Syntheses of 2,5-dimethyl-4-naphth-2'-yldioxolanes and their stereoselective isomerization to naphtho[1,2-c]pyrans, angular analogues of glucoside B, a cleavage product of the aphid insect pigments the protoaphins

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Dedicated to Professor Rod Rickards on the occasion of his 70th birthday
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Abstract
Benzynes were generated selectively through loss of ortho-bromotosylate from 1,2-dibromo-3-tosylates. Thus when treated with butyl lithium in the presence of furan rel-(2R,4S,5R)-4-(2',3'-dibromo-5'-methoxy-4'-toluene-p-sulfonloyxyphenyl)-2,5-dimethyl-1,3-dioxolane 21 was converted in two steps into rel-(2R,4S,5R)-4-(1'-bromo-4'-methoxynaphthalen-2'-yl)-2,5-dimethyl-1,3-dioxolane 8 in good yield. Attempted stereoselective isomerization of dioxolane 8 with titanium(IV) chloride at low temperature led to the recovery, almost exclusively, of starting material. The debrominated analogue rel-(2R,4S,5R)-4-(1'-methoxynaphthalen-3'-yl)-2,5-dimethyl-1,3-dioxolane 31, on the other hand, isomerized readily to give rel-(1R,3R,4S)– and rel-(1S,3R,4S)-3,4-dihydro-4-hydroxy-6-methoxy-1,3-dimethylnaphtho[1,2-c]pyrans 32 and 34 in a ratio (~1:3) that did not vary with reaction temperature.

Keywords: Selective benzyne formation, stereoselective synthesis of dioxolanes

Introduction

Reductive cleavage of the aphid insect pigments the protoaphins-fb 1 and –sl 2 affords glucoside B 3 in each case as well as, for the former, quinone A 4 and for the latter, quinone A' 5,1 as shown in Scheme 1. Routes to the enantiopure quinones 4 and 5 and their diastereoisomers have now been established.2,3 These rely on the intramolecular diastereoselective cyclisation of tethered phenolic lactaldehydes in reactions that provide the C-5 oxygen of the linear naphthopyranquinones 4 and 5. Glucoside B 3 lacks this oxygen and alternative routes are therefore being investigated. We have shown that phenyldioxolanes, which can be prepared in enantiopure form,4 can be isomerized to benzopyrans.5–7 In particular, all cis 4-aryl-2,5-
dimethyldioxolanes were found to provide the 1,3-trans-3,4-trans stereochemistry required for glucoside B since the stereochemistries at C-4 and C-5 in the dioxolanes were transferred unaltered to C-4 and C-3 respectively in the product benzo-and naphthopyrans. In an early study of this isomerization, the corresponding naphthylidioxolanes were shown to yield angular naphthopyrans readily as the sole products of isomerization, even when a peri-substituted bromine atom used as a blocking group was lost with an excess of the isomerization reagent. Having subsequently optimised the reaction conditions for this isomerization we now report on the further examination of the rearrangement of a naphthylidioxolane bearing a blocking bromine atom ortho to the dioxolane ring with a view to assembling linear naphthopyrans.

Scheme 1

The proposed method for the assembly of the target molecule required as a precursor the brominated linear naphthopyran and allowed for the possibility of generating a variety of naphthalenes with different substitution patterns in the second aromatic ring. This would be achieved through a Diels–Alder reaction of various dienes with a benzyne derived as a late intermediate in the synthetic sequence in order to avoid the potential for a series of lengthy reaction sequences. The retrosynthetic analysis considered is shown in Scheme 2. The choice of the naphthylidioxolane as the precursor to the naphthopyran followed from the smooth isomerization of 2-chloro-5-methoxyphenyldioxolanes to the corresponding 2-benzopyrans in high yield. A Diels–Alder reaction of furan with the benzyne would be manipulated to provide the naphthalene unsubstituted in the second aromatic ring. Alternatively, the possibility of the use of, for example, the protected (*) glucosidic diene with the related benzopyranoid benzyne might provide a precursor to glucoside B through a Diels–Alder reaction in which the regioselectivity would be controlled by the polarization of the 3-methoxybenzyne. Scheme 2 provides for the known phenolic benzaldehyde, obtained
from vanillin, as the starting material for each of the benzyynes 9 and 11. Benzyne 11 would be obtained from the starting material 10 via the precursor to benzyne 9.

Scheme 2

Results and Discussion

The phenolic group of aldehyde 10 was tosylated to form the derivative 13 with a view, ultimately, to generating the benzyynes 9 and 11. Benzyynes may be derived from, inter alia, either ortho-bromosulfonates or ortho-dibromides and since the aromatic ring of 13 is a 1,2-dibromo-3-tosylate, two different benzyynes might be produced. Since tosylate would be expected to be a better leaving group than bromide it was possible that the benzyynes 9 and 11 would, indeed, be the preferred or exclusive products. This hypothesis was tested by converting the aldehyde 13 into its ethylene acetal 14 and subjecting this to a lithium–halide exchange reaction with butyl lithium, which delivered the required benzyne. The presence of furan in the reaction mixture containing this benzyne afforded the epoxynaphthalene 19 as the sole product in a yield of 65%. The mass spectrum of 19 showed the expected molecular ion pair of equal intensity at m/z 326 and 324, confirming the presence of a single bromine atom, and the base peak at m/z 73 for the dioxolanium ion 20. The absence of resonances in the 1H NMR spectrum arising from the tosyl group established the formation of the benzyne solely through the loss of bromine and the ortho-tosylate. The position of the bromine on the aromatic nucleus of 19 was supported by nuclear Overhauser difference spectroscopy, where irradiation of the methoxy group led to a 19% enhancement of the aromatic singlet at δ 6.91. Irradiation of this aromatic proton indicated the proximity of both the methoxy group and the dioxolanyl proton 2-H.
Having established that the required benzyne is formed in the case just described, the aldehyde 13 was converted into the all cis dioxolane 21. Aldehyde 13 was treated with ethylidene triphenylphosphorane in a Wittig reaction that led to the formation of the mixture 15 of cis and trans alkenes in a yield of 95% and a ratio of approximately 1:1 as judged by $^1$H NMR spectroscopy. This mixture was converted into solely the trans isomer 16, obtained pure after recrystallization, in a yield of 79% through treatment with bisacetonitriledichloropalladium(II). In this product the two vicinal olefinic protons in the $^1$H NMR spectrum showed a mutual coupling constant of 15.5 Hz, whereas the coupling constant for the cis compound in the mixture 15 was 11.5 Hz. This alkene 16 was converted in 91% yield into the trans epoxide 17 using meta-chloroperbenzoic acid in the presence of anhydrous sodium bicarbonate. Whereas basic hydrolysis of 17 led preferentially to cleavage of the sulfonate ester, acidic hydrolysis in aqueous dimethyl sulfoxide achieved stereoselective ring opening of the epoxide 17 to give solely, after recrystallization, the erythro-diol 18 in 86% yield. Acetalation of this diol afforded the all cis dioxolane 21 as the sole product in 96% yield. The relative stereochemistry around the dioxolane ring was supported by two factors; first, a two dimensional NOESY spectrum that
indicated the mutual close proximity of the three heterocyclic ring protons 2-H, 4-H and 5-H, and, secondly, the same relative stereochemistry as observed for all the related dioxolanes prepared previously from erythro-diol precursors.\(^5\)\(^^-\)\(^8\) Thus the product 21 was obtained in an overall yield of 20\% in ten steps from vanillin.

Attempted isomerization of the aryldioxolane 21 to the 2-benzopyran 24 at −78 °C, using two equivalents\(^5\)\(^^-\)\(^7\) of titanium(IV) chloride, did not succeed, starting material being recovered together with some precursor diol 18. Repetition at −30 °C and 0 °C also gave none of the benzopyran 24 although increasing quantities of the diol 18 were produced as the temperature of the reaction was raised. A number of other Lewis acids and alternative conditions were also examined to no avail. The lack of reactivity towards isomerization might be due to either the relatively poor electron availability on the aromatic ring for the required electrophilic substitution to occur, or, perhaps less likely, the crowded nature of the aromatic ring of the target benzopyran 24. In order to increase the electron density on the aromatic ring, the tosyl group was removed through basic hydrolysis and the derived phenol 22 was converted into its \(\tau\)-butyldimethylsilyl ether 23. The yields for these successive reactions were 53\% and 86\% respectively. Treatment of this dioxolane 23 with two equivalents of titanium(IV) chloride gave the unwanted diastereoisomeric chlorohydrins 26 and 27 in a combined yield of 83\% in a ratio of approximately 2:1 with the threo diastereoisomer 26 predominating. It was possible to assign individual stereochemistries to the two compounds on the basis of the chemical shifts and associated coupling constants of the benzylic protons. It is known\(^1\)\(^3\) that the resonance for the erythro–isomer is characteristically deshielded and has a smaller coupling constant than for the corresponding threo compound. For the threo isomer 26 these values were \(\delta 5.44\) and 6.3 Hz while for the erythro-isomer 27 they were \(\delta 5.54\) and 4.8 Hz. This result is consistent with the alternative unwanted cleavage of the dioxolanyl O-3/C-4 bond cleavage in 23 on coordination of that oxygen atom with the Lewis acid catalyst. This cleavage is assisted by the increased electron availability provided by the silyloxy oxygen atom,\(^6\) as shown in structure 28, and the derived intermediate 29 undergoes subsequent attack at the benzylic position (Scheme 3) by chloride from the catalyst. Alternatively, increased activation at the benzylic carbon by the para-silyloxy substituent might allow direct displacement by chloride at this centre.

![Scheme 3](image-url)
Since it was not possible to isomerize either of the two phenyldioxolanes 21 or 23 to the corresponding 2-benzopyrans 24 and 25, the dioxolane 21 was converted into the naphthyldioxolane 8. This was achieved through initial generation from dioxolane 21 of the benzyne 9, using butyl lithium, in the presence of an excess of furan, whereupon the 1:1 pair of diastereoisomeric epoxides 30 (Scheme 4) was produced in 87% yield (based on consumed dioxolane 21). The correct high-resolution mass spectrometric molecular ion for adduct 30 was observed for each of the bromine-induced isotopic signals. Appropriate duplicate signals were observed in both the $^1$H and $^{13}$C NMR spectra for the structures 30. Once again, the absence of signals arising from the tosyl moiety supported the assignment.

Deoxygenation of the mixture of diastereoisomeric epoxides 30 with diiron nonacarbonyl in hot benzene, according to the method of Wege and co-workers,14,15 afforded the target naphthyldioxolane 8 as a single diastereoisomer in 86% yield (Scheme 4). A pair of molecular ions at m/z 338 and 336 and the observation of appropriate single, rather than duplicate, signals in the NMR spectra confirmed the assignment of a bromine-containing single diastereoisomer. Thus the naphthyldioxolane 8 was obtained in an overall yield of 75% from the phenyldioxolane 21.

![Scheme 4](image-url)

Attempted isomerization of the naphthyldioxolane 8 with two molar equivalents of titanium(IV) chloride at $-78$ °C led to the formation of the angular naphthopyran 32 (see below) in only 6%, the remainder being starting material. In particular, the single molecular ion in the mass spectrum at m/z 258 confirmed the absence of bromine and the chemical shift ($\delta$ 7.00) of the aromatic proton H-5 corresponded to those of related angular8 ($\sim\delta$ 6.8) rather than linear9 naphthopyrans such as 6 ($\delta$ 7.84). The formation of the angular naphthopyran can be attributed to the strong preference of naphthalenes to undergo electrophilic substitution at the $\alpha$- rather than the $\beta$-position, particularly at low temperatures. Presumably the dioxolane ring-opening occurs through reaction with titanium chloride but displacement of the bromonium through electrophilic substitution is discouraged under the reaction conditions that include a low reaction temperature and the bulk of the bromine atom. As a consequence, ring-closure to afford the starting material 8 occurred.

In order to support this view, the bromine atom was removed using butyl lithium at $-30$ °C to yield the naphthyldioxolane 31 in a yield of 74%. The loss of bromine was evident from the
mass spectrum of compound 31, which showed the molecular ion at m/z 258. The \(^1\)H NMR spectrum also supported the assigned structure with two \textit{meta}-coupled doublets (\(J\) 1.2 Hz) at \(\delta\) 6.76 and 7.29 for the protons 2'-H and 4'-H.

Isomerization of the dioxolane 31 afforded the two angular naphthopyrans 32 and 34 in a combined yield of 60\%, the major epimer 34 being obtained in 46\% and the minor one 32 in 14\% (Scheme 5). The product 32 was identical with that obtained earlier in low yield from the isomerization of the brominated naphthylidioxolane 8. Each product was acetylated to confirm that each was a naphthopyran rather than the isomeric naphthofuran with gross structure 36.\(^{1,5}\)

Strong deshielding of the signal due to proton H-4 was observed from \(\delta\) 4.46 in 32 to \(\delta\) 5.92 in 33 and from \(\delta\) 4.45 in 34 to \(\delta\) 5.89 in 35. For the naphthofuran 36 the alternative proton 1'-H would have been deshielded. For each naphthopyran 32 and 34 the mass spectral fragmentation patterns were very similar. In the \(^1\)H NMR spectrum of each compound the coupling constants between the \textit{vicinal} protons 3-H and 4-H (\(J\) 8.0 and 8.6 Hz respectively) indicated an almost \textit{trans}-diaxial arrangement between them and, therefore, that the the C-3 methyl group was equatorial and the C-4 hydroxy group was pseudoequatorial. For the products 32 and 34 the protons 3-H resonated at \(\delta\) 4.03 and 3.42, which indicated that the heterocyclic methyl substituents were \textit{trans} in the former and \textit{cis} in the latter.\(^{16}\) In product 32, therefore, the C-1 methyl was pseudoaxial while in product 34 it was pseudoequatorial. Support for the latter orientation was found in the long-range coupling constant of 2.0 Hz between the protons 1-H and 4-H, where no coupling was observed in the former.\(^{8,16-18}\)

![Scheme 5](image.png)
The naphthyldioxolane 31 was isomerized to the mixture of angular naphthopyrans at both −95 °C and −30 °C to determine whether the change in temperature would alter or reverse the ratio of the products 32 and 34.\textsuperscript{5,6} When these experiments were performed at different temperatures, however, there was no change in the ratio of the two products.

**Conclusions**

Generation of benzynes from the 1,2-dibromo-3-tosylates 14 and 21 arises exclusively through elimination of the ortho-bromotosylate rather than the ortho-dibromo substituents. Each of the derived benzynes reacts with furan in Diels–Alder reactions. The phenyldioxolane 21 does not isomerize to the target 2-benzopyran 24, either since the latter fully substituted aromatic system would be highly crowded, or since the aromatic ring of 21 is not sufficiently electron rich. On the other hand the more electron rich analogue 23 undergoes an alternative cleavage of the dioxolane ring on reaction with titanium(IV) chloride that leads to the unwanted chlorohydrins 26 and 27. The naphthyldioxolane 8 obtained from 21 does not isomerize to the required linear naphthopyran 7 and gives instead a very low yield (6\%) of the angular naphthopyran 32 through electrophilic substitution of the aromatic bromine substituent. Isomerization of the corresponding naphthyldioxolane 31 lacking this bromine substituent gives an approximately 1:3 mixture of the two angular naphthopyrans 32 and 34 in good yield and this ratio remains the same when the reaction is performed over a range of temperatures from −95 °C to −30 °C. As observed previously, the vicinal stereochemistry at C-4 and C-5 of the dioxolanes is transferred unaltered to C-4 and C-3, respectively, of the product 2-benzopyrans.\textsuperscript{6} While the factors that control the relative stereochemistry at C-1 in the products are complex and not yet understood, it is noteworthy that in the major isomer 34 the substituents at C-1 and C-4 are trans related, which differs from all earlier observations.\textsuperscript{6}

**Experimental Section**

**General Procedures.** Nuclear magnetic resonance (NMR) spectra were recorded using a Hitachi R-24B spectrometer (\textsuperscript{1}H, 60 MHz), a Bruker AM-300 spectrometer, a Bruker Avance DPX-300 spectrometer (\textsuperscript{1}H, 300 MHz; \textsuperscript{13}C, 75.5 MHz) or a Bruker ARX-500 spectrometer (\textsuperscript{1}H, 500 MHz; \textsuperscript{13}C, 126 MHz). All recorded spectra of purified products were measured on the Bruker AM-300 spectrometer or the Bruker Avance DPX-300 spectrometer, unless otherwise stated. The spectra were routinely run at ambient temperature in deuterochloroform (CDCl\textsubscript{3}) solution or, where indicated, \textsuperscript{2}H dimethyl sulfoxide (DMSO-d\textsubscript{6}) or \textsuperscript{2}H acetone (acetone-d\textsubscript{6}), with the internal standard being tetramethylsilane (TMS) (δ 0.00) for \textsuperscript{1}H NMR spectra and TMS δ 0.00) or chloroform δ 77.00) for \textsuperscript{13}C NMR spectra. The signals in the \textsuperscript{13}C NMR spectra were assigned with the help of the DEPT technique and assignments of signals with the same
superscripts are interchangeable. Melting points were determined either on a Riechert hot stage apparatus or an Electrothermal melting point apparatus and are uncorrected. Infrared spectra were recorded as KBr discs for solids and, as indicated in the text, as thin films between NaCl plates for oils, using a Perkin Elmer 1720-X Fourier Transform Spectrometer. Mass spectra were obtained either on a Hewlett Packard 5986 spectrometer operating in the electron impact mode at 35 eV or on a Perkin Elmer ITD Ion Trap Detector spectrometer in the electron impact mode at an emission current of 50 µA and an electron multiplier voltage of 2000 V. High-resolution mass spectra were obtained on a V.G. Autospec high resolution mass spectrometer. Elemental analyses were carried out by the Analytical Service Unit at the Australian National University, Canberra, Australia. Standard work-up refers to extraction with an organic solvent, then washing of the organic extracts with water and brine, drying the organic layer and concentration under reduced pressure. All drying of the organic extracts was performed using anhydrous magnesium sulfate (MgSO4). The yields recorded are unoptimised. Column chromatography refers to columns prepared as slurries of Merck silica gel 60 (70–230 mesh) in the eluent. Dry packed chromatography indicates dry-packed columns of the same stationary phase. Preadsorption was carried out on Merck silica gel 60 (35–70 mesh). Preparative thin layer chromatography (PLC) was performed using Camag silica gel as a 0.3 mm thick layer on glass plates (20 x 20 cm). Merck silica gel 60 F254 aluminium-backed sheets were used for thin layer chromatography (TLC). Compounds were routinely visualised under short wavelength (254 nm) ultraviolet light. All solvents were purified by distillation and, if required, were dried according to standard methods. The amount of residual water present in solvents was monitored using a Metrohm Karl Fischer Coulometer 684. The hydrocarbon solvent referred to as hexane routinely had a boiling point range of 65-70 °C. Ether refers to diethyl ether.

**2,3-Dibromo-4-formyl-6-methoxyphenyl toluene-p-sulfonate (13).** A solution of toluene-p-sulfonyl chloride (TsCl) (4.02 g, 21.1 mmol) in dry THF (25 mL) was added dropwise to a stirred solution of the dibromo phenol 10 (5.00 g, 16.2 mmol) and triethylamine (2.14 g, 21.1 mmol) in dry THF (60 mL) at 0 °C. After addition of the tosyl chloride, the mixture was allowed to warm to room temperature and was then heated under gentle reflux overnight. After cooling, the mixture was poured into water, the aqueous layer acidified with dilute hydrochloric acid (1 M) and then extracted with ethyl acetate. The combined organic extracts were washed with water and brine, dried and concentrated (under reduced pressure). To remove the excess of TsCl, hexane was added to the residue and the mixture boiled. After filtration, the filtrate, containing mostly tosyl chloride, was discarded and the residue (mostly product) was further purified by dry packed chromatography (20% ethyl acetate-hexane) to give the product 13 as a light brown solid (6.32 g, 84%). Recrystallisation from ethyl acetate-hexane afforded the tosylate 13 as cream plates, mp 140–141 °C (Found: C, 39.0; H, 2.5. C15H12Br2O5S requires C, 38.8; H, 2.6%); νmax/cm⁻¹ 1691 (C=O) and 1581 and 1448 (C=C); δH 2.49 (3H, s, Ar-CH3), 3.72 (3H, s, OCH3), 7.48 (1H, s, 5-H), 7.39 and 7.88 (each 2H, m, AA'BB', Ar-H) and 10.28 (1H, s, CHO);
δ_C 21.8 (Ar-CH_3), 56.3 (OCH_3), 111.5 (C-5), 121.4 (C-2),^a 124.3 (C-3),^a 128.4 (C-3' and C-5'),^b 129.6 (C-2' and C-6'),^b 133.5 (C-4), 134.7 (C-4'),^c 142.8 (C-1), 145.6 (C-1'),^c 152.9 (C-6) and 191.3 (CHO); m/z 466 (M^+ {2x^{81}Br}, 3%), 464 (M^+ {^{81}Br,^{79}Br}, 6%), 462 (M^+ {2x^{79}Br}, 3%), 309 (6), 155 (100), 91 (86) and 65 (15).

2-(2',3'-Dibromo-5'-methoxy-4'-toluenesulfonyloxyphenyl)-1,3-dioxolane (14). A solution of the aldehyde 13 (2.30 g, 4.96 mmol), ethylene glycol (375 mg, 6.00 mmol) and p-toluenesulfonic acid (20 mg, 0.10 mmol) in dry benzene (60 mL) was heated under reflux in a Dean–Stark apparatus for 24 h. The solution was cooled, poured into water and extracted with ether. The organic extracts were washed with saturated sodium hydrogen carbonate solution, water and brine, and then dried and evaporated. The crude product (2.46 g) was purified by column chromatography using 20–50% ethyl acetate-hexane as eluent to afford the dioxolane 14 (2.07 g, 82%). Recrystallisation from ethyl acetate gave white plates, mp 154–155 °C (Found: C, 40.1; H, 3.0. C_{17}H_{16}Br_2O_6S requires C, 40.2; H, 3.2%); ν_max/cm^-1 1608 and 1496 (C=C); δ_H 2.47 (3H, s, Ar-CH_3), 3.68 (3H, s, OCH_3), 4.07–4.16 (4H, m, CH_2–CH_2), 6.02 (1H, s, 2-H), 7.22 (1H, s, 6'-H) and 7.35 and 7.87 (each 2H, m, AA'BB', Ar-H); δ_C 21.7 (Ar-CH_3), 56.1 (OCH_3), 62.5 (CH_2CH_2), 102.8 (C-2), 110.5 (C-6'), 116.4 (C-2'),^a 123.1 (C-3'),^a 128.4 (C-3'' and C-5''),^b 129.5 (C-2'' and C-6''),^b 134.9 (C-4''),^c 137.4 (C-1'),^c 138.9 (C-1''),^d 145.2 (C-4')^d and 152.5 (C-5'); m/z 510 (M^+ {2x^{81}Br}, 3%), 508 (M^+ {^{81}Br,^{79}Br}, 6%), 506 (M^+ {2x^{79}Br}, 3%), 357 (27), 199 (54), 154 (34), 91 (100) and 73 (60).

2-(1'-Bromo-5',8'-dihydro-5',8'-epoxy-4'-methoxynaphthalen-2'-yl)-1,3-dioxolane (19). A solution of n-butyl lithium in hexane (460 µL, 1.29 M, 0.59 mmol) was added to a stirred solution of the dioxolane 14 (300 mg, 0.59 mmol) and furan (1.30 mL, 17.7 mmol) in dry THF (10 mL) at –78 °C in an atmosphere of nitrogen. The mixture was stirred at this temperature for 1 h, then allowed to warm to room temperature. After a further 3 h of reaction time, the mixture was poured into water containing a little sodium bicarbonate. Standard work-up (ethyl acetate) provided the crude product as a yellow oil (200 mg). This was purified by column chromatography (20% ethyl acetate-hexane) to furnish the adduct 19 (124 mg, 65%) as cream plates. Recrystallisation from ethyl acetate-hexane gave the epoxynaphthalene 19 as white plates, mp 122–124 °C (Found: C, 51.8; H, 4.1. C_{14}H_{13}BrO_4 requires C, 51.7; H, 4.0%); ν_max/cm^-1 1603 and 1465 (C=C); δ_H 3.83 (3H, s, OCH_3), 4.01–4.18 (4H, m, CH_2–CH_2), 5.82 and 5.99 (each 1H, d, J 1.0 Hz, 5'- and 8'-H), 5.97 (1H, s, 2-H), 6.91 (1H, s, 3'-H) and 7.08 (2H, m, 6'- and 7'-H); δ_C 55.9 (OCH_3), 65.3 (CH_2CH_2), 81.0 and 83.2 (C-5' and C-8'), 102.1 (C-2), 108.2 (C-1'), 110.7 (C-3'), 142.5 and 143.3 (C-6' and C-7'), 134.8 and 151.9 (C-4'a and C-4'')^a and 139.7 and 153.1 (C-2' and C-8'a)^a; m/z 326 (M^+ {^{81}Br}, 5%), 324 (M^+ {^{79}Br}, 5%), 226 (22), 145 (29), 115 (23), 73 (100) and 45 (47).

trans-1-(2',3'-Dibromo-5'-methoxy-4'-toluenesulfonyloxyphenyl)-1-propene (16). A solution of n-butyl lithium in hexane (3.60 mL, 2.34 M, 8.41 mmol) was added to a stirred suspension of ethyltriphenylphosphonium bromide (3.12 g, 8.41 mmol) [the ethyltriphenylphosphonium bromide was either prepared by heating a mixture of ethyl bromide and triphenylphosphine in
toluene in a sealed tube at 105 °C for 24 h, or purchased from Sigma-Aldrich. When the commercially available reagent was used, the yields for the Wittig reaction were increased] in dry THF (50 mL) at 0 °C under an atmosphere of nitrogen. The dark orange solution was stirred at 0 °C for 5 minutes and then cooled to −78 °C. The aldehyde 13 (3.00 g, 6.47 mmol) in dry THF (40 mL) was added dropwise at this temperature. After 15 minutes at −78 °C, the reaction mixture was allowed to warm to room temperature and was left stirring at this temperature overnight. Standard work-up with diethyl ether afforded an oily residue (4.74 g). This residue was purified by column chromatography using 10% ethyl acetate-hexane as eluent to afford a mixture (1:1) of the mixture of geometric isomers 15 (2.92 g, 95%) as a yellow oil. Following a modified procedure of Giles and Sargent, 12 a solution of this mixture (2.92 g, 6.12 mmol) and bisacetonitriledichloropalladium(II) (635 mg, 2.45 mmol) in dry dichloromethane (20 mL) was stirred overnight at room temperature. The catalyst was removed by filtration and the filtrate concentrated. The residue was purified by column chromatography using 10% ethyl acetate-hexane as eluent to provide the pure \textit{trans}-olefin 16 (2.29 g, 79%) as a yellow oil which crystallised as yellow plates upon standing. Repeated recrystallisation from ethanol-hexane furnished broad white needles, mp 115–116 °C (Found: C, 42.7; H, 3.3. C$_{17}$H$_{16}$Br$_{2}$O$_{4}$S requires C, 42.9; H, 3.4%); $\nu_{\text{max}}$/cm$^{-1}$ 1647 (alkene C=C) and 1584 (aromatic C=C); $\delta_{\text{H}}$ 1.93 (3H, dd, $J$ 6.7 and 1.7 Hz, CH=CHC$_{6}$H$_{3}$), 2.47 (3H, s, Ar-CH$_{3}$), 3.66 (3H, s, OCH$_{3}$), 6.12 (1H, dq, $J$ 15.5 and 6.7 Hz, 2-H), 6.69 (1H, dq, $J$ 15.5 and 1.7 Hz, 1-H), 6.97 (1H, s, 6'-H) and 7.35 and 7.87 (each 2H, m, AA'BB', Ar-H); $\delta_{\text{C}}$ 18.6 (CH=CHC$_{6}$H$_{3}$), 21.7 (Ar-CH$_{3}$), 56.0 (OCH$_{3}$), 109.5 (C-6'), 113.2 (C-2'),a 116.5 (C-3'),a 128.4 (C-3'' and C-5''),b 129.4 (C-2'' and C-6''),b 130.9 (CH=CHC$_{6}$H$_{3}$), 134.9 (C-4''),c 137.17 (C-1'), 138.7 (C-4'), 145.1 (C-1'')c and 152.2 (C-5'); m/z 478 (M$^+$ {2x$^{81}$Br}, 4%), 476 (M$^+$ {81Br, 79Br}, 7%), 474 (M$^+$ {2x$^{79}$Br}, 4%), 321 (100), 212 (20), 197 (15), 155 (15), 131 (51), 91 (52) and 65 (13).

\textit{trans}-1-(2',3'-Dibromo-5'-methoxy-4'-toluene-p-sulfonyloxyphenyl)-1,2-epoxypropane (17). A solution of \textit{m}-chloroperbenzoic acid (1.36 g, 7.86 mmol) in ice-cold dichloromethane (50 mL) was added to a suspension of the olefin 16 (2.20 g, 4.62 mmol) and anhydrous sodium hydrogen carbonate (830 mg, 9.88 mmol) in dry dichloromethane (30 mL) at 0 °C. The mixture was then stirred at room temperature for 24 h. The solid was removed by filtration and the filtrate poured into a saturated sodium hydrogen carbonate solution. Standard work-up with dichloromethane provided the crude product as a yellow oil (2.67 g). This crude oil was purified by column chromatography (20% ethyl acetate-hexane) to yield compound 17 as a pale yellow solid (2.06 g, 91%). Repeated recrystallisation from ethanol gave the epoxide 17 as white plates, mp 152–153.5 °C (Found: C, 41.1; H, 3.3. C$_{17}$H$_{16}$Br$_{2}$O$_{5}$S requires C, 41.5; H, 3.3%); $\nu_{\text{max}}$/cm$^{-1}$ 1588 and 1454 (C=C); $\delta_{\text{H}}$ 1.52 (3H, d, $J$ 5.1 Hz, CH$_{3}$), 2.48 (3H, s, Ar-CH$_{3}$), 2.85 (1H, dq, $J$ 2.1 and 5.1 Hz, 2-H), 3.68 (3H, s, OCH$_{3}$), 3.81 (1H, d, $J$ 2.1 Hz, 1-H), 6.85 (1H, s, 6'-H) and 7.36 and 7.88 (each 2H, m, AA'BB', Ar-H); $\delta_{\text{C}}$ 17.7 (CH$_{3}$), 21.7 (Ar-CH$_{3}$), 56.1 (OCH$_{3}$), 58.8 (C-2), 60.2 (C-1), 109.0 (C-6'), 115.3 (C-2'),a 122.3 (C-3'),a 128.4 (C-3'' and C-5''),b 129.5 (C-2'' and C-6''),b 134.9 (C-4''),c 137.7 (C-1'), 138.5 (C-4'), 145.1 (C-1'')c and 152.8 (C-5'); m/z
494 (M⁺ {2x^{81}Br}, 2%), 492 (M⁺ {^{81}Br, ^{79}Br}, 4%), 490 (M⁺ {2x^{79}Br}, 2%), 295 (54), 155 (47), 139 (36), 91 (100), 65 (34) and 43 (56).

Rel-(1S,2R)-1-(2',3'-Dibromo-5'-methoxy-4'-toluene-p-sulfonyloxyphenyl)-1,2-propanediol (18). The epoxide 17 (950 mg, 1.93 mmol) in 80% DMSO-20% water (50 mL) at 100 °C (oil bath temperature) was treated with an aqueous solution of 0.2 M sulfuric acid (19.3 mL, 3.86 mmol) and the mixture stirred at this temperature for 24 h. After cooling, the mixture was poured into water and extracted with ethyl acetate. The combined organic extracts were washed with water, saturated sodium hydrogencarbonate solution, water and brine, and then dried and concentrated. Purification of the crude product (1.03 g) by column chromatography using 30–50% ethyl acetate-hexane as eluent yielded the diol 18 as an off-white solid (847 mg, 86%). Recrystallisation from ethyl acetate-hexane afforded white plates, mp 162.5–164 °C.

Rel-(2R,4S,5R)-4-(2',3'-Dibromo-5'-methoxy-4'-toluene-p-sulfonyloxyphenyl)-2,5-dimethyl-1,3-dioxolane (21). A solution of the diol 18 (2.00 g, 3.92 mmol) in dry dichloromethane (100 mL) was treated with a slight excess of 1,1-dimethoxyethane (590 µL, 5.49 mmol) in the presence of (±)-camphorsulfonic acid (130 mg, 0.55 mmol) and the mixture heated under reflux overnight. After cooling, the mixture was poured into a saturated sodium hydrogencarbonate solution. Standard work-up (dichloromethane) furnished the crude product as a cream solid (2.06 g). Purification by column chromatography using 20% ethyl acetate-hexane as eluent provided the dioxolane 21 as an off-white solid (2.02 g, 96%). Recrystallisation from ethyl acetate afforded white plates, mp 151–153 °C.

Rel-(2R,4S,5R)-4-(2',3'-Dibromo-4'-hydroxy-5'-methoxyphenyl)-2,5-dimethyl-1,3-dioxolane (22). A solution of potassium hydroxide (0.54 M) in water and ethanol (1:1) was prepared.
alkaline solution (24 mL) was then added to the tosyl dioxolane 21 (500 mg, 0.93 mmol) in three 8 mL portions at 5 minute intervals. After the addition was complete the mixture was heated under reflux for 2 h. The solution was then cooled and concentrated. Standard work-up of the residual mixture with ethyl acetate gave the crude product as a cream solid (250 mg). Purification of this crude product by column chromatography using 5-20% ethyl acetate-hexane as eluent furnished the phenol 22 as a white solid (188 mg, 53%). Recrystallisation from ethyl acetate-hexane produced 22 as white plates, mp 138–140 °C (Found: M+ {2x81Br}, 383.9212 and M+ {2x79Br}, 379.9246; C12H14Br2O4 requires M+ {2x81Br}, 383.9218 and M+ {2x79Br}, 379.9259); νmax/cm−1 3379 (OH) and 1596, 1568, 1491 and 1468 (C=C); δH 0.88 (3H, d, J 6.3 Hz, 5-CH3), 1.57 (3H, d, J 4.8 Hz, 2-CH3), 3.93 (3H, s, OCH3), 4.52 (1H, dq, J 7.1 and 6.3 Hz, 5-H), 5.17 (1H, q, J 4.8 Hz, 2-H), 5.41 (1H, d, J 7.1 Hz, 4-H), 6.16 (1H, bs, OH) and 7.06 (1H, s, 6'-H); δc 16.5 (5-CH3), 19.7 (2-CH3), 56.3 (OCH3), 75.3 (C-5), 80.5 (C-4), 100.4 (C-2), 109.7 (C-6'), 111.9 (C-2),a 115.2 (C-3),a 131.0 (C-1'), 143.7 (C-4)b and 146.0 (C-5)b m/z 384 (M+ {2x81Br}, 40%), 382 (M+ {81Br, 79Br}, 80%), 380 (M+ {2x79Br}, 40%), 340 (55), 338 (100), 336 (53), 309 (46), 307 (52), 215 (66), 213 (62) and 77 (14).

Rel-(2R,4S,5R)-4-(2',3'-Dibromo-5'-methoxy-4'-t-butyldimethylsilyloxyphenyl)-2,5-dimethyl-1,3-dioxolane (23). Imidazole (84 mg, 0.98 mmol) was added to a solution of the phenol 22 (188 mg, 0.49 mmol) and t-butyldimethylsilyl chloride (112 mg, 0.74 mmol) in dry DMF (10 mL). The mixture was allowed to stir at room temperature overnight. Standard work-up (diethyl ether) followed by chromatography (5% ethyl acetate-hexane) yielded the silyl ether 23 (210 mg, 86%) as a white solid. Recrystallisation from hexane afforded white plates, mp 68–70 °C (Found: [(M-1) {81Br, 79Br}], 495.0028. C18H28Br2O4Si requires [(M-1), {81Br, 79Br}], 495.0025); νmax/cm−1 1588, 1553 and 1471 (C=C); δH 0.21 and 0.22 (each 3H, s, Si(CH3)2), 0.88 (3H, d, J 6.3 Hz, 5-CH3), 1.03 (9H, s, (CH3)3C), 1.55 (3H, d, J 4.8 Hz, 2-CH3), 3.83 (3H, s, OCH3), 4.52 (1H, dq, J 7.1 and 6.3 Hz, 5-H), 5.17 (1H, q, J 4.8 Hz, 2-H), 5.41 (1H, d, J 7.1 Hz, 4-H) and 7.03 (1H, s, 6'-H); δC –3.8 and –3.7 (Si(CH3)2), 16.4 (5-CH3), 19.7 (2-CH3), 26.0 (C(CH3)3), 55.1 (OCH3), 75.4 (C-5), 80.6 (C-4), 100.3 (C-2), 110.2 (C-6'), 115.0 (C-2),a 119.1 (C-3),a 131.9 (C-1'), 143.3 (C-4)b and 149.6 (C-5)b m/z 384 (M+ {2x81Br}, 40%), 382 (M+ {81Br, 79Br}, 80%), 380 (M+ {2x79Br}, 40%), 340 (55), 338 (100), 336 (53), 309 (47), 307 (52), 215 (66), 213 (62) and 77 (14).

Rel-(2R,4S,5R)-1-(2',3'-Dibromo-5'-methoxy-4'-t-butyldimethylsilyloxyphenyl)-1-chloropropan-2-ol (26) and Rel-(1S,2R)-1-(2',3'-dibromo-5'-methoxy-4'-t-butyldimethylsilyloxyphenyl)-1-chloropropan-2-ol (27). The dioxolane 23 (100 mg, 0.20 mmol) in dry dichloromethane (5 mL) was treated with titanium tetrachloride (50 µL, 0.40 mmol) at −78 °C in an atmosphere of nitrogen. The mixture was stirred at this temperature for 30 minutes. The reaction was then quenched with dry methanol (100 µL) and the mixture poured into saturated sodium hydrogencarbonate solution. Standard work-up (dichloromethane) yielded the products 26 and 27 as a colourless oil (88 mg). The crude product was isolated as a mixture of two inseparable diastereoisomers in a ratio of approximately 2:1. Purification by column chromatography (5-10% ethyl acetate-
hexane) gave the chlorohydrins 26 and 27 (82 mg, 83%) as a colourless oil (Found: [(M-OH) \(\{2x^{79}\text{Br}, 37\text{Cl}\}\)], 470.9563. \(\text{C}_{16}\text{H}_{25}\text{Br}_2\text{Cl}_3\text{Si}\) requires [(M-OH) \(\{2x^{79}\text{Br}, 37\text{Cl}\}\)], 470.9571); \(\nu_{\text{max}}/\text{cm}^{-1}\) 3408 (OH) and 1586, 1547 and 1472 (C=C); \(\delta_{\text{H}}\) (compound 26) 0.22 (6H, s, Si(CH\(_3\))\(_2\)), 1.03 (9H, s, C(CH\(_3\))\(_3\)), 1.23 (3H, d, J 6.3 Hz, CH\(_3\)), 2.43 (1H, d, J 4.3 Hz, 2-OH), 3.82 (3H, s, OCH\(_3\)), 4.04–4.16 (1H, m, 1-H) and 7.09 (1H, s, 6'-H); \(\delta_{\text{H}}\) (compound 27) 0.22 (6H, s, Si(CH\(_3\))\(_2\)), 1.03 (9H, s, C(CH\(_3\))\(_3\)), 1.24 (3H, d, J 5.3 Hz, CH\(_3\)), 2.11 (1H, d, J 5.3 Hz, 2-OH), 3.82 (3H, s, OCH\(_3\)), 4.19–4.29 (1H, m, 2-H), 5.54 (1H, d, J 4.8 Hz, 1-H) and 7.22 (1H, s, 6'-H); \(\delta_{\text{C}}\) (mixture of two isomers) –3.65 and –3.62 (Si(CH\(_3\))\(_2\)), 18.6 and 19.8 (2-CH\(_3\)), 19.0 (C(CH\(_3\))\(_3\)), 25.9 (C(CH\(_3\))\(_3\)), 55.3 (OCH\(_3\)), 68.0 and 70.1 (C-2),\(^{a}\) 70.8 and 71.6 (C-1),\(^{a}\) 110.8 and 111.4 (C-6'), 117.0 and 117.5 (C-2'),\(^{b}\) 119.1 and 119.2 (C-3'),\(^{b}\) 130.6 and 131.7 (C-1'), 144.3 and 144.3 (C-4')\(^{c}\) and 149.7 and 149.9 (C-5');\(^{c}\) m/z 492 (M\(^{+}\) \(\{2x^{81}\text{Br}\), \(37\text{Cl}\}\), 17%), 490 (M\(^{+}\) \(\{2x^{81}\text{Br}, 35\text{Cl}\}\), 81%),**, 488 (M\(^{+}\) \(\{2x^{79}\text{Br}, 37\text{Cl}\}\), ** 100%), 486 (M\(^{+}\) \(\{2x^{79}\text{Br}, 35\text{Cl}\}\), 44%), 475 (77), 473 (100), 445 (56), 443 (84), 433 (76), 431 (100), 372 (46) and 149 (70).

**Rel-(2R,4S,5R)-4-(1'-Bromo-5',8'-dihydro-5',8'-epoxy-4'-methoxynaphthalen-2'-yl)-2,5-dimethyl-1,3-dioxolane (30).** A solution of \(n\)-butyl lithium in hexane (1.20 mL, 2.34 M, 2.67 mmol) was added to a stirred solution of the dioxolane 21 (1.30 g, 2.43 mmol) and furan (5.30 mL, 72.9 mmol) in dry THF (20 mL) at –78 °C under an atmosphere of dry nitrogen. The mixture was stirred at this temperature for 1 h, after which it was allowed to warm to room temperature. The reaction was monitored by TLC. After approximately 4.5 h the amount of unreacted starting material was very small and the reaction was quenched by pouring the mixture into water containing a little sodium hydrogencarbonate. Standard work-up with ethyl acetate yielded a pale yellow oil. Purification of this crude oil by column chromatography (10% ethyl acetate-hexane) afforded the products 30, as a diastereomeric mixture (1:1), as a pale yellow oil (613 mg, 87%, based on amount of starting material consumed) and some of the dioxolane 21 (220 mg, 17% recovery). The product crystallised upon standing. Repeated recrystallisation from ethyl acetate-hexane yielded the epoxynaphthalenes 30 as white plates, mp 140–146 °C (Found: M\(^{+}\) \(\{81\text{Br}, 35\text{Cl}\}\), 354.0300 and M\(^{+}\) \(\{79\text{Br}\}\), 352.0317). \(\text{C}_{16}\text{H}_{17}\text{Br}_2\text{O}_4\) requires (M\(^{+}\) \(\{81\text{Br}\}\), 354.0290) and M\(^{+}\) \(\{79\text{Br}\}\), 352.0310); \(\nu_{\text{max}}/\text{cm}^{-1}\) 1596 and 1458 (C=C); \(\delta_{\text{H}}\) (500 MHz, mixture of the two isomers) 0.83 and 0.88 (each 3H, d, J 6.3 Hz, 5-CH\(_3\)), 1.54 (6H, d, J 4.8 Hz, 2-CH\(_3\)), 3.83 and 3.85 (each 3H, s, OCH\(_3\)), 4.496 and 4.498 (each 1H, dq, J 7.2 and 6.3 Hz, 5-H), 5.15 and 5.16 (each 1H, q, J 4.8 Hz, 2-H), 5.29 and 5.31 (each 1H, d, J 7.2 Hz, 4-H), 5.78–5.80 and 5.98–6.00 (each 2H, m, 8'- and 5'-H), 6.79 and 6.80 (each 1H, s, 3'-H) and 7.50–7.12 (4H, m, 6'- and 7'-H); \(\delta_{\text{C}}\) (126 MHz, mixture of two isomers) 16.5 and 16.6 (5-CH\(_3\)), 19.7 and 19.8 (2-CH\(_3\)), 55.9 (OCH\(_3\)), 75.0 and 75.3 (C-5), 79.2 and 79.3 (C-4), 81.07 and 81.11 (C-8'),\(^{a}\) 83.3 and 83.4 (C-5'),\(^{a}\) 100.3 and 100.4 (C-2), 105.3 and 105.5 (C-1'), 111.3 and 111.5 (C-3'), 136.3 and 136.4

\(^*\)Other isotopic combinations also contribute to these signals.
(C-4'a), b 137.0 and 137.1 (C-2'), c 143.6 and 143.7 (C-6'), c 151.8 and 152.0 (C-4')
d and 152.43 and 152.44 (C-8'a); d m/z 354 (M + {81Br}, 5%), 352 (M + {79Br}, 5%), 251 (27),
157 (53), 115 (31), 72 (55) and 43 (100).

**Rel-(2R,4S,5R)-4-(1'-Bromo-4'-methoxynaphthalen-2'-yl)-2,5-dimethyl-1,3-dioxolane (8).** A solution of the epoxynaphthalene 30 (500 mg, 1.42 mmol) in benzene (55 mL) was treated with diiron nonacarbonyl \(\text{[Fe}_2\text{(CO)}_9\text{]}\) (620 mg, 1.70 mmol) in an atmosphere of nitrogen. The mixture was stirred at 50–60 °C (oil bath) until all the solid \(\text{Fe}_2\text{(CO)}_9\) had dissolved (approx. 30 minutes). The bath temperature was then raised to 100 °C and the mixture heated under reflux for approximately 20 h. After cooling, the insoluble iron-containing by product was removed by filtration through a pad of celite which was then washed exhaustively with dichloromethane. The filtrate was evaporated under vacuum to give the naphthalene 8 as a brown oil (426 mg). Purification of this crude oil by column chromatography (hexane–5% ethyl acetate-hexane) yielded the title product 8 as a yellow oil (411 mg, 86%) (Found: C, 57.4; H, 5.05; M + {81Br}, 338.0334. \(\text{C}_{16}\text{H}_{17}\text{BrO}_3\) requires C, 57.0; H, 5.1%; M {81Br}, 338.0341); \(\nu_{\text{max/cm}^{-1}}\) 1595 and 1503 (C=C); \(\delta_{\text{H}}\) (500 MHz) 0.90 (3H, d, \(\text{J}_{6.3\text{ Hz}}\), 5-CH\(_3\)), 1.63 (3H, d, \(\text{J}_{4.8\text{ Hz}}\), 2-CH\(_3\)), 4.03 (3H, s, OCH\(_3\)), 4.63 (1H, dq, \(\text{J}_{7.3\text{ and 6.3 Hz}}\), 5-H), 5.25 (1H, \(\text{J}_{4.8\text{ Hz}}\), 2-H), 5.71 (1H, d, \(\text{J}_{7.3\text{ Hz}}\), 4-H), 7.05 (1H, s, 3'-H), 7.49–7.53 and 7.58–7.62 (each 1H, m, 6'- and 7'-H) and 8.24–8.27 (2H, m, 5'- and 8'-H); \(\delta_{\text{C}}\) (126 MHz) 16.5 (5-CH\(_3\)), 19.8 (2-CH\(_3\)), 55.6 (OCH\(_3\)), 75.6 (C-5), 80.5 (C-4), 100.6 (C-3'), 104.0 (C-2), 112.5 (C-1'), 122.3 (C-5'), a 125.9 (C-8'), a 126.4 (C-8'a), b 126.8 (C-6'), c 127.9 (C-7'), c 132.4 (C-4'a), b 136.1 (C-2') and 154.8 (C-4'); m/z 338 (M + {81Br}, 34%), 336 (M + {79Br}, 21%), 292 (49), 263 (91), 169 (100) and 126 (38).

**Rel-(2R,4S,5R)-4-(4'-Methoxynaphthalen-2'-yl)-2,5-dimethyl-1,3-dioxolane (31).** A solution of the bromonaphthyldioxolane 8 (760 mg, 2.26 mmol) in dry THF (10 mL), in an atmosphere of nitrogen, was cooled to –30 °C and a solution of \(\text{n}-\text{butyl lithium in hexane (1.10 mL, 2.29 M, 2.49 mmol)}\) added slowly. The reaction was quenched by the addition of water and the mixture was allowed to stir for a further 5 minutes at room temperature. Standard work-up with diethyl ether provided the product 31 as a yellow oil (650 mg). Purification of this oil by column chromatography using hexane–5% ethyl acetate-hexane as eluent afforded the naphthalene 31 (433 mg, 74%) as a pale yellow oil which crystallised upon standing. Repeat recrystallisation from hexane gave pale yellow plates, mp 69.5–71 °C (Found: C, 74.4; H, 6.95; M\(^+\), 258.1264. \(\text{C}_{16}\text{H}_{18}\text{O}_3\) requires C, 74.4; H, 7.0%; M, 258.1256); \(\nu_{\text{max/cm}^{-1}}\) 1631, 1579 and 1508 (C=C); \(\delta_{\text{H}}\) (500 MHz) 0.89 (3H, d, \(\text{J}_{6.4\text{ Hz}}\), 5-CH\(_3\)), 1.63 (3H, d, \(\text{J}_{4.8\text{ Hz}}\), 2-CH\(_3\)), 4.00 (3H, s, OCH\(_3\)), 4.41 (1H, dq, \(\text{J}_{7.2\text{ and 6.4 Hz}}\), 5-H), 5.13 (1H, d, \(\text{J}_{7.2\text{ Hz}}\), 4-H), 5.24 (1H, q, \(\text{J}_{4.8\text{ Hz}}\), 2-H), 6.76 (1H, d, \(\text{J}_{1.2\text{ Hz}}\), 3'-H), 7.29 (1H, d, \(\text{J}_{1.2\text{ Hz}}\), 1'-H), 7.43–7.49 (2H, m, 6'- and 7'-H) and 7.75–7.77 and 8.21–8.23 (each 1H, m, 5'- and 8'-H); \(\delta_{\text{C}}\) (126 MHz) 16.3 (5-CH\(_3\)), 19.9 (2-CH\(_3\)), 55.4 (OCH\(_3\)), 76.5 (C-5), 81.4 (C-4), 100.8 (C-3'), 103.2 (C-2), 118.4 (C-1'), 121.9 (C-5'), a 125.2 (C-8'), a 125.4 (C-4'a), b 126.7 (C-6'), c 127.5 (C-7'), c 134.0 (C-8'a), b 136.4 (C-2') and 155.4 (C-4'); m/z 258 (M\(^+\), 82%), 214 (100), 199 (78), 185 (54), 183 (47), 171 (31), 141 (35) and 115 (24).
Rel-(1R,3R,4S)-3,4-Dihydro-4-hydroxy-6-methoxy-1,3-dimethylnaphtho[1,2-c]pyran (32) and rel-(1S,3R,4S)-3,4-dihydro-4-hydroxy-6-methoxy-1,3-dimethylnaphtho[1,2-c]pyran (34). A solution of the naphthyldioxolane 31 (144 mg, 0.56 mmol) in dry dichloromethane (20 mL) was treated with titanium tetrachloride (130 µL, 1.12 mmol) at –78 °C in an atmosphere of nitrogen. The mixture was stirred at this temperature for 30 minutes and then quenched with dry methanol (490 µL) and poured into saturated sodium hydrogencarbonate solution. Standard work-up (dichloromethane) provided the crude product, a cream solid (87 mg, 60%), as a mixture of two isomers. Purification by column chromatography using 10–30% ethyl acetate-hexane as eluent yielded:

1. The pyran 34 (66 mg, 46%) as fine white needles, mp 156–157.5 °C (ethyl acetate-hexane) (Found: C, 73.95; H, 7.45. C₁₆H₁₈O₃ requires C, 74.4; H, 7.0%; νₘₐₓ/cm⁻¹ 3279 (OH), and 1592 and 1455 (C=C); δH 1.49 (3H, d, J 6.2 Hz, 3-CH₃), 1.58 (3H, d, J 6.1 Hz, 1-CH₃), 1.71 (1H, bs, OH), 3.42 (1H, dq, J 8.6 and 6.2 Hz, 3-H), 4.02 (3H, s, OCH₃), 4.46 (1H, dd, J 2.0 and 8.6 Hz, 4-H), 5.54 (1H, dq, J 2.0 and 6.1 Hz, 1-H), 7.08 (1H, s, 5-H), 7.43–7.53 (2H, m, 8- and 9-H), 7.73–7.76 (1H, m, 10-H) and 8.28–8.30 (1H, m, 7-H); δC 18.4 (3-CH₃) and 24.4 (1-CH₃), 55.6 (OCH₃), 71.6 (C-4), 71.6 (C-3), 74.0 (C-1), 100.6 (C-5), 122.6 (C-7), a 123.5 (C-8), a 124.8 (C-9), a 125.3 (C-6a), b 126.4 (C-10a), b 126.5 (C-10), a 130.3 (C-10b), c 135.5 (C-4a) c and 154.7 (C-6); m/z 258 (M⁺, 42%), 243 (74), 225 (8), 214 (64), 199 (100), 185 (28), 171 (39), 128 (33) and 43 (13).

2. The naphthopyran 32 (21 mg, 14%) which was recrystallised from hexane to give fine white needles, mp 188–189 °C (Found: C, 74.3; H, 7.35. C₁₆H₁₈O₃ requires C, 74.4; H, 7.0%; νₘₐₓ/cm⁻¹ 3397 (OH) and 1590 and 1509 (C=C); δH 1.44 (3H, d, J 6.2 Hz, 3-CH₃), 1.70 (3H, d, J 6.6 Hz, 1-CH₃), 1.72 (1H, bs partially obscured by the 1-CH₃ signal, OH), 4.01 (3H, s, OCH₃), 4.03 (1H, dq, partially obscured by OCH₃), 69.1 (C-3), 101.9 (C-5), 122.6 (C-7), a 123.0 (C-8), a 125.1 (C-9), a 125.3 (C-6a), b 126.8 (C-10), a 130.3 (C-10b), c 135.5 (C-4a) c and 154.9 (C-5); m/z 258 (M⁺, 29%), 243 (100), 225 (6), 199 (65), 171 (21), 128 (20) and 43 (14).

Rel-(1R,3R,4S)-4-Acetoxy-3,4-dihydro-6-methoxy-1,3-dimethylnaphtho-[1,2-c]pyran (33). The pyran 32 (10 mg, 0.04 mmol) in dry pyridine (2 mL) was treated with acetic anhydride (1 mL) at room temperature and the mixture allowed to stir overnight. Water (5 mL) and ether (5 mL) were then added and the mixture allowed to stir for a further 3 h. The two layers were then separated and a little more ether added. The ether layer was washed with water, dilute hydrochloric acid (1 M), water and brine, and then dried and evaporated to give the crude product as a pale yellow oil. Purification by column chromatography using 10% ethyl acetate-hexane as eluent afforded the acetate 33 as a cream solid (10 mg, 85%). Recrystallisation from hexane gave white plates, mp 117.5–119 °C (Found: C, 71.8; H, 6.7; M⁺, 300.1366. C₁₈H₂₀O₄ requires C, 72.0; H, 6.7%; M, 300.1362; νₘₐₓ/cm⁻¹ 1734 (C=O) and 1592 and 1513 (C=C); δH 1.32 (3H, d, J 6.3 Hz, 3-CH₃), 1.73 (3H, d, J 6.6 Hz, 1-CH₃), 2.23 (3H, s, OCH₃), 3.96 (3H, s,
OCH₃), 4.24 (1H, dq, J 7.2 and 6.3 Hz, 3-H), 5.52 (1H, q, J 6.6 Hz, 1-H), 5.89 (1H, d, J 7.2 Hz, 4-H), 6.58 (1H, s, 5-H), 7.46–7.57 (2H, m, 8- and 9-H), 7.73–7.76 (1H, m, 10-H) and 8.27–8.30 (1H, m, 7-H); δC 18.5 (3-CH₃), 21.3 (COCH₃), 21.4 (1-CH₃), 55.5 (OCH₃), 66.7 (C-4), 68.5 (C-3), 72.7 (C-1), 102.4 (C-5), 122.7 (C-7), a 123.0 (C-8), a 125.4 (C-9), a 125.6 (C-6a), b 126.9 (C-10), a 128.1 (C-10a), b 128.8 (C-10b), b 130.0 (C-4a), b 154.8 (C-6) and 171.4 (COCH₃); m/z 300 (M⁺, 24%), 285 (15), 256 (3), 240 (1), 226 (17), 225 (100), 167 (20) and 143 (43).

Rel-(1S, 3R, 4S)-4-Acetoxy-3,4-dihydro-6-methoxy-1,3-dimethylnaphtho-[1,2-c]pyran (35). Pyran 34 (32 mg, 0.12 mmol) was treated in the same manner as pyran 32 to obtain the acetate 35 (28 mg, 75%) as a cream solid. Recrystallisation from ethyl acetate-hexane gave white plates, mp 121–123 °C (Found: C, 71.7; H, 6.5; M⁺, 300.1369. C₁₈H₂₀O₄ requires C, 72.0; H, 6.7%; M, 300.1362); νmax/cm⁻¹ 1741 (C=O) and 1625, 1598 and 1512 (C=C); δH 1.36 (3H, d, J 6.1 Hz, 3-CH₃), 1.60 (3H, d, J 6.2 Hz, 1-CH₃), 2.22 (3H, s, COCH₃), 3.68 (1H, dq, J 8.6 and 6.1 Hz, 3-H), 3.96 (3H, s, OCH₃), 5.57 (1H, dq, J 1.6 and 6.2 Hz, 1-H), 5.92 (1H, dd, J 1.6 and 8.6 Hz, 4-H), 6.53 (1H, s, 5-H), 7.43–7.53 (2H, m, 8- and 9-H), 7.74–7.77 (1H, m, 10-H) and 8.26–8.29 (1H, m, 7-H); δC 18.3 (3-CH₃), 21.1 (COCH₃), 24.5 (1-CH₃), 55.5 (OCH₃), 71.5 (C-4), 71.5 (C-3), 72.2 (C-1), 100.6 (C-5), 122.6 (C-7), a 123.5 (C-8), a 125.0 (C-9), a 125.6 (C-6a), b 126.6 (C-10), a 127.2 (C-10a), b 130.4 (C-10b), b 134.7 (C-4a), b 154.5 (C-6) and 171.2 (COCH₃); m/z 300 (M⁺, 23%), 285 (6), 256 (6), 240 (19), 226 (17), 225 (100), 167 (14) and 149 (29).

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