cool slowly to 25 °C and were then filtered through 0.8-μM Millipore filters before use. The vesicle size was 700–800 Å by light scattering measurements.

Large vesicles (3000 ± 500 Å) were created by 1 mL/h slow injection (Sage Instruments Model 341A syringe pump) of a 1-mL, 1×10^{-3} M $CHCl_3$ solution of surfactant into 25 mL of buffer at 70 °C. Nitrogen was bubbled through the buffer solution during the injection to facilitate removal of the $CHCl_3$.

Chromatography. If required (see above), vesicle suspensions were passed through a column containing Sephadex G-75. Sephadex G-75 powder (2.5 g, Pharmacia, Inc.) was allowed to swell overnight in ~12 mL of 5×10^{-3} M aqueous KCl or 0.01 M Tris buffer at pH 8. The resulting slurry was degassed by gentle swirling under aspirator vacuum until bubbling ceased. This process required ~1.5 h. The slurry was then diluted to 200 mL with KCl or buffer solution, swirled several times, and set aside until the Sephadex particles had settled. The supernatant, which contained fine particles, was then decanted away. The residual slurry was suspended in a 1 cm × 27 cm glass chromatography column, care being taken to avoid trapped air bubbles. Sephadex particles were allowed to settle by gravity for ~15 min. The column was then *conditioned* by successive passage of 20 mL of buffer, 20 mL of an "empty" vesicle solution, and, finally, 20 mL of buffer.

Solutions of substrate-loaded vesicles were put onto the column in 2-mL volumes, permitted to absorb, and then eluted with buffer. Vesicles with entrapped substrate were obtained from the initial 8–12 mL of eluent, as visualized by light scattering. Free substrate (i.e., exovesicular or nonentrapped) was held up by the Sephadex and eluted after 22–30 mL of eluent, depending on the nature of the substrate.

Light Scattering. Light scattering data were collected at 25 °C and a 90° scattering angle with a Nicomp Model TC-100 computing autocorrelator, an argon laser light source (488 nm), and a Hazeltine microcomputer that used the cumulant program. The channel width was adjusted to produce a decay of 1.5-2.0 s. Vesicles were generated as described above.

Kinetic Studies. Faster reactions were followed on a Durrum/Dionex Model D-130 stopped-flow spectrophotometer coupled either to a Tektronix Model 5103N storage oscilloscope or, via a custom-built interface, to a Commodore Model 8032 computer. Slower reactions were monitored on a Gilford Model 250 spectrophotometer coupled to a Gilford Model 6051 recorder. Rate constants were obtained from computer-generated correlations of log $(A_\infty - A_t)$ with time. Temperature (±1 °C) was controlled by a circulating-water bath. All solutions of **2** were flushed under nitrogen and stored under a nitrogen atmosphere to prevent air oxidation.

The buildup or bleaching of anion **2** was followed at 412 nm (in buffer) or at 450 nm in vesicle solutions. Static UV spectra were recorded on an HP Model 8451A diode array spectrophotometer. Vesicle-containing solutions for either static or kinetic spectroscopy were corrected for background scatter by referencing against "empty" vesicle solutions under identical conditions of concentration and solvent. Kinetic results appear in Tables I–III. Further experimental details are given in the Results and in the table notes.

Acknowledgment. We thank Professor Hernan Chaimovich of the University of Sao Paulo for helpful discussions. We are grateful to the U.S. Army Research Office for financial support.

Regio- and Stereospecific Construction of Anthracyclinones: Total Syntheses of (±)-γ-Citromycinone and of (±)-Dimethyl-6-deoxydaunomycinone and (±)-Dimethyl-6-deoxyadriamycinone

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Abstract: Total syntheses of (±)-γ-citromycinone (**1**) and of the dimethyl ether derivatives of (±)-6-deoxydaunomycinone (**2a**) and (±)-6-deoxyadriamycinone (**2b**) are described. Key elements of these preparations were regiospecific construction of the anthraquinone **15** through condensation of the (phenylsulfonyl)isobenzofuranone **12** with the cyclohexenone **13**, ene cyclization of the anthraquinone aldehyde **17c** to the naphthacenone **18**, and use of the 7-hydroxyl group in **18** as a neighboring group to effect stereospecific cis epoxidation of the 9,13-olefinic moiety. Opening of the epoxide in **19** with phenyl selenide anion, followed by selenoxide elimination, furnished the allyic alcohol **20a**, which was selectively transformed to A-ring functionalization patterns present in (±)-γ-cytromycinone (**1**), (±)-6-deoxydaunomycinone (**2a**), and (±)-6-deoxyadriamycinone (**2b**).

A feature common to some of the most useful anthracyclines is an A ring with *cis*-7,9-dihydroxylation and a 9-acetyl- or 9-hydroxyacetyl functionality.[2] Stereospecific construction of this substitution pattern has been a continuing synthetic problem.[3] Typically, this fragment has been prepared by introducing the 7-hydroxyl group through bromination–solvolysis of a 9-hydroxyl-containing intermediate;[4-6] however, this approach has not been entirely satisfactory. Only moderate stereoselectivity has been achieved, and preparative scale has been limited by the low solubility of anthracyclinones in media that are compatible with the bromination step.[7] Also, attempted introduction of 7-hydroxyl groups in anthracyclines devoid of a 6-oxygen func-

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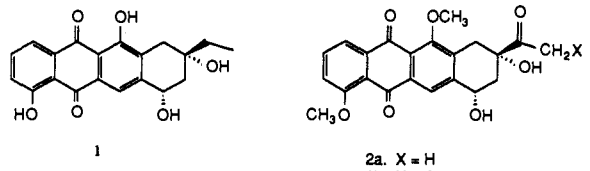
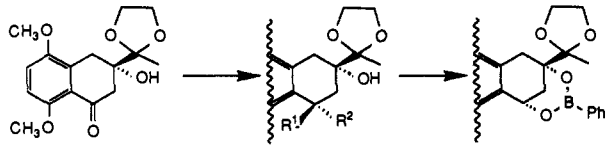


1 2a. X = H 2b. X = OH

Figure 1.



3 4a. R^1 = H, R^2 = OH 4b. R^1 = OH, R^2 = H 5

Figure 2.

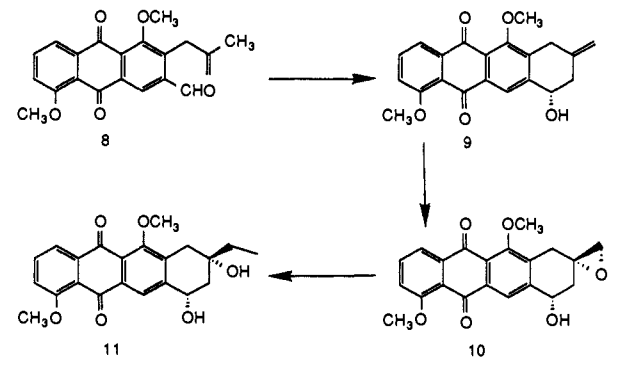
6 7

Figure 3.

tionality either resulted in modest yields[8] or, more usually, in complete failure of the reaction.[9,10]

The bromination solvolysis procedure can be employed for highly stereoselective introduction of the 7-hydroxyl group in anthracyclinone intermediates with A rings containing a 10-carbomethoxy group trans to a 9-hydroxyl functionality. This finding, originally reported by Rizza and Kende[11] and Confolone and Pizzolato,[12] has been exploited widely in subsequent syntheses of anthracyclinones with this type of substitution pattern.[13]

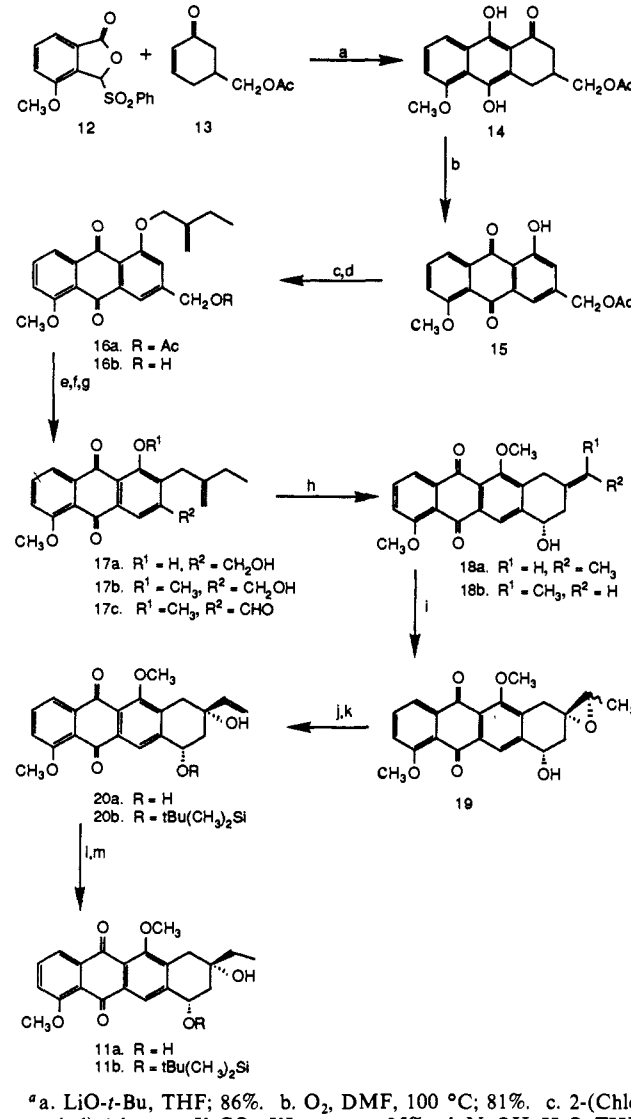
Hydronaphthalenes with *cis*-7,9-dihydroxyls and a *trans*-9-acetyl or 9-alkyl group have been stereoselectively prepared and used as intermediate to anthracyclinones. Hassall et al.[14] reported, as shown in Figure 2, that the epimeric mixture of diols **4** from reduction of the ketone **3** can be equilibrated with phenylboric acid to furnish selectively the *cis*-boronate **5**. In subsequent steps, this intermediate was converted to (+)-deoxydaunomycin. Swenton et al.[15] subsequently established that the ketone **3** could be stereoselectively reduced to **4a** with Selectride (Aldrich) and accomplished syntheses of (+)-daunomycinone and 4,6-dideoxydaunomycinone from this intermediate. In other work shown in Figure 3, Swenton et al.[16] found that reaction of the 10-ketohydronaphthalene **6** with potassium *tert*-butoxide and oxygen in the presence of trimethyl phosphite gave the 9-keto-*cis*-7,9-di-



8 9 10 11

Figure 4.

Scheme I[a]



12 13 14 15 16a. R = Ac 16b. R = H 17a. R^1 = H, R^2 = CH_2OH 17b. R^1 = CH_3, R^2 = CH_2OH 17c. R^1 = CH_3, R^2 = CHO 18a. R^1 = H, R^2 = CH_3 18b. R^1 = CH_3, R^2 = H 19 20a. R = H 20b. R = $tBu(CH_3)_2Si$ 11a. R = H 11b. R = $tBu(CH_3)_2Si$

[a] a. LiO-*t*-Bu, THF; 86%. b. O_2, DMF, 100 °C; 81%. c. 2-(Chloromethyl)-1-butene, K_2CO_3, KI, acetone; 95%. d. NaOH, H_2O–THF; 96%. e. $Na_2S_2O_4$, DMF, 100 °C; 96%. f. $(CH_3)_2SO_4$, K_2CO_3, acetone; 100%. g. $BaMnO_4$, CH_2Cl_2; 90%. h. $SnCl_4 \cdot 5H_2O$, CH_2Cl_2; 92%. i. *t*-BuOOH, $VO(AcAc)_2$, CH_2Cl_2; 89%. j. PhSeNa, EtOH–DME; 30% H_2O_2; 94%. k. *t*-$Bu(CH_3)_2SiCl$, imidazole, DMF; 91%. l. N_2H_4, H_2O_2, Cu^{2+}; 95%. m. HF, CH_3CN; 89%.

hydroxy compound **7**. This product was used for synthesis of α-citromycinone.[15b]

In a recent paper,[17] we described the first methodology for stereospecific synthesis of the *cis*-7,9-dihydroxy-9-ethyl A-ring substitution pattern, another fragment common in anthracycline

(8) Introduction of the 7-hydroxyl group in 4,6,7-trideoxydaunomycinone was accomplished by using the bromination–solvolysis procedure, though in modest yield. The product was converted to the 4,6-dideoxy analogue of daunorubicin and shown to have anticancer activity comparable with daunorubicin. Penco, S.; Angelucci, F.; Arcamone, F.; Ballabio, M.; Barchielli, G.; Grancheschi, G.; Franchi, G.; Suarato, A.; Vanoti, E. *J. Org. Chem.* **1983**, *48*, 405.

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antibiotics.[18] Included in that work was the total synthesis of citromycinone (**1**)[19] shown schematically in Figure 4. Key elements of that route[17] were intramolecular ene cyclization of the olefinic aldehyde **8** to the naphthacenone **9** and use of the antiperiplanar 7-hydroxyl group to stereospecifically cis epoxidize the homoallylic 9,13-olefinic moiety. Opening of the epoxide fragment in **10** with dimethylcopper gave **11**, which was demethylated to citromycinone (**1**).

We report here modifications that generalize this plan for stereospecific synthesis of A-ring substitution patterns with either a 9-acetyl or a 9-hydroxyacetyl group. Replacement of the methylpropenyl with an ethylpropenyl group provided the flexibility needed for synthesis of the acetyl fragments. Using this approach, we have performed efficient regio- and stereospecific syntheses of the dimethyl ether derivatives of (±)-6-deoxydaunomycinone (**2a**) and (±)-6-deoxyadriamycinone (**2b**) as well as a new synthesis of (±)-γ-citromycinone (**1**).

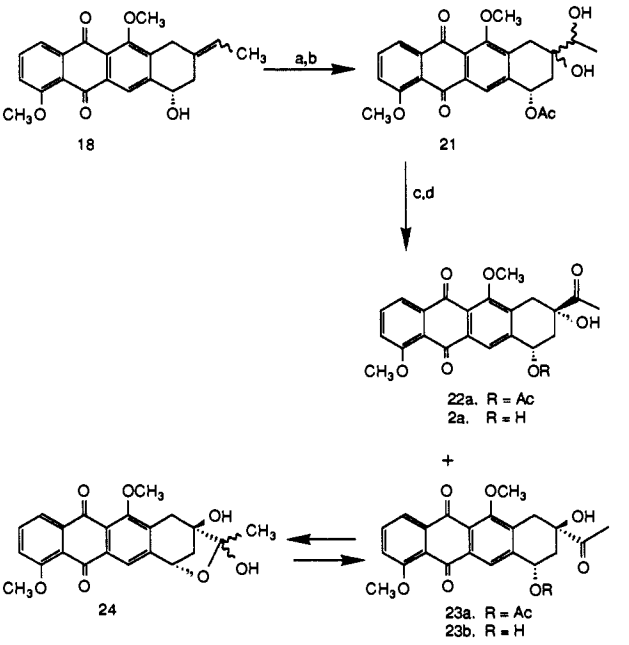
(±)-γ-Citromycinone (1). As shown in Scheme I, the aromatic annelation methodology that we developed previously was used to regiospecifically fabricate the anthracene intermediate **15**.[20] Condensation of the phthalide sulfone **12**[21] (3 equiv of LiO-*t*-Bu, THF, initially at −78 °C and then at room temperature) with the (acetoxymethyl)cyclohexenone **13**[22] gave the tetrahydroanthracenone **14**. Oxidative transformation to the anthraquinone **15** was accomplished by heating **14** in DMF under an oxygen atmosphere (81%).[17]

Chemospecific etherification of the phenolic group to furnish the allyl ether **16a** was achieved in 95% yield through reaction of **15** with 2-(chloromethyl)-1-butene[23] in acetone, potassium carbonate, and potassium iodide. Basic hydrolysis (NaOH, THF–H_2O) of the acetoxymethyl group in **16a** gave the hydroxymethyl product **16b** in 96% yield. In order to effect Claisen rearrangement, **16b** was heated in DMF and subjected to in situ reduction with dithionite.[24] Subsequent air oxidation of the anthrahydroquinone intermediate furnished the 2-ethylpropenyl-substituted quinone **17a** in 96% yield. The phenolic group in **17a** was methylated (Me_2SO_4, K_2CO_3, acetone; 100%) to furnish **17b**, and the hydroxymethyl group was then oxidized with barium manganate[25] to produce the aldehyde **17c** in 90% yield.

As in our earlier work with the methylpropenyl compound **8**, stannic chloride pentahydrate proved to be an effective catalyst for intramolecular ene reaction of the aldehyde and olefinic moieties. Thus treated, **17c** was regiospecifically converted to an *E,Z* mixture of 9,13-olefinic compounds **18** in 92% yield. Since the geometry of the C-9,13 olefin in **18** was of no consequence to the final products, the isomeric mixture was used in subsequent steps.

In the D_2O exchanged ^1H NMR spectra of the individual olefinic isomers of **18**, the C-7 protons were triplets, thereby establishing that the C-7 hydroxyl group was antiperiplanar with respect to the polycyclic aromatic ring system. This stereochemical feature was exploited to effect Sharpless epoxidation[26] (*t*-BuOOH, $VO(AcAc)_2$, CH_2Cl_2) of the 9,13-olefinic moiety in **18**, which stereospecifically furnished the *cis*-epoxide **19** in 89% yield. Although the presence of two epoxide products in the NMR spectrum of **19** was consistent with having used an *E,Z* olefinic mixture as the starting material, it was not entirely clear that the epoxidation had been stereospecific. This was established by opening the epoxide moiety in **19** with phenyl selenide anion and then oxidizing the selenium intermediate to effect elimination of phenyl selenoxide.[27] The sole product, obtained in 94% yield, was the *cis*-7,9-dihydroxy-9-vinyl compound **20a**.

Scheme II[a]



[a] a. AcCl, Py, CH_2Cl_2, 0 °C. b. OsO_4, TMNO, acetone–H_2O; 94%. c. $PySO_3$, DMSO, Et_3N; 85%. d. MeOH, K_2CO_3; 100%.

Reduction of the 13,14-olefinic moiety in **20a** to give the ethyl-substituted product **11a**, an established immediate precursor to citromycinone (**1**), proved unexpectedly difficult. While catalytic hydrogenation of the double bond could be accomplished under forcing conditions (Pd/C, H_2, EtOH, 80 psi), the yield of **11a** was unsatisfactory (43%). In their synthesis of rhodomycinone, Kende and Tsay[28] noted that a 9-vinylcarbinol moiety in a tetracyclic intermediate was resistant to hydrogenation and successfully overcame the problem by using a diimide reduction. Although we were able to reduce the 13,14-olefinic moiety in **20a** with diimide,[29] the yield of **11a** was again modest. With further work, it was found that the reduction proceeded in high yield (95%) when the 7-hydroxyl group was protected as the *tert*-butyldimethylsilyl derivative **20b**. Desilylation of **11b** with aqueous HF in acetonitrile[30] produced the dimethyl ether derivative **11a**, which was identical in all respects (melting point, TLC, IR, and ^1H and ^{13}C NMR) with the material prepared in our previous synthesis of citromycinone (**1**).[17]

(±)-Dimethyl-6-deoxydaunomycinone (2a). As shown in Scheme II, the 9,13-olefinic intermediate **18** was converted straightforwardly to 6-deoxydaunomycinone dimethyl ether (**2a**). Acetylation of the 7-hydroxyl group in **18**, followed by hydroxylation of the 9,13-olefinic moiety with excess trimethylamine *N*-oxide and a catalytic amount of osmium tetraoxide,[31] gave the diastereoisomeric 9,13-diols **21** in 94% yield. Oxidation of the C-13 alcohol in **21** with sulfur trioxide–pyridine complex[32] produced a mixture of the keto acetate derivative **22a** of dimethyl-6-deoxydaunomycinone and the corresponding 9-epi isomer **23a**. Since the products had similar R_f values on TLC, the mixture was deacetylated with methanolic potassium carbonate to dime-

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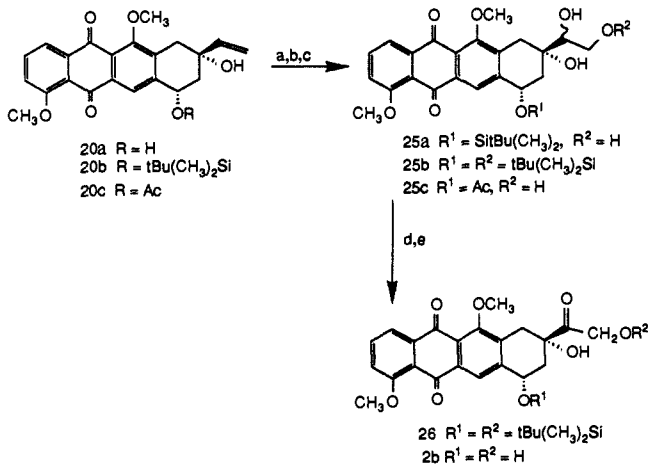
Scheme III[a]



[a] a. t-Bu$(CH_3)_2$SiCl, imidazole, DMF; 91%. b. OsO_4, TMNO, acetone–H_2O; 100%. c. t-Bu$(CH_3)_2$SiCl, DMAP, Et_3N, CH_2Cl_2; 100%. d. $PyrSO_3$, DMSO, Et_3N; 84%. e. HF–H_2O–CH_3CN; 87%.

thyl-6-deoxydaunomycinone (**2a**) and the epimeric C-9 isomer **23b** in order to facilitate chromatographic separation.

The assignment of stereochemistry to **2a** and **23b** was accomplished straightforwardly from their ^1H NMR spectra. The spectrum of **2a** was that of a single compound whereas that of **23b**, although homogeneous by TLC, indicated a mixture. Although addition of a drop of pyridine had little effect on the spectrum of **2a**, that of **23b** was radically altered. This behavior was consistent with the existence of an equilibrium between the acetyl form **23b** and the hemiacetal forms **24**. Such an equilibrium can occur only if the C-7 hydroxyl and 9-acetyl groups have a cis relationship. This supposition was chemically verified by quantitatively acetylating **23b** to the 7-acetoxy-9-epi product **23a**. The ^1H NMR spectrum was that of a single compound. The three-step preparation of **2a** from **18** was accomplished in 32% overall yield.

(±)-Dimethyl-6-deoxyadriamycinone (2b). The use of the 9-vinylcarbinol **20a** for stereospecific synthesis of (±)-dimethyl-6-deoxyadriamycinone (**2b**) was performed as shown in Scheme III. Initially, our plan was to cis hydroxylate the 13,14-olefinic moiety in **20c** and then oxidize the resultant diol fragment to an α-hydroxy ketone with one of the numerous reagents known to selectively oxidize secondary alcohols in the presence of primary alcohols.

Hydroxylation of the 13,14-olefinic entity in **20c** with a catalytic amount of osmium tetraoxide and trimethylamine N-oxide to regenerate the tetraoxide gave a mixture of the diastereoisomeric diols **25c** in quantitative yield. A variety of reagents [Ce$(NH_4)_2(NO_3)_2$–$NaBrO_3$,[33] $VO(AcAc)_2$–t-BOOH,[34] Ph_3CBF_4[35]] previously reported to effect selective oxidation of secondary alcohols in the presence of primary alcohols were examined for oxidation of **25c** to a keto alcohol, but in each instance complex mixtures were produced. Bis(tributyltin) oxide–bromine[36] seemed promising; however, the ketone product could not be separated completely from tin-containing contaminants.

It appeared that protection of the primary alcohol in **25a**, followed by oxidation of the secondary alcohol, would be a more viable approach. Protection of the 7-hydroxyl group in **20a** as its *tert*-butyldimethylsilyl derivative[37] (*tert*-butyldimethylsilyl chloride, imidazole, DMF; 91%) furnished **20b**, which was hydroxylated with osmium tetraoxide to give the diol **25a** as a mixture of diastereoisomers. Selective, quantitative protection of the primary alcohol in **25a** as the *tert*-butyldimethylsilyl derivative **25b** was accomplished with use of the silylating conditions described by Chaudhary and Hernandez[38] (*tert*-butyldimethylsilyl chloride, DMAP, Et_3N, CH_2Cl_2). Oxidation of the C-13 hydroxyl group with sulfur trioxide–pyridine complex[32] furnished the ketone **26** in 84% yield. Attempted desilyation of **26** with tetrabutylammonium fluoride resulted in *complete destruction of the molecule*; only intractable material was obtained. While we had previously noted the sensitivity of other intermediates in this sequence to base, the extreme sensitivity of **26** to fluoride was surprising. This problem was readily circumvented by treating **26** with aqueous HF in acetonitrile. Under these conditions, the deprotected product **2b** was obtained in 87% yield. The six-step sequence from the vinylcarbinol intermediate **20a** provides a stereospecific route to **2b** in 66% overall yield.

Conclusion

In summary, the efficient preparations of (±)-γ-citromycinone (**1**) and of (±)-dimethyl-6-deoxyadriamycinone (**2b**) presented herein demonstrate the unique capacity of this methodology for regio- and stereospecific syntheses of anthracyclinones with these A-ring substitution patterns. A notable feature of the 6-deoxyadriamycinone (**2b**) synthesis is that the intermediacy of a methyl ketone compound is not required. At present we are investigating the use of this approach for chiral syntheses of these anthracyclinones and for synthesis of anthracyclinones with other aromatic hydroxylation patterns.

Experimental Section

Melting points were taken on a Kofler hot-stage microscope and are uncorrected. IR spectra were measured on a Perkin-Elmer 1800 Fourier transform spectrophotometer and are expressed in wave numbers. Proton and ^{13}C NMR spectra were recorded on a JEOL FX90Q spectrometer. Chemical shifts are reported as δ values in ppm relative to TMS. Mass spectra were obtained on a VG 7070E spectrometer. Analytical TLC was conducted on 5 × 10 cm precoated TLC plates (silica gel 60 F-254, layer thickness 0.25 mm) manufactured by E. Merck and Co. Silica gel for chromatography was from E. Merck (60, 70–230 mesh ASTM). A stock solution of osmium tetraoxide (1 g, dissolved in 200 mL of 3:1 *tert*-butyl alcohol–carbon tetrachloride) was used for hydroxylations.

3-(Acetoxymethyl)-5-methoxy-9,10-dihydroxy-1,2,3,4-tetrahydroanthracen-1-one (14). A slurry of 4-methoxy-3-(phenylsulfonyl)-1-(3*H*)-isobenzofuranone (**12**)[21] (9.74 g, 32 mmol) in THF (30 mL) was added to a magnetically stirred, cold (−78 °C) solution of lithium *tert*-butoxide (96 mmol) prepared from *n*-butyllithium (43.6 mL of 2.2 M solution, 96 mmol) and *tert*-butyl alcohol (7.1 g, 96 mmol) in THF (200 mL). The cold yellow anion solution was stirred for 15 min, and then a solution of 5-(acetoxymethyl)-2-cyclohexen-1-one (**13**)[22] (7.0 g, 41.7 mmol) in THF (30 mL) was added slowly. Once the addition of **13** was finished, the reaction was maintained at −78 °C for 15 min. The cooling bath was then removed, and the reaction mixture was allowed to come to room temperature. The reaction mixture was stirred at room temperature for 2 h, cooled in an ice bath, and acidified with 3 N hydrochloric acid, whereupon a yellow solid precipitated. The THF was removed under reduced pressure, and the aqueous mixture was extracted with ethyl acetate (3 × 100 mL). The combined ethyl acetate extracts were successively washed with water and brine, dried ($MgSO_4$), filtered, and evaporated at reduced pressure. The syrupy residue was triturated with ether to give orange-red crystals of **14** (7.18 g, 68%), which were filtered and washed with ether. The filtrate and washings were combined and evaporated at reduced pressure. Chromatography of the residue (silica gel, 100 g, 50% EtOAc in hexanes) gave an additional 1.9 g of **14** (86% overall yield). A sample recrystallized from methylene chloride–hexanes had mp 128–129 °C: ^1H NMR ($CDCl_3$) δ 2.10 (s, 3 H), 2.60 (m, 4 H), 3.30 (m, 1 H), 4.07 (s, 3 H), 4.15 (d, 2 H, J = 5 Hz), 7.00 (dd, 1 H, J = 8, 1 Hz), 7.36 (t, 1 H, J = 8 Hz), 8.05 (dd, 1 H, J = 8, 1 Hz), 9.10 (s, 1 H), 13.35 (s, 1 H); mass spectrum, m/e 330 (M^+).

1-Hydroxy-3-(acetoxymethyl)-5-methoxyanthraquinone (15). Oxygen was bubbled through a solution of **14** (7.18 g, 21.7 mmol) in DMF (150 mL) heated at 100 °C for 12 h. The oxygen flow was terminated, and water (50 mL) was added to the hot solution. As the solution cooled, orange crystals of **15** precipitated, which were collected by filtration, washed with water, and dried to give 5.72 g (81%) of pure **15** with mp 179–180 °C: ^1H NMR ($CDCl_3$) δ 2.17 (s, 3 H), 4.05 (s, 3 H), 5.18 (s, 1 H), 7.21 (d, 1 H, J = 1 Hz), 7.37 (dd, 1 H, J = 8, 1 Hz), 7.71 (d, 1

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H, J = 1.76 Hz), 7.74 (dd, 1 H, J = 8, 8 Hz), 7.98 (dd, 1 H, J = 8, 1 Hz), 12.44 (s, 1 H); mass spectrum, m/e 326 (M^+). Anal. Calcd for $C_{16}H_{16}O_6$: C, 64.96; H, 4.52. Found: C, 65.02; H, 4.52.

1-*O*-(2-Methylenebutyl)-3-(hydroxymethyl)-5-methoxyanthraquinone (16b). To a magnetically stirred suspension of powdered anhydrous K_2CO_3 (1.2 g, 8.7 mmol) and potassium iodide (0.731 g, 4.4 mmol) in dry acetone (70 mL) under nitrogen was added successively a solution of **15** (1.34 g, 4.1 mmol) in acetone (30 mL) and 2-(chloromethyl)-1-butene[23] (0.65 g, 6.2 mmol). The mixture was heated at reflux for 24 h, cooled to room temperature, and filtered, and the filtrate was evaporated at reduced pressure. The residue was suspended in water (50 mL), and the mixture was extracted with ethyl acetate (2 × 50 mL). The combined organic solutions were washed successively with saturated $NaHSO_3$ (20 mL), water, and brine, dried (Na_2SO_4), filtered, and evaporated at reduced pressure to give 1.54 g (95%) of **16a**, which was used in the next step without purification.

A mixture of **16a** (1.54 g), THF (80 mL), water (20 mL), and 15% sodium hydroxide (2 mL) was stirred at room temperature for 1 h. The THF was removed at reduced pressure, and the aqueous phase was extracted with ethyl acetate (3 × 50 mL). The combined organic extracts were washed successively with 50-mL portions of water and brine, dried ($MgSO_4$), filtered, and evaporated at reduced pressure. Chromatography of the residue on silica gel (70 g, 80% ethyl acetate in hexanes) gave 1.32 g (96%) of pure **16b** with mp 125–126 °C: ^{1}H NMR ($CDCl_3$) δ 1.14 (t, 3 H, J = 7 Hz), 2.22 (q, 2 H, J = 7 Hz), 2.8 (br s, 1 H), 4.01 (s, 3 H), 4.62 (s, 2 H), 4.79 (s, 2 H), 5.08 (d, 1 H, J = 1 Hz), 5.40 (d, 1 H, J = 1 Hz), 7.24 (dd, 1 H, J = 7, 1 Hz), 7.29 (d, 1 H, J = 1 Hz), 7.66 (t, 1 H, J = 7 Hz), 7.75 (d, 1 H, J = 1 Hz), 7.89 (dd, 1 H, J = 7, 1 Hz); mass spectrum, m/e 352 (m^+).

1-Hydroxy-2-(2-methylenebutyl)-3-(hydroxymethyl)-5-methoxyanthraquinone (17a). A solution of **16b** (1.0 g, 2.85 mmol) and $Na_2S_2O_4$ (0.99 g, 5.7 mmol) in DMF (50 mL) and water (15 mL) was heated on a steam bath under nitrogen for 1.5 h. Oxygen was then bubbled through the hot solution for 0.5 h, and cold water (35 mL) was added. The solution was chilled in an ice bath, and the crystals of **17a** (643 mg, 64%) that precipitated were collected by filtration. The filtrate was extracted with methylene chloride (2 × 50 mL), and the combined organic extracts were dried ($MgSO_4$), filtered, and evaporated at reduced pressure. Chromatography of the residue (50 g of silica gel, 80% ethyl acetate in hexanes) gave an additional 323 mg of **17a** (combined yield of 96%). The product had mp 154–155 °C; ^{1}H NMR ($CDCl_3$) δ 1.10 (t, 2 H, J = 7 Hz), 2.12 (q, 2 H, J = 7 Hz), 2.24 (br s, 1 H), 3.50 (s, 2 H), 4.04 (s, 3 H), 4.36 (br s, 1 H), 4.75 (br s, 3 H), 7.33 (dd, 1 H, J = 8, 1 Hz), 7.7 (t, 1 H, J = 8 Hz), 7.90 (s, 1 H), 7.96 (dd, 1 H, J = 8, 1 Hz), 12.82 (s, 1 H); mass spectrum, m/e 352 (M^+). Anal. Calcd for $C_{21}H_{20}O_5$: C, 71.57; H, 5.72. Found: C, 71.54; H, 6.03.

1,5-Dimethoxy-2-(2-methylenebutyl)-3-(hydroxymethyl)anthraquinone (17b). A magnetically stirred suspension of **17a** (775 mg, 2.2 mmol), powdered anhydrous K_2CO_3 (1.5 g, 11 mmol), and dimethyl sulfate (2 mL) in dry acetone (100 mL) was heated at reflux under nitrogen for 6 h. The mixture was cooled to room temperature, and the potassium carbonate was removed by filtration. Triethylamine (10 mL) was added to the filtrate, and the mixture was allowed to stand for 2 h. The acetone and excess triethylamine were evaporated at reduced pressure. Water (50 mL) was added, and the mixture was extracted with methylene chloride (100 mL). The methylene chloride extract was washed successively with 50-mL portions of water and brine, dried ($MgSO_4$), filtered, and evaporated at reduced pressure. The residue was chromatographed (silica gel, 80% ethyl acetate in hexanes) to give 805 mg (100%) of pure **17b** with mp 50–52 °C; ^{1}H NMR ($CDCl_3$) δ 1.12 (t, 3 H, J = 7 Hz), 2.18 (q, 2 H, J = 7 Hz), 3.3 (br s, 1 H), 3.52 (s, 2 H), 3.83 (s, 3 H), 4.01 (s, 3 H), 4.22 (br s, 1 H), 4.75 (br s, 3 H), 4.75 (br s, 3 H), 7.24 (dd, 1 H, J = 8, 1 Hz), 7.64 (t, 1 H, J = 8 Hz), 7.82 (dd, 1 H, J = 8, 1 Hz), 8.19 (s, 1 H); mass spectrum, m/e 366 (M^+).

1,5-Dimethoxy-2-(2-methylenebutyl)-3-formylanthraquinone (17c). Barium manganate[25] (2.8 g, 10.9 mmol) was added portionwise to a magnetically stirred solution of **17b** (780 mg, 2.1 mmol) in dry methylene chloride (150 mL) under nitrogen. The suspension was stirred at room temperature for 3 h and then filtered, and the filtrate was evaporated at reduced pressure to give 702 mg (90%) of the pure aldehyde **17c** with mp 137–138 °C: ^{1}H NMR ($CDCl_3$) δ 1.16 (t, 3 H, J = 7 Hz), 2.24 (q, 2 H, J = 7 Hz), 3.92 (s, 2 H), 3.91 (s, 3 H), 4.05 (s, 3 H), 4.18 (br s, 1 H), 4.83 (br s, 1 H), 7.32 (dd, 1 H, J = 8, 1 Hz), 7.73 (t, 1 H, J = 8 Hz), 7.91 (dd, 1 H, J = 8, 1 Hz), 8.57 (s, 1 H), 10.23 (s, 1 H); mass spectrum, m/z 364 (M^+). Anal. Calcd for $C_{22}H_{20}O_5$: C, 72.51; H, 5.53. Found: C, 72.79; H, 5.38.

(±)-4,11-Dimethoxy-7-hydroxy-9-ethylidene-7,8,9,10-tetrahydro-5,12-naphthacenedione (18a and 18b). Stannic chloride pentahydrate (61 mg, 0.174 mmol) was added to a magnetically stirred solution of the aldehyde **17c** (217 mg, 0.596 mmol) in methylene chloride (80 mL) at room temperature, and the mixture was allowed to react for 15 min. The reaction mixture was chilled in an ice bath and then quenched with sodium bicarbonate solution (20 mL, 5%). The organic phase was separated and washed successively with 40-mL portions of water and brine, dried ($MgSO_4$), filtered, and evaporated. Recrystallization of the residue from methylene chloride–hexanes gave 200 mg (92%) of **18** as yellow crystals with mp 157–158 °C dec: ^{1}H NMR ($CDCl_3$) δ 1.24 (br s, 3 H), 1.70 (br d, 2 H), 2.0 (br m, 1 H), 2.70 (br m, 1 H), 3.90 (s, 3 H, OCH_3 of one isomer), 3.94 (s, 3 H, OCH_3 of the other isomer), 4.02 (s, 3 H, OCH_3 of both isomers), 4.86 (br m, 1 H), 5.62 (m, 1 H), 7.26 (dd, 1 H, J = 8, 1 Hz), 7.66 (t, 1 H, J = 8 Hz), 7.86 (dd, 1 H, J = 8, 1 Hz), 8.16 (s, 1 H); mass spectrum (FAB), m/e 365 (M + 1). Anal. Calcd for $C_{22}H_{20}O_5$: C, 72.51; H, 5.53. Found: C, 71.97; H, 5.44.

***cis*-(±)-3,4-Dihydro-7,12-dimethoxy-4-hydroxyspiro[naphthacene-2(1*H*),2′-(*E*,*Z*)-methyloxirane]-6,11-dione (19).** To a cold (0 °C) magnetically stirred solution of the homoallylic alcohol **18** (207 mg, 0.57 mmol) and vanadyl acetylacetonate (19 mg, 0.072 mmol) in dry methylene chloride (80 mL) under nitrogen was added *tert*-butyl hydroperoxide (474 μL, 1.42 mmol, 3.0 M solution in toluene).[26] The reaction was stirred for 4 h and then quenched with sodium sulfite solution (20 mL, 3%). The organic layer was separated and washed successively with 20-mL portions of water and brine, dried ($MgSO_4$), filtered, and evaporated. Chromatography of the residue (50 g silica gel, 2:1 ether–methylene chloride) furnished 192 mg of pure *cis*-epoxide **19** as a mixture of isomers. The product does not melt, but rather decomposes: ^{1}H NMR ($CDCl_3$) δ 1.38 (d, 3 H, J = 5 Hz), 1.96 (dd, 1 H, J = 14, 6 Hz), 2.26 (dd, 1 H, J = 14, 5 Hz), 2.96 (d, 1 H, J = 6 Hz), 3.08 (d, 1 H, J = 6 Hz), 3.4 (m, 1 H), 3.84 (s, 3 H, OCH_3 of one isomer), 3.90 (s, 3 H, OCH_3 of other isomer), 4.04 (s, 3 H, OCH_3 of both isomers), 7.24 (dd, 1 H, J = 8, 1 Hz), 7.64 (t, 1 H, J = 8 Hz), 7.82 (dd, 1 H, J = 8, 1 Hz), 8.18 (s, 1 H); mass spectrum (FAB), m/e 381 (M + 1). Anal. Calcd for $C_{22}H_{20}O_6$: C, 69.46; H, 5.30. Found: C, 69.25; H, 5.11.

(±)-4,11-Dimethoxy-*cis*-7,9-dihydroxy-9-ethenyl-7,8,9,10-tetrahydronaphthacene-5,12-dione (20a). Sodium borohydride (76 mg, 2 mmol) was added in small portions to a magnetically stirred solution of diphenyl diselenide (320 mg, 1.025 mmol) in absolute ethanol (40 mL) under nitrogen.[27] A slurry of the epoxide **19** (174 mg, 0.46 mmol) in dry DME (40 mL) was added, and the reaction was continued overnight. The solution was cooled in an ice bath, hydrogen peroxide (9 mL, 30%) was added dropwise, and the reaction mixture was allowed to warm to room temperature and stand overnight. Water (100 mL) was added, and the mixture was extracted with methylene chloride (3 × 50 mL). The combined organic extracts were washed successively with 50-mL portions of water and brine, dried ($MgSO_4$), filtered, and evaporated at reduced pressure. Chromatography of the residue (50 g of silica gel, 1:1 ether–methylene chloride) gave 163 mg (94%) of pure olefinic diol **20a** with mp 67–69 °C dec: ^{1}H NMR ($CDCl_3$) δ 2.0 (dd, 1 H, J = 14, 5 Hz), 2.32 (d, 1 H, J = 14 Hz), 2.72 (d, 1 H, J = 18 Hz), 3.22 (d, 1 H, J = 18 Hz), 3.4 (br s, 1 H), 3.90 (s, 3 H), 4.00 (s, 3 H), 4.40 (br m, 1 H), 4.9 (br s, 1 H), 5.20 (dd, 1 H, J = 10.5, 1 Hz), 5.40 (dd, 1 H, J = 17, 1 Hz), 6.1 (dd, 1 H, J = 17, 10.5 Hz), 7.20 (dd, 1 H, J = 8, 1 Hz), 7.62 (t, 1 H, J = 8 Hz), 7.80 (dd, 1 H, J = 8, 1 Hz), 8.20 (s, 1 H); mass spectrum (FAB), m/e 381 (M + 1).

(±)-4,11-Dimethoxy-*cis*-7-[(*tert*-butyldimethylsilyl)oxy]-9-hydroxy-9-ethenyl-7,8,9,10-tetrahydronaphthacene-5,12-dione (20b). A solution of the vinyl diol **20a** (112 mg, 0.295 mmol), imidazole (100 mg, 1.475 mmol), and *tert*-butydimethylsilyl chloride (134 mg, 0.89 mmol) in dry DMF (6 mL) under nitrogen was stirred for 24 h.[37] The excess silylating agent was destroyed by adding methanol (1 mL) to the reaction and stirring for 1 h. Water was added, and the mixture was extracted with methylene chloride (3 × 25 mL). The combined organic extracts were washed successively with 25-mL aliquots of water and brine, dried ($MgSO_4$), filtered, and evaporated at reduced pressure. Chromatography of the residue (20 g silica gel, 1:1 EtOAc–hexanes) furnished 132 mg (91%) of pure siloxy ether **20b** with mp 146–147 °C: ^{1}H NMR ($CDCl_3$) δ 0.28 (s, 6 H), 0.92 (s, 9 H), 2.12 (m, 2 H), 2.84 (d, 1 H, J = 18 Hz), 3.26 (d, 1 H, J = 18 Hz), 3.95 (s, 3 H), 4.06 (s, 3 H), 4.31 (s, 1 H), 5.04 (t, 1 H, J = 5 Hz), 5.16 (dd, 1 H, J = 10.5, 1.8 Hz), 5.40 (dd, 1 H, J = 17, 1.8 Hz), 6.04 (dd, 1 H, J = 17, 10.5 Hz), 7.32 (dd, 1 H, J = 8, 1 Hz), 7.71 (t, 1 H, J = 8 Hz), 7.93 (dd, 1 H, J = 8, 1 Hz), 8.10 (s, 1 H); mass spectrum (FAB), m/e 495 (M + 1).

(±)-4,11-Dimethoxy-*cis*-7-[(*tert*-butyldimethylsilyl)oxy]-9-hydroxy-9-ethyl-7,8,9,10-tetrahydronaphthacene-5,12-dione (11b). Hydrogen peroxide (30%, 3 mmol, 0.3 mL) was slowly added to a cold (0–5 °C), magnetically stirred solution of the vinylcarbinol **20b** (0.06 mmol, 30 mg) and hydrazine hydrate (100%, 3.0 mmol, 152 mg) in ethanol (2 mL) to which had been added one drop of a saturated solution of cupric sulfate.[29] The mixture was then warmed to room temperature and stirred for 16 h. Water (5 mL) was added, and the product was extracted with ether (3 × 15 mL). The combined organic extracts were successively washed

with water (15 mL) and brine (15 mL), dried ($MgSO_4$), filtered, and evaporated at reduced pressure. The residue was chromatographed (10 g of silica gel; 1:1 ethyl acetate–hexanes) to furnish 28.5 mg (95%) of pure **11b**: ^1H NMR ($CDCl_3$) δ 0.27 (s, 6 H), 0.89 (s, 9 H), 1.11 (t, J = 7 Hz, 3 H), 1.64 (q, J = 7 Hz, 2 H), 1.84 (dd, J = 5 Hz, J = 14 Hz, 1 H), 2.16 (dd, J = 5 Hz, J = 14 Hz, 1 H), 2.66 (d, J = 18 Hz, 1 H), 3.26 (d, J = 18 Hz, 1 H), 4.04 (s, 3 H), 4.12 (s, 3 H), 4.16 (s, 1 H), 5.12 (t, J = 5 Hz, 1 H), 7.29 (dd, J = 1 Hz, J = 8 Hz, 1 H), 7.69 (t, J = 8 Hz, 1 H), 7.96 (dd, J = 1 Hz, J = 8 Hz, 1 H), 8.12 (s, 1 H); mass spectrum (FAB), m/e 495 (M + 1).

(±)-4,11-Dimethoxy-*cis*-7,9-dihydroxy-9-ethyl-7,8,9,10-tetrahydro-5,12-naphthacenedione (11a). A solution of hydrogen fluoride (4 mL of a 5% solution in acetonitrile)[30] was added to a solution of the silyloxy ether **11b** (0.056 mmol, 28 mg) in acetonitrile (1 mL), and the reaction mixture was stirred at room temperature for 1 h. Water (20 mL) was added, and the mixture was extracted with methylene chloride (3 × 15 mL). The combined organic solutions were washed successively with water (15 mL) and brine (15 mL), dried ($MgSO_4$), filtered, and evaporated at reduced pressure. The residue was chromatographed (10 g silica gel; 2:1 ethyl acetate–methylene chloride) to furnish 19 mg (89%) of **11a** as a yellow solid with mp 194–195 °C: ^1H NMR ($CDCl_3$) δ 1.07 (t, J = 7 Hz, 3 H), 1.72 (q, J = 7 Hz, 2 H), 1.8 (br s, 1 H), 1.94 (dd, J = 5 Hz, J = 14 Hz, 1 H), 2.30 (d, J = 14 Hz, 1 H), 2.64 (d, J = 18 Hz, 1 H), 3.18 (d, J = 18 Hz, 1 H), 3.90 (s, 3 H), 3.95 (s, 1 H), 4.01 (s, 3 H), 4.92 (m, 1 H), 7.27 (dd, J = 1 Hz, J = 8 Hz, 1 H), 7.67 (t, J = 8 Hz, 1 H), 7.87 (dd, J = 1 Hz, J = 8 Hz, 1 H), 8.19 (s, 1 H); mass spectrum, m/e 382 (M^+). Anal. Calcd for $C_{22}H_{22}O_6$: C, 69.10; H, 5.80. Found: C, 68.81; H, 5.74.

(±)-4,11-Dimethoxy-*cis*-7,9-dihydroxy-9-acetyl-7,8,9,10-tetrahydronaphthacene-5,12-dione (2a). Acetyl chloride (1.1 mmol, 80 μL) was added dropwise to a cold (0 °C) solution of the alcohol **18** (53 mg, 0.145 mmol) and dry pyridine (120 μL) in dry methylene chloride (3 mL), and the resulting suspension was stirred under nitrogen for 2 h. The excess acetyl chloride was quenched with methanol (0.5 mL). Water (10 mL) and methylene chloride (15 mL) were added, and the layers were separated. The aqueous phase was further extracted with methylene chloride (2 × 15 mL). The combined organic extracts were washed with water (15 mL) and brine (15 mL), dried ($MgSO_4$), filtered, and evaporated at reduced pressure to give 63 mg of the acetate **18c**, which was used without further purification.

A solution of the olefinic acetate **18c** (63 mg), trimethylamine N-oxide monohydrate (0.29 mmol, 33 mg), and the osmium tetraoxide stock solution (0.007 mmol, 185 μL) in acetone (5 mL) and water (1.5 mL) was magnetically stirred 1.5 h. The mixture was cooled (0 °C), sodium bisulfite (10 mL, 10% solution) was added, and the mixture was stirred for 0.5 h to destroy excess osmium tetraoxide. The acetone was evaporated at reduced pressure, and water (10 mL) and ethyl acetate were added. The layers were separated, and the aqueous phase was further extracted with ethyl acetate (2 × 15 mL). The combined organic extracts were washed with water (15 mL) and brine (15 mL), dried ($MgSO_4$), filtered, and evaporated at reduced pressure. Chromatography of the residue (20 g of silica gel; ethyl acetate) furnished 60 mg (94% overall yield) of a diastereoisomeric mixture of diol acetates **21**.

Sulfur trioxide–pyridine complex[32] (108 mg, 0.68 mmol) in dimethyl sulfoxide (1 mL) was added to a solution of the diols **21** (60 mg, 0.136 mmol) and anhydrous triethylamine (2 mmol, 0.3 mL) in anhydrous dimethyl sulfoxide (1 mL), and the reaction mixture was stirred for 4 h at room temperature. Methylene chloride (15 mL) and water (10 mL) were added, the mixture was transferred to a separatory funnel, and the layers were separated. The organic phase was washed with brine (10 mL), dried ($MgSO_4$), filtered, and evaporated at reduced pressure. Chromatography of the residue (20 g of silica gel; 8:2 ethyl acetate–hexanes) gave 51 mg (85%) of the keto acetates **22a** and **23a**.

Powdered anhdrous potassium carbonate (90 mg, 0.7 mmol) was added to a solution of the acetates **22a** and **23a** (47 mg, 0.107 mmol) in anhydrous methanol (6 mL), and the mixture was stirred for 1 h. Saturated ammonium chloride solution (5 mL) and ethyl acetate (15 mL) were added. The layers were separated, and the aqueous phase was further extracted with ethyl acetate (15 mL). The combined organic solutions were washed with brine (10 mL), dried ($MgSO_4$), filtered, and evaporated at reduced pressure. The residue, a 3:2 diastereoisomeric mixture, was separated through column chromatography (20 g silica gel; 1:1 ethyl acetate–methylene chloride) to furnish 17 mg (40%) of **2a** with mp 204–205 °C: ^1H NMR ($CDCl_3$) δ 2.26 (d, J = 4.5 Hz, 2 H), 2.40 (s, 3 H), 2.95 (d, J = 18 Hz, 1 H), 3.18 (d, J = 18 Hz, 1 H), 3.87 (s, 3 H), 4.0 (s, 3 H), 4.16 (br d, 1 H), 4.59 (s, 1 H), 4.96 (m, 1 H), 7.27 (dd, J = 1 Hz, J = 8 Hz, 1 H), 7.67 (t, J = 8 Hz, 1 H), 7.86 (dd, J = 1 Hz, J = 8 Hz, 1 H), 8.19 (s, 1 H); mass spectrum, m/e 396 (M^+); IR (cm^{-1}) 3540–3620, 1720, 1675. Anal. Calcd for $C_{22}H_{20}O_7$: C, 66.66; H, 5.07. Found: C, 66.52; H, 5.14.

With continued elution there was obtained 26 mg (60%) of material, which was shown to be a mixture of the acetyl and hemiacetal forms **23b** and **24**.

(±)-4,11-Dimethoxy-*cis*-7-[(*tert*-butyldimethylsilyl)oxy]-9-hydroxy-9-[1-oxo-2-[(*tert*-butyldimethylsilyl)oxy]ethyl]-7,8,9,10-tetrahydro-5,12-naphthacenedione (26). A solution of the allylic alcohol **20b** (0.12 g, 0.243 mmol), trimethylamine N-oxide dihydrate (0.054 g, 0.49 mmol), and osmium tetraoxide stock solution (309 μL, 0.012 mmol) in acetone (7 mL) and water (3 mL) was stirred at room temperature for 16 h. The reaction was quenched with aqueous sodium sulfite solution (5 mL, 5% solution), and the acetone was removed by evaporation at reduced pressure. The residue was extracted with methylene chloride (50 mL), and the organic solution was successively washed with water (20 mL) and brine (20 mL), dried ($MgSO_4$), filtered, and concentrated to furnish a quantitative yield (129 mg) of the triol **25a**, which was used without further purification.

A solution of the triol **25a** (129 mg, 0.243 mmol), (dimethylamino)-pyridine (3 mg, 0.02 mmol), triethylamine (140 μL, 1 mmol), and *tert*-butyldimethylsilyl chloride (48 mg, 0.32 mmol) in dry methylene chloride (2 mL) was stirred at ambient temperature for 2 days. The excess *tert*-butyldimethylsilyl chloride was destroyed with methanol (1 mL). Water (10 mL) and methylene chloride (10 mL) were added, and the layers were separated. The organic solution was washed successively with water (10 mL) and brine (10 mL), dried ($MgSO_4$), filtered, and evaporated. The residue was chromatographed (25 g of silica gel; 4:6 ethyl acetate–hexanes) to give a quantitative yield (157 mg) of the bis(silyloxy) **25b** as a 1:1 diastereoisomeric mixture of yellow crystals with mp 127–129 °C dec: mass spectrum (FAB), m/e 643 (M + 1).

To the diol **25b** (157 mg, 0.243 mmol) in dry dimethyl sulfoxide (1 mL) and dry triethylamine (1 mL, 7.3 mmol) was added a solution of sulfur trioxide–pyridine complex[32] (386 mg, 2.43 mmol) in dry dimethyl sulfoxide (1 mL), and the mixture was stirred at room temperature under nitrogen for 48 h. Water (20 mL) was added, and the mixture was extracted with methylene chloride (3 × 25 mL). The combined organic extracts were washed successively with water (20 mL) and brine (20 mL), dried ($MgSO_4$), filtered, and evaporated at reduced pressure. The residue was chromatographed (30 g silica gel; 4:6 ethyl acetate–hexanes) to give 131 mg (84%) of pure α-hydroxy ketone **26** as yellow crystals with mp 113–115 °C dec: ^1H NMR ($CDCl_3$) δ 0.15 (s, 6 H), 0.25 (s, 3 H), 0.29 (s, 3 H), 0.90 (s, 9 H), 0.96 (s, 9 H), 2.19 (d, J = 4 Hz, 2 H), 3.05 (d, J = 18 Hz, 1 H), 3.31 (d, J = 18 Hz, 1 H), 3.92 (s, 3 H), 4.06 (s, 3 H), 4.89 (s, 1 H), 4.90 (s, 1 H), 5.04 (s, 1 H), 5.10 (t, J = 4 Hz, 1 H), 7.32 (dd, J = 1 Hz, J = 8 Hz, 1 H), 7.71 (t, J = 8 Hz, 1 H), 7.93 (dd, J = 1 Hz, J = 8 Hz, 1 H), 8.04 (s, 1 H); mass spectrum (FAB) m/e 641 (M + 1).

(±)-4,11-Dimethoxy-*cis*-7,9-dihydroxy-9-(1-oxo-2-hydroxyethyl)-7,8,9,10-tetrahydro-5,12-naphthacenedione (2b). Aqueous hydrofluoric acid (4 mL of a 5% solution in acetonitrile)[30] was added dropwise to a solution of the silyloxy ketone **26** (36 mg, 0.56 mmol) in acetonitrile (1 mL), and the mixture was stirred at room temperature for 1 h. Water (20 mL) was added, and the mixture was extracted with methylene chloride (3 × 15 mL). The combined organic extracts were washed successively with water (3 × 15 mL) and brine (15 mL), dried ($MgSO_4$), filtered, and evaporated. The residue was chromatographed (20 g of silica gel; 9.5:5 ethyl acetate–methanol) to give 20 mg (87%) of pure **2b** as yellow crystals with mp 143–145 °C dec: ^1H NMR: (pyridine-d_5) δ 1.94 (s, 1 H), 2.49 (dd, 1 H, J = 14, 6 Hz), 2.78 (dd, 1 H, J = 14, 6 Hz), 3.43 (d, 1 H, J = 17 Hz), 3.59 (s, 1 H), 3.86 (s, 3 H), 3.94 (s, 3 H), 5.22 (t, 1 H, J = 6 Hz), 5.29 (s, 2 H), 5.61 (s, 1 H), 7.26 (dd, 1 H, J = 8, 1 Hz), 7.62 (t, 1 H, J = 8 Hz), 7.98 (dd, 1 H, J = 8, 1 Hz), 8.67 (s, 1 H); mass spectrum (FAB), m/e 413 (M + 1); IR cm^{-1} 3550–3300, 1730, 1670. Anal. Calcd for $C_{22}H_{20}O_8$: C, 64.07; H, 4.88. Found: C, 64.06; H, 4.68.

Acknowledgment. This research was generously supported by the National Cancer Institute and the National Institutes of General Medical Sciences of the National Institutes of Health under Grant CA/GM 18141.

Registry No. 1, 79036-53-6; **2a**, 113452-56-5; **2b**, 113452-63-4; **11a**, 88945-98-6; **11b**, 113452-51-0; **12**, 74724-81-5; **13**, 113452-39-4; **14**, 113452-40-7; **15**, 88945-88-4; **16a**, 113452-41-8; **16b**, 113452-42-9; **17a**, 113452-43-0; **17b**, 113452-44-1; **17c**, 113452-45-2; **18a**, 113452-46-3; **18b**, 113452-47-4; **18c** (isomer 1), 113452-52-1; **18c** (isomer 2), 113452-53-2; **19** (isomer 1), 113452-48-5; **19** (isomer 2), 113531-27-4; **20a**, 113452-49-6; **20b**, 113452-50-9; **21**, 113474-69-4; **22a**, 113452-54-3; **23a**, 113452-55-4; **23b**, 113452-57-6; **24**, 113452-58-7; **25a** (isomer 1), 113452-59-8; **25a** (isomer 2), 113452-60-1; **25b** (isomer 1), 113452-61-2; **25b** (isomer 2), 113452-62-3; **26**, 113474-49-0; 2-(chloromethyl)-1-butene, 23010-02-8.