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

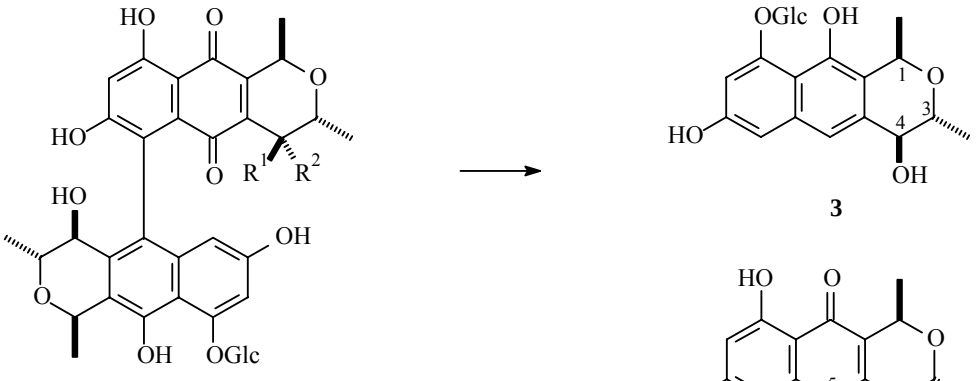
Benzynes were generated selectively through loss of *ortho*-bromotosylate from 1,2-dibromo-3-tosylates. Thus when treated with butyl lithium in the presence of furan *rel*-(2*R*,4*S*,5*R*)-4-(2',3'-dibromo-5'-methoxy-4'-toluene-*p*-sulfonyloxyphenyl)-2,5-dimethyl-1,3-dioxolane **21** was converted in two steps into *rel*-(2*R*,4*S*,5*R*)-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*-(2*R*,4*S*,5*R*)-4-(1'-methoxynaphthalen-3'-yl)-2,5-dimethyl-1,3-dioxolane **31**, on the other hand, isomerized readily to give *rel*-(1*R*,3*R*,4*S*)- and *rel*-(1*S*,3*R*,4*S*)-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.[6] In an early study[8] of this isomerization, the corresponding naphthyldioxolanes 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[5−7] we now report on the further examination of the rearrangement of a naphthyldioxolane bearing a blocking bromine atom *ortho* to the dioxolane ring with a view to assembling linear naphthopyrans.



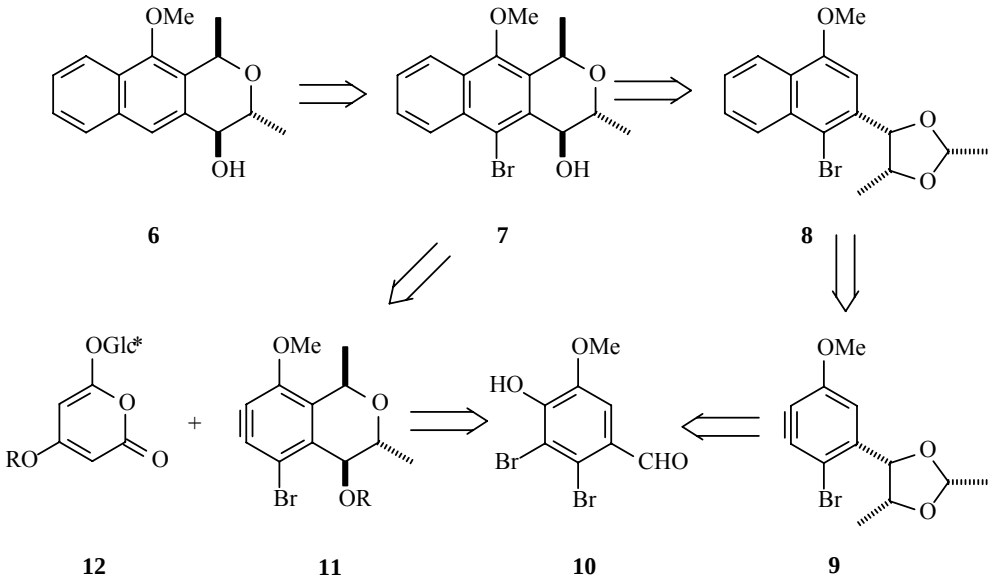
1 $R^1 = OH, R^2 = H$
2 $R^1 = H, R^2 = OH$

4 $R^1 = OH, R^2 = H$
5 $R^1 = H, R^2 = OH$

Scheme 1

The proposed method for the assembly of the target molecule[9] **6** required as a precursor the brominated linear naphthopyran **7** 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 naphthyldioxolane **8** as the precursor to the naphthopyran **7** followed from the smooth isomerization of 2-chloro-5-methoxyphenyldioxolanes to the corresponding 2-benzopyrans in high yield.[6] A Diels−Alder reaction of furan with the benzyne **9** would be manipulated to provide the naphthalene **8** unsubstituted in the second aromatic ring. Alternatively, the possibility of the use of, for example, the protected (*) glucosidic diene **12** with the related benzopyranoid benzyne **11** might provide a precursor to glucoside B **3** through a Diels−Alder reaction in which the regioselectivity would be controlled by the polarization of the 3-methoxybenzyne.[10] Scheme 2 provides for the known[11] phenolic benzaldehyde **10**, obtained

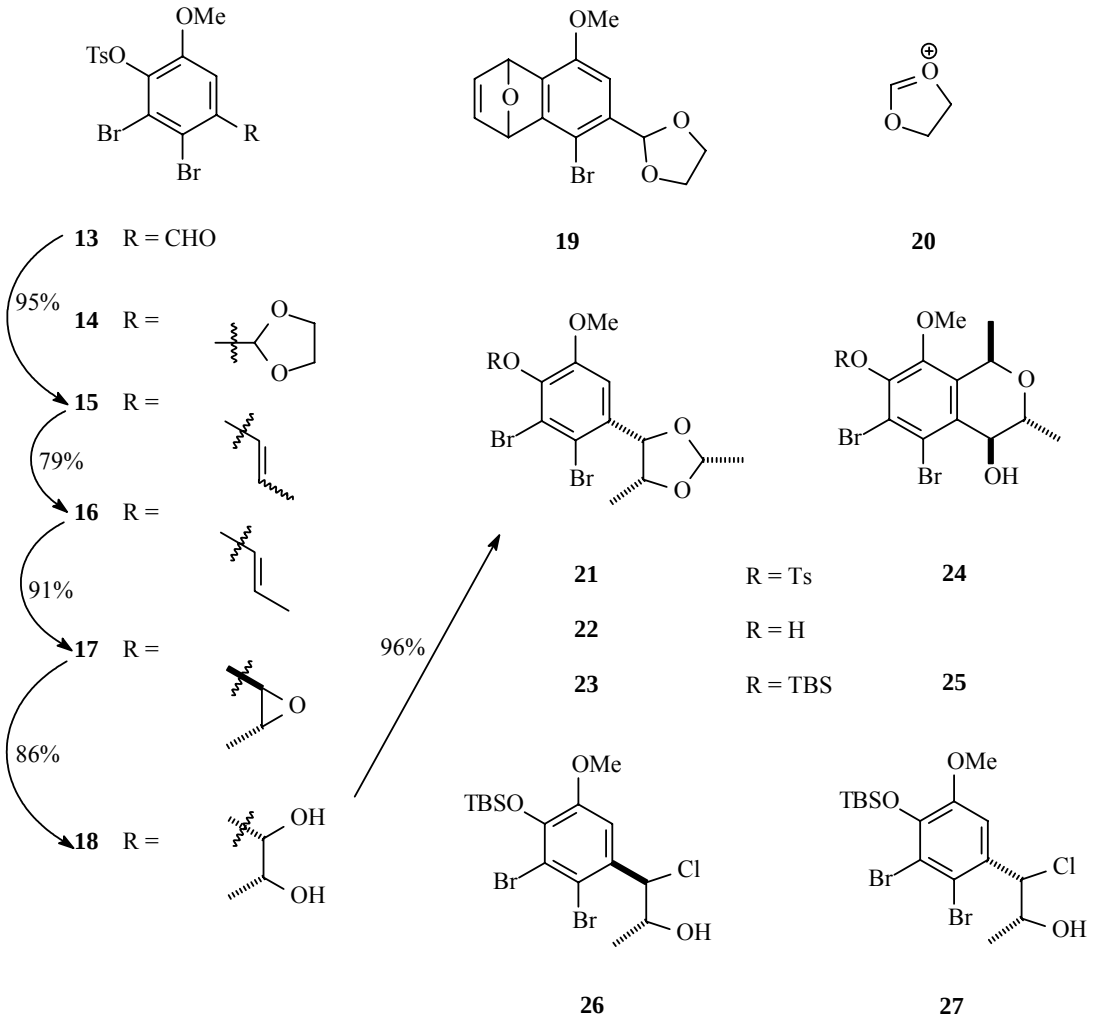
from vanillin, as the starting material for each of the benzynes **9** and **11**. Benzyne **11** would be obtained from the starting material **10** *via* the precursor to benzyne **9**.



Scheme 2

Results and Discussion

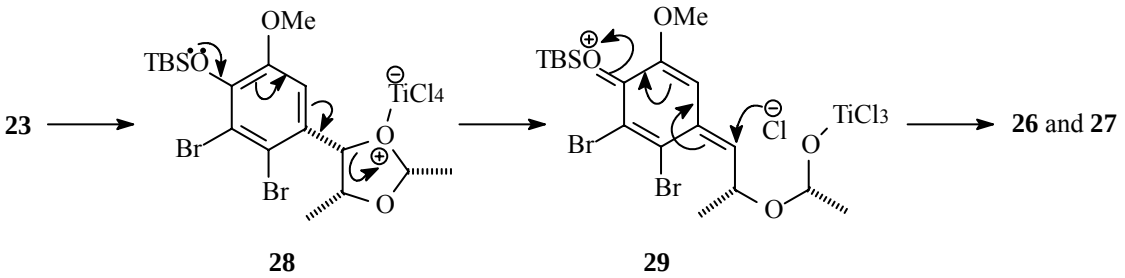
The phenolic group of aldehyde **10** was tosylated to form the derivative **13** with a view, ultimately, to generating the benzynes **9** and **11**. Benzynes may be derived from, *inter alia*, either *ortho*-bromosulfonates or *ortho*-dibromides and since the aromatic ring of **13** is a 1,2-dibromo-3-tosylate, two different benzynes might be produced. Since tosylate would be expected to be a better leaving group than bromide it was possible that the benzynes **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 ^{1}H 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).[12] 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.

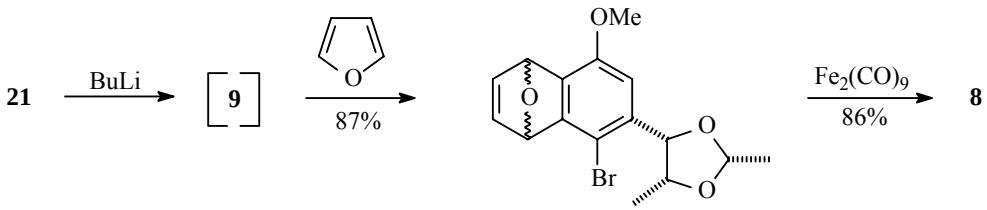
Attempted isomerization of the aryldioxolane **21** to the 2-benzopyran **24** at −78 °C, using two equivalents[5–7] of titanium(IV) chloride, did not succeed, starting material being recovered together with some precursor diol **18**. Repetition at −30 °C and 0 °C also gave none of the benzopyran **24** 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 *t*-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[13] 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 δ 5.44 and 6.3 Hz while for the *erythro*-isomer **27** they were δ 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

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 diasteoisomeric 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**.



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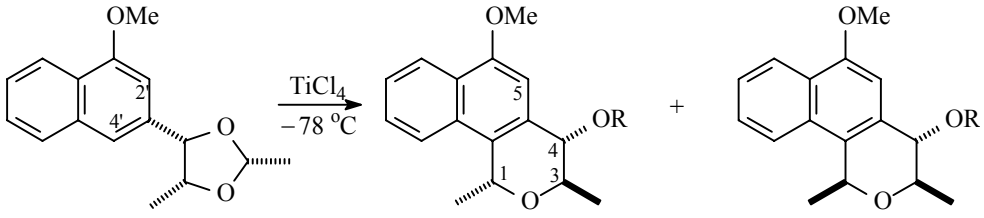
Scheme 4

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 (δ 7.00) of the aromatic proton H-5 corresponded to those of related angular[8] (~δ 6.8) rather than linear[9] naphthopyrans such as **6** (δ 7.84). The formation of the angular naphthopyran can be attributed to the strong preference of naphthalenes to undergo electrophilic substitution at the α- rather than the β-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 *meta*-coupled doublets (*J* 1.2 Hz) at δ 6.76 and δ 7.29 for the protons 2'-H and 4'-H.

Isomerization of the dioxolane **31** afforded the two angular naphthyopyrans **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 naphthyldioxolane **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 δ 4.46 in **32** to δ 5.92 in **33** and from δ 4.45 in **34** to δ 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 *vicinal* protons 3-H and 4-H (*J* 8.0 and 8.6 Hz respectively) indicated an almost *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 δ 4.03 and δ 3.42, which indicated that the heterocyclic methyl substituents were *trans* in the former and *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]

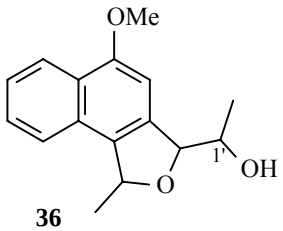


31 14% 46%

32 R = H **34**

33 R = Ac **35**

Scheme 5



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Scheme 5

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**.[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.[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.[6]

Experimental Section

General Procedures. Nuclear magnetic resonance (NMR) spectra were recorded using a Hitachi R-24B spectrometer (^{1}H, 60 MHz), a Bruker AM-300 spectrometer, a Bruker Avance DPX-300 spectrometer (^{1}H, 300 MHz; ^{13}C, 75.5 MHz) or a Bruker ARX-500 spectrometer (^{1}H, 500 MHz; ^{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 (CDCl3) solution or, where indicated, ^{2}H dimethyl sulphoxide (DMSO-d_6) or ^{2}H acetone (acetone-d_6), with the internal standard being tetramethylsilane (TMS) (δ 0.00) for ^{1}H NMR spectra and TMS δ 0.00) or chloroform δ 77.00) for ^{13}C NMR spectra. The signals in the ^{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 F_{254} 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. $C_{15}H_{12}Br_2O_5S$ requires C, 38.8; H, 2.6%); ν_{max}/cm^{-1} 1691 (C=O) and 1581 and 1448 (C=C); δ_H 2.49 (3H, s, Ar-CH_3), 3.72 (3H, s, OCH_3), 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'-toluene-*p*-sulfonyloxyphenyl)-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 hydrogencarbonate 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 (*C*H_2*C*H_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 (*C*H_2*C*H_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 *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. $C_{17}H_{16}Br_2O_4S$ requires C, 42.9; H, 3.4%); ν_{max}/cm^{-1} 1647 (alkene C=C) and 1584 (aromatic C=C); δ_H 1.93 (3H, dd, *J* 6.7 and 1.7 Hz, CH=CHC*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); δ_C 18.6 (CH=CH*C*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 (*C*H=*C*HCH$_3$), 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^+ {^{81}Br, ^{79}Br}, 7%), 474 (M^+ {2x^{79}Br}, 4%), 321 (100), 212 (20), 197 (15), 155 (15), 131 (51), 91 (52) and 65 (13).

***trans*-1-(2',3'-Dibromo-5'-methoxy-4'-toluene-*p*-sulfonyloxyphenyl)-1,2-epoxypropane (17).** A solution of *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 hydrogencarbonate (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 hydrogencarbonate 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. $C_{17}H_{16}Br_2O_5S$ requires C, 41.5; H, 3.3%); ν_{max}/cm^{-1} 1588 and 1454 (C=C); δ_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); δ_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*-(1*S*,2*R*)–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 (Found: C, 40.1; H, 3.7. $C_{17}H_{18}Br_2O_6S$ requires C, 40.0; H, 3.6%); ν_{max}/cm^{-1} 3433 and 3257 (OH), 1590 and 1571 (C=C); δ_H (500 MHz, DMSO-d_6) 1.01 (3H, d, *J* 6.3 Hz, CH_3), 2.44 (3H, s, Ar-CH_3), 3.47 (3H, s, OCH_3), 3.77 (1H, ddq, *J* 4.8, 5.4 and 6.3 Hz, 2-H), 4.69 (1H, d, *J* 5.4 Hz, 2-OH), 4.79 (1H, t, *J* 4.8 Hz, 1-H), 5.64 (1H, d, *J* 4.8 Hz, 1-OH), 7.22 (1H, s, 6'-H) and 7.49 and 7.82 (each 2H, m, AA'BB', Ar-H); δ_C (126 MHz) 18.0 (*C*H_3CH(OH)), 21.2 (Ar-CH_3), 55.9 (OCH_3), 69.0 (C-2), 76.8 (C-1), 112.1 (C-6'), 115.5 (C-2'),[a] 121.5 (C-3'),[a] 128.1 (C-3" and C-5"),[b] 129.8 (C-2" and C-6"),[b] 134.0 (C-4"),[c] 136.3 (C-1'), 144.5 (C-4'), 145.5 (C-1")[c] and 151.7 (C-5'); m/z 313 [(M^+ {2x^{81}Br} – 199), 47%], 311 [(M^+ {^{81}Br, ^{79}Br} – 199), 100%], 309 [(M^+ {2x^{79}Br} – 199), 53%], 202 (37), 155 (75), 91 (89) and 45 (34).

***Rel*-(2*R*,4*S*,5*R*)-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 (Found: C, 43.0; H, 3.6. $C_{19}H_{20}Br_2O_6S$ requires C, 42.6; H, 3.8%); ν_{max}/cm^{-1} 1584 and 1449 (C=C); δ_H 0.89 (3H, d, *J* 6.3 Hz, 5-CH_3), 1.55 (3H, d, *J* 4.8 Hz, 2-CH_3) , 2.48 (3H, s, Ar-CH_3), 3.67 (3H, s, OCH_3), 4.55 (1H, dq, *J* 7.1 and 6.3 Hz, 5-H), 5.17 (1H, q, *J* 4.8 Hz, 2-H), 5.40 (1H, d, *J* 7.1 Hz, 4-H), 7.12 (1H, s, 6'-H) and 7.36 and 7.88 (each 2H, m, AA'BB', Ar-H); δ_C 16.4 (5-CH_3), 19.6 (2-CH_3), 21.7 (Ar-CH_3), 55.9 (OCH_3), 75.2 (C-5), 80.4 (C-4), 100.5 (C-2), 111.4 (C-6'), 115.1 (C-2'),[a] 122.4 (C-3'),[a] 128.4 (C-3" and C-5"),[b] 129.4 (C-2" and C-6"),[b] 134.9 (C-4"),[c] 137.6 (C-1'), 139.0 (C-4'), 145.1, (C-1")[c] and 152.2 (C-5'); m/z 538 (M^+ {2x^{81}Br}, 2%), 536 (M^+ {^{81}Br, ^{79}Br}, 4%), 534 (M^+ {2x^{79}Br}, 2%), 295 (54), 155 (47), 139 (36), 91 (100), 65 (34) and 43 (56).

***Rel*-(2*R*,4*S*,5*R*)-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. This

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^+ {2x^{81}Br}, 383.9212 and M^+ {2x^{79}Br}, 379.9246. $C_{12}H_{14}Br_2O_4$ requires M {2x^{81}Br}, 383.9218 and M {2x^{79}Br}, 379.9259); ν_{max}/cm^{-1} 3379 (OH) and 1596, 1568, 1491 and 1468 (C=C); δ_H 0.88 (3H, d, *J* 6.3 Hz, 5-CH_3), 1.57 (3H, d, *J* 4.8 Hz, 2-CH_3), 3.93 (3H, s, OCH_3), 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); δ_c 16.5 (5-CH_3), 19.7 (2-CH_3), 56.3 (OCH_3), 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^+ {2x^{81}Br}, 40%), 382 (M^+ {^{81}Br, ^{79}Br}, 80%), 380 (M^+ {2x^{79}Br}, 40%), 340 (55), 338 (100), 336 (53), 309 (47), 307 (52), 215 (66), 213 (62) and 77 (14).

***Rel*-(2*R*,4*S*,5*R*)-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) {^{81}Br, ^{79}Br}], 495.0028. $C_{18}H_{28}Br_2O_4Si$ requires [(M-1), {^{81}Br, ^{79}Br}], 495.0025); ν_{max}/cm^{-1} 1588, 1553 and 1471 (C=C); δ_H 0.21 and 0.22 (each 3H, s, $Si(CH_3)_2$), 0.88 (3H, d, *J* 6.3 Hz, 5-CH_3), 1.03 (9H, s, $(CH_3)_3C$), 1.55 (3H, d, *J* 4.8 Hz, 2-CH_3), 3.83 (3H, s, OCH_3), 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); δ_C –3.8 and –3.7 ($Si(CH_3)_2$), 16.4 (5-CH_3), 19.0 ($C(CH_3)_3$), 19.7 (2-CH_3), 26.0 ($C(CH_3)_3$), 55.1 (OCH_3), 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 497 [(M-1) {2x^{81}Br}, 1%], 495 [(M-1) {^{81}Br, ^{79}Br}, 2%], 493 [(M-1) {2x^{79}Br}, 1%], 479 (3), 441 (14), 440 (58), 438 (100), 379 (47), 350 (13) and 73 (28).

***Rel*-(1*R*,2*R*)-1-(2',3'-Dibromo-5'-methoxy-4'-*t*-butyldimethylsilyloxyphenyl)-1-chloropropan-2-ol (26) and *Rel*-(1*S*,2*R*)-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}Br, ^{37}Cl}], 470.9563. $C_{16}H_{25}Br_2ClO_3Si$ requires [(M-OH) {2x^{79}Br, ^{37}Cl}], 470.9571); ν_{max}/cm^{-1} 3408 (OH) and 1586, 1547 and 1472 (C=C); δ_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), 4.07–4.16 (1H, m, 2-H), 5.44 (1H, d, *J* 6.3 Hz, 1-H) and 7.09 (1H, s, 6'-H); δ_H (compound **27**) 0.22 (6H, s, $Si(CH_3)_2$), 1.03 (9H, s, $C(CH_3)_3$), 1.24 (3H, d, *J* 6.3 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); δ_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}Br, ^{37}Cl}, 17%), 490 (M^+ {2x^{81}Br, ^{35}Cl}, 81%),** 488 (M^+ {2x^{79}Br, ^{37}Cl},** 100%), 486 (M^+ {2x^{79}Br, ^{35}Cl}, 44%), 475 (77), 473 (100), 445 (56), 443 (84), 433 (76), 431 (100), 372 (46) and 149 (70).

***Rel*-(2*R*,4*S*,5*R*)-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}Br}, 354.0300 and M^+ {^{79}Br}, 352.0317. $C_{16}H_{17}BrO_4$ requires (M {^{81}Br}, 354.0290) and M {^{79}Br}, 352.0310); ν_{max}/cm^{-1} 1596 and 1458 (C=C); δ_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), 3.833 and 3.835 (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); δ_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'),[b] 142.2 and 142.3 (C-7'),[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^+ {^{81}Br}, 5%), 352 (M^+ {^{79}Br}, 5%), 251 (27), 157 (53), 115 (31), 72 (55) and 43 (100).

***Rel*-(2*R*,4*S*,5*R*)-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 [$Fe_2(CO)_9$] (620 mg, 1.70 mmol) in an atmosphere of nitrogen. The mixture was stirred at 50–60 °C (oil bath) until all the solid $Fe_2(CO)_9$ 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^+ {^{81}Br}, 338.0334. $C_{16}H_{17}BrO_3$ requires C, 57.0; H, 5.1%; M {^{81}Br}, 338.0341); ν_{max}/cm^{-1} 1595 and 1503 (C=C); δ_H (500 MHz) 0.90 (3H, d, *J* 6.3 Hz, 5-CH_3), 1.63 (3H, d, *J* 4.8 Hz, 2-CH_3), 4.03 (3H, s, OCH_3), 4.63 (1H, dq, *J* 7.3 and 6.3 Hz, 5-H), 5.25 (1H, *J* 4.8 Hz, 2-H), 5.71 (1H, d, *J* 7.3 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); δ_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^+ {^{81}Br}, 34%), 336 (M^+ {^{79}Br}, 21%), 292 (49), 263 (91), 169 (100) and 126 (38).

***Rel*-(2*R*,4*S*,5*R*)-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 *n*-butyl lithium in hexane (1.10 mL, 2.29 M, 2.49 mmol) added slowly. The mixture was then stirred at –30 °C for approximately 20 minutes. 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. Repeated recrystallisation from hexane gave pale yellow plates, mp 69.5–71 °C (Found: C, 74.4; H, 6.95; M^+, 258.1264. $C_{16}H_{18}O_3$ requires C, 74.4; H, 7.0%; M, 258.1256); ν_{max}/cm^{-1} 1631, 1579 and 1508 (C=C); δ_H (500 MHz) 0.89 (3H, d, *J* 6.4 Hz, 5-CH_3), 1.63 (3H, d, *J* 4.8 Hz, 2-CH_3), 4.00 (3H, s, OCH_3), 4.41 (1H, dq, *J* 7.2 and 6.4 Hz, 5-H), 5.13 (1H, d, *J* 7.2 Hz, 4-H), 5.24 (1H, q, *J* 4.8 Hz, 2-H), 6.76 (1H, d, *J* 1.2 Hz, 3'-H), 7.29 (1H, d, *J* 1.2 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); δ_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*-(1*R*,3*R*,4*S*)-3,4-Dihydro-4-hydroxy-6-methoxy-1,3-dimethylnaphtho[1,2-*c*]pyran (32) and *rel*-(1*S*,3*R*,4*S*)-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. $C_{16}H_{18}O_3$ requires C, 74.4; H, 7.0%); ν_{max}/cm^{-1} 3279 (OH), and 1592 and 1455 (C=C); δ_H 1.49 (3H, d, *J* 6.2 Hz, 3-CH_3), 1.58 (3H, d, *J* 6.1 Hz, 1-CH_3), 1.71 (1H, bs, OH), 3.42 (1H, dq, *J* 8.6 and 6.2 Hz, 3-H), 4.02 (3H, s, OCH_3), 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 8.27–8.30 (1H, m, 7-H); δ_C 18.4 (3-CH_3) and 24.4 (1-CH_3), 55.6 (OCH_3), 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. $C_{16}H_{18}O_3$ requires C, 74.4; H, 7.0%); ν_{max}/cm^{-1} 3397 (OH) and 1590 and 1509 (C=C); δ_H 1.44 (3H, d, *J* 6.2 Hz, 3-CH_3), 1.70 (3H, d, *J* 6.6 Hz, 1-CH_3), 1.72 (1H, bs partially obscured by the 1-CH_3 signal, OH), 4.01 (3H, s, OCH_3), 4.03 (1H, dq, partially obscured by OCH_3, *J* 8.0 and 6.2 Hz, 3-H), 4.45 (1H, d, *J* 8.0 Hz, 4-H), 5.48 (1H, q, *J* 6.6 Hz, 1-H), 7.00 (1H, s, 5-H), 7.44–7.55 (2H, m, 8- and 9-H), 7.69–7.72 (1H, m, 10-H) and 8.27–8.30 (1H, m, 7-H); δ_C 18.7 (3-CH_3) and 21.2 (1-CH_3), 55.5 (OCH_3), 68.9 (C-4), 69.1 (C-3), 72.0 (C-1), 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] 127.0 (C-10a),[b] 130.0 (C-10b),[c] 132.8 (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*-(1*R*,3*R*,4*S*)-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. $C_{18}H_{20}O_4$ requires C, 72.0; H, 6.7%; M, 300.1362); ν_{max}/cm^{-1} 1734 (C=O) and 1592 and 1513 (C=C); δ_H 1.32 (3H, d, *J* 6.3 Hz, 3-CH_3), 1.73 (3H, d, *J* 6.6 Hz, 1-CH_3), 2.23 (3H, s, $COCH_3$), 3.96 (3H, s,

OCH_3), 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); δ_C 18.5 (3-CH_3), 21.3 (CO*C*H_3), 21.4 (1-CH_3), 55.5 (OCH_3), 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 (*C*OCH_3); m/z 300 (M^+, 24%), 285 (15), 256 (3), 240 (1), 226 (17), 225 (100), 167 (20) and 143 (43).

***Rel*-(1*S*, 3*R*, 4*S*)-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. $C_{18}H_{20}O_4$ requires C, 72.0; H, 6.7%; M, 300.1362); ν_{max}/cm^{-1} 1741 (C=O) and 1625, 1598 and 1512 (C=C); δ_H 1.36 (3H, d, *J* 6.1 Hz, 3-CH_3), 1.60 (3H, d, *J* 6.2 Hz, 1-CH_3), 2.22 (3H, s, $COCH_3$), 3.68 (1H, dq, *J* 8.6 and 6.1 Hz, 3-H), 3.96 (3H, s, OCH_3), 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); δ_C 18.3 (3-CH_3), 21.1 (CO*C*H_3), 24.5 (1-CH_3), 55.5 (OCH_3), 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] 131.7 (C-4a),[b] 154.5 (C-6) and 171.2 (*C*OCH_3); m/z 300 (M^+, 23%), 285 (6), 256 (6), 240 (19), 226 (17), 225 (100), 214 (16), 167 (14) and 149 (29).

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