A Unified Strategy for the Total Synthesis of the Angucycline Antibiotics SF 2315A, Urdamycinone B, and the Shunt Metabolite 104-2

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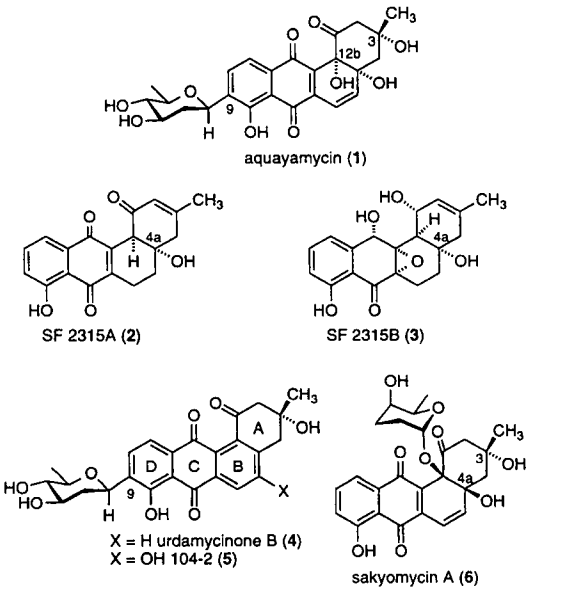
Abstract. Total syntheses of the angucycline antibiotics SF 2315A (**2**), urdamycinone B (**4**), and the shunt metabolite 104-2 (**5**) are described, as well as an approach toward the synthesis of SF 2315B (**3**). All four syntheses feature a Diels–Alder cycloaddition between a bromojuglone derivative and an optically active diene (**25a**), the latter derived from (–)-quinic acid. Subsequent key transformations include (i) stereocontrolled introduction of ring fusion oxygen functionality featured in SF 2315A (**2**) and SF 2315 B (**3**), (ii) preparation of C-glycosyl juglone **53**, and (iii) NMO mediated oxidative aromatization of **60**.

INTRODUCTION AND BACKGROUND

The antibiotic aquayamycin (**1**) was first reported without structure in 1968 and subsequently was assigned the structure shown in 1970.[1] Since this initial isolation, many related secondary metabolites of the *Actinomycete* group of microorganisms have been identified and collectively grouped as angucycline antibiotics.[2] The common structural feature shared by this family of antibiotics is an unsymmetrically assembled (angular) tetracyclic framework which is derived biosynthetically through a polyketide pathway. This angular pattern of ring assembly contrasts with the structurally and biosynthetically related tetracycline and anthracycline groups of linear tetracyclic decaketides. The diverging biosynthetic pathways leading to the production of angular and linear tetracycles have been proposed to be dependent upon the folding pattern of the respective decaketide synthases.[3a–d] An alternative pathway to an angular tetracycle entails initial assembly of a linear tetracycle, followed by a skeletal rearrangement to an unsymmetrical (angular) ring system.[3e] The angucycline group of antibiotics, which is represented by over one hundred group members, is further divided into subgroups with and without angular oxygens located at the AB ring fusion.[2a] Representatives of the former group include aquayamycin (**1**), SF 2315A (**2**), SF 2315B (**3**), and sakyomycin A (**6**),[1,2b–e] while urdamycinone B (**4**) and the shunt metabolite 104-2 (**5**) are representatives of the latter group.[2f–h] In the case of aquayamycin (**1**), labeling studies have demonstrated the C4a oxygen to be derived from an acetate unit, while the C12b oxygen is derived from molecular oxygen.[4] The latter oxidation is a late-stage biosynthetic transformation occurring subsequent to the formation of the carbon framework. Although no related studies have been reported for determining the origin of oxygens within SF 2315A (**2**) and SF 2315B



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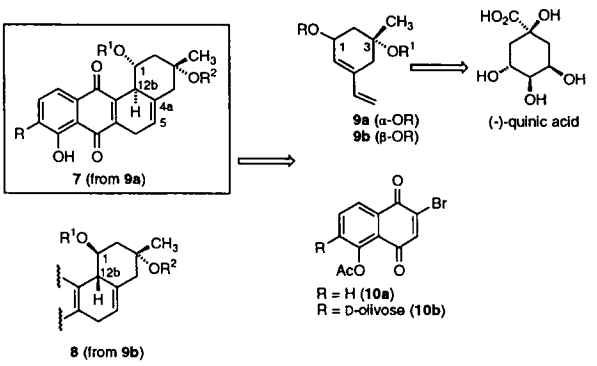
(**3**), a reasonable assumption is that the C4a oxygens of these antibiotics are also acetate derived.

A spectrum of biological activities has been associated with members of the angucycline group of antibiotics. The most frequently examined has been the cytotoxicity of various angucyclines.[5] For example, aquayamycin (**1**), urdamycinone B (**4**), and more highly glycosylated congeners of **1** and **4**, have been found to possess antitumor activity against adriamycin-sensitive and -resistant strains of P388 leukemia. On the other hand, SF 2315A (**2**) and SF 2315B (**3**) were found to be ineffective as antitumor agents when evaluated against similar cell lines.[2b] While the mechanism of cytotoxicity is not known for this class of antitumor agents, it is unlikely to involve DNA intercalation, as is the case for the well studied anthracycline class of anticancer agents.[6] However, alternative modes of binding to DNA (e.g., minor groove binders) have not been excluded.

In addition to exhibiting antitumor activity, aquayamycin (**1**) has been found to be a noncompetitive inhibitor of the enzymes tyrosine hydroxylase, dopamine β-hydroxylase, tryptophan 5-monooxygenase, and 2,3-dioxygenase.[7] A third biological activity, associated, in this case with heavily glycosylated derivatives of **1**, is the inhibition of blood platelet aggregation.[8] Interestingly, the latter activity appears to be dependent on the oligosaccharide conjugate rather than the aglycone. Finally, the antibiotics SF 2315A (**2**) and SF 2315B (**3**) are reported to be weakly active against Gram-positive bacteria and inhibit the reverse transcriptase of Avian myeloblastosis virus.[2b]

Synthetic investigations of the angucycline antibiotics have been directed toward group members with and without angular oxygen functionality. However, the former studies have frequently fallen short of satisfactory solutions and serve to illustrate the difficulty associated with the installation of angular hydroxyl groups located at C4a and C12b.[10] On the other hand, several total syntheses of angucyclines devoid of oxygens at these positions have been recorded.[10,11] These successes have served to highlight methods for the stereoselective introduction of beta-C-arylglycosides in the form of β-D-olivoside frequently located at the C9 position within the angucycline group [cf. aquayamycin (**1**) and urdamycinone B (**4**)] as well as the assembly of the common angular framework. Notable accomplishments in this area include the total synthesis of urdamycinone B, rabelomycin, and the antibiotic C104.[10a-e] We have developed a flexible synthetic strategy which has been applied to the total synthesis of SF 2315A (**2**), urdamycinone B (**4**), and the shunt metabolite 104-2 (**5**).[9d,10e] In this paper we detail our investigations leading to total syntheses of these three angucycline antibiotics and the stereocontrolled assembly of a fully functionalized SF 2315B (**3**) congener.[12]



Scheme 1

SYNTHETIC PLAN

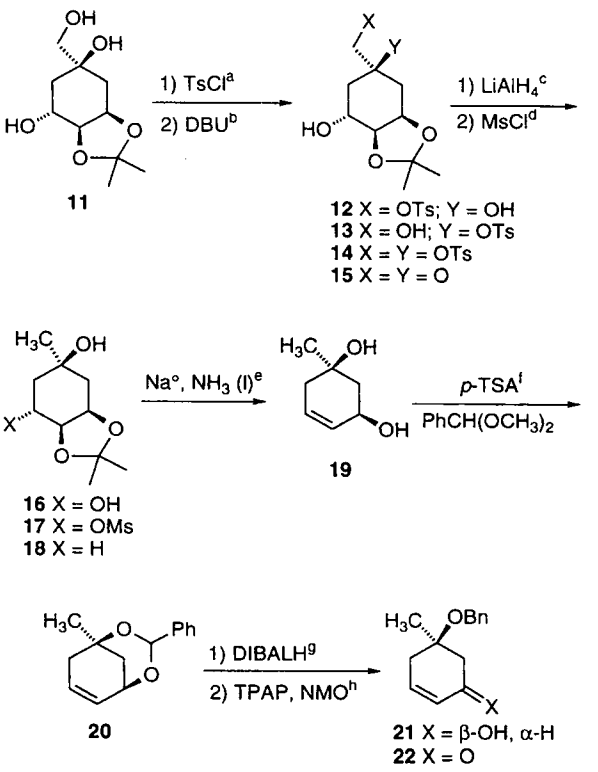
At the outset our goal was to develop a unified synthetic strategy which would provide access to many of the naturally occurring angucycline antibiotics. In this regard, the proposed biosynthesis of the angucycline antibiotics provided a useful paradigm in developing such a strategy. As discussed above, a range of angucyclines is derived through initial assembly of a tetracyclic carbon framework via a polyketide pathway, followed by a series of post-polyketide transformations including oxidation and glycosylation. This series of transformations leads to the generation of various functional and stereochemical arrangements, notably within the AB ring system. In cases where the C3 carbon is stereogenic, due to the positioning of an oxygen substituent as well as a common methyl group, the absolute stereochemistry of this center appears conserved throughout the angucycline group. On the other hand, secondary metabolites possessing either a cis or trans related C3-C4a 1,3-diol have been identified within the angucycline group (cf. **1** and **6**). A strategy which accommodates these structural variations is outlined in Scheme 1. Specifically, a tetracyclic ring system would be derived via a regio- and stereocontrolled Diels–Alder cycloaddition of diene **9** derived from (–)-quinic acid and a suitably functionalized bromojuglone derivative (**10**).[13,14] In this cycloaddition the diene component would possess the natural C3 absolute configuration and either a trans or cis related C1 alkoxy group. The latter would serve as a key structural feature since this would provide accessibility to either α,α-C1-C12b (**7**) or β,β-C1-C12b (**8**) configured angular quinones following dehydrobromination. *The topology conferred on tetracycle 7 prefers oxidation of the isolated olefin*

(C4a–C5) to occur from the alpha face or cis to the distant C3 alkoxy group, while 8 would lead to oxidation from the beta face or trans to the C3 alkoxy group. Thus, diene **9a** would provide an avenue for the assembly of cis related C3-C4a diols [cf. aquayamycin (**1**)], while **9b** would lead to the trans configured series [cf. sakyomycin (**6**)] (vide infra).

SYNTHESIS OF COMMON DIENE 25 FROM (–)-QUINIC ACID

Central to our synthetic strategy was the development of enantioselective syntheses of dienes **9a** and **9b**. For this purpose we sought the assembly of the corresponding dienone which, in turn, should be available from cyclohexenone **22**.[15] The synthesis of cyclohexenone **22** commenced with the preparation of triol **11** available from (–)-quinic acid in two steps and 76% yield.[16] Tosylation of **11** produced **12** as the major product (71%) accompanied by tertiary tosylate **13** (10%) and ditosylate **14** (16%). Sulfonates **13** and **14** are presumably derived via **12** through an internal migration of the tosyl group to the neighboring tertiary alcohol. Typically, sulfonation of **11** was carried out on a 2–3 gram scale since reaction scales larger than this led to higher yields of **13** and **14** at the expense of **12**. Following chromatographic purification, **12** was treated with base (DBU, PhH), to give rise to epoxide **15**, which on reduction with $LiAlH_4$, afforded diol **16** in 71% overall yield.[17] Next, secondary mesylate **17** derived from **16** (1.1 equiv MsCl) was subjected to dissolving metal conditions (Na°, NH_3 (l), THF). This reduction led to the elimination of the acetonide group to provide diol **19** (77–83%) as well as variable amounts of **18** (ca. 15%), the product of direct deoxygenation. Selective protection of the more hindered tertiary alcohol of diol **18** required initial derivatization of **19** (*p*-TSA, $PhC(OCH_3)_2$, CH_2Cl_2, 4 Å MS) to provide cyclic benzylidene **20** (one isomer). Reduction of **20** in dichloromethane at room temperature with DIBALH afforded benzyl ether **21** in 71–82% overall yield.[18] Ley oxidation (TPAP, NMO) of **21** produced enone **22** in near quantitative yield.[19]

The introduction of the remaining two carbons of the targeted diene (**25**) was accomplished by two reaction sequences. First, conjugate addition of a higher-order vinyl cuprate to **22**, followed by trapping of the intermediate enolate with trimethylsilyl chloride and DDQ oxidation of the resultant silyl enol ether produced (+)-**23**.[20,21] Alternatively, 1,2-addition of a vinyl cerium reagent provided bis-allylic alcohol **24**, which on oxidation with Jones reagent provided (–)-**23**.[22,23] Thus, depending on the sequence of reactions, either enantiomer of **23** may be produced starting from cyclohexenone **22**. Fortunately, the more efficient of the two routes leads to



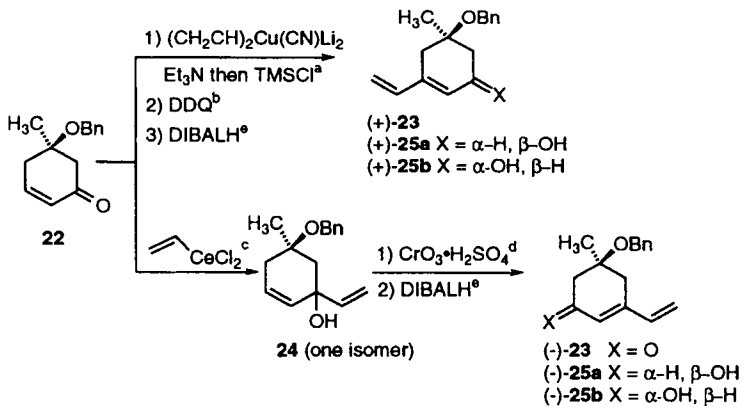
(a) pyridine, DMAP, CH_2Cl_2, 20 °C, 59-71%. (b) PhH, 20 °C, 92-98%. (c) THF, 0 °C to 20 °C, 92-98%. (d) CH_2Cl_2, 0 °C, 92-95%. (e) THF, -78 °C, 77-83%. (f) CH_2Cl_2, 4Å molecular sieves, 20 °C. (g) CH_2Cl_2, 0 to 20 °C, 72-82% from **19**. (h) CH_2Cl_2, 20 °C, 92-98%.

Scheme 2

dienone (+)-**23** possessing the absolute configuration common to the angucycline antibiotics (vide supra). Reduction of dienone **23** with DIBALH yielded a 9:1 mixture of diastereomers. The major isomer (**25a**) was assigned the cis configuration based upon a single-crystal X-ray analysis of the minor trans alcohol (**25b**). The optical purity of (+)- and (–)-**25b**, derived by the route outlined in Scheme 3, was determined to be greater than 95% by analysis of the derived Mosher esters.

TOTAL SYNTHESIS OF SF 2315A (2)

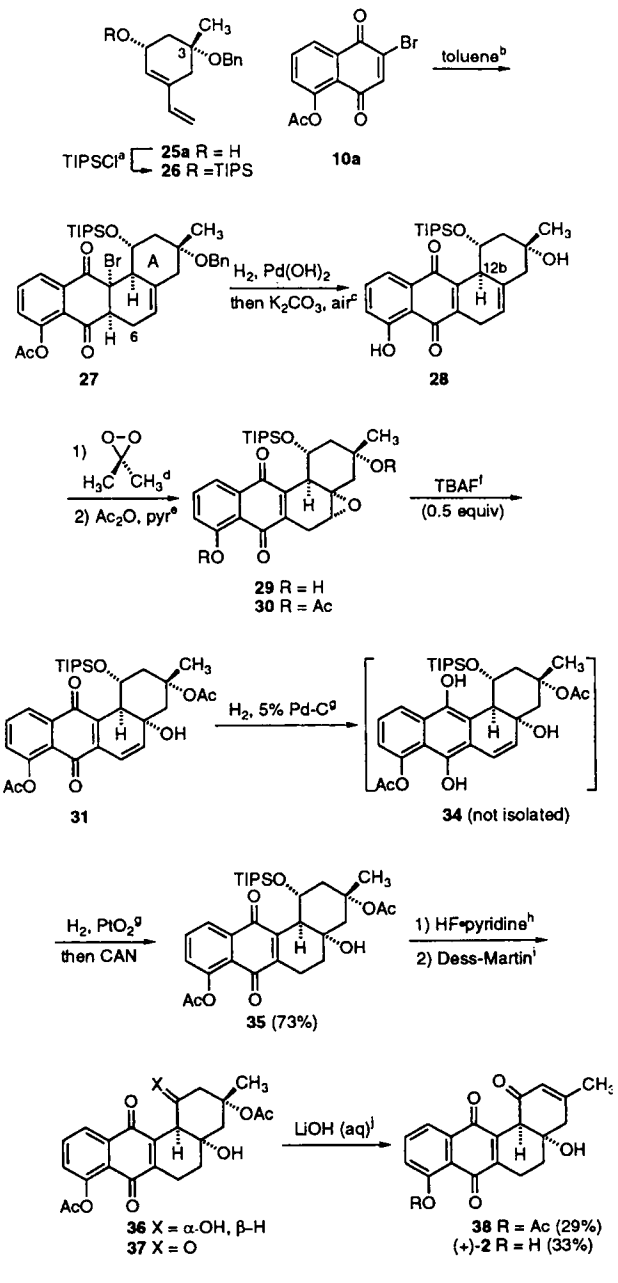
The TIPS-protected diene **26** was derived from **25** under standard conditions (TIPSCl, imidazole) and engaged in a Diels–Alder cycloaddition with 2-bromo-5-acetoxyjuglone **10a**.[24] The Diels–Alder reaction was performed by heating a toluene solution of **10a** (1.2 equiv) and diene **26** at reflux for 15 h. Under these



a (a) Et_2O, -78 to 0 °C. (b) PhH, 0 to 20°C, 67-72% from **22**. (c) THF, 0 °C, 83-93%. d) Me_2CO, 0 °C, 30-46%. (e) CH_2Cl_2, -78 °C, 90-98%.

Scheme 3

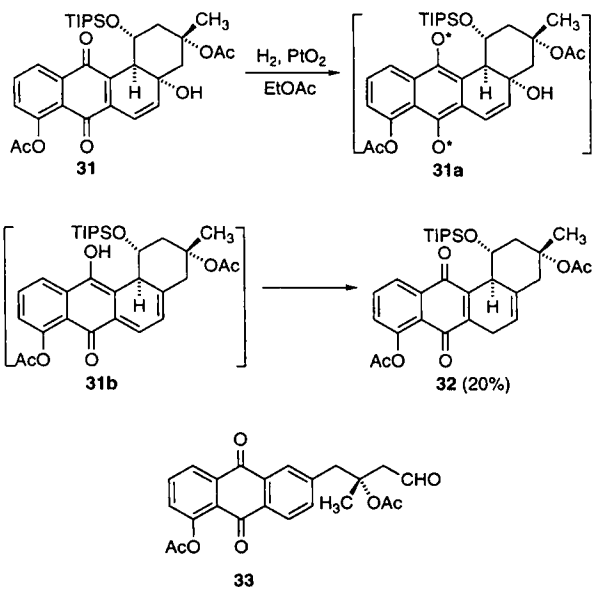
conditions cycloadduct **27** was obtained as a light yellow solid and no other isomers were isolated. The regiochemical relationship between the A ring and distant C8 acetoxy group of **27** was assigned based on the observed coupling between the C6 and C6a protons in the form of an apparent triplet ($J_{6,6a}$ = 7.2 Hz). The effects of the 2-bromo and 5-acetoxy groups of juglone derivatives on the regiochemical course of Diels–Alder cycloadditions is well documented.[13] However, previous literature examples have usually employed a diene with at least one strong electron releasing group in the form of a heteroatom. In this regard, the cycloaddition **26** + **10a**→**27** constitutes the first example which does not employ an electron-rich diene and proceeds with high regioselectivity.[10g] The stereochemical course of the reaction is predicted to occur by an endo approach of the dienophile from the side opposite the C1 TIPS ether (**26**).[14] In this way the configuration of the C12b stereocenter was defined, as well as tetracycle connectivity. Brief hydrogenation of **27** over palladium in ethanol, followed by the introduction of a catalytic amount of K_2CO_3, effected cleavage of the C3 benzyl ether, dehydrobromination, and removal of the C8 acetyl group to give rise to quinone **28** in 85–98% yield. Significantly, angular quinone **28** shows no tendency toward undergoing air oxidation to the corresponding anthraquinone via the dihydro anthraquinone.[25] We have attributed this kinetic stability to the positioning of the sterically demanding silyl ether (located at C1) which induces a ring conformation reluctant to undergo tautomerization to the dihydro anthraquinone.[12b] As discussed earlier, the topology of **28** reveals an expected preference for the delivery of oxidants from the less hindered alpha face, or cis to the C12b hydrogen and distant C3 oxygen. Indeed, epoxidation of **27** with dimethyl dioxirane provided, exclusively, alpha-epoxide **29** in nearly quantitative yield. In preparation for the eventual beta-elimination of the C3 oxygen, **29** was acetylated to provide diacetate **30**. Diacetate **30** underwent rearrangement to the corresponding allylic alcohol (**31**) on treatment with 0.5 equiv of TBAF in tetrahydrofuran. The use of alternative bases (Bu_4NOH, K_2CO_3 in MeOH) to effect this transformation provided discouraging results (decomposition and/or oxidation to an anthraquinone). Next, the deceptively simple reduction of the C5–C6 double bond proved problematic due to the tendency of the intermediate dihydro(semi)quinone to eliminate the newly installed C4a hydroxyl group.[26] For instance, elimination of the angular hydroxyl group to provide, following tautomerizations, quinone **32** was observed when **31** was directly hydrogenated over Adam's catalyst (PtO_2, EtOAc). On the other hand, hydrogenation over palladium (5% Pd-C, 1:1 hexane–EtOAc) for 1h followed by oxidative workup (CAN) produced aldehyde **33** (67%) plus starting quinone **31** (24%). The former could emerge through the pathway **31a** to **31b** which upon trans-silylation releases the C1 hydroxyl group leading to the eventual fragmentation of the C1–C12b bond.[1b,12a] Fortunately, brief hydrogenation over 5% palladium-carbon delivered dihydroquinone **34** without any structural disfigurement. Further hydrogenation over Adam's catalyst effected reduction of the C5–C6 double bond. On oxidation with CAN, **35** was obtained in 73% overall yield from **31**.



(a) Imidazole, DMAP, CH_2Cl_2, 20 °C, 98%. (b) reflux, 56-66%. (c) EtOH, 20 °C, 85-98%. (d) Me_2CO, 20 °C, 98%. (e) DMAP, CH_2Cl_2, 20 °C, 88%. (f) THF, 0 °C, 86%. (g) EtOAc, 20 °C. (h) CH_3CN 0 to 20 °C, 89%. (i) CH_2Cl_2, 20 °C, 93%. (j) EtOH, 0 °C.

Scheme 4

The remaining synthetic operations involved manipulation of the A ring functionality. To this end, removal of the C1 TIPS group (HF•pyr, CH_3CN) followed by Dess–Martin oxidation of the resultant alcohol provided ketone **37**.[27] Treatment of **37** with 10 equiv of



Scheme 5

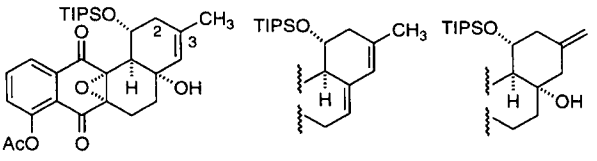
lithium hydroxide in THF produced an approximately equal mixture of **38** and SF 2315A (**2**). The former provided SF 2315A (**2**) on further treatment with aqueous lithium hydroxide in tetrahydrofuran. The ^1H and ^{13}C NMR spectra as well as the sign of optical rotation of synthetic and natural **2** were identical in all respects.[28a]

SYNTHETIC STUDIES DIRECTED TOWARDS SF 2315B (3)

Concurrent with the synthesis of SF 2315A (**2**), we examined the construction of SF 2315B (**3**) from angular quinone **28**. In this instance, the installation of an epoxy quinol functionality as well as the delicate C4a hydroxyl group was required. We previously described a stereoselective oxidation of an unsaturated angular quinone for the *simultaneous* introduction of a cis related quinone oxide and angular hydroxyl group.[12] This oxidation, which relies on a base mediated generation of a quinone methide, was applied to quinone **28**. An oxygenated tetrahydrofuran solution of **28** was cooled to −78 °C and treated with 1 equiv of TBAF leading to the generation of quinone methide **28a**, which on reaction with molecular oxygen led to the generation of epoxy alcohols **39** and **40**.[12,29] A third epoxy alcohol was isolated in less than 5% yield and assigned the structure **41**. Peracetylation of **41** provided triacetate **42**; spectral analysis of **42** supported the assigned structure of **41**. In particular, the ^{13}C NMR spectrum of **42** contains two

downfield carbonyl resonances (δ 181.6 and 181.4) which correspond to the quinone carbonyls. Secondly, inspection of the ^{1}H NMR spectrum of **41** and **42** revealed a significant downfield shift of the C6 proton upon acetylation of **41** (δ 5.35 to 6.43). The stereochemical assignment rests on the C5 proton assignment at δ 3.40 ($J_{12b,5}$ = 0.8 Hz and $J_{5,6}$ = 2.4 Hz). Long-range coupling between H_{12b} and H_5 is most consistent with a trans relationship between the epoxide oxygen and the neighboring C12b proton which induces a W configuration between H_{12b} and H_5. Finally, the epoxide oxygen and C6 hydroxyl group were assigned a cis relationship based on an observed coupling constant ($J_{5,6}$ = 2.4 Hz) consistent with a calculated coupling constant of 1.7 Hz ($J_{5,6}$ = 5.6 Hz was calculated for the C6 epimer of **41**).[30]

The major epoxy alcohol (**39**) was acetylated to provide **43**, which on hydrogenation over Adam's catalyst afforded **44**. At this point we examined the dehydration of **44** as a method of introducing the C2–C3 unsaturation common to SF 2315B (**3**). We found Martin sulfurane ([PhC(CF$_3$)$_2$O]$_2$SPh$_2$) to be an effective dehydrating agent; unfortunately only undesired alkenes **44a–c** were produced under these conditions.[31] We reasoned that reduction of the C12 keto group prior to dehydration may favor formation of the $\Delta_{2,3}$ alkene. To this end, removal of the C1 silyl protecting group (HF•pyr, CH$_3$CN) set the stage for a hydroxy-directed reduction of the C12 keto group.[32] In the event, reduction of **45** with tetramethylammonium triacetoxyborohydride gave rise to intermediate tetraol **46**, which was not isolated but acetylated to provide triacetate **47**. In support

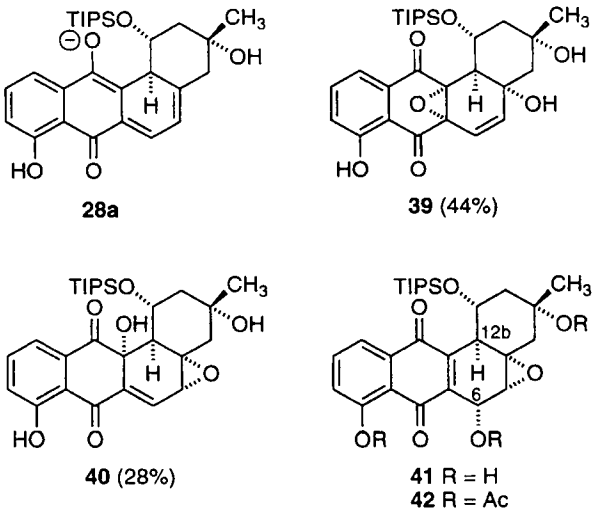


44a **44b** **44c**

of the hypothesized C1 hydroxyl-directed reduction of the C12 keto group, in model investigations, we found the use of sodium borohydride to lead to loss of stereo- as well as chemoselectivity (vis-à-vis C12 versus C7 keto reduction).[12b] Unfortunately, treatment of **47** with an excess of Martin sulfurane did not produce any dehydration products but instead generated an apparent adduct of Martin sulfurane and the starting substrate diol (**47**); while other dehydrating agents (Burgess reagent, $POCl_3$ and $BF{\bullet}OEt_2$) led to either decomposition or no reaction.

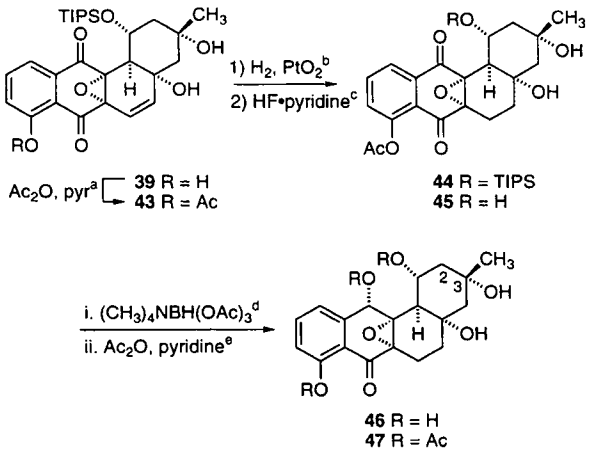
SYNTHESIS OF URDAMYCINONE B (4)

A large group of the angucycline antibiotics possess a C-aryl glycoside positioned at C9.[33] Our synthetic strategy readily accommodates this structural feature in the form of C-glycosyl juglone **53**. Several groups have recognized the versatility of C-glycosyl juglone derivatives in the construction of aryl C-glycoside antibiotics.[10d,11c,34] Our construction of **53** commencing from naphthol **48** is outlined in Scheme 6. While we have previously described the preparation of β-*C*-naphthylglycoside **50** from a sugar lactone, a more direct route to **50** entailed Lewis-acid-mediated ($BF_3{\bullet}OEt_2$, CH_2Cl_2) *C*-



28a **39** (44%) **40** (28%) **41** R = H, **42** R = Ac

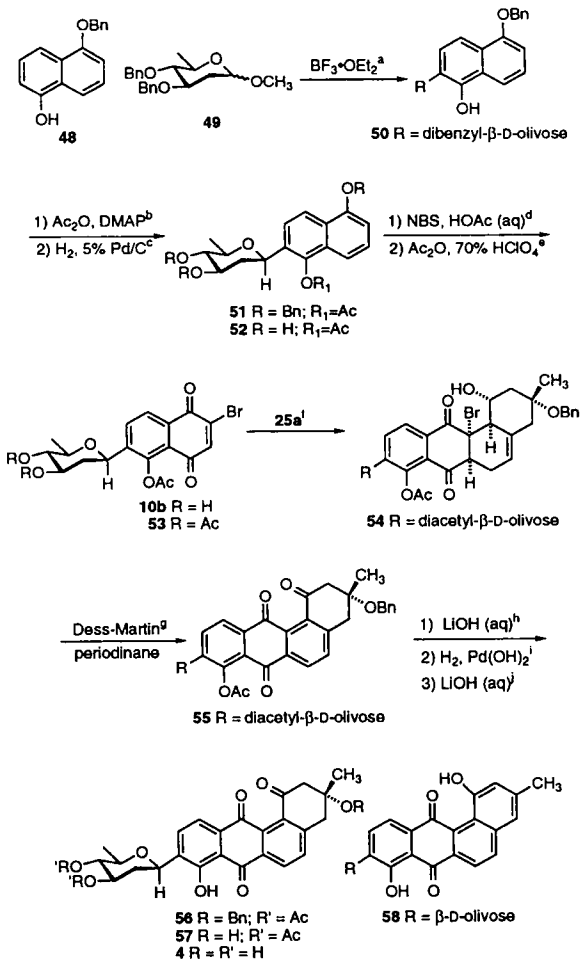
Scheme 6



39 R = H, **43** R = Ac; **44** R = TIPS, **45** R = H; **46** R = H, **47** R = Ac

[a] (a) DMAP, CH_2Cl_2, 20 °C, 93%. (b) 5:1 hexane-EtOAc, 20 °C, 83%. (c) CH_3CN, 0 to 20 °C, 98%. (d) 1:1 HOAc-CH_3CN, -10 °C. (e) DMAP, CH_2Cl_2, 20 °C, 41% from **45**.

Scheme 7



(a) CH_2Cl_2, 0 to 20 °C, 84-90%. (b) CH_2Cl_2, pyridine, 20 °C. (c) EtOH, 20 °C, 85-93% from **50**. (d) 70 °C, 73-94%. (e) EtOAc, 0 °C, 87-92%. (f) PhH, reflux, 12h, 72%. (g) CH_2Cl_2, 20 °C, 98%. (h) THF, 0 to 20 °C. (i) EtOAc-MeOH (1:1), 0 °C. (j) THF, 0 to 20 °C, 54% from **55**.

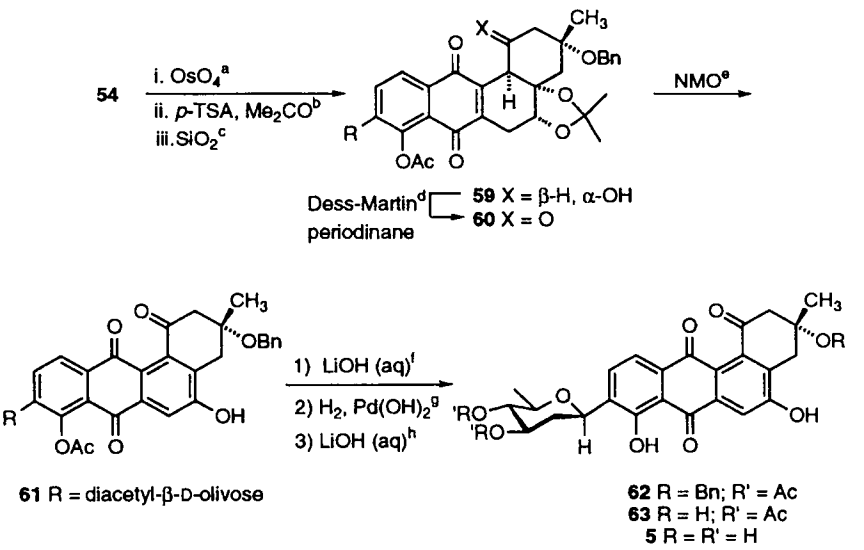
Scheme 8

arylglycosylation of 1-*O*-methyl-D-olivose **49** with naphthol **48**.[35] This regio- and stereoselective glycosylation occurs through the now well established *O*→*C*-glycoside rearrangement exploited by Suzuki and others.[36] Acetylation of **50**, followed by removal of the benzyl protecting groups (H_2, 5% Pd/C, EtOH), set the stage for oxidation of naphthol **52**. Oxidation of **52** utilizing conditions (NBS, HOAc (aq), 70 °C) described by Gruenwell and later modified by Jung provided bromoquinone **10b**.[24] Peracetylation of **10b** ($HClO_4$, Ac_2O, EtOAc) provided triacetate **53**. Notably, attempts to peracetylate **10b** under basic conditions led to decomposition.

The utility of **53** in the synthesis of aryl C-glycosides was first demonstrated by the assembly of urdamycinone B (**4**).[10c] Prior to our work the unnatural enantiomer of **1** was synthesized by Yamaguchi through a polyketide construction.[10a] More recently Toshima reported the synthesis of **4**.[10d] In line with our unified strategy, **53** was engaged in a Diels–Alder cycloaddition with diene **25a** (benzene, reflux, 12h) to afford **54** in 72% yield. Oxidation of **54** with Dess–Martin periodinane led to the production of anthraquinone **55**. Presumably, generation of the corresponding ketone triggered dehydrobromination and oxidation leading to **55**. At this point, removal of the acetyl and benzyl protecting groups were the remaining obstacles to completing urdamycinone B (**4**). Due to both the propensity for the C3 benzyl ether to undergo beta-elimination and the inherent insolubility of **55** in various solvents, the sequence of deprotection proved critical. For example, attempts at removing the C8 as well as C3' and C4' acetyl groups (LiOH (aq), THF) over an extended reaction period led to concomitant elimination of the C3 benzyl ether. On the other hand, initial hydrogenolysis of the benzyl group proved unworkable due to the insolubility of **55** in various solvents. Fortunately, we found brief saponification of **55** with aqueous lithium hydroxide led to removal of the C8 acetyl group (80%) without loss of the C3 benzyl ether as well as the C3' and C4' acetyl groups. Phenol **56** was then hydrogenated over Pearlman's catalyst to afford diacetate **57**. Careful removal of the remaining acetyl groups (2 equiv LiOH, THF, 0 °C) led to the isolation of urdamycinone B (67%) and 22% of diphenol **58**. The spectral data (^1H NMR, ^{13}C NMR, IR, CD) of synthetic and natural urdamcyinone B were identical.[28b]

SYNTHESIS OF SHUNT METABOLITE 104-2 (5)

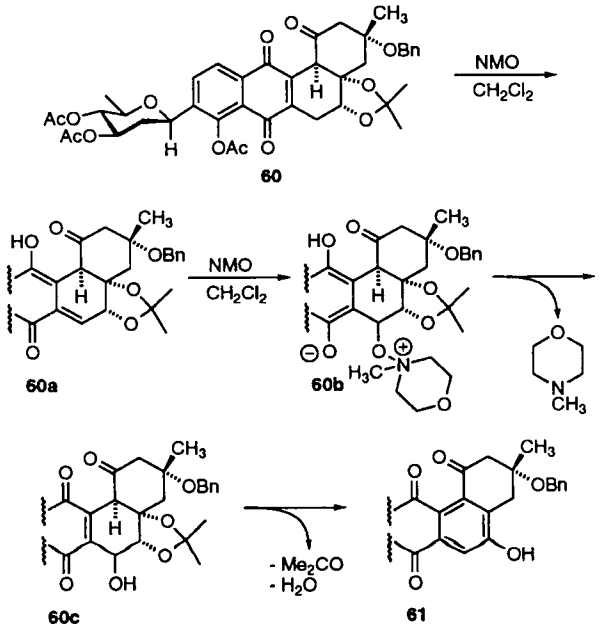
The shunt metabolite 104-2 (**5**) was isolated from a mutant strain of *streptomcyes* Fridae Tu 27.[2h] This metabolite differs from urdamycinone B (**4**) in the positioning of a second phenol group located at C5. Oxidation of quinone **60** with *N*-methylmorpholine *N*-oxide (NMO) produced **61**, a protected version of **5**.[37,10e] Quinone **60**, was in turn derived from cycloadduct **54** in four steps. First, oxidation with catalytic osmium tetroxide (NMO, Me_2CO (aq), *t*-butanol) produced a diol which was not isolated but protected as an acetonide derivative (*p*-TSA, Me_2CO) and subsequently dehydrobrominated in the presence of silica gel.[38] Dess–Martin oxidation of **59** furnished ketone **60** in quantitative yield. Treatment of a solution of **60** in dichloromethane with one equiv of NMO resulted in the production of anthraquinones **55** and **61** as yellow solids in 27 and 72% yield, respectively. The oxidation of **60** to **61** is proposed to arise through initial oxidation of the C6 position (Scheme 10)



[a](a) NMO, Me_2CO (aq), t-BuOH, 20 °C, 84-90%. (b) 20 °C. (c) EtOAc, 20 °C, 67% from **54**. (d) CH_2Cl_2, 20 °C, 98%. (e) CH_2Cl_2, 20 °C, 72%. (f) THF, 0 to 20 °C. (g) EtOAc-MeOH (1:1), 0 °C. (h) THF, 0 to 20 °C, 52% from **61**.

Scheme 9

via an intermediate quinone methide (**60a**).[36,39] Following formal loss of morpholine, **60c** is subject to beta-elimination of the acetonide group and dehydration to produce **61**. None of the intermediates on the pathway from **60** to **61** were isolated. With anthraquinone **61** in hand, the remaining obstacle to completing the synthesis of 104-2 (**2**) was the removal of protecting groups. Employing the three-step protocol developed in the synthesis of urdamycinone B (**4**), we obtained 104-2 (**5**) from **61** in 52% yield. The spectral data (^1H NMR, ^{13}C NMR, IR, CD) of synthetic and natural 104-2 were identical.[28b]



Scheme 10

EXPERIMENTAL SECTION

General Procedures

All starting materials and reagents were obtained from commercial suppliers and, where appropriate, were purified prior to use. All reactions were carried out under a nitrogen or argon atmosphere using dry glassware which had been flame-dried under a stream of nitrogen, unless otherwise noted. All necessary solvents were purified prior to use. Tetrahydrofuran and ethyl ether were distilled from sodium/benzophenone; dichloromethane and benzene were distilled from calcium hydride. *p*-Toluenesulphonyl chloride was recrystallized from chloroform. Pyridine and triethylamine were distilled from calcium hydride and stored over sodium hydroxide. Toluene was distilled from calcium hydride. *N*-bromosuccinimide was recrystallized from water and dried over P_2O_5. Trimethylsilyl chloride was freshly distilled from calcium hydride. Reactions were monitored by thin-layer chromatography (TLC) using 0.25-mm E. Merck precoated silica gel plates. Visualization 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

230–400 mesh) with the indicated solvent according to the method of Still.[41] Gas–liquid chromatography (GLC) analyses were performed with a Hewlett-Packard 5790A chromatograph equipped with a 30-m × 0.32-mm × 0.25-mm Hewlett-Packard Ultra (cross-linked methyl silicone) column. Yields refer to chromatographically and spectroscopically pure compounds unless otherwise stated. Melting points are uncorrected unless otherwise noted. ^{1}H and ^{13}C NMR spectra were recorded at 200 and 400 MHz at ambient temperature. ^{1}H and ^{13}C NMR data are reported as δ values relative to tetramethylsilane. Optical rotations were measured on a Jasco DIP-181 digital polarimeter at ambient temperature. High-resolution mass spectra were obtained at Texas A&M University Mass Spectrometry Service Center by Dr. Lloyd Sumner on a VG Analytical 70S high-resolution, double-focusing, sectored (EB) mass spectrometer. Combustion analyses were performed by Atlantic Mircrolab, Inc. (Norcross, GA). The single-crystal X-ray diffraction anaylsis was performed by Dr. Joseph Reibenspies of Texas A&M University using a R3m/V single-crystal X-ray diffractometer.

Tosylate ***12***

To a solution of triol **11** (2.0 g, 9.2 mmol) and a catalytic amount of DMAP (ca. 10 mg) in pyridine (10 mL) at 0 °C was added *p*-toluenesulfonyl chloride (1.9 g, 10.1 mmol) in 3 equal portions accompanied by a catalytic amount of DMAP (ca. 10 mg) over a 30 min period. The solution was allowed to warm to room temperature and stirred for 25 h. Additional *p*-toluenesulfonyl chloride (350 mg, 1.8 mmol) and DMAP (ca. 10 mg) were added and stirring was continued for 24 h. The solvent was removed in vacuo, and the resulting oil was diluted with methylene chloride (200 mL) and 20% aqueous $CuSO_4$ solution (75 mL). The mixture was extracted with methylene chloride (3 × 125 mL) and the combined organic extracts were washed with 20% aqueous $CuSO_4$ (50 mL), water (50 mL), brine (40 mL), dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash chromatography (gradient elution: 1:1 to 1:2 hexane/EtOAc) to afford 340 mg (10%) of tosylate **13** as a white solid, 769 mg (16%) of ditosylate **14** as a white solid, and 2.4 g (71%) of tosylate **12** as a white amorphous solid.

Tosylate **12**: TLC, R_f 0.46 (1:3 hexane/EtOAc); mp 88–93 °C; $[\alpha]^D_{20}$ –41.9° (*c* 1.7, $CHCl_3$); IR ($CHCl_3$) 3523, 2991, 2941, 1450 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.2 Hz, 2H, H_{arom}), 7.35 (d, *J* = 8.2 Hz, 2H, H_{arom}), 4.39 (m, 1H), 4.08 (m, 1H), 3.92 (t, *J* = 5.7 Hz, 1H), 3.84 (s, 2H), 3.47 (br s, 2H, both -OH), 2.44 (s, 3H), 2.15 (br d, *J* = 15.0 Hz, 1H),1.86 (dd, *J* = 15.5, 4.1 Hz, 2H), 1.49 (s superimposed m, 4H), 1.33 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 145.0, 132.3, 129.8, 127.8, 109.0, 80.1, 75.5, 73.8, 70.9, 68.3, 37.9, 33.0, 28.1, 25.6, 21.5. Anal. Calcd for $C_{17}H_{24}O_7S_1$: C, 54.82; H, 6.50. Found: C, 54.61; H, 6.48.

Epoxide ***15***

To a solution of tosylate **12** (8.8 g, 23.6 mmol) in benzene (80 mL) was added DBU (3.7 mL, 24.7 mmol) and the mixture stirred for 30 min at room temperature. The solution was concentrated in vacuo and the residue purified by flash chromatography (gradient elution: 1:2 to 1:3 hexane/EtOAc) to afford 4.7 g (99%) of epoxide **15** as a white amorphous solid: mp 60–63 °C; $[\alpha]^D_{20}$ –47.9° (*c* 1.8, $CHCl_3$); IR ($CHCl_3$) 3596, 3457, 2992, 2934, 1442 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.43 (m, 1H), 4.11 (m, 1H), 3.97 (t, *J* = 6.5 Hz, 1H), 3.18 (br s, 1H, –OH), 2.67 (d, *J* = 5.9 Hz, 1H, OCH_2), 2.63 (d, *J* = 5.9 Hz, 1H, OCH_2), 2.30 (dd, *J* = 15.5, 4.9 Hz, 1H), 1.90–1.60 (m 3H), 1.56 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 109.1, 79.8, 73.2, 69.6, 54.9, 51.7, 36.0, 33.1, 28.3, 25.8. Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.06. Found: C, 60.05; H, 8.02.

Diol ***16***

A solution of epoxide **15** (1.1 g, 5.5 mmol) in THF (10 mL) was added dropwise by cannula to a suspension of $LiAlH_4$ (270 mg, 7.1 mmol) in THF (10 mL) at 0 °C. The mixture was warmed to room temperature for 1 h. The resulting solution was cooled to 0 °C and quenched sequentially with water (270 mL), 15% aqueous NaOH (270 mL), and water (810 mL). Celite (25 g) was added and the suspension stirred for 2 h. The white suspension was filtered through a Celite plug and washed with Et_2O (ca. 400 mL). The filtrate was concentrated in vacuo and the residue purified by flash chromatography (gradient elution: 1:4 hexane/EtOAc to EtOAc) to afford 1.1 g (100%) of diol **16** as a white amorphous solid: mp 53–55 °C; $[\alpha]^D_{20}$ –90.3° (*c* 1.11, $CHCl_3$); IR ($CHCl_3$) 3513, 2991, 2938, 1373 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.32 (m, 1H), 4.02 (m, 1H), 3.82 (t, *J* = 7.1 Hz, 1H), 3.11 (br s, 2H, both –OH), 2.12 (br d, *J* = 15.5 Hz, 1H), 1.92 (m, 1H), 1.70 (dd, *J* = 15.8, 3.9 Hz, 1H), 1.46 (s, 3H), 1.29 (s, 3H), 1.18 (s superimposed on m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 108.9, 80.9, 74.9, 70.4, 69.2, 43.2, 37.8, 29.9, 28.5, 25.9. Anal. Calcd for $C_{10}H_{18}O_4$: C, 59.38; H, 8.97. Found: C, 59.16; H, 8.93.

Mesylate ***17***

A solution of diol **16** (6.6 g, 32.4 mmol) and triethylamine (5.4 mL, 40.8 mmol) in methylene chloride (110 mL) was cooled to 0 °C. Methanesulfonyl chloride (2.8 mL, 35.7 mmol) was added dropwise and the solution stirred for 40 min, quenched with water (20 mL) and saturated with NaCl. The mixture was extracted with EtOAc (3 × 150 mL), the extracts combined, washed with water (30 mL), brine (30 mL), dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The crude mesylate was purified by flash chromatography (gradient elution: 1:1 to 1:2 hexane/EtOAc) to afford 8.9 g (98%) of mesylate **17** as a white amorphous solid: mp 85–88 °C; $[\alpha]^D_{20}$ –89.9° (*c* 0.9, $CHCl_3$); IR ($CHCl_3$) 3531, 2990, 2937, 1355 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.03 (m, 1H), 4.44 (m, 1H), 4.10 (m, 1H), 3.15 (s, 3H), 3.02 (br s, 1H, –OH), 2.32-2.16 (m, 2H), 1.89–1.1.60 (m, 2H), 1,59 (s, 3H), 1.38 (s, 3H), 1.29 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 109.6, 81.9, 77.3, 75.1, 70.4, 42.2, 38.5, 37.3, 29.8, 28.1, 25.8; HRMS (FAB) *m/e* 281.1050 [$(M+H)^+$, calcd for $C_{11}H_{21}O_6S$: 281.1059].

Allylic Alcohol ***19***

A three-neck flask equipped with a mechanical stirrer and dry-ice condenser was charged with condensed ammonia gas (ca. 200 mL) at –78 °C. Mesylate **17** (6.9 g, 24.5 mmol) in tetrahydrofuran (25 mL), followed by sodium metal (ca. 1.2 g,

60 mmol) were added, and the deep blue mixture was maintained throughout the reaction. After 1.25 h the mixture was quenched with NH_4Cl (ca. 3 g) and the ammonia allowed to evaporate overnight. The residue was diluted with water (75 mL) and extracted with Et_2O (3 × 200 mL). The extracts were combined, washed with brine (20 mL), dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash chromatography (gradient elution: 1:2 to 1:3 hexane/EtOAc) to provide 192 mg (15%) of acetonide **18** as a colorless oil and 2.7 g (85%) of allylic alcohol **19** as a colorless oil .

Alcohol **19**: TLC, R_f 0.13 (1:2 hexane/EtOAc); $[\alpha]^D_{20}$ +126.8° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3599, 3408, 3001, 2972, 2927 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.92 (m, 1H), 5.77 (m, 1H), 4.23 (m, 1H), 3.33 (br s, 2H, both –OH), 2.22 (dd superimposed d, *J* = 9.8, 3.9 Hz, 2H), 2.00 (br d, *J* = 14.8 Hz, 1H), 1.77 (dd, *J* = 14.1, 4.8, Hz, 1H), 1.29 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 128.1, 127.0, 69.1, 64.9, 42.1, 39.4, 29.6; HRMS (EI) *m/e* 110.0724 [$(M-H_2O)^+$, calcd for $C_7H_{10}O$: 110.0732].

*Benzylidene **20***

A mixture of allylic alcohol **19** (980 mg, 7.7 mmol), benzaldehyde dimethylacetal (1.7 mL, 11.5 mmol), 4Å molecular sieves powder (7 g), and a catalytic amount of *p*-TSA (ca. 10 mg) in methylene chloride (25 mL) was stirred for 18 h. Additional *p*-TSA (ca. 10 mg) and molecular sieves (3 g) were added and stirring continued for 6 h. The suspension was filtered through Celite, washed with methylene chloride (ca. 125 mL), the filtrate concentrated in vacuo and the residue was purified by flash chromatography (6:1 hexane/EtOAc) to afford 138 mg (14%) of starting allylic alcohol **19** and 1.2 g (72%) of benzylidene **20** as a low-melting solid: mp 33–35 °C; $[\alpha]^D_{20}$ +86.8° (*c* 0.6, $CHCl_3$); IR ($CHCl_3$) 3000, 2959, 2933, 1062 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.55–7.25 (m, 5H, H_{arom}), 6.31 (dt, *J* = 9.9, 3.3 Hz, 1H), 6.09 (s, 1H), 5.91 (m, 1H), 4.60 (m, 1H), 2.55–2.18 (m, 3H), 1.61 (dd, *J* = 12.4 2.2 Hz, 1H), 1.29 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 139.2, 134.2, 128.5, 128.1, 126.4, 123.1, 90.8, 70.5, 66.7, 38.2, 36.8, 29.7. Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.60; H, 7.54.

*Allylic Alcohol **21***

A solution of benzylidene **20** (1.2 g, 5.6 mmol) in methylene chloride (55 mL) was cooled to 0 °C and treated with a solution of DIBAL (1 M in hexanes, 5.7 mL, 5.7 mmol). The reaction mixture was stirred at room temperature for 5h and quenched with a saturated solution of Rochelle's salt (25 mL). The quenched reaction mixture was allowed to stir for 20 min and was extracted with methylene chloride (4 × 100 mL). The combined organic extracts were washed with water (30 mL), brine (30 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (gradient elution: 3:1 to 2:1 hexane/EtOAc) to afford 1.2 g (99%) of benzyl ether **21** as a colorless oil: R_t 9.7 at 170 °C by GC; $[\alpha]^D_{20}$ +58.8° (*c* 0.8, $CHCl_3$); IR ($CHCl_3$) 3510, 3001, 2972, 2927 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.31–7.27 (m, 5H, H_{arom}), 5.95 (m, 1H), 5.68 (m, 1H), 4.42 (A of AB, J_{AB} = 10.8 Hz, 1H), 4.32 (B of AB, J_{AB} = 10.8 Hz, 1H), 4.07 (br s, 1H), 3.31 (br s, 1H, –OH), 2.56 (dd, *J* = 18.3, 4.9 Hz, 1H), 2.15 (br d, *J* = 14.1 Hz, 1H), 1.95 (dq, *J* = 18.2, 2.5 Hz, 1H), 1.82 (dd, *J* = 14.0, 5.2 Hz, 1H), 1.31 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 138.8, 130.0, 128.3, 127.3, 124.5, 74.4, 64.9, 63.8, 42.1, 33.7, 24.9; HRMS (FAB) *m/e* 219.1380 [$(M+H)^+$, calcd for $C_{14}H_{19}O_2$: 219.1385].

*Enone **22***

A solution of allylic alcohol **21** (1.0 g, 4.6 mmol), NMO (725 mg, 6.2 mmol) and TPAP (80 mg, 0.2 mmol) in methylene chloride (25 mL) was stirred until the reaction was judged complete by analytical gas chromatography (ca. 2 h). The mixture was filtered through Celite, concentrated in vacuo, and purified by flash chromatography (4:1 hexane/EtOAc) to afford 990 mg (100%) of enone **22** as a colorless oil: R_t 10.7 at 170 °C by GC; $[\alpha]^D_{20}$ –82.5° (*c* 0.8, $CHCl_3$); IR ($CHCl_3$) 3003, 2975, 1674 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.4–7.2 (m, 5H, H_{arom}), 6.84 (m, 1H), 6.09 (dt, *J* = 10.0, 1.1 Hz, 1H), 4.45 (A of AB, J_{AB} = 10.8 Hz, 1H), 4.37 (B of AB, J_{AB}, = 10.9 Hz, 1H), 2.85 (d, *J* = 16.1 Hz, 1H), 2.72 (dd, *J* = 18.8, 4.4 Hz, 1H), 2.55 (d, *J* = 19.8 Hz, 1H), 2.45 (dt, *J* = 15.4, 2.7 Hz, 1H), 1.40 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 198.3, 146.2, 138.5, 129.3, 128.3, 127.3, 127.3, 64.0, 49.3, 37.5, 24.1; HRMS (FAB) *m/e* 217.1210 [$(M+H)^+$, calcd for $C_{14}H_{17}O_2$: 217.1229].

*Cyclohexenol **24***

To a solution of anhydrous $CeCl_3$ (910 mg, 3.70 mmol) in THF (4 mL) at –78 °C was added vinylmagnesium bromide (1 M solution in THF, 3.9 mL, 3.9 mmol). After 1 h, a solution of **22** (400 mg, 1.85 mmol) in THF (5 mL) was added via cannula. The reaction mixture was stirred for 1 h, quenched with water (5 mL) and extracted with EtOAc (3 × 15 mL). The combined extracts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. Flash column chromatography (4:1 hexane/EtOAc) afforded 420 mg (93%) of **24** as a colorless oil: ^1H NMR (200 MHz, $CDCl_3$) δ 7.40–7.19 (m, 5H, H_{arom}), 5.91–5.64 (m, overlapping signals, 3H), 5.29 (dd, *J* = 17.0, 1.6 Hz, 1H), 5.06 (dd, *J* = 11.0, 1.6 Hz, 1H), 4.45 (A of AB, J_{AB} = 18.0 Hz, 1H), 4.35 (B of AB, J_{AB} = 18.0 Hz, 1H), 4.37 (s, 1H), 2.69–2.52 (m, 1H), 2.20–1.90 (m, 2H), 1.74 (d, *J* = 14 Hz, 1H), 1.35 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 143.4, 132.8, 128.4, 127.5, 127.4, 123.3, 112.5, 75.0, 70.4, 64.2, 46.9, 33.0, 25.4. Anal. Calcd for $C_{16}H_{20}O_2$: C, 78.64; H, 8.26. Found: C, 78.70; H, 8.28.

*Dienone (–)-**23***

To a solution of **24** (240 mg, 0.98 mmol) in acetone (2 mL) at 0 °C was added Jone's reagent (ca. 8 M solution, 1 mL, 8 mmol). After 0.5h, the reaction mixture was diluted with Et_2O (10 mL), quenched with water (5 mL), and extracted with Et_2O (3 × 10 mL). The combined extracts were washed with water (2 × 50 mL), saturated aqueous $NaHCO_3$ solution (3 × 50 mL), brine, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. Flash chromatography (4:1 hexane/EtOAc) furnished 110 mg (46%) of (–)-**23** as a colorless oil: TLC, R_f 0.33 (2:1 hexane/EtOAc); $[\alpha]^D_{20}$ –46.1° (*c* 1.4, $CHCl_3$); IR ($CHCl_3$) 1706, 1658 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.38–7.20 (m, 5H, H_{arom}), 6.54 (dd, *J* = 18.0, 11.0 Hz, 1H), 6.02 (d, *J* = 0.5 Hz, 1H), 5.68 (d, *J* = 18.0 Hz, 1H), 5.45 (d, *J* = 11.0 Hz, 1H), 4.48

(A of AB, J_{AB} = 17.0 Hz, 1H), 4.37 (B of AB, J_{AB}, J = 17.0 Hz, 1H), 2.88 (d, J = 17.7 Hz, 1H), 2.82 (d, J = 15.9 Hz, 1H), 2.57 (d, J = 16.0 Hz, 1H), 2.55 (d, J = 18.0 Hz, 1H), 1.43 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 198.8, 152.8, 138.5, 137.6, 128.3, 127.5, 127.4, 127.3, 120.6, 75.8, 64.1, 49.0, 36.2, 24.3; HRMS (FAB) *m/z* 243.1405 [(M+H)$^+$, calcd for $C_{16}H_{19}O_2$ 243.1385].

Dienone (+)-23

To a suspension of Cu(I)CN (640 mg, 7.1 mmol) in Et_2O (6 mL) was added vinyl lithium (2.3 M solution in THF, 6.2 mL, 14.3 mmol), and the black mixture stirred for 5 min at –45 °C, then 15 min at –78 °C. A solution of enone **22** (1.1 g, 5.1 mmol) in Et_2O (6 mL) was added by cannula, and the resulting dark solution stirred for 30 min at –78 °C, then gradually warmed to 0 °C . Triethylamine (2.5 mL, 18.0 mmol) followed by TMSCl (2.4 mL, 18.0 mol) were added, and the mixture gradually warmed to room temperature for 45 min. The solution was quenched with saturated aqueous NH_4Cl (5 mL), extracted with Et_2O (4 × 100 mL), and the combined organic extracts were washed with brine (30 mL), dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The crude silyl enol ether was dissolved in benzene (50 mL), cooled to 0 °C, and DDQ (1.5 g, 6.6 mmol) was added. The dark solution was stirred for 2 h and gradually allowed to warm to room temperature. The reaction was quenched with saturated aqueous $NaHCO_3$ (20 mL), extracted with EtOAc (3 × 100 mL), and the combined organic extracts were washed with saturated aqueous $NaHCO_3$ (3 × 50 mL), brine (30 mL), dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography (4:1 hexane/EtOAc) afforded 940 mg (76%) of dienone (+)-**23** as a colorless oil: $[\alpha]^D_{20}$ +39.8° (*c* 1.2, $CHCl_3$).

Allylic Alcohol 25

A solution of dienone (+)-**23** (790 mg, 3.3 mmol) in methylene chloride (17 mL) was cooled to –78 °C and treated with a solution of DIBAL (1 M in hexanes, 4.3 mL, 4.3 mmol). The reaction mixture was stirred for 30 min, quenched with a saturated solution of Rochelle's salt (5 mL), and stirred for 45 min, allowing the solution to gradually warm to room temperature. The mixture was extracted with methylene chloride (3 × 75 mL), and the combined organic extracts were washed with brine (30 mL), dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Flash chromatography (5:1 hexane/EtOAc) of the residue afforded 120 mg (15%) of allylic alcohol **25b** as a white solid and 680 mg (85%) of allylic alcohol **25a** as a colorless oil.

Alcohol **25a**: TLC, R_f 0.55 (4:1 × 4 hexane/EtOAc); $[\alpha]^D_{20}$ +187.9° (*c* 1.1, $CHCl_3$); IR ($CHCl_3$) 3510, 3001, 2971, 2926 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.38–7.20 (m, 5H, H_{arom}), 6.43 (dd, J = 17.4, 10.9 Hz, 1H), 5.96 (d, J = 3.4 Hz, 1H), 5.25 (d, J = 17.5 Hz, 1H), 5.07 (d, J = 10.8 Hz, 1H), 4.45 (A of AB, J_{AB} = 17.0 Hz, 1H), 4.30 (B of AB, J_{AB}, J = 17.0 Hz, 1H), 4.18 (br s, 1H), 3.30 (m, 1H, –OH), 2.76 (d, J = 17.8 Hz, 1H), 2.16 (br d, J = 13.9 Hz, 1H), 1.97 (br d, J = 17.6 Hz, 1H), 1.87 (dd, J = 14.2, 5.3 Hz, 1H), 1.39 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 139.0, 138.7, 133.3, 130.4, 128.4, 127.4, 112.6, 74.7, 65.3, 64.0, 42.1, 32.6, 25.0; HRMS (FAB) *m/e* 227.1406 [(M+H-H_2O)$^+$, calcd for $C_{16}H_{19}O$: 227.1436].

Diene 26

To a solution of allylic alcohol **25a** (1.49 g, 6.10 mmol), imidazole (1.26 g, 18.5 mmol), and a catalytic amount of DMAP (ca. 10 mg) in dichloromethane (20 ml) was added triisopropylsilyl chloride (1.97 mL, 9.21 mmol). After stirring for 3.6 h at room temperature, the mixture was quenched with saturated aqueous $NaHCO_3$ solution (10 mL), and extracted with dichloromethane (3 × 30 mL). The combined extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. Purification by flash chromatography (1:9 EtOAc/hexanes) afforded 2.44 g (100%) of diene **26** as a colorless oil: $[\alpha]^{25}_D$ +31.9° (*c* 2.0, $CHCl_3$); IR ($CDCl_3$) 1464, 1371 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.45–7.21 (m, 5H, H_{arom}), 6.41 (dd, J = 17.5, 10.8 Hz, 1H), 5.69 (br s, 1H), 5.18 (d, J = 17.5 Hz, 1H), 5.05 (d, J = 10.8 Hz, 1H), 4.62–4.40 (AB superimposed m, 3H), 2.45–2.35 (m, 2H), 2.21 (dd, J = 10.0, 7.8 Hz, 1H), 1.82 (app t, J = 8.0 Hz, 1H), 1.27 (s, 3H), 1.18–1.05 (m, 21H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 139.4, 138.9, 134.8, 131.5, 128.3, 127.4, 127.3, 112.8, 75.0, 68.2, 63.4, 43.2, 35.9, 23.2, 18.1, 12.3; HRMS(FAB) *m/z* 399.2702 [(M-H)$^+$, calcd for $C_{25}H_{39}O_2Si$ 399.2719].

Diels–Alder Adduct 27

A solution of diene **26** (300 mg, 0.84 mmol) and 5-acetoxy-2-bromojuglone **10a** (300 mg, 1.02 mmol) in toluene (15 mL) was heated at reflux overnight. The mixture was cooled to room temperature and concentrated in vacuo. Purification by flash chromatography (1:3 EtOAc/hexane) provided 360 mg (66% yield) of bromoketone **27** as a light yellow amorphous solid: mp 103–104 °C; $[\alpha]^{25}_D$ –34.5° (*c* 0.5, $CHCl_3$); IR ($CDCl_3$) 1769, 1707 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.00 (dd, J = 7.8, 1.16 Hz, 1H, H_{arom}), 7.73 (t, J = 7.8 Hz, 1H, H_{arom}), 7.40–7.20 (m, 6H, H_{arom}), 5.57 (m, 1H, H_5), 4.75 (m, 1H, H_1), 4.50 (s, 2H, –CH_2Ph), 3.61 (t, J = 7.2, 1H, H_{6a}), 3.09 (br d, J = 6.0 Hz, 1H, H_{12b}), 2.39 (s, 3H, –OAc), 2.57–2.30 (m, 5H), 1.85 (m, 1H), 1.29 (s, 3H, –CH_3), 1.09-0.80 (br s, 21H, –OTIPS); ^{13}C NMR (50 MHz, $CDCl_3$) δ 193.5, 189.7, 169.2, 149.0, 139.5, 135.5, 134.8, 133.8, 129.3, 128.3, 127.3, 127.2, 126.2, 120.6, 74.5, 70.0, 63.6, 59.3, 56.8, 46.2, 46.1, 22.8, 21.0, 18.4, 18.2, 13.5; HRMS(FAB) *m/z* 651.1802 [(M-C_3H_7)$^+$, calcd for $C_{34}H_{40}O_6BrSi$ 651.1778].

Quinone 28

Bromoketone **27** (750 mg, 1.08 mmol) was dissolved in anhydrous EtOH (60 mL), and 20% $Pd(OH)_2$ on carbon (ca. 5 mg) added. The flask was flushed three times with hydrogen and the mixture was stirred for 30 min under an atmosphere of hydrogen. Potassium carbonate (600 mg, 4.34 mmol) was added, and the hydrogen atmosphere replaced with a nitrogen atmosphere. The reaction mixture was stirred vigrously for 1h, and the dark red mixture quenched with saturated aqueous NH_4Cl solution, filtered through a Celite pad, and diluted with EtOAc. The aqueous layer was extracted with EtOAc (3 × 80 mL), and the combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. Flash column chromatography (1:3 EtOAc/hexane)

provided 520 mg (100%) of quinone **28** as a yellow powder: mp 51–53 °C; $[\alpha]^{25}_D$ +71.3° (*c* 1.5, $CHCl_3$); IR ($CDCl_3$) 3599, 1664, 1636, 1614, 1459 cm^{-1} ; ^1H NMR (200 MHz, $CDCl_3$) δ 12.02 (s, 1H, –OH), 7.62–7.43 (m, 2H, H_{arom}), 7.18 (dd, *J* = 7.3, 2.3 Hz, 1H, H_{arom}), 5.61 (br s, 1H, H_5), 3.77 (m, 1H, H_1), 3.58 (td, *J* = 10.5, 3.8 Hz, 1H, H_{12b}), 3.38 (A of AB, J_{AB} = 18.0 Hz, 1H, H_6), 3.05 (B of AB, J_{AB} = 18.0 Hz, 1H, H_6), 2.40–1.80 (m, overlapping signals, 5H), 1.23 (s, 3H, $-CH_3$), 0.90–0.78 (m, 21H, –OTIPS); ^{13}C NMR (50 MHz, $CDCl_3$) δ 189.3, 183.1, 161.0, 146.1, 140.8, 136.0, 133.7, 133.0, 123.3, 119.0, 118.4, 114.7, 74.8, 71.0, 51.7, 49.2, 45.0, 26.9, 25.1, 17.9, 17.8, 12.8; HRMS(FAB) *m/z* 483.2555 [(M+H)$^+$, calcd for $C_{28}H_{39}O_5Si$ 483.2567].

Epoxide 29

To a solution of quinone **28** (70 mg, 0.15 mmol) in acetone (1 mL) was added a 0.01 M solution of dioxirane in acetone (ca. 15 mL), and the mixture stirred for 10 min. The solvent was removed in vacuo. The residue was purified by flash chromatography (2:3 EtOAc/hexane) to afford epoxide **29** (72 mg, 100% yield) as a light yellow powder: mp 159–160 °C; $[\alpha]^{25}_D$ +63.8° (*c* 1.0, $CHCl_3$); IR ($CDCl_3$) 3599, 1667, 1642, 1618, 1459 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 12.00 (s, 1H, –OH), 7.68 (m, 2H, H_{arom}), 7.25 (m, 1H, H_{arom}), 3.85 (m, 2H, H_1 and H_{12b}), 3.60 (A of AB, J_{AB} = 19.0 Hz, 1H, H_6), 3.26 (s, 1H, H_5), 2.75 (B of AB, J_{AB} = 18.8 Hz, 1H), 2.42 (d, *J* = 12.0 Hz, 1H), 2.20 (d, *J* = 11.0 Hz, 1H), 2.05–1.85 (m, overlapping signals, 1H), 1.57 (m, 1H), 1.35 (s, 3H, $-CH_3$), 0.95–0.75 (m, 21H, –OTIPS); ^{13}C NMR (50 MHz, $CDCl_3$) δ 189.1, 182.2, 161.1, 145.9, 137.6, 136.1, 132.6, 123.6, 119.2, 114.6, 72.7, 69.5, 59.0, 56.2, 50.0, 46.9, 44.6, 27.9, 23.9, 17.9, 17.8, 12.9; HRMS(FAB) *m/z* 499.2527 [(M+H)$^+$, calcd for $C_{28}H_{39}O_6Si$ 499.2516].

Diacetate 30

A solution of epoxide **29** (75 mg, 0.15 mmol), acetic anhydride (0.21 mL, 2.23 mmol), pyridine (0.18 mL, 2.21 mmol), DMAP (ca. 10 mg) in dichloromethane (4 mL) was stirred overnight at room temperature. The reaction mixture was quenched with pH 7 buffer solution, extracted with $CHCl_3$ (3 × 50 mL) and the combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. Flash column chromatography (1:3 EtOAc/hexane) afforded 77 mg (88%) of **30** as a pale yellow amorphous solid: mp 63–64 °C; $[\alpha]^{25}_D$ +49.7° (c 0.6, $CHCl_3$); IR ($CDCl_3$) 1769, 1731, 1662, 1597 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 7.7, 1.3 Hz, 1H, H_{arom}), 7.69 (t, *J* = 8.1 Hz, 1H, H_{arom}), 7.31 (dd, *J* = 8.1, 1.3 Hz, 1H, H_{arom}), 3.80 (m, overlapping signals, 2H, H_1 and H_{12b}), 3.55 (A of AB, J_{AB} = 20.4 Hz, 1H), 3.26 (br s, 1H, H_5), 2.68 (B of AB superimiposed m, J_{AB} = 10.6 Hz, 2H), 2.44 (s superimposed m, 4H, –OAc), 2.02 (s superimposed m, 5H, –OAc), 1.61 (s, 3H, $-CH_3$), 0.93-0.75 (m, 21H, –OTIPS); ^{13}C NMR (50 MHz, $CDCl_3$) δ 182.5, 182.2, 170.1, 169.2, 149.2, 143.3, 138.7, 134.3, 134.1, 129.0, 124.9, 123.0, 79.1, 71.9, 58.4, 56.3, 46.4, 44.5, 43.7, 24.3, 23.9, 22.3, 21.1, 17.9, 17.8, 12.9; HRMS(FAB) *m/z* 583.2773 [(M+H)$^+$, calcd for $C_{32}H_{43}O_8Si$ 583.2727].

Allylic Alcohol 31

To a solution of **30** (140 mg, 0.24 mmol) in THF (15 mL) at 0 °C was added TBAF (1 M solution in THF, 0.12 mL, 0.12 mmol). After 5 min, the dark red solution was quenched with pH 7 buffer solution, extracted with EtOAc (3 × 50 mL), and the combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. Flash column chromatography (2:3 EtOAc/hexane) afforded 120 mg (86%) of **31** as a yellow amorphous solid: mp 73–75 °C; $[\alpha]^{25}_D$ –168.8° (*c* 0.5, $CHCl_3$); IR ($CDCl_3$) 3591, 1769, 1728, 1664, 1597 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (dd, *J* = 7.8, 1.1 Hz, 1H, H_{arom}), 7.73 (t, *J* = 7.8 Hz, 1H, H_{arom}), 7.34 (dd, *J* = 8.1, 1.0 Hz, 1H, H_{arom}), 6.94 (d, *J* = 9.6 Hz, 1H, H_5), 6.27 (dd, *J* = 9.6, 1.0 Hz, 1H, H_6), 3.72 (td, *J* = 10.5, 2.4 Hz, 1H, H_1), 3.51 (d, *J* = 9.7 Hz, 1H, H_{12b}), 2.65 (dd, *J* =13.1, 1.4 Hz, 1H), 2.45 (s, 3H, –OAc), 2.38 (m, 1H), 2.12 (d, *J* = 13.1 Hz, 1H), 2.02 (s superimposed m, 4H, –OAc), 1.57 (s, 3H, $-CH_3$), 0.94–0.70 (m, 21H, –OTIPS); ^{13}C NMR (50 MHz, $CDCl_3$) δ 182.7, 181.2, 170.2, 169.3, 149.4, 142.0, 139.8, 135.3, 134.5, 129.0, 124.8, 122.7, 120.1, 79.7, 70.8, 68.5, 47.7, 46.8, 45.7, 23.7, 22.4, 21.1, 17.8, 17.7, 12.9; HRMS(FAB) *m/z* 584.2813 [(M+2H)$^+$, calcd for $C_{32}H_{44}O_8Si$ 584.2806].

Carbinol 35

Quinone **31** (49 mg, 0.08 mmol) was dissolved in EtOAc (5 mL), and 5% palladium on carbon (ca. 2 mg) added. The flask was flushed three times with hydrogen and the mixture was stirred for 15 min under an atmosphere of hydrogen. Following filtration through a Celite pad, PtO_2 (ca. 3 mg) was added, the flask was again flushed three times with hydrogen, and the mixture stirred for 1.5 h under an atmosphere of hydrogen. The mixture was filtered through a Celite pad and CAN (86 mg, 0.16 mmol) was added. The light yellow solution was stirred for 20 min and quenched with saturated aqueous $NaHCO_3$ solution. The aqueous layer was extracted with EtOAc (3 × 50 mL), and the combined extracts washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. Flash column chromatography (2:3 EtOAc/hexane) furnished 36 mg (73%) of alcohol **35** as a light yellow powder: mp 75–77 °C; $[\alpha]^{25}_D$ +335° (*c* 0.2, $CHCl_3$); IR ($CDCl_3$) 1769, 1728, 1662, 1596 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 7.8, 1.2 Hz, 1H, H_{arom}), 7.70 (t, *J* = 8.0 Hz, 1H, H_{arom}), 7.33 (dd, *J* = 8.0, 1.2 Hz, 1H, H_{arom}), 4.90 (br s, 1H, –OH), 3.29 (br s, 1H, H_1), 2.80 (m, 1H, H_{12b}), 2.40 (s superimposed m, 5H), 2.00 (s, 3H, –OAc), 1.90 (m, 1H), 1.68 (m, 1H), 1.50 (s, 3H, –OAc), 1.6–1.4 (m, overlapping signals, 4H), 1.33–1.06 (m, 21H, –OTIPS); ^{13}C NMR (50 MHz, $CDCl_3$) δ 183.9, 182.9, 170.4, 169.5, 149.1, 146.5, 143.5, 134.8, 134.4, 129.0, 125.0, 123.0, 79.5, 70.8, 70.3, 47.8, 32.7, 27.3, 22.8, 22.7, 21.1, 16.1, 12.4, –1.27; HRMS(FAB) *m/z* 586.2962 [(M+2H)$^+$, calcd for $C_{32}H_{46}O_8Si$ 586.2962].

Diol 36

To a stirred solution of **35** (20 mg, 0.03 mmol) in acetonitrile (2 ml) at 0 °C was added HF–pyridine complex (ca. 1 mL). The mixture was stirred at room temperature for 30 min, diluted with EtOAc, neutralized with saturated aqueous

$NaHCO_3$, and extracted with EtOAc (3 × 50 mL). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. Flash column chromatography (4:1 EtOAc/hexane) furnished 13 mg (89%) of diol **36** as a yellow amorphous solid: mp 89–91 °C; $[\alpha]^{25}_D$ +60° (*c* 0.2, $CHCl_3$); IR ($CDCl_3$) 3594, 3505, 1769, 1729, 1662, 1595 cm^{-1} ^1H NMR (200 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 7.8, 1.3 Hz, 1H, H_{arom}), 7.70 (t, *J* = 8.1 Hz, 1H, H_{arom}), 7.33 (dd, *J* = 8.1, 1.3 Hz, 1H, H_{arom}), 3.65 (m, 1H, H_1), 3.08 (d, *J* = 8.6 Hz, 1H, H_{12b}), 2.85–2.65 (m, 3H), 2.44 (s, 3H, –OAc), 2.45–2.15 (m, overlapping signals, 4H), 2.00 (s, 3H, –OAc), 1.95-1.65 (m, 3H), 1.58 (s, 3H, $-CH_3$); ^{13}C NMR (50 MHz, $CDCl_3$) δ 186.2, 182.9, 170.4, 169.5, 149.3, 146.4, 141.9, 134.5, 134.0, 129.5, 125.3, 123.1, 80.1, 71.3, 69.7, 84.4, 45.5, 30.6, 26.3, 22.6, 21.7, 21.1; HRMS(FAB) *m/z* 430.1638 [(M+2H)$^+$, calcd for $C_{23}H_{26}O_8$ 430.1628].

Ketone 37

To a solution of **36** (10 mg, 0.02 mmol) in dichloromethane (2 mL) was added Dess–Martin periodinane (20 mg, 0.05 mmol), and the mixture was stirred for 10 min at room temperature. The mixture was quenched with pH 7 buffer solution and extracted with dichloromethane (3 × 10 mL). The combined extracts were washed with brine, dried over andhydrous Na_2SO_4, filtered and concentrated in vacuo. Flash column chromatography (7:3 EtOAc/hexane) afforded 9.3 mg (93%) of ketone **37** as a light yellow amorphous powder: mp 84–86 °C; $[\alpha]^{25}_D$ –94.3° (*c* 0.3, $CHCl_3$); IR ($CDCl_3$) 3590, 1764, 1723, 1665, 1596 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 7.7, 1.3 Hz, 1H, H_{arom}), 7.71 (t, *J* = 8.0 Hz, 1H, H_{arom}), 7.34 (dd, *J* = 8.1, 1.3 Hz, 1H, H_{arom}), 4.20 (br s, 1H, H_{12b}), 3.32 (dd, *J* = 16.7, 2.3 Hz, 1H), 2.83 (dd, *J* = 15.2, 2.6 Hz, 1H), 2.75–2.47 (m, 2H), 2.45 (s, 3H, –OAc), 2.23 (br s, 1H, –OH), 2.09 (s, 3H, –OAc), 2.10-1.84 (m, 2H), 1.62 (s, 3H, $-CH_3$), 1.60–1.40 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 204.8, 183.0, 182.7, 170.6, 169.5, 149.4, 146.4, 138.3, 134.6, 133.7, 129.5 125.1, 123.3, 81.9, 71.0, 54.5, 50.9, 47.5, 33.0, 26.1, 22.6, 21.1, 19.9; HRMS(FAB) *m/z* 367.1173 [(M-OAc)$^+$, calcd for $C_{21}H_{19}O_6$ 376.1181].

Acetate 38 and SF 2315A (2)

To a solution of **37** (4 mg, 0.01 mmol) in EtOH (1 mL) was added LiOH (0.1 M in water, 1 mL, 0.1 mmol) at 0 °C. After 1h, the dark red solution was quenched with pH 7 buffer solution, and extracted with EtOAc (3 × 10 mL). The combined extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. Flash chromatography (7:3 EtOAc/hexanes) afforded 1.0 mg (33%) of **2** as a light yellow solid and 1.0 mg (29%) of **38** as a light yellow solid.

Synthetic SF 2315A (**2**): R_f 0.27 (2:3 EtOAc/hexanes); $[\alpha]^{25}_D$ +112° (*c* 0.05, MeOH) [natural SF-2315A[28a] $[\alpha]^{25}_D$ +106° (*c* 0.05, MeOH)] [Lit[2b] $[\alpha]^{25}_D$ +229° (*c* 0.1, MeOH)]; ^1H NMR (400 MHz , $CDCl_3$) δ 12.10 (s, 1H, –OH), 7.68 (dd, *J* = 8.2, 1.2 Hz, 1H, H_{arom}), 7.59 (t, *J* = 8.2 Hz, 1H, H_{arom}), 7.23 (dd, *J* = 8.2, 1.2 Hz, 1H, H_{arom}), 5.89 (br s, 1H, H_2), 4.14 (br s, 1H, H_{12b}), 2.92 (br d, *J* = 18.1 Hz, 1H, H_4), 2.88–2.57 (m, overlapping signals, 2H, H_{5eq} and H_{6eq}), 2.52 (d, *J* = 18.2 Hz, 1H, H_4), 2.04 (s, 3H, $-CH_3$), 1.95 (m, 1H), 1.75 (m, 1H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 196.1, 189.1, 182.8, 161.0, 160.3, 143.4, 142.4, 136.6, 131.8, 123.8, 123.0, 118.7, 114.5, 68.9, 51.8, 45.7, 27.7, 23.8, 20.0; HRMS(FAB) *m/z* 325.1086 [(M+H)$^+$, calcd for $C_{19}H_{17}O_5$ 325.1076].

Epoxy Alcohols 39–41

To a solution of quinone **28** (280 mg, 0.58 mmol) in THF (150 mL) at –78 °C was added TBAF (1 M in THF, 0.58 mL, 0.58 mmol). A stream of oxygen was passed through the deep purple mixture which was allowed to warm to room temperature and quenched with saturated aqueous NH_4Cl. The mixture was extracted with EtOAc (3 × 100 mL). The combined extracts were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The products were separated by flash column chromatography (1:1 EtOAc/hexanes→1:3:6 hexanes/EtOAc/CH_2Cl_2) to afford 130 mg (44%) of **39**, 82 mg (28%) of **40** as light yellow amorphous solids and 5 mg (3%) of **41**.

The first to elute was **40**: TLC, R_f 0.53 (1:3:6 hexane/EtOAc/dichloromethane); mp 137–139 °C; $[\alpha]^{25}_D$ +90.8° (*c* 0.52, MeOH) ; IR ($CDCl_3$) 3595, 3423, 1705, 1641, 1449 cm^{-1}; ^1H NMR (200 MHz , $CDCl_3$) δ 12.80 (s, 1H, –OH), 7.77 (d superimposed m, *J* = 8.1 Hz, 2H, H_{arom} and H_6), 7.65 (app t, *J* = 8.0 Hz, 1H, H_{arom}), 7.27 (dd, *J* = 8.2, 1.3 Hz, 1H, H_{arom}), 4.49 (s, 1H, –OH), 3.65 (d, *J* = 4.5 Hz, 1H, H_5), 3.40–3.25 (m, 2H, H_1 and H_{12b}), 2.55 (d, *J* = 12.9 Hz, 1H), 2.20–1.82 (m, 3H), 1.28 (s, 3H, $-CH_3$), 0.88–0.60 (m, overlapping signals, 21H, –OTIPS); ^{13}C NMR (50 MHz, $CDCl_3$) δ 186.9, 186.5, 163.3, 139.6, 138.7, 136.9, 133.2, 123.9, 120.6, 117.0, 72.6, 70.6, 69.1, 63.5, 54.4, 49.7, 48.9, 46.2, 28.6, 17.9, 17.8, 13.5; HRMS (FAB) *m/z* 537.2303 [(M+Na)$^+$, calcd for $C_{28}H_{38}O_7SiNa$ 537.2284].

The second to elute was **39**: TLC, R_f 0.43 (1:3:6 hexane/EtOAc/dichloromethane); mp 62–64 °C; $[\alpha]^{25}_D$ –32.5° (c 0.28, MeOH) ; IR ($CDCl_3$) 3745, 1700, 1653, 1457 cm^{-1}; ^1H NMR (200 MHz , $CDCl_3$) δ 11.70 (s, 1H, –OH), 7.80–7.62 (m, 2H, H_{arom}), 7.29 (dd, *J* = 7.8, 1.8 Hz, 1H, H_{arom}), 6.96 (d, *J* = 9.9 Hz, 1H, H_5), 6.18 (dd, *J* = 9.9, 1.0 Hz, 1H, H_6), 3.64 (td, *J* = 6.5, 3.5 Hz, 1H, H_1), 3.35 (br d, *J* = 3.9 Hz, 1H, H_{12b}), 2.89 (s, 1H, –OH), 2.10–1.78 (m, overlapping signals, 4H), 1.23 (s, 3H, $-CH_3$), 0.95-0.60 (m, overlapping signals, 21H, –OTIPS); ^{13}C NMR (50 MHz, $CDCl_3$) δ 194.0, 182.7, 162.5, 141.4, 137.4, 131.5, 124.6, 120.2, 119.7, 113.7, 70.9, 69.7, 69.5, 69.0, 59.2, 51.2, 48.8, 45.8, 27.9, 17.9, 17.8, 13.4; HRMS (FAB) *m/z* 471.1828 [(M-C_3H_7)$^+$, calcd for $C_{25}H_{31}O_7Si$ 471.1839].

The third to elute was **41**: TLC, R_f 0.40 (1:3:6 hexane/EtOAc/dichloromethane); ^1H NMR (400 MHz , $CDCl_3$) δ11.8 (s, 1H, –OH), 7.75–7.60 (m, 2H, H_{arom}), 7.25 (dd, *J* = 7.7, 1.9 Hz, 1H, H_{arom}), 5.35 (br s, 1H, H_6), 4.66 (d, *J* = 2.2 Hz, 1H, –OH), 3.86 (d, *J* = 9.8 Hz, 1H, H_{12b}), 3.64 (td, *J* = 9.8, 3.7 Hz, 1H, H_1), 3.45 (br s, 1H, H_5), 2.33 (d, *J* = 13 Hz, 1H), 2.15 (br d *J* = 12 Hz, 1H), 1.93 (t, *J* = 12 Hz, 1H), 1.65 (dd, *J* = 13, 1 Hz, 1H), 1.35 (s, 3H, $-CH_3$), 1.0-0.8 (m, 21H, –OTIPS); LRMS (FAB) *m/z* 515 [(M+H)$^+$, calcd for $C_{28}H_{39}O_7Si$ 515].

Acetate 42

A solution of epoxy alcohol **41** (ca. 5 mg) and DMAP (ca. 1 mg) in dichloromethane (1 mL) and pyridine (0.01 mL) at

room temperature was treated with acetic anhydride (0.01 mL). After 6 h, the mixture was concentrated in vacuo. Flash chromatography, using 1:1 ethyl acetate/hexane as eluant, furnished 2 mg of **42**: ^{1}H NMR (400 MHz , $CDCl_3$) δ 8.01 (dd, J = 7.8, 1.3 Hz, 1H, H_{arom}), 7.70 (t, J = 7.8 Hz, 1H, H_{arom}), 7.43 (dd, J = 8.0, 1.3 Hz, 1H, H_{arom}), 6.43 (dd, J = 2.5, 1.0 Hz, 1H, H_6), 3.88 (br d, J = 9.7 Hz, 1H, H_{12b}), 3.61 (td, J = 11.3, 3.7 Hz, 1H, H_1), 3.40 (dd, J = 2.4, 0.8 Hz, 1H, H_5), 2.55 (m, 1H), 2.48 (d, J = 12 Hz, 1H), 2.38 (s, 3H, –OAc), 2.15 (s, 3H, –OAc), 2.02–2.09 (m, overlapping signals, 2H), 2.02 (s, 3H, –OAc), 1.60 (s, 3H, $-CH_3$), 0.81–0.91 (m, 21H, –OTIPS); ^{13}C NMR (125 MHz, $CDCl_3$) δ 181.6, 181.4, 170.2, 170.0, 168.9, 149.2, 145.1, 137.7, 134.4, 133.7, 129.4, 124.9, 123.5, 78.7, 74.1, 65.4, 58.3, 57.0, 46.1, 44.3, 43.1, 24.1, 22.3, 21.1, 20.7, 17.8, 17.7, 12.9; HRMS (FAB) *m/z* 671.2791 [(M+H)$^+$, calcd for $C_{34}H_{45}O_{10}Si$ 671.2782].

Acetate 43

A solution of epoxy alcohol **39** (22 mg, 0.04 mmol) and DMAP (ca. 2 mg) in dichloromethane (4 mL) and pyridine (0.01 mL) at room temperature was treated with acetic anhydride (0.01 mL, 0.11 mmol). After 20 min, the mixture was concentrated in vacuo. Flash chromatography (1:1 EtOAc/hexane) furnished 22 mg (92%) of **43** as a white amorphous solid: mp 73–75 °C; $[\alpha]^{25}_D$ –60° (c 0.16, MeOH); IR ($CDCl_3$) 3156, 1789, 1692, 1464 cm^{-1}; ^{1}H NMR (200 MHz , $CDCl_3$) δ 8.11 (dd, J = 7.8, 1.3 Hz, 1H, H_{arom}), 7.76 (t, J = 8.0 Hz, 1H, H_{arom}), 7.40 (dd, J = 8.0, 1.3 Hz, 1H, H_{arom}), 6.92 (d, J = 9.2 Hz, 1H, H_5), 6.13 (br d, J = 9.9 Hz, 1H, H_6), 3.63 (td, J = 10.1, 3.5 Hz, 1H, H_1), 3.31 (br d, J = 9.2 Hz, 1H, H_{12b}), 2.39 (s, 3H. –OAc), 2.10–1.75 (m, overlapping signals, 4H), 1.21 (s, 3H, $-CH_3$), 1.00–0.60 (m, overlapping signals, 21H, –OTIPS); ^{13}C NMR (50 MHz, $CDCl_3$) δ 187.2, 183.2, 169.1, 150.2, 140.8, 135.1, 133.2, 126.0, 122.9, 120.1, 70.8, 69.6, 69.3, 69.0, 59.7, 51.2, 48.8, 45.7, 27.9, 20.9, 17.9, 17.8, 13.3 ; HRMS (FAB) *m/z* 557.2594 [(M+H)$^+$, calcd for $C_{30}H_{41}O_8Si$ 557.2571].

Quinone Oxide 44

Acetate **43** (66 mg, 0.12 mmol) was dissolved in 6 mL of EtOAc/hexanes (1:5) and PtO_2 (ca. 2 mg) was added. The flask was flushed three times with hydrogen, and the mixture was stirred for 1 h at room temperature under an atmosphere of hydrogen. The mixture was diluted with EtOAc (10 mL), filtered through a Celite pad, and concentrated in vacuo. Flash column chromatography of the residue (1:1 EtOAc/hexane) afforded 55 mg (83%) of epoxy alcohol **44** as a white amorphous solid: mp 137–138 °C; $[\alpha]^{25}_D$ +69.6° (c 0.27, MeOH) ; IR ($CDCl_3$) 3526, 1755, 1682, 1453 cm^{-1}; ^{1}H NMR (400 MHz , $CDCl_3$) δ 7.89 (dd, J = 7.9, 1.2 Hz, 1H, H_{arom}), 7.71 (t, J = 8.0 Hz, 1H, H_{arom}), 7.37 (dd, J = 8.1, 1.2 Hz, 1H, H_{arom}), 6.28 (q, J = 2.9 Hz, 1H, H_1), 5.22 (s, 1H, –OH), 3.81 (s, 1H, –OH), 2.74 (br s, 1H, H_{12b}), 2.39 (s, 3H, –OAc), 2.50–2.35 (m, 2H), 2.19 (br d, J = 15.8 Hz, 1H), 1.76 (dt, J = 14.5, 1.8 Hz, 1H), 1.70–1.60 (m, 1H), 1.46 (dd, J = 15.1, 2.7 Hz, 1H), 1.30–1.22 (m, 2H), 1.21 (s, 3H, $-CH_3$), 1.19-1.13 (m, 21H, -OTIPS); ^{13}C NMR (50 MHz, $CDCl_3$) δ 190.8, 169.6, 148.8, 134.9, 134.8, 129.7, 126.0, 122.6, 70.1, 69.9, 65.7, 63.7, 48.7, 43.3, 41.1, 31.9, 31.6, 20.8, 19.6, 18.1, 12.0; HRMS (FAB) *m/z* 559.2730 [(M+H)$^+$, calcd for $C_{30}H_{43}O_8Si$ 559.2727].

Triol 45

To a stirred solution of **44** (24 mg, 0.04 mmol) in acetonitrile (3 mL) at 0 °C was added HF–pyridine complex (ca. 0.1 mL). The mixture was stirred at room temperature for 2 h, diluted with EtOAc (3 mL), quenched with pH 7 buffer solution, and extracted with chloroform (3 × 5 mL). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. Flash column chromatography (EtOAc) furnished 17 mg (98%) of triol **45**: $[\alpha]^{25}_D$ +32° (*c* 0.1, MeOH) ; IR ($CDCl_3$) 3854, 3688, 1734, 1700, 1684 cm^{-1}; ^{1}H NMR (400 MHz , $CDCl_3$) δ 7.89 (dd, J = 7.8, 1.2 Hz, 1H, H_{arom}), 7.73 (t, J = 7.9 Hz, 1H, H_{arom}), 7.39 (dd, J = 8.1, 1.2 Hz, 1H, H_{arom}), 4.45 (m, 1H, H_1), 3.45 (br s, 1H, –OH), 2.92 (d, J = 6.0 Hz, 1H, H_{12b}), 2.82 (br s, 1H, –OH), 2.48 (m, 2H), 2.38, (s, 3H, –OAc), 2.05 (m, 1H), 1.85 (m, 1H), 1.80–1.70 (m, overlapping signals, 4H), 1.28 (s, 3H, $-CH_3$); ^{13}C NMR (50 MHz, $CDCl_3$) δ 191.0, 190.2, 169.5, 149.1, 135.0, 134.2, 130.0, 125.9, 122.9, 71.0, 70.4, 68.0, 65.2, 64.8, 47.8, 47.3, 44.1, 31.6, 31.0, 20.9, 18.6; HRMS (FAB) *m/z* 425.1215 [(M+Na)$^+$, calcd for $C_{21}H_{22}O_8Na$ 425.1212].

Triacetate 47

To a solution of tetramethylammonium triacetoxyborohydride (26 mg, 0.10 mmol) in anhydrous acetonitrile (1.0 mL) and acetic acid (0.15 mL) at –10 °C was added a solution of triol **45** (10 mg, 0.02 mmol) in 1:1 CH_3CN/THF (1 mL) via cannula. The reaction mixture was stirred at –10 °C overnight and concentrated in vacuo. The residue was peracetylated without purification.

A solution of crude alcohol **46** and DMAP (ca. 2 mg) in dichloromethane (2 mL) and pyridine (0.4 mL) at room temperature was treated with Ac_2O (0.4 mL). After 3 h the mixture was concentrated in vacuo. Flash chromatography (EtOAc) furnished 5 mg (41%) of **47** as a white amorphous solid: mp 176–178 °C; $[\alpha]^{25}_D$ +36.9° (*c* 0.26, MeOH) ; IR ($CDCl_3$) 3654, 3154, 1738, 1466, 1371 cm^{-1}; ^{1}H NMR (400 MHz , $CDCl_3$) δ 7.58 (t, J = 8.1 Hz, 1H, H_{arom}), 7.11 (br d, J = 8.2 Hz, 2H, H_{arom}), 6.27 (s, 1H, H_{12}), 5.39 (br s, 1H, H_1), 3.36 (br s, 1H, –OH), 2.62 (br d, J = 1.5 Hz, 1H, H_{12b}), 2.41 (s, 3H, –OAc), 2.38 (s, 3H, –OAc), 2.40–2.34 (m, 2H), 2.19–2.11 (m, overlapping signals, 2H), 2.08 (s, 3H, –OAc), 1.83 (td, J = 13 , 6.2 Hz, 1H), 1.68 (d, J = 13.8 Hz, 1H), 1.60–1.49 (m, 3H), 1.31 (s, 3H, $-CH_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.8, 172.5, 170.0, 169.3, 149.7, 139.9, 134.8, 125.2, 124.6, 121.0, 71.5, 70.0, 68.3, 67.8, 63.3, 62.5, 46.2, 39.6, 39.3, 31.0, 29.2, 21.8, 21.1, 20.9, 19.8; LRMS (FAB) *m/z* 488 [(M)$^+$, calcd for $C_{25}H_{28}O_{10}$ 488].

Naphthylglycoside 50

A solution of naphthol **48** (658 mg, 2.63 mmol) and methyl acetal **49** (450 mg, 1.32 mmol) in dichloromethane (14 mL) was cooled to 0 °C, and BF_3•OEt_2 (324 mL, 2.63 mmol) added. The mixture was maintained at 0 °C for 15 min, warmed to room temperature and quenched with saturated aqueous $NaHCO_3$ (10 mL) after 1 h. The aqueous layer was separated and extracted with dichloromethane (3 × 20 mL). The combined organic extracts were washed with brine, dried over

anhydrous $MgSO_4$, filtered and concentrated in vacuo. Flash column chromatography of the residue (10:1 hexane/EtOAc) furnished 663 mg (90%) of naphthylglycoside **50** as a white amorphous solid: mp 98–105 °C; $[\alpha]^D_{20}$ +6.9° (*c* 0.8, $CHCl_3$); IR ($CHCl_3$) 3359, 3056, 2982 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.73 (s, 1H, –OH), 7.84 (dd, *J* = 15.3, 8.6 Hz, 2H, H_{arom}), 7.50 (d, *J* = 3.6 Hz, 1H, H_{arom}), 7.45–7.20 (m, 15H, H_{arom}), 6.95 (d, *J* = 8.6 Hz, 1H, H_{arom}), 6.86 (d, *J* = 7.6 Hz, 1H, H_{arom}), 5.19 (s, 2H, CH_2Ph), 5.00 (d, *J* = 10.8 Hz, 1H, CH_2Ph), 4.75 (dd, *J* = 11.6, 1.4 Hz, 1H, $H_{1'}$), 4.70 (d, *J* = 11.0 Hz, 2H, CH_2Ph), 4.60 (d, *J* = 11.6 Hz, 1H, CH_2Ph), 3.77 (m, 1H, $H_{3'}$), 3.59 (m, 1H, $H_{5'}$), 3.27 (app t, *J* = 8.9 Hz, 1H, $H_{4'}$), 2.43 (ddd, *J* = 13.6, 4.8, 2.1 Hz, 1H, $_{2'eq}$), 1.97 (app q, *J* = 12.6 Hz, 1H, $H_{2'ax}$), 1.43 (d, *J* = 6.1 Hz, 3H, $-CH_3$); ^{13}C NMR (50 MHz, $CDCl_3$) δ 154.2, 150.7, 138.3, 137.2, 128.5, 128.4, 128.1, 127.9, 127.8, 127.6, 127.3, 126.6, 126.3, 125.2, 123.5, 118.1, 114.7, 113.7, 105.8, 83.4, 80.3, 79.3, 75.5, 71.4, 70.1, 37.7, 18.6; HRMS (EI) *m/z* 560.2583 $[(M)^+$, calcd for $C_{37}H_{36}O_5$ 560.2563.

1-O-Benzyl-5-O-acetyl-naphthylglycoside 51

To a solution of *C*-naphthylglycoside **50** (3.0 g, 5.3 mmol) in pyridine (40 mL) was added a catalytic amount of DMAP (ca. 10 mg) and Ac_2O (30 mL). The mixture was stirred for 13 h, concentrated in vacuo and the residue dissolved in methylene chloride (400 mL). This solution was washed with 20% aqueous $CuSO_4$ solution (2 × 75 mL), brine (30 mL), dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. Flash chromatography of the residue (5:1 hexane/EtOAc) afforded 3.2 g (100%) of **51** as a white amorphous solid: mp 39–43 °C; $[\alpha]^D_{20}$ +114.9°; (*c* 5.2, $CHCl_3$); IR ($CHCl_3$) 3032, 3010, 1764 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.8 Hz, 1H, H_{arom}), 7.65–7.25 (m, 18H, H_{arom}), 6.86 (d, *J* = 7.3 Hz, 1H, H_{arom}), 5.22 (s, 2H, CH_2Ph), 5.02 (d, *J* = 10.9 Hz, 1H, CH_2Ph), 4.72 (d, *J* = 10.9 Hz, 1H, CH_2Ph), 4.70 (d, *J* = 11.6 Hz, 1H, CH_2Ph), 4.62 (d, *J* = 11.4 Hz, 1H, CH_2Ph), 4.59 (d, *J* = 10.6 Hz, 1H, $H_{1'}$), 3.76 (m, 1H, $H_{3'}$), 3.52 (dq, *J* = 9.2, 6.1 Hz, 1H, $H_{5'}$), 3.25 (t, *J* = 8.8 Hz, 1H, $H_{4'}$), 2.41 (s superimposed m, 4H, –OAc and $H_{2'eq}$), 1.84 (app q, *J* = 12.2 Hz, 1H, $H_{2'ax}$), 1.37 (d, *J* = 6.1 Hz, 3H, $-CH_3$); ^{13}C NMR (50 MHz, $CDCl_3$) δ 169.2, 154.5, 142.9, 138.6, 138.3, 136.9, 130.3, 128.6, 128.4, 128.3, 128.1, 128.0, 127.9, 127.7, 127.6, 127.6, 127.2, 126.9, 126.4, 123.2, 121.0, 113.7, 105.8, 83.9, 80.7, 75.9, 75.3, 72.6, 71.1, 70.1, 37.5, 20.6, 18.6; HRMS (FAB) *m/e* 602.2710 $[(M)^+$, calcd for $C_{39}H_{38}O_6$: 602.2668].

5-O-Acetyl-naphthylglycoside 52

1-*O*-Benzyl-5-*O*-acetylnaphthylglycoside **51** (1.6 g, 2.6 mmol) and a catalytic amount of 5% palladium on carbon (ca. 5 mg) in absolute ethanol (40 mL) were evacuated under hydrogen (4×). The reaction was stirred for 14 h under a hydrogen atmosphere, filtered through silica gel, and washed with EtOAc (ca. 300 mL). The filtrate was concentrated in vacuo and purified by flash chromatography (1:3 hexane/EtOAc) to afford 855 mg (99%) of 5-*O*-acetyl-naphthylglycoside **52** as a white amorphous solid: mp 76–81 °C; $[\alpha]^D_{20}$ +45.9° (*c* 5.7, acetone); IR (KBr) 3396, 2978, 2931, 2889, 1763, 1741 cm^{-1}; ^1H NMR (200 MHz, acetone-d_6) δ 8.95 (br s, 1H, –OH), 8.09 (d, *J* = 8.6 Hz, 1H, H_{arom}), 7.55 (d, *J* = 8.7 Hz, 1H, H_{arom}), 7.17 (m, 1H, H_{arom}) 6.82 (m, 1H, H_{arom}), 4.65 (dd, *J* = 11.4, 1.0 Hz, 1H, $H_{1'}$), 4.41 (br s, 2H, both –OH), 3.61 (m, 1H, $H_{3'}$), 3.38 (dq, *J* = 9.0, 6.1 Hz, 1H, $H_{5'}$), 2.98 (t, *J* = 8.7 Hz, 1H, $H_{4'}$), 2.28 (s, 3H, –OAc), 2.00 (m, 1H, $H_{2'eq}$), 1.63 (m, 1H, $H_{2'ax}$), 1.27 (d, *J* = 6.0 Hz, 3H, $-CH_3$); ^{13}C NMR (50 MHz, acetone-d_6) δ 169.7, 154.0, 143.6, 131.8, 129.2, 127.8, 126.0, 123.5, 121.1, 113.4, 109.3, 78.6, 76.9, 73.5, 73.1, 41.3, 20.6, 18.6; HRMS (FAB) *m/e* 332.1281 $[(M)^+$, calcd for $C_{18}H_{20}O_6$: 332.1260].

Bromoquinone 10b

To a solution of N-bromosuccinimide (670 mg, 3.8 mmol) in water (7.6 mL) and acetic acid (10 mL) was added a solution of 5-*O*-acetyl-naphthylglycoside **52** (315 mg, 1.0 mmol) in warm acetic acid (17 mL). The orange mixture was stirred at 70 °C for 4 h, quenched with water (20 mL), saturated with NaCl and extracted with EtOAc (4 × 50 mL). The combined extracts were washed with water (2 × 75 mL), cold saturated aqueous $NaHCO_3$ solution (4 × 35 mL), brine (30 mL), dried over andhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash chromatography (1:2 hexane/EtOAc) to afford 377 mg (94%) of bromoquinone **10b** as a light orange amorphous solid: mp 117–121 °C; $[\alpha]^D_{20}$ +54.8° (*c* 3.4, $CHCl_3$); IR ($CHCl_3$) 3609, 3028, 1773, 1682, 1662, 1596 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.2 Hz, 1H, H_{arom}), 7.96 (d, *J* = 8.2 Hz, 1H, H_{arom}), 7.36 (s, 1H), 4.65 (br d, *J* = 9.4 Hz, 1H, $H_{1'}$), 3.75 (m, 1H, $H_{3'}$), 3.62 (br s, 2H, both –OH), 3.45 (dq, *J* = 9.0, 6.1 Hz, 1H, $H_{5'}$), 3.16 (t, *J* = 8.7 Hz, 1H, $H_{4'}$), 2.46 (s superimposed m, 4H), 2.25 (m, 1H, $H_{2'ax}$), 1.37 (d, *J* = 6.0 Hz, 3H, $-CH_3$); ^{13}C NMR (50 MHz, Acetone-d_6) δ 180.7, 176.9, 168.4, 145.9, 142.7, 141.1, 138.0, 132.3, 131.0, 125.8, 122.2, 77.2, 75.9, 72.4, 71.4, 39.5, 20.6, 17.7; HRMS (FAB) *m/e* 409.0289, 411.0258 $[(M+H)^+$, calcd for $C_{18}H_{18}O_7Br$: 409.0287, 411.0267].

Triacetate 53

To a solution of bromoquinone **10b** (440 mg, 1.0 mmol) in EtOAc (20 mL) and acetic anhydride (2 mL) was added a catalytic amount of $HClO_4$ (1 drop), and the solution stirred for 20 min. Following cooling to 0 °C, the solution was quenched with cold saturated aqueous $NaHCO_3$ solution (5 mL), and extracted with EtOAc (3 × 75 mL). The combined extracts were washed with brine (20 mL), dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash chromatography (3:1 hexane/EtOAc) to afford 484 mg (92%) of the triacetyl bromoquinone **53** as a yellow amorphous solid: mp 192–194 °C; $[\alpha]^D_{20}$ +24.3° (*c* 3.7, $CHCl_3$); IR ($CHCl_3$) 3029, 1777, 1744, 1682, 1652 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.1 Hz, 1H, H_{arom}), 7.97 (d, *J* = 8.2 Hz, 1H, H_{arom}), 7.36 (s, 1H), 5.12 (td, *J* = 10.6, 5.4 Hz, 1H, $H_{3'}$), 4.85 (t, *J* = 9.5 Hz, 1H, $H_{4'}$), 4.72 (br d, *J* = 10.4 Hz, 1H, $H_{1'}$), 3.66 (dq, *J* = 9.6, 6.5 Hz, 1H, $H_{5'}$), 2.49 (s, 3H, –OAc), 2.09 (s, 3H, –OAc), 2.02 (s superimposed m, 4H, –OAc and $H_{2'eq}$), 1.63 (m, 1H, $H_{2'ax}$), 1.28 (d, *J* = 6.2 Hz, 3H, $-CH_3$); ^{13}C NMR (50 MHz, $CDCl_3$) δ 180.8, 177.1, 170.3, 170.0, 168.8, 142.0, 141.7, 141.4, 138.4, 132.3, 131.5, 126.2, 122.5, 74.5, 73.9, 71.7, 71.5, 37.1, 20.9, 20.9, 20.7, 17.8; HRMS (FAB) *m/e* 509.0413, 511.0445 $[(M+H)^+$, calcd for

$C_{22}H_{22}O_9Br$: 509.0448, 511.0428].

Diels–Alder Adduct 54

A solution of bromoquinone **53** (264 mg, 0.5 mmol) and diene **25a** (230 mg, 0.9 mmol) in benzene (3 mL) was heated at reflux for 12 h. Upon cooling, the mixture was concentrated in vacuo and purified by flash chromatography (gradient elution: 6:1 to 4:1 to 2:1 hexane/EtOAc) to afford 34 mg (13%) of recovered bromoquinone **53** and 282 mg (72%) of adduct **54** as an off-white amorphous solid: mp 124–126 °C; $[\alpha]^D_{20}$ +40.4° (*c* 1.3, acetone); IR ($CHCl_3$) 3029, 1745, 1706 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.2 Hz, 1H, H_{arom}), 7.93 (d, *J* = 8.2 Hz, 1H, H_{arom}), 7.35-7.22 (m, 5H, H_{arom}), 5.65 (br s, 1H, H_5), 5.09 (m, 1H, $H_{3'}$), 4.85 (t, *J* = 9.5 Hz, 1H, $H_{4'}$), 4.75 (m, 1H, $H_{1'}$), 4.44 (s, 2H, CH_2Ph), 3.65 (dq, *J* = 9.5, 6.2 Hz, 1H, $H_{5'}$), 3.58 (m, 1H, H_1), 2.99 (d, *J* = 9.0 Hz, 1H, H_{12b}), 2.85 (m, 1H, H_6), 2.54 (d, *J* = 16.0 Hz, 1H, H_6), 2.43 (s, 3H, –OAc), 2.38 (m, 2H), 2.08 (s superimposed m, 4H, –OAc, $H_{2'eq}$), 2.01 (s, 3H, –OAc), 1.69 (m, 2H, H_{6a} and $H_{2'ax}$), 1.28 (d, *J* = 6.1 Hz, 3H, $-CH_3$), 1.15 (s, 3H, $-CH_3$); ^{13}C NMR (50 MHz, $CDCl_3$) δ 170.4, 170.1, 140.1, 139.0, 128.3, 127.3, 127.3, 126.5, 121.3, 74.8, 74.6, 74.0, 71.9, 71.7, 63.6, 58.5, 58.5, 46.6, 46.5, 46.5, 46.4, 37.1, 22.1, 20.9, 20.8, 17.9; HRMS (FAB) *m/e* 735.1804, 737.1833 $[(M+H-H_2O)^+$, calcd for $C_{38}H_{40}O_{10}Br$: 735.1805, 737.1785].

Anthraquinone 55

Dess–Martin periodinane (21 mg, 0.05 mmol) was added to a solution of adduct **54** in methylene chloride (1 mL), and the mixture stirred for 2 h. The light yellow mixture was concentrated in vacuo and directly purified by flash chromatography (gradient elution: 3:1 to 2:1 to 1:1 hexane/EtOAc) to afford 22 mg (88%) of ketone **55** as an orange amorphous solid: mp 125 °C (Dec); $[\alpha]^D_{20}$ –56.1° (*c* 1.6, $CHCl_3$); IR ($CHCl_3$) 3028, 1773, 1682, 1662, 1596 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 8.1 Hz, 1H, H_{arom}), 8.18 (d, *J* = 8.0 Hz, 1H, H_{arom}), 8.11 (d, *J* = 8.1 Hz, 1H, H_{arom}), 7.99 (d, *J* = 8.1 Hz, 1H, H_{arom}), 7.25–7.12 (m, 5H, H_{arom}), 5.14 (m, 1H, $H_{3'}$), 4.86 (t, *J* = 9.5 Hz, 1H, $H_{4'}$), 4.76 (m, 1H, $H_{1'}$), 4.53 (A of AB, J_{AB} = 11.8 Hz, 1H), 4.39 (B of AB, J_{AB} = 11.8 Hz, 1H), 3.67 (dq, *J* = 9.6, 6.3 Hz, 1H, $H_{5'}$), 3.32 (d, *J* = 16.2 Hz, 1H), 3.28 (d, *J* = 15.6 Hz, 1H), 3.13 (d, *J* = 17.1 Hz, 1H), 3.05 (d, *J* = 14.9 Hz, 1H), 2.53 (s, 3H, –OAc), 2.16 (dd, *J* = 7.6, 6.5 Hz, 1H, $H_{2'eq}$), 2.09 (s, 3H, –OAc), 2.03 (s, 3H, –OAc), 1.56 (m, 1H, $H_{2'eq}$), 1.29 (d, *J* = 6.2 Hz, 3H, $-CH_3$), 1.25 (s, 3H, $-CH_3$); ^{13}C NMR (50 MHz, $CDCl_3$) δ 196.4, 170.5, 170.2, 147.0, 145.0, 140.4, 138.1, 136.3, 135.1, 134.2, 133.6, 132.7, 129.8, 128.3, 127.4, 125.6, 74.6, 74.2, 71.9, 71.7, 64.3, 64.1, 50.6, 42.3, 37.3, 24.7, 21.2, 21.0, 20.8, 17.9; HRMS (FAB) *m/e* 669.2327 $[(M+H)^+$, calcd for $C_{38}H_{37}O_{11}$: 669.2336].

Phenol 56

To a mixture of ketone **55** (6 mg, 0.01 mmol) in THF (250 mL) at 0 °C was added a solution of lithium hydroxide (0.1 M in water, 270 mL, 0.03 mmol), and the purple-colored mixture stirred for 40 min at room temperature. The reaction was quenched with saturated aqueous NH_4Cl (1 mL) and extracted with EtOAc (4 × 10 mL). The combined extracts were washed with brine (2 mL), dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash chromatography (gradient elution: 2:1 to 1:1 hexane/EtOAc) to afford 4.5 mg (80%) of ketone phenol **56** as a yellow-orange amorphous solid: ^1H NMR (400 MHz, $CDCl_3$) δ 12.2 (s, 1H, –OH), 8.26 (d, *J* = 8.0 Hz, 1H, H_{arom}), 7.89 (d, *J* = 7.9 Hz, 1H, H_{arom}), 7.70 (d, *J* = 7.8 Hz, 1H, H_{arom}), 7.49 (d, *J* = 8.1 Hz, 1H), H_{arom}, 7.24-7.1 (m, 5H, H_{arom}), 5.21 (m, 1H, $H_{3'}$), 4.97 (dd, *J* = 11.4, 1.6 Hz, 1H, $H_{1'}$), 4.86 (t, *J* = 9.4 Hz, 1H, $H_{4'}$), 4.53 (A of AB, J_{AB} = 11.0 Hz, 1H), 4.39 (B of AB, J_{AB} = 11.0 Hz, 1H), 3.71 (dq, *J* = 9.6, 6.1 Hz, 1H, $H_{5'}$), 3.38 (dd, *J* = 17.1, 1.6 Hz, 1H), 3.30 (dd, *J* = 14.9, 1.8 Hz, 1H), 3.13 (d, *J* = 17.1 Hz, 1H), 3.06 (d, *J* = 15.0 Hz, 1H), 2.63 (ddd, *J* = 12.7, 5.2, 2.0 Hz, 1H, $H_{2'eq}$), 2.09 (s, 3H, –OAc), 2.02 (s, 3H, -OAc), 1.60 (m, 1H, $H_{2'ax}$), 1.31 (d, *J* = 6.1 Hz, 3H, $-CH_3$), 1.25 (s, 3H, $-CH_3$); LRMS (FAB) *m/e* 627 $[(M+H)^+$, calcd for $C_{36}H_{35}O_{10}$: 627].

Diacetate 57

A solution of phenol **56** (13.5 mg, 0.02 mmol) dissolved in EtOAc (0.6 mL) was added by cannula to a suspension of a catalytic amount of 5% $Pd(OH)_2$ (ca. 5 mg) in methanol (0.5 mL) under a hydrogen atmosphere and maintained for 40 min at 0 °C. The black suspension was filtered through silica gel and washed with methanol (30 mL). The filtrate was concentrated in vacuo and purified by flash chromatography (20:1 $CHCl_3$:MeOH) to afford 12 mg (100%) of diol **57** as a yellow amorphous solid: ^1H NMR (400 MHz, $CDCl_3$) δ 12.62 (s, 1H, –OH), 8.29 (d, *J* = 8.0 Hz, 1H, H_{arom}), 7.88 (d, *J* = 7.8 Hz, 1H, H_{arom}), 7.68 (d, *J* = 7.7 Hz, 1H, H_{arom}), 7.54 (d, *J* = 8.0 Hz, 1H, H_{arom}), 5.20 (m, 1H, $H_{3'}$), 4.97 (dd, *J* = 11.4, 1.6 Hz, 1H, $H_{1'}$), 4.86 (t, *J* = 9.5 Hz, 1H, $H_{4'}$), 3.71 (dq, *J* = 9.6, 6.2 Hz, 1H, $H_{5'}$), 3.16 (s, 2H), 3.11 (d, *J* = 14.9 Hz, 1H), 3.01 (d, *J* = 15.0 Hz, 1H), 2.62 (ddd, *J* = 12.7, 5.3, 2.0 Hz, 1H, $H_{2'eq}$), 2.09 (s, 3H, –OAc), 2.02 (s, 3H, –OAc), 1.78 (m, 1H, $H_{2'ax}$), 1.31 (d, *J* = 6.1 Hz, 3H, $-CH_3$) 1.25 (s, 3H, $-CH_3$); LRMS (FAB) *m/e* 537 $[(M+H)^+$, calcd for $C_{29}H_{29}O_{10}$: 537].

Urdamycinone B (4)

To a mixture of alcohol **56** (11 mg, 0.02 mmol) in THF (500 mL) at 0 °C was added a solution of lithium hydroxide (0.1M in water, 210 mL, 0.02 mmol) and the purple-colored mixture stirred for 30 min at 0 °C, then at room temperature for 3.5 h. Additional lithium hydroxide was added at 10 min (210 mL, 0.02 mmol), 30 min (210 mL, 0.02 mmol), and 3 h (100 mL, 0.01 mmol). The purple mixture was quenched with a saturated aqueous NH_4Cl solution (2 mL), saturated with NaCl, and extracted with EtOAc (4 × 15 mL). The combined extracts were washed with brine (4 mL), dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash chromatography (gradient elution: 20:1 to 15:1 to 10:1 $CHCl_3$/methanol) to afford 2 mg (22%) of 1,8-diphenol **58** and 6 mg (67%) of urdamycinone B (**4**) as an orange amorphous solid mp 93–97 °C (Dec); $[\alpha]^D_{20}$ +52.0° (*c* 0.01, MeOH); CD $\lambda_{extreme}$ (MeOH) ($[\theta]_D \times 10^{-7}$): 273 (–2.51) nm [Lit[28] CD $\lambda_{extreme}$ (MeOH) ($[\theta]_D$): 495 (–2,000), 410 (+3,000), 325 (+2,000), 264 (–23,000) nm]; UV (MeOH) λ_{max} (log e): 269 (4.407), 406 (3.676) nm; IR (KBr) 3389, 1707, 1668, 1631, 1606 cm^{-1}; ^1H NMR (400 MHz, Acetone-d_6) δ 12.74 (s, 1H, –OH), 8.30 (d, *J* = 8.0 Hz, 1H, H_{arom}), 7.93 (dd, *J*

= 7.8, 0.7 Hz, 1H, H_{arom}), 7.73 (d, J = 8.1 Hz, 1H, H_{arom}), 7.60 (d, J = 7.9 Hz, 1H, H_{arom}), 4.90 (dd, J = 11.3, 1.7 Hz, 1H, $H_{1'}$), 4.16 (br s, 2H, both –OH), 3.74 (m, 1H, $H_{3'}$), 3.48 (dq, J = 9.1, 6.1 Hz, 1H, $H_{5'}$), 3.31 (d, J = 16.8 Hz, 1H), 3.21 (dd, J = 17.0, 1.6 Hz, 1H), 3.08 (m, overlapping signals, 2H), 2.89 (dd, J = 14.5, 1.7 Hz, 1H), 2.43 (ddd, J = 12.8, 4.8, 2.0 Hz, 1H, $H_{2'eq}$), 1.41 (m, 1H, $H_{2'ax}$), 1.48 (s, 3H, $-CH_3$), 1.36 (d, J = 6.2 Hz, 3H, $-CH_3$); ^{13}C NMR (50 MHz, acetone-d_6) δ 196.8, 189.0, 183.4, 158.8, 150.1, 138.0, 137.1, 135.1, 134.8, 134.3, 134.1, 129.4, 119.3, 115.8, 78.7, 77.2, 73.4, 72.6, 71.9, 54.1, 44.7, 40.9, 30.1, 18.7; HRMS (FAB) *m/e* 453.1513 [(M+H)$^+$, calcd for $C_{25}H_{24}O_8$: 453.1549].

Quinone 59

To a solution of adduct **54** (50 mg, 0.07 mmol) in acetone (150 mL), water (130 mL), and *t*-butyl alcohol (65 mL) at 0 °C was added a catalytic amount of OsO_4 (ca. 2 mg) and NMO (10 mg, 0.09 mmol), the mixture was stirred for 18 h and allowed to slowly warm to room temperature. The resulting yellow mixture was quenched with solid sodium hydrosulfite (ca. 100 mg) and stirred for 15 min. The resulting black mixture was diluted with water (5 mL) and EtOAc (5 mL) and saturated with NaCl. Next, the mixture was extracted with EtOAc (3 × 25 mL), and the combined organic extracts were washed with brine (10 mL), dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The crude diol was dissolved in acetone (2 mL), and a catalytic amount of *p*-TSA (ca. 5 mg) was added. The reaction was stirred for 5 h, then concentrated in vacuo. The residue was purified by flash chromatography (1:1 hexane/EtOAc) to afford a mixture of quinone **59** and the corresponding bromide. The bromide was dissolved in EtOAc (2 mL) and stirred in the presence of silica gel (ca. 700 mg) until the conversion of the bromide to quinone **59** was judged complete by TLC. The crude acetonide was filtered, the insolubles washed with EtOAc (20 mL) and purified by flash chromatography (gradient elution: 2:1 to 1:1 hexane/EtOAc) to afford 33 mg (67%) of quinone **58** as a yellow amorphous solid: mp 128–131 °C; $[\alpha]^D_{20}$ +98.5° (*c* 1.3, $CHCl_3$); IR ($CHCl_3$) 3029, 1772, 1745, 1663 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 8.1 Hz, 1H, H_{arom}), 7.94 (d, J = 8.2 Hz, 1H, H_{arom}), 7.40–7.26 (m, 5H, H_{arom}), 5.13 (m, 1H, $H_{3'}$), 4.85 (t, J = 9.5 Hz, 1H, $H_{4'}$), 4.75 (m, 1H, $H_{1'}$), 4.65 (AB superimposed m, 3H, H_5 and CH_2Ph), 3.66 (dq, J = 9.4, 6.2 Hz, 1H, $H_{5'}$), 3.58–3.41 (m, overlapping signals, 2H, H_1 and H_{12b}), 2.51 (s, 3H, –OAc), 2.45–2.20 (m, overlapping signals, 4H), 2.08 (s, 3H, –OAc), 2.02 (s, 3H, –OAc), 1.83 (m, 1H), 1.75–1.05 (m, overlapping signals, 4H), 1.36 (s, 3H, acetonide), 1.32 (s, 3H, acetonide), 1.28 (d, J = 6.2 Hz, 3H, $-CH_3$), 1.02 (s, 3H, $-CH_3$); ^{13}C NMR (50 MHz, $CDCl_3$) δ 183.8, 182.0, 170.4, 170.1, 169.1, 145.9, 144.3, 142.8, 140.7, 138.8, 132.7, 128.3, 127.7, 127.4, 127.4, 125.2, 122.8, 108.2, 82.9, 78.7, 74.5, 74.1, 73.8, 71.8, 71.6, 67.6, 63.3, 48.2, 47.1, 45.9, 37.2, 29.6, 27.8, 26.4, 24.1, 21.1, 20.9, 20.8, 17.9; HRMS (FAB) *m/e* 748.3154 [(M+2H)$^+$, calcd for $C_{41}H_{48}O_{13}$: 748.3094].

Ketone 60

Dess–Martin periodinane (41 mg, 0.10 mmol) was added to a solution of quinone **59** (55 mg, 0.07 mmol) in methylene chloride (3 mL), and the mixture stirred for 2 h. The reaction mixture was concentrated in vacuo and directly purified by flash chromatography (4:3 hexane/EtOAc) to afford 54 mg (100%) of ketone **60**: mp 120–125 °C; $[\alpha]^D_{20}$ +11.8° (*c* 1.3, $CHCl_3$); IR ($CHCl_3$) 3029, 1744, 1665 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.1 Hz, 1H, H_{arom}), 7.92 (d, J = 8.1 Hz, 1H, H_{arom}), 7.44 (d, J = 7.4 Hz, 2H, H_{arom}), 7.37 (d, J = 8.0 Hz, 2H, H_{arom}), 7.30 (d, J = 7.6 Hz, 1H, H_{arom}), 5.13 (m, 1H, $H_{3'}$), 4.90–4.84 (t, J = 9.4 Hz, 1H, $H_{4'}$), 4.78 (A of AB, J_{AB} = 10.4 Hz, 1H), 4.75 (m, 1H, H_1)4.49 (B of AB, J_{AB} = 10.4 Hz, 1H), 4.42 (t, J = 2.4 Hz, 1H, H_4), 3.65 (dq, J = 9.5, 6.4 Hz, 1H, $H_{5'}$), 3.45 (dd, J = 17.0, 2.3 Hz, 1H), 2.95 (d, J = 17.1 Hz, 1H), 2.71 (dd, J = 14.9, 1.5 Hz, 1H), 2.53 (m, 1H), 2.51 (s, 3H, –OAc), 2.41 (d, J = 16.8 Hz, 1H), 2.08 (s, 3H, –OAc), 2.03 (s, 3H, –OAc), 1.95 (dd, J = 17.2, 2.9 Hz, 3H), 1.70 (m, 1H, $H_{2'ax}$), 1.39 (s, 3H, acetonide), 1.36 (s, 3H, acetonide), 1.27 (d, J = 6.0 Hz, 3H, $-CH_3$), 1.09 (s, 3H, $-CH_3$); ^{13}C NMR (50 MHz, $CDCl_3$) δ 204.4, 181.8, 170.4, 170.1, 169.1, 146.0, 144.1, 140.6, 140.3, 138.6, 132.7, 131.9, 128.3, 127.7, 127.4, 125.2, 123.0, 109.0, 82.9, 80.1, 74.5, 74.3, 74.2, 71.8, 71.6, 64.6, 52.9, 52.7, 45.6, 37.2, 27.2, 26.3, 25.0, 24.3, 21.1, 20.9, 20.8, 17.9; HRMS (FAB) *m/e* 746.2919 [(M+H)$^+$, calcd for $C_{41}H_{45}O_{13}$: 746.2938].

Anthraquinone 61

To a solution of ketone **60** (5 mg, 0.007 mmol) in methylene chloride (150 mL) was added NMO (1 mg, 0.007 mmol), and the solution stirred for 3h. Purification by flash chromatography (1:1 hexane/EtOAc) afforded 1 mg (27%) of ketone **55** and 3 mg (72%) of phenol **61** as a yellow amorphous solid: mp 166 °C (Dec); $[\alpha]^D_{20}$ –96.7° (*c* 1.9, $CHCl_3$); IR ($CHCl_3$) 3380, 3029, 1745, 1711, 1673 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8.1 Hz, 1H, H_{arom}), 7.94 (d, J = 8.2 Hz, 1H, H_{arom}), 7.61 (br s, 1H, -OH), 7.18-7.05 (m, 5H, H_{arom}), 6.91 (br s, 1H, H_{arom}), 5.13 (m, 1H, $H_{3'}$), 4.88 (t, J = 9.6 Hz, 1H, $H_{4'}$), 4.78 (m, 1H, $H_{1'}$), 4.46 (A of AB, J_{AB} = 11.0 Hz, 1H), 4.29 (B of AB, J_{AB} = 10.4 Hz, 1H), 3.67 (dq, J = 9.6, 6.1 Hz, 1H, $H_{5'}$), 3.48 (m, 1H), 3.20-2.95 (m, 2H), 2.64 (br s, 3H, –OAc), 2.43 (m, 1H, $H_{2'eq}$), 2.10 (s, 3H, –OAc), 2.05 (s, 3H, –OAc), 1.67 (m, 1H, $H_{2'ax}$), 1.7–1.5 (m, 4H), 1.29 (d, J = 6.0 Hz, 3H, $-CH_3$), 1.25 (s, 3H, $-CH_3$); ^{13}C NMR (50 MHz, $CDCl_3$) δ 197.7, 170.6, 170.2, 158.1, 145.6, 139.7, 138.3, 137.8, 136.4, 134.9, 128.1, 127.5, 127.2, 125.8, 122.9, 112.9, 77.2, 74.6, 74.1, 72.1, 71.9, 63.8, 37.3, 35.7, 29.7, 25.2, 21.5, 21.0, 20.9, 18.0; HRMS (FAB) *m/e* 685.2285 [(M+H)$^+$, calcd for $C_{38}H_{37}O_{12}$: 685.2300].

Phenol 62

To a solution of ketone **61** (17 mg, 0.02 mmol) in THF (1 mL) at 0 °C was added a solution of lithium hydroxide (0.1M in water 500 mL, 0.05 mmol) and the purple-colored mixture stirred for 4 h at room temperature. Additional lithium hydroxide was added at 1.5 h (100 mL) and 3 h (50 mL). The reaction was quenched with saturated aqueous NH_4Cl (3 mL), extracted with EtOAc (4 × 15 mL), and the combined extracts were washed with brine (4 mL), dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash chromatography (gradient elution: 4:3 to 1:1 to 2:1 to

EtOAc hexane/EtOAc) to afford 1 mg (8%) of recovered **61** and 11 mg (68%) of phenol **62** as a yellow-orange amorphous solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.21 (s, 1H, –OH), 7.82 (d, J = 7.9 Hz, 1H, H_{arom}), 7.65 (d, J = 7.8 Hz, 1H, H_{arom}), 7.49 (br s, 1H, –OH), 7.33–7.12 (m, overlapping signals, 5H, H_{arom}), 6.63 (s, 1H, H_{arom}), 5.17 (m, 1H, $H_{3'}$), 4.83 (t, J = 9.5 Hz, 1H, $H_{4'}$), 4.74 (d, J = 10.2 Hz, 1H, $H_{1'}$), 4.65 (A of AB, J_{AB} = 9.9 Hz, 1H), 4.48 (B of AB, J_{AB} = 9.8 Hz, 1H), 3.68 (dq, J = 9.6, 6.1 Hz, 1H, $H_{5'}$), 3.48 (dd, J = 18.0, 1.8 Hz, 1H), 3.42 (dd, J = 14.6, 2.0 Hz, 1H), 3.02 (d, J = 14.6 Hz, 1H), 2.75 (d, J = 17.9 Hz, 1H), 2.63 (ddd, J = 1.8, 5.2, 12.9 Hz, 1H, $H_{2'eq}$), 2.10 (s, 3H, -OAc), 2.01 (s, 3H, –OAc), 1.35 (d superimposed m, J = 6.1 Hz, 4H, $H_{2'ax}$ and $-CH_3$), 1.25 (s, 3H, $-CH_3$); LRMS (FAB) *m/e* 644 [(M+2H)$^+$, calcd for $C_{36}H_{36}O_{11}$: 644].

Triol 63

A solution of phenol **62** (8 mg, 0.01 mmol) in EtOAc (3 mL) was added by cannula to a suspension of a catalytic amount of 5% $Pd(OH)_2$ (ca. 5 mg) in methanol (3 mL) under a hydrogen atmosphere and maintained for 40 min at 0 °C. The mixture was filtered through silica gel and the insolubles washed with methanol (20 mL). The filtrate was concentrated in vacuo and purified by flash chromatography (gradient elution: 3:4 to 1:2 hexane/EtOAc) to afford 5 mg (76%) of **63** as a yellow amorphous solid: ^{1}H NMR (400 MHz, acetone-d_6) δ 12.73 (br s, 1H, –OH), 7.95 (d, J = 7.9 Hz, 1H, H_{arom}), 7.78 (s, 1H, H_{arom}), 7.60 (d, J = 7.8 Hz, 1H, H_{arom}), 5.19 (m, 1H, $H_{3'}$), 5.05 (d, J = 10.2 Hz, 1H, $H_{1'}$), 4.82 (t, J = 9.5 Hz, 1H, $H_{4'}$), 3.81 (dq, J = 9.5, 6.2 Hz, 1H, $H_{5'}$), 3.26 (dd, J = 17.8, 1.5 Hz, 1H), 3.08 (d, J = 13.5 Hz, 1H), 3.00 (d, J = 17.8 Hz, 1H), 2.91 (dd, J = 13.7, 1.6 Hz, 1H), 2.58 (ddd, J = 12.6, 5.0, 2.1 Hz, 1H, $H_{2'eq}$), 2.05 (s, 3H, –OAc), 1.97 (s, 3H, –OAc), 1.60 (m, 1H, $H_{2'ax}$), 1.50 (s, 3H, $-CH_3$), 1.26 (d, J = 6.2 Hz, 3H, $-CH_3$); LRMS (FAB) *m/e* 553 [(M+H)$^+$, calcd for $C_{29}H_{29}O_{11}$: 553].

Shunt Metabolite 104-2 (5)

To a solution of alcohol **63** (5 mg, 0.009 mmol) in THF (0.5 mL) at 0 °C was added a solution of lithium hydroxide (0.1 M in water, 270 mL, 0.027 mmol), the mixture was stirred for 30 min at 0 °C and 3.5 h at room temperature. Additional lithium hydroxide was added upon recooling to 0 °C at 1 h (90 mL) and 2 h (45 mL). The purple mixture was quenched with a saturated aqueous NH_4Cl solution (3 mL), saturated with NaCl, and extracted with EtOAc (4 × 10 mL). The extracts were combined, washed with brine (3 mL), dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash chromatography (10:1 chloroform/methanol) to afford 5 mg (100%) of **5** as a yellow amorphous solid: mp 158 °C (dec) (lit.[2i] mp 177 °C dec); $[\alpha]^D_{20}$ +30.6° (*c* 0.1, MeOH) (lit.[2h] $[\alpha]^D_{20}$ +78° (*c* 0.0026, MeOH)); CD $\lambda_{extreme}$ (MeOH) ($[\theta]_D \times 10^{-6}$): 330 (–0.113), 298 (–8.231), 268 (–5.248), 253 (–0.108), 216 (+0.227) nm [Lit[2i] CD $\lambda_{extreme}$ (MeOH) ($[\theta]_D \times 10^{-5}$): 330 (–0.41), 298 (–1.17), 268 (–0.1), 253 (–0.49), 216 (+1.05) nm]; UV (MeOH) λ_{max} (log e): 258 (4.099), 284 (4.175), 388 (3.705) nm; IR (KBr) 3402, 3182, 2924, 2852, 1620 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.56 (s, 1H, –OH), 11.40 (br s, 1H, –OH), 7.80 (d, J = 7.8 Hz, 1H, H_{arom}), 7.64 (s, 1H, H_{arom}) 7.50 (d, J = 7.8 Hz, 1H, H_{arom}), 5.01 (d, J = 5.2 Hz, 1H, –OH), 4.93 (s, 2H, –OH), 4.77 (dd, J = 11.2, 1.4 Hz, 1H, $H_{1'}$), 3.51 (m, 1H, $H_{3'}$), 3.38 (m, 1H, $H_{5'}$), 3.05 (dd, J = 17.0, 1.2Hz, 1H), 3.03 (d, J = 12.9 Hz, 1H), 2.84 (d, J = 17.8 Hz, 1H), 2.88 (m, 1H, $H_{4'}$), 2.66 (dd, J = 13.1, 1.4 Hz, 1H), 2.22 (ddd, J = 12.7, 4.4, 1.8 Hz, 1H, $H_{2'eq}$), 1.34 (s superimposed m, 4H, $-CH_3$ and $H_{2'ax}$), 1.26 (d, J = 6.1 Hz, 3H, $-CH_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.4, 188.2, 181.4, 157.4, 138.3, 137.3, 136.4, 134.5, 134.2, 133.6, 118.8, 115.2, 112.3, 77.4, 76.5, 72.1, 71.9, 70.9, 53.3, 38.0, 29.5, 18.9; HRMS (FAB) *m/e* 469.1517 [(M+H)$^+$, calcd for $C_{25}H_{25}O_9$: 469.1499].

CONCLUSION

We have described a synthetic strategy of general applicability to a broad range of angucycline antibiotics. A notable feature of this approach is the accessibility of either antipode of cyclohexadienone **23** starting from (–)-quinic acid. This feature will allow entry into natural as well as unnaturally configured angucycline antibiotics. A second notable stereochemical feature of the synthesis is the availability of either cis (**25a**) or trans (**25b**) dienes leading to either cis or trans related C3–C4a diols (cf. **1** and **6**). Remaining challenges in this area include the installation of the C12b hydroxyl group common to aquayamycin (**1**) and sakyomycin (**6**), as well as the development of glycosylation methods for entry into the glycosylated derivatives of this group of natural products.[40]

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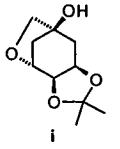

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