λ_{max} 288, 278, 270, 228, 220 nm; IR (KBr) ν(C≡N) 2250, ν(C=O) 1740, νC=N) 1668 cm^{-1}; EIMS (70 eV) m/e 352 ([M]$^+$, 15%), 284 (33%), 258 (31%), 252 (49%), 210 (28%), 185 ([$C_{11}H_9N_2O$]$^+$, 100%), 169 (74%), 168 ([$C_{11}H_8N_2$]$^+$, 84%; exact mass for $C_{19}H_{20}N_4O_3$, calcd 352.1535, found 352.1543; ^{1}H NMR (90 MHz, $CDCl_3$) δ 8.35 (s br, 1 H, N(11) H), 7.55–7.05 (m, 4 H, C(7)–C(10) H), 6.20 (s, 1 H, C(11b) H), 4.35 and 4.32 (2 q, 2 H, OCH_2CH_3), 3.80 (X part of ABX spectrum, $^3J_{AX}$ = 10.0 Hz, $^3J_{BX}$ = 5.0 Hz, 1 H, C(5) H), 3.15 and 3.05 (AB part of ABX spectrum, $^3J_{AX}$ = 10.0 Hz, $^3J_{BX}$ = 5.0 Hz, $^2J_{AB}$ = 12.5 Hz, 2 H, C(6) H_2), 1.70 (s, 6 H, $C(CH_3)_2$), 1.35 (t, 3 H, OCH_2CH_3). Anal. Calcd for $C_{19}H_{20}N_4O_3$ (MW 352.394): C, 64.76;, H, 5.72; N, 15.90. Found: C, 64.74; H, 5.73; N, 15.70.

2-(1-Cyano-2-phenylvinyl)-5-(ethoxycarbonyl)-9-methoxy-4,5,6,11b-tetrahydro-Δ^4-1,2,4-oxadiazolino[3,2-*a*]-β-carboline (14c). A solution of the nitrone **9** (1mmol, 288 mg) and the nitrile **12c**[27] (2.16 mmol, 330 mg) dissolved in toluene (15 mL) was kept at 65 °C for 7 h. The reaction was monitored by TLC (MeOH/$CHCl_3$, 7/93, v/v). Evaporation of the solvent, flash column chromatography of the residue (MeOH/CH_2Cl_2, 0.8/99.2, v/v, and recrystallization gave 400 mg of **14c**: 95%; mp 188–190 °C; R_f 0.60 (CH_2Cl_2/*n*-hexane); UV (MeOH) λ_{max} 307 (sh), 299, 228 nm; λ_{min} 251 nm; IR (KBr) ν(C≡N) 2200, ν(C=O) 1725, ν(C=N) 1642 cm^{-1}; EIMS (70 eV) m/e 442 ([M]$^+$, 42%), 369 ([$C_{22}H_{17}N_4O_2$]$^+$, 20%), 314 ([$C_{16}H_{16}N_3O_4$]$^+$, 10%), 198 ([$C_{12}H_{10}N_2O$]$^+$, 100%); exact mass for $C_{25}H_{22}N_4O_4$, calcd 442.1641, found 442.1635; ^{1}H NMR (90 MHz, $CDCl_3$) δ 8.27 (s br, 1 H, NH), 7.97–6.71 (m, 9 H, C(7)–C(8) H, C(10) H, C_6H_5, C=CH), 6.34 (s, 1 H, C(11b) H), 4.35 (q, 2 H, OCH_2CH_3), 3.90 (X part of ABX spectrum, 1 H, C(5) H–C(6) H_2), 3.83 (s, 1 H, OCH_3), 3.18 and 3.04 (AB part of ABX spectrum, 2 H, ^3J = 3.3 Hz, ^3J = 11.7 Hz, ^2J = 12.6 Hz, C(6) H_2–C(5) H), 1.35 (t, 3 H, OCH_2CH_3). Anal. Calcd for $C_{25}H_{22}N_4O_4$ (MW 442.476): C, 67,86; H, 5.01; N, 12.66. Found: C, 67.56; H, 4.85; N, 12.50.

2-Methyl-3-phenyl-5-(1-cyano-1-methylethyl)-Δ^4-1,2,4-oxadiazoline (15d). A solution of the nitrone **10**[19] (0.8 mmol, 108 mg) and the nitrile **12d** (0.81 mmol, 76 mg) in dry toluene (5 mL) was kept at 110 °C for 10 days. evaporation of the solvent and flash column chromatography of the residue (MeOH/CH_2Cl_2, 0.5/99.5 v/v) gave 156 mg of **15d** (85%) as an oil, which was homogeneous on TLC: R_f 0.35 (MeOH/$CDCl_3$, 7/93); CIMS (100 eV) m/e 230 ([M + 1), 28%), 161 ([$C_9H_9N_2O$], 100%); exact mass for $C_{13}H_{15}N_3O$, calcd 229.1215, found 229.1211; ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.23 (s, 5 H, C_6H_5), 5.61 (s, 1 H, C(3) H), 2.89 (s, 3 H, N(2) CH_3), 1.71 (s, 6H, C(1) $(CH_3)_2CN$).

2-(7-Cyanonorcaran-7-yl)-4,5,6,10b-tetrahydro-Δ^4-1,2,4-oxadiazolino[3,2-*a*]isoquinoline (16b). The nitrone **11**[14] (0.5 mmol, 74 mg) and the nitrile **12b**[27] (0.55 mmol, 80 mg) were dissolved in CH_2Cl_2 (1.5 mL). The solution was placed in a high-pressure vessel, which was placed in a high-pressure apparatus (12 kbar) for 7 days. After evaporation of the solvent and flash column chromatography (MeOH/CH_2Cl_2, 1/99, v/v) **16b** was obtained as an oil in 86% yield: 126 mg; R_f 0.30 (MeOH/CH_2Cl_2, 1/99, v/v); EIMS (70 eV) m/e 293 ([M]$^+$, 6%), 147 ([C_9H_9NO]$^+$, 100%); exact mass for $C_{18}H_{19}N_3O$, calcd 293.1528, found 293.1517; ^{1} H NMR (90 MHz, $CDCl_3$) δ 7.60–7.00 (m, 4 H, C(77)–C(10) H), 5.95 (s, 1 H, C(10b) H), 3.70–2.50 (m, 4 H, C(5) H_2–C(6) H_2, 2.40–1.10 (m, 10 H, cyclohexyl H).

1-[[(7-Cyanonorcaran-7-yl)carbonyl]amino]-3,4-dihydroisoquinoline (17b). The nitrone **11**[14] (0.5 mmol, 74 mg) and the nitrile **12b**[27] (0.55 mmol, 80 mg) were dissolved in toluene and heated (110 °C) for 2 days. Evaporation of the solvent and flash column chromatography of the residue (MeOH/CH_2Cl_2, 2/98, v/v) gave **17b** [115 mg (78%)], which was recrystallized from CH_2Cl_2/*n*-hexane: R_f 0.7 (MeOH/CH_2Cl_2, 1/99, v/v); mp 128–130 °C; UV (MeOH) λ_{max} 282, 210 nm; λ_{mi}(230 nm; IR (KBr) ν(C≡N) 2218 cm^{-1}; EIMS (70 eV) m/e 293 ([M]$^+$, 37%), 173 ([$C_{10}H_9N_2O$]$^+$, 100%), 130 ([C_9H_8N]$^+$, 18%); exact mass for $C_{18}H_{19}N_3O$, calcd 293.1528, found 293.1524; ^{1}H NMR (90 MHz, $CDCl_3$) δ 11.10 (s br, 1 H, CONH), 8.50–7.10 (m, 4 H, C75)–C(8) H), 3.60 (dt, 2 H, C(3) H_2), 2.95 (t, 2 H, C(4) H), 2.20–1.10 (m, 10 H, cyclohexyl H). Anal. Calcd for $C_{18}H_{19}N_3O$ (MW 293.370): C, 73.69; H, 6.53; N, 14.32. Found: C, 73.50; H, 6.54; N, 14.32.

Acknowledgment. We gratefully acknowledge Dr. J. W. Scheeren for advice and making available the high-pressure apparatus.

Registry No. **2**, 3189-13-7; **5**, 106544-16-5; **7**, 106544-17-6; **8**, 106544-20-1; **9**, 106544-18-7; **10**, 3376-23-6; **11**, 24423-87-8; **12a**, 6904-17-2; **12b**, 29782-28-3; **12c**, 2700-22-3; **12d**, 7321-55-3; **12e**, 6914-79-0; **12f**, 5500-21-0; **13a** (isomer 1), 106544-19-8; **13a** (isomer 2), 106622-86-0; **13b**, 106544-21-2; **13c**, 106544-22-3; **13d**, 106544-23-4; **14c**, 106544-24-5; **15d**, 106544-25-6; **16b**, 106568-14-3; **17b**, 106544-26-7; **18**, 74214-62-3; $BrCH_2C(=NOH)CO_2Et$, 73472-94-3.

Anthracyclinones. 2. Isosaccharinic Acid as Chiral Template for the Synthesis of (+)-4-Demethoxy-9-deacetyl-9-(hydroxymethyl)daunomycinone and (−)-4-Deoxy-γ-rhodomycinone[1]

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Chiral aldehyde derivatives **12**, **19**, and **22** were prepared in few steps from α-D-isosaccharino-1,4 lactone (**1a**). These derivative precursors of ring A of the title anthracyclinones were condensed with leucoquinizarin (**28**), the component of the BCD rings. Aldolization reactions afforded alkylanthraquinones **29**, **33**, and **34**, respectively. After suitable transformations of **29** and ring closure, the protected anthracyclinone **27** was obtained. Acetal cleavage of **27** led to the (+)-4-demethoxy-9-deacetyl-9-(hydroxymethyl)daunomycinone (**5**). Similarly suitable transformations of **33** or **34** followed by ring closure gave the (−)-4-deoxy-γ-rhodomycinone (**30**).

Rearrangement of hexoses by prolonged treatment with aqueous alkali leads primarily to the formation of "saccharinic acids" or deoxyaldonic acids, usually isolated as their crystalline lactones which are isomeric with the parent monosaccharides.[2]

In this way, for instance, α-D-isosaccharino-1,4-lactones **1a,b** and α-D-glucosaccharino-1,4-lactone (**2**) were prepared in high yield from lactose,[3] xylobiose or xylotriose,[4] and fructose,[5] respectively.

(1) Paper 1: Bennani, F.; Florent, J. C.; Koch, M.; Monneret, C. *Tetrahedron* **1984**, *40*, 4669.
(2) *Rodd's Chemistry of Carbon Compounds*; Coffey, S., Ed.; Elsevier: Amsterdam, 1967; Vol. IF, p 251.
(3) Whistler, R. L.; BeMiller, J. N. *Methods in Carbohydrate Chemistry* Academic: New York, 1963; Vol. II, p 477.
(4) Whistler, R. L.; BeMiller, J. N. *Adv. Carbohydr. Res.* **1958**, *13*, 289.
(5) Cf. ref 3, p 484.

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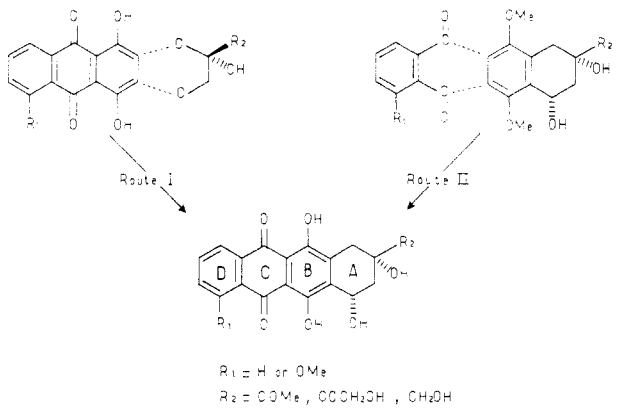
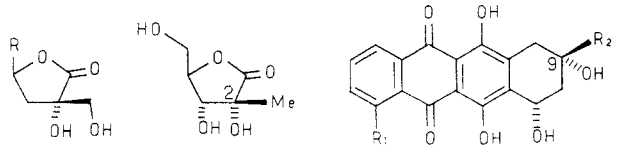
Scheme I



Interestingly, although such highly elaborated "chirons" as **1** and **2** are easily obtained from abundant and cheap starting materials by this well-known rearrangement, its potential in synthesis has been seldom exploited.[6-8]



1a R = CH_2OH **2** **3** R_1 = OMe R_2 = COMe
1b R = H **4** R_1 = OMe R_2 = $COCH_2OH$
5 R_1 = H R_2 = CH_2OH

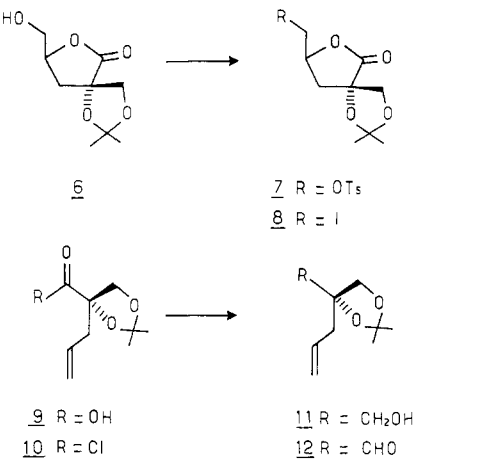
In our work toward the synthesis of analogs of daunomycinone **3** and adriamycinone **4**, the nonsugar moieties of the antitumour agents, daunorubicin, and doxorubicin,[9] it appeared attractive to use these compounds as precursor of ring A carbons 7–10 as the transfer of chirality of C-2 (sugar numbering) to C-9 (anthracycline numbering) would give rise to enantiomerically pure compounds. Construction of the tetracyclic nucleus of **3** or **4** or of analogues can be achieved by two routes as illustrated in Scheme I by assembling the subunits A + BCD or AB + CD.

Following route I we have recently reported[1] a synthesis of 4-demethoxy-9-deacetyl-9-(hydroxymethyl)daunomycinone (**5**) from isosaccharino-1,4-lactone (**1a**) and from leucoquinizarin as the BCD ring component. In this present paper we wish to describe as an extension of the route I (Scheme I), the synthesis of (−)-4-deoxy-γ-rhodomycinone[10] while following route II a new synthesis of **5** from hydroxytetralin intermediate will be presented in the accompanying paper.

Results and Discussion

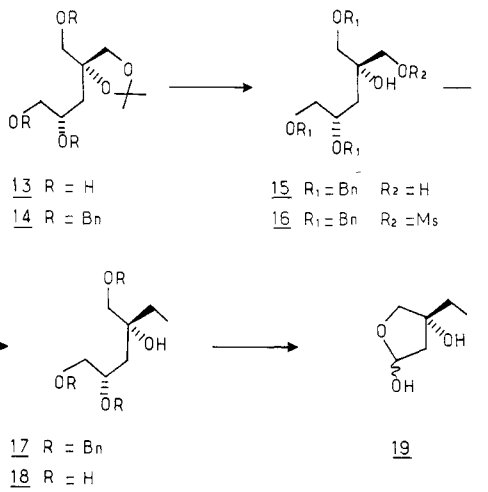
Syntheses of Aldehyde Derivatives. (a) Aldehyde 12. First, the *O*-isopropylidene lactone **6** derived from **1a** was transformed into the iodo derivative **8** in an overall yield of 62% in a two-step sequence involving reaction with tosyl chloride in pyridine to afford the tosylate **7** followed by reflux with sodium iodide in 2-butanone. Bernet and Vasella[12] reported that 6-deoxy-6-haloglycosides react with

Scheme II



6 **7** R = OTs
8 R = I
9 R = OH **11** R = CH_2OH
10 R = Cl **12** R = CHO

Scheme III



13 R = H **15** R_1 = Bn R_2 = H
14 R = Bn **16** R_1 = Bn R_2 = Ms

17 R = Bn **19**
18 R = H

zinc dust under mild conditions with glycoside cleavage and formation of hex-5-enoses. Later on [13] they also reported that under the same conditions fragmentation of a 6-bromo lactone gives an unsaturated acid in good yield (70%). As expected, application of the same procedure to **8** afforded a mixture containing the unsaturated carboxylic compound **9**. Formation of side products could be largely avoided, however, by replacing preactivated Zn and THF by nonpreactivated Zn and THF + HOAc as solvent. Lithium aluminum hydride reduction of **9** followed by oxidation of alcohol **11** with pyridinium dichromate according to Czernecky's procedure[14] gave the desired aldehyde **12** (overall yield **8** → **12**, 42%).

An alternative route was also attempted which consists in preparing aldehyde **12** from the corresponding acid chloride **10** according to Fleet.[15] However under these conditions, **10** reacts slowly and a mixture of **11** and **12** was obtained in a 1:1 ratio after 24 h. The sequence of reactions is summarized in Scheme II.

(b) Aldehydes 19 and 22. The triol compound **13**[1] obtained by LAH reduction of **1a** was protected as its tri-*O*-benzyl derivative **14** and the isopropylidene ring was cleaved by acid hydrolysis giving **15** in 50% overall yield. Transformation of the hydroxymethyl side chain into an ethyl group as occur in ring A of rhodomycins, involved

(6) Hanessian, S.; Roy, R. *Tetrahedron Lett.* **1981**, *22*, 1005; *Can. J. Chem.* **1985**, *63*, 163.
(7) Ireland, R. E.; Anderson, R. C.; Badoud, R.; Fitzsimmons, B. J.; McGarvey, G. J.; Thaisrivongs, S.; Wilcox, C. S. *J. Am. Chem. Soc.* **1983**, *105*, 1988.
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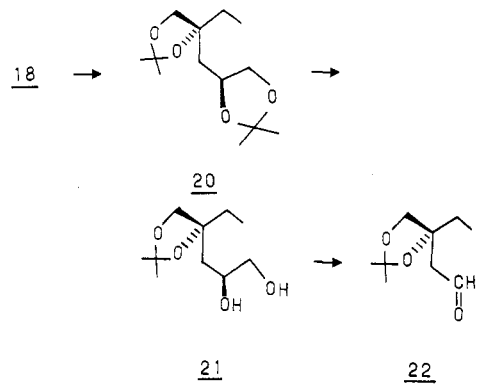
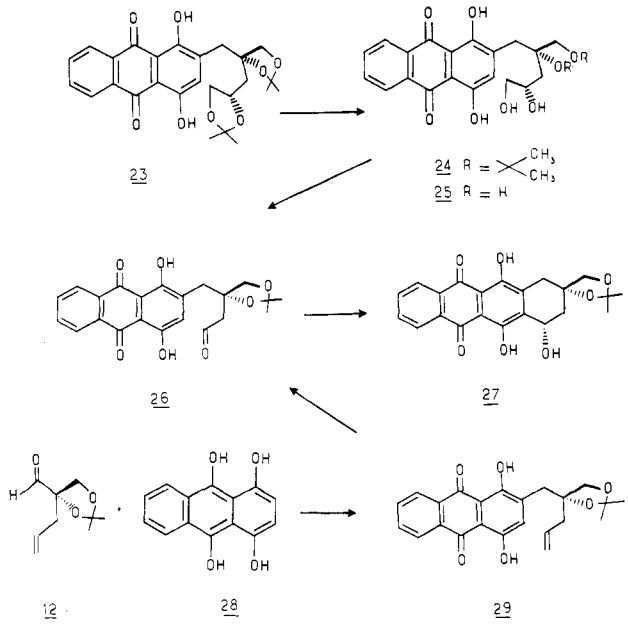
(15) Fleet, G. S.; Harding P. J. C. *Tetrahedron Lett.* **1979**, 975.

Scheme IV



Scheme V

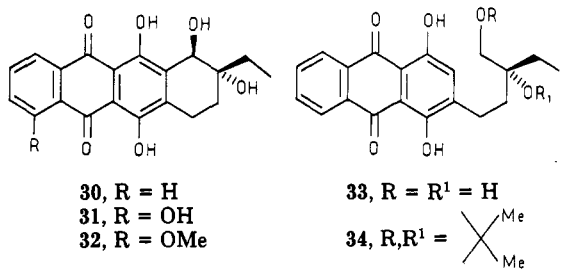


reaction of **15** with mesyl chloride in pyridine and reaction of the resultant mesylate **16** with Me_2CuLi in ether.[16] Compound **17** obtained in 65% yield was then treated under hydrogenolysis conditions, giving **18** in quantitative yield. Periodate oxidation of **18** led to the rather unstable aldehyde derivative **19** which exists as its hemiketal form as shown by examination of its IR and ^1H NMR spectra (Scheme III).

Alternatively (Scheme IV) acetalation of **18** followed by regioselective hydrolysis of the bisacetonide compound **20** led to **21** and subsequent periodate oxidation gave the aldehyde **22**, which was more stable than the corresponding unprotected analogue **19**.

Syntheses of Anthracyclinones. Since several glycosides of **5** have shown interesting cytotoxic activity[17] and original electrochemical behavior,[18] our efforts were turned toward a large-scale synthesis of this aglycon. Previous route to **5** or its monoisopropylidene derivative **27** included a regioselective hydrolysis of the diisopropylidene derivative **23** to give **24**, which, after periodate oxidation, led to aldehyde **26** as precursor of **27**. Unfortunatly when repeated on a larger scale, less regioselectivity was observed which led to a mixture of starting material **23** and monoacetal derivative **24** and also a large amount of tetrol **25**. To avoid such a delicate chromatography to isolate the

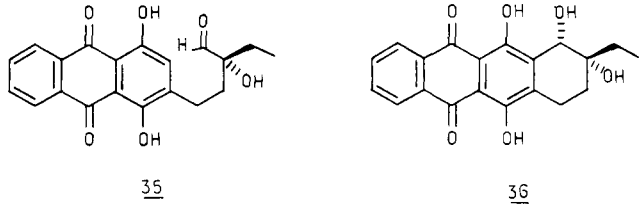
Scheme VI



30, R = H
31, R = OH
32, R = OMe

33, R = R¹ = H
34, R,R¹ =

Scheme VII



desired compound **24**, unsaturated aldehyde **12** appeared to be an appropriate starting material since the terminal double bond could act as a masked aldehyde. Actually on reacting **12** with leucoquinizarin **28** under Marschalk[19] (KOH, $Na_2S_2O_4$), Lewis[20] (piperidinium acetate) or Shaw[21] (DBU or DBN in THF) conditions, the alkylanthraquinone **29** was isolated in 75–80% yield (Scheme V). Ozonolysis of **29** afforded aldehyde **26** in 75–80% yield, which was then converted stereospecifically in 75% yield into the *cis* aglycon **27** (overall yield for the last three steps 42–48%). Acidic hydrolysis afforded in nearly quantitative yield **5**.

In planning an extension of the usefulness of saccharinic acids as precursors of other aglycons, we focused our attention toward γ-rhodomycinone. Closely related to the antitumour drugs daunorubicin and doxorubicin, the rhodomycins were isolated[22] from strains of *Streptomyces purpurascens*. In spite of their widespread occurence, relative few syntheses of the rhodomycinones, nonsugar moieties of rhodomycins have been published. (±)-4-Deoxy-γ-rhodomycinone (**30**) was elaborated first by means of Diels–Alder reactions[23] or as for (±)-γ-rhodomycinone (**31**) and its corresponding methyl ether **32** by intramolecular Marschalk reaction[10,24] (Scheme VI).

According to our general strategy as described in a previous publication,[1] the aldehydes **19** and **22** were precursors of optically active **30**. Their condensation with leucoquinizarin **28** afforded the alkylanthraquinones **33** and **34** in 10% and 45% yields, respectively. The low yield observed for the formation of **34** is understandable since, as mentioned above, the aldehyde **18** is very unstable. In fact, as hydrolysis of **34** giving **33** was almost quantitative, **33** can be prepared via **34**. Moffatt oxidation of **33** gives the aldehyde **35** (60%) (Scheme VII). Conversion of this α-hydroxy aldehyde to the tetracyclic (−)-4-deoxy-γ-rhodomycinone **30** and to a small amount of its cis epimer **36** was achieved at 0 °C under Marschalk conditions. The mp and spectroscopic data for **30** were in full agreement

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(24) Krohn, K.; Behnke, B. *Chem. Ber.* **1980**, *113*, 2994. Krohn, K.; Priyono, W. *Tetrahedron* **1984**, *40*, 4609.

with those previously reported by Krohn et al.[10]

Conclusions

The foregoing results are significant in several respects: First, the starting material, isosaccharino-1,4-lactone which already incorporates the desired functionality present at C-9 of the anthracyclinone products is prepared in a single step from readily available materials. Second, these syntheses avoid the delicate introduction of the labile 9-OH. Third, the aldol-type ring-closure step encountered in the synthesis of **5** is highly stereoselective giving the cis derivative **27** precursor of biologically active drugs.

The value of our synthetic approach is further enhanced by the fact that 4-demethoxydaunorubicin and doxorubicin cannot be produced by fermentation.

Transformation of α-D-glucosaccharino-1,4-lactone (**2**) into steffimycinone[25] and aranciamycinone[26] analogues is now under investigations.

Experimental Section

General Methods. Melting points (Kofler hot stage microscope) were uncorrected. IR spectra were recorded on a Perkin-Elmer Model 257 spectrophotometer, calibrated against polystyrene film, and were expressed in cm^{-1}. ^1H NMR spectra at 270 MHz were obtained on a Brucker HX 270 in $CDCl_3$ except when signaled. Chemical shifts were expressed in ppm downfield from internal Me_4Si with the notations indicating the multiplicity of the signal (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet). The coupling constants are expressed as J values in units of hertz. Mass spectra (DCI/NH_3 or EI) were recorded on a Nermag R 1010 (E.N.S.C.P.). For EI they were obtained at an ionizing voltage of 70 eV.

Silica gel for column chromatography or flash chromatography was Merck Silica Gel H 60 No. 7736. Analytical thin-layer chromatographies were performed on Merck Silica Gel 60 F_{254}.

Ether solvents (THF, ether, etc.) were dried over sodium benzophenone and distilled, while dry CH_2Cl_2 was prepared by distillation over CaH_2.

Microanalyses were performed by the Laboratoire de Microanalyse du CNRS, Gif sur Yvette and Lyon.

2,2′-*O*-Isopropylidene-5-*O*-tosyl-α-D-isosaccharino-1,4-lactone (7). To a solution of **6** (735 g, 3.7 mol) in pyridine (2500 mL) cooled at −25 °C was slowly added 900 g (4.7 mol) of *p*-toluenesulfonyl chloride. The reaction was allowed to reach room temperature and stirred for 72 h. The reaction mixture was then poured into crushed ice (5 kg) and water (10 L) with vigorous stirring. The white precipitate was filtered, washed with hot water, and washed quickly with cold ether. This affords 975 g of **7** (75%) as white crystals. Recrystallization from ether–CH_2Cl_2 gave an analytical sample: mp 110 °C; $[\alpha]^{20}_D$ + 57° (*c* 1, $CHCl_3$); IR (KBr) 1780 cm^{-1}; ^1H NMR δ 7.71 (d, 2 H, Ar), 7.31 (d, 2 H, Ar), 4.73 (m, 1 H, 4-H), 4.28 (d, 1 H, J = 9) and 4.02 (d, 1 H, J = 9) (AB, 2′-H), 4.19 (dd, 1 H, J = 11, J' = 4) and 4.09 (dd, 1 H, J = 11, J' = 4) (ABX, 5-H), 2.43 (s, 3 H, Me), 2.55–2.13 (m, 2 H, 3-H), 1.45 (s, 3 H) and 1.41 (s, 3 H) (CMe_2); EIMS; *m/z* (relative intensity) 357 (M + 1, <5), 341 ($M^{\bullet+}$ − 15, 100), 299 (13), 155 (50), 141 (75), 91(86). Anal. Calcd for $C_{16}H_{20}O_7S$: C, 53.01; H, 5.65. Found: C, 54.01; H, 5.59.

5-Iodo-2,2′-*O*-isopropylidene-α-D-isosaccharino-1,4-lactone (8). To a solution of **7** (712 g, 2 mol) in 2-butanone (3000 mL) was added NaI (357 g, 2.5 mol), and the suspension was heated under reflux for 15 h. After cooling and filtration, the resulting solution was evaporated under reduced pressure to ca. 300–400 mL, and the residue was extracted with ether (3 × 1000 mL). The combined ethereal extracts were washed with saturated aqueous solution of sodium thiosulfate and with water, dried (Na_2SO_4), and concentrated to give a pale yellow oil. Crystallization from hexane–ether (2:1) gave 512 g (82%) of **8** as a white crystalline solid: mp 65 °C; $[\alpha]^{20}_D$ + 52° (C 0.6, $CHCl_3$); IR (KBr) 1780 cm^{-1}; ^1H NMR δ 4.58 (m, 1 H, 4-H), 4.36 (d, 1 H, J = 9) and 4.01 (d, 1 H, J = 9) (AB, 2′-H), 3.40 (dd, 1 H, J = 10, J' = 5) and 3.29 (dd, 1 H, J = 10, J' = 7) (ABX, 5-H), 2.62 (dd, 1 H, J = 15, J' = 6) and 2.01 (dd, 1 H, J = 15, J' = 8) (ABX, 3-H), 1.45 (s, 3 H) and 1.43 (s, 3 H) (CMe_2); EIMS; *m/z* (relative intensity) 297 ($M^{\bullet+}$ − 15, 100), 255 (16), 237(13), 141(39). Anal. Calcd for $C_9H_{13}O_4I$: C, 34.6; H, 4.19. Found: C, 34.35; H, 4.22.

(−)-(2*S*)-2-Hydroxy-2-(hydroxymethyl)-2,2′-*O*-isopropylidenepent-4-enoic Acid (9). To a solution of iodo compound **8** (55 g, 176 mmol) in THF (300 mL), water (10 mL), and acetic acid (10 mL) at 0 °C was added zinc powder (20 g). The mixture was stirred vigorously at room temperature for 1 h. After filtration through a pad of Celite, the filtrate was diluted with water (500 mL) and neutralized with aqueous NaOH (1 N) and washed with dichloromethane (2 × 300 mL). The aqueous layer was then acidified with aqueous HCl (1 N) and extracted with ethyl acetate to give after evaporation under reduced pressure 26 g of compound **9** in a semicrystalline form (70%): $[\alpha]^{20}_D$ −17° (*c* 2, $CHCl_3$); IR (film) 1750 cm^{-1}; ^1H NMR δ 5.74 (m, 1 H, 4-H), 5.14 (d, 2 H, 5-H), 4.31 (d, 1 H, J = 9) and 3.92 (d, 1 H, J = 9) (AB, 2′-H), 2.64 (dd, 1 H, J = 15, J' = 7, 3a-H) and 2.49 (dd, 1 H, J = 15, J' = 7, 3b-H), 1.44 (s, 3 H) and 1.42 (s, 3 H) (CMe_2). Anal. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.57. Found: C, 58.25; H, 7.48.

(−)-(2*R*)-2-Hydroxy-2-(hydroxymethyl)-2,2′-*O*-isopropylidenepent-4-enol (11). To a solution of **9** (27 g, 145 mmol) in THF (500 mL) was added portionwise and at 0 °C LAH (8.26 g, 220 mmol). The suspension was stirred under reflux, overnight. The reaction mixture was then cooled and treated sequentially with 8 mL of water, 8 mL of 15% aqueous NaOH, and 24 mL of water. The mixture was stirred at room temperature for 2 h and filtered. Solids were washed with ether and the filtrate was concentrated under reduced pressure to give 24.9 g (80%) of **11** as a colorless oil: $[\alpha]^{20}_D$ −3° (*c* 3 $CHCl_3$); IR (film) 3450 cm^{-1}; ^1H NMR δ 5.74 (m, 1 H, 4-H), 5.11 (d, 1 H, J = 3) and 5.07 (br s) (5-CH_2), 3.88 (d, 1 H, J = 9) and 3.78 (d, 1 H, J = 9) (AB, 2′-H), 3.50 (m, 2 H, 1-H), 2.40 (m, 2 H, 3-H), 1.98 (dd, J = 5, OH), 1.41 (s, 6 H, CMe_2); EIMS, *m/z* (relative intensity) 173 (M + 1, 20), 157 ($M^{\bullet+}$ − 15, 10), 141 (20), 131 (25), 117 (42), 83 (100), 59 (100). Anal. Calcd for $C_9H_{16}O_3$: C, 61.31; H, 9.15. Found: C, 61.48; H, 9.32.

(−)-(2*S*)-2-Hydroxy-2-(hydroxymethyl)-2,2′-*O*-isopropylidenepent-4-enal (12). (1) From Alcohol 11. To a solution of alcohol **11** (20 g, 116 mmol) in dry dichloromethane (500 mL) at 0 °C were added 93 g of molecular sieves (3 Å); (activated 5 h at 320 °C) and pyridinium dichromate (65 g, 174 mmol). After dropwise addition of 10 mL of acetic acid,[14] the mixture was stirred at room temperature for 0.5 h. Ether (1000 mL) was then added, the suspension was filtered through a pad of Celite, and the filtrate was evaporated. The residue was dissolved in ether (500 mL) and the ethereal solution was filtered through silica gel (20 g, 230–400 mesh). Evaporation of ether under reduced pressure gave 14.8 g of aldehyde **12** (75%) as a pale yellow syrup: $[\alpha]^{20}_D$ −3° (*c* 3.2, $CHCl_3$); IR (film) 1730 cm^{-1}; ^1H NMR δ 9.59 (s, 1 H, 1-H), 5.70 (m, 1 H, 4-H), 5.14 (s, 1 H, 5a-H), 5.06 (d, 1 H, J = 10, 5b-H), 4.15 (d, 1 H, J = 9) and 3.78 (d, 1 H, J = 9) (AB, 2′-H), 3.17 (dd, 1 H, J = 15, J' = 7) and 2.62 (dd, 1 H, J = 15, J' = 7) (ABX, 3-H), 1.45 (s, 3 H) and 1.42 (s, 3 H) (CMe_2). Anal. Calcd for $C_9H_{14}O_3$: C, 63.52; H, 8.23. Found; C, 63.48; H, 8.45.

(2) From Acid Derivative 9 via the Acid Chloride 10. To a solution of **9** (3.8 g, 20.4 mmol) in a mixture of dichloromethane (25 mL) and pyridine (1.7 mL) was added dropwise oxalyl chloride (5.4 mL). After the mixture was stirred for 2 h at room temperature, the solution was concentrated under reduced pressure, and the residue was coevaporated twice with dichloromethane (25 mL). This afforded 4.2 g of **10**, which was not purified. To a solution of an aliquot part of this product (0.136 g, 1 mmol) in acetone (10 mL) were added triphenylphosphine (0.5 g, 2 mmol) and solid bis(triphenylphosphine)copper(I) borohydride (0.6 g, 1 mmol). After the mixture was stirred overnight, the white precipitate of tris(triphenylphosphine)copper chloride was removed and workup conducted as previously described.[15] This gave a mixture of alcohol **11** and of aldehyde **12** (ratio 1:1) as shown by TLC (hexane–acetone, 2:1) and by ^1H NMR spectrum.

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(−)-(2*R*)-1,4,5-Tri-*O*-benzyl-3-deoxy-2-*C*-(hydroxymethyl)-2,2′-*O*-isopropylidene-D-glyceropentitol (14). To a solution of **13**[1] (15 g, 73 mmol) in dry THF (150 mL) and dry DMF (150 mL) cooled into a ice bath were added in several portions 10 g (330 mmol) of NaH and in one portion 1 g (27 mmol) of tetrabutylammonium iodide. After the mixture was stirred at 0–5 °C for 30 min, benzyl bromide (40 mL, 336 mmol) was added over a period of ≃ 15 min. The mixture was allowed to reach room temperature, stirred for 72 h, then diluted with 500 mL of water, and extracted with ether. The combined extracts were dried (Na_2SO_4) and concentrated under reduced pressure to give a crude product (≃25 g). A flash chromatography with hexane–acetone (98:2) as eluent affords 19.2 g (55%) of **14** as a colorless syrup: $[\alpha]^{20}_D$ −21° (*c* 1.05, $CHCl_3$); IR (film) 1760 cm^{-1}; ^1H NMR δ 7.30 (m, 15 H, Ar), 4.70–4.30 (m, 6 H, CH_2Ar), 3.86 (d, 1 H, *J* = 9) and 3.79 (d, 1 H, *J* = 9) (AB, 1-H), 3.75 (m, 1 H, 4-H), 3.54 (m, 2 H, 5-H), 3.42 (d, 1 H, *J* = 10) and 3.35 (d, 1 H, *J* = 10) (AB, 2′-H), 2.03 (q, 1 H, *J* = 15, *J*′ = 4) and 1.92 (q, 1 H, *J* = 15, *J*′ = 9) (ABX, 3-H), 1.37 (s, 3 H) and 1.33 (s, 3 H) (CMe_2); EIMS, *m*/*z* (relative intensity) ($M^{\bullet+}$ − CH_2OCH_2Ph, 5), 107 (OCH_2Ph, 10), 91 (100).

(−)-(2*R*)-1,4,5-Tri-*O*-benzyl-3-deoxy-2-*C*-(hydroxymethyl)-D-glyceropentitol (15). To a solution of crude **14** (prepared from 7.5 g of **13** according to the preceeding procedure) in methanol (250 mL) was added aqueous HCl (1 N, 50 mL). The resulting solution was stirred at room temperature for 24 h, poured into 150 mL of saturated aqueous $NaHCO_3$, and concentrated under reduced pressure to ca. 200 mL. The residue was extracted with dichloromethane, and the organic layer was washed with water, dried (Na_2SO_4), and concentrated under reduced pressure to give 12 g of crude material. Flash chromatography with hexane–acetone (90:10) as eluent gave 8 g of **15** (50% overall yield): $[\alpha]^{20}_D$ −18° (*c*, 3, $CHCl_3$); IR (film) 3460, 1660, 1600, 1585 cm^{-1}; ^1H NMR δ 7.30 (m, 15 H, Ar), 4.66 (d, 1 H, *J* = 11) and 4.40 (d, 1 H, *J* = 11) (AB, CH_2Ar), 4.45 (s, 2 H) and 4.35 (s, 2 H) ($2CH_2Ar$), 3.95 (m, 1 H, 4-H), 3.86 (m, 1 H OH), 3.51 (m, 4 H, 1-H and 5-H), 3.44 (d, 1 H, *J* = 10) and 3.35 (d, 1 H, *J* = 10) (AB, 2′-H), 3.10 (m, 1 H, OH), 1.85 (m, 2 H, 3-H); EIMS, *m*/*z* (relative intensity) 315 ($M^{\bullet+}$ − CH_2OCH_2Ph, 5), 91 (CH_2Ph, 100). Anal. Calcd for $C_{27}H_{32}O_4$: C, 77.11; H, 7.66. Found: C, 77.25; H, 7.60.

(−)-(2*R*)-1,4,5-Tri-*O*-benzyl-3-deoxy-2-*C*-(hydroxymethyl)-2′-*O*-mesyl-D-glyceropentitol (16). To a solution of **15** (19 g, 43.6 mmol) in dry pyridine (250 mL) at 0 °C was added dropwise under inert atmosphere methanesulfonyl chloride (10 mL, 126 mmol). The mixture was allowed to reach room temperature and stirred for 15 h. It was then poured into ice–water and extracted with dichloromethane, and the organic layer was washed with 10% aqueous H_2SO_4, H_2O, and a saturated aqueous solution of $NaHCO_3$. The dichloromethane solution was dried (Na_2SO_4) and concentrated under reduced pressure to give 21 g (94%) of **16** as a colorless syrup: $[\alpha]^{20}_D$ −22° (*c* 1, $CHCl_3$); IR (film) 3400, 1600, 1585 cm^{-1}; ^1H NMR δ 7.28 (m, 15 H, Ar), 4.73 (d, 1 H, *J* = 10) and 4.25 (d, 1 H, *J* = 10) (AB, 2′-H), 4.53 (m, 4 H, CH_2Ph), 4.11 (d, 2 H, CH_2Ph), 4.05 (m, 1 H, 4-H), 3.55 (m, 2 H, 5-H), 3.44 (d, 1 H, *J* = 10) and 3.55 (d, 1 H, *J* = 10) (AB, 1-H), 2.88 (s, 3 H, Me), 1.85 (m, 2 H, 3-H); DCI/NH_3, *m*/*z* (relative intensity) 532 (M + NH_4^+, 100), 515 (M + H^+, 10), 204 (80), 91 (CH_2Ph, 20).

(−)-(2*S*,4*R*)-1,2,4′-Tri-*O*-benzyl-4-(hydroxymethyl)-1,2,4-hexanetriol (17). To a suspension of cuprous iodide (9.5 g, 50 mmol) in dry ether (25 mL) at 0 °C under argon atmosphere was added dropwise under vigorous stirring MeLi (62.5 mL, 100 mmol). The suspension was cooled to −40 °C, and after dropwise addition of **16** (5.14 g, 10 mmol) previously dissolved into dry THF (20 mL), stirring was continued for 4 h at −40 °C and then for 10 h at room temperature. The reaction mixture was poured into an aqueous NH_4Cl solution and extracted with ether. The ether layer was washed with H_2O, dried (Na_2SO_4), and concentrated under reduced pressure to give 3.5 g of crude material as a syrup. A flash chromatography with hexane–acetone (95:5) as eluent afforded **17** (2.83 g, 65%) as a colorless syrup: $[\alpha]^{20}_D$ −13° (*c* 1, $CHCl_3$); IR (film) 3490, 1600, 1585 cm^{-1}; ^1H NMR δ 7.25 (m, 15 H, Ar), 4.73 (d, 1 H, *J* = 11) and 4.51 (d, 1 H, *J* = 11) (CH_2Ph), 4.53 (s, 2 H) and 4.49 (s, 2 H) (CH_2Ph), 3.95 (m, 1 H, 2-H), 3.60 (dd, 1 H, *J* = 10, *J*′ = 6) and 3.51 (dd, 1 H, *J* = 10, *J*′ = 4) (ABX, 1-H), 3.37 (d, 1 H, *J* = 9) and 3.26 (d, 1 H, *J* = 9) (AB, 4′-H), 1.86 (dd, 1 H, *J* = 15, *J*′ = 9) and 1.75 (dd, 1 H, *J* = 15, *J*′ = 4) (ABX, 3-H), 1.57 (m, 2 H, 5-H), 0.84 (t, 3 H, 6-Me); EIMS, (relative intensity) *m*/*z* 313 ($M^{\bullet+}$ − CH_2OCH_2Ph, 35), 91 (CH_2Ph, 100). Anal. Calcd for $C_{28}H_{38}O_4$: C, 76.67; H, 8.73. Found: C, 76.85; H, 8.59.

(−)-(2*S*,4*R*)-4-(Hydroxymethyl)-1,2,4-hexanetriol (18). To a solution of **17** (8.9 g, 20 mmol) in 200 mL of methanol were added palladium on charcoal (10%, 3 g) and acetic acid (5 mL). After the mixture was stirred for 2 h under H_2 atmosphere, the catalyst was removed by filtration and the filtrate passed through a column of Amberlyst IR 45 OH^-. Evaporation of the solvent led to 3.3 g (98%) of **18** as a colorless syrup: $[\alpha]^{20}_D$ −2° (*c* 1, $CHCl_3$); IR (film) 3480 cm^{-1}; ^1H NMR ($CDCl_3$–pyridine) δ 6.5–5.5 (m, 4 H, OH), 4.45 (m, 1 H, 2-H), 3.79 (m, 4 H, 1-H and 4′-H), 2.00 (m, 2 H, 3-H), 1.88 (m, 2 H, 5-H), 1.02 (t, 3 H, *J* = 8, 6-Me). Anal. Calcd for $C_7H_{16}O_4$: C, 51.21; H, 9.75. Found: C, 51.38; H, 9.48.

(+)-(2*S*,4*R*)-4-(Hydroxymethyl)-1,2:4,4′-di-*O*-isopropylidene-1,2,4-hexanetriol (20). A solution of **18** (2.5 g, 15.2 mmol) in dry DMF (50 mL) and α-α-dimethoxypropane (10 mL) was stirred overnight at room temperature in the presence of camphorsulfonic acid (400 mg). The mixture was poured into an aqueous saturated solution of $NaHCO_3$ and extracted with ether. The ether layer was washed with water (4 × 25 mL), dried (Na_2SO_4), and evaporated under reduced pressure to give **20** (2.7 g, 73%) as a colorless syrup: $[\alpha]^{20}_D$ +2° (*c*, 1, $CHCl_3$); ^1H NMR δ 4.30 (m, 1 H, 2-H), 4.03 (d, 1 H, *J* = 9) and 3.78 (d, 1 H, *J* = 9) (AB, 4′-H), 4.12 (dd, 1H, *J* = 8, *J*′ = 5) and 3.53 (dd, 1 H, *J* = *J*′ = 8) (ABX, 1-H), 1.90 (dd, 1 H, *J* = 14, *J*′ = 6) and 1.82 (dd, 1 H, *J* = 14, *J*′ = 4) (ABX, 3-H), 1.62 (m, 2 H, 5-H), 1.42 (s, 3H), 1.39 (s, 6H), 1.34 (s, 3H) (CMe_2), 0.92 (t, 3 H, *J* = 8, 6-Me); DCI/NH_3; *m*/*z* (relative intensity) 245 (M + H^+, 5), 229 (M − 15, 30), 215 (10), 187 (M + H^+ − 58, 10), 129 (M + H^+ − 116, 80), 101 (100); HRMS, *m*/*e* calcd for $C_{13}H_{24}O_4$ 244.3302, found 244.3321.

(+)-(2*S*,4*R*)-4-(Hydroxymethyl)-4,4′-*O*-isopropylidene-1,2,4-hexanetriol (21). To a solution of **20** (1g, 4.0 mmol) in MeOH (20 mL) was added a mixture of H_2O (10 mL) and AcOH (1 mL). After the mixture was stirred for 12 h at room temperature, acetic acid was added (1 mL) and the stirring continued for 18 h. The solution was poured into a saturated aqueous $NaHCO_3$ solution (10 mL) and extracted with dichloromethane. The dichloromethane extract was washed with water, dried (Na_2SO_4), and evaporated under reduced pressure to give 0.85 g of crude product. A flash chromatography with dichloromethane and then dichloromethane–methanol (95:5) as eluents afforded successively starting material **20** (550 mg), monoacetal derivative **21** (220 mg), and then a small amount of tetrol **18** (20 mg). Compound **21**: syrup; $[\alpha]^{20}_D$ +16° (*c* 1, $CHCl_3$); ^1H NMR δ 4.04 (m, 1 H, 2-H), 3.88 (d, 1 H, *J* = 9) and 3.77 (d, 1 H, *J* = 9) (AB, 4′-H), 3.57 (dd, 1 H, *J* = 12, *J*′ = 4) and 3.46 (dd, 1 H, *J* = 12, *J*′ = 6) (ABX, 1-H), 2.48 (s, 1 H, OH), 1.95 (s, 1 H, OH), 1.88–1.60 (m, 4H, 3-H and 5-H), 1.44 (s, 3 H) and 1.40 (s, 3 H) (CMe_2), 0.88 (t, 3 H, *J* = 8, 6-Me); EIMS, *m*/*z* (relative intensity) 205 ($M\bullet^+$ + 1, 25), 189 (M − 15, 30), 129 (M − 15 − 60, 100); HRMS, *m*/*e* calcd for $C_{10}H_{20}O_4$ 204.2656, found 204.2647.

(3*R*)-3-Hydroxy-3-(hydroxymethyl)-3,3′-*O*-isopropylidenepentanal (22). To a stirred solution of **21** (230 mg, 1.12 mmol) in MeOH (10 mL) at room temperature was added a solution of sodium periodate (250 mg, 1.17 mmol). After 15 min, the mixture was filtered and the filtrate concentrated under reduced pressure to ca. 4 mL. After dilution with water, extraction with dichloromethane gave 150 mg of **22** as a colorless syrup (92%): IR (film) 1720 cm^{-1} (CH=O); ^1H NMR δ 9.73 (dd, 1 H, *J* = 3, *J*′ = 2, CHO), 3.88 (1 H, *J* = 7) and 3.82 (d, 1 H, *J* = 7) (AB, CH_2O), 2.71 (dd, 1 H, *J* = 16, *J*′ = 2) and 2.62 (dd, 1 H, *J* = 16, *J*′ = 3) (ABX, 2-H), 1.75 (m, 2 H, 4-H), 1.42 (s, 3 H) and 1.40 (s, 3 H) (CMe_2), 0.93 (t, 3 H, *J* = 7, 5-Me). No satisfactory analysis could be obtained for this compound.

(−)-(2*R*)-1,4-Dihydroxy-2-[2-hydroxy-2-(hydroxymethyl)-2,2′-*O*-isopropylidene-4-pentenyl]-9,10-anthraquinone (29). To a solution of piperidinium acetate [prepared from piperidine (6.9 mL, 69 mmol) and acetic acid (4 mL, 69 mmol) in *i*-PrOH (250 mL) at 0 °C] was added leucoquinizarin **28** (7.8 g, 32 mmol) and **12** (6 g, 35 mmol) in solution in *i*-PrOH (100 mL). The mixture was stirred at reflux under argon until TLC (hexane–CH_2Cl_2, 1:1) showed complete disapearance of

starting material **12**. After cooling the mixture was poured into ice–water (50 mL). The precipitate was removed by filtration and the filtrate washed with water and dried (P_2O_5) to give 13 g of precipitate. Flash chromatography with hexane–CH_2Cl_2 (9:1) as eluent afforded quinizarin (resulting from unreacted leucoquinizarin), while elution with hexane–CH_2Cl_2 (8:2 and then 1:1) as eluent gave 10 g (80%) of **29** as a red gum: $[\alpha]^{20}_D$ −31° (*c*, 0.07, $CHCl_3$); IR ($CHCl_3$) 1620 and 1590 cm^{-1}; ^1H NMR δ 13.38 (s, 1 H) and 12.74 (s, 1 H) (OH phenol), 8.25 (m, 2 H, Ar) and 7.73 (m, 2 H, Ar), 7.28 (s, 1 H, Ar) 5.87 (m, 1 H, 4-H), 5.11 (m, 2 H, 5-H), 3.87 (d, 1 H, J = 9) and 3.78 (d, 1 H, J = 9) (AB, 3-H), 3.01 (s, 2 H, CH_2Ph), 2.39 (m, 2 H, 2′-H), 1.39 (s, 3 H) and 1.23 (s, 3 H) (CMe_2); DCI/NH_3, *m/z* (relative intensity) 395 (M + H^+, 100), 379 (M^+ − 15, 30); HRMS, *m/e* calcd for $C_{23}H_{22}O_6$ 394.4232, found, 394.4227.

(+)-(3*S*)-4-(1,4-Dihydroxy-9,10-anthraquinon-2-yl)-3-hydroxy-3-(hydroxymethyl)-3,3′-*O*-isopropylidenebutanal (26). A solution of **29** (3.8g, 3.65mmol) in dichloromethane (50 mL) was cooled at −78 °C, and ozone was introduced through the liquid until TLC (hexane–EtOAc, 4:1) showed the complete disappearance of the starting material (≃1.5 h). Nitrogen was passed through the solution (15 min) and after warming to −10 °C, dimethyl sulfide added (5 mL). The solution was allowed to reach room temperature, stirred overnight, and concentrated under reduced pressure to give a colorless oily residue. A flash chromatography with hexane–EtOAc (4:1) as eluent led to 2.5 g (65%) of pure **26** identical in all respects with a sample previously synthesized.[1]

(+)-(1*S*,3*S*)-1,2,3,4,6,11-Hexahydro-1,3,5,12-tetrahydroxy-3-(hydroxymethyl)-3,3′-*O*-isopropylidene-6,11-naphthacenedione (27). A solution of **26** (5 g, 12.6mmol) in tetrahydrofuran was treated as previously reported[1] to give 3.6 g of **27** (≃70%), under Marschalk conditions at −10 °C.

(+)-(1*S*,3*S*)-1,2,3,4,6,11-Hexahydro-1,3,5,12-tetrahydroxy-3-(hydroxymethyl)-6,11-naphthacenedione (5). To a stirred solution of **27** (4 g) in a mixture of tetrahydrofuran (150 mL) and methanol (150 mL) were added water (50 mL) and then HCl concentrated (1 mL). The mixture was stirred under reflux overnight and then concentrated under reduced pressure to remove organic solvents. After addition of crushed ice and stirring for 2 h, the crystals were collected and dried over phosphoric anhydride. This gave 1.6 g of **5**, identical in all respects with a sample previously analyzed.[1]

(−)-(3*R*)-1,4-Dihydroxy-2-[3-hydroxy-3-(hydroxymethyl)-pentyl]-9,10-anthraquinone (33). A solution of **18** (214 mg, 1.3 mmol) was treated as described previously for the preparation of **19**. After filtration, the filtrate was added dropwise to a solution of leucoquinizarin **28** (629 mg, 2.6 mmol) in THF (1.5 mL) and MeOH (10 mL) under argon atmosphere, containing also KOH (923 mg), sodium dithionite (279 mg), and H_2O (5 mL). The mixture was stirred at 40 °C for 3 h. The reaction mixture was reoxidized by stirring with air for 30 min and then was acidified with cold 1 N HCl and extracted with ethyl acetate. The organic solution was washed with water, dried (Na_2SO_4), and concentrated under reduced pressure. The red-brown residue (800 mg) was chromatographed on silica gel. Elution with dichloromethane–methanol (95:5) gave 48 mg (10%) of pure **33** as a red syrup: $[\alpha]^{20}_D$ −20°; IR ($CHCl_3$) 3700, 3620, 1620, 1590 cm^{-1}; ^1H NMR δ 13.40 (s, 1 H) and 12.90 (s, 1 H) (2 OH, phenol), 8.33 (m, 2 H, Ar), 7.80 (2 H, Ar), 7.10 (s, 1 H, Ar), 3.57 (s, 2 H, 3′-H), 2.77 (t, 2 H, J = J' = 8, 1-H), 1.82 (m, 2 H, 2-H), 1.64 (q, 2 H, J = 7, 4′-H), 2.1–1.5 (m, 2 H, OH), 0.97 (t, 3 H, J = 7, 5-Me); DCI/NH_3, *m/z* (relative intensity) 374 (M + NH_4^+, 5), 357 (M + H^+, 100), 339 (M + H^+ − H_2O, 15), 321 (M + H^+ − $2H_2O$, 3), HRMS, *m/e* calcd for $C_{20}H_{20}O_6$ found 356.3748.

(3*R*)-1,4-Dihydroxy-2-[3-hydroxy-3-(hydroxymethyl)-3,3′-*O*-isopropylidenepentyl]-9,10-anthraquinone (34). To a stirred solution of piperidine (3 mL, 30 mmol) in isopropyl alcohol (10 mL) at 0 °C under argon atmosphere were successively added acetic acid (0.9 mL, 15.3 mmol), a solution of **22** (150 mg, 0.87 mmol) in *i*-PrOH (2 mL), and then a suspension of leucoquinizarin **28** (400 mg, 1.6 mmol) in *i*-PrOH (10 mL). The mixture was warmed to reflux for 20 h, cooled to room temperature, and aerated for 15 min. After addition of water (50mL) and concentration to ca. 60 mL, extraction with dichloromethane gave a crude compound (≃600 mg). Chromatography on silica gel with hexane–THF (90:10) afforded 160 mg (46%) of **34** as a syrup: IR ($CHCl_3$) 1620, 1590 cm^{-1}; ^1H NMR δ 13.39 (s, 1 H) and 12.97 (s, 1 H) (2 OH, phenol), 8.35 (m, 2 H, Ar), 7.84 (m, 2 H, Ar), 7.20 (s, 1 H, Ar), 3.86 (s, 2 H, 3′-H), 2.80 (m, 2 H, 1-H), 1.91 (t, 2 H, J = J' = 8, 2-H), 1.75 (q, 2 H, J = 7, 4-H), 1.46 (s, 3 H) and 1.42 (s, 3 H) (CMe_2), 0.97 (t, 3 H, J = 7, 5-Me); DCI/NH_3 *m/z* (relative intensity) 414 (M + NH_4^+, 10), 397 (M + H^+, 30); HRMS, *m/e* calcd for $C_{23}H_{24}O_6$ 396.4390, found 396.4398.

(−)-(2*R*)-4-(1,4-Dihydroxy-9,10-anthraquinon-2-yl)-2-ethyl-2-hydroxybutanal (35). To a solution of **33** (107 mg, 0.3 mmol) in a mixture of dry Me_2SO (2.5 mL) and anhydrous toluene (4.5 mL) were successively added pyridine (0.12 mL, 1.4 mmol), trifluoroacetic acid (0.027 mL, 0.34 mmol), and dicyclohexylcarbodiimide (558 mg, 2.7 mmol). The mixture was stirred at room temperature for 20 h and taken up in ether. The ether layer was washed with water, dried (Na_2SO_4), and concentrated under reduced pressure to afford 100 mg of crude material. Flash chromatography on silica gel and elution with hexane–acetone (3:1) as eluent gave 65 mg (60%) of pure **35** as a syrup: $[\alpha]^{20}_D$ −56° (*c*, 0.08, $CHCl_3$); IR ($CHCl_3$) 3680, 3610, 1730 cm^{-1}; ^1H NMR δ 13.34 (s, 1 H) and 12.90 (s, 1 H) (2 OH, phenol), 9.58 (s, 1 H, CHO), 8.32 (m, 2 H, Ar), 7.85 (m, 2 H, Ar), 7.18 (s, 1 H, Ar), 2.66 (m, 2 H, 4-H), 2.13 (m, 2 H, 3-H), 1.88 (q, 2 H, J = 7, 2-H), 0.98 (t, 3 H, J = 7, 3-Me); DCI/NH_3 *m/z* (relative intensity) 372 (M + NH_4^+, 25), 355 (M + H^+, 100), 337 (M + H^+ − H_2O, 5). No correct analysis could be obtained with this derivative.

(−)-4-Deoxy-γ-rhodomycinone (30). The aldehyde derivative **35** (30 mg, 0.085 mmol) was treated under Marschalk conditions as previously described by K. Krohn et al.[10] Extraction with ethyl acetate gave 28 mg of crude product and TLC (hexane–ethyl acetate, 3:1) showed disappearance of the starting material and formation of two more polar compounds. Chromatography on silica gel and elution with hexane–EtOAc (4:1) afforded successively 9 mg (30%) of trans diol 4-deoxy-γ-rhodomycinone (**30**) and then a mixture of **30** with the corresponding cis diol **36**, which was not purified. (−)-4-Deoxy-γ-rhodomycinone (**30**) was recrystallized from ether: mp 195 °C (lit.[10] mp 214 °C); $[\alpha]^{20}_D$ −11° (*c*, 0.18, $CHCl_3$); IR ($CHCl_3$) 3620, 1600, 1585 cm^{-1}; ^1H NMR (pyridine-d_5) δ 14.4 (s, 1 H) and 13.7 (s, 1 H) (OH, phenol), 8.29 (m, 2 H, Ar), 7.66 (m, 2 H, Ar), 5.44 (s, 1 H, 10-H), 3.21 (m, 2 H, 7-H), 2.37 (m, 1 H, 8a-H), 2.28 (q, 1 H, J = 7, 13a-H), 2.13 (m, 3 H, 8b-H and 13b-H), 1.37 (t, 1 H, J = 7, 14-Me); DCI/NH_3, *m/z* (relative intensity) 372 (M + NH_4^+, 5), 355 (M + H^+, 70), 337 (2), 225 (100). Anal. Calcd. for $C_{20}H_{18}O_6$: C, 67.79; H, 5.12. Found: C, 67.95; H, 5.02.

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