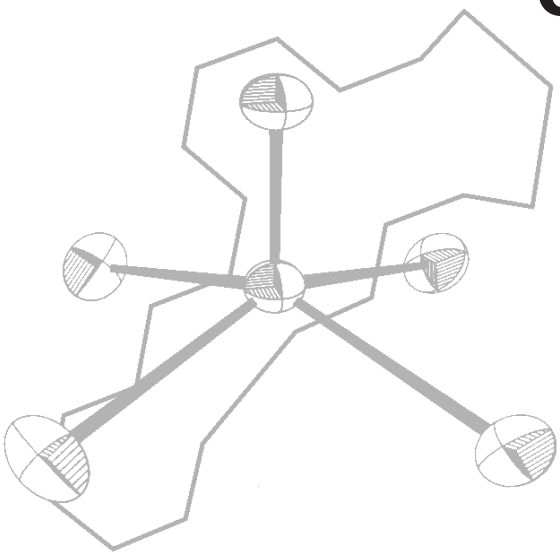
CSIRO PUBLISHING

# Australian Journal of Chemistry



Volume 52, 1999


A journal for the publication of original research
in all branches of chemistry and chemical technology

**www.publish.csiro.au/journals/ajc**

All enquiries and manuscripts should be directed to
The Managing Editor
*Australian Journal of Chemistry*
**CSIRO** PUBLISHING
PO Box 1139 (150 Oxford St)
Collingwood Telephone: 61 3 9662 7630
Vic. 3066 Facsimile: 61 3 9662 7611
Australia Email: john.zdysiewicz@publish.csiro.au

Published by **CSIRO** PUBLISHING
for CSIRO Australia and
the Australian Academy of Science

*Aust. J. Chem.*, 1999, **52**, 1165–1171

# Reaction of 2-Acetoxy-3-chloro and 2,3-Diacetoxy Naphthoquinones with 1,3-Dioxy and 1,1,3-Trioxy Butadienes

*Donald W. Cameron*[A,B] *and Andrew G. Riches*[A]

[A] School of Chemistry, The University of Melbourne, Parkville, Vic. 3010.
[B] Author to whom correspondence should be addressed.

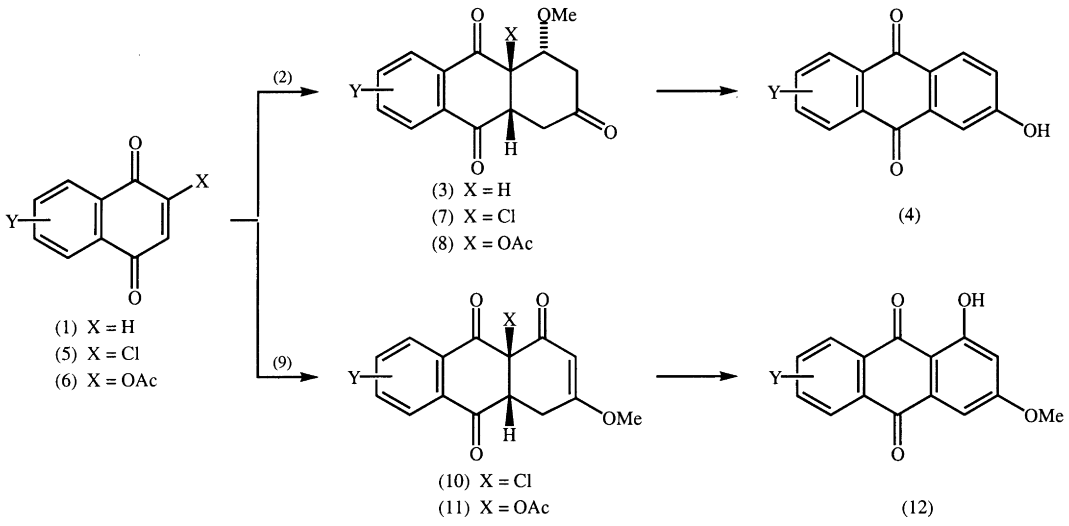
Reaction of 2-acetoxy-3-chloro naphthoquinones towards the 1,3-dioxy diene (2) and the 1,1,3-trioxy diene (9) was examined. The competing influence of the acetoxy and chloro substituents was assessed from the regiochemistry of the resulting Diels–Alder chemistry, as was competition between that process and Michael addition/elimination. Reaction of the same dienes towards the less reactive 2,3-diacetoxy naphthoquinone (25) was also investigated.

## Introduction

2,3-Unsubstituted naphthoquinones (1) undergo cycloaddition to the polarized buta-1,3-diene (2), with established regiochemistry dictated by the benzenoid substituent.[1] This follows from oxidative aromatization of the derived products (3) to identifiable anthraquinones (4). A 2-chloro or 2-acetoxy substituent on the naphthoquinone, as in structures (5) and (6), leads to analogous cycloaddition but regiochemistry is then largely controlled by the quinonoid substituent, giving the respective products (7) and (8), and thence anthraquinones (4) by elimination. Use of the more reactive 1,1,3-trioxy diene (9) in place of (2) leads to analogous outcomes. In particular, cycloaddition of (9) with quinones (5) and (6) leads to the relatively unstable products (10) and (11), which undergo aromatization to 1,3-dioxy anthraquinones (12) (Scheme 1).[2,3]

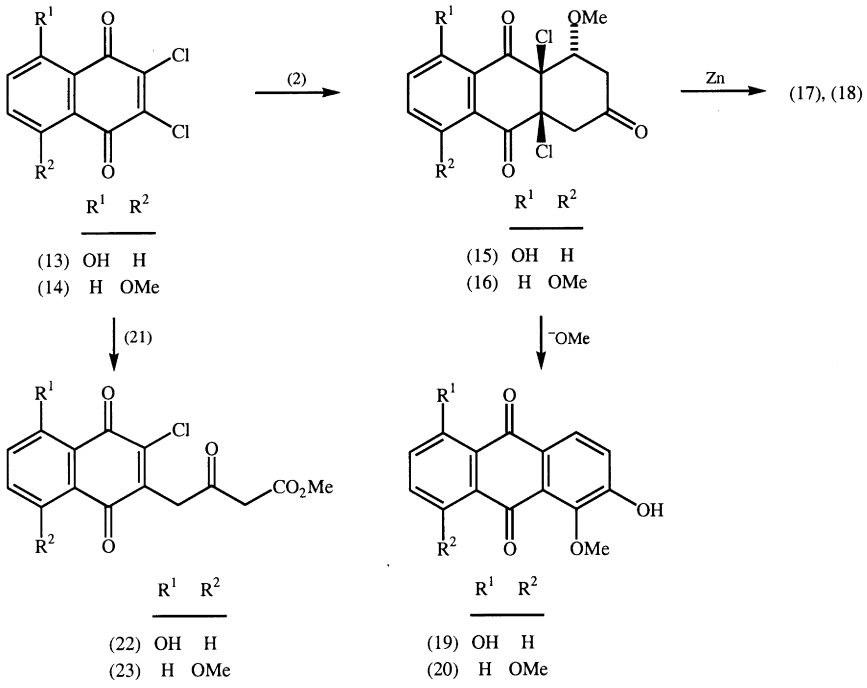
Earlier work here has shown that the 2,3-dichloro naphthoquinones (13) and (14) react with diene (2), albeit less readily. Regiochemistry was controlled by the benzenoid substituent, giving the respective products (15) and (16). These underwent reductive aromatization to anthraquinones (17) and (18), allowing the orientation of addition to be confirmed. They also underwent useful, non-reductive aromatization on treatment with nucleophiles like sodium methoxide, giving the respective 1,2-disubstituted anthraquinones (19) and (20).[4] However, towards the more polarized 1,1,3-trioxy diene (21), the quinones (13) and (14) reacted only by Michael addition/elimination to give esters (22) and (23) (Scheme 2).[5,6]

The paper seeks to extend the chemistry of Scheme 2 by replacing one or both of the quinonoid chloro groups by acetoxy, to assess whether such substrates could then be used




Scheme 1

Manuscript received 16 December 1999  10.1071/CH99179 0004-9425/99/121165



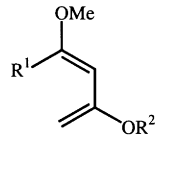

| | $R^1$ | $R^2$ |
|---|---|---|
| (13) | OH | H |
| (14) | H | OMe |

| | $R^1$ | $R^2$ |
|---|---|---|
| (15) | OH | H |
| (16) | H | OMe |

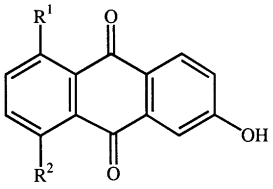
| | $R^1$ | $R^2$ |
|---|---|---|
| (22) | OH | H |
| (23) | H | OMe |

| | $R^1$ | $R^2$ |
|---|---|---|
| (19) | OH | H |
| (20) | H | OMe |

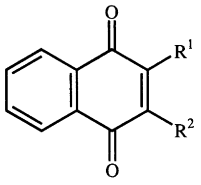
Scheme 2



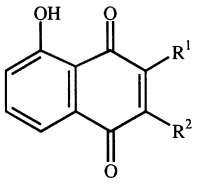
| | $R^1$ | $R^2$ |
|---|---|---|
| (2) | H | $SiMe_3$ |
| (9) | $OSiMe_3$ | Me |
| (21) | $OSiMe_3$ | $SiMe_3$ |



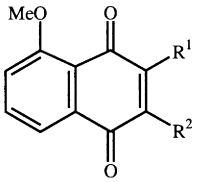
| | $R^1$ | $R^2$ |
|---|---|---|
| (17) | OH | H |
| (18) | H | OMe |
| (36) | H | H |
| (37) | H | OH |
| (41) | OMe | H |



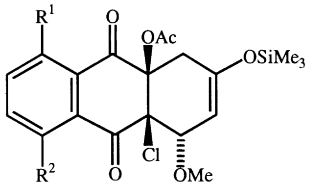
| | $R^1$ | $R^2$ |
|---|---|---|
| (24) | OAc | Cl |
| (25) | OAc | OAc |
| (44) | Cl | Cl |



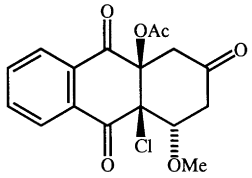
| | $R^1$ | $R^2$ |
|---|---|---|
| (26) | OH | Cl |
| (27) | Cl | OH |
| (28) | OAc | Cl |
| (29) | Cl | OAc |



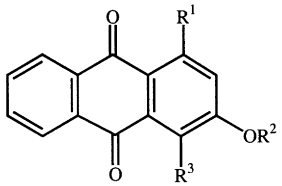
| | $R^1$ | $R^2$ |
|---|---|---|
| (30) | OAc | Cl |
| (31) | Cl | OAc |
| (32) | OH | Cl |



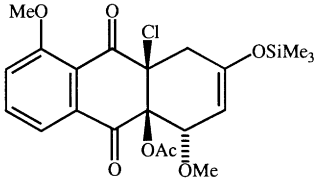
| | $R^1$ | $R^2$ |
|---|---|---|
| (33) | H | H |
| (38) | OH | H |
| (39) | H | OH |
| (40) | OMe | H |
| (42) | H | OMe |



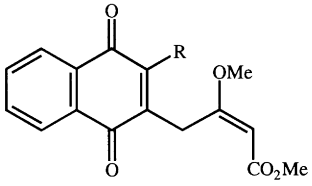
(34)



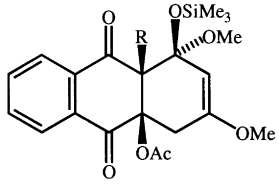
| | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|
| (35) | H | H | OMe |
| (48) | OH | Me | H |



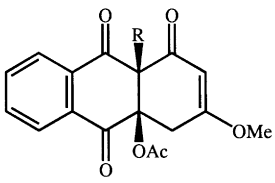
(43)



(45) R = Cl
(49) R = OAc



(46) R = Cl
(51) R = OAc



(47) R = Cl
(50) R = OAc

for forming cycloadducts containing angular oxy substituents, such as occur in natural products.[7,8]

## Results and Discussion

At the start of this work, the simple 2-acetoxy-3-chloro and 2,3-diacetoxy quinones (24) and (25) were known.[9,10] New analogues of the former, containing a 5(8)-oxy substituent, were synthesized from dichlorojuglone (13).[4,11] This was first converted into the isomeric chloro dihydroxy quinones (26) and (27) by literature procedures.[12,13] Their regiochemistry was confirmed by $^1$H n.m.r. spectroscopy, the chelated hydroxy proton of (27) (δ 12.03) being considerably deshielded relative to that of (26) (δ 11.00). For analogous isomeric naphthoquinones, such deshielding of an α-hydroxy proton has been associated with conjugative electron donation to its chelated carbonyl partner by the electronically significant 2(3)-hydroxy group.[14]

Selective acetylation of (26) and (27) gave the new monoacetates (28) (79%) and (29) (54%) respectively. Their $^1$H n.m.r. spectra each contained a single acetoxy resonance and retained a chelated hydroxy resonance. Again, they were differentiated by deshielding of the chelated proton for (29) (δ 11.69) relative to that of (28) (δ 11.49), its magnitude diminished following acetylation.

The isomeric methoxy quinones (30) and (31) were then obtained, the latter by *O*-methylation of (29) with iodomethane/silver(I) oxide (72%). Analogous direct methylation of (28) to give (30) proved unsuccessful, however, because of particularly easy hydrolysis of the acetate group in the weakly basic environment. The desired (30) was obtained instead from 2,3-dichloro-5-methoxy-1,4-naphthoquinone (14).[4,15] This underwent displacement of the 3-chloro group to give the known hydroxy compound (32), which on acetylation gave (30) (90%).

The acetoxy chloro substrates (28)–(31) were then treated separately with diene (2), after elaborating preliminary work here that showed that the parent acetoxy chloro quinone (24) reacted with (2) to give the stoichiometric adduct (33) (79%). Its regiochemistry was confirmed by X-ray crystallography, consistent with orientational control of cycloaddition having been dominated by the chloro group (Scheme 1).[16]

Mild hydrolysis of adduct (33) with dilute hydrochloric acid gave the trione (34) (86%). Its chemistry qualitatively resembled that of analogous dichloro products of Scheme 2. It reacted with sodium methoxide to give 2-hydroxy-1-methoxy-9,10-anthraquinone (35) (53%), whose $^1$H n.m.r. spectrum contained a new methoxy singlet (δ 4.04) and two *ortho*-coupled doublets (δ 8.14, 7.36). No intermediate retaining an angular substituent could be identified and attempts at deliberately hydrolysing the acetate group of (34) prior to aromatization, by milder treatment, were unsuccessful.

Reductive aromatization of (34) also paralleled the dichloro series (Scheme 2), treatment with zinc in acetic acid giving 2-hydroxy-9,10-anthraquinone (36) (54%). This mode of aromatization was then used to establish the regiochemistry of cycloaddition of the α-substituted quinones (28)–(31).

On separate reaction of the α-hydroxy quinones (28) and (29) with an excess of diene (2) in benzene, each detectably gave a single stoichiometric cycloadduct, based on the $^1$H n.m.r. spectrum of the crude product. Without purification, each was treated with zinc in acetic acid to give the 1,7-dihydroxy anthraquinone (37) from (28) and its 1,6-isomer (17) from (29). In each case identity was confirmed by spectroscopic comparison with independently synthesized material.[17] The α-hydroxy resonance of (17) (δ 12.70) was deshielded relative to its counterpart in the spectrum of (37) (δ 12.37), reflecting the conjugative influence of the ß-hydroxy group.

These outcomes are consistent with reaction of (28) and (29) proceeding through the respective stoichiometric adducts (38) and (39). The orientation of cycloaddition was thus parallel to that observed for formation of (33), dominated by the chloro group and relatively unaffected by the hydroxyl. This was particularly noteworthy for the conversion of (28) into (38), where the α-hydroxy group in isolation would have facilitated the opposite regiochemistry.

The α-methoxy quinone (30) reacted analogously with (2) to give a single adduct within the limits of $^1$H n.m.r. spectroscopic detection. Its structure was assigned as (40), since it underwent reductive aromatization to give the anthraquinone (18), whose structure was confirmed by demethylation to (37).

These parallel outcomes contrasted with the behaviour of the isomeric methoxy quinone (31) towards (2). Analysis of the crude product by $^1$H n.m.r. spectroscopy showed a 1 : 1 mixture of stoichiometric cycloadducts. On reductive aromatization this gave a mixture of two anthraquinones formulated as (18) and (41), since demethylation led to a 1 : 1 mixture of the dihydroxy isomers (37) and (17). This supports the two adducts from (31) being the isomeric systems (42) and (43). Competitive formation of the latter product unpredictably could reflect the isolated electronic influences of the methoxy and acetoxy groups of (31) outweighing that of the chloro group.

By comparison with the reactivity of these acetoxy chloro quinones towards diene (2), the diacetoxy quinone (25) could not be made to react at all; heating the mixture eventually led to decomposition. The relative importance of electronic and steric effects in impeding addition is unclear. Modifying acetate (25) as the analogous formate, trifluoroacetate or oxalate, in the hope of improving its dienophilicity, proved unsatisfactory owing to the ease with which these derivatives underwent decomposition.

Attention was then directed towards treating the parent acetoxy chloro quinone (24) with the more highly polarized 1,1,3-trioxy diene (9). In regard to the dichloro–quinone chemistry of Scheme 2, this diene was expected to behave like (21) except for greater stability of the ß-methoxy group over ß-trimethylsilyloxy.

To establish a benchmark, diene (9) was first treated with 2,3-dichloro-1,4-naphthoquinone (44) at room temperature. This gave the anticipated Michael addition/elimination product (45) (45% after isolation) as the only observed outcome. Its $^1$H n.m.r. spectrum indicated that it was a single

isomer of undetermined geometry, showing an olefinic proton (δ 5.18), two equivalent methylene protons (δ 4.51) and two *O*-methyl groups (δ 3.74, 3.57). Its mass spectrum showed an appropriate molecular ion incorporating a monochloro isotope pattern.

In marked contrast to this Michael chemistry, reaction of diene (9) with the acetoxy chloro quinone (24) followed by careful workup gave the cycloadduct (46) (45%) as the only detected product. This is the first such cycloadduct to be observed from reaction between a 1,1,3-trioxy diene and a 2,3-disubstituted quinone. Its $^1$H n.m.r. spectrum showed signals for the trimethylsilyloxy (δ 0.20), α- and β-methoxy groups (δ 2.83, 3.66), the olefinic proton (δ 4.58), and two differentiated methylene protons (δ 3.76, 2.58) of appropriate multiplicity. Its acetoxy signal (δ 1.75) was shielded by 0.70 ppm relative to that of (24). The regiochemistry of addition was inferred by analogy with the parallel cycloaddition of (24) to diene (2), leading to (33).

Mild acidic hydrolysis of this adduct (46) gave the trione (47). Its $^1$H n.m.r. spectrum lacked any trimethylsilyloxy resonance, while the olefinic (δ 5.35) and β-methoxy signals (δ 3.80) were both deshielded relative to their counterparts of (46). The spectrum showed conformational mobility. The olefinic, methylene and acetoxy signals all were broad at room temperature and were sharpened considerably at 45°.

The trione (47) was subjected to each of the two aromatizing conditions developed for the dichloro adducts of Scheme 2. Treatment with zinc in acetic acid gave parallel behaviour, efficiently giving 1-hydroxy-3-methoxy-9,10-anthraquinone (48). Its $^1$H n.m.r. spectrum showed *meta*-coupled doublets for H 2 (δ 6.72) and H 4 (δ 7.39), together with appropriate hydroxy (δ 12.91) and methoxy (δ 3.95) resonances. However treatment of (47) with sodium methoxide was not straightforward, even brief contact giving an intractable mixture of products as shown by chromatographic analysis.

Reaction of 2,3-diacetoxy-1,4-naphthoquinone (25) with the trioxy diene (9) was slower than for (24). Two products were isolated by chromatography. The major, yellow component (49) corresponded to Michael addition/elimination. Its $^1$H n.m.r. spectrum resembled that of its chloro analogue (45) but showed an additional acetoxy signal (δ 2.32). Its mass spectrum contained an appropriate molecular ion (*m/z* 344).

The minor, colourless product (5%) was the trione (50), presumably derived by hydrolysis of a stoichiometric cycloadduct (51) during chromatography. Its $^1$H n.m.r. spectrum contained one methoxy resonance (δ 3.78), two acetoxy resonances (δ 2.29, 2.25), and resonances corresponding to olefinic (δ 5.37) and differentiated methylene (δ 3.15, 2.96) protons. Its mass spectrum contained an appropriate molecular ion (*m/z* 372). Direct spectroscopic evidence for the cycloadduct (51) was obtained following trituration of the crude reaction mixture prior to chromatography but, because of its low yield and instability, it could not be purified.

As for the related trione (47), treatment of (50) with sodium methoxide led to an intractable mixture of products. In contrast to (47), however, treatment with zinc in acetic acid did not lead to aromatization, resulting only in recovery of unreacted trione. This stability could be useful in synthesizing angular dioxy-substituted polycycles, if cycloaddition chemistry leading to products such as (50) could be made preparatively more efficient. However, a major limitation to doing so remains the unpredictability of cycloaddition versus Michael outcomes for reaction combinations involving a polarized diene like (9). The fine balance between these competing processes is illustrated by the three reactions of (9) with the dichloro (44), acetoxy chloro (24) and diacetoxy (25) quinones; the first led only to Michael chemistry, the second only to cycloaddition and the third to a mixture of the two.

## Experimental

*General*

Melting points were determined on a Kofler hot stage and are uncorrected. Microanalyses were carried out by National Analytical Laboratories, Melbourne, or Chemical and Microanalytical Services, Geelong. Electronic spectra were recorded in ethanol containing 1% formic acid (v/v), unless otherwise stated, on a Varian Superscan 3 spectrophotometer. Infrared spectra were recorded on a Perkin Elmer 983-G grating spectrophotometer. Solids were recorded as potassium bromide disks and liquids as films between sodium chloride plates. Proton nuclear magnetic resonance ($^1$H n.m.r.) spectra were recorded at 399.65 MHz on a JEOL JNM-GX400 spectrometer. The solvent was (D)chloroform unless otherwise stated. High- and low-resolution mass spectra were recorded by using a V.G. Micromass 7070F instrument or a JEOL JMS-AX505H mass spectrometer at 70 eV, unless otherwise stated. In general, only peaks greater than 20% are quoted. Analytical and preparative thin-layer chromatography (t.l.c.) were carried out on glass plates coated with a layer of silica gel [Merck Kieselgel 60 $GF_{254}$ or Merck Kieselgel 60 $GF_{254}$ containing 2% oxalic acid (oxalated silica)]. The separated components were extracted from the silica with ethyl acetate or dichloromethane. Oxalic acid was removed by washing the extracts with water and then drying over magnesium sulfate prior to evaporation. Flash chromatography was carried out using Merck Kieselgel No. 9385. All solvents were of A.R. grade or were redistilled prior to use. Petrol refers to the hydrocarbon fraction boiling in the range 60–80°. All diene preparations and reactions were performed under dry nitrogen in flame-dried glassware. Acid-sensitive cycloadditions were performed in glassware which had been previously washed with aqueous ammonia solution followed by distilled water. Organic extracts were generally dried over magnesium sulfate before evaporation at reduced pressure.

*2-Acetoxy-3-chloro-1,4-naphthoquinone (24)*

This was prepared from 2-chloro-3-hydroxy-1,4-naphthoquinone according to the literature, m.p. 142–143° (lit.[9] 142°). δ 8.22–8.18, m, H 5 or H 8; 8.16–8.12, m, H 5 or H 8; 7.82–7.57, m, H 6, H 7; 2.45, s, OAc.

*2-Chloro-3,5-dihydroxy-1,4-naphthoquinone (26)*

This was prepared from 2,3-dichloro-5-hydroxy-1,4-naphthoquinone (13)[11] according to the literature, m.p. 191–193° (lit.[12] 191°). δ 11.00, s, 5-OH; 7.76, dd, *J* 7.3, 1.5 Hz, H 8; 7.69, app. t, spacings 7.9 Hz, H 7; 7.55, br s, 3-OH; 7.27, dd, *J* 8.4, 1.5 Hz, H 6.

*3-Chloro-2,5-dihydroxy-1,4-naphthoquinone (27)*

This was prepared from 2-anilino-3-chloro-5-hydroxy-1,4-naphthoquinone[12] by the method of Thomson, m.p. 221–224° (lit.[13] 224°). δ 12.03, s, 5-OH; 7.72, dd, *J* 7.3, 1.1 Hz, H 8; 7.61, app. t, spacings 8.3 Hz, H 7; 7.35, dd, *J* 8.3, 1.2 Hz, H 6. *m/z* 226 (M [$^{37}$Cl], 32%), 224 (M [$^{35}$Cl], 100), 196 (44), 168 (21), 121 (24).

*3-Acetoxy-2-chloro-5-hydroxy-1,4-naphthoquinone (28)*

A mixture of the dihydroxy naphthoquinone (26)[12] (185 mg) and acetic anhydride (3 $cm^3$) was heated to 100° for 5 h and then cooled.

Water (30 $cm^3$) was added and the mixture was stirred vigorously until the excess of acetic anhydride was hydrolysed. The mixture was then extracted with ether (2×20 $cm^3$). The extract was washed with water (100 $cm^3$), brine (100 $cm^3$), and then dried and evaporated. Recrystallization of the orange residue from ethyl acetate/petrol gave the *acetoxy naphthoquinone* (28) (173 mg, 79%) as orange blocks, m.p. 138–140° (Found: C, 53.9; H, 2.5. $C_{12}H_7C1O_5$ requires C, 54.1; H, 2.7%). $\lambda_{max}$ (log ε) 239, 433 nm (4.21, 3.72). $\nu_{max}$ 1778, 1674, 1644, 1615 $cm^{-1}$. δ 11.49, s, OH; 7.76, dd, *J* 7.3, 1.3 Hz, H 8; 7.67, app. t, spacings 7.9 Hz, H 7; 7.32, dd, *J* 8.4, 1.3 Hz, H 6; 2.45, s, OAc. *m/z* 268 (M [$^{37}$Cl], 2%), 266 (M [$^{35}$Cl], 8), 224 (30).

*2-Acetoxy-3-chloro-5-hydroxy-1,4-naphthoquinone (29)*

Quinone (27) (504 mg) was added to acetic anhydride (7 $cm^3$) and the mixture was heated to 70° for 3 h. The excess of acetic anhydride was evaporated under reduced pressure and the residue was recrystallized from dichloromethane/petrol to give the *acetoxy naphthoquinone* (29) (324 mg, 54%) as yellow needles, m.p. 140–142° (Found: C, 54.0; H, 2.6. $C_{12}H_7C1O_5$ requires C, 54.1; H, 2.7%). $\lambda_{max}$ (log ε) ($CHCl_3$) 383, 434 nm (4.19, 3.69). $\nu_{max}$ 1779, 1678, 1641 $cm^{-1}$. δ 11.69, s, OH; 7.71–7.64, m, H 7, H 8; 7.33, dd, *J* 8.1, 1.4 Hz, H 6; 2.44, s, OAc. *m/z* 268 (M [$^{37}$Cl], 2%], 266 (M [$^{35}$Cl], 7), 224 (85), 196 (20).

*2-Chloro-3-hydroxy-5-methoxy-1,4-naphthoquinone (32)*

To a solution of 2,3-dichloro-5-methoxy-1,4-naphthoquinone (14)[15] (92 mg) in methanol (15 $cm^3$) was added a solution of potassium hydroxide (200 mg) in water (15 $cm^3$) and the mixture was stirred at room temperature for 1 h. It was then poured into cold water (75 $cm^3$) and acidified with concentrated hydrochloric acid. The precipitate was collected, washed with water and dried to give the hydroxy naphthoquinone (32) (85 mg, 100%) as yellow needles, m.p. 253–255° (lit.[15] 261°). δ 7.99, br s, OH; 7.88, br d, *J* 7.8 Hz, H 8; 7.76, app. t, spacings 8.1 Hz, H 7; 7.31, br d, *J* 8.4 Hz, H 6; 4.06, s, OMe.

*3-Acetoxy-2-chloro-5-methoxy-1,4-naphthoquinone (30)*

To the naphthoquinone (32) (85 mg) was added acetic anhydride (5 $cm^3$) and sulfuric acid (1 drop) and the mixture was gently warmed over a steam bath until homogeneous. Water (50 $cm^3$) was then added and the mixture was stirred vigorously until the acetic anhydride had completely hydrolysed. The mixture was then extracted with ether (2×25 $cm^3$) and the extract was washed with water (2×50 $cm^3$), brine (50 $cm^3$), and then dried and evaporated. The residue was recrystallized from ethyl acetate/petrol to give the *acetoxy naphthoquinone* (30) (90 mg, 90%) as yellow needles, m.p. 112–114° (Found: C, 55.6; H, 3.4. $C_{13}H_9ClO_5$ requires C, 55.6; H, 3.2%). $\lambda_{max}$ (log ε) ($CHCl_3$) 250sh, 277, 410 nm (4.06, 4.21, 3.67). $\nu_{max}$ 1772, 1671, 1627, 1582 $cm^{-1}$. δ 7.86, d, *J* 8.3 Hz, H 8; 7.73, app. t, spacings 8.3 Hz, H 7; 7.35, d, *J* 8.3 Hz, H 6; 4.02, s, OMe; 2.43, s, OAc. *m/z* 280 (M [$^{35}$Cl], 1%), 240 (40), 238 (100).

*2-Acetoxy-3-chloro-5-methoxy-1,4-naphthoquinone (31)*

To a solution of the naphthoquinone (27) (163 mg) in dichloromethane (10 $cm^3$) was added iodomethane (1 $cm^3$) and silver(I) oxide (753 mg) and the mixture was stirred vigorously at room temperature for 6 h, then filtered through Celite and evaporated. Recrystallization of the residue from ethyl acetate/petrol gave the *acetoxy naphthoquinone* (31) (124 mg, 72%) as yellow needles, m.p. 150–151° (Found: C, 55.8; H, 3.1. $C_{13}H_9ClO_5$ requires C, 55.6; H, 3.2%). $\lambda_{max}$ (log ε) ($CHCl_3$) 250sh, 278, 409 nm (3.99, 4.14, 3.57). $\nu_{max}$ 1761, 1674, 1628, 1581 $cm^{-1}$. δ 7.79, dd, *J* 7.7, 1.2 Hz, H 8; 7.71, dd, *J* 8.5, 7.7 Hz, H 7; 7.35, dd *J* 8.5, 1.2 Hz, H 6; 4.03, s, OMe; 2.42, s, OAc. *m/z* 280 (M [$^{35}$Cl], 5%), 240 (22), 238 (50).

*2,3-Diacetoxy-1,4-naphthoquinone (25)*

To a suspension of 2,3-dihydroxy-1,4-naphthoquinone[10] (129 mg) in acetic anhydride (5 $cm^3$) was added concentrated sulfuric acid (2 drops) and the mixture was warmed on the steam bath until solution was complete. It was then cooled, water (20 $cm^3$) was added and the mixture was stirred vigorously until hydrolysis of the acetic anhydride was complete. It was then extracted into ether (2×30 $cm^3$) and the extract was washed with water (2×50 $cm^3$), brine (50 $cm^3$), and then dried and evaporated. Crystallization of the residue from ethyl acetate/petrol gave 2,3-diacetoxy-1,4-naphthoquinone (25) (172 mg, 92%) as pale yellow needles, m.p. 113–114° (lit.[10] 105–106°). δ 8.11, m, H 5, H 8; 7.76, m, H 6, H 7; 2.37, s, 2×OAc. *m/z* (24 eV) 232 (43%), 190 (36), 162 (86).

*(1α,4aβ,9aβ)-4a-Acetoxy-9a-chloro-1-methoxy-3-trimethylsilyloxy-1,4,4a,9a-tetrahydroanthracene-9,10-dione (33)*

Diene (2)[18] (796 mg) was added to a solution of quinone (24) (241 mg) in benzene (2 $cm^3$) and the mixture was stirred at room temperature for 5 days. The solvent was removed and the residue was crystallized from petrol to give the *anthracenedione* (33) (320 mg, 79%) as colourless needles, m.p. 124–129° (Found: C, 56.9; H, 5.6. $C_{20}H_{23}ClO_6Si$ requires C, 56.8; H, 5.5%). $\lambda_{max}$ (log ε) ($CHCl_3$) 239, 256, 300 nm (4.07, 4.01, 3.21). $\nu_{max}$ 1749, 1722, 1707, 1653 $cm^{-1}$. δ 8.15, dd, *J* 6.4, 2.2 Hz, H 5 or H 8; 7.89, dd, *J* 6.5, 2.2 Hz, H 5 or H 8; 7.73–7.69, m, H 6, H 7; 5.03, ddd, *J* 5.4, 2.0, 1.0 Hz, H 2; 4.23, d, *J* 5.4 Hz, H 1; 3.69, dd, *J* 17.1, 1.0 Hz, H 4α; 2.48, dd, *J* 17.1, 2.0 Hz, H 4β; 2.89, s, OMe; 1.76, s, OAc; 0.31, s, $OSiMe_3$. *m/z* 422 (M [$^{35}$Cl], 0.3%), 363 (42), 333 (21), 331 (53), 328 (23), 327 (88), 297 (44), 281 (25), 224 (31), 172 (54), 163 (27), 157 (71), 147 (28), 141 (41).

*(4α,4aβ,9aβ)-9a-Acetoxy-4a-chloro-4-methoxy-3,4,4a,9a-tetrahydroanthracene-2,9,10(1*H*)-trione (34)*

To a solution of adduct (33) (308 mg) in tetrahydrofuran (7 $cm^3$) was added 0.1 M hydrochloric acid (20 drops) and the mixture was stirred at room temperature for 3 h. It was then diluted with water (30 $cm^3$) and extracted with ethyl acetate (2×20 $cm^3$). The extract was washed with water (50 $cm^3$), brine (50 $cm^3$), and then dried and evaporated. The residue was crystallized from ethyl acetate/petrol to give the *anthracenetrione* (34) (220 mg, 86%) as colourless prisms, m.p. 162–163° (Found: C, 58.0; H, 4.4. $C_{17}H_{15}ClO_6$ requires C, 58.2; H, 4.3%). $\lambda_{max}$ (log ε) ($CHCl_3$) 238, 259, 302 nm (4.15, 4.04, 3.35). $\nu_{max}$ 1752, 1730, 1696, 1632, 1592 $cm^{-1}$. δ 8.18, m, H 5 or H 8; 7.93, m, H 5 or H 8; 7.76, m, H 6, H 7; 4.13, dd, *J* 4.1, 2.0 Hz, H 4; 4.01, dd, *J* 15.1, 2.0 Hz, H 1α; 3.08, dd, *J* 16.6, 4.1 Hz, H 3β; 2.92, s, OMe; 2.83, d, *J* 15.1 Hz, H 1β; 2.77, app. dt, spacings 16.6, 2.0 Hz, H 3α; 1.80, s, OAc. *m/z* 350 (M [$^{35}$Cl], 1%), 241 (28), 199 (31).

*Reaction of Trione (34) with Sodium Methoxide*

To a solution of trione (34) (70 mg) in methanol (10 $cm^3$) was added a solution of sodium methoxide in methanol (5% w/v, 2 $cm^3$), whereupon the solution became deeply coloured. The mixture was stirred at room temperature for 1 h, acidified with 2 M hydrochloric acid (75 $cm^3$) and extracted with ethyl acetate (2×50 $cm^3$). The extract was washed with water (75 $cm^3$), brine (75 $cm^3$), and then dried and evaporated. The residue was crystallized from ethyl acetate/petrol to give 2-hydroxy-1-methoxy-9,10-anthraquinone (35) (27 mg, 53%) as yellow needles, m.p. 180–182° (lit.[19] 182–184°). δ 8.27, m, H 5, H 8; 8.14, d, *J* 8.4 Hz, H 4; 7.78, m, H 6, H 7; 7.36, d, *J* 8.4 Hz, H 3; 6.67, br s, OH; 4.04, s, OMe.

*Reductive Aromatization of Trione (34)*

To a solution of trione (34) (67 mg) in glacial acetic acid (7 $cm^3$) was added zinc dust (200 mg) and the mixture was stirred vigorously at room temperature for 3 h. It was then filtered through Celite and evaporated. Subjecting the residue to preparative t.l.c., with ethyl acetate/toluene (1 : 9) as eluent, gave 2-hydroxy-9,10-anthraquinone (36) (23 mg, 54%) as yellow needles from ethyl acetate/toluene, m.p. 293° (subl.) (lit.[19] 306°). $\lambda_{max}$ (log ε) 244, 268, 327sh, 373 nm (4.21, 4.24, 3.44, 3.25). δ [$(CD_3)_2SO$] 8.18–8.14, m, H 5, H 8; 8.08, d, *J* 8.5 Hz, H 4; 8.00–7.80, m, H 6, H 7; 7.50, d, *J* 1.8 Hz, H 1; 7.24, dd, *J* 8.5, 1.8 Hz, H 3.

*Reaction of Diene (2) with Quinone (28)*

To a solution of quinone (28) (154 mg) in benzene (3 $cm^3$) was added diene (2) (307 mg). The mixture was stirred at 50° for 4 days. The solvent was evaporated and the residue was treated with zinc dust and acetic acid as for the formation of (36). Subjecting the residue to column

chromatography, with an ethyl acetate/toluene (5 : 95 → 20 : 80) solvent gradient as eluent, gave 1,7-dihydroxy-9,10-anthraquinone (37) (71 mg, 50%) as yellow needles, m.p. 293° (dec.) (lit.[17] 291–293°). $\lambda_{max}$ (log ε) 270, 283 inf., 390 nm (4.54, 4.38, 3.97). δ [$(CD_3)_2SO$] 12.37, s, 1-OH; 11.17, br s, 7-OH; 8.06, d, *J* 8.6 Hz, H 5; 7.78, app. t, spacings 7.8 Hz, H 3; 7.67, dd, *J* 7.6, 1.0 Hz, H 4; 7.52, d, *J* 2.6 Hz, H 8; 7.33, dd, *J* 8.2, 1.0 Hz, H 2; 7.25, dd, *J* 8.6, 2.6 Hz, H 6.

*Reaction of Diene (2) with Quinone (30)*

To a solution of quinone (30) (51 mg) in benzene (3 $cm^3$) was added diene (2) (300 mg) and the mixture was stirred at 50° for 4 days. It was then evaporated and the residue was treated with zinc dust in acetic acid as for the formation of (36). The residue was crystallized from ethyl acetate/petrol to give 7-hydroxy-1-methoxy-9,10-anthraquinone (18) (22 mg, 48%) as a yellow microcrystalline solid, m.p. 271° (dec.) (lit.[20] 273°, lit.[21] 186–187°) (Found: $M^{+\bullet}$, 254.0577. Calc. for $C_{15}H_{10}O_4$: $M^{+\bullet}$, 254.0579). δ [$(CD_3)_2SO$, 35°] 7.91, m, ArH; 7.82–7.70, m, 2×ArH; 7.51, m, ArH; 7.28, br s, ArH; 7.03, br m, ArH; 3.92, s, OMe. *m/z* 254 (M, 100%), 225 (38), 139 (30).

*Demethylation of 7-Hydroxy-1-methoxy-9,10-anthraquinone (18)*

The anthraquinone (18) (10 mg) was added to a molten mixture of aluminium chloride (5 g) and sodium chloride (1 g) at 140°. After 5 min the reaction mixture was poured onto a mixture of ice (100 g) and concentrated hydrochloric acid (5 $cm^3$). The resultant suspension was then extracted with ethyl acetate (2×50 $cm^3$). The combined extracts were washed with water (2×50 $cm^3$), brine (100 $cm^3$), and then dried and evaporated. The residue was subjected to column chromatography, with a solvent gradient of ethyl acetate/toluene/acetic acid (0 : 99 : 1 → 20 : 79 : 1) as eluent, to afford 1,7-dihydroxy-9,10-anthraquinone (37) (4 mg, 42%) as yellow needles, indistinguishable in chromatographic and spectroscopic properties from material obtained above.

*Reaction of Diene (2) with Quinone (29)*

To a solution of quinone (29) (79 mg) in benzene (2 $cm^3$) was added diene (2) (342 mg) and the mixture was stirred at room temperature for 4 days. The solvent was removed and the residue was treated with zinc dust in acetic acid as for the formation of (36). The product was subjected to column chromatography as for (37) to give 1,6-dihydroxy-9,10-anthraquinone (17) (37 mg, 52%) as yellow needles, m.p. >270° (dec.) (lit.[17] 270–272°). $\lambda_{max}$ (log ε) 271, 408 nm (4.45, 3.90). δ [$(CD_3)_2SO$] 12.70, s, 1-OH; 11.22, br s, 6-OH; 8.10, d, *J* 8.5 Hz, H 8; 7.75, app. t, spacings 7.9 Hz, H 3; 7.67, dd, *J* 7.5, 1.0 Hz, H 4; 7.48, d, *J* 2.5 Hz, H 5; 7.34, dd, *J* 8.5, 1.0 Hz, H 2; 7.24, dd, *J* 8.5, 2.5 Hz, H 7.

*Reaction of Diene (2) with Quinone (31)*

To a solution of quinone (31) (93 mg) in benzene (3 $cm^3$) was added diene (2) (523 mg) and the mixture was stirred at 50° for 3 days and then evaporated. Examination of the residue by $^1$H n.m.r. spectroscopy showed it to consist of a mixture of two stoichiometric cycloadducts (1 : 1). This mixture was treated with zinc and acetic acid as for the formation of (36). The crude aromatized product was then directly demethylated by treatment with molten aluminium chloride/sodium chloride as above. Column chromatography afforded a 1 : 1 mixture of 1,6-dihydroxy-9,10-anthraquinone (17) and 1,7-dihydroxy-9,10-anthraquinone (37) [35 mg, 44% from (31)], as shown by $^1$H n.m.r. spectroscopy.

*Methyl 4-(3′-Chloro-1′,4′-dioxo-1′,4′-dihydronaphthalen-2′-yl)-3-methoxybut-2-enoate (45)*

To a solution of 2,3-dichloro-1,4-naphthoquinone (44) (93 mg) in benzene (2 $cm^3$) was added diene (9)[2] (150 mg) and the mixture was stirred for 12 h. Further diene (83 mg) was added and stirring was continued for 8 h. The solvent was then evaporated and the residue crystallized from ethyl acetate/petrol to give the *ester* (45) (59 mg, 45%) as pale yellow bars, m.p. 132–133° (Found: C, 60.0; H, 4.1. $C_{16}H_{13}ClO_5$ requires C, 59.9; H, 4.1%). $\lambda_{max}$ (log ε) 243, 275, 337 nm (4.33, 4.20, 3.40). $\nu_{max}$ 1703, 1673, 1614, 1589sh $cm^{-1}$. δ 8.15, m, H 5′, H 8′; 7.76, m, H 6′, H 7′; 5.18, br s, H 2; 4.51, br s, $CH_2$; 3.74, 3.57, s, s, 2×OMe. *m/z* 322 (M [$^{37}$C1], 14%), 320 (M [$^{35}$C1], 39), 290 (20), 289 (33), 288 (46), 263 (34), 262 (33), 261 (100), 260 (57).

*(1β,4aβ,9aβ)-4a-Acetoxy-9a-chloro-1,3-dimethoxy-1-trimethylsilyloxy-1,4,4a,9a-tetrahydroanthracene-9,10-dione (46)*

To a solution of quinone (24) (101 mg) in benzene (5 $cm^3$) was added diene (9) (167 mg) and the mixture was stirred at room temperature for 32 h. The solvent was evaporated and the residue was recrystallized from ether/petrol to give the *anthracenedione* (46) (82 mg, 45%) as colourless needles, m.p. 176–180° (dec.) (Found: C, 55.6; H, 5.6. $C_{21}H_{25}ClO_7Si$ requires C, 55.7; H, 5.6%). $\lambda_{max}$ (log ε) ($CHCl_3$) 242, 260sh nm (4.39, 4.29). δ 8.13, m, H 8 or H 5; 7.88, m, H 8 or H 5; 7.67, m, H 6, H 7; 4.58, br s, H 2; 3.76, dd, *J* 16.9, 0.7 Hz, H 4α; 3.66, s, 3-OMe; 2.83, s, 1-OMe; 2.58, dd, *J* 16.9, 1.7 Hz, H 4β; 1.75, s, OAc; 0.20, s, $OSiMe_3$. *m/z* 421 (M [$^{35}$Cl] – 31,13%), 393 (24), 363 (37), 289 (42), 202 (94), 187 (42), 183 (22), 171 (39), 163 (68), 98 (43), 75 (34), 73 (100).

*(4aβ,9aβ)-4a-Acetoxy-9a-chloro-3-methoxy-4a,9a-dihydroanthracene-1,9,10(4*H*)-trione (47)*

To a solution of adduct (46) (87 mg) in tetrahydrofuran (3 $cm^3$) was added 0.1 M hydrochloric acid (10 drops) and the mixture was stirred for 8 h. It was then diluted with water (20 $cm^3$) and extracted into dichloromethane (2×10 $cm^3$). The extract was washed with water (2×20 $cm^3$), brine (20 $cm^3$), and then dried and evaporated. Recrystallization of the pale yellow residue from ethyl acetate/petrol gave the *anthracenetrione* (47) (57 mg, 86%) as colourless bars, m.p. 170–173° (Found: C, 58.5; H, 3.9. $C_{17}H_{13}ClO_6$ requires C, 58.6; H, 3.8%). $\lambda_{max}$ (log ε) ($CHCl_3$) 243, 259sh nm (4.33, 4.28). $\nu_{max}$ 1753, 1713, 1663, 1600 $cm^{-1}$. δ 8.17, m, H 5 or H 8; 7.99, m, H 5 or H 8; 7.81–7.73, m, H 6, H 7; 5.35, br s, H 2; 3.85, br s, H 4α; 3.80, s, 3-OMe; 3.19, br s, H 4β; 1.96, s, OAc. δ (45°, partial) 5.35, br s, H 2; 3.85, br d, *J* 17.3 Hz, H 4α; 3.80, s. OMe; 3.19, br d, *J* 17.3 Hz, H 4β; 1.95, s, OAc. *m/z* (15 eV) 305 (M [$^{35}$Cl] – $COCH_3$, 24%), 254 (62), 98 (100).

*Reductive Aromatization of (47)*

Trione (47) (13 mg) was treated with zinc dust in acetic acid as for the formation of (36) to afford 1-hydroxy-3-methoxy-9,10-anthraquinone (48) (8 mg, 84%) as a yellow solid, m.p. 187–190° (lit.[19] 193–194°). δ 12.91, s, OH; 8.32–8.27, m, H 5, H 8; 7.83–7.76, m, H 6, H 7; 7.39, d, *J* 2.7 Hz, H 4; 6.72, d, *J* 2.7 Hz, H 2; 3.95, s, OMe.

*Reaction of Quinone (25) with Diene (9)*

To a solution of the naphthoquinone (25) (103 mg) in benzene (1 $cm^3$) was added diene (9) (286 mg) and the mixture was stirred at room temperature for 48 h. The solvent was evaporated. Trituration of the residue with ether/petrol gave (1β,4aβ,9aβ)-4a,9a-diacetoxy-1,3-dimethoxy-1-trimethylsilyloxy-1,4,4a,9a-tetrahydroanthracene-9,10-dione (51) (2 mg, 1%) as a colourless solid. δ 8.17, m, H 5, H 8; 7.82, m, H 6, H 7; 4.59, br s, H 2; 3.73, dd, *J* 16.9, 0.6 Hz, H 4α; 3.67, s, 3-OMe; 2.82, s, 1-OMe; 2.39, d, *J* 16.9, 1.7 Hz, H 4β; 2.19, 1.67, s, s, 2×OAc; 0.24, s, $OSiMe_3$. The remainder of the residue was subjected to preparative t.l.c., with ethyl acetate/petrol (1 : 1) as eluent, to give two bands.

The more mobile, yellow band gave *methyl 4-(3′-acetoxy-1′,4′-dioxo-1′,4′-dihydronaphthalen-2′-yl)-3-methoxybut-2-enoate* (49) (45 mg, 32%) as pale yellow needles from ethyl acetate/petrol, m.p. 154–158° (Found: C, 62.7; H, 4.9. $C_{18}H_{16}O_7$ requires C, 62.8; H, 4.7%). $\lambda_{max}$ 247, 252, 267, 271, 340 nm. $\nu_{max}$ 1765, 1742, 1707, 1671, 1642, 1620, 1592sh $cm^{-1}$. δ 8.16–8.08, m, H 5′, H 8′; 7.78–7.71, m, H 6′, H 7′; 5.13, br s, H 2; 4.29, br s, $CH_2$; 3.72, 3.54, s, s, 2×OMe; 2.32, s, OAc. *m/z* 344 (M, 9%), 302 (23), 285 (26), 271 (21), 270 (24), 243 (100), 242 (40), 214 (24), 199 (39), 183 (31), 128 (21), 127 (29), 115 (40), 105 (22), 104 (26), 102 (24).

The less mobile, colourless band gave *(4aβ,9aβ)-4a,9a-diacetoxy-3-methoxy-4a,9a-dihydroanthracene-1,9,10(4*H*)-trione* (50) (7 mg, 5%) as colourless crystals from ethyl acetate/petrol, m.p. 163–165° (Found: C, 61.3; H, 4.4. $C_{19}H_{16}O_8$ requires C, 61.3; H, 4.3%). $\lambda_{max}$ (log ε) 240, 275sh nm (4.23, 3.87). δ 8.13, d, *J* 7.9 Hz, H 5 or H 8; 7.76–7.69, m, H 5 or H 8, H 6 or H 7; 7.55, app. dt, *J* 8.0, 1.9 Hz, H 6 or

H 7; 5.37, d, *J* 1.6 Hz, H 2; 3.78, s, OMe; 3.15, dd, *J* 18.3, 1.6 Hz, H 4α; 2.96, d, *J* 18.3 Hz, H 4β; 2.29, 2.25, s, s, 2×OAc. *m/z* 372 (M, 4%), 371 (16), 329 (30), 288 (68), 285 (21), 244 (23), 243 (100), 229 (22).

## Acknowledgments

We thank Dr P. G. Griffiths for helpful discussion. We acknowledge the financial support of the Australian Research Council and an Australian Postgraduate Research Award (to A.G.R.). Early experiments involving adduct (33) were carried out by Ms S. Pasterk.

## References

[1] Boeckman, R. K., Dolak, T. M., and Culos, K. O., *J. Am. Chem. Soc.*, 1978, **100**, 7098.
[2] Savard, J., and Brassard, P., *Tetrahedron*, 1984, **40**, 3455.
[3] Bell, S. H., Cameron, D. W., Feutrill, G. I., Skelton, B. W., and White, A. H., *Tetrahedron Lett*., 1985, **26**, 6519.
[4] Cameron, D. W., Feutrill, G. I., and Keep, P. L. C., *Tetrahedron Lett.*, 1989, **30**, 5173.
[5] Cameron, D. W., Crosby, I. T., and Feutrill, G. I., *Tetrahedron Lett.*, 1992, **33**, 2855.
[6] Cameron, D. W., Feutrill, G. I., and Keep, P. L. C., unpublished data.
[7] Weber, W. H., Zähner, H., Siebers, J., Schröder, K., and Zeeck, A., *Arch. Mikrobiol*., 1979, **121**, 111.
[8] Anderson, M. G., Khoo, C. K. Y., and Rickards, R. W., *J. Antibiot.*, 1989, **42**, 640.
[9] Eistert, B., and Klein, L., *Chem. Ber.*, 1968, **101**, 391.
[10] Weygand, F., *Ber. Dtsch. Chem. Ges.*, 1942, **75**, 625.
[11] Thomson, R. H., *J. Org. Chem.*, 1948, **13**, 377.
[12] Wheeler, A. S., Dawson, P. R., and McEwen, J. L., *J. Am. Chem. Soc.*, 1923, **45**, 1970.
[13] Thomson, R. H., *J. Org. Chem.*, 1948, **13**, 870.
[14] Lillie, T. J., and Musgrave, O. C., *J. Chem. Soc., Perkin Trans. 1*, 1977, 355.
[15] Belitskaya, L. D., and Kolesnikov, V. T., *Zh. Org. Khim.*, 1984, **20**, 1920.
[16] White, J. M., Riches, A. G., Cameron, D. W., and Griffiths, P. G., *Acta Crystallogr., Sect. C*, 1997, **53**, 386.
[17] Evans, R. L., M.Sc. Thesis, The University of Melbourne, 1982.
[18] Danishefsky, S., and Kitahara, T., *J. Am. Chem. Soc.*, 1974, **96**, 7807.
[19] Thomson, R. H., 'Naturally Occurring Quinones', 2nd Edn (Academic Press: London and New York 1971).
[20] Cameron, D. W., Evans, R. L., and Feutrill, G. I., unpublished data.
[21] Beagley, B., Curtis, A. D. M., Pritchard, R. G., and Stoodley, R. J., *J. Chem. Soc., Perkin Trans. 1*, 1992, 1981.