Synthetic Anthracyclines: Regiospecific Total Synthesis of D-Ring Thiophene Analogues of Daunomycin

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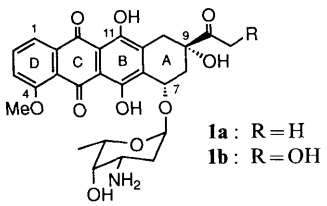
The key anhydride 2-acetoxy-[2-carboxy-5-(trimethylsilyl)thiophen-3-yl]acetic acid anhydride (8), prepared from (2-carboxythiophen-3-yl)acetic acid (5), underwent a strong base-induced cycloaddition reaction with the chloroquinone acetal (11) to give the 7,7-ethylenedioxy-2-trimethylsilyl-6,7,8,9-tetrahydroanthra[2,3-*b*]thiophene-5,10-dione (12) regioselectively. Similarly, the regioisomeric 8,8-ethylenedioxy-2-trimethylsilyl-6,7,8,9-tetrahydroanthra[2,3-*b*]thiophene-5,10-dione (30) was obtained by the strong base-induced cycloaddition reaction of 8 with the chloroquinone acetal (29). These cycloadducts (12 and 30) were converted to D-ring thiophene analogues (28 and 38) of daunomycin (1a). Another D-ring thiophene analogue (42) which has a trimethylsilyl substitutent in the D-ring was also prepared.

Keywords daunomycin analogue; heteroanthracycline; D-ring thiophene analogue; cycloaddition; antitumor agent

Anthracycline antibiotics, daunomycin (**1a**) and adriamycin (**1b**), are powerful antitumor agents in the treatment of a broad spectrum of human cancers,[1,2] but their severe cardiotoxicities have limited their usefulness.[3] This may be in part explained by the easy one-electron reduction of these agents to the corresponding radical anion which is able to react with oxygen to afford reactive oxygen species such as $O_2^{\cdot-}$, H_2O_2 or $OH^{\cdot}$.[4] It has been suggested that the quinone moiety might take part in the redox reaction, and some C-ring modified anthracyclines show antitumor activity with low cardiotoxicity.[5] Modification of the redox potential may be of importance to obtain more information about structure–activity relationships. Thus, synthetic anthracyclines, 11-deoxy-[6] and 4-demethoxyanthracyclines,[6b,7] exhibit higher values of therapeutic index than natural anthracyclines. It would be interesting to synthesize anthracycline analogues of **1a, b** in which the B- or D-ring is heteroaromatic, since the heteroaromatic ring would change the redox potential and provides a useful bioisosteric replacement of the benzene ring in some drugs.[8] Although numerous efforts have been made to prepare anthracyclines themselves, only a few successful examples have so far been directed toward the synthesis of heteroanthracyclines involving modifications within the D-ring due to the synthetic difficulty.[9] As part of our continuing studies of the practical synthesis of anthracyclines and their analogues, we have reported the first total synthesis of D-ring indole[10] and thiophene analogues of **1a**.[11] We now report in detail the regiospecific total synthesis of D-ring thiophene analogues.

Recently we have reported an efficient, regiospecific synthesis of 7,7-ethylenedioxy-11-hydroxy-6,7,8,9-tetrahydroanthra[2,3-*b*]thiophene-5,10-dione (**2**).[12] Therefore, we initially attempted to obtain the key *para*-acetoxylated cycloaddition product (**3**) by a similar method to that described for 4-demethoxydaunomycinone and daunomycinone.[13] Thus, *para*-oxidation of **2** with lead tetraacetate (LTA) gave the *para*-acetoxylated compound (**3**) in 22% yield. Treatment of **3** with trifluoroacetic acid (TFA) caused deacetalization, deacetylation, and enol-keto isomerization in the B/C rings at the same time to give a 92% yield of the triketone (**4**). Although we could thus get the key intermediate (**4**), the yield of the oxidation step of **2** was quite low. Therefore, an alternative synthesis of **3** by utilizing a cycloaddition of the previously C_2-acetoxylated heterohomophthalic anhydride to the chloroquinone acetal (**11**) was examined. The desired anhydride (**8**) was prepared in excellent yield from (2-carboxythiophen-3-yl)acetic acid (**5**)[14] through LTA oxidation of the tetra-trimethylsilylated ketene acetal intermediate (**6**).[15] Treatment of **5** with a fourfold excess of lithium diisopropylamide (LDA) gave the tetraanion, which was quenched with an excess of trimethylsilyl chloride to give **6**. Subsequent oxidation of **6** with LTA yielded 2-acetoxy-2-[2-carboxy-5-(trimethylsilyl)-thiophen-3-yl]acetic acid (**7**) in 99% yield. Dehydration of **7** with (trimethylsilyl)ethoxyacetylene[16] in dichloromethane gave **8** in a quantitative yield. The desilylated anhydride (**10**) was obtained from **7**. Treatment of **7** with tetrabutylammonium fluoride (TBAF) gave the desilylated dicarboxylic acid (**9**) in 97% yield, and this was dehydrated with (trimethylsilyl)ethoxyacetylene to give **10** in a quantitative yield (Chart 1).

Treatment of the sodium salt generated from **8** and 1.1 eq of sodium hydride in tetrahydrofuran (THF) with the chloroquinone acetal (**11**)[17] at room temperature gave the regiospecific cycloadduct (**12**) in 58% yield. Acid hydrolysis of both acetoxy and acetal groups of **12** with aqueous TFA led to a 93% yield of the triketone (**13**). Side chain elaboration of the enolizable 7-keto group of **13** was accomplished by use of (trimethylsilyl)ethynyl cerium(III) chloride.[15,18] Treatment of **13** with 20 eq of (trimethylsilyl)ethynylcerium(III) chloride [prepared from (trimethylsilyl)ethynyllithium and cerium(III) chloride in THF] at −78 °C gave 7-(trimethylsilyl)ethynyl alcohol (**14**) in a quantitative yield. Direct conversion of the (trimethylsilyl)ethynyl group of **14** into the methyl ketone group was accomplished by treatment with mercury(II) oxide and dilute sulfuric acid in boiling THF, which gave the α-hydroxyketone compound (**15**) in 91% yield. Acetali-



1a: R = H
1b: R = OH

Fig. 1

zation of **15** with ethylene glycol in the presence of a catalytic amount of *p*-toluenesulfonic acid in boiling benzene gave the acetal (**16**) in 98% yield. Desilylation of **16** with TBAF in THF gave the desilylated acetal (**17**) in a quantitative yield. An attempt to convert **17** into the desired aglycone (**20**) having *cis*-stereochemistry of the 7- and 9-hydroxy functions by the standard procedure[19] unexpectedly gave the *trans*-diol (**18**) as a major product. Thus, bromination of **17** with bromine and 2,2′-azobisisobutyronitrile (AIBN) in a mixture of water, carbon tetrachloride and chloroform under reflux and subsequent hydrolysis with 80% aqueous TFA at 0 °C gave **18** in 82% yield. The *trans*-stereochemistry was deduced from the coupling constant [δ 5.37 (br t, J=8.0 Hz, $\nu_{1/2}$=19.0 Hz, H-9)][20] and the following chemical behavior. Reaction of **18** with 2,2-dimethoxypropane in the presence of a catalytic amount of *p*-toluenesulfonic acid in dichloromethane at room temperature resulted in a formation of the ketal (**23**). If the stereochemistry of **18** was *cis*, **18** would be converted into the acetonide (**23′**) by this reaction. Epimerization was successfully accomplished when **18** was treated with benzeneboronic acid in the presence of TFA[17,21] and the resulting *cis*-boronate was deprotected with 2-methylpentane-2,4-diol and acetic acid. This gave the pure **20** in 86% yield (33% overall yield from **8**). Alternatively, **20** was also obtained from the desilylated anhydride (**10**) by a series of similar reactions (**10**→**3**→**4**→**21**→**22**→**17**→**18**→**20**) in rather poor yield (13% overall yield from **10**) (Charts 2 and 3).

With this aglycone in hand, there remained the glycosidation with appropriately protected L-daunosamine as the target. First, we examined the useful glycosidation method developed by Terashima *et al.*[22] The aglycone (**20**) and suitably modified L-daunosamine (**24**) were treated with trimethylsilyl trifluoromethanesulfonate (TMSOTf) and

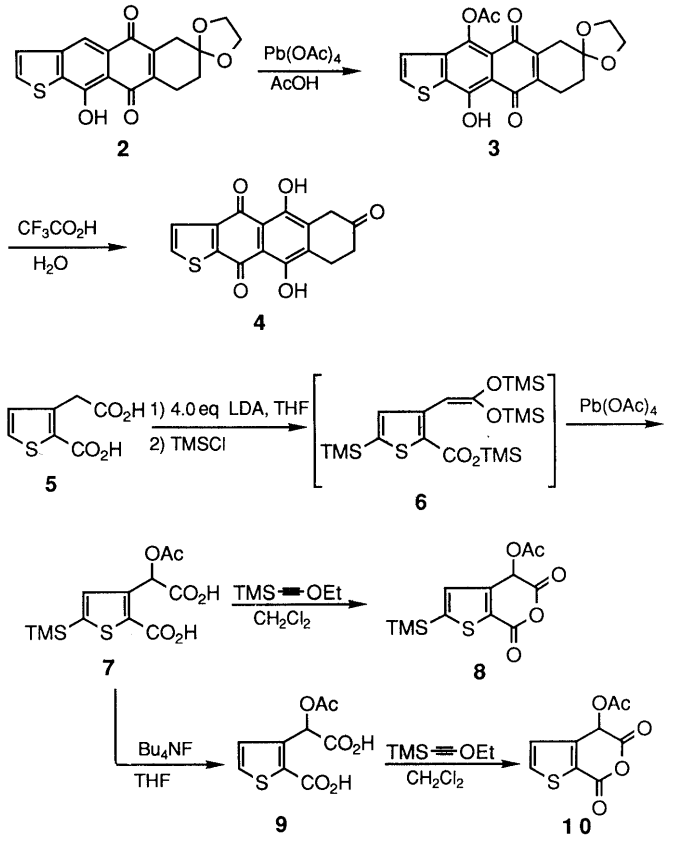


Chart 1

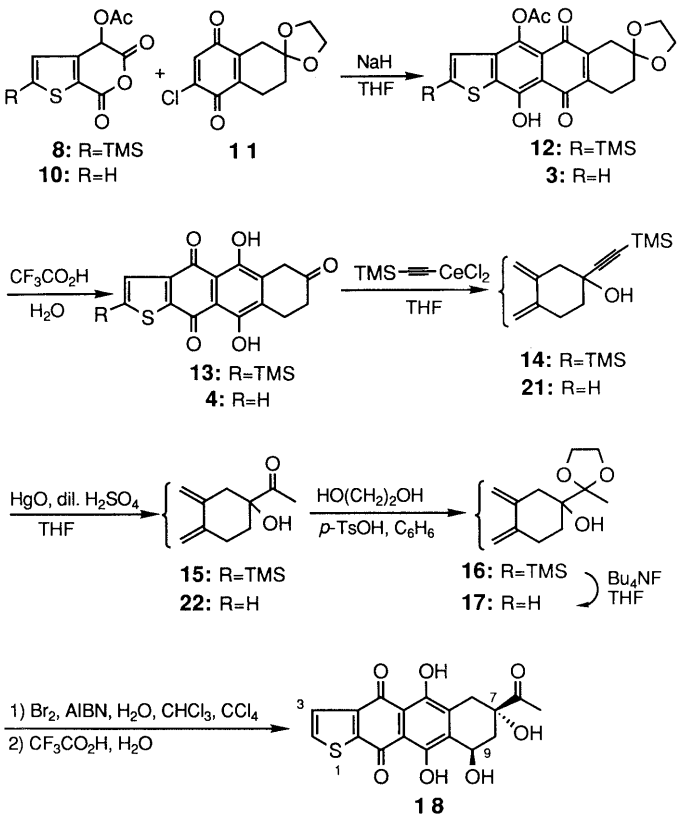


Chart 2

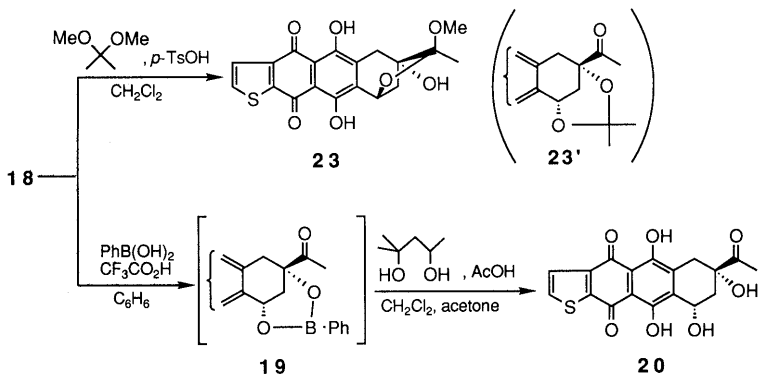


Chart 3

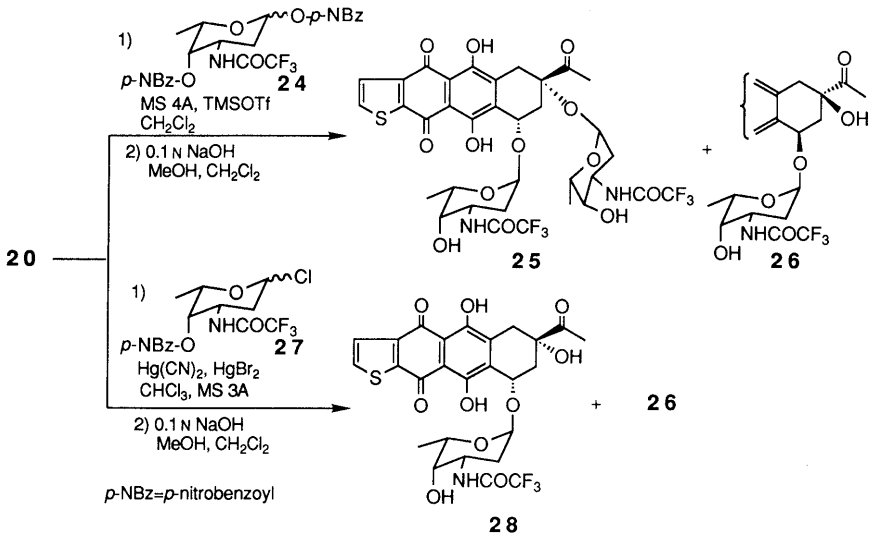


Chart 4

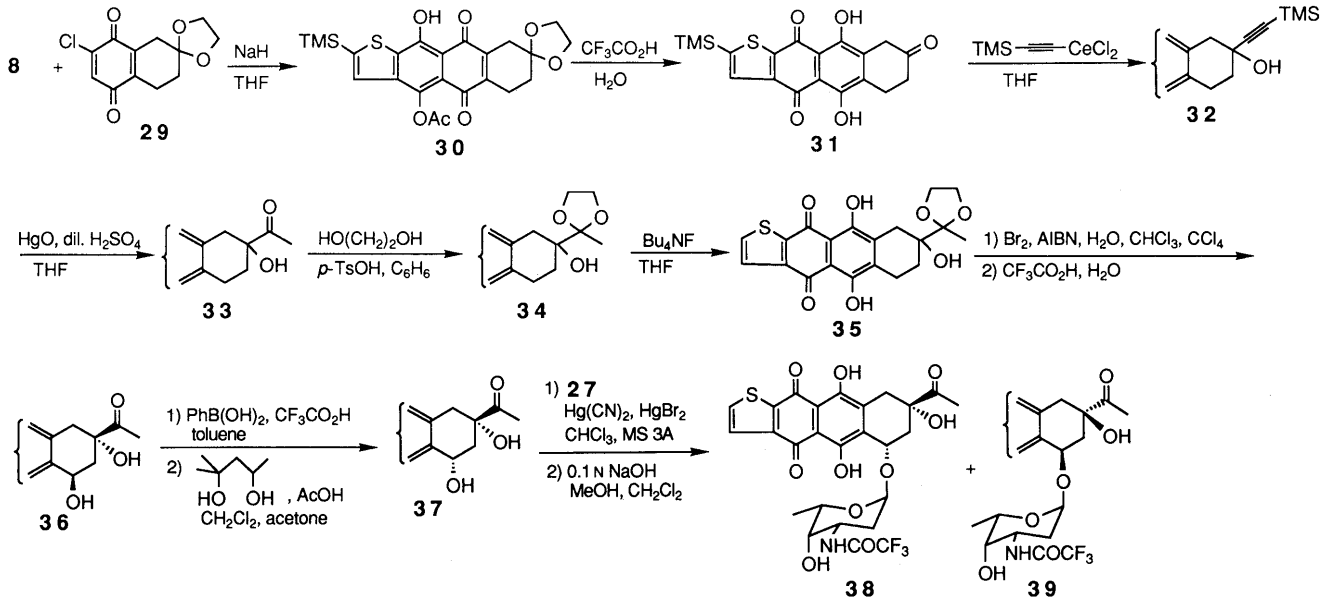


Chart 5

molecular sieves 4A in a mixed solvent of anhydrous dichloromethane and anhydrous ether at $-15\,^{\circ}C$ to give two α-glycosides. These glycosides were separated by preparative thin layer chromatography (TLC) on silica gel and deprotected with an equivalent amount of 0.1 N sodium hydroxide at $0\,^{\circ}C$ to give a natural-type (7*S*,9*S*)-α-bisglycoside (**25**) (45% from **20**), and the (7*R*,9*R*)-α-monoglycoside (**26**) (40% from **20**). Employment of the classical Koenigs–Knorr method for the glycosidation gave a better result. Thus, **20** and the 1-chloro sugar (**27**) were treated with mercury(II) cyanide, mercury(II) bromide, and molecular sieves 3A in chloroform to give two α-glycosides. They were separated by preparative TLC and deprotected with 0.1 N sodium hydroxide to give the desired natural-type (7*S*,9*S*)-α-monoglycoside (**28**) (28% from **20**), and the (7*R*,9*R*)-α-monoglycoside (**26**) (36% from **20**). The absolute structures of these glycosides were adequately supported by the spectral data [circular dichroism (CD) and ^{1}H-nuclear magnetic resonance (^{1}H-NMR), see experimental section]. The similarity of the CD curves of **25** and **28** to that of natural daunomycin (**1a**) $[[\theta]_{287} = -1.72 \times 10^4$ (MeOH)][23] indicated that they had natural configurations (7*S*,9*S*), whereas the CD curve of **26** indicated the opposite configuration (7*R*,9*R*), and the small $v_{1/2}$ value (7.0 Hz) of the ^{1}H-NMR signals due to the anomeric protons indicated that they were α-glycosides[24] (Chart 4).

Similarly, regioisomeric α-glycosides (**38** and **39**) were prepared from the adduct (**30**) obtained by the reaction of **8** and the chloroquinone acetal (**29**)[15] through a similar series of reactions (**30**→**31**→**32**→**33**→**34**→**35**→**36**→**37**→**38**+**39**) (Chart 5).

Next we planned to synthesize the heteroanthracycline which has a trimethylsilyl substituent in the D-ring, because some silicon-containing medicinal agents retain and/or improve their biological profile in comparison with that of the corresponding carbon isoster.[24] We could obtain the *trans*-7,9-diol (**40**) by bromination of **16** with bromine and AIBN in a mixture of water, chloroform and carbon

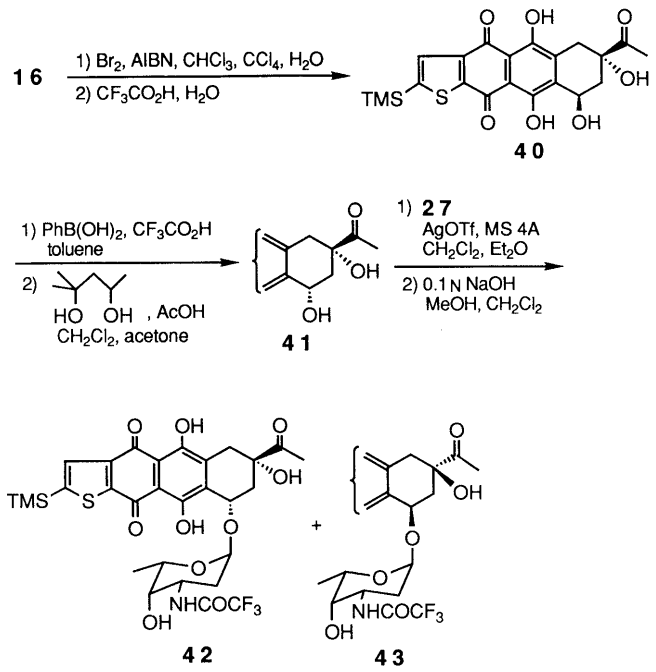


Chart 6

tetrachloride followed by hydrolysis with 80% aqueous TFA in 66% yield. The *trans*-diol (**40**) was converted into the desired *cis*-diol (**41**) in 77% yield by the same procedure as described for the epimerization of **18**. The glycosidation of **41** by the Koenigs–Knorr method as described for the preparation of **28** gave α-monoglycosides in poor yield. Better yields of α-monoglycosides (**42** and **43**) were obtained when silver trifluoromethanesulfonate (AgOTf)[25] was used instead of the Hg salts. Thus, the aglycone (**41**) and **27** were treated with AgOTf and molecular sieves 4A in anhydrous dichloromethane and ether at room temperature to give two α-glycosides. These glycosides were separated by preparative TLC on silica gel and deprotected by the same procedure as described for the preparation of **28** to give the (7*S*,9*S*)-α-monoglycoside (**42**) (19% yield from **41**) and (7*R*,9*R*)-α-monoglycoside (**43**) (17% yield from **41**) (Chart 6).

The D-ring thiophene analogues (**28**, **38**, and **42**) show inhibitory activity against L-1210 cell growth (*in vitro*) comparable to that of adriamycin (**1b**) and the biological results including those of *in vivo* testing will be described in detail in the near future.

Experimental

All melting points are uncorrected. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. Infrared (IR) absorption spectra were recorded on a JASCO HPIR-102 spectrophotometer, ^{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. Mass spectra (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- 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 mm, 70—230 mesh ASTM) and E. Merck pre-coated TLC plates, Silica gel 60 F_{254} were used for column chromatography and for preparative TLC, respectively.

4-Acetoxy-7,7-ethylenedioxy-11-hydroxy-6,7,8,9-tetrahydroanthra-[2,3-*b*]thiophene-5,10-dione (3) A solution of **2** (38.9 mg, 0.114 mmol) in AcOH (6 ml), CH_2Cl_2 (3 ml), and $ClCH_2CH_2Cl$ (1.5 ml) was treated with $Pb(OAc)_4$ (200 mg, 0.451 mmol) at 40 °C for 23 h. The mixture was concentrated *in vacuo*. The residue was purified by column chromatography (hexane : Et_2O = 1 : 2) to give a 22% yield (10.1 mg) of **3** as yellow crystals, mp 245—250 °C (C_6H_6–Et_2O). IR ($CHCl_3$) ν cm^{-1}: 1770, 1670, 1620. ^{1}H-NMR ($CDCl_3$) δ: 1.8—2.0 (m, 2H, H-8 × 2), 2.47 (s, 3H, $COCH_3$), 2.7—3.1 (m, 4H, H-6 × 2, H-9 × 2), 4.04 (s, 4H, OCH_2CH_2O), 7.59 (d, 1H, J = 5.0 Hz, ArH), 7.72 (d, 1H, J = 5.0 Hz, ArH), 13.10 (s, 1H, ArOH). Exact MS Calcd for $C_{20}H_{16}O_7S$: 400.0614. Found: 400.0608.

5,10-Dihydroxy-6,7,8,9-tetrahydroanthra[2,3-*b*]thiophene-4,7,11-trione (4) A solution of **3** (13.0 mg, 0.0325 mmol) in CF_3CO_2H (2.0 ml) and water (0.5 ml) was heated at 50 °C for 8 h, then concentrated *in vacuo*, and the residue was partitioned between CH_2Cl_2 (20 ml) and water. The aqueous layer was extracted with CH_2Cl_2 (20 ml × 2). The combined extract was washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by preparative TLC ($CHCl_3$) to give a 92% yield (9.4 mg) of **4** as red crystals, mp 287—289 °C (hexane–$CHCl_3$). IR (KCl) ν cm^{-1}: 1710, 1597, 1400. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 2.66 (t, 2H, J = 7.0 Hz, H-8 × 2), 3.24 (t, 2H, J = 7.0 Hz, H-9 × 2), 3.65 (s, 2H, H-6 × 2), 7.73 (d, 1H, J = 5.0 Hz, ArH), 7.80 (d, 1H, J = 5.0 Hz, ArH), 13.13 (s, 1H, ArOH), 13.24 (s, 1H, ArOH). Exact MS Calcd for $C_{16}H_{10}O_5S$: 314.0247. Found: 314.0247.

2-Acetoxy-[2-carboxy-5-(trimethylsilyl)thiophen-3-yl]acetic Acid (7) A solution of (2-carboxythiophen-3-yl)acetic acid (**5**) (186 mg, 1.0 mmol) in dry THF (5 ml) was added dropwise to a solution of LDA (4.64 mmol) in THF over a few minutes at −78 °C under a nitrogen atmosphere and the reaction mixture was stirred for 30 min under the same conditions. After addition of Me_3SiCl (1.0 ml, 8.0 mmol), the reaction mixture was stirred at −78 °C for 1.5 h, allowed to warm to room temperature, and stirred for an additional 30 min. The reaction mixture was concentrated under reduced pressure and pentane (25 ml) was added to the residue. The mixture was filtered rapidly and the filtrate was concentrated *in vacuo* to give the ketene silyl acetal intermediate (**6**), which was used for the next oxidation reaction without purification. A solution of **6** in dry C_6H_6 (5 ml) was added to a stirred suspension of $Pb(OAc)_4$ (600 mg, 1.22 mmol) in dry C_6H_6 (5 ml) at room temperature under a nitrogen atmosphere. The resulting slurry was stirred for 1 h under the same conditions and filtered to remove $Pb(OAc)_2$. The filtrate was poured into 10% HCl (20 ml), and extracted with Et_2O (30 ml × 2). The extract was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a 99% yield (313 mg) of **7** as colorless crystals, mp 180—188 °C (hexane–Et_2O). IR ($CHCl_3$) ν cm^{-1}: 3400—2400, 1725. ^{1}H-NMR ($CDCl_3$) δ: 0.35 (s, 9H, $SiMe_3$), 2.20 (s, 3H, $COCH_3$), 7.01 (s, 1H, CH), 7.35 (s, 1H, ArH).

2-Acetoxy-[2-carboxy-5-(trimethylsilyl)thiophen-3-yl]acetic Acid Anhydride (8) A solution of **7** (266 mg, 0.84 mmol) and (trimethylsilyl)ethoxyacetylene (179 mg, 1.26 mmol) in dry CH_2Cl_2 (7 ml) was stirred at room temperature for 3 h. After concentration of the reaction mixture in a rotary evaporator, the residue was dried under reduced pressure [90 °C (0.2 mmHg)] for 1 h to give a quantitative yield (252 mg) of **8** as a colorless oil. IR ($CHCl_3$) ν cm^{-1}: 1800, 1750. ^{1}H-NMR ($CDCl_3$) δ: 0.38 (s, 9H, $SiMe_3$), 2.27 (s, 3H, $COCH_3$), 6.45 (s, 1H, CH), 7.17 (s, 1H, ArH).

2-Acetoxy-(2-carboxythiophen-3-yl)acetic Acid (9) A solution of **7** (75 mg, 0.237 mmol) and $Bu_4NF \cdot 3H_2O$ (200 mg) in THF (5 ml) was stirred at room temperature for 1 h. The reaction mixture was diluted with 10% HCl (1 ml) and extracted with Et_2O (20 ml × 2). The extract was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give a 97% yield (57 mg) of **9** as colorless crystals, mp 55—60 °C (CCl_4–$CHCl_3$). IR ($CHCl_3$) ν cm^{-1}: 3400—2400, 1730. ^{1}H-NMR ($CDCl_3$) δ: 1.77 (s, 3H, $COCH_3$), 6.75 (s, 1H, CH), 6.94 (d, 1H, J = 5.0 Hz, ArH), 7.48 (d, 1H, J = 5.0 Hz, ArH).

2-Acetoxy-(2-carboxythiophen-3-yl)acetic Acid Anhydride (10) According to the same procedure as described for the preparation of **8**, a quantitative yield (51 mg) of **10** was obtained from **9** (55 mg, 0.225 mmol) as colorless crystals, mp 110—113 °C (CCl_4–$CHCl_3$). IR ($CHCl_3$) ν cm^{-1}: 1800, 1760. ^{1}H-NMR ($CDCl_3$) δ: 2.12 (s, 3H, $COCH_3$), 6.53 (s, 1H, CH), 7.23 (d, 1H, J = 5.0 Hz, ArH), 8.11 (d, 1H, J = 5.0 Hz, ArH).

4-Acetoxy-7,7-ethylenedioxy-11-hydroxy-2-trimethylsilyl-6,7,8,9-tetrahydroanthra[2,3-*b*]thiophene-5,10-dione (12) A mixture of **8** (298 mg, 1.0 mmol) and NaH (60% in mineral oil, 48 mg, 1.2 mmol) in dry THF (7 ml) was stirred at room temperature for 15 min under a nitrogen atmosphere, then a solution of **11** (245 mg, 1.0 mmol) in dry THF (9 ml) was added. The reaction mixture was stirred at room temperature for 5 h, then quenched with saturated aqueous NH_4Cl (5 ml) and extracted with CH_2Cl_2 (20 ml × 3). The extract was washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was subjected to column chromatography on silica gel (C_6H_6 : AcOEt = 4 : 1) to give a 58% yield (272 mg) of **12** as yellow crystals, mp 169—175 °C (C_6H_6–Et_2O). IR

($CHCl_3$) ν cm^{-1}: 1760, 1660, 1620. ^{1}H-NMR ($CDCl_3$) δ: 0.39 (s, 9H, $SiMe_3$), 1.8—2.0 (m, 2H, H-8×2), 2.46 (s, 3H, $COCH_3$), 2.8—3.1 (m, 4H, H-6×2, H-9×2), 4.04 (s, 4H, OCH_2CH_2O), 7.71 (s, 1H, ArH), 13.14 (s, 1H, ArOH). Exact MS Calcd for $C_{23}H_{24}O_7SSi$: 472.1012. Found: 472.1012.

5,10-Dihydroxy-2-trimethylsilyl-6,7,8,9-tetrahydroanthra[2,3-*b*]thiophene-4,7,11-trione (13) A solution of **12** (235 mg, 0.498 mmol) in CF_3CO_2H (40 ml) and water (10 ml) was heated at 50 °C for 3 h, then concentrated *in vacuo*, and the residue was partitioned between CH_2Cl_2 (20 ml) and water. The aqueous layer was extracted with CH_2Cl_2 (10 ml×2). The combined extract was washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (CH_2Cl_2 : AcOEt = 30 : 1) to give a 93% yield (179 mg) of **13** as red crystals, mp 228—231 °C (AcOEt). IR ($CHCl_3$) ν cm^{-1}: 1720, 1610, 1510. ^{1}H-NMR ($CDCl_3$) δ: 0.43 (s, 9H, $SiMe_3$), 2.64 (t, 2H, J=7.0 Hz, H-8×2), 3.18 (t, 2H, J=7.0 Hz, H-9×2), 3.57 (s, 2H, H-6×2), 7.74 (s, 1H, ArH), 13.03 (s, 1H, ArOH), 13.09 (s, 1H, ArOH). MS *m/z*: 386 (M^+). *Anal.* Calcd for $C_{19}H_{18}O_5SSi$: C, 59.05; H, 4.69; S, 8.30. Found: C, 59.08; H, 4.58; S, 8.34.

(±)-5,7,10-Trihydroxy-2-trimethylsilyl-7-(trimethylsilyl)ethynyl-6,7,8,9-tetrahydroanthra[2,3-*b*]thiophene-4,11-dione (14) Anhydrous $CeCl_3$ (2.3 g, 9.3 mmol) was heated *in vacuo* (0.1 mmHg) at 140 °C for 2 h, and cooled under a nitrogen atmosphere, then dry THF (10 ml) was added. The resulting suspension was stirred at room temperature for 1 h and cooled to −78 °C. Lithium (trimethylsilyl)acetylide [prepared from (trimethylsilyl)acetylene (1.20 ml, 8.44 mmol) and BuLi (1.6 N in hexane, 5.1 ml, 8.15 mmol) in dry THF (8 ml) at −40 °C for 30 min] was added to the cooled suspension with stirring. The mixture was stirred at −78 °C for 1 h and then used as a dry THF solution of (trimethylsilyl)ethynylcerium(III) chloride. To this solution was added a solution of **13** (180 mg, 0.466 mmol) in dry THF (30 ml) at −78 °C for 1 h under a nitrogen atmosphere. The mixture was stirred for 2 h under the same conditions and then quenched with water (50 ml), made acidic by addition of diluted HCl, and extracted with CH_2Cl_2 (20 ml×3). The extract was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. Purification of the residue by column chromatography on silica gel ($CHCl_3$) gave a quantitative yield (293 mg) of **14** as red crystals, mp 108—110 °C (C_6H_6–hexane). IR ($CHCl_3$) ν cm^{-1}: 1600, 1510. ^{1}H-NMR ($CDCl_3$) δ: 0.16 (s, 9H, C≡CSiMe_3), 0.42 (s, 9H, $SiMe_3$-2), 1.9—2.4 (m, 2H, H-8×2), 2.9—3.2 (m, 4H, H-6×2, H-9×2), 7.75 (s, 1H, ArH), 13.08 (s, 1H, ArOH), 13.27 (s, 1H, ArOH). Exact MS Calcd for $C_{24}H_{28}O_5SSi$: 484.1197. Found: 484.1215.

(±)-7-Acetyl-5,7,10-trihydroxy-2-trimethylsilyl-6,7,8,9-tetrahydroanthra[2,3-*b*]thiophene-4,11-dione (15) A mixture of **14** (265 mg, 0.548 mmol), HgO (273 mg, 1.096 mmol), and 20% H_2SO_4 (5 ml) in THF was heated under reflux for 1.5 h and then cooled to room temperature. The reaction mixture was diluted with 10% HCl (3 ml) and extracted with CH_2Cl_2 (20 ml×2). The extract was washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (CH_2Cl_2 : Et_2O = 10 : 1) to give a 91% yield (213 mg) of **15** as red crystals, mp 197—201 °C (C_6H_6). IR ($CHCl_3$) ν cm^{-1}: 1710, 1605, 1510. ^{1}H-NMR ($CDCl_3$) δ: 0.42 (s, 9H, $SiMe_3$), 1.8—2.1 (m, 2H, H-8×2), 2.40 (s, 3H, $COCH_3$), 2.7—3.1 (m, 4H, H-6×2, H-9×2), 7.74 (s, 1H, ArH), 13.06 (s, 1H, ArOH), 13.22 (s, 1H, ArOH). MS *m/z*: 430 (M^+). *Anal.* Calcd for $C_{21}H_{22}O_6SSi$: C, 58.58; H, 5.15; S, 7.45. Found: C, 58.39; H, 4.99; S, 7.41.

(±)-7-[1,1-(Ethylenedioxy)ethyl]-5,7,10-trihydroxy-2-trimethylsilyl-6,7,8,9-tetrahydroanthra[2,3-*b*]thiophene-4,11-dione (16) A mixture of **15** (210 mg, 0.61 mmol), ethylene glycol (0.04 ml, 0.70 mmol), and *p*-toluenesulfonic acid (40 mg) in C_6H_6 (15 ml) was refluxed for 3 h with azeotropic removal of water formed using a Dean-Stark apparatus. After being cooled, the reaction 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 (10 ml×2), and the combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (CH_2Cl_2) to give a 98% yield (227 mg) of **16** as red crystals, mp 198—201 °C (hexane–Et_2O). IR ($CHCl_3$) ν cm^{-1}: 1600, 1510. ^{1}H-NMR ($CDCl_3$) δ: 0.42 (s, 9H, $SiMe_3$), 1.46 (s, 3H, H-13×3), 2.11 (s, 2H, H-6×2), 2.7—3.0 (m, 4H, H-8×2, H-9×2), 4.08 (s, 4H, OCH_2CH_2O), 7.76 (s, 1H, ArH), 13.14 (s, 1H, ArOH), 13.35 (s, 1H, ArOH). Exact MS Calcd for $C_{23}H_{26}O_7SSi$: 474.1165. Found: 474.1153.

(±)-7-[1,1-(Ethylenedioxy)ethyl]-5,7,10-trihydroxy-6,7,8,9-tetrahydroanthra[2,3-*b*]thiophene-4,11-dione (17) a) A solution of **16** (59 mg, 0.124 mmol) and $Bu_4NF \cdot 3H_2O$ (50 mg) in THF (10 ml) was stirred at room temprature for 15 min. The reaction mixture was diluted with water (6 ml) and extracted with $CHCl_3$ (15 ml×2). The extract was washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel ($CHCl_3$: AcOEt = 2 : 1) to give a quantitative yield (50 mg) of **17** as red crystals, mp 188—192 °C (hexane–$CHCl_3$). IR (KCl) ν cm^{-1}: 1605, 1510. ^{1}H-NMR ($CDCl_3$) δ: 1.46 (s, 3H, H-13×3), 1.8—2.1 (m, 2H, H-8×2), 2.7—3.1 (m, 4H, H-6×2, H-9×2), 7.71 (d, 1H, J=5.0 Hz, ArH), 7.76 (d, 1H, J=5.0 Hz, ArH), 13.19 (s, 1H, ArOH), 13.42 (s, 1H, ArOH). Exact MS Calcd for $C_{20}H_{18}O_7S$: 402.0771. Found: 402.0771.

b) By a procedure similar to that described for the preparation of **16**, **22** (25 mg, 0.070 mmol) was treated with ethylene glycol (52.1 mg, 0.840 mmol) and *p*-toluenesulfonic acid (9 mg). The reaction mixture was worked up as usual and purified by column chromatography on silica gel ($CHCl_3$: AcOEt = 5 : 1) to give an 84% yield (23.5 mg) of **17**, which was identical with an authentic sample obtained from **16**.

(7*RS*,9*SR*)-7-Acetyl-5,7,9,10-tetrahydroxy-6,7,8,9-tetrahydroanthra-[2,3-*b*]thiophene-4,11-dione (18) A solution of bromine (100 mg, 0.625 mmol) in CCl_4 (5 ml) was added to a two-phase solution of **17** (34.5 mg, 0.086 mmol) and AIBN (40 mg, 0.24 mmol) in a mixture of $CHCl_3$ (70 ml), CCl_4 (5 ml), and H_2O (8 ml). The reaction mixture was refluxed for 2 h. After being cooled, the mixture was quenched with saturated aqueous $Na_2S_2O_3$ (10 ml), and the organic layer was separated. The aqueous layer was extracted with $CHCl_3$ (15 ml×2), and the combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was dissolved in aqueous 80% CF_3CO_2H (25 ml) and stirred at 0 °C for 1.5 h. The reaction mixture was poured into ice-water, and extracted with $CHCl_3$ (30 ml×3). The extract was washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by preparative TLC (CH_2Cl_2 : Et_2O = 10 : 1) to give an 82% yield (26 mg) of **18** as red crystals, mp 171—176 °C (hexane–C_6H_6). IR ($CHCl_3$) ν cm^{-1}: 1710, 1600. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 2.17 (dd, 1H, J=12.5, 9.5 Hz, H-8), 2.34 (ddd, 1H, J=12.5, 6.5, 2.5 Hz, H-8), 2.41 (s, 3H, $COCH_3$), 2.91 (dd, 1H, J=18.0, 2.5 Hz, H-6), 3.08 (dd, 1H, J=18.0, 1.5 Hz, H-6), 5.37 (br t, J=8.0 Hz, $\nu_{1/2}$=19 Hz, H-9), 7.71 (d, 1H, J=5.0 Hz, ArH), 7.81 (d, J=5.0 Hz, ArH), 13.16 (s, 1H, ArOH), 13.54 (s, 1H, ArOH). Exact MS Calcd for $C_{18}H_{14}O_7S$: 374.0461. Found: 374.0464.

(7*RS*,9*RS*)-7-Acetyl-5,7,9,10-tetrahydroxy-6,7,8,9-tetrahydroanthra-[2,3-*b*]thiophene-4,11-dione (20) Under a nitrogen atmosphere, a mixture of **18** (5.6 mg, 0.015 mmol) and benzeneboronic acid (5.5 mg, 0.045 mmol) in CF_3CO_2H (0.17 ml) and dry toluene (1.4 ml) was stirred at 0 °C for 3 h, then gradually warmed to room temperature, and stirred for an additional 12 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 (5 ml) and saturated aqueous $NaHCO_3$ (4 ml) was added. The organic layer was separated, washed with water, dried over Na_2SO_4, and concentrated *in vacuo* to give crude **19**. Crude **19** was stirred in a mixture of 2-methyl-2,4-pentanediol (0.1 ml), AcOH (0.1 ml), CH_2Cl_2 (3 ml), and acetone (3 ml) at room temperature for 12 h. This mixture was poured into a mixture of CH_2Cl_2 (5 ml) and saturated aqueous $NaHCO_3$ (2 ml). The organic layer was separated, washed with water, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was washed with pentane (4 ml×2) and purified by preparative TLC (CH_2Cl_2 : Et_2O = 10 : 1) to give an 86% yield (4.8 mg) of **20** as red crystals, mp 192—198 °C (CCl_4–$CHCl_3$). IR ($CHCl_3$) ν cm^{-1}: 1705, 1605. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 2.18 (dd, 1H, J=14.0, 4.5 Hz, H-8), 2.35 (dd, 1H, J=14.0, 2.0 Hz, H-8), 2.43 (s, 3H, $COCH_3$), 2.96 (d, 1H, J=18.0 Hz, H-6), 3.19 (dd, 1H, J=18.0, 2.0 Hz, H-6), 3.7—3.8 (br s, 1H, OH-9), 4.5—4.6 (br s, 1H, OH-7). 5.30 (br d, 1H, J=2.0 Hz, $\nu_{1/2}$=10.0 Hz, H-9), 7.73 (d, 1H, J=4.0 Hz, ArH), 7.81 (d, 1H, J=4.0 Hz, ArH), 13.21 (s, 1H, ArOH), 13.26 (s, 1H, ArOH). Exact MS Calcd for $C_{18}H_{14}O_7S$: 374.0459. Found: 374.0471.

4-Acetoxy-7,7-ethylenedioxy-11-hydroxy-6,7,8,9-tetrahydroanthra-[2,3-*b*]thiophene-5,10-dione (3) By the same procedure as described for the preparation of **12**, a 30% yield (27 mg) of **3** was obtained from **10** (57 mg, 0.225 mmol) and **11** (50.9 mg, 0.225 mmol). This product was identical with an authentic sample obtained from **2**.

(±)-5,7,10-Trihydroxy-7-(trimethylsilyl)ethynyl-6,7,8,9-tetrahydroanthra[2,3-*b*]thiophene-4,11-dione (21) By a procedure similar to that as described for the preparation of **14**, a solution of **4** (10 mg, 0.032 mmol) in dry THF (25 ml) was added to a solution of (trimethylsilyl)ethynylcerium(III) chloride in dry THF, prepared from anhydrous $CeCl_3$ (192 mg, 0.779 mmol), (trimethylsilyl)acetylene (0.11 ml, 0.778 mmol), BuLi (1.6 N in hexane, 0.48 ml, 0.768 mmol), and dry THF (4 ml) at −78 °C under a nitrogen atmosphere. The reaction mixture was stirred for 2.5 h under the

same conditions, worked up as usual, and purified by preparative TLC ($CHCl_3$) to give a quantitative yield (13.9 mg) of **21** as red crystals, mp 184—186 °C (hexane–$CHCl_3$). IR ($CHCl_3$) ν cm^{-1}: 1655, 1605. ^{1}H-NMR ($CDCl_3$) δ: 0.16 (s, 9H, $SiMe_3$), 2.0—2.3 (m, 2H, H-8 × 2), 2.8—3.2 (m, 4H, H-6 × 2, H-9 × 2), 7.60 (d, 1H, J = 5.0 Hz, ArH), 7.67 (d, 1H, J = 5.0 Hz, ArH), 13.03 (s, 1H, ArOH), 13.24 (s, 1H, ArOH). Exact MS Calcd for $C_{21}H_{20}O_5SSi$: 412.0801. Found: 412.0808.

(±)-7-Acetyl-5,7,10-trihydroxy-6,7,8,9-tetrahydroanthra[2,3-*b*]thiophene-4,11-dione (22) By the same procedure as described for the preparation of **15**, **21** (13.9 mg, 0.034 mmol) was treated with HgO (18.5 mg, 0.0854 mmol) and 6 N H_2SO_4 (0.5 ml). The reaction mixture was worked up as usual and purified by column chromatography on silica gel ($CHCl_3$: acetone = 50 : 1) to give an 82% yield (9.9 mg) of **22** as red crystals, mp 243—246 °C (hexane–$CHCl_3$). IR ($CHCl_3$) ν cm^{-1}: 1700, 1595. ^{1}H-NMR ($CDCl_3$) δ: 1.8—2.1 (m, 2H, H-8 × 2), 2.83 (s, 3H, $COCH_3$), 2.8—3.2 (m, 4H, H-6 × 2, H-9 × 2), 3.79 (s, 1H, OH-7), 7.71 (d, 1H, J = 5.0 Hz, ArH), 7.76 (d, 1H, J = 5.0 Hz, ArH), 13.13 (s, 1H, ArOH), 13.34 (s, 1H, ArOH). Exact MS Calcd for $C_{18}H_{14}O_6S$: 358.0508. Found: 358.0502.

(±)-9,12-Epoxy-5,7,10-trihydroxy-7-(1-methoxyethyl)-6,7,8,9-tetrahydroanthra[2,3-*b*]thiophene-4,11-dione (23) Freshly distilled 2,2-dimethoxypropane (30 mg) was added to a solution of **18** (6.0 mg, 0.015 mmol) and *p*-toluenesulfonic acid (1 mg) in dry CH_2Cl_2 (10 ml) under a nitrogen atmosphere at room temperature. The solution was stirred under the same conditions for 24 h, washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by preparative TLC (CH_2Cl_2 : Et_2O = 3 : 1) to give a 40% yield (2.3 mg) of **23** as red crystals, mp 120—125 °C (CCl_4–$CHCl_3$). IR ($CHCl_3$) ν cm^{-1}: 1600. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.29 (s, 3H, H-13 × 3), 1.92 (d, 1H, J = 11.0 Hz, H-8), 2.66 (ddd, 1H, J = 11.0, 6.0, 1.5 Hz, H-8), 3.10 (d, 1H, J = 19.0 Hz, H-6), 3.24 (dd, 1H, J = 19.0, 1.5 Hz, H-6), 3.37 (s, 3H, OMe), 5.48 (d, 1H, J = 6.0 Hz, H-9), 7.72 (d, 1H, J = 5.0 Hz, ArH), 7.78 (d, 1H, J = 5.0 Hz, ArH), 12.90 (s, 1H, ArOH), 13.07 (s, 1H, ArOH). Exact MS Calcd for $C_{19}H_{16}O_7S$: 388.0617. Found: 388.0634.

(−)-(7*S*,9*S*)-7,9-*O*-Bis(3′-*N*-trifluoroacetyl-α-L-daunosaminyl)-7-acetyl-5,10-dihydroxy-6,7,8,9-tetrahydroanthra[2,3-*b*]thiophene-4,11-dione (25) and (−)-(7*R*,9*R*)-9-*O*-(3′-*N*-Trifluoroacetyl-α-L-daunosaminyl)-7-acetyl-5,7,10-trihydroxy-6,7,8,9-tetrahydroanthra[2,3-*b*]thiophene-4,11-dione (26) Under a nitrogen atmosphere, TMSOTf (0.007 ml, 0.034 mmol) was added to a stirred suspension of molecular sieves 4A (0.2 g) and **24** (9 mg, 0.017 mmol) in dry CH_2Cl_2 (1.5 ml) and dry Et_2O (0.5 ml) at −40 °C. The mixture was stirred at −5 °C for 1 h and then cooled to −15 °C, and a solution of (±)-**20** (4.8 mg, 0.013 mmol) in dry CH_2Cl_2 (3 ml) was added. After being stirred for 4 h under the same conditions, the mixture was poured into a vigorously stirred mixture of AcOEt (15 ml) and aqueous $NaHCO_3$ (8 ml). The organic layer was separated and the aqueous layer was extracted with AcOEt (10 ml). The combined organic layer was washed twice with brine, dried over Na_2SO_4, and concentrated *in vacuo*. Separation of the residue by preparative TLC (CH_2Cl_2: Et_2O = 10 : 1) gave two crude products. Each of them was dissolved in CH_2Cl_2 (1 ml) and MeOH (10 ml) under a nitrogen atmosphere, and 0.1 N NaOH (0.012 ml) was added to each solution at 0 °C. The reaction mixture was stirred for 30 min, then one drop of AcOH was added. The resulting mixture was partitioned between AcOEt (20 ml) and brine (10 ml). The organic layer was separated and the aqueous layer was extracted with AcOEt (8 ml). The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. Purification of the residue by preparative TLC (CH_2Cl_2: Et_2O = 10 : 1) gave a 45% yield (5.0 mg) of **25**. A 40% yield (3.1 mg) of **26** was obtained by the same procedure. Each of them was obtained as red crystals. **25**; mp over 300 °C (CCl_4–$CHCl_3$). $[\alpha]_D^{25}$ −3° (c = 0.05, $CHCl_3$). IR ($CHCl_3$) ν cm^{-1}: 1720, 1600. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.55 (d, 3H, J = 6.5 Hz, H-6″ × 3), 1.37 (d, 3H, J = 6.5 Hz, H-6′ × 3), 1.81—2.02 (m, 5H, H-2′ × 2, H-2″ × 2, H-8), 2.34 (s, 3H, $COCH_3$), 2.57 (d, 1H, J = 14.5 Hz, H-8), 3.02 (d, 1H, J = 19.0 Hz, H-6), 3.72 (dd, 1H, J = 19.0, 2.0 Hz, H-6), 3.78 (dd, 1H, J = 7.0, 1.5 Hz, H-4″), 3.88 (q, 1H, J = 6.5 Hz, H-5′), 3.94 (dd, 1H, J = 8.0, 1.5 Hz, H-4′), 4.24—4.33 (m, 1H, H-3″), 4.36—4.43 (m, 1H, H-3′), 4.57 (q, 1H, J = 6.5 Hz, H-5″), 4.96 (m, 2H, $\nu_{1/2}$ = 6.0 Hz, H-9, H-1″), 5.44 (br d, 1H, J = 4.0 Hz, $\nu_{1/2}$ = 7.0 Hz, H-1′), 6.75 (d, 1H, J = 8.0 Hz, NH-3′), 6.82 (d, 1H, J = 8.0 Hz, NH-3″), 7.60 (d, 1H, J = 4.5 Hz, ArH), 7.71 (d, 1H, J = 4.5 Hz, ArH), 13.30 (s, 1H, ArOH), 13.37 (s, 1H, ArOH). FAB-MS (negative) m/z: 855 [(M−H)$^-$]. CD (EtOH) $[\theta]_{max}$ (nm): -1.08×10^4 (295). **26**; mp 109—115 °C (CCl_4–$CHCl_3$). $[\alpha]_D^{25}$ −258° (c = 0.05, $CHCl_3$). IR ($CHCl_3$) ν cm^{-1}: 1720, 1600. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 1.28 (d, 3H, J = 6.5 Hz, H-6′ × 3), 1.88 (td, 1H, J = 13.5, 5.0 Hz, H-2′), 1.95 (dd, 1H, J = 15.5, 4.0 Hz, H-8), 1.85—2.0 (m, 1H, H-2′), 2.40 (s, 3H, $COCH_3$), 2.44 (br d, 1H, J = 15.5 Hz, H-8), 3.04 (d, 1H, J = 19.0 Hz, H-6), 3.30 (dd, 1H, J = 19.0, 1.5 Hz, H-6), 3.61 (br s, 1H, H-4′), 4.27—4.34 (m, 1H, H-3′), 4.46 (s, 1H, OH), 4.47 (q, 1H, J = 6.5 Hz, H-5′), 5.34 (br d, 1H, J = 4.0 Hz, $\nu_{1/2}$ = 7.0 Hz, H-1′), 5.52 (br t, 1H, J = 3.0 Hz, $\nu_{1/2}$ = 7.0 Hz, H-9), 6.67 (br d, 1H, J = 8.0 Hz, NH), 7.75 (d, 1H, J = 5.0 Hz, ArH), 7.81 (d, 1H, J = 5.0 Hz, ArH), 13.24 (s, 1H, ArOH), 13.42 (s, 1H, ArOH). FAB-MS (negative) m/z: 598 [(M−H)$^-$]. CD (EtOH) $[\theta]_{max}$ (nm): $+5.83 \times 10^4$ (298).

(+)-(7*S*,9*S*)-9-*O*-(3′-*N*-Trifluoroacetyl-α-L-daunosaminyl)-7-acetyl-5,7,10-trihydroxy-6,7,8,9-tetrahydroanthra[2,3-*b*]thiophene-4,11-dione (28) and 26 Under a nitrogen atmosphere, a mixture of (±)-**20** (11 mg, 0.029 mmol), $Hg(CN)_2$ (22.7 mg, 0.09 mmol), $HgBr_2$ (12.6 mg, 0.035 mmol), and molecular sieves 3A (300 mg) in freshly distilled anhydrous $CHCl_3$ (10 ml) was stirred at room temperature for 30 min, then a solution of **27** [prepared from **24** (32 mg, 0.059 mmol) according to the reported method[26]] in freshly distilled anhydrous $CHCl_3$ (10 ml) was added. The mixture was stirred for 24 h under the same condition and treated again with the same quantities of $Hg(CN)_2$, $HgBr_2$, molecular sieves 3A, and **27**. After 24 h the mixture was filtered. The filtrate was washed with water and brine, dried over $MgSO_4$, and concentrated *in vacuo*. Separation of the residue by preparative TLC (CH_2Cl_2 : Et_2O = 10 : 1) gave two crude products. One of them was dissolved in CH_2Cl_2 (1 ml) and MeOH (10 ml) under nitrogen, and 0.1 N NaOH (0.11 ml) was added into this solution at 0 °C. By the same procedure as described for **25**, a 28% yield (4.9 mg) of **28** was obtained as red crystals. A 36% yield (6.3 mg) of **26** was obtained from the other crude product by the same procedure: **28**; mp 145—150 °C (CCl_4–$CHCl_3$). $[\alpha]_D^{25}$ +152° (c = 0.05, $CHCl_3$). IR ($CHCl_3$) ν cm^{-1}: 1720, 1600. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 1.31 (d, 1H, J = 6.5 Hz, H-6′ × 3), 1.84 (td, 1H, J = 13.5, 4.0 Hz, H-2′), 2.01 (dd, 1H, J = 13.5, 5.0 Hz, H-2′), 2.14 (dd, 1H, J = 15.5, 4.5 Hz, H-8), 2.33 (dt, 1H, J = 15.5, 2.0 Hz, H-8), 2.42 (s, 3H, $COCH_3$), 2.98 (d, 1H, J = 19.0 Hz, H-6), 3.27 (dd, 1H, J = 19.0, 2.0 Hz, H-6), 3.68 (br s, 1H, H-4′), 4.2—4.3 (m, 1H, H-3′), 4.28 (q, 1H, J = 6.5 Hz, H-5′), 5.24 (dd, 1H, J = 4.5, 2.0 Hz, $\nu_{1/2}$ = 8.0 Hz, H-9), 5.48 (br d, 1H, J = 4.0 Hz, $\nu_{1/2}$ = 7.0 Hz, H-1′), 6.65 (br d, 1H, J = 8.0 Hz, NH), 7.74 (d, 1H, J = 5.0 Hz, ArH), 7.80 (d, 1H, J = 5.0 Hz, ArH), 13.23 (s, 1H, ArOH), 13.27 (s, 1H, ArOH). FAB-MS (negative) m/z: 598 [(M−H)$^-$]. CD (EtOH) $[\theta]_{max}$ (nm): -1.54×10^4 (295).

4-Acetoxy-8,8-ethylenedioxy-11-hydroxy-2-trimethylsilyl-6,7,8,9-tetrahydroanthra[2,3-*b*]thiophene-5,10-dione (30) By a procedure similar to that described for the preparation of **12**, a 51% yield (122 mg) of **30** was obtained from **8** (152 mg, 0.51 mmol), **29** (130 mg, 0.51 mmol), and NaH (60% in a mineral oil, 24.5 mg, 0.61 mmol) as yellow crystals, mp 188—192 °C (C_6H_6–Et_2O). IR ($CHCl_3$) ν cm^{-1}: 1770, 1660, 1620, ^{1}H-NMR ($CDCl_3$) δ: 0.39 (s, 9H, $SiMe_3$), 1.9—2.0 (m, 2H, H-7 × 2), 2.46 (s, 3H, $COCH_3$), 2.8—3.1 (m, 4H, H-6 × 2, H-9 × 2), 4.04 (s, 4H, OCH_2CH_2O), 7.72 (s, 1H, ArH), 13.14 (s, 1H, ArOH). Exact MS Calcd for $C_{23}H_{24}O_7SSi$: 472.1012. Found: 472.1009.

5,10-Dihydroxy-2-trimethylsilyl-6,7,8,9-tetrahydroanthra[2,3-*b*]thiophene-4,8,11-trione (31) Compound **30** (100 mg, 0.212 mmol) was hydrolyzed with 80% aqueous CF_3CO_2H (20 ml) by the same procedure as described for the conversion of **12** to **13**, to give an 80% yield (65.5 mg) of **31** as red crystals, mp 218—222 °C. IR ($CHCl_3$) ν cm^{-1}: 1720, 1610, 1510. ^{1}H-NMR ($CDCl_3$) δ: ($CDCl_3$) δ: 0.44 (s, 9H, $SiMe_3$), 2.64 (t, 2H, J = 7.0 Hz, H-7 × 2), 3.17 (t, 2H, J = 7.0 Hz, H-6 × 2), 3.55 (s, 2H, H-9 × 2), 7.73 (s, 1H, ArH), 12.90 (s, 1H, ArOH), 13.18 (s, 1H, ArOH). Exact MS Calcd for $C_{19}H_{18}O_5SSi$: 386.0645. Found: 386.0648.

(±)-5,8,10-Trihydroxy-2-trimethylsilyl-8-(trimethylsilyl)ethynyl-6,7,8,9-tetrahydroanthra[2,3-*b*]thiophene-4,11-dione (32) By a procedure similar to that described for the preparation of **14**, a quantitative yield (28 mg) of **32** was obtained from **31** (22 mg, 0.057 mmol) as red crystals, mp 86—89 °C (hexane–C_6H_6). IR ($CHCl_3$) ν cm^{-1}: 1600, 1510. ^{1}H-NMR ($CDCl_3$) δ: 0.17 (s, 9H, C≡C$SiMe_3$), 0.42 (s, 9H, $SiMe_3$-2), 1.9—2.4 (m, 2H, H-7 × 2), 2.7—3.3 (m, 4H, H-6 × 2, H-9 × 2), 7.74 (s, 1H, ArH), 13.06 (s, 1H, ArOH), 13.23 (s, 1H, ArOH). Eact MS Calcd for $C_{24}H_{28}O_5SSi$: 484.1196. Found: 484.1208.

(±)-8-Acetyl-5,8,10-trihydroxy-2-trimethylsilyl-6,7,8,9-tetrahydroanthra[2,3-*b*]thiophene-4,11-dione (33) By a procedure similar to that described for the preparation of **15**, a 90% yield (20.2 mg) of **33** was obtained from **32** (25 mg, 0.025 mmol) as red crystals, mp 218—221 °C (CCl_4). IR ($CHCl_3$) ν cm^{-1}: 1710, 1600, 1510. ^{1}H-NMR ($CDCl_3$) δ: 0.42 (s, 9H, $SiMe_3$), 1.9—2.0 (m, 2H, H-7 × 2), 2.40 (s, 3H, $COCH_3$), 2.8—3.1 (m, 4H, H-6 × 2, H-9 × 2), 3.78 (br s, 1H, OH-8), 7.77 (s, 1H, ArH), 13.07 (s, 1H, ArOH), 13.26 (s, 1H, ArOH). Exact MS Calcd for $C_{21}H_{22}O_6SSi$: 430.0906. Found: 430.0918.

(±)-8-[1,1-(Ethylenedioxy)ethyl]-5,8,10-trihydroxy-2-trimethylsilyl-

6,7,8,9-tetrahydroanthra[2,3-*b*]thiophene-4,11-dione (34) By a procedure similar to that described for the preparation of **16**, a 98% yield (19.5 mg) of **34** was obtained from **33** (18 mg, 0.0419 mmol) as red crystals, mp 248—250 °C (hexane–C_6H_6). IR ($CHCl_3$) ν cm^{-1}: 1600, 1510. ^{1}H-NMR ($CDCl_3$) δ: 0.42 (s, 9H, $SiMe_3$), 1.6—2.3 (m, 2H, H-7 × 2), 2.6—3.2 (m, 4H, H-6 × 2, H-9 × 2), 4.07 (s, 4H, OCH_2CH_2O), 7.75 (s, 1H, ArH), 13.15 (s, 1H, ArOH), 13.31 (s, 1H, ArOH). Exact MS Calcd for $C_{23}H_{26}O_7SSi$: 474.1165. Found: 474.1168.

(±)-8-[1,1-(Ethylenedioxy)ethyl]-5,8,10-trihydroxy-6,7,8,9-tetrahydroanthra[2,3-*b*]thiophene-4,11-dione (35) By a procedure similar to that described for the preparation of **17** from **16**, a quantitative yield (51 mg) of **35** was obtained from **34** (59 mg, 0.124 mmol) as red crystals, mp 243—247 °C (CCl_4). IR ($CHCl_3$) ν cm^{-1}: 1605, 1510. ^{1}H-NMR ($CDCl_3$) δ: 1.47 (s, 3H, H-13 × 3), 1.8—2.1 (m, 2H, H-7 × 2), 2.7—3.1 (m, 4H, H-6 × 2, H-9 × 2), 4.08 (s, 4H, OCH_2CH_2O), 7.67 (d, 1H, J = 5.0 Hz, ArH), 7.80 (d, 1H, J = 5.0 Hz, ArH), 13.22 (s, 1H, ArOH), 13.40 (s, 1H, ArOH). Exact MS Calcd for $C_{20}H_{18}O_7S$: 402.0771. Found: 402.0771.

(6*RS*,8*SR*)-8-Acetyl-5,6,8,10-tetrahydroxy-6,7,8,9-tetrahydroanthra-[2,3-*b*]thiophene-4,11-dione (36) By a procedure similar to that described for the preparation of **18**, a 71% yield (20.6 mg) of **36** was obtained from **35** (31.1 mg, 0.077 mmol) as red crystals, mp 110—115 °C (CCl_4). IR ($CHCl_3$) ν cm^{-1}: 1710, 1600. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 2.18 (dd, 1H, J = 13.0, 9.5 Hz, H-7), 2.35 (ddd, 1H, J = 13.0, 7.0, 3.0 Hz, H-7), 2.41 (s, 3H, $COCH_3$), 2.92 (dd, 1H, J = 18.0, 3.0 Hz, H-9), 3.11 (dd, 1H, J = 18.0, 1.5 Hz, H-9), 5.39 (br t, 1H, J = 8.0 Hz, $\nu_{1/2}$ = 19.0 Hz, H-6), 7.75 (d, 1H, J = 5.0 Hz, ArH), 7.82 (d, 1H, J = 5.0 Hz, ArH), 13.00 (s, 1H, ArOH), 13.80 (s, 1H, ArOH). Exact MS Calcd for $C_{18}H_{14}O_7S$: 374.0461. Found: 374.0458.

(6*RS*,8*RS*)-8-Acetyl-5,6,8,10-tetrahydroxy-6,7,8,9-tetrahydroanthra-[2,3-*b*]thiophene-4,11-dione (37) By a procedure similar to that described for the preparation of **20**, a 68% yield (5.3 mg) of **37** was obtained from **36** (7.8 mg, 0.021 mmol) as red crystals, mp 203—206 °C (CCl_4). IR ($CHCl_3$) ν cm^{-1}: 1705, 1605. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 2.18 (dd, 1H, J = 14.0, 4.5 Hz, H-7), 2.35 (dd, 1H, J = 14.0, 2.0 Hz, H-7), 2.42 (s, 3H, $COCH_3$), 2.95 (d, 1H, J = 18.0 Hz, H-9), 3.15 (dd, 1H, J = 18.0, 2.0 Hz, H-9), 3.65—3.95 (br, 1H, OH-6), 4.45—4.60 (br, 1H, OH-8), 5.31 (br d, 1H, J = 4.5 Hz, $\nu_{1/2}$ = 10.0 Hz, H-6), 7.74 (d, 1H, J = 5.0 Hz, ArH), 7.81 (d, 1H, J = 5.0 Hz, ArH), 13.01 (s, 1H, ArOH), 13.47 (s, 1H, ArOH). Exact MS Calcd for $C_{18}H_{14}O_7S$: 374.0459. Found: 374.0464.

(+)-(6*S*,8*S*)-6-*O*-(3′-*N*-Trifluoroacetyl-α-L-daunosaminyl)-8-acetyl-5,8,10-trihydroxy-6,7,8,9-tetrahydroanthra[2,3-*b*]thiophene-4,11-dione (38) and Its (−)-(6*R*,8*R*)-Diastereomer (39) By a procedure similar to that described for the preparation of **28**, a 30% yield (5.9 mg) of **38** and a 39% yield (7.7 mg) of **39** were obtained from **37** (12.5 mg, 0.033 mmol), each as red crystals. **38**: mp 147—155 °C (CCl_4–$CHCl_3$). $[\alpha]_D^{25}$ +34° (c = 0.05, $CHCl_3$). IR ($CHCl_3$) ν cm^{-1}: 1720, 1610. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.31 (d, 1H, J = 6.5 Hz, H-6′ × 3), 1.83 (td, 1H, J = 13.5, 5.5 Hz, H-2′), 2.02 (dd, 1H, J = 13.5, 5.5 Hz, H-2′), 2.14 (dd, 1H, J = 14.5, 4.5 Hz, H-7), 2.33 (td, 1H, J = 14.5, 2.0 Hz, H-7), 2.42 (s, 3H, $COCH_3$), 2.98 (d, 1H, J = 19.0 Hz, H-9), 3.27 (dd, 1H, J = 19.0, 2.0 Hz, H-9), 3.67 (br d, 1H, J = 5.0 Hz, H-4′), 4.20—4.31 (m, 2H, H-3′ and H-5′), 5.25 (dd, 1H, J = 4.5, 2.0 Hz, $\nu_{1/2}$ = 8.0 Hz, H-6), 5.49 (br d, 1H, J = 4.0 Hz, $\nu_{1/2}$ = 7.0 Hz, H-1′), 6.64 (br d, 1H, J = 9.0 Hz, NH), 7.74 (d, 1H, J = 5.0 Hz, ArH), 7.81 (d, 1H, J = 5.0 Hz, ArH), 13.04 (s, 1H, ArOH), 13.48 (s, 1H, ArOH). FAB-MS (negative) m/z: 598 [(M − H)$^-$]. CD (EtOH) $[\theta]_{max}$ (nm): −3.97 × 10^3 (295). **39**: mp 137—142 °C (CCl_4–$CHCl_3$). $[\alpha]_D^{25}$ −270° (c = 0.06, $CHCl_3$). IR ($CHCl_3$) ν cm^{-1}: 1720, 1600. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.28 (d, 3H, J = 6.5 Hz, H-6′ × 3), 1.84—1.98 (m, 3H, H-2′ × 2, H-7), 2.40 (s, 3H, $COCH_3$), 2.45 (br d, 1H, J = 14.0 Hz, H-7), 3.03 (d, 1H, J = 19.0 Hz, H-9), 3.29 (dd, 1H, J = 19.0, 1.5 Hz, H-9), 3.61 (br d, 1H, J = 5.0 Hz, H-4′), 4.27—4.34 (m, 1H, H-3′), 4.48 (q, 1H, J = 6.5 Hz, H-5′), 5.34 (br d, 1H, J = 3.0 Hz, $\nu_{1/2}$ = 7.0 Hz, H-1′), 5.52 (br t, 1H, J = 2.0 Hz, $\nu_{1/2}$ = 7.0 Hz, H-6), 6.66 (br d, 1H, J = 9.0 Hz, NH), 7.74 (d, 1H, J = 5.0 Hz, ArH), 7.82 (d, 1H, J = 5.0 Hz, ArH), 13.04 (s, 1H, ArOH), 13.63 (s, 1H, ArOH). FAB-MS (negative) m/z: 598 [(M − H)$^-$]. CD (EtOH) $[\theta]_{max}$ (nm): +8.10 × 10^3 (295).

(7*RS*,9*SR*)-7-Acetyl-5,7,9,10-tetrahydroxy-2-trimethylsilyl-6,7,8,9-tetrahydroanthra[2,3-*b*]thiophene-4,11-dione (40) A solution of Br_2 (90 mg, 0.563 mmol) in CCl_4 (4.5 ml) was added to the two-layered solution of **16** (30 mg, 0.063 mmol) and AIBN (45 mg, 0.27 mmol) in a mixture of $CHCl_3$ (5 ml), CCl_4 (1.5 ml), and H_2O (1.5 ml). The mixture was stirred at 40 °C for 16 h, then quenched with saturated aqueous $Na_2S_2O_3$ (10 ml). Work-up and subsequent treatment with CF_3CO_2H as described for the preparation of **18** gave a 66% yield (18.5 mg) of **40** as red crystals, mp 176—181 °C (hexane–Et_2O). IR ($CHCl_3$) ν cm^{-1}: 1710, 1610, 1510. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.42 (s, 9H, $SiMe_3$), 2.17 (dd, 1H, J = 12.5, 9.5 Hz, H-8), 2.33 (ddd, 1H, J = 12.5, 6.5, 2.5 Hz, H-8), 2.40 (s, 3H, $COCH_3$), 2.91 (dd, 1H, J = 18.0, 2.5 Hz, H-6), 3.08 (dd, 1H, J = 18.0, 1.5 Hz, H-6), 5.37 (m, 1H, $\nu_{1/2}$ = 19.0 Hz, H-9), 7.82 (s, 1H, ArH), 13.21 (s, 1H, ArOH), 13.64 (s, 1H, ArOH). Exact MS Calcd for $C_{21}H_{22}O_7SSi$: 446.0855. Found: 446.0855.

(7*RS*,9*RS*)-7-Acetyl-5,7,9,10-tetrahydroxy-2-trimethylsilyl-6,7,8,9-tetrahydroanthra[2,3-*b*]thiophene-4,11-dione (41) By a procedure similar to that described for the preparation of **20**, a 77% yield (10.9 mg) of **41** was obtained from **40** (14.2 mg, 0.032 mmol) as red crystals, mp 121—126 °C (CCl_4). IR ($CHCl_3$) ν cm^{-1}: 1710, 1610. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.41 (s, 9H, $SiMe_3$), 2.17 (dd, 1H, J = 14.0, 5.0 Hz, H-8), 2.34 (dt, 1H, J = 14.0, 2.0 Hz, H-8), 2.43 (s, 3H, $COCH_3$), 2.95 (d, 1H, J = 18.0 Hz, H-6), 3.18 (dd, 1H, J = 18,0, 2.0 Hz, H-6), 5.30 (m, 1H, $\nu_{1/2}$ = 9.0 Hz, H-9), 7.81 (s, 1H, ArH), 13.21 (s, 1H, ArOH), 13.30 (s, 1H, ArOH). Exact MS Calcd for $C_{21}H_{22}O_7SSi$: 446.0854. Found: 446.0854.

(+)-(7*S*,9*S*)-9-*O*-(3′-*N*-Trifluoroacetyl-α-L-daunosaminyl)-7-acetyl-5,7,10-trihydroxy-2-trimethylsilyl-6,7,8,9-tetrahydroanthra[2,3-*b*]thiophene-4,11-dione (42) and Its (−)-(7*R*,9*R*)-Diastereomer (43) Compound **41** (5.8 mg, 0.013 mmol) was dissolved in anhydrous CH_2Cl_2 (5 ml), and then molecular sieves 4A (0.2 g) and a solution of **27** [prepared from **24** (14 mg, 0.026 mmol) according to the reported method[26]] in anhydrous CH_2Cl_2 (5 ml) were added under a nitrogen atmosphere at room temperature. A solution of silver trifluoromethanesulfonate (6.7 mg, 0.026 mmol) in Et_2O (4 ml) was further added to this solution in the dark and the whole was stirred for 12 h under the same conditions, then poured into a vigorously stirred mixture of CH_2Cl_2 (15 ml) and saturated aqueous $NaHCO_3$ (7 ml). The solution was filtered and the aqueous layer was extracted with CH_2Cl_2 (10 ml × 2). The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. Separation of the residue by preparative TLC (CH_2Cl_2 : Et_2O = 10 : 1) gave two crude products. Each of them was treated with 0.1 N NaOH in the same way as described for the preparation of **25** to give a 19% yield (1.7 mg) of **42** and a 17% yield (1.5 mg) of **43**. Each of them was obtained as red crystals. **42**: mp 89—92 °C (CCl_4–C_6H_6). $[\alpha]_D^{25}$ +118° (c = 0.1, $CHCl_3$). IR ($CHCl_3$) ν cm^{-1}. 1720, 1610. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.42 (s, 9H, $SiMe_3$), 1.31 (d, 3H, J = 6.5 Hz, H-6′ × 3), 1.84 (td, 1H, J = 13.0, 4.5 Hz, H-2′), 2.01 (dd, 1H, J = 13.0, 5.0 Hz, H-2′), 2.14 (dd, 1H, J = 14.5, 4.5 Hz, H-8), 2.32 (dt, 1H, J = 14.5, 2.0 Hz, H-8), 2.42 (s, 3H, $COCH_3$), 2.98 (d, 1H, J = 19.0 Hz, H-6), 3.27 (dd, 1H, J = 19.0, 2.0 Hz, H-6), 3.68 (br d, 1H, J = 4.0 Hz, H-4′), 4.20—4.30 (m, 2H, H-3′, H-5′), 4.29 (s, 1H, OH), 5.24 (dd, 1H, J = 4.5, 2.0 Hz, $\nu_{1/2}$ = 8.0 Hz, H-9), 5.49 (br d, 1H, J = 4.5 Hz, $\nu_{1/2}$ = 7.0 Hz, H-1′), 6.65 (br d, 1H, J = 9.0 Hz, NH), 7.83 (s, 1H, ArH), 13.27 (s, 1H, ArOH), 13.32 (s, 1H, ArOH). FAB-MS (negative) m/z: 671 [(M − H)$^-$]. CD (EtOH) $[\theta]_{max}$ (nm): −2.77 × 10^4 (298). **43**: mp 113—117 °C (CCl_4–C_6H_6). $[\alpha]_D^{25}$ −275° (c = 0.1, $CHCl_3$). IR ($CHCl_3$) ν cm^{-1}: 1720, 1610. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 0.43 (s, 9H, $SiMe_3$), 1.28 (d, 3H, J = 6.5 Hz, H-6 × 3), 1.83—1.98 (m, 3H, H-2′ × 2, H-8), 2.40 (s, 3H, $COCH_3$), 2.44 (br d, 1H, J = 15.0 Hz, H-8), 3.04 (d, 1H, J = 19.0 Hz, H-6), 3.30 (dd, 1H, J = 19.0, 2.0 Hz, H-6), 3.61 (br d, 1H, J = 3.0 Hz, H-4′), 4.27—4.34 (m, 1H, H-3′), 4.46 (s, 1H, OH), 4.48 (q, 1H, J = 6.5 Hz, H-5′), 5.34 (br d, 1H, J = 3.0 Hz, $\nu_{1/2}$ = 7.0 Hz, H-1′), 5.51 (br s, 1H, $\nu_{1/2}$ = 6.0 Hz, H-9), 6.68 (br d, 1H, J = 9.0 Hz, NH), 7.84 (s, 1H, ArH), 13.26 (s, 1H, ArOH), 13.47 (s, 1H, ArOH). FAB-MS (negative) m/z: 671 [(M − H)$^-$]. CD (EtOH) $[\theta]_{max}$ (nm): +5.83 × 10^4 (298).

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