Synthetic Studies of the Angucycline Antibiotics. Stereocontrolled Assembly of the SF 2315B Ring System

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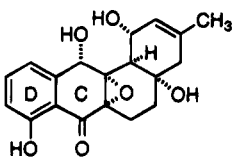
The stereocontrolled assembly of epoxy quinol **2** is described. Diels–Alder cycloaddition between 2-bromo-5-acetoxyjuglone (**5**) and 3-[(triisopropylsilyl)oxy]-1-vinylcyclohexene (**6c**) followed by saponification provided quinone **11b** in good overall yield. Oxygenation of a tetrahydrofuran solution of **11b** in the presence of tetrabutylammonium fluoride resulted in the production of epoxy alcohols α-**12b** and α-**13b**. Epoxy alcohol α-**12b** was converted to epoxy quinol **2** in five steps. A key transformation of the latter reaction sequence was a C1 hydroxyl-directed reduction of the C12 keto group (**20** → **21**). The assigned structure of **2** was confirmed by single-crystal X-ray analysis.

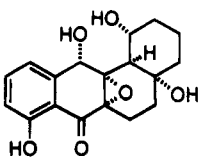
Introduction

The angucycline family of antibiotics comprises over 100 secondary metabolites of the *Actinomycete* group of microorganisms.[1] A structural feature shared by this group of antibiotics is an angular tetracyclic (benz[*a*]-anthracene) framework which is derived biosynthetically through a polyketide pathway. Further structural classification divides this family of antibiotics into two subgroups, angucyclines and angucyclinones. The former group members possess hydrolyzable sugars while the latter term refers to group members devoid of acid-labile sugars. In addition to diverse structural features these natural products also display a broad range of biological activities such as antitumor, enzyme inhibitory, and blood platelet aggregation inhibitory activity.[2]

To date, synthetic investigations of the angucycline antibiotics have been mostly limited to angucyclinone antibiotics possessing an anthraquinone chromophore.[3] Notable accomplishments in this area include the total synthesis of urdamycinone B and rabelomycin by Yamaguchi and Krohn, respectively.[4 a,b] We have described in a preliminary communication an oxidation which is potentially useful in the assemblage of SF 2315B (**1**), an angucyclinone which does not bear an anthraquinone chromophore.[5] This antibiotic was isolated from a soil microorganism of the *Actinomycete* strain *Excellospora viridilutea*.[6] Furthermore, SF 2315B (**1**) was reported to be weakly active against Gram-positive bacteria and inhibited the reverse transcriptase of Avian myeloblastosis virus (IC_{50} 40 μg/mL). As part of a program directed toward the synthesis of angucycline antibiotics, we have recently completed the synthesis of epoxy quinol **2**, which bears the complete array of stereogenic centers present in SF 2315B (**1**). In this paper we detail our investigations leading to the synthesis of **2**.



SF 2315B (1)



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Our approach to epoxy quinol **2** featured the construction of the angular carbon framework through a Diels–Alder reaction between 2-bromo-5-acetoxyjuglone and a protected derivative of 3-vinyl-2-cyclohexen-1-ol.[7,8] Careful dehydrobromination of the resulting cycloadduct then affords quinone **4**.[9] In this manner the correct relative stereochemistry between C1 and C12b as well as the regiochemistry of the benz[*a*]anthracene framework of SF-2315B (**1**) can be established. Stereocontrolled installation of the epoxide ring as well as the angular hydroxyl group then delivers keto epoxide **3**. Finally, the remaining C12 stereocenter can be introduced utilizing the favorable disposition of the C1 hydroxyl group (cf. **3**) in a hydroxyl directed reduction of the C12 keto group.[10]

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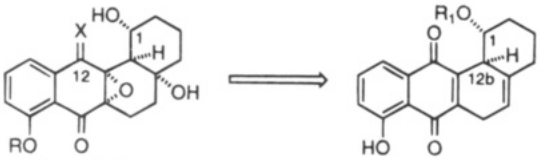

2 X = α-OH, β-H; R = H
3 X = O; R=Ac

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Results and Discussion

Construction of Angular Quinone 8 and Oxidation Studies. Our starting point was to examine the Diels–Alder cycloaddition between bromojuglone **5** and diene **6** to provide bromo ketone **7**. In this case three dienes (**6a–c**), differing in the identity of the C1 hydroxyl-protecting group, were examined. Dienes **6a–c** engaged in a cycloaddition with bromojuglone **5** to provide a single isomeric cycloadduct (**7a–c**) in 41, 74, and 71% yield, respectively (Scheme 1). However, base-induced dehydrobromination of **7a** and **7b** led to different reaction products. On the one hand, dehydrobromination of **7a** with 1,8-diazabicyclo[5.4.0]undecene (DBU) produced only anthraquinone **10a** in 48% yield. The product of elimination, quinone **8a**, was not detected but apparently tautomerizes to dihydro quinone **9** which upon air oxidation produced anthraquinone **10a**.[5b] In contrast dehydrobromination of **7b** afforded only quinone **8b**. Anthraquinone **10b** was not detected. We attribute the latter observation to the steric inhibition of dihydro quinone formation (**8b** → **9b**) through the sterically demanding C1 silyl ether which induces a distortion of the AB ring system resulting in a stereochemical misalignment of the C12b hydrogen and the neighboring π-system (Figure 1).[11a] On the other hand, the relatively small C1 methoxymethoxy group (**8a**) presumably accommodates the structural reorganization to dihydro quinone **9a** and its subsequent air oxidation to **10a**.

As discussed above, quinone **8b** was reluctant to undergo air oxidation to anthraquinone **10b**; however air oxidation of the quinone methide generated from the corresponding phenol (**11a**) yielded epoxy alcohols α-**12a** and α-**13a**.[5a,12] Phenol **11a** was generated directly from **7b** upon treatment with 2 equiv of tetrabutylammonium hydroxide in THF. Quinone methide generation was effected by treating a tetrahydrofuran solution of quinone **11a** at −78 °C with 1 equiv of tetrabutylammonium fluoride. The resulting purple solution was then slowly warmed to room temperature while a stream of oxygen was passed through the mixture. In the case of TBS ether **11a**, epoxy alcohols α-**12a** and α-**13a** were produced in 29 and 24% yield, respectively (Scheme 2). The assigned structures (α-**12a** and α-**13a**) were based initially on NMR analysis and subsequently confirmed by single-crystal X-ray analysis.[5a] In addition to α-**12a** and α-**13a**, up to 26% of starting quinone **11a** was recovered. Similarly TIPS ether **11b** provided epoxy alcohols α-**12b** and α-**13b** in 33 and 16% yields plus recovered **11b** (20%). Notably the major epoxy alcohol in both cases (α-**12**) possesses five of the six stereocenters common to SF 2315B (**1**). In this regard, oxidation of **11b** proved to be more preparatively useful than oxidation of **11a**.

(11) (a) All modeling calculations reported in this article were carried out using molecular mechanics (MM2) calculations as implemented by Macromodel Version 4.0. (b) In estimating the lowest energy conformation of **16**α and **16**β the corresponding dienol was employed.

(12) Oxidation of the quinone methide generated from acetate **8b** also produced a mixture of epoxy alcohols. However the oxidation of phenol **11b** proved to be more synthetically useful. See ref 5a.

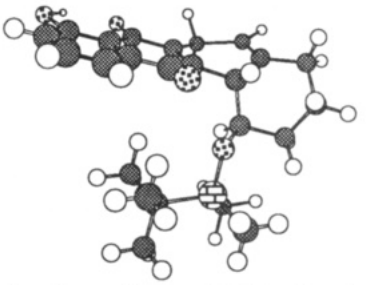
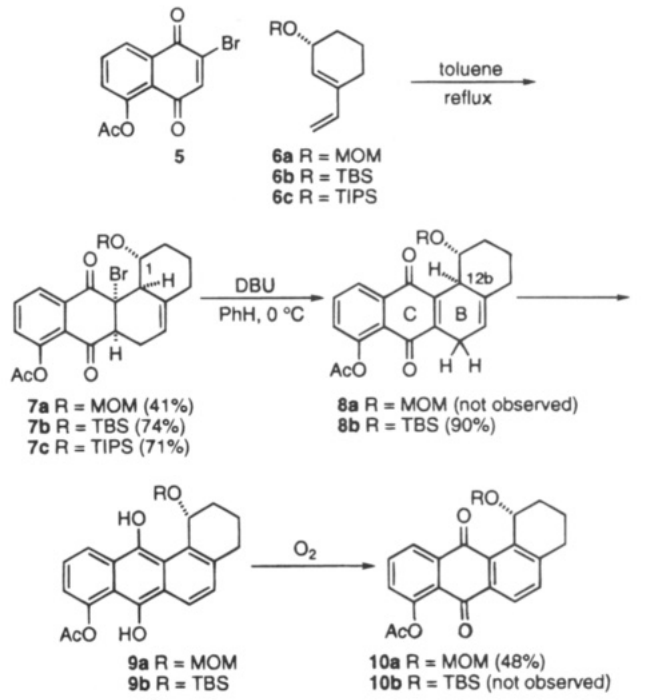
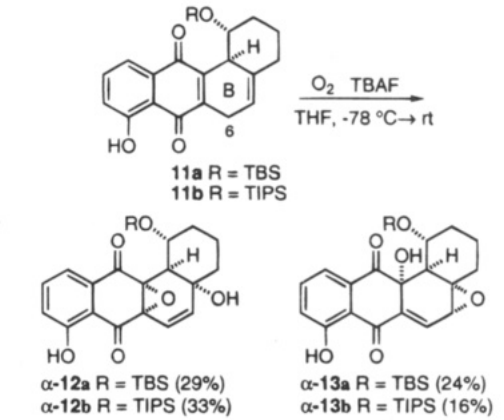


Figure 1. Molecular mechanics (MM2) estimate of the lowest energy conformation of quinone **8b**.

Scheme 1



Scheme 2



A mechanism which accounts for the oxidation of **11a** to α-**12a** and α-**13a** is outlined in Scheme 3. The oxidation process commences with deprotonation at the C6 position of **11a** by fluoride ion to generate the corresponding quinone methide, which upon loss of one electron to molecular oxygen affords semiquinone methide **14**.[13] Molecular oxygen addition to **14** then generates peroxy radical **15**α which cyclizes to intermediate endoperoxides **16**α.[14,15] One-electron reduction of **16**α by a second equivalent of quinone methide serves to gener-

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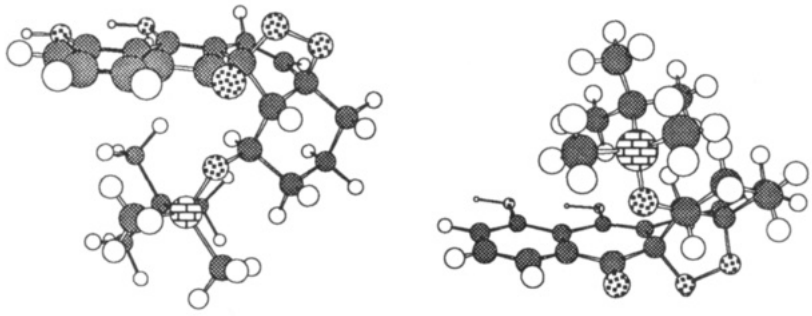
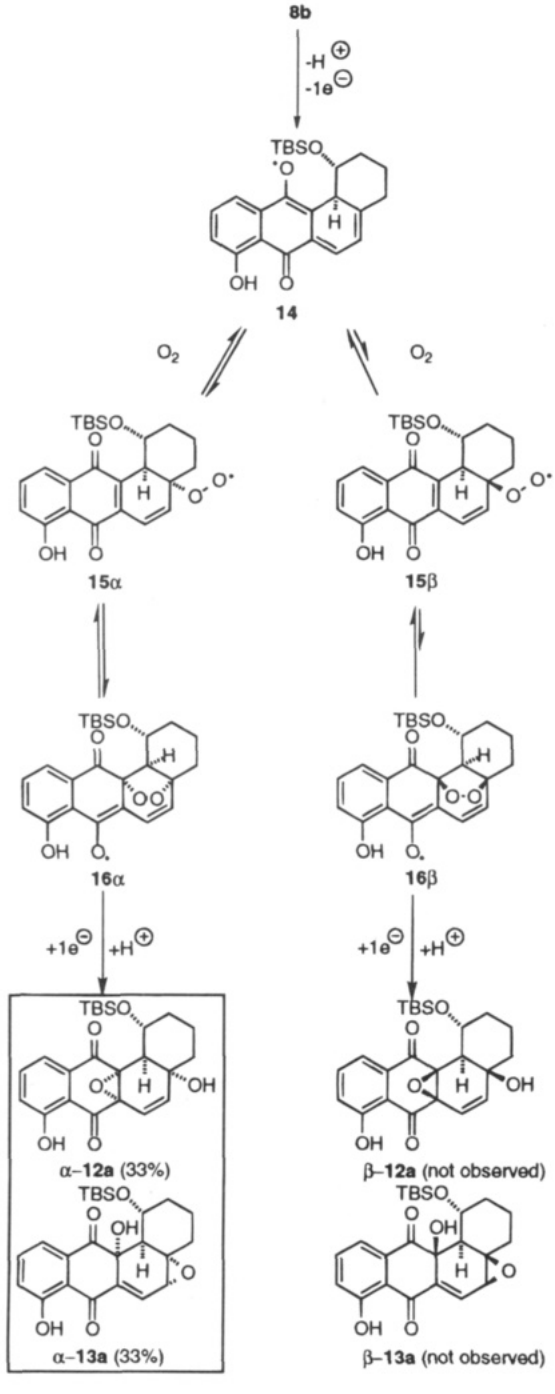


Figure 2. Molecular mechanics (MM2) estimate of the lowest energy conformations of endoperoxides **16**α and **16**β. Endoperoxide **16**α is 5 kcal/mol lower in energy than **16**β.

Scheme 3

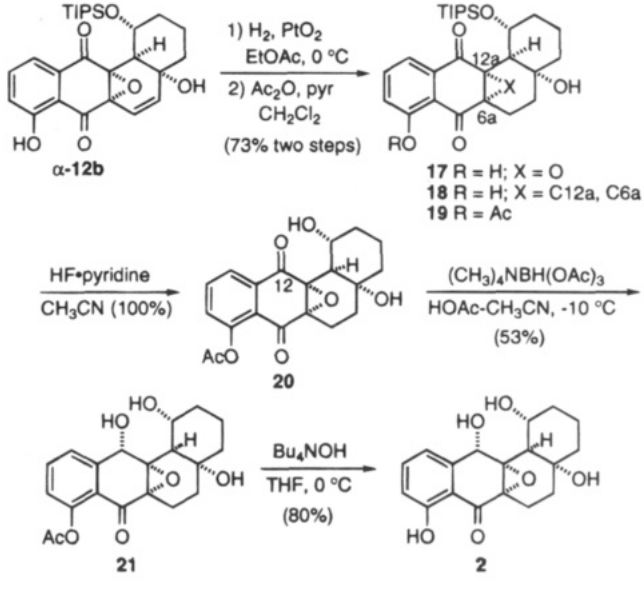


ate the corresponding dienolate as well as replenish starting semiquinone methide **14**. Finally, collapse of the dienolate intermediate produces epoxy alcohols α-**12a** and α-**13a**. The intramolecularity of the mechanism outlined in Scheme 3 accounts for the observed cis relationship between the newly formed epoxide and hydroxyl groups of α-**12a** and α-**13a**.

In principle, a second reaction pathway leading to the production of β-**12a** and β-**13a** is possible. This would require the addition of molecular oxygen to the β face of **14** to produce intermediate peroxy radical **15**β, which would cyclize to endoperoxide **16**β. However, examination of molecular models suggests this addition−cyclization sequence to be unfavorable due to a conformational change amplifying the steric congestion between the bulky C1 silyl ether group and the C12 keto group. In contrast, addition of oxygen to the α face (**14** to **16**α) requires little structural reorganization.[15] An estimate of the lowest energy conformations of endoperoxides **16**α and **16**β is shown in Figure 2.[11a] Endoperoxide **16**α is an estimated 5 kcal/mol lower in energy relative to **16**β. This leads to the conclusion that the conversion of **14** to **16**β must mount a more substantial energy barrier relative to the conversion of **14** to **16**α.

Completion of Epoxy Quinol 2. The remaining obstacles to completing the synthesis of **2** were the stereoselective reduction of the C12 keto group and reduction of the C5−C6 double bond. For these studies we employed epoxy alcohol α-**12b** (vide supra). Hydrogenation of an ethyl acetate solution of α-**12b** at 0 °C over Adam's catalyst (PtO_2) provided quinone oxide **17** (Scheme 4). When methanol was used as a solvent, overreduction

Scheme 4



to provide quinone **18** was observed. Quinone oxide **17** and quinone **18** were differentiated on the basis of differences in their ^{13}C NMR spectra. In particular the C6a and C12a carbon resonances for **17** were at δ 65.8 and 64.6, respectively, while the corresponding resonances in **18** were δ 146.9 and 144.4. Significant differences in the carbonyl carbon resonances were also noted. Next, as prelude to the stereoselctive reduction of the C12 carbonyl group, the C8 phenol was acetylated to suppress undesired reduction of the C7 keto group. Following acetylation of the C8 phenol group, the triisopropylsilyl protecting group was removed using a hydrogen fluoride-pyridine complex to provide **20**. The stage was now set for the C1 hydroxyl-directed reduction of the C12 keto group. To this end, treatment of diol **20** with tetramethylammonium triacetoxyborohydride in 1:1 acetonitrile/acetic acid at −10 °C for 20 h afforded triol **21** (53%) plus 38% of recovered starting material.[9] Finally, removal of the acetyl group produced phenol **2**. The assigned stereochemistry of **2** was unequivocally assigned on the basis of single-crystal X-ray analysis.[16]

Conclusion. We have completed the stereocontrolled assembly of epoxy quinol **2**. The synthesis of **2** illustrates methodology for the introduction of all six stereocenters of SF 2315B (**1**).

Experimental Section

General. All reactions were carried out under a nitrogen atmosphere using dry glassware which had been flame dried under a stream of nitrogen, unless otherwise noted. When necessary, solvents were purified prior to use. Tetrahydrofuran was distilled from sodium/benzophenone; dichloromethane and benzene were distilled from calcium hydride. Toluene was distilled from sodium. Pyridine was distilled from calcium hydride and stored over potassium hydroxide. Reactions were monitored by thin-layer chromatography (TLC) using 0.25-mm E. Merck precoated silica gel plates. Visualizatoin was accomplished with UV light and aqueous ceric ammonium molybdate solution or anisaldehyde stain followed by charring on a hot plate. Flash chromatography was perfomed with the indicated solvents using silica gel 60 (particle size 0.040−0.063 mm). Yields refer to chromatographically and spectroscopically pure compounds unless otherwise stated. Melting points are uncorrected unless otherwise noted. High-resolution mass spectra were obtained at Texas A&M University Mass Spectrometry Service Center by Dr. Llyod Sumners on a VG Analytical 70S high-resolution, double-focusing, sectored (EB) mass spectrometer. Combustion analyses were performed by Atlantic Mircrolab, Inc. (Norcross, GA).

Diels−Alder Adduct 7a. A mixture of 3-[(methoxymethyl)oxy]-1-vinylcyclohexene (210 mg, 1.25 mmol), 2-bromo-5-acetoxyjuglone (370 mg, 1.25 mmol), and toluene (50 mL) was heated at reflux for 7 h. The solution was cooled to room temperature and concentrated *in vacuo*. Flash chromatography with 3:7 ethyl acetate/hexane as eluant provided 240 mg (41% yield) of bromo ketone **7a** as a yellow solid: mp 158−159 °C; IR ($CDCl_3$) 1771, 1707, 1604 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.0−1.4 (m, 2H), 1.6−2.0 (m, 2H), 2.1−2.3 (m, 2H), 2.33 (s, 3H), 2.35−2.60 (m, 1H), 2.7−3.0 (m, 3H), 3.03 (s, 3H), 3.3−3.5 (m, 1H), 3.5−3.7 (m, 2H), 5.5−5.6 (m, 1H), 7.29 (dd, J = 8.0, 1.0 Hz, 1H), 7.73 (t, J = 8.0 Hz, 1H), 8.15 (dd, J = 8.0, 1.0 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 20.8, 22.7, 24.8, 34.4, 35.8, 55.2, 55.3, 57.3, 70.3, 80.1, 96.0, 117.7, 126.0, 126.1, 128.7, 134.5, 134.8, 135.8, 148.6, 169.3, 188.7, 191.3; HRMS (FAB) m/z 401.0380 [$(M - OCH_2OCH_3)^+$, calcd for $C_{20}H_{18}O_4Br$ 401.0388].

Diels−Alder Adduct 7b. A mixture of 3-[(*tert*-butyldimethylsilyl)oxy]-1-vinylcyclohexene (2.96 g, 12.4 mmol), 2-bromo-5-acetoxyjuglone (3.66 g, 12.4 mmol), and toluene (100 mL) was heated at reflux for 12 h. The solution was cooled to room temperature and concentrated in vacuo. Flash chromatography with 1:5 ethyl acetate/hexane as eluant provided 4.90 g (74%) of bromo ketone **7b** as a white solid: mp 161−163 °C; IR ($CHCl_3$) 1769, 1700, 1591 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ −0.04 (s, 3H), −0.03 (s, 3H), 0.77 (s, 9H), 1.35−1.55 (m, 2H), 1.64−1.80 (m, 1H), 2.01−2.41 (m, 8H), 3.02−3.06 (m, 1H), 3.54 (t, J = 8.0 Hz, 1H), 4.45−4.60 (m, 1H), 5.41−5.50 (m, 1H), 7.32 (dd, J = 8.0, 1.2 Hz, 1H), 7.71 (t, J = 8.0 Hz, 1H), 7.96 (dd, J = 8.0, 1.2 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ −4.3, −3.8, 18.1, 21.0, 21.5, 26.0, 27.3, 33.1, 34.5, 57.6, 59.3, 65.5, 72.1, 117.5, 123.9, 126.1, 129.3, 134.8, 135.6, 137.0, 149.0, 169.2, 189.4, 193.8. high-resolution mass spectrum (EI) m/z 475.0590 [$(M - C_4H_9)^+$, calcd for $C_{22}H_{24}O_5SiBr$ 475.0576].

Diels−Alder Adduct 7c. A mixture of 3-[(triisopropylsilyl)oxy]-1-vinylcyclohexene (1.92 g, 6.85 mmol), 2-bromo-5-acetoxyjuglone (2.02 g, 6.85 mmol), and toluene (100 mL) was heated at reflux for 12 h. The solution was cooled to room temperature and concentrated *in vacuo*. Flash chromatography using 3:7 ethyl acetate/hexane as eluant provided 2.79 g (71%) of **7c** as a pale yellow solid: mp 102−104 °C; IR ($CDCl_3$) 1765, 1707, 1598 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.03 (s, 21H), 1.40−1.90 (m, 4H), 2.15−2.30 (m, 4H), 2.38 (s, 3H), 3.05 (m, 1H), 3.57 (t, J = 7.0 Hz, 1H), 4.69 (m, 1H), 5.41 (m, 1H), 7.34 (dd, J = 8.0, 1.2 Hz, 1H), 7.71 (t, J = 8.0 Hz, 1H), 7.98 (dd, J = 8.0, 1.2 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.1, 18.3, 18.4, 20.4, 21.0, 27.7, 31.8, 32.2, 57.6, 59.4, 66.6, 71.7, 117.2, 123.7, 126.1, 129.5, 134.8, 135.1, 137.4, 149.2, 169.2, 189.0, 193.6; HRMS (FAB) m/z 575.1776 [$(M + H)^+$, calcd for $C_{29}H_{40}O_5SiBr$ 575.1828].

Anthraquinone 10a. To a solution of **7a** (100 mg, 0.23 mmol) in benzene (5 mL) at 0 °C was added 1,8-diazabicyclo-[5.4.0]undec-7-ene (40 μL, 0.25 mmol). After 1h, the reaction was quenched with saturated NH_4Cl solution (5 mL), and the solution was extracted with diethyl ether (3 × 20 mL). The combined extracts were washed with water, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Flash column chromatography using 1:3 ethyl acetate/hexane as eluant afforded 35 mg of anthraquinone **10a** (43%) as an orange-yellow solid: mp 131−133 °C; IR ($CDCl_3$) 1768, 1668, 1594 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.7−1.9 (m, 2H), 2.0−2.2 (m, 1H), 2.3−2.4 (m, 1H), 2.48 (s, 3H), 2.8−3.1 (m, 2H), 3.37 (s, 3H), 4.78 (d, J = 6.9 Hz, 1H), 5.17 (d, J = 6.9 Hz, 1H), 5.9−6.0 (m, 1H), 7.36 (dd, J = 8.0, 1.2 Hz, 1H), 7.50 (d, J = 8.0 Hz, 1H), 7.75 (t, J = 8.0 Hz, 1H), 8.1−8.2 (m, 2H); HRMS (FAB) m/z 319.0975 [$(M - OCH_2OCH_3)^+$, calcd for $C_{20}H_{15}O_4$ 319.0970].

Quinone 8b. To a solution of **7b** (300 mg, 0.56 mmol) in anhydrous benzene (4.0 mL) at 0 ° C was added 1,8-diazabicyclo-[5.4.0]undec-7-ene (90 μL, 0.60 mmol). After 5 min, the reaction was quenched with saturated NH_4Cl solution, and the solution was extracted with diethyl ether (3 × 15 mL). The combined extracts were washed with water, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Flash column chromatography using 1:9 ethyl acetate/hexane as eluant provided 230 mg (90%) of quinone **8b** as a yellow solid: mp 128−130 °C; IR ($CHCl_3$) 1768, 1660, 1621, 1590 cm^{-1} ; ^1H NMR (200 MHz, $CDCl_3$) δ −0.36 (s, 3H), −0.12 (s, 3H), 0.73 (s, 9H), 1.20−2.36 (m, 6H), 2.45 (s, 3H), 2.91−3.12 (m, 1H), 3.24−3.44 (m, 2H), 3.64−3.78 (m, 1H), 5.51−5.61 (m, 1H), 7.32 (dd, J = 8.0, 1.3 Hz, 1H), 7.71 (t, J = 8.0 Hz, 1H), 8.01 (dd, J = 8.0, 1.3 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ −4.9, 17.9, 21.1, 25.3, 25.6, 26.2, 34.3, 37.0, 44.9, 78.1, 115.2, 123.2, 125.1, 128.7, 134.2, 134.6, 137.7, 142.1, 144.0, 149.1, 169.4, 183.1, 183.3. Anal. Calcd for $C_{26}H_{32}O_5Si$: C, 69.00; H, 7.13. Found: C, 69.09; H, 7.17.

Quinone 11a. To a solution of bromo ketone **7b** (0.60g, 1.13 mmol) in THF (10 mL) cooled to 0 °C was added 2 mL of a 40 wt % tetrabutylammonium hydroxide solution (6.55 mmol).

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(16) The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.

After 5 min of stirring, the reaction was quenched with saturated NH_4Cl, and the solution was extracted with diethyl ether (3 × 15 mL). The combined organic extracts were combined, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Flash column chromatography using 1:13 ethyl acetate/hexane as eluant provided 410 mg (89%) of phenol **11a** as a yellow solid: mp 192–194 °C; IR ($CHCl_3$) 1659, 1630, 1610 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ −0.33 (s, 3H), −0.11 (s, 3H), 0.74 (s, 9H), 1.20–2.20 (m, 6H), 3.00–3.20 (m, 1H), 3.29–3.45 (m, 2H), 3.65–3.80 (m, 1H), 5.57 (br s, 1H), 7.16–7.25 (m, 1H), 7.54–7.60 (m, 2H), 12.1 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ −4.8, 17.9, 24.8, 25.6, 26.2, 34.3, 37.0, 45.1, 78.1, 114.7, 114.9, 119.2, 123.3, 133.0, 136.0, 138.0, 141.1, 146.2, 161.1, 183.4, 189.7. Anal. Calcd for $C_{24}H_{30}O_4Si$: C, 70.21; H, 7.37. Found: C, 70.17; H, 7.37.

Quinone 11b. To a solution of bromo ketone **7c** (130 mg, 0.23 mmol) in 1:1 THF/MeOH (4 mL) at 0 °C was added 5 mL of a 0.1 M LiOH solution (0.5 mmol). After 0.5 h, the reaction was quenched with saturated NH_4Cl solution, and the solution was extracted with dichoromethane (3 × 30 mL). The combined extracts were washed with brine (50 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Flash column chromatography using 1:4 ethyl acetate/hexane as eluant provided 72 mg (70%) of quinone **11b** as a yellow solid: mp 142–144 °C; IR ($CDCl_3$) 1662, 1635, 1614 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.87 (m, 21H), 1.15–1.45 (m, 2H), 1.60–2.34 (m, 4H), 2.95–3.80 (m, 4H), 5.55 (br s, 1H), 7.10–7.29 (m, 1H), 7.50–7.59 (m, 2H), 12.06 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.9, 17.9, 18.0, 24.8, 26.2, 34.3, 37.4, 45.4, 78.7, 114.7, 114.8, 118.9, 123.1, 133.2, 135.9, 138.3, 141.0, 146.5, 161.0, 183.3, 189.6; HRMS (FAB) m/z 453.2438 [$(M + H)^+$, calcd for $C_{27}H_{37}O_4Si$ 453.2461].

Epoxy Alcohols α-12a and α-13a. To a solution of **11a** (61 mg, 0.15 mmol) in THF (4.0 mL) at −78 °C was added 0.15 mL of a 1 M solution of tetrabutylammonium fluoride in THF (0.15 mmol). Oxygen was passed through the reaction mixture which was allowed to warm to room temperature and the reaction quenched with saturated NH_4Cl solution. The mixture was extracted with ethyl acetate (3 × 15 mL), and the extracts were combined, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Flash column chromatography using 1:6 ethyl acetate/hexane as eluant afforded 16 mg (26%) of **11a**, 19 mg (29%) of α-**12a** as a yellow solid, and 16 mg (24%) of α-**13a** as a yellow solid.

The first to elute was α-**12a**: TLC, R_f 0.23 (17:3 hexane/EtOAc); mp 204–206 ° C; IR ($CHCl_3$) 3520, 1700, 1654, 1602, 1574 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ −0.44 (s, 3H), −0.16 (s, 3H), 0.66 (s, 9H), 1.0–2.0 (m, 6H), 2.98 (br s, 1H), 3.22–3.55 (m, 2H), 6.14 (dd, J = 10.0, 1.1 Hz, 1H), 7.01 (d, 9.9 Hz, 1H), 7.03 (dd, J = 7.8, 1.8 Hz, 1H), 7.62–7.80 (m, 2H), 11.7 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ −4.2, −4.1, 17.9, 20.1, 25.6, 34.7, 37.2, 45.7, 59.6, 69.8, 70.8, 73.2, 113.9, 120.6, 120.9, 124.5, 131.7, 137.4, 141.9, 162.4, 183.2, 194.3; high-resolution mass spectrum (EI) m/z 442.1813 [$(M)^+$, calcd for $C_{24}H_{30}O_6Si$ 442.1812].

The second to elute was α-**13a** : TLC, R_f 0.17 (17:3 hexane/EtOAc); ^1H NMR (200 MHz, $CDCl_3$) δ −0.55 (s, 3H), −0.23 (s, 3H), 0.63 (s, 9H), 1.2–2.2 (m, 6H), 3.02–3.28 (m, 2H), 3.61 (d, J = 4.4 Hz, 1H), 4.52 (s, 1H), 7.23–7.30 (m, 1H), 7.65 (t, J = 8.1 Hz, 1H), 7.74–7.82 (m, 2H), 12.8 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ −4.2, −3.8, 18.2, 21.1, 25.7, 32.0, 34.9, 49.7, 54.3, 66.5, 72.7, 74.1, 117.2, 120.9, 123.8, 133.4, 137.0, 139.3, 139.5, 163.4, 186.9, 187.2; low-resolution mass spectrum (CI) m/z 442 [$(M)^+$, calcd for $C_{24}H_{30}O_6Si$ 442].

Epoxy Alcohols α-12b and α-13b. Following the above procedure, quionone **11b** (230 mg, 0.51 mmol) in THF (100 mL) at −78 °C was treated with 0.51 mL of a 1 M solution of tetrabutylammonium fluoride in THF (0.51 mmol) and oxygenated. Flash column chromatography using 1:4 ethyl acetate/hexane as eluant afforded 47 mg (20%) of **11b**, 80 mg (33%) of α-**12b** as a yellow solid, and 40 mg (16%) of α-**13b** as a yellow solid.

The first to elute was α-**12b**: TLC, R_f 0.73 (4:1 hexane/EtOAc); mp 190–192 °C; IR ($CDCl_3$) 3538, 1712, 1649 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.7–0.9 (m, 21H), 1.0–1.3 (m, 2H), 1.4–1.95 (m, 4H), 2.97 (s, 1H), 3.26 (d, J = 9.0 Hz, 1H), 3.51 (td, J = 10.0, 4.0 Hz, 1H), 6.12 (dd, J = 10.0, 1.0 Hz, 1H), 6.98 (d, J = 10.0 Hz, 1H), 7.28 (dd, J = 8.0, 0.9 Hz, 1H), 7.65 (t, J = 8.0 Hz, 1H), 7.73 (dd, J = 8.0, 0.9 Hz, 1H), 11.69 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.4, 17.8, 20.3, 34.7, 37.2, 45.9, 59.6, 69.8, 70.8, 73.8, 113.8, 120.2, 120.9, 124.5, 131.6, 137.2, 141.9, 162.4, 182.8, 194.3; HRMS (FAB) m/z 484.2329 [$(M)^+$, calcd for $C_{27}H_{36}O_6Si$ 484.2281].

The second to elute was α-**13b**: TLC, R_f 0.60 (4:1 hexane/EtOAc); mp 172–174 °C; IR ($CDCl_3$) 1643, 1707, 3425 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.8–1.0 (m, 21H), 1.2–2.2 (m, 6H), 2.3–2.4 (m, 1H), 2.79–2.85 (m, 1H), 3.6–3.8 (m, 1H), 5.3–5.4 (m, 1H), 5.7–5.8 (m, 1H), 7.2–7.3 (m, 1H), 7.5–7.7 (m, 2H), 11.9 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.5, 17.8, 17.9, 21.3, 32.1, 34.6, 49.6, 54.3, 66.6, 72.7, 74.6, 117.1, 119.2, 120.6, 123.7, 136.4, 136.7, 139.4, 163.3, 186.9, 187.2; HRMS (FAB) m/z 441.1723 [$(M - C_3H_7)^+$, calcd for $C_{24}H_{29}O_6Si$ 441.1733].

Epoxy Alcohol 17. Epoxy alcohol α-**12b** (64 mg, 0.13 mmol) was dissolved in ethyl acetate (5 mL) and cooled to 0 °C, and PtO_2 (ca. 2 mg) was added. The flask was flushed three times with hydrogen, and the mixture was stirred for 30 min at 0 °C under an atmosphere of hydrogen. The mixture was diluted with ethyl acetate, filtered through a Celite pad, and concentrated *in vacuo*. Flash column chromatography using 1:4 ethyl acetate/hexane as eluant furnished 49 mg (76%) of epoxy alcohol **17** as a white solid: mp 131–132 °C; IR ($CDCl_3$) 3407, 1697, 1649 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.0 (s, 21H), 1.30–2.09 (m, 8H), 2.15–2.45 (m, 1H), 2.56–2.72 (m, 1H), 2.80–2.89 (m, 1H), 4.90–5.10 (m, 2H), 7.20–7.30 (m, 1H), 7.60–7.70 (m, 2H), 11.63 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.7, 17.2, 18.0, 19.1, 29.6, 32.2, 35.0, 47.3, 64.6, 65.8, 70.4, 70.6, 113.7, 120.1, 124.3, 132.2, 137.1, 161.9, 186.2, 197.2; HRMS (FAB) m/z 443.1930 [$(M - C_3H_7)^+$, calcd for $C_{24}H_{31}O_6Si$ 443.1890].

Quinone 18. Epoxy alcohol α-**12b** (110 mg, 0.23 mmol) was dissolved in methanol (5 mL), and PtO_2 (ca. 2 mg) was added. The flask was flushed three times with hydrogen, and the mixture was stirred for 30 min under an atmosphere of hydrogen. The mixture was diluted with ethyl acetate, filtered through a Celite pad, and concentrated *in vacuo*. Flash column chromatography using 1:4 ethyl acetate/hexane as eluant furnished 85 mg (80%) of quinone **18** as a white solid: ^1H NMR (200 MHz, $CDCl_3$) δ 0.8–1.0 (m, 21H), 1.2–2.0 (m, 9H), 2.6–2.8 (m, 2H), 3.1–3.2 (m, 1H), 4.6 (br s, 1H), 7.15–7.25 (m, 1H), 7.5–7.6 (m, 2H), 12.0 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.6, 17.8, 17.9, 18.0, 31.0, 36.0, 48.6, 70.7, 73.5, 114.7, 119.0, 123.4, 133.2, 136.0, 144.4, 146.9, 161.0, 183.9, 189.7.

Acetate 19. A solution of epoxy alcohol **17** (210 mg, 0.43 mmol) and DMAP (catalytic amount) in dichloromethane (2 mL) and pyridine (0.11 mL) at room temperature was treated with acetic anhydride (0.12 mL, 1.29 mmol). After 30 min the mixture was concentrated *in vacuo*. Flash chromatography, using 1:4 ethyl acetate/hexane as eluant, furnished 220 mg (96%) of **19** as a white solid: mp 55–57 °C; IR ($CDCl_3$) 3398, 1771, 1700 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.05 (s, 21H), 1.30–2.09 (m, 8H), 2.30–2.50 (m, 5H), 2.71 (d, J = 5.0 Hz, 1H), 5.20–5.49 (m, 2H), 7.35 (dd, J = 8.0, 1.2 Hz, 1H), 7.70 (t, J = 8.0 Hz, 1H), 7.95 (dd, J = 8.0, 1.2 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.5, 16.4, 18.0, 19.2, 20.8, 30.2, 31.6, 34.2, 47.9, 64.9, 65.5, 69.8, 70.1, 122.7, 125.9, 129.7, 134.4, 134.7, 149.1, 169.4, 188.7, 190.8; HRMS (FAB) m/z 485.2011 [$(M - C_3H_7)^+$, calcd for $C_{26}H_{33}O_7Si$ 485.1966].

Diol 20. To a solution of acetate **19** (220 mg, 0.42 mmol) in acetonitrile (10 mL) at 0 ° C was added an HF–pyridine complex (1.0 mL). The mixture was allowed to warm to room temperature and stirred for 2 h. The reaction of the pale yellow solution was quenched with saturated $NaHCO_3$ solution, and the solution was extracted with dichloromethane (30 mL x 3), washed with brine (100 mL x 2), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Flash column chromatography, with 7:3 ethyl acetate/hexane as eluant, afforded 140 mg (100%) of diol **20** as a white solid: mp 196–197 °C; IR ($CDCl_3$) 3553, 1778, 1694 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.20–2.00 (m, 10H), 2.31 (s, 3H), 2.54–2.65 (m, 2H), 2.88 (dd, J = 11.0 Hz, 1.2 Hz, 1H), 3.71 (td, J = 11.0, 4.0 Hz, 1H), 7.39 (dd, J = 8.0, 1.2 Hz, 1H), 7.72 (t, J = 8.0 Hz, 1H), 8.03 (dd, J

= 8.0, 1.2 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 17.3, 20.2, 20.9, 27.4, 35.8, 38.2, 46.7, 64.5, 66.9, 71.1, 71.9, 123.2, 126.0, 130.4, 132.9, 134.8, 149.6, 169.4, 189.4, 189.7; HRMS (FAB) m/z 373.1304 [$(M + H)^+$, calcd for $C_{20}H_{21}O_7$ 373.1287].

Triol 21. To a solution of 90 mg (0.34 mmol) of tetramethylammonium triacetoxyborohydride in anhydrous acetonitrile (1.0 mL) and acetic acid (1.0 mL) at −10 °C was added a solution of diol **20** (85 mg, 0.23 mmol) in 1:1 CH_3CN/THF (10 mL) via cannula. The reaction mixture was stirred at −10 °C for 20 h and concentrated *in vacuo*. Purification of the residue by flash column chromatography using 2:1 ethyl acetate/hexane as eluant afforded 32 mg of diol **20** (38%) and 45 mg (53%) of triol **21** as a white solid: mp 69−71 °C; IR ($CDCl_3$) 3494, 1764, 1691 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.20−2.20 (m, 9H), 2.35 (s, 3H), 2.46 (d, J = 10.0 Hz, 1H), 2.90−3.03 (m, 1H), 3.11 (m, 1H), 3.50−3.57 (m, 1H), 4.33 (s, 1H), 4.50 (d, J = 6.0 Hz, 1H), 6.16 (d, J = 5.0 Hz, 1H), 7.03 (d, J =8.0 Hz, 1H), 7.60 (t, J = 8.0 Hz, 1H), 7.71 (d, J = 8.0 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 15.8, 19.0, 21.0, 28.0, 36.2, 38.8, 47.1, 64.4, 68.1, 68.7, 69.5, 71.3, 120.7, 122.7, 124.1, 134.2, 141.7, 148.7, 170.6, 192.1; HRMS (FAB) m/z 375.1442 [$(M + H)^+$, calcd for $C_{20}H_{23}O_7$ 375.1441].

Epoxy Quinol 2. To a solution of triol **21** (45 mg, 0.12 mmol) in THF (3 mL) at 0 °C was added 0.2 mL of a 40 wt % aqueous solution of tetrabutylammonium hydroxide (0.31 mmol). The reaction was quenched with saturated NH_4Cl solution, the solution was extracted with ethyl acetate (4 × 10 mL), and the extracts were combined, washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Flash column chromatography using 4:1 ethyl acetate/hexane as eluant afforded 32 mg (80%) of **2** as a white solid. A sample of **2** was recrystallized from dichloromethane and subjected to single-crystal X-ray analysis: mp 197−198 °C; IR ($CDCl_3$) 3694, 3495, 1733 cm^{-1}; ^{1}H NMR (200 MHz , DMSO-d_6) δ 1.15−2.35 (m, 11H), 4.49 (m, 1H), 4.88 (s, 1H), 5.00 (m, 1H), 5.43 (d, J = 5.0 Hz, 1H), 6.02 (d, J = 9.0 Hz, 1H), 6.84 (d, J = 8.0 Hz, 1H), 7.12 (d, J = 8.0 Hz, 1H), 7.55 (t, J = 8.0 Hz, 1H), 11.35 (s, 1H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 16.1, 18.6, 30.6, 31.8, 34.5, 48.0, 63.2, 65.9, 66.3, 66.9, 70.0, 112.5, 115.6, 118.3, 136.5, 144.2, 160.1, 199.3; HRMS (FAB) m/z 337.1347 [$(M + H)^+$, calcd for $C_{18}H_{21}O_6$ 333.1338].

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of compounds **7−13**, **17−21**, and **2** and ORTEP presentation of **2** (35 pages). This material is contained in libraries on microfiche, immediately following this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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