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Synthetic Anthracyclinones, XXIX[1)]

Quinone Antibiotics with Five Substituents at the Hydroaromatic Ring

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From the adduct **8**, obtained from naphthazarin (**6**) and the diene **7**, the olefin **25** is synthesized *via* epoxidation (→**15**) and treatment with base. Cleavage of the silyl ethers **25** yields the allylic alcohol **26** which can be epoxidized to give **28** and **30** and subsequently cleaved with methanol to yield the methyl ethers **32** and **33**. The relative configuration of the acetonide **36** obtained from **33** is confirmed by X-ray analysis; consequently, the relative configuration **1a** of altersolanol A is proved. Furthermore, the mass spectrometrical investigations support the stereochemistry of the isomers **31** – **33**. The tetracyclic anthracyclinones **40** – **42** are synthesized by Diels-Alder reaction of **31**, **33**, and **36** with 1-methoxy-1,3-butadiene.

Synthetische Anthracyclinone, XXIX[1)]. – Chinon-Antibiotica mit fünf Substituenten am hydroaromatischen Ring

Das aus Naphthazarin (**6**) und dem Dien **7** erhältliche Addukt **8** wird zu **15** epoxidiert und durch Basenbehandlung zum Olefin **25** umgesetzt. Der durch Spaltung des Silylethers **25** erhältliche Allylalkohol **26** wird zu **28** und **30** epoxidiert und mit Methanol zu den Methylethern **32** und **33** geöffnet. Die relative Konfiguration des aus **33** erhältlichen Acetonids **36** wird durch Röntgenstrukturanalyse abgesichert; damit ist auch die relative Konfiguration **1a** des Altersolanols A bewiesen. Ferner bestätigen massenspektrometrische Untersuchungen die Stereochemie der Isomeren **31** – **33**. Die tetracyclischen Anthracyclinone **40** – **42** werden durch Diels-Alder-Reaktion von **31**, **33** und **36** mit 1-Methoxy-1,3-butadien erhalten.

The clinically important antitumor antibiotics of the anthracycline family such as daunorubicin or aclacinomycin A possess three or four substituents at the hydroaromatic part of the molecule with two or three chiral centers, respectively. There are, however, several stereochemically more complex quinoid antibiotics with five substituents at ring A. This group is represented not only by the tetracyclic anthracyclinones aranciamycinone[2)] (**3**),

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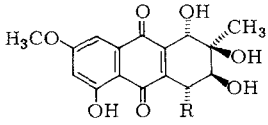
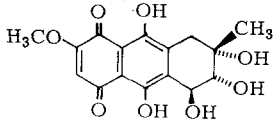
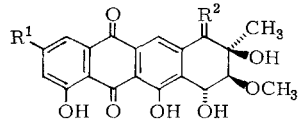
steffimycinone[3] **(4)**, or steffimycinol[3] **(5)** but also by tricyclic quinone antibiotics such as altersolanol A[4] **(1a)***, dactylariol[4] **(1b)**, and bostrycin[5] **(2)**.



	R
Altersolanol (**1a**)	OH
Dactylariol (**1b**)	H



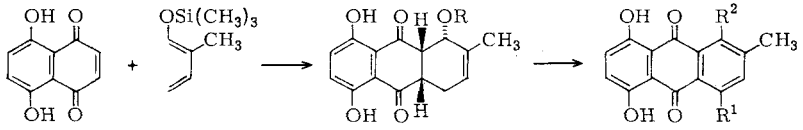
Bostrycin (**2**)



	R^1	R^2
Aranciamycinon (**3**)	H	=O
Steffimycinon (**4**)	OCH_3	=O
Steffimycinol (**5**)	OCH_3	H,OH

Racemic 3-demethoxyaranciamycinone[6]** and 3-demethoxysteffimycinone[7] have been prepared, and with the exception of aranciamycinone[8] no total synthesis of quinone antibiotics with five substituents in the chiral part of the aglycone has been published. However, the chemical transformation of natural products like daunomycinone into 3-methoxydaunomycinone[9] and ε-rhodomycinone into 3-methoxy-ε-rhodomycinone[10] were reported.

We now describe a stereoselective method for the synthesis of these more complex derivatives which gives access to some tri- and tetracyclic members of quinone antibiotics. The principle of the synthesis is the successive addition of different dienes to naphthazarin[11] **(6)**, a principle which has been successfully applied to the synthesis of daunomycinone[12,13].



6 **7** **8**: R = $Si(CH_3)_3$ **9**: R = H

	R^1	R^2
10	H	H
11	H	OH
12	OH	OH

In a related study of the synthesis of 6-demethoxybostrycin we have investigated the Diels-Alder reaction of naphthazarin **(6)** with 3-methyl-1-trimethylsiloxy-1,3-butadiene[14]. A retrosynthetic analysis showed the similar 2-methyl-1-trimethylsiloxy-1,3-butadiene **(7)** to be a suitable reagent for the introduction of both benzylic substituents present in altersolanol A **(1a)** at a later stage of the synthesis. Diene **7** was prepared from the readily available tiglic aldehyde[15] using the silylation method employed for 3-methyl-1-trimethylsiloxy-1,3-butadiene[14]. The Diels-Alder reaction of naphthazarin

*) Only the relative configurations of **1a** and **1b** are known.
**) IUPAC and Chem. Abstr. numbering are used in this communication.

(**6**) and the diene **7** gave one single crystalline adduct **8** in 83% yield. The relative stereochemistry of **8** conforms to the *endo* rule of Alder[16], and corresponding stereochemistry has been postulated for related adducts[17]. However, the configuration cannot unambiguously be determined on the basis of ^{1}H NMR alone. An X-ray analysis definitely proved the *trans* orientation of the silylether group to the neighboring proton at C-9a in addition to the *cis* connection of ring A and B[18].

The silyl ether **8** crystallizes in the orthorombic space group $P2_12_12_1$ with four molecular units $C_{18}H_{22}O_5Si$ in the cell (final $R = 0.047$). Half-chair conformations are observed in the hydroaromatic ring A as well as in the quinoid ring B, whereas ring C is approximately planar. There are no intermolecular hydrogen bonds in the structure, which consists of discrete molecules held together by van der Waals interactions (see Figure 1).

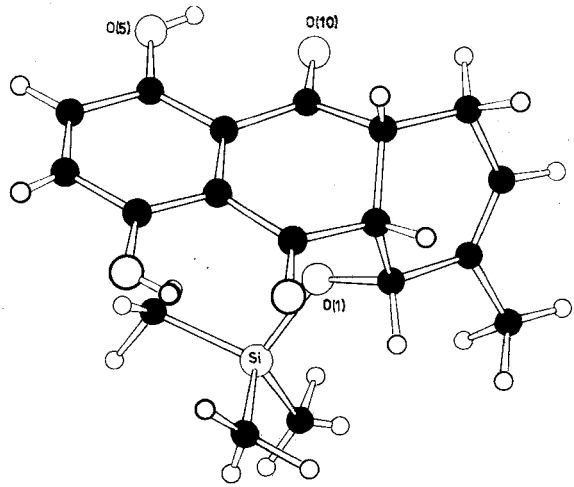


Fig. 1. Perspective view of the molecule **8**

Figure 1 clearly demonstrates that the *cis*-decalin-like shape of the molecule together with the large *endo* silyl ether grouping makes attack of the double bond from the *endo* side very difficult. This fact is of great importance for stereoselective epoxidations (see below). First of all, however, the chemistry of the adduct **8** had to be studied.

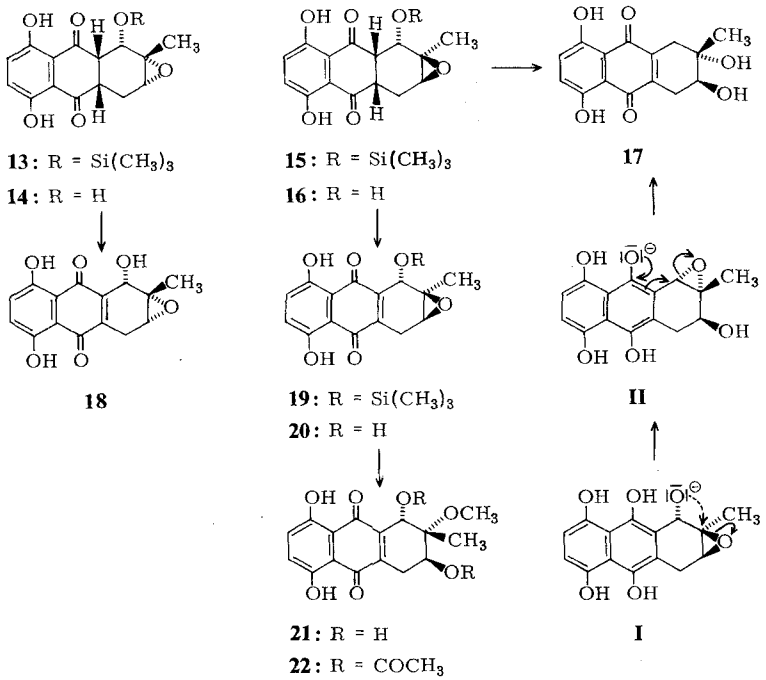
The cleavage of the silyl ether **8** could be effected at low temperatures using 0.01 N hydrochloric acid in methanol to give the alcohol **9** in 96% yield. Stronger acid, as well as base or heating above the melting point (112 °C) gave rise to elimination of the silyl ether group, and subsequent air oxidation afforded the anthraquinone **10** almost quantitatively. The hydroxy group at C-1 could be preserved by oxidation of **9** with pyridinium chlorochromate to afford 1,5,8-trihydroxy-2-methyl-9,10-anthraquinone (**11**). Further, oxidation of **11** with manganese dioxide yielded the naturally occuring anthraquinone cynodontine (**12**) in moderate yield[19].

Next, the epoxidation of the olefins **8** and **9** and the chemistry of the resulting epoxides were investigated. Treatment of the silyl ether **8** with 3-chloroperbenzoic acid at room temperature gave the *exo* epoxide **15** almost exclusively (^{1}H NMR: **15**:**13** =

20:1). The selectivity was further improved by reaction at lower temperature (4°C) affording the pure *exo* epoxide **15** after only one crystallization from methanol in 89% yield. In contrast, an approximately 1:1 mixture of the expoxides **14** and **16** was obtained from the reaction of the allylic alcohol **9**. Obviously, in spite of the steric hindrance, some *endo* epoxide was formed as a result of complexation of the peracid with the allylic alcohol. It is known from many examples in the literature, that cyclic allylic alcohols predominately yield the *cis* epoxides with peracids[20]. The isomeric epoxides **14** and **16**, whose relative configurations were unambiguously established at a later stage, could easily be distinguished by TLC. However, the separation by chromatography failed due to partial oxidation to the corresponding quinones **18** and **20** during chromatography. Experiments were conducted in order to obtain the pure *trans* epoxide **16** by selective cleavage of the silyl ether **15**. Although no *cis* epoxide **14** was present in the reaction product, some oxidation to **20** and cleavage to **21** always occurred, even under mild fluoride-promoted reaction conditions.

The corresponding quinones **18** and **20** could best be obtained by air oxidation in the presence of a mild base such as potassium carbonate. The oxidized products **18** and **20** were stable enough to be separated by TLC chromatography.

An unexspected result was observed on treating the mixture of **14** and **16** with sodium methoxide under strict exclusion of air. On oxidative workup – in addition to the quinoid epoxides **18** and **20** – a new product of constitution **17** was obtained. In separate experiments it could be shown that the new compound was exclusively formed from the *trans* epoxide **16**.



The structure of the product was shown to be the *trans* diol **17** by comparison with a corresponding *cis* diol prepared earlier[14]. Surprisingly, the epoxide had not been opened by methoxide and furthermore elimination of the benzylic substituent had occurred. The formation of **17** can best be mechanistically explained by successive enolization, Payne rearrangement[21], and reductive opening of the oxirane (see formulas **I** and **II**), which is a well known reaction in quinone chemistry[22].

The transformation of the epoxide **20** under acidic conditions was more in accord with expectation. Thus, the addition of methanol occurred selectively at the tertiary position to yield **21**. The constitution of **21** was confirmed by acetylation of the two secondary hydroxy groups to give the diacetate **22**. The chelated phenolic groups did not react under mild acidic conditions.

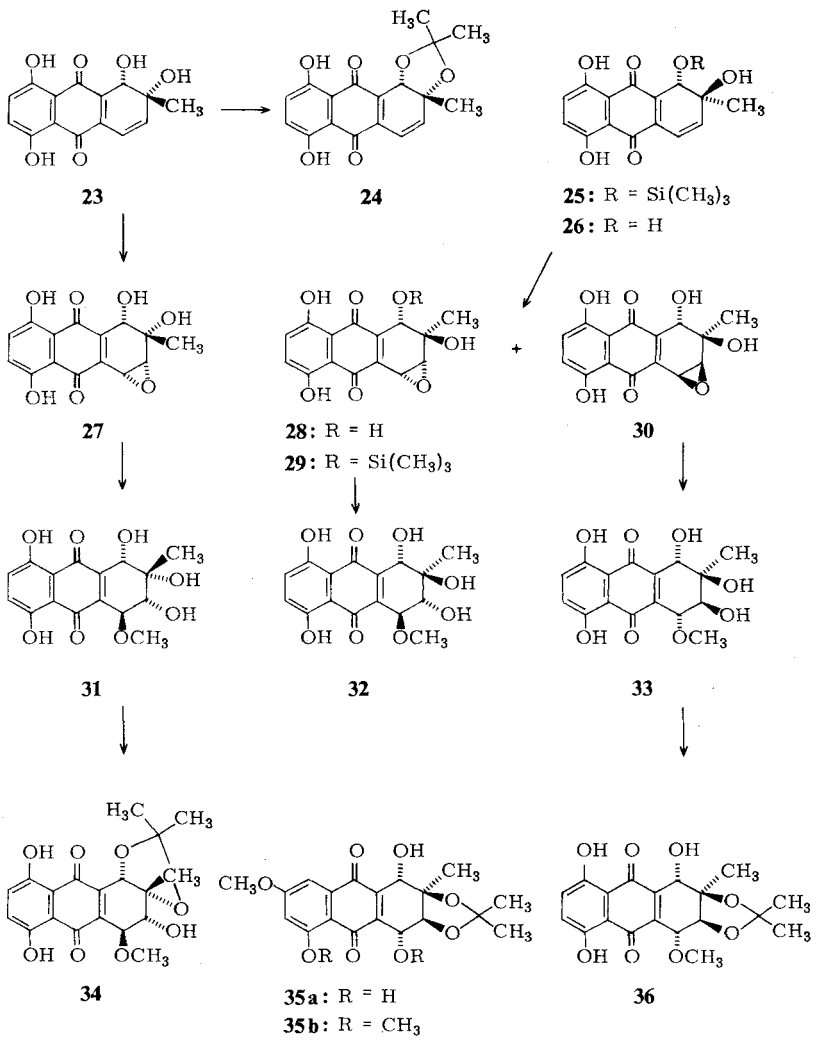
Thus far, the reactions studied did not bring much progress towards pentasubstituted derivatives, since in the natural products the tertiary hydroxy group at C-2 is not alkylated. However, base treatment of the oxidized *cis* and *trans* epoxides **18** and **20** smoothly formed the *cis* and *trans* enediols **23** and **26**, respectively. This rearrangement occurred under surprisingly mild conditions with various bases and solvents. The formation of the olefins **23** and **26** can easily be explained by base-induced deprotonation of the acidic benzylic position followed by opening of the epoxide. In fact, the prior oxidation of the epoxides **14** – **16** to the quinones **18** – **20** is a prerequisite for olefin formation (generating sufficiently acidic benzylic protons)[23]. As has been shown earlier, base treatment of **14** and **16** with exclusion of air gave only the epoxyquinones **18** and **20** and the rearranged *trans* diol **17**, even with prolonged reaction times.

The configurations of the epoxides **14** and **16** could now be determined, since only the less polar enediol **23** derived from **14** gave an isopropylidene ether **24**, thus confirming the *cis* orientation of the hydroxy groups. Furthermore, in TLC experiments, the *cis* diol **23** gave non-polar cyclic complexes on addition of phenylboronic acid to the eluant, whereas **26** did not. The silyl ether **15** was also efficiently converted *via* the oxidized form **19** (not isolated) into the olefinic silyl ether **25** by simple treatment with two drops of triethylamine in dichloromethane in the presence of air.

For the introduction of the last substituents the olefins **23**, **25**, and **26** could again be epoxidized. On treatment with 3-chloroperbenzoic acid the olefin **23** was converted into only one single epoxide **27**. The configuration was expected to be all *cis* due to chelation of the peracid with both hydroxy groups. This was later confirmed by comparison with products derived from **26**.

On the other hand, two epoxides **28** and **30** were obtained from the *trans* diol **26** in a much slower reaction. Inspection of models showed that chelation of the peracid is possible with both the allylic and homoallylic hydroxy groups, directing the addition of oxygen from both sides of the molecule.

Surprisingly, the silyl ether **25** did not give the *cis* epoxide **30**, but exclusively the *trans* epoxide **29** which could quantitatively be cleaved to give the epoxy alcohol **28**. Epoxidation occurred extremely slow (3 days) and obviously the tertiary hydroxy group did not have an axial position (due to the large equatorial silyl ether grouping), thus losing the ability of anchimeric assistance.



The epoxides **28** and **30** could be separated by TLC, but an unambiguous determination of their configuration was not possible by ^{1}H NMR alone. The problem was solved by further chemical transformations (see below). All three epoxides **27**, **28**, and **30** gave in a highly selective reaction one product on treatment with acidic methanol. Only two of them, **31** and **33**, formed isopropylidene ethers making the all-*trans* configuration of **32** probable. In order to definitely establish the relative stereochemistry of the methyl ethers **31** – **33** an X-ray structure analysis of the nicely crystalline acetonide **36** (derived from the most polar triol **33**) was performed. Figure 2 confirms the relative orientation of the substituents of **36**. Ring A has a boat conformation and the envelope conformation of the dioxolane ring is nearly undistorted.

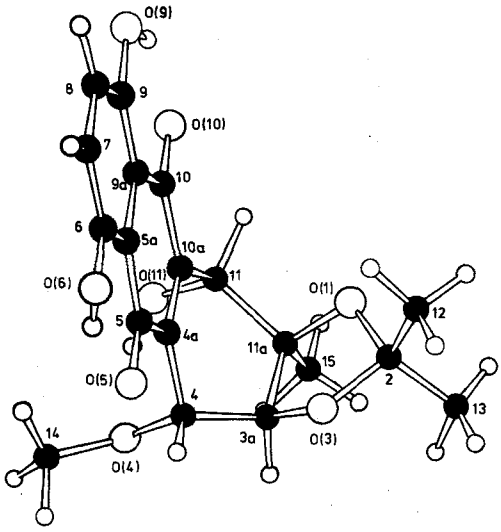


Figure 2. Perspective view of the molecule **36**

The isopropylidene ether crystallizes in the monocline space group $P2_1/n$ with four formular units $C_{19}H_{20}O_8$ in the cell. All H atoms were fixed at $U = 0.04$ Å, the final R being 0.063 for 1310 observed reflections, based on unit weights. In addition to intramolecular hydrogen bonds of the phenolic protons a weak intermolecular interaction of O-1 and H-11 can be observed.

Thus, not only the ralative configurations of the epoxides **28** and **30** (and by exclusion of **27**), but also the expected stereoselective *trans* opening of the oxirane ring and the regioselective addition of methanol to the benzylic position are confirmed. The chemical shifts and the coupling constants of the ^{1}H NMR spectra are in agreement with the assigned configurations of **31**–**33**. Of special value is the 1,5-coupling (W-conformation) of 1.3 Hz of 1- and 3-H in **32**, thus showing the *cis* relationship of 1- and 3-OH.

The all-*cis* triol **31** could possibly form two isomeric acetonides. The structure **34** was assigned based on the downfield shift of 1-H in the ^{1}H NMR spectrum on transformation of **31** into the isopropylidene ether **34**. Furthermore, the mass spectra of the acetonides of **34** and **36** differ considerably. The characteristic RDA fragment at $m/z = 262$ (see below) is missing in **34**, since the possible fragments are held together by the isopropylidene bridge. Such a fragment does likewise not appear in the mass spectrum of the 1,2-acetonide **24**.

At this stage of the investigation a comparison of the natural and synthetic products can be made. Altersolanol A (**1a**) has been transformed into the acetonide **35a** which in turn was selectively methylated to give the dimethyl ether **35b** due to steric hindrance of 1-OH[4a]. Table 1 compares the ^{1}H NMR data of **35b** and **36**. The closely corresponding chemical shifts and coupling constants prove the identity of the chiral part of the molecules, thus confirming **1a** as the correct structure of altersolanol A[4a].

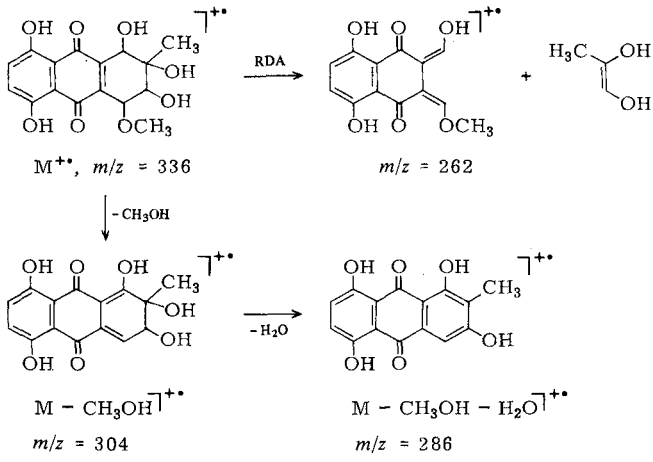
Table 1. ^{1}H NMR data of the altersolanol A derivative **35b** (**A**; 100 MHz)[4a] and the synthetic product **36** (**B**; 400 MHz) ($CDCl_3$, δ values, TMS = 0, *J*[Hz])

	CH_3	CH_3	CH_3	OH	OCH_3	3-H	1-H	4-H
A:	1.00	1.38	1.72	3.30 (13)	3.46	4.50 (2.8)	4.78 (13)	5.04 (2.8)
B:	0.95	1.37	1.74	3.44 (12.6)	3.47	4.54 (2.6)	4.90 (12.6)	5.03 (2.6)

The isomeric triols **31** – **33** can readily be separated by TLC. In addition to the reaction of the isomerically pure epoxides **27**, **28**, and **30** the whole sequence of reactions starting from **9** can be conducted without purification of any intermediates separating the isomers **31** – **33** at the final step. On the other hand, starting from the silyl ether **8** several highly selective reactions lead to the all-*trans* configurated triol **32** without any chromatographic separation of the isomers.

The stereochemistry of the isomeric triols **31** – **33** being established, we have studied the mass spectra of **31** – **33** in some detail in order to see what effect the configurational differences may have. As expected, the 70 eV mass spectra show peaks for the same fragment ions (see Table 2). The molecular ions (*m/z* = 336) are of relatively low intensity due to rapid elimination of water and methanol to give the fragment ion *m/z* = 286. A further characteristic ion of *m/z* = 262 of all three compounds **31** – **33** is due to a retro Diels-Alder reaction (RDA) as shown in Scheme 1. This process is equally well known from anthracyclinones[24].

Scheme 1



However, the intensities of the fragment ions differ considerably, for instance of ($M^{+\bullet} - H_2O$) in **33**. In analogy to stereoisomeric cyclohexane polyols a clear relationship between relative configuration and fragment ion intensities can be expected for the ions ($M^{+\bullet} - H_2O$) and ($M^{+\bullet} - CH_3OH$), specially of weekly excited ions[25]. This is the case using the FIK method or investigating metastable ions by MIKE spectroscopy[26,27]. The decomposition of the low-energy metastable ions in the MIKE spectra

accurately reflects the stereochemistry, whereas corresponding fragment ions of stereoisomers vary only if they have different structure due to different mechanisms of formation. In fact, these expectations are fulfilled for the MIKE spectra of the ions in the 70-eV mass spectra (see Table 3). The fragment ions $m/z = 262$ give identical MIKE spectra of all three isomers **31** – **33**, since the steric differences have been reduced or fully eliminated by ring cleavage. Minor deviations are observed in the ion $m/z = 286$ ($M^{+\cdot} - H_2O - CH_3OH$) whereas the MIKE spectra of the molecular ions are distinctly different specially for **33**.

The main degradation pathways of the metastable ions of **31** and **32** are elimination of H_2O ($m/z = 318$), CH_3OH ($m/z = 304$) as well as loss of the OCH – $\dot{C}$HOH radical ($m/z = 263$). The *trans*-1,4 configuration of the hydroxy and methoxy groups facilitates 1,4-elimination of H_2O and CH_3OH and the MIKE spectra of these ions differ only slightly. In contrast, the MIKE spectrum of **33** shows only one intense signal for H_2O elimination (see Table 3).

Table 2. Characteristic ions in the 70-eV mass spectra of the tricyclic quinones **31** – **33** (relative intensity in % of the base peak)

m/z	ion	**31**	**32**	**33**
336	$M^{+\cdot}$	6	5	4
318	$-H_2O$	1	1	7
304	$-CH_3OH$	2	2	2
286	$-H_2O$ $-CH_3OH$	21	18	40
263		44	35	41
262		48	58	33
244		75	100	100
243		33	47	63
231		69	41	84
230		100	87	96

Table 3. MIKE spectra of the molecular ion $m/z = 336$ and the fragment ion $m/z = 286$ in the 70-eV mass spectra of **31** – **33** (relative to the most intense signal = 100%)

m/z	ion	**31**	**32**	**33**
mother ion m/z = 336				
318	$-H$	100	100	100
304	$-CH_3OH$	85	68	12
286	$-H_2O$ $-CH_3OH$	16	15	3
263		48	47	7
244		12	18	2
mother ion m/z = 286				
268	$-H_2O$	29	88	73
258	$-CO$	52	77	93
244	$-H_2O$ $-CO$	100	100	100
240		–	10	10
231 + 1		–	17	11

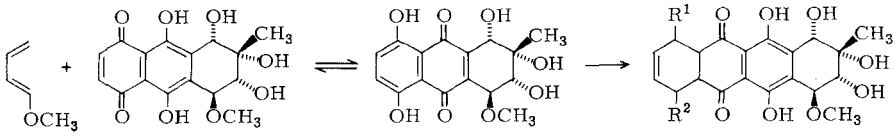
The *cis*-1,4 configuration of 1-OH and 4-OCH_3 excludes an energetically favorable transannular 1,4-elimination, whereas the 1,3-elimination of H_2O still can proceed easily[25].

Steric differences of cyclic compounds with polar substituents can further be established by mass spectroscopy using chemical ionization (CI) methods[28,29]. The differences are especially clear, if protonated substrates MH^+ of low energy are formed by slightly exothermic protonation. Accordingly, the diastereoisomers **31** – **33** give very similar CI mass spectra with high intensity fragment ions $MH^+ - H_2O - CH_3OH$ at $m/z = 287$ using CH_4 as reagent gas. However, using isobutane as reagent gas, the CI spectra are dominated by the ions MH^+ ($m/z = 337$), $MH^+ - H_2O$ ($m/z = 319$), and $MH^+ - CH_3OH$ ($m/z = 305$) showing distinct differences of intensities (see Table 4).

Table 4. CI (isobutane) mass spectra of the stereoisomers **31** – **33** (relative intensity in % of the base peak)

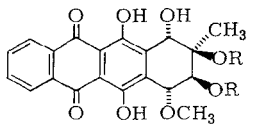
m/z	ion	**31**	**32**	**33**
337	MH^+	100	49	100
319	$-H_2O$	30	100	6
305	$-CH_3OH$	7	30	45
287	$-H_2O$ $-CH_3OH$	83	50	48

Especially striking is the high intensity of the ion m/z = 319 in **32** relative to the intensity of the MH^+ ions. In this isomer a twofold *cis*-1,2 relationship between the methyl group and the two neighboring hydroxy groups leads to increased H_2O elimination which can also be observed in the CI mass spectra of *cis*-2-methylcyclohexanols[30]. In contrast, the stereoisomers **31** and **33** behave oppositely with respect to the elimination of H_2O and CH_3OH from the MH^+ ions. A plausible reason for this effect can only be given by further investigation of model compounds. In summary, the general rules deduced from cycloalkanols can equally well be applied to the somewhat more complicated system **31** – **33** and thus independently confirm the configuration of these isomers.



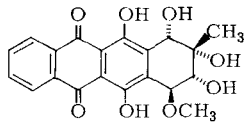
37 **31a** **31**

	R^1	R^2
38	H	OCH_3
39	OCH_3	H



41: R = H

42: R = $>C(CH_3)_2$



40

Next to the synthesis of altersolanol A analogues we turned our attention to the construction of tetracyclic anthracycline-like antibiotics. Naphthazarin derivatives like **31** exist in tautomeric forms as **31a** which can be trapped by reactive diens[11]. Thus, reaction of **31** with 1-methoxy-1,3-butadiene (**37**) smoothly gave two regioisomeric adducts **38** and **39**, which were not isolated but treated with base in the presence of air to afford the tetracycle **40** almost quantitatively. This mild procedure does not affect the stereochemistry of ring A, as is shown by the similar ^1H NMR spectra of **31** and **40**.

Similarly, **33** was transformed into the tetracyclic compound **41** which gave an acetonide on treatment with 2,2-dimethoxypropane. An identical product was obtained on treatment of **36** with the diene **37** followed by aromatization to **42**.

The tetracyclic compounds **40** – **42** have the relative configuration of aranciamycinone (**3**) or steffimycinone (**4**). The final methylation of the secondary hydroxy group at C-3 and the oxidation of 1-OH as well as the synthesis of *meta*-substituted derivatives (altersolanol A) is the subject of further investigations. It is worth noting that the syntheses described in this paper may be conducted in an enantioselective manner using chiral dienes[17,31].

Financial support from the *Deutsche Forschungsgemeinschaft* is greatefully acknowledged.

Experimental

Melting points were determined with a Kofler heating block apparatus and are corrected. – Infrared (IR) spectra were obtained with a Perkin-Elmer spectral photometer 1420 and are reported in wavenumbers (KBr, cm^{-1}). – Nuclear magnetic resonance (^1H NMR) spectra were recorded with Bruker HFX 90 (90 MHz), WM 270 (270 MHz), AM 300 (300 MHz), and WM 400 (400 MHz) spectrometers. Chemical shifts are reported in δ values downfield relative to tetramethylsilane as standard (in $CDCl_3$). – Ultraviolett/visible (UV/VIS) spectra were recorded with a Beckman UV 5230 spectral photometer in methanol; λ_{max} in nm (lg ε). – Mass spectra were obtained with a Varian MAT CH 7 mass spectrometer (70 eV); for compounds **31** – **33** a MAT 311 A mass spectrometer was used (electron current 200 A, temperature of the ion source 180°C, direct probe inlet at 110 – 150°C; MIKE spectra: VG ZAB-2F mass spectrometer, 70 eV, ion current 200 A, ion source temperature 180°C, direct probe inlet at 110 – 140°C); CI mass spectra: Finnigan 1020 B, CI gas methane or isobutane (0.5 Torr), ion source temperature 200°C, direct probe inlet with heating rates of 30°C/min between 40 – 170°C at cyclic scan. – Analytical TLC was performed on silica gel plates (0.25 mm; Merck), preparative TLC on silica gel plates (1 mm; Schleicher & Schüll), and column chromatography with silica gel 60 (230 – 400 mesh, Merck). – Elemental analyses were performed by the microanalytical laboratory of the Institute of Pharmaceutical Chemistry, D-3300 Braunschweig. – X-ray structural analysis: Enraf-Nonius CAD-4 diffractometer with graphite-monochromatized Cu-*K*α radiation, max. $\sin\Theta/\lambda = 0.562$ $Å^{-1}$, Θ – 2Θ scan technique, zig-zag mode. The structures were solved by direct methods with MULTAN[32], the full-matrix least square refinements were done with SHELX[33].

2-Methyl-1-trimethylsiloxy-1,3-butadiene (**7**): A solution of 8.4 g (0.1 mol) of 2-methyl-2-butenal (tiglic aldehyde)[15] in 50 ml of benzene was added to a suspension of 1 g of $ZnCl_2$ in 13.0 ml (0.13 mol) of triethylamine. The stirred suspension was treated within 1 h with 13.0 g (0.12 mol) of trimethylsilyl chloride and stirred for additional 18 h at 35°C. The suspension was filtered after addition of 100 ml of dry diethyl ether and evaporated to a volume of ca. 15 ml. 100 ml of petrol ether was then added and the suspension filtered again. After evaporation of the solvent the residue was distilled at reduced pressure to afford 10.8 g (69%) of diene **7**; b. p. (8 Torr) 54°C; $n_D^{\alpha} = 1.4538$. – IR (CCl_4): 3100, 2965 – 2800, 1650, 1610, 1450, 1420, 1175 cm^{-1}. – ^1H NMR (90 MHz): δ = 0.20 [s; 9H, $Si(CH_3)_3$], 1.71 (broad s, 3H, CH_3), 4.82 (dd, J = 2, J = 10 Hz; 1H, $=CH_2$), 4.98 (dd, J = 2, J = 18 Hz; 1H, $=CH_2$), 6.12 – 6.50 (m; 2H, 1-, 3-H).

(1SR,4aSR,9aSR)-1,4,4a,9a-Tetrahydro-5,8-dihydroxy-2-methyl-1-trimethylsiloxy-9,10-anthraquinone (**8**): A solution of 12.4 g (65 mmol) of naphthazarin (**6**) in 100 ml of CH_2Cl_2 was treated with 16.6 g (106 mmol) of diene **7**. After 18 h at room temperature the solution was rapidly

filtered through a short column of silica gel (elution with CH_2Cl_2). The first fraction of 350 ml was evaporated at reduced pressure and crystallized from 20 ml of petrol ether (−20 °C) to afford 14.5 g (65%) of adduct **8**; m. p. 112 °C. – IR: 1640 (quinone), 1582 cm^{-1}. – ^1H NMR (300 MHz): δ = −0.28 [s; 9H, $Si(CH_3)_3$], 1.75 (mc; 3H, CH_3), 2.15 (dm; 1H, 4-H), 3.20 (dd; 2H), 3.26 (m; 1H), 3.28 (q; 1H), 4.24 (d, J = 3.1 Hz; 1H, 1-H), 5.56 (mc; 1H, 3-H), 7.20 (AB signal; 2H, 6-, 7-H), 11.54 (s; 1H, OH), 12.07 (s; 1H, OH). – UV: 212 (4.10), 228 (4.14), 258 (3.99), 394 nm (3.87).

$C_{18}H_{22}O_5Si$ (346.5) Calc. C 62.40 H 6.40 Found C 62.27 H 6.44

(1SR,4aSR,9aSR)-1,4,4a,9a-Tetrahydro-1,5,8-trihydroxy-2-methyl-9,10-anthraquinone (**9**): A solution of 3.47 g (10 mmol) of silyl ether **8** in a mixture of 10 ml of CH_2Cl_2 and 10 ml of CH_3OH was treated with 0.1 ml of 1 N HCl and stirred for 1 h. The solution was evaporated to dryness at reduced pressure, and the residue was stirred with 20 ml of diethyl ether and filtered to afford 2.63 g (96%) of **9**; m. p. 170–173 °C. – IR: 3500 (OH), 1664 and 1642 (quinone), 1587 cm^{-1}. – ^1H NMR (300 MHz): δ = 2.08 (mc; 3H, CH_3), 2.47 (dm; 1H), 3.33 (dm; 1H), 3.59 (m; 2H), 4.48 (d, J = 3.3 Hz; 1H, 1-H), 5.85 (mc; 1H, 3-H). – UV: 213 (4.14), 229 (4.16), 258 (4.03), 393 nm (3.89).

$C_{15}H_{14}O_5$ (274.3) Calc. C 65.69 H 5.14 Found C 65.43 H 5.27

1,4-Dihydroxy-6-methyl-9,10-anthraquinone (**10**): A solution of 346 mg (1 mmol) of adduct **8** in 10 ml of CH_2Cl_2 was treated with 0.1 ml of triethylamine and stirred for 1 h. The solvent was evaporated at reduced pressure and the residue crystallized from petrol ether to afford 239 mg (94%) of **10** identical with an authentic sample[14].

1,5,8-Trihydroxy-2-methyl-9,10-anthraquinone (**11**): A suspension of 548 mg (2 mmol) of allyl alcohol **9** in 100 ml of dry CH_2Cl_2 was treated with 0.54 (25 mmol) of pyridinium chlorochromate (PCC) and stirred for 5 h at 20 °C. The solution was filtered through a short column of silica gel (20 g, CH_2Cl_2) and the first fraction was evaporated. Crystallization of the residue from ether afforded 383 mg (71%) of anthraquinone **11**; m. p. 209–211 °C. – IR: 1612 (quinone), 1595 cm^{-1}. – ^1H NMR (300 MHz): δ = 240 (s; 3H, CH_3), 7.29 (AB signal; 2H, 7-, 8-H), 7.57 (d, J = 7.5 Hz; 1H, 3-H), 7.80 (d, J = 7.5 Hz; 1H, 4-H), 12.30 (s; 1H, 8-OH), 12.57 (s; 1H, 1-OH), 13.08 (s, 1H, 5-OH). – UV: 230 (4.58), 2.52 (4.29), 270 sh, 286 (3.93), 464 sh, 476 (4.13), 488 (4.15), 508 (4.04), 522 nm (3.94).

$C_{15}H_{10}O_5$ (270.2) Calc. C 66.67 H 3.73 Found C 66.85 H 3.69

cis- and trans-2,3-Epoxy-1,2,3,4,4a,9a-hexahydro-1,5,8-trihydroxy-2-methyl-9,10-anthraquinone (**14/16**): A solution of 2.74 g (810 mmol) of olefin **9** in 200 ml of CH_2Cl_2 was treated with 2.22 g (13 mmol) of 3-chloroperbenzoic acid and stirred for about 12 h. The solvent was evaporated at reduced pressure and the residue stirred with 10 ml of dry ether to remove the 3-chlorobenzoic acid. The suspension was filtered after standing for 3 h at 4 °C to afford 2.52 g (87%) of a ca. 2:3 mixture of **14** and **16**; m. p. 163–167 °C. – IR: 3510 (OH), 1664, 1638 (C=O), 1589 cm^{-1}. – UV: 213 (4.16), 227 (4.16), 258 (4.61), 394 nm (3.87).

$C_{15}H_{14}O_6$ (290.3) Calc. C 62.07 H 4.86 Found C 61.86 H 4.83

(1SR,2SR,3SR,4aSR,9aSR)-2,3-Epoxy-1,2,3,4-tetrahydro-5,8-dihydroxy-2-methyl-1-trimethylsiloxy-9,10-anthraquinone (**15**): A solution of 1.04 g (3 mmol) of adduct **8** in 20 ml of dry CH_2Cl_2 was stirred for 12 h with 0.67 (3.9 mmol) of 3-chloroperbenzoic acid at 4 °C and then stored for another 12 h at −20 °C. The solution was filtered to remove most of the 3-chlorobenzoic acid, evaporated to dryness and crystallized from 3 ml of methanol (4 °C) to afford 0.97 g (89%) of epoxide **15**; m. p. 150–152 °C. – ^1H NMR (300 MHz): δ = −0.28 [s; 9H, $Si(CH_3)_3$], 1.35 (s, 3H, CH_3), 2.06 (dd, J_{gem} = 16.3, $J_{3,4}$ = 9.7 Hz; 1H, 4-H), 3.05 (ddd, $J_{4,4a}$ = 9.7, $J_{4a,9a}$ = 6.3, $J_{4,4a}$ = 1.3 Hz; 1H, 4a-H), 3.12 (d, $J_{3,4}$ = 3.8 Hz; 1H, 3-H), 3.19 (ddd, J_{gem} = 16.3, $J_{3,4}$ = 3.8,

$J_{4,4a}$ = 1.3 Hz; 1H, 4-H), 3.50 (dd, $J_{4,4a}$ = 6.3, $J_{1,9a}$ = 2.3 Hz; 1H, 9a-H), 4.36 (d, $J_{1,9a}$ = 2.3 Hz; 1H, 1-H), 7.20 (AB signal; 2H, 6-, 7-H), 11.52 (s; 1H, OH), 12.11 (s; 1H, OH).

$C_{18}H_{22}O_6Si$ (362.5) Calc. C 59.65 H 6.12 Found C 59.45 H 6.05

(1SR,2RS,3RS)-1,2,3,4-Tetrahydro-1,5,8-trihydroxy-2-methyl-9,10-anthraquinone (**18**): A suspension of 560 mg (1.9 mmol) of the epoxides **14**/**16** in 20 ml of CH_3OH was treated at 4 °C with 1 ml of a 0.3 N aquous solution of potassium carbonate and stirred for 10 min (TLC control). The solution was neutralized by addition of 1 N acetic acid, diluted with 100 ml of water and extracted with 100 ml of CH_2Cl_2. The solution was dried with Na_2SO_4, evaporated to dryness and the residue separated by TLC (1 mm silica gel, CH_2Cl_2/2% CH_3OH). From the less polar zone 186 mg (33%) of dark red brown plates crystallized from ether; m. p. 160–163 °C (dec.). – IR: 3520 (OH), 1595 (C=O), 1575 cm^{-1}. – UV: 215 (4.26), 2.31 (4.23), 5.11 (3.82), 5.27 (3.82), 5.67 nm sh. – ^1H NMR (270 MHz): δ = 1.67 (s; 3H, CH_3), 2.81 (dm, J = 21.8 Hz; 1H, 4-H), 3.43 (mc; 1H, 3-H), 3.48 (dt, J_{gem} = 21.8 Hz; 1H, 4-H), 4.09 (d, J = 3.6 Hz; 1H, OH), 5.13 (mc; 1H, 1-H), 7.25 (s; 2H, 6-, 7-H), 12.43 (s; 1H, OH), 12.49 (s; 1H, OH).

$C_{15}H_{12}O_6$ (288.3) Calc. C 62.50 H 4.20 Found C 62.32 H 4.20

(1SR,2SR,3SR)-2,3-Epoxy-1,2,3,4-tetrahydro-1,5,8-trihydroxy-2-methyl-9,10-anthraquinone (**20**): From the polar zone of the TLC (see **18**) 279 mg (50%) of the quinone **20** were isolated; m. p. 153–156 °C (dec.). – IR: 3500 (OH), 1615 (quinone), 1580 cm^{-1}. – UV: See **18**. – ^1H NMR (270 MHz): δ = 1.62 (s; 3H, CH_3), 2.84 (d, J = 4.8 Hz; 1H, OH), 2.96 (ddd, J_{gem} = 21.1, J = 2.4, J = 1.6 Hz; 1H, 4-H), 3.48 (dt, J = 21.1, 1H, 4-H), 5.21 (mc; 1H, 1-H), 7.40 (s; 2H, 6-, 7-H), 12.45 (s; 1H, OH), 12.48 (s; 1H, OH). – MS (120 °C): m/z = 289 (26%, M^+ + 1), 288 (91, M^+), 270 (100, $M^+ - H_2O$), 254 (35), 245 (94), 228 (91).

$C_{15}H_{12}O_6$ (288.3) Calc. C 62.50 H 4.20 Found C 62.07 H 4.18

(2SR,3SR)-1,2,3,4-Tetrahydro-2,3,5,8-tetrahydroxy-2-methyl-9,10-anthraquinone (**17**): A suspension of 200 mg (0.7 mmol) of the epoxides **14**/**16** in 3 ml of dry methanol was treated under N_2 with 5 ml of 1 N sodium methanolate in methanol. After stirring 2.5 h at 20 °C with strict exclusion of oxygen the solution was stirred for 5 min with an access of air. TLC analysis showed a mixture of compounds consisting of **18**, **20**, traces of **23** and **26**, and the polar *trans*-diol **17** which was separated by TLC; yield 46 mg (23%); m. p. 179–180 °C. – IR: 3530, 3400 (OH), 1610 (quinone), 1582 cm^{-1}. – ^1H NMR (270 MHz): δ = 1.35 (s; 3H, CH_3), 1.38 (s; 1H, OH), 2.13 (m; 1H, OH), 2.74 (dm, J_{gem} = 19.8 Hz; 1H, 4-H), 2.74 (dt, J_{gem} = 19.3 Hz; 1H, 1-H), 3.00 (dt, J = 19.3 Hz; 1H, 1-H), 3.21 (dm, J = 19.8 Hz; 1H, 4-H), 3.98 (mc; 1H, 3-H), 7.22 (s; 2H, 6-, 7-H), 12.53 (s; 2H, 2 OH). – MS (150 °C): m/z = 290 (100%, M^+), 272 (17, $M^+ - H_2O$), 257 (22), 254 (31, $M^+ - 2\,H_2O$), 247 (38), 243 (22), 229 (57), 219 (64), 217 (65).

$C_{15}H_{14}O_6$ (290.3) Calc. C 62.07 H 4.86 Found C 61.78 H 4.87

(1SR,2RS,3SR)-1,2,3,4-Tetrahydro-1,3,5,8-tetrahydroxy-2-methoxy-2-methyl-9,10-anthraquinone (**21**): A solution of 57 mg (0.2 mmol) of epoxide **20** in 10 ml of CH_3OH was treated with 1 drop of conc. H_2SO_4 and stirred for 30 min (TLC control). The solution was poured into 50 ml of water and extracted twice with 20 ml of CH_2Cl_2. The solution was dried with Na_2SO_4 and evaporated to dryness. The residue was washed with 3 ml of ether and filtered to afford 51 mg (80%) of diol **21**; m. p. 116–120 °C. – IR: 3530 (broad, OH), 1609 (quinone), 1573 cm^{-1}. – UV: 216 (4.46), 279 (3.91), 491 (3.77), 508 (3.80), 545 nm (3.58). – ^1H NMR (270 MHz): δ = 1.59 (s; 3H, CH_3), 1.74 (broad s; 1H, 3-OH), 2.90 (ddd, J_{gem} = 19.8, J = 4.2, J = 1.0 Hz; 1H, 4-H), 3.45 (s; 3H, OCH_3), 3.59 (dt, J = 4.2, J = 1.2 Hz; 1H, 3-H), 3.71 (d, J = 9.1 Hz; 1H, 1-OH), 4.57 (broad d, J = 9.1 Hz; 1H, 1-H), 7.24 (s; 2H, 6-, 7-H), 12.53 (s; 1H, OH), 12.60 (s; 1H, OH). – MS (120 °C): m/z = 320 (66%, M^+), 302 (14, $M^+ - H_2O$), 284 (17, $M^+ - 2\,H_2O$), 270 (33), 260 (86), 259 (100), 259 (77), 233 (89), 228 (63), 217 (60), 204 (83), 189 (67).

(1SR,2RS,3SR)-1,3-Diacetoxy-1,2,3,4-tetrahydro-5,8-dihydroxy-2-methoxy-2-methyl-9,10-anthraquinone (**22**): A suspension of 32 mg (0.1 mmol) of **21** in 2 ml of acetic anhydride was treated with 1 drop of conc. H_2SO_4 and stirred for 2 – 3 h (TLC control). The solution was poured into ice/water and stirred until the anhydride was hydrolized (ca. 2 h). The red precipitate was collected by filtration and purified by TLC to afford 26 mg (65%) of the diacetate **22**; m. p. 194 – 198 °C (dec.). – IR: 1745, 1732 (C=O), 1615 (quinone), 1573 cm^{-1}. – UV: See **21**. – ^1H NMR (400 MHz): δ = 1.63 (s; 3 H, CH_3), 1.98 (s; 3 H, $COCH_3$), 2.14 (s; 3 H, $COCH_3$), 2.65 (ddd, J = 20.0, J = 4.4, J = 1.5 Hz; 1 H, 4-H), 3.13 (dd, J = 20.0, J = 3.7; 1 H, 4-H), 3.45 (s; 3 H, OCH_3), 4.57 (t; 1 H, 3-H), 6.41 (broad s; 1 H, 1-H), 7.26 (s; 2 H, 6-, 7-H), 12.52 (s; 1 H, OH), 12.54 (s; 1 H, OH). – MS (130 °C): m/z = 404 (2%, M^+), 344 (40), 302 (91), 284 (93), 271 (100), 254 (91), 242 (75), 228 (64).

$C_{20}H_{20}O_9$ (404.4) Calc. C 59.40 H 4.99 Found C 59.33 H 4.97

(1SR,2RS)-1,2-Dihydro-1,2,5,8-tetrahydroxy-2-methyl-9,10-anthraquinone (**23**): A solution of 288 mg (1 mmol) of epoxide **18** in 10 ml of CH_3OH was treated with 0.2 ml of 1 N sodium methanolate and stirred for 20 – 30 min (TLC control) with an access of air. The solution was neutralized with equivalent amounts of acetic acid and evaporated to dryness at reduced pressure. The residue was dissolved in dry CH_2Cl_2, filtered, and crystallized from ether to afford 181 mg of *cis*-enediol **23**; m. p. 175 – 179 °C (dec.). Triethylamine in CH_2Cl_2 was equally suited for the rearrangement of the epoxides (see **25**). – IR: 3450 (broad, OH), 1607 (quinone), 1573 cm^{-1}. – UV: 232 (4.26), 286 sh, 501 (3.81), 526 (3.82), 568 sh, 622 nm sh. – ^1H NMR (270 MHz): δ = 1.35 (s; 3 H, CH_3), 3.05 (broad d, 1 H, OH), 3.19 (s; 1 H, 2-OH), 4.82 (mc; 1 H, 1-H), 6.42 (dd, $J_{3,5}$ = 8.7, J = 1.0 Hz; 1 H, 3-H), 6.83 (d, $J_{3,4}$ = 8.7 Hz; 1 H, 4-H), 7.23 (s; 2 H, 6-, 7-H), 12.60 (s; 1 H, OH), 12.66 (s; 1 H, OH).

(3aSR,11bSR)-3a,11b-Dihydro-7,10-dihydroxy-2,2,3a-trimethyl-1H-anthra[1,2-d]dioxol-6,11-dione (**24**): A solution of 29 mg (0.1 mmol) of *cis*-enediol **23** in 5 ml of 2,2-dimethoxypropane was treated with 10 mg of *p*-toluenesulfonic acid. After 3 h at 20 °C the solution was evaporated at reduced pressure to 0.5 ml, diluted with 10 ml of CH_2Cl_2, and shaken with aqueous sodium hydrogen carbonate. The organic phase was dried with Na_2SO_4, evaporated to dryness, and crystallized from 0.5 ml of CH_3OH (– 20 °C) to afford 24 mg (73%) of **24**; m. p. 124 – 125 °C. – ^1H NMR (300 MHz): δ = 1.39 (s; 3 H, CH_3), 1.56 (s; 6 H, 2 CH_3), 4.97 (d, $J_{4,11b}$ = 1.2 Hz; 1 H, 11b-H), 6.32 (dd, $J_{4,11b}$ = 1.2 Hz, $J_{4,5}$ = 9.8 Hz; 1 H, 4-H), 6.83 (d, $J_{4,5}$ = 9.8 Hz; 1 H, 5-H), 7.21 (AB signal; 2 H, 8-, 9-H), 12.61 (s; 1 H, OH), 12.78 (s; 1 H, OH). – MS (70 °C): m/z = 328 (20%, M^+), 271 (98), 270 (100), 255 (64), 254 (51), 253 (56), 242 (56), 224 (27), 149 (47).

$C_{18}H_{16}O_6$ (328.3) Calc. C 65.85 H 4.91 Found C 65.92 H 5.02

(1SR,2SR)-1,2-Dihydro-1,2,5,8-tetrahydroxy-2-methyl-9,10-anthraquinone (**26**): As described for **23**, 300 mg of the *trans*-epoxide **20** was rearranged by base treatment to afford 195 mg (65%) of *trans*-enediol **26**: m. p. 105 – 107 °C (dec.). Alternatively a solution of 120 mg (0.3 mmol) of silyl ether **25** in 2 ml of CH_2Cl_2 and 2 ml of CH_3OH was treated with 1 drop of 1 N methanolic HCl for 5 min. Evaporation of the solvent at reduced pressure afforded 101 mg (quantitative) of enediol **26**. – IR: 3540 (broad, OH), 1603 cm^{-1} (quinone). – UV: 231 (4.27), 293 (3.72), 501 (3.81), 525 (3.81), 564 sh, 622 nm sh. – ^1H NMR (270 MHz): δ = 1.48 (s, 3 H, CH_3), 2.13 (s; 1 H, 2-OH), 4.09 (d, $J_{1,1\text{-OH}}$ = 3.0 Hz; 1 H, 1-OH), 5.09 (d, $J_{1,1\text{-OH}}$ = 3.0 Hz; 1 H, 1-H), 6.43 (d, $J_{3,4}$ = 9.9 Hz; 1 H, 3-H), 6.86 (d; $J_{3,4}$ = 9.9 Hz; 1 H, 4-H), 7.23 (s; 2 H, 6-, 7-H), 12.58 (s; 1 H, OH), 12.60 (s; 1 H, OH).

$C_{15}H_{14}O_6$ (288.3) Calc. C 62.50 H 4.20 Found C 62.21 H 4.17

(1SR,2SR)-1,2-Dihydro-2,5,8-trihydroxy-2-methyl-1-trimethylsiloxy-9,10-anthraquinone (**25**): A solution of 362 mg (1 mmol) of epoxide **15** in 10 ml of dry CH_2Cl_2 was treated with 2 drops of

triethylamine and stirred for 3 h. The formation of the red coloured intermediate quinone **19** could be observed by TLC. Quinone **19** smoothly rearranged to the violett olefin **25**. After 6 h (TLC control) the solution was rapidly filtered through a short (3 × 2 cm) column of silca gel. The first fraction (CH_2Cl_2) contained some aromatization product and the product **25** was next eluated with CH_2Cl_2/15% $O(C_2H_5)_2$. Crystallization from 2 ml of petrol ether gave **25** as dark violett plates; yield 264 mg (73%); m. p. 145–146°C. – IR: 3425 (OH), 1604 (quinone), 1577 cm^{-1}. – UV: See **26**. – ^1H NMR (300 MHz): δ = 0.16 [s; 9H, $Si(CH_3)_3$], 1.56 (s; 3H, CH_3), 4.81 (d, $J_{1,3}$ = 1.3 Hz; 1H, 1-H), 6.30 (dd, $J_{1,3}$ = 1.3, $J_{3,4}$ = 9.7 Hz; 1H, 3-H), 6.93 (d, $J_{3,4}$ = 9.7 Hz; 1H, 4-H), 7.24 (AB signal, 2H, 6-, 7-H), 12.60 (s; 1H, OH), 12.80 (s; 1H, OH).

$C_{18}H_{22}SiO_6$ (362.5) Calc. C 59.65 H 6.12 Found C 59.67 H 5.60

(1SR,2SR,3RS,4RS)-3,4-Epoxy-1,2,3,4-tetrahydro-1,2,5,8-tetrahydroxy-2-methyl-9,10-anthraquinone (**27**): A solution of 144 mg (0.5 mmol) of enediol **23** and 120 mg (0.7 mmol) of 3-chloroperbenzoic acid in 10 ml of CH_2Cl_2 was stirred for about 12 h. The solution was extracted twice with aqueous $NaHCO_3$, dried with Na_2SO_4, evaporated to dryness, and crystallized from diethyl ether to afford 126 mg (83%) of **27**; m. p. 170–173°C (dec.). – IR: 3480 (OH), 1612, 1608 (quinone), 1260, 840 cm^{-1}. – UV: 218 (4.45), 287 (3.87), 4.95 (3.78), 524 (3.80), 561 (3.59), 603 nm (2.91). – ^1H NMR (270 MHz): δ = 1.13 (s, 3H, CH_3), 2.74 (d, $J_{1,1\text{-OH}}$ = 11.9 Hz; 1H, 1-OH), 3.70 (s; 1H, 2-OH), 3.79 (dd, $J_{3,4}$ = 4.1, $J_{1,3}$ = 2.7 Hz; 1H, 1-H), 4.64 (d, $J_{3,4}$ = 4.1 Hz; 1H, 4-H), 4.76 (dd, $J_{1,1\text{-OH}}$ = 11.9, $J_{1,3}$ = 2.7 Hz; 1H, 1-H), 7.19 (s; 2H, 6-, 7-H), 12.61 (s; 1H, OH), 12.64 (s; 1H, OH).

(1SR,2RS,3RS,4RS)-3,4-Epoxy-1,2,3,4-tetrahydro-1,2,5,8-tetrahydroxy-2-methyl-9,10-anthraquinone (**28**): A solution of 202 mg (0.7 mmol) of *trans*-enediol **26** was treated with 170 mg (1 mmol) of 3-chloroperbenzoic acid for 24 h as described for **27**. The resulting mixture of epoxides was separated by TLC (1 mm silica gel, CH_2Cl_2/2% CH_3OH, three developments). From the polar zone 117 mg of **28** were obtained [50% of **28** were isolated as copper-coloured plates (ether); m. p. 136–138°C]. Alternatively 121 mg (0.3 mmol) of silyl ether **25** was dissolved in 10 ml of CH_2Cl_2 and treated with 171 mg (1 mmol) of 3-chloroperbenzoic acid. After 3 d 5 ml of CH_3OH and 1 drop of 2 N HCl was added. After 10 min the solution was shaken with aqueous $NaHCO_3$, dried with Na_2SO_4, evaporated to dryness at reduced pressure, and separated by TLC to afford 64 mg (70%) of epoxide **28**. – IR: 3460 (OH), 1603 (quinone), 1570, 1240, 850 cm^{-1}. – UV: See **27**. – ^1H NMR ($CDCl_3/CD_3OD$): δ = 1.25 (s; 3H, CH_3), 3.75 (dd, $J_{1,3}$ = 2.3, $J_{3,4}$ = 3.9 Hz; 1H, 3-H), 4.58 (d, $J_{3,4}$ = 3.9 Hz; 1H, 4-H), 4.70 (d, $J_{1,3}$ = 2.3 Hz; 1H, 1-H), 7.28 (AB signal; 2H, 6-, 7-H).

(1SR,2RS,3SR,4SR)-3,4-Epoxy-1,2,3,4-tetrahydro-1,2,5,8-tetrahydroxy-2-methyl-9,10-anthraquinone (**30**): From the less polar zone of the TLC separation (see **28**) 86 mg (41%) of the epoxide **30** were isolated; m. p. 157–160°C (dec.). – IR: 3470, 3380 (OH), 1600 (quinone), 1567, 837 cm^{-1}. – UV: See **27**. – ^1H NMR (270 MHz): δ = 1.27 (s; 3H, CH_3), 2.66 (broad s; 1H, OH), 3.75 (d, $J_{3,4}$ = 4.3 Hz; 1H, 3-H), 4.50 (d, $J_{3,4}$ = 4.3 Hz; 1H, 4-H), 4.98 (broad s; 1H, 1-H), 5.16 (broad s; 1H, OH), 7.26 (s; 2H, 6-, 7-H), 12.53 (s; 1H, OH), 12.60 (s; 1H, OH).

(1SR,2SR,3RS,4SR)-1,2,3,4-Tetrahydro-1,2,3,5,8-pentahydroxy-4-methoxy-2-methyl-9,10-anthraquinone (**31**): A solution of 101 mg (0.3 mmol) of **27** in 5 ml of CH_2Cl_2 was added to 5 ml of methanol which contained 0.2 ml of 5% methanolic H_2SO_4. After 20–30 min (TLC control) 0.1 g of $NaHCO_3$ was added and the solution was filtered after stirring and evaporated to dryness at reduced pressure. The residue was washed with 1 ml of dry ether to afford 91 mg (90% of crude **31**. An analytical sample was purified by TLC (CH_2Cl_2/4% CH_3OH, 1 mm silica gel, zone of medium polarity); m. p. 189–193°C. – IR: 3430 (OH), 1618 (quinone), 1573 cm^{-1}. – UV: 216 (4.46), 276 (3.88), 490 (3.79), 515 (3.82), 552 (3.59), 593 nm (2.69). – ^1H NMR (270 MHz): δ =

1.33 (s; 3H, CH_3), 2.86 (d, $J_{3,3\text{-OH}}$ = 6.7 Hz, 1H, 3-OH), 3.45 (d, $J_{1,1\text{-OH}}$ = 6.3 Hz; 1H, 1-OH), 3.57 (s; 1H, 2-OH), 3.66 (s; 3H, OCH_3), 3.99 (ddd, $J_{3,3\text{-OH}}$ = 6.7, $J_{3,4}$ = 2.8, $J_{1,3}$ = 0.8 Hz; 1H, 3-H), 4.63 (d, $J_{3,4}$ = 2.8 Hz; 1H, 4-H), 4.74 (dd, $J_{1,1\text{-OH}}$ = 6.3, $J_{1,3}$ = 0.8 Hz; 1H, 1-H), 7.26 (s; 2H, 6-, 7-H), 12.51 (s; 1H, OH), 12.63 (s; 1H, OH).

$C_{16}H_{16}O_8$ (336.3) Calc. C 57.14 H 4.80 Found C 56.89 H 4.71

(1SR,2RS,3RS,4SR)-1,2,3,4-Tetrahydro-1,2,3,5,8-pentahydroxy-4-methoxy-2-methyl-9,10-anthraquinone (**32**): 61 mg (0.2 mmol) of **28** was treated as described for **31** to afford 50 mg (75%) of the triol **32** after TLC separation (least polar zone); m. p. 189–193 °C. – IR: 3490, 3455 (OH), 1609 (quinone), 1575 cm^{-1}. – UV: See **31**. – ^1H NMR (270 MHz): δ = 1.65 (s; 3H, CH_3), 3.13 (d, $J_{3,3\text{-OH}}$ = 6.5 Hz; 1H, 3-OH), 3.14 (broad s; 1H, 1-OH), 3.70 (s; 3H, OCH_3), 4.04 (ddd, $J_{3,3\text{-OH}}$ = 6.5, $J_{3,4}$ = 2.4, $J_{1,3}$ = 1.3 Hz; 1H, 1-H), 4.19 (s; 1H, 2-OH), 4.65 (d, $J_{3,4}$ = 2.4 Hz; 1H, 4-H), 4.77 (broad, d after deuterium exchange, $J_{1,3}$ = 1.3 Hz; 1H, 1-H), 7.27 (s; 2H, 6-, 7-H), 12.50 (s; 1H, OH), 12.61 (s; 1H, OH).

$C_{16}H_{16}O_8$ (336.3) Calc. C 57.14 H 4.80 Found C 56.75 H 4.76

(1SR,2RS,3SR,4RS)-1,2,3,4-Tetrahydro-1,2,3,5,8-pentahydroxy-4-methoxy-2-methyl-9,10-anthraquinone (**33**): Similar treatment of 61 mg (0.2 mmol) of **30** (see **31**) yielded 48 mg (72%) of triol **33** from the most polar fraction of the TLC separation; m. p. 202–206 °C. – IR: 3408 (OH), 1618 (quinone), 1578 cm^{-1}. – UV: See **31**. – ^1H NMR (270 MHz; acidic H exchanged with CD_3OD): δ = 1.43 (s; 3H, CH_3), 2.39 (broad, exchangable; 1H, OH), 2.69 (broad, exchangable; 1H, OH), 3.67 (s; 3H, OCH_3), 4.07 (s, exchangable; 1H, 2-OH), 4.07 (d after exchange, $J_{3,4}$ = 5.4 Hz; 1H, 3-H), 4.45 (dd, $J_{1,4}$ = 0.5, $J_{3,4}$ = 5.4 Hz; 1H, 4-H), 4.92 (s after exchange; 1H, 1-H), 7.26 (AB signal; 2H, 6-, 7-H), 12.39 (s; 1H, OH), 12.64 (s; 1H, OH).

$C_{16}H_{16}O_8$ (336.3) Calc. C 57.14 H 4.80 Found C 57.10 H 4.76

(3aSR,4RS,5SR,11bSR)-3a,4,5,11b-Tetrahydro-4,7,10-trihydroxy-5-methoxy-2,2,3a-trimethyl-1H-anthra[1,2-d]dioxol-6,11-dione (**34**). A suspension of 34 mg (0.1 mmol) of triol **31** and 10 mg of *p*-toluenesulfonic acid in 2 ml of 2,2-dimethoxypropane was stirred for 2 h. The solution was diluted with 10 ml of CH_2Cl_2, shaken with aqueous $NaHCO_3$, dried with Na_2SO_4, and evaporated at reduced pressure to afford 34 mg (90%) of acetonide **34**; m. p. (CH_3OH) 160–163 °C. – ^1H NMR (400 MHz): δ = 1.57 (s; 6H, 2 CH_3), 1.66 (s; 3H, CH_3), 2.65 (s; 1H, OH), 3.60 (s; 3H, OCH_3), 4.02 (dd, *J* = 1.6, *J* = 2.8 Hz; 1H, 4-H), 4.84 (d, *J* = 2.8 Hz; 1H, 5-H), 5.01 (s; 1H, 11b-H), 7.28 (s; 2H, 8-, 9-H), 12.57 (s; 1H, OH), 12.61 (s; 1H, OH). – MS (130 °C): *m/z* = 376 (20%, M^+), 361 (36), 318 (3), 300 (9), 286 (35), 273 (51), 258 (77), 257 (100), 244 (57), 241 (57), 230 (21).

(3aSR,4RS,11SR,11aRS)-3a,4,11,11a-Tetrahydro-4,6,9-trihydroxy-11-methoxy-2,2,3a-trimethyl-2H-anthra[2,3-d]dioxol-5,10-dione (**36**): Similar treatment of 336 mg (1 mmol) of triol **33** (see **34**) yielded 316 mg (84%) of the acetonide **36** after column chromatography [5 g of silica gel, CH_2Cl_2/5% $O(C_2H_5)_2$]; m. p. 143–146 °C. – IR: 3460 (OH), 1613 (quinone), 1570 cm^{-1}. – ^1H NMR (300 MHz): δ = 0.95, 1.37, 1.74 (each s; each 3H, 3 CH_3), 3.44 (d, $J_{1,OH}$ = 12.6; 1H, 1-OH), 3.47 (s; 3H, OCH_3), 4.54 (d, $J_{3,4}$ = 2.6 Hz; 1H, 3-H), 4.91 (d, $J_{1,OH}$ = 12.6 Hz; 1H, 1-H), 5.03 (d, $J_{3,4}$ = 2.6 Hz; 1H, 4-H), 7.19 (s; 2H, 6-, 7-H), 12.62 (s; 1H, OH), 12.64 (s; 1H, OH). – MS (140 °C): *m/z* = 376 (9%, M^+), 361 (11), 344 (7, $M^+ - CH_3OH$), 318 (12), 301 (21), 286 (58), 276 (10), 270 (9), 262 (29), 257 (50), 244 (100), 243 (98), 230 (62).

(7SR,8SR,9RS,10SR)-7,8,9,10-Tetrahydro-6,7,8,9,11-pentahydroxy-10-methoxy-8-methyl-5,12-naphthacenequinone (**40**): A suspension of 34 mg (0.1 mmol) of **31** in 0.4 ml of 1-methoxy-1,3-butadiene was stirred for about 12 h at 20 °C. One drop of triethylamine was added and stirring was continued for 10 min. The reagents were evaporated at reduced pressure and the

residue was washed with 1 ml of ether to afford 38 mg (98%) of the tetracycle **40**; m. p. 272–273°C. – IR: 3330 (OH), 1630 (quinone), 1587 cm^{-1}. – ^1H NMR (300 MHz, [D_5]-pyridine): δ = 1.66 (s; 3H, CH_3), 3.73 (s; 3H, OCH_3), 4.58 (mc; 1H, 9-H), 5.15 (d, $J_{3,4}$ = 2.5 Hz; 1H, 10-H), 5.40 (broad s; 1H, 7-H), 7.72 (m; 2H, 2-, 3-H), 8.34 (m; 2H, 1-, 4-H), 13.87 (broad; 2H, 2-OH).

$C_{20}H_{18}O_8$ (386.4) Calc. C 62.18 H 4.70 Found C 62.02 H 4.63

(7SR,8RS,9SR,10RS)-7,8,9,10-Tetrahydro-6,7,8,9,11-pentahydroxy-10-methoxy-8-methyl-5,12-naphthacenequinone (**41**): Similar treatment of 40 mg (0.12 mmol) of **33** (see **40**) gave 43 mg (94%) of **41**; m. p. 264–265°C. – IR: 3450 (OH), 1623 (quinone), 1583 cm^{-1}. – MS (210°C): *m/z* = 386 (10%, M^+), 368 (4, $M^+ - H_2O$), 354 (27, $M^+ - CH_3OH$), 336 (44), 320 (45), 312 (83), 293 (100), 280 (64).

(3aSR,4RS,13SR,13aRS)-3a,4,13,13a-Tetrahydro-4,5,12-trihydroxy-13-methoxy-2,2,3a-trimethyl-2H-naphthacene[8,9-d]dioxol-6,11-dione (**42**): Similarly, using the procedure for **40**, 38 mg of **36** was converted into 40 mg (94%) of **42**; **42** could also be prepared by acetalization of **41** (procedure see **34**); m. p. 213–214°C. – ^1H NMR (400 MHz): δ = 0.78, 1.34, 1.75 (each s; each 3H, 3 CH_3), 3.45 (s; 3H, OCH_3), 3.63 (s, $J_{7,OH}$ = 12.7 Hz; 1H, OH), 4.57 (d, $J_{13,13a}$ = 2.7 Hz; 1H, 13a-H), 5.05 (d, $J_{4,OH}$ = 12.7 Hz; 1H, 1-H), 5.17 (d, $J_{13,13a}$ = 2.7 Hz; 1H, 13-H), 7.87 (mc; 2H, 8-, 9-H), 8.40 (mc; 2H, 7-, 10-H), 13.27 (s; 1H, OH), 13.36 (s; 1H, OH). – MS (100°C): *m/z* = 426 (12%, M^+), 411 (5), 394 (7, $M^+ - CH_3OH$), 368 (6), 351 (12), 336 (37), 320 (19), 312 (70, RDA fragment), 307 (57), 294 (82), 293 (100), 280 (48).

$C_{23}H_{22}O_8$ (426.4) Calc. C 64.78 H 5.20 Found C 64.39 H 5.09

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