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SYNTHETIC ANTHRACYCLINONES—XXVII ANTHRACYCLINONES BY INTRAMOLECULAR MARSCHALK REACTION

SYNTHESIS OF THE FEUDOMYCINONES AND RHODOMYCINONES

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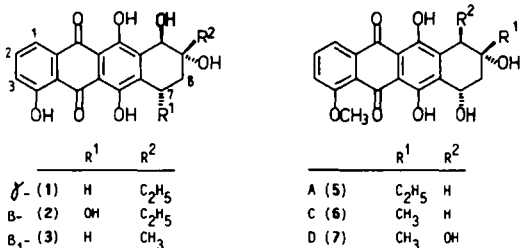
Abstract—1,4,5-Trihydroxy-9,10-anthraquinone is transformed regioselectively to the α-hydroxy dichlorides **18–21**, which are cyclized to yield predominantly the naturally configurated 9,10-*trans*-diols **1**, **3**, **26**, and **27** (80 to 96% d.e.). The monotrifluoroacetates **38–40** derived from the *trans*-diols are hydroxylated via bromination at C-7 to yield almost exclusively the 7,9-*cis*-9,10-*trans*-triols α_1-rhodomycinone (**4**), feudomycinone D (**7**), and 4-*O*-methyl-β-rhodomycinone (**42**). The feudomycinones A (**5**) and C (**6**) are obtained with less chemo- and stereoselectivity by hydroxylation of the 10-deoxycompounds **33** and **34**.

INTRODUCTION

THE rhodomycinones **1–4**, which are closely related to the clinically important antitumor drug daunorubicin, belong to a long known and well characterized family of anthracyclinones.[1,2] The red pigments are produced by various strains of *Streptomyces*, and are biosynthetically derived from the ε-rhodomycionones by 10-decarbomethoxylation.[3] More recently, a similar group of anthracyclinones, the feudomycinones, were isolated from the mutant *S. coeruleorubidus* ME 130-A4.[4] Feudomycinone D (**7**) has also been produced from auramycinone by microbial conversion by another mutant of *S. coeruleorubidus*.[5] Chemically, they resemble the daunomycinones in having a methyl ether at C-4, and as daunomycinone, the feudomycinones A (**5**) and C (**6**) lack a substituent at the benzylic position C-10.



Scheme 1

In spite of their widespread occurrence, relatively few syntheses of the rhodomycinones of type A (type A without, type B with carbomethoxy group at C-10[6]) have been published.[7–10] Diels–Alder reactions were successfully applied for the construction of the linearly condensed ring system,[7,8] but an even more efficient solution of the problem of regioselectivity and the introduction of functional groups has been found in an intramolecular version of the Marschalk reaction.[9,10]

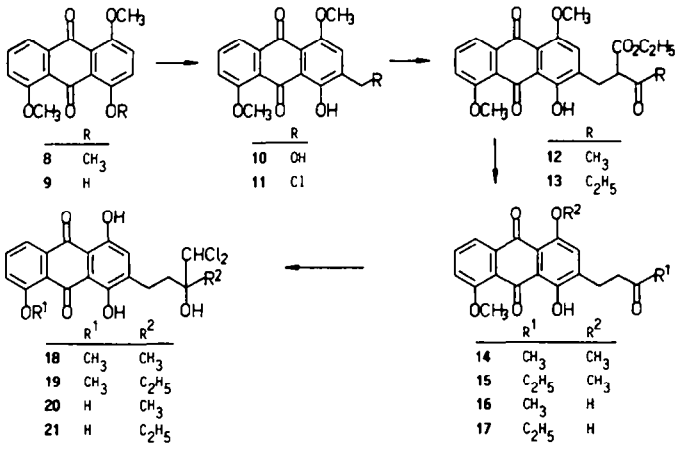
In this paper we shall describe the first syntheses of the racemic feudomycinones A (**5**), C (**6**), D (**7**), and several new derivatives of the rhodomycinones via the intramolecular version of the Marschalk reaction. In addition, new results of the stereochemical outcome of the cyclization and hydroxylation steps are reported.

Starting materials

Three of the four rings of anthracyclinones are already assembled in anthraquinones such as 1,4,5-trihydroxy-9,10-anthraquinone, which is readily available from industrial production. In order to make use of this simple building block, a functionalized side chain had to be attached regiospecifically at C-3. Further transformation yielded α-hydroxy aldehydes, that could be cyclized directly to anthracyclinones such as γ-rhodomycinones (**1**).[9,10]

The regioselectivity was effected by partial methylation to 4-hydroxy-1,5-dimethoxy-9,10-anthraquinone (**9**) via boroacetates.[9] An even shorter and equally selective route has recently been described using boron trifluoride etherate to cleave the methyl ether **8** to yield **9** in good yield.[11] Sequential conversion of **9** into **10–13** by the Marschalk reaction with formaldehyde, treatment of **10** with thionyl chloride, and alkylation with ethyl acetoacetate or ethyl 3-oxovalerate to give **12** or **13** has been reported (Scheme 2).[9] An improvement has been made in the saponification and decarboxylation step to yield the ketones **14** and **15** by simply treating **12** and **13** with 0.3N ethanolic alkali for two days. The thermal decarboxylation at 160° occasionally gave some loss of material. All these steps are operationally simple and could be routinely done on a 10 g scale to give **14** and **15** in 50–55% overall yield starting from **8**.

A further improvement was the employment of BCl_3[12,13] at low temperatures instead of aluminium chloride[9] to selectively cleave the second methyl ether at C-1 to afford the new compounds **16** and **17** in over 90% yield. Various acyl anion equivalents have been tried in our laboratory to convert the ketones **14** and **15** to the corresponding α-hydroxy aldehydes **24** and **25**.[10] The most selective reagent was a carbenoid, lithium dichloromethane, which can be generated by treatment of dichloromethane with butyl lithium at −100° by the procedure of Köbrich.[14] The corresponding adducts **18–21** were isolated in almost quantitative yield and no addition to the quinoid carbonyls could observed.



Scheme 2

Cylization of the α-hydroxy aldehydes

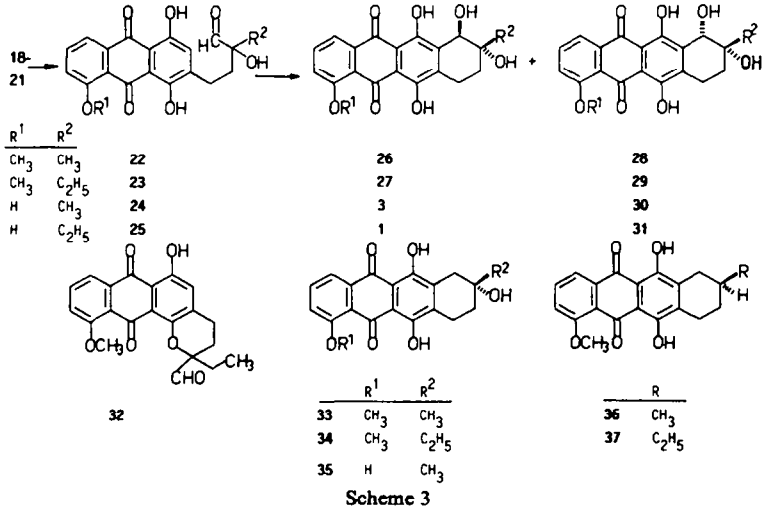
In the orginal paper of Marschalk *et al.*,[15] the reaction of hydroxylated hydroanthraquinones with aldehydes at elevated temperatures to yield alkylated anthraquinones is described. The primary addition of the aldehyde is followed by elimination of the benzylic hydroxy group, reoxidizing the hydroquinone to the anthraquinone. However, the OH group can be preserved by immediately quenching the reaction by reoxidation[16] or by lowering the reaction temperature.[17] Thus, one of the two benzylic OH groups of many anthracyclinones can be introduced simultaneously during the cyclization step.

In a recent investigation, we have studied the saponification of the α-hydroxy dichlorides **20** and **21** to the corresponding α-hydroxy aldehydes in some detail.[10] Optimal results were obtained by a phase transfer procedure. The main concern of the present study was to elucidate a possible dependence of the *cis/trans* ratio of the tetracyclic 9,10-diols formed in the cyclization reaction on solvent, catalyst, and temperature (Scheme 3). Previously, the cyclisation of the α-hydroxy aldehydes in aqueous alkali invariably gave a *cis/trans* ratio of 1:2.3 to 3.0.[9,10] Was it possible to further improve the ratio in favour of the naturally occurring 9,10-*trans* diols?

Thus, the α-hydroxy dichlorides **18–21** were transformed to the α-hydroxy aldehydes **22–25**, which were immediately reduced by alkaline dithionite without any prior isolation. Cyclization to the anthracylinones proceeded very rapidly (10 min) even at −10°, as shown by TLC monitoring. The main differences to similar previous reactions[10] were the lowering of the reaction temperature to −10°, the direct cyclization in the phase transfer system, and the variation of the phase transfer catalyst. Table 1 shows a representative selection of the reaction conditions.

As can be seen from Table 1, less protic solvents such as THF with a minimum amount of water to bring the sodium dithionite into solution favor the formation of the *cis*-9,10-diols. In analogy to the cyclic model of Cram[18] chelation of the α-hydroxy aldehyde with the counter ion in a 5-membered ring and attack from behind may be responsible for the *cis*-orientation. In contrast, in more protic solvents chelation plays only a minor role. Especially in the presence of voluminous bases such as Triton B, which are too large to fit into a 5-membered cycle, the developing negative charge on the aldehyde CO is repelled by the alcoholate group (dipolar model of Cornforth)[19] and the *trans*-diol is formed preferentially.

Two of the primary cyclization products are



Scheme 3

Table 1. Conversion of the α-hydroxy dichlorides **18–21** to the tetracyclic *trans*-(**1, 3, 26, 27**) and *cis*-diol (**28–31**) at −10°

α-hydroxy dichloride	Solvent system	Catalyst	*trans*-diol	*cis*-diol	Ratio *trans*/*cis*
18	MeOH/THF/0.5N NaOH (8:1:1)	—	29%	21%	1.1:1
	MeOH/THF/0.5N NaOH (7:2:1)	—	22%	40%	1:1.7
	CH_2Cl_2/0.5N NaOH	Triton B	47%	1.8%	25:1
	CH_2Cl_2/0.5N NaOH	tetrabutyl-ammonium-hydrogensulfate	43%	18%	2.4:1
	CH_2Cl_2/0.5N NaOH	benzyltrimethyl-ammonium chloride	37%	12%	3.0:1
	CH_2Cl_2/0.5N NaOH	[18] crown-6	21%	28%	1:1.35
19	MeOH/THF/0.5N NaOH (8:1:1)	—	17%	40%	1:2.3
	CH_2Cl_2/0.5N NaOH	Triton B	60%	trace (< 1%)	—
20	MeOH/THF/0.5N NaOH (8:1:1)	—	10%	56%	1:5.5
	CH_2Cl_2/0.5N NaOH	Triton B	52%	8%	7:1
21	CH_2Cl_2/0.2N NaOH (0°C)	tetrabutyl-ammonium-hydrogensulfate	59%	22%	2.7:1[10]
	CH_2Cl_2/0.5N NaOH	Triton B	67%	trace (< 1%)	—

naturally occurring [β_1-rhodomycinone (**3**)[2] and γ-rhodomycinone (**1**)[1]] but it is not unlikely, that the corresponding methyl ethers **26** and **27** will be isolated from natural sources. The 9,10-*cis*-diols are normally not natural products, but **28–31** can serve as reference samples for spectroscopic and chemical studies.

In the saponification and cyclization procedure always some of the nonpolar starting ketones **14–17** are formed, which can be easily separated by crystallization and recycled. The alkali treatment of **19** in homogeneous phase always gave some of the yellow coloured cyclic ether of structure **32**. (A corresponding ether with Me side chain was also observed by TLC, but could not be isolated in pure form). The formation of these minor side products could be avoided in the phase transfer procedure.

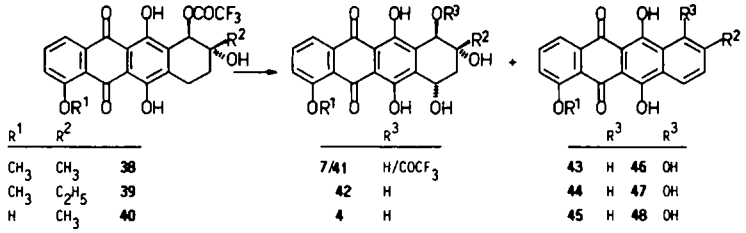
In order also to make available those anthracyclines of the feudomycinone and rhodomycinone families lacking substituents at C-10, the dichlorides **18–20** were cyclized as usual in homogeneous phase and then the reaction mixture was briefly heated to 60°. The tetracyclic tertiary alcohols were obtained in 60–75% yield, the only byproducts being some of the ketones **14–16** and the tetracyclic compounds **36** and **37**, where both aliphatic hydroxy groups have been eliminated.

Many of the natural anthracyclinones are hydroxylated at the benzylic position at C-7, and the introduction of this OH group was the next step in our synthesis.

In the first synthesis of 4-demethoxydaunomycinone[20] and daunomycinone,[21] Wong *et al.* have introduced the benzylic OH group via homolytic bromination. Since that time this reaction has found wide-spread application in anthracyclinone chemistry. However, methanolysis[20,21] as well as treatment with silver salts[7,21] yielded both epimers in an approximately 1:1 ratio. In connection with the synthesis of β-rhodomycinone we observed the exclusive formation of the natural 7,9-*cis*-diols by solvolysis of the intermediate bromides with dilute alkali.[9] Anchimeric assistance from the neighbouring axial OH group was considered to be responsible for the high stereoselectivity. A further preriquisite was the unprotected peri phenolic OH group. The stereochemistry and the chemical yield strongly depend on the nature of the side chain at C-9 (CH_3,C_2H_5, or $COCH_3$) and the substituents at C-10 (see for example: CH_2,[23] CHOH,[9] C=O,[24,25] or $CHCO_2CH_3$[26–28]). The optimal solvolysis conditions (dilute NaOH, $NaHCO_3$, H_2O, etc) have to be found for every single compound.

First, the *trans*-diols **3**, **26**, and **27** were transformed quantitatively to the monotrifluoroacetates **38–40** by treatment with trifluoroacetic anhydride. The trifluoroacetates were brominated in the presence of light with 1.6 equivalents of bromine in tetrachloromethane. The labile intermediate bromides were immediately treated with a dilute solution of sodium hydrogen carbonate in THF/H_2O. In all cases the main products were naturally configured 7,9-*cis*,9,10-*trans*-triols feudomycnione D (**7**) (81%), α_1-rhodomycinone (**4**) (66%), and 4-*O*-methyl-β-rhodomycinone (**42**) (75%). Only traces of the more polar and presumably 7,9-*trans*-orientated triols could be detected by TLC, but some aromatisation always accompanied the hydroxylation procedure. The 1:3 mixtures of the violet aromatic compounds **46–48** hydroxylated at C-1 (R^3 = OH) could not be separated from the red main napthacenequinones **43–45** (R^3 = H). Treatment of the bromide obtained from **38** with water afforded the monotrifluoroacetate **41** (38%), which is an attractive

substrate for monoglycosidation at C-7.



R^1	R^2		R^3		R^3	R^3	
CH_3	CH_3	**38**	**7/41**	$H/COCF_3$	**43**	H	**46** OH
CH_3	C_2H_5	**39**	**42**	H	**44**	H	**47** OH
H	CH_3	**40**	**4**	H	**45**	H	**48** OH

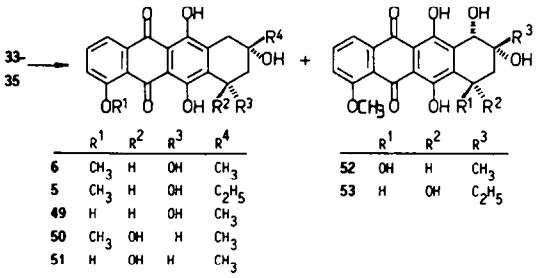
Scheme 4

Next, the 10-deoxy-anthracyclinones **33–35** were subjected to the same sequence of bromination and solvolysis. In contrast to the highly selective 7,9-*cis*-hydroxylation of the 9,10-*trans*-diols, rather complex mixtures were obtained. From the light-induced bromination of the methyl ether **33** only minor amounts of the 7,9-*cis* diol **6** (feudomycinone C) could be isolated. In addition to the 7,9-*trans*-diol **50** the triol of configuration **52** was formed. The 7,9-*cis*-diols **5**, **6**, and **49** could easily be distinguished from the 7,9-*trans*-diols **50** and **51** by formation of unpolar complexes with phenylboronic acid in TLC experiments.

phenolic OH groups at C-6 and C-11 were of special diagnostic value. The chemical shift characteristically depends on the axial or equatorial orientation of the neighbouring benzylic OH group.[29] The data in Table 2 show that the signals for the 6-OH or 11-OH neighbouring an equatorial benzylic OH group appear downfield in comparison to the axial alcohols.

EXPERIMENTAL

M.ps were determined on a Büchi 510 m.p. apparatus and are uncorrected. IR spectra were obtained on a Perkin–Elmer spectral photometer 1420 and are reported in wavenumbers



	R^1	R^2	R^3	R^4
6	CH_3	H	OH	CH_3
5	CH_3	H	OH	C_2H_5
49	H	H	OH	CH_3
50	CH_3	OH	H	CH_3
51	H	OH	H	CH_3

	R^1	R^2	R^3
52	OH	H	CH_3
53	H	OH	C_2H_5

Scheme 5

However, the bromination catalysed by azo-bis-isobutyronitril (AIBN) produced the desired feudomycinone C (**6**) (7%) together with the *trans*-diol **50** (8%) and the already known 9,10-*cis*-diol **28** (22%). In all cases in the hydroxylation of the 10-deoxy compounds substantial amounts of the aromatization products **43–45** were formed. A somewhat different result was obtained from the treatment of compound **34** with an Et side chain. The light-induced reaction produced the all-*cis*-triol **53** together with 39% of the aromatisation product **44**. Again, the milder procedure using AIBN as catalyst gave 18% of feudomycinone A (**5**). The higher selectivity in favour of the naturally configured 7.9-*cis*-diols in the Et series may be due to the more stabilized conformation with the equatorial side chain and the axial OH group at C-9. Furthermore, the Et group does more effectively protect the benzylic position at C-10 during bromination.

It should be mentioned, that anthracyclinones of the not naturally occurring configurations **52** and **53** have not been described before and they represent the last two of the four possible rhodomycinone stereoisomers (as racemates). The structure assignment has been made on the basis of the previously outlined ^{1}H-NMR parameters.[8,10,29] In addition to vicinal coupling constants and the possible 1,5-coupling of 8e-H and 10e-H in a W-conformation, the chemical shifts of the

(KBr, cm^{-1}). (^{1}H-NMR) spectra were recorded on Bruker AM 300 (300 MHz) and WM (400 MHz) spectrometers. Chemical shifts are reported in ppm (δ) downfield relative to TMS as standard (in $CDCl_3$). UV/VIS spectra were recorded on a Beckman UV 5230 spectral photometer in methanol; λ_{max} (lg ε); n.m. Mass spectra were obtained on a Varian MAT CH 7 mass spectrometer (70 eV). Analytical TLC was performed on silica gel plates (0.25 mm, E. Merck), preparative TLC on 1 mm silica gel plates (Schleicher & Schüll), and column chromatography with E. Merck silica gel 60 (230–400 mesh). Elemental analyses were performed by Ilse Beetz, Mikronanalytisches Lab. D-8640 Kronach. With the exception of optical rotation all spectroscopic data of compounds **4–7** were identical with the natural products.[1,4]

1,4-Dihydroxy-5-methoxy-2-(3-oxobutyl)-9,10-anthraquinone (**16**)

A soln of 8.03 g (20 mmol) ether **12**[10] in 250 ml of dry CH_2Cl_2 was cooled to −78° and 5.7 ml of a 1M soln of BCl_3 in CH_2Cl_2 was added dropwise. The complex was destroyed after 1 hr (TLC control) with excess $NaHCO_3$ aq and the organic phase was washed with water. The soln was dried over $MgSO_4$ and filtered over a short (20 × 4 cm) column of silica gel. 6.45 g (86%) of brown-red plates crystallized from the unpolar fraction, m.p. 197° (ether). 1.37 g of starting material **12** could be isolated from the polar fraction; IR 1718, 1622, 1578 cm^{-1}; UV 239 (4.53), 245 (4.30), 284 (3.92), 476 (4.00), 493 (3.99), 527 (3.71), 575 nm (sh); ^{1}H-NMR δ 2.19 (s; 3H, CH_3), 2.85 (t; 2H, CH_2), 3.02 (t; 2H, CH_2), 4.09 (s; 3H, OCH_3), 7.14 (s; 1H, 3-H), 7.37 (dd, J = 8.5 Hz, J = 1.0 Hz; 1H, 7-H), 7.77 (t; 1H, 6-H),

Table 2. Chemical shifts of the phenolic protons 6-OH and 11-OH in ^{1}H-NMR (δ, TMS = 0) of rhodomycinones and feudomycinones

	26	**28**	**6**	**50**	**7**	**52**	**3**	**30**
6-OH	13.79 (13.76)	13.72	14.06	14.35	13.91	14.15	12.76	12.71
11-OH	13.76 (13.79)	13.87	13.35	13.32	13.41	13.80	13.87	14.05
	27	**29**	**1**	**31**	**42**	**53**		
6-OH	13.74	13.72 (13.74)	12.73	12.70	13.91	13.93		
11-OH	13.67	13.74 (13.72)	13.84	14.04	13.42	13.85		

8.02 (dd, J = 7.5, J = 1.0 Hz, 1H, 5-H), 12.89 (s; 1H, OH), 13.68 (s; 1H, OH); mass spectrum (160°) 340 (47%, M^+), 322 (20, $M^+ - H_2O$), 311 (47), 297 (75), 284 ($M^+ - CH_3OH$), 265 (59), 255 (68), 237 (59). (Found: C, 66.95; H, 4.86. Calc for $C_{19}H_{16}O_6$: C, 67.06; H, 4.70%).

1,4-Dihydroxy-5-methoxy-2-(3-oxopentyl)-9,10-anthraquinone (**17**)

In a similar reaction 3.01 g (8.2 mmol) of **13**[9] afforded 2.60 g (89%) of ether **17**[9] (m.p. 170–171°).

(RS)-2-(4,4-Dichloro-3-hydroxy-3-methylbutyl)-1,4-dihydroxy-9,10-anthraquinone (**18**)

According to the general procedure given in the lit.,[10] 3.50 g (9.9 mmol) of **16** were treated with $LiCHCl_2$ at −100° to afford 3.45 g (82%) of **18** m.p. 128–130° (ether); IR 3470 (broad), 1616, 1578 cm^{-1}; UV 231 (4.59), 249 (4.38), 284 (4.06), 380 (sh), 477 (4.06), 494 (4.05), 527 nm (3.79); ^{1}H-NMR (300 MHz) δ 1.51 (s; 3H, CH_3), 2.10 (m; 2H, CH_2), 4.09 (s; 3H, OCH_3), 5.75 (s; 1H, $CHCl_2$), 7.16 (s; 1H, 3-H), 7.41 (dd, J = 8.5, J = 1.0 Hz; 1H, 5-H), 7.77 (t; 1H, 6-H), 8.03 (dd, J = 8.0, J = 1.0 Hz; 1H, 7-H), 12.93 (s; 1H, OH), 13.77 (s; 1H, OH). (Found: C, 56.73; H, 4.18; Cl, 16.57. Calc for $C_{20}H_{18}O_6Cl_2$: C, 56.45; H, 4.26 Cl, 16.67%).

(RS)-2-(3-Dichloromethyl-3-hydroxypentyl)-1,4-dihydroxy-8-methoxy-9,10-anthraquinone (**19**)

Similarly from 1.22 g of **17**[9] 1.33 g (90%) of **19** m.p. 124° (ether) were obtained. IR 3440, 1670, 1576 cm^{-1}; UV see 18; ^{1}H-NMR δ 1.03 (t, J = 7.6 Hz; 3H, CH_3), 1.94 (q, J = 7.6 Hz; 2H, CH_2), 2.10 (m; 2H, CH_2), 2.24 (s; 1H, OH), 2.84 (m; 2H, CH_2), 4.10 (s; 3H, OCH_3), 7.15 (s; 1H, 3-H), 7.40 (dd, J = 8.7, J = 1.0 Hz; 1H, 5-H), 7.79 (t; 1H, 6-H), 8.04 (dd, J = 8.0, J = 1.0 Hz; 1H, 7-H), 12.93 (s; 1H, OH), 13.79 (s; 1H, OH); mass spectrum (155°) 440 (59%), 439 (28), 438 (M^+, 78), 429 (17), 420 (17, $M^+ - H_2O$), 409 (19), 385 (81), 366 (21) 3.55 (27), 349 (76) 337 (100), 323 (46), 305 (39), 297 (96), 283 (76), 266 (58), 255 (64). (Found: C, 57.45; H, 4.52, Cl, 16.32. Calc for $C_{21}H_{20}O_6Cl_2$: C, 57.53: H, 4.56 Cl, 15.98%).

General phase transfer procedure for the transformation of the α-hydroxy dichlorides **18–21** *to the tetracycles* **26–31**

Method A. A soln of 2 mmol of dichlorides **18–21** in CH_2Cl_2 was cooled to 10° and treated under N_2 with 0.2 ml of a 40% soln of triton B in MeOH and 60 ml of 0.5N NaOH. After complete saponification (about 1 hr), the soln was cooled to −10° and a soln of 4 mmol of sodium dithionite in 15 ml of water was added. The colour of the mixture turned from blue to brown-yellow. After complete conversion of the starting material (about 15 min), the hydroquinones were reoxidized by stirring with air, the colour changing again to dark blue. The mixture was acidified with cold 1N HCl and 100 ml of CH_2Cl_2 were added.

The organic phase was washed with water and dried over Na_2SO_4. Crystallization of the crude product from CH_2Cl_2 afforded the main yield of 9,10-*trans*-diols and preparative TLC of the mother liquor gave a second crop of *trans*-diols together with minor amounts of the 9,10-*cis*-diols **28–31** and the ketones **14–17**. For yields of *cis*- and *trans*-diols by method A and B see Table 1.

rac-7-Deoxyfeudomycinone D (**26**). The reaction of 800 mg of **18** afforded 327 mg (47%) *trans*-**26** m.p. 210–212°, 13 mg (2%) *cis*-**28** and 125 mg ketone **14** were isolated; IR 3550, 1614, 1584 cm^{-1}; UV 218 (4.25), 234 (4.42), 250 (4.35), 288 (3.81), 375 (sh), 482 (3.96), 4.94 (3.99), 529 (3.79), 571 nm (sh); ^{1}H-NMR δ 1.49 (s; 3H, CH_3), 1.89 (dddd, J = 13.5, J = 6.0, J = 4.5, J = 1.0 Hz; 1H, 8e-H), 2.02 (ddd; J = 13.5, J = 9.5, J = 6.5 Hz; 1H, 8a-H), 3.93–3.96 (m; 2H, 7-H), 3.11 (d; J = 3.5 Hz; 1H, 10-OH), 4.07 (s; 1H, 9-OH), 4.11 (s; 3H, OCH_3), 4.78 (dd, J = 3.5, J = 1.0 Hz; 1H, 10e-H), 7.41 (dd, J = 8.5, J = 1.0 Hz; 1H, 3-H), 7.79 (t; 1H, 2-H), 8.05 (dd, J = 7.8, J = 1.0 Hz; 1H, 1-H), 13.74 (s; 1H, OH), 13.76 (s; 1H, OH); mass spectrum (195°) 370 (44%, M^+), 352 (25, $M^+ - H_2O$), 342 (16, $M^+ - CO$), 334 (55, $M^+ - 2H_2O$), 316 (55), 312 (36), 309 (100), 294 (53), 284 (61), 226 (56), 241 (26), 217 (24) 202 (28). (Found: C, 64.73; H, 5.70. Calc for $C_{20}H_{18}O_7$: C, 64.86; H, 4.90%).

rac- 10-epi-7-Deoxyfeudomycinone D (**28**; m.p. 247–249°). IR 3500, 3450, 1612, 1584 cm^{-1}; UV see 26; ^{1}H-NMR δ 1.48 (s; 3H, CH_3), 1.74 (dt, J = 13.1, J = 6.5 Hz; 1H, 8e-H), 2.12 (dt, J = 13.1, J = 6.5 Hz; 1H, 8a-H), 2.77 (dt, J = 19.5, J = 6.5 Hz; 1H, 7a-H), 2.92 (s; 1H, 9-OH), 3.06 (dt, J = 19.5, J = 6.5 Hz; 1H, 7e-H), 3.89 (d, J = 3.5 Hz; 1H, 10-OH), 4.09 (s; 3H, OCH_3), 4.79 (d, J = 3.5 Hz; 1H, 10a-H), 7.40 (dd, J = 8.0, J = 1.0 Hz; 1H, 3-H), 7.78 (t; 1H, 2-H), 8.05 (dd, J = 7.9, J = 1.0 Hz; 1H, 1-H), 13.72 (s; 1H, OH), 13.85 (s; 1H, OH); mass spectrum (220°), 370 (68%, M^+), 352 (23, $M^+ - H_2O$), 342 (16, $M^+ - CO$), 334 (60, $M^+ - 2H_2O$), 323 (54), 316 (51), 312 (50), 305 (100), 295 (26), 284 (66), 266 (47), 251 (22), 217 (21), 202 (20). (Found: C, 64.36; H, 4.84. Calc for $C_{20}H_{18}O_7$: C, 64.66; H, 4.90%).

General procedure for the cyclization of the α-hydroxy-dichlorides in homogeneous phase

Method B. A soln of 1mmol **18–21** in a mixture of 160 ml THF and 20 ml MeOH was treated at 15° with 20 ml of 0.5N NaOH for 2 hr under N_2. A soln of 2 mmol of sodium dithionite in 4 ml of H_2O was added with vigorous stirring. After 30 min stirring was continued in the presence of air (reoxidation) and after another 15 min 250 ml of cold 0.05N HCl was added. The mixture was extracted twice with each 100 ml of CH_2Cl_2. The combined organic phases were washed with water, dried over Na_2SO_4, evaporated i. vac., and the residue separated by preparative TLC. For yields see below and Table 1.

rac-4-O-Methyl-γ-rhodomycinone (**27**). The cyclization of 137 mg (0.31 mmol) of **19** by method B afforded 21 mg of the *trans*-**27** (17%), m.p. 227°, 48 mg (40%) *cis*-**29**, 4 mg (4%) of the cyclic ether **32**, and 19 mg (17%) of ketone **15**.[9] Method A gave 164 mg (60%) **27** and 34 mg (13%) of **29** starting from 313 mg (0.71 mmol) **19**. IR 3470, 1615, 1582 cm^{-1}; UV 219 (4.33), 234 (4.51), 251 (4.44), 288 (3.90), 377 (sh), 468 (4.06), 481 (4.07), 495 (4.10), 509 (sh), 529 nm (3.88); ^{1}H-NMR (300 MHz) δ 1.10 (t, J = 7.3 Hz; 3H, CH_3), 1.64 (sextett, J = 15.0, J = 7.3 Hz; 1H, 13-H), 1.68 (sextett, J = 15.0, J = 7.3 Hz; 1H, 13-H), 1.91 (ddd,

J = 14.1, J = 10.2, J = 6.0 Hz; 1H, 8a-H), 1.96 (ddd, J = 14.1, J = 6.7, J = 3.0 Hz; 1H, 8e-H), 2.83 (ddd; J = 19.5, J = 10.2, J = 6.7 Hz; 1H, 7a-H), 2.84 (d, J = 3.5 Hz; 1H, 10-OH), 2.99 (ddd, J = 19.5, J = 6.0, J = 3.0 Hz; 1H, 7e-H), 4.09 (s; 3H, OCH_3), 4.80 (d, J = 3.5 Hz; 1H, 10-H), 7.37 (dd, J = 8.3, J = 1.0 Hz; 1H, 3-H), 7.77 (t; 1H, 2-H), 8.02 (dd, J = 7.8, J = 1.0 Hz; 1H, 1-H), 13.67 (s; 1H, OH), 13.74 (s; 1H, OH); mass spectrum (180°), 384 (45%, M^+), 366 (37, $M^+ - H_2O$), 348 (25, $M^+ - 2H_2O$), 337 (46), 330 (17), 323 (23), 312 (33), 309 (100). 284 (65), 266 (48), 251 (17), 241 (24), 217 (24).

rac-4-O-Methyl-10-epi-γ-rhodomycinone (**29**; m.p. 212–213°), IR 3470, 1618, 1585 cm^{-1}; UV 221 (4.31), 233 (4.49), 250 (4.39), 288 (3.88), 377 (sh), 481 (4.02), 499 (4.05), 529 (3.83), 570 nm (3.80); ^{1}H-NMR (300 MHz) δ 1.10 (t, J = 7.5 Hz; 3H, CH_3), 1.82–2.06 (m; 4H, 2 CH_2), 2.81–2.90 (m; 2H, CH_2), 3.10 (d, J = 3.4 Hz; 1H, 10-OH), 4.09 (s; 3H, OCH_3), 4.77 (d, J = 3.4 Hz; 1H, 10-H), 7.39 (dd, J = 8.0, J = 1.4 Hz; 1H, 3-H), 7.77 (t; 1H, 2-H), 8.03 (dd, J = 7.2, J = 1.4 Hz; 1H, 1-H), 13.72 (s; 1H, OH), 13.74 (s; 1H, OH); mass spectrum (166°), 384 (56%, M^+), 366 (26, $M^+ - H_2O$), 356 (16), 348 (60), 337 (55), 321 (24), 312 (33), 309 (100), 299 (32), 284 (68), 266 (61), 251 (27), 241 (28), 217 (37).

(RS)-2-*Ethyl-2-formyl-3,4-dihydro-6-hydroxy-8-methoxy-2H-anthra*[1,2-*b*]*pyran-7,12-dion* (**32**; m.p. 174°)

IR 1737, 1660, 1634, 1575 cm^{-1}; UV 229 (4.53), 249 (4.30), 270 (4.05), 330 (sh), 400 (sh), 465 nm (3.95); ^{1}H-NMR (300 MHz) δ 1.12 (t, J = 7.5 Hz; 3H, CH_3), 1.89 (dddd, J = 17.8, J = 13.5, J = 3.0, J = 1.0 Hz; 1H, 3a-H), 1.91 (sextett, J = 15.0, J = 7.5 Hz; 1H, 13-H), 1.99 (sextett, J = 15.0, J = 7.5 Hz; 1H, 13-H), 2.29 (dt, J = 13.5, J = 6.0 Hz; 1H, 3e-H), 2.77 (dddd, J = 20.0, J = 6.0, J = 3.0, J = 1.0 Hz; 1H, 4e-H), 2.78 (dddd, J = 20.0, J = 17.8, J = 6.0, J = 1.0 Hz; 1H, 4a-H), 4.02 (s; 3H, OCH_3), 6.95 (t, J = 1.0 Hz; 1H, 5-H), 7.33 (dd, J = 8.5 Hz, J = 0.9 Hz; 1H, 10-H), 7.67 (t; 1H, 9-H), 7.92 (dd, J = 7.9, J = 0.9 Hz; 1H, 8-H), 9.78 (d, J = 1.0 Hz; 1H, CHO), 12.65 (s; 1H, OH); mass spectrum (110°) 366 (16%, M^+), 354 (19), 337 (81), 319 (22), 309 (100), 297 (25), 283 (28).

Cyclization of the α-hydroxy dichlorides **18–20** *to the* 10-*deoxyanthracyclinones* **33–37**

General procedure. A soln of 1 mmol α-hydroxy dichloride (**18–20**) in a mixture of 100 ml of THF and 150 ml MeOH was treated as described by the general procedure B. The mixture was then heated to 60° for 10 min and worked up as in method B. Crystallization from 4 ml of CH_2Cl_2 afforded the pure **33–35**. By preparative TLC chromatography of the mother liquor another small amount of **33–35** and the unpolar products **36** and **37** could be isolated.

rac-7-Deoxyfeudomycinone C (**33**). 500 mg (1.17 mmol) of **18** were treated as described by the general procedure to afford 257 mg (62%) of **33** m.p. 177–178°. IR 3450, 1612, 1584 cm^{-1}; UV 216 (4.30), 234 (4.41), 252 (4.43), 289 (3.86), 380 (sh), 469 (3.99), 481 (3.99), 499 (4.03), 529 (3.82), 567 nm (sh); ^{1}H-NMR δ 1.48 (s; 3H, CH_3), 1.80 (dt, J = 13.5, J = 8.5 Hz; 1H, 8a-H), 1.99 (ddt, J = 13.5, J = 5.2, J = 2.0 Hz; 1H, 8e-H), 2.80 (dd, J = 18.5, J = 2.0 Hz; 1H, 10e-H), 2.98 (m; 2H, CH_2), 2.99 (d, J = 18.5 Hz; 1H, 10a-H), 4.11 (s; 3H, OCH_3), 7.38 (dd, J = 8.4, J = 0.9 Hz; 1H, 3-H), 7.76 (t; 1H, 2-H), 8.04 (dd, J = 8.0, J = 0.9 Hz; 1H, 1-H), 13.52 (s; 1H, OH), 13.88 (s; 1H, OH); mass spectrum (200°) 354 (100%, M^+), 336 (59, $M^+ - H_2O$), 321 (40), 311 (79), 296 (65). (Found: C, 67.65; H, 5.04. Calc for $C_{20}H_{18}O_6$: C, 67.80; H. 5.08).

rac-7,9-Dideoxyfeudomycinone C (**36**). From the unpolar fraction (see above) 64 mg (16%) of **36** m.p. 201° were isolated. IR 1605, 1579 cm^{-1}; UV 219 (4.36), 234 (4.44), 252 (4.50), 287 (3.94), 366 (3.50), 470 (4.04), 492 (4.10), 528 nm (3.92); ^{1}H-NMR δ (300 MHz) 1.13 (d, J = 6.9 Hz; 3H, CH_3), 1.34 (ddt, J = 13.0, J = 11.0, J = 5.3 Hz; 1H, 8a-H), 1.74–1.88 (m; 1H, 9a-H), 1.96 (dddd, J = 13.0, J = 6.0, J = 3.0, J = 1.0Hz; 1H, 8e-H), 2.20 (dddd, J = 18.5, J = 10.2, J = 2.5, J = 1.2 Hz; 1H, 10a-H), 2.63 (dddd, J = 18.5, J = 5.0, J = 2.5, J = 1.2 Hz; 1H, 10e-H), 2.96–3.08 (m, 2H, CH_2), 4.07 (s; 3H, OCH_3), 7.34 (dd, J = 8.7, J = 1.0 Hz; 1H, 3-H), 7.73 (t; 1H, 2-H), 8.02 (dd, J = 7.7, J = 1.0 Hz; 1H, 1-H), 13.53 (s; 1H, OH), 13.89 (s; 1H, OH); mass spectrum (150°), 339 (51%, $M^+ + 1$), 338 (100, M^+), 323 (60, $M^+ - CH_3$), 320 (38), 309 (37), 305 (65), 291 (41), 278 (18), 277 (18), 263 (14), 253 (15), 237 (12), 225 (14), 217 (19), 203 (22).

rac-7-Deoxyfeudomycinone A (**34**). According to the general procedure, 302 mg (0.69 mmol) of **19** were transformed to afford 175 mg (69%) of **34** m.p. 248° and 24 mg (9%) of **37** m.p. 126°. IR 3540, 1610, 1578 cm^{-1}; UV see **33**; ^{1}H-NMR (300 MHz) δ 1.08 (t, J = 7.8 Hz; 3H, CH_3), 1.36 (s; 1H, 9-OH), 1.68 (sextett, J = 15.5, J = 7.8 Hz; 1H, 13-H), 1.69 (sextett, J = 15.5, J = 7.8 Hz; 1H, 13-H), 1.73 (dd, J = 13.1, J = 7.0 Hz; 1H, 8a-H), 1.96 (dddd, J = 13.1, J = 6.0, J = 4.0, J = 2.0 Hz; 1H, 8e-H), 2.75 (d, J = 18.5 Hz; 1H, 10a-H), 2.92 (dd, J = 18.5, J = 2.0 Hz; 1H, 10e-H), 2.97 (m; 2H, CH_2), 4.11 (s; 3H, OCH_3), 7.36 (dd, J = 8.8, J = 1.0 Hz; 1H, 3-H), 7.76 (t; 1H, 2-H), 8.04 (dd, J = 7.8, J = 1.0 Hz; 1H, 1-H), 13.52 (s; 1H, OH), 13.89 (s; 1H, OH); mass spectrum (150°), 369 (36%, $M^+ + 1$), 368 (100, M^+), 350 (42, $M^+ - H_2O$), 339 (28), 321 (62), 311 (97), 296 (64), 278 (39), 269 (25), 253 (32), 237 (19), 221 (24). (Found: C, 68.58; H, 5.39. Calc for $C_{21}H_{20}O_6$: C, 68.48; H, 5.43).

7,9-*Dideoxyfeudomycinone* A (**37**). IR 3000–2900, 1608, 1578 cm^{-1}; mass spectrum (110°), 352 (100%, M^+), 338 (83), 323 (75), 309 (85), 305 (77), 291 (62), 284 (75), 266 (73), 252 (42), 238 (58), 217 (67). ^{1}H-NMR (400) MHz δ 1.03 (t, J = 7.0 Hz; 3H, CH_3), 1.35 (ddd, J = 13.0, J = 11.5, J = 5.8 Hz; 1H, 8a-H), 1.34–1.55 (m; 2H, CH_2), 1.93–2.06 (m; 1H, 9a-H), 2.23 (dddd, J = 18.0, J = 10.0, J = 2.2, J = 1.2 Hz; 1H, 10a-H), 2.32 (ddd, J = 18.0, J = 8.0, J = 2.0 Hz; 10e-H), 2.54–2.65 (m; 1H, 8e-H), 3.00–3.11 (m; 2H, CH_2), 4.10 (s; 3H, CH_3), 7.48 (dd, J = 8.0, J = 1.0 Hz; 1H, 3-H), 7.73 (t; 1H, 2-H), 8.02 (dd, J = 7.4, J = 1.0 Hz; 1H, 1-H), 13.57 (s; 1H, OH); 13.90 (s; 1H, OH).

10-*Deoxy-β*$_1$*-rhodomycinone* (**35**). According to the general procedure, 610 mg (1.49 mmol) of **20** were transformed to 380 mg (75%) of **35** m.p. 225°. IR 3540, 1600, 1584 cm^{-1}; UV 219 (4.30), 235 (4.47), 254 (4.52), 293 (3.94), 387 (sh), 411 (3.53), 465 (4.07), 490 (4.20), 510 (4.05), 525 (4.08), 561 nm (sh); ^{1}H-NMR (300 MHz) δ 1.47 (s; 3H, CH_3), 1.77 (dt, J = 13.5, J = 8.0 Hz; 1H, 8a-H), 1.98 (ddt, J = 13.5, J = 5.0, J = 2.6 Hz; 1H, 8e-H), 2.78 (dd, J = 19.0, J = 2.0 Hz; 1H, 10e-H), 2.95 (m; 2H, CH_2), 2.98 (dd, J = 19.0, J = 1.8 Hz; 1H, 10a-H), 7.29 (dd, J = 8.3, J = 1.0 Hz; 1H, 3-H), 7.68 (t; 1H, 2-H), 7.87 (dd, J = 7.7, J = 1.0 Hz; 1-H), 12.30 (s; 1H, OH), 13.65 (s; 1H, OH); mass spectrum (150°), 341 (57%, $M^+ + 1$), 340 (100, M^+), 322 (93, $M^+ - H_2O$), 307 (88), 297 (78), 282 (93), 265 (26), 253 (33), 237 (32), 226 (25), 202 (56). (Found: C, 66.99; H, 4.75. Calc for $C_{19}H_{16}O_6$: C, 67.06; H, 4.70%).

rac-7-Deoxyfeudomycinone D-10-trifluoroacerate (**38**). A soln of 50 mg (0.13 mmol) *trans*-**26** in 30 ml of CH_2Cl_2 was treated with 2 ml of trifluoroacetic anhydride for 2.5 hr. The solvent was evaporated i. vac. and the residue crystallized from petrol ether to afford 52 mg (82%) of **38** m.p. 184–185°. IR 3440, 1782, 1612, 1579 cm^{-1}; ^{1}H-NMR (400 MHz) δ 1.47 (s; 3H, CH_3), 1.73 (s; 1H, 9-OH), 1.95 (ddd; J = 14.0, J = 11.0, J = 6.0 Hz; 1H, 8a-H), 2.01 (ddt, J = 14.0, J = 6.0, J = 2.0 Hz; 1H, 8e-H), 2.92 (ddd, J = 20.0, J = 11.0, J = 6.0 Hz; 1H, 7a-H), 3.12 (ddd, J = 20.0, J = 6.0, J = 2.0 Hz; 1H, 7e-H), 4.11 (s; 3H, OCH_3), 6.25 (d, J = 2.0 Hz, 1H, 10e-H), 7.40 (dd, J = 8.0, J = 1.0 Hz; 1H, 3-H), 7.80 (t; 1H, 2-H), 8.03 (dd, J = 7.5, J = 1.0 Hz; 1H, 1-H), 13.37 (s; 1H, OH), 13.66 (s; 1H, OH).

rac-4-O-Methyl-γ-rhodomycinone-10-trifluoroacetate (**39**). Similarly, treatment of 16 mg of the *trans*-**27** gave 18 mg (95%) of **39** m.p. 200°. IR 3500, 1787, 1615, 1586 cm^{-1}; ^{1}H-NMR (400 MHz) δ 1.11 (t, J = 7.5 Hz; 3H, CH_3), 1.52 (s; 1H, 9-OH), 1.65 (sextett, J = 15.0, J = 7.5 Hz; 1H, 13-H), 1.77 (sextett, J = 15.0, J = 7.5 Hz; 1H, 13-H), 1.89 (ddd, J = 14.1, J = 12.0, J = 6.2 Hz; 1H, 8a-H), 2.11 (ddt, J = 14.1, J = 6.5, J = 2.0 Hz; 1H, 8e-H), 2.85 (ddd, J = 19.8, J = 12.0, J = 6.5 Hz; 1H, 7a-H), 3.14 (ddd, J = 19.8, J = 6.2, J = 2.0 Hz; 1H, 7e-H), 4.11 (s; 3H, OCH_3), 6.26 (d, J = 2.0 Hz; 1H, 10e-H), 7.40 (dd, J = 8.1, J = 1.0 Hz; 1H, 3-H), 7.82 (t; 1H, 2-H), 8.04 (dd, J = 7.5, J = 1.0 Hz; 1H, 1-H), 13.42 (s; 1H, OH), 13.67 (s; 1H, OH).

General procedure for the hydroxylation of the monotrifluoro acetates **38–40** *to the triols* **4**, **7**, *and* **42**

The *trans*-**3**, **26**, and **27** were converted to acetates **38–40** without isolation. Solns of 0.3 mmol of **38–40** in 80 ml of CCl_4

were irridiated (500 Watt) in the presence of 0.5 mmol Br_2. After 20 min the solutions were evaporated i. vac. (bath below 30°). The residue was dissolved in 40 ml of THF and stirred with 40 ml of a 0.1N soln of $NaHCO_3$ at 15°. After 30 min the soln was extracted twice each with 50 ml of CH_2Cl_2. The organic phase was dried over Na_2SO_4, filtered, and evaporated. The residue crystallized from 2 ml of CH_2Cl_2 to afford the triols **4**, **7**, and **42**. A second small amount of product can be obtained by TLC separation from the polar fraction. The unpolar fractions consisted of mixtures of the naphthacenequinones **43–45** and **46–48** (3 : 1).

rac-Feudomycinone D (**7**). Hydroxylation of 100 mg (0.27 mmol) of **26** afforded 85 mg (81%) of 7 m.p. 267–268°. IR 3480, 3418, 1614, 1572, cm^{-1}; UV 207 (4.21), 232 (4.58), 249 (4.35), 286 (3.91), 380 (sh), 477 (4.05), 493 (4.06), 529 (3.81), 565 nm (sh); ^{1}H-NMR (400 MHz) δ 1.26 (s; 3H, CH_3), 2.19 (ddd, J = 15.0, J = 2.0, J = 1.0 Hz; 1H, 8e-H), 2.28 (ddd, J = 15.0, J = 5.0, J = 1.5 Hz; 1H, 8a-H), 2.72 (d, J = 4.0 Hz; 1H, 10-OH), 3.49 (dd, J = 4.0, J = 1.5 Hz; 1H, 7-OH), 3.60 (s; 1H, 9-OH), 4.12 (s; 3H, OCH_3), 4.85 (dd, J = 4.0, J = 1.0 Hz; 1H, 10e-H), 5.27 (ddd, J = 5.0, J = 4.0, J = 2.0 Hz; 1H, 7e-H), 7.44 (dd, J = 8.0, J = 1.0 Hz; 1H, 3-H), 7.82 (t; 1H, 2-H), 8.07 (dd, J = 7.5, J = 1.0 Hz; 1H, 1-H), 13.41 (s; 1H, OH), 13.91 (s; 1H, OH); mass spectrum (210°), 386 (20%, M^+), 368 (96, $M^+ - H_2O$), 350 (87), 334 (73), 328 (100), 321 (53), 316 (63), 311 (85), 297 (71), 285 (65), 267 (37). (Found: C, 62.04; H, 4.58. Calc for $C_{20}H_{18}O_8$: C, 62.17; H, 4.66%).

rac-7-Trifluoroacetyl-feudomycinone D (**41**). 81 mg (0.22 mmol) of **23** were converted to acetate **38** and brominated as described above. Solvolysis with THF/H_2O and TLC separation gave 40 mg (38%) of acetate **41** m.p. 170°. IR 3470, 1789, 1618, 1580 cm^{-1}; UV see 7; ^{1}H-NMR (400 MHz) δ 1.42 (s; 3H, CH_3), 2.19 (dt, J = 15.5, J = 5.0 Hz; 1H, 8a-H), 2.31 (dt, J = 15.5, J = 1.0 Hz; 1H, 8e-H), 3.50 (d, J = 2 Hz; 1H, 7-OH), 4.06 (s; 3H, 9-OH), 4.09 (s; 3H, OCH_3), 5.35 (ddd, J = 5.0, J = 2 Hz; 1H, 7e-H), 6.35 (d, J = 1.0 Hz; 1H, 10e-H), 7.42 (dd, J = 8.5, J = 1.0 Hz; 1H, 3-H), 7.82 (t, 1H, 2-H), 8.05 (dd, J = 7.5, J = 1.0 Hz; 1H, 1-H), 13.15 (s; 1H, OH), 13.81 (s; 1H, OH).

rac-4-O-Methyl-β-rhodomycinone (**42**). Hydroxylation of 36 mg (0.09 mmol) of **27** by the general procedure yielded 27 mg (75%) of **42** m.p. 220°. IR 3575, 3450, 1617, 1583 cm^{-1}; UV see 7; ^{1}H-NMR δ (400 MHz) 1.15 (t, J = 7.0 Hz; 3H, CH_3), 1.77 (sextett, J = 14.1, J = 7.0 Hz; 1H, CH_2), 18.9 (sextett, J = 14.1, J = 7.0 Hz, 1H, CH_2), 2.15 (dd, J = 14.2, J = 5.0 Hz; 1H, 8a-H), 2.32 (ddd, J = 14.2, J = 2.0, J = 1.0 Hz; 1H, 8e-H), 2.46 (d, J = 4 Hz; 1H, 10-OH), 3.46 (s; 1H, 9-OH), 3.49 (d, J = 5.0 Hz, 1H, 7-OH), 4.11 (s; 3H, OCH_3), 4.91 (dd, J = 4, J = 1 Hz; 1H, 10e-H), 5.27 (m; 1H, 7e-H), 7.43 (dd, J = 8.5, J = 1.0 Hz; 1H, 3-H), 7.82 (t; 1H, 2-H), 8.06 (dd, J = 8.0, J = 1.0 Hz; 1H, 1-H), 13.42 (s; 1H, OH), 13.91 (s; 1H, OH); mass spectrum (200°), 400 (31%, M^+), 382 (94), 364 (93), 348 (72), 335 (61), 328 (100), 326 (97), 311 (85), 310 (85), 297 (72), 292 (44), 285 (62), 267 (45), 257 (43), 235 (38), 225 (29), 211 (27).

rac-α$_1$-Rhodomycinone (**4**). From 51 mg (0.14 mmol) of **3**, 36 mg (66%) of **4** m.p. 231–232° were obtained. IR 3550, 3400, 1598, 1576 cm^{-1}; UV 211 (4.18), 233 (4.59), 253 (4.39), 385 (sh), 470 (4.06), 485 (0.12), 494 (4.16), 512 (4.04), 528 (4.01), 598 nm (3.33); ^{1}H-NMR (400 MHz) δ 1.50 (s; 3H, CH_3), 2.18 (ddd, J = 15.0, J = 2.0, J = 1.0 Hz; 1H, 8e-H), 2.27 (ddd, J = 15.0, J = 5.0 Hz; 1H, J = 1.0 Hz; 1H, 8a-H), 2.73 (d, J = 4.0 Hz, 1H, 10-OH), 3.37 (s; 1H, 9-OH), 3.48 (dd, J = 5.0, J = 1.0 Hz; 7-OH), 4.83 (dd, J = 4.0, J = 1.0 Hz; 1H, 10e-H), 5.23 (dd, J = 5.0, J = 2.0 Hz; 1H, 7e-H), 7.39 (dd, J = 8.4, J = 1.0 Hz; 1H, 3-H), 7.73 (t; 1H, 2-H), 7.91 (dd, J = 7.4, J = 1.0 Hz; 1H, 1-H), 12.12 (s; 1H; OH), 12.89 (s; 1H, OH); 13.58 (s; 1H, OH); mass spectrum (210°), 372 (7%, M^+), 352 (40), 336 (92), 320 (100), 314 (33), 296 (50), 283 (21), 270 (58), 263 (21), 255 (18), 249 (16), 235 (18), 218 (17), 205 (21).

Photobromination and solvolysis of 7-deoxyfeudomycinone D (**33**)

A soln of 100 mg (0.28 mmol) of **33** in 100 ml of CCl_4 was treated with 90 mg (0.56 mmol) of Br_2 at 40° for 25 min in the presence of light (500 Watt). Solvolysis with $NaHCO_3$ and workup was as described in the general procedure for **38–40**. Preparative TLC separation (CH_2Cl_2/5% CH_3OH) afforded with decreasing polarity: 6 mg (5%) of **52**, 6 mg (6%) of **50**, and 24 mg (25%) of **43**.

Data for **52**: m.p. 218–219°; IR 3525, 3480, 3420, 1619, 1583 cm^{-1}; UV see 7; ^{1}H-NMR (400 MHz) δ 1.48 (s, 3H, CH_3), 1.83 (dd, J = 14.0, J = 7.7 Hz; 1H, 8a-H), 2.53 (dd, J = 14.0, J = 6.7 Hz; 1H, 8e-H), 2.74 (d, J = 2.0 Hz; 1H, 7-OH), 4.03 (s; 1H, 9-OH), 4.10 (s; 3H, OCH_3), 4.22 (d, J = 1.8 Hz; 1H, 10-OH), 4.83 (d, J = 1.8 Hz; 1H, 10a-H), 5.32 (td, J = 7.7, J = 6.7, J = 2.0 Hz; 1H, 7a-H), 7.42 (dd, J = 8.9, J = 1.0 Hz; 1H, 3-H), 3-H), 7.81 (t; 1H; 2-H), 8.05 (dd, J = 7.6, J = 1.0 Hz; 1H, 1-H), 13.80 (s; 1H, OH), 14.15 (s; 1H, OH); mass spectrum (180°), 386 (17%, M^+), 368 (77), 350 (100), 332 (90), 328 (98), 321 (39), 316 (61), 310 (78), 304 (54), 297 (51), 292 (42), 285 (53), 279 (39), 264 (32), 257 (35), 239 (25), 205 (27). (Found: C, 62.04; H, 4.58. Calc for $C_{20}H_{18}O_8$: C, 62.17; H, 4.66%).

Data for **50**: m.p. 197°; IR 3530, 3460, 1615, 1587 cm^{-1}; UV see 6; ^{1}H-NMR δ 1.34 (s; 1H, 9-OH), 1.91 (dd, J = 13.5, J = 9.0 Hz; 1H, 8a-H), 2.42 (ddd, J = 13.5, J = 6.6, J = 2.5 Hz; 1H, 8e-H), 2.80 (d, J = 18.5 Hz; 10a-H), 3.01 (dd, J = 18.5, J = 2.5 Hz; 1H, 10e-H), 4.10 (s; 3H, OCH_3), 4.20 (d, J = 2.5 Hz; 1H, 7-OH), 5.36 (ddd, J = 9.0, J = 6.6, J = 2.5 Hz; 1H, 7a-H), 7.40 (dd, J = 8.0, J = 1.0 Hz; 1H, 3-H), 7.80 (t; 1H, 2-H), 8.05 (dd, J = 8.0, J = 1.0 Hz; 1H, 1-H), 13.32 (s; 1H, OH), 14.35 (s; 1H, OH); mass spectrum 370 (81%, M^+), 352 (100), 337 (96), 334 (80), 328 (41), 329 (63), 316 (66), 312 (34), 295 (64), 291 (48), 284 (70), 277 (32), 266 (62), 251 (28), 241 (37), 217 (35); high-resolution mass spectrum. (Found 370.10516; Calc for $C_{20}H_{18}O_7$, 370.10524).

Data for **43**: m.p. 263–265°; ^{1}H-NMR (300 MHz) δ 2.58 (s; 3H, CH_3), 4.10 (s; 3H, OCH_3), 7.31 (dd, J = 8.1, J = 1.0 Hz; 1H, 9-H), 7.61 (dd, J = 8.2, J = 1.5 Hz; 1H, 2-H), 7.75 (t; 1H, 3-H), 8.14 (dd, J = 8.0, J = 1.0 Hz; 1H, 4-H), 8.26 (d, J = 1 Hz; 1H, 7-H), 8.38 (d, J = 8.1 Hz; 1H, 10-H), 15.29 (s; 1H, OH), 16.10 (s; 1H, OH).

Bromination and solvolysis of 7-deoxyfeudomycinone D (**33**) *in the presence of 2,2'-azo-bis-isobutyronitrile* (AIBN). 70 mg of **33** in 100 ml CCl_4 were brominated at 40° in the presence of 50 mg of AIBN. Solvolysis and workup were as described before. Preparative TLC separation afforded with decreasing polarity 6 mg (8%) of **50**, 16 mg (22%) of **28**, 5 mg (7%) of rac-feudomycinone C (**6**) and 5 mg (7%) of **43**.

Data for feudomycinone C (**6**): m.p. 264°; IR 3515, 3490, 1620, 1573 cm^{-1}; UV 220 (4.31), 233 (4.50), 250 (4.35), 380 (sh), 479 (4.03), 495 (4.04), 530 nm (3.80); ^{1}H-NMR (400 MHz) δ 1.28 (s; 3H, CH_3), 1.95 (dd, J = 15.0, J = 5.0 Hz; 1H, 8a-H), 2.39 (dt, J = 15.0, J = 2.5 Hz; 1H, 8e-H), 2.61 (d, J = 18.0 Hz; 1H, 10a-H), 3.26 (dd, J = 18.0, J = 2.5 Hz; 1H, 10e-H), 3.44 (s; 1H, 9-OH), 3.57 (d, J = 1.6 Hz; 1H, 7-OH), 4.11 (s; 3H, OCH_3), 5.32 (ddd, J = 5.0, J = 2.5, J = 1.6 Hz; 1H, 7e-H), 7.42 (dd, J = 8.2, J = 1.0 Hz; 1H, 3-H), 7.80 (t, 1H, 2-H), 8.07 (dd, J = 7.7, J = 1.0 Hz; 1H, 1-H), 13.35 (s; 1H, OH), 14.06 (s; 1H, OH); mass spectrum (180°), 370 (85%, M^+), 352 (98), 334 (82), 323 (56), 316 (77), 312 (98), 309 (100), 295 (77), 284 (64), 277 (48), 266 (65), 251 (30), 241 (33), 217 (45), 203 (44); high-resolution mass spectrum. (Found 370.10516; Calc for $C_{20}H_{18}O_7$, 370.10524).

Photobromination and solvolysis of **34**. 100 mg (0.27 mmol) of **34** were treated as described for **33**. Preparative TLC separation afforded 6 mg (7%) of **53** and 37 mg (39%) of 8-ethyl-6,11-dihydroxy-1-methoxy-5,12-naphthacenequinone **44**.

Data for **53**: m.p. 225°; IR 3540, 1620, 1584 cm^{-1}; UV 210 (4.31), 232 (4.61), 248 (4.38), 283 (3.97), 380 (sh), 450 (sh), 477 (4.08), 493 (4.07), 529 nm (3.81); ^{1}H-NMR (300 MHz) δ 1.05 (t, J = 7.5 Hz; 3H, CH_3), 1.76 (sextett, J = 15.0, J = 7.5 Hz; 1H, 13-H), 1.84 (dd, J = 15.0, J = 4.0 Hz; 1H, 8a-H); 1.86 (sextett, J = 15.0, J = 7.5 Hz; 1H, 13-H), 2.46 (dd, J = 15.0, J = 3.5 Hz; 1H, 8e-H), 3.33 (s; 1H, 9-OH), 4.10 (s; 3H, OCH_3), 4.47 (d, J = 2.5 Hz; 1H, 10-OH), 4.69 (d, J = 8.0 Hz; 1H, 7-OH), 4.82 (d, J = 2.5 Hz, 1H, 10a-H), 5.10 (ddd, J = 8.0, J = 4.0, J = 3.5 Hz; 1H, 7e-H), 7.40 (dd, J = 8.0, J = 1.0 Hz; 1H, 3-H), 7.79 (t; 1H, 2-H), 8.02 (dd, J = 7.6, J = 1.0 Hz; 1H, 1-H), 13.85 (s; 1H, OH), 13.91 (s; 1H, OH); mass spectrum (130°), 400 (14%, M^+), 382 (45, $M^+ - H_2O$), 364 (90), 348 (97), 330 (100), 318 (44), 311 (67), 303 (59), 292 (59), 285 (44), 262 (37), 239 (20), 217 (27).

Data for **44**: m.p. 226°; ^{1}H-NMR (400 MHz) δ 1.39 (t, J

= 7.5 Hz; 3H, CH_3), 2.88 (q, J = 7.5 Hz; 2H, CH_2), 7.29 (dd, J = 8.5, J = 1.5 Hz; 1H, 9-H), 7.64 (dd, J = 8.5, J = 1.9 Hz; 1H, 2-H), 7.75 (t; 1H, 3-H), 8.13 (dd, J = 7.9, J = 1.0 Hz; 1H, 4-H), 8.22 (d, J = 1.5 Hz; 1H, 7-H), 8.40 (d, J = 8.5 Hz; 1H, 10-H), 15.31 (s; 1H, OH), 16.09 (s; 1H, OH).

Bromination and solvolysis of **34** *in the presence of AIBN.* 60 mg of **34** were treated as described for **33**. Preparative TLC separation afforded 11 mg (18%) of feudomycinone A (**5**) and 21 mg of **44**.

Data for feudomycinone A (**5**): m.p. 248°; IR 3500, 1614, 1572 cm^{-1}; UV see 5; ^{1}H-NMR (300 MHz) δ 1.07 (t, J = 7.2 Hz; 3H, CH_3), 1.72 (sextett, J = 14.4, J = 7.2 Hz; 1H, 13-H), 1.74 (sextett, J = 14.4, J = 7.2 Hz; 1H, 13-H), 1.85 (ddd, J = 14.8, J = 5.0, J = 1.0 Hz; 1H, 8a-H), 2.36 (dt, J = 14.8, J = 2.0 Hz; 1H, 8e-H), 2.57 (d, J = 19.0 Hz; 1H, 10a-H), 3.20 (dd, J = 4.4, J = 1.0 Hz; 1H, 7-OH), 4.10 (s; 3H, OCH_3), 5.29 (td, J = 5.0, J = 4.4, J = 2.0 Hz; 1H, 7e-H), 7.40 (dd, J = 8.5, J = 1.0 Hz; 1H, 3-H), 7.79 (t; 1H, 2-H), 8.05 (dd, J = 7.8, J = 1.0 Hz; 1H, 1-H), 13.35 (s; 1H, OH), 14.04 (s; 1H, OH); mass spectrum (180°), 385 (30%, $M^+ + 1$), 384 (79, M^+), 366 (93), 348 (76), 337 (85), 330 (53), 319 (42), 312 (47), 310 (100), 295 (78), 284 (68), 277 (49), 266 (68), 241 (53), 217 (63). (Found: C, 65.61; H, 5.12. Calc for $C_{21}H_{20}O_7$: C, 65.62; H, 5.21%).

Photobromination and solvolysis of **35**. 90 mg of **35** were treated as described for **33** to afford after preparative TLC separation 5 mg (7%) of rac-10-deoxy-α_1-rhodomycinone **49** and 8 mg (12%) of 1,6,11-trihydroxy-8-methyl-5,12-naphthacenequinone (**45**).

Data for **49**: m.p. 239°; IR 3420, 3350, 1604, 1594 cm^{-1}; UV 210 (4.19), 234 (4.55), 254 (4.45), 292 (3.91), 472 (4.08), 480 (4.12), 492 (4.18), 510 (4.04), 526 (4.07), 560 nm (2.90); ^{1}H-NMR (300 MHz) δ 1.50 (s; 3H, CH_3), 1.93 (dd, J = 15.0, J = 5.0 Hz; 1H, 8a-H), 2.39 (dt, J = 15.0, J = 2.0 Hz; 1H, 8e-H), 2.69 (d, J = 19.0 Hz; 1H, 10a-H), 3.17 (s; 1H, 9-OH), 3.28 (dd, J = 19.0, J = 2.0 Hz; 1H, 10e-H), 3.63 (d, J = 5.0 Hz; 1H, 7-OH), 5.35 (td, J = 5.0, J = 2.0 Hz; 1H, 7e-H), 7.32 (dd, J = 8.2, J = 1.0, Hz; 1H, 3-H), 7.71 (t; 1H, 2-H), 7.90 (dd, J = 7.6, J = 1.0 Hz; 1H, 1-H), 12.19, 12.99, 13.50 (3s, 3-OH); mass spectrum (160°), 356 (41%, M^+), 338 (96), 320 (100), 296 (84), 280 (88), 270 (53), 203 (40). (Found: C, 63.76; H, 4.59. Calc for $C_{19}H_{16}O_7$: C, 64.04; H, 4.49%).

Data for **45**: m.p. 253–254°; IR 1600, 1582 cm^{-1}; UV 211 (4.29), 227 (sh), 267 (4.53), 470 (sh), 495 (4.06), 528 (4.13), 562 (4.13), 590 nm (4.04); ^{1}H-NMR (300 MHz), 2.55 (s; 3H, CH_3), 7.28 (dd, J = 8.0, J = 0.9 Hz; 1H, 2-H), 7.62 (dd, J = 8.1, J = 1.3 Hz; 1H, 9-H), 7.69 (t, 1H, 3-H), 7.93 (dd, J = 8.0, J = 0.9 Hz; 1H, 4-H), 8.28 (d, J = 1.3 Hz; 1H, 7-H), 8.37 (d, J = 8.1 Hz; 1H, 10-H), 12.40, 14.27, 15.35 (3s; 3-OH); mass spectrum (160°), 320 (100%, M^+), 303 (20), 291 (15), 263 (18), 249 (15), 235 (15), 218 (15), 200 (15).

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