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λ^3-Iodane-mediated arenol dearomatization. Synthesis of five-membered ring-containing analogues of the aquayamycin ABC tricyclic unit and novel access to the apoptosis inducer menadione

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Abstract—The λ^3-iodane [bis(trifluoroacetoxy)]iodobenzene (BTI)-mediated oxidative dearomatization of 2-alkoxyarenols with soft external carbon-based nucleophiles constitutes a rapid access to highly functionalized naphthoid cyclohexa-2,4-dienones. These synthons can serve as valuable intermediates in the construction of the angularly-oxygenated benz[*a*]naphthalene ABC ring system of aquayamycin- and SS-228Y-type antibiotic angucyclinones, and analogues thereof. This methodology led to the elaboration of five-membered A ring-containing analogues of this ABC tricyclic unit. In addition, the BTI-mediated oxidative activation of 2-methylnaphthol can be exploited to prepare menadione (i.e. vitamin K_3), known to induce apoptosis and autoschizis, a novel type of cancer cell death.

1. Introduction

Angucyclines and angucyclinones are structurally characterized by their benz[*a*]anthraquinone ABCD cyclic skeleton and constitute an important class of microbial antibiotics exhibiting a wide variety of biological activities, including antitumor, antifungal, and antiviral properties.[1,2] The high structural diversity that these natural products feature, especially on their angular ABC ring system, gave impetus to many studies aimed at their total synthesis. Until now, most efforts have been directed toward angucyclinones in which the B ring is aromatic. In most cases, the strategy followed for constructing the benz[*a*]anthracene framework was based on Diels-Alder reactions.[3–13] The repertoire of other approaches that have been examined encompass Michael-type cyclization,[14] phthalide anion-based annulation,[15,16] Friedel–Crafts reactions,[17–19] chromium carbenoid-mediated benzannulation,[20] benzyne-furan cycloaddition,[21] metal-induced free radical annulation,[22] cobalt-catalyzed [2+2+2] triyne cycloaddition[23] and biomimetic polyketide condensation reactions.[1,24,25] Despite this enormous amount of work, the synthesis of angucyclinones bearing two hydroxy groups in a *cis*-configuration at the AB ring junction (i.e. positions **4a** and **12b**), as exemplified by aquayamycin (**1**)[26,27] and SS-228Y (**2**)[28] remains a challenge for synthetic organic chemists. A further justification for tackling this challenge is found in the fact that most angucyclines or angucyclinones of this subclass display therapeutically-significant activities.[29–35]

Only two relevant model studies have been reported,[25,36] and two syntheses of angucyclinones of this subclass have been described; the first total synthesis of (+)-**1**, in more than 50 steps,[37–39] and the synthesis of the racemic 8-deoxy analogue of WP 3688-2 (**3**).[40] In both cases, the key A ring annulation step relied on a biomimetic pinacolic-type coupling. Our previous investigation on the regioselective formation of naphthoid cyclohexa-2,4-dienones by oxidative dearomatization of naphthols using the λ^3-iodane bis(trifluoroacetoxy)]iodobenzene (BTI) in the presence of soft carbon-based nucleophiles[41,42] led us to examine a novel approach to the polycyclic core of aquayamycin-type angucyclinones (Scheme 1). The first key to the success of this approach resides in the use of either naphthoid or an anthranoid cyclohexa-2,4-dienone orthoquinol of type **5** that can be generated from the corresponding arenol **6** by the aforementioned BTI-mediated oxidative nucleophilic substitution reaction. In this event, the silyl enol ether **7b** constitutes an ideal second reaction partner, since it adds a

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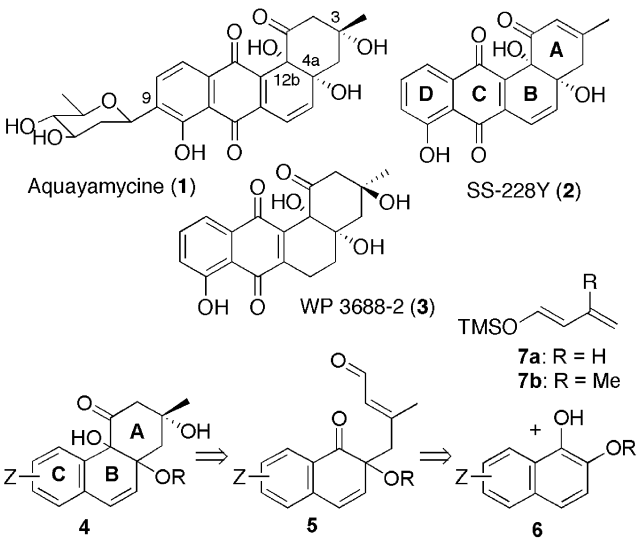
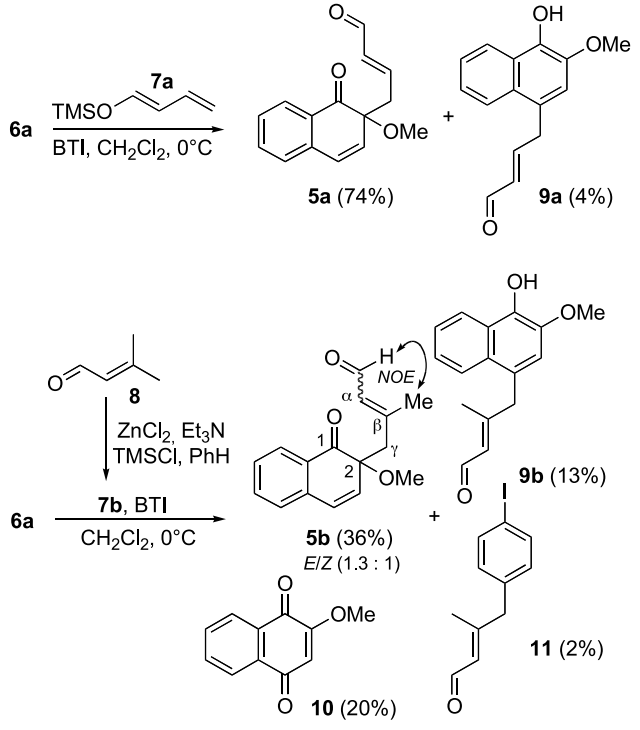


Scheme 1.

four-carbon appendage adequately functionalized for making the A ring in one step. We wish to report in full detail the work carried out so far on this orthoquinol route toward the synthesis of aquayamycin-type angucyclinones and model compounds thereof.

2. Results and Discussion

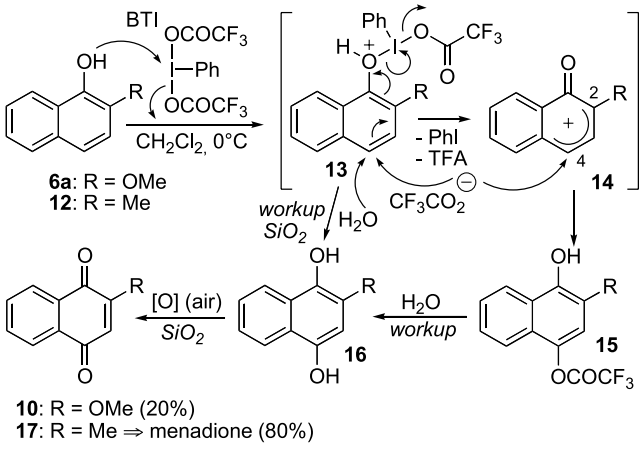
The first task to accomplish was to ascertain the possibility of generating an orthoquinol of type **5** using the silyl enol ether **7b** in our BTI-mediated arenol dearomatization reaction. We previously used a simpler and commercially available silyl enol ether (i.e. **7a**, 1-trimethylsilyloxybuta-1,3-diene) to prepare naphthoid orthoquinols, such as **5a**, in



Scheme 2.

good yields (Scheme 2).[41,42] The diene **7b** has the advantage of bearing an additional methyl group prefiguring that of the aquayamycin-type A cycle. It was prepared in one step in 63% as the (*E*)-isomer from methyl-3-but-2-enal (**8**).[43] A mixture of 2-methoxynaphthol (**6a**, Z=H, R=Me, Scheme 1) and **7b** was then treated with BTI (1.8 equiv) in CH_2Cl_2 at 0 °C for 2 h to furnish both the orthoquinol **5b** and the naphthol **9b** in moderate yields, together with the paraquinone **10**[44] (20%) and the iodoaryl compound **11** (2%) (Scheme 2). The desired and major orthoquinol product **5b** was obtained as a 1.3:1 mixture of the *E* and *Z* isomers; their assignment was determined by NOE spectroscopy that revealed a correlation between the aldehydic proton and the methyl group only for the *E* geometry. We were much intrigued by the formation of **10** in such a significant yield (i.e. 20%), for this type of paraquinone was not obtained in previous reactions performed with 2-methoxy- and 2-benzyloxynaphth-1-ols in the presence of silyl enol ethers or allylsilane.[41,42]

The only case in which we observed such an oxidative oxygenation was when we used 2-methylnaphth-1-ol (**12**). The treatment of this arenol with BTI led to the formation of menadione (**17**, i.e. vitamin K_3) as a bright yellow solid in an excellent yield of 80% (Scheme 3). Vitamin K_3, which displays the antihemorrhagic activity of the naturally occurring vitamin K, has also recently been found to induce cell death via apoptosis[45] and autoschizis, a new type of cancer cell death.[46] Vitamin K_3 is produced on industrial scale by stoichiometric oxidation of 2-methylnaphthalene with chromium trioxide in sulfuric acid,[47] but the environmental concerns linked to the use of chromium and the interesting pharmacological properties recently unveiled for this 1,4-naphthoquinone[45] encouraged the development of novel procedures of varying preparative values.[48–51] Although 2-methylnaphth-1-ol (**12**) is a more expensive starting material than 2-methylnaphthalene and CH_2Cl_2 is not the most appropriate solvent from an environmental point of view, the use of a λ^3-iodane oxidizing agent such as BTI, nevertheless, constitutes an alternative preparation of vitamin K_3 (**17**). Several reports have described the use of λ^3-iodanes in aqueous solvent systems to efficiently generate paraquinones from phenols,[52–58] but, to the best of our knowledge, none were concerned with the preparation of **17**.

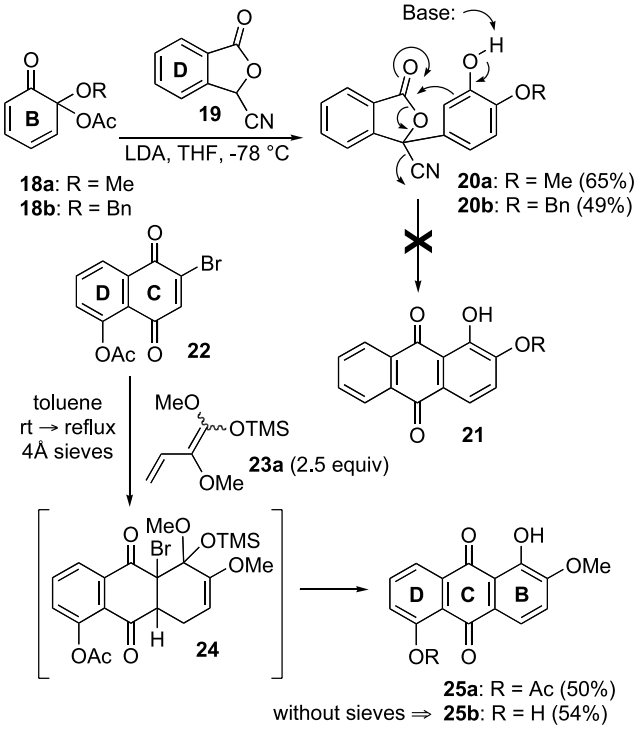


Scheme 3.

For the desired conversion of **6a** into **5b** (Scheme 2), we chose to use BTI to prevent any competing nucleophilic attack by the trifluoroacetate anion released during the reaction. This anion has a relatively low nucleophilic power and its participation in displacing the λ^3-iodanyl unit of the initial ligand exchange product **13**, either directly or by quenching an arenoxenium ion intermediate of type **14** (Scheme 3), was not expected to be a favored process in the presence of other nucleophilic species. Furthermore, special care was taken to ensure that the reaction was run under strictly anhydrous conditions to avoid any competitive substitution reaction with water. Hence, the possibility that the formation of **10** and **17** might be derived from the nucleophilic attack of the trifluoroacetate anion at the 4-position of **13** or **14** cannot be disregarded. The resulting trifluoroacetate esters of type **15** would then be hydrolysed during the aqueous workup and rapidly air oxidized during silica gel chromatography to furnish paraquinones **10** or **17** (Scheme 3). The attack of the trifluoroacetate anion onto 2-naphthol derivatives has previously been reported in special cases.[59] However, our experimental observations and NMR analyses of the crude products, which contain small amounts of paraquinones **10** or **17**, do not allow us to confirm the formation of trifluoroacetate esters of type **15**. Another possibility would be that the λ^3-iodanyl conjugate base of **13** remains intact in significant amounts during the reaction and that their conversion into paraquinones **10** or **17** occurs via the attack of H_2O to give the hydroquinone intermediate **16** during the aqueous workup and silica gel chromatography (Scheme 3).

The only explanation we can propose for the minor formation of the iodoaryl compound **11** in the reaction between **6a** and **7b** (Scheme 2) is that iodobenzene released from BTI underwent an initial one-electron oxidation by excess BTI to generate a phenyl radical cation species, which was then quenched by the nucleophile **7b**. The resulting radical intermediate could then be further one-electron oxidized to furnish **11** after proton loss. Despite the decrease in chemical yield, chemo- and regioselectivity as compared to the results obtained using the simpler silyl enol ether **7a**, we were nevertheless satisfied to have developed a rapid access to the highly functionalized orthoquinol **5b** (Scheme 2) that we could subsequently use to investigate modes of cyclization onto the aquayamycin ABC ring system. Only the *Z* isomer of **5b** had a chance to cyclize into the desired angular polycycle.

First, we decided to examine the possibility of performing the same type of oxidative nucleophilic substitution reaction on an anthranoid derivative in order to build directly an aquayamycin BCD ring system appended by a four-carbon precursor of the A ring (Scheme 1). Using 2-alkoxy-1-hydroxyanthraquinones as starting arenols, the first approach we tried to build such anthraquinones was that of Mitchell and Russell,[15,60] which, involved a conjugated addition of the phtalide anion derived from **19** to non-dimerizing orthoquinol acetates such as **18a/b** (Scheme 4).[61] Unfortunately, the rapid rearomatizing departure of AcOH from the Michael-type adduct intermediate prevented the desired annulation into **21** to occur in situ, and led to the formation of phenols **20a/b**. Several attempts to induce

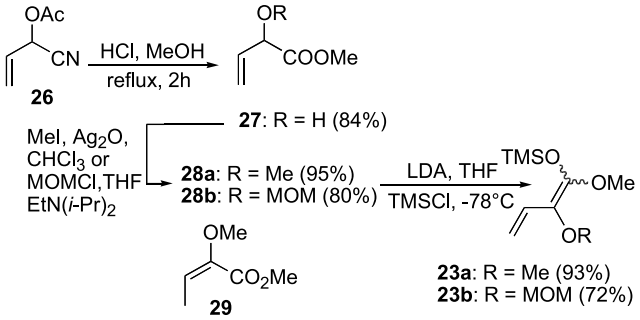


Scheme 4.

cyclization into **21** by treating these phenols with a base (eg. LDA, LHMDS) failed.[42]

The solution came from annulating the B ring to a CD bicyclic unit via a cycloaddition process.[62,63] The bromonaphthoquinone CD unit **22** was prepared in 97% yield over two steps from 1,5-dihydroxynaphthalene, as previously described,[64,65] and was used as the dienophile in a Diels-Alder reaction with diene **23a** (Schemes 4 and 5). We were particularly eager to carry out this reaction, for a *C*-glycosylated version of this dienophile bearing the aquayamycin D-olivose at the appropriate position has already been synthesized by Sulikowski and his co-workers.[9] The silyl ketene acetal **23a** was prepared as a 2:1 mixture of geometric isomers in 74% yield over three steps from 1-cyano-2-propenylacetate **26**, as previously described (Scheme 5).[62,66,67] Of particular note is the fact that it was crucial to maintain the reaction mixture at low temperature to avoid isomerization of **28a** to **29**.

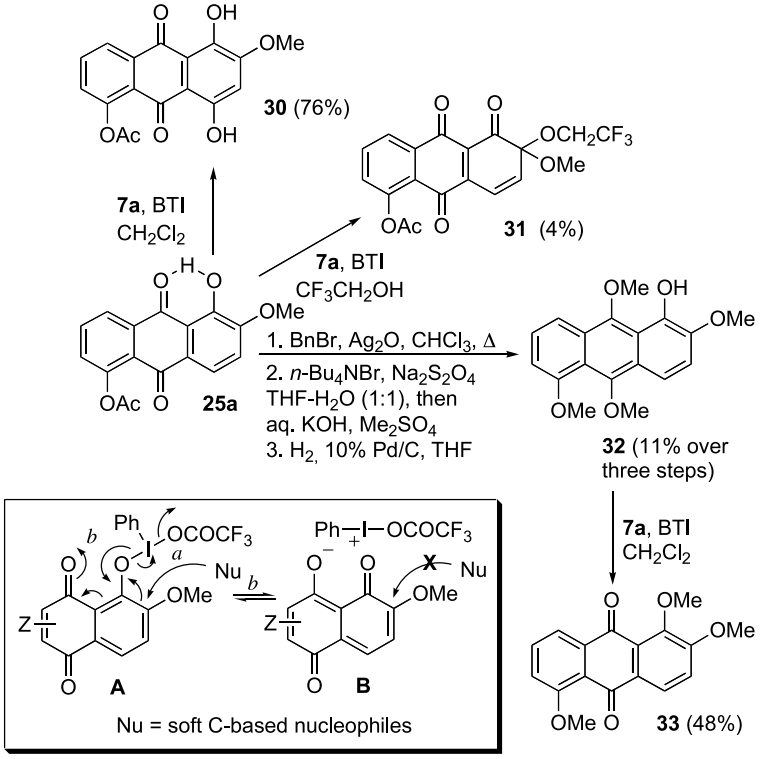
The Diels–Ader reaction between **22** and **23a** was first carried out at room temperature in toluene to afford, after



Scheme 5.

silica gel flash chromatography, an undefined and unstable mixture that slowly (ca. 7 days) and completely evolved into the deacetylated anthraquinone **25b**[68] (Scheme 4). The mixture probably contained some anthraquinone **25b** together with the initial cycloadduct **24** still in significant amounts, as suggested by the observation of a phenolic acetate group by NMR analysis. Furthermore, TLC analysis of this mixture did not show evidence of any formation of **25a**. The elimination of HBr and concomitant aromatization of the B ring, possibly induced by a bromine-mediated cleavage of the acetal *O*-Si bond, occurred slowly upon standing, but the bromine anion then also mediated deacetylation via a nucleophilic addition-elimination at the carbonyl acetate carbonyl group. Attempts to carry out the reaction in the presence of a base (e.g. Et_3N, DBU) in order to promote elimination of HBr, while quenching it in situ, failed. The introduction of 4 Å molecular sieves in the reaction medium brought to reflux after 1 h at room temperature solved this problem, and the desired anthraquinone **25a** was thus obtained as an orange powder in 50% yield (Scheme 4). The role of the molecular sieves remains unknown, but they must in some way trap the bromine anion before it cleaves the acetate group. In any event, access to this novel 5-acetoxy-1-hydroxy-2-methoxyanthraquinone (**25a**) allowed us to proceed as planned to mount a four-carbon tether at its 2-position. Unfortunately, the only product isolated after performing the BTI-mediated reaction between **25a** and **7a** in CH_2Cl_2 at various temperatures was the 1,4-dihydroxy compound **30** (Scheme 6). Again, this hydroxylation must have arisen either from an in situ attack of the trifluoroacetate anion released from BTI or from a λ^3-iodanyl displacement by water during reaction processing (Scheme 3).

The use of fluorinated solvents such as 2,2,2-trifluoroethanol (TFE) and hexafluoroisopropanol (HFIP), as first recommended by Kita and co-workers in place of CH_2Cl_2 for similar iodane-mediated reactions with phenolic compounds and their simple ethers,[69–71] did not help and resulted only in complex reaction mixtures. Interestingly, the only product we could extract from these mixtures, albeit in a very low yield (i.e. 4%), was the anthranoid orthoquinone monoketal **31** that resulted from attack of TFE at the 2-position of **25a**. Although TFE is recommended because of its low nucleophilicity, similar solvolyses have been observed in such a solvent.[59,71] We then tried to augment the electrophilicity of the iodine(III) by adding a Lewis acid to the medium in the form of complexes of BTI or iodosylbenzene (PhIO) with BF_3 etherate,[70,72,73] as well as PhIO with HBF_4,[74,75] but no better formation of the desired C–C bond was observed. Another option was to reduce **25a** into its corresponding dimethyl hydroquinone **32** before performing the BTI-mediated reaction. This was accomplished by reductive methylation of the benzyl ether of **25a**. The difficulty of performing this preliminary benzylation, which necessitated the use of silver(I) oxide with benzyl bromide in refluxing $CHCl_3$ (Scheme 6), is probably due to the participation of the free phenol function of **25a** in a hydrogen-bond with the adjacent carbonyl function. This lowering of the nucleophilic power of the phenolic oxygen, however, had no major effect on its reactivity towards the iodane reagent used, since the BTI-mediated hydration of **25a** into **30** occurred in high yield (Scheme 6). Nevertheless, it is conceivable that the electron-withdrawing effect of the paraquinone motif of the ligand exchange reaction intermediate (e.g. **A**, Scheme 6) sufficiently disfavors any displacement of the iodanyl unit by soft carbon-based nucleophiles such as **7a**

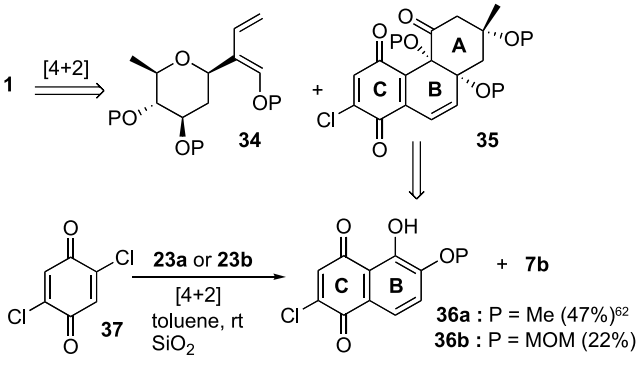


Scheme 6.

(path a), while augmenting its phenyliodonium **B** character (path b).

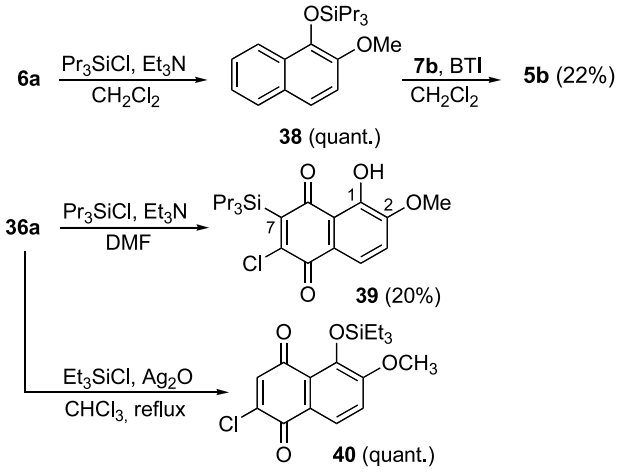
Reduction with sodium dithionite, methylation with dimethyl sulfate in aqueous potassium hydroxide and a final hydrogenolytic cleavage of the benzyl ether bond furnished the tetramethoxylated anthranol **32** (Scheme 6). Unfortunately, all attempts to promote the attack of the silyl enol ether **7a** onto **32** with BTI failed because of rapid oxidation of the dimethyl ether hydroquinone unit with concomitant displacement of a methyl group onto the free hydroxy group, giving rise to the formation of the anthraquinone **33**[76] in 48% yield (Scheme 6).

These recurring problems caused by the extreme sensitivity of the anthracene unit toward oxidation led us to envisage another approach to the benz[*a*]anthraquinone skeleton of angucyclinones. Since the BTI-mediated C–C bond-forming dearomatization of 2-alkoxynaphthols was successful (Scheme 2),[41,42] we thought of first constructing a paraquinonic ABC ring system of type **35**, on which the D ring would then be added by a Diels–Alder reaction with a *C*-glycosidic diene of type **34** (Scheme 7). With this in mind, the synthesis of the required naphthoquinone **36** was carried out also via a Diels–Alder reaction between the commercially available 1,4-benzoquinone **37** and **23**, according to the method of Brassard and co-workers.[62] Both the methoxylated **23a** and the more labile methoxymethoxylated **23b** were used in these reactions. In these cases, complete B ring aromatization was ensured before purification by stirring the crude cycloaddition product with SiO_2 in CH_2Cl_2 for 6 h (Scheme 7).[62]



Scheme 7.

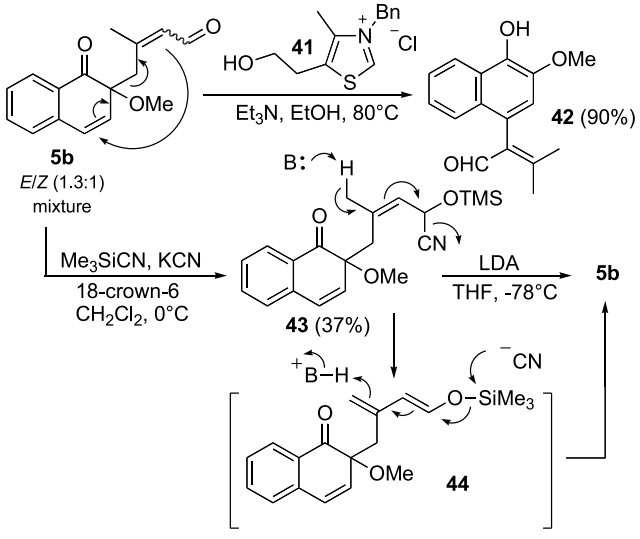
Before submitting **36a/b** to the BTI-mediated dearomatization reaction in the presence of **7b**, its phenolic group was silylated in the hope of improving the yield of the desired C–C bond forming reaction. Indeed, such silylations, in particular those using a tripropylsilyl group, have been proven beneficial in similar iodane-mediated transformations reported by Kita[77] and McKillop.[78] Although 2-methoxynaphthol **6a** was quantitatively converted into the corresponding tripropylsilyl phenyl ether **38** and to the orthoquinol methyl ether **5b**, albeit with no yield improvement, the tripropylsilylation of **36a** did not occur at the phenolic locus, but, surprisingly, at the C-7 center to furnish **39** (Scheme 8). Once again, we had to rely on more drastic conditions using silver(I) oxide and a smaller silylating



Scheme 8.

reagent to enable the reaction to occur at the phenolic function, the nucleophilicity of which was also lowered by its participation into an intramolecular hydrogen bond with the neighboring carbonyl group. Unfortunately, all attempts to dearomatize **40**, as well as the free phenol **36a**, with BTI into the desired orthoquinol in the presence of **7b** mainly gave back the staring material **36a**, plus up to 8% of the iodoaryl compound **11** as the only isolated compounds.

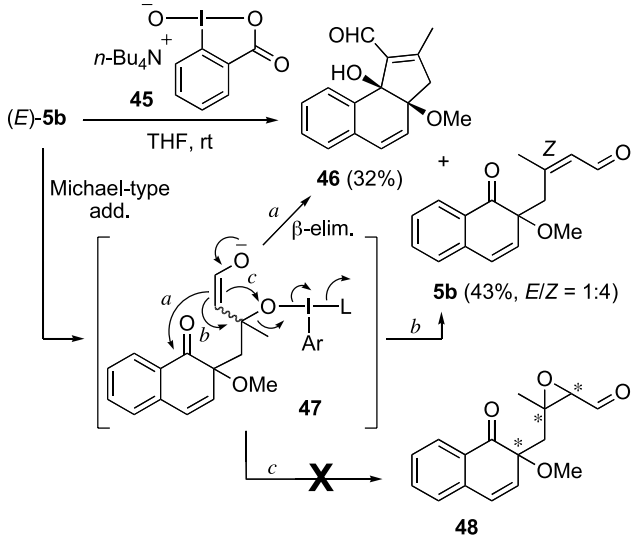
We thus decided to investigate the possibilities of converting the bicyclic orthoquinol ether **5b** into an angucyclinone ABC ring model system. The first tactic we examined for annulating its four-carbon enal unit onto the A ring part was a thiazolium ion-catalyzed benzoin-type coupling,[79,80] but the heating of **5b** in absolute ethanol at 80 °C in the presence of 3-benzyl-5-(2-hydroxyethyl)-4-methyl-1,3-thiazolium chloride (**41**) and triethylamine only gave **42**, after enal isomerization and aromatization of the thermally-induced Cope rearrangement product (Scheme 9).[81–83] The cyanohydrin-based cyclisation approach reported by Kraus[25] for making similar ring systems was then tried. The cyanohydrin **43** was generated as a 1:1 diastereomeric mixture in a moderate yield of 37% by treating **5b** with trimethylsilyl



Scheme 9.

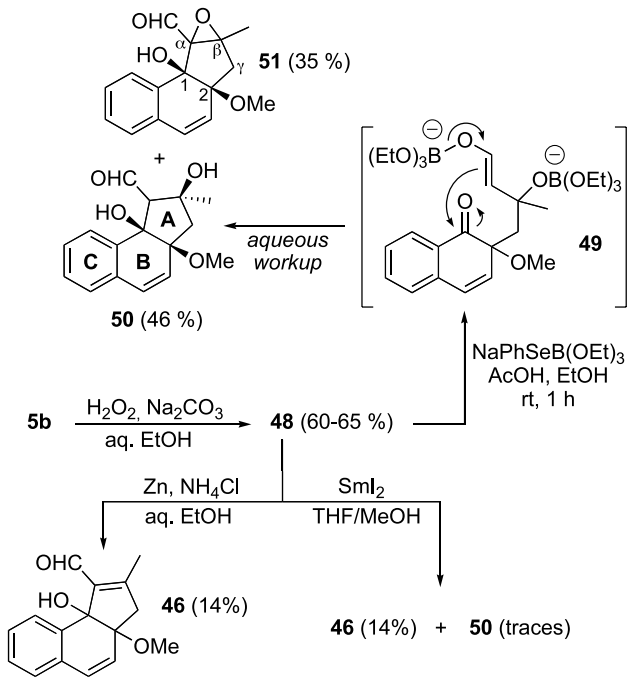
cyanide in the presence of catalytic amounts of KCN and 18-crown-6,[84,85] but treatment of **43** with LDA in THF at −78 °C gave no cyclized product. In fact, the starting aldehydic orthoquinol ether **5b** was quantitatively recovered, probably via a mechanism involving an initial deprotonation at a γ-allylic position of the reacting tether (Scheme 9).

The last draw of this study led us to results of value for the synthesis of angucyclinone analogues. Since the presence of a double bond on the four-carbon tether allowed other reactions to compete with the desired cyclization, the alternative was to transform the enal unit of **5b** into a β-hydroxyaldehyde before cyclization. Furthermore, such a transformation would convert both the (*E*)- and (*Z*)-enal tethers of the 1.3:1 product mixture **5b** into cyclizing motifs. Reductive opening of an α,β-epoxyaldehyde was the tactic chosen to elaborate the desired tertiary alcohol function. In the context of this study, we felt obliged to use the oxido-λ^3-iodane reagent **45**, recently reported by Ochiai and co-workers to epoxidize α,β-unsaturated carbonyl compounds.[86] Treatment of pure (*E*)-**5b** with **45** in THF at room temperature did not lead to the desired epoxide, but to the five-membered ring-containing tricycle **46** (32%), together with the starting **5b** (43%), now enriched in the (*Z*)-isomer (Scheme 10). The high nucleofugality of the λ^3-aryl-iodanyl[87] group did not force the enolate intermediate **47** to follow the epoxidation path (route *c*), usually driven by reductive elimination at the iodine(III) center, and this enolate instead evolved through the intramolecular aldol reaction path (route *a*) and the isomerizing reversal of the initial Michael-type addition (route *b*).



Scheme 10.

We had to rely on a more classic methodology to prepare the required epoxide. Treatment of **5b** with H_2O_2/Na_2CO_3 in aqueous EtOH afforded the epoxyaldehyde **48** as a diastereomeric mixture in 60–65% yield (Scheme 11).[88] Various reaction conditions known to reduce regioselectively α,β-epoxyketones[88–90] were then examined for opening the epoxide moiety of **48**.



Scheme 11.

The first conditions tried were those proposed by Miyashita and co-workers[90] by using a phenylseleno(triethyl)borate complex to initiate epoxide opening by a one-electron reduction of the aldehydic carbonyl. These conditions are known to preclude dehydration of the resulting β-hydroxy-carbonyl product.[90] Opening of the epoxide was indeed successful, but the boron enolate intermediate **49** generated under these conditions, like enolate **47**, quickly followed the intramolecular aldol reaction path before being quenched during workup. The five-membered ring-containing tricycle **50** was thus obtained in 46% yield, together with the related epoxide **51** in 35% yield, the formation of which remains unclear (Scheme 11). Stereochemical assignments of **50** were deduced from the observation of strong NOE signals between the two hydroxyl hydrogens. Reduction of **48** using zinc in aqueous EtOH containing ammonium chloride[88] gave the dehydrated analogue **46** in 14% yield. Samarium diiodide reduction in THF in the presence of MeOH as a proton source[89] furnished only traces of **50** and **46** in 14% yield (Scheme 11). Although these epoxide-opening reactions did not lead to the formation of a six-membered A ring, the five-membered ring cyclization path they unveiled constitutes a valuable approach for the synthesis of aquayamycin-type angucyclinone analogues. In particular, the use of Miyashita's selenoborate complex on an orthoquinol epoxide such as **48** affords two related angularly oxygenated tricyclic analogues (i.e. **50** and **51**) of the aquayamycin ABC ring system in good yields.

In conclusion, the synthesis studies described here in full details on the orthoquinol route to aquayamycin-type angucyclinones and related compounds led to a novel and convenient access to five-membered ring-containing analogues of their ABC tricylic system. This work has confirmed the value of λ^3-iodane-mediated arenol dearomatization reactions for the direct elaboration of highly functionalized synthetic intermediates. We are actively

pursuing our efforts with the aim of fully synthesizing five-membered ring-containing analogues of aquayamycin, while investigating other transformations of orthoquinols of type **48** into benz[*a*]naphthoquinones en route to aquayamycin. Furthermore, the use of the λ^3-iodane BTI reagent for dearomatizing arenols allowed us to propose a novel and rapid preparation of the apoptosis inducer menadione (i.e. vitamine K_3).

3. Experimental

3.1. General

Tetrahydrofuran (THF) and diethyl ether (Et_2O) were purified by distillation from sodium/benzophenone under N_2 immediately before use. CH_2Cl_2 was distilled from CaH_2. Light petroleum refers to the 40–60 °C boiling range. Moisture and oxygen sensitive reactions were carried out in flame-dried glassware under N_2. Evaporations were conducted under reduced pressure at temperatures less than 45 °C unless otherwise noted. Column chromatography was carried out under positive pressure using 40–63 μm silica gel (Merck). Preparative layer chromatography (PLC) was performed using glass-coated silica gel plates (SILG-100 UV 254, Macherey-Nagel). Melting points are uncorrected. NMR spectra of samples in the indicated solvent were run at 200, 250 or 300 MHz. Carbon multiplicities were determined by DEPT135 experiments. Diagnostic bond connectivities and stereochemical assignments were obtained by two-dimensional HMQC, HMBC and NOESY experiments run on Bruker 200- and 400-DPX spectrometers. Electron impact mass spectra (EIMS) were obtained at 50–70 eV. Low and high resolution electron impact and liquid secondary ion mass spectrometry data (EIMS, and LSIMS, HRMS) were obtained from the mass spectrometry laboratory at the CESAMO, Université Bordeaux 1.

3.1.1. Bis(trifluoroacetoxy)]iodobenzene-mediated transformation of 2-methoxynaphthol (6a) in the presence of 1-trimethylsilyloxy-3-methylbuta-1,3-diene (7b). To a stirring ice-cold solution of **6a** (1.0 g, 5.7 mmol)[42] and **7b** (2.6 g, 16.6 mmol)[43] in CH_2Cl_2 (17 mL) was added BTI (4.4 g, 10.2 mmol) as a solid, in one portion. The mixture was stirred at rt for 2 h, after which time it was diluted with CH_2Cl_2 (20 mL), washed with saturated aqueous $NaHCO_3$ (2×20 mL), 1M H_3PO_4 (20 mL), brine (20 mL), dried over Na_2SO_4, and evaporated at rt. The resulting brownish oil was purified by column chromatography, eluting with light petroleum/Et_2O (1:1), to furnish a 1.3:1 mixture *E*/*Z* mixture of **5b** (532 mg, 36%) as a red oil, **9b** (192 mg, 13%) as a pale yellow gum, **10** (216 mg, 20%) as a yellow solid and **11** (32.8 mg, 2%) as a brownish oil.

3.1.2. 1,2-Dihydro-2-(3-formylprop-2-enyl)-2-methoxy-1-oxonaphthalene (5b). (*E*)-**5b**: IR (KBr) 2938, 1670, 1596, 1120 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 2.20 (s, 3H, β-CH_3), 2.57 (s, 2H, γ-CH_2), 3.16 (s, 3H, OCH_3), 5.74 (d, J=8.0 Hz, 1H, H-α), 6.08 (d, J=10.1 Hz, 1H, H-3), 6.76 (d, J=10.1 Hz, 1H, H-4), 7.23 (dd, J=1.2, 7.6 Hz, 1H, H-5), 7.37 (m, 1H, H-7), 7.58 (m, 1H, H-6), 7.98 (m, 1H, H-8), 9.89 (d, J=8.0 Hz, 1H, CHO); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 199.5, 190.8, 157.8, 136.9, 135.3, 134.8, 131.3, 129.8, 129.6, 128.7, 127.9, 127.2, 82.3, 53.7, 49.6, 19.7. (*Z*)-**5b**: ^1H NMR ($CDCl_3$, 300 MHz) δ 1.93 (s, 3H, β-CH_3), 2.79 (d, J=13.2 Hz, 1H, γ-CH_2), 2.91 (d, J=13.2 Hz, 1H, γ-CH_2), 3.09 (s, 3H, OCH_3), 5.69 (d, J=7.9 Hz, 1H, H-α), 6.02 (d, J=9.8 Hz, 1H, H-3), 6.71 (d, J=9.8 Hz, 1H, H-4), 7.17 (m, 1H, H-5), 7.30 (m, 1H, H-7), 7.52 (m, 1H, H-6), 7.92 (d, J=7.5 Hz, 1H, H-8), 9.61 (d, J=7.9 Hz, 1H, CHO); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 199.4, 190.7, 156.8, 136.7, 135.3, 134.8, 131.3, 129.7, 129.5, 128.7, 127.9, 127.1, 82.0, 53.7, 41.3, 27.7. LSIMS *m*/*z* (rel intensity) 279 (MNa^+, 58), 257 (MH^+, 41), 256 (M^+, 35), 225 (59); HMRS (LSIMS) calcd for $C_{16}H_{16}O_3$ 256.1099, found 256.1091.

3.1.3. 4-(*E*-3-Formylprop-2-enyl)-2-methoxynaphthol (9b). IR (KBr) 3292, 1649 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 2.20 (s, 3H), 3.88 (s, 2H), 3.94 (s, 3H), 5.75 (br d, J=8.1 Hz, 1H), 6.20 (s, 1H), 7.07 (s, 1H), 7.41 (m, 2H), 7.73 (d, J=8.1 Hz, 1H), 8.20 (d, J=7.9 Hz, 1H), 9.98 (d, J=8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 191.4, 162.9, 140.6, 139.4, 131.9, 128.3, 127.9, 125.4, 124.8, 124.6, 123.6, 122.0, 115.6, 57.3, 43.7, 17.8; LSIMS *m*/*z* (rel intensity) 279 (MNa^+, 18), 256 (M^+, 100); HMRS (LSIMS) calcd for $C_{16}H_{16}O_3$ 256.1099, found 256.1098.

3.1.4. 2-Methoxy-1,4-naphthoquinone (10).[44] IR (NaCl) 1685, 1651 cm^{-1}; 1H NMR ($CDCl_3$, 250 MHz) δ 3.91 (s, 3H), 6.18 (s, 1H), 7.71–7.76 (m, 2H), 8.07–8.15 (m, 2H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 184.8, 180.1, 160.4, 133.3, 132.0, 131.0, 126.1, 109.8, 56.4; EIMS *m*/*z* (rel intensity) 188 (M^+, 100), 174 (40); HMRS (EIMS) calcd for $C_{11}H_8O_3$ 188.0473, found 188.0471.

3.1.5. 4-(4-Iodophenyl)-3-methyl-but-2-enal (11). IR (NaCl) 1670 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.10 (s, 3H), 3.42 (s, 2H), 5.84 (d, J=7.9 Hz, 1H), 6.90 (d, J=6.8 Hz, 2H), 7.62 (q, J=6.8 Hz, 2H), 9.97 (d, J=7.9 Hz, 1H), ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 191.1, 161.2, 137.7, 136.5, 131.1, 128.6, 92.3, 46.2, 17.3; EIMS *m*/*z* (rel intensity) 286 (M^+, 35), 159 (100); HMRS (EIMS) calcd for $C_{11}H_{11}OI$ 285.9855, found 285.9851.

3.1.6. 2-Methyl-1,4-naphthoquinone (17, menadione). To a stirring ice-cold solution of 2-methylnaphthol **12** (100 mg, 0.63 mmol) in CH_2Cl_2 (5 mL) was added dropwise a solution of BTI (408 mg, 0.95 mmol) in CH_2Cl_2 (5 mL). The mixture was stirred at rt for 45 min, after which time it was diluted with CH_2Cl_2 (20 mL), washed with saturated aqueous $NaHCO_3$ (2×20 mL), 1M H_3PO_4 (20 mL), brine (20 mL), dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography, eluting with light petroleum/Et_2O (1:1), to furnish **17** (87 mg, 80%) as a bright yellow solid: mp 103–104 °C; IR (KBr) 1664 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 2.17 (d, J=1.5 Hz, 3H), 6.82 (q, J=1.5 Hz, 1H), 7.7–7.8 (m, 2H), 8.0–8.1 (m, 3H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 185.6, 185.0, 148.2, 135.7, 133.6, 133.6, 132.3, 132.2, 126.5, 126.1, 16.5; EIMS *m*/*z* (rel intensity) 172 (M^+, 100).

3.1.7. 5-Acetoxy-1-hydroxy-2-methoxyanthraquinone (25a). To a stirring solution of 2-bromo-5-acetoxynaphthoquinone **22** (666 mg, 2.26 mmol)[64,65] in toluene (7 mL) was added dropwise a solution of 1,2-dimethoxy-1-trimethylsilyloxy-1,3-butadiene **23a** (1.14 g, 5.64 mmol)[62] in toluene

(3 mL). The mixture was stirred in the presence of 4 Å molecular sieves at rt for 1 h and then heat to reflux overnight. The residue was evaporated, dissolved in CH_2Cl_2, adsorbed on silica gel and purified by column chromatography, eluting with EtOAc/hexane [(1:2)→(1:1)], to afford **25a** (354 mg, 50%) as an orange powder, which was crystallized from EtOAc/hexane: mp 180–181 °C; IR (KBr) 3420, 1759, 1661, 1637, 1590 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 2.49 (s, 3H), 4.01 (s, 3H), 7.17 (d, J=8.5 Hz, 1H), 7.43 (dd, J=1.2, 7.9 Hz, 1H), 7.79 (t, J=7.9 Hz, 1H), 7.79 (d, J=8.5 Hz, 1H), 8.30 (dd, J=1.2, 7.9 Hz, 1H), 12.88 (s, 1H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 188.2, 180.1, 169.5, 153.6, 152.4, 150.4, 135.1, 134.5, 130.6, 125.8, 125.4, 125.3, 121.0, 116.1, 115.5, 56.3, 21.1; LSIMS m/z (rel intensity) 335 (MNa^+, 3), 313 (MH^+, 36), 312 (M^+, 5), 271 (100); HMRS (LSIMS) calcd for $C_{17}H_{13}O_6$ 313.0712, found 313.0704.

3.1.8. 1,5-Dihydroxy-2-methoxyanthraquinone (25b).[68] To a stirring solution of 2-bromo-5-acetoxynaphthoquinone **22** (509 mg, 1.73 mmol)[64,65] in toluene (6 mL) was added dropwise a solution of 1,2-dimethoxy-1-trimethylsilyloxy-1,3-butadiene **23a** (700 mg, 3.46 mmol)[62] in toluene (3 mL). The mixture was stirred at rt for 4 days. The residue was evaporated, dissolved in CH_2Cl_2, adsorbed on silica gel and purified by column chromatography, eluting with Et_2O/hexane (1:1), to afford **25b** (290 mg, 54%) as orange needles after crystallization from EtOAc/hexane: mp 227 °C; IR (KBr) 3464, 1624 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 4.03 (s, 3H), 7.16 (d, J=8.4 Hz, 1H), 7.30 (dd, J=1.1, 8.4 Hz, 1H), 7.65 (t, J=8.4 Hz, 1H), 7.83 (dd, J=1.1, 8.4 Hz, 1H), 7.86 (d, J=8.4 Hz, 1H), 12.84 (s, 1H), 13.07 (s, 1H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 188.4, 187.0, 162.7, 154.5, 153.1, 136.2, 133.3, 125.0, 124.8, 121.0, 119.2, 116.3, 115.9, 115.6, 56.4; EIMS m/z (rel intensity) 271 (MH^+, 18), 270 (M^+, 100); HMRS (EIMS) calcd for $C_{15}H_{10}O_5$ 270.0528, found 270.0518.

3.1.9. Methyl 2-methoxymethyl-3-butenoate (28b). To a stirred solution of methyl 2-hydroxy-3-butenoate (2 g, 17.2 mmol) in THF (25 mL) was added dropwise at 0 °C diisopropylethylamine (6.6 mL, 32.8 mmol) and chloromethylmethylether (3.9 mL, 51.6 mmol). The mixture was allowed to warm up to rt and stirred for 6 days, after which time it was diluted with Et_2O (40 mL), washed with 0.1 M HCl (30 mL), saturated aqueous $NaHCO_3$ (30 mL), brine (30 mL), dried over Na_2SO_4, and evaporated to afford a colorless oil (2.2 g, 80%), which was used without any further purification: IR (NaCl) 2964, 2900, 2830, 1762 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.4 (s, 3H), 3.75 (s, 3H), 4.64 (d, J=6.4 Hz, 1H), 4.70 (s, 2H), 5.32 (d, J=10.6 Hz, 1H), 5.46 (d, J=17.9 Hz, 1H), 5.82–5.94 (m, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 170.9, 132.3, 119.1, 95.0, 75.7, 55.8, 52.9; EIMS m/z (rel intensity) 160 (M^+, 0.5), 101 (24), 45 (100); HMRS (EIMS) calcd for $C_7H_{12}O_4$ 160.0735, found 160.0738.

3.1.10. 5-Acetoxy-1,4-dihydroxy-2-methoxyanthraquinone (30). To a stirring ice-cold solution of BTI (76 mg, 0.18 mmol) in dry CH_2Cl_2 (3 mL) was added dropwise a solution of 1-hydroxy-2-methoxy-5-acetoxyanthraquinone (**25a**) (50 mg, 0.16 mmol) in dry CH_2Cl_2 (2 mL) and diene **7a** (56 μL, 0.32 mmol). After 3 h at rt, the mixture was diluted with CH_2Cl_2 (20 mL), washed with saturated aqueous $NaHCO_3$ (10 mL), 1M H_3PO_4 (10 mL), brine (10 mL), dried over Na_2SO_4, filtered, and evaporated at rt. The residue was purified by column chromatography, eluting with hexane/EtOAc [(4:1)→(2:1)], to afford **30** (40 mg, 76%) as red needles. The same result was obtained without allyltrimethylsilane. **30**: mp 176–177 °C; IR (KBr) 3442, 1763, 1614, 1587 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 2.47 (s, 3H), 4.00 (s, 3H), 6.70 (s, 1H), 7.44 (dd, J=1.5, 7.9 Hz, 1H), 7.81 (t, J=7.9 Hz, 1H), 8.34 (dd, J=1.5, 7.9 Hz, 1H), 13.43 (s, 1H), 13.43 (s, 1H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 186.3, 183.8, 169.7, 161.1, 157.4, 150.6, 150.2, 135.1, 134.6, 130.5, 125.6, 125.4, 112.0, 107.4, 106.6, 56.6, 21.2; EIMS m/z (rel intensity) 328 (MH^+, 28); HMRS (LSIMS) calcd for $C_{17}H_{12}O_7$ 328.0583, found 328.0572.

3.1.11. 5-Acetoxy-1,6-dihydro-6-methoxy-6-(2,2,2-trifluoroethoxy)-1-oxoanthraquinone (31). To a stirring ice-cold solution of BTI (90 mg, 0.21 mmol) in CF_3CH_2OH (3 mL) was added dropwise a solution of 5-acetoxy-1-hydroxy-2-methoxyanthraquinone (**25a**) (60 mg, 0.19 mmol) in dry CF_3CH_2OH (2 mL). After 2 min, the diene **7a** (47 μL, 0.27 mmol) was added dropwise. After 30 min, an another portion of diene **7a** (47 μL, 0.27 mmol) was added dropwise. After 1 h at rt, the mixture was diluted with CH_2Cl_2 (20 mL), washed with saturated aqueous $NaHCO_3$ (10 mL), 1M H_3PO_4 (10 mL), brine (10 mL), dried over Na_2SO_4, filtered, and evaporated. The residue was purified by column chromatography, eluting with hexane/EtOAc (2:1), to afford **31** (3 mg, 4%): IR (NaCl) 1759, 1715, 1687 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 2.38 (s, 3H), 3.36 (s, 3H), 3.86–4.01 (m, 2H), 6.00 (d, J=10.3 Hz, 1H), 6.24 (d, J=10.3 Hz, 1H), 7.35 (d, J=7.9 Hz, 1H), 7.68 (d, J=7.9 Hz, 1H), 7.95 (d, J=7.9 Hz, 1H); LSIMS m/z (rel intensity) 433 (MNa^+, 85), 411 (MH^+, 30).

3.1.12. 2,5,9,10-Tetramethoxyanthracenol (32). A mixture of **25a** (173 mg, 0.55 mmol), Ag_2O (514 mg, 2.22 mmol) and benzyl bromide (196 μL, 1.65 mmol) in $CHCl_3$ (8 mL) was heat to reflux for 4 h. The mixture was cooled down to rt, filtered through Celite and evaporated. The residue was submitted to column chromatography, eluting with CH_2Cl_2/Et_2O (50:1), to give 5-acetoxy-1-benzyloxy-2-methoxy-anthraquinone (150 mg, 68%): mp 146.7–147.4 °C; IR (KBr) 1759, 1675 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 2.48 (s, 3H), 3.92 (s, 3H), 5.11 (s, 2H), 7.21 (d, J=8.8 Hz, 1H), 7.33–7.45 (m, 4H), 7.66 (dd, J=1.5, 7.9 Hz, 2H), 7.73 (t, J=7.9 Hz, 1H), 8.04 (d, J=8.5 Hz, 1H), 8.20 (dd, J=1.5, 7.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 181.7, 180.9, 169.5, 158.8, 149.5, 147.5, 137.0, 136.8, 134.4, 129.0, 128.6, 128.2, 128.0, 127.7, 126.6, 125.6, 125.2, 124.2, 116.1, 75.0, 56.1, 21.1; EIMS m/z (rel intensity) 402 (M^+, 6), 91 (Bn^+, 100); HMRS (EIMS) calcd for $C_{24}H_{18}O_6$ 402.1103, found 402.1107.

To a stirred solution of this anthraquinone in THF (6 mL) and H_2O (2.5 mL) were added n-Bu_4NBr (35 mg, 5%) and $Na_2S_2O_4$ (4×555 mg, 12.75 mmol) portionwise over 1 h. The mixture was then treated with aqueous KOH (3.5 mL, 42.5 mmol) and stirred for 15 min, after which time Me_2SO_4 (4 mL, 42.5 mmol) was added dropwise. The reaction mixture was stirred at rt overnight. It was then diluted in

CH_2Cl_2 (20 mL) and quenched with H_2O (50 mL). The aqueous phase was extracted with CH_2Cl_2 (3×40 mL). The combined organic layers were washed with brine (80 mL), dried over Na_2SO_4, and evaporated. The crude mixture was purified by column chromatography, eluting with hexane/EtOAc [(5:1)→(1:1)], to give 1-benzyloxy-2,5,9,10-tetramethoxyanthracene (303 mg, 35%): mp 130–131 °C; IR (KBr) 2931, 2831 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 3.95 (s, 3H), 4.01 (s, 3H), 4.02 (s, 3H), 4.08 (s, 3H), 5.08 (s, 2H), 6.74 (d, J=7.6 Hz, 1H), 7.32–7.48 (m, 5H), 7.68 (m, 2H), 8.12 (d, J=8.9 Hz, 1H), 8.27 (dd, J=1.9, 9.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 156.2, 149.6, 149.2, 146.4, 140.3, 138.1, 129.0, 128.8, 128.2, 127.7, 125.3, 124.2, 121.8, 120.7, 116.8, 115.5, 115.1, 103.1, 76.6, 63.4, 63.3, 57.0, 56.0; LSIMS *m/z* (rel intensity) 404 (M^+, 33), 405 (MH^+, 17), 313 (M-Bn^+, 100); HMRS (LSIMS) calcd for $C_{25}H_{24}O_5$ 404.1624, found 404.1618.

A solution of this anthracene (238 mg, 0.70 mmol) in THF (23 mL) was stirred for 24 h in the presence of 10% wt Pd-C (87 mg) under an atmosphere of hydrogen. This mixture was filtered through Celite, and evaporated to give a residue, which was purified by column chromatography, eluting with hexane/EtOAc (4:1), to give **32** (67 mg, 30%): mp 134 °C; IR (KBr) 3341, 2934, 2838 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 3.99 (s, 3H), 4.05–4.07 (m, 9H), 6.70 (d, J=7.6 Hz, 1H), 7.26–7.39 (m, 2H), 7.72 (d, J=8.9 Hz, 1H), 7.94 (d, J=9.6 Hz, 1H), 9.56 (s, 1H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 156.4, 149.8, 145.2, 141.7, 139.5, 126.3, 125.6, 123.5, 117.1, 116.8, 116.4, 114.8, 113.5, 102.9, 63.7, 63.3, 57.2, 56.0; LSIMS *m/z* (rel intensity) 314 (M^+, 33) 337 (MNa^+, 17), 299 (M-Me^+, 100).

3.1.13. 1,2,5-Trimethoxyanthraquinone (33).[76] To a stirring ice-cold solution of **33** (50 mg, 0.16 mmol) in CH_2Cl_2 (10 mL) was added BTI (75 mg, 0.17 mmol) as a solid, in one portion. After 2 min, the diene **7a** (33 μL, 0.19 mmol) in solution in CH_2Cl_2 (200 μL) was added dropwise. The mixture was stirred at rt for 1 h, after which time it was diluted with CH_2Cl_2 (20 mL), washed with saturated aqueous $NaHCO_3$ (2×20 mL), 1M H_3PO_4 (20 mL), brine (20 mL), dried over Na_2SO_4, and evaporated at rt. The resulting brownish oil was purified by column chromatography, eluting with hexane/Et_2O (1:1), to furnish **33** (21 mg, 48%) as a red solid: mp 186–188 °C; IR (KBr) 1663 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 3.88 (s, 3H), 4.03 (s, 3H), 4.05 (s, 3H), 6.49 (d, J=10.3 Hz, 1H), 7.13 (d, J=7.4 Hz, 1H), 7.57 (dd, J=8.1, 8.1 Hz, 1H), 7.98 (dd, J=1.0, 8.4 Hz, 1H), 8.10 (d, J=10.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 181.0, 178.7, 160.0, 157.1, 152.8, 140.9, 133.8, 129.8, 126.4, 122.5, 119.0, 118.1, 117.5, 111.6, 64.1, 62.7, 54.4; LSIMS *m/z* (rel intensity) 298 (M^+, 21), 299 (MH^+, 97), 321 (MH^+, 100).

3.1.14. 2-Chloro-5-hydroxy-6-methoxymethylnaphthoquinone (36b). To a solution of *i*-Pr_2NH (184 μL, 1.3 mmol) in THF (1 mL) was added dropwise at −78 °C *n*-BuLi (576 μL, 1.44 mmol). After 40 min at this temperature, the mixture was allowed to warm up to rt for 10 min, and then cooled down again to −78 °C. To this solution of LDA was added dropwise methyl 2-methoxymethyl-3-butenoate (**28b**, 200 mg, 1.25 mmol) in solution in THF (1 mL). After 40 min, TMSCl (793 μL, 6.25 mmol) in solution in THF (1 mL) was added and the resulting mixture was stirred for 1 h. The THF solvent was then removed by evaporation and replaced with pentane. The mixture was filtered through Celite and evaporated to furnish a *ca*. 3:1 mixture of **23b** and **28b**, as estimated by ^1H NMR analysis. A solution of this mixture thus estimated to contain 114 mg of **23b** (0.49 mmol) in toluene (2 mL) was added dropwise to a stirred solution of commercial 2,5-dichlorobenzoquinone (44 mg, 0.25 mmol) in toluene (1 mL). The reaction mixture was stirred at rt for 24 h, after which time the solvent was evaporated, the residue was diluted in CH_2Cl_2 and treated with silica gel for 6 h. After filtration and extensive trituration of the silica gel with CH_2Cl_2, evaporation gave a red solid, which was purified by column chromatography, eluting with light petroleum/Et_2O (4:1), to give **36b** (14.7 mg, 22%): IR (NaCl) 1668, 1634, 1584 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 3.53 (s, 3H), 5.36 (s, 2H), 7.18 (s, 1H), 7.40 (d, J=8.5 Hz, 1H), 7.72 (d, J=8.5 Hz, 1H), 12.22 (s, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 188.2, 152.5, 152.3, 145.4, 135.6, 124.0, 122.3, 119.7, 119.2, 116.0, 95.1, 56.8; EIMS *m/z* (rel intensity) 268 (M^+, 100), 237 (27); HMRS (EIMS) calcd for $C_{12}H_9O_5Cl$ 268.0138, found 268.0140.

3.1.15. 2-Methoxy-1-(tripropylsilyloxy)-naphthalene (38). To a stirred solution of 2-methoxynaphthol **6a** (500 mg, 2.87 mmol)[42] in CH_2Cl_2 (30 mL) was added dropwise at 0 °C the triethylamine (0.5 mL, 3.37 mmol). After stirring for 30 min, Pr_3SiCl (609 mg, 3.16 mmol) was added dropwise at 0 °C. The mixture was stirred at rt for 100 min, after which time it was diluted with CH_2Cl_2 (20 mL), washed with 1M H_3PO_4 (30 mL), water (30 mL), dried over Na_2SO_4, and evaporated at rt to furnish pure **38** in quantitative yield (1 g): IR (NaCl) 3062, 2952, 2865, 1626 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.72 (m, 6H), 0.87 (m, 9H), 1.34 (m, 6H), 3.81 (s, 3H), 7.15 (d, J=8.1 Hz, 1H), 7. 23 (m, 1H), 7.34 (m, 2H), 7.63 (d, J=8.1 Hz, 1H), 7.99 (dd, J=8.2, 1.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 145.4, 139.0, 129.8, 128.8, 127.5, 125.3, 123.8, 121.9, 121.1, 114.5, 56.3, 18.5, 17.6, 16.8; EIMS *m/z* (rel intensity) 330 (M^+, 41), 272 (100); HMRS (EIMS) calcd for $C_{20}H_{30}O_2Si$ 330.2015, found 330.2012.

3.1.16. 2-Chloro-5-hydroxy-6-methoxy-3-tripropylsilanyl-[1,4]naphthoquinone (39). To a stirred ice-cooled solution of naphthoquinone **36a** (40 mg, 0.17 mmol) in DMF (5 mL) was added triethylamine (47 μL, 0.34 mmol). After stirring for 30 min, Pr_3SiCl (74 μL, 0.34 mmol) was added dropwise at 0 °C. The mixture was stirred at rt for 90 min, after which time it was diluted with water (20 mL). The aqueous phase was extracted with ether (3×20 mL), and the combined organic layers were dried over Na_2SO_4, and evaporated at rt. The residue was purified by column chromatography, eluting with hexane/Et_2O (2:1), to afford **39** (13.3 mg, 20%): IR (NaCl) 3408, 2925, 2854, 1668, 1632 cm^{-1}; ^1H NMR (CDCl3, 300 MHz) δ 0.87 (m, 6H, CH_2-Pr), 1.04 (m, 9H, CH_3-Pr), 1.62 (m, 6H, CH_2-Pr), 4.00 (s, 3H, OCH_3), 7.08 (d, J=8.5 Hz, 1H, H-4), 7.75 (d, J=8.5 Hz, 1H, H-3), 12.43 (s, 1H, OH); ^{13}C NMR (CDCl3, 75.5 MHz) δ 188.2, 176.1, 154.6, 152.4, 148.0, 144.9, 123.1, 121.9, 115.0, 114.5, 56.4, 29.8, 21.3, 14.3; EIMS *m/z* (rel intensity) 280 (M^+, 100), 265 [(M-Pr_3)$^+$, 65].

3.1.17. 2-Chloro-6-methoxy-5-triethylsilanyloxy-[1,4]-naphthoquinone (40). A solution of naphthoquinone **36a** (40 mg, 0.17 mmol), Ag_2O (158 mg, 0.26 mmol) and Et_3-SiCl (42.8 μL, 0.26 mmol) in $CHCl_3$ (5 mL) was refluxed for 12 h. The mixture was filtered through Celite and evaporated at rt to afford quantitatively **40** (71 mg), which was used without any further purification: ^{1}H NMR (CDCl3, 300 MHz) δ 0.81 (m, 6H), 0.97 (m, 9H), 3.90 (s, 3H), 7.01 (s, 1H), 7.07 (d, J=8.7 Hz, 1H), 7.83 (d, J=8.7 Hz, 1H); ^{13}C NMR (CDCl3, 75.5 MHz) δ 180.9, 175.5, 156.5, 145.4, 143.6, 136.7, 123.9, 122.1, 121.0, 113.1, 54.7, 5.7, 4.6.

3.1.18. 2-(4-Hydroxy-3-methoxynaphtalen-1-yl)-3-methylbut-2-enal (42). 3-Benzyl-5-(2-hydroxyethyl)-4-methylthiazolium chloride (**41**, 1.4 mg, 0.005 mmol) and Et_3N (4 μL, 0.03 mmol) were successively added to a solution of **5b** (25 mg, 0.098 mmol) in absolute ethanol (2 mL). The reaction mixture was heated at 80 °C for 2.5 h, after which time ethanol was evaporated. The residue was then diluted with CH_2Cl_2 (10 mL), washed with saturated aqueous Na_2CO_3 (10 mL), brine (20 mL), dried over Na_2SO_4, and evaporated. The resulting crude oil was purified by column chromatography, eluting with light petroleum/Et_2O (1:1), to give **42** as a light red gum (23 mg, 90%): IR (NaCl) 3408, 2928, 1694, 1350 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.71 (s, 3H, CH_3), 2.47 (s, 3H, CH_3), 3.97 (s, 3H, OCH_3), 6.03 (s, 1H, H-3), 6.94 (s, 1H), 7.30 (d, J=8.3 Hz, 1H), 7.42 (m, 2H), 8.17 (d, J=7.6 Hz, 1H), 10.36 (s, 1H, CHO); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 190.7, 158.7, 140.8, 139.5, 137.1, 128.0, 125.8, 125.4, 124.8, 124.7, 124.3, 121.8, 115.0, 57.2, 25.3, 19.9; LSIMS m/z (rel intensity) 279 (MNa^+, 28); 256 (M^+, 100); HMRS (LSIMS) calcd for $C_{16}H_{16}O_3$ 256.1099, found 256.1101.

3.1.19. 5-(2-Methoxy-1-oxo-1,2-dihydro-naphthalen-2-yl)-4-methyl-trimethylsilanyloxy-pent-3-enenitrile (43). To a stirred solution of **5b** (150 mg, 0.59 mmol), KCN (3 mg, 0.08 mmol) and 18-crown-6 (8 mg, 0.05 mmol) in CH_2Cl_2 (6 mL) was added dropwise at 0 °C Me_3SiCN (94 μl, 0.71 mmol). The reaction mixture was stirred at 0 °C for 45 min, after which time it was evaporated and directly submitted to column chromatography, eluting with light petroleum/Et_2O (2:1), to give **43** as a pale yellow oil (77 mg, 37%): IR (NaCl) 2935, 2360, 1686 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.16 (s, 9H, TMS), 1.67 (s, 3H, β-CH_3), 1.79 (s, 3H, β-CH_3), 2.46 (s, 2H, γ-CH_2), 2.50 (s, 2H, γ-CH_2), 3.17 (s, 3H, OCH_3), 3.18 (s, 3H, OCH_3), 4.93 (d, J=8.5 Hz, 1H, CHCN), 4.99 (d, J=7.9 Hz, 1H, CHCN), 5.26 (d, J=8.5 Hz, 1H, H-α), 5.32 (d, J=7.3 Hz, 1H, H-α), 6.09 (d, J=10.1 Hz, 1H, H-4), 6.79 (d, J=10.1 Hz, 1H, H-3), 7.24 (d, J=7.6 Hz, 1H, H-5), 7.37 (t, J=7.6 Hz, 1H, H-7), 7.59 (t, J=7.6 Hz, 1H, H-6), 8.02 (d, J=7.6 Hz, 1H, H-8); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 200.0, 137.1, 136.9, 135.0, 135.0, 134.9, 134.9, 129.9, 129.3, 129.1, 128.3, 126.9, 126.8, 125.8, 82.3, 57.9, 53.4, 48.6, 48.3, 18.7, 18.5, -0.4; EIMS m/z (rel intensity) 355 (M^+, 7), 173 (100); HMRS (EIMS) calcd for $C_{20}H_{25}NO_3Si$ 355.1603, found 355.1601.

3.1.20. 9b-Hydroxy-3a-methoxy-2-methyl-3a,9b-dihydro-3*H*-cyclopenta[*a*]naphthalene-1-carbaldehyde (46)—treatment of enal 5b with tetra-*n*-butylammonium oxido-λ^3-iodane (45). Tetrabutylammonium fluoride (270 μL in THF, 0.3 mmol) was added to a suspension of 1-hydroxy-1,2-benziodoxol-3(1*H*)-one (80 mg, 0.3 mmol) in THF (2 mL). To the resulting colorless solution was added dropwise at rt a solution of enal **5b** (63 mg, 0.25 mmol) in THF (2 mL). The resulting mixture gradually became blue and then black. After 2 h, it was diluted with Et_2O (10 mL), washed with saturated aqueous $NaHCO_3$ (2×5 mL), 10% HCl (10 mL), brine (10 mL), dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography, eluting with light petroleum/acetone (4:1), to give **46** (20 mg, 32%): IR (KBr) 3430, 2930, 1680, 1608, 753 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 2.19 (s, 3H, β-CH_3), 2.63 (d, J=17.4 Hz, 1H, γ-CH_2), 3.12 (d, J=17.4 Hz, 1H, γ-CH_2), 3.17 (s, 3H, OCH_3), 3.48 (s, 1H, OH), 5.73 (d, J=9.8 Hz, 1H, H-3), 6.73 (d, J=9.8 Hz, 1H, H-4), 7.25–7.28 (m, 1H), 7.32–7.36 (m, 1H), 7.95 (d, J=7.6 Hz, 1H), 9.51 (s, 1H, CHO); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 189.4, 160.9, 136.6, 136.3, 132.7, 130.4, 128.7, 128.1, 127.3, 127.1, 126.9, 80.9, 80.2, 52.3, 49.8, 16.4; EIMS m/z (rel intensity) 256 (M^+, 55), 224 (100), 195 (73); HMRS (EIMS) calcd for $C_{16}H_{16}O_3$ 256.1099, found 256.1103.

3.1.21. Treatment of epoxide 48 with zinc. A suspension of **48** (17 mg, 0.06 mmol), zinc powder (20 mg, 0.31 mmol), ammonium chloride (10 mg, 0.18 mmol) in a 4:1 mixture of EtOH/H_2O (7 mL) was heated at 80 °C for 20 min, after which time it was filtered. The filtration pellet was rinsed with Et_2O, and the filtrates were washed with brine (10 mL), dried over Na_2SO_4 and evaporated at rt. The residue was purified by PLC, eluting with light petroleum/Et_2O (2:3), to afford **46** (17 mg, 14%).

3.1.22. Treatment of epoxide 48 with SmI_2. To a slurry suspension of Sm powder (84 mg, 0.55 mmol) and molecular sieves 4 Å in THF (4 mL) was added at rt diiodomethane (30 μL, 0.37 mmol). The resulting olive-green slurry was stirred for 2 h, after which time the deep blue solution of SmI_2 thus formed was cooled to −90 °C, and treated with a solution of **48** (100 mg, 0.37 mmol) in THF/MeOH (4:1, 2.5 mL). The resulting brown mixture was stirred for 10 min at −90 °C, quenched at this temperature with H_2O and then warmed to rt. The mixture was then further diluted in H_2O and extracted four times with Et_2O (4×10 mL). The combined organic layers were washed with saturated aqueous sodium thiosulfate (5 mL) and H_2O (2×5 mL), dried over Na_2SO_4, and evaporated to give a residue which was purified by column chromatography, eluting with light petroleum/Et_2O (1:1), to furnish **46** (13 mg, 14%).

3.1.23. Epoxide 48. To a suspension of **5b** (120 mg, 0.47 mmol) and Na_2CO_3 (49.8 mg, 0.47 mmol) in a mixture of EtOH/H_2O (4:1, 7 mL) was added dropwise at 0 °C a 30% aqueous solution of H_2O_2 (400 μL). After the addition was complete, the ice-bath was removed and the mixture was stirred at rt for 3 h. The mixture was then evaporated, and the residue was diluted with CH_2Cl_2 (10 mL), washed with H_2O (10 mL), brine (10 mL), dried over Na_2SO_4, and evaporated at rt. The resulting oil was purified by column chromatography, eluting with ligth petroleum/Et_2O (2:3), to afford the epoxide **48** as a 1:1 mixture of diastereosomers (85 mg, 67%, light yellow oil). These isomers were separated by PLC, eluting with light petroleum/acetone (3:1), to furnish **48a** as the fastest moving isomer and **48b**.

48a: ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.42 (s, 3H, γ-CH_3), 2.10 (d, J=14.6 Hz, 1H), 2.31 (d, J=14.6 Hz, 1H), 3.18 (s, 3H, OCH_3), 6.13 (d, J=10.0 Hz, 1H, H-3), 6.72 (d, J=10.0 Hz, 1H, H-4), 7.24 (d, J=7.9 Hz, 1H), 7.39 (m, 1H), 7.60 (t, J=1.5, 7.8 Hz, 1H), 7.99 (d, J=8.5 Hz, 1H), 9.28 (d, J=5.2 Hz, 1H, CHO); EIMS *m/z* (rel intensity) 272 (M^+, 15), 157 (100). **48b**: ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.48 (s, 3H, γ-CH_3), 1.88 (d, J=14.6 Hz, 1H), 2.20 (d, J=14.6 Hz, 1H), 3.18 (s, 3H, OCH_3), 6.18 (d, J=10.0 Hz, 1H, H-3), 6.82 (d, J=10.0 Hz, 1H, H-4), 7.24 (d, J=6.1 Hz, 1H), 7.39 (m, 1H), 7.60 (t, J=1.5, 7.8 Hz, 1H), 8.03 (d, J=8.5 Hz, 1H), 9.37 (d, J=4.9 Hz, 1H, CHO); EIMS *m/z* (rel intensity) 272 (M^+, 15), 157 (100).

3.1.24. β-Hydroxyaldehyde 50 and β-epoxyaldehyde 51. $NaBH_4$ (38 mg, 1.00 mmol) was added portionwise to a solution of diphenyldiselenide (160 mg, 0.51 mmol) in absolute EtOH (2 mL). Once the gas evolution ceased, the yellow solution was cooled down to 0 °C in an ice-water bath, treated with AcOH (9.8 μL), and then added at rt to a solution of the epoxide **48** (90 mg, 0.33 mmol) in EtOH (2 mL). The reaction mixture turned to blue and was stirred for 2.5 h, after which time it was diluted with EtOAc and bubbled with oxygen gas for several minutes to convert the remaining selenium reagent to $(PhSe)_2$. The organic layer was washed with brine (10 mL), dried over Na_2SO_4, and evaporated at rt. The resulting crude oil was purified by column chromatography, eluting with light petroleum/acetone (3:1), to furnish **50** (42 mg, 46%) and **51** (32 mg, 35%). **50**: IR (KBr) 3447, 2933, 1716 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.39 (s, 3H, β-CH_3), 2.40 (d, J=14.9 Hz, 1H, γ-CH_2), 2.54 (d, J=2.1 Hz, 1H, H-α), 2.58 (d, J=15.5 Hz, 1H, γ-CH_2), 3.08 (s, 3H, OCH3), 3.88 (s, 1H, β-OH), 4.08 (s, 1H, 1-OH), 5.75 (d, J=9.8 Hz, 1H, H-3), 6.73 (d, J=9.8 Hz, 1H, H-4), 7.16 (d, J=7.1 Hz, 1H), 7.26–7.30 (m, 2H), 7.70 (d, J=7.5 Hz, 1H), 9.90 (d, J=2.5 Hz, 1H, CHO); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 203.3, 137.7, 131.2, 129.9, 129.1, 128.6, 128.2, 127.8, 125.1, 82.4, 80.3, 78.1, 66.3, 54.8, 52.0, 28.2; LSIMS *m/z* (rel intensity) 297 (MNa^+, 100); HMRS (LSIMS) calcd for $C_{16}H_{18}O_4Na$ 297.1103, found 297.1106. **51:** mp 129.0–130 °C; IR (KBr) 3408, 2924, 1716 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.33 (s, 3H, β-CH_3), 2.24 (d, J=14.3 Hz, 1H, γ-CH_2), 2.47 (d, J=14.3 Hz, 1H, γ-CH_2), 3.03 (s, 3H, OCH3), 3.35 (s, 1H, 1-OH), 5.61 (d, J=10.0 Hz, 1H, H-3), 6.93 (d, J=9.8 Hz, 1H, H-4), 7.25 (m, 1H), 7.34 (m, 2H), 7.80 (d, J=7.0 Hz, 1H), 8.81 (s, 1H, CHO); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 193.9, 134.6, 133.1, 131.4, 130.0, 128.9, 127.6, 127.5, 125.4, 84.9, 77.5, 77.0, 72.3, 51.7, 46.1, 16.1; EIMS *m/z* (rel intensity) 272 (M^+, 5), 174 (100); HMRS (EIMS) calcd for $C_{16}H_{16}O_4$ 272.1048, found 272.1052.

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References and notes

1. Krohn, K.; Rohr, J. *Top. Curr. Chem.* **1997**, *188*, 127–195.
2. Rohr, J.; Thiericke, R. *Nat. Prod. Rep.* **1992**, *9*, 103–137.
3. Guingant, A.; Barreto, M. M. *Tetrahedron Lett.* **1987**, *28*, 3107–3110.
4. Larsen, D. S.; O'Shea, M. D. *J. Chem. Soc. Perkin Trans 1* **1995**, 1019–1028.
5. Larsen, D. S.; O'Shea, M. D.; Brooker, S. *Chem. Comm.* **1996**, 203–204.
6. Krohn, K.; Khanbabaee, K. *Liebigs Ann. Chem.* **1994**, 1109–1112.
7. Krohn, K.; Khanbabaee, K.; Micheel, J. *Liebigs Ann.* **1995**, 1529–1537.
8. Carreño, C. M.; Urbano, A.; Di Vitta, C. *Chem. Comm.* **1999**, 817–818.
9. Kim, K.; Boyd, V. A.; Sobti, A.; Sulikowski, G. A. *Isr. J. Chem.* **1997**, *37*, 3–22.
10. Matsumoto, T.; Sohma, T.; Yamaguchi, H.; Kurata, S.; Suzuki, K. *Tetrahedron* **1995**, *51*, 7347–7360.
11. Boyd, V. A.; Sulikowski, G. A. *J. Am. Chem. Soc.* **1995**, *117*, 8472–8473.
12. Landells, J. S.; Larsen, D. S.; Simpson, J. *Tetrahedron Lett.* **2003**, *44*, 5193–5196.
13. Matsuo, G.; Miki, Y.; Nakata, M.; Matsumura, S.; Toshima, K. *Chem. Commun.* **1996**, 225–226.
14. Brown, P. M.; Thomson, R. H. *J. Chem. Soc. Perkin Trans. 1* **1976**, *1976*, 997–1000.
15. Mitchell, A. S.; Russell, R. A. *Tetrahedron* **1997**, *53*, 4387–4410.
16. Mal, D.; Roy, H. N.; Hazra, N. K.; Adhikari, S. *Tetrahedron* **1997**, *53*, 2177–2184.
17. Katsuura, K.; Snieckus, V. *Can J. Chem.* **1987**, *65*, 124–130.
18. Katsuura, K.; Snieckus, V. *Tetrahedron Lett.* **1985**, *26*, 9–12.
19. Uemura, M.; Nishikawa, N.; Take, K.; Ohnishi, M.; Hirotsu, K.; Higushi, T.; Hayashi, Y. *J. Org. Chem.* **1983**, *48*, 2349–2356.
20. Gordon, D. M.; Danishefsky, S. J. *J. Org. Chem.* **1992**, *57*, 7052–7055.
21. Matsumoto, T.; Sohma, T.; Yamaguchi, H.; Kurata, S.; Suzuki, K. *Synlett* **1995**, 263–266.
22. Chuang, C.-P.; Wang, S.-V. *Tetrahedron Lett.* **1994**, *35*, 4365–4366.
23. Kalogerakis, A.; Groth, U. *Org. Lett.* **2003**, *5*, 843–844.
24. Yamaguchi, M.; Okuma, T.; Horiguchi, A.; Ikeura, C.; Minami, T. *J. Org. Chem.* **1992**, *57*, 1647–1649.
25. Kraus, G. A.; Wan, Z. *Tetrahedron Lett.* **1997**, *38*, 6509–6512.
26. Sezaki, M.; Hara, T.; Ayukawa, S.; Takeuchi, T.; Okami, Y.; Hamada, M.; Nagatsu, T.; Umezawa, H. *J. Antibiot.* **1968**, *21*, 91–97.
27. Sezaki, M.; Kondo, S.; Maeda, K.; Umezawa, H.; Ohno, M. *Tetrahedron* **1970**, *26*, 5171–5190.
28. Okazaki, T.; Kitahara, T.; Okami, Y. *J. Antibiot.* **1975**, *28*, 176–184.

29. Nagatsu, T.; Ayukawa, S.; Umezawa, K. *J. Antibiot.* **1968**, *21*, 354–357.
30. Ayukawa, S.; Takeuchi, T.; Sezaki, M.; Hara, T.; Umezawa, K.; Nagatsu, T. *J. Antibiot.* **1968**, *21*, 350–353.
31. Hayaishi, O.; Okuno, S.; Fujisawa, H. *Biochem. Biophys. Res. Commun.* **1970**, *39*, 643–650.
32. Nozaki, M.; Okuno, S.; Fujisawa, H. *Biochem. Biophys. Res. Commun.* **1971**, *44*, 1109–1116.
33. Tanaka, N.; Okabe, T.; Tanaka, N.; Take, K.; Inouye, Y.; Nakamura, S.; Nakashima, H.; Yamamoto, Y.; Jpn *J. Cancer Res.* **1986**, *77*, 324–326.
34. Henkel, T.; Zeeck, A. *J. Antibiot.* **1990**, *43*, 830–837.
35. Sekisawa, R.; Iinuma, H.; Naganawa, H.; Hamada, S.; Takeuchi, T.; Yamaizumi, J.; Umezawa, K. *J. Antibiot.* **1996**, *49*, 487–490.
36. Nicolas, T. E.; Franck, R. W. *J. Org. Chem.* **1995**, *60*, 6904–6911.
37. Matsumoto, T.; Yamaguchi, H.; Hamura, T.; Tanabe, M.; Kuriyama, Y.; Suzuki, K. *Tetrahedron Lett.* **2000**, *41*, 8383–8387.
38. Matsumoto, T.; Yamaguchi, H.; Tanabe, M.; Yasui, Y.; Suzuki, K. *Tetrahedron Lett.* **2000**, *41*, 8393–8396.
39. Yamaguchi, H.; Konegawa, T.; Tanabe, M.; Nakamura, T.; Matsumoto, T.; Suzuki, K. *Tetrahedron Lett.* **2000**, *41*, 8389–8392.
40. Krohn, K.; Frese, P.; Flörke, U. *Chem. Eur. J.* **2000**, *6*, 3887–3896.
41. Quideau, S.; Looney, M. A.; Pouységu, L. *Org. Lett.* **1999**, *1*, 1651–1654.
42. Quideau, S.; Pouységu, L.; Oxoby, M.; Looney, M. *Tetrahedron* **2001**, *57*, 319–329.
43. Colvin, E. W.; Thom, I. G. *Tetrahedron* **1986**, *42*, 3137–3146.
44. Millefiori, S.; Gulino, A.; Casarin, M. *J. Chim. Phys.* **1990**, *87*, 317–330.
45. Chen, C.; Liu, Y.-Z.; Shia, K.-S.; Tseng, H.-Y. *Bioorg. Med. Chem.* **2002**, *12*, 2729–2732.
46. Verrax, J.; Cadrobbi, J.; Delvaux, M.; Jamison, J. M.; Gilloteaux, J.; Summers, J. L.; Taper, H. S.; Calderon, P. B. *Eur. J. Med. Chem.* **2003**, *38*, 451–457.
47. Fieser, L. F. *J. Biol. Chem.* **1940**, *133*, 391–396.
48. Narayanan, S.; Murthy, K.V.V.S.B.S.R.; Reddy, K. M.; Premchander, N. *Appl. Catal.* **2002**, *228*, 161–165.
49. Herrmann, W. A.; Haider, J. J.; Fischer, R. W. *J. Mol. Catal.* **1999**, *138*, 115–121.
50. Song, R.; Sorokin, A.; Bernadou, J.; Meunier, B. *J. Org. Chem* **1997**, *62*, 673–678.
51. Adam, W.; Herrmann, W. A.; Lin, J.; Saha-Möller, C. R.; Fischer, R. W.; Correia, J. D. G. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2475–2477.
52. Akai, S.; Kita, Y. *Org. Prep. Proc. Int.* **1998**, *30*, 605–629.
53. Kato, N.; Sugaya, T.; Mimura, T.; Ikuta, M.; Kato, S.; Kuge, Y.; Tomioka, S.; Kasai, M. *Synthesis* **1997**, 625–627.
54. Barret, R.; Daudon, M. *Tetrahedron Lett.* **1990**, *31*, 4871–4872.
55. Barret, R.; Daudon, M. *Synth. Commun.* **1990**, *20*, 2907–2912.
56. Saitz, B. C.; Valderrama, J. A.; Tapia, R.; Farina, F.; Paredes, C. *Synth. Commun.* **1992**, *22*, 955–960.
57. Bergeron, D.; Brassard, P. *Heterocycles* **1992**, *34*, 1835–1845.
58. Pelter, A.; Elgendy, S. M. A. *J. Chem. Soc. Perkin Trans. 1* **1993**, 1891–1896.
59. Bodajla, M.; Jones, G. R.; Ramsden, C. A. *Tetrahedron Lett.* **1997**, *38*, 2573–2576.
60. Mitchell, A. S.; Russell, R. A. *Tetrahedron Lett.* **1993**, *34*, 545–548.
61. Quideau, S.; Looney, M. A.; Pouységu, L.; Ham, S.; Birney, D. M. *Tetrahedron Lett.* **1999**, *40*, 615–618.
62. Savard, J.; Brassard, P. *Tetrahedron* **1984**, *40*, 3455–3464.
63. Bauman, J. G.; Hawley, R. C.; Rapoport, H. *J. Org. Chem.* **1985**, *50*, 1569–1573.
64. Heinzman, S. W.; Grunwell, J. R. *Tetrahedron Lett.* **1980**, *21*, 4305–4308.
65. Jung, M. E.; Hagenah, J. A. *J. Org. Chem.* **1983**, *48*, 5359–5361.
66. Savard, J.; Brassard, P. *Tetrahedron Lett.* **1979**, 4911–4914.
67. Palm, R.; Ohse, H.; Cherdron, H. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 994–1000.
68. Lee, S.-W.; Kuo, S.-C.; Chen, Z.-T.; Liu, Z.-S. *J. Nat. Prod.* **1994**, *57*, 1313–1315.
69. Kita, Y.; Takada, T.; Tohma, H. *Pure Appl. Chem.* **1996**, *68*, 627–630.
70. Takada, T.; Arisawa, M.; Gyoten, M.; Hamada, R.; Tohma, H.; Kita, Y. *J. Org. Chem.* **1998**, *63*, 7698–7706.
71. Braun, N. A.; Ousmer, M.; Bray, J. D.; Bouchu, D.; Peters, K.; Peters, E.-M.; Ciufolini, M. A. *J. Org. Chem.* **2000**, *65*, 4397–4408.
72. Kita, Y.; Gyoten, M.; Ohtsubo, M.; Tohma, H.; Takada, T. *Chem. Commun.* **1996**, 1481–1482.
73. Moriarty, R. M.; Prakash, O.; Duncan, M. P.; Vaid, R. K.; Musallam, H. A. *J. Org. Chem.* **1987**, *52*, 150–153.
74. Zhdankin, V. V.; Mullikin, M.; Tykwinski, R. R.; Berglund, B.; Caple, R.; Zefirov, N. S.; Koz'min, A. S. *J. Org. Chem.* **1989**, *54*, 2605–2608.
75. Zhdankin, V. V.; Tykwinski, R. R.; Berglund, B.; Mullikin, M.; Caple, R.; Zefirov, N. S.; Koz'min, A. S. *J. Org. Chem.* **1989**, *54*, 2609–2612.
76. Fischer, O.; Ziegler, H. *J. Prakt. Chem.* **1912**, *86*, 297–305.
77. Kita, Y.; Yakura, T.; Tohma, H.; Kikuchi, K.; Tamura, Y. *Tetrahedron Lett.* **1989**, *30*, 1119–1120.
78. McKillop, A.; McLauren, L.; Taylor, R. J. K. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2047–2048.
79. Hachisu, Y.; Bode, J. W.; Suzuki, K. *J. Am. Chem. Soc.* **2003**, *125*, 8432–8433.
80. Stetter, H. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 639–712.
81. Miller, B.; Lin, W.-O. *J. Org. Chem.* **1978**, *43*, 4441–4446.
82. Miller, B.; Saidi, M. R. *J. Am. Chem. Soc.* **1976**, 2227–2238.
83. Takuwa, A.; Naruta, Y.; Soga, O.; Maruyama, K. *J. Org. Chem.* **1984**, *49*, 1857–1864.
84. Corey, E. J.; Schimdt, G. *Tetrahedron Lett.* **1980**, *21*, 731–734.
85. Li, J.; Lan, J.; Liu, Z.; Li, Y. *J. Nat. Prod.* **1998**, *61*, 92–95.
86. Ochiai, M.; Nakanishi, A.; Suefuji, T. *Org. Lett.* **2000**, *2*, 2923–2926.
87. Ochiai, M. *Top. Curr. Chem.* **2003**, *224*, 5–68.
88. Singh, V.; Porichu, M. *Tetrahedron* **1996**, *52*, 7087–7126.
89. Molander, G. A.; Hahn, G. *J. Org. Chem.* **1986**, *51*, 2596–2599.
90. Miyashita, M.; Suzuki, T.; Hoshino, M.; Yoshikoshi, A. *Tetrahedron* **1997**, *33*, 12469–12486.