



Asymmetric diastereoselective syntheses of the aphid insect pigment derivatives quinone **A** and quinone **A'**

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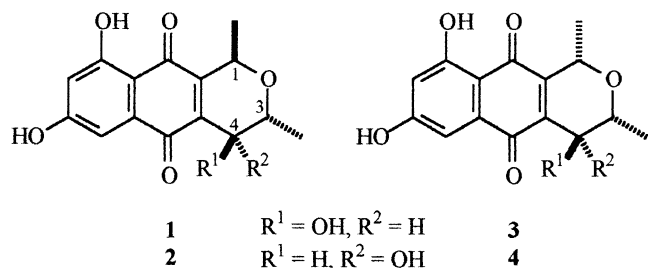
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Abstract—Commercially available (*R*)-lactate has been used to provide the chiral source for the asymmetric diastereoselective syntheses of all four stereoisomers of 3,4-dihydro-4,7,9-trihydroxy-1,3-dimethylnaphtho[2,3-*c*]pyran-5,10-quinone based on *3R* stereochemistry. The (1*R*,3*R*,4*S*) and (1*R*,3*R*,4*R*) stereoisomers were identical with the natural derivatives of the aphid insect pigments quinone **A** and quinone **A'**, while the (1*S*,3*R*,4*S*) and (1*S*,3*R*,4*R*) stereoisomers were found to be the enantiomers of two hitherto unreported naturally derived quinones from alternative aphid insect sources. A key-step is the titanium tetraisopropoxide-induced intramolecular diastereoselective cyclization of *meta*-hydroxybenzyl protected lactaldehydes to afford benzo[*c*]pyran-4,5-diols. © 2001 Elsevier Science Ltd. All rights reserved.

The quinones **A** **1** and **A'** **2** are a pair of C-4 epimeric naphthopyranols derived through reduction of the bean and willow aphid insect pigments protoaphin-*fb* and protoaphin-*sl*, respectively.¹ These quinones have been synthesized previously in racemic form;² we now describe their first diastereoselective asymmetric syntheses, together with those of their C-1 epimers **3** and **4**. These comprise all four stereoisomers based on *3R* stereochemistry. Following the completion of these four syntheses, discussions with Professor Cameron revealed that compounds **3** and **4** are the enantiomers of two further, unreported, derivatives of naturally occurring aphid pigments.³



The enantiopure phenolic aldehyde **5**⁴ was cyclized in 69% yield to afford the benzopyran **7** as a single

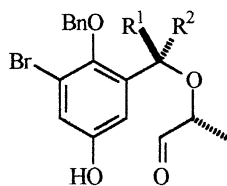
Keywords: asymmetric syntheses; naphthopyranquinones; intramolecular diastereoselective cyclizations.

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diastereomer using titanium tetraisopropoxide.^{5,6} Debenzylation⁷ of **7** through hydrogenolysis followed by immediate oxidation of the intermediate hydroquinone **8** with cerium(IV) ammonium nitrate gave the quinone **16** in 41% overall yield for the two steps. The benzopyranquinone **17**, the C-4 epimer of **16**, was obtained through methylation of the phenolic benzopyran **7** to afford the methyl ether **9**. The C-4 pseudo-equatorial stereochemistry of this alcohol was reversed through treatment of **9** with phosphorus pentachloride followed by silver nitrate in aqueous acetonitrile² to afford the epimeric C-4 pseudoaxial alcohol **10** in 87% from diol **7**. Debenzylation⁷ of **10** followed by cerium(IV) ammonium nitrate oxidation of the product **11** afforded the target benzopyranquinone **17** in 50% overall yield.

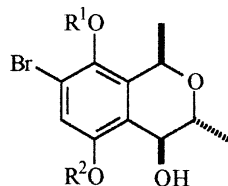
The related cyclization of the benzyl-epimeric aldehyde **6** yielded a mixture of the C-4 epimeric benzopyrans **12** (51%) and **13** (30%). Each of these was individually debenzylated⁷ to afford the intermediate hydroquinones **14** and **15**, respectively, and these were oxidized as before to give the separate benzopyranquinones **18** and **19** in overall yields of 43 and 42% respectively.

In Diels–Alder reactions in which bromine controlled the regiochemistry,⁸ each of the quinones **16**–**19** was separately treated with 1-methoxy-1,3-trimethylsilyloxy-1,3-butadiene,⁹ from which each of the naphthopyranquinones **1**–**4**¹⁰ was obtained in yields of 20–30%.



5 $R^1 = \text{Me}, R^2 = \text{H}$

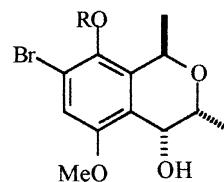
6 $R^1 = \text{H}, R^2 = \text{Me}$



7 $R^1 = \text{Bn}, R^2 = \text{H}$

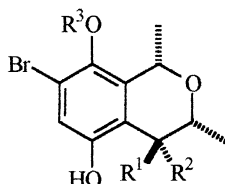
8 $R^1 = R^2 = \text{H}$

9 $R^1 = \text{Bn}, R^2 = \text{Me}$



10 $R = \text{Bn}$

11 $R = \text{H}$

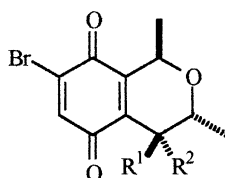


12 $R^1 = \text{OH}, R^2 = \text{H}, R^3 = \text{Bn}$

13 $R^1 = \text{H}, R^2 = \text{OH}, R^3 = \text{Bn}$

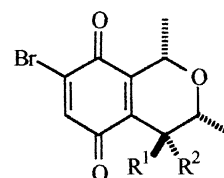
14 $R^1 = \text{OH}, R^2 = R^3 = \text{H}$

15 $R^1 = R^3 = \text{H}, R^2 = \text{OH}$



16 $R^1 = \text{OH}, R^2 = \text{H}$

17 $R^1 = \text{H}, R^2 = \text{OH}$



18

19

References

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- We greatly appreciate Professor D. W. Cameron's personal communication, more details of which will appear subsequently.
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- ¹H NMR spectroscopic studies⁶ using Eu(hfc)₃ on precursors to the aldehydes **5** and **6** showed that these possessed enantiomeric excesses of >98%. Specific rotations measured for the quinones **A 1** and **A' 2** obtained through synthesis (+37 and +262°) corresponded closely to those obtained for the naturally derived compounds³ (+41 and +258°, respectively).