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Syntheses in enantiopure form of four diastereoisomeric naphthopyranquinones derived from aphid insect pigments†‡

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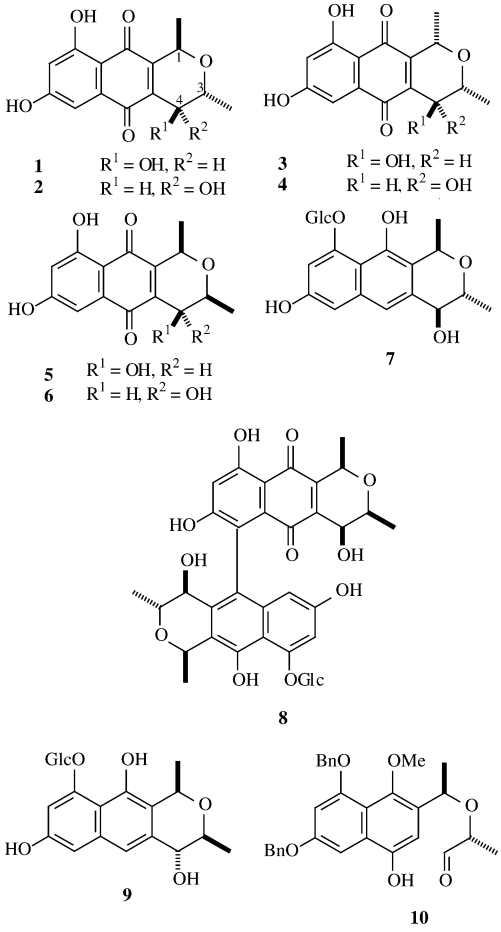
The first syntheses are described of the four enantiopure naphthopyranquinones (1*R*,3*R*,4*S*)- and (1*R*,3*R*,4*R*)-3,4-dihydro-4,7,9-trihydroxy-1,3-dimethylnaphtho[2,3-*c*]pyranquinone (quinone A **1** and quinone A′ **2**) and their two C-3 epimers, the (1*R*,3*S*,4*S*)- and (1*R*,3*S*,4*R*)-diastereoisomers **5** and **6**, using enantiopure lactate as the source of asymmetry. Key factors in these syntheses are the maintenance of stereochemical integrity throughout the sequences and intramolecular diastereoselective cyclisations of the titanium phenolates of phenolic lactaldehydes. For these cyclisations the differing degree of diastereoselectivity is explained as are the stereochemistries of the product 2-benzopyran-4,5-diols.

Introduction

Quinone A **1** and glucoside B **7** are the products of reductive cleavage of the bean aphid insect pigment protoaphin-*fb*,[1] while the C-4 epimeric quinone A′ **2** and the same glucoside **7** are obtained similarly from the willow aphid pigment protoaphin-*sl*.[1] These quinones are of interest, *inter alia*, since they have been nominated as potential bioreductive dialkylating agents.[2] Cameron *et al.* have shown[3] that each of these protoaphins can be reconstituted through oxidative coupling of the individual quinones with glucoside B **7**. The assembly of these components **1**, **2** and **7** in enantiopure form would be required for syntheses of the parent protoaphins to avoid diastereomeric mixtures. While we have previously synthesised[4] the racemates of the quinones **1** and **2**, this method did not lend itself to the assembly of the individual enantiomers.[5] In a preliminary publication we have recently reported[6] the first syntheses of each of these enantiopure quinones, as well as those of their C-1 epimers **3** and **4**. These compounds **1–4** comprise all four stereoisomers based on *3R* stereochemistry. After the completion of this work,[6] discussions with Professor Cameron revealed[7] preliminary observations suggesting that the compounds **3** and **4** are the enantiomers of two further, unreported, derivatives of naturally occurring aphid pigments. The remainder of this paragraph summarizes the hitherto unpublished results of Banks and Cameron.[7] These new naturally derived quinones are the C-3 epimers **5** and **6** of the quinones A **1** and A′ **2**. Quinone **5** was isolated[7] together with glucoside B **7** through reductive cleavage[1] of a new protoaphin-*pm*[7] **8** that co-occurred with protoaphin-*fb* in aphid insect species of the Pemphigidae. The most practical source of protoaphin-*pm*, however, was found to be *Eriosoma lanigerum* Hausmann, the common woolly apple aphid.[7] Furthermore, a new glucoside **9**, diastereoisomeric with glucoside B **7** at both C-3 and C-4, was obtained[7] on examination of constituents of *Periphyllus acericola* Walker from the aphid insect family Chaitophoridae. The new glucoside **9** was converted[7] into quinone **6** through Fremy salt oxidation followed by treatment of the glycosidic quinonoid intermediate with enzymic extracts of *Aphis fabae* using the method pioneered by Cameron and Craik[8] for the conversion of glucoside B **7** into quinone A **1**.



Our model experiments had shown[9] that the completely diastereoselective cyclisation of an enantiopure *meta*-hydroxybenzyl ether of lactaldehyde ultimately afforded the target benzopyranquinone in monochiral form. The extension of these ideas to the present study required, as one option, the assembly of the naphtholic lactaldehyde **10**, but this proved problematic. As an alternative, the retrosynthetic analysis shown in Scheme 1 was considered based on methyl (*R*)-lactate **15** as the chiral

† Dedicated to Professor Don Cameron for his outstanding contribution to research and teaching in organic chemistry.

‡ Electronic supplementary information (ESI) available: additional experimental details. See http://www.rsc.org/suppdata/ob/b4/b414213f/

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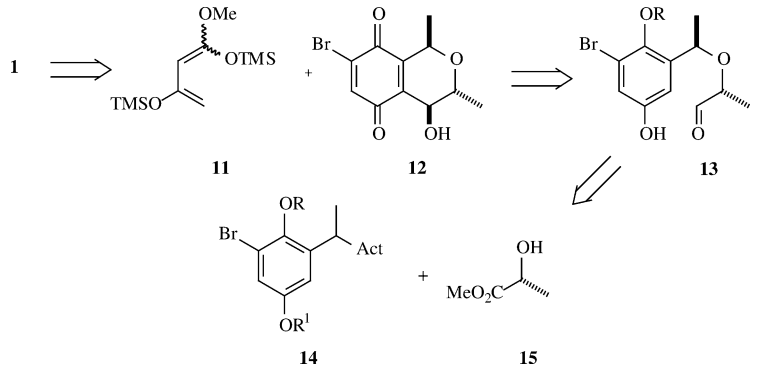


Scheme 1

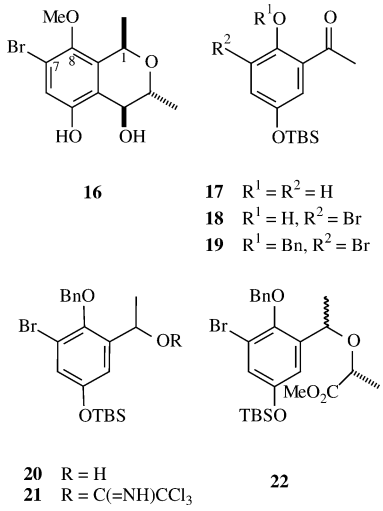
pool source of asymmetry for C-3 of the derived naphthopyranquinones **1** and **2**. The other starting material required would be the benzyl activated regioselectively brominated hydroquinone diether **14**. The bromine atom in benzopyranquinone **12** was necessary to direct the Diels–Alder regioselectivity[10] in the forward sense to yield quinone A **1**. The use of bromine rather than chlorine was imperative since recent studies had shown[11] that brominated, but not chlorinated, *meta*-hydroxybenzyl lactaldehydes cyclise (with complete diastereoselectivity) to yield benzopyran-4,5-diols as potential precursors to quinones such as **12**. The Diels–Alder reaction of the diene **11** with the non-brominated analogue of quinone **12** would be anticipated to favour the alternative regioisomer of quinone **1** (the 4,6,8-naphthopyrantriol rather than the required 4,7,9-regioisomer) through hydrogen bonding between the C-4 alcohol hydrogen and the C-5 carbonyl oxygen atoms.[12] We report here in detail on the first syntheses of the four naturally derived enantiopure quinones A **1** and A′ **2** and their C-3 epimers **5** and **6**.

Results and discussion

Syntheses of phenolic lactaldehydes 25 and 28

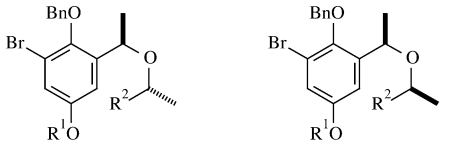
Attempted oxidative dealkylation of the benzopyran-4,5-diol **16**[11] with either ceric ammonium nitrate[13] or argentic oxide[14] did not afford the target quinone **12**. Other oxidants investigated either failed to react or led to decomposition of starting material. A comparison of the failure of this diol **16** to undergo oxidation using argentic oxide with the smooth oxidation of its non-brominated enantiomer[9] suggested that the environment of the C-8 methoxy substituent between the C-7 bromine and the C-1 methyl was too crowded to permit this oxidative dealkylation. Alternative protection of the hydroquinone diether **14** was therefore established.

The non-hydrogen bonded, less crowded hydroxy group of commercially available 2,5-dihydroxyacetophenone was regioselectively silylated to give solely the *t*-butyldimethylsilyl ether **17** in 96% yield, for which, *inter alia*, the hydrogen bonded hydroxyl hydrogen was observed in the ^{1}H NMR spectrum at δ 11.85. This was in turn regioselectively monobrominated, using bromine in dichloromethane containing pyridine, *ortho* to the phenolic and *meta* to the acetyl substituents to afford the bromobenzene **18** in 96% yield, for which the ^{1}H NMR spectrum showed two *meta*-coupled aromatic protons. Benzylation of the remaining phenolic oxygen using benzyl bromide in the presence of anhydrous potassium carbonate yielded the differently protected hydroquinone diether **19** in 95% yield. Reduction of the ketone function gave the benzylic alcohol **20** in 94% yield. This was converted into its trichloroacetimidate **21** in a yield of 88% using trichloroacetonitrile and a catalytic quantity of sodium hydride.[15] The infrared spectrum of the product showed an imine absorption at 1661 cm^{-1} and, in the ^{1}H NMR spectrum, the characteristic resonances of the NH and benzylic methine protons at δ 8.35 and δ 6.25 respectively, the latter strongly deshielded from its value of δ 5.03 for the alcohol **20**. Imidate **21** was in turn treated with methyl (*R*)-lactate **15** in the presence of a catalytic amount of boron trifluoride diethyl etherate[16] to yield an inseparable mixture of the benzyl epimeric lactates **22** in a yield of 91% and in a ratio of 1.3 : 1, as judged by ^{1}H NMR spectroscopy. The overall yield of this mixture **22** from 2,5-dihydroxyacetophenone was 51% in six steps.

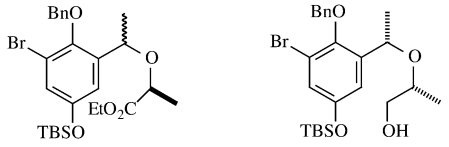


Just sufficient lithium aluminium hydride (monitored by thin layer chromatography) was added to the ester mixture **22** to effect complete conversion into the chromatographically separable benzyl-epimeric alcohols **23** and **30**, obtained in a combined yield of 91% and individual yields of 52% and 39% respectively. An excess of the reducing agent also removed the bromine atom from the aromatic ring. Individual assignments were not possible to make at this stage, but followed from the ^{1}H NMR spectra of the derived benzopyrans (see below). In order to establish that no epimerisation of the lactate asymmetric centre had occurred during either its benzylation or the subsequent reduction, the enantiomeric excess for each of these alcohols **23** and **30** was investigated. This was achieved by preparing their enantiomers **31** and **26** respectively as above from the trichloroacetimidate **21** and ethyl (*S*)-lactate *via* the inseparable mixture of esters **29**. These were obtained in a ratio of 1 : 1. The values for the specific rotations of these alcohols corresponded closely to those expected for their enantiomers **23** and **30** (see Experimental). Mixtures of the enantiomeric pairs **23**/**31** and **26**/**30** were assembled, each in a 60 : 40 ratio, and examined both by ^{1}H NMR spectroscopy using the lanthanide shift reagent europium tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate] (Eu(hfc)$_3$)[9,17] and by chiral high pressure liquid chromatography. In each procedure good separation was achieved for signals attributable to each enantiomer within each mixture, whereas for the enantiopure **23** and **26** required for the assembly of the natural derivatives virtually none of the

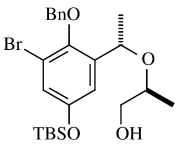
alternative enantiomers were observed (and likewise for the enantiopure **30** and **31**).



23 R^1 = TBS, R^2 = CH_2OH **26**
24 R^1 = TBS, R^2 = CHO **27**
25 R^1 = H, R^2 = CHO **28**



29 **30**



31

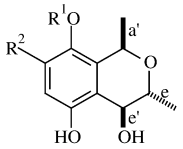
Swern oxidation[18] of the alcohol **23** afforded the aldehyde **24** in 88% yield. Pyridinium chlorochromate[19] could also be used, but the yields were lower. Evidence for the aldehyde was observed in the infrared spectrum, in which the hydroxyl absorption of the alcohol **23** was replaced by a carbonyl absorption at 1735 cm^{-1}, and in the ^1H NMR spectrum the aldehydic proton appeared as a doublet at δ 9.60 (J 1.7 Hz). Similar oxidation of the alcohol **26** derived from ethyl (*S*)-lactate gave, in 85% yield, the aldehyde **27** for which the corresponding aldehydic proton was observed at δ 9.49 (J 1.2 Hz). Two observations confirmed that no epimerisation of the carbon α to the aldehydic carbonyl had occurred during the oxidation step. First, such epimerisation of the aldehyde **24** would yield the epimeric aldehyde **27**, but this was not observed in its ^1H NMR spectrum. Secondly, the aldehyde **24** was reduced back to its precursor alcohol **23** for which the specific rotation agreed with the value for material obtained directly through reduction of the ester **22**. The same two observations were made for the epimeric aldehyde **27**.

Removal of the silyl protecting group in aldehyde **24** was achieved using a mixture (1 : 1) of saturated solutions of sodium fluoride and ammonium chloride, whereupon the crude phenolic aldehyde **25** was obtained in 73% yield after rapid chromatography. Deprotection of the epimeric aldehyde **27** was similarly accomplished in 76% yield to afford the crude benzyl epimeric lactaldehyde **28**.

Syntheses of benzopyranquinones 12 and 58–64

The phenolic lactaldehyde **25** was immediately cyclised with titanium tetraisopropoxide[9,20] using ultrasound. This afforded solely the benzopyran-4,5-diol **32** in a completely diastereoselective reaction in 55% yield for the two steps from the silyloxyphenyl lactaldehyde **24**. The stereochemistry of pyran **32** was determined from its ^1H NMR spectrum, which showed, first, that the coupling constant between the protons 3-H and 4-H was 8.7 Hz. This required an almost *trans*-diaxial arrangement for the two protons and therefore the C-3 methyl to be equatorial and the C-4 hydroxyl to be pseudoequatorial. Secondly, the chemical shift of the proton 3-H was δ 3.86. A comparison of this with the related values for the two benzopyran-4,5-diols from the alternative lactaldehyde **28** (see below) showed it to be significantly deshielded from these, and, therefore, that the product **32** possessed a *trans* arrangement[21] of the two methyl substituents at C-1 and C-3. It followed that the C-1 methyl was pseudoaxial.

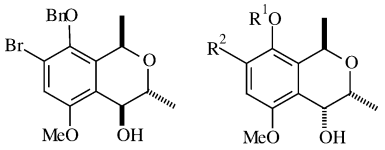
The benzyl protecting group in compound **32** was removed through hydrogenolysis, using the catalyst palladium on carbon in ethyl acetate, to afford the required hydroquinone **33** together with the analogue **34** arising from unavoidable debromination. The oily mixture was immediately oxidized with ceric ammonium nitrate to the chromatographically separable bromobenzopyranquinone **12** and its debrominated analogue **58**, the enantiomer of the latter being known,[9] in yields of 41% and 17% over the two steps. The stereochemistry of each was confirmed as the same from the chemical shifts of the proton 3-H (δ 3.84), the large 3-H/4-H coupling constants (7.7 and 7.8 Hz respectively) and, in addition, the long range homoallylic couplings between the protons 1-H and 4-H. These values (J 1.4 and 1.6 Hz respectively) are typical for such coupling between a pseudoequatorial and a pseudoaxial proton and are consistent with that observed for the natural derivative quinone A.[9,22,23] This hydrogenolytic debromination was useful in that it provided the parent 2-benzopyranquinone **58** itself, although for the natural derivative quinone A selective debenzylation to give solely the brominated quinone **12** was necessary and was achieved by a change in solvent from ethyl acetate to tetrahydrofuran. Here the debenzylation afforded solely the rapidly chromatographed hydroquinone **33** in virtually quantitative yield and this was then oxidised to the quinone **12** in a yield of 84% over the two steps.



32 R^1 = Bn, R^2 = Br
33 R^1 = H, R^2 = Br
34 R^1 = R^2 = H

The brominated quinone **59**, the C-4 pseudoaxial epimer of **12** required for the synthesis of quinone A′, could not be obtained readily by the cyclisation of the magnesium phenolate[20] of phenolic lactaldehyde **25**, presumably owing to the inability of the magnesium to coordinate effectively to both the carbonyl and lactaldehyde oxygen atoms. The benzopyranquinone **59** was obtained through phenolic methylation of the benzopyran **32** to afford the methyl ether **35** in 96% yield. The C-4 pseudoequatorial stereochemistry of this alcohol was reversed through treatment of **35** with phosphorus pentachloride followed by silver nitrate in aqueous acetonitrile[4] to afford the epimeric C-4 pseudoaxial alcohol **36** in 72% yield, together with a 21% recovery of the starting material **35**. This represented an overall yield of 87% over the two steps from the alcohol **35** based on unrecovered alcohol **35**. Debenzylation of this hydroquinone dialkyl ether in ethyl acetate (see above) afforded the monomethyl ether **37**, together with the corresponding product of debromination **38**. This 5-methoxybenzopyran-4,8-diol **37** was a structurally isomeric analogue of the 8-methoxybenzopyran-4,5-diol **16** above which could not be oxidized. In contrast, the mixture containing this new isomer underwent smooth oxidative demethylation to afford the separable mixture of benzopyranquinones **59** and **60** in yields of 51% and 22% for the two steps from alcohol **36**. The ready oxidation of the 5-methoxy compound **37** confirmed the earlier assumption that steric crowding prevented the oxidation of its isomer **16**. The new benzopyranquinones **59** and **60** possessed the same stereochemistry for the pyran ring. This was evident from chemical shifts of the proton 3-H in each case (δ 3.96 and δ 3.97 respectively), the identical 3-H/4-H coupling constant (J 2.2 Hz) and the lack of long range homoallylic coupling between the two pseudoequatorial protons 1-H and 4-H.[9,22,23] Selective debenzylation without debromination was

achieved again using the alternative solvent tetrahydrofuran, giving solely the bromoquinone **59**, after oxidation, in a yield of 73% for the two steps from benzopyran **36**.

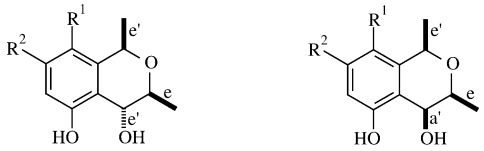


35 **36** R^1 = Bn, R^2 = Br
37 R^1 = H, R^2 = Br
38 R^1 = R^2 = H

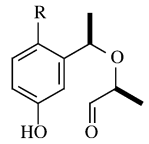
Immediate cyclisation of the diastereomeric lactaldehyde **28** with titanium tetraisopropoxide and ultrasound was only partially diastereoselective, with the formation of the two chromatographically separable C-4 epimeric benzopyran-4,5-diols **39** and **44** being obtained in a combined yield of 62% over the two steps from the silyl-protected aldehyde **27** and respective yields of 51% and 30% for the cyclisation step. Individual stereochemistries were established, first, from the coupling constants between 3-H and 4-H for the two stereoisomers, these being 8.8 Hz and 1.6 Hz respectively. For the major isomer **39** this required that the C-3 methyl was equatorial and the C-4 hydroxy group pseudoequatorial. For the minor diastereoisomer, the smaller coupling constant indicated a smaller dihedral angle between the two protons and therefore, with the C-3 methyl still equatorial, the C-4 hydroxy group was pseudoaxial. Secondly, the chemical shifts for 3-H for the two diastereoisomers **39** and **44** were δ 3.39 and δ 3.59, both at significantly lower chemical shift than that (δ 3.86) for the 1,3-*trans*-dimethyl stereoisomer **32** above. Both these values were consistent with the alternative 1,3-*cis*-dimethyl stereochemistry,[21] which required the C-1 methyl in each case to be pseudoequatorial.

In a recent study[24,25] we showed that the phenolic lactaldehyde **49** unsubstituted *para* to the phenolic hydroxyl group cyclised with complete diastereoselectivity to give the *cis*-1,3-dimethylbenzopyran-4,5-diol **42** in good yield, none of the epimeric C-4 diol **47** being formed, whereas an earlier study[9] showed that the corresponding methoxy lactaldehyde **50** cyclised with lower diastereoselectivity to afford the pair of C-4 epimeric *cis*-1,3-dimethylbenzopyran-4,5-diols **43** and **48** in a ratio of 75 : 25, with the pseudoequatorial alcohol still predominating. In the present study the diastereoselectivity is even less, with cyclisation of the corresponding brominated benzyloxy derivative yielding the two C-4 epimeric *cis*-1,3-dimethylbenzopyrans **39** and **44** in a ratio of 62 : 38. For the corresponding three benzyl-epimeric lactaldehydes **25**, **51** and **52**, (the first with the enantiomeric stereochemistry of the latter two) the cyclisations to the *trans*-1,3-dimethyl compounds were all completely diastereoselective. We propose that in the conformation for the transition state **55**§ (numbering for the developing benzopyran ring-system) leading to all the *trans*-1,3-dimethylbenzopyrans **32**, **53** and **54** the developing C-4 alcohol oxygen assumes the pseudoequatorial orientation to minimize the inter-oxygen distance for titanium coordination, the C-3 methyl is equatorial to avoid 1,3-diaxial interactions and the C-1 methyl is pseudoaxial, which minimizes the 1,8-*peri*-interactions with the neighbouring alkoxy group in the first and third cases. The exclusive products in these two cases are therefore **32** and **54**. The transition state for the conversion of the lactaldehyde **51** into the pyranol **53** and the possible inversion of the dihydropyran ring of the latter has recently been published elsewhere.[24,25]

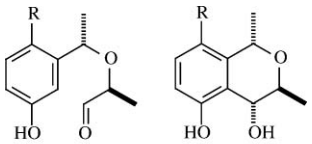
§ The transition state **55** is drawn for the conversion of the lactaldehyde **25** into the benzopyran **16**. For the conversions of the lactaldehydes **51** and **52** into the benzopyrans **53** and **54** the transition states would have the enantiomeric stereochemistry.



39 R^1 = OBn, R^2 = Br **44**
40 R^1 = OH, R^2 = Br **45**
41 R^1 = OH, R^2 = H **46**
42 R^1 = R^2 = H **47**
43 R^1 = OMe, R^2 = H **48**



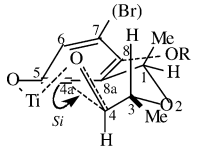
49 R = H
50 R = OMe



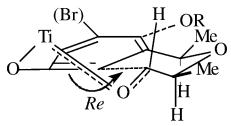
51 R = H **53** R = H
52 R = OMe **54** R = OMe

For that leading from lactaldehyde **49** to pyran **42**, the C-1 methyl is pseudoequatorial, which is preferred since there are no significant 1,8-*peri*-interactions with the neighbouring hydrogen and a single diastereomer is therefore formed. For those transition states **56** involved in the conversions of the lactaldehydes **28** and **50** into the remaining *cis*-1,3-dimethylbenzopyrans **39** and **43**, however, the pseudoequatorial C-1 methyl orientation leads to significant 1,8-*peri*-interactions with the neighbouring alkoxy substituents. Here, intramolecular arylation occurs at the *Re* face of the aldehyde.[9] The alternative conformation **57** of the transition state is therefore adopted by ~38% and ~25%, respectively, of the molecules in the cyclisations to the minor C-4 epimers **44** and **48**, in which the incipient C-4 alcohol retains the pseudoequatorial orientation to minimize the inter-oxygen distance through coordination. The C-1 methyl becomes pseudoaxial to reduce these 1,8-*peri*-interactions with the neighbouring C-8 alkoxy group at the expense of the C-3 methyl becoming axial,[24] and intramolecular arylation in **57** occurs at the *Si* face of the aldehyde. Upon hydrolysis of the titanium complex the conformation of the derived dihydropyran rings in **44** and **48** invert so that the C-1 and C-3 methyl groups become pseudoequatorial and equatorial respectively, and the C-4 alcohol becomes pseudoaxial. The dihydropyrans **44** and **48** obtained from this alternative transition state are therefore the C-4 epimers of dihydropyrans **39** and **43**. The greater the steric demand of the C-8 substituent in the developing benzopyran the greater the proportion of molecules adopting this alternative conformation leading to the pseudoaxial C-4 alcohols. In the case of **44** this steric compression may be increased by the buttressing effect of the additional bromine atom.

The benzopyran **39** was debenzylated over palladium on charcoal in ethyl acetate to afford the hydroquinone **40** mixed with its debrominated analogue **41**. This mixture was oxidized immediately with ceric ammonium nitrate to give the chromatographically separable benzopyranquinones **63** and **64** in yields of 43% and 40%. Once again, the stereochemistry was shown to be the same for both products. The chemical shifts for the protons 3-H were at δ 3.57 and δ 3.69 respectively, the 3-H/4-H coupling constants identical (J 8.3 Hz), and the large long range homoallylic coupling between 1-H and 4-H (J 2.9 Hz) further confirmation that both these protons were pseudoaxial in each of the product 2-benzopyranquinones.[9,23]



55



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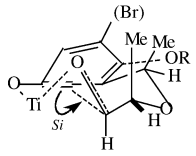
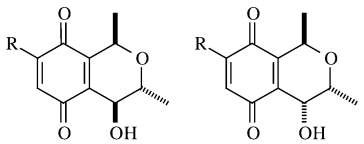
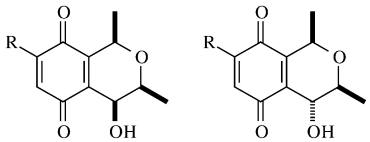


57

Similar debenzylation of the all *cis* benzopyran **44** followed by oxidation afforded the separable mixture of benzopyranquinones **61** and **62** (the latter known as the racemate[26]) in yields of 42% and 33%. The identical values for the chemical shifts of the protons 3-H (δ 3.59), the 3-H/4-H coupling constants (J 1.6 Hz), and the long range homoallylic coupling constants (J 1.4 Hz) between the pseudoaxial 1-H and pseudoequatorial 4-H confirmed the same stereochemistry for each product. This latter value is very close to that (J 1.6 Hz) for compounds **12** and **58** above, where 1-H is pseudoequatorial and 4-H pseudoaxial.



12 R = Br **59**
58 R = H **60**

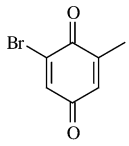


61 R = Br **63**
62 R = H **64**

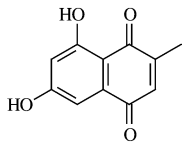
Once again, selective debenzylation with retention of the aromatic bromine atom could be achieved using tetrahydrofuran as the solvent for each of the *O*-benzyl-protected 2-benzopyrans **39** and **44**, giving, respectively, the hydroquinones **40** and **45**. Ceric ammonium nitrate oxidation of these individual hydroquinones afforded the brominated 2-benzopyranquinones **63** and **61**, which were obtained in yields of 70% and 77% respectively.

Syntheses of quinone A 1, quinone A′ 2, and their two C-3 epimers 5 and 6

2-Bromo-6-methyl-1,4-benzoquinone **65**[27] was used as a readily available model to optimize conditions for the reaction of bromobenzopyranquinones such as **12** with the diene **11**.[28] After considerable experimentation, modification of a literature method[29] was used with this model to afford 6,8-dihydroxy-2-methyl-1,4-naphthoquinone **66** in 73% yield. When these conditions were used for the Diels–Alder reaction of diene **11** with the benzopyranquinone **12**, quinone A **1** was crystallized directly from the solution (as were the quinones **2**, **5** and **6** below) in a 30% yield. Combustion data and a high-resolution mass spectrum confirmed the molecular formula. Similar reaction of the diene **11** with the C-4 epimeric benzopyranquinone **59** afforded quinone A′ **2** in a yield of 20%. The chromatographic behaviour of each of these quinones **1** and **2** was identical with that of each natural derivative. Likewise diene **11** reacted with each of the brominated 2-benzopyranquinones **61** and **63** to form the hitherto unreported quinones **5** and **6** in yields of 24% and 23% respectively.



65



66

The NMR data for the four naturally derived quinones **1**, **2**, **5** and **6** have not been reported and we determined these in acetone-d_6 and methanol-d_4. In subsequent discussions with Professor Cameron it transpired that he had obtained the ^{1}H NMR spectra for these four compounds in dimethyl sulfoxide-d_6.[7] In comparing the combined data, provided in Table 1, three factors in particular confirm the stereochemistries of the dihydropyran rings in each case; the chemical shifts of the protons 3-H, the coupling constants between the protons 3-H and 4-H and the long-range homoallylic coupling between the protons 1-H and 4-H. This long-range coupling is largest for two pseudoaxial protons (~3 Hz), less for one pseudoaxial and one pseudoequatorial proton (~1.5–2 Hz) and negligible for two pseudoequatorial protons. The proton chemical shifts for the corresponding brominated and parent non-brominated 2-benzopyranquinones are given in Table 2.

The specific rotations of each of the synthetic materials compared very well with the hitherto unreported[7] values for the natural derivatives, as shown in Table 3. The signs of our rotations support the assignment of absolute stereochemistries for quinones A and A′ **1** and **2** already made[1] and also the absolute stereochemistries for quinones **5** and **6** assumed by Banks and Cameron[7] through a comparison with both the values for **1** and **2**[7] and also the literature values for eleutherin and isoeleutherin[30] and related materials.

Conclusions

The first routes have been developed for the syntheses, in principle, of all eight possible enantiopure diastereoisomers of 3,4-dihydro-4,7,9-trihydroxy-1,3-dimethylnaphtho[2,3-*c*]pyran-5,10-quinones. This paper describes the assembly of four of these, quinones A **1**[1] and A′ **2**[1] and their hitherto unreported C-3 epimers, the quinones **5**[7] and **6**,[7] all of which have been isolated from natural sources as derivatives of a variety of different aphid insect pigments. The quinones **1**, **5** and **6** were obtained in thirteen, and quinone **2** in sixteen, consecutive steps from the commercially available starting materials 2,5-dihydroxyacetophenone and lactate, the latter as the source of asymmetry from the chiral pool. Although the yield of the last step in each sequence, a Diels–Alder reaction between the diene **11** and diastereoisomers of the 2-benzopyranquinone **12**, was only moderate, all other yields were gratifyingly high. Key factors that enabled these achievements were, first, the successful maintenance of stereochemical integrity throughout each sequence even when the asymmetric centres were α to ester and aldehydic carbonyl groups. Secondly, cyclisation of the phenolic lactaldehyde **25** to the benzopyran-4,5-diol **32** was completely diastereoselective while the related process for the benzyl-epimeric lactaldehyde **28** into the pair of C-4 epimeric benzopyrans **39** and **44** was almost completely non-stereoselective. These stereochemical differences for these two related reactions have been rationalised in terms of the differences in *peri*-interactions in the transition states involved.

Experimental

General

Melting points were determined on a Reichert hot stage apparatus and are uncorrected. Optical rotations were measured using

Table 1 ^{1}H NMR spectral chemical shifts (δ) and coupling constants (J Hz) for the quinones **1**, **2**, **5** and **6** measured in the solvents acetone-d_6, methanol-d_4 and dimethyl sulfoxide-d_6[7]

	Quinone A **1**			Quinone A′ **2**			Quinone **5**			Quinone **6**		
Solvent	Acetone-d_6	Methanol-d_4	DMSO-d_6	Acetone-d_6	Methanol-d_4	DMSO-d_6	Acetone-d_6	Methanol-d_4	DMSO-d_6	Acetone-d_6	Methanol-d_4	DMSO-d_6
3-CH_3 (δ)	1.09	1.30		1.11	1.30		1.31	1.31		1.15	1.36	
1-CH_3 (δ)	1.36	1.58		1.35	1.51		1.56	1.59		1.31	1.51	
3-H (δ)	3.66	3.89	3.84	3.84	3.97	3.97	3.64	3.58	3.60	3.23	3.40	>3.6[a]
4-H (δ)	4.15	4.35	4.33	4.41	4.38	4.35	4.44	4.42	4.38	4.18	4.33	4.33
1-H (δ)	4.61	4.83[a]	4.80	4.75	4.91[a]	4.83	4.76	4.74	4.72	4.60	4.77	4.74
8-H (δ)	6.40	6.50		6.48	6.51		6.62	6.51		6.42	6.51	
6-H (δ)	6.85	7.00		6.98	7.04		7.10	7.03		6.87	7.01	
7-OH[b] (δ)	4.05	—		2.72	—		3.40	—		4.22	—	
9-OH (δ)	11.89	—		12.05	—		12.16	—		11.92	—	
J H-3/H-4	7.2	7.2	7.4	1.90	1.90	2	1.2	1.2	1.5	8.2	8.3	9
J H-1/H-4	1.2	1.2	1.5	0	0	0	1.2	1.2	1.5	2.5	2.6	3

[a] Partially obscured by solvent. [b] Broad signal.

an Optical Activity PolAAr 2001 polarimeter for chloroform solutions of c 1.0 at 20 °C, unless otherwise stated, and are given in 10^{-1} deg cm^2 g^{-1}. Infrared (IR) spectra were recorded as a nujol mull for solids and as thin films between NaCl plates for oils, using a Perkin Elmer 1720-X Fourier Transform Spectrometer. The sonication bath used was a Branson B3200-E4, operating at a frequency of 44 kHz. Mass spectra were obtained on a VG Autospec spectrometer operating in the electron impact mode at 70 eV. Elemental analyses were determined by the Canadian Microanalytical Service Ltd. Unless otherwise stated, nuclear magnetic resonance (NMR) spectra were recorded using a Bruker AM-300 spectrometer (^{1}H, 300 MHz; ^{13}C, 75.5 MHz). These were run at ambient temperature in deuterochloroform ($CDCl_3$) solution, with tetramethylsilane (TMS) (δ 0.00) for ^{1}H NMR spectra and TMS (δ 0.00) and chloroform (δ 77.00) for ^{13}C NMR spectra as internal standards. Assignments of signals with the same superscripts are interchangeable. All solvents were purified by distillation and, if necessary, were dried according to standard methods. The amount of residual water present in solvents was determined using a Metrohm Karl Fischer Calorimeter 684. The hydrocarbon solvent referred to as hexane routinely had a bp range of 65–70 °C. Chromatography refers to dry-packed columns of Merck silica gel 60 (70–230 mesh). Preadsorption was carried out on Merck silica gel 60 (35–70 mesh). The adsorbent for radial chromatography was Merck silica gel 60 PF_{254}. Merck silica gel 60 F_{254} aluminium backed sheets were used for thin layer chromatography (TLC). The phrase "residue obtained upon work-up" refers to the residue when the organic layer was separated, dried with anhydrous magnesium sulfate ($MgSO_4$) and concentrated under reduced pressure.

5′-*t*-Butyldimethylsilyloxy-2′-hydroxyacetophenone 17

t-Butyldimethylsilyl chloride (5.94 g, 39 mmol) and imidazole (2.68 g, 39 mmol) were added to a solution of 2,5-dihydroxyacetophenone (5 g, 33 mmol) in dry dimethylformamide (80 cm^3). The mixture was stirred under argon for 12 h at room temperature after which water was added and the mixture exhaustively extracted with ethyl acetate. The residue obtained upon work-up was chromatographed (10% ethyl acetate–hexane) to give product **17** as a yellow oil (8.5 g, 97%) (Found: C, 62.9; H, 8.4; M$^+$, 266.1336. $C_{14}H_{22}O_3Si$ requires C, 63.1; H, 8.3%; M, 266.1338); υ_{max}(film)/cm^{-1} 1648 (C=O) and 1616, 1588 and 1481 (C=C); δ_H 0.21 (6H, s, OSi(CH_3)$_2$C(CH$_3$)$_3$), 0.99 (9H, s, OSi(CH$_3$)$_2$C(CH_3)$_3$), 2.59 (3H, s, COCH$_3$), 6.86 (1H, d, J 8.9 Hz, 3′-H), 7.02 (1H, dd, J 2.9 and 8.9 Hz, 4′-H), 7.16 (1H, d, J 2.9 Hz, 6′-H) and 11.85 (1H, s, OH); δ_C −4.6 (OSi(CH_3)$_2$C(CH$_3$)$_3$), 17.1 (OSi(CH$_3$)$_2$C(CH$_3$)$_3$), 24.7 (OSi(CH$_3$)$_2$C(CH_3)$_3$), 25.6 (COCH$_3$), 118.0 (C-1′), 118.4 (C-6′), 119.1 (C-3′), 128.3 (C-4′), 146.2 (C-2′), 155.7 (C-5′) and 202.9 (COCH$_3$); m/z 266 (M$^+$, 60%), 209 (100), 181 (20), 167 (10), 86 (11) and 84 (17).

3′-Bromo-5′-*t*-butyldimethylsilyloxy-2′-hydroxyacetophenone 18

Bromine (2.40 g, 15 mmol) was added to a solution of 5′-*t*-butyldimethylsilyloxy-2′-hydroxyacetophenone **17** (4 g, 15 mmol) and pyridine (4.75 g, 60 mmol) in dry dichloromethane (150 cm^3) at 0 °C. The solution was stirred at this temperature for 5 min and then at room temperature for 3 h. The reaction was then quenched with hydrochloric acid (1 M) and the mixture was exhaustively extracted with dichloromethane. The organic extracts were washed further with hydrochloric acid (1 M) and saturated sodium chloride, after which the residue obtained upon work-up was chromatographed (10% ethyl acetate–hexane) to give product **18** (5 g, 96%) as light yellow prisms mp 66–67 °C (hexane) (Found: C, 49.0; H, 6.2; M$^+$, 344.0443. $C_{14}H_{21}BrO_3Si$ requires C, 48.7; H, 6.15%; M(^{79}Br), 344.0443); υ_{max}/cm^{-1} 1654 (C=O) and 1447 (C=C); δ_H 0.21 (6H, s, OSi(CH_3)$_2$C(CH$_3$)$_3$), 0.99 (9H, s, OSi(CH$_3$)$_2$C(CH_3)$_3$), 2.61 (3H, s, COCH$_3$). 7.15 (1H, d, J 2.8 Hz, 4′-H), 7.30 (1H, d, J 2.8 Hz, 6′-H) and 12.49 (1H, s,

Table 2 Chemical shifts (δ) and coupling constants (J) for the 2-benzopyrans **12, 58–64** in deuterochloroform

Compound	**12**	**58**	**59**	**60**	**61**	**62**	**63**	**64**
3-CH_3	1.37	1.37	1.37	1.37	1.37	1.37	1.41	1.41
1-CH_3	1.54	1.52	1.47	1.45	1.54	1.53	1.46	1.45
4-OH	3.43	3.52	2.25	2.22	2.13	2.08	3.57	3.69
3-H	3.84	3.84	3.96	3.97	3.59	3.59	3.41	3.42
4-H	4.35	4.35	4.35	4.36	4.37	4.37	4.38	4.38
1-H	4.80	4.75	4.89	4.85	4.67	4.64	4.70	4.67
6-H	7.27	6.73	7.32	6.75[a]	7.32	6.73[b]	7.25	6.72
7-H	—	6.73	—	6.80[a]	—	6.80[b]	—	6.72
J 3-H/4-H	7.7	7.8	2.2	2.2	1.6	1.6	8.3	8.3
J 1-H/4-H	1.4	1.6	0	0	1.4	1.4	2.9	2.9

[a,b]Assignments with identical superscripts may be interchanged.

Table 3 A comparison of the specific rotations of the naturally derived quinones **1**, **2**, **5** and **6** with those of the synthesised compounds $[\alpha]_D^{20}$ (c 1.0, 1% AcOH in MeOH)

Quinone	**1**	**2**	**5**	**6**
Natural derivative	+41	+258	+278	+568
Synthetic product	+40	+262	+260	+550

OH); δ_C −4.5 (OSi(CH_3)$_2$C(CH_3)$_3$), 18.2 (OSi(CH_3)$_2$*C*(CH_3)$_3$), 25.6 (OSi(CH_3)$_2$C(*C*H_3)$_3$), 26.7 (CO*C*H_3), 111.8 (C-1′), 119.7 (C-3′), 119.9 (C-4′), 132.2 (C-6′), 147.3 (C-2′), 153.7 (C-5′) and 203.7 (*C*OCH$_3$); *m*/*z* 346 [M$^+$ (^{81}Br), 24%], 344 [M$^+$ (^{79}Br), 22%], 289 (39), 287 (37), 97 (15), 95 (11), 84 (100), 83 (18), 81 (12) and 71 (18).

2′-Benzyloxy-3′-bromo-5′-*t*-butyldimethylsilyloxyacetophenone 19

Anhydrous potassium carbonate was added to a solution of compound **18** (1.00 g, 2.9 mmol) in dry acetone at 45 °C under nitrogen. Benzyl bromide (0.497 g, 2.9 mmol) was added dropwise to the reaction mixture over a period of 10 min. The mixture was stirred at that temperature until completion of the reaction as monitored by TLC (30–60 min) and then filtered through Celite, whereupon the filtrate was concentrated under reduced pressure. The residue was chromatographed (5% ethyl acetate–hexane) to give the benzyl ether **19** (1.23 g, 97%) as pale yellow needles, mp 89–90 °C (dichloromethane). Found: M$^+$, 434.0923. $C_{21}H_{27}BrO_3Si$ requires M(^{79}Br), 434.0912; υ_{max}(film)/cm^{-1} 1677 (C=O) and 1591 and 1495 (C=C); δ_H 0.24 (6H, s, OSi(C*H*$_3$)$_2$C(CH$_3$)$_3$), 1.01 (9H, s, OSi(CH$_3$)$_2$C(C*H*$_3$)$_3$), 2.55 (3H, s, COCH$_3$), 4.95 (2H, s, OCH$_2$), 7.01 (1H, d, J 3.0 Hz, 4′-H), 7.24 (1H, d, J 3.0 Hz, 6′-H) and 7.38–7.51 (5H, m, C$_6$H$_5$); δ_C −4.1 (OSi(*C*H$_3$)$_2$C(CH$_3$)$_3$), 18.5 (OSi(CH$_3$)$_2$*C*(CH$_3$)$_3$), 26.0 (OSi(CH$_3$)$_2$C(*C*H$_3$)$_3$), 31.0 (CO*C*H$_3$), 70.1 (OCH$_2$), 119.1 (C-1′), 120.0 (C-3′), 128.6 (C-6′), 128.7 (C-4″), 128.9 (C-2″ and C-6″), 129.0 (C-3″ and C-5″), 136.3 (C-4′), 136.5 (C-1″), 148.9 (C-5′), 152.8 (C-2′) and 199.9 (*C*OCH$_3$); *m*/*z* 436 [M$^+$ (^{81}Br), 5%], 434 [M$^+$ (^{79}Br), 5%], 394 (9), 392 (9), 345 (6), 343 (5), 289 (8), 287 (8), 115 (11), 91 (100) and 73 (52).

1-(2′-Benzyloxy-3′-bromo-5′-*t*-butyldimethylsilyloxyphenyl)-ethanol 20

To a stirred slurry of sodium borohydride (570 mg, 1.5 mmol) in dry ethanol (30 cm^3) was added drop-wise a solution of the compound **19** in dry ethanol (10 cm^3). The mixture was stirred at room temperature for 1 h, after which a saturated ammonium chloride solution was added drop-wise, followed by anhydrous magnesium sulfate. Filtration through Celite and concentration of the filtrate followed by chromatography (radial, 10–20% ethyl acetate–hexane) yielded alcohol **20** (525 mg, 91%) as a light yellow oil. (Found: C, 57.8; H, 6.6; M$^+$, 436.1082. $C_{21}H_{29}BrO_3Si$ requires C, 57.65; H, 6.7%; M(^{79}Br), 436.1069); υ_{max}(film)/cm^{-1} 3409 (OH), and 1599 and 1496 (C=C); δ_H 0.21 (6H, s, OSi(C*H*$_3$)$_2$C(CH$_3$)$_3$), 0.98 (9H, s, OSi(CH$_3$)$_2$C(C*H*$_3$)$_3$), 1.38 (3H, d, J 6.4 Hz, 1-CH$_3$), 1.94 (1H, d, J 2.9 Hz, OH), 4.99 (2H, s, OCH$_2$), 5.03 (1H, dq, J 2.9 and 6.4 Hz, 1-H), 6.88 (1H, d, J 2.9 Hz, 6′-H), 7.00 (1H, d, J 2.9 Hz, 4′-H) and 7.34–7.48 (5H, m, C$_6$H$_5$); δ_C −4.5 (OSi(*C*H$_3$)$_2$C(CH$_3$)$_3$), 18.2 (OSi(CH$_3$)$_2$*C*(CH$_3$)$_3$), 23.9 (C-2), 25.6, (OSi(CH$_3$)$_2$C(*C*H$_3$)$_3$), 65.1 (C-1), 75.6 (OCH$_2$), 117.0 (C-6′), 117.1 (C-3′), 123.8 (C-2″ and C-6″), 125.9 (C-4″), 128.4 (C-4′), 128.6 (C-3″ and C-5″), 136.5 (C-1″), 141.1 (C-1′), 146.6 (C-2′) and 152.7 (C-5′); *m*/*z* 438 [M$^+$ (^{81}Br), 6%], 436 [M$^+$ (^{79}Br), 6%], 347 (10), 345 (10), 330 (57), 328 (55), 273 (30), 271 (26), 115 (28), 91 (84) and 73 (100).

2′-Benzyloxy-3′-bromo-5′-*t*-butyldimethylsilyloxy-α′-methylbenzyl-2,2,2-trichloroethanimidate 21

The benzyl alcohol **20** (3 g, 6.9 mmol) in dry diethyl ether (10 cm^3) was added drop-wise to a stirred suspension of sodium hydride (60% dispersion in mineral oil) (110 mg, 4.6 mmol) in diethyl ether (15 cm^3). The mixture was stirred for 10 min under argon at −10 °C. Trichloroacetonitrile (1.94 g, 13.7 mmol) was added drop-wise over 10 min and the reaction mixture stirred for a further 30 min at that temperature, after which it was allowed to reach room temperature. The solution was concentrated and chromatographed (radial, 5% ethyl acetate–hexane) to afford the imidate **21** (3.5 g, 88%) as a light yellow oil. (Found: C, 47.9; H, 5.1; N, 2.3; M$^+$, 579.0165. $C_{23}H_{29}BrCl_3NO_3Si$ requires C, 47.5; H, 5.05; N, 2.4%; M(^{79}Br and ^{35}Cl), 579.0165); υ_{max}(film)/cm^{-1} 3337 (N–H), 1661 (C=N) and 1600, 1562 and 1464 (C=C); δ_H 0.18 (6H, s, OSi(C*H*$_3$)$_2$C(CH$_3$)$_3$), 0.96 (9H, s, OSi(CH$_3$)$_2$C(C*H*$_3$)$_3$), 1.54 (3H, d, J 6.5 Hz, α′-CH$_3$), 5.10 and 5.14 (each 1H, d, J 10.6 Hz, OCH$_2$), 6.25 (1H, q, J 6.5 Hz, α′-H), 6.94 (1H, d, J 2.9 Hz, 6′-H), 7.02 (1H, d, J 2.9 Hz, 4′-H), 7.32–7.44 (5H, m, C$_6$H$_5$) and 8.35 (1H, br s, NH); δ_C −4.5 (OSi(*C*H$_3$)$_2$C(CH$_3$)$_3$), 18.1 (OSi(CH$_3$)$_2$*C*(CH$_3$)$_3$), 22.1 (OSi(CH$_3$)$_2$C(*C*H$_3$)$_3$), 25.6 (α′-CH$_3$), 72.7 (C-α′), 74.8 (OCH$_2$), 91.6 (CCl$_3$), 116.4 (C-6′), 117.3 (C-3′), 124.1 (C-4′), 127.8 (C-4″), 128.2 (C-2″ and C-6″), 128.5 (C-3″ and C-5″), 137.1 (C-1″), 137.6 (C-1′), 146.5 (C-2′), 152.7 (C-5′) and 161.2 (C-1); *m*/*z* 581 [M$^+$ (^{81}Br^{35}Cl), 4%], 579 [M$^+$ (^{79}Br^{35}Cl), 2%], 420 (34), 418 (31), 363 (17), 361 (16), 329 (38), 327 (34), 272 (11), 270 (13), 248 (18), 191 (100) and 91 (77).

Methyl (α′*S* and *R*,2*R*)-2-(2′-benzyloxy-3′-bromo-5′-*t*-butyldimethylsilyloxy-α′-methylbenzyloxy)propanoate 22

Boron trifluoride diethyl etherate (79 mg, 0.56 mmol) was added dropwise to a solution of imidate **21** (1.61 g, 2.8 mmol) and methyl (*R*)-lactate **15** (577 mg, 5.5 mmol) in dry hexane–dichloromethane (20 cm^3, 2 : 1). The reaction was stirred under nitrogen for 40 min. Solid sodium hydrogencarbonate was added to the reaction and the resulting suspension was filtered through Celite. The clear solution was then concentrated and chromatographed (radial, 10% ethyl acetate–hexane) to afford the yellow, oily inseparable mixture of diastereoisomeric esters **22** (1.33 g, 91%) (Found: M$^+$, 522.1426. $C_{25}H_{35}BrO_5Si$ requires M(^{79}Br), 522.1437); υ_{max}(film)/cm^{-1} 1754 (C=O) and 1598 and 1498 (C=C); δ_H (mixture of two diastereoisomers)

0.21 (12H, s, OSi(CH_3)$_2$C(CH$_3$)$_3$), 0.98 and 0.99 (each 9H, s, OSi(CH$_3$)$_2$C(CH_3)$_3$), 1.33 and 1.35 (each 3H, d, *J* 6.8 Hz, 2-CH$_3$), 1.36 and 1.40 (each 3H, d, *J* 6.5 Hz, α′-CH$_3$), 3.61 and 3.65 (each 3H, s, CO$_2$CH$_3$), 3.80 and 3.88 (each 1H, q, *J* 6.8 Hz, 2-H), 4.70–5.11 (6H, m, α′-H and OCH$_2$), 6.88, 6.93, 6.99 and 7.02 (each 1H, d, *J* 2.9 Hz, 4′ and 6′-H) and 7.33–7.51 (10H, m, 2 × C$_6$H$_5$); δ_C (mixture of two diastereoisomers) −4.57 and −4.56 (OSi(*C*H$_3$)$_2$C(CH$_3$)$_3$), −4.48 (2 × (OSi(*C*H$_3$)$_2$C(CH$_3$)$_3$), 18.06 and 19.0 (C-3), 18.14 and 18.2 (OSi(CH$_3$)$_2$*C*(CH$_3$)$_3$), 23.2 and 23.6 (α′-CH$_3$), 25.6 (OSi(CH$_3$)$_2$C(*C*H$_3$)$_3$), 51.8 and 51.9 (OCH$_3$), 70.9 and 71.4 (C-α′), 72.2 and 72.5 (C-2), 75.4 and 75.6 (OCH$_2$Ph), 116.9 and 117.3 (C-3′), 117.1 and 117.9 (C-6′),[a] 124.0 and 124.2 (C-4′),[a] 128.0 (C-2″ and C-6″), 128.2 (C-4″), 128.5 and 128.6 (C-3″ and C-5″), 136.7 and 136.9 (C-1′),[b] 138.9 and 139.0 (C-1″),[b] 147.0 and 147.6 (C-2′),[c] 152.8 and 152.9 (C-5′),[c] 173.0 and 173.9 (C=O); *m*/*z* 524 [M$^+$ (^{81}Br), 5%], 522 [M$^+$ (^{79}Br), 5%], 433 (46), 431 (43), 330 (41), 328 (38), 272 (16), 270 (16), 191 (29) and 91 (100).

(α′*R*,2*R*)-2-(2′-Benzyloxy-3′-bromo-5′-*t*-butyldimethylsilyloxy-α′-methyl-benzyloxy)propanol 23 and (α′*S*,2*R*)-2-(2′-benzyloxy-3′-bromo-5′-*t*-butyldimethylsilyloxy-α′-methylbenzyloxy)propanol 30

Lithium aluminium hydride was added portion-wise to a solution of the methyl esters **22** (600 mg, 1.15 mmol) in dry diethyl ether (25 cm^3) until TLC indicated no starting material remained. A saturated ammonium chloride solution was added drop-wise to the reaction mixture followed by anhydrous magnesium sulfate. Filtration through Celite and concentration of the filtrate gave crude product, which was chromatographed (radial, 5–50% ethyl acetate–hexane) to afford two products as colourless oils. The product of higher R_f was identified as compound **30** (224 mg, 39%); $[\alpha]_D$ −58.0 (*c* 1.0 in CHCl$_3$) (Found: C, 58.55; H, 7.0; M$^+$, 494.1474. C$_{24}$H$_{35}$BrO$_4$Si requires C, 58.3; H, 7.15%; M(^{79}Br), 494.1487); υ_{max}(film)/cm^{-1} 3466 (OH), 1598 and 1495 (C=C); δ_H 0.21 (6H, s, OSi(CH_3)$_2$C(CH$_3$)$_3$), 0.98 (9H, s, OSi(CH$_3$)$_2$C(CH_3)$_3$), 1.08 (3H, d, *J* 5.7 Hz, 2-CH$_3$), 1.33 (3H, d, *J* 6.4 Hz, α′-CH$_3$), 1.85 (1H, br s, OH), 3.34–3.48 (3H, m, CH_2OH and 2-H), 4.90 (1H, q, *J* 6.4 Hz, α′-H), 4.93 and 4.96 (each 1H, d, *J* 11.0 Hz, OCH$_2$), 6.86 (1H, d, *J* 2.9 Hz, 6′-H), 7.01 (1H, d, *J* 2.9 Hz, 4′-H) and 7.35–7.51 (5H, m, C$_6$H$_5$); δ_C −4.5, (OSi(*C*H$_3$)$_2$C(CH$_3$)$_3$), 15.8 (C-3), 18.2 (OSi(CH$_3$)$_2$*C*(CH$_3$)$_3$), 23.8 (α′-CH$_3$), 25.6 (OSi(CH$_3$)$_2$C(*C*H$_3$)$_3$), 66.7 (C-1), 68.7 (C-2), 73.1 (C-α′), 75.9 (OCH$_2$), 117.2 (C-6′), 124.0 (C-4′), 125.9 (C-3′), 128.0 (C-2″ and C-6″), 128.3 (C-4″), 128.6 (C-3″ and C-5″), 136.8 (C-1″), 139.6 (C-1′), 147.3 (C-2′) and 152.9 (C-5′); *m*/*z* [M$^+$ 496 (^{81}Br), 5%], 494 [M$^+$ (^{79}Br), 5%], 421 (7), 419 (7), 330 (87), 328 (84), 273 (41), 271 (36), 192 (18) and 91 (100). The product of lower R_f was identified as compound **23** (298 mg, 52%); $[\alpha]_D$ +23.5 (*c* 1.0 in CHCl$_3$); (Found: C, 58.35; H, 7.15; M$^+$, 494.1475. C$_{24}$H$_{35}$BrO$_4$Si requires C, 58.3; H, 7.15%; M(^{79}Br), 494.1487); υ_{max}(film)/cm^{-1} 3447 (OH) and 1598 and 1496 (C=C); δ_H 0.21 (6H, s, OSi(CH_3)$_2$C(CH$_3$)$_3$), 0.98 (3H, d, *J* 6.3 Hz, 2-CH$_3$), 0.99 (9H, s, OSi(CH$_3$)$_2$C(CH_3)$_3$), 1.33 (3H, d, *J* 6.4 Hz, α′-CH$_3$), 1.90 (1H, br s, OH), 3.36–3.62 (3H, m, CH$_2$OH and 2-H), 4.87 (1H, q, *J* 6.4 Hz, α′-H), 4.95 (2H, s, OCH$_2$), 6.90 (1H, d, *J* 2.9 Hz, 6′-H), 7.00 (1H, d, *J* 2.9 Hz, 4′-H) and 7.34–7.51 (5H, m, C$_6$H$_5$); δ_C −4.5, (OSi(*C*H$_3$)$_2$C(CH$_3$)$_3$), 17.4 (OSi(CH$_3$)$_2$*C*(CH$_3$)$_3$), 18.2 (C-3), 23.7 (α′-CH$_3$), 25.6 (OSi(CH$_3$)$_2$C(*C*H$_3$)$_3$), 65.7 (C-1), 70.6 (C-2), 74.4 (C-α′), 75.6 (OCH$_2$), 117.0 (C-3′), 117.5 (C-6′), 123.9 (C-4′), 128.5 (C-2″ and C-6″), 128.7 (C-4″), 129.0 (C-3″ and C-5″), 136.8 (C-1″), 140.4 (C-1′), 146.9 (C-2′) and 152.7 (C-5′); *m*/*z* 496 [M$^+$ (^{81}Br), 4%], 494 [M$^+$ (^{79}Br), 4%], 421 (7), 419 (6), 330 (80), 328 (76%), 274 (15), 272 (15), 191 (18) and 91 (100).

(α′*R*,2*R*)-2-(2′-Benzyloxy-3′-bromo-5′-*t*-butyldimethylsilyloxy-α′-methybenzyloxy)propanal 24

To a solution of oxalyl chloride (453 mg, 3.57 mmol) in dry dichloromethane (10 cm^3) at 70 °C under an atmosphere of argon was added dropwise a solution of dimethyl sulfoxide (558 mg, 7.14 mmol) in dry dichloromethane (2 cm^3) keeping the temperature below −65 °C. After stirring for 15 min, a solution of the (α′*R*,2*R*)-alcohol **23** (354 mg, 0.71 mmol) in dry dichloromethane (2 cm^3) was added drop-wise keeping the temperature below −65 °C and the stirring continued for a further 15 min at that temperature. Dry diisopropylamine (1.11 g, 8.59 mmol) was added slowly and the reaction stirred for a further 10 min at −70 °C before being allowed to warm to room temperature over 1 h. The reaction mixture was quenched with water and exhaustively extracted with dichloromethane. The residue obtained upon work-up was chromatographed (radial, 10–20% ethyl acetate–hexane) to give aldehyde **24** (312 mg, 88%) as a colourless oil. $[\alpha]_D$ +46.6 (*c* 1.0 in CHCl$_3$); (Found: M,$^+$ 492.1333. C$_{24}$H$_{33}$BrO$_4$Si requires M(^{79}Br), 492.1331); υ_{max}(film)/cm^{-1} 1735 (C=O) and 1596 and 1496 (C=C); δ_H 0.21 (6H, s, OSi(CH_3)$_2$C(CH$_3$)$_3$), 0.99 (9H, s, OSi(CH$_3$)$_2$C(CH_3)$_3$), 1.18 (3H, d, *J* 7.0 Hz, 2-CH$_3$), 1.39 (3H, d, *J* 6.4 Hz, α′-CH$_3$), 3.59 (1H, dq, *J* 1.7 and 7.0 Hz, 2-H), 4.80 (1H, q, *J* 6.4 Hz, α′-H), 4.84 and 4.95 (each 1H, d, *J* 10.9 Hz, OCH$_2$), 6.88 (1H, d, *J* 2.9 Hz, 6′-H), 7.03 (1H, d, *J* 2.9 Hz, 4′-H), 7.32–7.48 (5H, m, C$_6$H$_5$) and 9.60 (1H, d, *J* 1.7 Hz, CHO); δ_C −4.5, (OSi(*C*H$_3$)$_2$C(CH$_3$)$_3$), 15.8 (C-3), 18.2 (OSi(CH$_3$)$_2$*C*(CH$_3$)$_3$, 23.6 (α′-CH$_3$), 25.6 (OSi(CH$_3$)$_2$C(*C*H$_3$)$_3$), 71.8 (C-2), 75.6 (OCH$_2$), 77.9 (C-α′), 117.0 (C-6′), 117.2 (C-3′), 124.3 (C-4′), 128.2 (C-2″ and C-6″), 128.4 (C-4″), 128.6 (C-3″ and C-5″), 136.6 (C-1″), 138.7 (C-1′), 147.3 (C-2′), 152.8 (C-5′) and 203.3 (C-1); *m*/*z* 494 [M$^+$ (^{81}Br), 1%], 492 [M$^+$ (^{79}Br), 1%], 420 (15), 418 (14), 359 (13), 357 (13), 329 (32), 248 (11), 191 (66), 149 (21), 91 (88) and 73 (100).

(α′*R*,2*R*)-2-(2′-Benzyloxy-3′-bromo-5′-hydroxy-α′-methylbenzyloxy)propanal 25

A mixture of the aldehyde **24** (300 mg, 0.61 mmol), tetrahydrofuran (20 cm^3) and saturated solutions of aqueous ammonium chloride and sodium fluoride (40 cm^3, 1 : 1) was stirred for 16 h at room temperature. The reaction mixture was exhaustively extracted with diethyl ether and the residue obtained upon work-up was rapidly chromatographed (radial, 35% ethyl acetate–hexane) to afford the potentially unstable phenolic aldehyde **25** (168 mg, 73%) as a colourless oil. (Found: (M − H$_2$O)$^+$, 360.0353. C$_{18}$H$_{17}$BrO$_3$ requires M(^{79}Br), 360.0361); υ_{max}(film)/cm^{-1} 3383 (OH), 1730 (C=O) and 1603 and 1497 (C=C); δ_H 1.19 (3H, d, *J* 7.0 Hz, 2-CH$_3$), 1.39 (3H, d, *J* 6.4 Hz, α′-CH$_3$), 3.64 (1H, dq, *J* 1.5 and 7.0 Hz, 2-H), 4.80 (1H, *J* 6.4 Hz, α′-H), 4.85 and 4.93 (each 1H, d, *J* 10.8 Hz, OCH$_2$), 6.40 (1H, br s, OH), 6.90 (1H, d, *J* 2.9 Hz, 6′-H), 7.03 (1H, d, *J* 2.9 Hz, 4′-H), 7.35–7.48 (5H, m, C$_6$H$_5$) and 9.58 (1H, d, *J* 1.5 Hz, CHO); δ_C 16.1 (C-3), 23.8 (α′-CH$_3$), 74.4 (C-2), 76.2 (OCH$_2$), 78.4 (C-α′), 113.0 (C-6′), 118.0 (C-3′), 120.2 (C-4′), 128.7 (C-2″ and C-6″), 128.8 (C-4″), 129.0 (C-3″ and C-5″), 136.9 (C-1″), 139.4 (C-1′), 146.9 (C-2′), 153.7 (C-5′) and 203.8 (C-1); *m*/*z* 362 [(M − H$_2$O)$^+$ (^{81}Br), 4%], 360 [(M − H$_2$O)$^+$ (^{79}Br), 4%], 167 (8) 149 (27) and 91 (100).

(1*R*,3*R*,4*S*)-8-Benzyloxy-7-bromo-3,4-dihydro-4,5-dihydroxy-1,3-dimethylbenzo[*c*]pyran 32

Fresh neat titanium tetraisopropoxide (253 mg, 0.89 mmol) was added to a solution of the crude (prior to chromatography) (α′*R*,2*R*) phenolic aldehyde **25** (240 mg, 0.63 mmol) in dry dichloromethane (15 cm^3) at 0 °C, under an atmosphere of argon. After standing for 10 min at 0 °C, the reaction mixture was sonically irradiated at 8–35 °C for 5 h, after which dichloromethane (30 cm^3) and saturated solutions of aqueous sodium fluoride and ammonium chloride (60 cm^3, 1 : 1) were added. The mixture was stirred until the yellow colour had discharged. The aqueous layer was extracted with dichloromethane and the residue obtained upon work-up was rapidly chromatographed (radial, 30–50% ethyl acetate–hexane) to give the potentially

unstable cyclised product **32** (180 mg, 75%) as white prisms mp 149–150 °C (dichloromethane–hexane) $[a]_D$ −46.5 (*c* 1.0 in $CHCl_3$); (Found: M^+, 378.0472. $C_{18}H_{19}BrO_4$ requires M(^{79}Br), 378.0466); υ_{max}/cm^{-1} 3450 and 3292 (OH) and 1581 and 1496 (C=C); δ_H 1.36 (3H, d, *J* 6.1 Hz, 3-CH_3), 1.54 (3H, d, *J* 6.7 Hz, 1-CH_3), 3.86 (1H, dq, *J* 6.1 and 8.7 Hz, 3-H), 4.20–5.20 (2H, br s, 4- and 5-OH), 4.51 (1H, d, *J* 8.7 Hz, 4-H), 4.71 and 5.12 (each 1H, d, *J* 10.7 Hz, OCH_2), 4.96 (1H, q, *J* 6.7 Hz, 1-H), 6.99 (1H, s, 6-H) and 7.34–7.48 (5H, m, C_6H_5); δ_C 18.3 (3-CH_3), 19.8 (1-CH_3), 67.3 (C-3), 69.0 (C-4), 70.7 (C-1), 75.0 (OCH_2), 117.0 (C-8), 119.4 (C-6), 120.6 (C-7), 128.4 (C-2″ and C-6″), 128.7 (C-4″), 129.0 (C-3″ and C-5″), 135.5 (C-1″), 136.7 (C-8a), 144.4 (C-4a) and 152.9 (C-5); *m/z* 380 [M^+ (^{81}Br), 22%], 378 [M^+ (^{79}Br), 22%], 363 (17), 361 (20), 299 (42), 287 (17), 282 (14), 270 (77), 253 (30), 227 (96) and 148 (100).

(1*R*,3*R*,4*S*)-7-Bromo-3,4-dihydro-4-hydroxy-1,3-dimethylbenzo[*c*]pyran-5,8-quinone 12 and (1*R*,3*R*,4*S*)-3,4-dihydro-4-hydroxy-1,3-dimethylbenzo[*c*]pyran-5,8-quinone 58

A solution of the diol **32** (165 mg, 0.44 mmol) in dry ethyl acetate (15 cm^3) was stirred with 10% palladium on carbon catalyst (165 mg) under a hydrogen atmosphere until one molar equivalent had been consumed (1.5 h). The mixture was filtered through Celite, concentrated and purified through rapid chromatography (radial, 35% ethyl acetate–hexane) to afford unstable hydroquinones **33** and **34** as an oily mixture (126 mg). This was immediately dissolved in acetonitrile (15 cm^3) and cerium(IV) ammonium nitrate (342 mg, 0.62 mmol) in water (3 cm^3) was added drop-wise to the solution. After stirring for 20 min the reaction was quenched with water and exhaustively extracted with dichloromethane. The residue obtained upon work-up was chromatographed (radial, 15–25% ethyl acetate–hexane) to give a mixture of the brominated quinone **12** and the debrominated quinone **58**, each as bright yellow crystals. The product of higher R_f was identified as **12** (51 mg, 41%) mp 140–142 °C (dichloromethane–hexane) $[a]_D$ −156 (*c* in 1.0 $CHCl_3$); (Found: C, 46.4; H, 3.95; M^+, 285.9843. $C_{11}H_{11}BrO_4$ requires C, 46.15; H, 3.9%; M(^{79}Br), 285.9843); υ_{max}/cm^{-1} 3505 (OH), 1677 and 1652 (C=O) and 1590 (C=C); δ_H 1.37 (3H, d, *J* 6.2 Hz, 3-CH_3), 1.54 (3H, d, *J* 6.8 Hz, 1-CH_3), 3.43 (1H, d, *J* 2.6 Hz, OH), 3.84 (1H, dq, *J* 6.2 and 7.7 Hz, 3-H), 4.35 (1H, ddd, *J* 1.4, 2.6 and 7.7 Hz, 4-H), 4.80 (1H, dq, *J* 1.4 and 6.8 Hz, 1-H) and 7.27 (1H, s, 6-H); δ_C 18.8 (3-CH_3), 19.2 (1-CH_3), 67.5 (C-3), 67.6 (C-4), 67.8 (C-1), 138.1 (C-7), 138.3 (C-6), 139.7 (C-8a), 145.7 (C-4a), 178.7 (C-8) and 186.0 (C-5); *m/z* 270 [$M^+ - H_2O$ (^{81}Br), 20%], 268 [$M^+ - H_2O$ (^{79}Br), 13%], 244 (100), 242 (98), 216 (40), 214 (41), 163 (12), 134 (23) and 107 (34). The product of lower R_f was identified as 58 (15 mg, 17%) mp 95–97 °C (dichloromethane–hexane) (Lit.[9] for enantiomer 96.5–99.5 °C) $[a]_D$ −307.7 (*c* in 1.0 $CHCl_3$) (Lit.[9] for enantiomer +313.1 °); (Found: C, 63.7; H, 6.2; $(M + 2)^+$, 210.0879. $C_{11}H_{12}O_4$ requires C, 63.45; H, 5.8%; M, 210.0892); υ_{max}/cm^{-1} 3492 (OH) and 1650 (C=O); δ_H 1.37 (3H, d, *J* 6.2 Hz, 3-CH_3), 1.52 (3H, d, *J* 6.8 Hz, 1-CH_3), 3.52 (1H, d, *J* 2.5 Hz, OH), 3.84 (1H, dq, *J* 7.8 and 6.2 Hz, 3-H), 4.35 (1H, ddd, *J* 1.6, 2.5 and 7.8 Hz, 4-H), 4.75 (1H, dq, *J* 1.6 and 6.8 Hz, 1-H) and 6.73 (2H, s, 6- and 7-H); δ_C 18.8 (3-CH_3), 19.3 (1-CH_3), 67.2 (C-3), 67.3 (C-4), 67.6 (C-1), 136.8 (C-6), 137.3 (C-7), 138.3 (C-8a), 146.5 (C-4a), 186.3 (C-8) and 188.8 (C-5); *m/z* 210 [$(M + 2)^+$, 100%], 208 (12), 193 (74), 191 (20), 175 (32), 165 (11) and 147 (11).

(1*R*,3*R*,4*S*)-7-Bromo-3,4-dihydro-4-hydroxy-1,3-dimethylbenzo[*c*]pyran-5,8-quinone 12

A solution of the diol **32** (150 mg, 0.4 mmol) in dry tetrahydrofuran (8 cm^3) was stirred with 10% palladium on carbon catalyst (200 mg) at room temperature for 3 h and the mixture was then hydrogenated until one mole equivalent of the gas had been consumed (30–60 min). The mixture was filtered through Celite, concentrated and then chromatographed rapidly (radial, 35% ethyl acetate–hexane) to afford the hydroquinone (115 mg) as an oil. This was immediately dissolved in acetonitrile (10 cm^3) and cerium(IV) ammonium nitrate (420 mg, 0.762 mmol) in water (4 cm^3) was added drop-wise to the solution. After stirring for 20 min the reaction was exhaustively extracted with dichloromethane. The residue obtained upon work-up was chromatographed (15–25% ethyl acetate–hexane) to give the product **12** (95 mg, 84%), identical to that reported above.

(1*R*,3*R*,4*S*)-8-Benzyloxy-7-bromo-4-hydroxy-3,4-dihydro-1,3-dimethyl-5-methoxybenzo[*c*]pyran 35

Diol **32** (450 mg, 1.19 mmol) in dry dimethylformamide (15 cm^3) was treated with an excess of potassium carbonate (819 mg, 5.93 mmol) and iodomethane (843 mg, 5.93 mmol) and the mixture refluxed under an atmosphere of argon for 1 h. The reaction mixture was then cooled, filtered, concentrated and chromatographed (radial, 15% ethyl acetate—hexane) to give the methylated product **35** as a light yellow oil (450 mg, 96%) $[a]_D$ −47.7 (*c* 1.0 in $CHCl_3$); (Found: C, 58.6; H, 5.45; M^+, 392.0636. $C_{19}H_{21}BrO_4$ requires C, 58.15; H, 5.4%; M (^{79}Br), 392.0623); υ_{max}(film)/cm^{-1} 3569 (OH) and 1580 and 1498 (C=C); δ_H 1.35 (3H, d, *J* 6.2 Hz, 3-CH_3), 1.59 (3H, d, *J* 6.6 Hz, 1-CH_3), 3.64 (1H, d, *J* 2.5 Hz, OH), 3.86 (3H, s, OCH_3), 3.96 (1H, dq, *J* 7.5 and 6.2 Hz, 3-H), 4.50 (1H, dd, *J* 2.5 and 7.5 Hz, 4-H), 4.75 and 5.12 (each 1H, d, *J* 10.8 Hz, OCH_2), 4.96 (1H, q, *J* 6.6 Hz, 1-H), 7.01 (1H, s, 6-H) and 7.32–7.49 (5H, m, C_6H_5); δ_C 19.6 (3-CH_3), 20.6 (1-CH_3), 56.9 (OCH_3), 68.4 (C-3), 68.7 (C-4), 69.1 (C-1), 75.7 (OCH_2), 114.6 (C-6), 116.9 (C-8), 125.8 (C-7), 128.8 (C-4″), 129.1 (C-2″ and C-6″), 129.4 (C-3″ and C-5″), 137.2 (C-1″), 137.6 (C-8a), 146.3 (C-4a) and 155.4 (C-5); *m/z* 394 [M^+ (^{81}Br), 2%], 392 [M^+ (^{79}Br), 2%], 302 (10), 300 (10), 286 (8), 284 (8), 149 (19) and 91 (100).

(1*R*,3*R*,4*R*)-8-Benzyloxy-7-bromo-3,4-dihydro-4-hydroxy-1,3-dimethyl-5-methoxybenzo[*c*]pyran 36

Phosphorus pentachloride (100 mg, 0.48 mmol) was added to a stirred solution of compound **35** (94 mg, 0.24 mg), in dry diethyl ether (10 cm^3). The mixture was stirred for 10 min at room temperature under an atmosphere of argon, then quenched with water (20 cm^3), extracted with diethyl ether and concentrated. The residue obtained was immediately redissolved in acetonitrile (10 cm^3) and then deionised water (1 cm^3) containing silver nitrate (222 mg, 1.31 mmol) was added. The mixture was stirred for a further 3.5 h at room temperature during which time a white precipitate formed. The reaction mixture was extracted with diethyl ether, dried, concentrated and chromatographed (radial, 15% ethyl acetate–hexane) to afford, first, starting material **35** (20 mg, 22%) followed by its C-4 epimeric alcohol **36** (67 mg, 72%) as white plates mp 81.5–82 °C (hexane–dichloromethane) $[a]_D$ −50 (*c* 1.0 in $CHCl_3$); (Found: C, 58.4; H, 5.1; M^+, 392.0637. $C_{19}H_{21}BrO_4$ requires C, 58.15; H, 5.4%; M(^{79}Br), 392.0623); υ_{max}(film)/cm^{-1} 3466 (OH) and 1577 and 1498 (C=C); δ_H 1.38 (3H, d, *J* 6.4 Hz, 3-CH_3), 1.51 (3H, d, *J* 6.7 Hz, 1-CH_3), 2.13 (1H, br s, OH), 3.85 (3H, s, OCH_3), 4.03 (1H, q, *J* 1.9 and 6.4 Hz, 3-H), 4.49 (1H, d, *J* 1.9 Hz, 4-H), 4.71 and 5.13 (each 1H, d, *J* 10.7 Hz, OCH_2), 5.06 (1H, q, *J* 6.7 Hz, 1-H), 7.01 (1H, s, 6-H) and 7.32–7.49 (5H, m, C_6H_5); δ_C 18.7 (3-CH_3), 20.8 (1-CH_3), 58.0 (OCH_3), 64.1 (C-3), 68.0 (C-4), 71.1 (C-1), 76.9 (OCH_2), 115.6 (C-6), 118.9 (C-7), 127.1 (C-8), 129. 9 (C-4″), 130.2 (C-2″ and C-6″), 130.5 (C-3″ and C-5″), 137.2 (C-1″), 138.7 (C-8a), 147.3 (C-4a) and 156.3 (C-5); *m/z* 394 [M^+ (^{81}Br), 1%), 392 [M^+ (^{79}Br), 1%], 376 (3), 374 (3), 302 (8), 300 (8), 286 (17), 284 (17), 149 (36), 91 (100) and 65 (11).

6,8-Dihydroxy-2-methyl-1,4-naphthoquinone 66

To a stirred solution of 2-bromo-6-methyl-1,4-benzoquinone **65**[27] (150 mg, 0.75 mmol) in dry tetrahydrofuran (10 cm^3) at 0 °C was added drop-wise a solution of the diene **11** (1.29 g,

4.96 mmol) in tetrahydrofuran (5 cm^3). The green coloured mixture was stirred for 24 h during which time a bright yellow solution was obtained. The reaction mixture was diluted with dichloromethane (100 cm^3) and the mixture poured into water (150 cm^3) and exhaustively extracted with dichloromethane. The residue obtained upon work-up was chromatographed (radial, 30% ethyl acetate–hexane) and recrystallised (dichloromethane–hexane) to give **66** (110 mg, 73%) as bright orange plates, mp 190° C (decomp.) (hexane). (Found: C, 64.15; H, 3.9; M,$^+$ 204.0415. $C_{11}H_8O_4$ requires C, 64.7; H, 3.9%; M, 204.0422); υ_{max}/cm^{-1} 3405 (OH), 1637 and 1616 (C=O) and 1490 (C=C); δ_H (acetone-d_6) 2.09 (3H, d, *J* 1.5 Hz, 2-CH_3), 6.54 (1H, d, *J* 2.4 Hz, 7-H), 6.74 (1H, q, *J* 1.5 Hz, 3-H), 6.96 (1H, d, *J* 2.4 Hz, 5-H), 9.86 (1H, br s, 6-OH) and 12.21 (1H, br s, 8-OH); δ_C 18.1 (2-CH_3), 107.8 (C-8), 110.3 (C-5), 110.6 (C-3), 112.3 (C-8a), 138.6 (C-4a), 137.6 (C-7), 151.7 (C-2), 167.6 (C-6), 186.8 (C-1) and 192.0 (C-4); *m/z* 204 (M^+, 64%), 149 (40), 91 (16) and 57 (100).

(1*R*,3*R*,4*S*)-3,4-Dihydro-4,7,9-trihydroxy-1,3-dimethylnaphtho[2,3-*c*]pyran-5,10-quinone [Quinone A] 1

To a stirred solution of bromoquinone **12** (100 mg, 0.35 mmol) in dry tetrahydrofuran (10 cm^3) at 0 °C was added drop-wise a solution of the diene **11** (181 mg, 0.70 mmol) in tetrahydrofuran (5 cm^3). The green coloured mixture was stirred for 24 h during which time a bright yellow solution was obtained. The reaction mixture was diluted with dichloromethane (100 cm^3) and the mixture poured into water (150 cm^3) and exhaustively extracted with dichloromethane. The residue obtained upon work-up was chromatographed (radial, 30% ethyl acetate–hexane) and recrystallised to give quinone A **1** (30 mg, 30%) as bright orange plates, mp 200 °C (decomp.) (benzene) (Lit.,[1] 200 °C) $[\alpha]_D$ +40 (*c* 1.0 in 1% CH_3CO_2H–CH_3OH) (Lit.[7] +41) (Found: C, 61.75; H, 4.4; $(M - H)^+$, 289.0702. $C_{15}H_{14}O_6$ requires C, 62.05; H, 4.85%; (M − H), 289.0712); υ_{max}/cm^{-1} 3402 (OH), 1641 (C=O) and 1552 (C=C); δ_H (acetone-d_6) 1.09 (3H, d, *J* 6.3 Hz, 3-CH_3), 1.36 (3H, d, *J* 6.8 Hz, 1-CH_3), 2.60–2.70 (1H, br s, 4-OH), 3.66 (1H, dq, *J* 6.3 and 7.2 Hz, 3-H), 4.00–4.10 (1H, br s, 7-OH), 4.15 (1H, dd, *J* 1.2 and 7.2 Hz, 4-H), 4.61 (1H, dq, *J* 1.2 and 6.8 Hz, 1-H), 6.40 (1H, d, *J* 2.4 Hz, 8-H), 6.85 (1H, d, *J* 2.4 Hz, 6-H) and 11.89 (1H, s, 9-OH); δ_C 18.5 (3-CH_3), 19.5 (1-CH_3), 66.9 (C-3), 67.2 (C-1), 69.0 (C-4), 108.4 (C-8), 108.9 (C-6), 126.8 (C-4a), 135.0 (C-10a), 142.5 (C-5a), 148.5 (C-9a), 165.3 (C-7), 165.7 (C-9), 185.0 (C-5) and 188.0 (C-10).

(1*R*,3*R*,4*R*)-3,4-Dihydro-4,7,9-trihydroxy-1,3-dimethylnaphtho[2,3-*c*]pyran-5,10-quinone [Quinone A′] 2

Bromoquinone **59** (100 mg, 0.35 mmol) was treated with the diene **11** (181 mg, 0.70 mmol), as described above for the conversion of **12** to the naphthoquinone **1**, to give quinone A′ **2** (20 mg, 20%) as bright orange plates, mp 234 °C (decomp.) (benzene) (Lit.,[1] 236 °C) $[\alpha]_D$ +262 (*c* 1.0 in 1% CH_3CO_2H–CH_3OH) (Lit.,[7] +258) (Found: C, 62.4; H, 5.05; $(M - H)^+$, 289.0724. $C_{15}H_{14}O_6$ requires C, 62.05; H, 4.85%; (M − H), 289.0712); υ_{max}/cm^{-1} 3438 (OH) and 1643 (C=O); δ_H (acetone-d_6) 1.11 (3H, d, *J* 6.3 Hz, 3-CH_3), 1.35 (3H, d, *J* 6.8 Hz, 1-CH_3), 2.64–2.80 (2H, br s, 4- and 7-OH), 3.84 (1H, dq, *J* 1.9 and 6.3 Hz, 3-H), 4.41 (1H, d, *J* 1.9 Hz, 4-H), 4.75 (1H, q, *J* 6.8 Hz, 1-H), 6.48 (1H, d, *J* 2.4 Hz, 8-H), 6.98 (1H, d, *J* 2.4 Hz, 6-H) and 12.05 (1H, br s, 9-OH); δ_C 16.7 (3-CH_3), 18.5 (1-CH_3), 61.6 (C-3), 68.0 (C-1), 68.3 (C-4), 108.4 (C-8), 109.5 (C-6), 110.1 (C-4a), 135.2 (C-10a), 142.53 (C-5a), 148.2 (C-9a), 165.8 (C-7), 166.7 (C-9), 183.8 (C-5) and 188.6 (C-10); *m/z* 290 ($M,^+$ 20%), 275 (13), 183 (100) and 90 (22).

(1*R*,3*S*,4*S*)-3,4-Dihydro-4,7,9-trihydroxy-1,3-dimethylnaphtho[2,3-*c*]pyran-5,10-quinone 5

Bromoquinone **61** (60 mg, 0.21 mmol) was treated with the diene **11** (108 mg, 0.42 mmol), as described above for the conversion of the benzoquinone **12** into the naphthopyranquinone **1**, to give the product **5** (14 mg, 23%) as bright orange plates, mp 102–103 °C (decomp.) (benzene) $[\alpha]_D$ +260 (*c* 1.0 in 1% CH_3CO_2H–CH_3OH) (Lit.[7] +278) (Found: $(M - H)^+$, 289.0711. $C_{15}H_{14}O_6$ requires (M − H), 289.0712); υ_{max}/cm^{-1} 3444 (OH), 1639 (C=O) and 1463 (C=C); δ_H (acetone-d_6) 1.31 (3H, d, *J* 6.3 Hz, 3-CH_3), 1.56 (3H, d, *J* 6.5 Hz, 1-CH_3), 3.20–3.60 (2H, br s, 4- and 7-OH), 3.64 (1H, dq, *J* 1.2 and 6.3 Hz, 3-H), 4.44 (1H, t, *J* 1.2 Hz, 4-H), 4.76 (1H, dq, *J* 1.2 and 6.5 Hz, 1-H), 6.62 (1H, d, *J* 2.3 Hz, 8-H), 7.10 (1H, d, *J* 2.3 Hz, 6-H) and 12.16 (1H, br s, 9-OH); δ_C 17.0 (3-CH_3), 21.8 (1-CH_3), 62.4 (C-3), 70.6 (C-1), 73.1 (C-4), 108.7 (C-8), 109.2 (C-6), 110.1 (C-4a), 135.3 (C-10a), 143.9 (C-5a), 148.6 (C-9a), 165.7 (C-7), 166.3 (C-9), 183.5 (C-5) and 189.5 (C-10).

(1*R*,3*S*,4*R*)-3,4-Dihydro-4,7,9-trihydroxy-1,3-dimethylnaphtho[2,3-*c*]pyran-5,10-quinone 6

Bromoquinone **63** (84 mg, 0.29 mmol) was treated with the diene **11** (152 mg, 0.58 mmol), as described above for the conversion of quinone **12** into quinone A **1**, to give the naphthopyranquinone **6** (20 mg, 23%) as bright orange plates, mp 196–198 °C (decomp.) (benzene) $[\alpha]_D$ +550 (*c* 1.0 in 1% CH_3CO_2H–CH_3OH) (Lit.,[7] +568) Found: M^+, 290.0815. $C_{15}H_{14}O_6$ requires M, 290.0790; υ_{max}/cm^{-1} 3492 and 3222 (OH), 1631 (C=O) and 1497 (C=C); δ_H (acetone-d_6) 1.15 (3H, d, *J* 6.2 Hz, 3-CH_3), 1.31 (3H, d, *J* 6.6 Hz, 1-CH_3), 2.60–2.80 (1H, br s, 4-OH), 3.23 (1H, dq, *J* 6.2 and 8.2 Hz, 3-H), 4.15–4.30 (1H, br s, 7-OH), 4.18 (1H, dd, *J* 2.5 and 8.2 Hz, 4-H), 4.60 (1H, dq, *J* 2.5 and 6.6 Hz, 1-H), 6.42 (1H, d, *J* 2.3 Hz, 8-H), 6.87 (1H, d, *J* 2.3 Hz, 6-H) and 11.92 (1H, br s, 9-OH); δ_C 21.1 (3-CH_3), 23.8 (1-CH_3), 68.6 (C-3), 71.1 (C-1), 74.3 (C-4), 111.0 (C-8), 111.3 (C-6), 127.3 (C-4a), 137.4 (C-10a), 147.5 (C-5a), 150.7 (C-9a), 167.7 (C-7), 168.1 (C-9), 187.6 (C-5) and 191.1 (C-10).

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