 Hz, 1H; Ar-H), 7.64 ppm (dd, J=7.8, 0.9 Hz, 1H; Ar-H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=10.3, 24.5, 24.9, 55.9, 60.2, 61.8, 62.6, 99.4, 114.3, 119.0, 124.6, 125.6, 126.6, 127.0, 129.1, 129.5, 136.4, 145.2, 151.3, 157.0, 184.8 ppm; IR (KBr): $\tilde{\nu}$=2932, 1673, 1591, 1271, 1054, 861, 747 cm^{-1}; MS (EI, 70 eV): m/z (%): 384.2 (14) $[M]^+$, 326.2 (100) $[M-C_3H_6O]^+$, 298.2 (25), 267.1 (24), 149.1 (40); HRMS: calcd for $C_{22}H_{24}O_6$: 384.1573; confirmed.

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