Synthesis and Acetylation of Naphthols as Precursors to Naturally Derived Naphthoquinones; Crystal Structure of the Aphin-related 7-*O*-Methyl Quinone A

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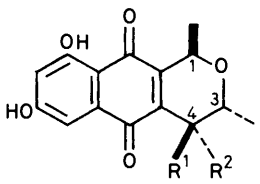
A route is described to 1,5,7-trialkoxy-4-naphthols.† A method has been established to convert these compounds into the corresponding 3-acetyl-4-naphthols, in good yield, with a view to synthesizing naturally derived naphtho[2,3-*c*]pyran-5,10-quinones. Boron trichloride-induced monodemethylation of racemic Quinone A dimethyl ether was effected without perturbation of the pyran ring stereochemistry; this was confirmed by an *X*-ray crystallographic investigation.

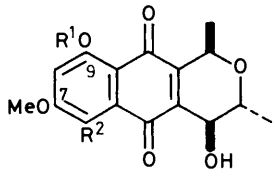
We recently undertook syntheses of Quinone A (**1**), Quinone A′ (**2**), and Deoxyquinone A (**3**), derivatives of the aphid pigments protoaphin-*fb*,[1] protoaphin-*sl*,[1] and deoxyprotoaphin.[2] Two phases of these syntheses are complete. First, the construction of the ring system common to the three quinones was investigated so as to include the pyran ring with the correct relative stereochemistry at C-1, C-3, and (where appropriate) C-4, but without effecting regiochemical oxygenation of the aromatic ring. Two methods were pioneered.[3,4] The second phase was to establish the correct regiochemistry of the aromatic oxygen atoms relative to the pyran rings by synthesis of 3-acetyl-5,7-dimethoxy-1,4-naphthoquinone,[5] which was then elaborated to give the dimethyl ethers of Quinones A and A′ and Deoxyquinone A,[6] identical with the naturally derived compounds (except that the synthetic materials were racemic). However, as expected, it was not possible to remove smoothly both *O*-methyl groups without disruption of the pyran ring. To complete the desired syntheses, alternative protecting groups for at least one of the phenolic groups were required which could be removed readily in a final step, and which would survive the reactions leading to the penultimate products. This paper describes the formation of 1,4,5,7-tetraoxygenated naphthalenes with each oxygen substituent suitably protected,[7] followed by a study of the most convenient conditions to effect acetylation of these products at C-3. For this latter reaction, the Lewis acid-catalysed Fries rearrangement[5] could not be used with *O*-protecting groups other than methyl. The following paper describes the conversion of these acylated naphthalenes into the racemates of Quinones A and A′ and Deoxyquinone A.

Results and Discussion

It was first necessary to establish that methyl could be retained as a protecting group at O-9 for the syntheses of Quinone A (**1**), Quinone A′ (**2**), and Deoxyquinone A (**3**) without disruption of the pyran ring or the relative stereochemistry of its substituents. Quinone A dimethyl ether (**4**) in dichloromethane was therefore treated at −78 °C with boron trichloride. Two products were obtained, the ^{1}H n.m.r. spectra of which showed them to be the *peri*-demethylated Quinone A monomethyl ether (**5**) (44%), previously obtained as a single enantiomer from natural material,[1] and also 6-chloro-Quinone A dimethyl ether (**6**) (45%). That the stereochemistry in both products had been maintained was shown by the retention of the large coupling constant (*J* 8 Hz) between 3-H and 4-H, and the long-range coupling constant (*J* 1.5 Hz) between 1-H and 4-H.



(**1**) R^1 = OH, R^2 = H
(**2**) R^1 = H, R^2 = OH
(**3**) R^1 = R^2 = H



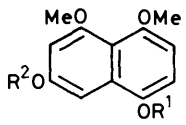
(**4**) R^1 = Me, R^2 = H
(**5**) R^1 = R^2 = H
(**6**) R^1 = Me, R^2 = Cl

The structure of compound (**5**) was confirmed by *X*-ray crystallography (see later). The formation of the novel but unwanted chloro compound (**6**) was suppressed by conducting the reaction at 0 °C, the yield of (**5**) thereby rising to 72%. In attempts to remove the remaining *O*-methyl group, it was found that a range of demethylating reagents, including aluminium trichloride,[8] boron tribromide,[9] boron trifluoride,[10] trimethylsilyl iodide,[11] and sodium ethanethiolate in dimethylformamide[12] either effected no reaction or destroyed the substrate. For our purposes, methyl was therefore deemed a suitable protecting group at O-5, but not at O-7, in naphthalenes such as (**7**).

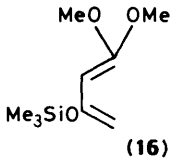
In earlier work,[5] we found that 1,4,5,7-tetramethoxynaphthalene (**7**) underwent acetylation at both C-3 (22%) and C-8 (66%), and we suggested that the use of more bulky protecting roups at O-1 and -7 might increase the proportion of the C-3 isomer through crowding. This possibility was investigated, using isopropyl or benzyl as an alternative protecting group. These two substituents, in addition to being bulkier than methyl, were considered potentially suitable for use in the synthesis of the desired quinones (**1**)—(**3**) for a number of reasons. First, it appeared that both might be removed from O-7 in precursors to the quinones, since isopropyl has been reported[13] as being removed from aromatic oxygen by boron trichloride without the requirement of an *ortho*- or a *peri*-carbonyl group and should therefore be removable from O-7 in the analogue of the quinone (**4**). Benzyl, on the other hand, is known[14] to suffer cleavage from oxygen by hydrogenolysis, conditions which have been used to derive the quinones (**1**)—(**3**) from the protoaphins and to which these quinones must therefore be stable. Secondly, both protecting groups are known to be stable to reasonably acidic and also basic conditions, both of which were to be used for the formation of the quinones.

Brassard's diene (**16**)[15] was treated with 1,4-benzoquinone and the intermediate adduct (**17**) was alkylated directly with isopropyl bromide and potassium carbonate in dimethylformamide to afford the naphthol (**18**) (71%). Alternative alkylation with benzyl bromide gave the naphthol (**19**) (42%);

† For clarity, the oxy substituents in all tetraoxygenated naphthalenes referred to here are numbered 1,4,5,7, although strictly speaking a principal group (*e.g.* -ol) should be assigned lowest locant (as *e.g.* 4,6,8-trialkoxy-1-naphthol).



(7) $R^1 = R^2 = Me$
(8) $R^1 = R^2 = Pr^i$
(9) $R^1 = R^2 = CH_2Ph$
(10) $R^1 = R^2 = Ac$
(11) $R^1 = R^2 = Me_3CSiMe_2$
(12) $R^1 = Me$, $R^2 = Me_3CSiMe_2$
(13) $R^1 = Me$, $R^2 = CH_2Ph$
(14) $R^1 = Me$, $R^2 = H$
(15) $R^1 = Me$, $R^2 = Ac$



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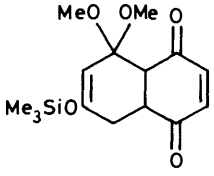

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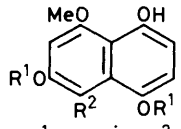
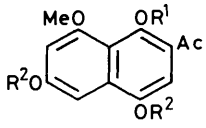
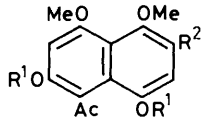


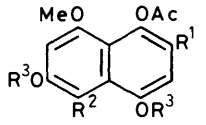
(18) $R^1 = Pr^i$, $R^2 = H$
(19) $R^1 = CH_2Ph$, $R^2 = H$
(20) $R^1 = R^2 = CH_2Ph$
(21) $R^1 = Ac$, $R^2 = H$
(22) $R^1 = Me_3CSiMe_2$, $R^2 = H$



(23) $R^1 = Me$, $R^2 = Pr^i$
(24) $R^1 = Me$, $R^2 = CH_2Ph$
(25) $R^1 = Ac$, $R^2 = Pr^i$
(26) $R^1 = Ac$, $R^2 = CH_2Ph$
(27) $R^1 = H$, $R^2 = Pr^i$
(28) $R^1 = H$, $R^2 = CH_2Ph$



(29) $R^1 = Pr^i$, $R^2 = H$
(30) $R^1 = CH_2Ph$, $R^2 = H$
(31) $R^1 = Ac$, $R^2 = H$
(32) $R^1 = Pr^i$, $R^2 = Ac$



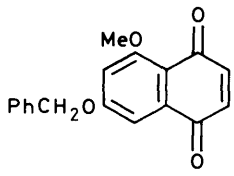
(33) $R^1 = R^2 = H$, $R^3 = Pr^i$
(34) $R^1 = H$, $R^2 = Ac$, $R^3 = Pr^i$
(35) $R^1 = R^2 = H$, $R^3 = Me$

the C-8 benzylated compound (**20**) was a minor product (9%). The naphthols (**18**) and (**19**) were converted into their methyl ethers (**8**) and (**9**), respectively.

Acetylation of the bisisopropoxynaphthalene (**8**) with premixed acetic acid and trifluoroacetic anhydride gave the 3-acetyl isomer (**23**) (18%) and the 8-acetyl isomer (**29**) (61%); thus there was little change from the mode of acetylation of the tetramethoxynaphthalene (**7**) on increasing the bulk of the alkyl groups at O-1 and O-7 (from methyl to isopropyl). The diacetylnaphthalene (**32**) was obtained as a minor product. On the other hand, similar acetylation of the 1,7-bisbenzyloxy analogue (**9**) changed the distribution of products somewhat to yield the 3-acetyl compound (**24**) (28%) and the corresponding 8-isomer (**30**) (38%). However, the latter still predominated.

No reaction was observed between either (**8**) or (**9**) and the alternative acylating mixtures of acetic anhydride with pyridine or dimethylaminopyridine.

The isolation of naphthols related to (**18**) and (**19**), but protected at O-1 and O-7 by groups other than alkyl, was also investigated. Treatment of the intermediate Diels–Alder adduct (**17**) with acetic anhydride and pyridine afforded the 1,7-diacetoxy derivative (**21**) (53%), which on methylation afforded 1,7-diacetoxy-4,5-dimethoxynaphthalene (**10**) in high yield (88%). Acetylation of this compound with premixed acetic acid and trifluoroacetic anhydride gave the 8-acetyl derivative (**31**)



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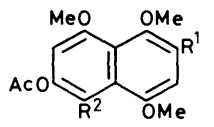

(37) $R^1 = Ac$, $R^2 = H$
(38) $R^1 = H$, $R^2 = Ac$

as the sole product. Alternative treatment of the adduct (**17**) with t-butyldimethylsilyl chloride and imidazole followed by 1,5-diazabicyclo[5.4.0]non-5-ene gave a solid which was assigned structure (**22**) on the basis of its ^1H n.m.r. spectrum. This was directly methylated with dimethyl sulphate and potassium carbonate in acetone to afford the dimethyl ether (**11**) as the minor product (30%) followed (chromatographically) by a compound formulated as either 7-t-butyldimethylsilyloxy-1,4,5-trimethoxynaphthalene (**12**) or its isomer, 1-t-butyldimethylsilyloxy-4,5,7-trimethoxynaphthalene, as the major product (60%). Because of the known sensitivity of this protecting silyl group to acids, neither (**11**) nor the trimethoxy compound was acetylated by the mixed anhydride method.

The naphthol (**18**) was acylated with pyridine and acetic anhydride to afford the acetate (**33**), acetylation of which with the mixed anhydride afforded solely the 8-acetyl compound (**34**) (80%). Since replacement of the methyl group on O-4 in compound (**8**) with acetyl [in (**33**)] resulted in the suppression of acetylation at C-3, presumably at least in part because acetoxy, while electron-releasing, is somewhat less so than methoxy,[16] thereby discouraging electrophilic substitution at C-3, the question arose as to whether replacement of methyl at O-7 in compound (**7**) by acetyl as in compound (**15**) would cause acetylation preferentially, or even exclusively, at C-3. The 7-acetoxy derivative (**15**) was prepared from the bisbenzyloxynaphthol (**19**), which was oxidised to yield the crude quinone (**36**), and this was in turn reductively dimethylated to afford the benzyl trimethyl ether (**13**). The benzyl group was hydrogenolysed to yield the crude 7-naphthol (**14**) and acetylation with pyridine and acetic anhydride afforded the desired acetate (**15**). A comparison of the chemical shifts of the four aromatic protons in compounds (**7**), (**35**), (**14**), and (**15**) was made (Table 1). In particular, the fact that 8-H in the 7-acetoxynaphthalene (**15**) was deshielded (δ 7.56) relative to the same proton in the 7-naphthol (**14**) (δ 7.16) and the 7-methoxynaphthalene (**7**) (δ 7.19) lent credence to the possibility that substitution of methoxy at C-7 by acetoxy might well reduce the capacity of C-8 to suffer electrophilic attack, particularly as the deshielding of 6-H was considerably less. However, when the 7-acetoxy compound (**15**) was acetylated using the mixed anhydride method the 8-isomer (**38**) was still dominant (67%), the yield of the 3-isomer (**37**) being only 11%.

Success was achieved in acylating the naphthalenes at C-3 in the following way. The 4-naphthol (**18**) was acylated with premixed acetic acid and trifluoroacetic anhydride in boiling chloroform. Under these conditions four products were obtained (after chromatography), in addition to some starting material. The 3-acetyl-4-acetoxynaphthalene (**25**) predominated (56%), and this was readily hydrolysed to afford the desired 3-acetyl-4-naphthol (**27**). This naphthol was also obtained from the acetylation reaction, but was contaminated by the acetate (**33**) already described. Separation of this mixture was however possible by treatment with dilute methanolic potassium hydroxide, which hydrolysed the acetate (**33**) to starting material, and the two naphthols were then readily separated. A fourth minor product (3%) was the 4-acetoxy-8-acetylnaphthalene (**34**) already mentioned.

This reaction was highly successful since it provided the

Table 1. Comparison of the chemical shifts (δ)[a] [and coupling constants (Hz)] of the aromatic protons in compounds (**7**), (**35**), (**14**), and (**15**)

Compound	2-H	3-H	6-H	8-H
(**7**)	6.74[8]	6.63[8]	6.57[2]	7.19[2]
(**35**)	6.73[8]	6.85[8]	6.54[2]	7.19[2]
(**14**)	6.93[b]	6.93[b]	6.50[2]	7.16[2]
(**15**)	6.72[b]	6.72[b]	6.63[2]	7.56[2]

[a] 0.15M Solutions in $CDCl_3$. [b] Singlets.

Table 2. Crystal data, and experimental and refinement parameters for structure (**5**)

Molecular formula	$C_{16}H_{16}O_6$
M	304.30
Space group	$P\bar{1}$
a/Å	7.260(4)
b/Å	7.887(4)
c/Å	26.65(1)
α/°	92.63(2)
β/°	93.13(2)
γ/°	113.30(2)
V/Å^3	1 396
D_c/g m^{-3}	1.45 for Z = 4
μ(Mo-K_α)/mm^{-1}	6.9
F(000)	640
Data collection	
Crystal dimensions (mm)	0.36 × 0.25 × 0.20
Scan mode	ω—2θ
Scan width (θ/°)	0.34
Scan speed (° s^{-1})	0.14
Range scanned [(2θ)/°]	6—46°
Stability of standard reflections (%)	1.1
Reflections collected	3 916
Observed reflections	1 996
Refinement	
Variables	417
$R = \Sigma\|\|F_o\| - \|F_c\|\|/\Sigma\|F_o\|$	0.119
U_{iso} of H atoms: methyl (Å^2)	0.09(2)
CH_2, CH (Å^2)	0.02(2)

Table 3. Fractional atomic co-ordinates (× 10^4) for non-hydrogen atoms

Atom	x/a	y/b	z/c
	Molecule A		
C(1)	3 812(25)	9 411(21)	1 438(6)
C(11)	1 911(31)	9 257(30)	1 693(7)
O(2)	5 090(17)	8 828(14)	1 763(4)
C(3)	4 351(26)	6 831(20)	1 768(6)
C(31)	5 800(34)	6 534(31)	2 145(7)
C(4)	4 269(25)	5 906(21)	1 264(6)
O(4)	3 090(20)	3 987(14)	1 285(4)
C(4′)	3 466(24)	6 743(20)	855(6)
C(5)	3 008(26)	5 782(22)	343(6)
O(5)	3 072(21)	4 257(14)	277(4)
C(5′)	2 432(24)	6 675(19)	−90(5)
C(6)	2 102(26)	5 785(22)	−550(6)
C(7)	1 736(23)	6 687(20)	−976(6)
O(7)	1 488(20)	5 768(15)	−1 418(4)
C(71)	1 069(29)	6 613(25)	−1 859(7)
C(8)	1 711(24)	8 449(21)	−887(6)
C(9)	2 050(25)	9 319(22)	−419(6)
O(9)	2 053(17)	11 037(13)	−373(4)
C(9′)	2 411(24)	8 438(20)	7(5)
C(10)	2 801(24)	9 337(23)	514(6)
O(10)	2 744(18)	10 885(14)	595(4)
C(10′)	3 341(25)	8 379(20)	934(5)
	Molecule B		
C(1)	2 062(26)	6 290(22)	6 456(6)
C(11)	4 159(29)	6 716(27)	6 716(7)
O(2)	878(17)	6 972(14)	6 758(4)
C(3)	1 582(27)	8 930(21)	6 796(6)
C(31)	215(32)	9 417(26)	7 150(7)
C(4)	1 353(27)	9 646(21)	6 275(6)
O(4)	2 558(20)	11 600(14)	6 320(4)
C(4′)	1 972(24)	8 640(19)	5 854(5)
C(5)	2 199(27)	9 397(22)	5 357(6)
O(5)	2 062(21)	10 867(14)	5 293(4)
C(5′)	2 468(25)	8 265(19)	4 922(5)
C(6)	2 552(25)	8 883(19)	4 465(6)
C(7)	2 658(27)	7 770(23)	4 050(6)
O(7)	2 647(20)	8 485(15)	3 588(4)
C(71)	2 824(34)	7 432(25)	3 166(7)
C(8)	2 717(24)	6 029(20)	4 109(5)
C(9)	2 727(25)	5 435(23)	4 600(7)
O(9)	2 742(18)	3 736(13)	4 653(4)
C(9′)	2 580(24)	6 521(19)	5 015(5)
C(10)	2 514(26)	5 901(23)	5 511(6)
O(10)	2 636(18)	4 420(14)	5 611(4)
C(10′)	2 224(25)	7 062(21)	5 943(5)

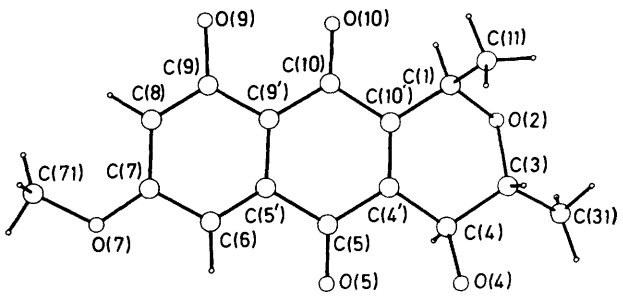

Figure 1.

required 3-acetyl-4-naphthol (**27**) directly, and also indirectly by hydrolysis of the acetate (**25**). In addition, since the acetate (**33**) could be hydrolysed to starting material (**18**), this could be combined with the starting material recovered directly by chromatography, and the whole could be re-acetylated, thereby giving a high overall yield of the acetylnaphthol (**27**).

The corresponding 1,7-bisbenzyloxy-4-naphthol (**19**) was similarly acetylated to yield the 3-acetyl 4-acetate (**26**) in 51% yield. This product was hydrolysed to the corresponding naphthol (**28**) under the conditions used for the hydrolysis of the acetate (**25**) to the naphthol (**27**), but the yield (50%) was lower.

The formation of the 3-acetyl 4-acetates (**25**) and (**26**) no doubt arises through initial *C*-acetylation of the naphthols (**18**) and (**19**) respectively followed by *O*-acetylation. The formation of the 8-acetyl derivative (**34**) as a minor product in the former of these two reactions would arise from acylation of the acetate (**33**) with the mixed anhydride.

On the basis of starting benzoquinone, the yield of the bisisopropoxynaphthol (**27**) was 48%, whereas the corresponding yield of the bisbenzyloxy analogue (**28**) was considerably less (12%). In view of the fact that the benzyl-protected naphthol (**28**) was much more difficult to obtain in quantity, investigations in this series were discontinued in favour of the isopropyl series. Compound (**27**) was therefore used for the synthesis of Quinones A and A′ and Deoxyquinone A described in the following paper.

Table 4. Conformational analysis of the hetero rings: asymmetry and pucker parameters[a]

	Asymmetry parameters				Pucker parameters[b]		
	A	B	Ref. 19		A	B	Ref. 19
$\Delta C_2(C_2C_3)$	17	11	1	Q/Å	0.45	0.47	0.49
$\Delta C_s(O_2)$	15	15	24	θ/°	46	47	49
$\Delta C_s(C_3)$	25	24	22	φ/°	83	81	93
					$^3H_2$		

[a] Only the values for one enantiomer of each independent molecule are quoted; the values for the other are complementary. [b] The total degree of pucker is described by the radial co-ordinate Q; the angular co-ordinates θ and φ describe the shape of the ring. The order used in the conformational nomenclature is C(1)–O(2)–C(3)–C(4)–C(4¹)–C(10¹).

Table 5. Non-bonded O–H · · · O interactions

Atoms	d(O · · · O)/Å	Symmetry operation applied to second atom	C–O · · · O angle (°)
O(5A)–O(4A)[a]	2.70(2)	x, y, z	79.3
O(10A)–O(4A)	2.91(2)	$x, y + 1, z$	129.5
O(5B)–O(4B)	2.75(2)	x, y, z	78.5
O(10B)–O(4B)	2.97(2)	$x, y + 1, z$	128.6
O(5A)–O(9A)	2.82(2)	$x, y - 1, z$	145.0
O(10A)–O(9A)[b]	2.62(2)	x, y, z	85.5
O(5B)–O(9B)	2.80(2)	$x, y + 1, z$	145.6
O(10B)–O(9B)	2.60(2)	x, y, z	85.9

[a] For ref. 19, this value is 2.721(6) Å. [b] For ref. 19, this value is 2.589(9) Å.

Crystal Structure of 7-O-*Methyl Quinone A* (**5**).—A perspective view of the compound (single illustration representative of both molecules A and B) is shown with atomic numbering in Figure 1. The crystal structure analysis confirmed unequivocally that the gross structure and stereochemistry for compound (**5**) are as predicted by spectroscopic means. A comparison of the two independent molecules reveals that all corresponding bond lengths, angles, and torsion angles are the same within the standard deviations obtained. The general similarity between the two independent molecules allows the mean value to be quoted for each respective bonding parameter in the ensuing discussion.

The major features of the molecular geometry are those expected for an alicyclic ring fused to a 1,4-naphthoquinone. Carbon–carbon distances in the benzenoid ring are in the range 1.34(2)—1.43(2), Å, indicative of π-electron delocalisation.

The two-ring naphthoquinonoid moiety is notably planar, with a maximum deviation from its least-squares plane of 0.09 Å for its constituent atoms. However, an examination of the least-squares planes calculated for the benzenoid and quinonoid rings individually shows that they have even greater planarity (maximum deviation of a constituent atom <0.05 Å). All bond lengths and angles in the hetero-ring are of the expected magnitudes, and Table 4 presents its conformation in terms of asymmetry parameters[17] and parameters of pucker.[18] A half-chair situation obtains.

Hydrogen bonding. All relevant intra- and inter-molecular O · · · O close contacts (<3 Å) involving the O–(H) · · · O groups are given in Table 5. A packing diagram (Figure 2) shows these close contacts. Regrettably, the hydroxylic hydrogen atoms could not be located in a difference map and were not included in the final model. However, we postulate that the intermolecular H-bonding is probably more favourable [the relative positions of O(4)/O(5) and O(9)/O(10) within one molecule make intra-molecular H-bonding unlikely].

Table 6. Torsion angles (°) of the hetero ring

τ	Molecule A	Molecule B	Ref. 19
C(11)–C(1)–O(2)–C(3)	77	70	76.2
C(10′)–C(1)–O(2)–C(3)	−49	−54	−49.3
C(1)–O(2)–C(3)–C(4)	62	65	68.1
C(1)–O(2)–C(3)–C(31)	−177	−177	−169.1
O(2)–C(3)–C(4)–C(4′)	−42	−42	−48.9
C(31)–C(3)–C(4)–C(4′)	−159	−158	−168.0
O(2)–C(3)–C(4)–O(4)	−166	−165	−171.2
C(31)–C(3)–C(4)–O(4)	77	79	69.8
C(3)–C(4)–C(4′)–C(5)	−171	−169	−164.5
C(3)–C(4)–C(4′)–C(10′)	15	14	17.6
O(4)–C(4)–C(4′)–C(5)	−50	−49	−44.5
O(4)–C(4)–C(4′)–C(10′)	136	133	137.7
C(10)–C(10′)–C(1)–C(11)	79	83	70.6
C(10)–C(10′)–C(1)–O(2)	−156	−152	−163.8
C(4′)–C(10′)–C(1)–C(11)	−103	−102	−109.8
C(4′)–C(10′)–C(1)–O(2)	22	23	15.7
	σ = 2°		

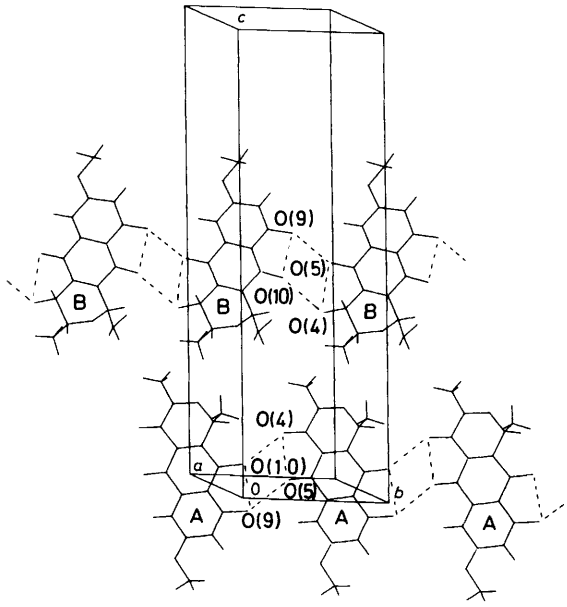

Figure 2.

A detailed comparison between the crystal structures of the synthetic quinone (**5**) and the aphin-derived pigment Quinone A (**1**)[19] has been carried out. With allowance for standard deviations, all intramolecular bond lengths and angles are the same in the two structures. Differences in the conformations of the hetero-rings are apparent (Table 6); however, that they are similar is evidenced by a residual $R = 0.06$ calculated according to $R = \Sigma\|\tau_o| - |\tau_T\|/\Sigma|\tau_o|$, where τ_o is a torsion angle value for the synthetic compound and τ_T the corresponding value for Quinone A (**1**). In contrast, White[19] does not report any evidence of intermolecular O–H · · · O hydrogen bonding involving the hydroxy groups.

Experimental

All ^{1}H n.m.r. spectra were measured for solutions in [^{2}H]chloroform, with tetramethylsilane as internal reference;

i.r. spectra were measured for Nujol mulls, unless otherwise stated. Preparative layer chromatography (p.l.c.) was performed on glass plates coated with Merck Kieselgel 60 F_{254}; column chromatography refers to dry-packed columns of the same gel (70—230 mesh). Light petroleum refers to the fraction of b.p. 60—80 °C and 'ether' to diethyl ether. The phrase 'residue obtained upon work-up' refers to the material remaining when the organic layer was separated, dried ($MgSO_4$), and evaporated under reduced pressure.

(1R,3R,4S)-3,4-*Dihydro*-4,9-*dihydroxy*-7-*methoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran*-5,10-*quinone* (**5**) *and its Enantiomer* [(±)-7-O-*Methyl Quinone A*] *and* (1R,3R,4S)-6-*Chloro*-3,4-*dihydro*-4-*hydroxy*-7,9-*dimethoxy*-1,3-*dimethyl*-1H-*naphtho*[2,3-c]*pyran*-5,10-*quinone* (**6**) *and its Enantiomer*.—A solution of the quinone (**4**) (105 mg, 0.33 mmol) in methylene dichloride (5 ml) was cooled to −78 °C and boron trichloride (233 mg, 2 mmol) dissolved in methylene dichloride (10 ml) was added at a fast drip. The solution was stirred for 30 min and then warmed to room temperature. Water and more methylene dichloride were added. The residue obtained upon work-up was subjected to flash chromatography (25—50% ethyl acetate–light petroleum) and yielded first the *product* (**5**) (25 mg, 25%; 45% based on starting material consumed) as orange plates, m.p. 165—166.5 °C (from propan-2-ol) (Found: C, 62.9; H, 5.4. $C_{16}H_{16}O_6$ requires C, 63.2; H, 5.3%); $\nu_{max.}$ 3 500 (OH), 1 640 (C=O), and 1 620 and 1 570 cm^{-1} (C=C); δ 1.42 (3 H, d, *J* 6 Hz, 3-CH_3), 1.64 (3 H, d, *J* 7 Hz, 1-CH_3), 3.85 (1 H, d, *J* 2 Hz, OH, D_2O-exchangeable), *ca.* 3.90 (1 H, dq, *J* 6 and 8 Hz, 3-H largely obscured by OCH_3 and OH), 3.95 (3 H, s, OCH_3), 4.48 (1 H, ddd, *J* 8, 2, and 1.5 Hz, 4-H, collapses to dd, *J* 8 and 1.5 Hz on D_2O exchange), 4.97 (1 H, dq, *J* 1.5 and 7 Hz, 1-H), 6.68 (1 H, d, *J* 2.5 Hz, 8-H), 7.20 (1 H, d, *J* 2.5 Hz, 6-H), and 11.67 (1 H, s, OH, D_2O-exchangeable); *m/z* 304 (M^+, 2%), 287 (5), 260 (100), and 231 (75).

The second compound isolated was starting material (45 mg, 43%); this was followed by the 6-*chloroquinone* (**6**) (30 mg, 25%; 45% based on starting material consumed) as bright yellow needles, m.p. 200—201 °C (from propan-2-ol) (Found: M^+, 352.07813. $C_{17}H_{17}{}^{35}ClO_6$ requires *M*, 352.07136); $\nu_{max.}$ 3 500 (OH), 1 670 and 1 640 (C=O), and 1 590 cm^{-1} (C=C); δ 1.40 (3 H, d, *J* 6 Hz, 3-CH_3), 1.56 (3 H, d, *J* 7 Hz, 1-CH_3), 3.51 (1 H, d, *J* 3 Hz, OH), 3.98 (1 H, dq, *J* 8 and 6 Hz, 3-H), 4.00 and 4.01 (each 3 H, s, OCH_3), 4.47 (1 H, ddd, *J* 8, 3, and 1.5 Hz, 4-H), 4.92 (1 H, dq, *J* 7 and 1.5 Hz, 1-H), and 6.72 (1 H, s, 8-H); *m/z* 354 (M^+, 5%), 352 (M^+, 15%), 334 (10), 319 (13), 308 (100), and 279 (25).

The reaction was repeated on the quinone (**4**) (48 mg, 0.15 mmol) at 0 °C to afford exclusively the demethylation product (**5**) (33 mg, 72%), m.p. 165—166 °C (from propan-2-ol), identical with that just described.

1,7-*Bisisopropoxy*-5-*methoxy*-4-*naphthol* (**18**).—A solution of 1,4-benzoquinone (12.17 g, 0.113 mol) and freshly distilled Brassard's diene (30.00 g, 0.149 mol) in dry benzene (120 ml) was boiled for 1.25 h under nitrogen (or until the dark red solution turned yellow) to afford the adduct, which was not purified beyond evaporation of the solvent. Immediately upon isolation the crude adduct was dissolved in dry dimethylformamide (310 ml); isopropyl bromide (92.30 g, 0.75 mol) and anhydrous potassium carbonate (103.70 g, 0.75 mol) were then added. The mixture was vigorously stirred in a bath heated to 60 °C under nitrogen for 9 h, before being quenched with water (600 ml) and extracted with ether (8 × 100 ml); the extracts were washed with water. The residue obtained upon work-up was chromatographed (eluant 3% ethyl acetate–light petroleum) to afford the *product* (23.14 g, 71%), which crystallised as colourless plates, m.p. 52—53 °C (from 25% water–methanol) (Found: C, 70.0; H, 7.8. $C_{17}H_{22}O_4$ requires C, 70.3; H, 7.6%); $\nu_{max.}$ 3 430 (OH) and 1 620 cm^{-1} (C=C); δ 1.36 and 1.39 [each 6 H, d, *J* 6 Hz, CH(CH_3)$_2$], 3.96 (3 H, s, OCH_3), 4.46 and 4.72 [1 H each, sept, *J* 6 Hz, CH(CH$_3$)$_2$], 6.43 (1 H, d, *J* 2 Hz, 6-H), 6.56 and 6.78 (each 1 H, d, *J* 9 Hz, 2- and 3-H), 7.11 (1 H, d, *J* 2 Hz, 8-H), and 8.76 (1 H, s, OH); *m/z* 290 (M^+, 60%), 247 (35), and 205 (100).

1,7-*Bisbenzyloxy*-5-*methoxy*-4-*naphthol* (**19**) *and* 8-*Benzyl*-1,7-*bisbenzyloxy*-5-*methoxy*-4-*naphthol* (**20**).—The adduct, prepared similarly from benzoquinone (1.00 g, 9.26 mmol) and Brassard's diene (12 mmol), was dissolved in dry dimethylformamide (60 ml) under nitrogen and treated with benzyl bromide (11.08 g, 63 mmol) and anhydrous potassium carbonate (8.94 g, 63 mmol) with vigorous stirring at 60 °C. After 8 h the mixture was quenched with water, cooled, extracted with 30% ether–ethyl acetate, and worked up in the usual manner. The crude residue was passed down a filtration column (25% light petroleum–methylene dichloride) and purified further by crystallisation to afford the *product* (**19**). Chromatography (20—30% ether–light petroleum) of the supernatant followed by recrystallisation afforded additional product (**19**) (combined yield 1.52 g, 42%) as silver flakes, m.p. 159—160 °C (from 20% ethanol–chloroform) (Found: C, 77.6; H, 5.8. $C_{25}H_{22}O_4$ requires C, 77.7; H, 5.7%); $\nu_{max.}$ 3 450 (OH) and 1 630 cm^{-1} (C=C); δ 3.97 (3 H, s, OMe), 5.13 (4 H, s, CH_2), 6.58 (1 H, d, *J* 2 Hz, 6-H) 6.60 and 6.85 (each 1 H, d, *J* 8 Hz, 2- and 3-H), 7.30 (1 H, d, *J* 2 Hz, 8-H), 7.42 (10 H, s, C_6H_5), and 8.73 (1 H, s, OH); *m/z* 386 (M^+, 17%), 385 (18), 294 (90), and 91 (100). 8-*Benzyl*-1,7-*bisbenzyloxy*-5-*methoxy*-4-*naphthol* (**20**) (411 mg, 9%) was the second compound isolated by chromatography, as colourless plates, m.p. 126—127 °C (from propan-2-ol) (Found: C, 80.6; H, 5.8. $C_{32}H_{28}O_4$ requires C, 80.7; H, 5.9%); $\nu_{max.}$ 3 400 (OH) and 1 620 and 1 590 cm^{-1} (C=C); δ 3.94 (3 H, s, OCH_3), 4.76, 4.80, and 5.02 (each 2 H, s, CH_2), 6.55 (1 H, d, *J* 8 Hz, 2- or 3-H), 6.66 (1 H, s, 6-H), 6.72 (1 H, d, *J* 8 Hz, 2- or 3-H), 6.73—7.16 (10 H, m, C_6H_5), 7.40 (5 H, s, C_6H_5), and 9.13 (1 H, s, OH); *m/z* 476 (M^+, 6%), 385 (20), 295 (15), and 91 (100).

The alkylation was repeated in boiling acetone and in boiling acetonitrile. Reaction was faster but more 8-benzyl compound (**20**) was formed, which reduced the yield of the desired product to less than 30%.

1,7-*Bisisopropoxy*-4,5-*dimethoxynaphthalene* (**8**).—A mixture of the naphthol (**18**) (2.34 g, 8.1 mmol), dimethyl sulphate (5.08 g, 40.5 mmol), and anhydrous potassium carbonate (5.57 g, 40.5 mmol) in dry acetone (80 ml) was vigorously stirred and boiled for 16 h. The mixture was cooled, filtered, evaporated to an oil then taken up in ether and washed successively with concentrated ammonia, water, dilute hydrochloric acid, and finally water. The residue obtained upon work-up was chromatographed (eluant 15% ethyl acetate–light petroleum) to yield the *product* (**18**) (1.89 g, 77%) as white needles, m.p. 74.5—75 °C (from light petroleum) (Found: C, 71.3; H, 7.8. $C_{18}H_{24}O_4$ requires C, 71.0; H, 8.0%); $\nu_{max.}$ 1 620 and 1 600 cm^{-1} (C=C); δ 1.39 [12 H, d, *J* 6 Hz, CH(CH_3)$_2$], 3.88 and 3.92 (each 3 H, s, OCH_3), 4.54 and 4.74 [each 1 H, sept, *J* 6 Hz, CH(CH$_3$)$_2$], 6.52 (1 H, d, *J* 2 Hz, 6-H), 6.56 and 6.79 (each 1 H, d, *J* 8 Hz, 2- and 3-H), and 7.19 (1 H, d, *J* 2 Hz, 8-H); *m/z* 304 (M^+, 65%), 261 (50), and 219 (100).

1-7-*Bisbenzyloxy*-4,5-*dimethoxynaphthalene* (**9**).—The naphthol (**19**) (464 mg, 1.16 mmol) was similarly methylated over 3 days. Similar work-up and chromatography (30% ethyl acetate–light petroleum) afforded the *product* (**9**) (390 mg, 84%) as white needles, m.p. 116—117 °C (from propan-2-ol) (Found: C, 77.9; H, 6.2. $C_{26}H_{22}O_4$ requires C, 78.0; H, 6.0%); $\nu_{max.}$ 1 610 cm^{-1} (C=C); δ 3.90 and 3.95 (each 3 H, s, OCH_3), 5.16 and 5.17

(each 2 H, s, CH_2), 6.65 (1 H, d, *J* 2 Hz, 6-H), 6.61 and 6.80 (each 1 H, d, *J* 8 Hz, 2- and 3-H), 7.34 (1 H, d, *J* 2 Hz, 8-H), and 7.3—7.6 (10 H, m, C_6H_5); *m/z* 400 (M^+, 15%), 309 (60), and 91 (100).

3-*Acetyl*-4,5-*dimethoxy*-1,7-*bisisopropoxynaphthalene* (**23**), 8-*Acetyl*-4,5-*dimethoxy*-1,7-*bisisopropoxynaphthalene* (**29**), *and* 3,8-*Diacetyl*-4,5-*dimethoxy*-1,7-*bisisopropoxynaphthalene* (**32**).—The naphthalene (**8**) (156 mg, 0.51 mmol), stirred in dry methylene dichloride (2 ml) at room temperature, was treated with premixed glacial acetic acid (34 mg, 0.56 mmol) and trifluoroacetic anhydride (119 mg, 0.56 mmol). The solution quickly darkened but little reaction was observed (t.l.c.). Further portions of the mixed anhydride were added to 1, 4, and 20 h before the starting material was consumed. The mixture was quenched after 36 h with dilute aqueous sodium hydrogen carbonate and extracted with methylene dichloride. The residue obtained upon work-up was chromatographed (10—25% ethyl acetate–light petroleum) to yield first the *naphthalene* (**23**) (32 mg, 18%) as a colourless oil (Found: M^+, 346.1796. $C_{20}H_{26}O_5$ requires *M*, 346.1780); $\nu_{max.}$ 1 670 (C=O), and 1 620 and 1 590 cm^{-1} (C=C); δ 1.43 [12 H, d, *J* 6 Hz, $CH(CH_3)_2$], 2.78 (3 H, s, $COCH_3$), 3.83 and 4.03 (3 H each, s, OCH_3), 4.77 and 4.82 [1 H each, sept, *J* 6 Hz, $CH(CH_3)_2$], 6.67 (1 H, d, *J* 2 Hz, 6-H), 7.23 (1 H, s, 2-H), and 7.43 (1 H, d, *J* 2 Hz, 8-H); *m/z* 346 (M^+, 80%), 303 (38), 261 (88), 247 (25), and 42 (100). The *isomer* (**29**) (108 mg, 61%) was recovered next as white rosettes, m.p. 109—110 °C (from methanol) (Found: C, 69.2; H, 7.6. $C_{20}H_{26}O_5$ requires C, 69.3; H, 7.6%); $\nu_{max.}$ 1 710 (C=O) and 1 590 cm^{-1} (C=C); δ 1.33 [12 H, br d, *J* 6 Hz, $CH(CH_3)_2$], 2.60 (3 H, s, $COCH_3$), 3.93 and 4.00 (3 H each, s, OCH_3), 4.67 [2 H, br sept, *J* 6 Hz, $CH(CH_3)_2$], 6.77 (1 H, s, 6-H), and 6.80 (2 H, s, 2- and 3-H); *m/z* 346 (M^+, 100%), 304 (60), 262 (70), and 247 (80). The third compound isolated was the *diacetylnaphthalene* (**32**) (36 mg, 10%), as white rhombic crystals, m.p. 137—138 °C (from methanol) (Found: C, 67.8; H, 7.2%; M^+, 388.1874. $C_{22}H_{28}O_6$ requires C, 68.0; H, 7.3%; *M*, 388.1856); $\nu_{max.}$ 1 720 and 1 670 (C=O) and 1 610 and 1 590 cm^{-1} (C=C); δ 1.33 [12 H, br, d, *J* 6 Hz, $CH(CH_3)_2$], 2.55 (3 H, s, 8-$COCH_3$), 2.72 (3 H, s, 3-$COCH_3$), 3.77 and 4.02 (3 H each, s, OCH_3), 4.63 and 4.73 [1 H each, sept, *J* 6 Hz, $CH(CH_3)_2$], 6.67 (1 H, s, 6-H), and 7.07 (1 H, s, 2-H); *m/z* 388 (M^+, 100%), 346 (40), 304 (45), and 266 (36).

The reaction was also attempted in methylene dichloride (at 0 °C and at its b.p.) and in boiling chloroform. In all cases the product ratio remained unchanged.

3-*Acetyl*-1,7-*bisbenzyloxy*-4,5-*dimethoxynaphthalene* (**24**) *and* 8-*Acetyl*-1,7-*bisbenzyloxy*-4,5-*dimethoxynaphthalene* (**30**).—The naphthalene (**9**) (157 mg, 0.39 mmol) was acylated with the mixed anhydride in the usual manner but for a total time of 17 h. The residue obtained upon work-up was chromatographed (p.l.c. eluant 4 × 15% ethyl acetate–light petroleum) to afford starting material (15 mg, 10%) as the front band, followed by 3-*acetyl*-1,7-*bisbenzyloxy*-4,5-*dimethoxynaphthalene* (45 mg, 28% based on starting material consumed) as cream cubes, m.p. 118.5—119.5 °C (from propan-2-ol) (Found: C, 76.1; H, 6.0. $C_{28}H_{26}O_5$ requires C, 76.0; H, 5.9%); $\nu_{max.}$ 1 660 (C=O) and 1 620 and 1 590 cm^{-1} (C=C); δ 2.77 (3 H, s, $COCH_3$), 3.80 and 4.00 (each 3 H, s, OCH_3), 5.17 and 5.22 (each 2 H, s, CH_2), 6.72 (1 H, d, *J* 2 Hz, 6-H), 7.23 (1 H, s, 2-H), 7.37 (1 H, d, *J* 2 Hz, 8-H), and 7.45 (10 H, s, C_6H_5); *m/z* 442 (M^+, 15%), 400 (5), 351 (40), 309 (15), and 91 (100). The band of lowest R_F value afforded 8-*acetyl*-1,7-*bisbenzyloxy*-4,5-*dimethoxynaphthalene* (62 mg, 38% based on starting material consumed) as white needles, m.p. 137 °C (10% chloroform–methanol) (Found: C, 75.6; H, 6.0. $C_{28}H_{26}O_5$ requires C, 76.0; H, 5.9%); $\nu_{max.}$ 1 710 (C=O) and 1 590 cm^{-1} (C=C); δ 2.33 (3 H, s, $COCH_3$), 3.88 and 3.90 (each 3 H, s, OCH_3), 5.08 and 5.20 (each 2 H, s, CH_2), 6.65 and 6.88 (each 1 H, d, *J* 8 Hz, 2- and 3-H), 6.70 (1 H, s, 6-H), and 7.43 and 7.47 (each 5 H, s, C_6H_5); *m/z* 442 (M^+, 25%), 351 (65), 260 (75), and 91 (100).

In boiling chloroform the reaction was faster but the product ratio was unaltered.

1,7-*Diacetoxy*-5-*methoxy*-4-*naphthol* (**21**).—The adduct, prepared in the usual manner from benzoquinone (0.50 g, 4.6 mmol) and Brassard's diene (1.21 g, 6.0 mmol), was dissolved in dry chloroform (15 ml) under nitrogen, treated with acetic anhydride (1.18 g, 10 mmol) and pyridine (0.91 g, 10 mmol), and boiled for 0.25 h. Stirring was continued while the solution was allowed to cool for a further 0.5 h; the reaction was quenched with methanol (1 ml) and dilute hydrochloric acid. The residue obtained on work-up was recrystallised (chloroform) and chromatographed (eluant 30% ethyl acetate–light petroleum) to give the *product* (713 mg, 53%) as white cubes, m.p. 137.5—138.5 °C (from ethanol) (Found: C, 61.9; H, 4.8. $C_{15}H_{14}O_6$ requires C, 62.1; H, 4.9%); $\nu_{max.}$ 3 440 (OH), 1 760 (OAc), and 1 620 and 1 600 cm^{-1} (C=C); δ 2.35 and 2.42 (each 3 H, s, $COCH_3$), 3.97 (3 H, s, OCH_3), 6.58 (1 H, d, *J* 2 Hz, 6-H), 6.83 and 7.17 (each 1 H, d, *J* 8 Hz, 2- and 3-H), 7.13 (1 H, d, *J* 2 Hz, 8-H), and 9.07 (1 H, s, OH); *m/z* 290 (M^+, 15%), 248 (40), and 206 (100).

1,7-*Diacetoxy*-4,5-*dimethoxynaphthalene* (**10**).—The naphthol (**21**) (373 mg, 1.3 mmol) was methylated as before over 4 h. The usual work-up and chromatography (eluant 30% ethyl acetate–light petroleum) afforded the *product* (344 mg, 88%) as white needles, m.p. 135.5—136 °C (from ethanol) (Found: C, 63.1; H, 5.4. $C_{16}H_{16}O_6$ requires C, 63.2; H, 5.3%); $\nu_{max.}$ 1 760 (OAc) and 1 630 and 1 590 cm^{-1} (C=C); δ 2.32 and 2.42 (each 3 H, s, $COCH_3$), 3.95 (6 H, s, OCH_3), 6.62 (1 H, d, *J* 2 Hz, 6-H), 6.73 and 7.17 (each 1 H, d, *J* 8 Hz, 2- and 3-H), and 7.12 (1 H, d, *J* 2 Hz, 8-H); *m/z* 304 (M^+, 22%), 262 (60), and 220 (100).

1,7-*Diacetoxy*-8-*acetyl*-4,5-*dimethoxynaphthalene* (**31**).—The naphthalene (**10**) (97 mg, 0.32 mmol) was acylated with the mixed anhydride in the usual manner but for a total time of 48 h. The mixture was quenched with methanol (2 ml) then chromatographed (p.l.c. eluant 2 × 30% ethyl acetate–light petroleum) without further work-up to afford starting material (8 mg, 8%) as the front band, followed by 1,7-*diacetoxy*-8-*acetyl*-4,5-*dimethoxynaphthalene* (78 mg, 77% based on starting material consumed) as the sole indentifiable product, as white cubes, m.p. 173—174 °C (from methanol) (Found: C, 62.55; H, 5.15. $C_{18}H_{18}O_7$ requires C, 62.45; H, 5.25%); $\nu_{max.}$ 1 775 (OAc), 1 700 (CAc), and 1 630 and 1 590 cm^{-1} (C=C); δ 2.25 and 2.28 (each 3 H, s, $OCOCH_3$), 2.50 (3 H, s, $CCOCH_3$), 4.10 (6 H, s, OCH_3), 6.80 (1 H, s, 6-H), and 6.95 and 7.33 (each 1 H, d, *J* 8 Hz, 2- and 3-H); *m/z* 346 (M^+, 42%), 304 (70), 262 (100), 247 (56), and 244 (40).

1,7-*Di-t-butyldimethylsilyloxy*-4,5-*dimethoxynaphthalene* (**11**).—The adduct, prepared in the usual manner from benzoquinone (0.50 g, 4.6 mmol) and Brassard's diene (1.31 g, 6.5 mmol), was dissolved in *N*,*N*-dimethylformamide (20 ml) under nitrogen. t-Butyldimethylsilyl chloride (2.09 g, 13.9 mmol) and imidazole (1.58 g, 23.1 mmol) were added and the solution was stirred with gentle warming (bath temp. 42 °C). Initially there was no evidence of reaction (t.l.c.), but after the addition of diazabicyclononene (0.1 ml) the reaction proceeded rapidly. After 5 h the mixture was quenched with water, extracted with ether, and worked up as usual. T.l.c. and ^1H n.m.r. spectroscopy showed the presence of the naphthol (**22**) with several very minor impurities; δ 0.2 br (12 H, s, $SiCH_3$), 0.95 br (18 H, s, CCH_3), 3.9 (3 H, s, OCH_3), 6.3 (1 H, d, *J* 2 Hz, 6-H), 6.5 and 6.7 (each 1 H, d, *J* 8 Hz, 2- and 3-H), 7.1 (1 H, d, *J* 2 Hz, 8-H), and 8.8 (1 H, s, OH). The naphthol (2.01 g, 4.6 mmol)

was methylated as before over 22 h. The usual work-up and chromatography (eluant 5% ethyl acetate–light petroleum) yielded two products. The *naphthalene* (**11**) (621 mg, 30%) was isolated first as white, waxy, photosensitive plates, m.p. 82—83 °C (from methanol) (Found: C, 63.7; H, 8.9. $C_{24}H_{40}Si_2O_4$ requires C, 64.0; H, 9.0%); $\nu_{max.}$ 1 620, 1 605, and 1 590 cm^{-1} (C=C); δ 0.24 (12 H, s, $SiCH_3$), 1.02 and 1.09 (each 9 H, s, CCH_3), 3.89 and 3.93 (each 3 H, s, OCH_3), 6.47 (1 H, d, *J* 2 Hz, 6-H), 6.53 and 6.73 (each 1 H, d, *J* 8 Hz, 2- and 3-H), and 7.12 (1 H, d, *J* 2 Hz, 8-H); *m/z* 449 (M^+, 100%), 391 (18), and 73 (90). *Compound* (**12**) (or 1-t-butyldimethylsilyloxy-4,5,7-trimethoxynaphthalene?) (946 mg, 60%) was isolated as the second product, as white needles, m.p. 113—113.5 °C (from ethanol) (Found: C, 65.2; H, 8.3. $C_{19}H_{28}SiO_4$ requires C, 65.5; H, 8.1%); $\nu_{max.}$ 1 630, 1 610, and 1 600 cm^{-1} (C=C); δ 0.16 (6 H, s, $SiCH_3$), 1.02 (9 H, s, CCH_3), 3.90, 3.92, and 3.93 (each 3 H, s, OCH_3), 6.53 (1 H, d, *J* 2 Hz, 6-H), 6.67 (2 H, s, 2- and 3-H), and 7.25 (1 H, d, *J* 2 Hz, 8-H); *m/z* 348 (M^+, 100%), 333 (60), and 291 (23).

4-*Acetoxy*-1,7-*bisisopropoxy*-5-*methoxynaphthalene* (**33**).—The naphthol (**18**) (366 mg, 1.26 mmol), acetic anhydride (257 mg, 2.5 mmol), and pyridine (2 ml) were boiled together for 2 h then poured on to ice. The solid was filtered off, washed with water, dried, and chromatographed (eluant 15% ethyl acetate–light petroleum) to afford the *product* (364 mg, 87%) as white rectangular plates, m.p. 139.5—140 °C (from methanol) (Found: C, 69.0; H, 7.4. $C_{19}H_{24}O_5$ requires C, 68.7; H, 7.3%); $\nu_{max.}$ 1 770 (OAc) and 1 630 and 1 610 cm^{-1} (C=C); δ 1.39 and 1.40 [each 6 H, d, *J* 6 Hz, $CH(CH_3)_2$], 2.30 (3 H, s, $COCH_3$), 3.83 (3 H, s, OCH_3), 4.60 and 4.70 [each 1 H, d, *J* 6 Hz, $CH(CH_3)_2$], 6.50 (1 H, d, *J* 2 Hz, 6-H), 6.73 (2 H, s, 2- and 3-H), and 7.22 (1 H, d, *J* 2 Hz, 8-H); *m/z* 332 (M^+, 65%), 290 (55), 247 (95), and 204 (100).

4-*Acetoxy*-8-*acetyl*-1,7-*bisisopropoxy*-5-*methoxynaphthalene* (**34**).—The acetate (**33**) (86 mg, 0.26 mmol) was acylated with the mixed anhydride in the usual manner but for a total time of 36 h. Quenching with methanol (1 ml) followed immediately by chromatography (eluant 20% ethyl acetate–light petroleum) afforded the *product* (78 mg, 80%) as colourless plates, m.p. 176.5—177 °C (from methanol) (Found: C, 67.3; H, 7.0. $C_{21}H_{26}O_6$ requires C, 67.4; H, 7.0%); $\nu_{max.}$ 1 760 (OAc), 1 720 (CAc), and 1 630 and 1 600 cm^{-1} (C=C); δ 1.33 and 1.40 [each 6 H, d, *J* 6 Hz, $CH(CH_3)_2$], 2.33 (3 H, s, $OCOCH_3$), 2.43 (3 H, s, $CCOCH_3$), 3.90 (3 H, s, OCH_3), 4.56 and 4.67 [each 1 H, sept, *J* 6 Hz, $CH(CH_3)_2$], 6.62 (1 H, s, 6-H), and 6.70 and 6.87 (each 1 H, d, *J* 8 Hz, 2- and 3-H); *m/z* 374 (M^+, 55%), 332 (23), 290 (92), 248 (100), and 233 (35).

7-*Benzyloxy*-1,4,5-*trimethoxynaphthalene* (**13**).—1,7-Bisbenzyloxy-5-methoxy-4-naphthol (300 mg, 0.78 mmol) was dissolved in dioxane (15 ml), and silver(II) oxide (385 mg, 3.1 mmol) was added. Nitric acid (6M; 1.0 ml) was dripped into the vigorously stirred solution until the oxidant dissolved. Stirring was continued for 2 min before quenching with methylene dichloride and water. T.l.c. upon work-up showed that all the starting material had been consumed.

The crude quinone (**36**) in ether (20 ml) was shaken with an excess of saturated aqueous sodium dithionite (4 × 20 ml). The organic layer was dried and evaporated to give a light brown oil which was immediately dissolved in dry acetone (30 ml), and anhydrous potassium carbonate (1.10 g, 8 mmol) and dimethyl sulphate (1.00 g, 8 mmol) were added. The mixture was stirred and boiled under nitrogen for 18 h. The usual work-up and chromatography (eluant 12% ethyl acetate–light petroleum) afforded the *product* (200 mg, 79%) as white needles, m.p. 140—142 °C (from propan-2-ol) (Found: C, 73.9; H, 6.2. $C_{20}H_{20}O_4$ requires C, 74.0; H, 6.2%); $\nu_{max.}$ 1 600 cm^{-1} (C=C); δ 3.92 (3 H, s, OCH_3), 3.95 (6 H, s, OCH_3), 5.20 (2 H, s, CH_2), 6.72 (1 H, d, *J* 2 Hz, 6-H), 6.75 (2 H, s, 2- and 3-H), 7.38 (1 H, d, *J* 2 Hz, 8-H), and 7.3—8.5 (5 H, m, C_6H_5); *m/z* 324 (M^+, 64%), 309 (8), 205 (97), and 91 (100).

7-*Acetoxy*-1,4,5-*trimethoxynaphthalene* (**15**).—The benzyl ether (**13**) (390 mg, 1.3 mmol) was dissolved in ethyl acetate and 10% Pd–C (0.26 g) was added followed by a drop of concentrated hydrochloric acid. The solution was stirred under hydrogen for 15 min at atmospheric pressure. The catalyst was removed by filtration and the solvent by evaporation. The crude product was chromatographed (eluant 40% ethyl acetate–light petroleum) to yield the naphthol (**14**) (219 mg, 75%), δ 3.83 (3 H, s, OCH_3), 3.90 (6 H, s, OCH_3), 5.5 br (1 H, OH), 6.50 (1 H, d, *J* 2 Hz, 6-H), 6.93 (2 H, s, 2- and 3-H), and 7.16 (1 H, d, *J* 2 Hz, 8-H).

Because of its instability, the naphthol (219 mg, 0.9 mmol) was quickly treated with acetic anhydride (2.0 ml) and dry pyridine (2.0 ml) on a hot water-bath for 1 h. The mixture was quenched with methanol (1 ml) followed by dilute hydrochloric acid, and extracted with methylene dichloride. The usual work-up and chromatography (40% ethyl acetate–light petroleum) afforded the *product* (178 mg, 69%) as light brown needles, m.p. 75 °C (from methylene dichloride–light petroleum) (Found: C, 65.2; H, 5.8. $C_{15}H_{16}O_5$ requires C, 65.2; H, 5.8%); $\nu_{max.}$ 1 770 (OAc) and 1 620 and 1 605 cm^{-1} (C=C); δ 2.30 (3 H, s, $COCH_3$), 3.88 (6 H, s, OCH_3), 3.91 (3 H, s, OCH_3), 6.63 (1 H, d, *J* 2 Hz, 6-H), 6.72 (2 H, s, 2- and 3-H), and 7.56 (1 H, d, *J* 2 Hz, 8-H); *m/z* 276 (M^+, 58%), 234 (78), and 219 (100).

7-*Acetoxy*-3-*acetyl*-1,4,5-*trimethoxynaphthalene* (**37**) *and* 7-*Acetoxy*-8-*acetyl*-1,4,5-*trimethoxynaphthalene* (**38**).—The acetate (**15**) (104 mg, 0.4 mmol) was acylated with the mixed anhydride as before for a total of 40 h. The mixture was quenched with methanol (4 ml) then immediately adsorbed on silica gel and chromatographed (25—35% ethyl acetate–light petroleum) to afford starting material (3 mg, 3% followed by the *product* (**37**) (13 mg, 11% based on starting material consumed) as an oil (Found: M^+, 318.11398. $C_{17}H_{18}O_6$ requires *M*, 318.10032); $\nu_{max.}$ 1 770 (OAc), 1 680 (CAc), and 1 630 and 1 590 cm^{-1} (C=C); δ 2.33 (3 H, s, $OCOCH_3$), 2.74 (3 H, s, $CCOCH_3$), 3.76, 3.90, and 3.96 (each 3 H, s, OCH_3), 6.67 (1 H, d, *J* 2 Hz, 6-H), 7.03 (1 H, s, 2-H), and 7.52 (1 H, d, *J* 2 Hz, 8-H); *m/z* 318 (M^+, 80%), 304 (5), 276 (100), and 261 (65). The *product* (**38**) (78 mg, 65%; 67% based on starting material consumed) was recovered last as colourless needles, m.p. 131—132 °C (from methanol) (Found: C, 64.2; H, 5.7. $C_{17}H_{18}O_6$ requires C, 64.2; H, 5.7%); $\nu_{max.}$ 1 770 (OAc), 1 720 (CAc), and 1 600 cm^{-1} (C=C); δ 2.30 (3 H, s, $OCOCH_3$), 2.47 (3 H, s, $CCOCH_3$), 3.83, 3.92, and 3.97 (each 3 H, s, OCH_3), 6.70 (1 H, s, 6-H), and 6.90 (2 H, s, 2- and 3-H); *m/z* 318 (M^+, 55%), 276 (100), 261 (65), and 245 (45).

4-*Acetoxy*-3-*acetyl*-1,7-*bisisopropoxy*-5-*methoxynaphthalene* (**25**).—The naphthol (**18**) (13.63 g, 47 mmol) in a flask fitted with an efficient condenser and drying tube was boiled in dry chloroform (400 ml). Premixed glacial acetic acid (4.23 g, 70.5 mmol) and trifluoroacetic anhydride (17.77 g, 85 mmol) were added rapidly and boiling was maintained for 10 min after which a second portion of the mixed anhydride was added. After a further 10 min boiling, the dark red solution was quenched with methanol (15 ml) and the products were isolated directly by chromatography (eluant 15—50% ethyl acetate–light petroleum). The early fractions contained starting material (5.00 g, 37%), followed by a mixture of the yellow-green *naphthol* (**27**) and the colourless naphthyl acetate (**33**) (1.5 g); these were followed by 4-*acetoxy*-3-*acetyl*-1,7-*bisisopropoxy*-5-*methoxynaphthalene* (**25**) (7.04 g, 63% based on starting material consumed) as white needles, m.p. 104—105 °C from methanol) (Found: C, 67.5; H, 6.9. $C_{21}H_{26}O_6$ requires C, 67.4; H, 7.0%);

$\nu_{max.}$ 1 750 (OAc), 1 670 (CAc), and 1 630 and 1 600 cm^{-1} (C=C); δ 1.40 and 1.43 [each 3 H, d, *J* 6 Hz, $CH(CH_3)_2$], 2.38 (3 H, s, $OCOCH_3$), 2.60 (3 H, s, $CCOCH_3$), 3.88 (3 H, s, OCH_3), 4.74 and 4.75 [each 1 H, septet, *J* 6 Hz, $CH(CH_3)_2$], 6.50 (1 H, d, *J* 2 Hz, 6-H), 7.15 (2 H, s, 2- and 3-H), and 7.19 (1 H, d, *J* 2 Hz, 8-H); *m/z* 374 (M^+, 40%), 332 (80), 289 (65), and 247 (75). The last compound isolated was the *product* (**34**) (0.40 g, 3% based on starting material consumed) as white plates, m.p. 176.5—177 °C (from methanol) (no depression in admixture with authentic material). Hydrolysis of the mixture of compounds (**27**) and (**33**) with methanolic potassium hydroxide (1.5 mol equiv. as a 1% w/v solution) enhanced their separation. Reacylation of the derived naphthol (**18**) increased the overall yield of the product (**27**) to 75% after one recycle followed by hydrolysis of (**25**) to afford (**27**) as described later.

3-*Acetyl*-1,7-*bisisopropoxy*-5-*methoxy*-4-*naphthol* (**27**).—Potassium hydroxide (2.92 g, 52.1 mmol) dissolved in methanol (292 ml) was added to the ester (**25**) (13.00 g, 34.8 mmol) which, upon vigorous stirring, dissolved; the solution turned green. The reaction was quenched after 10 min with water (500 ml), dilute hydrochloric acid, and methylene dichloride (180 ml). The residue obtained upon work-up was chromatographed (eluant 15% ethyl acetate–light petroleum) to afford the *product* (10.35 g, 90%) as green cubes, m.p. 91—92 °C (from propan-2-ol) (Found: C, 68.7; H, 7.3. $C_{19}H_{24}O_5$ requires C, 68.7; H, 7.2%); $\nu_{max.}$ 3 600 (OH), 1 630 (C=O), and 1 615 and 1 590 cm^{-1} (C=C); δ 1.42 (12 H, d, *J* 6 Hz, $CH(CH_3)_2$], 2.64 (3 H, s, $COCH_3$), 4.00 (3 H, s, OCH_3), 4.55 and 4.78 [each 1 H, septet, *J* 6 Hz, $CH(CH_3)_2$], 6.53 (1 H, d, *J* 2 Hz, 6-H), 7.00 (1 H, s, 2-H), 7.12 (1 H, d, *J* 2 Hz, 8-H), and 14.10 (1 H, s, OH); *m/z* 332 (M^+, 93%), 290 (60), 247 (100), and 233 (35).

4-*Acetoxy*-3-*acetyl*-1,7-*bisbenzyloxy*-5-*methoxynaphthalene* (**26**).—The naphthol (**19**) (780 mg, 2.12 mmol), dissolved in boiling dry chloroform (8 ml), was treated with premixed glacial acetic acid (280 mg, 4.67 mmol) and trifluoroacetic anhydride (1.25 g, 5.9 mmol). The mixture was quenched after 15 min by careful addition of methanol (2 ml) and purified directly by chromatography (eluant 25—40% ethyl acetate–light petroleum) to afford the *product* (487 mg, 51%) as grey cubes, m.p. 143 °C (methylene dichloride–ethanol) (Found: C, 73.7; H, 5.6. $C_{29}H_{26}O_6$ requires C, 74.0; H, 5.6%); $\nu_{max.}$ 1 760 (OAc), 1 670 (CAc), and 1 630 and 1 615 cm^{-1} (C=C); δ 2.37 (3 H, s, $OCOCH_3$), 2.57 (3 H, s, $CCOCH_3$), 3.83 (3 H, s, OCH_3), 5.13 and 5.20 (each 2 H, s, CH_2), 6.67 (1 H, d, *J* 2 Hz, 6-H), 7.30 (1 H, s, 2-H), 7.37 (1 H, d, *J* 2 Hz, 8-H), and 7.43 and 7.47 (each 5 H, s, C_6H_5); *m/z* 470 (M^+, 5%), 424 (2), 337 (40), 295 (3), and 91 (100).

3-*Acetyl*-1,7-*bisbenzyloxy*-5-*methoxy*-4-*naphthol* (**28**).—The ester (**26**) (119 mg, 0.25 mmol) was dissolved in dioxane (2 ml). Potassium hydroxide (21 mg, 0.38 mmol) dissolved in ethanol (21 ml) was added rapidly and the solution was stirred for 2 min, then quenched with hydrochloric acid (0.5M). Partitioning with methylene dichloride and chromatography (eluant 30% ethyl acetate–light petroleum) of the residue obtained upon work-up afforded the *product* (58 mg, 54%) as pale yellow-green needles, m.p. 145 °C (from methylene dichloride–ethanol) (Found: C, 75.6; H, 5.7. $C_{27}H_{24}O_5$ requires C, 75.7; H, 5.7%); $\nu_{max.}$ 3 600 (OH), 1 630 (CAc), and 1 610 and 1 590 cm^{-1} (C=C); δ 2.58 (3 H, s, CCH_3), 3.97 (3 H, s, OCH_3), 5.13 (4 H, s, CH_2), 6.60 (1 H, d, *J* 2 Hz, 6-H), 6.94 (1 H, s, 2-H), 7.30 (1 H, d, *J* 2 Hz, 8-H), 7.38 (10 H, s, C_6H_5), and 14.05 (1 H, s, OH); *m/z* 428 (M^+, 10%), 337 (55), and 91 (100).

Crystal Structure of 7-O-*Methyl Quinone A* (**5**).—Preliminary photography of single crystals of compound (**5**) established a triclinic lattice. Accurate cell dimensions were obtained by least squares techniques from the settings of 25 high-order reflections measured with a Philips PW1100 four-circle diffractometer with graphite-monochromated Mo-K_α radiation (λ 0.7107 Å). Intensities were collected by the ω—2θ scan technique. The intensities of three reference reflections were monitored periodically to ascertain crystal stability. Lorentz-polarization corrections were applied but no correction was made for absorption. Crystal data and experimental details of the data collection are listed in Table 2.

Solution and refinement of the structure. An examination of *E* statistics obtained on data reduction indicated that the space group is $P\bar{1}$. Regrettably, no solution could be obtained by the various direct methods available in SHELX-76;[20] this is most likely because the structure is a very planar molecule in a symmorphic space group. However, all non-hydrogen atom co-ordinates were ultimately obtained from an *E*-map generated using a preliminary version of SHELX-84[21] on default settings of the direct-methods routine. Difference syntheses and refinements were carried out using SHELX-76.[20] Owing to the large number of independent atoms, final refinements in which all non-hydrogen atoms were treated anisotropically were carried out using the blocked-matrix technique; methyl groups were refined as rigid systems; all other C–H hydrogen atoms were placed at calculated positions dictated by the geometry of the molecules (C–H 1.00 Å). The variety of O(–H)···O non-bonded inter- and intra-molecular distances < 3.0 Å (see main text) indicated that a number of H-bonding schemes are probable, each of which optimized with a different hydroxy-H location. As no significant electron density in these areas was revealed in the Fourier analyses, these hydrogen atoms have been omitted from the final model.

Details of the final refinements are shown in Table 2. In the final cycles, the mean e.s.d. of the parameters of the non-hydrogen atoms were > 50 times the average parameter shift; the final difference map was smooth with the largest residual electron density 0.5 e $Å^{-3}$.

Complex neutral atom scattering factors were used for C and O,[22] and for H,[23] with dispersion corrections.[24] Table 3 lists the final fractional atomic co-ordinates and temperature factors for all the non-hydrogen atoms. Calculations on the molecular geometry were carried out using XANADU[25] and illustrations were obtained using PLUTO.[26] Co-ordinates of all the atoms, including hydrogen, anisotropic temperature factors, all bond lengths and angles, selected torsion angles, and parameters of the least squares planes calculated, have been deposited at the Cambridge Crystallographic Data Centre.*

Acknowledgements

Financial support from the Council for Scientific and Industrial Research and from the Council of the University of Cape Town is gratefully acknowledged. M. L. N. thanks the organisers and participants of the School on Direct Methods and Macromolecular Crystallography, July 1983, held at the Medical Foundation of Buffalo Inc. Research Laboratories, N.Y., U.S.A., where assistance in the solution of the crystal structure was received.

* See Instructions for Authors, *J. Chem. Soc., Perkin Trans. 1*, Issue 1, 1988.

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Received 20*th July* 1987; *Paper* 7/1308