Total Synthesis of Angucyclines, Part 14[+]

Biomimetic Synthesis of the Racemic Angucyclinones of the Aquayamycin and WP 3688-2 Types

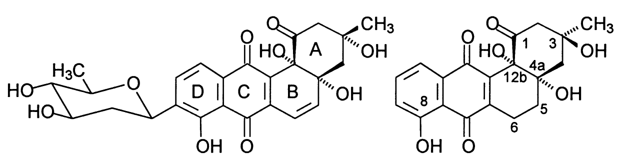
Karsten Krohn,* Peter Frese, and Ulrich Flörke[a]

Abstract: The first synthesis of the racemic 8-deoxy WP 3688-2 angucycline antibiotic (**3**), with characteristic *cis*-hydroxy groups at C-4a and C-12b, is reported. Key steps involve the coupling, mediated by samarium diiodide, of the bicyclic trione **37** to the tricyclic *cis*-diol **39**. Biomimetic aldol cyclization of the corresponding dione **41** gave a mixture of the tetracyclic *cis*- and *trans*-3,4a-diols **42** and **43**, which were oxidized by cerium ammonium nitrate to the quinones **45** and **3**. The synthetic compounds **45** and **3** corresponded in configuration to the angucycline antibiotics aquayamicin (**1**) and WP 3688-2 (**2**), respectively.

Keywords: aldol reactions · angucyclines · antibiotics · biomimetic synthesis · enediolates · samarium

Introduction

The angucycline antibiotics exhibit a great variety of interesting biological activities.[2, 3] They may be classified into the simpler representatives, with an aromatic ring B in the benz[*a*]anthracene skeleton, and the complex and relatively unstable[4] compounds with hydroaromatic rings A and B. Of particular importance are those derivatives bearing two hydroxy groups in a *cis* configuration at the ring junction positions C-4a and C-12b, such as aquayamycin (**1**) and WP 3688-2 (**2**).[5] Remarkably, the tertiary hydroxy group at C-12b does not originate from the polyketide chain, but



rather from atmospheric oxygen, as found by Rohr et al.[6] The *C*-glycosidic aquayamycin (**1**) is known as a potent inhibitor of tyrosine[7] and dopamine hydrolases.[8] In WP 3688-2 (**2**), the hydroxy groups at C-3 and C-4a are assumed to be in a *trans* configuration, as opposed to the more common *cis* arrangement in aquayamycin (**1**) and related congeners.[2, 3] From comparison of optical rotation values, WP 3688-2 (**2**)[9] is postulated to have opposite configurations at the relevant stereogenic centres at C-3, C-4a and C-12b, as was proven by X-ray analysis for sakyomicin A.[10]

The assembly of the SF 2315B ring system, which lacks the hydroxy group at C-12b in **2**, was achieved by Sulikowski et al.[11] and by our group,[12, 13] using strategies based on Diels–Alder reactions. Recently, we reported on an alternative approach of biomimetic type.[14] However, with the exception of model studies in which only parts of the systems were constructed,[15, 16] no synthesis has been reported of the entire benz[*a*]anthracene system, including the two hydroxy groups at C-4a and C-12b. We now disclose the first synthesis of racemic 8-deoxy WP 3688-2 (**3**) and also of 3,4a-*cis* compounds related to aquayamycin (**1**).

Results and Discussion

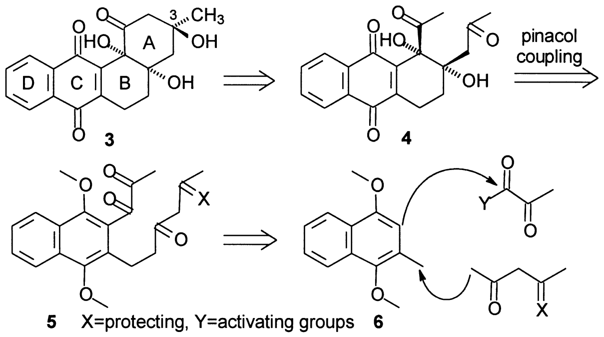
The background to the biomimetic-type synthesis of these aromatic polyketides, catalyzed by the polyketide synthetase II complex,[17] is detailed in the preceding communication.[14] The introduction of the additional hydroxy group at C-12b required a modified approach, as shown in the

[a] Prof. K. Krohn, Dipl.-Chem. P. Frese, Dr. U. Flörke
Fachbereich Chemie und Chemietechnik
der Universität Paderborn
Warburger Strasse 100, 33098 Paderborn (Germany)
Fax: (+49) 5251-603245
E-mail: kk@chemie.uni-paderborn.de

[+] Part 13: see ref. [1].

Supporting information for this article (experimental details and spectroscopic information for compounds **7**–**33**) is available on the WWW under http://www.wiley-vch.de/home/chemistry/ or from the author.

retrosynthetic analysis in Scheme 1. It was envisaged that a pinacol reaction would bring about the coupling of the opposed electrophilic carbonyl groups in **5** to give the *cis*-diol **4**. For the synthesis of **5**, appropriately functionalized and



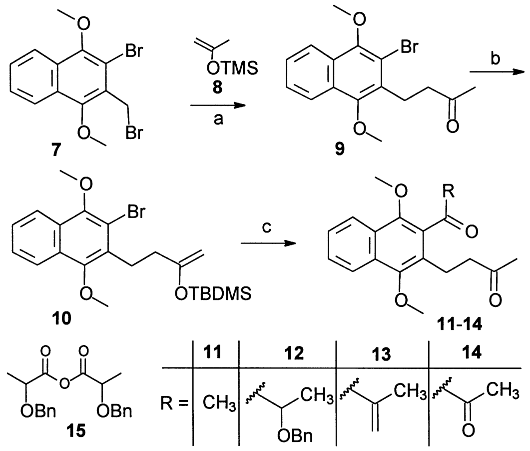
Scheme 1. Retrosynthetic scheme using a biomimetic strategy.

protected side chains would have to be attached to the naphthalene core **6**. The reductive conditions for the cyclization step would require hydroquinone dimethyl ethers such as **5** instead of the previously used quinones.[14] This synthetic scheme is appealing in its simplicity. However, during its execution, numerous surprises and obstacles were to emerge, revealing an interesting spectrum of reactions on the path to these unstable target compounds.

The pinacol reaction is an efficient method for the reductive coupling of dicarbonyl compounds.[18] Various metals such as magnesium,[19] low-valent titanium,[20] and several lanthanide halides[21] have successfully been employed for this purpose. More recently, samarium diiodide has emerged as the reagent of choice for high-yield, stereoselective pinacol couplings, as pioneered by Kagan et al.[22] and Molander.[23, 24] However, with a very few exceptions,[25–27] substrates with neighboring functional groups, as required for our purpose (see Scheme 1), have seldom been investigated. Therefore, prior to the conversion of the fully functionalized substrate, a number of model compounds were prepared in order to test the scope and limitations of the coupling reaction with α-functionalized ketones.

Abstract in German: *Die erste chemische Synthese des racemischen Angucyclin Antibiotikums 8-Desoxy WP 3688-2 (**3**), das sich durch cis-ständige Hydroxygruppen an C-4a und C-12b auszeichnet, wird vorgestellt. Eine Samariumdiiodid-vermittelte Kupplung des bicyclischen Trions **37** bildet den Schlüsselschritt beim Aufbau des tricyclischen cis-Diols **39**. Die anschließende biomimetische Aldol-Cyclization des entsprechenden Dions **41** lieferte ein Gemisch der tetracyclischen cis- und trans-3,4a-Diole **42** and **43**, die mit Ceriumammoniumnitrat zu den Chinonen **45** and **3** oxidiert wurden. Die syntheischen Verbindungen **45** and **3** entsprechen in ihrer Konfiguration den Angucyclin Antibiotika Aquayamicin (**1**) und WP 3688-2 (**2**).*

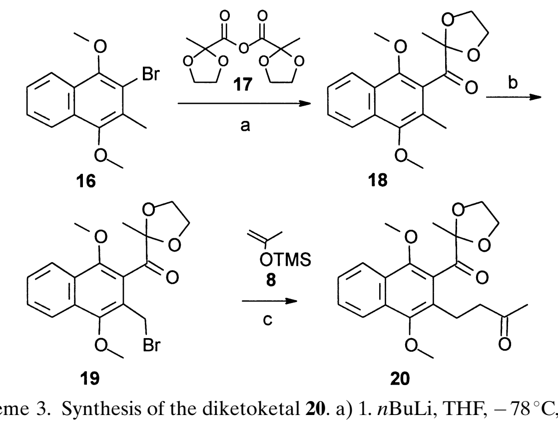
Preparation of starting materials: In principle, there are two possible reaction sequences for attachment of the side chains to give **5**: either the bottom side chain or the top one may be coupled on first. A C-3 ketone was coupled at the bottom benzylic bromide of the known dibromide **7**[28] to yield **9**, using the acetone silyl enol ether **8** (Scheme 2) and tetrabutylammonium difluorotriphenylstannate ($[nBu_4N][Ph_3SnF_2]$)[29] as



Scheme 2. Synthesis of model compounds for studying the pinacol reaction. a) **8**, $[nBu_4N][Ph_3SnF_2]$, TBAI, THF, −78 to 20 °C, 91%; b) TBDMSOTf, Et_3N, CH_2Cl_2, 87%; c) 1. *n*BuLi, THF, −78 °C, 2. electrophile (see text), 3. 2 N HCl.

the fluoride source to generate the enolate of **8**. To avoid reaction with *n*BuLi in the subsequent bromine–lithium exchange, the carbonyl group was protected as the silyl enol ether **10** (mixture of olefinic isomers). The lithium salt derived from the bromide **10** was then treated with a number of electrophiles in the form of acid anhydrides or chlorides (acetic acid anhydride, 2-benzyloxypropionic acid anhydride (**15**), methacrylic acid anhydride, pyruvic acid chloride) to yield the respective tetrasubstituted naphthalenes **11**–**14**.

For the synthesis of the ketal **20**, we explored the possibility of reversing the reaction sequence (Scheme 3). Thus, the monobromide **16** was lithiated and then treated with 2-methyl-[1,3]dioxolane-2-carboxylic acid anhydride (**17**) to afford



Scheme 3. Synthesis of the diketoketal **20**. a) 1. *n*BuLi, THF, −78 °C, 2. **17** (70%); b) NBS, CCl_4, 83%; c) $[nBu_4N][Ph_3SnF_2]$, TBAI, THF, −78 to 20 °C **8**, 49%.

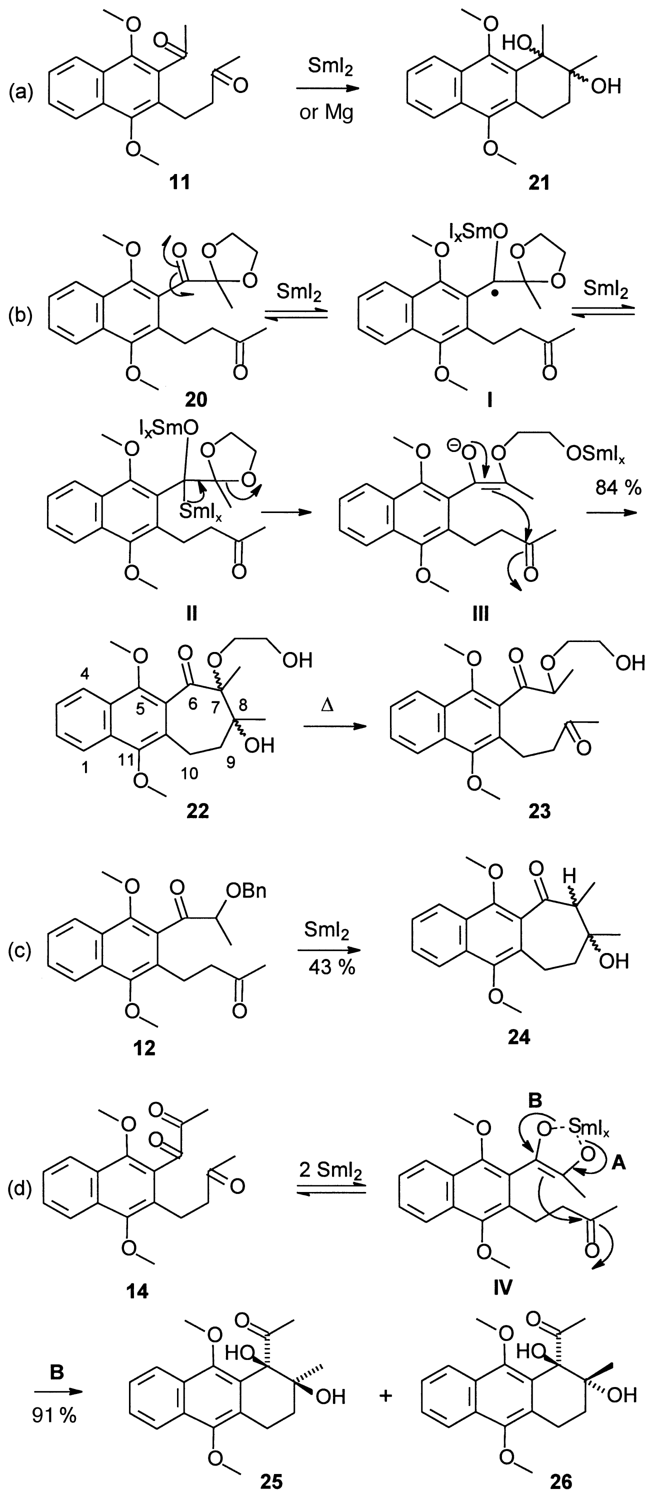
the acylated naphthalene **18**. Radical bromination with *N*-bromosuccinimide (NBS) at the aromatic methyl group proceeded in 83% yield without affecting the ketal group. The bromide **19** was then coupled with the silyl ether **8**, using tetrabutylammonium difluorotriphenylstannate as the mediator as described above, to yield the diketone **20**. Because of steric hindrance, the yields for the attachment of the second side chains were relatively low (39–49%, non-optimized) but sufficient quantities of the model compounds **11**–**14** and **20** were obtained to study the crucial pinacol coupling.

Cyclization of model compounds: For testing the pinacol coupling, the simplest model in this series was the dimethoxynaphthalene dione **11**. The reaction was performed with SmI_2[22, 24] and with activated magnesium[19] as single-electron transfer reagents. With SmI_2, the anticipated diol **21** was obtained as a single isomer in 27% yield, while with magnesium, 21% of a 1:1 mixture of isomers of **21** (unknown relative configuration) resulted (Scheme 4, path a). Some colored by-products indicated that the dimethoxynaphthalene core might have been attacked. However, in spite of the low yield, the experiment demonstrated that the coupling was possible in principle and that the study of more highly functionalized substrates would be worthwhile.

The next target was the ketal **20**. Interestingly, the reaction with SmI_2 at $-78\,^{\circ}C$ was much cleaner and only one major product was isolated, in 84% yield. The spectral data soon revealed that the dioxolane ring had been opened and that the seven-membered cyclization product **22** had been formed, as a single isomer of unknown relative stereochemistry. In an investigation of pinacol coupling with sugar-derived dialdehydes, Hanessian et al.[27] stated that "the presence of a ketal function next to one of the reducible aldehyde groups appears to cause side reactions." We propose that the major side reaction is the result of two successive electron transfer reactions via intermediates **I** and **II**, followed by β-elimination to **III** and aldol reaction to **22**, as outlined in Scheme 4, path b. This mechanism is analogous to the tetrahydropyran ring-opening reactions promoted by SmI_2[30] or the deoxygenation of α-oxygenated esters by β-elimination.[31] In NMR investigations, the seven-membered ring of **22**, on heating to $100\,^{\circ}C$ in DMSO, underwent retro-aldol ring-opening to **23**, further confirming the structure of **22**.

β-Elimination and formation of a seven-membered ring, giving **24**, was also the principal outcome of the SmI_2-mediated reaction of the α-benzyloxydione **12** (Scheme 4, path c).

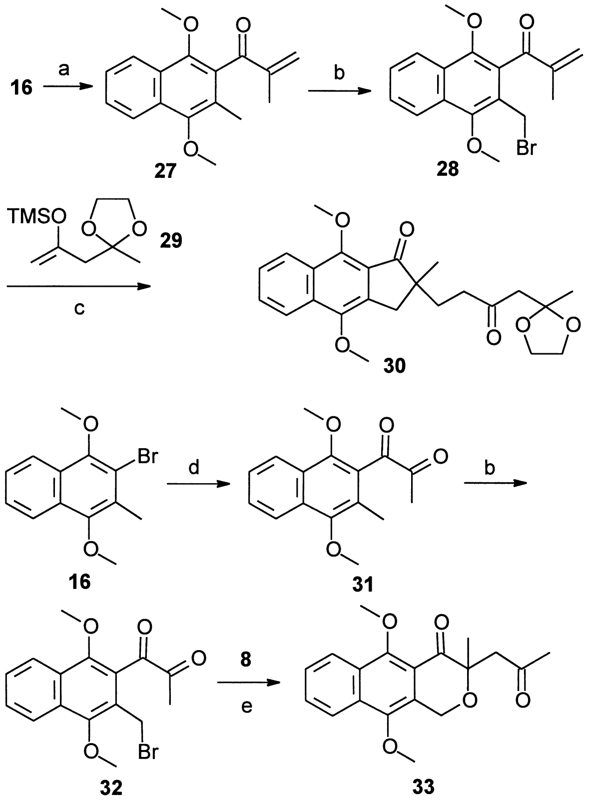
How could the problem of unwanted seven-membered ring formation be circumvented? Evidently, the efficacy of the α-substituent as a leaving group had to be drastically reduced. Therefore, we turned our attention to the triketone **14**, hoping that rapid twofold electron transfer might lead to a samarium enediolate that could not undergo β-elimination. These considerations were encouraged by some findings of Schobert[32] and of Fürstner et al.,[25] who observed the formation of enediolates with "activated titanocene" or in titanium-mediated cyclizations to coumarins. Aldol reactions promoted by samarium ion were also recently studied by Fang et al..[33]



Scheme 4. SmI_2-mediated cyclization of model diones.

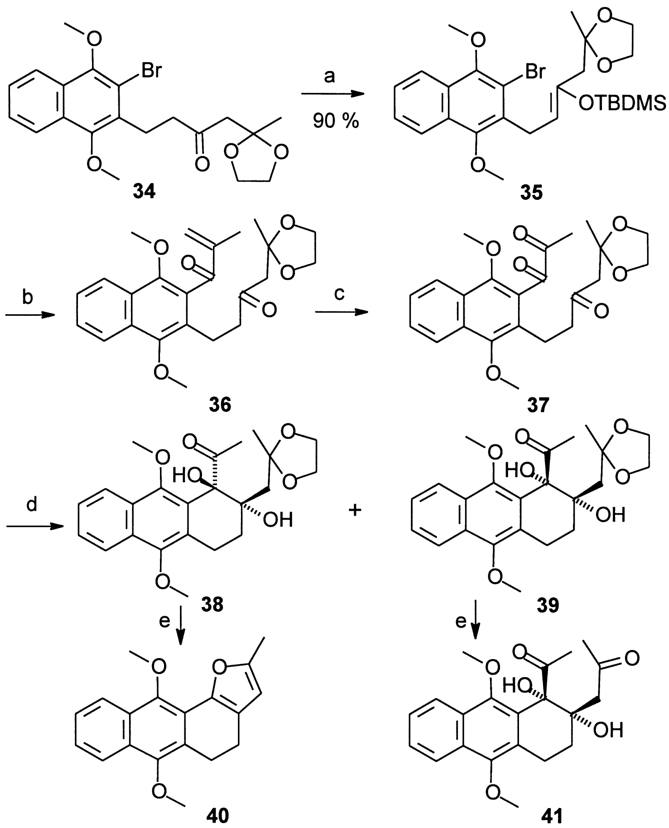
In the event, the SmI_2-mediated reaction of the trione **14** gave a 91% yield of a 1.7:1 diastereoisomeric mixture of the diols **25** and **26**. In principle, the samarium enediolate **IV** could undergo two modes of cyclization: A or B (Scheme 4, path d). Evidently, the formation of the desired six-membered ring via B is entropically favored. We believe that the facile SmI_2-mediated formation of enediolates and subsequent reactions with electrophiles will prove to be of general utility, particularly in the construction of ketodiol functionalities.

Encouraged by these excellent results for SmI_2-mediated cyclizations by the ionic pathway, we next examined the matter of the optimal route to fully functionalized precursors of the triketo structure **5**. In particular, it was not known which reaction sequence (attachment of the top or the bottom side chain first) would give the best results. Two starting materials—the benzylic bromides **28** and **32**—were selected in order to study the first option. They were prepared via **16**, **27** and **31**, in analogy to the methodology (lithiation, acylation, followed by NBS bromination) outlined earlier in the preparation of **11**–**14** (see Scheme 2). Reaction of **28** with the silyl enol ether **29**, and of acetone silyl ether **8** with **32**, resulted in the formation of the cyclization products **30** and **33**, respectively (Scheme 5). The formation of products **30** and **33** can easily be explained by Michael addition or 1,2-addition of the enolate to the top side chain, followed by nucleophilic substitution of the benzylic bromide. Therefore, this reaction sequence was abandoned and we selected the naphthalene bromide **34**[1] as the starting material to attach the top side chain in the second step.



Scheme 5. "Top side chain first" strategy leading to naphthocyclopentane **30** and naphthopyranone **33**. a) 1. *n*BuLi, THF, −78 °C, 2. methacrylic acid anhydride, 57 %; b) NBS, CCl_4 (43 % of **28**, 67 % of **32**); c) **29**, $[nBu_4N][Ph_3SnF_2]$, TBAI, THF, 25 %; d) 1. *n*BuLi, THF, −78 °C, 2. pyruvyl chloride, 21 %; e) **8**, $[nBu_4N][Ph_3SnF_2]$, TBAI, THF, 12 %.

Lithiation of the silyl ether **35** and reaction with methacrylic acid anhydride afforded the unsaturated acylation product **36** in 47 % yield, together with the debromination product of **35** (35 %). The double bond was relatively electron deficient, and osmium tetroxide proved to react too slowly. Therefore, the much more reactive ruthenium tetroxide in conjunction with sodium periodate was employed to cleave the double bond.[34] Fortunately, the naphthalene core was deactivated by the acylation. Nonetheless, the reaction time had to be carefully monitored to avoid cleavage of the naphthalene ring. In this way, the triketone **37** could be isolated in 77 % yield (Scheme 6). The crucial SmI_2-mediated cyclization gave the



Scheme 6. Synthesis of the triketone **37** and its aldol cyclization. a) TBDMSOTf, Et_3N, CH_2Cl_2, 90 %; b) 1. *n*BuLi, THF, −78 °C, 2. methacrylic acid anhydride, 47 %; c) RuO_4, $NaIO_4$, 77 %, d) SmI_2, THF, 18 °C (83 % **38** + **39**, see Table 1), e) SiO_2, diluted H_2SO_4/CH_2Cl_2 (80 % of **41**).

stereoisomeric diols **38** and **39** in 69–83 % yield. The remote ketal remained completely unaffected. Interestingly, a high degree of dependence of the isomer ratio on reaction temperature was observed, as shown in Table 1. At −100 °C, the *trans*-diol **38** predominated by 2:1, whereas at 18 °C the desired *cis*-diol **39** was favored by 9:1. The assignment of the relative configurations of the two tertiary stereogenic centres in the cyclization products lacking indicative protons was difficult by NMR methods. Fortunately, the *trans*-diol **38** crystallized nicely and the structure was proven by X-ray analysis (Figure 1).

Table 1. Temperature-dependent *cis*:*trans* ratio in the SmI_2-mediated cyclization of **37**.

Temp. [°C]	**39**:**38**	Yield [%]
−100	1:2	72
−78	1:1.7	69
0	8:1	79
18	9:1	83

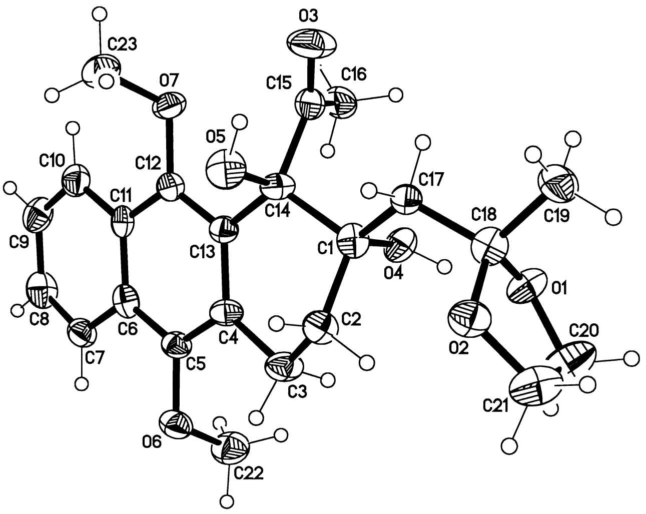
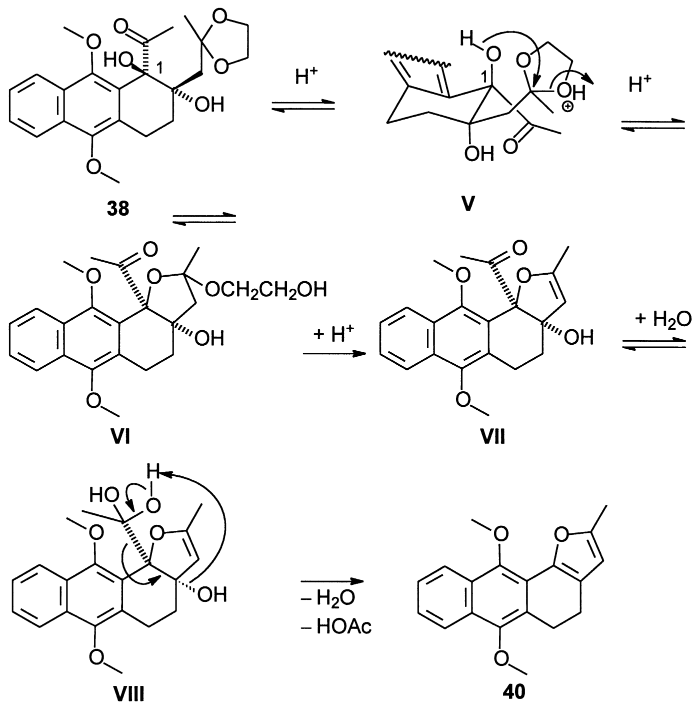


Figure 1. Crystal structure of *trans*-diol **38**.

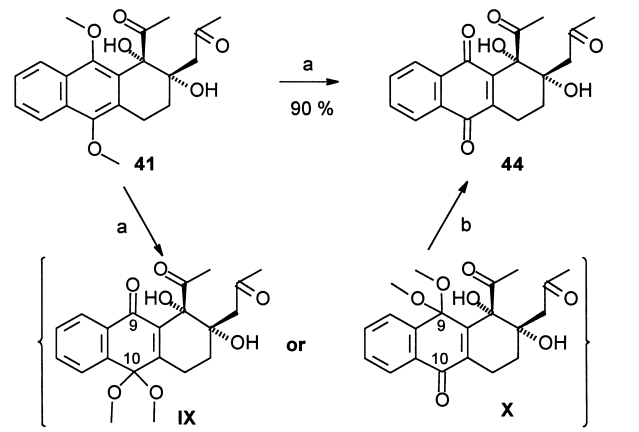
In chelation-controlled reactions with low-valent titanium, McMurry, Rico, and Lecta[35] observed the predominance of *cis*-diols, as did Molander and Kenny[23] in related SmI_2-mediated reactions. However, in the SmI_2-initiated coupling of biaryl dialdehydes, the selective formation of the *trans*-diol has recently been observed.[36, 37] (For the effect of Lewis acids and the nature of the substrates see reference [38].)

The acid-catalyzed cleavage on silica gel of the *cis*-diol **39** according to the procedure of Huet et al.[39] proceeded without decomposition, and the dione **41** was isolated in 80% yield. A totally different behaviour was observed with the corresponding *trans*-diol **38**, which decomposed to the highly non-polar anthrafuran **40**. How can this remarkable difference be explained? We assume that the increase in the electrophilicity of the dioxolane ring induced by protonation enables the axial hydroxy group at C-1 to attack the oxonium ion of the dioxolane ring (Scheme 7, **V**), to form the tetrahydrofuran **VI**. A series of plausible eliminations via **VII** and **VIII** then leads to the very stable anthrafuran **40**. Only the *trans*-diol **38** can assume a relatively favorable conformation, as shown in **V**. From an experimental viewpoint, the decomposition of the *trans*-diol proved to be highly advantageous. The 9:1 mixture of the diols **38** and **39** (of similar polarities) was directly subjected to the acidic ketal cleavage, and the highly non-polar furan **40** could then easily be separated by flash chromatography. It is also worth noting that, in the family of non-aromatic angucyclinones, the AB *cis*-connected natural products (e.g. **1** or **2**) are found exclusively.

The next step in the synthesis was to decide whether the oxidative cleavage of the hydroquinone dimethyl ether, mediated by cerium(IV), had to take place at the stage of the three- or of the four-membered ring systems. Firstly, the readily available *cis*-diol **40** was treated with cerium ammonium nitrate (CAN) under the usual conditions in acetonitrile solution.[40] Only decomposition to complex mixtures was observed using this method. Tanoue and Terada[41] recommended a modified procedure, using solid CAN in CH_2Cl_2 in the presence of a phase transfer catalyst and traces of water. Indeed, a clean conversion was observed under these conditions. However, the NMR spectrum of the product mixture still showed the presence of methoxy groups, despite complete conversion of the starting material. Careful analysis of the NMR data revealed the presence of the quinone monoacetals **IX** or **X** in an inseparable mixture with the quinone **4** (Scheme 8). Similar behaviour has previously only been observed in the conversion of hydroquinone methyl ethers with thallium(III) nitrate.[42] Since the reaction conditions were free of methanol, we assume an intramolecular shift, during the CAN oxidation, of the methoxy group in one of the postulated cationic intermediates.[41] Fortunately, the *cis*-diol proved to be relatively stable to acid, and treatment of the crude reaction mixture with sulfuric acid on silica gel[39]



Scheme 7. Mechanistic considerations relating to the acidic decomposition of the *cis*-diol **38** to the anthrafurane **40**.

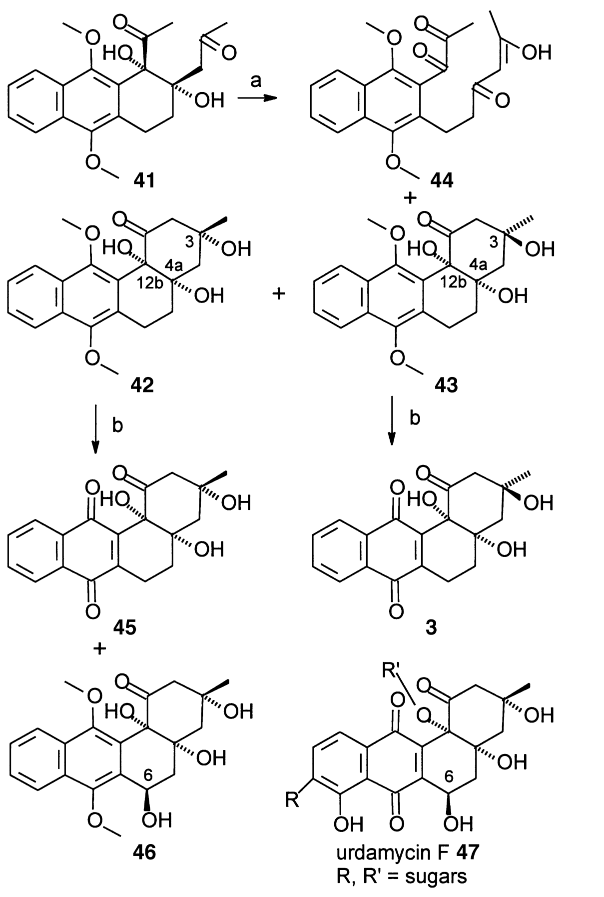


Scheme 8. CAN oxidation of the hydroquinone dimethyl ether **41**. a) 1. CAN, $nBu_4NHSO_4/CH_2Cl_2/H_2O$, b) SiO_2, H_2SO_4, 90% of **4**.

completely converted the quinone monoketal **IX** or **X** to the quinone **4**, which was now isolated in 90% overall yield.

Only one step to the final targets remained now. In analogy with previous successful cyclization experiments using related substrates lacking the C-1 hydroxy group,[14] the dione **4** was treated with dilute KOH in methanol at low temperatures. However, in complete contrast to the related experiments,[14] only a bright yellow, fluorescent mixture of three inseparable isomers resulted from the treatment of **4** with base! The NMR spectra showed the absence of the hydroxy groups at C-1 and C-2, supporting the assumption that the treatment with base had caused proton abstraction from the acidic pseudo-benzylic position, followed by vinylogous β-elimination of 1-OH, forming highly reactive *ortho*-quinonemethide intermediates. Use of other bases led to the same result. Consequently, base treatment of quinones of type **4** had to be strictly avoided and cyclization to tetracyclic compounds had to be undertaken at the hydroquinone dimethyl ether stage. Thus, dione **41** was subjected to treatment with dilute alkali in methanol and a very clean reaction to three compounds was observed. The major compounds were the desired tetracyclic 3,4a-*cis*-and 3,4a-*trans*-triols **42** and **43**, which were formed in a ratio of about 1.7:1, and small amounts of the open chain retro-aldol product **44**. The mixture could easily be separated by preparative TLC (Scheme 9). A preliminary stereochemical assignment of the 3,4a-*cis*- and 3,4a-*trans*-triols **42** and **43** was made by comparison of the NMR spectra (in particular the chemical shift of the methyl protons) of related previously prepared 12b-deoxy compounds, the structures of which had been correlated by an X-ray analysis.[14]

The stage was now set for the final oxidative CAN deprotection of the tetracyclic compounds. In the oxidation of the 3,4a-*trans*-diol **43**, formation of small amounts of the quinone hemiketals analogous to **IX** or **X** was again observed. Mild acid treatment of the crude mixture cleaved the ketal and the quinone **3** was isolated as the main product (70%). A similar result was observed with the 3,4a-*cis*-diol **42**, affording quinone **45** (36%, ca. 15% impurity). The stereochemical assignments of **45** and **3** were unambiguously confirmed by comparison with the published NMR spectra of the natural products aquayamycin (**1**) and WP 3688-2 (**2**). Finally, a very interesting by-product, **46**, was isolated from an incomplete CAN oxidation of 3,4a-*cis*-diol **42**. The spectral data unambiguously indicated the presence of a benzylic hydroxy group. The stereochemistry at C-6 was deduced by the close analogy of the relevant nonaromatic part of the NMR spectra with those of the natural product urdamycin F (**47**).[43] The small impurity found in the cerium (IV) oxidation of **42**, not separable from **45** by TLC, most probably corresponded to a quinone derived from the hydroquinone dimethyl ether **46**, as deduced from corresponding signals in the ^{1}H NMR spectrum.



Scheme 9. Biomimetic-type aldol cyclization of **41** and CAN oxidation to 8-deoxy angucyclines. a) 0.2 N KOH/CH_3OH; b) CAN, nBu_4NHSO_4/CH_2Cl_2/H_2O.

Conclusion

The SmI_2-mediated cyclization of ketides of type **5** via samarium enediolates proved to be an excellent strategy for the stereoselective construction of the ketodiol function present in the majority of angucycline antibiotics. The procedure offers the option to use low cost "Mischmetall" as coreductant[44] and also, in the presence of chiral amines, volunteers an enantioselective version.[45, 46] The subsequent aldol cyclization has to take place at the stage of the non-acidic hydroquinone dimethyl ethers such as **41**. Under chelate-breaking methanolic alkaline conditions, both naturally occurring stereoisomers **42** and **43** were formed. This biomimetic approach enabled, for the first time, the chemical synthesis of 8-deoxy WP 3688-2 (**3**) and the 8-deoxy-5,6-dihydro analogue (**45**) of aquayamycin. Starting from readily accessible materials, this approach may open the door to other aquayamycin- and urdamycin-type angucyclines.

Experimental Section

For general methods and instrumentation see ref. [47].

General procedure I: alkylation of benzyl bromides with silyl enol ethers: The silyl enol ether (2.2 mmol) was added at −78°C to a solution of naphthyl bromide (1 mmol) and tetrabutylammonium iodide (TBAI, 0.3 mmol) in THF (10 mL) under argon. After this, $[nBu_4N][Ph_3SnF_2]$[29] (1.2 mmol) was added in one portion. The cooling bath was removed after 15 min and the mixture was stirred at 20°C for the time indicated for the individual compounds (TLC monitoring). If the conversion was incomplete, another portion of $[nBu_4N][Ph_3SnF_2]$ (0.6 mmol) was added at

$-78\,^{\circ}C$. The solution was then filtered through a short silica gel column (5 g, CH_2Cl_2) and the solvent was removed under reduced pressure.

General procedure II: formation of silyl enol ethers from ketones: A solution of the ketone (4 mmol) in CH_2Cl_2 (10 mL) was treated at 0 °C with triethylamine (12 mmol) and *tert*-butyldimethylsilyl (TBDMS) triflate (4.6 mmol). The solution was then stirred for 1 h (TLC monitoring) under argon. The reaction was quenched by addition of saturated aqueous $NaHCO_3$ solution (20 mL), the phases were separated, and the aqueous phase extracted with CH_2Cl_2 (2 × 20 mL). The combined organic phases were washed with brine (20 mL), dried ($MgSO_4$), filtered and the solvent removed under reduced pressure.

General procedure III: addition of electrophiles to lithiated naphthalenes: A solution of *n*BuLi in hexane (3.3 mmol) was added at $-78\,^{\circ}C$ to a solution of the naphthyl bromide (3 mmol) in THF (20 mL) under argon. After 15 min of stirring at $-78\,^{\circ}C$, the electrophile (3.6 mmol) was added (solid electrophiles in THF (2 mL) solution). After a further 30 min at $-78\,^{\circ}C$, the reaction was quenched by addition of Et_2O (20 mL) and saturated NH_4Cl solution (20 mL). The phases were separated, the aqueous phase extracted with Et_2O (3 × 20 mL) and the combined organic phases washed with water (20 mL) and brine (20 mL). The solutions were dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure.

General procedure IV: bromination of benzylic positions using NBS: A solution of the methyl naphthalene (5 mmol), NBS (5.1 mmol) and azobisisobutyronitrile (AIBN) (20 mg) was refluxed in CCl_4 (20 mL) for the times indicated. After cooling the mixture, the succinimide was filtered off, the solvent removed under reduced pressure, and the residue purified by column chromatography on silica gel.

General procedure V: acidic cleavage of TBDMS enol ethers: A solution of the functionalized silyl enol ethers (crude products from electrophilic addition) was vigorously stirred in a mixture of CH_2Cl_2 and 2 N aqueous HCl (4:1, 125 mL, TLC monitoring) at 20 °C. The phases were separated, the organic phase was washed with aqueous $NaHCO_3$ solution (30 mL), water (30 mL) and brine (30 mL), dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure.

General procedure VI: coupling of diketones using samarium diiodide: A 0.1 M solution of SmI_2 in THF was prepared according to a literature procedure.[48] This solution (10 mL, 1 mmol) was treated under argon at the temperatures and times indicated with a solution of the diketone (0.4 mmol) in THF (2 mL) (TLC monitoring). After conversion of the starting material, the reaction was quenched by addition of saturated NH_4Cl solution (10 mL). Et_2O (20 mL) was added, the phases separated, and the aqueous phase extracted twice with Et_2O (20 mL). The combined organic phases were washed with water (20 mL) and brine (20 mL), dried ($MgSO_4$), filtered, and the solvent was removed under reduced pressure.

[3-(3-Bromo-1,4-dimethoxynaphthalen-2-yl)-1-(2-methyl-[1,3]dioxolan-2-ylmethyl)-propenyloxy]-*tert*-butyldimethylsilane (35): Ketone **34**[1] (2.55 g, 6.1 mmol) was converted to the TBDMS ether **35** as described in general procedure II. The crude product was purified by column chromatography on silica gel (80 g, petroleum ether/diethyl acetate (PE/EA) 9:1, 0.5% Et_3N) to afford silyl enol ether **35** (2.95 g, 90%) as white needles (hexane). M.p. 91–92 °C; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 0.26$ (s, 6H; $Si(CH_3)_2$), 1.05 (s, 9H; $SiC(CH_3)_3$), 1.34 (s, 3H; dioxolane-CH_3), 2.35 (s, 2H; 1-H), 3.76 (d, $J = 6.0$ Hz, 2H; 4-H), 3.86 (s, 4H; OCH_2CH_2O), 3.91 (s, 3H; OCH_3), 3.97 (s, 3H; OCH_3), 4.67 (t, $J = 6.0$ Hz, 1H; 3-H), 7.48–7.54 (m, 2H; 6′-H, 7′-H), 8.04–8.10 (m, 2H; 5′-H, 8′-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = -3.19$ (q; $Si(CH_3)_2$), 18.77 (s; $SiC(CH_3)_3$), 24.79 (q; dioxolane-CH_3), 26.35 (q; $SiC(CH_3)_3$), 27.81 (t; C-4), 46.09 (t; C-1), 61.71/62.91 (2 × q; 2 × OCH_3), 64.96 (t; OCH_2CH_2O), 109.70 (s; dioxolane-OCO), 110.33 (d; C-3), 117.25 (s; C-3′), 122.83/123.06 (2 × d; C-5′, C-8′), 126.69/126.85 (2 × d; C-6′, C-7′), 128.18/128.46/131.22 (3 × s; C-2′, C-4a′, C-8a′), 146.97 (s; C-2), 150.42/151.13 (2 × s; C-1′, C-4′).

1-(1,4-Dimethoxy-3-[4-(2-methyl-[1,3]dioxolan-2-yl)-3-oxobutyl]-naphthalen-2-yl)-2-methylpropenone (36): The TBDMS ether **35** (2.47 g, 4.6 mmol) was treated with methacrylic acid anhydride (0.83 g, 5.4 mmol) as described in general procedure III. The crude product was desilylated according to general procedure V. The residue was purified by column chromatography on silica (130 g, PE/EA 3:1) to afford a mixture of the acylation product **36** (900 mg, 47%) and the debrominated starting material (710 mg, 45%). The products were separated by preparative TLC on silica gel to yield pure **36** as a faint yellow oil. ^1H NMR (200 MHz, $CDCl_3$): $\delta = 1.42$ (s, 3H; dioxolane-CH_3), 2.08 (s, 3H; 4-H), 2.74 (s, 2H; 4″-H), 2.81 (s, 4H; 1″-H, 2″-H), 3.85 (s, 3H; OCH_3), 3.92 (s, 3H; OCH_3), 3.96 (s, 4H; OCH_2CH_2O), 5.63 (s, 1H; 3-H), 6.00 (s, 1H; 3-H), 7.45–7.60 (m, 2H; 6′-H, 7′-H), 8.03–8.08 (m, 2H; 5′-H, 8′-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 17.12$ (q; C-4), 22.11 (t; C-1″), 25.02 (q; dioxolane-CH_3), 45.61 (t; C-2″), 51.88 (t; C-4″), 61.44/62.69 (2 × q; 2 × OCH_3), 65.05 (t; OCH_2CH_2O), 108.28 (s; dioxolane-OCO), 122.89/123.01/126.58/127.36 (4 × d; C-5′, C-6′, C-7′, C-8′), 127.58/127.75/129.49/131.29 (4 × s; C-2′, C-3′, C-4′a, C-8′a), 130.73 (t; C-3), 146.14 (s; C-2), 149.39/150.92 (2 × s; C-1′, C-4′), 199.51 (s; C-1), 207.08 (s; C-3″); UV (methanol): λ_{max} (lgε) = 223 nm (3.82), 264 (4.02), 328 (3.70); MS (EI, 70 eV): *m/z* (%): 412 (32) $[M]^+$, 268 (14) $[M - C_3H_5 - CH_3C(CH_2)OCH_2CH_2O]^+$, 253 (25) $[M - C_3H_5 - CH_3C(CH_2)OCH_2CH_2O - CH_3]^+$, 87 (100) $[CH_3COCH_2CH_2O]^+$, 43 (19) $[CH_3CO]^+$; IR (KBr): $\tilde{\nu}$ = 3429, 2939 (CH), 2838 (CH), 1703 (C=O), 1656 (C=O), 1582, 1354, 1058 cm^{-1}; HRMS found: 412.1867; $C_{24}H_{28}O_6$ calcd 412.1886; elemental analysis calcd for $C_{24}H_{28}O_6$ (412.48) (%): C 69.87, H 6.85; found: C 70.43, H 7.18.

1-(1,4-Dimethoxy-3-[4-(2-methyl-[1,3]dioxolan-2-yl)-3-oxobutyl]-naphthalen-2-yl)-propane-1,2-dione (37): A solution of the olefin **36** (1.29 g, 3.14 mmol) in a mixture of $CH_3CN/CCl_4/H_2O$ (10:10:15 mL) at 20 °C was treated first with $NaIO_4$ (1.99 g, 9.4 mmol) and then with $RuCl_3 \cdot H_2O$ (14 mg, 0.06 mmol). The suspension was stirred for about 30–45 min (TLC monitoring, PE/EA 2:1). When the color changed to green-brown, an additional quantity of $NaIO_4$ (0.66 g, 3.1 mmol) was added and stirring was continued for a further 30 min. CH_2Cl_2 (50 mL) and H_2O (50 mL) were then added, the phases were separated and the aqueous phase extracted with CH_2Cl_2 (2 × 30 mL). The combined organic phases were washed with water (30 mL) and brine (30 mL), dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure. The residue was dissolved in Et_2O (20 mL), filtered through a batch of celite (Et_2O, ca. 60 mL) and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (150 g, PE/EA 3:1) to afford the triketone **37** (1.00 g, 77%) as a yellow oil. ^1H NMR (300 MHz, $CDCl_3$): $\delta =$ 1.43 (s, 3H; dioxolane-CH_3), 2.53 (s, 3H; 3-H), 2.76 (s, 2H; 4″-H), 2.81–2.89 (m, 2H; 2″-H), 3.01–3.07 (m, 2H; 1″-H), 3.87 (s, 3H; OCH_3), 3.91 (s, 3H; OCH_3), 3.94 (s, 4H; OCH_2CH_2O), 7.51–7.64 (m, 2H; 6′-H, 7′-H), 8.03 (d, $J = 8.0$ H; 1H; 5′-H/8′-H), 8.07 (d, $J = 8.4$ Hz, 1H; 5′-H/8′-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 19.07$ (t; C-1″), 22.40 (q; dioxolane-CH_3), 22.77 (q; C-3), 43.46 (t; C-2″), 49.65 (t; C-4″), 60.42/61.76 (2 × q; 2 × OCH_3), 62.78 (t; OCH_2CH_2O), 106.08 (s; dioxolane-OCO), 121.12/121.15/124.56/126.62 (4 × d; C-5′, C-6′, C-7′, C-8′), 124.22/124.71/127.08/129.21 (4 × s; C-2′, C-3′, C-4′a, C-8′a), 149.28/152.07 (2 × s; C-1′, C-4′), 194.04/196.57 (2 × s; C-1, C-2), 204.74 (s; C-3″); UV (methanol): λ_{max} (lg ε) = 225 nm (4.10), 263 (3.94), 322 (3.52); MS (EI, 70 eV): *m/z* (%): 414 (4) $[M]^+$, 371 (5) $[M - CH_3CO]^+$, 243 (8) $[M - CH_3CO - CH_3COCH_2CH_2O - CHCO]^+$, 213 (4), 129 (3), 87 (100) $[CH_3COCH_2CH_2O]^+$, 43 (29) $[CH_3CO]^+$; IR (KBr): $\tilde{\nu}$ = 2939 (CH), 2885 (CH), 2845 (CH), 1716 (C=O), 1676 (C=O), 1669 (C=O), 1582, 1354, 1058, 958, 776 cm^{-1}; HRMS found: 414.1674; $C_{23}H_{26}O_7$ calcd 414.1679; elemental analysis calcd for $C_{23}H_{26}O_7$ (414.46) (%): C 66.64, H 6.33; found C 66.10, H 6.16.

1-[1,2-Dihydroxy-9,10-dimethoxy-2-(2-methyl-[1,3]dioxolan-2-ylmethyl)-1,2,3,4-tetrahydroanthracen-1-yl]-ethanone *cis* and *trans* isomers (*cis*-39, polar fraction) and (*trans*-38, less polar fraction): The triketone **37** was treated with a solution of samarium diiodide as described in general procedure VI. The crude product was separated by chromatography on silica gel (PE/EA 3:1) to afford the pure isomers **38** and **39** (yields 69–83%). For reaction temperatures, ratio of isomers and combined yields see Table 1.

Data for the *trans*-diol 38: M.p. 142 °C; ^1H NMR (300 MHz, $CDCl_3$): $\delta =$ 1.40 (s, 3H; 3″-H), AB signal ($\Delta\delta = 0.34$, $\delta_A = 2.20$, $\delta_B = 1.86$, $J_{A,B} = 15.3$ Hz, 2H; 1″-H), 2.15–2.24 (m, 1H; 3′-H), 2.29 (s, 3H; 2-H), 2.37–2.44 (m, 1H; 3′-H), 3.11–3.16 (m, 2H; 4′-H), 3.75 (s, 3H; OCH_3), 3.93 (s, 3H; OCH_3), 4.01 (brs, 4H; OCH_2CH_2O), 4.17 (s, 1H; OH), 5.04 (s, 1H; OH), 7.40–7.52 (m, 2H; 6′-H, 7′-H), 7.97 (dd, $^3J = 7.4$ Hz, $^4J = 1.0$ Hz, 1H; 5′-H/8′-H), 8.06 (dd, $^3J = 7.6$ Hz, $^4J = 1.1$ Hz, 1H; 5′-H/8′-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 18.08$ (t, C-4′), 24.35 (q, C-3″), 26.26 (q, C-2), 27.01 (t, C-3′), 39.34 (t, C-1″), 58.95/60.84 (2 × q , 2 × OCH_3), 61.94/62.02 (2 × t, OCH_2CH_2O), 72.60 (s, C-2′), 77.96 (s, C-1′), 109.51 (s, C-2″) 120.26/120.67 (2 × d, C-5′, C-8′), 123.36/124.56 (2 × d, C-6′, C-7′), 124.96/125.29/126.28/126.66 (4 × s, C-4′a, C-8′a, C-9′a, C-10′a), 147.39/148.98 (2 × s, C-9′, C-10′), 208.97 (s, C-1); UV (methanol): λ_{max} (lg ε) = 217 nm (4.31), 225 (4.02), 235 (3.90), 292

(3.52); IR (KBr): $\tilde{\nu} = 3443$ (OH), 2932 (CH), 2838 (CH), 1690 (C=O), 1448, 1354, 1273, 1058, 944, 776 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 416 (4) $[M]^+$ 373 (42) $[M - CH_3CO]^+$, 355 (31) $[M - CH_3CO - H_2O]^+$, 271 (73) $[M - CH_3CO - CH_3COCH_2CH_2O - CH_3]^+$, 213 (9), 185 (4), 87 (100) $[CH_3COCH_2CH_2O]^+$, 43 (26) $[CH_3CO]^+$; HRMS found: 416.1823; $C_{23}H_{28}O_7$ calcd: 416.1835.

Crystallographic data for 38: $C_{23}H_{28}O_7$, colorless crystal, size 0.58 × 0.16 × 0.08 mm, $M_r = 416.4$, monoclinic, space group *C*2, $a = 27.278(5)$, $b = 5.810(2)$, $c = 15.875(2)$ Å, $\beta = 125.45(1)^\circ$, $V = 2049.5(8)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.350$ Mg cm^{-3}, $\lambda(Mo_{K\alpha}) = 0.71073$ Å, $\mu = 0.099$ mm^{-1}, omega scan, $T = 203(2)$ K, $-1 \le h \le 33$, $-7 \le k \le 1$, $-19 \le l \le 16$, $2.6 \le \Theta \le 26^\circ$, 2807 reflections collected, LP correction, no absorption correction, 2634 unique reflections ($R_{int} = 0.017$); structure solution by direct and conventional Fourier methods, structure refinement based on F^2 and 278 parameters, all but hydrogen atoms refined anisotropically, H atoms located from ΔF maps and refined with riding model, refinement converged at $R1$ ($F > 4\sigma(F)$) = 0.054, $wR2$(all data) = 0.107, $S = 1.029$, max. $(\delta/\sigma) = 0.001$, min/max height in final ΔF map $-0.23/0.22$ e Å^{-3}. Structure solution and refinement program: SHELXTL NT V5.10.[49] Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-140462. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

Data for the *cis*-diol 39 (oil): ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.42$ (s, 3H; 3″-H), AB signal ($\Delta\delta = 0.27$, $\delta_A = 2.16$, $\delta_B = 1.89$, $J_{A,B} = 14.8$ Hz, 2H; 1″-H), 2.10–2.19 (m, 1H; 3′-H), 2.44 (s, 3H; 2-H), 2.43–2.51 (m, 1H; 3′-H), 3.07–3.22 (m, 2H; 4′-H), 3.92 (s, 3H; OCH_3), 3.96 (s, 3H; OCH_3), 4.05 (brs, 4H; OCH_2CH_2O), 4.44 (s, 1H; OH), 4.86 (s, 1H; OH), 7.43–7.52 (m, 2H; 6′-H, 7′-H), 7.99 (dd, $^3J = 7.6$ Hz, $^4J = 1.1$ Hz, 1H; 5′-H/8′-H), 8.05 (dd, $^3J = 7.4$ Hz, $^4J = 1.1$ Hz, 1H; 5′-H/8′-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 20.75$ (t, C-4′), 25.65 (q, C-3″), 28.41 (q, C-2), 28.69 (t, C-3′), 40.30 (t, C-1″), 60.64/63.01 (2 × q, 2 × OCH_3), 63.55/63.93 (2 × t, OCH_2CH_2O), 73.96 (s, C-2′), 82.03 (s, C-1′), 110.66 (s, C-2″), 121.87/122.48 (2 × d, C-5′, C-8′), 125.00/126.19 (2 × d, C-6′, C-7′), 126.50/126.96/128.33/129.10 (4 × s, C-4′a, C-8′a, C-9′a, C-10′a), 148.80/151.35 (2 × s, C-9′, C-10′), 211.01 (s, C-1); UV (methanol): λ_{max} (lg ε) = 218 nm (4.21), 247 (4.31), 262 (3.92), 338 (3.44); IR (KBr): $\tilde{\nu} = 3449$ (OH), 2939 (CH), 2845 (CH), 1710 (C=O), 1663, 1589, 1454, 1360, 1045, 776, 736 cm^{-1}; elemental analysis (%) calcd for $C_{23}H_{28}O_7$ (416.47): C 66.32, H 6.78; found: C 66.76, H 6.87.

***cis*-1-(1-Acetyl-1,2-dihydroxy-9,10-dimethoxy-1,2,3,4-tetrahydroanthracen-2-yl)propan-2-one (41)**: A solution of the ketal *cis*-**39** (198 mg, 0.48 mmol) in CH_2Cl_2 (2 mL) was added at 20 °C to a suspension of silica gel (1 g) and 15% H_2SO_4 (0.1 g) in CH_2Cl_2 (10 mL). The suspension was stirred vigorously for 1.5 h, filtered, and the filtrate was washed with water (20 mL), saturated aqueous $NaHCO_3$ solution (20 mL), and brine (20 mL). The organic phase was dried ($MgSO_4$), filtered, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (25 g, PE/EA 3:1) to yield the diketone **41** (142 mg, 80%) as faint yellow crystals. M.p. 140 °C; ^1H NMR (300 MHz, $CDCl_3$): δ = ABMN signal ($\delta_A = 3.20$, dt, $^2J = 17.9$ Hz, $^3J = 5.6$ Hz, 4′-H_{eq}; $\delta_B = 3.06$, ddd, $^2J = 17.9$ Hz, $^3J = 4.4$, 5.6 Hz, 4′-H_{ax}; $\delta_M = 2.30$, ddd, $^2J = 13.4$ Hz, $^3J = 4.4$, 5.6 Hz, 3′-H_{ax}; $\delta_N = 1.94$, dt, $^2J = 13.4$ Hz, $^3J = 5.6$, 5.8 Hz, 3′-H_{eq}), 2.19 (s, 3H; 3-H), 2.45 (s, 3H; 2″-H), AB signal ($\Delta\delta = 0.54$, $\delta_A = 3.03$, $\delta_B = 2.49$, $J_{AB} = 16.4$ Hz, 2H; 1-H), 3.90 (s, 3H; OCH_3), 3.97 (s, 3H; OCH_3), 4.84 (s, 1H; OH), 5.36 (s, 1H; OH), 7.41–7.52 (m, 2H; 6′-H, 7′-H), 7.98 (dd, $^3J = 7.6$ Hz, $^4J = 1.3$ Hz, 1H; 5′-H/8′-H), 8.04 (dd, $^3J = 7.5$ Hz, $^4J = 1.0$ Hz, 1H; 5′-H/8′-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 20.53$ (t, C-4′), 28.30 (q, C-2″), 30.42 (t, C-3′), 31.82 (q, C-3), 45.63 (t, C-1), 60.73/63.18 (2 × q, 2 × OCH_3), 74.52 (s, C-2′), 81.09 (s, C-1′), 121.95/122.58 (2 × d, C-5′, C-8′), 125.28/126.43 (2 × d, C-6′, C-7′), 125.21/127.08/128.46/128.76 (4 × s, C-4′a, C-8′a, C-9′a, C-10′a), 149.07/151.33 (2 × s, C-9′, C-10′), 211.28 (s, C-1″), 212.67 (s, C-2); UV (methanol): λ_{max} (lg ε) = 215 nm (4.09), 255 (4.21), 270 (4.04), 340 (3.64); MS (EI, 70 eV): *m/z* (%): 372 (14) $[M]^+$, 329 (100) $[M - CH_3CO]^+$, 311 (53) $[M - CH_3CO - H_2O]^+$, 283 (35) $[M - CH_3CO - H_2O - CO]^+$, 271 (58) $[M - CH_3CO - CH_2COCH_3 - H]^+$, 239 (32), 201 (29), 43 (47) $[CH_3CO]^+$; IR (KBr): $\tilde{\nu} = 3456$ (OH), 2939 (CH), 2838 (CH), 1703 (C=O), 1689 (C=O), 1455, 1360, 1099, 1038, 763 cm^{-1}; HRMS found: 372.1570: $C_{21}H_{24}O_6$ calcd: 372.1573; elemental analysis (%) calcd for $C_{21}H_{24}O_6$ (372.42): C 67.71, H 6.50; found: C 67.04, H 6.32.

6,11-Dimethoxy-2-methyl-4,5-dihydroanthra[1,2-*b*]furan (40): The *trans*-ketal **38** (40 mg, 0.11 mmol) was treated with sulfuric acid on silica gel as described for **41** to afford after column chromatography on silica gel the anthrafuran derivative **40** (20 mg, 62%) as a yellow oil. ^1H NMR (200 MHz, $CDCl_3$): $\delta = 2.44$ (s, 3H; 2-CH_3), 2.68–2.75 (m, 2H; 4-H), 3.11–3.18 (m, 2H; 5-H), 3.88 (s, 3H; OCH_3), 3.99 (s, 3H; OCH_3), 6.02 (s, 1H; 3-H), 7.43–7.51 (m, 2H; 8-H, 9-H), 7.99–8.15 (m, 2H; 7-H, 10-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 14.52$ (q, 2-CH_3), 21.28 (t, C-5), 23.36 (t, C-4), 61.81/62.67 (2 × q, 2 × OCH_3), 107.43 (d, C-3), 118.55 (s, C-3a), 122.48/122.68/125.91/126.29 (4 × d, C-7, C-8, C-9, C-10), 123.86/125.48/128.07/129.27 (4 × s, C-5a, C-6a, C-10a, C-11a), 144.92 (s, C-2), 146.78/149.41 (2 × s, C-6, C-11), 153.25 (s, C-11b); UV (methanol): λ_{max} (lg ε) = 210 nm (4.02), 252 (4.27), 272 (4.10), 341 (3.76); MS (EI, 70 eV): *m/z* (%): 294 (76) $[M]^+$, 279 (100) $[M - CH_3]^+$, 263 (38) $[M - 2 \times CH_3]^+$, 221 (15) $[M - 2 \times CH_3 - CH_3CO]^+$, 104 (10), 77 (11), 43 (42) $[CH_3CO]^+$; IR (KBr): $\tilde{\nu} = 2929$ (CH), 2852 (CH), 1450, 1357, 1269, 1067, 741 cm^{-1}; HRMS found: 294.1266; $C_{19}H_{18}O_3$ calcd: 294.1256.

1-Acetyl-1,2-dihydroxy-2-(2-oxopropyl)-1,2,3,4-tetrahydroanthraquinone (4): To a suspension of CAN (433 mg, 0.79 mmol) and nBu_4NHSO_4 (268 mg, 0.79 mmol) in dry CH_2Cl_2 (50 mL) was added a solution of the dimethoxynaphthalene **41** (147 mg, 0.39 mmol) in CH_2Cl_2 (2 mL). Water was then added dropwise over 15 min until the starting material had been completely consumed (TLC monitoring). The suspension was filtered over a batch of Celite (Et_2O), the filtrate was washed with water (2 × 20 mL) and brine (20 mL), the organic phase was dried ($MgSO_4$), filtered, and the solvent was removed under reduced pressure. The NMR spectrum of the crude product revealed the presence of quinone hemiketals (ca. 50%, see below). The crude product from the CAN reaction (ca. 160 mg) was treated with sulfuric acid on silica gel as described for **41** to yield the tetrahydroanthraquinone **4** (121 mg, 90%), as yellow crystals.

Data for 4: M.p. 128 °C; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.96$–2.17 (m, 2H; 3-H), 2.23 (s, 3H; 3″-H), AB signal ($\Delta\delta_{AB} = 0.64$, $\delta_A = 3.01$, $\delta_B = 2.37$, $J_{AB} = 15.9$ Hz, 2H; 1″-H), 2.57 (s, 3H; 2′-H), 2.72–2.77 (m, 2H; 4-H), 4.80/4.93 (2 × brs, 2H; 2 × OH), 7.66–7.71 (m, 2H; 6-H, 7-H), 7.97–8.06 (m, 2H; 5-H, 8-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 20.22$ (t, C-4), 27.74 (q, C-2′), 27.80 (t, C-3), 32.08 (q, C-3″), 45.94 (t, C-1″), 73.29 (s, C-2) 80.71 (s, C-1), 126.15/126.24 (2 × d, C-5, C-8) 133.66/133.78 (2 × d, C-6, C-7), 131.56/131.76 (2 × s, C-8a, C-10a), 143.25/146.80 (2 × s, C-4a, C-9a), 184.11/184.82 (2 × s, C-9, C-10), 210.00 (s, C-1′), 211.76 (s, C-2″); UV (methanol): λ_{max} (lg ε) = 218 nm (4.02), 253 (4.19), 270 (4.10), 353 (3.82); MS (EI, 70 eV): *m/z* (%): 342 (1) $[M]^+$, 314 (2) $[M - CO]^+$, 281 (6) $[M - CH_3CO - H_2O]^+$, 253 (5) $[M - CO - CH_3CO - H_2O]^+$, 241 (14) $[M - CH_3CO - CH_2COCH_3 - H]^+$, 43 (88) $[CH_3CO]^+$, 18 (100) $[H_2O]^+$; IR (KBr): $\tilde{\nu} = 3452$ (OH), 2924 (CH), 2847 (CH), 1709 (C=O), 1662 (C=O), 1590, 1357, 1290, 1083, 716 cm^{-1}; HRMS found: 342.1107; $C_{19}H_{18}O_6$ calcd: 342.1103; elemental analysis (%) calcd for $C_{19}H_{18}O_6$ (342.35): C 66.65, H 5.30; found: C 66.22, H 5.17.

Data for the tetrahydroanthraquinone monoketal (IX or X): ^1H NMR (200 MHz, $CDCl_3$): $\delta = 2.01$–2.18 (m, 2H; 3-H), AB signal ($\Delta\delta_{AB} = 0.87$, $\delta_A = 3.11$, $\delta_B = 2.24$, $J_{AB} = 14.4$ Hz, 2H; 1″-H), 2.27 (s, 3H; 3″-H), 2.55 (s, 3H; 2′-H), 2.57–2.69 (m, 2H; 4-H), 2.93 (s, 3H; OCH_3), 2.95 (s, 3H; OCH_3), 7.47–7.59 (m, 1H; 5-H), 7.65–7.77 (m, 2H; 6-H, 7-H), 8.03 (d, $J = 6.7$ Hz, 1H; 8-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 20.52$ (t, C-4), 27.32 (t, C-3), 28.22 (q, C-2′), 33.06 (q, C-3″), 47.88 (t, C-1″), 51.69/51.93 (2 × q, 2 × OCH_3), 73.52/82.50 (2 × s, C-1, C-2), 97.65 (s, C-9 or C-10), 126.67/126.98/30.03/134.59 (24 d, C-5, C-8, 1, C-6, C-7), 132.73/139.04/139.94 (3 × s, C-8a, C-9a, C-10a), 157.51 (s, C-4a), 184.97 (s, C-9 or C-10), 209.48 (s, C-1′), 212.25 (s, C-2″).

Aldol cyclization of 41: A solution of the diketone **41** (130 mg, 0.38 mmol) in CH_2Cl_2 (4 mL), was added dropwise at 0 °C to a 0.2 M solution of KOH (450 mg) in MeOH (40 mL) and stirred for 30 min at 0 °C and for 80 min at 20 °C (TLC monitoring). The reaction was quenched by addition of 2 N HCl (4 mL) and saturated NH_4Cl solution (20 mL). CH_2Cl_2 (20 mL) was added, the phases were separated, and the aqueous phase was extracted twice with CH_2Cl_2 (20 mL). The combined organic phases were washed with H_2O (2 × 50 mL), saturated $NaHCO_3$ solution (50 mL), and brine (50 mL), dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure. The crude product was purified by preparative TLC chromatography on silica gel (2 plates, 2 mm, CH_2Cl_2/MeOH 97:3) to yield the diastereomeric 3,4a-*cis*-benz[*a*]anthracene **42** (43 mg, 33%, less polar fraction, white solid), the

3,4a-*trans* isomer **43** (26 mg, 20%, polar fraction), and the open-chain retro-aldol product **44** (13 mg, 10%).

3,4a-*cis*-3,4a,12b-Trihydroxy-7,12-dimethoxy-3-methyl-3,4,4a,5,6,12b-hexahydro-2*H*-benz[a]anthracen-1-one (42): ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.19$ (s, 3H; 3-CH_3), ABMN signal ($\delta_A = 3.34$, dd, $^2J = 18.7$ Hz, $^3J = 6.1$ Hz, 6-H_{eq}; $\delta_B = 2.98$, ddd, $^2J = 18.7$ Hz, $^3J = 5.6$, 7.2 Hz, 6-H_{ax}; $\delta_M = 2.28$, ddd, $^2J = 13.2$ Hz, $^3J = 6.1$, 7.2 Hz, 5-H_{ax}; $\delta_N = 1.95$, dd, $^3J = 6.6$ Hz, 5-H_{eq}), 1.97 (brs, 2H; 4-H), AB signal ($\Delta\delta = 0.06$, $\delta_A = 2.78$, 2-H_{ax}, $\delta_B = 2.72$, $^4J = 1.2$ Hz, $J_{AB} = 12.6$ Hz, 2H; 2-H), 3.15 (brs, 1H; OH), 3.80 (s, 3H; OCH_3), 3.94 (s, 3H; OCH_3), 4.34 (s, 1H; OH), 5.12 (s, 1H; OH), 7.49–7.60 (m, 2H; 9-H, 10-H), 8.01 (d, $J = 8.2$ Hz, 1H; 8-H/11-H), 8.07 (d, $J = 8.6$ Hz, 1H; 8-H/11-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 21.83$ (t, C-6), 30.02 (q, 3-CH_3), 30.49 (t, C-5), 40.93 (t, C-4), 50.39 (t, C-2), 60.74/62.61 (2 × q, 2 × OCH_3), 75.12/77.41/79.12 (3 × s, C-3, C-4a, C-12b), 121.92/122.56 (2 × d, C-8, C-11), 125.79/127.00 (2 × d, C-9, C-10), 123.96/127.25/127.32/128.82 (4 × s, C-6a, C-7a, C-11a, C-12a), 150.09 (s+s, C-7, C-12), 207.24 (s, C-1); UV (methanol): λ_{max} (lg ε) = 218 nm (4.12), 246 (4.08), 263 (3.88), 322 (3.72); IR (KBr): $\tilde{\nu} = 3369$ (OH), 2932 (CH), 2852 (CH), 1703 (C=O), 1453, 1359, 1264, 1052, 740 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 372 (100) $[M]^+$, 344 (26) $[M - CO]^+$, 326 (17) $[M - CO - H_2O]^+$, 293 (24) $[M - CO - 2H_2O - CH_3]^+$, 271 (54) $[M - CO - CH_2C(OH)(CH_3)CH_2 - H]^+$, 225 (22), 213 (21), 125 (22), 57 (19), 43 (28) $[CH_3CO]^+$; HRMS found: 372.1570: $C_{21}H_{24}O_6$ calcd: 372.1573.

3,4a-*trans*-3,4a,12b-Trihydroxy-7,12-dimethoxy-3-methyl-3,4,4a,5,6,12b-hexahydro-2*H*-benz[a]anthracen-1-one (43): ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.48$ (s, 3H; 3-CH_3), 1.68 (s, 1H; OH), ABMN signal ($\delta_A = 3.33$, dd, $^2J = 18.8$ Hz, $^3J = 6.2$ Hz, 6-H_{eq}; $\delta_B = 2.97$, ddd, $^2J = 18.8$ Hz, $^3J = 5.6$, 7.1 Hz, 6-H_{ax}; $\delta_M = 2.20$, ddd, $^2J = 12.6$ Hz, $^3J = 5.6$, 6.2 Hz, 5-H_{ax}; $\delta_N = 1.93$, dd, $^2J = 12.6$ Hz, $^3J = 7.1$ Hz, 5-H_{eq}), AB signal ($\Delta\delta = 0.09$, $\delta_A = 2.06$, 4-H_{ax}, $\delta_B = 1.97$, $^4J = 2.2$, 2-H_{eq}, $J_{AB} = 16.5$ Hz), AB signal ($\Delta\delta = 0.20$, $\delta_A = 2.89$, 2-H_{ax}, $\delta_B = 2.69$, dd, $^4J = 2.2$ Hz, 2-H_{eq}, $J_{AB} = 11.6$ Hz), 3.79 (s, 3H; OCH_3), 3.93 (s, 3H; OCH_3), 5.04 (s, 1H; OH), 7.47–7.58 (m, 2H; 9-H, 10-H), 7.99 (d, $J = 7.9$ Hz, 1H; 8-H/11-H), 8.06 (d, $J = 8.4$ Hz, 1H; 8-H/11-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 22.00$ (t, C-6), 29.43 (q, 3-CH_3), 31.32 (t, C-5), 43.27 (t, C-4), 50.66 (t, C-2), 60.67/62.48 (2 × q, 2 × OCH_3), 73.85/74.38/77.18 (3 × s, C-3, C-4a, C-12b), 121.91/122.48 (2 × d, C-8, C-11), 125.70/126.90 (2 × d, C-9, C-10), 124.05/127.28/127.58/128.76 (4 × s, C-6a, C-7a, C-11a, C-12a), 150.01/150.09 (2 × s, C-7, C-12), 206.39 (s, C-1); UV (methanol): λ_{max} (lg ε) = 218 nm (4.22), 248 (4.12), 266 (3.97), 324 (3.60); IR (KBr): $\tilde{\nu} = 3429$ (OH), 2932 (CH), 2845 (CH), 1713 (C=O), 1453, 1359, 1273, 1106, 1064, 741 cm^{-1}; elemental analysis (%) calcd for $C_{21}H_{24}O_6$ (372.42): C 67.71, H 6.50; found for **43**: C 67.54, H 6.41; found for **42**: C 66.89, H 6.28.

1-[3-(5-Hydroxy-3-oxohexen-4-yl)-1,4-dimethoxynaphthalen-2-yl]-propane-1,2-dione (44): ^{1}H NMR (200 MHz, $CDCl_3$): enol: $\delta = 2.04$ (s, 3H; 6″-H), 2.55 (s, 3H; 3-H), 2.53–2.63 (m, 2H; 2″-H), 3.02–3.16 (m, 2H; 1″-H), 3.88 (s, 3H; OCH_3), 3.94 (s, 3H; OCH_3), 5.53 (s, 1H; 4″-H), 7.48–7.66 (m, 2H; 6′-H, 7′-H), 8.02–8.11 (m, 2H; 5′-H, 8′-H), 15.40 (brs, 1H; OH); ^{1}H NMR (200 MHz, $CDCl_3$): ketone: $\delta = 2.25$ (s, 3H; 6″-H), 2.55 (s, 3H; 3-H), 2.80–2.94 (m, 2H; 2″-H), 3.02–3.16 (m, 2H; 1″-H), 3.59 (s, 2H; 4″-H), 3.88 (s, 3H; OCH_3), 3.91 (s, 3H; OCH_3), 7.48–7.66 (m, 2H; 6′-H, 7′-H), 8.02–8.11 (m, 2H; 5′-H, 8′-H); ^{13}C NMR (50 MHz, $CDCl_3$): enol: $\delta = 23.18$ (t, C-1″), 24.70 (q, C-3), 25.11 (q, C-6″), 39.96 (t, C-2″), 62.80/64.08 (2 × q, 2 × OCH_3), 100.20 (d, C-4″), 123.48 (2 d, C-5′, C-8′), 126.95/129.04 (2 × d, C-6′, C-7′), 126.07/126.89/129.00/131.57 (4 × s, C-2′, C-3′, C-4′a, C-8′a), 151.65/154.72 (2 × s, C-1′, C-4′), 190.86/194.14 (2 × s, C-3″, C-5″), 196.51/199.03 (2 × s, C-1, C-2); IR (KBr): $\tilde{\nu} = 3405$ (OH), 2940 (CH), 2841 (CH), 1719 (C=O), 1683 (C=O), 1616 (C=O), 1419, 1357, 1062, 964, 778 cm^{-1}.

3,4a,12b-Trihydroxy-3-methyl-3,4,4a,5,6,12b-hexahydro-2*H*-benz[*a*]anthracene-1,7,12-trione (3,4a-*trans*-3, 8-deoxy WP 3688-2): A solution of the 3,4a-*trans*-triol **43** (120 mg, 0.32 mmol) in CH_2Cl_2 (2 mL) was oxidized by using CAN (348 mg, 0.63 mmol) and nBu_4NHSO_4 (215 mg, 0.63 mmol) in dry CH_2Cl_2 (10 mL) as described for **4**. The crude product contained about 20% of unidentified quinone monoacetals (NMR) that were cleaved with sulfuric acid on silica gel as described for **41**. The crude product was purified by preparative TLC chromatography on silica gel (0.5 mm, CH_2Cl_2/MeOH 97:3) to afford the quinone **3** (84 mg, 70%) as a yellow solid. M.p. 128 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.47$ (s, 3H; 3-CH_3), 1.91–2.09 (m, 3H; 5-H and OH), AB signal ($\Delta\delta = 0.11$, $\delta_A = 2.14$, dd, $^4J = 1.5$ Hz, 4-H_{eq}; $\delta_B = 2.03$, 4-H_{ax}, $^2J = 14.4$ Hz), AB signal ($\Delta\delta = 0.51$, $\delta_A = 3.03$, 2-H_{eq}; $\delta_B = 2.52$, 2-H_{ax}, $^2J = 12.1$ Hz), 2.68 (brs, 1H; OH), 2.66–2.78 (m, 1H; 6-H), 2.92–3.03 (m, 1H; 6-H), 5.35 (brs, 1H; OH), 7.72–7.79 (m, 2H; 9-H, 10-H), 8.04–8.13 (m, 2H; 8-H, 11-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 22.51$ (t, C-6), 30.32 (q, 3-CH_3), 30.37 (t, C-5), 45.02 (t, C-4), 51.16 (t, C-2), 73.11/73.79/78.62 (3 × s, C-3, C-4a, C-12b), 126.53/126.77 (2 × d, C-8, C-11), 131.72/131.92 (2 × s, C-7a, C-11a), 134.11/134.33 (2 d, C-9, C-10), 140.81/147.58 (2 × s, C-6a, C-12a), 184.37/184.90 (2 × s, C-7, C-12), 205.59 (s, C-1).

3,4a,12b-Trihydroxy-3-methyl-3,4,4a,5,6,12b-hexahydro-2*H*-benz[*a*]anthracene-1,7,12-trione (3,4a-*cis*-45): The *cis*-triol **42** (16 mg, 0.04 mmol) was oxidized by using CAN (47 mg, 0.08 mmol) and nBu_4NHSO_4 (29 mg, 0.08 mmol) in CH_2Cl_2 (8 mL) as described above for **3**, to afford the 3,4a-*cis*-triol **45** (5 mg, 36%) as a yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.30$ (s, 3H; 3-CH_3), AB signal ($\Delta\delta = 0.08$, $\delta_A = 2.03$, dd, $^4J = 2.6$ Hz, 4-H_{eq}; $\delta_B = 1.95$, 4-H_{ax}, $^2J = 14.8$ Hz), 1.95–2.04 (m, 2H; 5-H), AB signal ($\Delta\delta = 0.32$, $\delta_A = 2.83$, dd, $^4J = 2.6$ Hz, 2-H_{eq}; $\delta_B = 2.51$, 2-H_{ax}, $^2J = 12.6$ Hz), 2.62–2.75 (m, 1H; 6-H), 2.99 (s, 1H; OH), 3.08 (ddd, $^2J = 21$ Hz, $^3J = 4.8$, 1.6 Hz, 1H; 6-H), 4.11 (brs, 1H; OH), 5.07 (s, 1H; OH), 7.73–7.80 (m, 2H; 9-H, 10-H), 8.03–8.13 (m, 2H; 8-H, 11-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 23.40$ (t, C-6), 30.63 (q, 3-CH_3), 30.68 (t, C-5), 41.66 (t, C-4), 51.98 (t, C-2), 75.59/75.96/78.99 (3 × s, C-3, C-4a, C-12b), 126.96/127.34 (2 × d, C-8, C-11), 131.92/132.17 (2 × s, C-7a, C-11a), 134.78/134.80 (2 × d, C-9, C-10), 142.11/147.18 (2 × s, C-6a, C-12a), 183.53/184.94 (2 × s, C-7, C-12), 205.94 (s, C-1).

3,4a,6,12b-Tetrahydroxy-7,12-dimethoxy-3-methyl-3,4,4a,5,6,12b-hexahydro-2*H*-benz[*a*]anthracen-1-one (46): After one incomplete oxidation of **45** (16 mg, 0.04 mmol) and $(nBu)_4NHSO_4$ (29 mg, 0.08 mmol) by CAN (47 mg, 0.08 mmol), 2 mg (14%) of the 6-hydroxylated tetraol **46** was isolated. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.19$ (s, 3H; 3-CH_3), AB signal ($\Delta\delta = 0.34$, $\delta_A = 2.42$, 4-H_{ax}; $\delta_B = 2.08$, dd, $^4J = 2.7$ Hz, 4-H_{eq}, $^2J = 15.7$ Hz), ABX signal ($\Delta\delta = 0.33$, $\delta_A = 2.51$, dd, $^3J = 6.4$ Hz, 5-H_{ax}; $\delta_B = 2.18$, 5-H_{eq}, $^2J = 14.5$ Hz), AB signal ($\Delta\delta = 0.08$, $\delta_A = 2.79$, 2-H_{ax}; $\delta_B = 2.71$, dd, $^4J = 2.7$ Hz, 2-H_{eq}, $^2J = 12.6$ Hz), 3.25 (brs, 1H; OH), 3.38 (brs, 1H; OH), 3.79 (s, 3H; 12-OCH_3), 4.00 (brs, 1H; OH), 4.08 (s, 3H; 7-OCH_3), 5.35 (s, 1H; OH), 5.42 (d, $^3J = 6.4$ Hz, 1H; 6-H_{eq}), 7.56–7.65 (m, 2H; 9-H, 10-H), 8.04–8.11 (m, 2H; 8-H, 11-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 30.09$ (q, 3-CH_3), 38.15 (t, C-5), 43.30 (t, C-4), 50.68 (t, C-2), 62.07/62.73 (2 × q, 2 × OCH_3), 63.82 (d, C-6), 75.39/77.55/78.47 (3 × s, C-3, C-4a, C-12b), 122.12/122.83 (2 × d, C-8, C-11), 125.79/127.03/128.65/128.96 (4 × s, C-6a, C-7a, C-11a, C-12a), 126.82/127.36 (2 × d, C-9, C-10), 149.91/151.45 (2 × s, C-7, C-12), 207.19 (s, C-1).

Acknowledgements

We thank the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for financial support.

[1] K. Krohn, P. Frese, C. Freund, *Tetrahedron* **2000**, in press.
[2] J. Rohr, R. Thiericke, *Nat. Prod. Rep.* **1992**, *9*, 103–137.
[3] K. Krohn, J. Rohr, *Top. Curr. Chem.* **1997**, *188*, 128–195.
[4] M. Hatsu, T. Sasaki, S. Gomi, Y. Kodama, M. Sezaki, S. Inouye, S. Kondo, *J. Antibiot.* **1992**, *45*, 325–330.
[5] S. J. Gold, X. C. Cheng, *J. Org. Chem.* **1994**, *59*, 400.
[6] G. Udvarnoki, T. Henkel, R. Machinek, J. Rohr, *J. Org. Chem.* **1992**, *57*, 1274–1276.
[7] S. Ayukawa, T. Takeuchi, M. Sezaki, T. Hara, H. Umezawa, T. Nagatsu, *J. Antibiot.* **1968**, *21*, 350–353.
[8] T. Nagatsu, S. Ayukawa, T. Nagatsu, *J. Antibiot.* **1968**, *21*, 354–357.
[9] S. J. Gould, X.-C. Cheng, *J. Org. Chem.* **1994**, *59*, 400–405.
[10] H. Irie, Y. Mizuno, I. Kuono, T. Nagasawa, Y. Tani, H. Yamada, T. Taga, K. Osaki, *J. Chem. Soc. Chem. Commun.* **1983**, 174–175.
[11] K. Kim, Y. Guo, G. A. Sulikowski, *J. Org. Chem.* **1995**, *60*, 6866–6871.
[12] R. Faust, B. Göbelt, *J. Prakt. Chem.* **1998**, *340*, 90–93.
[13] K. Krohn, J. Micheel, *Tetrahedron* **1998**, *54*, 4827–4838.
[14] K. Krohn, U. Flörke, C. Freund, N. Hayat, *Eur. J. Org. Chem.* **2000**, in press.
[15] G. A. Kraus, Z. Wan, *Tetrahedron Lett.* **1997**, *38*, 6509–6512.
[16] T. E. Nicolas, R. W. Franck, *J. Org. Chem.* **1995**, *60*, 6904–6911.
[17] D. O'Hagan, *The Polyketide Metabolites*, Ellis Horwood, Chichester, **1991**.
[18] R. A. Smiley, *J. Org. Chem.* **1958**, *23*, 1115–1117.

[19] R. T. Arnold, S. T. Kulenovic, *Synthetic Communications* **1977**, *7*, 223–232.
[20] J. E. McMurry, *Chem. Rev.* **1989**, *89*, 1513–1524.
[21] G. A. Molander, *Chem. Rev.* **1992**, *92*, 29–68.
[22] J. L. Namy, J. Souppe, H. B. Kagan, *Tetrahedron Lett.* **1983**, *24*, 765–766.
[23] G. A. Molander, C. Kenny, *J. Org. Chem.* **1988**, *53*, 2132–2136.
[24] G. A. Molander, C. R. Harris, *Chem. Rev.* **1996**, *96*, 307–338.
[25] A. Fürstner, D. N. Jumbam, N. Shi, *Z. Naturfosch. B* **1995**, *50*, 326–332.
[26] A. Chénedé, P. Pothier, M. Sollogoub, A. J. Fairbanks, P. Sinay, *J. Chem. Soc. Chem. Commun.* **1995**, 1373–1374.
[27] J. L. Chiara, W. Cabri, S. Hanessian, *Tetrahedron Lett.* **1991**, *32*, 1125–1128.
[28] L. Syper, J. Mlochowski, K. Kloc, *Tetrahedron* **1983**, *39*, 781–792.
[29] M. Gingras, *Tetrahedron Lett.* **1991**, *32*, 7381–7384.
[30] E. J. Enholm, J. A. Schreier, *J. Org. Chem.* **1995**, *60*, 1110–1111.
[31] K. Kusuda, J. Inanaga, M. Yamaguchi, *Tetrahedron Lett.* **1989**, *30*, 2945–2948.
[32] R. Schobert, *Angew. Chem.* **1988**, *100*, 869–871; *Angew. Chem. Int. Ed.* **1988**, *27*, 855-856.
[33] L Lu., H.-Y. Chang, J.-M. Fanf, *J. Org. Chem.* **1999**, *64*, 843–853.
[34] P. H. J. Carlsen, T. Katsuki, V. S. Martin, K. B. Sharpless, *J. Org. Chem.* **1981**, *46*, 3936–3938.
[35] J. E. McMurry, J. G. Rico, T. C. Lecta, *J.Org. Chem.* **1989**, *54*, 3748.
[36] K. Ohmori, M. Kitamura, K. Suzuki, *Angew. Chem.* **1999**, *111*, 1304–1307; *Angew. Chem. Int. Ed.* **1999**, *38*, 1226–1229.
[37] N. Taniguchi, T. Hata, M. Uemura, *Angew. Chem.* **1999**, *111*, 1311–1314; *Angew. Chem. Int. Ed.* **1999**, *38*, 1232–1235.
[38] R. Annunziata, M. Benaglia, C. Cinquini, L. Raimondi, *Eur. J. Org. Chem.* **1999**, 3369–3374.
[39] F. Huet, A. Lechevallier, M. Pellet, J. M. Conia, *Synthesis* **1978**, 63–65.
[40] L. Syper, K. Kloc, J. Mlochowski, Z. Szulc, *Synthesis* **1979**, 521–522.
[41] Y. Tanoue, A. Terada, *Bull. Chem. Soc. Jpn.* **1988**, *61*, 2039–2043.
[42] A. McKillop, D. H. Perry, M. Edwards, S. Antus, L. Farkas, M. Nógrádi, E. C. Taylor, *J. Org. Chem.* **1976**, *41*, 282–287.
[43] J. Rohr, A. Zeeck, *J. Antibiot.* **1987**, *40*, 459–467.
[44] F. Hélion, J.-L. Namy, *J. Org. Chem.* **1999**, *64*, 2944–2946.
[45] S. Matubara, Y. Hashimoto, t. Okano, K. Utimoto, *Synlett* **1999**, 1411–1412.
[46] D. Hoppe, T. Hense, *Angew. Chem.* **1997**, *109*, 2376–2410; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2282–2316 .
[47] K. Krohn, A. Michel, U. Flörke, H.-J. Aust, S. Draeger, B. Schulz, *Liebigs Ann. Chem.* **1994**, 1093–1097.
[48] P. Girard, J. L. Namy, H. B. Kagan, *J. Am. Chem. Soc.* **1980**, *102*, 2693–2698.
[49] SHELXTL NT, Ver. 5.10, Bruker Analytical X-ray Systems, Madison, Wisconsin, USA.

Received: March 1, 2000 [F2328]

