

## Anthracyclonones. Part 3.<sup>1</sup> Use of Di-isopropylidene-D-glucose and a Modified Marschalk Reaction to Introduce a Tertiary Carbinol Function into Ring D of Anthracyclonones

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Reaction of 3-*C*-ethynyl-1,2-*O*-isopropylidene- $\alpha$ -D-*ribo*-pentodialdo-1,4-furanose (**2b**) with *leuco*-quinizarin (**4**) in alkaline solution gave a mixture of (5*S*)- and (5*R*)-3-*C*-ethynyl-1,2-*O*-isopropylidene-5-(quinizarin-2-yl)- $\alpha$ -D-ribofuranose (**11a**) and (**11b**) respectively and the corresponding 5-deoxyderivative (**11c**). Acid-catalysed hydrolysis of the furanoses (**11a**) and (**11b**) furnished the quinizarinyl pyranoses (**13a**) and (**14**) respectively. Similarly, 3-*O*-benzyl-3-*C*-ethynyl-1,2-*O*-isopropylidene- $\alpha$ -D-*ribo*-pentodialdo-1,4-furanose (**2c**) with *leuco*-quinizarin gave a good yield of a mixture of the two diastereoisomers (5*S*)- and (5*R*)-3-*O*-benzyl-3-*C*-ethynyl-1,2-*O*-isopropylidene-5-(quinizarin-2-yl)- $\alpha$ -D-ribofuranose (**11d**) and (**11e**) respectively and reaction of each with boron trichloride resulted in the loss of the benzyl and isopropylidene groups to give the quinizarinylpyranoses (**13a**) and (**14**) respectively. Hydrolysis of compound (**11d**) with acid produced the crystalline (5*S*)-3-*O*-benzyl-3-*C*-ethynyl-5-(quinizarin-2-yl)- $\alpha$ -( $\beta$ )-D-ribofuranose (**13b**) which, with periodate, afforded (4*S*)-2-*O*-benzyl-2-*C*-ethynyl-3-*O*-formyl-4-(quinizarin-2-yl)- $\alpha$ -( $\beta$ )-D-*erythro*-tetrahydrofuranose (**15**). Reduction of compound (**15**) with zinc and methanolic acetic acid and treatment of the resulting *leuco*-derivative with 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) in DMF produced the (10*S*)-8-benzyloxy-8-ethynylhexahydroxyanthracyclonone (**17a**) and the corresponding deoxy derivative (**18a**), debenylation of each of which with boron trichloride gave the corresponding anthracyclonones (**17b**) and (**18b**) respectively. Structures of the compounds were confirmed by u.v., mass, i.r., c.d., and <sup>1</sup>H n.m.r. spectroscopy.

In the previous paper<sup>1</sup> in this series we described the use of 3-*O*-benzyl-1,2:5,6-di-*O*-isopropylidene- $\alpha$ -D-glucofuranose (**1a**) via the derived 3-*O*-benzyl-1,2-*O*-isopropylidene- $\alpha$ -D-*xyl*o-pentodialdo-1,4-furanose (**2a**) as an inexpensive chiral template precursor of the fourth (A) ring in a novel anthracyclonone synthesis using a modified Marschalk-type reaction<sup>2</sup> to produce compound (**3**) from *leuco*-quinizarin (**4**).

However, most of the naturally occurring anthracycline antibiotics are characterised by the presence of a tertiary carbinol group in ring A. The alkyl moiety of the carbinol is usually an ethyl or modified ethyl group as with adriamycin (**5**), daunomycin (**6**), and carminomycin (**7**) but may also be methyl as in aranciamycin (**8**).<sup>3-6</sup> We have therefore been anxious to extend our new synthesis to include compounds of this type. Suitable chiral templates of the required type are readily available by addition of Grignard reagents or alkyl-lithium derivatives to the carbonyl group in the ketone (**9**) which is readily produced<sup>7</sup> by oxidation of 1,2:5,6-di-*O*-isopropylidene- $\alpha$ -D-glucofuranose (**1b**) with dimethyl sulphoxide (DMSO) and acetic anhydride. During the anion-addition reactions to compound (**9**) both the *allo* and the *gluco* forms are produced but generally the *allo* form predominates.

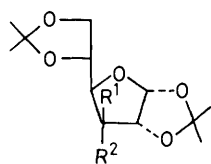
Of special interest to us was the acetylenic carbinol (**1c**), a potential precursor of most of the required C<sub>2</sub> systems, which is readily available in the *allo* form by reaction of the ketone (**9**) with ethynylmagnesium bromide.<sup>8</sup> The acetylenic carbinol (**1c**) is readily converted into the diol (**10a**) by treatment with aqueous acetic acid overnight at room temperature, and the diol, on reaction with sodium metaperiodate, furnishes the aldehyde (**2b**) in almost quantitative yield.

Reactions of the aldehyde (**2b**) with *leuco*-quinizarin (**4**) and aqueous sodium hydroxide in methanolic tetrahydrofuran (THF) at 0°C for 1 h under nitrogen followed by aerial oxidation gave a good yield of (5*S*)-3-*C*-ethynyl-1,2-*O*-isopropylidene-5-(quinizarin-2-yl)- $\alpha$ -D-ribofuranose (**11a**) which

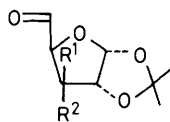
readily crystallised after a single chromatographic purification on silica gel. It was accompanied by smaller amounts of the (5*R*)-isomer (**11b**) and the deoxy derivative (**11c**), also obtained in crystalline form, and these three compounds were readily separated from each other by chromatography.

The structure assigned to compound (**11a**) was confirmed by elemental analysis, by its i.r. [*e.g.*,  $\nu_{\max}$ , 2110 (C≡CH) and 1380 cm<sup>-1</sup> (CMe<sub>2</sub>)], mass [*e.g.*,  $m/z$  452 (*M*<sup>+</sup>), 437 (*M* - 15), and 269 (characteristic breakdown fragment Q - CH=OH<sup>+</sup>; Q = quinizarin-2-yl)] and <sup>1</sup>H n.m.r. [*e.g.*, absence of signal for 2'-H, signals at  $\delta$  3.29 (d, 5-OH), 5.4 (d, 5-H), and 7.56 (s, 3'-H), and full assignment of all other protons] spectra, and by its subsequent reactions. Similar analytical and spectroscopic data were obtained for the (5*R*)-isomer (**11b**). The spectroscopic data and homogeneity of compounds (**11a**) and (**11b**) on t.l.c. in different solvent systems suggested that they were pure single diastereoisomers and this and the assigned (5*S*) and (5*R*) configurations were confirmed by comparison of the c.d. spectra of the two compounds (Figure) with those of compounds (**3**) and (**12**) whose structures have been earlier confirmed<sup>9</sup> by X-ray crystal studies and which were shown in each case to have the *S* configuration at the 5-position. The structure assigned to the deoxy derivative (**11c**) was similarly confirmed by elemental analysis and mass [*e.g.*,  $m/z$  436 (*M*<sup>+</sup>), 253 (characteristic breakdown fragment Q - CH<sub>2</sub>), and absence of a peak at  $m/z$  269] and <sup>1</sup>H n.m.r. [*e.g.*, absence of signals for 2-H and 5-OH, signal at  $\delta$  2.7 (s, C≡CH)] spectra.

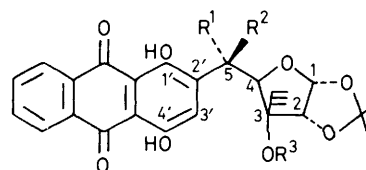
The isopropylidene groups in compounds (**11a**) and (**11b**) were readily removed with aqueous acetic acid to furnish in each case single products, homogeneous on t.l.c., to which the pyranose structures (**13a**) and (**14**) were assigned. These structures were confirmed by elemental analyses and mass [*e.g.*,  $m/z$  412 (*M*<sup>+</sup>) in each case] and <sup>1</sup>H n.m.r. spectra. Thus whereas in the furanose (**11a**) the benzylic hydrogen signal of 5-H is a



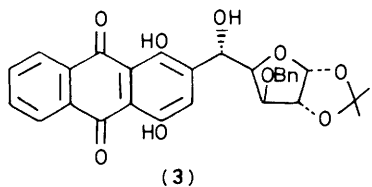
- (1) a;  $R^1 = \text{OBn}$ ,  $R^2 = \text{H}$   
 b;  $R^1 = \text{OH}$ ,  $R^2 = \text{H}$   
 c;  $R^1 = \text{C}\equiv\text{CH}$ ,  $R^2 = \text{OH}$   
 d;  $R^1 = \text{C}\equiv\text{CH}$ ,  $R^2 = \text{OBn}$



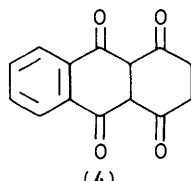
- (2) a;  $R^1 = \text{OBn}$ ,  $R^2 = \text{H}$   
 b;  $R^1 = \text{C}\equiv\text{CH}$ ,  $R^2 = \text{OH}$   
 c;  $R^1 = \text{C}\equiv\text{CH}$ ,  $R^2 = \text{OBn}$



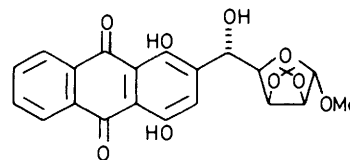
- (11) a;  $R^1 = \text{OH}$ ,  $R^2 = R^3 = \text{H}$   
 b;  $R^1 = R^3 = \text{H}$ ,  $R^2 = \text{OH}$   
 c;  $R^1 = R^2 = R^3 = \text{H}$   
 d;  $R^1 = \text{OH}$ ,  $R^2 = \text{H}$ ,  $R^3 = \text{Bn}$   
 e;  $R^1 = \text{H}$ ,  $R^2 = \text{OH}$ ,  $R^3 = \text{Bn}$



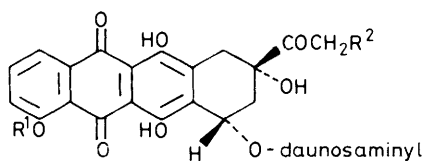
(3)



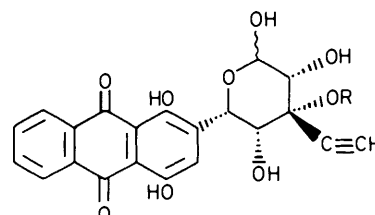
(4)



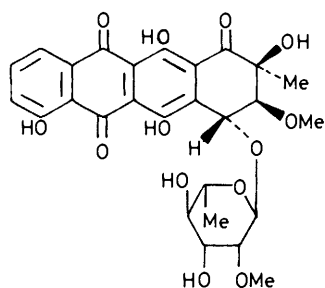
(12)



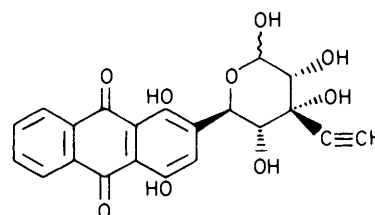
- (5)  $R^1 = \text{Me}$ ,  $R^2 = \text{OH}$   
 (6)  $R^1 = \text{Me}$ ,  $R^2 = \text{H}$   
 (7)  $R^1 = \text{H}$ ,  $R^2 = \text{Me}$



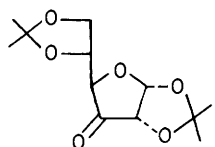
- (13) a;  $R = \text{H}$   
 b;  $R = \text{Bn}$



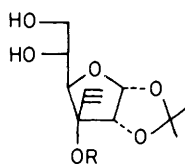
(8)



(14)



(9)

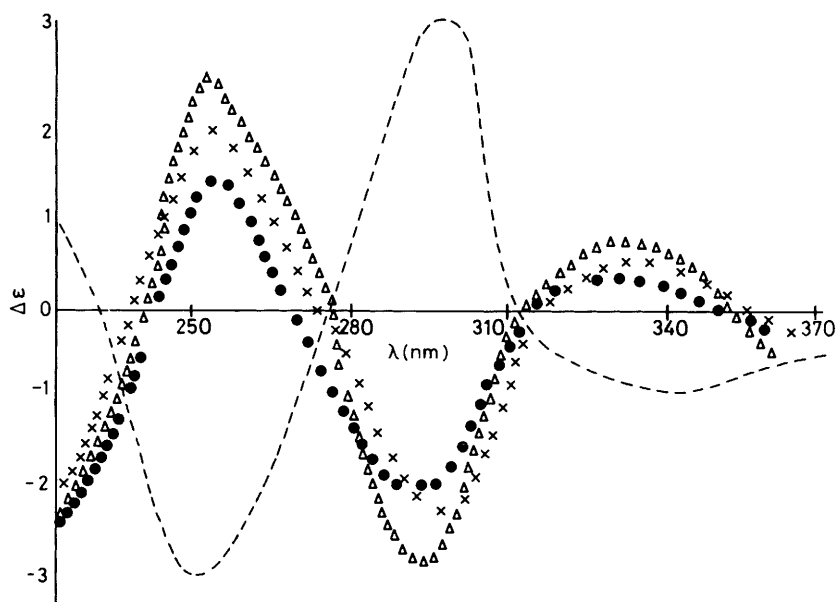


- (10) a;  $R = \text{H}$   
 b;  $R = \text{Bn}$

doublet ( $\delta$  5.4) coupled to the 5-OH proton, in the pyranose (13a) the corresponding 5-H proton signal is attributed to a one-proton singlet ( $\delta$  5.2). Similar spectral data were obtained for compound (14). The configuration at the anomeric centre in the pyranoses (13a) and (14) cannot be assigned with certainty but the data would indicate in each case the presence of a single anomer only.

It was hoped that periodate oxidation of the pyranose (13a) or (14) might occur exclusively or to a large extent at the terminal diol system. However, treatment of a solution of the quinizarinyl pyranose (13a) in THF with one equivalent of aqueous sodium metaperiodate at 0 °C during 1.5 h gave a mixture of products which was not examined further but which resulted presumably from random attack at the three diol systems available; the behaviour of the products on t.l.c. was consistent with this.

Accordingly, in order to isolate the required diol system, the *O*-benzyl derivative (1d) was prepared in high yield by benzylation of the acetylenic carbinol (1c) with benzyl chloride and sodium hydride in DMSO. The structure was confirmed by  $^1\text{H}$  n.m.r. [*e.g.*,  $\delta$  1.7 (C $\equiv$ CH) and 7.3 (5 H, m, Ph)], i.r. [*e.g.*,  $\nu_{\text{max}}$ . 2 110 (C $\equiv$ CH) and 1 380  $\text{cm}^{-1}$  (CMe $_2$ )], and mass [*e.g.*,  $m/z$  359 ( $M - \text{CH}_3$ ) and 91 (C $_7\text{H}_7^+$ , 100%)] spectra. Removal of the 5,6-isopropylidene group from compound (1d) with 70% aqueous acetic acid at room temperature, followed by periodate oxidation of the resulting diol (10b), produced the aldehyde (2c),



**Figure.** C.d. spectra of some hydroxyglycyl anthraquinones. ---- (5*R*)-3-*C*-Ethynyl-1,2-*O*-isopropylidene-5-(quinizarin-2-yl)- $\alpha$ -D-ribofuranose (11*b*). ●●● (5*S*)-3-*C*-Ethynyl-1,2-*O*-isopropylidene-5-(quinizarin-2-yl)- $\alpha$ -D-ribofuranose (11*a*). ××× (5*S*)-3-*O*-Benzyl-1,2-*O*-isopropylidene-5-(quinizarin-2-yl)- $\alpha$ -D-xylofuranose (3).  $\Delta\Delta\Delta\Delta$  Methyl(5*S*)-2,3-*O*-isopropylidene-5-(quinizarin-2-yl)- $\alpha$ -D-lyxofuranoside (12)

$\nu_{\max}$ . 1 380 (CMe<sub>2</sub>), 1 735 (CHO), and 2 110 cm<sup>-1</sup> (C≡CH), which with *leuco*-quinizarin (4) in aqueous sodium hydroxide and methanolic THF at 0 °C during 1.5 h under nitrogen, followed by aerial oxidation and acidification, gave, in addition to some unchanged quinizarin, a good yield of a mixture of two compounds, one of which was formed in greater quantity than the other. The compounds were readily separated by chromatography on silica gel and were shown to be the 5*R* and 5*S* isomers of 3-*O*-benzyl-3-*C*-ethynyl-1,2-*O*-isopropylidene-5-(quinizarin-2-yl)- $\alpha$ -D-ribofuranose, (11*e*) and (11*d*) respectively, formed in the ratio 1:3. The structures assigned to the compounds were in each case confirmed by elemental analysis, by their mass [e.g., *m/z* 542 (*M*<sup>+</sup>), 527 (*M* - CH<sub>3</sub>), 269, 240, and 91 (C<sub>7</sub>H<sub>7</sub><sup>+</sup>, 100%)] and <sup>1</sup>H n.m.r. [e.g., (major product first)  $\delta$  2.87, 2.91 (s, C≡CH), 3.35, 3.26 (br, 5-OH, exch. D<sub>2</sub>O), 4.5, 4.55 (d, *J* 10 Hz; CH<sub>2</sub>Ph), 5.24, 5.55 (d, *J*<sub>5,5-OH</sub> 7.5, 7 Hz, 5-H), and 5.98, 5.9 (d, *J*<sub>1,2</sub> 3, 3.5 Hz, 1-H)] spectra, and by full assignment of all other proton signals in both compounds.

The 5*R* and 5*S* configurations assigned to (11*e*) and (11*d*) were confirmed in each case by debenylation with boron trichloride in chloroform at -78 °C when the isopropylidene groups were also lost on work-up with formation of the quinizarinylpyranoses (13*a*) and (14) respectively, identical (i.r., t.l.c., mass spectra) with the compounds prepared by the earlier, direct route.

The (5*S*)-derivative (11*d*) was readily converted in high yield, on being heated with 70% aqueous acetic acid, into a single product, homogeneous on t.l.c., and this may be assigned the pyranose structure (13*b*). The structure was confirmed by elemental analysis and mass [e.g., *m/z* 502 (*M*<sup>+</sup>), 269, 240, and 91 (C<sub>7</sub>H<sub>7</sub><sup>+</sup>, 100%)] and <sup>1</sup>H n.m.r. spectra. In particular, whereas in both furanose isomers (11*e*) and (11*d*) the 5-H proton signal is a doublet coupled to the 5-OH proton, in the pyranose (13*b*) where the OH has disappeared into the pyranose ring the 5-H proton signal is attributed to a one-proton singlet.

Definitive assignments of all protons in the <sup>1</sup>H n.m.r. spectrum of compound (13*b*) was made possible by decoupling difference spectra, the results of which are presented in Table 1. Furthermore, the fact that there is no positive response

**Table 1.** <sup>1</sup>H N.m.r. decoupling difference spectra of compound (13*b*)

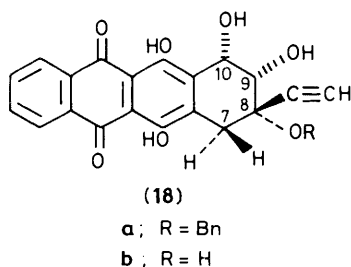
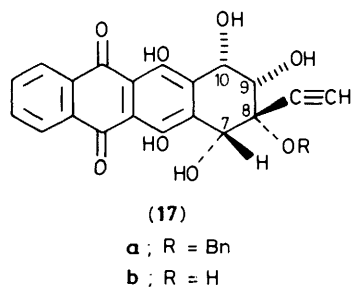
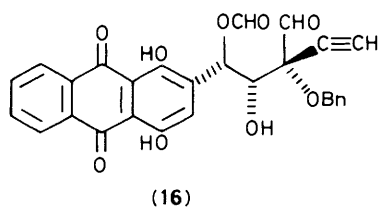
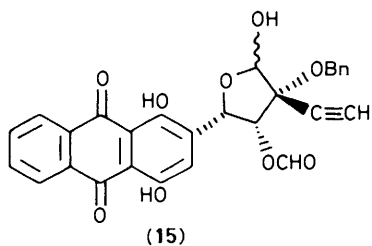
Hydrogen atom irradiated	$\delta$ (multiplicity)*	Response (assignment)
5-H	5.45 (s)	7.7 (3'-H), 7.4 (Ph), 5.25 (1-H), 4.35 (4-H)
4-H	4.4 (d)	4.07 (2-H), 5.45 (5-H)
2-H	4.07 (d)	4.4 (4-H), 5.3 (1-H)
1-H	5.3 (d)	7.4 (Ph), 4.07 (2-H), 5.45 (5-H)

\* p.p.m. from TMS; solvent CDCl<sub>3</sub>.

for 2-H when 5-H is decoupled provides confirmation of the pyranose structure, since if the furanose form existed one would expect to see a positive result for 1-H and 2-H when 5-H was decoupled (both 1-H and 2-H being 3 atoms away from 5-H in the furanose form). The configuration at the anomeric centre cannot be assigned with certainty but the data would indicate the presence of a single anomer.

Reaction of the pyranose derivative (13*b*) with sodium metaperiodate in aqueous acetic acid gave a compound to which the *O*-formyl  $\alpha$ -( $\beta$ )-D *erythro*-furanose structure (15) [produced either by rearrangement of the first formed 4-*O*-formyl aldehyde (16) or alternatively by initial reaction of periodate with the isomeric furanose form of (13*b*) which although present in solution in very small amounts would presumably be more reactive towards periodate than is compound (13*b*)] may be assigned, the anomers being present in the ratio 3:1. This was confirmed by mass [e.g., *m/z* 500 (*M*<sup>+</sup>), 269, and 267 (*Q* - CO<sup>+</sup>, 100%)], i.r. [e.g.,  $\nu_{\max}$ . 1 735 cm<sup>-1</sup> (OCHO) (single absorption band indicating absence of aldehyde)], and <sup>1</sup>H n.m.r. (showing 2 anomers) [e.g.,  $\delta$  2.95-3.1 (1 H, signal split in ratio 1:2), 4.6-4.8 (2 H, m, OCH<sub>2</sub>Ph), 5.82-6.18 (1 H, dd, *J*<sub>3,4</sub> 4 Hz, 3- or 4-H), 6.0-6.2 (1 H, dd, *J*<sub>4,3</sub> 4 Hz, 4- or 3-H) the latter signals being in the ratio 2:1, and no signal at  $\delta$  ca. 10 corresponding to a free aldehyde proton, and full assignment of all other protons] spectra. The *O*-formyl

derivative (15) was reduced to the *leuco*-derivative with zinc, acetic acid, and methanol. Treatment of this derivative with a solution of 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) in *NN*-dimethylformamide (DMF) for 45 min at 0 °C, followed by aeration and acidification, and hydrolysis of the crude product with aqueous sodium hydroxide, followed by acidification, produced one major and one minor product which were separated on silica gel plates, and shown to be the anthracyclinones (17a) and (18a) respectively. The structure assigned to compound (17a) was confirmed by elemental



analysis and mass [*e.g.*,  $m/z$  472 ( $M^+$ ), 298 (retro-Diels–Alder fragment characteristic of a 2,3-disubstituted quinizarins), and 91 ( $C_7H_7^+$ )], u.v. (characteristic of a 2,3-disubstituted quinizarin), and  $^1H$  n.m.r. (*e.g.*, absence of signal for 3'-H and assignment of all other protons) spectra. Similarly, the structure of the deoxy derivative (18a) was confirmed by elemental analysis and mass [*e.g.*,  $m/z$  456 ( $M^+$ ), 282 (retro-Diels–Alder fragment), and 91 ( $C_7H_7^+$ , 100%)],  $^1H$  n.m.r. (*e.g.*, absence of signal for 3'-H and assignment of all other protons) spectra. The same products (17a) and (18a) were also produced, but less efficiently, from the furanose (15) with an alkaline solution of

Table 2. N.O.E. data for compound (17a)

Hydrogen atom irradiated ( $\delta$ ) <sup>a</sup>	Observed enhancement
9-H (5.15)	10-H, Ph <sup>b</sup>
10-H (4.5)	9-H
7-H (5.25)	10-H
H <sub>a</sub> (PhCH <sub>2</sub> H <sub>b</sub> ) (4.85)	H <sub>b</sub>
H <sub>b</sub> (PhCH <sub>2</sub> H <sub>a</sub> ) (5.0)	Ph <sup>b</sup>

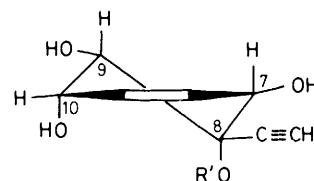
<sup>a</sup> p.p.m. from SiMe<sub>4</sub>; solvent CDCl<sub>3</sub>.

<sup>b</sup> Small enhancement ( $\delta$  7.2).

sodium dithionite under nitrogen at 0 °C followed by aeration and acidification.

Treatment of both anthracyclinones (17a) and (18a) with boron trichloride in chloroform at -78 °C rapidly produced the corresponding debenzylated anthracyclinones (17b) and (18b) respectively.

The signal for 7-H in compound (17a) occurs as a singlet ( $J < 0.1$  Hz) and the absence of coupling between 7-H and 9-H suggests that the benzyl ether (17a) and the related hexaol (17b) may have the 7*R* configuration as in structure (19).



This was confirmed by a series of n.O.e. experiments the results of which are presented in Table 2. Firstly however, confirmation that the signals at  $\delta$  4.5 and 5.15 represent two adjacent protons (9-H, 10-H) comes from the fact that irradiation at  $\delta$  4.5 results in the doublet signal at  $\delta$  5.15 collapsing to a singlet. Assignment of 9-H to the signal at  $\delta$  5.15 and hence 10-H to the signal at  $\delta$  4.5 was confirmed by the n.O.e. data (Table 2) where irradiation of the signal at  $\delta$  5.15 results in enhancement of the phenyl (derived from the benzyl group) signal in addition to enhancement of the signal at  $\delta$  4.5. Irradiation of the latter signal only produces enhancement of the signal at  $\delta$  5.15. Space filling models show clearly that 9-H is much closer to the phenyl group than is 10-H. Irradiation of 7-H produces an enhancement of the 10-H signal as expected for the 7*R* configuration. Additionally, no enhancement of the benzyl (CH<sub>2</sub>) signals was observed suggesting that the ethynyl group must be on the same side of the ring as 7-H, the ethynyl proton being too far removed from 7-H to show any effect. Similarly, irradiation of the benzyl (CH<sub>2</sub>) signals produced no enhancement of the 7-H signal.

### Experimental

Evaporations were carried out under water-pump vacuum with a flask temperature below 40 °C, unless otherwise stated. U.v. spectra were measured with a Unicam SP800 spectrophotometer, i.r. spectra with a Perkin-Elmer 681 spectrophotometer,  $^1H$  n.m.r. (100 MHz) spectra with a JEOL JNM-MH-100 spectrometer (tetramethylsilane as internal standard), unless otherwise stated, and mass spectra with an A.E.I. MS 903 spectrometer. We thank the S.E.R.C. High Field n.m.r. service, Sheffield University, for high-resolution  $^1H$  n.m.r. spectra and

Dr. P. M. Scopes, Westfield College, and Dr. A. Drake, King's College, London, for c.d. spectra. Silica gel (0.05–0.2 mm, 70–270 mesh; Machery-Nagel and Co.) was used for column chromatography. T.l.c. was run on Silica Gel 60 F<sub>254</sub> (0.2 mm thick) pre-coated aluminium plates (Merck) and Cellulose F<sub>254</sub> (0.1 mm thick) pre-coated aluminium plates (Merck) in the systems (A) toluene–ethyl acetate (2:1); (B) toluene–ethyl acetate (1:1); (C) toluene–ethyl acetate (4:1); (D) chloroform–n-butyl alcohol (4:1).

(5S)-3-C-Ethynyl-1,2-O-isopropylidene-5-(quinizarin-2-yl)- $\alpha$ -D-ribofuranose (**11a**).—A solution of 3-C-ethynyl-1,2:5,6-di-O-isopropylidene- $\alpha$ -D-allofuranose (**1c**)<sup>8</sup> (2 g) ( $R_F$  0.75, System C) in 70% aqueous acetic acid (50 cm<sup>3</sup>) was set aside at 45 °C for 4.5 h and then evaporated to afford a pale yellow syrup, homogeneous on t.l.c. ( $R_F$  0.06, System C), of 3-C-ethynyl-1,2-O-isopropylidene- $\alpha$ -D-allofuranose (**10a**) (1.95 g). To a solution of this compound in methanol (30 cm<sup>3</sup>) at 0 °C was added a solution of sodium metaperiodate (1.88 g) in water (25 cm<sup>3</sup>). The mixture was set aside at room temperature for 2 h, when t.l.c. examination (System A) indicated that the starting material ( $R_F$  0.06) had been completely replaced by a single homogeneous product ( $R_F$  0.2). The filtered solution was evaporated (bath temperature < 30 °C) and the remaining solution was saturated with salt and extracted with chloroform (3  $\times$  25 cm<sup>3</sup>). The combined extracts were dried (MgSO<sub>4</sub>) and evaporated to afford a pale straw-coloured syrup of 3-C-ethynyl-1,2-O-isopropylidene- $\alpha$ -D-ribo-pentodialdo-1,4-furanose (**2b**) (1.4 g, 83%),  $\nu_{\max}$ . 3 450 (OH), 1 740 (CHO), 2 110 (C $\equiv$ C), and 1 380 cm<sup>-1</sup> (CMe<sub>2</sub>). The syrup was added to a solution of leuco-quinizarin (**3**) (1.5 g) in methanol (35 cm<sup>3</sup>) and THF (45 cm<sup>3</sup>) at 0 °C under nitrogen and the mixture was then treated with 8M-sodium hydroxide (1.7 cm<sup>3</sup>). After 45 min t.l.c. examination (System A) showed the presence of one major product ( $R_F$  0.18) in addition to a lesser amount of a second compound ( $R_F$  0.4 and traces of compounds with  $R_F$  0.08 and 0.0) and quinizarin ( $R_F$  0.82). A steady stream of air was passed through the mixture for 1.5 h and the resultant purple solution added dropwise to a rapidly stirred mixture of 2M-hydrochloric acid (40 cm<sup>3</sup>) and crushed ice (50 g). The solid red precipitate was collected, washed with water, and air-dried. A solution of the solid (2.9 g) in toluene–ethyl acetate (4:1) was filtered and applied to a silica gel column (7  $\times$  20 cm) and eluted with the same solvent system. The major product ( $R_F$  0.18) readily separated from quinizarin and the other products of the reaction. Evaporation of the appropriate fractions gave a crystalline solid residue of (5S)-3-C-Ethynyl-1,2-O-isopropylidene-5-(quinizarin-2-yl)- $\alpha$ -D-ribofuranose (**11a**) (0.9 g, 31%), which was crystallised from ethanol as orange-red needles, m.p. 229 °C (Found: C, 63.8; H, 4.8%;  $M^+$ , 452. C<sub>24</sub>H<sub>20</sub>O<sub>9</sub> requires C, 63.7; H, 4.45%;  $M$ , 452);  $m/z$  437 ( $M - \text{CH}_3$ ), 269, and 240;  $\nu_{\max}$ . 3 475 (OH), 2 110 (C $\equiv$ C), 1 625 and 1 690 (quinone), and 1 380 cm<sup>-1</sup> (CMe<sub>2</sub>);  $\delta$ (CDCl<sub>3</sub>; 400 MHz) 1.32 and 1.62 (2  $\times$  3 H, CMe<sub>2</sub>), 2.81 (1 H, s, C $\equiv$ CH), 2.95 (1 H, s, 3-OH, exch. D<sub>2</sub>O), 3.29 (1 H, d,  $J_{5,5\text{-OH}}$  5 Hz, 5-OH, exch. D<sub>2</sub>O), 4.43 (1 H, d,  $J_{4,5}$  5 Hz, 4-H), 4.63 (1 H, d,  $J_{2,1}$  4 Hz, 2-H), 5.4 (1 H, d,  $J_{5,5\text{-OH}}$  5 Hz, 5-H), 6.0 (1 H, d, H-1,  $J_{1,2}$  4 Hz, 1-H), 7.56 (1 H, s, 3'-H), an AA'-BB' signal [ $\delta_A$  7.82–7.90 (6'- and 7'-H),  $\delta_B$  8.3–8.4 (5'- and 8'-H)], 12.88 (1 H, s, 4'-OH, exch. D<sub>2</sub>O), and 13.62 (1 H, s, 1'-OH, exch. D<sub>2</sub>O);  $\lambda_{\max}$ . (MeOH) (log  $\epsilon$ ) 322 (4.43), 285 (3.93), 256 (4.45), 250 (4.54), and 228 nm (4.27).

(5R)-3-C-Ethynyl-1,2-O-isopropylidene-5-(quinizarin-2-yl)- $\alpha$ -D-ribofuranose (**11b**).—The minor product isolated in the foregoing reaction  $R_F$  0.08 (System C) by evaporation of the appropriate eluates was obtained as orange-red needles (0.3 g, 10%), m.p. 189 °C, which retained a little toluene (Found: C, 64.6; H, 4.8%;  $M^+$ , 452. C<sub>24</sub>H<sub>20</sub>O<sub>9</sub>· $\frac{1}{8}$  C<sub>7</sub>H<sub>8</sub> requires C, 64.4; H,

4.55%;  $M$ , 452);  $m/z$  437 ( $M - 15$ ), 269, and 240;  $\delta$  (CDCl<sub>3</sub>; 400 MHz) 1.36 and 1.56 (2  $\times$  3 H, CMe<sub>2</sub>), 2.85 (1 H, s, C $\equiv$ CH), 3.42 (1 H, d, 3-OH, exch. D<sub>2</sub>O), 3.61 (1 H, d, 5-OH, exch. D<sub>2</sub>O), 4.33 (1 H, s,  $J_{4,5}$  8.5 Hz, 4-H), 4.69 (1 H, d,  $J_{2,1}$  3.5 Hz, 2-H), 5.36 (1 H, dd,  $J_{5,4}$  8.5 Hz, 5-H), 5.88 (1 H, d,  $J_{1,2}$  3.5 Hz, 1-H), 7.42 (1 H, s, 3'-H), an AA'-BB' signal [ $\delta_A$  7.75–7.83 (6'- and 7'-H),  $\delta_B$  8.24–8.3 (5'- and 8'-H)], 12.79 (1 H, s, 4'-OH, exch. D<sub>2</sub>O), and 13.66 (1 H, s, 1'-OH, exch. D<sub>2</sub>O).

5-Deoxy-3-C-ethynyl-1,2-O-isopropylidene-5-(quinizarin-2-yl)- $\alpha$ -D-ribofuranose (**11c**).—The second compound ( $R_F$  0.4, System C) obtained in the preparation of compound (**11a**) was isolated by evaporation of the appropriate chromatographic fraction. The hydrated deoxy derivative (**11c**) (0.3 g) crystallised from toluene–ethyl acetate as orange-red needles, m.p. 248 °C (Found: C, 65.5; H, 4.7%;  $M^+$ , 436. C<sub>24</sub>H<sub>20</sub>O<sub>8</sub>· $\frac{1}{4}$ H<sub>2</sub>O requires C, 65.4; H, 4.7%;  $M$ , 436);  $m/z$  378 ( $M - \text{CMe}_2 - \text{H}_2\text{O}$ ), 283 ( $Q - \text{CH}_2\text{CHOH}$ ), 253 ( $Q - \text{CH}_2^+$ ), 254, and 59 (Me<sub>2</sub>COH, 100%);  $\lambda_{\max}$ . (MeOH) (log  $\epsilon$ ) 227 (4.31), 250 (4.61) 255 (4.53), 327 (3.34), and 285 nm (3.96);  $\delta$  (CDCl<sub>3</sub>; 400 MHz) 1.35 and 1.58 (2  $\times$  3 H, CMe<sub>2</sub>), 2.7 (1 H, s, C $\equiv$ CH), 2.9 (1 H, s, 3-OH, exch. D<sub>2</sub>O), 3.2 (2 H, m, CH<sub>2</sub>), 4.2 (1 H, m, 4-H), 4.5 (1 H, d,  $J_{2,1}$  4.5 Hz, 2-H), 5.9 (1 H, d,  $J_{1,2}$  4.5 Hz, 1-H), 7.3 (1 H, s, 3'-H), an AA'-BB' signal [ $\delta_A$  7.5–7.75 (6'- and 7'-H),  $\delta_B$  8.24–8.4 (5'- and 8'-H)], 12.6 (1 H, s, 4'-OH, exch. D<sub>2</sub>O), and 13.2 (1 H, s, 1'-OH, exch. D<sub>2</sub>O).

(5S)-3-C-Ethynyl-5-(quinizarin-2-yl)- $\alpha$ -( $\beta$ )-D-ribofuranose (**13a**).—A solution of (5S)-3-C-ethynyl-1,2-O-isopropylidene-5-(quinizarin-2-yl)- $\alpha$ -D-ribofuranose (**11a**) (0.5 g) in aqueous acetic acid (200 cm<sup>3</sup>; 70%) was heated under reflux for 2 h, when t.l.c. examination (System B) indicated complete disappearance of starting material ( $R_F$  0.8) and the presence of a single product ( $R_F$  0.12). The solution was evaporated to dryness and repeatedly evaporated with toluene to give a solid orange-red residue, (5S)-3-C-Ethynyl-5-(quinizarin-2-yl)- $\alpha$ -( $\beta$ )-D-ribofuranose hemihydrate (0.45 g), which was crystallised from toluene–ethyl acetate as orange-red needles, m.p. 158 °C (Found: C, 59.45; H, 4.1%;  $M^+$ , 412. C<sub>21</sub>H<sub>16</sub>O<sub>9</sub>· $\frac{1}{2}$ H<sub>2</sub>O requires C, 59.55; H, 4.07%;  $M$ , 412)  $\delta$ [(CD<sub>3</sub>)<sub>2</sub>SO] 2.5 (1 H, s, C $\equiv$ CH), 3.57 (1 H, d,  $J$  7 Hz, 2- or 4-H), 3.82 (1 H, d,  $J$  8 Hz, 4- or 2-H), 5.0 (1 H, d,  $J$  8 Hz, 4- or 2-OH exch. D<sub>2</sub>O), 5.12 (1 H, d,  $J_{1,1\text{-OH}}$  8.5 Hz, 1-H), 5.2 (1 H, s, 5-H), 5.4 (1 H, d,  $J$  7 Hz, 2- or 4-OH, exch. D<sub>2</sub>O), 5.8 (1 H, s, 3-OH, exch. D<sub>2</sub>O), 6.8 (1 H, d,  $J$  8.5 Hz, 1-OH exch. D<sub>2</sub>O), 7.4 (1 H, s, 3'-H), an AA'-BB' signal [ $\delta_A$  7.4–7.7 (6' and 7'-H),  $\delta_B$  8.2–8.37 (5'- and 8'-H)], 12.66 (1 H, s, 4'-OH, exch. D<sub>2</sub>O), and 13.27 (1 H, s, 1'-OH, exch. D<sub>2</sub>O). When a solution of the pyranose derivative in THF–acetone was treated with aqueous sodium metaperiodate at 0 °C during 1.5 h, t.l.c. examination (System A) showed that the starting material had been completely converted into a mixture of products ( $R_F$  0.6, 0.5, and 0.9) which were not investigated further.

(5R)-3-C-Ethynyl-5-(quinizarin-2-yl)- $\alpha$ -( $\beta$ )-D-ribofuranose (**14**).—A solution of (5R)-3-C-ethynyl-1,2-O-isopropylidene-5-(quinizarin-2-yl)- $\alpha$ -D-ribofuranose (**11b**) (52.2 mg) in 70% aqueous acetic acid (15 cm<sup>3</sup>) was heated under reflux for 3 h. T.l.c. examination (System D) indicated the complete disappearance of starting material ( $R_F$  0.89) and the presence of a single product ( $R_F$  0.36). The solution was evaporated to dryness to yield an orange-red residue of (5R)-3-C-ethynyl-5-(quinizarin-2-yl)- $\alpha$ -( $\beta$ )-D-ribofuranose (**14**) (45 mg, 94%) which was crystallised from acetic acid as needles, m.p. 212 °C (decomp.) (Found: C, 58.4; H, 4.1%;  $M^+$ , 412. C<sub>21</sub>H<sub>16</sub>O<sub>9</sub>·H<sub>2</sub>O requires C, 58.6; H, 4.18%;  $M$ , 412);  $m/z$  394 ( $M - \text{H}_2\text{O}$ ), 376 ( $M - 2 \text{H}_2\text{O}$ ), 269, and 240 (100%);  $\delta$  (CDCl<sub>3</sub>; 400 MHz) 2.45 (1 H, s, C $\equiv$ CH), 3.72 (d, 1 H,  $J$  5 Hz, 2- or 4-H), 4.69 (1 H, t, 4- or 2-H), 5.06 (2  $\times$  1 H, d, 1- and 5-H), 5.48 (1 H, s, 3-OH, exch. D<sub>2</sub>O), 5.09–6.78 (3 H,

1-, 2-, and 4-OH, all exch. D<sub>2</sub>O), 7.55 (1 H, s, 3'-H), and AA'-BB' signal [ $\delta_A$  7.88—8.05 (6'- and 7'-H),  $\delta_B$  8.2—8.35 (5'- and 8'-H)], 12.75 (1 H, s, 4'-OH, exch. D<sub>2</sub>O), and 13.33 (1 H, s, 1'-OH, exch. D<sub>2</sub>O).

**3-O-Benzyl-3-C-ethynyl-1,2:5,6-di-O-isopropylidene- $\alpha$ -D-allofuranose (1d).**—A suspension of sodium hydride (16.28 g) and 3-C-ethynyl-1,2:5,6-di-O-isopropylidene- $\alpha$ -D-allofuranose (1c) (16.26 g) in dry DMSO (150 cm<sup>3</sup>) was stirred for 1.5 h at 45 °C. Benzyl chloride (14.49 g) was added and the mixture was heated for 1.5 h at 55 °C and then poured into ice-water and extracted with chloroform (5 × 50 cm<sup>3</sup>). The combined extracts were washed with water (3 × 50 cm<sup>3</sup>), dried (MgSO<sub>4</sub>), and evaporated to leave a pale yellow syrup of 3-O-benzyl-3-C-ethynyl-1,2:5,6-di-O-isopropylidene- $\alpha$ -D-allofuranose (1d) (20.5 g, 95%),  $R_F$  (System A) 0.72;  $\nu_{\max}$ . 2 110 (C≡C) and 1 380 cm<sup>-1</sup> (CMe<sub>2</sub>);  $m/z$  359 ( $M - CH_3$ ), 101, and 91 (C<sub>7</sub>H<sub>7</sub><sup>+</sup>, 100%);  $\delta$  (CDCl<sub>3</sub>; 60 MHz) 1.3 and 1.5 (2 × 3 H, CMe<sub>2</sub>), 1.7 (1 H, s, C≡CH), 4.0—5.0 (7 H, m, unresolved), 5.8 (1 H, d, 1-H), and 7.3 (5 H, m, Ph). The compound was sufficiently pure to be used in the following experiment.

**3-O-Benzyl-3-C-ethynyl-1,2-O-isopropylidene- $\alpha$ -D-ribo-pentodialdo-1,4-furanose (2c).**—A solution of the foregoing diisopropylidene derivative (1d) (11 g) in aqueous acetic acid (70%; 200 cm<sup>3</sup>) was set aside at room temperature for 24 h, when t.l.c. (System A) examination revealed that the starting material had been replaced by a single major product ( $R_F$  0.38). To the solution was added a solution of sodium metaperiodate (6.9 g) in water (75 cm<sup>3</sup>) and the mixture was stirred for 30 min at 0 °C, diluted with water (250 cm<sup>3</sup>), and extracted with chloroform (5 × 50 cm<sup>3</sup>). The combined extracts were washed with water (3 × 25 cm<sup>3</sup>), dried (MgSO<sub>4</sub>), and evaporated to dryness. The aldehyde (2c) was obtained as a pale yellow syrup (8.7 g, 98%), homogeneous on t.l.c. [ $R_F$  (System A) 0.58];  $\nu_{\max}$ . 1 380 (CMe<sub>2</sub>), 1 735 (C=O), and 2 110 cm<sup>-1</sup> (C≡CH).

**(5S)-3-O-Benzyl-3-C-ethynyl-1,2-O-isopropylidene-5-(quinizarin-2-yl)- $\alpha$ -D-ribofuranose (11d).**—The foregoing 3-O-benzyl-3-C-ethynyl-1,2-O-isopropylidene- $\alpha$ -D-ribo-pentodialdo-1,4-furanose (2c) (8.7 g) was added to a solution of leuco-quinizarin (3) (7.66 g) in methanol (85 cm<sup>3</sup>) and THF (150 cm<sup>3</sup>) at 0 °C and the mixture was then treated under nitrogen with a solution of sodium hydroxide (32%; 7.6 cm<sup>3</sup>) and set aside for 1.5 h, when t.l.c. examination (System A) revealed the presence of a single major product ( $R_F$  0.45) accompanied by a smaller quantity of a second compound ( $R_F$  0.69), quinizarin ( $R_F$  0.82), and a trace of a fourth substance ( $R_F$  0.0). A steady stream of air was passed through the reaction mixture for 2 h and the resultant purple solution was added dropwise to a rapidly stirred mixture of 2M-hydrochloric acid (50 cm<sup>3</sup>) and crushed ice (50 g). The resultant solid red precipitate (10.5 g) was collected by filtration, washed thoroughly with water, and air-dried. A filtered solution of the solid in toluene-ethyl acetate (2:1) was applied to a silica gel column (7 × 60 cm) and eluted by the same solvent system. The major product [ $R_F$  0.45 (System A)] readily separated from quinizarin and the minor products of the reaction and was obtained in solid form after evaporation of the appropriate column fractions. (5S)-3-O-Benzyl-3-C-ethynyl-1,2-O-isopropylidene-5-(quinizarin-2-yl)- $\alpha$ -D-ribofuranose hemihydrate (11d) was obtained as an orange-red solid, m.p. 96 °C (5.7 g, 36%) (Found: C, 67.8; H, 5.0%;  $M^+$ , 542. C<sub>31</sub>H<sub>26</sub>O<sub>9</sub>·½H<sub>2</sub>O requires C, 67.5; H, 4.9%;  $M$ , 542);  $m/z$  527 ( $M - CH_3$ ), 269, 240, and 91 (C<sub>7</sub>H<sub>7</sub><sup>+</sup>, 100%);  $\nu_{\max}$ . (KBr) 3 475 (OH), 1 625 (quinone), 2 110 (C≡C), and 1 380 cm<sup>-1</sup> (CMe<sub>2</sub>);  $\lambda_{\max}$ . (MeOH) (log  $\epsilon$ ) 205 (4.42) and 250 nm (4.4);  $\delta$  (CDCl<sub>3</sub>; 400 MHz) 1.35 and 1.6 (2 × 3 H, CMe<sub>2</sub>), 2.87 (1 H, s, C≡CH), 3.35 (1 H, br, 5-OH, exch. D<sub>2</sub>O), 4.45 and 4.55 (2 × 1 H, d,  $J$  10 Hz, OCH<sub>2</sub>Ph), 4.66 (1 H, d, 2-H), 4.68 (1 H, d, 4-H), 5.24 (1 H, d,  $J_{5,5-OH}$  7.5 Hz, 5-H), 5.98 (1 H, d,  $J_{1,2}$  3 Hz, 1-H),

6.95 (5 H, m, Ph), 7.28 (1 H, s, 3'-H), AA'-BB' signal [ $\delta_A$  7.83—7.85 (6'- and 7'-H),  $\delta_B$  8.28—8.35 (5'- and 8'-H)], 12.78 (1 H, s, 4'-OH, exch. D<sub>2</sub>O), and 13.5 (1 H, s, 1'-OH, exch. D<sub>2</sub>O).

The minor fraction from the foregoing reaction [ $R_F$  0.69 (System A)] was isolated as a red solid after evaporation of the appropriate fractions. (5R)-3-O-Benzyl-3-C-ethynyl-1,2-O-isopropylidene-5-(quinizarin-2-yl)- $\alpha$ -D-ribofuranose hemihydrate (11e) (1.8 g) was crystallised from toluene-ethyl acetate as orange-red needles, m.p. 150 °C (Found: C, 67.9; H, 4.8%;  $M^+$ , 542);  $m/z$  527 ( $M - CH_3$ ), 269, 240, and 91 (C<sub>7</sub>H<sub>7</sub><sup>+</sup>, 100%);  $\delta$  (CDCl<sub>3</sub>; 400 MHz) 1.35 and 1.55 (2 × 3 H, CMe<sub>2</sub>), 2.91 (1 H, s, C≡CH), 3.26 (1 H, br, 5-OH, exch. D<sub>2</sub>O), 4.55 (2 H, s, CH<sub>2</sub>), 4.7 (1 H, d,  $J_{2,1}$  3.5 Hz, 2-H), 4.77 (1 H, d, 4-H), 5.55 (1 H, d,  $J_{5,5-OH}$  7 Hz, 5-H), 5.9 (1 H, d,  $J_{1,2}$  3.5 Hz, 1-H), 7.15 (5 H, m, Ph), 7.6 (1 H, s, 3'-H), AA'-BB' signal [ $\delta_A$  7.78—7.85 (6'- and 7'-H),  $\delta_B$  8.27—8.35 (5'- and 8'-H)], 12.9 (1 H, s, 4'-OH, exch. D<sub>2</sub>O), and 13.6 (1 H, s, 1'-OH, exch. D<sub>2</sub>O).

**Debenzylation of (5S)- and (5R)-3-O-Benzyl-3-C-ethynyl-1,2-O-isopropylidene-5-(quinizarin-2-yl)- $\alpha$ -D-ribofuranose (11d and e).**—A few milligrams of (5S)-3-O-benzyl-3-C-ethynyl-1,2-O-isopropylidene-5-(quinizarin-2-yl)- $\alpha$ -D-ribofuranose were dissolved in chloroform and the solution was treated with a few drops of BCl<sub>3</sub> at -78 °C. After 10 min the solution was allowed to warm to 0 °C and water was added. The mixture was then evaporated to dryness. The residue was treated with water and the insoluble fraction was collected by centrifugation and isolated as an orange-red solid,  $m/z$  412 ( $M^+$ ); 394 ( $M - H_2O$ ), 376 ( $M - 2H_2O$ ), and 240 (100%). The compound was identical (i.r., t.l.c., mass spectra) with (5S)-3-C-ethynyl-5-(quinizarin-2-yl)- $\alpha$ -( $\beta$ )-D-ribofuranose (13a) (see above).

A similar debenzoylation of (5R)-3-O-benzyl-3-C-ethynyl-1,2-O-isopropylidene-5-(quinizarin-2-yl)- $\alpha$ -D-ribofuranose with boron trichloride gave (5R)-3-C-ethynyl-5-(quinizarin-2-yl)- $\alpha$ -( $\beta$ )-D-ribofuranose (14), identical (i.r., t.l.c., mass spectra) with the compound prepared above.

**(5S)-3-O-Benzyl-3-C-ethynyl-5-(quinizarin-2-yl)- $\alpha$ -( $\beta$ )-D-ribofuranose (13b).**—A solution of (5S)-3-O-benzyl-3-C-ethynyl-1,2-O-isopropylidene-5-(quinizarin-2-yl)- $\alpha$ -D-ribofuranose (11d) (4 g) in aqueous acetic acid (70%; 120 cm<sup>3</sup>) was heated under reflux for 2 h, when t.l.c. examination (System A) revealed the complete disappearance of starting material ( $R_F$  0.46) and the presence of a single new compound ( $R_F$  0.32). The solution was evaporated to dryness, and added toluene was repeatedly evaporated off to give a red solid residue of (5S)-3-O-benzyl-3-C-ethynyl-5-(quinizarin-2-yl)- $\alpha$ -( $\beta$ )-D-ribofuranose (3.26 g, 88%) which was crystallised from toluene as deep red needles which retained a little toluene, m.p. 168 °C (Found: C, 67.5; H, 4.7%;  $M^+$ , 502. C<sub>28</sub>H<sub>22</sub>O<sub>9</sub>·¼C<sub>7</sub>H<sub>8</sub> requires C, 67.45; H, 4.5%;  $M$ , 502);  $m/z$  350 ( $M - 2H_2O - OCH_2Ph - C\equiv CH$ ), 269, 240, and 91 (C<sub>7</sub>H<sub>7</sub><sup>+</sup>, 100%);  $\delta$  (CDCl<sub>3</sub>) 2.95 (1 H, s, C≡CH), 3.07 (1 H, d,  $J$  6.5 Hz, 4-OH, exch. D<sub>2</sub>O), 3.6 (1 H, d,  $J$  7.5 Hz, 2-OH, exch. D<sub>2</sub>O), 4.05 (1 H, d,  $J_{2,2-OH}$  7.5 Hz, 2-H), 4.14 (1 H, d,  $J_{1,1-OH}$  12 Hz, 1-OH), 4.41 (1 H, d,  $J_{4,4-OH}$  6.5 Hz, 4-H), 4.85 (2 H, d, OCH<sub>2</sub>Ph), 5.3 (1 H, d,  $J_{1,1-OH}$  12 Hz, 1-H), 5.45 (1 H, s, 5-H), 7.4 (5 H, m, Ph), 7.69 (1 H, s, 3'-H), an AA'-BB' signal [ $\delta_A$  7.81—7.85 (6'- and 7'-H),  $\delta_B$  8.32—8.37 (5'- and 8'-H)], and 12.9 and 13.45 (2 × 1 H, 1'- and 4'-OH, both exch. D<sub>2</sub>O).

**(4S)-2-O-Benzyl-2-C-ethynyl-3-O-formyl-4-(quinizarin-2-yl)- $\alpha$ -( $\beta$ )-D-erythroterofuranose (15).**—To a solution of the aforementioned ribopyranosyl quinizarin (13b) ( $R_F$  0.45) (2 g) in acetic acid (235 cm<sup>3</sup>) at room temperature was added a solution of sodium metaperiodate (0.87 g) in water (100 cm<sup>3</sup>). The progress of the reaction was monitored by t.l.c. (System B) which revealed the complete disappearance of starting material ( $R_F$  0.36) and the presence of a new single product ( $R_F$  0.43) after

35 min. Water (100 cm<sup>3</sup>) was added and the mixture was extracted with chloroform (3 × 50 cm<sup>3</sup>). The combined extracts were washed with water, dried (MgSO<sub>4</sub>), and evaporated to give the  $\alpha$ -( $\beta$ )-D-erythrose derivative (15) as an orange-red solid (1.8 g, 90%), homogeneous on t.l.c., m.p. 184 °C, which retained a little chloroform (Found: C, 63.54; H, 3.9%; M<sup>+</sup>, 500. C<sub>28</sub>H<sub>20</sub>O<sub>9</sub>· $\frac{1}{4}$ CHCl<sub>3</sub> requires C, 63.4; H, 3.85%; M, 500); m/z 269, 267 (quinizarin - CO<sup>+</sup>, 100%);  $\nu_{\max}$ , 3 440 (OH), 1 735 (OCHO), 1 635 (quinone), and 1 590 cm<sup>-1</sup>;  $\delta$  (CDCl<sub>3</sub>; 400 MHz) 2.95–3.1 (1 H, singlet split in ratio 1:2, C≡CH), 3.5 (1 H, br, 2-OH, exch. D<sub>2</sub>O), 4.6–4.8 (2 H, m, OCH<sub>2</sub>Ph), 5.55 (1 H, s, 2-H), [5.82–6.18 (1 H, dd, J 4 Hz, 3- or 4-H) and 6.0–6.2 (1 H, dd, J 3 Hz, 4- or 3-H)—the signals are in the ratio 2:1], 7.3 (5 H, m, Ph), 7.6 (1 H, s, 3'-H), 7.85 (3 H, m, 6'- and 7'-H and OCHO), 8.35 (2 H, m, 5'- and 8'-H), and 12.9 and 13.3 (2 × 1 H, 1'- and 4'-OH, both exch. D<sub>2</sub>O).

(7R,8R,9S,10S)-8-Benzoyloxy-8-ethynyl-7,8,9,10-tetrahydro-6,7,9,10,11-pentahydroxynaphthacene-5,12-dione (17a).—(a) To a solution of the foregoing O-benzyl erythrose derivative (15) (0.5 g) in acetic acid (50 cm<sup>3</sup>) were added methanol (15 cm<sup>3</sup>) and zinc powder. The mixture was shaken at room temperature for 3 h and was then filtered and the yellow filtrate was evaporated to ca. 20 cm<sup>3</sup> and extracted with chloroform (3 × 25 cm<sup>3</sup>). The combined extracts were washed successively with water and dil. hydrochloric acid, dried (MgSO<sub>4</sub>), and evaporated to afford a yellow solid (0.5 g). A solution of the solid (0.5 g) in dimethylformamide (DMF) (8 cm<sup>3</sup>) at 0 °C was treated with a solution of DBN (0.2 cm<sup>3</sup>) in DMF (4 cm<sup>3</sup>) during 45 min under nitrogen, when t.l.c. examination (System B) showed that the starting material (R<sub>F</sub> 0.6) had been completely replaced by one major product (R<sub>F</sub> 0.5) and a small amount of a second component (R<sub>F</sub> 0.43) in addition to a trace of material with R<sub>F</sub> 0.0. The mixture was aerated for 1 h and the resultant purple solution was poured into a mixture of 2M-hydrochloric acid (25 cm<sup>3</sup>) and crushed ice (50 g) to produce an orange-red solid precipitate which was collected, washed thoroughly with water, and dissolved in THF (15 cm<sup>3</sup>)-methanol (5 cm<sup>3</sup>); the solution was basified with M-sodium hydroxide (12 cm<sup>3</sup>) followed by acidification with hydrochloric acid to afford a solid orange-red precipitate (0.43 g). T.l.c. examination of the solid (System B) showed that the major starting material (R<sub>F</sub> 0.5) had completely disappeared and had been replaced by a new product (R<sub>F</sub> 0.2) in addition to the compound (R<sub>F</sub> 0.43) which was unaffected by the treatment with alkali. The two compounds were separated on thick layer plates (20 × 20 cm) to give the first product (R<sub>F</sub> 0.2) (0.175 g) and the second product (R<sub>F</sub> 0.43) (0.112 g). The naphthacenedione hydrate (17a) (R<sub>F</sub> 0.2) was obtained as orange-red needles, m.p. 158 °C (Found: C, 65.9; H, 4.4%; M<sup>+</sup>, 472. C<sub>27</sub>H<sub>20</sub>O<sub>8</sub>·H<sub>2</sub>O requires C, 66.1; H, 4.5%; M, 472); m/z 454 (M - H<sub>2</sub>O), 363 (M - H<sub>2</sub>O - C<sub>7</sub>H<sub>7</sub>), 346 (M - C<sub>7</sub>H<sub>7</sub>OH - H<sub>2</sub>O, 100%), 298 (retro-Diels-Alder fragment), 280 (298 - H<sub>2</sub>O), and 91 (C<sub>7</sub>H<sub>7</sub><sup>+</sup>);  $\lambda_{\max}$  (MeOH) 252, 281, and 400–550 nm (characteristic of a 2,3-disubstituted quinizarin);  $\delta$  (CDCl<sub>3</sub>; 400 MHz) 2.65, 3.05, and 4.25 (3 × 1 H, 7-, 9-, and 10-OH, all exch. D<sub>2</sub>O), 2.9 (1 H, s, C≡CH), 4.5 and 5.15 (2 × 1 H, d, J<sub>9,10</sub> 7.5 Hz, 10- and 9-H respectively), 4.85 and 5.0 (2 × 1 H, d, J 12 Hz, CH<sub>2</sub>Ph), 5.25 (1 H, s, 7-H), 7.2 (5 H, m, Ph), an AA'-BB' signal [ $\delta_A$  7.83–7.87 (2- and 3-H),  $\delta_B$  8.32–8.36 (1- and 4-H)], and 13.3 and 13.8 (2 × 1 H, s, 6- and 11-OH, both exch. D<sub>2</sub>O).

(b) To a solution of the foregoing erythrose derivative (15) (10 mg) in THF (0.75 cm<sup>3</sup>)-methanol (0.5 cm<sup>3</sup>) under nitrogen at 0 °C was added a solution of sodium dithionite (18 mg) in water (0.5 cm<sup>3</sup>) followed by 0.5M-sodium hydroxide (0.5 cm<sup>3</sup>). The reaction mixture was monitored by aeration, acidification of a small sample and collection of the resultant red solid precipitate by centrifugation followed by t.l.c. examination (System B). After 1 h the starting material had been completely

replaced by a major product (R<sub>F</sub> 0.43) and a minor one (R<sub>F</sub> 0.2). The products had identical behaviour on t.l.c. in several solvent systems to the two products isolated under (a) but were produced in different amounts. They were not examined further.

(7R,8R,9S,10S)-8-Ethynyl-7,8,9,10-tetrahydro-6,7,8,9,10,11-hexahydroxynaphthacene-5,12-dione (17b).—To a solution of the foregoing O-benzyl derivative (17a) (50 mg) in dry chloroform (30 cm<sup>3</sup>) cooled to -78 °C was added boron trichloride (2 cm<sup>3</sup>). The solution was allowed to reach room temperature and was then poured into rapidly stirred ice-water. The mixture was evaporated to remove chloroform and the resulting red solid precipitate was filtered off from the aqueous phase, washed with water, and dried. The anthracyclinone (17b) (25 mg), m.p. 240 °C, was homogeneous on t.l.c. (R<sub>F</sub> 0.06, System B) (Found: M<sup>+</sup>, 382. C<sub>20</sub>H<sub>14</sub>O<sub>8</sub> requires M, 382); m/z 364 (M - H<sub>2</sub>O), 347 (M - 2H<sub>2</sub>O), 298 (retro-Diels-Alder fragment, 100%), 280 (298 - H<sub>2</sub>O); peak m/z 91 (benzyl) was absent.

(8S,9S,10S)-8-Benzoyloxy-8-ethynyl-7,8,9,10-tetrahydro-6,9,10,11-tetrahydroxynaphthacene-5,12-dione (18a).—The product (R<sub>F</sub> 0.43, System B) produced in the foregoing preparation of compound (17a) formed orange-red needles, m.p. 110 °C, which retained chloroform (Found: C, 62.4; H, 4.2%; M<sup>+</sup>, 456. C<sub>27</sub>H<sub>20</sub>O<sub>7</sub>·0.65 CHCl<sub>3</sub> requires C, 62.2; H, 3.9%; M, 456); m/z 365 (M - C<sub>7</sub>H<sub>7</sub>), 330 (M - C<sub>7</sub>H<sub>7</sub>OH - H<sub>2</sub>O), 282 (retro-Diels-Alder fragment), and 91 (C<sub>7</sub>H<sub>7</sub><sup>+</sup>, 100%);  $\lambda_{\max}$  (MeOH) 252, 281, and 440–550 nm (characteristic of a 2,3-disubstituted quinizarin);  $\delta$  (CDCl<sub>3</sub>; 400 MHz) 2.8 (1 H, s, C≡CH), 2.9 and 3.9 (2 × 1 H, 9- and 10-OH, both exch. D<sub>2</sub>O), 3.15 and 3.45 (2 × 1 H, d, J 18 Hz, 7-H<sub>eq</sub> and 7-H<sub>ax</sub>), 4.24 (1 H, d, J 5 Hz, 9- or 10-H), 5.2 (1 H, d, J 5 Hz, 10- or 9-H), 4.72 and 4.9 (2 H, d, J 11.5 Hz, CH<sub>2</sub>Ph), 7.25 (5 H, m, Ph), an AA'-BB' signal [ $\delta_A$  7.8–7.87 (2- and 3-H),  $\delta_B$  8.28–8.33 (1- and 4-H)], and 13.27 (2 H, s, 6- and 11-OH, both exch. D<sub>2</sub>O).

(8S,9S,10S)-8-Ethynyl-7,8,9,10-tetrahydro-6,8,9,10,11-pentahydroxynaphthacene-5,12-dione (18b).—Debenzylation of the foregoing O-benzylanthracyclinone (18a) was carried out by the method used for the preparation of compound (17b). The anthracyclinone (18b) (75% yield) was obtained as an orange-red solid, m.p. 230 °C, homogeneous on t.l.c. (Found: M<sup>+</sup>, 366. C<sub>20</sub>H<sub>14</sub>O<sub>7</sub> requires M, 366); m/z 348 (M - H<sub>2</sub>O), 330 (M - 2H<sub>2</sub>O), 282 (retro-Diels-Alder fragment, 100%); peak at m/z 91 (benzyl) was absent.  $\delta$  [(CD<sub>3</sub>)<sub>2</sub>CO; 250 MHz] 3.05 (1 H, s, C≡CH), 3.15 and 3.35 (2 × 1 H, d, J 18 Hz, 7-H<sub>eq</sub> and 7-H<sub>ax</sub>), 4.1 (1 H, t, 9-H), 4.35 (1 H, d, 9- or 10-OH, exch. D<sub>2</sub>O), 4.7 (1 H, d, 10- or 9-OH, exch. D<sub>2</sub>O), 4.95 (1 H, s, 8-OH, exch. D<sub>2</sub>O), 5.05 (1 H, t, 10-H), an AA'-BB' signal [ $\delta_A$  7.95–8.05 (2- and 3-H),  $\delta_B$  8.3–8.4 (1- and 4-H)] and 13.45 and 13.75 (2 × 1 H, s, 6- and 11-OH, both exch. D<sub>2</sub>O).

#### Acknowledgements

We thank the Yorkshire Cancer Research Campaign for a research grant (to S. Q.).

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*Received 23rd August 1984; Paper 4/1468*