[Chem. Pharm. Bull. 36(10)3897—3914(1988)]

Total Synthesis of 11-Deoxyanthracyclines: 4-Demethoxy-11-deoxydaunomycin, 11-Deoxydaunomycin, and Their Analogues

YASUMITSU TAMURA,* SHUJI AKAI, HISAKAZU KISHIMOTO, MANABU SASHO, MASAYUKI KIRIHARA, and YASUYUKI KITA*

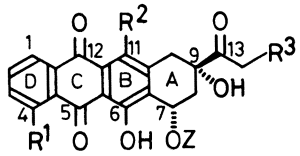
Faculty of Pharmaceutical Sciences, Osaka University, 1-6, Yamada-oka, Suita, Osaka 565, Japan

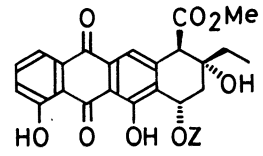
(Received April 20, 1988)

Practical total synthesis of 11-deoxyanthracyclinones (**8** and **9**) was accomplished on the basis of two effective syntheses of the key intermediates (**14** and **15**) and the subsequent highly stereoselective introduction of a C-7 *cis*-hydroxyl group. Glycosidation of **8** with a suitably protected L-daunosamine (**37**) followed by deprotection provided 4-demethoxy-11-deoxydaunomycin (**5**). The C-13 acetal derivative (**34**) of **9** was successfully employed for the glycosidation to achieve the first total synthesis of 11-deoxydaunomycin (**6**). Two novel synthetic 11-deoxyanthracyclines (**10** and **11**) possessing a neutral sugar instead of L-daunosamine were also synthesized.

Keywords——11-deoxyanthracycline; 4-demethoxy-11-deoxydaunomycin; 11-deoxydaunomycin; 5,6,7,8-tetrahydrohomophthalic anhydride; cycloaddition; ethynylcerium(III) reagent; 11-deoxyanthracycline analogue

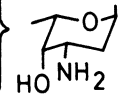
Anthracycline antibiotics, daunomycin (**1**) and adriamycin (**2**), are powerful antitumor agents in the treatment of a broad spectrum of human cancers, but their severe cardiotoxicities have often prevented their safe administration.[1,2] On the other hand, recently developed 11-deoxyanthracyclines such as aclacinomycin A (**3**), alkalvin (**4**), 4-demethoxy-11-deoxydaunomycin (**5**), and 11-deoxydaunomycin (**6**) show stronger antineoplastic activity and/or less cardiotoxicity than the ordinary agents (**1** and **2**),[3-5] so that much attention has been directed to synthetic studies of these 11-deoxy agents, especially to the regioselective





1 : R^1=OMe, R^2=OH, R^3=H
2 : R^1=OMe, R^2=R^3=OH
5 : R^1=R^2=R^3=H
6 : R^1=OMe, R^2=R^3=H

Z=

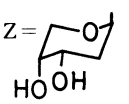


8 : R^1=R^2=R^3=H
9 : R^1=OMe, R^2=R^3=H

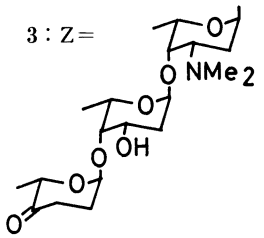
Z=H

10 : R^1=R^2=R^3=H
11 : R^1=OMe, R^2=R^3=H

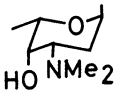
Z=



3 : Z=



4 : Z=



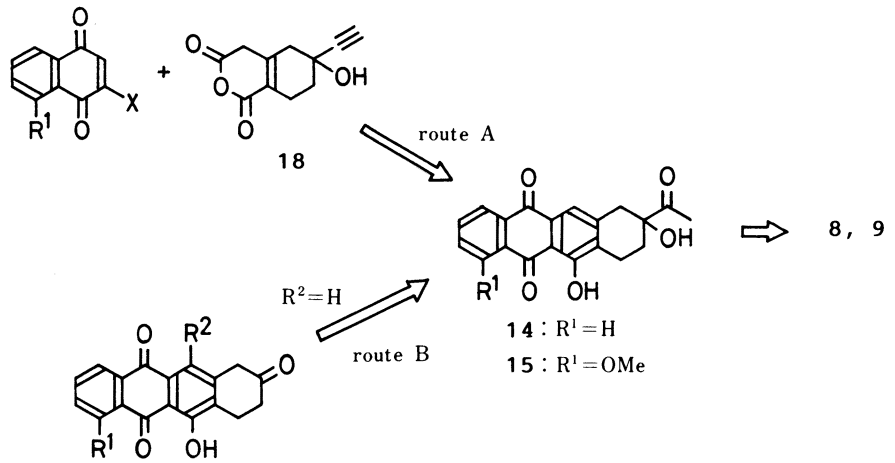
7 : Z=H

syntheses of their aglycones, 11-deoxyanthracyclinones.[2] Total syntheses of aklavinone (**7**),[6] 4-demethoxy-11-deoxydaunomycinone (**8**),[4] and 11-deoxydaunomycinone (**9**)[7] have been accomplished in recent years. Although syntheses of **4** and **5** have been achieved through the glycosidation of their aglycones (**7** and **8**) with L-daunosamine derivatives by Kishi *et al.*[6b] and Umezawa *et al.*,[4] respectively, the glycosidation of **9** or its derivatives has not yet been reported. As a part of our continuing studies on the practical synthesis of anthracyclines[8] and their analogues,[9] we have briefly reported the effective total synthesis of **8** and **9** and the first total synthesis of **6**.[10] We present here the full details of that work and a novel synthesis of 11-deoxyanthracycline analogues (**10** and **11**) in which L-daunosamine was replaced by a neutral sugar.

Results and Discussion

Effective Synthesis of 4-Demethoxy-11-deoxydaunomycinone (8) and 11-Deoxydaunomycinone (9)

In planning the effective synthesis of the aglycones (**8** and **9**), two critical problems must be overcome: (i) the regioselective construction of the tetracyclic quinone framework and (ii) the stereoselective introduction of the substituents on ring A. Many elegant approaches have been employed to solve these problems and extensive literature, including our method, exists concerning the preparation of the tetracyclic triones (**12** and **13**).[8c,d,11] There remains, however, the need for some improvements in the side chain elaboration at the C-9 carbonyl group, since the reported method for **13** using a large excess of ethynylmagnesium bromide is inadequate in yield (30% yield), probably due to the ready enolization of the C-9 carbonyl group by the basic Grignard reagent.[7b,d] Therefore, our attention was first focused on the effective synthesis of the pivotal intermediates (**14** and **15**) to the aglycones (**8** and **9**). Attempts to elaborate the C-9 side chain on **13** by other existing methodologies using acyl anion equivalents such as 1-lithio-1-methoxyethene, 2-lithio-2-methyl-1,3-dithiane, and (trimethylsilyl)ethynyllithium did not give any satisfactory results. The preliminary application of the method using the organocerium(III) reagent,[12] which has worked dramatically



12 : $R^1=R^2=H$
13 : $R^1=OMe$, $R^2=H$
16 : $R^1=H$, $R^2=OH$
17 : $R^1=OMe$, $R^2=OH$

Chart 1

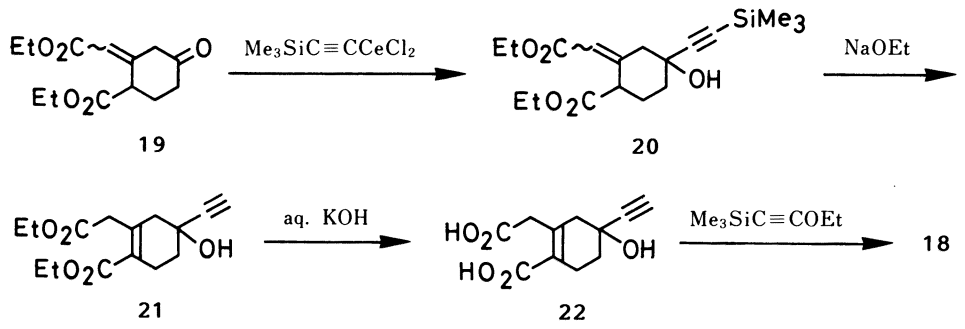


Chart 2

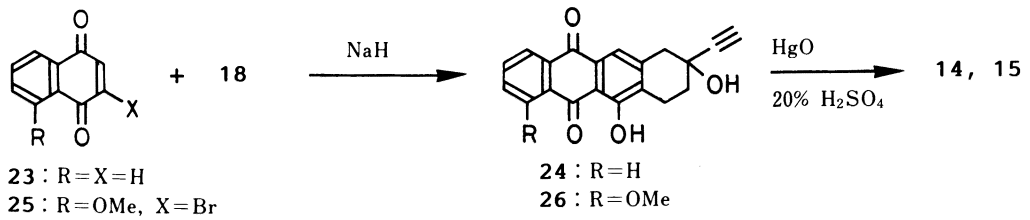


Chart 3

in the same elaboration of the C-9 side chain on 11-hydroxytriones (**16** and **17**),[8e,f,13] to these 11-deoxy systems initially failed to give the desired adducts (*vide infra*). After many unsuccessful attempts, two effective syntheses of **14** and **15** were developed: a convergent synthesis of **14** and **15** by the strong base-induced cycloaddition[8] of suitably functionalized tetrahydrohomophthalic anhydride (**18**) to naphthoquinones (route A), and an elaboration of the C-9 side chain on **13** by the reverse addition of (trimethylsilyl)ethynylcerium(III) reagent (route B) (Chart 1).

The anhydride (**18**) required for route A was prepared from the known ketone (**19**)[8d] in 4 steps in a 60% overall yield (Chart 2). Reaction of **19** with 2 eq of (trimethylsilyl)ethynylcerium(III) chloride, prepared from (trimethylsilyl)ethynyllithium and anhydrous $CeCl_3$, in anhydrous tetrahydrofuran (THF) at −78 °C for 2 h gave the diester (**20**) possessing appropriate (trimethylsilyl)ethynyl and hydroxyl groups in 89% yield, although treatment of **19** with a large excess of (trimethylsilyl)ethynyllithium instead of the cerium reagent at −78 C for 2 h gave only an 11% yield of **20** together with a 73% yield of recovered **19**. Treatment of **20** with NaOEt in EtOH caused *exo–endo* olefin isomerization and desilylation at the same time to give the *endo*-olefin (**21**). The overall yield of **21** from **19** was 71%. The alkaline hydrolysis of **21** with aqueous KOH in refluxing EtOH gave the diacid (**22**) in 85% yield, and this was cyclized with (trimethylsilyl)ethoxyacetylene[14] into the desired anhydride (**18**) in 99% yield.[15]

The cycloaddition of **18** to naphthoquinone (**23**) proceeded readily under mild conditions. Thus, the sodio anion of **18**, generated by the treatment with 2 eq of NaH, reacted with **23** at room temperature for 2 h to give the tetracyclic adduct (**24**) possessing ethynyl and hydroxyl groups at the C-9 position in 66% yield. Similarly, **18** reacted with the bromonaphthoquinone (**25**) in a regiocontrolled manner to give the adduct (**26**) as a sole product in 73% yield.[16] These products (**24** and **26**) were hydrated by a standard method (HgO, 20% H_2SO_4) to give the 9-acetyl-9-hydroxy compounds (**14** and **15**) in 88% and 99% yields, respectively (Chart 3).

An alternative route to **15** (route B) was developed as follows. Recently we have reported

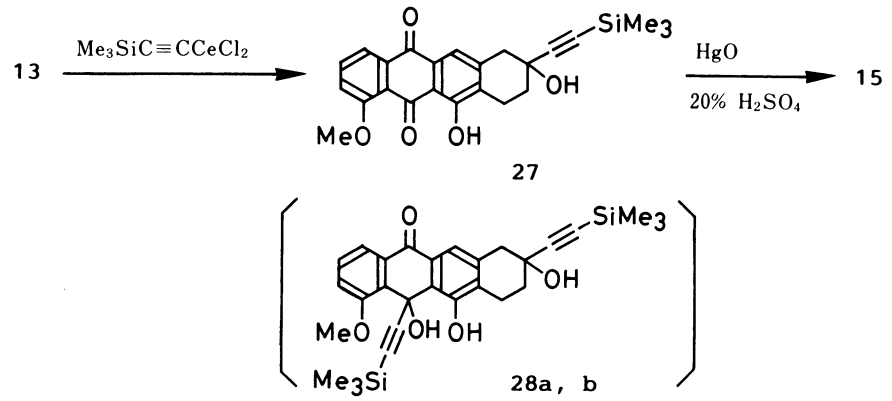


Chart 4

an effective method for C-9 side chain elaboration on 11-hydroxytriones (**16** and **17**) using (trimethylsilyl)ethynylcerium(III) chloride.[8e,f] The application of the same method to the 11-deoxy analogue (**13**) did not give the desired 9-hydroxy-9-(trimethylsilyl)ethynyl compound (**27**) but gave a mixture of two unexpected diastereomers (**28a, b**). Thus, a solution of **13** in THF was added to a solution of the cerium reagent (16 eq) in THF at −78 °C to give **28a** and **28b** in 43% and 41% yields, respectively. The following spectral data indicated that two (trimethylsilyl)ethynyl groups had been introduced into the C-5 (not C-12) and C-9 positions, though the relative configurations have not been elucidated[17]: (i) in the infrared (IR) spectra the presence of the absorption band at about 1660 cm^{-1} due to the C-12 carbonyl group and the disappearance of the absorption band at about 1620 cm^{-1} due to intramolecular hydrogen bonding of the C-5 carbonyl group, (ii) in the proton nuclear magnetic resonance (^{1}H-NMR) spectra the presence of two signals of trimethylsilyl groups (about δ 0.08 and 0.13 ppm) and the disappearance of the characteristic signal (about δ 13 ppm) due to intramolecular hydrogen bonding of the hydroxyl group (C-6 OH) of *peri*-hydroxyanthraquinones, and (iii) in the mass spectra (MS) the presence of the strong fragment ion peak at *m/z* 500 arising from $(M-H_2O)^+$ (the loss of H_2O from the parent molecule has often been observed in *o*-hydroxybenzyl alcohol structures[18]).

Among various reaction conditions examined, changing the amount of the cerium reagent, concentration, the addition rate, and so on, the reverse addition method was found to overcome this problem and gave a good yield of the desired **27**: 4 eq of (trimethylsilyl)ethynylcerium(III) chloride was gradually added to a stirred solution of **13** in CH_2Cl_2 over 4 h at −78 °C to give **27** in 59% yield (94% yield based on the reacted **13**). Direct hydration of **27** with HgO–20% H_2SO_4 in refluxing THF gave the key intermediate (**15**) quantitatively (Chart 4).

Introduction of a C-7 *cis*-hydroxyl group into **14** and **15** has already been performed by bromination with bromine at the C-7 position of them or their C-13 acetal derivatives (**29** and **30**) and subsequent hydrolysis.[4,7a,b,d] This method, however, provides unsatisfactory results, low yields of the products and/or the formation of a fair amount of the C-7 epimers, 7,9-*trans*-diols, which require tedious chromatographic separation. Better results were obtained by the following sequence, with high yields and stereoselectivities (Chart 5). Bromination of **29** with *N*-bromosuccinimide (NBS) and azobisisobutyronitrile (AIBN) in refluxing anhydrous CCl_4 and subsequent hydrolysis with silica gel in wet THF at 0 °C gave the 7,9-*cis*-diol (**31**) stereospecifically in 77% yield. The relative configuration of **31** was determined from its ^{1}H-NMR spectral data [δ 5.329 (m, 1H, $\nu_{1/2}$ = 9.5 Hz, H-7eq)][19] and the facile formation of the corresponding acetonide (**32**). Reaction of **31** with benzeneboronic acid in CF_3CO_2H–an-

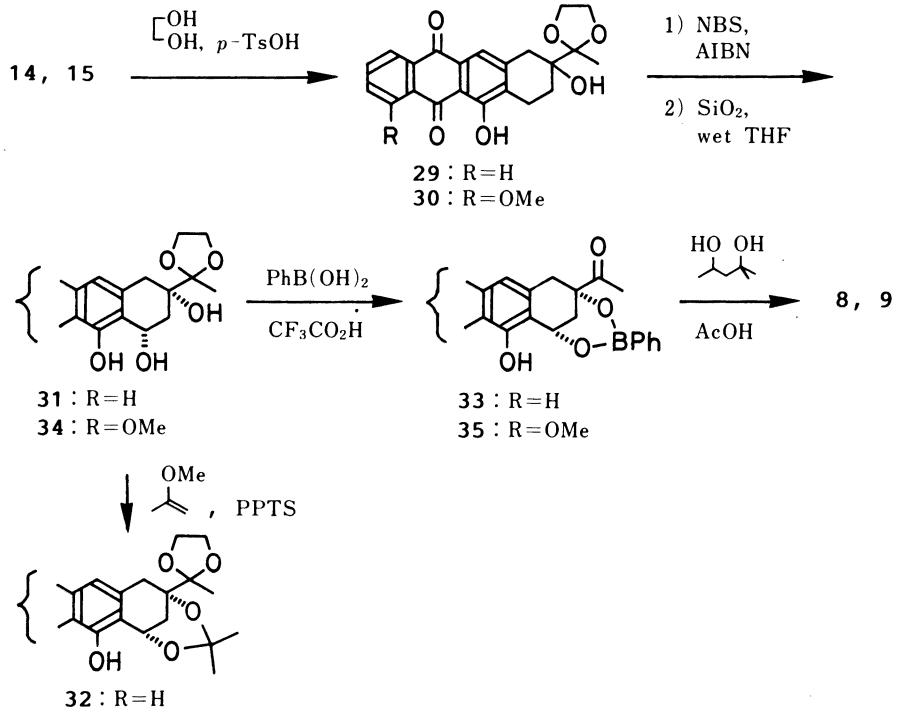


Chart 5

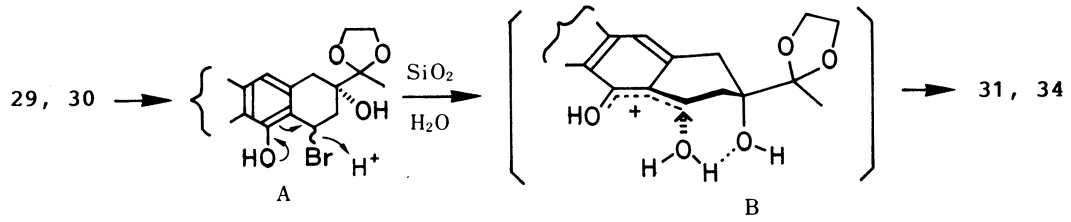


Chart 6

hydrous toluene[21] at 0 °C to room temperature caused deacetalization and formation of the cyclic *cis*-boronate at the same time to give **33**, which was hydrolyzed under mild conditions (2-methyl-2,4-pentanediol, AcOH) to give 4-demethoxy-11-deoxydaunomycinone (**8**) in 83% yield. This **8** was identical with an authentic sample.[4] The same sequence from **30** readily provided 11-deoxydaunomycinone (**9**). The bromination-hydrolysis of **30** gave a mixture (15 : 1) of the 7,9-*cis*-diol (**34**) and 7,9-*trans*-diol in 81% yield. The mixture was converted into **35** in 61% yield, from which pure **9** was obtained in a quantitative yield. Since **9** was extraordinarily insoluble in both organic solvents and water, the present method is more convenient for the purification of **9** than the reported C-7 hydroxylation procedure.[7a,b,d] The aglycone (**9**) gave a satisfactory exact mass spectral analysis, and its IR and ^{1}H-NMR spectral data were identical with those of the authentic sample generously provided by Professor Arcamone.

The following reasons are proposed to explain the high yield and stereoselectivity in the present C-7 hydroxylation method: (i) C-13 acetalization of **14** and **15** prevented the bromination at the C-10 and C-14 positions, (ii) under weakly acidic conditions the C-7 brominated products (A) readily provided the cation (B), into which water came stereospecifi-

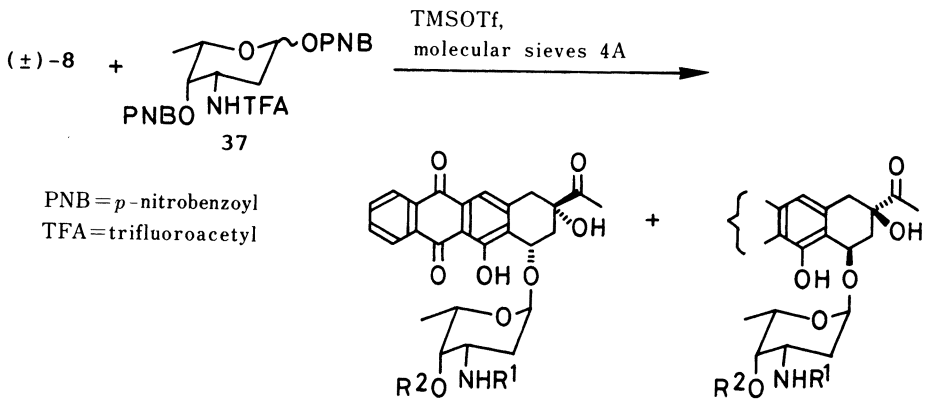
cally from the same side as the C-9 axial-hydroxyl group owing to hydrogen bonding, and (iii) contaminating *trans*-diol could be converted to *cis*-boronate by epimerization *via* a cation similar to B in CF_3CO_2H (Chart 6).[22]

Total Synthesis of 4-Demethoxy-11-deoxydaunomycin (5), 11-Deoxydaunomycin (6), and Their Analogues (10 and 11)

The following four methods have been reported for the glycosidation of the ordinary anthracyclinones with L-daunosamine: condensation of an aglycone (a) with a 1-halo sugar by Hg(II) salt or Ag(I) salt (Koenigs–Knorr method), (b) with glycal by a protic acid, (c) with 1-*O*-acyl sugar by a Lewis acid or protic acid, and (d) with 1-*O*-acyl sugar by trimethylsilyl trifluoromethanesulfonate (TMSOTf).[23] The last method (method d), recently developed by Terashima *et al.*, provided only the α-anomer in high yield, and was effectively used in the total synthesis of 4-demethoxydaunomycin.

The glycosidation of **8** was reported by Umezawa *et al.*,[4] who found that glycosidation of racemic **8** by method b gave a mixture of four glycosides as two anomers for each enantiomer of the aglycone, from which a 19% yield of **36** possessing the natural absolute configuration was isolated. By employing method d for the glycosidation of (±)-**8**, **5** was obtained in high stereoselectivity (Chart 7). Thus, (±)-**8** and suitably modified L-daunosamine (**37**) were treated with TMSOTf and molecular sieves 4A in a mixed solvent of anhydrous CH_2Cl_2 and anhydrous ether at −15 °C to give two α-glycosides (**36** and **38**) in 46% and 49% yields, respectively. Their absolute structures were adequately supported by their spectral data (circular dichroism (CD) and ^{1}H-NMR) (Table I); the similarity of the CD curve of **36** to that of natural daunomycin (**1**) ($[\theta]_{287}$ -1.72×10^4 (MeOH)) indicated that **36** had the natural configuration (7*S*,9*S*), whereas the CD curve of **38** indicated the opposite configuration (7*R*,9*R*), and small coupling constants (<3.7 Hz) of the ^{1}H-NMR signals due to both of their anomeric protons indicated that they were α-glycosides.[24] Further confirmation was obtained by comparison of the physical data (melting point and specific rotation) of **36** and **38** with those of authentic samples reported by Umezawa *et al.*[4] Deprotection of **36** to 4-demethoxy-11-deoxydaunomycin (**5**) has already been done in 94% yield by them.

On the other hand, total synthesis of **6** contains a crucial problem in the glycosidation step. There has been no report on the glycosidation of **9** or its derivatives. Our preliminary study on the glycosidation of (±)-**9** with suitably protected L-daunosamine by Terashima's



36 : R^1=TFA, R^2=PNB
5 : $R^1=R^2$=H

38 : R^1=TFA, R^2=PNB

Chart 7

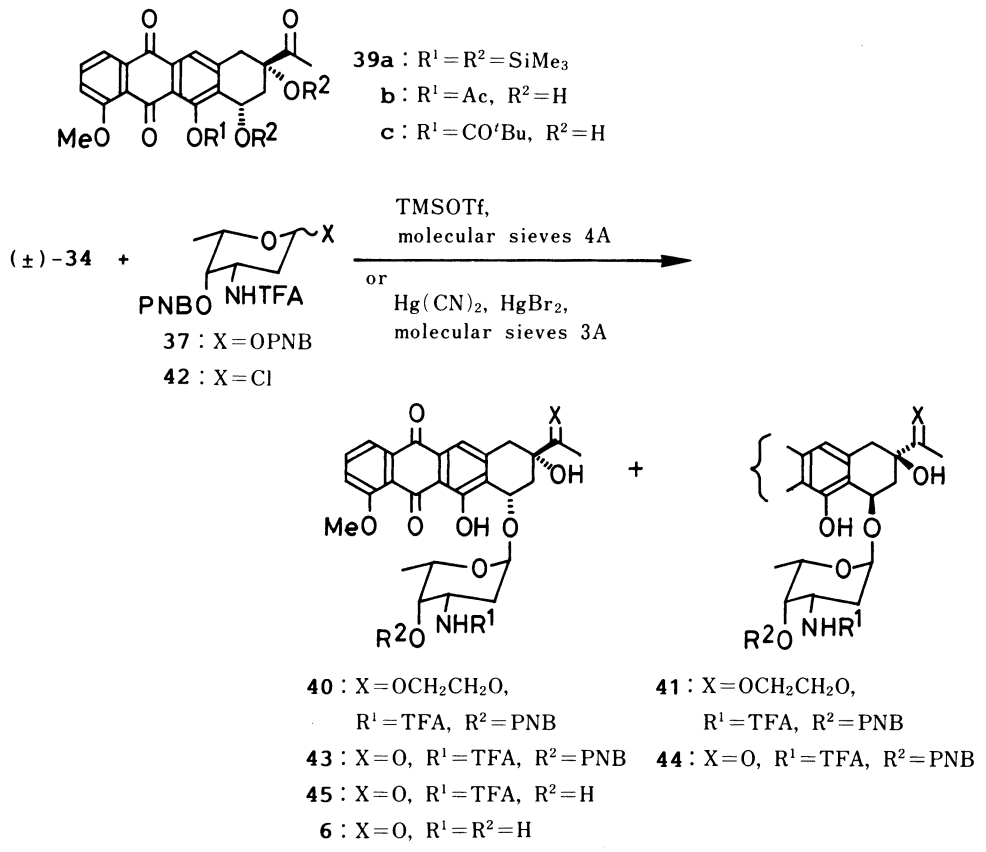
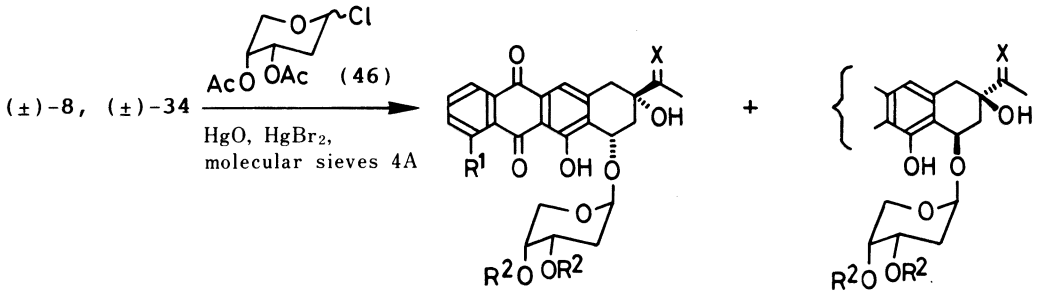


Chart 8

method or the usual Koenigs–Knorr method did not provide any glycosides at all, probably due to the extremely low solubility of (±)-**9** in common organic solvents. Condensation using more soluble derivatives (**39a**—**c**) whose hydroxyl groups were protected with trimethylsilyl or acyl groups failed to give glycosides. After many unsuccessful attempts, condensation of the C-13 acetal derivative ((±)-**34**) with **37** by Terashima's method gave a 42% yield of a mixture of the expected α-glycosides (**40** and **41**) and a 29% yield of recovered (±)-**34**. A slightly better result was obtained by the condensation of (±)-**34** and the 1-chloro sugar (**42**)[26] under Koenigs–Knorr conditions. Thus, (±)-**34** and **42** were treated with $Hg(CN)_2$, $HgBr_2$, and molecular sieves 3A in $CHCl_3$ to give a mixture (1 : 1) of **40** and **41** in 56% yield. Careful deacetalization of these glycosides in aqueous 80% AcOH gave **43** and **44** in 41% and 53% yields (85% and 84% yields based on reacted **40** and **41**), respectively. The absolute configurations of these novel glycosides (**40**, **41**, **43**, and **44**) were deduced from their CD and ^{1}H-NMR spectral data similarly to the case of **36** and **38** (Table I), and finally confirmed by the direct conversion of **43** into **6**. Thus, hydrolysis of **43** with an equivalent amount of 0.1 N NaOH at 0 °C gave *N*-trifluoroacetyl-11-deoxydaunomycin (**45**) in 82% yield, which was stirred in an excess of 0.1 N NaOH at room temperature to give 11-deoxydaunomycin (**6**) in 95% yield (Chart 8). The hydrochloride of **6** was identical with the authentic sample generously provided by Professor Arcamone.

Recent investigations have revealed that some novel synthetic anthracyclines, in which L-daunosamine was replaced by neutral sugars such as 2,6-dideoxy-L-*lyxo*-hexose or 2-deoxy-D-*erythro*-pentose, show stronger antineoplastic activities and/or reduced cardiotoxicities.[27]



47 : R^1=H, R^2=Ac, X=O
10 : R^1=R^2=H, X=O
49 : R^1=OMe, R^2=Ac, X=OCH_2CH_2O
51 : R^1=OMe, R^2=Ac, X=O
11 : R^1=OMe, R^2=H, X=O

48 : R^1=H, R^2=Ac, X=O
50 : R^1=OMe, R^2=Ac, X=OCH_2CH_2O
52 : R^1=OMe, R^2=Ac, X=O

Chart 9

TABLE I. Spectral Data (CD and ^{1}H-NMR) for **6**, **10**, **11**, **36**, **38**, **40**, **41**, **43**—**45**, **47**—**51**, and **52**

Compound	CD (MeOH) $[\theta]_{max} \times 10^4$ (nm):	^{1}H-NMR (500 MHz, $CDCl_3$) δ: H-7	H-1′
36	−5.32 (268) +0.66 (339)	5.377 (dd, J=4.4, 2.2 H)	5.695 (d, J=3.7 Hz)
38	+0.91 (273) −0.91 (338)	5.634 (dd, J=2.9, 2.2 Hz)	5.530 (d, J=3.7 Hz)
40	−1.81 (265) +0.49 (332)	5.222 (dd, J=4.0, 1.5 Hz)	5.635 (br s, $\nu_{1/2}$=4 Hz)
41	+0.43 (285) −0.33 (334)	5.616 (dd, J=3.7, 2.0 Hz)	5.560 (d, J=3.5 Hz)
43	−3.24 (266) +0.80 (331)	5.356 (dd, J=4.0, 2.0 Hz)	5.682 (br s, $\nu_{1/2}$=4 Hz)
44	+0.96 (287) −0.60 (335)	5.648 (dd, J=3.5, 1.5 Hz)	5.512 (d, J=3.7 Hz)
45	−1.10 (286) +0.74 (333)	5.298 (dd, J=4.4, 2.0 Hz)	5.515 (d, J=4.0 Hz)
6·HCl	−0.85 (286) +0.66 (332)	5.003 (dd, J=5.5, 4.0 Hz)	5.295 (br d, J=3.5 Hz)
47	−1.64 (282) +0.50 (336)	5.317 (dd, J=4.4, 2.2 Hz)	5.539 (dd, J=3.7, 2.9 Hz)
48	+1.53 (283) −0.30 (339)	5.555 (dd, J=3.7, 2.2 Hz)	5.438 (br d, J=3.7 Hz)
10	−1.09 (284) +0.52 (340)	5.313 (dd, J=3.7, 2.2 Hz)	5.486 (t, J=3.7 Hz)
49	−0.86 (287) +0.55 (334)	5.263 (dd, J=4.4, 1.5 Hz)	5.557 (t, J=2.9 Hz)
50	+0.98 (286) −0.75 (331)	5.558 (dd, J=4.0, 2.0 Hz)	5.480 (br d, J=3.7 Hz)
51	−0.92 (285) +0.55 (335)	5.318 (dd, J=4.0, 2.0 Hz)	5.551 (t, J=3.7 Hz)
52	+0.70 (284) −0.25 (333)	5.575 (dd, J=3.7, 2.0 Hz)	5.432 (br d, J=3.7 Hz)
11	−0.94 (287) +0.56 (332)	5.312 (dd, J=4.0, 2.2 Hz)	5.490 (t, J=3.7 Hz)

Such developments drew our attention to the glycosidation of **8** and **9** with neutral sugars, and the condensation of these aglycones with commercially available 2-deoxy-D-*erythro*-pentose was carried out as a preliminary study.

Among several methods tried to combine (±)-**8** and 2-deoxy-D-*erythro*-pentose, a successful result was obtained by the Koenigs–Knorr method. Thus, (±)-**8** and the 1-chloro sugar (**46**)[26,28] were treated with HgO, $HgBr_2$, and molecular sieves 4A in CH_2Cl_2 to give two β-glycosides (**47** and **48**) each in 19% yield.[29] Their CD and ^{1}H-NMR spectral data unambiguously supported their absolute configurations (Table I), and **47** having the same configuration as natural anthracyclines was hydrolyzed by NaOMe at 0 °C to give **10** in 84% yield.

The C-13 acetal derivative (**34**) was also efficiently used for the synthesis of the 11-deoxydaunomycin analogue (**11**), although direct treatment of (±)-**9** with **46** could not afford

the glycosides. Thus, (±)-**34** and **46** were treated under Koenigs–Knorr conditions to give two β-glycosides (**49** and **50**) in 29% and 26% yields, respectively.[29] Deacetalization of **49** and **50** was carried out in aqueous 80% AcOH at 45 °C to give the C-13 keto glycosides (**51** and **52**) in 52% and 57% yields (71% and 97% yields based on reacted **49** and **50**), respectively. Hydrolysis of **51** with NaOMe gave **11** in 61% yield (Chart 9).

The CD and ^{1}H-NMR spectral data of other intermediates (**45**, **49**—**51**, and **52**) and final products (**6**, **10**, and **11**) are also given in Table I, revealing the general effectiveness of these data for predicting the absolute configuration of 11-deoxyanthracyclines.

Extended studies on the synthesis of 11-deoxyanthracyclines and their analogues following these synthetic schemes are currently in progress.

Experimental

All boiling and melting points are uncorrected. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. IR absorption spectra were recorded on a JASCO HPIR-102 spectrophotometer with $CHCl_3$ as a solvent unless otherwise noted. ^{1}H-NMR spectra were determined on a Hitachi R-22 (90 MHz), a JEOL JNM FX-90Q (90 MHz), or a JEOL JNM-GX500 (500 MHz) spectrometer with tetramethylsilane as an internal standard. MS were obtained by the electron impact (EI) method unless otherwise noted on an ESCO EMD-05A (for EI-MS), a JEOL JMS-D300 (for EI-, chemical ionization (CI)-, and exact MS), or a JEOL HX-100 (for fast atom bombardment (FAB)-MS) mass spectrometer. CD spectra were obtained on a JASCO J-500A spectropolarimeter. E. Merck silica gel 60 (0.063—0.200 nm, 70—230 mesh ASTM) and E. Merck pre-coated TLC plates, silica gel 60 F_{254} were used for column chromatography and for preparative thin layer chromatography (prep. TLC), respectively. Organic layers were dried with anhydrous $MgSO_4$. Known compounds were prepared by rhe reported methods: **19**,[8d] (trimethylsilyl)ethoxyacetylene,[14b] **25**,[30] **37**,[23] **42**.[26]

Ethyl (±)-2-Ethoxycarbonyl-5-hydroxy-5-(trimethylsilyl)ethynyl-1-cyclohexylideneacetate (20)——(i) Preparation Using (Trimethylsilyl)ethynylcerium(III) Chloride: Anhydrous $CeCl_3$ (5.2 g, 21 mmol) was heated *in vacuo* (5 Torr) at 140 °C for 2 h, and cooled under a nitrogen atmosphere, then anhydrous THF (35 ml) was added. The resulting suspension was stirred at room temperature for 1 h and cooled to −78 °C. To this suspension was added a THF solution of (trimethylsilyl)ethynyllithium [prepared from (trimethylsilyl)acetylene (2.9 ml, 21 mmol) and *n*-BuLi (1.6 N, 11.3 ml, 18 mmol) in anhydrous THF (30 ml) at −40 °C for 30 min], and the mixture was stirred at −78 °C for 1 h then used as a THF solution of (trimethylsilyl)ethynylcerium(III) chloride. To this solution was added a solution of **19** (3.07 g, 12.1 mmol) in anhydrous THF (30 ml) at −78 °C. The mixture was stirred for 2 h under the same conditions, quenched with saturated aqueous NH_4Cl (50 ml), made acidic with 1 N HCl, and extracted with CH_2Cl_2 (100 ml × 3). The combined extract was washed with brine, dried, and concentrated *in vacuo*. Purification of the residue by column chromatography on silica gel (AcOEt : *n*-hexane = 1 : 3) gave an 89% yield (3.80 g) of **20** as a colorless oil: IR: 2160, 1725 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.17 (s, 9H, $Si(CH_3)_3$), 1.31 (t, 6H, J = 7 Hz, CH_2CH_3 × 2), 1.95—2.2 (m, 4H, H-3 × 2 and H-4 × 2), 3.06 (d, 1H, J = 16 Hz, H-6), 3.20 (d, 1H, J = 16 Hz, H-6), 3.25—3.35 (m, 1H, H-2), 4.17 (q, 2H, J = 7 Hz, CO_2CH_2), 4.18 (q, 2H, J = 7 Hz, CO_2CH_2), 5.81 (br s, 1H, CH = C). Exact MS Calcd for $C_{18}H_{28}O_5Si$: 352.1703. Found: 352.1696.

(ii) Preparation Using (Trimethylsilyl)ethynyllithium: A solution of (trimethylsilyl)ethynyllithium in THF was prepared from (trimethylsilyl)acetylene (0.15 ml, 1.06 mmol) and *n*-BuLi (1.6 N, 0.6 ml, 0.96 mmol) in anhydrous THF (3 ml) similarly to the above procedure. To this solution was added a solution of **19** (127 mg, 0.5 mmol) in anhydrous THF (3 ml) at −78 °C, and the mixture was stirred at −78 °C for 2 h and then at room temperature for 30 min. The same work-up as described above gave an 11% yield (19 mg) of **20** and a 73% yield (93 mg) of recovered **19**.

Ethyl (±)-2-Ethoxycarbonyl-5-ethynyl-5-hydroxycyclohex-1-enylacetate (21)——A crude product (4.0 g) obtained from anhydrous $CeCl_3$ (5.9 g, 24 mmol), (trimethylsilyl)acetylene (3.6 ml, 26 mmol), *n*-BuLi (1.6 N, 14.5 ml, 23 mmol), and **19** (3.0 g, 11.8 mmol) by the same procedure (i) as described above was dissolved in anhydrous EtOH (35 ml). This solution was added to an ice-cooled solution of NaOEt in EtOH [freshly prepared from Na (0.51 g, 22 mmol) in anhydrous EtOH (35 ml)]. After stirring of the reaction mixture at room temperature for 50 min, AcOH (2 ml) was added at 0 °C and the whole was concentrated *in vacuo* below room temperature. The residue was partitioned between brine (20 ml) and ether (100 ml), and the organic layer was separated, dried, and concentrated *in vacuo*. Purification of the residue by column chromatography on silica gel (AcOEt : *n*-hexane = 1 : 3) gave a 71% yield (2.36 g) of **21** as a colorless oil: bp 170—175 °C (0.2 Torr) (bath temp.). IR: 3300, 1720, 1705, 1640 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.26 (t, 3H, J = 7 Hz, CH_2CH_3), 1.28 (t, 3H, J = 7 Hz, CH_2CH_3), 1.94 (br t, 2H, J = 7 Hz, H-4 × 2), 2.45—2.7 (m, 4H, H-3 × 2 and H-6 × 2), 2.47 (s, 1H, C≡CH), 3.47 (br s, 2H, $COCH_2$), 4.15 (q, 2H, J = 7 Hz, CO_2CH_2), 4.18 (q, 2H, J = 7 Hz, CO_2CH_2). CI-MS *m/z*: 281 [(M + H)$^+$]. *Anal.* Calcd for $C_{15}H_{20}O_5$: C, 64.27; H, 7.19. Found: C, 63.96; H, 7.42.

(±)-2-Carboxy-5-ethynyl-5-hydroxycyclohex-1-enylacetic Acid (22)——A solution of **21** (0.71 g, 2.53 mmol) and

KOH (0.57 g, 10 mmol) in EtOH (18 ml) and water (6 ml) was heated at reflux for 1 h, concentrated *in vacuo*, and washed with ether (10 ml). The residue was taken up in ether (30 ml) and the mixture was acidified to pH 2—3 with 10% HCl at 0 °C, saturated with NaCl, and extracted with ether (30 ml × 3). The combined organic layer was washed with brine, dried, and concentrated *in vacuo* to give an 85% yield (0.48 g) of **22** as pale brown crystals: mp 161—163 °C (AcOEt). IR (KCl): 3600—2400, 3260, 1710, 1680, 1630 cm^{-1}. ^{1}H-NMR (acetone-d_6) δ: 1.8—2.0 (m, 2H, H-4×2), 2.4—2.7 (m, 4H, H-3×2 and H-6×2), 2.80 (s, 1H, C≡CH), 3.55 (br s, 2H, $COCH_2$). CI-MS *m/z*: 225 [$(M+H)^+$]. Exact MS Calcd for $C_{11}H_{10}O_4$ [$(M-H_2O)^+$]: 206.0576. Found: 206.0565.

(±)-6-Ethynyl-6-hydroxy-5,6,7,8-tetrahydrohomophthalic Anhydride (18)——The experimental details were as reported.[14b]

(±)-9-Ethynyl-6,9-dihydroxy-7,8,9,10-tetrahydronaphthacene-5,12-dione (24)——Under a nitrogen atmosphere, a mixture of **18** (40 mg, 0.195 mmol) and NaH (60% oil suspension, 16 mg, 0.39 mmol) in anhydrous THF (4 ml) was stirred at 0 °C for 5 min, then a solution of **23** (31 mg, 0.195 mmol) in anhydrous THF (3 ml) was added. After being stirred at 0 °C for 20 min and then at room temperature for 2 h, the mixture was quenched with saturated aqueous NH_4Cl (10 ml) and partitioned between 1 N HCl (1 ml) and CH_2Cl_2 (15 ml). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (15 ml × 2). The combined organic layer was washed with brine, dried, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (ether : CH_2Cl_2 = 1 : 20) to give a 66% yield (41 mg) of **24** as yellow crystals: mp 243—245.5 °C ($CHCl_3$). IR (KCl): 3425, 3250, 1665, 1620, 1590, 1575 (sh) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.16 (t, 2H, J=7 Hz, H-8×2), 2.48 (s, 1H, C≡CH), 3.03 (t, 2H, J=7 Hz, H-7×2), 3.16 (d, 1H, J=17.5 Hz, H-10), 3.31 (d, 1H, J=17.5 Hz, H-10), 7.57 (s, 1H, H-11), 7.7—7.85 (m, 2H, H-2 and H-3), 8.2—8.35 (m, 2H, H-1 and H-4), 13.04 (s, 1H, OH-6). MS *m/z*: 318 (M^+). *Anal.* Calcd for $C_{20}H_{14}O_4$: C, 75.40; H, 4.43. Found: C, 75.22; H, 4.21.

(±)-9-Ethynyl-6,9-dihydroxy-4-methoxy-7,8,9,10-tetrahydronaphthacene-5,12-dione (26)——By the same procedure as described for the preparation of **24**, a 73% yield (50 mg) of **26** was obtained from **18** (40 mg, 0.195 mmol), NaH (0.39 mmol), and **25** (52 mg, 0.195 mmol) as yellow crystals: mp 250—252 °C (CH_2Cl_2–MeOH) (lit.[7d] 247—249 °C). IR (KCl): 3470, 3260, 1660, 1620, 1580 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.15 (br t, 2H, J=7 Hz, H-8×2), 2.47 (s, 1H, C≡CH), 3.03 (br t, 2H, J=7 Hz, H-7×2), 3.14 (d, 1H, J=17 Hz, H-10), 3.28 (d, 1H, J=17 Hz, H-10), 4.07 (s, 3H, OCH_3-4), 7.35 (dd, 1H, J=8, 1.5 Hz, H-3), 7.50 (s, 1H, H-11), 7.72 (t, 1H, J=8 Hz, H-2), 7.96 (dd, 1H, J=8, 1.5 Hz, H-1), 13.39 (s, 1H, OH-6). MS *m/z*: 348 (M^+). Exact MS Calcd for $C_{21}H_{16}O_5$: 348.0998. Found: 348.1008.

(±)-9-Acetyl-6,9-dihydroxy-7,8,9,10-tetrahydronaphthacene-5,12-dione (14)——A mixture of **24** (59 mg, 0.19 mmol), yellow HgO (80 mg, 0.37 mmol), and 20% H_2SO_4 (1 ml) in THF (7 ml) was heated at reflux for 5 h. After cooling, the mixture was diluted with 1 N HCl (10 ml) and extracted with CH_2Cl_2 (20 ml × 5). The combined organic layer was washed with brine, dried, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (CH_2Cl_2 to ether : CH_2Cl_2 = 1 : 20) to give an 88% yield (55 mg) of **14** as yellow crystals: mp 219—220 °C (CH_2Cl_2) [lit.[4] 208—214 °C (dec.), lit.[31] 212—214 °C (dec.), lit.[32] 213—215 °C, lit.[33] 214 °C (dec.)]. IR: 1710, 1670, 1630, 1590 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.9—2.15 (m, 2H, H-8×2), 2.37 (s, 3H, H-14×3), 2.81 (d, 1H, J=18 Hz, H-10), 2.9—3.15 (m, 2H, H-7×2), 3.31 (d, 1H, J=18 Hz, H-10), 7.56 (s, 1H, H-11), 7.7—7.85 (m, 2H, H-2 and H-3), 8.2—8.4 (m, 2H, H-1 and H-4), 13.04 (s, 1H, OH-6). MS *m/z*: 336 (M^+).

(±)-9-Acetyl-6,9-dihydroxy-4-methoxy-7,8,9,10-tetrahydronaphthacene-5,12-dione (15)——(i) Preparation from **26**: By the same procedure as described for the preparation of **14**, a 99% yield (55 mg) of **15** was obtained from **26** (53 mg, 0.15 mmol) as yellow crystals: mp 218—219.5 °C ($CHCl_3$) (lit.[7a,d,34,35] 209—211 °C, lit.[36] 210—211 °C). IR: 1715, 1670 (sh), 1620, 1585 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.85—2.1 (m, 2H, H-8×2), 2.37 (s, 3H, H-14×3), 2.78 (d, 1H, J=17.5 Hz, H-10), 2.9—3.1 (m, 2H, H-7×2), 3.30 (d, 1H, J=17.5 Hz, H-10), 4.07 (s, 3H, OCH_3-4), 7.34 (dd, 1H, J=7.5, 1.5 Hz, H-3), 7.47 (s, 1H, H-11), 7.72 (t, 1H, J=7.5 Hz, H-2), 7.94 (dd, 1H, J=7.5, 1.5 Hz, H-1), 13.38 (s, 1H, OH-6). MS *m/z*: 366 (M^+).

(ii) Preparation from **27**: By the same procedure as described for the preparation of **14**, a quantitative yield (14 mg) of **15** was obtained from **27** (16 mg, 0.038 mmol) as yellow crystals, mp 218.5—220 °C ($CHCl_3$). This product was identical with the authentic sample obtained from **26**.

(±)-5,9-Bis[(trimethylsilyl)ethynyl]-5,6,9-trihydroxy-4-methoxy-7,8,9,10-tetrahydronaphthacene-12(5*H*)-one (28a and b)——Similarly to the procedure (i) described for the preparation of **20**, a solution of **13** (27.5 mg, 0.085 mmol) in anhydrous THF (50 ml) was added to a solution of (trimethylsilyl)ethynylcerium(III) chloride in THF, prepared from anhydrous $CeCl_3$ (0.52 g, 2.1 mmol), (trimethylsilyl)acetylene (0.30 ml, 2.1 mmol), and *n*-BuLi (1.6 N, 0.87 ml, 1.4 mmol) in anhydrous THF (13 ml), at −78 °C. After being stirred at −78 °C for 3 h, the mixture was worked up as usual and purified by column chromatography on silica gel (ether : CH_2Cl_2 = 1 : 40 to 1 : 20) to give a 43% yield (19 mg) of **28a** and a 41% yield (18 mg) of **28b**, each as colorless crystals: **28a**, TLC Rf=0.50 (silica gel, ether : CH_2Cl_2 = 1 : 20). mp 183.5—185 °C (C_6H_6). IR: 1660, 1590 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.085 (s, 9H, $Si(CH_3)_3$), 0.133 (s, 9H, $Si(CH_3)_3$), 2.09—2.20 (m, 2H, H-8×2), 2.96—3.08 (m, 2H, H-7×2), 3.146 (d, 1H, J=16.1 Hz, H-10), 3.262 (d, 1H, J=16.1 Hz, H-10), 4.105 (s, 3H, OCH_3-4), 5.964 (s, 1H, OH), 7.286 (dd, 1H, J=8.1, 1.5 Hz, H-3), 7.528 (t, 1H, J=8.1 Hz, H-2), 7.621 (s, 1H, H-11), 7.973 (dd, 1H, J=8.1, 1.5 Hz, H-1), 8.425 (s, 1H, OH). MS *m/z*: 500 [$(M-H_2O)^+$]. *Anal.* Calcd for $C_{29}H_{34}O_5Si_2$: C, 67.15; H, 6.61. Found: C, 66.97; H, 6.52. **28b**, TLC Rf=0.33 (*vide supra*). mp 163—165 °C (C_6H_6). IR: 1665, 1595 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.069 (s, 9H,

$Si(CH_3)_3$), 0.122 (s, 9H, $Si(CH_3)_3$), 2.09—2.19 (m, 2H, H-8 × 2), 2.97—3.09 (m, 2H, H-7 × 2), 3.113 (d, 1H, J = 16.2 Hz, H-10), 3.269 (d, 1H, J = 16.2 Hz, H-10), 4.103 (s, 3H, OCH_3-4), 5.953 (s, 1H, OH), 7.284 (dd, 1H, J = 8.0, 1.2 Hz, H-3), 7.529 (t, 1H, J = 8.0 Hz, H-2), 7.615 (s, 1H, H-11), 7.971 (d, 1H, J = 8.0, 1.2 Hz, H-1), 8.470 (s, 1H, OH). MS m/z: 500 [$(M-H_2O)^+$]. Exact MS Calcd for $C_{29}H_{32}O_4Si_2$ [$(M-H_2O)^+$]: 500.1839. Found: 500.1830.

(±)-6,9-Dihydroxy-4-methoxy-9-(trimethylsilyl)ethynyl-7,8,9,10-tetrahydronaphthacene-5,12-dione (27)——A solution of (trimethylsilyl)ethynylcerium(III) chloride in THF, prepared from anhydrous $CeCl_3$ (108 mg, 0.44 mmol), (trimethylsilyl)acetylene (0.06 ml, 0.44 mmol), and *n*-BuLi (1.6 N, 0.21 ml, 0.34 mmol) in anhydrous THF (2 ml) by the same procedure as described for the preparation of **20**, was added to a solution of **13** (25.6 mg, 0.080 mmol) in anhydrous CH_2Cl_2 (10 ml) at −78 °C over 3 h. After being stirred for 1 h under the same conditions, the reaction mixture was worked up as usual and purified by prep. TLC (MeOH : CH_2Cl_2 = 1 : 100) to give a 59% yield (20 mg) of **27** as yellow crystals and a 37% yield (9.6 mg) of recovered **13**: mp 203.5—205 °C ($CHCl_3$). IR: 1665, 1625, 1590 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.131 (s, 9H, $Si(CH_3)_3$), 2.12—2.15 (m, 2H, H-8 × 2), 2.93—3.05 (m, 2H, H-7 × 2), 3.117 (d, 1H, J = 17.5 Hz, H-10), 3.259 (d, 1H, J = 17.5 Hz, H-10), 4.072 (s, 3H, OCH_3-4), 7.348 (dd, 1H, J = 8.0, 1.2 Hz, H-3), 7.498 (s, 1H, H-11), 7.728 (t, 1H, J = 8.0 Hz, H-2), 7.958 (dd, 1H, J = 8.0, 1.2 Hz, H-1), 13.387 (s, 1H, OH-6). Exact MS Calcd for $C_{24}H_{24}O_5Si$: 420.1390. Found: 420.1378.

(±)-9-[1,1-(Ethylenedioxy)ethyl]-6,9-dihydroxy-7,8,9,10-tetrahydronaphthacene-5,12-dione (29)——A mixture of **14** (120 mg, 0.36 mmol), ethylene glycol (0.2 ml, 3.6 mmol), and *p*-toluenesulfonic acid (10 mg) in C_6H_6 (8 ml) was refluxed for 3 h with azeotropic removal of water formed using a Dean–Stark apparatus. After cooling, the mixture was partitioned between CH_2Cl_2 (20 ml) and saturated aqueous $NaHCO_3$ (10 ml), and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (15 ml × 2), and the combined organic layer was washed with brine, dried, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (ether : CH_2Cl_2 = 1 : 20 to 1 : 5) to give a quantitative yield (135 mg) of **29** as yellow crystals: mp 215.5—216.5 °C (CH_2Cl_2). IR (KCl): 3440, 1665, 1625, 1590, 1575 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.44 (s, 3H, H-14 × 3), 1.7—2.2 (m, 2H, H-8 × 2), 2.7—3.3 (m, 4, H-7 × 2 and H-10 × 2), 4.06 (s, 4H, OCH_2CH_2O), 7.52 (s, 1H, H-11), 7.7—7.85 (m, 2H, H-2 and H-3), 8.15—8.35 (m, 2H, H-1 and H-4), 12.97 (s, 1H, OH-6). Exact MS Calcd for $C_{22}H_{20}O_6$: 380.1260. Found: 380.1265.

(±)-9-[1,1-(Ethylenedioxy)ethyl]-6,9-dihydroxy-4-methoxy-7,8,9,10-tetrahydronaphthacene-5,12-dione (30)——By the same procedure as described for the preparation of **29**, a quantitative yield (62 mg) of **30** was obtained from **15** (55 mg, 0.15 mmol) as yellow crystals: mp 267—270 °C ($CHCl_3$–*n*-hexane) (lit.[7a] 258—260 °C). IR: 1665, 1625, 1585 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.43 (s, 3H, H-14 × 3), 1.9—2.1 (m, 2H, H-8 × 2), 2.8—3.2 (m, 4H, H-7 × 2 and H-10 × 2), 4.07 (s, 7H, OCH_3-4 and OCH_2CH_2O), 7.33 (dd, 1H, J = 8, 1.5 Hz, H-3), 7.52 (s, 1H, H-11), 7.71 (t, 1H, J = 8 Hz, H-2), 7.95 (dd, 1H, J = 8, 1.5 Hz, H-1), 13.38 (s, 1H, OH-6). MS m/z: 410 (M^+).

(±)-9-[(1,1-Ethylenedioxy)ethyl]-*cis*-6,7,9-trihydroxy-7,8,9,10-tetrahydronaphthacene-5,12-dione (31)——Under a nitrogen atmosphere, a mixture of **29** (105 mg, 0.28 mmol), NBS (54 mg, 0.30 mmol), and AIBN (23 mg, 0.14 mmol) in anhydrous CCl_4 (55 ml) was heated at 80 °C for 35 min. After ice-cooling under a nitrogen atmosphere, silica gel (for column chromatography, 15 g) and ice-cooled wet THF (containing about 3% water, 15 ml) were successively added to the reaction mixture and stirred at room temperature for 1.5 h. Silica gel was separated by suction filtration and washed several times with MeOH–CH_2Cl_2 (1 : 10). The combined organic layer was concentrated *in vacuo*, and the residue was dissolved in CH_2Cl_2. This solution was washed twice with water, dried, and concentrated *in vacuo* to give crude **31**, which was purifed by column chromatography on silica gel (ether : CH_2Cl_2 = 1 : 5 to MeOH : ether : CH_2Cl_2 = 1 : 10 : 50) to give a 77% yield (85 mg) of pure **31**: mp 230—231 °C ($CHCl_3$). IR (KCl): 3350, 1665, 1625, 1595, 1575 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.468 (s, 3H, H-14 × 3), 2.046 (dd, 1H, J = 14.7, 5.1 Hz, H-8ax), 2.483 (ddd, 1H, J = 14.7, 2.0, 1.5 Hz, H-8eq), 3.095 (d, 1H, J = 17.6 Hz, H-10ax), 3.128 (dd, 1H, J = 17.6, 1.5 Hz, H-10eq), 4.03—4.13 (m, 4H, OCH_2CH_2O), 5.329 (m, 1H, $v_{1/2}$ = 9.5 Hz, H-7eq), 7.664 (s, 1H, H-11), 7.80—7.85 (m, 2H, H-2 and H-3), 8.29—8.34 (m, 2H, H-1 and H-4), 13.275 (s, 1H, OH-6). Exact MS Calcd for $C_{22}H_{20}O_7$: 396.1207. Found: 396.1204.

(±)-9-[(1,1-Ethylenedioxy)ethyl]-6-hydroxy-*cis*-7,9-isopropylidenedioxy-7,8,9,10-tetrahydronaphthacene-5,12-dione (32)——Under a nitrogen atmosphere, a mixture of **31** (21.0 mg, 0.053 mmol), 2-methoxypropene (0.2 ml), and pyridinium *p*-toluenesulfonate (2 mg) in anhdrous CH_2Cl_2 (3 ml) was stirred at room temperature for 40 min. The mixture was partitioned between CH_2Cl_2 (5 ml) and saturated aqueous $NaHCO_3$ (3 ml), and the separated organic layer was washed with water, dried, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (CH_2Cl_2) to give a 74% yield of **32** (17.1 mg) as yellow crystals: mp 210—215 °C (C_6H_6–*n*-hexane). IR: 1670, 1630, 1595 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.02, 1.44, and 1.53 (s × 3, 3H × 3, H-14 × 3 and $C(CH_3)_2$), 1.72 (dd, 1H, J = 13, 3 Hz, H-8), 2.67 (dd, 1H, J = 13, 3 Hz, H-8), 3.14 (br s, 2H, H-10 × 2), 4.06 (br s, 4H, OCH_2CH_2O), 5.51 (t, 1H, J = 3 Hz, H-7), 7.58 (s, 1H, H-11), 7.7—7.9 (m, 2H, H-2 and H-3), 8.2—8.4 (m, 2H, H-1 and H-4), 13.12 (s, 1H, OH-6). MS m/z: 436 (M^+). *Anal.* Calcd for $C_{25}H_{24}O_7$: C, 68.80; H, 5.54. Found: C, 68.77; H, 5.44.

(±)-9-Acetyl-6-hydroxy-5,12-dioxo-7,8,9,10-tetrahydronaphthacene-*cis*-7,9-diyl Phenylboronate (33)——Under a nitrogen atmosphere, a mixture of **31** (17.2 mg, 0.043 mmol) and benzeneboronic acid (16 mg, 0.13 mmol) in CF_3CO_2H (0.5 ml) and anhydrous toluene (0.5 ml) was stirred at 0 °C for 3 h, gradually warmed to room temperature, and stirred for an additional 10 h. The reaction mixture was concentrated *in vacuo* at room temperature to give a

residue, to which an ice-cooled mixture of CH_2Cl_2 (3 ml) and saturated aqueous $NaHCO_3$ (2 ml) was added. The organic layer was separated, washed twice with water, dried, and concentrated *in vacuo* to give crude **33** (25 mg) as orange crystals; this product was used for the next step without further purification. Analytically pure **33** was obtained by recrystallization from C_6H_6–*n*-hexane: mp 261—265 °C (dec.). IR: 1720, 1670, 1635, 1595, 1570 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.3—2.4 (m, 2H, H-8 × 2), 2.55 (s, 3H, H-14 × 3), 3.28 (d, 1H, J = 18.5 Hz, 10-H), 3.52 (d, 1H, J = 18.5 Hz, 10-H), 5.84 (t, 1H, J = 2.5 Hz, H-7), 7.3—7.45 (m, 3H, ArH × 3), 7.63 (s, 1H, H-11), 7.75—7.9 (m, 4H, ArH × 4), 8.2—8.4 (m, 2H, H-1 and H-4), 13.23 (s, 1H, OH-6). MS *m/z*: 437 (M^+), 438 (M^+). *Anal.* Calcd for $C_{26}H_{19}BO_6$: C, 71.26; H, 4.37. Found: C, 71.40; H, 4.28.

(±)-4-Demethoxy-11-deoxydaunomycinone (8)——Crude **33** (25 mg) obtained above was stirred in a mixture of 2-methyl-2,4-pentanediol (0.2 ml), AcOH (0.1 ml), CH_2Cl_2 (1.5 ml), and acetone (1.5 ml) at room temperature for 46 h. This mixture was poured into an ice-cooled mixture of CH_2Cl_2 (10 ml) and saturated aqueous $NaHCO_3$ (5 ml). The organic layer was separated, washed with water, dried, and concentrated *in vacuo*. The residue was washed with *n*-pentane (15 ml × 2) and purified by prep. TLC (ether : CH_2Cl_2 = 1 : 5) to give an 83% yield (12.7 mg) of **8** as yellow crystals: mp 201—208 °C (CH_2Cl_2) [lit.[4] 199—207 °C (dec.)]. IR (KCl): 3600—3100, 1720, 1665, 1630, 1590, 1575 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 2.200 (dd, 1H, J = 14.7, 5.1 Hz, H-8ax), 2.380 (dt, 1H, J = 14.7, 2.2 Hz, H-8eq), 2.430 (s, 3H, H-14 × 3), 3.029 (dd, 1H, J = 17.6, 2.2 Hz, H-10eq), 3.284 (d, 1H, J = 17.6 Hz, H-10ax), 5.36 (m, 1H, $\nu_{1/2}$ = 12 Hz, H-7eq), 7.643 (s, 1H, H-11), 7.81—7.86 (m, 2H, H-2 and H-3), 8.29—8.34 (m, 2H, H-1 and H-4), 13.273 (s, 1H, OH-6). Exact MS Calcd for $C_{20}H_{16}O_6$: 352.0947. Found: 352.0948.

(±)-9-[(1,1-Ethylenedioxy)ethyl]-*cis*-6,7,9-trihydroxy-4-methoxy-7,8,9,10-tetrahydronaphthacene-5,12-dione (34)——Similarly to the procedure described for the preparation of **31**, **30** (81 mg, 0.20 mmol) was treated with NBS (39 mg, 0.22 mmol) and AIBN (16 mg, 0.10 mmol) in anhydrous CCl_4 (50 ml), and then with silica gel (15 g) in wet THF (25 ml) to give a mixture (15 : 1, determined from the ^{1}H-NMR spectral data) of **34** and its C-7 epimer, the *trans*-7,9-diol, in 81% yield (69 mg); mp 180—222 °C. This product was used for the next step without further purification. Analytically pure **34** was obtained by recrystallization from CH_2Cl_2: mp 220—222 °C. IR: 1665, 1625, 1600 (sh), 1585 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.455 (s, 3H, H-14 × 3), 2.018 (dd, 1H, J = 14.7, 5.1 Hz, H-8ax), 2.454 (ddd, 1H, J = 14.7, 2.2, 1.5 Hz, H-8eq), 3.047 (d, 1H, J = 17.6 Hz, H-10ax), 3.093 (dd, 1H, J = 17.6, 1.5 Hz, H-10eq), 4.03—4.10 (m, 4H, OCH_2CH_2O), 4.075 (s, 3H, OCH_3-4), 5.316 (m, 1H, $\nu_{1/2}$ = 9 Hz, H-7eq), 7.362 (dd, 1H, J = 8.0, 1.0 Hz, H-3), 7.579 (s, 1H, H-11), 7.743 (t, 1H, J = 8.0 Hz, H-2), 7.954 (dd, 1H, J = 8.0, 1.0 Hz, H-1), 13.610 (s, 1H, OH-6). Exact MS Calcd for $C_{23}H_{22}O_8$: 426.1312. Found: 426.1299. Characteristic ^{1}H-NMR (500 MHz, $CDCl_3$) data of the C-7 epimer, (±)-9-[(1,1-ethylenedioxy)ethyl]-*trans*-6,7,9-trihydroxy-4-methoxy-7,8,9,10-tetrahydronaphthacene-5,12-dione measured on a mixture of **34** and this compound were as follows: δ: 1.433 (s, 3H, H-14 × 3), 1.935 (dd, 1H, J = 13.0, 10.5 Hz, H-8ax), 2.502 (ddd, 1H, J = 13.0, 7.5, 2.5 Hz, H-8eq), 2.905 (dd, 1H, J = 17.0, 2.5 Hz, H-10eq), 3.171 (d, 1H, J = 17.0 Hz, H-10ax), 5.364 (m, 1H, $\nu_{1/2}$ = 18 Hz, H-7ax), 7.563 (s, 1H, H-11), 13.921 (s, 1H, OH-6).

(±)-9-Acetyl-6-hydroxy-4-methoxy-5,12-dioxo-7,8,9,10-tetrahydronaphthacene-cis-7,9-diyl Phenylboronate (35)——By the same procedure as described for the preparation of **33**, a mixture (15 : 1) of **34** and its C-7 epimer (21 mg, 0.049 mmol) was treated with benzeneboronic acid (12 mg, 0.099 mmol) to give crude **35** (30 mg), which was recrystallized from C_6H_6–*n*-hexane to give pure **35** in 61% yield (14 mg) as yellow crystals: mp 243—247 C. IR: 1710, 1665, 1625, 1660, 1585 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.25—2.4 (m, 2H, H-8 × 2), 2.55 (s, 3H, H-14 × 3), 3.24 (d, 1H, J = 18.5 Hz, H-10), 3.48 (d, 1H, J = 18.5 Hz, H-10), 4.07 (s, 3H, OCH_3-4), 5.83 (t, 1H, J = 2.7 Hz, H-7), 7.25—8.0 (m, 9H, ArH × 9), 13.57 (s, 1H OH-6). MS *m/z*: 467 (M^+), 468 (M^+). Exact MS Calcd for $C_{27}H_{21}BO_7$: 468.1377. Found: 468.1370.

(±)-11-Deoxydaunomycinone (9)——By the same procedure as described for the preparation of **8**, **35** (2.0 mg, 0.0043 mmol) was treated with 2-methyl-2,4-pentanediol (0.04 ml) and AcOH (0.01 ml) to give pure **9** in quantitative yield (1.6 mg) after usual work-up. An analytically pure sample was obtained by recrystallization from $ClCH_2CH_2Cl$ as yellow crystals: mp 250—251 °C (dec.) (lit.[7a,d] 210—213 °C, lit.[5] 213—215 °C. IR (KCl): 3480, 1700, 1665, 1620, 1580 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 2.180 (dd, 1H, J = 15.0, 5.0 Hz, H-8ax), 2.376 (ddd, 1H, J = 15.0, 2.5, 2.0 Hz, H-8eq), 2.426 (s, 3H, H-14 × 3), 3.018 (dd, 1H, J = 17.5, 2.5 Hz, H-10eq), 3.270 (d, 1H, J = 17.5 Hz, H-10ax), 4.099 (s, 3H, OCH_3-4), 5.382 (m, 1H, $\nu_{1/2}$ = 11 Hz, H-7eq), 7.396 (d, 1H, J = 8.0 Hz, H-3), 7.617 (s, 1H, H-11), 7.779 (t, 1H, J = 8.0 Hz, H-2), 7.989 (d, 1H, J = 8.0 Hz, H-1), 13.690 (s, 1H, OH-6). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 2.039 (dd, 1H, J = 14, 5 Hz, H-8), 2.142 (br d, 1H, J = 14 Hz, H-8), 2.282 (s, 3H, H-14 × 3), 3.042 (d, 1H, J = 17.5 Hz, H-10), 3.155 (d, 1H, J = 17.5 Hz, H-10), 3.991 (s, 3H, OCH_3-4), 5.111 (m, 1H, $\nu_{1/2}$ = 16 Hz, H-7eq), 7.469 (s, 1H, H-11), 7.647 and 7.833 (d × 2, 1H × 2, each J = 8 Hz, H-1 and H-3), 7.892 (t, 1H, J = 8 Hz, H-2), 13.596 (s, 1H, OH-6). Exact MS Calcd for $C_{21}H_{18}O_7$: 382.1050. Found: 382.1037.

(−)-4′-*O*-*p*-Nitrobenzoyl-3′-*N*-trifluoroacetyl-4-demethoxy-11-deoxydaunomycin (36) and Its (7*R*,9*R*) Diastereomer (38)——Under a nitrogen atmosphere, TMSOTf (0.014 ml, 0.074 mmol) was added to a stirred suspension of molecular sieves 4A (0.4 g) and **37** (20.0 mg, 0.037 mmol) in anhydrous CH_2Cl_2 (6 ml) and anhydrous ether (2 ml) at −40 °C. The mixture was stirred at −5 °C for 1 h and cooled to −15 °C, then a solution of (±)-**8** (10.0 mg, 0.028 mmol) in anhydrous CH_2Cl_2 (5 ml) was added. After being stirred for 4 h under the same conditions, the mixture was poured into a vigorously stirred mixture of AcOEt (8 ml) and saturated aqueous $NaHCO_3$ (16 mg). The

organic layer was separated and the aqueous layer was extracted with AcOEt (8 ml). The combined organic layer was washed twice with brine, dried, and concentrated *in vacuo*. Purification of the residue by prep. TLC (AcOEt : C_6H_6 = 1 : 4) gave a 46% yield (9.6 mg) of **36** and a 49% yield (10.1 mg) of **38**, each as yellow crystals: **36**, mp 162—164 °C (C_6H_6); $[\alpha]_D^{20}$ −123° (*c* = 0.08, acetone) [lit.[4] mp 153—156 °C; $[\alpha]_D^{24}$ −125° (*c* = 0.2, acetone)]. IR: 1730, 1670, 1630, 1610, 1595, 1570, 1530 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.278 (d, 3H, *J* = 6.6 Hz, H-6′ × 3), 2.074 (td, 1H, *J* = 13.2, 3.7 Hz, H-2′ax), 2.121 (br dd, 1H, *J* = 13.2, 5.5 Hz, H-2′eq), 2.230 (dd, 1H, *J* = 14.7, 4.4 Hz, H-8ax), 2.394 (ddd, 1H, *J* = 14.7, 2.2, 1.5 Hz, H-8eq), 2.434 (s, 3H, H-14 × 3), 3.158 (dd, 1H, *J* = 17.6, 1.5 Hz, H-10eq), 3.313 (d, 1H, *J* = 17.6 Hz, H-10ax), 4.474 (br q, 1H, *J* = 6.6 Hz, H-5′ax) 4.513 (m, 1H, $\nu_{1/2}$ = 28 Hz, H-3′ax), 5.377 (dd, 1H, *J* = 4.4, 2.2 Hz, H-7eq), 5.511 (d, 1H, *J* = 2.0 Hz, H-4′eq), 5.695 (d, 1H, *J* = 3.7 Hz, H-1′eq), 6.246 (d, 1H, *J* = 7.3 Hz, NH-3′), 7.682 (s, 1H, H-11), 7.83—7.87 (m, 2H, H-2 and H-3), 8.28—8.38 (m, 2H, H-1 and H-4), 8.297 (d, 2H, *J* = 8.8 Hz, ArH × 2), 8.364 (d, 2H, *J* = 8.8 Hz, ArH × 2), 13.367 (s, 1H, OH-6). FAB-MS (negative) *m/z*: 725 [(M − H)$^-$]. CD (MeOH) $[\theta]_{max}$ (nm): -5.32×10^4 (268), $+0.66 \times 10^4$ (339). **38**, mp 165—169 °C (C_6H_6), $[\alpha]_D^{20}$ −240° (*c* = 0.03, acetone) [lit.[4] mp 148—152 C; $[\alpha]_D^{25}$ −225° (*c* = 0.2, acetone)]. IR: 1735, 1670, 1630, 1610, 1590, 1575, 1530 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.267 (d, 3H, *J* = 6.6 Hz, H-6′ × 3), 1.997 (br dd, 1H, *J* = 13.2, 4.4 Hz, H-2′eq), 2.030 (dd, 1H, *J* = 15.4, 2.9 Hz, H-8ax), 2.147 (td, 1H, *J* = 13.2, 3.7 Hz, H-2′ax), 2.396 (s, 3H, H-14 × 3), 2.505 (ddd, 1H, *J* = 15.4, 2.2, 1.0 Hz, H-8eq), 3.238 (br d, 1H, *J* = 17.6 Hz, H-10eq), 3.312 (d, 1H, *J* = 17.6 Hz, H-10ax), 4.600 (m, 1H, $\nu_{1/2}$ = 27 Hz, H-3′ax), 4.717 (br q, 1H, *J* = 6.6 Hz, H-5′ax), 5.422 (br s, 1H, H-4′eq), 5.530 (d, 1H, *J* = 3.7 Hz, H-1′eq), 5.634 (dd, 1H, *J* = 2.9, 2.2 Hz, H-7eq), 6.348 (d, 1H, *J* = 7.3 Hz, NH-3′), 7.690 (s, 1H, H-11), 7.83—7.90 (m, 2H, H-2 and H-3), 8.25—8.39 (m, 2H, H-1 and H-4), 8.293 (d, 2H, *J* = 8.8 Hz, ArH × 2), 8.354 (d, 2H, *J* = 8.8 Hz, ArH × 2), 13.480 (s, 1H, OH-6). FAB-MS (negative) *m/z*: 725 [(M − H)$^-$]. CD (MeOH) $[\theta]_{max}$ (nm): $+0.91 \times 10^4$ (273), -0.91×10^4 (338).

(−)-(7*S*,9*S*)-9-[(1,1-Ethylenedioxy)ethyl]-6,9-dihydroxy-4-methoxy-7-[(4′-*O*-*p*-nitrobenzoyl-3′-*N*-trifluoroacetyl-α-L-daunosaminyl)oxy]-7,8,9,10-tetrahydronaphthacene-5,12-dione (40) and Its (7*R*,9*R*) Diastereomer (41)——(i) By the Glycosidation of (±)-**34** with **37** Using TMSOTf: By the same procedure as described for the preparation of **36**, (±)-**34** (19.6 mg, 0.046 mmol) was treated with TMSOTf (0.025 ml, 0.132 mmol), **37** (31.8 mg, 0.058 mmol), and molecular sieves 4A (0.16 g) for 7.5 h. The reaction mixture was worked up as usual and purified by prep. TLC (ether : CH_2Cl_2 = 1 : 10) to give a 22% yield (8.0 mg) of **40** and a 20% yield (7.5 mg) of **41**, each as yellow crystals: **40**, mp 195—199 C (C_6H_6-*n*-hexane); $[\alpha]_D^{20}$ −105 (*c* = 0.04, $CHCl_3$). IR: 1735, 1670, 1625, 1610, 1585, 1530 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.260 (d, 3H, *J* = 6.6 Hz, H-6′ × 3), 1.459 (s, 3H, H-14 × 3), 2.01—2.10 (m, 3H, H-8ax and H-2′ × 2), 2.480 (dt, 1H, *J* = 14.7, 1.5 Hz, H-8eq), 3.068 (d, 1H, *J* = 17.6 Hz, H-10ax), 3.140 (dd, 1H, *J* = 17.6, 1.5 Hz, H-10eq), 4.046 (s, 3H, OCH_3-4), 4.05—4.11 (m, 4H, OCH_2CH_2O), 4.472 (m, 1H, $\nu_{1/2}$ = 29 Hz, H-3′ax), 4.543 (br q, 1H, *J* = 6.6 Hz, H-5′ax), 5.222 (dd, 1H, *J* = 4.0, 1.5 Hz, H-7eq), 5.476 (d, 1H, *J* = 2.0 Hz, H-4′ax), 5.635 (br s, 1H, $\nu_{1/2}$ = 4 Hz, H-1′eq), 6.260 (br d, 1H, *J* = 7.3 Hz, NH-3′), 7.360 (d, 1H, *J* = 8.1 Hz, H-3), 7.574 (s, 1H, H-11), 7.751 (t, 1H, *J* = 8.1 Hz, H-2), 7.957 (d, 1H, *J* = 8.1 Hz, H-1), 8.285 (d, 2H, *J* = 8.8 Hz, ArH × 2), 8.335 (d, 2H, *J* = 8.8 Hz, ArH × 2), 13.636 (s, 1H, OH-6). FAB-MS (negative) *m/z*: 799 [(M − H)$^-$]. CD (MeOH) $[\theta]_{max}$ (nm): -1.81×10^4 (265), $+0.49 \times 10^4$ (332). **41**, mp 179—183 °C (C_6H_6-*n*-hexane); $[\alpha]_D^{20}$ −208° (*c* = 0.05, $CHCl_3$). IR: 1730, 1670, 1625, 1605, 1585, 1530 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.227 (d, 3H, *J* = 6.6 Hz, H-6′ × 3), 1.447 (s, 3H, H-14 × 3), 1.818 (dd, 1H, *J* = 15.4, 3.7 Hz, H-8ax), 1.940 (br dd, 1H, *J* = 13.2, 4.4 Hz, H-2′eq), 2.105 (td, 1H, *J* = 13.2, 3.5 Hz, H-2′ax), 2.635 (dd, 1H, *J* = 15.4, 2.0 Hz, H-8eq), 3.212 (br s, 2H, H-10 × 2), 4.03—4.09 (m, 4H, OCH_2CH_2O), 4.093 (s, 3H, OCH_3-4), 4.567 (m, 1H, $\nu_{1/2}$ = 28 Hz, H-3′ax), 4.774 (br q, 1H, *J* = 6.6 Hz, H-5′ax), 5.399 (d, 1H, *J* = 1.5 Hz, H-4′eq), 5.560 (d, 1H, *J* = 3.5 Hz, H-1′eq), 5.616 (dd, 1H, *J* = 3.7, 2.0 Hz, H-7eq), 6.263 (br d, 1 Hz, *J* = 7.3 Hz, NH-3′), 7.391 (d, 1H, *J* = 8.1 Hz, H-3), 7.609 (s, 1H, H-11), 7.768 (t, 1H, *J* = 8.1 Hz, H-2), 7.978 (d, 1H, *J* = 8.1 Hz, H-1), 8.265 (d, 2H, *J* = 8.8 Hz, ArH × 2), 8.322 (d, 2H, *J* = 8.8 Hz, ArH × 2), 13.829 (s, 1H, OH-6). FAB-MS (negative) *m/z*: 799 [(M − H)$^-$]. CD (MeOH) $[\theta]_{max}$ (nm): $+0.43 \times 10^4$ (285), -0.33×10^4 (334). A 29% yield (5.6 mg) of (±)-**34** was recovered in this reaction.

(ii) By the Glycosidation of (±)-**34** with **42** Using Hg(II) Salts: Under a nitrogen atmosphere, a mixture of (±)-**34** (18.0 mg, 0.042 mmol), $Hg(CN)_2$ (32 mg, 0.13 mmol), $HgBr_2$ (18 mg, 0.050 mmol), and molecular sieves 3A (0.2 g) in freshly distilled anhydrous $CHCl_3$ (6 ml) was stirred at room temperature for 30 min. Then a solution of **42** (0.085 mmol) [prepared from 1,4-di-*O*-*p*-nitrobenzoyl-3-*N*-trifluoroacetyl-L-daunosamine (46 mg, 0.085 mmol) according to the reported method[26]] in freshly distilled anhydrous $CHCl_3$ (4 ml) was added. After being stirred at room temperature for 38 h, the reaction mixture was filtered and the filtrate was successively washed with diluted aqueous KI and water, dried, and concentrated *in vacuo*. Purification of the residue by prep. TLC (ether : CH_2Cl_2 = 1 : 5) to give a 28% yield (9.4 mg) of **40** and a 28% yield (9.3 mg) of **41**. These products were identical with the authentic samples obtained by procedure (i).

(−)-4′-*O*-*p*-Nitrobenzoyl-3′-*N*-trifluoroacetyl-11-deoxydaunomycin (43)——**40** (3.1 mg, 0.039 mmol) was stirred in aqueous 80% AcOH (0.5 ml) at 45 C. After 40 h, the formation of a trace amount of **9** was observed by TLC (silica gel, ether : CH_2Cl_2 = 1 : 5) analysis and the reaction mixture was diluted with CH_2Cl_2 (10 ml), washed successively with saturated aqueous $NaHCO_3$ and brine, dried, and concentrated *in vacuo*. Purification of the residue by prep. TLC (ether : CH_2Cl_2 = 1 : 10) gave a 41% yield (1.2 mg) of **43** as yellow crystals: mp 174.5—177.5 °C (C_6H_6-*n*-hexane); $[\alpha]_D^{20}$ −81° (*c* = 0.05, $CHCl_3$). IR: 1730 (sh), 1720, 1665, 1625, 1585, 1530 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.259

(d, 3H, J=6.6 Hz, H-6′×3), 2.01—2.08 (m, 2H, H-2′×2), 2.212 (dd, 1H, J=14.7, 4.0 Hz, H-8ax), 2.367 (dt, 1H, J=14.7, 2.0 Hz, H-8eq), 2.418 (s, 3H, H-14×3), 3.116 (dd, 1H, J=18.3, 2.0 Hz, H-10eq), 3.273 (d, 1H, J=18.3 Hz, H-10ax), 4.090 (s, 3H, OCH_3-4), 4.452 (br q, 1H, J=6.6 Hz, H-5′ax), 4.485 (m, 1H, $\nu_{1/2}$=25 Hz, H-3′ax), 5.356 (dd, 1H, J=4.0, 2.0 Hz, H-7eq), 5.502 (d, 1H, J=2.0 Hz, H-4′eq), 5.682 (br s, 1H, $\nu_{1/2}$=4 Hz, H-1′eq), 6.192 (br d, 1H, J=7.3 Hz, NH-3′), 7.394 (d, 1H, J=8.8 Hz, H-3), 7.605 (s, 1H, H-11), 7.781 (t, 1H, J=8.8 Hz, H-2), 7.988 (d, 1H, J=8.8 Hz, H-1), 8.285 (d, 2H, J=8.8 Hz, ArH×2), 8.354 (d, 2H, J=8.8 Hz, ArH×2), 13.739 (s, 1H, OH-6). FAB-MS (negative) m/z: 755 [$(M-H)^-$]. CD (MeOH) $[\theta]_{max}$ (nm): -3.24×10^4 (266), $+0.80\times10^4$ (331). A 52% yield (1.6 mg) of **40** was recovered in this reaction.

(−)-4′-*O*-*p*-Nitrobenzoyl-3′-*N*-trifluoroacetyl-7,9-bis-*epi*-11-deoxydaunomycin (44)——By the same procedure as described for the preparation of **43**, a 53% yield (5.2 mg) of **44** was obtained from **41** (10.3 mg, 0.013 mmol) as yellow crystals: mp 170—174 °C (C_6H_6–*n*-hexane): $[\alpha]_D^{20}$ −202° (c=0.03, $CHCl_3$). IR: 1735 (sh), 1725, 1670, 1625, 1605, 1585, 1530 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.253 (d, 3H, J=6.6 Hz, H-6′×3), 1.988 (dd, 1H, J=13.2, 4.5 Hz, H-2′eq), 2.015 (dd, 1H, J=15.4, 3.5 Hz, H-8ax), 2.134 (td, 1H, J=13.2, 3.7 Hz, H-2′ax), 2.390 (s, 1H, H-14×3), 2.486 (dt, 1H, J=15.4, 1.5 Hz, H-8eq), 3.207 (dd, 1H, J=17.6, 1.5 Hz, H-10eq), 3.286 (d, 1H, J=17.6 Hz, H-10ax), 4.114 (s, 3H, OCH_3-4), 4.583 (m, 1H, $\nu_{1/2}$=27 Hz, H-3′ax), 4.742 (br q, 1H, J=6.6 Hz, H-5′ax), 5.384 (br s, 1H, H-4′eq), 5.512 (d, 1H, J=3.7 Hz, H-1′eq), 5.648 (dd, 1H, J=3.5, 1.5 Hz, H-7eq), 6.345 (br d, 1H, J=7.3 Hz, NH-3′), 7.415 (d, 1H, J=8.1 Hz, H-3), 7.624 (s, 1H, H-11), 7.797 (t, 1H, J=8.1 Hz, H-2), 8.003 (d, 1H, J=8.1 Hz, H-1), 8.292 (d, 2H, J=8.8 Hz, ArH×2), 8.355 (d, 2H, J=8.8 Hz, ArH×2), 13.870 (s, 1H, OH-6). FAB-MS (negative) m/z: 755 [$(M-H)^-$]. CD(MeOH) $[\theta]_{max}$ (nm): $+0.96\times10^4$ (287), -0.60×10^4 (335). A 37% yield (3.8 mg) of **41** was recovered in this reaction.

(+)-3′-*N*-Trifluoroacetyl-11-deoxydaunomycin (45)——Under a nitrogen atmosphere, 0.1 N NaOH (0.082 ml, 0.0082 mmol) was added to an ice-cooled solution of **43** (6.2 mg. 0.0082 mmol) in CH_2Cl_2 (0.05 ml) and MeOH (3 ml). The reaction mixture was stirred at 0 °C for 20 min, then one drop of AcOH was added. The resulting mixture was partitioned between AcOEt (10 ml) and brine (5 ml) and the separated organic layer was washed with brine, dried, and concentrated *in vacuo*. Purification of the residue by prep. TLC (ether : CH_2Cl_2 = 1 : 1) gave an 82% yield (4.1 mg) of **45** as yellow crystals: mp 151—155 °C (C_6H_6–*n*-hexane); $[\alpha]_D^{20}$ +86° (c=0.05, $CHCl_3$). IR: 1720, 1670, 1625, 1585, 1530 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.320 (d, 3H, J=6.6 Hz, H-6′×3), 1.831 (td, 1H, J=13.2, 4.0 Hz, H-2′ax), 1.994 (dd, 1H, J=13.2, 5.1 Hz, H-2′eq), 2.330 (dd, 1H, J=14.7, 4.4 Hz, H-8ax), 2.351 (dt, 1H, J=14.7, 2.0 Hz, H-8eq), 2.405 (s, 3H, H-14×3), 3.105 (dd, 1H, J=17.6, 2.0 Hz, H-10eq), 3.269 (d, 1H, J=17.6 Hz, H-10ax), 4.090 (s, 3H, OCH_3-4), 4.237 (m, 1H, $\nu_{1/2}$=30 Hz, H-3′ax), 4.286 (br q, 1H, J=6.6 Hz, H-5′ax), 4.307 (s, 1H, H-4′eq), 5.298 (dd, 1H, J=4.4, 2.0 Hz, H-7eq), 5.515 (d, 1H, J=4.0 Hz, H-1′eq), 6.636 (br d, 1H, J=8.8 Hz, NH-3′), 7.392 (d, 1H, J=8.1 Hz, H-3), 7.599 (s, 1H, H-11), 7.778 (t, 1H, J=8.1 Hz, H-2), 7.989 (d, 1H, J=8.1 Hz, H-1), 13.691 (s, 1H, OH-6). FAB-MS (negative) m/z: 606 [$(M-H)^-$]. CD (MeOH) $[\theta]_{max}$ (nm): -1.10×10^4 (286), $+0.74\times10^4$ (333).

(+)-11-Deoxydaunomycin (6)——Under a nitrogen atmosphere, **45** (2.0 mg, 0.0033 mmol) was stirred in 0.1 N NaOH (0.4 ml) at room temperature for 20 min. The mixture was diluted with CH_2Cl_2 (5 ml) and neutralized to pH about 8 with 0.1 N HCl under ice-cooling and vigorous stirring. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (5 ml×3). The combined organic layer was washed with water, dried with anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification of the residue by prep. TLC (Et_3N : MeOH : CH_2Cl_2 = 1 : 100 : 1000) gave a 95% yield (1.6 mg) of **6** as yellow crystals. Treatment of **6** with an equimolar amount of 0.1 N HCl in a mixture (9 : 1) of $CHCl_3$ and MeOH gave **6**·HCl as yellow crystals mp 215—220 °C (dec.), mmp 197—210 °C (dec.)[37]; $[\alpha]_D^{20}$ +135° (c=0.01, MeOH) [lit.[5] mp 175—176 °C (dec.); $[\alpha]_D^{23}$ +139° (c=0.2, MeOH)]. IR (KCl): 3600—2500, 1710, 1670, 1625, 1585 cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 1.162 (d, 3H, J=6.6 Hz, H-6′×3), 1.689 (dd, 1H, J=13, 4.5 Hz, H-2′eq), 1.890 (td, 1H, J=13, 3.5 Hz, H-2′ax), 2.122 (dd, 1H, J=14, 4 Hz, H-8), 2.21—2.26 (m, 1H, H-8), 2.235 (s, 3H, H-14×3), 2.998 (d, 1H, J=17 Hz, H-10), 3.160 (d, 1H, J=17 Hz, H-10), 3.2—3.4 (m, 1H, H-3′ax, overlapped by H_2O signal), 3.548 (m, 1H, $\nu_{1/2}$=10 Hz, H-4′eq), 3.990 (s, 3H, OCH_3-4), 4.150 (q, 1H, J=6.6 Hz, H-5′ax), 5.003 (dd, 1H, J=5.5, 4 Hz, H-7eq), 5.295 (br d, 1H, J=3.5 Hz, H-1′eq), 7.466 (s, 1H, H-11), 7.649 (d, 1H, J=8 Hz, H-3), 7.830 (d, 1H, J=8 Hz, H-1), 7.898 (t, 1H, J=8 Hz, H-2), 13.638 (s, 1H, OH-6). CD (MeOH) $[\theta]_{max}$ (nm): -0.85×10^4 (286), $+0.66\times10^4$ (332).

(+)-(7*S*,9*S*)-7-*O*-(3′,4′-Di-*O*-acetyl-2′-deoxy-β-D-*erythro*-pentopyranosyl)-4-demethoxy-11-deoxydaunomycinone (47) and Its (7*R*,9*R*) Diastereomer (48)——Under a nitrogen atmosphere, a mixture of (±)-**8** (10.0 mg, 0.028 mmol), yellow HgO (15.2 mg, 0.070 mmol), $HgBr_2$ (12.1 mg, 0.034 mmol), and molecular sieves 4A (0.5 g) in anhydrous CH_2Cl_2 (10 ml) was stirred at room temperature for 1 h. Then a solution of **46** (0.071 mmol) [prepared from 1,3,4-tri-*O*-acetyl-2-deoxy-D-*erythro*-pentopyranose[28] (15.9 mg, 0.071 mmol) similarly to the reported method[26]] in anhydrous CH_2Cl_2 (5 ml) was added. Under stirring at room temperature, the same amounts of yellow HgO, $HgBr_2$, molecular sieves 4A, and **46** as described above were added to the reaction mixture twice every 15 h. After 40 h, the mixture was worked up as described for the preparation of **40** (procedure ii) to give a 19% yield (3.0 mg) of **47** and a 19% yield (3.1 mg) of **48**, each as yellow crystals: **47**, mp 107.5—108.5 °C (C_6H_6–*n*-hexane); $[\alpha]_D^{20}$ +50° (c=0.12, $CHCl_3$). IR: 1740, 1720 (sh), 1670, 1630, 1595, 1575 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.908 (br d, 1H, J=13.2 Hz, H-2′eq), 2.014 (s, 3H, $OCOCH_3$), 2.137 (s, 3H, $OCOCH_3$), 2.143 (dd, 1H, J=14.7, 4.4 Hz, H-8ax), 2.170 (ddd, 1H, J=13.2, 10.0, 3.7 Hz, H-2′ax), 2.417 (s, 3H, H-14×3), 2.465 (ddd, 1H, J=14.7, 2.2, 1.5 Hz, H-8eq), 3.115 (dd, 1H, J=18.3,

1.5 Hz, H-10eq), 3.283 (d, 1H, J=18.3 Hz, H-10ax), 3.886 (dd, 1H, J=13.0, 4.0 Hz, H-5′), 4.111 (dd, 1H, J=13.0, 2.0 Hz, H-5′), 5.15—5.20 (m, 2H, H-3′ax and H-4′eq), 5.317 (dd, 1H, J=4.4, 2.2 Hz, H-7eq), 5.539 (dd, 1H, J=3.7, 2.9 Hz, H-1′eq), 7.648 (s, 1H, H-11), 7.81—7.85 (m, 2H, H-2 and H-3), 8.30—8.34 (m, 2H, H-1 and H-4), 13.300 (s, 1H, OH-6). MS m/z: 552 (M^+). CD (MeOH) $[\theta]_{max}$ (nm): -1.64×10^4 (282), $+0.50\times10^4$ (336). **48**, mp 115—116 °C (C_6H_6–*n*-hexane); $[\alpha]_D^{20}$ −257° (c=0.08, $CHCl_3$). IR: 1745, 1720, 1670, 1635, 1595, 1575 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.831 (br d, 1H, J=13.2 Hz, H-2′eq), 1.969 (dd, 1H, J=14.7, 3.7 Hz, H-8ax), 1.974 (s, 3H, $OCOCH_3$), 2.156 (s, 3H, $OCOCH_3$), 2.266 (ddd, 1H, J=13.2, 11.7, 3.7 Hz, H-2′ax), 2.383 (s, 3H, H-14×3), 2.462 (ddd, 1H, J=14.7, 2.2, 1.5 Hz, H-8eq), 3.192 (dd, 1H, J=18.3, 1.5 Hz, H-10eq), 3.288 (d, 1H, J=18.3 Hz, H-10ax), 3.808 (dd, 1H, J=13.0, 2.2 Hz, H-5′), 4.426 (d, 1H, J=13.0 Hz, H-5′), 5.16—5.20 (m, 2H, H-3′ax and H-4′eq), 5.438 (br d, 1H, J=3.7 Hz, H-1′eq), 5.555 (dd, 1H, J=3.7, 2.2 Hz, H-7eq), 7.650 (s, 1H, H-11), 7.81—7.85 (m, 2H, H-2 and H-3), 8.29—8.36 (m, 2H, H-1 and H-4), 13.400 (s, 1H, OH-6). MS m/z: 552 (M^+). CD (MeOH) $[\theta]_{max}$ (nm): $+1.53\times10^4$ (283), -0.30×10^4 (339). Exact MS Calcd for $C_{29}H_{28}O_{11}$: 552.1632. Found: 552.1633.

(+)-(7*S*,9*S*)-7-*O*-(2′-Deoxy-β-D-*erythro*-pentopyranosyl)-4-demethoxy-11-deoxydaunomycinone (10)——A solution of NaOMe (about 28% in MeOH, 0.06 ml, 0.3 mmol) was added to an ice-cooled solution of **47** (5.9 mg, 0.0107 mmol) in MeOH (0.6 ml) and THF (0.6 ml), and the mixture was stirred at 0 °C for 1 h. After addition of AcOH (0.09 ml), the mixture was worked up similarly to the procedure described for the preparation of **21** to give crude **10**, which was purified by prep. TLC (MeOH : CH_2Cl_2 = 1 : 20) to give an 84% yield (4.2 mg) of **10** as yellow crystals: mp 188—190 °C (C_6H_6–*n*-hexane); $[\alpha]_D^{20}$ +31° (c=0.05, $CHCl_3$). IR: 1710, 1670, 1630, 1595, 1575 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.859 (ddd, 1H, J=13.2, 4.4, 3.7 Hz, H-2′eq), 2.026 (ddd, 1H, J=13.2, 9.5, 3.7 Hz, H-2′ax), 2.114 (dd, 1H, J=14.7, 3.7 Hz, H-8ax), 2.408 (s, 3H, H-14×3), 2.496 (dt, 1H, J=14.7, 2.2 Hz, H-8eq), 3.101 (dd, 1H, J=18.3, 2.2 Hz, H-10eq), 3.285 (d, 1H, J=18.3 Hz, H-10ax), 3.85—3.90 (m, 2H, H-4′eq and H-5′), 3.97—4.01 (m, 1H, H-3′ax), 4.024 (dd, 1H, J=13.9, 4.4 Hz, H-5′), 5.313 (dd, 1H, J=3.7, 2.2 Hz, H-7eq), 5.486 (t, 1H, J=3.7 Hz, H-1′eq), 7.640 (s, 1H, H-11), 7.81—7.85 (m, 2H, H-2 and H-3), 8.28—8.35 (m, 2H, H-1 and H-4), 13.278 (s, 1H, OH-6). FAB-MS (negative) m/z: 468 (M^-). CD (MeOH) $[\theta]_{max}$ (nm): -1.09×10^4 (284), $+0.52\times10^4$ (340).

(+)-(7*S*,9*S*)-7-[(3′,4′-Di-*O*-acetyl-2′-deoxy-β-D-*erythro*-pentopyranosyl)oxy]-9-[(1,1-ethylenedioxy)ethyl]-6,9-dihydroxy-4-methoxy-7,8,9,10-tetrahydronaphthacene-5,12-dione (49) and Its (7*R*,9*R*) Diastereomer (50)——According to the procedure described for the preparation of **47** and **48**, (±)-**34** (43.6 mg, 0.12 mmol) was treated with yellow HgO (52 mg, 0.24 mmol), $HgBr_2$ (43 mg, 0.12 mmol), molecular sieves 4A (0.5 g), and **46** (0.24 mmol) for 19 h. The reaction mixture was worked up as usual and purified by prep. TLC (AcOEt : C_6H_6 = 1 : 2) to give a 29% yield (18.8 mg) of **49** and a 26% yield (16.8 mg) of **50**, each as yellow crystals: **49**, mp 138—145 °C (C_6H_6–*n*-hexane); $[\alpha]_D^{20}$ (c=0.1, $CHCl_3$). IR: 1735, 1670, 1625, 1585 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.452 (s, 3H, H-14×3), 1.87—1.91 (m, 1H, H-2′), 1.979 (s, 3H, $OCOCH_3$), 2.022 (dd, 1H, J=14.7, 4.4 Hz, H-8ax), 2.10—2.17 (m, 1H, H-2′), 2.133 (s, 3H, $OCOCH_3$), 2.529 (dt, 1H, J=14.7, 1.5 Hz, H-8eq), 3.064 (d, 1H, J=17.6 Hz, H-10ax), 3.155 (dd, 1H, J=17.6, 1.5 Hz, H-10eq), 3.863 (dd, 1H, J=13.2, 3.7 Hz, H-5′), 4.00—4.09 (m, 4H, OCH_2CH_2O), 4.080 (s, 3H, OCH_3-4), 4.171 (dd, 1H, J=13.2, 2.2 Hz, H-5′), 5.126 (ddd, 1H, J=11.0, 4.4, 2.9 Hz, H-3′ax), 5.183 (br s, 1H, $\nu_{1/2}$=8 Hz, H-4′eq), 5.263 (dd, 1H, J=4.4, 1.5 Hz, H-7eq), 5.557 (t, 1H, J=2.9 Hz, H-1′eq), 7.372 (d, 1H, J=8.1 Hz, H-3), 7.589 (s, 1H, H-11), 7.753 (t, 1H, J=8.1 Hz, H-2), 7.969 (d, 1H, J=8.1 Hz, H-1), 13.636 (s, 1H, OH-6). FAB-MS (negative) m/z: 626 (M^-). CD (MeOH) $[\theta]_{max}$ (nm): -0.86×10^4 (287), $+0.55\times10^4$ (334). **50**, mp 140—144 °C (C_6H_6–*n*-hexane); $[\alpha]_D^{20}$ −188° (c=0.08, $CHCl_3$). IR: 1735, 1665, 1620, 1580 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.449 (s, 3H, H-14×3), 1.77—1.82 (m, 1H, H-2′eq), 1.789 (dd, 1H, J=15.4, 4.0 Hz, H-8ax), 1.953 (s, 3H, $OCOCH_3$), 2.154 (s, 3H, $OCOCH_3$), 2.230 (td, 1H, J=12.5, 3.7 Hz, H-2′ax), 2.602 (dd, 1H, J=15.4, 2.0 Hz, H-8eq), 3.195 (s, 2H, H-10×2), 3.770 (dd, 1H, J=13.2, 2.2 Hz, H-5′), 4.00—4.10 (m, 4H, OCH_2CH_2O), 4.090 (s, 3H, OCH_3-4), 4.491 (d, 1H, J=13.2 Hz, H-5′), 5.14—5.18 (m, 2H, H-3′ax and H-4′eq), 5.480 (br d, 1H, J=3.7 Hz, H-1′eq), 5.558 (dd, 1H, J=4.0, 2.0 Hz, H-7eq), 7.383 (d, 1H, J=8.1 Hz, H-3), 7.600 (s, 1H, H-11), 7.761 (t, 1H, J=8.1 Hz, H-2), 7.976 (d, 1H, J=8.1 Hz, H-1), 13.771 (s, 1H, OH-6). FAB-MS (negative) m/z: 626 (M^-). CD (MeOH) $[\theta]_{max}$ (nm): $+0.98\times10^4$ (286), -0.75×10^4 (331).

(+)-(7*S*,9*S*)-7-*O*-(3′,4′-Di-*O*-acetyl-2′-deoxy-β-D-*erythro*-pentopyranosyl)-11-deoxydaunomycinone (51)——By the same procedure as described for the preparation of **43**, a 52% yield (3.8 mg) of **51** was obtained from **49** (7.8 mg, 0.013 mmol) as yellow crystals: mp 190—194 °C (C_6H_6–*n*-hexane); $[\alpha]_D^{20}$ +33° (c=0.1, $CHCl_3$). IR: 1735, 1710, 1670, 1625, 1585 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.890 (dt, 1H, J=13.2, 3.7 Hz, H-2′eq), 2.025 (s, 3H, $OCOCH_3$), 2.139 (s, 3H, $OCOCH_3$), 2.12—2.17 (m, 2H, H-2′ax and H-8ax), 2.423 (s, 3H, H-14×3), 2.461 (dt, 1H, J=15.4, 2.0 Hz, H-8eq), 3.091 (dd, 1H, J=18.0, 2.0 Hz, H-10eq), 3.263 (d, 1H, J=18.0, H-10ax), 3.882 (dd, 1H, J=13.0, 3.7 Hz, H-5′), 4.098 (s, 3H, OCH_3-4), 4.105 (dd, 1H, J=13.0, 1.5 Hz, H-5′), 5.15—5.19 (m, 2H, H-3′ax and H-4′eq), 5.138 (dd, 1H, J=4.0, 2.0 Hz, H-7eq), 5.551 (t, 1H, J=3.7 Hz, H-1′eq), 7.395 (d, 1H, J=8.8 Hz, H-3), 7.593 (s, 1H, H-11), 7.779 (t, 1H, J=8.8 Hz, H-2), 7.989 (d, 1H, J=8.8 Hz, H-1), 13.693 (s, 1H, OH-6). FAB-MS (negative) m/z: 582 (M^-). CD (MeOH) $[\theta]_{max}$ (nm): -0.92×10^4 (285), $+0.55\times10^4$ (335). A 27% yield (2.1 mg) of **49** was recovered in this reaction.

(+)-(7*R*,9*R*)-7-*O*-(3′,4′-Di-*O*-acetyl-2′-deoxy-β-D-*erythro*-pentopyranosyl)-11-deoxydaunomycinone (52)——By the same procedure as described for the preparation of **43**, a 57% yield (4.5 mg) of **52** was obtained from **50** (8.5 mg, 0.015 mmol) as yellow crystals: mp 218—220 °C (C_6H_6–*n*-hexane); $[\alpha]_D^{20}$ −254° (c=0.07, $CHCl_3$). IR: 1735, 1670,

1625, 1585 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.823 (br d, 1H, J=13.2 Hz, H-2′eq), 1.974 (dd, 1H, J=15.4, 3.7 Hz, H-8ax), 1.978 (s, 3H, $OCOCH_3$), 2.163 (s, 3H, $OCOCH_3$), 2.263 (td, 1H, J=13.2, 3.7 Hz, H-2′ax), 2.387 (s, 3H, H-14×3), 2.448 (dt, 1H, J=15.4, 2.0 Hz, H-8eq), 3.172 (dd, 1H, J=17.6, 2.0 Hz, H-10eq), 3.273 (d, 1H, J=17.6 Hz, H-10ax), 3.781 (dd, 1H, J=13.2, 2.2 Hz, H-5′), 4.102 (s, 3H, OCH_3-4), 4.444 (d, 1H, J=13.2 Hz, H-5′), 5.14—5.19 (m, 2H, H-3′ax and H-4′eq), 5.432 (br d, 1H, J=3.7 Hz, H-1′eq), 5.575 (dd, 1H, J=3.7, 2.0 Hz, H-7eq), 7.401 (d, 1H, J=8.8 Hz, H-3), 7.600 (s, 1H, H-11), 7.782 (t, 1H, J=8.8 Hz, H-2), 7.992 (d, 1H, J=8.8 Hz, H-1), 13.803 (s, 1H, OH-6). FAB-MS (negative) m/z: 582 (M^-). CD (MeOH) $[\theta]_{max}$ (nm): $+0.70\times10^4$ (284), -0.25×10^4 (333). A 41% yield (3.5 mg) of **50** was recovered in this reaction.

(+)-(7*S*,9*S*)-7-*O*-(2′-Deoxy-β-D-*erythro*-pentopyranosyl)-11-deoxydaunomycinone (11)——By the same procedure as described for the preparation of **10**, a 61% yield (1.3 mg) of **11** was obtained from **51** (2.5 mg, 0.0043 mmol) as yellow crystals: mp 222—224 °C (CH_2Cl_2); $[\alpha]_D^{20}$ +16.4° (c=0.09, $CHCl_3$). IR: 1710, 1675, 1620, 1580 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.844 (dt, 1H, J=13.5, 3.7 Hz, H-2′eq), 1.991 (ddd, 1H, J=13.5, 10.0, 3.7 Hz, H-2′ax), 2.109 (dd, 1H, J=14.7, 4.0, H-8ax), 2.401 (s, 3H, H-14×3), 2.474 (dt, 1H, J=14.7, 2.2 Hz, H-8eq), 3.074 (dd, 1H, J=17.6, 2.2 Hz, H-10eq), 3.260 (d, 1H, J=17.6 Hz, H-10ax), 3.84—3.88 (m, 2H, H-4′eq and H-5′), 3.969 (m, 1H, $\nu_{1/2}$=19 Hz, H-3′ax), 4.019 (dd, 1H, J=13.2, 3.7 Hz, H-5′), 4.086 (s, 3H, OCH_3-4), 5.312 (dd, 1H, J=4.0, 2.2 Hz, H-7eq), 5.490 (t, 1H, J=3.7 Hz, H-1′eq), 7.373 (dd, 1H, J=8.0, 1.5 Hz, H-3), 7.578 (s, 1H, H-11), 7.765 (t, 1H, J=8.0 Hz, H-2), 7.974 (dd, 1H, J=8.0, 1.5 Hz, H-1), 13.667 (s, 1H, OH-6). FAB-MS (negative) m/z: 498 (M^-). CD (MeOH) $[\theta]_{max}$ (nm): -0.94×10^4 (287), $+0.56\times10^4$ (332).

Acknowledgement We are grateful to Professor F. Arcamone for providing a sample of **6** and spectroscopic data of **6** and **9**, and also to Mr. M. Morita for the measurement of FAB-MS performed at the Faculty of Pharmaceutical Sciences of Kinki University. We thank Mr. Yong-Zhong Da for technical assistance.

References and Notes

1) Reviews on the biological activites: *a*) S. T. Crooke and S. D. Reich (eds.), "Anthracyclines: Current Status and New Developments," Academic Press, New York, 1980; *b*) F. Arcamone, "Doxorubicin," ed. by G. Stevens, Academic Press, New York, 1981; *c*) H. S. E. Khadem (ed.), "Anthracycline Antibiotics," Academic Press, New York, 1982; *d*) T. Oki and T. Takeuchi, *Yuki Gosei Kagaku Kyokai Shi*, **40**, 2 (1980); *e*) F. Arcamone, *Med. Res. Rev.*, **4**, 153 (1984).

2) Reviews on the synthetic studies: *a*) S. Terashima, *Yuki Gosei Kagaku Kyokai Shi*, **40**, 20 (1982); *b*) Tetrahedron Symposia-in-Print Number 17, T. R. Kelly (ed.), "Recent Aspects of Anthracyclinone Chemistry," *Tetrahedron*, **40**, 4537 (1984); *c*) M. J. Broadhurst, C. H. Hassall, and G. J. Thomas, *Chem. Ind.* (London), **1985**, 106; *d*) K. Krohn, *Angew. Chem. Int. Ed. Engl.*, **25**, 790 (1986); Y. Tamura and Y. Kita, *Yuki Gosei Kagaku Kyokai Shi*, **46**, 205 (1988).

3) *a*) T. Oki, Y. Matsuzawa, A. Yoshimoto, K. Numata, I. Kitamura, S. Hori, A. Takamatsu, H. Umezawa, M. Ishizuka, H. Naganawa, H. Suda, M. Hamada, and T. Takeuchi, *J. Antibiot.*, **28**, 830 (1975); *b*) S. Hori, M. Shirai, S. Hirano, T. Oki, T. Inui, S. Tsukagoshi, M. Ishizuka, T. Takeuchi, and H. Umezawa, *Gann*, **68**, 685 (1977).

4) H. Umezawa, Y. Takahashi, M. Kinoshita, H. Naganawa, K. Tatsuta, and T. Takeuchi, *J. Antibiot.*, **33**, 1581 (1980).

5) *a*) F. Arcamone, G. Cassinelli, F. D. Matteo, S. Forenza, M. C. Ripamonti, G. Rivola, A. Vigevani, J. Clardy, and T. McCabe, *J. Am. Chem. Soc.*, **102**, 1462 (1980); *b*) G. Cassinelli, F. D. Matteo, S. Forenza, M. C. Ripamonti, G. Rivola, F. Arcamone, A. D. Marco, A. M. Casazza, C. Soranzo, and G. Pratesi, *J. Antibiot.*, **33**, 1468 (1980).

6) *a*) A. S. Kende and J. P. Rizzi, *J. Am. Chem. Soc.*, **103**, 4247 (1981); *b*) B. A. Pearlman, J. M. McNamara, I. Hasan, S. Hatakeyama, H. Sekizaki, and Y. Kishi, *ibid.*, **103**, 4248 (1981); *c*) P. N. Confalone and G. Pizzolato, *ibid.*, **103**, 4251 (1981); *d*) T.-T. Li and Y. L. Wu, *ibid.*, **103**, 7007 (1981); *e*) R. K. Boeckman, Jr. and F.-W. Sum, *ibid.*, **104**, 4604 (1982); *f*) K. Maruyama, H. Uno, and Y. Naruta, *Chem. Lett.*, **1983**, 1767; *g*) F. M. Hauser and D. Mal, *J. Am. Chem. Soc.*, **106**, 1098 (1984).

7) *a*) S. D. Kimball, D. R. Walt, and F. Johnson, *J. Am. Chem. Soc.*, **103**, 1561 (1981); *b*) J. P. Gesson and M. Mondon, *J. Chem. Soc., Chem. Commun.*, **1982**, 421; *c*) H. Sekizaki, M. Jung, J. M. McNamara, and Y. Kishi, *J. Am. Chem. Soc.*, **104**, 7372 (1982); *d*) A. A. Abdallah, J. P. Gesson, J. C. Jacquesy, and M. Mondon, *Bull. Soc. Chim. Fr.*, **1986**, 93.

8) *a*) Y. Tamura, A. Wada, M. Sasho, K. Fukunaga, H. Maeda, and Y. Kita, *J. Org. Chem.*, **47**, 4376 (1982); *b*) Y. Tamura, M. Sasho, K. Nakagawa, T. Tsugoshi, and Y. Kita, *ibid.*, **49**, 473 (1984); *c*) Y. Tamura, S. Akai, M. Sasho, and Y. Kita, *Tetrahedron Lett.*, **25**, 1167 (1984); *d*) Y. Tamura, M. Sasho, S. Akai, A. Wada, and Y. Kita, *Tetrahedron*, **40**, 4539 (1984); *e*) Y. Tamura, M. Sasho, S. Akai, H. Kishimoto, J. Sekihachi, and Y. Kita, *Tetrahedron Lett.*, **27**, 195 (1986); *f*) *Idem, Chem. Pharm. Bull.*, **35**, 1405 (1987).

9) *a*) Y. Tamura, M. Kirihara, J. Sekihachi, R. Okunaka, S. Mohri, T. Tugoshi, S. Akai, M. Sasho, and V. Kita,

Tetrahedron Lett., **28**, 3971 (1987); *b*) Y. Tamura, M. Kirihara, M. Sasho, S. Akai, J. Sekihachi, R. Okunaka, and Y. Kita, *J. Chem. Soc., Chem. Commun.*, **1987**, 1474.

10) *a*) Y. Tamura, M. Sasho, H. Ohe, S. Akai, and Y. Kita, *Tetrahedron Lett.*, **26**, 1549 (1985); *b*) Y. Tamura, S. Akai, H. Kishimoto, M. Kirihara, M. Sasho, and Y. kita, *ibid.*, **28**, 4583 (1987).

11) *a*) J. P. Gesson, J. C. Jacquesy, and M. Mondon, *Tetrahedron Lett.*, **21**, 3351 (1980); *b*) J. G. Bauman, R. B. Barber, R. D. Gless, and H. Rapoport, *ibid.*, **21**, 4777 (1980); *c*) J. Alexander, D. L. Flynn, L. A. Mitscher, and T. Veysoglu, *ibid.*, **22**, 3711 (1981); *d*) M. E. Jung, M. Node, R. W. Pfluger, M. A. Lyster, and J. A Lowe, III, *J. Org. Chem.*, **47**, 1150 (1982); *e*) F. M. Hauser, S. Prasanna, and D. W. Combs, *ibid.*, **48**, 1328 (1983); *f*) E. Vedejs, W. H. Miller, and J. R. Pribish, *ibid.*, **48**, 3611 (1983); *g*) P. N. Preston, T. Winwick, and J. O. Morley, *J. Chem. Soc., Perkin Trans. 1*, **1985**, 39; and references cited therein.

12) The weakly basic alkylcerium(III) reagents were shown to have greater nucleophilicity than the parent organolithium reagents. See *a*) T. Imamoto, T. Kusumoto, and M. Yokoyama, *J. Chem. Soc., Chem. Commun.*, **1982**, 1042; *b*) T. Imamoto, T. Kusumoto, Y. Tawarayama, Y. Sugiura, T. Mita, Y. Hatanaka, and M. Yokoyama, *J. Org. Chem.*, **49**, 3904 (1984).

13) *a*) M. Suzuki, Y. Kimura, and S. Terashima, *Chem. Lett.*, **1984**, 1543; *b*) *Idem, Chem. Pharm. Bull.*, **34**, 1531 (1986).

14) *a*) Y. Kita, S. Akai, M. Yoshigi, Y. Nakajima, H. Yasuda, and Y. Tamura, *Tetrahedron Lett.*, **25**, 6027 (1984); *b*) Y. Kita, S. Akai, N. Ajimura, M. Yoshigi, T. Tsugoshi, H. Yasuda, and Y. Tamura, *J. Org. Chem.*, **51**, 4150 (1986).

15) Treatment of **20** with aqueous KOH in refluxing EtOH followed by acidification with concentrated HCl caused saponification, desilylation, and *exo–endo* olefin isomerization to give the diacid (**22**), which was cyclized with (trimethylsilyl)ethoxyacetylene into the syrupy anhydride (**18**) in 92% overall yield. However, the following cycloaddition to naphthoquinones (**23** and **25**) with NaH gave fairly low yields (32—42%) of the adducts (**24** and **26**), probably due to small amounts of inseparable contaminants formed in the saponification step.[10a)]

16) Fully controlled regiochemistry dominated by the position of halogen substituents in the quinone rings is generally seen in our strong base-induced cycloaddition of homophthalic anhydrides and their analogues to haloquinones.[8)]

17) Recently Gesson *et al.* reported a similar unsucessful result in C-9 side chain elaboration. Treatment of **13** with ethynylcerium(III) chloride gave a mixture of two diastereomers with two ethynyl groups at the C-5 and C-9 positions.[7d)]

18) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Interpretation of Mass Spectra of Organic Compounds," Holden-Day, Inc., San Francisco, 1964.

19) In the ^{1}H-NMR spectra of anthracyclinones, relatively small $v_{1\,2}$ values (7—12 Hz) for 7,9-*cis*-diols and larger $v_{1\,2}$ values (18—20 Hz) for 7,9-*trans*-diols were reported for the C-7 proton.[20)]

20) *a*) N. Tanno and S. Terashima, *Chem. Pharm. Bull.*, **31**, 821 (1983); *b*) D. Dominguez, R. J. Ardecky, and M. P. Cava, *J. Am. Chem. Soc.*, **105**, 1608 (1983).

21) *a*) M. J. Broadhurst, C. H. Hassall, and G. J. Thomas, *J. Chem. Soc., Perkin Trans. 1*, **1982**, 2239; *b*) K. Ravichandran, F. A. J. Kerdesky, and M. P. Cava, *J. Org. Chem.*, **51**, 2044 (1986).

22) Treatment of the 7,9-*trans* isomer of **8** with CF_3CO_2H in the absence of benzeneboronic acid gave **8**, along with a small amount of the fully aromatized product. Similar conversion was also effective in the synthesis of heteroanthracyclines.[9a)]

23) *a*) Y. Kimura, M. Suzuki, T. Matsumoto, R. Abe, and S. Terashima, *Chem. Lett.*, **1984**, 501; *b*) *Idem, Bull. Chem. Soc. Jpn.*, **59**, 423 (1986); and references cited therein.

24) Spectral data (CD and ^{1}H-NMR) have been efficiently employed for the determination of the absolute configuration of anthracyclines.[4,25)]

25) *a*) J. P. Marsh, Jun., R. H. Iwamoto, and L. Goodman, *J. Chem. Soc., Chem. Commun.*, **1968**, 589; *b*) S. Penco, F. Angelucci, M. Ballabio, G. Barchielli, A. Suarato, E. Vanotti, A. Vigevani, and F. Arcamone, *Tetrahedron*, **40**, 4677 (1984).

26) T. H. Smith, A. N. Fujiwara, W. W. Lee, H. Y. Wu, and D. W. Henry, *J. Org. Chem.*, **42**, 3653 (1977).

27) *a*) D. Horton, W. Priebe, and W. R. Turner, *Carbohydr. Res.*, **94**, 11 (1981); *b*) D. Horton, W. Priebe, and O. Varela, *J. Antibiot.*, **37**, 853 (1984); *c*) *Idem, ibid.*, **37**, 1635 (1984); *d*) T. Tsuchiya, Y. Takagi, K.-D. Ok, S. Umezawa, T. Takeuchi, N. Wako, and H. Umezawa, *ibid.*, **39**, 731 (1986); *e*) K. Ishizumi, N. Ohashi, and N. Tanno, *J. Org. Chem.*, **52**, 4477 (1987).

28) J. Davoll and B. Lythgoe, *J. Chem. Soc.*, **1949**, 2526.

29) Formation of small amounts ($< 10\%$ yields) of two corresponding α-glycosides was also observed.

30) Y. Tamura, A. Wada, M. Sasho, and Y. Kita, *Chem. Pharm. Bull.*, **31**, 2691 (1983).

31) A. V. Rama Rao, A. R. Mehendale, and K. Bal Reddy, *Tetrahedron Lett.*, **24**, 1093 (1983).

32) A. V. Rama Rao, B. M. Chanda, and H. B. Borate, *Synth. Commun.*, **14**, 257 (1984).

33) V. H. Deshpande, K. Ravichandran, and B. Ramamohan Rao, *Synth. Commun.*, **14**, 477 (1984).

34) A. V. Rama Rao, A. R. Mehendale, and K. Bal Reddy, *Indian J. Chem.*, **23B**, 1154 (1984).

35) J.-M. Tornare and P. Vogel, *Helv. Chim. Acta*, **68**, 1069 (1985).
36) J. Yadav, P. Corey, C.-T. Hsu, K. Perlman, and C. J. Sih, *Tetrahedron Lett.*, **22**, 811 (1981).
37) The melting point of the authentic sample generously given by Prof. Arcamone measured by us was 195—213 °C (dec.), and the crude **6**·HCl prepared from crude **6**, which contained a small amount of aromatized compounds, decomposed at 170—177 °C.