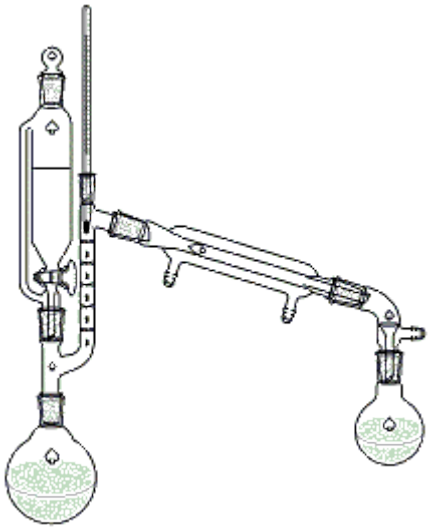
General Experimental Details



Ethyl acetate and hexanes were distilled prior to use. Dry solvents used in the experiments were prepared as follows: dichloromethane was distilled off calcium hydride or phosphorus(v) oxide and stored over 4å molecular sieves; hexanes were distilled off phosphorus(v) oxide; THF, diethyl ether, benzene and toluene were distilled off sodium benzophenone ketyl; xylene was dried and stored over sodium hydroxide pellets. Dry diethyl ether used for the trituations and crystallisations was prepared by allowing the solvent to stand over sodium wire for a minimum of one week. 'Analar' toluene was considered dry toluene. Deuteriochloroform, used as a solvent for the determination of NMR spectra, was stored over tin granules. Zinc chloride was fused in a nickel crucible immediately before use.

Unless otherwise stated, all reactions were carried out at room temperature (*ca.* 20 °C). Evaporations were conducted under reduced pressure (using a water-pump or an oil pump) with a Büchi rotary evaporator (<40 °C). Reactions which involved sonication were carried out using a Sonicor Instruments Corporation SC-220H sonicator filled with water.

TLC (Thin Layer Chromatography) was carried out on Merck plastic plates coated with silica gel (60 F_{254}). The plates were either observed under UV light (Mineralight UVG2-58 lamp) or developed with iodine vapour or a sulfuric acid stain (EtOH: conc. H_2SO_4:p-$MeOC_6H_4CHO$, 95:4:1). Column chromatography was performed under pressure (ca. 7 x 10^4 Pa) using either Merck Kieselgel H Type 60 or Crossfield Sorbsil C60 flash silica. Low temperature silica-gel chromatography was carried out using cooled (Me_2CO-solid CO_2) solvents. Thus the material to be purified was loaded onto the column (which had been prewashed with the cooled eluant) in dichloromethane; the column was then eluted with the cooled mobile

phase. When the strengths of the eluant was varied during the chromatography, the first ratio was used and then more of the second solvent used to change the strength until the final ratio was used; product fractions monitored by TLC.

Melting points were determined using a Büchi 512 melting point apparatus. Optical rotations, measured at *ca.* 20 °C using either a Thorn Type 243 or an Optical Activity 1000 polarimeter, are given in 10^{-1}deg cm^2 g^{-1}. IR spectra were recorded using a Perkin-Elmer 783 spectrometer. A Perkin-Elmer Lambda 15 was used to determine UV spectra; extinction coefficients (ε) are presented in cm^2 mmol^{-1}. ^{1}H NMR spectra were measured at room temperature at 300 MHz using a Brucker AC 300 spectrometer or at 220 MHz using a Perkin-Elmer R34 spectrometer or at 200 MHz using a Brucker AC 200 spectrometer. A Kratos MS45 spectrometer was used to obtain EI and CI mass spectra (NH_3 as the carrier gas); FAB mass spectra (*p*-$NO_2C_6H_4CH_2OH$ as matrix) was measured using a Kratos Concept IS spectrometer. Elemental analyses were performed with a Carlo-Erba Model 1106 analyser.

For the NMR spectra, *s* represents a singlet, *d* represents a doublet, *dd* represents a doublet of doublets , *t* a triplet and *q* a quartet.

When an experiment was using 'refluxing under argon' conditions, a round-bottomed flask (in a hot oil bath), with a vertical liebig condenser was kept under a constant atmosphere of argon by placing a balloon of argon on top of the condenser through a suba-seal rubber bung. A two mouthed round-bottomed flask could contain a suba-seal bung for syringe insertion of solutions and the other mouth containing the balloon. A three-mouthed round-bottomed flask could contain a thermometer also, for example. All glassware 'Quickfit' jointed and dried in an oven before use.

The experimental part of the *thesis* is 63 pages of A4 print; this is a condensed version, but full experimental details are the same for all of the experiments listed below.

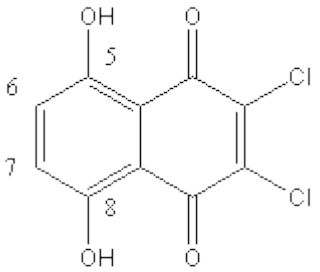
In some browsers, you may see 10-Hα or 10-Hβ instead of the better formatted 10-Hα and 10-Hβ respectively (e.g. in the NMR analysis).

Exp. 1

Reaction of Dichloromaleic Anhydride with 1,4-Dimethoxybenzene

To a molten mass of 1,4-dimethoxybenzene (45.56 g, 0.33 mol), aluminium chloride (205.8 g, 0.17 mol) and sodium chloride (39.72 g, 0.68 mol) at 170 °C was added, in portions, finely ground dichloromaleic anhydride (55.29 g, 0.33 mol). The temperature was kept at *ca.* 175-180 °C for 2 min and then the melt was allowed to cool. The mixture was treated with water (1.5 dm^3)

and conc. hydrochloric acid (100 cm^3) and allowed to stand overnight. The insoluble material was collected by filtration, dried (P_2O_5; *in vacuo*) and subjected to a soxhlet extraction with ethyl acetate as the solvent. Evaporation of the extract and crystallisation of the residue from ethyl acetate afforded dichloronaphthazarin (**1**)(22.58 g, 53%) as deep-red crystals;



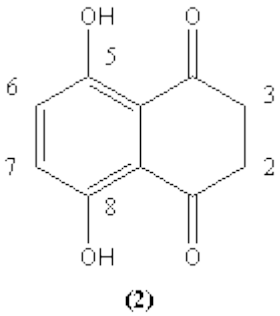
(1)

m.p. 198-200 °C (lit.[1] 198-199 °C),
δ(300 MHz; $CDCl_3$) 7.32 (2 H, s, 6- and 7-H) and 12.34 (2 H, s, 5- and 8-OH).

Exp. 2

*Reduction of Dichloronaphthazarin (**1**) with Tin(II) Chloride*

To a hot solution of tin(II) chloride (39.11 g, 0.17 mol) in 4M hydrochloric acid (300 cm^3) was added dichloronapththazarin (**1**) (5.18 g, 0.02 mmol). The mixture was heated under reflux for 3 h and filtered (while hot) through Celite. Extraction of the cooled filtrate with dichloromethane and evaporation of the dried ($MgSO_4$) extract left a residue (2.41 g) which was crystallised from ethyl acetate to afford dihydronaphthazarin (**2**) (1.71 g, 45%) as a dark-yellow solid;



(2)

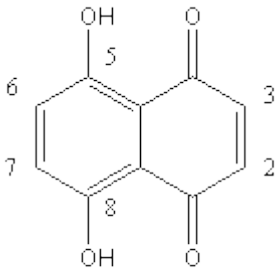
m.p. 148-149 °C (lit.[1] 148-151 °C),
δ (300 MHz; $CDCl_3$) 3.07 (4 H, s, 2- and 3-H_2), 7.27 (2 H, s, 6- and 7-H) and 11.93 (2 H, s, 5- and 8-OH).

Exp. 3

*Preparation of Naphthazarin (**3**)*

A solution of dihydronaphthazarin (**2**) (1.01 g, 5.31 mmol) in 5M sodium

hydroxide (500 cm^3) was warmed for 2.5 h; the reaction being monitored by TLC. The mixture was cooled to 0 °C (by the addition of crushed ice), acidified with conc. hydrochloric acid and extracted with dichloromethane. Evaporation of the dried ($MgSO_4$) extract and crystallisation of the residue from dichloromethane afforded naphthazarin (**3**) (0.68 g, 68 %) as dark-red crystals;



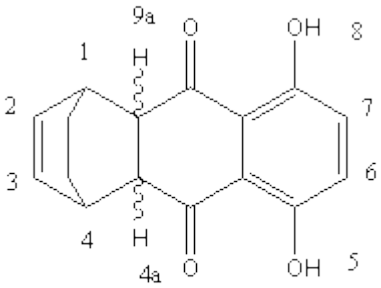
(3)

m.p. 235-238 °C (with sublimination) [lit.[1] 230-240 °C (with sublimination)], δ (300 MHz; $CDCl_3$) 7.15 (4 H, s, 2-, 3-, 6- and 7-H) and 12.42 (2 H, s, 5- and 8-OH).

Exp. 4

*Reaction of Naphthazarin (**3**) with Cyclohexa-1,3-diene*

To a solution of naphthazarin (**3**)(1.9 g, 10 mmol) in toluene (40 cm^3) was added cyclohexa-1,3-diene (2.43 g, 30 mmol). The mixture was heated at reflux under argon for 3 days. After removal of the solvent and residual diene by evaporation, the crude cycloadduct (2.62 g) was obtained. Crystallisation from chloroform afforded 1,4,4a,9a-*tetrahydro*-5,8-*dihydroxy*-1,4-*ethano*-9,10-*anthraquinone* (**4**) (1.67 g, 62%) as a brown solid;



(4)

m.p. 128-132 °C,

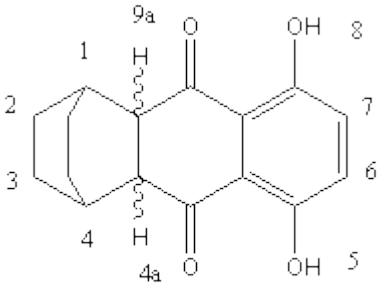
ν_{max} (KBr) 1620 (C=O) and 1580 cm^{-1}.

λ_{max} (EtOH) 213 (ε 13 600), 232 (16 300) and 398 nm (7700),

δ (300 MHz; $CDCl_3$) 1.41-1.48 and 1.77-1.84 (each 2 H, m, CH2CH2), 3.19 (2 H, s, 4a- and 9a-H), 3.42 (2 H, br s, 1- and 4-H), 6.22 (2 H, dd, J 4.5 and 3 Hz, 2- and 3-H), 7.22 (2 H, s, 6- and 7-H) and 12.8 (2 H, s, 5- and 8-OH) (irradiation at δ 3.4 caused the dd at δ 6.22 to collapse to a s; irradiation at

δ 3.19 caused no change),
m/z (EI) 270 (M^+, 100%),
(CI, NH_3) 271 (MH^+, 100%).
Found: C, 70.9; H, 5.0. $C_{16}H_{14}O_4$ requires C, 71.2; H, 5.2%.

Exp. 5
Reduction of 1,4,4a,9a-*Tetrahydro*-5,8-*dihydroxy*-1,4-*ethano*-9,10-*anthraquinone (**4**) with Hydrogen*
The cycloadduct (**4**) (0.305 g, 1.128 mmol) was stirred with 10% palladium on charcoal (0.15 g, 0.5 mass equiv.) in dry dichloromethane (10 cm^3) under an atmosphere of hydrogen for 1 day (the reaction being monitored by 220 MHz ^1H NMR spectroscopy). After filtration through celite and removal of the solvent from the filtrate, the crude reduced product (0.28 g) was obtained. Crystallisation from 1:1 chloroform-hexanes afforded 1,2,3,4,4a,9a-*hexahydro*-5,8-*dihydroxy*-1,4-*ethano*-9,10-*anthraquinone* (**5**) (0.10 g, 32.5%) as a light-yellow solid;

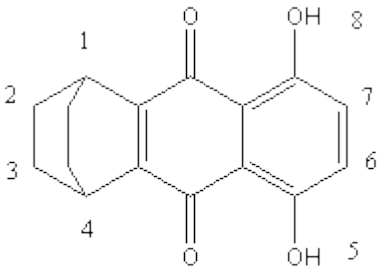


(5)

m.p. 153-153.5 °C,
ν_{max} (KBr) 1610 cm^{-1} (C=O),
λ_{max} (EtOH) 213 (ε 12 700), 233 (16 300), 256 (9200) and 398 nm (7400),
δ (300 MHz; $CDCl_3$) 1.45 and 1.75 (each 4 H, br s, together CH_2CH_2), 2.39 (2 H, br s, 1- and 4-H), 3.12 (2 H, s, 4a- and 9a-H), 7.29 (2 H, s, 7- and 8-H) and 12.77 (2 H, s, 5- and 8-OH) (irradiation at δ 2.30 caused the signals at δ 1.45 and 3.12 to sharpen; irradiation at δ 3.12 caused no change),
m/z (EI) 272 (M^+, 100%) and 192 (92),
(CI, NH_3) 273 (MH^+, 100%) and 272 (M^+, 36).
Found: C, 70.9; H, 5.7. $C_{16}H_{14}O_4$ requires C, 70.6; 5.9%.

Exp. 6
Oxidation of 1,2,3,4,4a,9a-*Hexahydro*-5,8-*dihydroxy*-1,4-*ethano*-9,10-*anthraquinone (**5**) with Air/Sodium Hydroxide*
A solution of compound (**5**) (4.28 g, 15.73 mmol) was warmed with 5M sodium hydroxide (500 cm^3) in the presence of air for 6 h (the process being followed by TLC). Acidification at °C with hydrochloric acid and filtration afforded a red solid. After washing with water and drying (P_2O_5; *in*

vacuo), the material (3.75 g) was crystallised from ethyl acetate to give 1,2,3,4-*tetrahydro*-5,8-*dihydroxy*-1,4-*ethano*-9,10-*anthraquinone* (**6**) (2.94 g, 69%) as a red solid;



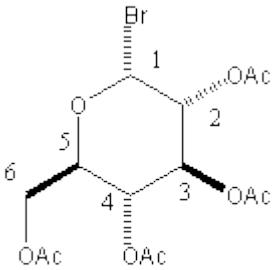
(6)

m.p. 182-183 °C,
ν_{max} (KBr) 1610 (C=O) and 1570 cm^{-1} (C=C),
λ_{max} (EtOH) 217 (ε 31 000), 287 (7900), 51 (6900) and 549 nm (4800),
δ (300 MHz; $CDCl_3$) 1.35 and 1.81 (each 4 H, br d, separation 7 Hz, 2 x CH_2CH_2), 3.58 (2 H, br s, 1- and 4-H), 7.20 (2 H, s, 6- and 7-H) and 12.73 (2 H, s, 5- and 8-OH),
m/z (EI) 270 (M^+, 83%) and 242 (M^+-C_2H_4, 100),
(CI, NH_3) 273 (MH_3^+, 100%).
Found: C, 70.8; H, 5.1. $C_{16}H_{14}O_4$ requires C, 71.1; 5.2%.

Exp. 7

*Preparation of Acetobromoglucose (**7**)*[2]

To stirred ice-cold acetic anhydride (1.2 dm^3) in a three litre reaction vessel, was added dropwise perchloric acid (8 cm^3, 60%) and the solution allowed to warm to room temperature. Anhydrous α-D-glucose (300 g, 1.66 mmol) was then added to the stirred mixture at such a rate that the reaction temperature was maintained at 30-45 °C. After cooling to 20 °C, red phosphorus (90 g, 2.90 mol) was introduced followed by bromine (178 cm^3, 3.45 mol) at such a rate that the temperature was maintained at <30 °C. Water (108 cm^3) was then added over 0.5 h (the temperature was not allowed to rise above 25 °C). After the addition was complete, the mixture was left to stir for 2 h, dichloromethane (ca. 750 cm^3) was then added and the mixture filtered through Celite. The filtrate was poured into ice-cold water (2 dm^3) contained in a separating funnel. After shaking, the organic layer was separated and the aqueous layer re-extracted with dichloromethane (x3). The combined organic phase was washed with aqueous sodium carbonate, dried ($MgSO_4$) and evaporated. The crude product was crystallised from diethyl ether-light petroleum to give *acetobromoglucose* (**7**) (426.8 g, 63%) as a white powder;



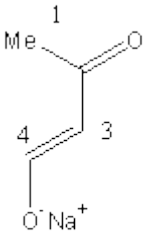
(7)

m.p. 76-78 °C (lit.,[2] 88 °C),
$[\alpha]_D$ +192 (1% in $CHCl_3$) [lit.,[2] +191 ($CHCl_3$)],
δ (300 MHz; $CDCl_3$) 2.04, 2.06, 2.10 and 2.11 (each 3 H, s, 4 x $MeCO_2$), 4.13 (1 H, br d, separation 11 Hz, 6-H), 4.27-4.37 (2 H, m, 5- and 6-H), 4.84 (1 H, dd, *J* 10 and 4 Hz, 2-H), 5.17 (1 H, t, *J* 10 Hz, 4-H), 5.51 (1 H, t, *J* 10 Hz, 3-H) and 6.62 (1 H, d, *J* 4 Hz, 1-H).

Exp. 8

Preparation of (E)-4-*Hydroxybut*-3-*en*-2-*one Sodium Salt*[2]

Sodium methoxide was prepared by the addition of sodium (23.5 g, 1.05 mol) to methanol (400 cm^3). Excess methanol was removed by azeotropic distillation with toluene (2 x 100 cm^3) under reduced pressure. Diethyl ether (600 cm^3) was added and the slurry cooled in an ice-bath. A mixture of ethyl formate (100 cm^3, 1.2 mol) and acetone (80 cm^3, 1.1 mol) was slowly added. The mixture was allowed to warm to room temperature, stirred overnight (under anhydrous conditions) and then filtered. The solid was washed well with diethyl ether and dried *in vacuo* to give the *title* (**8**) compound (79.7 g, 70 %) as a pale cream solid;



(8)

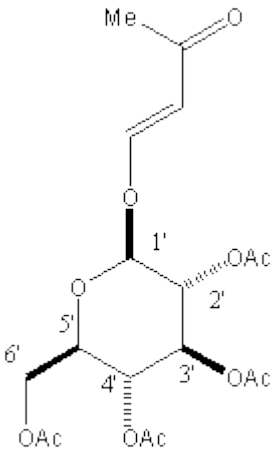
δ(200 MHz; D_2O) 2.00 (3 H, s, 1-H^3), 5.10 (1 H, d, *J* 12 Hz, 3-H) and 8.77 (1 H, d, *J* 12 Hz, 4-H).

Exp. 9

Preparation of (E)-4-(2′,3′,4′,6-*Tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*)*but*-3-*en*-2-*one* (***9***)[2]

Acetobromoglucose (**7**) (60.0 g, 0.15 mol) and the sodium salt (**8**) (31.9 g, 0.29 mmol) were dissolved in dry dimethyl sulfoxide (200 cm^3). The mixture was stirred for 3 h and then poured onto ice (200 cm^3). The aqueous phase

was extracted with dichloromethane (x 3), washed with water (x 6), dried ($MgSO_4$) and filtered. Evaporation *in vacuo* gave the crude butenone (27.5 g). Crystallisation of the product from dichloromethane-diethyl ether afforded the butenone (**9**) (19.5 g, 31 %) as fine needles;



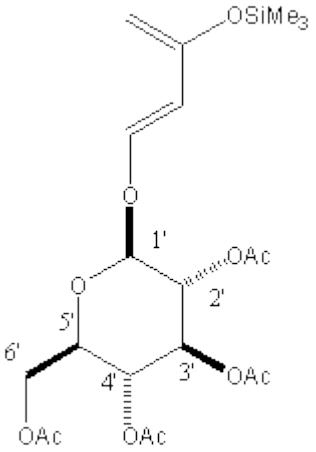
(9)

m.p. 149-150 (lit.[2], 149-150 °C),
δ(300 MHz; $CDCl_3$) 2.02, 2.04, 2.06 and 2.09 (each 3 H, s, 4 x $MeCO_2$), 2.12 (3 H, s, MeCO), 3.82 (1 H, dd, *J* 10, 5 and 2 Hz, 5'-H), 4.14 (1 H, dd, *J* 12.5 and 2 Hz, 6'-H), 4.27 (1 H, dd, *J* 12.5 and 5 Hz, 6'-H), 4.92 (1 H, d, *J* 8 Hz, 1'-H), 5.11 (1 H, t, *J* 9 Hz, 4'-H), 5.13 (1 H, dd, *J* 9 and 8 Hz, 2'-H), 5.25 (1 H, t, *J* 9 Hz, 3'-H) 5.84 (1 H, d, *J* 12.5 Hz, 3-H) and 7.42 (1 H, d, *J* 12.5 Hz, 4-H).

Exp. 10

Preparation of (E)-4-(2',3',4',6-*Tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*)-3-*trimethylsilyloxy*
buta-1,3-*diene (**10**)*[2]

(a) To a stirred mixture of fused zinc chloride (1.6 g, 11.7 mmol) and triethylamine (40 cm^3, 0.29 mmol) was added a slurry of the butenone (**9**) (16 g, 38 mmol) in dry benzene (100 cm^3) followed by trimethylsilyl chloride (7.5 cm^3, 160 mmol). The mixture was stirred at 55 °C for 2 days and the solvent removed *in vacuo*. Diethyl ether was added to the residue and the mixture filtered to afford the crude diene. The crude diene was triturated with dichloromethane-diethyl ether to afford a residue (17 g) and a mother liquor. Crystallisation of this mother liquor and combination of the material obtained (12.8 g) with the residue (17 g) and subjection of this mixture to low-temperature silica-gel chromatography [hexanes-EtOAc (3:1 to 1:3) then EtOAc as eluants] afforded two fractions.
The first-eluted material (14.34 g) afforded, after crystallisation from chloroform-diethyl-hexanes, the *title* compound (**10**) (10.21 g, 55 %) as a fine-white powder;



(10)

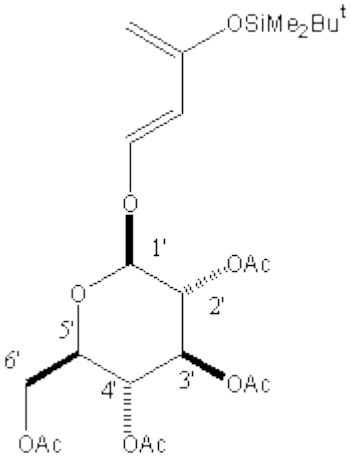
m.p. 98-99.5 °C (lit.[2], 104-106 °C),
$[\alpha]_D$ -18 (0.5% in EtOAc) [lit.,[2] -19 (EtOH)],
δ (300 MHz; $CDCl_3$) 0.22 (9 H, s, $SiMe_3$), 2.00, 2.02, 2.03 and 2.06 (each 3 H, s, 4 x $MeCO_2$), 3.75-3.82 (1 H, m, 5'-H), 4.13 (1 H, dd, *J* 12.5 and 2.5 Hz, 6'-H), 4.14 (2 H, s, 4-H_2), 4.24 (1 H, dd, *J* 12.5 and 5 Hz, 6'-H), 4.77 (1 H, d, *J* 8 Hz, 1'-H), 5.09 (1 H, dd, *J* 9 and 8 Hz, 2'-H), 5.09 *[or possibly 5.13(?) see ref. 2]*(1 H, t, *J* 4 Hz, 4'-H), 5.22 (1 H, t, *J* 9 Hz, 3'-H), 5.63 (1 H, d, *J* 12 Hz, 2-H) and 6.66 (1 H, d, *J* 12 Hz, 1-H).
The second-eluted material (10.2 g) was the butenone.
(b). To a stirred mixture of anhydrous zinc chloride (1.1 g, 8.1 mmol) and triethylamine (25 cm^3, 0.18 mmol) was added a slurry of the butenone (**9**) (10.1 g, 20.4 mmol) in dry benzene (140 cm^3) followed by trimethylsilyl chloride (15 cm^3, 320 mmol). The mixture was stirred at 50 °C for 2 days and the solvent removed *in vacuo*. The material obtained was washed with dry diethyl ether (300 cm^3) and the filtrate washed with water (3 x 250 cm^3), dried ($MgSO_4$) and evaporated to afford the crude diene (10.0 g). Crystallisation from dichloromethane-hexanes gave the *title* compound (6.55 g, 66%) as an off-white powder; whose ^{1}H NMR spectrum was identical to that of the diene obtained in part (a).

Exp. 11

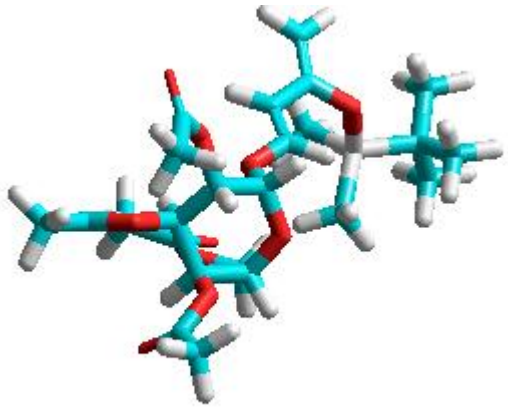
Preparation of (E)-1-(2',3',4',6'-*Tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*)-3-tert-
bytyldimethylsilyloxybuta-1,3-*diene (**11**)*[3]

(a) To a solution of the butenone (**9**) (5.0 g, 12 mmol) and triethylamine (3.4 cm^3 24 mmol) in dry dichloromethane (100 cm^3) was added tert-butyldimethylsilyl triflate (5.5 cm^3, 24 mmol) slowly at room temperature; an immediate darkening in colour was observed. After 80 min, triethylamine (10 cm^3) was added and the mixture was transferred to a separating funnel and diluted with dichloromethane (*ca.* 200 cm^3). The solution was washed with saturated aqueous sodium hydrogen carbonate and dried ($MgSO_4$). Removal of the solvent gave a light-brown solid (7.76 g). Purification by low

temperature silica-gel chromatography (diethyl ether-light petroleum (2:3) as eluant] gave the *title* compound (**11**) (3.18 g, 49 %) as a white solid after recrystallisation from dichloromethane-diethyl ether-hexanes;



(11)



Structure of the TBDMS-ether (trans diene)

m.p. 113-114 °C (lit.[3], 112-114 °C),
$[\alpha]_D$ -12.8 (0.01% in CH_2Cl_2) [lit.,[3] -12 (0.9% in CH_2Cl_2)],
δ (300 MHz; $CDCl_3$) 0.23 (6 H, s, $SiMe_2$), 1.0 (9 H, s, Me3C), 2.03, 2.05, 2.07 and 2.10 (each 3 H, s, 4 x $MeCO_2$), 3.82 (1 H, dd, J 10, 5 and 2 Hz, 5'-H), 4.15 (1 H, dd, *J* 12 and 2 Hz, 6'-H), 4.17 (2 H, s, 4-H_2), 4.27 (1 H, dd, *J* 12 and 4 Hz, 6'-H), 4.80 (1 H, d, *J* 8 Hz, 1'-H), 5.13 (2 H, t, *J* 9 Hz, 2'- and 4'-H), 5.26 (1 H, t, *J* 9 Hz, 3'-H), 5.65 (1 H, d, *J* 12 Hz, 2-H) and 6.75 (1 H, d, *J* 12 Hz, 1-H).

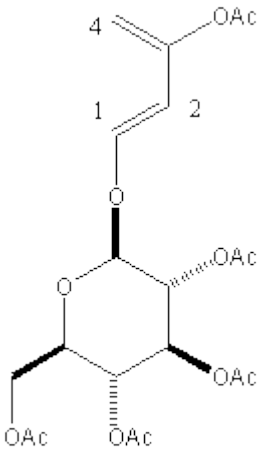
Exp. 12

Preparation of
(E)-1-(2',3',4',6'-*Tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*)-3-*acetoxybuta*-1,3-*diene (**12**)*

Acetic anhydride (0.210 g, 2.1 mmol) in dry THF (1cm^3) was added to a solution of the diene (**10**) (0.750 g, 1.53 mmol) in dry THF (25 cm^3),followed by 1.0M tetrabutylammonium fluoride in THF (1.65 cm^3) and the mixture stirred at room temperature for 1.5h. The mixture was then added to saturated aqueous ammonium chloride and extracted with dichloromethane. The organic extract was washed with brine, dried ($MgSO_4$) and evaporated to afford a white solid (0.619 g) which, on the basis of NMR spectroscopy comprised mainly a 5:2 mixture of the butenone and the diene. Fractional recrystallisation from diethyl-ether-dichloromethane-hexanes failed to effectively separate the two components. Subjection of this mixture to low-temperature silica-gel chromatography [hexanes-EtOAc (2:1 to 1:2) as eluant] gave three fractions.

The first-eluted material (0.126 g), identified as the diene in a slightly

impure state failed to crystallise from diethyl-ether-dry dichloromethane, but, on trituration with hexanes, afforded the *title* compound (**12**) (0.053 g, 8 %) as a pale-yellow solid;

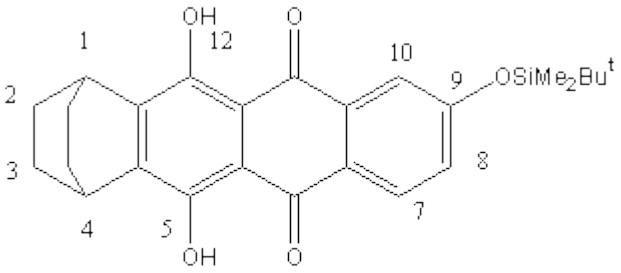


(12)

m.p. 92.5-96 °C;
$[\alpha]_D$ -17 (0.5% in EtOH)
ν_{max} (KBr) 1755 (ester C=O), 1670 and 1620 cm^{-1} (C=C),
λ_{max} (EtOH) 205 nm (ε 18 200),
δ (300 MHz; $CDCl_3$) 2.01, 2.03, 2.04 and 2.08 (each 3 H, s, 4 x $MeCO_2$), 2.21 (3 H, s, 3-OAc), 3.76-3.81 (1 H, m, 5'-H), 4.10 (1 H, dd, *J* 12.5 and 2 Hz, 6'-H), 4.27 (1 H, dd, *J* 12.5 and 5 Hz, 6'-H), 4.73 (1 H, d, *J* 1.5 Hz, 4-H), 4.79 (1 H, d, *J* 8 Hz, 1'-H), 4.84 (1 H, d, *J* 1.5 Hz, 4-H), 5.06-5.16 (2 H, m, 2'- and 4'-H), 5.22 (1 H, t, *J* 9 Hz, 3'-H), 5.72 (1 H, d, *J* 12.5 Hz, 2-H) and 6.53 (1 H, d, *J* 12.5 Hz, 1-H) (in a COSY 90° experiment, the following connectivities were established: δ 4.27 to 4.10 to 3.76-3.81 to 5.06-5.16 to 5.22 to 5.06-5.16 to 4.79; δ 5.72 to 6.53; d 4.73 to 4.84),
m\z (FAB) 789 ($M(331)^+$, 13%), 481 (MNa^+, 6), 457 (M^+-H, 6), 415 (M^+-MeCO, 2), 399 (M^+-$MeCO_2$, 5), 331 ($C_{14}H_{19}O_9^+$, 100) and 169 (100).
Found: M^+-H, 457.1358 $C_{20}H_{26}O_{12}$ requires 457.1345.
Found: C, 52.4; H, 6.3. $C_{20}H_{26}O_{12}$ requires C, 52.4; H, 5.7%.

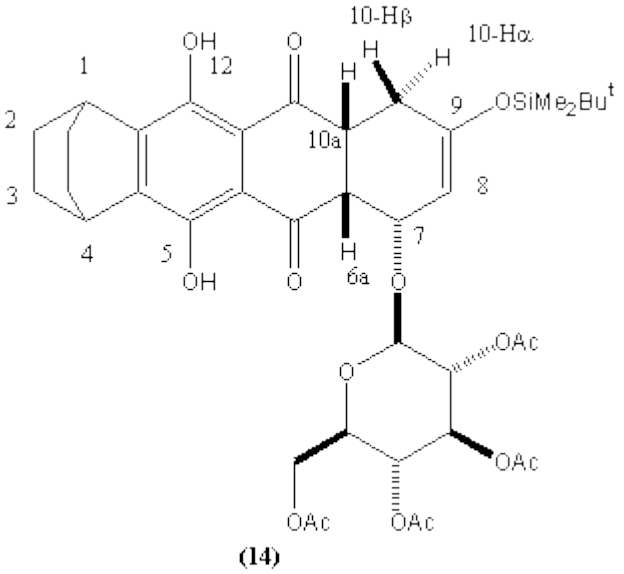
Exp. 13
Reaction of 1,2,3,4-*Tetrahydro*-5,8-*dihydroxy*-1,4-*ethano*-9,10-*anthraquinone (**6**) with the* D-*Glucose-based diene (**11**)*
A solution of the quinol (**6**) (0.09 g, 0.333 mmol) and the D-glucose based diene (**10**) (0.36 g, 0.680 mmol) in 'analar' toluene (8 cm^3) was refluxed under argon for 2.5 days. Removal of the solvent afforded a red-brown solid (0.46 g), which comprised of the cycloadduct together with a trace of compound (**13**) and the butenone from it's 300 MHz ^{1}H NMR spectrum. Subjection of this material to silica-gel chromatography [hexanes-ethyl acetate (8:1 to 2:1) as eluant] afforded three fractions.

The first-eluted material (0.015 g, 10%) was 1,2,3,4-*tetrahydro*-5,12-*dihydroxy*-9-tert-*butyldimethylsilyloxy*-1,4-*ethano*-6,11-*dione* (***13***);



(13)

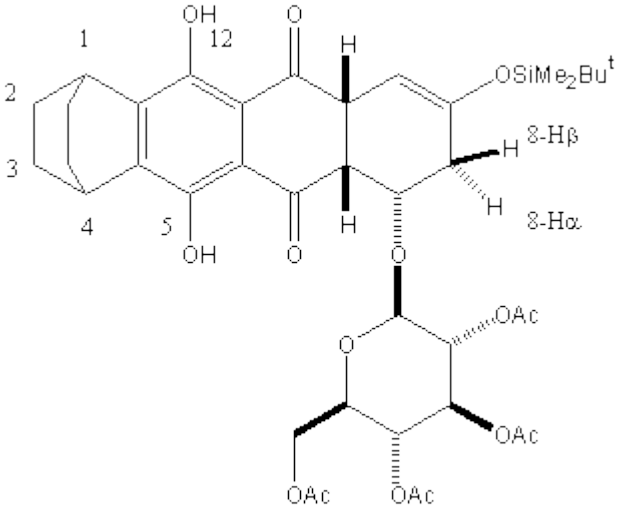
m.p. 191-192 °C;
ν_{max} (KBr) 1750 and 1585 cm^{-1} (C=O),
λ_{max} (EtOH) 214 (ε 15 200), 232 (12 800), 268 (23 100), 481 (7200) and 518 nm (4800),
δ (300 MHz; $CDCl_3$) 0.31 (6 H, s, Me_2Si), 1.02 (9 H, s, Me_3C), 1.39 and 1.85 (each 4 H, br d, separation 7 Hz, 2 x CH_2CH_2), 3.70 (2 H, br s, 1- and 4-H), 7.20 (1 H, dd, *J* 8.5 and 2.5 Hz, 9-H), 7.70 (1 H, d, *J* 8.5 Hz, 10-H) and 13.35 & 13.52 (each 1 H, s, 6- and 11-OH),
m/z (EI) 450 (M^+, 100%), 383 (M^+-Me_3C, 79) and 338 (12),
(CI) 451 (MH^+, 100%),
(FAB) 451 (MH^+, 100%).
Found: C, 69.0; H, 6.8; Si, 5.9. $C_{26}H_{30}O_5Si$ requires C, 69.3; H, 6.78; Si, 6.2%.
The second-eluted material (0.133 g) was crystallised from chloroform-hexanes followed by dichloroform-hexanes to give (6aR,7S,10aR)-1,2,3,4,6a,7,10,10a-*octahydro*-5,12-*dihydroxy*-7-(2',3',4',6'-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*)-9-tert-*butyldimethylsilyloxy*-1,4-*ethanonaphthacene*-6,11-*dione* (**14**) (0.062 g, 25%) as a pale-yellow solid;



(14)

m.p. 179-180 °C,
$[\alpha]_D$ +281 (0.05% in CH_2Cl_2),
ν_{max} (KBr) 1750 (ester C=O) and 1670 cm^{-1} (ketone C=O),
λ_{max} (EtOH) 205 (ε 19 200), 243 (24 300), 273 (7300), 396 (9400), 484 (275) and 518 nm (180),
δ (300 MHz; $CDCl_3$) 0.18 and 0.22 (each 3 H, s, Me_2Si), 0.95 (9 H, s, Me_3C), 1.29 and 1.47 (each 2 H, br d, separation 8 Hz, CH_2CH_2), 1.80 (4 H, br d, separation 9 Hz, CH_2CH_2), 1.73, 1.88, 1.97 and 2.09 (each 3 H, s, 4 x $MeCO_2$), 2.16 (1 H, dd, *J* 18.5 and 8 Hz, 10-Hβ), 3.1-3.2 (1 H, m, 6a-H), 3.38 (1 H, t, *J* 7, 10a-H), 3.52-3.58 (1 H, m, 5'-H), 3.61-3.65 (each 1 H, br s, 1- and 4-H), 4.04 (1 H, dd, *J* 12 and 2.5 Hz, 6'-H), 4.17 (1 H, d, J 12 and 2.5 Hz, 6'-H), 4.36-4.44 (2H, m, 1'- and 2'-H), 4.56 (1 H, t, *J* 5 Hz, 7-H), 4.94-4.96 (2 H, m, 3'- and 4'-H), 5.15 (1 H, d, *J* 4.5 Hz, 8-H), 11.66 and 12.28 (each 1 H, s, 5- and 12-OH)(irradiation at δ 4.56 caused the m at δ 3.1-3.2 to simplify and the d at δ 5.15 to collapse to a s),
m/z (FAB) 800 (M^+, 1.5%), 453 (M^+-$C_{14}H_{19}O_{10}$, 36) and 73 (100).
Found: C, 59.2; H, 6.4; Si, 3.4. $C_{40}H_{52}O_{15}Si$ requires C, 60.0; H, 6.7; Si, 3.6%.
The third-eluted fraction (0.001 g) was identified as the butenone (**9**).
(b) A stirred solution of the quinol (**6**) (0.486 g, 1.8 mmol) and the D-glucose-based diene (**11**) (1.024 g, 1.93 mmol) in 'analar' toluene (30 cm^3) was heated at 98 °C under argon. The reaction was followed by 300 MHz ^1H NMR spectroscopy and, after 3 days, a further quantity of the diene (0.30 g, 0.57 mmol) dissolved in 'analar' toluene (30 cm^3) was added [to react with the unchanged quinol]. This mixture was heated at 98 °C for a further 24 h. Removal of the solvent *in vacuo* afforded mainly a 3:1 mixture of a 60% d.e. of the cycloadduct (**14**) and the quinol (**6**), together with a trace of compound (**13**). Crystallisation of the mixture from diethyl ether-hexanes gave mainly the cycloadduct (**14**) (0.53 g, 36%)[δ (300 MHz;

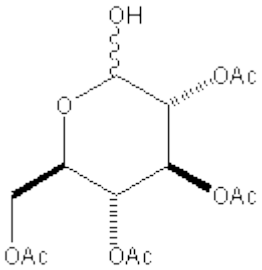
$CDCl_3$) *inter alia* 11.60 and 12.26 (5- and 12-OH)]. Evaporation of the mother liquor left a residue (1.14 g).
Attempted recrystallisation of the impure cycloadduct (**14**) from diethyl ether-hexanes gave an oil, which was subjected to silica-gel chromatography [hexanes-EtOAc (8:1 to 1:1) as eluant] to afford three fractions.
The first eluted material (0.337 g) was observed as a 5.7:4:3.1 mixture of compounds (**15**), (**17**) and (**14**). Recrystallisation of this mixture from dichloromethane-hexanes afforded a mixture; it's 300 MHz ^{1}H NMR revealed that partial hydrolysis to the dihydroxytrione (**17**) had occurred. A final recrystallisation of this material afforded a yellow solid (0.165 g, 10%) which contained a 11:2 mixture of (6aR,7S,10aR)-1,2,3,4,6a,7,8,10a-*octahydro*-5,12-*dihydroxy*-(2',3',4',6'-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*)-9-tert-*butyldimethylsilyloxy*-1,4-*ethanonaphthacene*-6,11-*dione* (**15**) and (6aR,7S,10aR)-1,2,3,4,6a,7,10,10a-*octahydro*-5,12-*dihydroxy*-(2',3',4',6'-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*)-9-tert-*butyldimethylsilyloxy*-1,4-*ethanonaphthacene*-6,11-*dione* (**14**)*;*



(15)

m.p. 177.5-179 °C,
$[\alpha]_D$ +231 (0.05% in CH_2Cl_2),
ν_{max} (KBr) 1750 cm^{-1}(C=O),
λ_{max} (EtOH) 205 (ε 20 000), 244 (25 800), 274 (7500), 294 (4800), 347 (10 000), 483 (8800) and 517 nm (5600),
For isomerised cycloadduct (**15**) δ (300 MHz; $CDCl_3$) 0.21 (6 H, s, Me_2Si), 0.93 (9 H, s, Me_3C), 1.31 and 1.38 (each 2 H, d, *J* 9 and 6.5 Hz, 2 x CH_2CH_2), 1.81 (4 H, d, *J* 6.5Hz, CH_2CH_2), 1.58, 1.89, 1.97 and 2.09 (each 3 H, s, 4 x $MeCO_2$), 2.41-2.61 (2 H, m, 8-Hα and 8-Hβ), 3.10 (1 H, dd, *J* 9 and 2 Hz, 6a-H), 3.54-3.60 (1 H, m, 5'-H), 3.64-3.66 (3 H, m, 1-,4- and 10a-H), 4.05 (1 H, dd, *J* 12 and 2.5 Hz, 6'-H), 4.19 (1 H, dd, *J* 12 and 5 Hz, 6'-

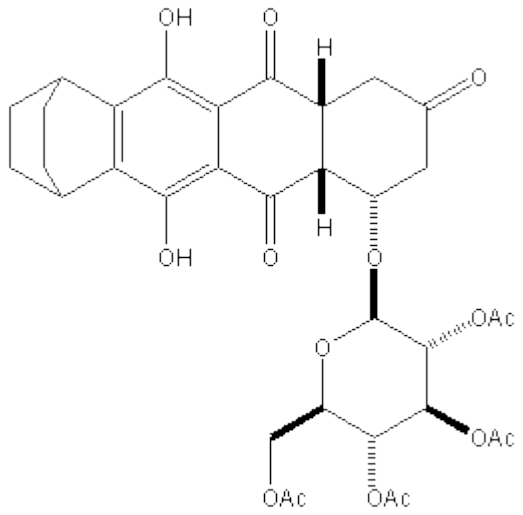
H), 4.41-4.47 (2 H, m, 7- and 1'-H), 4.58 (1 H, m, 2'-H), 4.94-4.97 (2 H, m, 3'- and 4'-H), 5.26 (1 H, dd, *J* 5 and 1.5 Hz, 10-H), 12.02 and 12.48 (each 1H, s, 5- and 12-OH) (irradiation at δ 3.10 caused the two br s at δ 3.6-3.64 to split into 3 signals and the m at δ 4.44 to simplify; irradiation of the m at δ 3.58 caused the dd at δ 4.02 and 4.18 to collapse to two d (J 12 Hz) and the m at δ 4.96 to simplify; irradiation of the m at δ 4.58 caused the m at δ 4.41-4.47 and 4.96 to simplify; irradiation at δ 5.26 caused the two br s at δ 3.6-3.64 to split into three signals and a minor change in the range δ 2.45-2.61),
m\z (FAB) 800 (M^+, 18%), 743 (M^+-Me_3C, 1) and 453 (M^+-$C_{14}H_{19}O_{10}$, 100). Found: C, 60.0; H, 6.6; Si, 3.6. $C_{40}H_{52}O_{15}Si$ requires C, 60.0; H, 6.6; Si, 3.5%.
The second-eluted material (0.150 g) was tetra-acetylglucose (**16**).
Attempted recrystallisation of the residue (from the mother liquor) from dichloromethane-hexanes gave a dark-brown oil, which was subjected to low-temperature silica-gel column chromatography [hexanes-EtOAc (8:1 to 2:1) as eluant] to afford three fractions.
The first-eluted fraction (0.113 g) was shown to be a 1:1.5 mixture of aromatised compound (**13**) and the quinol.
The third-eluted fraction was detected mainly as the isomerised compound (**15**). Recrystallisation of this material from dichloromethane-hexanes afforded a buff solid (0.27 g), detected as a 2:1 mixture of isomerised cycloadduct (**15**) and the dihydroxytrione (**17**); δ (300 MHz; $CDCl_3$) for (**15**) *inter alia* 12.02 and 12.48 (each 1 H, s , 5- and 12-OH); for (**13**) *inter alia* 11.87 and 12.37 (each 1 H, s, 5- and 12-OH).
The residue (0.10 g) from the mother liquor was shown to contain the isomerised cycloadduct (**15**) as the only identifiable component.



(16)

Exp. 14
Hydrolysis of a 60% Diastereomeric Excess of (6aR,7S,10aR)-1,2,3,4,6a,7,10,10a-*Octahydro*-5,12-*dihydroxy*-(2',3',4',6'-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*)-9-tert-*butyldimethylsilyloxy*-1,4-*ethanonaphthacene*-6,11-*dione* (**14**)
(a) A solution containing a 60% d.e. of the cycloadduct (**14**) (0.301 g, 0.37 mmol) in chloroform (15 cm^3) was treated with 3 drops of conc. hydrochloric acid and stirred at room temperature for 35 min (when TLC

had shown disappearance of the starting material). The mixture was diluted with water and extracted with chloroform (x 2). Evaporation of the dried ($MgSO_4$) organic layer afforded an oil containing an 8:2:1 ratio of the dihydroxytrione (**17**), a diastereomer and the aromatised compound (**13**), [δ (200 MHz; $CDCl_3$) major diastereomer: 11.87 and 12.37 (5- and 12-OH); minor diastereomer 11.84 and 12.28 (5- and 12-OH) (the ratio was estimated by the integrals of the 5- and 12-OH singlets)].
Subjection of this mixture to low-temperature silica-gel chromatography [hexanes-EtOAc (4:1 to 3:2) as eluant] gave a solid (0.88 g) which was crystallised from chloroform-ethanol-hexanes to afford (6aR,7S,10aR)-1,2,3,4,6a,7,8,9,10,10a-*decahydro*-5,12-*dihydroxy*-7-(2',3',4',6'-tetra-O-*acetyl*-β-D-*glucopyranosyloxy*)-1,4-*ethanonaphthacene*-5,9,12-*trione* (**17**) (0.045 g, 30%) as a yellow solid;



(17)

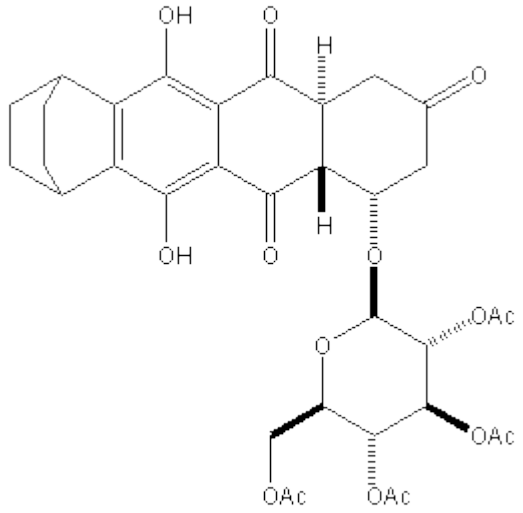
m.p. 185-186 °C;
$[\alpha]_D$ +105 (0.5% in CH_2Cl_2)
ν_{max} (KBr) 1750 (ester C=O) and 1630 cm^{-1}(C=O),
λ_{max} (EtOH) 243 (ε 22 800), 274 (11 000), 294 (5800), 399 (8900), 482 (22 00) and 516 nm (1400),
δ (300 MHz; $CDCl_3$) 1.20 and 1.83 (each 4 H, separation 8 Hz, 2 x CH_2CH_2), 1.62, 1.88, 1.97 and 2.10 (each 3 H, s, 4 x $MeCO_2$), 2.44 (1 H, dd, *J* 16.5 and 8 Hz, 10-Hβ), 2.52 (1 H, dd, *J* 18 and 4 Hz, 8-Hβ), 3.0 (1 H, br d, separation 18 Hz, 8-Hα), 3.18 (1 H, dd, *J* 7.5 and 2 Hz, 6a-H), 3.26 (1 H, dd, *J* 16.5 and 8.5 Hz, 10-Hα), 3.54-3.62 (2 H, m, 10a- and 5'-H), 3.65 and 3.70 (2 H, br s, 1- and 4-H), 4.07 (1 H, dd, *J* 12 and 2.5 Hz, 6'-H), 4.20 (1 H, dd, *J* 12 and 5.5 Hz, 6'-H), 4.38 (1 H, d, *J* 8 Hz, 1'-H), 4.36-4.40 (2 H, m, 2'-H), 4.88 (1 H, q, *J* 8 Hz, 7-H), 4.90-5.00 (2 H, m, 3'- and 4'-H), 11.87 and 12.37 (each 1H, s, 5- and 12-OH) [irradiation at δ 3.54-3.62 caused the m at δ 2.43-2.56 to simplify, the dd at δ 3.18 to collapse to a d (*J* 2.2 Hz); the dd at δ3.26 to collapse to a d (*J* 16.5 Hz), the dd at δ 4.07 to collapse to

a d (*J* 12.2 Hz) and the dd at δ 4.20 to collapse to a d (*J* 12.2 Hz); irradiation at δ 3.18 caused the m at δ 3.54-3.62 to simplify and the q at δ 4.88 to simplify],
m\z (FAB) 686 (M^+, 100%), 356 (M^+-$C_{14}H_{18}O_9$, 4), 339 (M^+-$C_{14}H_{19}O_{10}$, 8) and 331 ($C_{14}H_{19}O_9^+$, 18).
Found: C, 59.2; H, 5.3. $C_{34}H_{38}O_{15}$ requires C, 59.5; H, 5.6%.
(b) Hydrolysis [using 9 drops of conc. HCl in $CHCl_3$ (20 cm^3) for 40 min] of the crude product [obtained from the reaction of the quinol (**6**) (2 mmol) and the D-glucose-based diene (**11**) (4 mmol) in the presence of the lanthanide shift reagent Eu(fod)$_3$ (*ca.* 1.2 mol%) in refluxing toluene for at least one day[4]] afforded an inseparable mixture of the dihydroxytrione (**17**) and tetraacetylglucose (**16**) [the 10a-H epimers formed were separable by low-temperature silica-gel chromatography (2:1 to 1:5 hexanes:EtOAc as eluant)].

Exp. 15
Hydrolysis of (6aR,7S,10aR)-1,2,3,4,6a,7,8,10a-*Octahydro*-5,12-*dihydroxy*-(2',3',4',6'-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*)-9-tert-*butyldimethylsilyloxy*-1,4-*ethanonaphthacene*-6,11-*dione* (**15**)
The isomerised cycloadduct (**15**) (0.017 g, 0.022 mmol) was dissolved in chloroform (5 cm^3) and the solution was treated with 3 drops of conc. hydrochloric acid. The mixture was stirred for *ca.* 40 min (until TLC had shown disappearance of the starting material). Dilution with dichloromethane, followed by a wash with water, drying of the organic layer ($MgSO_4$) and evaporation afforded the dihydroxytrione (**17**) (0.010 g, 65 %) as a buff solid, whose ^{1}H NMR spectrum was identical to that obtained for the dihydroxytrione (**17**) obtained in the previous experiment.

Exp. 16
Hydrolysis of a 2:1 Mixture of (6aR,7S,10aR)-1,2,3,4,6a,7,8,10a-*Octahydro*-5,12-*dihydroxy*-(2',3',4',6'-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*)-9-tert-*butyldimethylsilyloxy*-1,4-*ethanonaphthacene*-6,11-*dione* (**15**) and 1,2,3,4-*tetrahydro*-5,12-*dihydroxy*-9-tert-*butyldimethylsilyloxy*-1,4-*ethano*-6,11-*dione* (**13**)
A solution containing a 2:1 mixture of the isomerised cycloadduct (**15**) and compound (**13**) (0.44 g, 0.37 mmol) in chloroform (10 cm^3) was treated with 5 drops of conc. hydrochloric acid and stirred at room temperature for 40 min (when TLC had shown disappearance of the starting material). The mixture was diluted with water and extracted with chloroform (x 2). After washing with water, the organic phase was dried ($MgSO_4$) and concentrated in vacuo to afford a solid (0.39 g), containing a 1:1 ratio of compounds (**18**) and (**13**). Subjection of this mixture to low-temperature silica-gel chromatography [hexanes:EtOAc (3:1 to 1:1) as eluant] afforded

two fractions.
The first-eluted material (0.150 g) was the aromatic compound (**13**), identified by its 300 MHz ^{1}H NMR spectrum.
The second-eluted material (0.19 g) was recrystallised twice from ethanol-chloroform to afford (6aR,7S,10aR)-1,2,3,4,6a,7,8,9,10,10a-*decahydro*-5,12-*dihydroxy*-(2',3',4',6'-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*)-1,4-*ethanonaphthacene*-5,9,12-*trione* (**18**) (0.121 g, 48 %) as a pale-yellow solid;

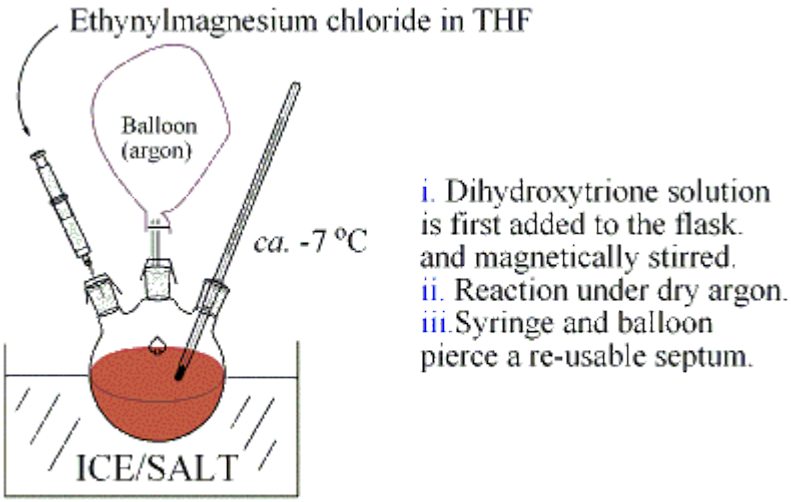


(18)

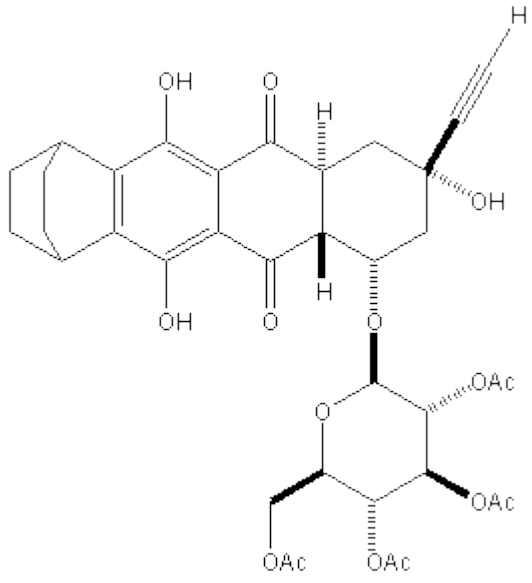
m.p. 215-217 °C;
$[\alpha]_D$ +38 (0.5% in CH_2Cl_2)
ν_{max} (KBr) 1750 (ester C=O) and 1630 cm^{-1}(C=O),
λ_{max} (EtOH) 217 (ε 20 000), 236 (25 500), 272 (23 200), 297 (8900), 341 (3320), 401 (7000) and 516 nm (4300),
δ (300 MHz; $CDCl_3$) 1.31 and 1.78 (each 4 H, separation 8 Hz, 2 x CH_2CH_2), 1.68, 1.96, 2.02 and 2.14 (each 3 H, s, 4 x $MeCO_2$), 2.36-2.60 (2 H, m, 8- and 10-Hβ), 2.98-3.16 (3 H, m, 6a-, 8α-, 10a-H), 3.56-3.80 (3 H, m, 1-, 4- and 5'-H), 4.18-4.23 (2 H, m, 6'-H_2), 4.78-4.90 (2 H, m, 1'- and 2'-H), 4.95-5.07 (2 H, m, 4'- and 7-H), 5.15-5.25 (1 H, t, *J* 9 Hz, 3'-H) and 11.96 and 12.25 (each 1H, s, 5- and 12-OH),
δ (300 MHz; C_6D_6) 1.41 and 1.70 (each 4 H, d, *J* 7.7 and 8.3 Hz, 2 x CH_2CH_2), 1.88, 1.90, 1.95 and 2.03 (each 3 H, s, 4 x $MeCO_2$), 2.14-2.20 (2 H, m, 8- and 10-Hβ), 3.1-3.25 (3 H, m, 6a-, 8α- and 10-Hα), 3.48 (1 H, m, 5'-H), 3.75 (1 H, dt, *J* 13 and 4 Hz, 10a-H), 3.97 (2 H, br s, 1- and 4-H), 4.39-4.41 (2 H, m, 6'-H_2), 4.78-4.81 (2 H, m, 1'- and 2'-H), 5.33 (1 H, t, *J* 9 Hz, 3'-H), 5.41 (1 H, t, *J* 9 Hz, 4'-H), 5.66 (1 H, t, *J* 9 Hz, 7-H), 12.67 and 13.06 (each 1 H, s, 5- and 12-OH)
[irradiation at δ 3.1-3.25 caused the m at δ 2.14-2.20 to simplify and the dt at δ 3.75 to simplify; irradiation of the m at δ 3.48 caused the m at δ 4.39-4.41 to collapse to a s and the t at δ 5.41 to collapse to a d (*J* 9 Hz);

irradiation at δ 3.75 caused the m at δ 2.14-2.20 to simplify and the m at δ 3.1-3.25 to collapse to a br t (*J* 17 Hz); irradiation at δ 4.39-4.41 caused the m at δ 3.48 to collapse to a d (*J* 10 Hz); irradiation at δ 4.78-4.81 caused the t at δ 5.33 to collapse to a d (*J* 9 Hz)];
m\z (FAB) 709 (*M*Na^+, 11%), 686 (*M*$^+$, 40), 356 (*M*$^+$-$C_{14}H_{18}O_9$, 15), 340 (*M*H^+-$C_{14}H_{19}O_{10}$, 40) and 331 ($C_{14}H_{19}O_9^+$, 84).
Found: C, 59.3; H, 5.4. $C_{34}H_{38}O_{15}$ requires C, 59.5; H, 5.6%.

Exp. 17
Reaction of (6aR,7S,10aR)-1,2,3,4,6a,7,8,9,10,10a-*Decahydro*-5,12-*dihydroxy*-(2',3',4',6'-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*)-1,4-*ethanonaphthacene*-5,9,12-*trione* (**18**) *with Ethynylmagnesium Chloride Followed by Lead(IV) Acetate*

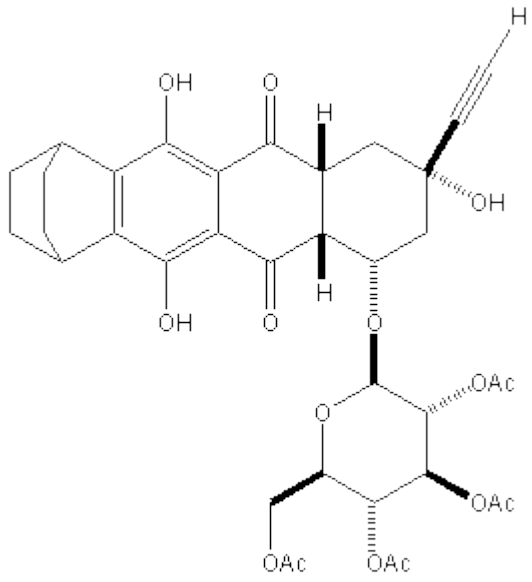


A solution of ethynylmagnesium chloride in THF (*ca.* 0.5 mol dm^{-3}, 34 cm^3, *ca.* 19 mmol) (via a glass syringe) was added to a stirred solution of the dihydroxytrione (**18**) (0.424 g, 0.62 mmol) in freshly distilled THF (37 cm^3) at *ca.* -7 °C under argon. After 30 min, the mixture was poured onto ice-cold saturated aqueous ammonium chloride and extracted with dichloromethane. The organic extract was washed with water, dried ($MgSO_4$) and evaporated to afford a glassy red solid (0.395 g). On the basis of 300 MHz ^{1}H NMR spectroscopy, a complex mixture was present, containing predominantly the ethynylcarbinol (**20**), with a smaller amount of the ethynylcarbinol (**19**), the aromatised compound (**21**) and the tetraacetylglucose;



(19)

δ(300 MHz; $CDCl_3$) (**19**) *inter alia* 2.50 (1H, s, $^{C\equiv CH}$), 12.32 and 12.42 (each 1 H, s, 5- and 12-OH),

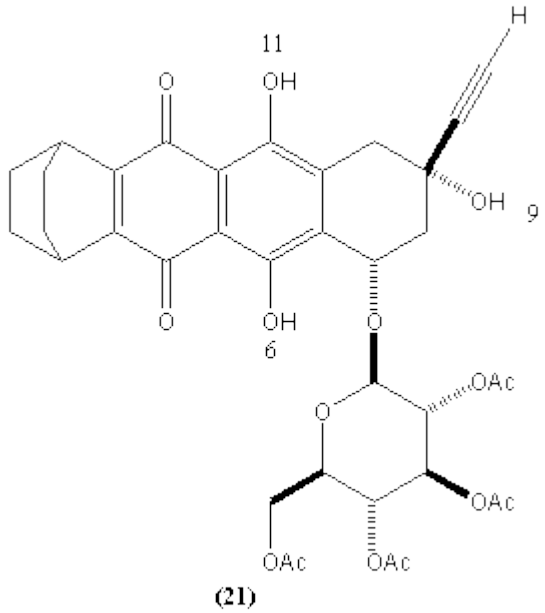


(20)

δ (300 MHz; $CDCl_3$) (**20**) *inter alia* 2.20 (1H, s, $^{C\equiv CH}$), 12.36 and 12.42 (each 1 H, s, 5- and 12-OH).

The residue (0.390 g) was treated with a solution of lead(IV) acetate (0.30 g, 0.68 mmol) in acetic acid (50 cm^3) and the mixture stirred for 2 days. After this time, the red solution was diluted with water and extracted with aqueous sodium hydrogen carbonate and water, dried ($MgSO_4$) and evaporated to afford a solid (0.226 g) comprising mainly a mixture of the crude anthracycline (**21**) and the tetraacetylglucose (**16**). This mixture was subjected to silica-gel chromatography [hexanes-EtOAc (5:1 to 1:1) as eluant] to afford a solid (*ca.* 0.050 g), which was crystallised from ethyl

acetate-hexanes to give an orange solid (0.034 g) containing predominantly the anthracycline (**21**) [*ca.* 8% based on the dihydroxytrione (**18**)];



(21)

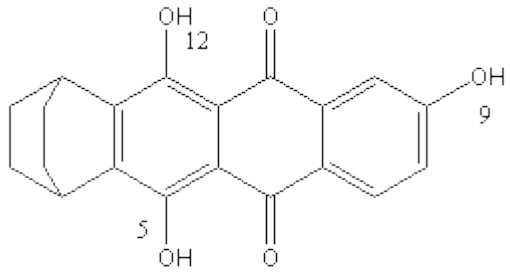
δ (300 MHz; $CDCl_3$) *inter alia* 2.52 (1H, s, $C{\equiv}CH$), 13.02 and 13.20 (each 1 H, s, 6- and 11-OH).

Exp. 18

Reaction of a Mixture of (6aR,7S,10aR)-1,2,3,4,6a,7,8,9,10,10a-*Decahydro*-5,12-*dihydroxy*-(2',3',4',6'-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*)-1,4-*ethanonaphthacene*-5,9,12-*trione* (**17**) *and* (6aR,7S,10aS)-1,2,3,4,6a,7,8,9,10,10a-*Decahydro*-5,12-*dihydroxy*-(2',3',4',6'-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*)-1,4-*ethanonaphthacene*-5,9,12-*trione* (**18**) *with Ethynylmagnesium Chloride Followed by Lead(IV) Acetate*

A solution of ethynylmagnesium chloride in THF (*ca.* 0.5 mol dm^{-3}, 5.4 cm^3, *ca.* 2.7 mmol) was added to a stirred solution containing a 2:1 mixture of the dihydroxytriones (**17**) and (**18**) (0.062 g, 0.090 mmol) in freshly distilled dry THF (5 cm^3) at ca. -13 °C under argon. After 30 min, the mixture was poured onto ice-cold saturated aqueous ammonium chloride and extracted with dichloromethane. The organic extract was washed with water, dried ($MgSO_4$) and evaporated to afford a red-brown solid (0.071 g). On the basis of 300 MHz ^1H NMR spectroscopy, the sample contained a 4:2:1:1 ratio of the ethynylcarbinols (**20**), (**19**), the aromatised material (**22**) and the tetraacetylglucose (**16**). The residue (0.068 g) was stirred with a solution of lead(IV) acetate (0.047 g, 0.105 mmol) in acetic acid (30 cm^3) for 2.5 days. After this time, the red mixture was diluted with water and extracted with ethyl acetate. The organic extract was washed with saturated aqueous sodium carbonate, treated with *N,N*-diethylhydroxylamine (0.3 cm^3) (to reduce any over-oxidised material) and then quickly washed with dilute

hydrochloric acid, brine and water. Evaporation of the dried ($MgSO_4$) organic layer left a residue (0.062 g), which was subjected to silica-gel chromatography [hexanes-EtOAc (5:1 to 1:1) as eluant] to afford two fractions.
The first-eluted material was identified as the aromatised compound (**22**) (0.004 g, 12%),



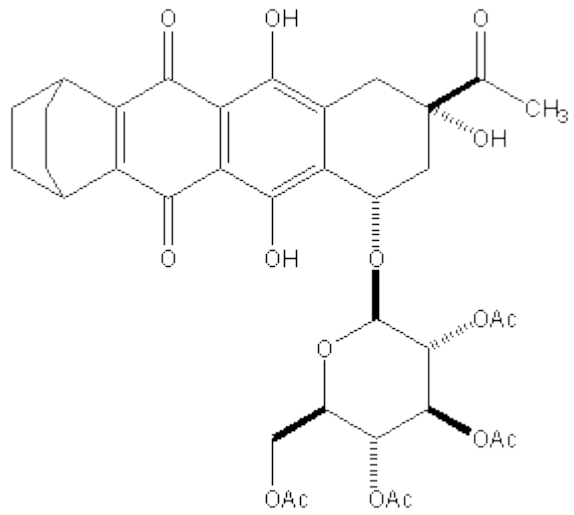
(22)

δ (300 MHz; $CDCl_3$) *inter alia* 13.31 and 13.51 (each 1 H, s, 6- and 11-OH).
The second-eluted material (0.024 g) was crystallised from chloroform-hexanes to afford (7S,9S)-9-*ethynyl*-1,2,3,4,7,8,9,10-*octahydro*-6,9,11-*trihydroxy*-7-(2',3',4',6'-*tetra*-O-*acetyl*-b-D-*glucopyranosyloxy*)-1,4-*ethanonaphthacene*-5,12-*dione* (**21**) (0.007 g, 10%) as a red solid;
m.p. 103-105 °C;
$[\alpha]_D$ +55 (0.2% in CH_2Cl_2)
ν_{max} (KBr) 3480 (OH), 2100 (C≡CH), 1750 cm^{-1} (ester C=O),
δ (300 MHz; $CDCl_3$) 1.42 and 1.81 (each 4 H, br d, separation 7 Hz, 2 x CH_2CH_2), 1.88, 1.98, 2.00 and 2.14 (each 3 H, s, 4 x $MeCO_2$), 2.18 (1 H, dd, *J* 15 and 5 Hz, 8-Hβ), 2.48 (1 H, d, *J* 15 Hz, 8-Hα), 2.52 (1 H, d, *J* 19 Hz, 10-Hβ), 3.44 (1 H, d, *J* 19 Hz, 10-Hα), 3.61 (2 H, br s, 1- and 4-H), 3.70 (1 H, br s, 9-OH), 3.81-3.85 (1 H, m, 5'-H), 4.20-4.30 (2 H, m, 6'-H_2), 4.91 (1 H, dd, *J* 9.5 and 8.5 Hz, 2'-H), 5.03-5.09 (2 H, m, 1'- and 4'-H), 5.15 (1 H, m, 7-H), 5.27 (1 H, t, *J* 9 Hz, 3'-H) and 13.02 and 13.20 (each 1 H, s, 6- and 11-OH) (addition of D_2O caused the signals at δ 3.70, 13.02 and 13.20 to disappear),
m/z (FAB) 710 (M^+, 10%), 522 (58), 419 (60), 391 (M^+-$C_{13}H_{19}O_9$, 100), 363 (M^+-$C_{14}H_{19}O_{10}$, 12) and 149 (87).
Found: MH^+, 710.2230. $C_{36}H_{38}O_{15}$ requires *m/z*, 710.2211.

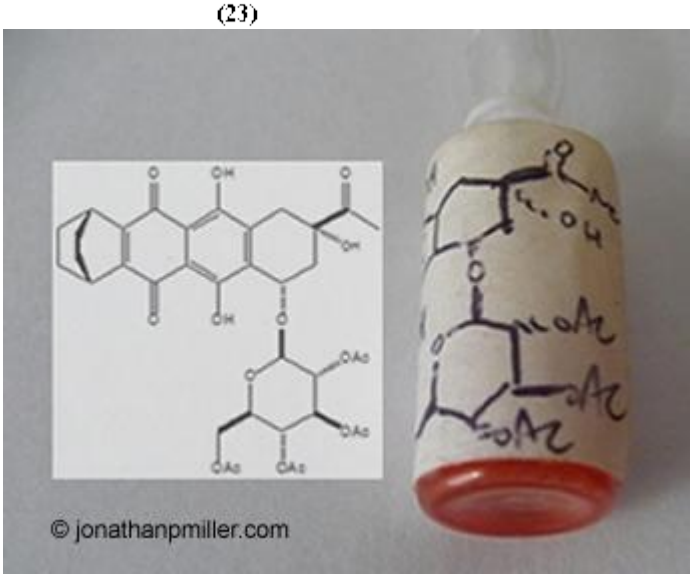
Exp. 19
Hydration of (7S,9S)-9-*Ethynyl*-1,2,3,4,7,8,9,10-*octahydro*-6,9,11-*trihydroxy*-7-(2',3',4',6'-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*)-1,4-*ethanonaphthacene*-5,12-*dione* (**21**) to (7S,9S)-9-*Acetyl*-1,2,3,4,7,8,9,10-*octahydro*-6,9,11-*trihydroxy*-7-(2',3',4',6'-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*)-1,4-*ethanonaphthacene*-5,12-*dione*

(**23**)

A solution of the anthracycline (**21**) (0.013 g, 0.018 mmol) in acetone (3 cm^3) was treated with red mercury(II) oxide (0.015 g, 0.064 mmol) and 7% aqueous sulfuric acid (3 cm^3). The mixture was heated under reflux for 10 min and allowed to cool to room temperature. After dilution with 2M hydrochloric acid (3 cm^3), the mixture was extracted with dichloromethane. The organic extract was washed with 0.1M hydrochloric acid, dried ($MgSO_4$) and evaporated to leave a red solid (0.012 g) which comprised mainly the *title* compound (**23**);



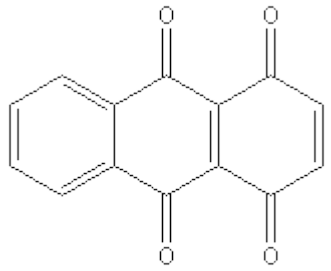
(23)



δ (300 MHz; $CDCl_3$) 1.34-1.37 and 1.81-1.83 (each 4 H, br d, separation 8 Hz, 2 x CH_2CH_2), 1.89, 1.99, 2.04 and 2.10 (each 3 H, s, 4 x $MeCO_2$), 2.42 (3 H, s, MeCO), 2.54 (1 H, d, *J* 15 Hz, 8-Hα), 2.85 (1 H, d, *J* 19 Hz, 10-Hβ), 3.13 (1 H, d, *J* 19 Hz, 10-Hα), 3.62-3.66 (2 H, m, 1- and 4-H), 3.80-3.84 (1 H, m, 5'-H), 4.14 (1 H, br s, 9-OH), 4.25-4.26 (2H, m, 6'-H_2), 4.90-5.30 (5H, m, 1'-,2'-,3'-,4'- and 7-H) and 13.05 and 13.22 (each 1 H, s, 6 and 11-OH) [the signals for the 8-Hβ proton, expected in the 2.00-2.20 region were

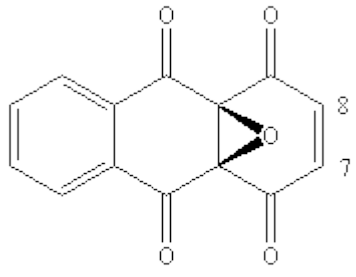
obscured by the $MeCO_2$ signals] (addition of D_2O caused the signals at δ 4.14, 13.05 and 13.22 to disappear),
m/z (FAB) 751 (*M*Na^+, 11%), 750 (22), 729 (*M*H^+, 49), 728 (M^+, 12), 397 (M^+-$C_{14}H_{19}O_9$, 32), 381 (80), 363 (95), 337 (97), 331 ($C_{14}H_{19}O_9^+$, 89), 321 (100) and 169 (51).
Found: *M*H^+, 729.2366. $C_{36}H_{40}O_{16}$ requires *m/z*, 729.2395.

Exp. 20
Preparation of 4a,10a-*Epoxy*-4a,10a-*dihydroanthracene*-1,4,9,10-*tetraone*(**25**)[5]
Quinizarin (30.0 g, 0.125 mmol), lead(IV) acetate (57.0 g, 0.129 mol) and acetic acid (60 cm^3) were ground in a mortar for 15 min, where upon the mixture turned a dark-brown colour. The mixture was filtered and the insoluble material washed with water. The brown solid obtained was dried (P_2O_5; *in vacuo*) to give the crude tetraone (**24**) (24.4 g, *ca.* 80%).



(24)

To a stirred cold solution of the tetraone (**24**) (24.4 g, *ca.* 0.10 mmol) in dry dichloromethane (500 cm^3) *m*-chlorobenzoic acid (20.2 g, 0.12 mmol) was added in portions over 5 min. The mixture was allowed to warm up to room temperature and stirred for 2 h. The mixture was filtered, washed with ice-cold saturated aqueous sodium hydrogen carbonate and dried ($MgSO_4$). The solvent was evaporated and the crude oxirane (**25**) (20.7 g) dissolved in the minimum volume of hot chloroform. The solution was left at 0 °C overnight, from which the title compound (**25**) (11.56 g, 36%) was obtained as yellow needles;
δ (300 MHz; $CDCl_3$) 6.76 (2 H, s, 7- and 8-H), 7.80-7.85 and 8.0-8.1 (each 2 H, s, 1-,2-,3- and 4-H).

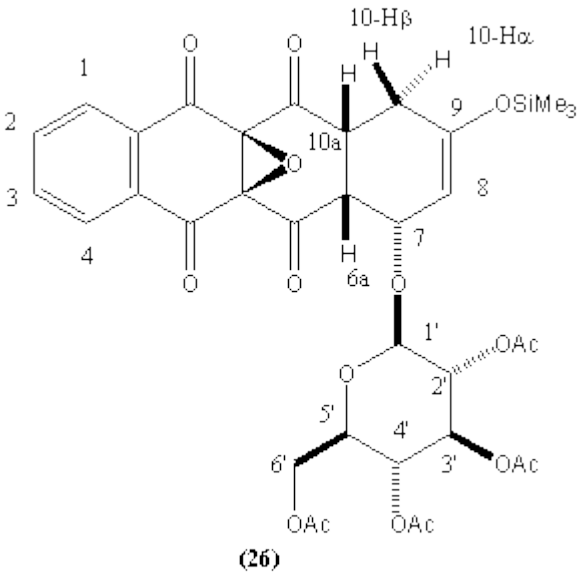


(25)

Exp. 21

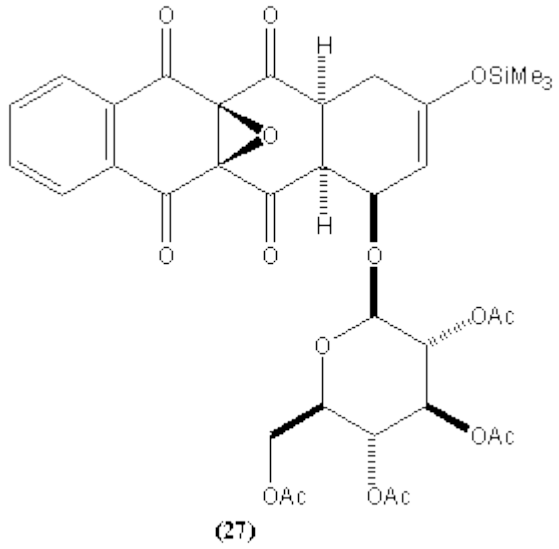
Preparation of (5aS,6aR,7S,10aR,11aR)-5a,11a-*Epoxy*-5a,6a,7,10,10a,11a-*hexahydro*-7-(2',3',4',6'-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy)-9-trimethylsilyloxy-naphthacene*-5,6,11,12-*tetraone* (**26**)

(a)[6] A solution of the oxirane (**25**) (2.0 g, 7.93 mmol) and the D-glucose-based diene (**10**) (4.0 g, 7.93 mmol) was kept in the dark at 4 °C for 3 days in acetone (45 cm^3). Evaporation of the solvent left a residue comprised as a 85:15 mixture of the cycloadduct (**26**) and its diastereomer (**27**) [the ratio was estimated from the integrals of the doublets at δ 2.73 and 2.84 (ascribed to H-10a) and the double doublets at δ 3.07 and 3.10 (ascribed to H-6a)], which was triturated with dry diethyl ether to afford the title compound (**26**) (3.79 g, 64 %) as a cream solid;



(26)

δ (300 MHz; $CDCl_3$) 0.26 (9H, s, $SiMe_3$), 1.78, 1.86, 1.96 and 2.06 (each 3 H, s, 4 x $MeCO_2$), 2.09 (1 H, dd, *J* 18.5 and 8.5 Hz, 10-Hβ), 2.84 (1 H, br d, *J* 18.5 Hz, 10-Hα), 3.08 (1 H, dd, *J* 7.5 and 4 Hz, 6a-H), 3.54-3.56 (1 H, m, 5'-H), 3.96 (1 H, dt, *J* 8, 8 and 1 H, 10a-H), 4.04 (1 H, dd, *J* 12 and 2.5 Hz, 6'-H), 4.16 (1 H, dd, *J* 12 and 4.5 Hz, 6'-H), 4.44 (1 H, d, *J* 8 Hz, 1'-H), 4.56 (1 H, dd, *J* 9 and 8 Hz, 2'-H), 4.64 (1 H, dd, *J* 6 and 4 Hz, 7-H), 4.90 (1 H, t, *J* 9.5 and 9.5 Hz, 4'-H), 5.04 (1 H, t, *J* 9.5 and 9.5 Hz, 3'-H), 5.05 (1 H, d, *J* 6 Hz, 8-H), 7.75-7.79, 8.04-8.06 and 8.09-8.12 (2, 1 and 1 H, each m, 1-,2-,3- and 4-H).



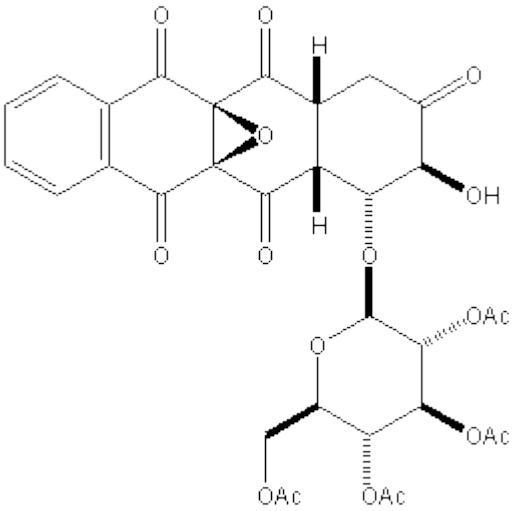
(27)

(b)[2] A solution of the oxirane (**25**) (3.10 g, 12.46 mmol) and the diene (**10**) (6.20 g, 12.7 mmol) in dry benzene (90 cm^3) was left at room temperature for 18 h. After this time, an additional quantity of the diene (**10**) (1.55 g, 3.18 mmol) was added to react with the unchanged oxirane (**25**) and the mixture was stirred for a further 24 h. Evaporation left a residue which contained predominantly a 60% d.e. of the cycloadduct (**25**). Addition of dry diethyl ether to the residue gave the crude cycloadduct (**25**) (7.837 g), which was crystallised twice from dry dichloromethane-hexanes to afford the *title* compound (**25**) (4.61 g, 60%) as a cream solid.

Exp. 22

Reaction of (5aS,6aR,7S,10aR,11aR)-5a,11a-*Epoxy*-5a,6a,7,10,10a,11a-*hexahydro*-7-(2',
3',4',6'-*tetra*-O-*acetyl*-β-D-*glucopyransyloxy)-9-trimethylsilyloxynaphthacene*-
5,6,11,12-*tetraone* (**26**) *with Dimethyldioxirane*

(a) The cycloadduct (**26**) (0.50 g, 0.67 mmol) was added to a stirred solution of dimethyldioxirane (DMDO) in acetone (*ca.* 1 mol dm^{-3}, 13 cm^3, 1.27 mmol). After having been left overnight, the solution was evaporated and the residue crystallised from dry dichloromethane-dry diethyl ether-hexanes to afford (5aS,6aR,7R,8S,10aR,11aR)-5a,11a-*Epoxy*-5a,6a,7,8,9,10,10a,11a-*octahydro*-8-*hydroxy*-7-(2',3',4',6'-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy)naphthacene*-5,6,9,11,12-*pentaone* (**28**) (0.295 g, 64%) as a cream solid;

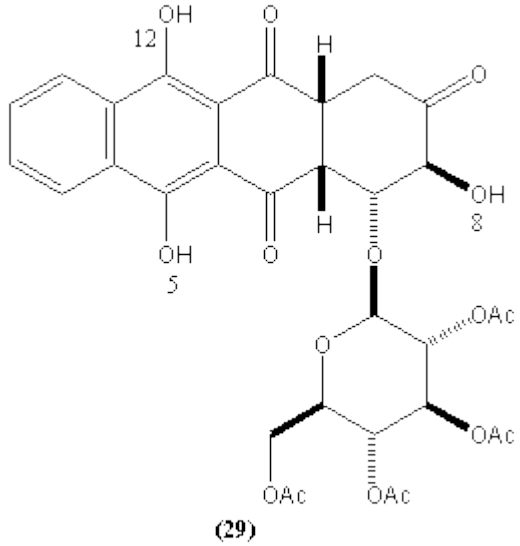


(28)

m.p. 202-203 °C (with decomp.) [lit.,[7] 222 °C (with decomp.)],
$[\alpha]_D$ -42 (0.44% in CH_2Cl_2) [lit.,[7] -100 (0.28% in CH_2Cl_2)],
δ (300 MHz; $CDCl_3$) 1.70, 1.89, 2.00 and 2.08 (each 3 H, s, 4 x $MeCO_2$), 2.43 (1 H, dd, *J* 13.5 and 8 Hz, 10-Hβ), 3.16 (1 H, br s, 8-OH), 3.17 (1 H, dd, *J* 11 and 2 Hz, 6a-H), 3.57 (1 H, dd, *J* 13.5 and 10 Hz, 10-Hα), 3.66-3.73 (1 H, m, 5'-H), 4.06-4.18 (3 H, m, 6'-H_2 and 10a-H), 4.42 (1 H, d, *J* 1.5 Hz, 8-H), 4.64-4.66 (1 H, m, 7-H), 4.69 (2 H, apparent dd, separation 5 and 2 Hz, 1'- and 2'-H), 4.95 (1 H, br d, *J* 9.5 Hz, 4'-H), 5.13 (1 H, dt, *J* 9.5, 9.5 and 2 Hz, 3'-H) and 7.82-7.86 and 8.17-8.22 (each 2 H, m, 1-,2-,3- and 4-H).
(b) The cycloadduct (**26**) (3.89 g, 5.25 mmol) was subjected to the aforementioned conditions [using 10.49 mmol of DMDO for 21 h] to afford, after crystallisation of the crude material (3.66 g) from dry dichloromethane-hexanes the epoxypentaone (**28**) (3.5 g, 97%).

Exp. 23
Reduction of (5aS,6aR,7R,8S,10aR,11aR)-5a,11a-*Epoxy*-5a,6a,7,8,9,10,10a,11a-*octahydro*-8-*hydroxy*-7-(2',3',4',6'-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy)naphthacene*-5,6,9,11,12-*pentaone* (**28**) *with Zinc-Acetic Acid*
A solution of the epoxypentaone (**28**) (0.46 g, 0.67 mmol) in acetic acid (50 cm^3) and dichloromethane (50 cm^3) was cooled to -20 °C and activated zinc[8] (2.53 g, 38.9 mmol) was added. The reaction was followed by TLC and after 35 min, the mixture was filtered and washed once with water. Evaporation of the dried ($MgSO_4$) organic phase afforded a mixture containing an 8:1 ratio of the trihydroxytrione (**29**) [δ (300 MHz; $CDCl_3$) *inter alia* 13.15 and 13.77 (each 1 H, s, 5- and 12-OH)] and an identified material [δ (300 MHz; $CDCl_3$) *inter alia* 12.76 and 13.74 (each 1 H, s, 5- and 12-OH)]. Crystallisation of this mixture from ethanol afforded (5aS,6aR,7R,8S,10aR,11aR)-5a,6a,7,8,9,10,10a,11a-*octahydro*-5,8,12-

trihydroxy-7-(2',3',4',6'-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy)naphthacene*-6,9,11-*trione* (**29**) (0.193 g 29%) as fine-yellow needles;



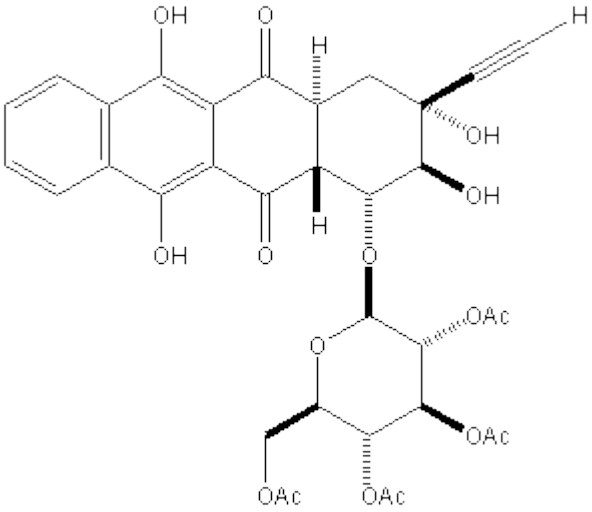
(29)

m.p. 164-165 °C (lit.,[7] 169 °C),
$[\alpha]_D$ +25 (0.5% in CH_2Cl_2) [lit.,[7] +26 (0.31% in CH_2Cl_2)],
δ (300 MHz; $CDCl_3$) 1.29, 1.85, 1.98 and 2.09 (each 3 H, s, 4 x $MeCO_2$), 2.89 (1 H, dd, *J* 14.5 and 8.5 Hz, 10-Hβ), 3.31 (1 H, dd, *J* 6.5 and 2 Hz, 6a-H), 3.39 (1 H, dd, *J* 14.5 and 8 Hz, 10-Hα), 3.56 (1 H, q, *J* 8 Hz, 10a-H), 3.63-3.70 (1 H, m, 5'-H), 4.11-4.21 (2 H, m, 6'-H_2), 4.39-4.41 (1 H, m, 7-H), 4.58 (1 H, d, *J* 2 Hz, 8-H), 4.61 (1 H, d, *J* 8 Hz, 1'-H), 4.71 (1 H, dd, *J* 8.5 and 8 Hz, 2'-H), 4.93-5.03 (2 H, m, 3'- and 4'-H), 7.76-7.85 and 8.47-8.52 (each 2 H, m, 1-, 2-, 3- and 4-H) and 13.15 and 13.78 (each 1 H, s, 5- and 12-OH).

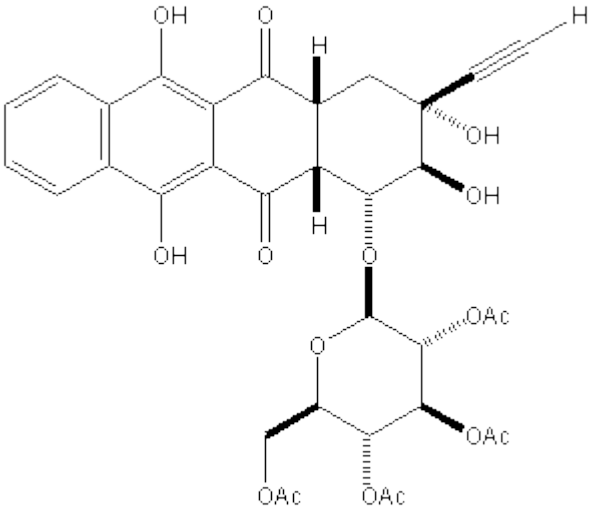
Exp. 24

Reaction of (5aS,6aR,7R,8S,10aR,11aR)-5a,6a,7,8,9,10,10a,11a-*octahydro*-5,8,12-*trihydroxy*-7-(2',3',4',6'-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy)naphthacene*-6,9,11-*trione* (**29**) *with Ethynylmagnesium Chloride*

To a stirred solution of the trihydroxytrione (**29**) (0.265 g, 0.40 mmol) in freshly distilled dry THF (30 cm^3) at 0 °C was added a solution of ethynylmagnesium chloride in THF (*ca.* 0.5 mol dm^{-3}, 24cm^3, 12 mmol). After 30 min, the mixture was poured onto ice-cold saturated aqueous ammonium chloride and extracted with dichloromethane (x 2). The organic extracts were washed with water, dried ($MgSO_4$) and concentrated to afford a solid (0.270 g) which on the basis of 300 MHz ^{1}H NMR spectroscopy contained a mixture of ethynylated materials. Attempted crystallisation of this material from dry dichloromethane-dry diethyl ether-hexanes afforded a precipitate (0.245 g, *ca.* 88%) which contained a 3:1 mixture of the C-10a epimers (**30**) and (**31**);



(30) Major Epimer



(31) Minor Epimer

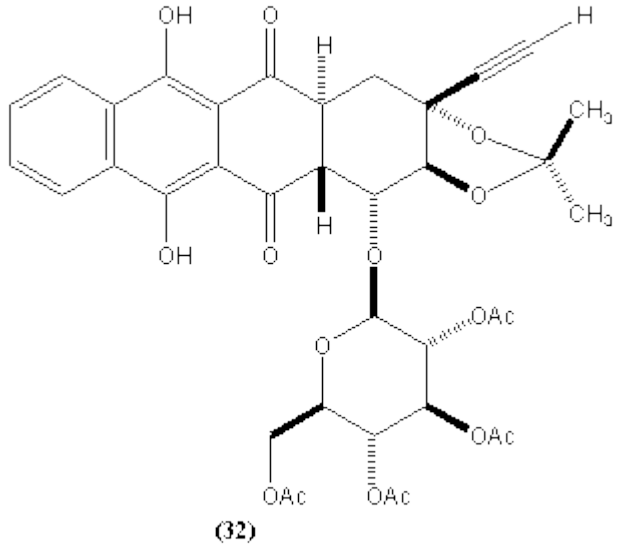
m.p. 130-138 °C,
δ (300 MHz; $CDCl_3$) *inter alia* 2.45 (1 H, s, C≡CH), 2.70 (1 H, d, *J* 17 Hz, 10-Hα), 4.64 (1 H, d, *J* 8 Hz, 8-H), 7.77-7.81 and 8.45-8.49 (each 2 H, m, 1-,2-,3- and 4-H) and 13.32 and 13.53 (each 1 H, br s, 5- and 12-OH), *m/z* (FAB) 721 (*M*Na^+, 16%), 698 (*M*$^+$, 32), 331 ($C_{14}H_{19}O_{10}^+$, 95) and 169 (100).

Exp. 25

Reaction of (6aR,7R,8S,9S,10aS)-9-*Ethynyl*-6a,7,8,9,10,10a-*hexahydro*-5,8,9,12-*tetrahydroxy*-7-(2',3',4',6'-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*) *naphthacene*-6,11-*dione* (**30**) *with* 2,2-*Dimethoxypropane and* p-*Toluenesulfonic Acid*

To a stirred solution of a mixture containing predominantly the ethynyltetraol (**30**) (0.019 g, 0.026 mmol) in freshly distilled dry benzene (2

cm^3) was added *p*-toluenesulfonic acid (0.007 g, 0.04 mmol) followed by 3 drops of 2,2-dimethoxypropane (0.024 g, 0.23 mmol). After 5 h, the mixture was added to water and extracted with dichloromethane. The organic extract was washed with water, dried ($MgSO_4$) and concentrated to give a residue (0.014 g) containing a 5:1 mixture of (6aR,7R,8S,9S,10aS)-9-*Ethynyl*-6a,7,8,9,10,10a-*hexahydro*-5,12-*dihydroxy*-8,9-O-*isopropylidene*-7-(2',3',4',6'-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*) *naphthacene*-6,11-*dione* (**32**) and an unidentified material;



(32)

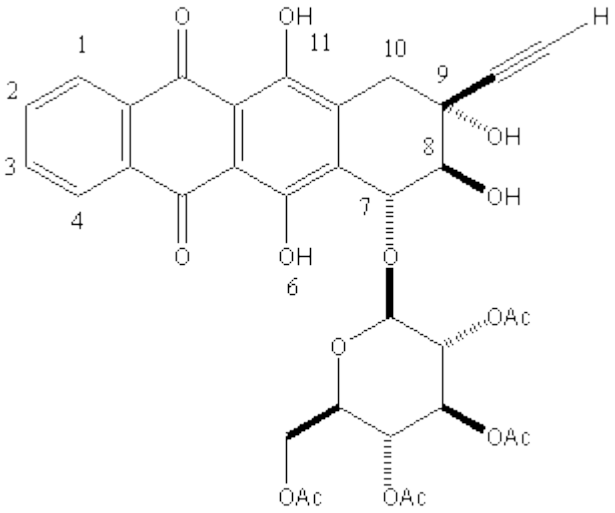
δ(300 MHz; $CDCl_3$) [for (**32**)] 1.71, 1.86, 2.00 and 2.11 (each 3 H, s, 4 x $MeCO_2$), 1.51 and 1.64 (each 3 H, s, Me_2C), 2.50 (1 H, dd, *J* 15 and 11 Hz, 10-Hβ), 2.58 (1 H, s, C≡CH), 2.75 (1 H, dd, *J* 15 and 6 Hz, 10-Hα), 3.34-3.51 (2 H, m, 6a- and 10a-H), 3.67-3.73 (1 H, m, 5'-H), 4.18-4.21 (2 H, m, 6'-H_2), 4.51-4.57 (2 H, m, 1- and 7-H), 4.73 (1 H, dd, *J* 9 and 8 Hz, 2'-H), 4.79 (1 H, d, *J* 3 Hz, 8-H), 4.99 (1 H, t, *J* 9.5 Hz, 4'-H), 5.06 (1 H, t, *J* 9 Hz, 3'-H), 7.77-7.81 and 8.45-8.52 (each 2 H, m, 1-,2-,3- and 4-H) and 14.11 and 14.27 (each 1 H, s, 5-and 12-OH) (addition of D_2O caused the signals at δ 14.11 and 14.27 to disappear),
m/z (FAB) 738 (M^+, 16%), 331 ($C_{14}H_{19}O_{10}^+$, 100) and 169 (99).

Exp. 26

Oxidation of (6aR,7R,8S,9S,10aS)-9-*Ethynyl*-6a,7,8,9,10,10a-*hexahydro*-5,12-*dihydroxy*-8,9-O-*isopropylidene*-7-(2',3',4',6'-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*) *naphthacene*-5,12-*dione* (**30**) *to* (7R,8S,9S)-9-*Ethynyl*-7,8,9,10-*tetrahydro*-6,8,9,11-*tetrahydroxy*-8,9-7-(2',3',4',6'-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy*) *naphthacene*-6,11-*dione* (**33**)

A solution of the ethynyltetraol (**30**) (0.121 g, 0.13 mmol) in freshly distilled dry benzene (25 cm^3) was treated with activated manganese(IV) oxide[9]

(1.03 g, 11.85 mmol) and the mixture was heated under reflux. The oxidation was followed by TLC and, after 18 h, the mixture was filtered through Celite (the residue being washed by dichloromethane). The filtrate and washings were combined and evaporated to afford a residue (0.046 g, ca. 51%) containing predominantly the anthracycline (**33**) and a small amount of an unidentified material. Crystallisation of the mixture from hot ethanol afforded the title compound (**33**) (0.009 g, 10%) {in a separate experiment, subjection of the crude material to silica-gel column chromatography [hexanes:EtOAc (1:1 to 1:4) then EtOAc as eluant] failed to separate the two components};

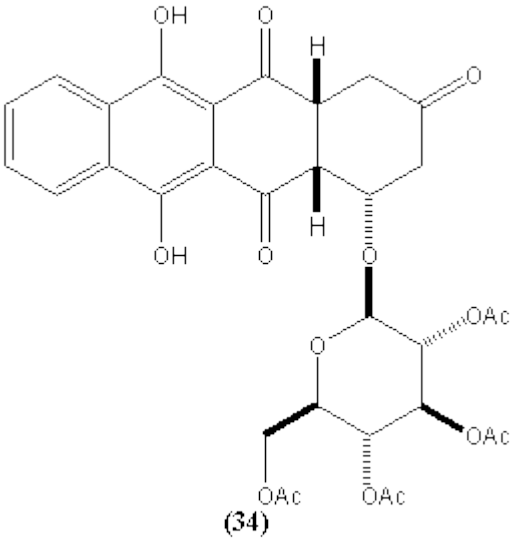


(33)

m.p. 279-282 °C;
$[\alpha]_D$ +163 (0.09% in CH_2Cl_2)
ν_{max} (KBr) 3520-3360 (OH), 3270 (chelated OH), 1755 (ester C=O), 1625 (chelated C=O) and 1590 cm^{-1}(C=O),
λ_{max} (EtOH) 204 (ε 22 600), 251 (29 800), 287 (10 900) and 484 nm (9500),
δ (300 MHz; $CDCl_3$) 1.89, 2.01, 2.07 and 2.16 (each 3 H, s, 4 x $MeCO_2$), 2.61 (1 H, s, C≡CH), 2.94 (1 H, s, 9-OH), 3.06 (1 H, d, *J* 18.5 Hz, 10-Hβ), 3.62 (1 H, d, *J* 18.5 Hz, 10-Hα), 3.93-3.98 (1 H, m, 5'-H), 4.16-4.23 (2 H, m, 6'- and 8-H), 4.33 (1 H, dd, *J* 13 and 2 Hz, 6'-H), 4.61 (1 H, s, 8-OH), 4.85 (1 H, d, *J* 6 Hz, 7-H), 5.01-5.14 (2 H, m, 2'- and 4'-H), 5.19 (1 H, d, *J* 8 Hz, 1'-H), 5.37 (1 H, t, *J* 9.5 Hz, 3'-H), 7.82-7.86 and 8.34-8.36 (each 2 H, m, 1-, 2-, 3-, and 4-H) and 13.28 and 13.64 (each 1 H, s, 6- and 11-OH) (addition of D_2O caused the signals at δ 2.94, 4.61, 13.28 and 13.64 to disappear) (in a 2D COSY 45° experiment the following connectivities were established: δ 3.06 to 3.62; δ 4.33 to 4.17-4.23 to 3.93-3.98 to 5.01-5.14 to 5.37; δ 4.17-4.23 to 4.85; and δ 5.19 to 5.01-5.14),
m/z (FAB) 719 (*M*Na^+, 16%), 697 (*M*H^+, 39), 696 (M^+, 37), 331 ($C_{14}H_{19}O_{10}^+$, 100) and 169 (27).

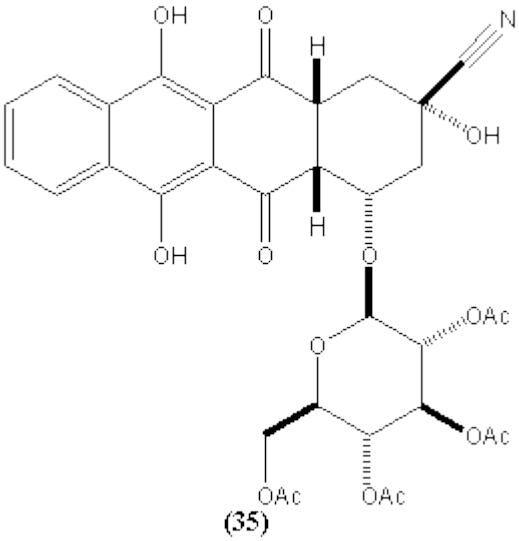
Found: MH^+, 697.1789. $C_{34}H_{32}O_{16}$ requires *m/z*, 697.1769.
Found: C, 57.0; H, 4.2. $C_{34}H_{32}O_{16}$ requires C, 58.62; H, 4.63%.

Exp. 27
Exploratory reactions of (6aR,7S,10aR)-6a,7,8,9,10,10a-*Hexahydro*-5,12-*dihydroxy*-7-(2',
3',4',6'-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy)naphthacene*-6,9,11-*trione* (**34**) *with Trimethylsilyl Cyanide in the Presence of Lewis Acids*



(34)

(a) To the dihydroxytrione (**34**)[2] (0.103 g, 0.157 mmol) in dry dichloromethane (10 cm^3) was added a solution of trimethylsilyl cyanide (0.52 g, 5.2 mmol) in dry dichloromethane (3 cm^3), followed by titanium(IV) chloride (0.893 g, 4.7 mmol) in dry dichloromethane (3 cm^3). The mixture was stirred under argon for 9.5 h and the purple mixture poured onto saturated aqueous ammonium chloride. Extraction with dichloromethane then washing of the organic layer with water, drying ($MgSO_4$), filtration and condensation *in vacuo* afforded an orange solid (0.040 g). Subjection of the mixture to low-temperature silica-gel chromatography [hexanes-EtOAc (5:1 to 1:2) as eluant] gave a solid (0.032 g) which, after crystallisation from chloroform-hexanes, afforded (6aR,7S,9S,10aR)-9-cyano-6a,7,8,9,10,10a-*hexahydro*-5,9,12-*trihydroxy*-7-(2',
3',4',6'-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy)naphthacene*-6,11-*dione* (**35**) (0.018 g, 17%) as a dark-orange solid;



(35)

m.p. 209-211.5 °C,
$[\alpha]_D$ +122 (0.5% in CH_2Cl_2),
δ(300 MHz; $CDCl_3$) 1.60, 1.80, 1.87 and 2.18 (each 3 H, s, 4 x $MeCO_2$), 1.98 (1 H, m, 10-Hβ), 2.16 (1 H, m, 8-Hβ), 2.88 (1 H, br d, separation 15 Hz, 8-Hα), 3.21 (1 H, dd, *J* 6.2 and 3.3 Hz, 6a-H), 3.41 (1 H, dt, *J* 7.6 and 2 Hz, 10a-H), 3.58 (1 H, br d, separation 15 Hz, 10-Hα), 3.73 (1 H, m, 5'-H), 4.00 (1 H, dd, *J* 7.6 and 12.3 Hz, 6'-H), 4.20-4.30 (2H, m, 9-OH and 6'-H), 4.45-4.54 (3 H, m, 1'-, 2'- and 7-H), 4.84 (1 H, t, *J* 9.7 Hz, 4'-H), 4.98 (1 H, t, *J* 9.7 Hz, 3'-H), 7.75-7.84 (2 H, m, 1- and 4-H), 8.48 (2 H, ddd, *J* 17.6, 6.9 and 2.3 Hz, 2- and 3-H), 13.45 and 13.81 (2 H, s, 5- and 12-OH) [addition of D_2O caused the m at δ 4.20-4.30 to simplify and the signals at δ 13.45 and 13.81 to disappear] [a ^1H-^1H COSY experiment established the following observations; no connectivity was established between the m a δ 1.98 (10-Hβ) and the br d at δ 3.58 (10-Hα); the br d at δ 2.88 (8-Hα) and the br d at δ 3.58 (10-Hα) were not connected],
m/z (FAB) 706 (MNa$^+$, 4%), 683 (M^+, 45), 353 (MH$^+$-$C_{14}H_{19}O_9$, 10) and 331 ($C_{14}H_{19}O_{10}^+$, 100).

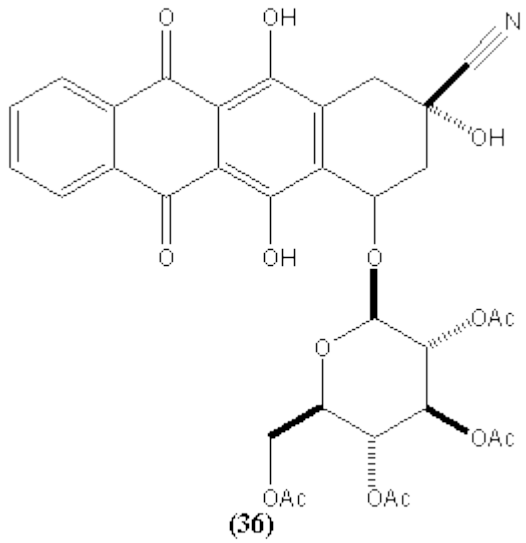
(b) To the dihydroxytrione (**34**)[2] (0.020 g, 0.031 mmol) in dry dichloromethane (2 cm^3) was added a solution of trimethylsilyl cyanide (0.090 g, 0.91 mmol) in dry dichloromethane (2 cm^3), followed by titanium(IV) chloride (0.035 g, 0.21 mmol) in dry dichloromethane (1 cm^3). The mixture was refluxed for 25 h and allowed to cool. The dark-purple solution was poured onto saturated aqueous ammonium chloride, extracted with dichloromethane, washed once with water, dried ($MgSO_4$), filtered and the solvent evaporated *in vacuo* to afford a light-brown solid (0.012 g), shown by 300 MHz ^1H NMR spectroscopy to contain an 8:11 mixture of the dihydroxytrione (**34**) and the cyanohydrin (**35**).

(c) To the dihydroxytrione (**34**)[2] (0.020 g, 0.031 mmol) in dry dichloromethane (2 cm^3) was added a solution of trimethylsilyl cyanide (0.090 g, 0.91 mmol) in dry dichloromethane (2 cm^3), followed by *tert*-butyldimethylsilyl triflate (0.066 g, 0.023 mmol) in dry dichloromethane (1 cm^3) at 0 ^oC and stirred at room temperature for 24 h. The red solution was then added to saturated aqueous ammonium chloride, extracted with dichloromethane, washed once with water, dried ($MgSO_4$), filtered and the solvent evaporated *in vacuo* to afford an orange solid (0.019 g). The product comprised a 3:1:3 ratio of the cyanohydrin (**35**), an unidentified material [δ (200 MHZ; $CDCl_3$) *inter alia* 13.08 and 13.56 (each 1 H, s, 5- and 12-OH)] and the tetra-acetylglucose (**16**).

Exp. 28

Oxidation of (6aR,7S,9S,10aR)-9-Cyano-6a,7,8,9,10,10a-*hexahydro*-5,9,12-*trihydroxy*-7-(2', 3',4',6'-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy)naphthacene*-6,11-*dione* (**35**) to (7S,9S)-9-Cyano-6a,7,8,9,10-*tetrahydro*-6,9,11-*trihydroxy*-7-(2', 3',4',6'-*tetra*-O-*acetyl*-β-D-*glucopyranosyloxy)naphthacene*-5,12-*dione* (**36**)

A solution of the cyanohydrin (**35**) (0.223 g, 0.33 mmol) in acetic acid (45 cm^3) was treated with lead(IV) acetate (0.190 g, 0.43 mmol) and the mixture stirred at room temperature for 22 h. The resultant orange precipitate was filtered, washed with water and dried. The crude anthracycline (**36**) (0.151 g) was crystallised from chloroform-methanol-hexanes to afford a solid (0.104 g) which was further recrystallised from chloroform-ethyl acetate-hexanes to afford the *title* compound (**36**) (0.045 g, 23%) as a bright orange solid;



(36)

m.p. 227.5-229 °C,
$[\alpha]_D$ +86 (0.47% in CH_2Cl_2),

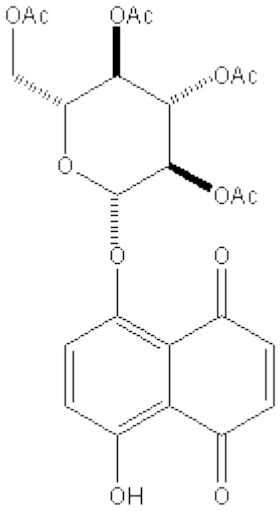
ν_{max} (KBr) 3460 (OH), 1755 (ester C=O) and 1620 cm^{-1}(C=O),
λ_{max} (EtOH) 251 (ε 30 000), 273 (19 300) and 480 nm (10 300),
δ(300 MHz; $CDCl_3$) 1.89, 2.00, 2.06 and 2.18 (each 3 H, s, 4 x $MeCO_2$), 2.33 (1 H, dd, *J* 15 and 4.5 Hz, 8-Hβ), 2.98 (1 H, d, *J* 15 Hz, 8-Hα), 3.03 (1 H, d, *J* 19 Hz, 10-Hβ), 3.72 (1 H, d, *J* 19 Hz, 10-Hα), 3.87 (1 H, m, 5'-H), 4.28-4.31 (3 H, m, 9-OH and 6'-H_2), 4.92 (1 H, t, *J* 9 Hz, 2'-H), 5.06-5.11 (2 H, m, 4'- and 1'-H), 5.29-5.32 (2 H, m, 3'- and 7-H), 7.82-7.92 and 8.34-8.42 (each 2 H, m, 1-, 2-, 3- and 4-H) and 13.26 and 13.61 (each 1 H, s, 6- and 11-OH) (addition of D_2O caused the m at δ 4.28-4.31 to simplify and those at δ 13.26 and 13.61 to disappear),
m/z (FAB) 682 (*M*H^+, 10%), 681 (*M*$^+$, 12), 334 (*M*$^+$-$C_{14}H_{19}O_{10}$, 100), 331 ($C_{14}H_{19}O_9^+$, 97), 307 (68), 287 (82) and 169 (22).
Found: *M*H+, 682.1783. $C_{33}H_{31}NO_{15}$ requires *M*H+, 682.1772.
Found: C, 57.2; H, 4.7; N, 2.1. $C_{33}H_{31}NO_{15}$ requires C, 58.1; H, 4.6; N, 2.1%.
Found: C, 57.2; H, 4.7; N, 2.1. $C_{33}H_{31}NO_{15}0.5H_2O$ requires C, 57.3; H, 4.8; N, 2.1%.

Exp. 29

Preparation of 8-*Hydroxy*-5-(2',3',4',6'-*tetra*-O-β-D-*glucopyranosyloxy*)-1,4-*naphthoquinone* (37)[10]

(a) Silver(I) oxide (0.974 g, 4 mmol) was added to a solution of naphthazarin (**3**) (0.50 g, 3.36 mmol) and the acetobromoglucose (**7**) (1.38 g, 3.36 mmol) in 'HPLC grade' acetonitrile (7 cm^3). The mixture was subjected to sonication for 2 h and left at room temperature for a further 45 min. The mixture was diluted with dichloromethane to which Celite was added. This slurry was filtered through silica-gel which was subsequently washed with dichloromethane and diethyl ether. The combined filtrate and washings were condensed *in vacuo* to afford a solid (0.67 g), which was subjected to the same work-up procedure.

Attempted separation of the glucoside (**37**) from naphthazarin (**3**) by fractional crystallisation using dichloromethane-hexanes was unsuccessful. The resultant solid (0.289 g) was subjected to silica-gel column chromotography [hexanes-EtOAc (1:1) then EtOAc as eluant] to give a solid (0.289 g) which was crystallised from dry dichloromethane-dry diethyl ether-hexanes to afford the *title* compound (**37**) (0.133 g, 10%) as a bright-orange solid;



(37)

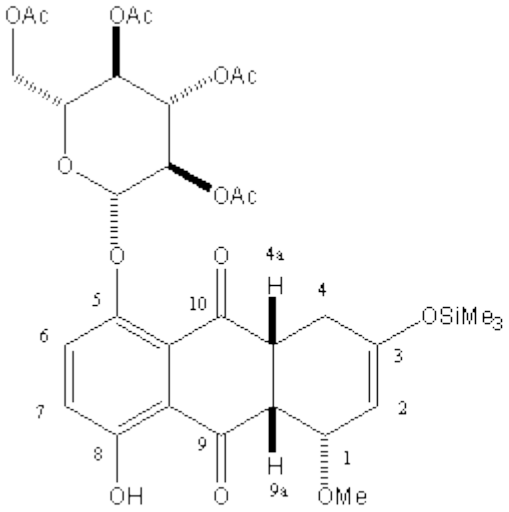
m.p. 164-165 °C (with decomp.) (lit.,[10] 143-144 °C),
$[\alpha]_D$ -107.5 (5.3% in CH_2Cl_2) [lit.,[10] -53 (2.5% in $CHCl_3$)],
δ (300 MHz; $CDCl_3$) 2.03, 2.05, 2.08 and 2.16 (each 3 H, s, 4 x $MeCO_2$), 3.76-3.82 (1 H, m, 5'-H), 4.18 (1 H, dd, *J* 12.5 and 2.5 Hz, 6'-H), 4.26 (1 H, dd, *J* 12.5 and 5 Hz, 6'-H), 5.01 (1 H, d, *J* 8 Hz, 1'-H), 5.17 (1 H, t, *J* 10 Hz, 4'-H), 5.31 (1 H, t, *J* 9 Hz, 3'-H), 5.40 (1 H, dd, *J* 9.5 and 8 Hz, 2'-H), 6.83 and 6.89 (each 1 H, d, *J* 5 Hz, 2- and 3-H), 7.24 and 7.54 (each 1 H, *J* 9.5 Hz, 6- and 7-H) and 12.43 (1 H, s, 8-OH).

(b) Silver(I) oxide (1.96 g, 8.45 mmol) was added to a solution of naphthazarin (**3**) (1.02 g, 5.36 mmol) and the acetobromoglucose (**7**) (2.75 g, 6.7 mmol) in 'HPLC grade' acetonitrile (16 cm^3). The mixture was subjected to sonication for 2 h and left at room temperature for 30 min. Celite was added and the mixture was filtered through silica-gel which was then washed with dichloromethane and diethyl ether. Concentration of the combined filtrate and washings gave a dark-orange residue (2.37 g) which was subjected to silica-gel column chromatography [hexanes-EtOAc (1:1) then EtOAc as eluant] and crystallised twice from ethyl acetate-hexanes to afford the *title* compound (**37**) (0.592 g, 21%) as an orange solid.

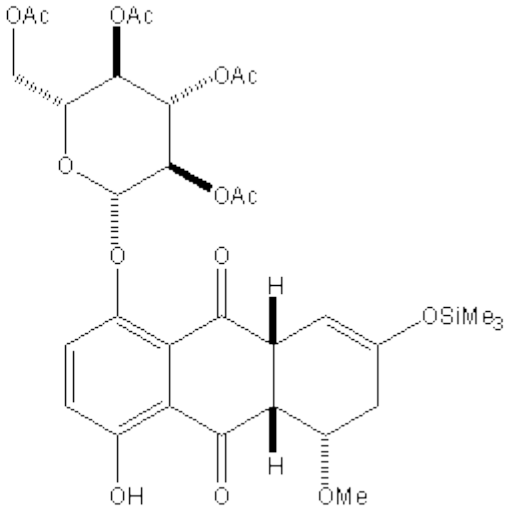
Ex. 30

Reaction of 8-*Hydroxy*-5-(2',3',4',6'-*tetra*-O-β-D-*glucopyranosyloxy*)-1,4-*naphthoquinone* (**37**) *with Danishefsky's Diene* (**40**)

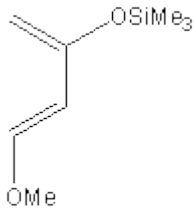
(a) To a solution of the glucoside (**37**) (0.174 g, 0.334 mmol) in dry dichloromethane (10 cm^3) was added a solution of Danishefsky's diene (**40**) (0.184 g, 1.06 mmol) in dry dichloromethane (2 cm^3). Evaporation, after 4 h, afforded predominantly the cycloadduct (**38**) (0.232 g). Crystallisation from dichloromethane-diethyl ether-hexanes gave a mixture containing a 7:2 ratio f the cycloadduct (**38**) and the presumed isomer (**39**) (0.179 g, 77%) as a buff solid;



(38)



(39)



(40)

δ (300 MHz; $CDCl_3$) [for (**38**)] *inter alia* 0.27 (9 H, s, Me_3Si), 2.95 (3 H, s, MeO), 7.09 and 7.54 (each 1 H, d, *J* 9.5 Hz, 6- and 7-H) and 12.44 (1 H, s, 8-OH).

δ (300 MHz; $CDCl_3$) [for (**39**)] *inter alia* 0.25 (9 H, s, Me_3Si), 3.06 (3 H, s, MeO), 7.11 and 7.58 (each 1 H, d, *J* 9.5 Hz, 6- and 7-H) and 12.61 (1 H, s, 8-OH).

(b) A solution of the glucoside (**37**) (0.009 g, 0.017 mmol) and Danishefsky's diene (**40**) (0.023 g, 0.134 mmol) in dry benzene (3 cm^3) was heated at reflux for 1.5 h. Evaporation of the solvent afforded (1S,4aR,9aR)-1,4,4a,9a-*tetrahydro*-8-*hydroxy*-1-*methoxy*-5-(2',3',4',6'-*tetra*-O-β-D-*glucopyranosyloxy*)-3-*trimethylsilyloxy*-9,10-*anthraquinone* (**38**) (0.014 g) as a light brown solid;

δ (200 MHz; $CDCl_3$) 0.27 (9 H, s, Me_3Si), 2.03, 2.05 and 2.13 (6, 3 and 3-H, each s, 4 x $MeCO_2$), 2.16-2.22 (1 H, m, 4-Hβ), 2.95 (3 H, s, MeO), 2.95-3.00 (1 H, m, 4-Hα), 3.21 (1 H, dd, *J* 6 and 4 Hz, 9a-H), 3.34 (1 H, t, *J* 6 Hz, 4a-H), 3.70-3.74 (1 H, apparent d, separation 9.5 Hz, 5'-H), 4.17-4.23 (3 H, m, 1- and 6'-H_2), 4.75 (1 H, d, *J* 7 Hz, 1'-H), 5.02-5.40 (4 H, m, 2-,2'-,3'- and 4'-H), 7.09 and 7.54 (each 1 H, d, *J* 9 Hz, 6- and 7-H) and 12.43 (1 H, s, 8-OH).

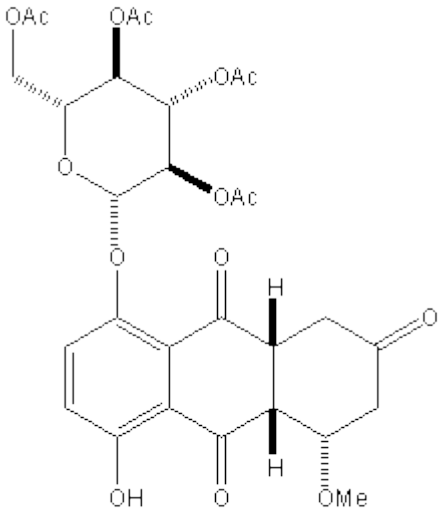
(c) To the glucoside (**37**) (0.015 g, 0.029 mmol) was added a solution of tetraacetyldiborate (0.005 g, 0.036 mmol) in dry dichloromethane (2 cm^3) followed by a solution of Danishefsky's diene (**40**) (0.017 g, 0.1 mmol) in

dry dichloromethane (1 cm^3). The reaction was followed by 300 MHz ^1H NMR spectroscopy and, after 10 min, a mixture containing a 2:1 ratio of 4-methoxybut-1-ene-3-one and the cycloadduct (**38**) was detected. Evaporation, after 20 h, afforded a dark-orange material (0.024 g) that contained a 6:4:3 ratio of the cycloadduct (**38**), the isomerised cycloadduct (**39**) and 4-methoxybut-1-ene-3-one, together with a small amount of aromatic material.

Exp. 31

Preparation of (1S,4aR,9aR)-1,2,3,4,4a,9a-*Hexahydro*-9-*hydroxy*-1-*methoxy*-5-(2',3',4',6'-*tetra*-O-β-D-*glucopyranosyloxy*)*anthracene*-3,9,10-*trione* (**41**)

A mixture of compounds (**38**) and (**39**) (0.428 g, 0.62 mmol) was dissolved in THF (14 cm^3) containing 0.1M hydrochloric acid (1.4 cm^3). After 2 h, the mixture was diluted with dichloromethane and washed with water. Evaporation of the dried ($MgSO_4$) organic phase gave a residue (0.424 g) which was crystallised twice from dry dichloromethane-dry diethyl ether-hexanes to afford the *title* compound (**41**) (0.169 g, 44%) as a pale-cream solid;



(41)

m.p. 228-229 °C,

$[\alpha]_D$ -45 (1% in CH_2Cl_2),

ν_{max} (KBr) 1750br (ester CO), 1700 (ketone CO) and 1650 cm^{-1}(quinone CO),

λ_{max} (EtOH) 206 (ε 13 350), 228 (15 500), 251 (14 500) and 367 nm (7100),

δ (300 MHz; $CDCl_3$) 2.031, 2.037, 2.08 and 2.20 (each 3-H, each s, 4 x $MeCO_2$), 2.35 (1 H, dd, *J* 15 and 7 Hz, 4-Hβ), 2.46 (1 H, dd, *J* 15.5 and 3 Hz, 2-Hβ), 2.90 (1 H, br d, separation 15.5 Hz, 2-Hα), 3.03 (1 H, s, MeO), 3.30 (1 H, br d, separation 15 Hz, 4-Hα), 3.48 (1 H, dd, *J* 7 and 2.5 Hz, 9a-H), 3.59 (1 H, dt, separation 7, 7 and 2.5 Hz, 4a-H), 3.66-3.72 (1 H, m, 5'-

H), 4.16-4.27 (3 H, m, 1-H and 6'-H_2), 4.72-4.75 and 5.10-5.25 (1 and 3 H, each m, 1'-,2'-,3'- and 4'-H), 7.13 (1 H, d, *J* 9 Hz, 6-H), 7.59 (1 H, d, *J* 9 Hz, 7-H) and 12.39 (1 H, s, 8-OH) (in a 2D COSY experiment, the following connectivities were established: δ 3.48 to 3.59 to 2.35 to 3.30 to 2.90 to 2.46 to 4.16-4.29; δ 4.16-4.29 to 3.70 to 5.10-5.25 to 4.72-4.75),
m/z (FAB) 642 [(*M*-H)Na^+, 4%)], 620 (M^+, 2), 460 (10), 331 ($C_{14}H_{19}O_9^+$, 18), 169 (44) and 43 ($MeCO^+$, 100).

Exp. 32

Reaction of (1S,4aR,9aR)-1,2,3,4,4a,9a-*Hexahydro*-9-*hydroxy*-1-*methoxy*-5-(2',3',4',6'-*tetra*-O-β-D-*glucopyranosyloxy*)*anthracene*-3,9,10-*trione* (**41**) *with Ethynylmagnesium Chloride Followed by Lead(IV) acetate*

(a) A solution of ethynylmagnesium chloride in THF (*ca.* 0.5 mol dm^{-3}, 1.1cm^3, 0.55 mmol) was added to a stirred solution of the hydroxytrione (**41**) (0.0115 g, 0.018 mmol) in freshly distilled dry THF (3 cm^3) at -10 °C. After 25 min, the solution was poured onto ice-cold saturated ammonium chloride and extracted with dichloromethane. The organic extract was washed with water, dried ($MgSO_4$) and evaporated to afford a yellow solid (*ca.* 0.007 g) shown to be a complex mixture by 300 MHz ^{1}H NMR spectroscopy;
δ (300 MHz; $CDCl_3$) *inter alia* 2.43, 2.47, 2.70 and 2.76 (each s, C≡CH), 2.92 (s, MeO) and 12.39 (s, 8-OH),
m/z (FAB) 650 (17%), 331 ($C_{14}H_{19}O_9^+$, 100) and 169 (75).

The residue (0.007 g, *ca.* 0.011 mmol) was stirred with a solution of lead(IV) acetate (0.008 g, 0.019 mmol) in acetic acid (1.7 cm^3) for 22 h. After this time, the solution was diluted with water and extracted with ethyl acetate. The organic extract was washed with aqueous sodium hydrogen carbonate and water, dried ($MgSO_4$) and evaporated to afford a dark-yellow solid (0.004 g) shown by 300 MHz ^{1}H NMR spectroscopy to be a complex mixture;
δ(300 MHz; $CDCl_3$) *inter alia* 3.09 (s, MeO) (the 8-OH signal expected around 12.40 ppm was not detected),
m/z (FAB) 648 (5%), 331 ($C_{14}H_{19}O_9^+$, 90) and 169 (100).

(b) A solution of ethynylmagnesium chloride in THF (*ca.* 0.5 mol dm^{-3}, 1.2cm^3, 0.6 mmol) was added to a stirred solution of the hydroxytrione (**41**) (0.0127 g, 0.020 mmol) in freshly distilled dry THF (3 cm^3) at -room temperature. After 25 min, the solution was poured onto ice-cold saturated ammonium chloride and extracted with dichloromethane. The organic extract was washed with water, dried ($MgSO_4$) and evaporated to afford a yellow solid (*ca.* 0.006 g) shown to be a complex mixture by 300 MHz ^{1}H NMR spectroscopy;
δ(300 MHz; $CDCl_3$) *inter alia* 2.27, 2.48, 2.58 and 2.71 (each s, C≡CH), 3.19 (s, MeO) and 13.23 (s, 8-OH),

m/z (FAB) 649 (20%), 331 ($C_{14}H_{19}O_9^+$, 84) 219 (100) and 169 (87).

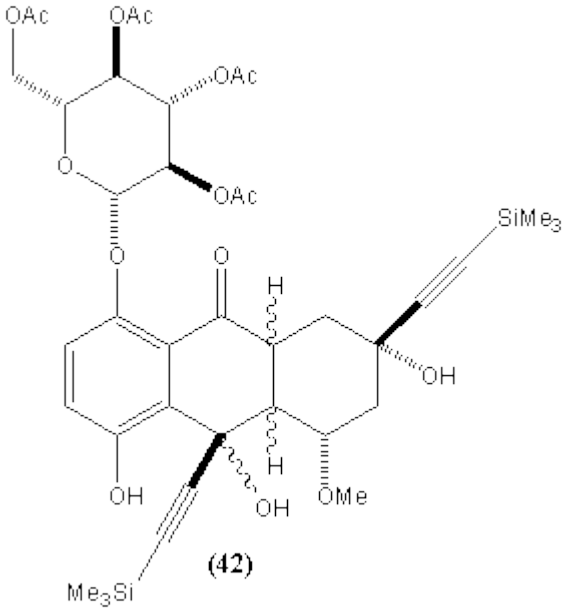
The residue (0.004 g, *ca.* 0.006 mmol) was stirred with a solution of lead(IV) acetate (0.0044 g, 0.01 mmol) in acetic acid (1 cm^3) for 22 h. After this time, the solution was diluted with water and extracted with ethyl acetate. The organic extract was washed with aqueous sodium hydrogen carbonate and water, dried ($MgSO_4$) and evaporated to afford a dark-yellow solid (0.004 g) shown by 300 MHz ^1H NMR spectroscopy to be a complex mixture;
δ (300 MHz; $CDCl_3$) *inter alia* 2.41, 2.59, 2.65 and 2.67 (each s, C≡CH) and 3.26 (s, MeO) (the 8-OH signal expected around 12.40 ppm was not detected),
m/z (FAB) 649 (12%), 331 ($C_{14}H_{19}O_9^+$, 80) and 169 (100).

Exp. 33

Reaction of (1S,4aR,9aR)-1,2,3,4,4a,9a-*Hexahydro*-9-*hydroxy*-1-*methoxy*-5-(2',3',4',6'-*tetra*-O-β-D-*glucopyranosyloxy*)*anthracene*-3,9,10-*trione* (**41**) *with* 2-*Trimethylsilylethynylcerium Dichloride*

Anydrous cerium(III) chloride (0.150 g, 0.61 mmol) (dried in vacuo at 145 °C for 1h) was added to freshly distilled dry THF (3 cm^3) and the slurry was stirred at room temperature for 19 h.

To a cooled (-78 °C) stirred solution of trimethylsilylacetylene (0.086 g, 0.82 mmol) in dry THF (1 cm^3) was added a solution of butylithium in hexanes (*ca.* 2.5 mol dm^{-3}, 0.25cm^3, 0.63 mmol) under argon. After 30 min at the same temperature, the stirred suspension of anhydrous cerium(III) chloride in dry THF at -78 °C was added. After 30 min, a solution of the hydroxytrione (**41**) (0.012 g, 0.02 mmol) in THF (*ca.* 2 cm^3) was added to the flask. After a further 4 h, the mixture was allowed to warm to -15 °C and kept in a freezer for 21 h. The resultant mixture was poured onto saturated aqueous ammonium chloride and acidified with 10% aqueous hydrochloric acid. After extraction (x 2) with ethyl acetate, the organic phase was washed once with water, dried ($MgSO_4$) and evaporated to give a yellow solid (0.016 g) which comprised a complex mixture containing the bis ethynylated compound (**42**);



(42)

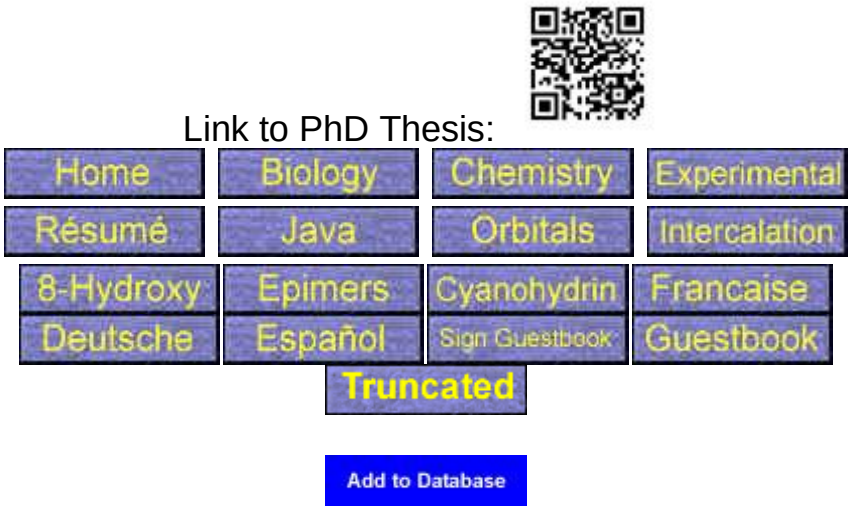
δ (300 MHz; $CDCl_3$) *inter alia* 0.06-0.25 (s, Me_3Si), 3.39 (br s, MeO) and 12.39 (1 H, s, 8-OH),
m/z (FAB) 839 ($C_{39}H_{52}O_{15}Si_2Na^+$, 100%), 331 ($C_{14}H_{19}O_9^+$, 60) and 169 (92).

REFERENCES

General techniques and reference
J. T. Sharp, I. Gosney and A. G. Rowley, *Practical Organic Chemistry*, Chapman and Hall publishers, London, 1989, ISBN 0 412 28230 5.
D. H. Williams and I. Fleming, *Spectroscopic Methods in Organic Chemistry*, McGraw-Hill Book Company (UK) publishers, **4th Edition**, 1989, ISBN 0 07 707212 X.
1. R. Hart and P. Brassard, *Can. J. Chem.*, 1974, **52**, 838; J. R. Lewis and J. Paul, *Z. Naturforsch.*, 1977, **32b**, 1473.
2. R. C. Gupta, P. A. Harland and R. J. Stoodley, *Tetrahedron*, 1984, **40**, 4657.
3. D. S. Larsen and R. J. Stoodley, *J. Chem. Soc., Perkin Trans. 1*, 1989. 1841.
4. *Based on the exploratory experiment (J. P. Miller and R. J. Stoodley, Ph.D. thesis, 1994):* To a stirred solution of the quinol (**6**) (0.013 g, 0.048 mmol), was added the D-glucose-based diene (**11**) (0.039 g, 0.074 mmol) and $Eu(fod)_3$ (0.002 g, 4 mol%) in 'analar' toluene (5 cm^3) and was heated at reflux under argon. After 2 days, a further quantity of the diene (0.017 g, 0.032 mmol) was added. After 4 h, a 1:1.1:1:0.4 ratio of compounds (**6**), (**14**), (**11**) and (**13**) was present; after 21 h, a 1:2.4:0.2:0.4 ratio of compounds (**6**), (**14**), (**13**) and (**16**) was detected; after 3 days only the aromatic compound (**13**) and the TAG (**16**) were observed by NMR spectroscopy.

5. M. Chandler and R. J. Stoodley, *J. Chem. Soc., Perkin Trans. 1*, 1980, 1007.
6. M. M. L. Crilley and R. J. Stoodley, "Synthesis of Anticancer Anthracyclines", *Report No. 1*, 1984.
7. F. T. Escribano and R. J. Stoodley, "Synthetic approaches to 8/10-Hydroxyidarubicins", *Report No. 2*, 1991.
8. B. S. Furniss, A. J. Hannaford, P. W. Smith and A. R. Totchell eds., "Vogel's Textbook of Practical Organic Chemistry", Longmann Scientific and Technical, 1978, London, 4th Edition, p. 302. ISBN 0-582-44250-8 or 5th Edition, 1989, p. 467.
9. Ref. 8, 4th Edition, p. 318 or 5th Edition, p. 445.
10. A. D. Curtis and R. J. Stoodley, *Ph.D. Thesis*, University of Manchester, 1990.
11. Some of these original experimental procedures have been discussed/reported elsewhere, e.g. J. P. Miller, *ChemInform*, 2013, **44** (48) DOI: 10.1002/chin.201348243: see cited (original) references therein.

Link to PhD Thesis:



jonathan@jonathanpmiller.com