C-Glycosylation of tri-*O*-benzyl-2-deoxy-D-glucose: synthesis of naphthyl-substituted 3,6-dioxabicyclo[3.2.2]nonanes

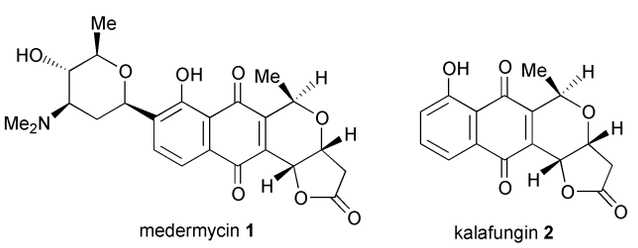
Margaret A. Brimble *† and Timothy J. Brenstrum

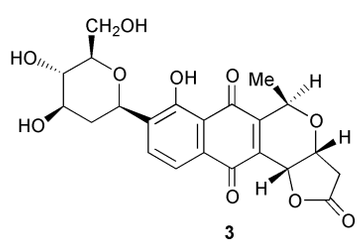
School of Chemistry, F11, University of Sydney, Camperdown, NSW 2006, Australia

Received (in Cambridge, UK) 27th March 2001, Accepted 22nd May 2001
First published as an Advance Article on the web 5th July 2001

The syntheses of naphthol **7**, naphthol **8**, naphthol **11** and naphthol **12** are described, starting from juglone **13**. *C*-Glycosylation of naphthol **8** with benzyl-protected glycosyl donor **10** using trimethylsilyl trifluoromethanesulfonate and silver perchlorate or boron trifluoride–diethyl ether affords rearranged product **36** in which the glycosyl donor has undergone an unusual 1,6-hydride shift. Use of the corresponding naphthol **12** as the glycosyl acceptor under the same conditions affords the expected *C*-glycoside **34**. Use of the naphthol **7** and naphthol **11** affords predominantly rearranged products **35** and **37** respectively, albeit in much lower yield than the reactions using the corresponding bromonaphthols. The study described herein establishes that introduction of an acetyl group to C-3, as in *C*-glycosylnaphthoquinone **4**, as required for conversion to analogues of medermycin **1** such as **3**, necessitates that the *C*-glycosylation step be effected before regioselective introduction of the acetyl group.

Medermycin **1** was isolated from *Streptomyces tanashiensis*[1] and is highly active against gram-positive organisms including many species of *Staphylococcus* and *Bacillus*.[2] It is also effective against neoplastic cells *in vitro*, antibiotic-resistant cell lines of L5178Y lymphoblastoma and Ehrlich carcinoma in mice, and has shown 50% inhibition of human leukaemia K-562 cells at a concentration of 0.03 μg mL^{-1}.[3] Another property of medermycin **1** is its ability to act as a bioreductive alkylating agent *in vivo via* quinone methide intermediates, as postulated by Moore.[4] Medermycin **1** possesses the same pyranonaphthoquinone ring skeleton as kalafungin **2**[5] with an additional β *C*-glycoside linkage at C-8 to an amino sugar, D-angolosamine. Given the reported improvement in anthelmintic activity reported for kalafungin **2** in the presence of various natural sugars,[6] an efficient and flexible method for the introduction of a *C*-glycoside linkage at C-8 of the kalafungin molecule was sought, such that a range of *C*-glycosidic pyranonaphthoquinones could be prepared for biological evaluation.





To date only one (lengthy) synthesis of medermycin **1** has been reported[7] in which a pyranonaphthalene skeleton was assembled by addition of a sulfonylphthalide to an enone. The sulfonylphthalide was prepared in a seventeen-step sequence in which *C*-glycosylation was effected by addition of a substituted aryllithium species to a bromolactone derived from D-rhamnal. Our synthetic effort to date has focused on the synthesis of a 2-deoxyglycosyl analogue of medermycin, compound **3**,[8] using a furofuran annulation–oxidative rearrangement strategy that we have successfully used for the synthesis of kalafungin **2**[9] and related aglycones.[10] Initial studies,[11] focused on developing an efficient synthesis of the key benzyl-protected 2-acetyl-2′-deoxyglucosyl-1,4-naphthoquinone **4**, unveiled an extensive rearrangement of the tri-*O*-benzyl-2-deoxyglucosyl moiety. We therefore herein report the full details of the formation of naphthyl *C*-glycosides derived from this rearranged tri-*O*-benzyl-2-deoxyglucosyl skeleton.

Results and discussion

A synthesis of the 2-acetyl-7-deoxyglucosyl-1,4-naphthoquinone **4** was required in order to realise a synthesis of a 2-deoxyglucosyl analogue of medermycin, compound **3**, based on the retrosynthesis outlined in Scheme 1. Preliminary studies had indicated that direct *C*-glycosylation[12] of kalafungin **2**, which contains a 5-hydroxy-1,4-naphthoquinone (juglone) skeleton, was not feasible given the low reactivity of this glycosyl acceptor due to the strong hydrogen bonding between the hydroxy group and the neighbouring quinone carbonyl group. Mindful of these limitations[13] we decided to focus our attention on the synthesis of *C*-glycosylnaphthalenes **5** and **6** which would serve as suitable precursors to the key *C*-glycosylnaphthoquinone **4**. In turn *C*-glycosylnaphthalenes **5** and **6** were envisaged to be prepared *via* *C*-glycosylation of the acetylnaphthol **7** or the bromonaphthol **8**.

It transpired that the reactivity of 3-functionalised naphthalenes **7** and **8** towards the 2-deoxyglucosyl donors **9** and **10** differed markedly from the reactivity of the corresponding 2-functionalised naphthols **11** and **12**. Thus the starting point for the synthetic work reported herein is the synthesis of naphthols **7** and **8**, together with their regioisomers **11** and **12**, starting from juglone **13** (Scheme 2).

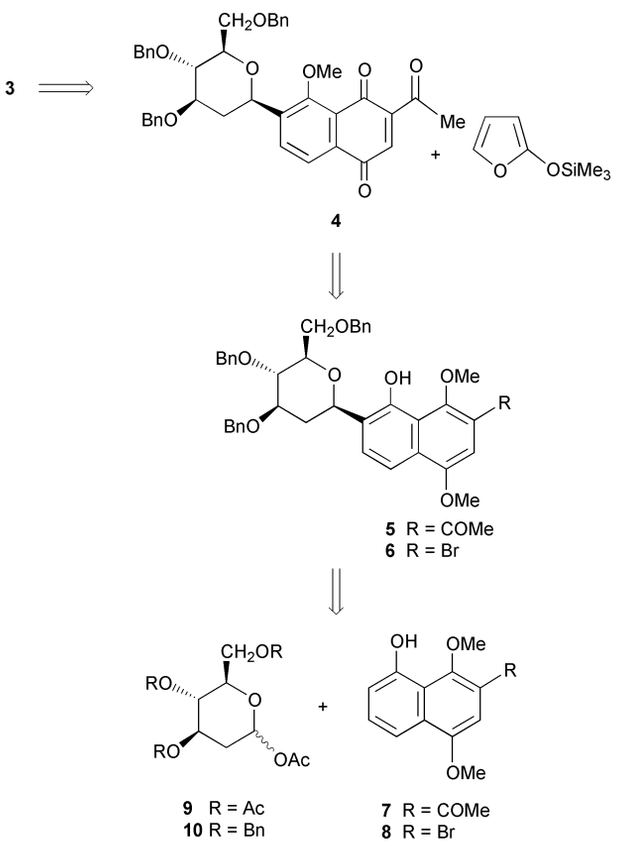
The first step in the synthesis was the bromination of juglone **13**.[14] Bromination of juglone **13** in chloroform at 0 °C followed by the addition of a trace of glacial acetic acid afforded a 3.6:1 mixture of **14** and **15** in an overall yield of 97%. 3-Bromo-

† *Present address:* Department of Chemistry, University of Auckland, Private Bag 92019, Auckland, New Zealand. Fax: +64 9 3737422; email: m.brimble@auckland.ac.nz

 DOI: 10.1039/b102807n

juglone **14** was the less polar of the two regioisomers and melted at 171–172 °C, in good agreement with the literature.[15] The more polar 2-bromojuglone **15** melted at 135–136 °C which was also in good agreement with the literature value.[15]

With 3-bromojuglone **14** in hand, attention turned to the benzylation and reductive methylation steps (Scheme 2). A solution of 3-bromojuglone **14** in chloroform was treated with benzyl bromide and silver(I) oxide. The yellow crystalline benzyl ether **16** was obtained in 89% yield after work-up and chromatography. The 2-bromo isomer **15** was subjected to the same conditions, affording the crystalline benzyl ether **17** in 84% yield.



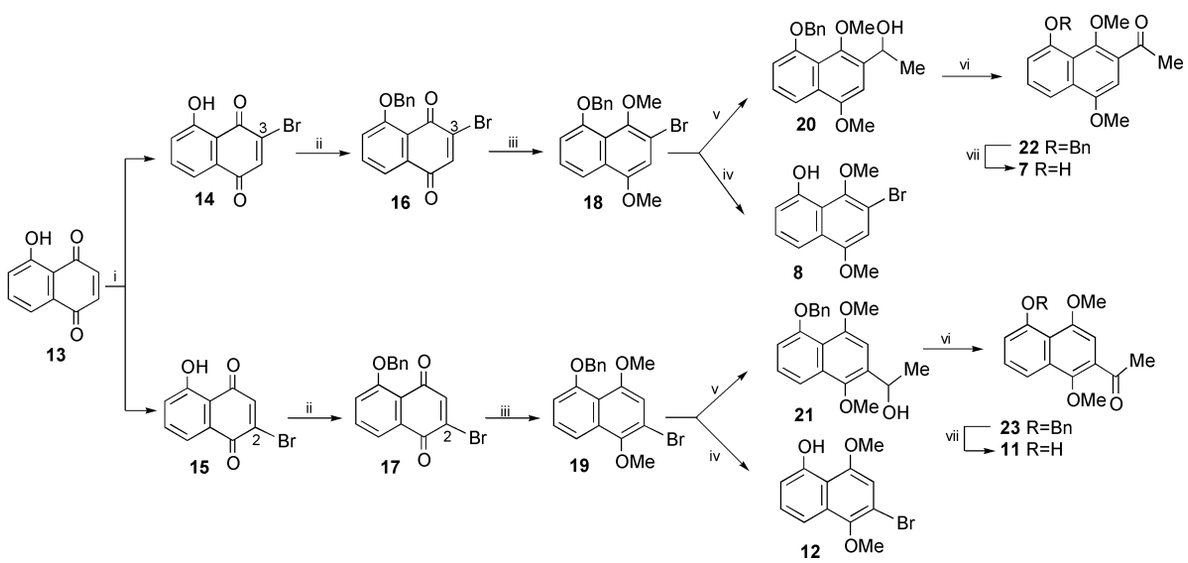
Scheme 1

With the hydroxy group at C-5 protected as a benzyl ether, reductive methylation of the quinone was next undertaken. Naphthoquinone **16** was reduced with aq. disodium dithionite to give an air-sensitive hydroquinone, which underwent methylation using dimethyl sulfate and potassium carbonate to give the dimethoxynaphthalene **18** in 76% yield. The 2-bromo isomer **17** reacted under the same conditions to give the dimethylated product **19** in 79% yield. The final step in the synthesis of bromonaphthol **8** was the removal of the benzyl protecting group which was effected in 98% yield by hydrogenolysis over 10% palladium on charcoal in ethyl acetate. Likewise, the 2-bromo isomer **12** was readily afforded by hydrogenolysis of benzyl ether **19** in 94% yield.

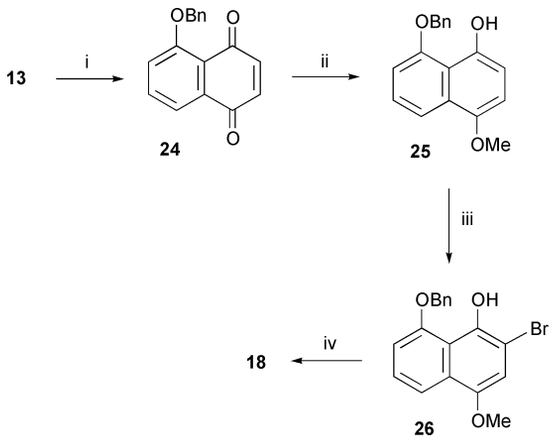
It was hoped that the acetyl group in naphthol **7** could be installed in one step by reaction of the lithiated anion of bromide **18** with acetyl chloride; however, treatment of a solution of **18** in tetrahydrofuran at −78 °C with *n*-butyllithium (1.35 equiv.) followed by quenching with freshly distilled acetyl chloride afforded only protonated material. More success was realised when using acetaldehyde as the electrophile, taking care to add the acetaldehyde immediately after generation of the organolithium reagent. This procedure afforded the benzylic alcohol **20** in 98% yield. The regioisomeric bromide **19** was converted to alcohol **21** in 97% yield using these optimum conditions.

Oxidation of alcohol **20** to ketone **22** was initially attempted using manganese dioxide; however, no reaction took place even after stirring for a day. Use of tetra-*n*-propylammonium perruthenate (TPAP), in combination with *N*-methylmorpholine *N*-oxide (NMO) as the reoxidant, and powdered molecular sieves (4 Å) in dichloromethane afforded ketone **22** in 80% yield after flash chromatography.[16] The regioisomeric alcohol **21** was also conveniently oxidised to ketone **23** in 78% yield using these reagents.

Finally, treatment of a solution of **22** in ethyl acetate with palladium on charcoal (50 mg $mmol^{-1}$) under an atmosphere of hydrogen gave acetylnaphthol **7**, in 53% yield after purification by flash chromatography. Similarly, the regioisomeric ketone **23** underwent debenzylation in 58% yield. Formation of more polar benzylic alcohol by-products accounted for the poor yields from this reaction. Re-oxidation using TPAP–NMO allowed recycling of these unwanted by-products to the desired ketones **7** and **11**, thereby increasing the overall yield to approximately 70%.



Scheme 2 *Reagents, conditions and yields:* (i) Br_2, AcOH, $CHCl_3$, 70 min: **14** (76%), **15** (21%) (ii) BnBr, Ag_2O, $CHCl_3$, 2 h: **16** (89%), **17** (84%) (iii) aq. $Na_2S_2O_4$, CH_2Cl_2–Et_2O; then Me_2SO_4, K_2CO_3, acetone, heat, 48 h: **18** (76%), **19** (79%) (iv) H_2, Pd/C, EtOAc, 8 h: **8** (98%), **12** (94%) (v) ^{n}BuLi, −78 °C, THF, 0.5 min; then AcH: **20** (98%), **21** (97%) (vi) TPAP, NMO, CH_2Cl_2, 3 h, 4 Å mol. sieves: **22** (80%), **23** (78%) (vii) H_2, Pd/C, EtOAc, 8 h: **7** (53%), **11** (58%). The juglone numbering scheme is presented here, and is used for NMR assignments of all compounds described in the Experimental section.



Scheme 3 *Reagents, conditions and yields:* (i) BnBr, Ag_2O, $CHCl_3$, 2 h (80%) (ii) aq. $Na_2S_2O_4$, Me_2SO_4, K_2CO_3, acetone, heat, 4 h (75%) (iii) Br_2, CCl_4, 5 min (99%) (iv) NaH, MeI, DMF, 12 h (74%).

Due to the initial problems encountered with the regioselective bromination of juglone **13**, an alternative synthesis of bromide **8** (*via* benzyl ether **18**) was developed (Scheme 3). Juglone **13** was first converted to benzyl ether **24**[17] by treatment with benzyl bromide and silver(I) oxide. Reductive methylation of benzyl juglone **24** was then carried out, as for bromide **16**, by reduction to the hydroquinone using aqueous dithionite, followed by methylation using dimethyl sulfate and potassium carbonate in acetone under reflux. In this case, the reaction was worked up before methylation of the second, more hindered, hydroxy group at C-4 took place, affording methoxynaphthol **25** in 75% yield.

Regioselective bromination of naphthol **25** was then possible due to the strong *ortho*-directing effect of the hydroxy group. Thus, treatment of the naphthol **25** with bromine in tetrachloromethane gave the crystalline bromonaphthol **26** in essentially quantitative yield after purification by flash chromatography. The hydroxy group of bromonaphthol **26** was then methylated by treatment with sodium hydride and iodomethane in dimethylformamide to give methyl ether **18** in 74% yield after chromatography. Methyl ether **18** was identical in all respects to the material prepared by the original method and was converted to 3-bromonaphthol **8** as described above.

The acetate-protected 2-deoxypyranoside **9** was prepared by acetylation of 2-deoxyglucose according to the procedure of Overend *et al.*,[18] affording glycosyl acetate **9** (α : β, 10 : 1) in 73% yield. Alternatively, the procedure of Mioskowski *et al.*[19] required treatment tri-*O*-acetyl-D-glucal with triphenylphosphine hydrobromide and acetic acid, affording the desired acetate **9** (α : β, 9 : 1) in 72% yield. The benzyl-protected 2-deoxypyranoside **10** was also prepared from tri-*O*-benzyl-D-glucal according to the procedure of Mioskowski *et al.*,[19] affording glycosyl acetate **10** (α : β, 9 : 1) in 86% yield.

With naphthols **7**, **8**, **11** and **12** in hand, our initial attention focused on their *C*-glycosylation using the acetate-protected glycosyl donor **9**. Trimethylsilyl triflate (TMSOTf) in combination with silver perchlorate has been used to effect *C*-glycosylation of β-naphthol in excellent yield[20] and acetonitrile has been recommended as the solvent of choice for effecting *C*-glycosylation of 5,8-dimethoxy-1-naphthol using $BF_3{\cdot}Et_2O$.[21] Attempted *C*-glycosylation of acetylnaphthols **7** and **11** with glycosyl acetate **9** using either $BF_3{\cdot}Et_2O$ (1.5–2.0 equiv.) in acetonitrile or TMSOTf (1.5 equiv.) and silver perchlorate (5 mol%) in acetonitrile afforded neither of the desired *C*-glycosides **27** and **31** (Table 1). The bromonaphthol **12** proved more reactive than bromonaphthol **8**, affording *C*-glycoside **33** in 48–57% yield using the same Lewis acids. The corresponding *C*-glycoside **29** derived from bromonaphthol **8** was obtained in only 5% yield using TMSOTf and silver perchlorate. In all of the above cases much of the starting naphthol was recovered and deacetylation at the anomeric position of the sugar was observed.

Formation of the β-*C*-glycoside **29** was established by the ^{1}H NMR spectrum in which the anomeric proton, 1′-H, resonated at δ 5.12 as a doublet of doublets, with coupling constants $J_{1',2'ax}$ 11.3 and $J_{1',2'eq}$ 2.0 Hz consistent with β-stereochemistry at the anomeric position. Doublets of doublets of doublets at δ 1.78 and 2.52 were assigned to 2′ax-H, with coupling constants, J_{gem} 12.7, $J_{2'ax,3'}$ 11.3 and $J_{2'ax,1'}$ 11.3 Hz, and 2′eq-H, with coupling constants, J_{gem} 12.7, $J_{2'eq,3'}$ 4.8 and $J_{2'eq,1'}$ 2.0 Hz, respectively. The three three-proton singlets at δ 2.02, 2.07 and 2.09 were assigned to the acetate methyl protons of the glycoside, and the hydroxy proton resonated as a singlet at δ 9.70. The ^{1}H NMR spectrum of β-*C*-glycoside **33** was similarly supportive of the proposed structure. The anomeric proton, 1′-H, resonated at δ 5.12 as a doublet of doublets, with coupling constants $J_{1',2'ax}$ 11.3 and $J_{1',2'eq}$ 2.0 Hz, while the hydroxy proton resonated as a singlet at δ 9.49.

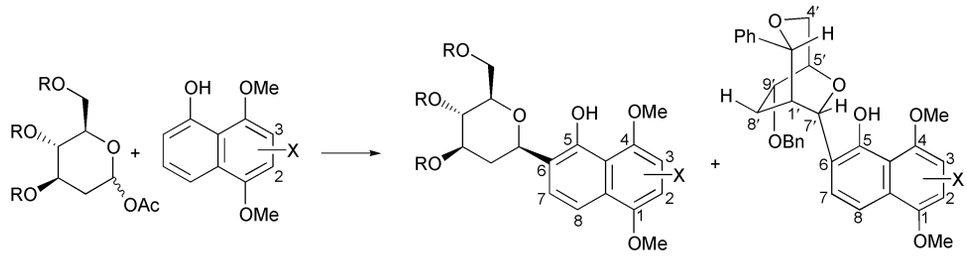
Disappointed by the poor recovery of β-*C*-glycoside **29** from attempted *C*-glycosylation of the bromonaphthol **8** with acetate-protected glycosyl acetate **9**, our attention next turned to use of the benzyl-protected sugar **10**. Accordingly, trimethylsilyl triflate (1.5 equiv.) and silver perchlorate (5 mol%) were added to a solution of bromonaphthol **8** and glycosyl acetate **10** in dry acetonitrile at 0 °C. After 1 hour the reaction was quenched with aqueous sodium bicarbonate and a mixture containing β-*C*-glycoside **30** and the rearranged product **36** (1 : 6) was isolated after flash chromatography. Upon attempting to separate these two products by semi-preparative HPLC (0.375% ^{i}PrOH–hexane; Partisil 10 column, 50 cm × 9.4 mm I.D., flow rate 4 mL min^{-1}), the rearranged product **36** was obtained in 48% yield, while the less stable *C*-glycoside **30** decomposed and was not isolated. The use of boron trifluoride–diethyl ether gave a similar result, affording the rearranged product **36** in a slightly better yield (59%).

In the ^{1}H NMR spectrum of the rearranged product **36** two singlets at δ 5.06 and 5.86 were assigned to 7′-H and 2′-H respectively. Doublets of doublets of doublets at δ 1.43 and 1.98 corresponded to the geminal protons 8′-H_A and 8′-H_B respectively. The doublet of doublets at δ 2.19 was assigned as 1′-H with couplings of $J_{1',8'A}$ 4.8 and $J_{1',8'B}$ 2.2 Hz, and the resonances at δ 3.85 and 3.94 corresponded to the two methoxy groups. 4′-H_A resonated as a doublet at δ 4.08 with coupling constant J_{gem} 13.4 Hz, while 4′-H_B resonated as a doublet of doublets at δ 4.21 showing an additional coupling constant, $J_{4'B,5'}$ 5.5 Hz. The 9′-H proton resonated as a doublet of doublets at δ 4.16 with coupling constants $J_{9',8'A}$ 9.7 and $J_{9',8'B}$ 4.8 Hz. 2-H resonated as a singlet at δ 6.70, while 8-H and 7-H resonated as a pair of doublets at δ 7.64 and 8.04 with a coupling constant, $J_{7,8}$ 8.7 Hz.

The assignment of **36** was aided by comparison with compound **39**, which bears essentially the same structure as the rearranged glycosyl moiety of **36** (Table 2). The literature[22] compound **39** has a β-benzyloxy substituent at C-7′, whereas in our rearranged product **36** the lack of coupling with 1′-H suggests that 7′-H is *exo* and the aryl moiety is therefore *endo*. This assignment of stereochemistry was confirmed by obtaining an X-ray crystal structure of the acetate derivative of the rearranged product **36**.[23]

The formation of rearranged *C*-glycoside **36** can be rationalised (Scheme 4) by initial generation of an oxacarbenium ion followed by a 1,6-hydride shift to regenerate a glycal producing a benzylic oxacarbenium ion. Attack of the glycal on this latter ion followed by trapping with the appropriate substituted naphthol affords the unusual *C*-glycosides. An analogous rearrangement has been observed by Steel *et al.*[22] during investigations of the dimerisation of tri-*O*-benzyl-D-glucal using acetyl perchlorate. These authors also carried out deuterium-labelling studies which provided evidence for the critical 1,6-hydride shift.

Table 1 *C*-Glycosylation of naphthols **7**, **8**, **11**, **12**, with the naphthol moiety given the juglone numbering system



9 R=Ac
10 R=Bn

7 X=COMe (C-3)
8 X=Br (C-3)
11 X=COMe (C-2)
12 X=Br (C-2)

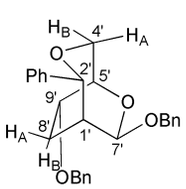
27 X=COMe (C-3); R=Ac
28 X=COMe (C-3); R=Bn
29 X=Br (C-3); R=Ac
30 X=Br (C-3); R=Bn
31 X=COMe (C-2); R=Ac
32 X=COMe (C-2); R=Bn
33 X=Br (C-2); R=Ac
34 X=Br (C-2); R=Bn

35 X=COMe (C-3)
36 X=Br (C-3)
37 X=COMe (C-2)
38 X=Br (C-2)

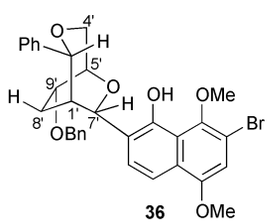
				2-Deoxyglycoside		Rearranged product	
Entry	Glycosyl donor	Naphthol	Lewis acid	Yield (%)		Yield (%)	
1	**9**	**7**	TMSOTf, $AgClO_4$				
2	**9**	**11**	TMSOTf, $AgClO_4$				
3	**9**	**8**	TMSOTf, $AgClO_4$	**29**	5		
4	**9**	**8**	$BF_3{\cdot}Et_2O$				
5	**9**	**12**	TMSOTf, $AgClO_4$	**33**	57		
6	**9**	**12**	$BF_3{\cdot}Et_2O$	**33**	48		
7	**10**	**8**	TMSOTf, $AgClO_4$	**30**	5[a]	**36**	48
8	**10**	**8**	$BF_3{\cdot}Et_2O$	**30**	9[a]	**36**	59
9	**10**	**12**	$BF_3{\cdot}Et_2O$	**34**	53		
10	**10**	**7**	$BF_3{\cdot}Et_2O$	**28**	7	**35**	12
11	**10**	**11**	$BF_3{\cdot}Et_2O$	**32**	9	**37**	23

[a] Not isolated (estimated yield from analysis of ^{1}H NMR spectrum of crude product mixture).

Table 2 ^{1}H and ^{13}C NMR shifts for **36** and **39**



39



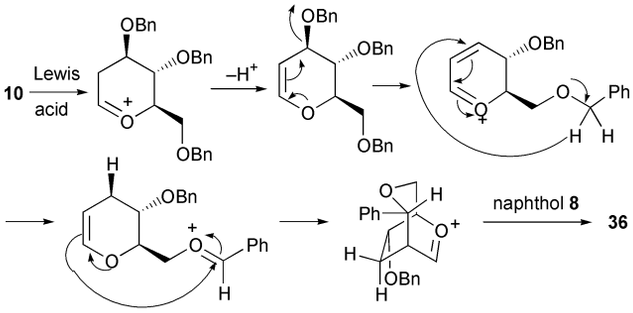
36

	39				**36**			
	δ_H (ppm)	m	*J*/Hz	δ_C (ppm)	δ_H (ppm)	m	*J*/Hz	δ_C (ppm)
1′	2.35	m		44.8	2.19	dd	4.8, 2.2	45.5
2′	5.47	s		76.0	5.86	s		76.2
4′A	4.00	d	7.1	71.4	4.08	d	13.4	71.1
4′B	4.10	dd	13.1, 5.2		4.21	dd	13.4, 5.5	
5′	4.35	d	5.0	77.4	4.36	d	5.5	76.6
7′	5.18	d	4.4	98.4	5.06	s		86.2
8′A	1.44	m		25.6	1.43	ddd	14.4, 4.8, 4.8	22.4
8′B	2.38	m			1.98	ddd	14.4, 9.7, 2.2	
9′	4.17	dd	9.2, 4.0	73.0	4.16	dd	9.7, 4.8	73.7

By way of contrast, the bromonaphthol **12** coupled smoothly with glycosyl acetate **10** using boron trifluoride–diethyl ether as promoter to give β-*C*-glycoside **34** in 53% yield after flash chromatography with none of the rearranged *C*-glycoside **38** being formed. The ^{1}H NMR spectrum of **34** was consistent with formation of a β-*C*-glycoside, featuring doublets of doublets of doublets at δ 1.63 and 2.59 corresponding to 2′ax-H and 2′eq-H. 1′-H resonated as a doublet of doublets at δ 4.98 with a coupling constant $J_{1'ax,2'ax}$10 Hz, establishing the β-stereochemistry at the anomeric carbon.

As was observed for glycosylation reactions employing the acetate-protected glycosyl donor **9**, the reactivity that the 6-bromonaphthol **12** exhibited towards the benzyl-protected glycosyl donor **10** was greater than was displayed by the 7-bromonaphthol **8**. The lack of reactivity in the latter case resulted in the Lewis acid-mediated 1,6-hydride shift rearrangement reaction to afford the unusual bicyclic acetal **36**. In light of these results, it was decided to investigate the *C*-glycosylation of acetylnaphthol **7** with the same glycosyl donor **10**. It was hoped that replacement of the bulky bromine atom by an acetyl group may alter the outcome of the critical *C*-glycosylation reaction.

Boron trifluoride–diethyl ether was added to a solution of the acetylnaphthol **7** and glycosyl acetate **10** in dry acetonitrile



Scheme 4

at 0 °C. After 20 min the reaction was quenched with water and a mixture of β-*C*-glycoside **28** and the rearranged product **35** (≈ 1 : 3 from the crude ^{1}H NMR spectrum) was isolated after chromatography. Semi-preparative HPLC (1.5% ^{i}PrOH–hexane; Partisil 10 column, 50 cm × 9.4 mm I.D.; flow rate 4 mL min^{-1}) allowed isolation of the pure compounds, in yields of 7 and 12% respectively.

The ^{1}H NMR spectrum of the major product **35** featured characteristic singlets at δ 5.15 and 5.98, assigned to 7′-H and 2′-H, respectively. The ^{1}H NMR spectrum of the minor product **28** featured a characteristic doublets of doublets of doublets at δ 1.65 and 2.57 assigned to 2′$_{ax}$-H and 2′$_{eq}$-H respectively. 1′-H resonated as a doublet of doublets at δ 5.04 with a large axial–axial coupling constant, $J_{1'ax,2'ax}$ 11.4 Hz, confirming the β-stereochemistry of the *C*-glycoside **28**.

Use of the regioisomeric acetylnaphthol **11** as the glycosyl acceptor with glycosyl acetate **10** and boron trifluoride–diethyl ether in acetonitrile also afforded a mixture of *C*-glycoside **32** and rearranged product **37** in low yield. Semi-preparative HPLC (1.5% ^{i}PrOH–hexane; Partisil 10 column, 50 cm × 9.4 mm I.D.; flow rate = 4 mL min^{-1}) was required to isolate the pure components **32** and **37**, in yields of 9 and 23% respectively.

A number of trends emerge from the *C*-glycosylations described herein. Slightly better results were obtained with the acetate-protected sugar **9** using the trimethylsilyl triflate–silver perchlorate system rather than with boron trifluoride–diethyl ether (Table 1, entries 1–6). The reverse was true for the benzyl-protected sugar **10**, where boron trifluoride–diethyl ether gave slightly improved results (entries 7, 8). More important, however, was the reactivity of the naphthols. Using the acetate-protected sugar **9** poor reactivity was observed with naphthols **7** and **8** (entries 1, 3, 4) and naphthol **11** (entry 2), only forming *C*-glycosides in reasonable yield using the bromonaphthol **12** (entries 5, 6). Likewise, using the more reactive benzyl-protected glycosyl donor **10**, poor yields were obtained for naphthols **7** and **8** (entries 7, 8, 10) with the sugar undergoing substantial rearrangement to give the rearranged compounds **35** and **36**. Again, reasonable yields of *C*-glycosides were only obtained using naphthol **12** (entry 9).

The work reported herein provides the first example of the *C*-glycosylation of this unusual rearranged tri-*O*-benzyl-D-glucal skeleton. The different reactivity and product profiles that are observed, depending upon whether the substituent in the right-hand ring of the naphthalene is at C-2 or C-3, illustrate the subtle nature of these *C*-glycosylations. These differences may be attributed to the ability of the 3-bromonaphthol **8**, compared with the 2-bromonaphthol **12**, to better stabilise the positive charge that develops when *C*-glycosylation occurs. For our purposes the results described herein indicate that in order to synthesise the 3-acetyl-*C*-glycosylnaphthoquinone **4** required for synthesis of the 2-deoxyglucosyl analogue of medermycin **3**, a naphthol which is unsubstituted at C-3 must be used in the *C*-glycosylation step. The required acetyl group at C-3 must then be introduced regioselectively after the critical *C*-glycosylation has been effected. This strategy did result in a successful synthesis of the 2-deoxyglucosyl analogue of medermycin **3**.[24]

Experimental

Mps were determined on a Kofler hot-stage apparatus and are uncorrected. IR spectra were recorded using a Perkin-Elmer 1600 Fourier Transform IR spectrophotometer as thin films between sodium chloride plates. Absorption spectra are expressed in wavenumbers (cm^{-1}) with the following abbreviations: s = strong, m = medium, w = weak and br = broad. ^{1}H NMR spectra were recorded on a Bruker AC 200 (200 MHz) or a Bruker DRX 400 (400 MHz) spectrometer at ambient temperature. All *J*-values are given in Hz. Chemical shifts are expressed in parts per million downfield shift from tetramethylsilane as internal standard, and reported as position (δ_H), relative integral, multiplicity (s = singlet, br s = broad singlet, d = doublet, dd = double doublet, ddd = double double doublet, t = triplet, q = quartet, m = multiplet) and assignment. ^{13}C NMR spectra were recorded on a Bruker AC 200 (50.3 MHz) or a Bruker DRX 400 (100.5 MHz) spectrometer at ambient temperature with complete proton decoupling. Chemical shifts are expressed in parts per million downfield shift from tetramethylsilane as internal standard and reported as position (δ_C), multiplicity (aided by DEPT 135, DEPT 90, COSY and HETCOR experiments) and assignment. Low-resolution mass spectra were recorded on a VG70-250S, a VG70-SD or an AEI model MS902 double-focusing magnetic sector mass spectrometer operating with an ionisation potential of 70 eV (EI, DEI, CI and DCI). High-resolution mass spectra were recorded at a nominal resolution of 5000 or 10 000 as appropriate. Major fragments are given as percentages relative to the base peak and assigned where possible. Ionisation methods employed were either electron impact or chemical ionisation with ammonia or methane as reagent gas (CI). Low-resolution chemical ionisation mass spectra were also recorded on a Hewlett Packard 5989A mass spectrometer using ammonia as reagent gas with the sample dissolved in methanol. Flash chromatography was performed using Merck Kieselgel 60 (230–400 mesh) with the indicated solvents. TLC was performed using 0.2 mm thick precoated silica gel plates (Merck Kieselgel 60 F_{254} or Riedel-de Haen Kieselgel S F_{254}). Compounds were visualised by UV fluorescence or by staining with iodine or vanillin in methanolic sulfuric acid. High-performance liquid chromatography (HPLC) was carried out using a Waters Associates system consisting of a Model M-6000A pump, a millipore model U6K injector, a model 440 UV detector at 256 nm and an R401 differential refractometer. Separation was carried out using the indicated solvents on a Partisil 10 M9 semipreparative column of the following dimensions; outer diameter 12.80 mm, inner diameter 9.40 mm, length 500.0 mm and particle size 10.0 μm. Optical rotations were recorded on an Optical Activity POLAAR 2001 polarimeter using a 5 mL cell. Samples were prepared in the solvent indicated at the concentration specified (measured in g/100 mL). $[\alpha]_D$-Values are given in units of 10^{-1} deg cm^2 g^{-1}.

3-Bromo-5-hydroxy-1,4-naphthoquinone (3-bromojuglone) 14 and 2-bromo-5-hydroxy-1,4-naphthoquinone (2-bromojuglone) 15

A solution of bromine (400 mg, 2.50 mmol) in chloroform (5 mL) was added to a stirred solution of juglone **13**[25] (400 mg, 2.30 mmol) and acetic acid (4 drops) in chloroform (5 mL) at 0 °C. Stirring was continued for 70 min, after which the solvent was removed at reduced pressure. Flash chromatography of the resulting orange solid (juglone dibromide) using toluene–hexane (4 : 1) as eluent afforded 3-bromojuglone **14** (442 mg, 76%) and the more polar 2-bromojuglone **15** (122 mg, 21%). Alternatively, the orange solid was redissolved in a mixture of ethanol (10 mL) and boron trifluoride–diethyl ether (1 mL) and heated for 15 min on a steam-bath. The reaction mixture was cooled, diluted with both water (10 mL) and chloroform (30 mL), then filtered and the residue was washed well with chloro-

form (15 mL). The phases were separated and the aqueous phase was extracted with chloroform (2 × 40 mL). The combined organic fractions were washed with water (100 mL), dried (sodium sulfate), and the solvent was removed at reduced pressure. Purification of the residue by flash chromatography using toluene–hexane (4 : 1) as eluent gave 3-bromojuglone **14** (343 mg, 59%) as the sole product, which was recrystallised from ethanol to give orange needles, mp 171–172 °C (lit.,[15] 172 °C); ν_{max}/cm^{-1} 3050 (OH), 1656, 1631 (C=O, quin.), 1459 (C-O); δ_H (200 MHz; $CDCl_3$) ‡ 7.31 (1H, dd, $J_{6,7}$ 6.9 and $J_{6,8}$ 2.8, 6-H), 7.50 (1H, s, 2-H), 7.62–7.72 (2H, m, 7-H and 8-H), 11.74 (1H, s, OH); δ_C (50 MHz; $CDCl_3$) ‡ 114.2 (quat., C-4a), 119.8 (CH, C-8), 124.6 (CH, C-6), 131.9 (quat., C-8a), 137.3 (CH, C-7), 141.5 (CH, C-2), 142.4 (quat., C-3), 162.2 (quat., C-5), 181.7 (quat., C-1), 183.1 (quat., C-4); *m*/*z* (EI) 254, 252 (M^+, 26%), 173 (M − Br, 100).

2-Bromojuglone **15** (122 mg, 21%) was recrystallised from hexane to give orange plates, 135–136 °C (lit.,[15] 136 °C); ν_{max}/cm^{-1} 1675, 1633 (C=O, quin.), 1589 (C-O); δ_H (200 MHz; $CDCl_3$) ‡ 7.32 (1H, dd, $J_{6,7}$ 8.3 and $J_{6,8}$ 1.4, 6-H), 7.50 (1H, s, 3-H), 7.64 (1H, dd, $J_{7,6}$ 8.3 and $J_{7,8}$ 7.4, 7-H), 7.75 (1H, dd, $J_{8,7}$ 7.4 and $J_{8,6}$ 1.4, 8-H), 11.77 (1H, s, OH); δ_C (50 MHz; $CDCl_3$) ‡ 114.6 (quat., C-4a), 121.0 (CH, C-8), 125.1 (CH, C-6), 130.7 (quat., C-8a), 136.4 (CH, C-7), 140.3 (CH, C-3), 140.9 (quat., C-2), 161.7 (quat., C-5), 176.0 (quat., C-1), 187.5 (quat., C-4); *m*/*z* (EI) 254, 252 (M^+, 25%), 173 (M − Br, 100).

The intermediate 2,3-dibromo-2,3-dihydro-5-hydroxy-1,4-naphthoquinone (juglone dibromide) could be isolated by filtration as an orange solid, mp 104 °C (lit.,[26] 109 °C); δ_H (200 MHz; $CDCl_3$) ‡ 4.92, 4.96 (2H, d, $J_{2,3}$ 3.2 Hz, 2-H and 3-H), 7.36 (1H, dd, $J_{6,7}$ 8.0 and $J_{6,8}$ 1.4, 6-H), 7.65 (1H, dd, $J_{8,7}$ 7.4 and $J_{8,6}$ 1.4, 8-H), 7.74 (1H, dd, $J_{7,6}$ 8.0 and $J_{7,8}$ 7.4, 7-H), 11.42 (1H, s, OH); δ_C (50 MHz; $CDCl_3$) ‡ 45.4, 45.5 (CH, C-2 and C-3), 113.0 (quat., C-4a), 120.2 (CH, C-8), 125.4 (CH, C-6), 130.2 (quat., C-8a), 138.0 (CH, C-7), 162.6 (quat., C-5), 185.7, 192.7 (quat., C-1 and C-4); *m*/*z* (EI) 336, 334, 332 (M^+, 20, 40, 20%), 255, 254, 253, 252 (M − Br, 100), 173 (M − 2Br, 95), 145 (75), 118 (40), 63 (60).

5-Benzyloxy-3-bromo-1,4-naphthoquinone 16

Silver(I) oxide (5.5 g, 23.7 mmol) was added to a stirred solution of 3-bromojuglone **14** (1.50 g, 5.93 mmol) and benzyl bromide (1.41 mL, 11.9 mmol) in chloroform (15 mL). After 2 h the solution was filtered through a Celite pad to remove silver salts and the solvent was removed at reduced pressure. The resultant orange oil was purified by flash chromatography using hexane–ethyl acetate (18 : 1 to 9 : 1) as eluent to afford *5-benzyloxy-3-bromo-1,4-naphthoquinone* **16** (1.82 g, 89%), which was recrystallised from ethanol to give yellow needles, mp 107–108 °C [Found (FAB): M^+, 343.9875, 341.9893. $C_{17}H_{11}BrO_3$ requires *M*, 343.9871, 341.9892]; ν_{max}/cm^{-1} 1672 (C=O, quin.), 1583 (C-O); δ_H (400 MHz; $CDCl_3$) ‡ 5.30 (2H, s, CH_2Ph), 7.34 (1H, d, J_o 7.3, *p*-Ph), 7.35 (1H, dd, $J_{6,7}$ 8.7 and $J_{6,8}$ 0.7, 6-H), 7.43 (2H, t, J_o 7.3, *m*-Ph), 7.45 (1H, s, 2-H), 7.58 (2H, d, J_o 7.3, *o*-Ph), 7.66 (1H, dd, $J_{7,6}$ 8.1 and $J_{7,8}$ 8.1, 7-H), 7.73 (1H, dd, $J_{8,7}$ 7.8 and $J_{8,6}$ 1.0, 8-H); δ_C (100 MHz; $CDCl_3$) ‡ 70.1 (CH_2, CH_2Ph), 119.6, 119.7 (CH, C-6, C-8), 120.1 (quat., C-4a), 126.7 (CH, *o*-Ph), 128.1 (CH, *p*-Ph), 128.7 (CH, *m*-Ph), 133.3 (quat., C-8a), 135.4 (CH, C-7), 135.7 (quat., *ipso*-Ph), 138.3 (CH, C-2), 142.6 (quat., C-3), 159.2 (quat., C-5), 176.0, 182.5 (quat., C-1, C-4); *m*/*z* (EI) 344, 342 (M^+, 9%), 253, 251 (M − C_7H_7, 12), 91 (C_7H_7, 100).

5-Benzyloxy-2-bromo-1,4-naphthoquinone 17

Silver(I) oxide (9.25 g, 39.9 mmol) was added to a stirred solution of 2-bromojuglone **15** (2.02 g, 7.98 mmol) and benzyl bromide (7.8 mL, 11.2 mmol) in chloroform (15 mL). After 2 h the solution was filtered through a Celite pad to remove silver salts and the solvent was removed at reduced pressure. The resultant orange oil was purified by flash chromatography using hexane–ethyl acetate (18 : 1 to 9 : 1) as eluent to afford *5-benzyloxy-2-bromo-1,4-naphthoquinone* **17** (2.30 g, 84%), which was recrystallised from ethanol to give yellow needles, mp 122–123 °C [Found (EI): M^+, 343.9875, 341.9893. $C_{17}H_{11}BrO_3$ requires *M*, 343.9871, 341.9892]; ν_{max}/cm^{-1} 1676, 1656 (C=O, quin.); δ_H (400 MHz; $CDCl_3$) ‡ 5.30 (2H, s, CH_2Ph), 7.33–7.43 (5H, m, 6-H, 3-H, *p*-Ph, *m*-Ph), 7.58 (2H, dd, J_o 7.3 and J_m 0.8, *o*-Ph), 7.66 (1H, dd, $J_{7,8}$ 8.5 and $J_{7,6}$ 8.1, 7-H), 7.73 (1H, dd, $J_{8,7}$ 8.5 and $J_{8,6}$ 1.1, 8-H); δ_C (100 MHz; $CDCl_3$) ‡ 70.9 (CH_2, CH_2Ph), 119.8 (quat., C-4a), 120.9, 120.1 (CH, C-6, C-8), 126.7 (CH, *o*-Ph), 128.1 (CH, *p*-Ph), 128.7 (CH, *m*-Ph), 133.1 (quat., C-8a), 135.9 (CH, C-7), 135.7, 136.9 (quat., C-2, *ipso*-Ph), 142.3 (CH, C-3), 158.8 (quat., C-5), 178.2, 181.3 (quat., C-1, C-4); *m*/*z* (EI) 344, 342 (M^+, 90%), 91 (C_7H_7, 100).

5-Benzyloxy-3-bromo-1,4-dimethoxynaphthalene 18

The naphthoquinone **16** (2.7 g, 7.87 mmol) was dissolved in dichloromethane–diethyl ether (1 : 3) (200 mL) and shaken with a freshly prepared solution of sodium dithionite (12 g, 55 mmol) in water (120 mL) for 10 min. The organic layer was separated, washed with brine (80 mL), and dried (magnesium sulfate). The solvent was removed under reduced pressure to give the crude hydroquinone as a pale brown oil. This was dissolved in dry acetone (45 mL) and transferred by double-ended needle to a reaction vessel containing a stirred suspension of potassium carbonate (13.0 g, 94 mmol) in dry acetone (130 mL). Dimethyl sulfate (5.2 mL, 55 mmol) was added in one portion and the solution was stirred and heated at reflux for 48 h. The mixture was then cooled, filtered through Celite, and the solvent was removed at reduced pressure. The resultant red oil was redissolved in diethyl ether (100 mL) and stirred with triethylamine (8.78 mL, 63 mmol). After 20 min the solution was washed successively with hydrochloric acid (1 M; 2 × 50 mL), water (50 mL) and brine (50 mL). The organic extract was then dried (sodium sulfate), and concentrated *in vacuo* to give an oily residue, which was purified by flash chromatography using hexane–ethyl acetate (6 : 1) as eluent to afford *5-benzyloxy-3-bromo-1,4-dimethoxynaphthalene* **18** (2.16 g, 76%) as a brown solid, which was recrystallised from hexane–ethyl acetate to give tan needles, mp 93.5–94.5 °C [Found (FAB): M^+, 372.0363. $C_{19}H_{17}{}^{79}BrO_3$ requires *M*, 372.0361); ν_{max}/cm^{-1} 1577, 1508 (C-O); δ_H (400 MHz; $CDCl_3$) ‡ 3.71, 3.95 (each 3H, s, 2 × OCH_3), 5.19 (2H, s, CH_2Ph), 6.95 (1H, s, 2-H), 7.03 (1H, d, $J_{6,7}$ 7.7, 6-H), 7.30–7.46 (4H, m, 7-H, *m*-Ph, *p*-Ph), 7.58 (2H, d, J_o 7.8, *o*-Ph), 7.85 (1H, dd, $J_{8,7}$ 8.4 and $J_{8,6}$ 0.8, 8-H); δ_C (100 MHz; $CDCl_3$) ‡ 56.6, 62.5 (CH_3, 2 × OCH_3), 72.4 (CH_2, CH_2Ph), 109.7 (CH, C-2), 110.1 (CH, C-6), 115.0 (quat., C-3), 116.1 (CH, C-7), 122.3 (quat., C-4a), 126.7 (CH, C-8), 128.4–129.2 (CH, Ph), 128.9 (quat., C-8a), 137.6 (quat., *ipso*-Ph), 147.5 (quat., C-5), 152.5, 155.2 (quat., C-1, C-4); *m*/*z* (EI) 374, 372 (M^+, 4%), 283, 281 (M − C_7H_7, 6), 202 (M − C_7H_7 − Br, 11), 174 (10), 91 (C_7H_7, 67), 83 (17), 72 (55), 59 (100).

5-Benzyloxy-2-bromo-1,4-dimethoxynaphthalene 19

Using the above conditions, the 2-bromonaphthoquinone **17** (1.35 g, 3.94 mmol) was reduced to the hydroquinone and then methylated. Purification by flash chromatography using hexane–ethyl acetate (6 : 1) as eluent afforded *5-benzyloxy-2-bromo-1,4-dimethoxynaphthalene* **19** (1.12 g, 79%) as a tan solid, which was recrystallised from hexane–ethyl acetate to give colourless needles, mp 90.4–90.9 °C [Found (EI): M^+, 374.0330, 372.0368. $C_{19}H_{17}BrO_3$ requires *M*, 374.0341, 372.0361]; ν_{max}/cm^{-1} 1578 (C-O); δ_H (400 MHz; $CDCl_3$) ‡ 3.91, 3.93 (each 3H, s, 2 × OCH_3), 5.20 (2H, s, CH_2Ph), 6.91 (1H, s, 3-H), 6.97 (1H, d, $J_{6,7}$ 7.7, 6-H), 7.33 (1H, t, J_o 7.4, *p*-Ph), 7.40 (2H, t, J_o 7.4,

‡ Juglone numbering scheme (see Scheme 2).

m-Ph), 7.45 (1H, dd, $J_{6,7}$ 7.7 and $J_{7,8}$ 8.4, 7-H), 7.57 (2H, br d, J_o 7.4, *o*-Ph), 7.71 (1H, br d, $J_{8,7}$ 8.4, 8-H); δ_C (400 MHz; $CDCl_3$)‡ 55.6, 61.2 (CH_3, 2 × OCH_3), 71.4 (CH_2, *C*H_2Ph), 109.2 (CH, C-3), 109.7 (CH, C-6), 115.1 (CH, C-8), 118.1 (quat., C-4a), 126.9 (CH, *o*-Ph), 127.5, 127.6 (CH, *p*-Ph, C-7), 128.4 (CH, *m*-Ph), 131.8 (quat., C-8a), 137.3 (quat., *ipso*-Ph), 146.6 (quat., C-1), 154.0, 156.5 (quat., C-4, C-5); *m*/*z* (EI) 374, 372 (M^+, 27%), 283, 281 (M − C_7H_7, 10), 174 (15), 91 (C_7H_7, 100).

3-Bromo-5-hydroxy-1,4-dimethoxynaphthalene 8

A solution of benzyl ether **18** (1.00 g, 2.68 mmol) in ethyl acetate (15 mL) was stirred under an atmosphere of hydrogen gas over palladium on charcoal (10%; 140 mg, 50 mg $mmol^{-1}$). After 8 h the reaction was complete and the mixture was filtered through Celite. The solvent was removed at reduced pressure and the resultant green oil was purified by flash chromatography using hexane–ethyl acetate (4 : 1) as eluent to afford *3-bromo-5-hydroxy-1,4-dimethoxynaphthalene* **8** (745 mg, 98%) as a pale green solid, which was recrystallised from ethanol to give colourless needles, mp 75.5–76.5 °C (Found: C, 51.42; H, 3.71. $C_{12}H_{11}BrO_3$ requires C, 51.07; H, 3.93%); ν_{max}/cm^{-1} 3362 br (OH), 1595, 1583 (C=C), 1381, 1335 (C-O); δ_H (400 MHz; $CDCl_3$)‡ 3.95, 4.01 (each 3H, s, 2 × OCH_3), 6.84 (1H, s, 2-H), 6.99 (1H, dd, $J_{6,7}$ 7.7 and $J_{6,8}$ 1.1, 6-H), 7.39 (1H, dd, $J_{7,6}$ 7.7 and $J_{7,8}$ 8.3, 7-H), 7.70 (1H, dd, $J_{8,7}$ 8.3 and $J_{8,6}$ 1.1, 8-H), 9.39 (1H, s, OH); δ_C (100 MHz; $CDCl_3$)‡ 56.6, 63.2 (CH_3, 2 × OCH_3), 108.9 (CH, C-2), 111.1 (quat., C-3), 113.1, 114.4 (CH, C-6, C-7), 118.7 (quat., C-4a), 127.5 (quat., C-8a), 128.1 (CH, C-8), 146.8 (quat., C-5), 153.5, 153.6 (quat., C-1, C-4); *m*/*z* (EI) 284, 282 (M^+, 70%), 269, 267 (M − CH_3, 100), 173 (M − CH_3Br, 30).

2-Bromo-5-hydroxy-1,4-dimethoxynaphthalene 12

A solution of benzyl ether **19** (500 mg, 1.34 mmol) in ethyl acetate (8 mL) was stirred over palladium on charcoal (10%; 67 mg, 50 mg $mmol^{-1}$) under an atmosphere of hydrogen gas. After 8 h the reaction was complete and the mixture was filtered through Celite. The solvent was removed at reduced pressure and the resultant green oil was purified by flash chromatography using hexane–ethyl acetate (4 : 1) as eluent to afford *2-bromo-5-hydroxy-1,4-dimethoxynaphthalene* **12** (356 mg, 94%) as a pale green solid, which was recrystallised from ethanol to give colourless needles, mp 140.5–141.5 °C [Found (EI): M^+, 283.9874, 281.9884. $C_{12}H_{11}BrO_3$ requires *M*, 283.9871, 281.9892]; ν_{max}/cm^{-1} 3362br (OH); δ_H (200 MHz; $CDCl_3$)‡ 3.92, 4.05 (each 3H, s, 2 × OCH_3), 6.86 (1H, s, 3-H), 6.93 (1H, dd, $J_{6,7}$ 7.7 and $J_{6,8}$ 1.1, 6-H), 7.43 (1H, dd, $J_{7,8}$ 8.3 and $J_{7,6}$ 7.7, 7-H), 7.57 (1H, dd, $J_{8,7}$ 8.3 and $J_{8,6}$ 1.1, 8-H), 9.19 (1H, s, OH); δ_C (100 MHz; $CDCl_3$)‡ 56.5, 61.1 (CH_3, 2 × OCH_3), 107.7 (CH, C-3), 111.5 (CH, C-6 and quat., C-2), 113.1 (CH, C-8), 114.9 (quat., C-4a), 128.7 (CH, C-7), 131.1 (quat., C-8a), 147.7 (quat., C-1), 152.6, 154.9 (quat., C-4, C-5); *m*/*z* (EI) 284, 282 (M^+, 70%), 269 (100), 267 (100), 173 (30).

5-Benzyloxy-3-(1-hydroxyethyl)-1,4-dimethoxynaphthalene 20

A solution of 5-benzyloxy-3-bromo-1,4-dimethoxynaphthalene **18** (300 mg, 0.804 mmol) in tetrahydrofuran (10 mL) was stirred at −78 °C under an atmosphere of nitrogen. *n*-Butyllithium (1.36 M solution in hexane; 800 μL, 1.09 mmol) was added, followed immediately by an excess of acetaldehyde (>32 μL) [any delay before the addition of acetaldehyde resulted in the formation of considerable amounts of the protonated by-product, 5-benzyloxy-1,4-dimethoxynaphthalene]. The solution was allowed to warm to room temperature over a period of 1 h, then was quenched with saturated aq. ammonium chloride (5 mL) and extracted with dichloromethane (3 × 20 mL). The combined organic fractions were washed with water (30 mL) and dried (sodium sulfate). The solvent was removed at reduced pressure and the residue was purified by flash chromatography using hexane–ethyl acetate (4 : 1 to 2 : 1) as eluent to afford *5-benzyloxy-3-(1-hydroxyethyl)-1,4-dimethoxynaphthalene* **20** (266 mg, 98%) as a colourless oil which slowly turned yellow on storage [Found (FAB): M^+, 338.1526. $C_{21}H_{22}O_4$ requires *M*, 338.1518]; ν_{max}/cm^{-1} 3405br (OH), 2968, 2929 (C-H), 1600, 1579, 1510 (C=C), 1361, 1262, 1067 (C-O); δ_H (200 MHz; $CDCl_3$)‡ 1.57 (3H, d, J_{vic} 6.4, CH_3), 2.30 (1H, br s, OH), 3.68, 3.98 (each 3H, s, 2 × OCH_3), 5.20 (2H, s, C*H*$_2$Ph), 5.50 (1H, q, J_{vic} 7.1, C*H*OH), 6.94 (1H, s, 2-H), 6.99 (1H, dd, $J_{6,7}$ 7.7 and $J_{6,8}$ 0.9, 6-H), 7.30–7.46 (4H, m, *m*-Ph, *p*-Ph, 7-H), 7.56 (2H, dd, J_o 7.6 and J_m 1.5, *o*-Ph), 7.88 (1H, dd, $J_{8,7}$ 8.4 and $J_{8,6}$ 0.9, 8-H); δ_C (50 MHz; $CDCl_3$)‡ 24.4 (CH_3, CH_3), 55.7 (CH_3, OCH_3), 63.3 (CH, *C*HOH), 64.6 (CH_3, OCH_3), 71.5 (CH_2, *C*H_2Ph), 102.0 (CH, C-2), 109.2 (CH, C-6), 115.3 (CH, C-8), 120.7 (quat., C-4a), 125.5 (CH, C-7), 127.6 (CH, *o*-Ph), 127.8 (CH, *p*-Ph), 128.4 (quat., C-8a), 128.5 (CH, *m*-Ph), 134.3 (quat., C-3), 137.1 (quat., *ipso*-Ph), 146.0 (quat., C-4), 151.9, 155.0 (quat., C-1, C-5); *m*/*z* 338 (M^+, 100%), 217 (M − C_7H_7 − Me − Me, 65), 91 (C_7H_7, 100).

5-Benzyloxy-2-(1-hydroxyethyl)-1,4-dimethoxynaphthalene 21

Using the conditions described above for **18**, 5-benzyloxy-2-bromo-1,4-dimethoxynaphthalene **19** (300 mg, 0.804 mmol) afforded *5-benzyloxy-2-(1-hydroxyethyl)-1,4-dimethoxynaphthalene* **21** (287 mg, 97%) as a tan oil [Found (EI): M^+, 338.1520. $C_{21}H_{22}O_4$ requires *M*, 338.1518]; ν_{max}/cm^{-1} 3410br (OH), 1583 (C-O), 1511, 1454, 1385; δ_H (400 MHz; $CDCl_3$)‡ 1.55 (3H, d, J_{vic} 6.5, CH_3), 2.45 (1H, br s, OH), 3.86, 3.92 (each 3H, s, 2 × OCH_3), 5.18 (2H, s, C*H*$_2$Ph), 2.41 (1H, q, J_{vic} 6.5, C*H*OH), 6.92 (1H, s, 3-H), 6.92 (1H, br d, $J_{6,7}$ 7.7, 6-H), 7.30–7.45 (4H, m, *m*-Ph, *p*-Ph, 7-H), 7.58 (2H, br d, J_o 7.5, *o*-Ph), 7.65 (1H, dd, $J_{8,7}$ 8.5 and $J_{8,6}$ 0.9, 8-H); δ_C (100 MHz; $CDCl_3$)‡ 24.2 (CH_3, CH_3), 56.5, 62.4 (CH_3, 2 × OCH_3), 64.7 (CH, *C*HOH), 71.5 (CH_2, *C*H_2Ph), 103.4 (CH, C-3), 108.9 (CH, C-6), 115.2 (CH, C-8), 118.4 (quat., C-4a), 126.7 (CH, C-7), 126.9 (CH, *o*-Ph), 127.5 (CH, *p*-Ph), 128.3 (CH, *m*-Ph), 131.2 (quat., C-8a), 133.8 (quat., C-2), 137.5 (quat., *ipso*-Ph), 145.5 (quat., C-1), 154.0, 156.4 (quat., C-4, C-5); *m*/*z* 338 (M^+, 100%), 217 (65), 91 (C_7H_7, 100), 43 (12).

3-Acetyl-5-benzyloxy-1,4-dimethoxynaphthalene 22

Tetrapropylammonium perruthenate (26 mg, 0.074 mmol) was added to a stirred solution of benzylic alcohol **20** (290 mg, 0.858 mmol), *N*-methylmorpholine *N*-oxide (260 mg, 2.22 mmol) and powdered molecular sieves (4 Å, 30 mg) in dry dichloromethane (3 mL). When the reaction was complete (2–3 h) the mixture was filtered through a pad of silica using dichloromethane as eluent. The mixture was evaporated and the residue was purified by flash chromatography using hexane–ethyl acetate (4 : 1) as eluent to afford *3-acetyl-5-benzyloxy-1,4-dimethoxynaphthalene* **22** (230 mg, 80%) as a pale yellow oil [Found (EI): M^+, 336.1361. $C_{21}H_{20}O_4$ requires *M*, 336.1362]; ν_{max}/cm^{-1} 2933, 2842 (C-H), 1685 (C=O, ketone), 1615, 1573, 1508, 1410 (C=C), 1366, 1265, 1224, 1065 (C-O); δ_H (200 MHz; $CDCl_3$)‡ 2.78 (3H, s, $COCH_3$), 3.71, 3.99 (each 3H, s, 2 × OCH_3), 5.25 (2H, s, C*H*$_2$Ph), 7.06 (1H, dd, $J_{6,7}$ 7.8 and $J_{6,8}$ 0.9, 6-H), 7.07 (1H, s, 2-H), 7.36–7.60 (6H, m, Ph, 7-H), 7.91 (1H, dd, $J_{8,7}$ 8.3 and $J_{8,6}$ 0.9, 8-H); δ_C (50 MHz; $CDCl_3$)‡ 31.4 (CH_3, *C*O*C*H$_3$), 55.7, 64.1 (CH_3, 2 × OCH_3), 71.4 (CH_2, *C*H_2Ph), 103.2 (CH, C-2), 109.3 (CH, C-6), 115.2 (CH, C-8), 120.6 (quat., C-4a), 127.6 (CH, *o*-Ph, *p*-Ph), 128.0 (CH, C-7), 128.5 (CH, *m*-Ph), 129.1 (quat., C-3), 131.2 (quat., C-8a), 136.7 (quat., *ipso*-Ph), 151.3, 152.2, 156.1 (quat., C-1, C-4, C-5), 201.3 (quat., *C*OCH$_3$); *m*/*z* (EI) 336 (M^+, 65%), 245 (M − C_7H_7, 38), 91 (C_7H_7, 100), 43 ($COCH_3$, 18).

2-Acetyl-5-benzyloxy-1,4-dimethoxynaphthalene 23

Using the conditions described above for **20**, benzylic alcohol **21** (290 mg, 0.858 mmol) was oxidised to afford *2-acetyl-5-*

benzyloxy-1,4-dimethoxynaphthalene **23** (224 mg, 78%) as a yellow solid, which was recrystallised from ethanol to give colourless needles, mp 109–110 °C [Found (EI): M^+, 336.1363. $C_{21}H_{20}O_4$ requires *M*, 336.1362]; ν_{max}/cm^{-1} 2934 (C-H), 1668 (C=O, ketone), 1593 (C=C), 1375 (C-O); δ_H (400 MHz; $CDCl_3$) ‡ 2.79 (3H, s, $COCH_3$), 3.92, 3.97 (each 3H, s, 2 × OCH_3), 5.21 (2H, s, CH_2Ph), 7.07 (1H, br d, $J_{6,7}$ 7.7, 6-H), 7.10 (1H, s, 3-H), 7.34 (1H, t, J_o 7.4, *p*-Ph), 7.42 (2H, t, J_o 7.4, *m*-Ph), 7.47 (1H, dd, $J_{7,8}$ 8.4 and $J_{7,6}$ 7.7, 7-H), 7.59 (2H, br d, J_o 7.4, *o*-Ph), 7.82 (1H, dd, $J_{8,7}$ 8.4 and $J_{8,6}$ 0.7, 8-H); δ_C (100 MHz; $CDCl_3$) ‡ 30.9 (CH_3, $COCH_3$), 56.3, 63.6 (CH_3, 2 × OCH_3), 71.6 (CH_2, CH_2Ph), 103.9 (CH, C-3), 111.3 (CH, C-6), 116.4 (CH, C-8), 121.2 (quat., C-4a), 126.9 (CH, *o*-Ph), 126.9 (quat., C-2), 127.3 (CH, C-7), 127.6 (CH, *p*-Ph), 128.4 (CH, *m*-Ph), 131.8 (CH, C-8a), 137.2 (quat., *ipso*-Ph), 151.2, 153.5, 156.4 (quat., C-1, C-4, C-5), 199.9 (quat., $COCH_3$); *m*/*z* (EI) 336 (M^+, 59%), 245 (M − C_7H_7, 35), 91 (C_7H_7, 100), 43 ($COCH_3$, 12).

3-Acetyl-5-hydroxy-1,4-dimethoxynaphthalene 7

A solution of benzyl ether **22** (223 mg, 0.664 mmol) in ethyl acetate (5 mL) was stirred under an atmosphere of hydrogen over palladium on charcoal (10%; 33 mg, 50 mg $mmol^{-1}$). After 8 h the reaction was incomplete, therefore the mixture was filtered through Celite and the solvent was removed *in vacuo*. The residue was redissolved in ethyl acetate and the hydrogenation procedure repeated with the reaction going to completion almost immediately. The mixture was filtered through Celite and the solvent was evaporated off at reduced pressure. The oily green residue was purified by flash chromatography using hexane–ethyl acetate (4 : 1) as eluent to afford *ketone* **7** (86 mg, 53%) as a pale yellow oil [Found (FAB): M^+, 246.0894. $C_{14}H_{14}O_4$ requires *M*, 246.0892]; ν_{max}/cm^{-1} 3357br (OH), 2939, 2843 (C-H), 1672 (C=O), 1627, 1598, 1512 (C=C), 1367, 1240 (C-O); δ_H (200 MHz; $CDCl_3$) ‡ 2.76 (3H, s, $COCH_3$), 3.94, 4.00 (3H, s, 2 × OCH_3), 6.95 (1H, s, 2-H), 7.00 (1H, dd, $J_{6,7}$ 7.8 and $J_{6,8}$ 0.9, 6-H), 7.47 (1H, dd, $J_{7,6}$ 7.8 and $J_{7,8}$ 8.3, 7-H), 7.75 (1H, dd, $J_{8,7}$ 8.3 and $J_{8,6}$ 0.9, 8-H), 9.49 (1H, s, OH); δ_C (50 MHz; $CDCl_3$) ‡ 30.3 (CH_3, $COCH_3$), 55.7, 65.5 (CH_3, 2 × OCH_3), 102.4 (CH, C-2), 112.4, 113.5 (CH, C-6, C-8), 117.1 (quat., C-4a), 126.6 (quat., C-3), 129.3 (CH, C-7), 130.2 (quat., C-8a), 151.3, 152.2, 154.7 (quat., C-1, C-4, C-5), 199.4 (quat., $COCH_3$); *m*/*z* (EI) 246 (M^+, 70%), 231 (M − CH_3, 100), 203 (M − $COCH_3$, 45), 175 (25), 145 (20), 115 (30), 89 (18), 43 ($COCH_3$, 27).

5-Hydroxy-3-(1-hydroxyethyl)-1,4-dimethoxynaphthalene (43 mg, 26%), a colourless oil, although not characterised, was identified on the basis of its ^1H NMR spectrum; δ_H (200 MHz; $CDCl_3$) ‡ 1.54 (3H, d, J_{vic} 6.4, CH_3), 2.27 (1H, br s, CHO*H*), 3.86, 4.00 (3H, s, 2 × OCH_3), 5.43 (1H, q, J_{vic} 6.4, C*H*OH), 6.82 (1H, s, 2-H), 6.88 (1H, dd, $J_{6,7}$ 7.5 and $J_{6,8}$ 1.2, 6-H), 7.38 (1H, dd, $J_{7,8}$ 8.3 and $J_{7,6}$ 7.5, 7-H), 7.49 (1H, dd, $J_{8,7}$ 8.3 and $J_{8,6}$ 1.2, 8-H), 9.35 (1H, s, OH).

A solution of this diol (43 mg, 0.173 mmol) in dry dichloromethane (1 mL) was treated with tetrapropylammonium perruthenate (3 mg, 0.009 mmol), *N*-methylmorpholine *N*-oxide (30 mg, 0.260 mmol) and molecular sieves (4 Å, 10 mg) and stirred for 2 h. The mixture was filtered through silica and the solvent was removed at reduced pressure. Purification by flash chromatography using hexane–ethyl acetate (4 : 1) as eluent afforded ketone **7** (35 mg, 83%).

2-Acetyl-5-hydroxy-1,4-dimethoxynaphthalene 11

A solution of benzyl ether **23** (205 mg, 0.610 mmol) was debenzylated using the conditions described above for **22** to afford *ketone* **11** (87 mg, 58%), which was recrystallised from hexane–ethyl acetate to give colourless needles, mp 96.5–97.5 °C [Found (FAB): M^+, 246.0894. $C_{14}H_{14}O_4$ requires *M*, 246.0892]; ν_{max}/cm^{-1} 3362br (OH), 1660 (C=O, ketone), 1611 (C=C), 1375, 1214 (C-O); δ_H (400 MHz; $CDCl_3$) ‡ 2.79 (3H, s, $COCH_3$), 3.93, 4.01 (each 3H, s, 2 × OCH_3), 7.01 (1H, br d, $J_{6,7}$ 7.7, 6-H), 7.06 (1H, s, 3-H), 7.47 (1H, dd, $J_{7,8}$ 8.4 and $J_{7,6}$ 7.7, 7-H), 7.67 (1H, dd, $J_{8,7}$ 8.4 and $J_{8,6}$ 0.6, 8-H), 9.37 (1H, s, OH); δ_C (100 MHz; $CDCl_3$) ‡ 30.9 (CH_3, $COCH_3$), 56.4, 63.6 (CH_3, 2 × OCH_3), 102.0 (CH, C-3), 113.6, 114.6 (CH, C-6, C-8), 117.8 (quat., C-4a), 126.9 (quat., C-2), 128.6 (CH, C-7), 131.1 (quat., C-8a), 152.4, 152.8, 154.9 (quat., C-1, C-4, C-5), 199.3 (quat., $COCH_3$); *m*/*z* (EI) 246 (M^+, 70%), 231 (M − CH_3, 100), 203 (M − $COCH_3$, 45), 175 (25), 145 (20), 115 (30), 89 (18), 43 ($COCH_3$, 27).

5-Hydroxy-2-(1-hydroxyethyl)-1,4-dimethoxynaphthalene (32 mg, 21%), a colourless oil, was identified on the basis of its ^1H NMR spectrum; δ_H (200 MHz; $CDCl_3$) 1.52 (3H, d, J_{vic} 6.5, Me), 2.68 (1H, br s, CHO*H*), 3.83, 3.93 (3H, s, 2 × OCH_3), 5.41 (1H, q, J_{vic} 6.5, C*H*OH), 6.77 (1H, s, 3-H), 6.86 (1H, dd, $J_{6,7}$ 7.4 and $J_{6,8}$ 1.2, 6-H), 7.36 (1H, dd, $J_{7,8}$ 8.3 and $J_{7,6}$ 7.4, 7-H), 7.45 (1H, dd, $J_{8,7}$ 8.3 and $J_{8,6}$ 1.2, 8-H), 9.32 (1H, s, OH).

This diol (32 mg, 0.129 mmol) was oxidized as described above to give ketone **11** (28 mg, 89%).

5-Benzyloxy-1,4-naphthoquinone 24

Silver(I) oxide (14 g, 62 mmol) was added to a stirred solution of juglone **13** (2.70 g, 15.5 mmol) and benzyl bromide (5.5 mL, 46.6 mmol) in chloroform (50 mL). After 2 h the solution was filtered through a Celite pad to remove silver salts and the solvent was removed at reduced pressure. The oily residue was purified by flash chromatography using hexane–ethyl acetate (18 : 1 to 9 : 1) as eluent to afford 5-benzyloxy-1,4-naphthoquinone **24** (3.28 g, 80%) as fine orange needles, mp 111–111.5 °C (lit.,[17] 113 °C); ν_{max}/cm^{-1} 1659 (C=O, quin.); δ_H (400 MHz; $CDCl_3$) ‡ 5.30 (2H, s, CH_2Ph), 6.89 (2H, s, 2-H and 3-H), 7.33–7.37 (2H, m, 6-H, *p*-Ph), 7.42 (2H, t, J_o 7.3, *m*-Ph), 7.58 (2H, d, J_o 7.3, *o*-Ph), 7.65 (1H, dd, $J_{6,7}$ 8.0 and $J_{7,8}$ 7.6, 7-H), 7.74 (1H, dd, $J_{8,7}$ 7.6 and $J_{8,6}$ 0.9, 8-H); δ_C (100 MHz; $CDCl_3$) ‡ 70.9 (CH_2, CH_2Ph), 119.5, 119.6 (CH, C-7, C-8), 126.6 (CH, *o*-Ph), 128.0 (CH, *p*-Ph), 128.7 (CH, *m*-Ph), 130.2, 134.1 (quat., C-8a, C-4a), 134.8, 136.2, 140.9 (CH, C-6, C-2, C-3), 136.0 (quat., *ipso*-Ph), 158.5 (quat., C-5), 184.1, 185.2 (quat., C-1, C-4); *m*/*z* (EI) 264 (M^+, 25%), 91 (C_7H_7, 100).

5-Benzyloxy-4-hydroxy-1-methoxynaphthalene 25

The naphthoquinone **24** (1.01 g, 3.78 mmol) was dissolved in dichloromethane–diethyl ether (1 : 3) (60 mL) and shaken with a freshly prepared solution of sodium dithionite (4.6 g, 26.5 mmol) in water (30 mL) for 10 min. The organic layer was washed with water (30 mL), dried (magnesium sulfate), and the solvent was removed under reduced pressure to give the crude hydroquinone as a brown foam. This was dissolved in dry acetone (50 mL) and transferred by double-ended needle to a reaction vessel containing a slurry of potassium carbonate (1.57 g, 11.3 mmol) and dry acetone (20 mL). Dimethyl sulfate (1.43 mL, 15.0 mmol) was added and the solution was stirred and then heated at reflux until the reaction was complete (2–3 h). The mixture was then cooled, filtered through Celite, and the solvent was removed at reduced pressure. The resultant red oil was dissolved in diethyl ether (100 mL) and stirred with triethylamine (2.3 mL, 16.6 mmol) for 20 min. The ethereal solution was washed successively with hydrochloric acid (1 M; 2 × 50 mL), water (50 mL), and brine (50 mL), then dried (sodium sulfate), and concentrated *in vacuo*. The oily residue was purified by flash chromatography using hexane–ethyl acetate (4 : 1) as eluent to afford 5-benzyloxy-4-hydroxy-1-methoxynaphthalene **25** (761 mg, 75%) as a brown solid, which was recrystallised from ethanol to give tan needles, mp 108–108.5 °C (lit.,[17] 108 °C); ν_{max}/cm^{-1} 3407br (OH); δ_H (200 MHz; $CDCl_3$) ‡ 3.91 (3H, s, OCH_3), 5.23 (2H, s, CH_2Ph), 6.75 (2H, s, 2-H and 3-H), 6.90 (1H, d, $J_{7,6}$ 7.9, 6-H), 7.31 (1H, dd, $J_{7,8}$ 8.1 and $J_{6,7}$ 7.9, 7-H), 7.34–7.50 (5H, m, Ph), 7.86 (1H, dd, $J_{7,8}$ 8.1 and $J_{8,6}$ 0.8, 8-H), 8.98 (1H, s, OH); δ_C (50 MHz; $CDCl_3$) ‡ 56.0 (CH_3, OCH_3), 71.7 (CH_2, CH_2Ph), 106.3 (CH, C-2 and C-3), 109.1, 116.2, 125.1 (CH, C-6, C-7, C-8), 115.7 (quat., C-4a),

126.0 (quat., C-8a), 128.0 (CH, *o*-Ph), 128.8 (CH, *p*-Ph), 129.0 (CH, *m*-Ph), 135.3 (quat., *ipso*-Ph), 147.9 (quat., C-1), 148.1 (quat., C-5), 155.1 (quat., C-4); *m*/*z* (EI) 280 (M^+, 20%), 189 ($M - C_7H_7$, 100), 91 (C_7H_7, 40).

5-Benzyloxy-3-bromo-4-hydroxy-1-methoxynaphthalene 26

A solution of bromine (190 mg, 1.18 mmol) in tetrachloromethane (1.0 mL) was added dropwise to a solution of the naphthol **25** (300 mg, 1.07 mmol) in tetrachloromethane (6.0 mL) at 0 °C. The reaction mixture was stirred for a further 2 min before being quenched with saturated aq. sodium thiosulfate (5 mL) and diluted with dichloromethane (50 mL). The organic layer was washed with water (50 mL) and the aqueous layer was extracted twice with dichloromethane (2 × 50 mL). The combined organic phases were dried (magnesium sulfate) and the solvent was removed under reduced pressure. The residue was purified by flash chromatography using hexane–ethyl acetate (6 : 1) as eluent to afford *5-benzyloxy-3-bromo-4-hydroxy-1-methoxynaphthalene* **26** (380 mg, 99%), which was recrystallised from hexane–ethyl acetate to give red needles, mp 132.5–133.5 °C [Found (FAB): M^+, 358.0207. $C_{18}H_{15}{}^{79}BrO_3$ requires *M*, 358.0205]; ν_{max}/cm^{-1} 3343br (OH); δ_H (400 MHz; $CDCl_3$)‡ 3.86 (3H, s, OCH_3), 5.17 (2H, s, CH_2Ph), 6.87 (1H, s, 2-H), 6.91 (1H, dd, $J_{7,6}$ 7.8 and $J_{6,8}$ 1.0, 6-H), 7.28 (1H, dd, $J_{6,7}$ 8.9 and $J_{8,7}$ 7.8, 7-H), 7.33–7.43 (5H, m, Ph), 7.77 (1H, dd, $J_{8,7}$ 8.9 and $J_{8,6}$ 1.0, 8-H), 9.58 (1H, s, OH); δ_C (100 MHz; $CDCl_3$)‡ 56.7 (CH_3, OCH_3), 72.6 (CH_2, CH_2Ph), 103.6 (quat., C-3), 107.9 (CH, C-2), 110.8, 117.0, 126.2 (CH, C-6, C-7, C-8), 116.4 (quat., C-4a), 128.0 (quat., C-8a), 128.9 (CH, *o*-Ph), 129.7 (CH, *p*-Ph), 129.7 (CH, *m*-Ph), 135.4 (quat., *ipso*-Ph), 145.0 (quat., C-1), 148.8 (quat., C-5), 155.0 (quat., C-4); *m*/*z* (EI) 360, 358 (M^+, 15%), 279 (M − Br, 20), 269, 267 ($M - C_7H_7$, 100), 91 (C_7H_7, 60).

5-Benzyloxy-3-bromo-1,4-dimethoxynaphthalene 18 (alternative preparation)

A slurry of oil-free sodium hydride (259 mg, 10.8 mmol) in dry dimethylformamide (2 mL) was added dropwise to a stirred solution of the bromonaphthol **26** (1.94 g, 5.40 mmol) in dimethylformamide (15 mL) at 0 °C. The mixture was stirred for 15 min at 0 °C, then iodomethane (3.36 mL, 54 mmol) was added and the reaction mixture was allowed to warm to room temperature overnight before being quenched with water (1 mL) and extracted with dichloromethane (3 × 50 mL). The combined organic extracts were washed with water (50 mL), dried (magnesium sulfate), and the solvent was removed under reduced pressure. The residue was purified by flash chromatography using hexane–ethyl acetate (4 : 1) as eluent to afford *5-benzyloxy-3-bromo-1,4-dimethoxynaphthalene* **18** (1.49 g, 74%), which was recrystallised from hexane–ethyl acetate to give tan needles, mp 93.5–94 °C. The spectroscopic data were identical to those reported above.

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-D-*arabino*-hexopyranoside 9

(i) Using 2-deoxyglucose.[18] 2-Deoxy-D-glucose (1.5 g, 9.14 mmol) was suspended in dry pyridine (25 mL) at 0 °C and freshly distilled acetic anhydride (20 mL) was added. The reaction mixture was kept at 0 °C for 4 days, at the end of which time the starting material had completely dissolved. The solution was diluted with water and then extracted with chloroform. The combined extracts were washed successively with sulfuric acid (0.01 M; 3 × 50 mL), dilute aq. sodium bicarbonate (50 mL) and water (50 mL). After drying (calcium chloride), the solvent was removed at reduced pressure and the residue was triturated with ethanol–diethyl ether (3 : 1). The resulting solid was recrystallised several times from ethanol to give 1,3,4,6-tetra-*O*-acetyl-2-deoxy-D-*arabino*-hexopyranoside **9** (2.21 g, 73%) (α : β, 10 : 1) as white needles, mp 92–93 °C; $[a]_D^{18}$ +10.9 (*c* 1.01, ethanol) {lit.,[18] mp 91 °C; $[a]_D^{20}$ +12.3 (*c* 0.325, ethanol)}; ν_{max}/cm^{-1} 1745 (C=O), 1376 (C-O); *α-anomer*: δ_H (200 MHz; $CDCl_3$) 1.87 (1H, ddd, J_{gem} 12.3, $J_{2ax,3}$ 11.3, $J_{2ax,1}$ 10.0, 2_{ax}-H), 2.04, 2.05, 2.09, 2.12 (each 3H, s, 4 × $COCH_3$), 2.36 (1H, ddd, J_{gem} 12.3, $J_{2eq,3}$ 4.7, $J_{2eq,1}$ 2.3, 2_{eq}-H), 3.75 (1H, ddd, $J_{5,4}$ 9.4, $J_{5,6B}$ 4.7 and $J_{5,6A}$ 2.3, 5-H), 4.09 (1H, dd, J_{gem} 12.4, $J_{6A,5}$ 2.3, 6-H_A), 4.32 (1H, dd, J_{gem} 12.4, $J_{6B,5}$ 4.7, 6-H_B), 4.97–5.14 (2H, m, 3-H, 4-H), 5.80 (1H, dd, $J_{1,2ax}$ 10.0 and $J_{1,2eq}$ 2.3, 1-H); δ_C (50 MHz; $CDCl_3$) 20.6, 20.7, 20.8, 20.9 (CH_3, 4 × $COCH_3$), 34.7 (CH_2, C-2), 61.9 (CH_2, C-6), 68.2, 70.1, 72.3 (CH, C-3, C-4, C-5), 91.0 (CH, C-1), 168.7, 169.7, 170.0, 170.6 (quat., 4 × $COCH_3$); *β-anomer*: δ_H (200 MHz; $CDCl_3$) 5.78 (1H, dd, $J_{1,2ax}$ 10.5 and $J_{1,2eq}$ 2.5, 1-H).

(ii) Using tri-*O*-acetyl-D-glucal.[19] Distilled glacial acetic acid (351 mL, 5.51 mol) was added to a stirred solution of tri-*O*-acetyl-D-glucal (1.002 g, 3.67 mmol) and triphenylphosphine hydrogen bromide[27] (63 mg, 0.184 mmol) in anhydrous dichloromethane (18 mL). The mixture was stirred for 2 days at room temperature, then the solvent was removed at reduced pressure. The resultant oil was purified by flash chromatography using hexane–ethyl acetate (4 : 1) as eluent to give 1,3,4,6-tetra-*O*-acetyl-2-deoxy-D-*arabino*-hexopyranoside **9** as a mixture of anomers (α : β, 9 : 1) (879 mg, 72%). The spectroscopic data were in agreement with those reported above.

3,4,6-Tri-*O*-benzyl-2-deoxy-D-*arabino*-hexopyranosyl acetate 10

Glacial acetic acid (0.432 g, 7.2 mmol) was added to a stirred solution of tri-*O*-benzyl-D-glucal[28] (2.0 g, 4.80 mmol) and triphenylphosphine hydrogen bromide (82 mg, 0.240 mmol) in dry dichloromethane (35 mL). The mixture was stirred overnight at room temperature. Removal of the solvent under reduced pressure and purification of the residue by flash chromatography using hexane–ethyl acetate (4 : 1) as eluent gave 3,4,6-tri-*O*-benzyl-2-deoxy-D-*arabino*-hexopyranosyl acetate **10** (α : β, 9 : 1) (1.97 g, 86%) as a colourless oil, $[a]_D^{20}$ +71.2 (*c* 0.876, $CHCl_3$); the spectroscopic data were in agreement with those reported in the literature;[19] *α-anomer*: δ_H (200 MHz; $CDCl_3$) 1.84 (1H, ddd, J_{gem} 13.6, $J_{2ax,3}$ 11.4, $J_{2ax,1}$ 3.4, 2_{ax}-H), 2.03 (3H, s, $COCH_3$), 2.28 (1H, ddd, J_{gem} 13.5, $J_{2eq,3}$ 4.9, $J_{2eq,1}$ 1.7, 2_{eq}-H), 3.53–4.02 (5H, m, 3-H, 4-H, 5-H, 6-H_A, 6-H_B), 4.47–4.71 (5H, m, 5 × C*H*Ph), 4.91 (1H, d, J_{gem} 10.7, C*H*Ph), 6.26 (1H, d, $J_{1,2}$ 1.7, 1-H), 7.16–7.34 (15H, m, Ph); δ_C (50 MHz; $CDCl_3$) 21.0 (CH_3, $COCH_3$), 34.1 (CH_2, C-2), 68.3 (CH_2, C-6), 71.7 (CH_2, CH_2Ph), 73.3 (CH, C-3), 73.4, 75.0 (CH_2, 2 × CH_2Ph), 76.7 (CH, C-5), 77.4 (CH, C-4), 92.0 (CH, C-1), 127.5–128.5 (CH, Ph), 138.0, 138.1, 138.2 (quat., 3 × *ipso*-Ph), 169.1 (quat., $COCH_3$).

β-Anomer: δ_H (200 MHz; $CDCl_3$) 1.77 (1H, m, 2_{ax}-H), 2.09 (3H, s, $COCH_3$), 2.36 (1H, m, 2_{eq}-H), 3.53–4.02 (5H, m, 3-H, 4-H, 5-H, 6-H_A, 6-H_B), 4.47–4.71 (5H, m, 5 × C*H*Ph), 4.87 (1H, d, J_{gem} 10.8, C*H*PH), 5.67 (1H, dd, $J_{1,2ax}$ 10.0 and $J_{1,2eq}$ 2.2, 1-H), 7.16–7.34 (15H, m, Ph-H); δ_C (50 MHz; $CDCl_3$) 21.1 (CH_3, $COCH_3$), 35.4 (CH_2, C-2), 68.5 (CH_2, C-6), 71.7, 73.5, 75.0 (CH_2, 3 × CH_2Ph), 75.8 (CH, C-3), 77.3 (CH, C-5), 78.9 (CH, C-4), 92.2 (CH, C-1), 127.5–128.5 (CH, Ph), 138.0, 138.1, 138.2 (quat., 3 × *ipso*-Ph), 169.1 (quat., $COCH_3$).

3-Bromo-5-hydroxy-1,4-dimethoxy-6-(3′,4′,6′-tri-*O*-acetyl-2′-deoxy-β-D-*arabino*-hexopyranosyl)naphthalene 29

Trimethylsilyl trifluoromethanesulfonate (51 μL, 0.266 mmol) and silver perchlorate (2 mg, 5 mol%) were added to a stirred solution of 3-bromo-5-hydroxy-1,4-dimethoxynaphthalene **8** (50 mg, 0.177 mmol) and tetra-*O*-acetyl-2-deoxy-D-glucoside **9** (100 mg, 210 mmol) in dry acetonitrile (5 mL) at 0 °C. The mixture was stirred for 1 h, then was quenched with aq. sodium bicarbonate (5 mL). The reaction mixture was extracted with dichloromethane (3 × 50 mL), washed with water (100 mL) and dried (magnesium sulfate). The solvent was removed at reduced

pressure and the oily residue was purified by flash chromatography using hexane–ethyl acetate (6 : 1) as eluent to give *the title compound* **29** (5 mg, 5%) as a colourless oil [Found (EI): M^+, 554.0785. $C_{24}H_{27}{}^{79}BrO_{10}$ requires *M*, 554.0788]; ν_{max}/cm^{-1} 3345 (OH), 1741 (C=O), 1631 (C=C), 1391 (C-O); δ_H (200 MHz; $CDCl_3$)‡ 1.78 (1H, ddd, J_{gem} 12.7, $J_{2'ax,1'}$ 11.3 and $J_{2'ax,3'}$ 11.3, $2'_{ax}$-H), 2.02, 2.07, 2.09 (each 3H, s, 3 × $COCH_3$), 2.52 (1H, ddd, J_{gem} 12.7, $J_{2'eq,3'}$ 4.8 and $J_{2'eq,1'}$ 2.0, $2'_{eq}$-H), 3.84 (1H, ddd, $J_{5',4'}$ 9.7, $J_{5',6'B}$ 4.8 and $J_{5',6'A}$ 2.3, 5′-H), 3.95, 3.99 (each 3H, s, 2 × OCH_3), 4.20 (1H, dd, J_{gem} 12.2 and $J_{6'A,5'}$ 2.3, 6′-H_A), 4.35 (1H, dd, J_{gem} 12.2 and $J_{6'B,5'}$ 4.8, 6′-H_B), 5.12 (1H, dd, $J_{1',2'ax}$ 11.3 and $J_{1',2'eq}$ 2.0, 1′-H), 5.14 (1H, dd, $J_{4',3'}$ 9.7 and $J_{4',5'}$ 9.7, 4′-H), 5.25 (1H, ddd, $J_{3',2'ax}$ 11.3, $J_{3',4'}$ 9.7, $J_{3',2'eq}$ 4.8, 3′-H), 6.83 (1H, s, 2-H), 7.57 (1H, d, $J_{8,7}$ 8.8, 8-H), 7.72 (1H, d, $J_{7,8}$ 8.8 Hz, 7-H), 9.70 (1H, s, OH); *m/z* (EI) 556, 554 (M^+, 38%), 43 (100).

2-Bromo-5-hydroxy-1,4-dimethoxy-6-(3′,4′,6′-tri-*O*-acetyl-2′-deoxy-β-D-*arabino*-hexopyranosyl)naphthalene 33

Under the same conditions as described above for the preparation of **29**, 2-bromo-5-hydroxy-1,4-dimethoxynaphthalene **12** (50 mg, 0.177 mmol) and tetra-*O*-acetyl-2-deoxy-D-glucoside **9** (100 mg, 210 mmol) reacted to afford *2-bromo-5-hydroxy-1,4-dimethoxy-6-(3′,4′,6′-tri-O-acetyl-2′-deoxy-β-D-arabino-hexopyranosyl)naphthalene* **33** (71 mg, 57%) as a colourless oil; $[\alpha]_D^{22}$ +17.49 (*c* 0.27, $CHCl_3$) [Found (EI): M^+, 556.0774 and 554.0777. $C_{24}H_{27}BrO_{10}$ requires *M*, 556.0767 and 554.0788]; ν_{max}/cm^{-1} 3346 (OH), 2938 (C-H), 1742 (C=O), 1631 (C=C), 1391 (C-O); δ_H (200 MHz; $CDCl_3$)‡ 1.26 (1H, ddd, J_{gem} 12.7, $J_{2'ax,1'}$ 11.3 and $J_{2'ax,3'}$ 11.3, $2'_{ax}$-H), 2.02, 2.08, 2.10 (each 3H, s, 3 × $COCH_3$), 2.52 (1H, ddd, J_{gem} 12.7, $J_{2'eq,3'}$ 4.8 and $J_{2'eq,1'}$ 2.0, $2'_{eq}$-H), 3.84 (1H, ddd, $J_{5',4'}$ 9.7, $J_{5',6'B}$ 4.8 and $J_{5',6'A}$ 2.3, 5′-H), 3.91, 4.04 (each 3H, s, 2 × OCH_3), 4.20 (1H, dd, J_{gem} 12.2 and $J_{6'A,5'}$ 2.3, 6′-H_A), 4.35 (1H, dd, J_{gem} 12.2 and $J_{6'B,5'}$ 4.8, 6′-H_B), 5.12 (1H, dd, $J_{1',2'ax}$ 11.3 and $J_{1',2'eq}$ 2.0, 1′-H), 5.14 (1H, dd, $J_{4',3'}$ 9.7 and $J_{4',5'}$ 9.7, 4′-H), 5.25 (1H, ddd, $J_{3',2'ax}$ 11.3, $J_{3',4'}$ 9.7, $J_{3',2'eq}$ 4.8, 3′-H), 6.86 (1H, s, 3-H), 7.58 (1H, d, $J_{8,7}$ 8.8, 8-H), 7.64 (1H, d, $J_{7,8}$, 7-H), 9.49 (1H, s, OH); δ_C (50 MHz; $CDCl_3$)‡ 20.8, 20.9, 21.0 (CH_3, 3 × $COCH_3$), 36.7 (CH_2, C-2′), 56.7, 61.2 (CH_3, 2 × OCH_3), 62.9 (CH_2, C-6′), 69.6 (CH, C-4′), 71.7 (CH, C-1′), 72.5 (CH, C-3′), 76.2 (CH, C-5′), 108.2 (CH, C-3), 113.4 (CH, C-7), 114.5 (quat., C-2), 122.5 (quat., C-4a), 125.9 (CH, C-8), 130.1 (quat., C-8a), 133.5 (quat., C-6), 147.8, 150.5, 152.7 (quat., C-1, C-4, C-5), 170.0, 170.4, 170.9 (quat., 3 × $COCH_3$); *m/z* (EI) 556, 554 (M^+, 42%), 321, 319 (48), 43 ($COCH_3$, 100).

(1′*R*,2′*R*,5′*R*,7′*S*,9′*S*)-6-(9′-Benzyloxy-2′-phenyl-3′,6′-dioxabicyclo[3.2.2]nonan-7′-yl)-3-bromo-5-hydroxy-1,4-dimethoxynaphthalene 36

Trimethylsilyl trifluoromethanesulfonate (51 μL, 0.266 mmol) and silver perchlorate (2 mg, 5 mol%) were added to a stirred solution of 3-bromo-5-hydroxy-1,4-dimethoxynaphthalene **8** (50 mg, 0.177 mmol) and tri-*O*-benzyl-2-deoxy-D-glucosyl acetate **10** (101 mg, 210 mmol) in dry acetonitrile (5 mL) at 0 °C. The mixture was stirred for 1 h, then was quenched with aq. sodium bicarbonate (5 mL). The reaction mixture was extracted with dichloromethane (3 × 50 mL), washed with water (100 mL) and dried (magnesium sulfate). The solvent was removed at reduced pressure and the oily residue was purified by flash chromatography using hexane–ethyl acetate (4 : 1) as eluent to give a mixture of the *rearranged compound* **36** and *β-C-glycoside* **30** (71 mg; 6 : 1). These were subjected to HPLC. Analytical HPLC established the optimal separation conditions (0.375% ^{i}PrOH–hexane; Partisil 5 column, 25 cm × 4.6 mm I.D.; flow rate 1.5 mL min^{-1}), but on a semi-preparative scale (0.375% ^{i}PrOH–hexane; Partisil 10 column, 50 cm × 9.4 mm I.D.; flow rate 4 mL min^{-1}) the unstable β-*C*-glycoside **30** decomposed. The more stable rearranged product **36** (59 mg, 48%) was recovered as a colourless oil; $[\alpha]_D^{22}$ −105 (*c* 0.24, $CHCl_3$) [Found (LSIMS): M^+, 590.1295. $C_{32}H_{31}{}^{79}BrO_6$ requires *M*, 590.1304]; ν_{max}/cm^{-1} 3329 (OH), 2934 (C-H), 1591 (C=C), 1508, 1453 (C-O); δ_H (400 MHz; $CDCl_3$)‡ 1.43 (1H, ddd, J_{gem} 14.4, $J_{8'A,9'}$ 4.8 and $J_{8'A,1'}$ 4.8, 8′-H_A), 1.98 (1H, ddd, J_{gem} 14.4, $J_{8'B,9'}$ 9.7 and $J_{8'B,1'}$ 2.2, 8′-H_B), 2.19 (1H, dd, $J_{1',8'A}$ 4.8 and $J_{1',8'B}$ 2.2, 1′-H), 3.85 (3H, s, 1-OCH_3), 3.94 (3H, s, 4-OCH_3), 4.08 (1H, d, J_{gem} 13.4, 4′-H_A), 4.16 (1H, dd, $J_{9',8'B}$ 9.7 and $J_{9',8'A}$ 4.8, 9′-H), 4.21 (1H, dd, J_{gem} 13.4 and $J_{4'B,5'}$ 5.5, 4′-H_B), 4.36 (1H, d, $J_{5',4'B}$ 5.5, 5′-H), 4.48 (1H, d, J_{gem} 11.9, C*H*Ph), 4.52 (1H, d, J_{gem} 11.9, C*H*PH), 5.06 (1H, s, 7′-H), 5.86 (1H, s, 2′-H), 6.70 (1H, s, 2-H), 7.14 (1H, t, J_o 7.2, *p*-Ph), 7.24 (2H, t, J_o 7.2, *m*-Ph), 7.29–7.35 (7H, m, *o*-Ph, CH_2*Ph*), 7.64 (1H, d, $J_{7,8}$ 8.7, 8-H), 8.04 (1H, d, $J_{7,8}$ 8.7, 7-H), 9.68 (1H, s, OH); δ_C (100 MHz; $CDCl_3$)‡ 22.4 (CH_2, C-8′), 45.5 (CH, C-1′), 55.9 (CH_3, 1-OCH_3), 62.6 (CH_3, 4-OCH_3), 70.2 (CH_2, *C*H_2Ph), 71.1 (CH_2, C-4′), 73.7 (CH, C-9′), 76.2 (CH, C-2′), 76.6 (CH, C-5′), 86.2 (CH, C-7′), 107.6 (CH, C-7), 110.3 (quat., C-3), 113.0 (CH, C-8), 117.4 (quat., C-8a), 125.5 (CH, Ph), 126.1 (CH, C-2), 126.4, 126.6 (quat., C-2, C-4a), 127.0–128.4 (CH, Ph), 138.6 (quat., *ipso*-Ph), 142.4 (quat., *ipso*-Ph), 146.0 (quat., C-5), 148.5, 152.8 (quat., C-1, C-4); *m/z* (EI) 592, 590 (M^+, 27%), 321 (11), 91 (C_7H_7, 100).

Although not able to be fully characterised, ^{1}H NMR shifts for β-*C*-glycoside **30** were identified from the spectrum of the mixture; δ_H (400 MHz; $CDCl_3$)‡ 2.50 (1H, ddd, J_{gem} 12.7, $J_{2'eq,3'}$ 4.8 and $J_{2'eq,1'}$ 1.8, $2_{eq}'$-H), 7.59 (1H, d, $J_{8,7}$ 8.0, 8-H), 6.74 (1H, s, 2-H), 7.66 (1H, d, $J_{7,8}$ 8.0, 7-H), 9.60 (1H, s, OH).

Triethylamine (0.50 mL, 3.59 mmol), acetic anhydride (0.25 mL, 2.65 mmol) and a catalytic quantity of 4-(dimethylamino)-pyridine were added to a solution of **36** (98 mg, 0.166 mmol) in dichloromethane (2 mL). The solution was stirred overnight, then the solvent was removed at reduced pressure. The residue was purified by flash chromatography using hexane–ethyl acetate (4 : 1) to give the *acetate derivative* (99 mg, 94%), which was recrystallised from hexane–ethyl acetate (1:1) to give white needles, mp 204–205 °C (from which a crystal structure was obtained[23]); $[\alpha]_D^{20}$ −192 (*c* 0.45, $CHCl_3$) [Found (LSIMS): M^+, 632.1422. $C_{34}H_{33}{}^{79}BrO_7$ requires *M*, 632.1410]; ν_{max}/cm^{-1} 2933 (C-H), 1769 (C=O, ester), 1587 (C=C), 1506, 1453, 1411 (C-O); δ_H (400 MHz; 360 K; C_7D_8) 1.63 (1H, ddd, J_{gem} 14.4, $J_{8'B,9'}$ 4.6 and $J_{8'B,1'}$ 4.6, 8′-H_B), 2.01 (1H, ddd, J_{gem} 14.4, $J_{8'A,9'}$ 9.7 and $J_{8'A,1'}$ 2.2, 8′-H_A), 2.14 (3H, s, $COCH_3$), 2.31 (1H, dd, $J_{1',8'B}$ 4.6 and $J_{1',8'A}$ 2.2, 1′-H), 3.37, 3.66 (each 3H, s, 2 × OCH_3), 3.91 (1H, d, J_{gem} 13.4, 4′-H_A), 3.98 (1H, dd, J_{gem} 13.4 and $J_{4'B,5'}$ 5.1, 4′-H_B), 4.09 (1H, dd, $J_{9',8'A}$ 9.7 and $J_{9',8'B}$ 4.6, 9′-H), 4.24 (1H, d, $J_{5',4'B}$ 5.1, 5′-H), 4.34 (1H, d, J_{gem} 12.2, C*H*PH), 4.37 (1H, d, J_{gem} 12.2, C*H*PH), 4.92 (1H, s, 7′-H), 5.81 (1H, s, 2′-H), 6.68 (1H, s, 2-H), 7.03–7.09 (2H, m, *p*-Ph), 7.15–7.20 (4H, m, *m*-Ph), 7.30 (2H, d, J_o 7.7, *o*-Ph), 7.44 (2H, d, J_o 7.7, *o*-Ph), 8.14 (1H, d, $J_{7,8}$ 8.9, 8-H), 8.45 (1H, d, $J_{7,8}$ 8.9, 7-H); *m/z* (CI) 634, 632 (M^+, 10%), 91 (C_7H_7, 100).

2-Bromo-5-hydroxy-1,4-dimethoxy-6-(3′,4′,6′-tri-*O*-benzyl-2′-deoxy-β-D-*arabino*-hexopyranosyl)naphthalene 34

Boron trifluoride–diethyl ether (43 μL, 0.350 mmol) was added dropwise to a stirred solution of naphthol **12** (50 mg, 0.177 mmol) and tri-*O*-benzyl-2-deoxy-D-glucosyl acetate **10** (100 mg, 210 mmol) in dry acetonitrile (5 mL) at 0 °C. The mixture was stirred for 20 min, then was quenched with water (5 mL). The reaction mixture was extracted with dichloromethane (3 × 50 mL), washed with water (100 mL) and dried (magnesium sulfate). The solvent was removed at reduced pressure and the oily residue was purified by flash chromatography using hexane–ethyl acetate (6 : 1) as eluent to give the *title compound* **34** (65 mg, 53%) as a colourless glass; $[\alpha]_D^{22}$ +29.3 (*c* 0.3, $CHCl_3$) [Found (FAB): M^+, 700.1855, 698.1872. $C_{39}H_{39}BrO_7$ requires *M*, 700.1859, 698.1879]; ν_{max}/cm^{-1} 3384 (OH), 3056 (C-H), 1643 (C=C), 1419 (C-O); δ_H (200 MHz; $CDCl_3$)‡ 1.63 (1H, ddd, J_{gem} 12.9, $J_{2'ax,1'}$ 11.6 and $J_{2'ax,3'}$ 11.6, $2_{ax}'$-H), 2.59 (1H, ddd, J_{gem} 12.9, $J_{2'eq,3'}$ 5.0 and $J_{2'eq,1'}$ 1.0, $2_{eq}'$-H), 3.66–4.02 (5H, m, 3′-H, 4′-H, 5′-H, 6′-H_A, 6′-H_B), 3.90, 3.98 (each 3H, s, 2 × OCH_3),

4.58–4.74 (5H, m, 5 × C*H*Ph), 4.97 (1H, d, J_{gem} 10.8, C*H*Ph), 4.98 (1H, dd, $J_{1',2'ax}$ 10.0 and $J_{1',2'eq}$ 1.0 Hz, 1′-H), 6.82 (1H, s, 3-H), 7.21–7.41 (15H, m, Ph), 7.59 (1H, d, $J_{8,7}$ 8.7, 8-H), 7.73 (1H, d, $J_{7,8}$ 8.7, 7-H), 9.47 (1H, s, OH); δ_C (50 MHz; $CDCl_3$)‡ 38.5 (CH_2, C-2′), 56.5, 61.1 (CH_3, 2 × OCH_3), 69.6 (CH_2, C-6′), 71.1 (CH_2, *C*H_2Ph), 71.6 (CH, C-1′), 73.4, 75.0 (CH_2, 2 × *C*H_2Ph), 78.4, 79.4, 81.3 (CH, C-3′, C-4′, C-5′), 108.0 (CH, C-7), 111.1 (quat., C-2), 113.3 (CH, C-8), 114.5 (quat., C-4a), 124.0 (quat., C-8a), 126.4 (CH, C-3), 127.4–128.3 (CH, Ph), 130.2 (quat., C-6), 138.5, 138.6, 138.6 (quat., 3 × *ipso*-Ph), 147.8, 150.1, 152.7 (quat., C-1, C-4, C-5); *m*/*z* (EI) 700, 698 (M^+, 12%), 592, 590 (20), 91 (C_7H_7, 100).

(1′*R*,2′*R*,5′*R*,7′*S*,9′*S*)-3-Acetyl-6-(9′-benzyloxy-2′-phenyl-3′,6′-dioxabicyclo[3.2.2]nonan-7′-yl)-5-hydroxy-1,4-dimethoxynaphthalene 35 and 3-acetyl-5-hydroxy-1,4-dimethoxy-6-(3′,4′,6′-tri-*O*-benzyl-2′-deoxy-β-D-*arabino*-hexopyranosyl)-naphthalene 28

Boron trifluoride–diethyl ether (40 μL, 0.325 mmol) was added dropwise to a stirred solution of tri-*O*-benzyl-2-deoxy-D-glucosyl acetate **10** (93 mg, 0.195 mmol) and naphthol **7** (40 mg, 0.163 mmol) in dry acetonitrile (3 mL) at 0 °C. The mixture was stirred for 1 h at 0 °C, then was quenched with water (2 mL). The crude reaction mixture was extracted with dichloromethane (3 × 25 mL), washed with water (50 mL) and dried (magnesium sulfate). The solvent was removed at reduced pressure and the oily residue was purified by flash chromatography using hexane–ethyl acetate (4 : 1) as eluent to give the starting naphthol **7** (24 mg, 60% recovery) as well as a (1 : 2) mixture of the *β-C-glycoside* **28** and the *rearranged product* **35** (29 mg). These products were separated by semipreparative HPLC (1.5% ^{i}PrOH–hexane; Partisil 10 column, 50 cm × 9.4 mm I.D.; flow rate 4 mL min^{-1}) to give *title compound* **35** (11 mg, 12%) as a yellow oil; $[\alpha]_D^{22}$ −147.5 (*c* 0.24, $CHCl_3$) [Found (EI): M^+, 554.2294. $C_{34}H_{34}O_7$ requires *M*, 554.2305]; ν_{max}/cm^{-1} 3328br (OH), 2956, 2917, 2851 (C-H), 1667 (C=O), 1602, 1514 (C=C), 1366 (s, C-O); δ_H (400 MHz; $CDCl_3$)‡ 1.52 (1H, ddd, J_{gem} 14.5, $J_{8'B,1'}$ 4.9 and $J_{8'B,9'}$ 4.8, 8′-H_B), 2.09 (1H, ddd, J_{gem} 14.5, $J_{8'A,9'}$ 9.7 and $J_{8'A,1'}$ 2.3, 8′-H_A), 2.29 (1H, dd, $J_{1',8'B}$ 4.9 and $J_{1',8'A}$ 2.3, 1′-H), 2.76 (3H, s, $COCH_3$), 3.96, 3.99 (each 3H, s, 2 × OCH_3), 4.17 (1H, d, J_{gem} 13.5, 4′-H_A), 4.25 (1H, dd, $J_{9',8'A}$ 9.7 and $J_{9',8'B}$ 4.8, 9′-H), 4.31 (1H, dd, J_{gem} 13.5 and $J_{4'B,5'}$ 5.3, 4′-H_B), 4.45 (1H, d, $J_{5',4'B}$ 5.3, 5′-H), 4.58 (1H, d, J_{gem} 11.9, C*H*Ph), 4.62 (1H, d, J_{gem} 11.9, C*H*Ph), 5.15 (1H, s, 7′-H), 5.98 (1H, s, 2′-H), 6.91 (1H, s, 2-H), 7.24 (1H, t, J_o 7.4, *p*-Ph), 7.33 (2H, t, J_o 7.4, *m*-Ph), 7.38–7.46 (7H, m, Ph), 7.78 (1H, d, $J_{7,8}$ 8.7, 8-H), 8.21 (1H, d, $J_{7,8}$ 8.7, 7-H), 9.88 (1H, s, OH); δ_C (100 MHz; $CDCl_3$)‡ 22.4 (CH_2, C-8′), 30.5 (CH_3, CO*C*H_3), 45.5 (CH, C-1′), 55.8, 65.6 (CH_3, 2 × OCH_3), 70.2 (CH_2, *C*H_2Ph), 71.2 (CH_2, C-4′), 73.7 (CH, C-9′), 76.2 (CH, C-2′), 76.6 (CH, C-5′), 86.2 (CH, C-7′), 101.9 (CH, C-7), 112.9 (CH, C-8), 116.6 (quat., C-4a), 125.5 (CH, Ph), 126.4, 126.7 (quat., C-6, C-8a), 127.0, 127.5, 127.6, 128.1, 128.2, 128.4 (CH, Ph, C-2), 129.3 (quat., C-3), 138.6 (quat., *ipso*-Ph), 142.5 (quat., *ipso*-Ph), 150.4, 151.3, 152.4 (quat., C-1, C-5, C-4), 199.6 (quat., *C*OCH_3); *m*/*z* (EI) 554 (M^+, 4%), 285 (17), 91 (C_7H_7, 100) and *title compound* **28** (8 mg, 7%) as a yellow oil; $[\alpha]_D^{22}$ +40.0 (*c* 0.40, $CHCl_3$) [Found (EI): M^+, 662.2868. $C_{41}H_{42}O_8$ requires *M*, 662.2880]; ν_{max}/cm^{-1} 3327br (OH), 2921, 2853 (C-H), 1672 (C=O), 1604, 1514, 1453 (C=C), 1368 (s, C-O); δ_H (400 MHz; $CDCl_3$)‡ 1.65 (1H, ddd, J_{gem} 12.7, $J_{2'ax,3'}$ 11.5 and $J_{2'ax,1'}$ 11.5, 2′$_{ax}$-H), 2.57 (1H, ddd, J_{gem} 12.7, $J_{2'eq,3'}$ 4.8 and $J_{2'eq,1'}$ 1.8, 2′$_{eq}$-H), 2.76 (3H, s, $COCH_3$), 3.65–4.20 (5H, m, 3′-H, 4′-H, 5′-H, 6′-H_A, 6′-H_B), 3.93, 3.99 (each 3H, s, 2 × OCH_3), 4.61 (1H, d, J_{gem} 12.4, C*H*Ph), 4.65 (1H, d, J_{gem} 11.6, C*H*Ph), 4.66 (1H, d, J_{gem} 10.9, C*H*Ph), 4.70 (1H, d, J_{gem} 12.4, C*H*Ph), 4.74 (1H, d, J_{gem} 11.6, C*H*Ph), 4.97 (1H, d, J_{gem} 10.9, C*H*Ph), 5.04 (1H, dd, $J_{1',2'ax}$ 11.4 and $J_{1',2'eq}$ 1.6, 1′-H), 6.92 (1H, s, 2-H), 7.20–7.50 (15H, m, Ph), 7.75 (1H, d, $J_{8,7}$ 8.7, 8-H), 7.79 (1H, d, $J_{7,8}$ 8.7, 7-H), 9.78 (1H, s, OH); δ_C (100 MHz; $CDCl_3$)‡ 30.5 (CH_3, CO*C*H_3), 37.4 (CH_2, C-2′), 55.8, 65.6 (CH_3, 2 × OCH_3), 69.6 (CH_2, C-6′), 71.3 (CH_2, *C*H_2Ph), 71.7 (CH, C-1′), 73.4, 75.1 (CH_2, 2 × *C*H_2Ph), 78.5, 79.5, 81.4 (CH, C-3′, C-4′, C-5′), 102.3 (CH, C-2), 113.7 (CH, C-8), 116.8 (quat., C-4a), 124.9, 125.5 (quat., C-3, C-6), 127.1 (CH, C-7), 127.5–128.3 (CH, Ph), 129.4 (quat., C-8a), 138.5, 138.6, 138.6 (quat., 3 × *ipso*-Ph), 150.1, 151.3, 152.3 (quat., C-1, C-8, C-5), 199.7 (quat., *C*OCH_3); *m*/*z* (EI) 662 (M^+, 0.5%), 554 (1), 272 (12), 91 (C_7H_7, 100).

(1′*R*,2′*R*,5′*R*,7′*S*,9′*S*)-2-Acetyl-6-(9′-benzyloxy-2′-phenyl-3′,6′-dioxabicyclo[3.2.2]nonan-7′-yl)-5-hydroxy-1,4-dimethoxynaphthalene 37 and 2-acetyl-5-hydroxy-1,4-dimethoxy-6-(3′,4′,6′-tri-*O*-benzyl-2′-deoxy-β-D-*arabino*-hexopyranosyl)-naphthalene 32

Boron trifluoride–diethyl ether (40 μL, 0.325 mmol) was added dropwise to a stirred solution of tri-*O*-benzyl-2-deoxy-D-glucosyl acetate **10** (93 mg, 0.195 mmol) and 2-acetyl-1,4-dimethoxy-5-hydroxynaphthalene **11** (40 mg, 0.163 mmol) in dry acetonitrile (3 mL) at 0 °C. The mixture was stirred for 1 h at 0 °C, then was quenched with water (2 mL). The crude reaction mixture was extracted with dichloromethane (3 × 25 mL), washed with water (50 mL) and dried (magnesium sulfate). The solvent was removed at reduced pressure and the oily residue was purified by flash chromatography using hexane–ethyl acetate (4 : 1) as eluent to give the starting naphthol **11** (17 mg, 43% recovery) as well as a (1 : 2) mixture of *β-C-glycoside* **32** and the *rearranged product* **37** (60 mg). These were separated by HPLC (1.5% ^{i}PrOH–hexane; Partisil 5 column; rt; 45 min) to give *(1′R,2′R,5′R,7′S,9′S)-2-acetyl-6-(9′-benzyloxy-2′-phenyl-3′,6′-dioxabicyclo[3.2.2]-nonan-7′-yl)-5-hydroxy-1,4-dimethoxynaphthalene* **37** (21 mg, 23%) as a colourless oil; $[\alpha]_D^{22}$ −201 (*c* 0.38, $CHCl_3$) [Found (EI): M^+, 554.2317. $C_{34}H_{34}O_7$ requires *M*, 554.2305]; ν_{max}/cm^{-1} 3366br (OH), 2938, 2855 (C-H), 1668 (C=O), 1608 (C=C), 1371 (C-O); δ_H (400 MHz; $CDCl_3$)‡ 1.52 (1H, ddd, J_{gem} 14.3, $J_{8'B,9'}$ 4.7 and $J_{8'B,1'}$ 4.6, 8′-H_B), 2.09 (1H, ddd, J_{gem} 14.3, $J_{8'A,9'}$ 9.6 and $J_{8'A,1'}$ 2.3, 8′-H_A), 2.29 (1H, dd, $J_{1',8'B}$ 4.6 and $J_{1',8'A}$ 2.3, 1′-H), 2.79 (3H, s, $COCH_3$), 3.93, 4.11 (each 3H, s, 2 × OCH_3), 4.17 (1H, d, J_{gem} 13.5, 4′-H_A), 4.26 (1H, dd, $J_{9',8'A}$ 9.6 and $J_{9',8'B}$ 4.7, 9′-H), 4.31 (1H, dd, J_{gem} 13.5 and $J_{4'B,5'}$ 5.4, 4′-H_B), 4.46 (1H, d, $J_{5',4'B}$ 5.4, 5′-H), 4.61 (2H, s, CH_2Ph), 5.14 (1H, s, 7′-H), 5.94 (1H, s, 2′-H), 7.08 (1H, s, 3-H), 7.24 (1H, t, J_o 7.4, *p*-Ph), 7.33 (2H, t, J_o 7.4, *m*-Ph), 7.35–7.45 (7H, m, Ph), 7.70 (1H, d, $J_{7,8}$ 8.7, 8-H), 8.21 (1H, d, $J_{7,8}$ 8.7, 7-H), 9.72 (1H, s, OH); δ_C (100 MHz; $CDCl_3$)‡ 23.2 (CH_2, C-8′), 31.6 (CH_3, CO*C*H_3), 45.9 (CH, C-1′), 57.1, 64.3 (CH_3, 2 × OCH_3), 71.0 (CH_2, *C*H_2Ph), 71.9 (CH_2, C-4′), 74.5 (CH, C-9′), 76.9 (CH, C-2′), 77.2 (CH, C-5′), 86.1 (CH, C-7′), 102.7 (CH, C-7), 114.5 (CH, C-8), 118.1 (quat., C-4a), 126.2 (CH, Ph), 127.0 (quat., C-6), 127.7, 128.0, 128.2, 128.3 (CH, Ph, C-3), 128.4 (quat., C-8a), 128.7, 129.1 (CH, Ph), 130.8 (quat., C-2), 139.3 (quat., *ipso*-Ph), 143.1 (quat., 3 × *ipso*-Ph), 151.3, 153.1, 153.8 (quat., C-1, C-5, C-4), 199.8 (quat., *C*OCH_3); *m*/*z* (EI) 554 (M^+, 3%), 285 (18), 91 (C_7H_7, 100) and *2-acetyl-5-hydroxy-1,4-dimethoxy-6-(3′,4′-',6′-tri-O-benzyl-2′-deoxy-β-D-arabino-hexopyranosyl)naphthalene* **32** (10 mg, 9%) as a colourless oil; $[\alpha]_D^{22}$ +45.0 (*c* 0.16, $CHCl_3$) [Found (EI): M^+, 662.2898. $C_{41}H_{42}O_8$ requires *M*, 662.2880]; ν_{max}/cm^{-1} 3359br, (OH), 2955, 2922, 2863 (C-H), 1668 (C=O), 1610 (C=C), 1454, 1372 (C-O); δ_H (400 MHz; $CDCl_3$)‡ 1.62 (1H, ddd, J_{gem} 12.7, $J_{2'ax,3'}$ 11.4 and $J_{2'ax,1'}$ 11.4, 2′$_{ax}$-H), 2.62 (1H, ddd, J_{gem} 12.7, $J_{2'eq,3'}$ 4.9 and $J_{2'eq,1'}$ 1.7, 2′$_{eq}$-H), 2.79 (3H, s, $COCH_3$), 3.65–3.92 (5H, m, 3′-H, 4′-H, 5′-H, 6′-H_A, 6′-H_B), 3.93, 4.08 (each 3H, s, 2 × OCH_3), 4.61 (1H, d, J_{gem} 12.4, C*H*Ph), 4.65 (1H, d, J_{gem} 11.6, C*H*Ph), 4.66 (1H, d, J_{gem} 10.9, C*H*Ph), 4.71 (1H, d, J_{gem} 12.4, C*H*Ph), 4.73 (1H, d, J_{gem} 11.6, C*H*Ph), 4.97 (1H, d, J_{gem} 10.9, C*H*Ph), 5.00 (1H, dd, $J_{1',2'ax}$ 11.4 and $J_{1',2'eq}$ 1.7, 1′-H), 7.08 (1H, s, 3-H), 7.25–7.40 (15H, m, Ph), 7.71 (1H, d, $J_{8,7}$ 8.7, 8-H), 7.77 (1H, d, $J_{7,8}$ 8.7, 7-H), 9.65 (1H, s, OH); δ_C (100 MHz; $CDCl_3$)‡

30.9 (CH_3, $COCH_3$), 37.2 (CH_2, C-2′), 56.4, 63.6 (CH_3, 2 × OCH_3), 69.7 (CH_2, C-6′), 71.2 (CH_2, CH_2Ph), 71.7 (CH, C-1′), 73.4, 75.1 (CH_2, 2 × CH_2Ph), 78.4, 79.5, 81.3 (CH, C-3′, C-4′, C-5′), 102.4 (CH, C-3), 114.8 (CH, C-8), 117.5 (quat., C-4a), 126.2 (CH, C-7), 126.3, 126.6 (quat., C-2, C-6), 127.5–128.4 (CH, Ph), 130.2 (quat., C-8a), 138.6, 138.6, 138.6 (quat., 3 × *ipso*-Ph), 150.2, 152.5, 152.9 (quat., C-1, C-4, C-5), 199.1 (quat., $COCH_3$); *m*/*z* (EI) 662 (M^+, 0.5%), 554 (0.2), 272 (8), 181 (5), 149 (7), 91 (C_7H_7, 100).

Acknowledgements

We thank Dr Patrick Steel (University of Durham, UK) for supplying NMR spectra for compounds related to the rearranged *C*-glycosides reported herein.

References

1 S. Takano, K. Hasuda, A. Ito, Y. Koide, F. Ishii, I. Haneda, S. Chihara and T. Koyami, *J. Antibiot.*, 1976, **29**, 765.
2 (*a*) T. Okabe, K. Namoto, H. Funabashi, S. Okuda, H. Suzuki and N. Tanaka, *J. Antibiot.*, 1985, **38**, 1333; (*b*) N. Tanaka, T. Okabe, F. Isono, M. Kashiwagi, K. Namoto, M. Takahashi, A. Shimazu and T. Nishimura, *J. Antibiot.*, 1985, **38**, 1327.
3 N. Tanaka, *Jap. Pat.*, 62 10086, 1987 (*Chem. Abstr.*, 1987, **106**, 212564u).
4 H. W. Moore and R. Czerniak, *Med. Res. Rev.*, 1981, **1**, 1249.
5 H. Hoeksama and W. C. Kruger, *J. Antibiot.*, 1976, **29**, 704.
6 E. L. Rosenfield and H. E. Laubach, *J. Parasitol.*, 1986, **72**, 770.
7 K. Tatsuka, H. Ozeki, M. Yamaguchi, M. Tanaka and T. Okui, *Tetrahedron Lett.*, 1990, **31**, 5495.
8 M. A. Brimble and T. J. Brenstrum, *Tetrahedron Lett.*, 2000, **41**, 2991.
9 M. A. Brimble and S. J. Stuart, *J. Chem. Soc., Perkin Trans. 1*, 1990, 881.
10 M. A. Brimble, S. J. Phythian and H. Prabaharan, *J. Chem. Soc., Perkin Trans. 1*, 1995, 2855.
11 For a preliminary communication on this work see: M. A. Brimble and T. J. Brenstrum, *Tetrahedron Lett.*, 2000, **41**, 1107.
12 For recent reviews on *C*-glycosylation see: (*a*) M. H. D. Postema, *Tetrahedron*, 1992, **48**, 8545; (*b*) C. Jaramillo and S. Knapp, *Synthesis*, 1994, 1; (*c*) D. E. Levy and C. Tang, *The Chemistry of C-Glycosides*, Pergamon Press, Oxford, 1995; (*d*) Y. Du and R. J. Lindhardt, *Tetrahedron*, 1998, **54**, 9913.
13 The lack of reactivity of juglone towards *C*-glycosylation has been observed previously. See: G. Matsuo, Y. Miki, M. Nakata, S. Matsumura and K. Toshima, *J. Org. Chem.*, 1999, **64**, 7101.
14 H. Rappoport, R. L. Hannan and R. B. Barber, *J. Org. Chem.*, 1979, **44**, 2153.
15 R. H. Thompson, *J. Org. Chem.*, 1948, **13**, 377.
16 S. V. Ley, W. P. Griffith, J. Norman and S. P. Marsden, *Synthesis*, 1994, 639.
17 H. Laatsch, *Liebigs Ann. Chem.*, 1980, 1321.
18 W. G. Overend, M. Stacey and J. Stanek, *J. Chem. Soc.*, 1949, 2841.
19 C. Mioskowski, V. Bolitt, S.-G. Lee and J. R. Falck, *J. Org. Chem.*, 1990, **55**, 5812.
20 K. Toshima, G. Matsuo and K. Tatsuka, *Tetrahedron Lett.*, 1992, **33**, 2175.
21 D. S. Larsen and F. L. Andrews, *Tetrahedron Lett.*, 1994, **35**, 8693.
22 P. G. Steel, A. L. J. Byerly, A. M. Kenwright and C. W. Lehman, *J. Org. Chem.*, 1998, **63**, 193.
23 T. J. Brenstrum, M. A. Brimble and P. Turner, *Acta Crystallogr., Sect. E*, 2001, **57**, 28.
24 M. A. Brimble and T. J. Brenstrum, *J. Chem. Soc., Perkin Trans. 1*; following paper, DOI 10.1039/b103080a.
25 T. Wakamatsu, N. Takahide, T. Ohnuma and B. Yoshio, *Synth. Commun.*, 1984, **14**, 1167.
26 A. S. Wheeler and J. W. Scott, *J. Am. Chem. Soc.*, 1919, **41**, 833.
27 J. D. Surmatis and A. Ofner, *J. Org. Chem.*, 1963, **28**, 2735.
28 I. D. Blackburne, P. M. Fredericks and R. D. Guthrie, *Aust. J. Chem.*, 1976, **29**, 381.