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Synthetic Anthracyclinones, XXXI[1]

Total Synthesis of Racemic ε-Rhodomycinones *via* Keto-Ester Cyclization

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The keto esters **15**–**17b** were prepared by regioselective alkylation of the anthraquinone acetals **12**–**14** followed by cleavage of the acetals and methyl ethers and esterification. The tetracyclic *trans*-β-hydroxy esters **25**–**27b** were formed predominantly upon treatment of **15**–**17b** with Triton B in pyridine, whereas lithium amides in THF gave only the *cis*-hydroxy esters **28** and **29a**. Stereoselective hydroxylation of **25**–**27b** afforded the rhodomycinones **38**–**40a** and **6** of natural configuration (*cis*-2,4-diols), while that of **28**–**30b** gave the not naturally occurring *trans*-2,4-diols **41**–**43b**.

Synthetische Anthracyclinone, XXXI[1]. – Totalsynthese racemischer ε-Rhodomycinone durch Ketoester-Cyclisierung

Die Ketoester **15**–**17b** wurden durch regioselektive Alkylierung der Chinonacetale **12**–**14** gefolgt von Spaltung der Acetale und Methylether sowie Veresterung hergestellt. Vorwiegend die *trans*-β-Hydroxyester **25**–**27b** wurden durch Behandlung von **15**–**17b** mit Triton B in Pyridin erhalten, während Lithiumamide in THF nur die *cis*-Hydroxyester **28** und **29a** ergaben. Die stereoselektive Hydroxylierung von **25**–**27b** lieferte die Rhodomycinone **38**–**40a** und **6** mit natürlicher Konfiguration (*cis*-2,4-Diole) und die von **28**–**30b** die nicht natürlich vorkommenden *trans*-2,4-Diole **41**–**43b**.

The biosynthesis of anthracyclinones from nine acetate and one propionate units *via* intermediate polyketides is well documented by incorporation of labeled precusors[2]. The nature of the side chain depends on the starting molecule (acetate, propionate, butyrate, or acetoacetate) and accordingly anthracyclinones with methyl[3], ethyl[3], propyl[4], and acetonyl[3c] side chains have been isolated. A general view is depicted in Scheme 1: the polyketide **1** is cyclized to give a hypothetical intermediate **2** which is further transformed into glycosides **3b** of aklavinone (**3a**). These glycosides are established precursors of the clinically important anticancer drug daunorubicin (**4**). – Recently it has been found that white mutants of daunorubicin-producing strains of *Streptomyces griseus* convert aklanoic acid (**5**) into ε-rhodomycinone[5] (**6**) (Scheme 1).

Six years before anthraquinones such as **5** were shown to be intermediates in anthracyclinone biosynthesis, we realized the general plan outlined in Scheme 2 for the synthesis of the model compound 4-deoxy-α-rhodomycinone Ist 299[6] and later of ε-rhodomycinone[7] (**6**) using *ortho*-dialkylated anthraquinone precursors of type **II**.

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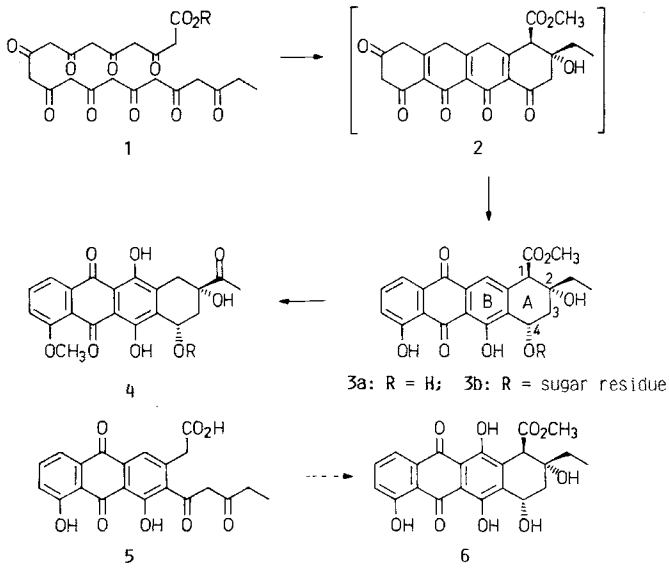
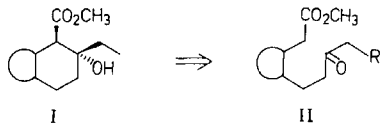
Scheme 1



Scheme 2



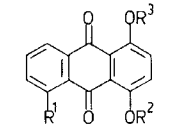
We now report the synthetic work related to ε-rhodomycinone in full detail with special emphasis on the stereochemical outcome of the cyclization and hydroxylation steps.

In previous papers[6,7] we have outlined our general strategy in converting the readily available hydroxylated anthraquinones into anthracyclinones. The advantage of this method is that three of the four linearly condensed rings are already assembled in these starting materials. However, the application of this method implies solution of three major problems: (i) Monoalkylations of symmetrically substituted anthraquinones [*e. g.*, quinizarine (**7a**)]; (ii) regioselective monoalkylation of not symmetrically substituted anthraquinones (*e. g.*, 5-hydroxyquinizarine); (iii) regioselektive second alkylation at the sterically hindered position *ortho* to the first side chain.

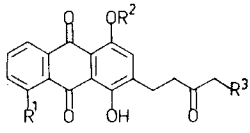
A straightforward solution of the first two problems can be achieved by selective removal of protecting groups leading to monophenols which can be alkylated in *ortho* position to the free phenol function by the *Marschalk* reaction[8]. Thus, the monomethyl ether **7b** of quinizarine (**7a**) is obtained by the method of *Laatsch*[9], and 1,4,5-trimethoxy-9,10-anthraquinone (**8a**) can be selectively cleaved to give **8b** or **8c** by successive treatment with diethyl ether – boron trifluoride[10] or boron

trichloride[11], respectively. The synthesis of the corresponding (3-oxoalkyl)anthraquinones **9a–11b** *via* hydroxymethylation and chain elongation with different 3-oxo esters has been reported earlier[12,13].

The third problem of regioselective second alkylation was greatly facilitated by the selective cleavage of the C-1 methyl ether in **10a** and **11a** affording **10b** and **11b**[13], respectively. The protection of the phenolic hydroxy group at C-5 is a prerequisite for the second alkylation step, which was next investigated.



	R^1	R^2	R^3
7a	H	H	H
7b	H	H	CH_3
8a	OCH_3	CH_3	CH_3
8b	OCH_3	H	CH_3
8c	OCH_3	H	H



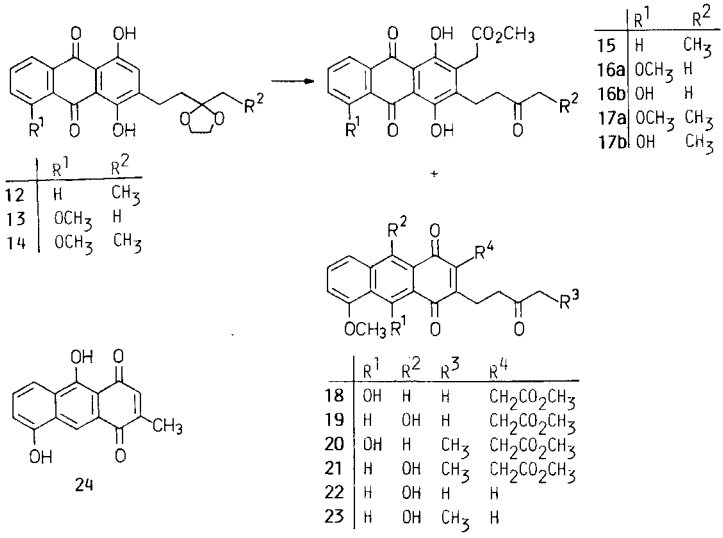
	R^1	R^2	R^3
9a	H	CH_3	CH_3
9b	H	H	CH_3
10a	OCH_3	CH_3	H
10b	OCH_3	H	H
11a	OCH_3	CH_3	CH_3
11b	OCH_3	H	CH_3

In the course of our initial studies[6,7] we had observed the difficulties in the second alkylation at the sterically congested center at C-3 in compounds like **11b**.

First the carbonyl group of the side chain had to be protected. This was best achieved by acetalization with ethylene glycol to afford the corresponding acetals **12–14** in essentially quantitative yield. The reaction of glyoxylic acid was next studied employing the method of *Marschalk*[8] (aqueous alkali) as well as that of *Lewis*[14] using piperidine acetate as catalyst in boiling 2-propanol.

Unfortunately, the reaction conditions of *Lewis*[14] led to decarboxylation of the acetic acid residue when glyoxylic acid was treated with **12**. We have therefore further improved the second alkylation reaction by using a large excess of glyoxylic acid and by the continuous addition of the reducing agent sodium dithionite at high reaction temperatures (80 °C) in order to constantly maintain a high concentration of the nucleophilic hydroquinone. Thus, the keto esters **15, 16a**, and **17a** were prepared in over 60% yield by deacetalization and esterification of the primary Marschalk products from **12–14**. However, under the somewhat vigorous reaction conditions the new, interesting reduction products **18–23** could be isolated in about 10% yield. Prolonged reaction times and larger excess of reducing agent favored the formation of **19** and **21** (about 30%), whereas the reaction mixture always contained less than 1% of the isomeric phenolic 1,4-anthraquinones **18** and **20**.

It was not previously known that dithionite reduction and reoxidation converted quinizarine derivatives into 1,4-anthraquinones. However, very similar 1,4-anthraquinone structures have simultaneously been isolated by dithionite and also by enzymatic reduction of daunorubicine (**4**) by *Fisher* et al.[15]. These observations give new insight into the metabolism of this important anticancer drug.



	R^1	R^2
12	H	CH_3
13	OCH_3	H
14	OCH_3	CH_3

	R^1	R^2
15	H	CH_3
16a	OCH_3	H
16b	OH	H
17a	OCH_3	CH_3
17b	OH	CH_3

	R^1	R^2	R^3	R^4
18	OH	H	H	$CH_2CO_2CH_3$
19	H	OH	H	$CH_2CO_2CH_3$
20	OH	H	CH_3	$CH_2CO_2CH_3$
21	H	OH	CH_3	$CH_2CO_2CH_3$
22	H	OH	H	H
23	H	OH	CH_3	H

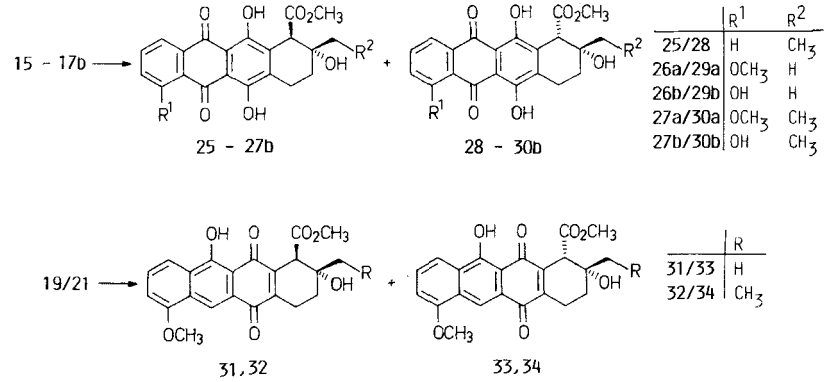
24

The structures of the four regioisomeric dialkylated 1,4-anthraquinones **18**–**21** and of the two monoalkylated products **22** and **23** could be determined by comparison of the ^{1}H NMR spectra with that of the 1,4-anthraquinone **24** prepared following the unambiguous pathway of *Behnke*[16,17]. The chemical shifts of the phenolic protons at C-10 and of 9-H of **24** at δ = 13.75 and 8.52 are in excellent agreement with the corresponding signals of the analogues **19** and **21**–**23** (δ = 13.71–13.75 and 8.52–8.57, respectively). In contrast, the signals of the phenolic proton in the isomers **18** and **20** appear at considerably lower field (δ = 15.11) due to the deshielding effect of the two neighboring oxygens.

The 1,4-anthraquinones are readily detected by a deep red violet color on thin-layer chromatography (TLC) plates. The major products **19** and **21** are valuable models for the investigation of the cyclization step and serve as precursors for novel, not naturally occurring anthraquinones (see below).

With sufficient amounts of the keto esters **15**–**17b** and also of the corresponding 1,4-anthraquinones **19** and **21** at hand, the cyclization was next studied. Various bases and solvents such as Triton B in dichloromethane/methanol[18] or in methanol[19], potassium carbonate in methanol[20], 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) in tetrahydrofuran (THF)[21], and magnesium methoxide in methanol[22] have been used in the aklavinone synthesis. The best system for the cyclization of the *rhodomycinone* precursors **15**–**17b**, having an additional phenolic hydroxy group at C-1 proved to be Triton B in pyridine. This system has already been used in previous investigations[6,7]. However, in order to avoid direct additions of nucleophiles[6] the methanol of the Triton B solution was carefully evaporated. The reaction was conducted at −10 °C for 15 minutes to improve the *trans/cis* ratio of the cyclization products. In order to obtain more information concerning the factors that determine the stereochemical outcome, the same cyclization reaction was also run in dimethyl formamide (DMF) at room temperature, using

sodium hydride as base, and at low temperature (−78 °C) in THF with lithium amides. Separate epimerization experiments were performed to see to what degree equilibration might take place during the reaction. Thus, the pure *cis*- and *trans*-β-hydroxy esters **25** and **28** were treated under the same reaction conditions used for the cyclization procedures and the reactions were monitored by TLC. As expected, no epimerization could be observed at −78 °C, very little at −10 °C, and only about 10% at room temperature, with reaction times of 20 minutes.



Mechanisms for the epimerization process have been proposed by *Essery* and *Doyle*[23] as well as *Kishi* et al.[21]. An ester enolate, and not the open-chained retroaldol product was postulated for aklavinone[21], while the participation of the neighboring phenolic hydroxy group was proposed for ε-rhodomycinone[23]. Our preliminary equilibration experiments suggest that at lower temperatures and relatively short reaction times the cyclization proceeds under essentially kinetically controlled conditions.

The diastereomers obtained from the cyclizations can be separated chromatographically and Table 1 shows the *trans/cis* ratios and the isolated yields of various cyclization experiments using the three conditions already mentioned to give the tetracycles **25**−**34**. A striking result is the formation of the pure *cis*-hydroxy esters **28** and **29a** by treatment of **15** and **16a** with the lithium salt of (*S*)-(+)-2-(methoxymethyl)pyrrolidine in THF at −78 °C. The low yield is due to slow reaction with recovery of the starting material. The *cis* product is also predominant in the sodium hydride/DMF cyclization, in which the *trans/cis* ratio ranges from 1.2 to 0.3. Due to equilibration to some extent the initial excess of the *cis* product may be even higher under these conditions. The rhodomycinones corresponding to the natural *trans* configuration are mainly obtained from the Triton B catalyzed reaction (*trans/cis* ratio ranging from 8.4 to 15.6). Exceptions are the 7-deoxy compounds and the 1,4-anthraquinones, in which the excess of the *trans*-hydroxy esters is decreased. Thus, stereochemical control of the cyclization is possible leading entirely to the *cis*-hydroxy esters or to the *trans* products in the order of 10 : 1. This result is in contrast to the cyclization of the corresponding aklavinone precursors, which leads to only a 2 : 1 ratio in pyridine or to an approximate 4 : 1 ratio in protic solvents[18] or with magnesium methoxide[22].

Table 1. *trans/cis* ratio and yields in the cyclization reaction of the keto esters **15**–**17b** and **19**/**21**

Keto ester	Triton B/pyridine, −10 °C			NaH/DMF, 20 °C			Li amide[a]/ THF, −78 °C
	trans (%)	*cis* (%)	ratio	*trans* (%)	*cis* (%)	ratio	*cis* (%)
15	62	19	3.3	12	37	0.3	21
16a	80	7	11.4	19	37	0.5	28
16b	76	7	10.8	16	13	1.2	
17a	78	5	15.6	15	26	0.6	
17b	76	9	8.4	9	28	0.3	
19	70	23	3.0				
21	77	9	8.5				

[a] (*S*)-(+)-1-Lithio-2-(methoxymethyl)pyrrolidine.

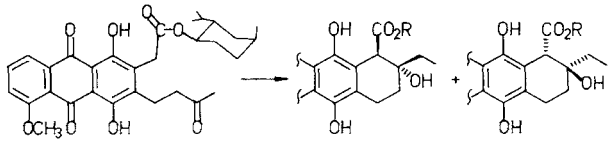
It is reasonable to assume that the conditions favoring or disfavoring chelation of the intermediate ester enolates play an important role in the stereochemical outcome of the keto-ester cyclization as discussed by *Boeckman*[18].

The presence of the neighboring phenolic hydroxy group is the only difference between ε-rhodomycinone (**6**) and aklavinone (**3a**) and chelation control is favored in the reactions with sodium hydride or lithium amides leading predominantly to *cis*-hydroxy esters in nonprotic solvents (for model considerations see ref.[18]). On the other hand, *trans* products are formed mainly using nonchelating counter ions such as the benzyltrimethylammonium ion of Triton B.

Some of the spectroscopic properties of the 9-deoxyanthracyclinones are noteworthy and may be used to distinguish between *cis* and *trans* compounds. In contrast to the anthracyclinones of type A (no ester group) no retro Diels-Alder fragments can be detected in the mass spectra of **25**–**34**[24]. In the ^{1}H NMR spectra however, the 1,3 coupling of 1*e*-H and 3*e*-H (*W* coupling) is a common feature in both series A and B (ester group at C-1) confirming the pseudo-axial position of the ester group in the *trans*-hydroxy esters **25**–**27b**. The signals of 2-OH in the *cis*-hydroxy esters **28**–**30b** appear as sharp singlets at $\delta = 2.45-2.46$ and are shifted downfield by almost 1 ppm compared with the signals of the corresponding *trans* compounds **25**–**27b**. This characteristic effect is due to deshielding by an intramolecular hydrogen bond to the ester carbonyl which is only possible in the *cis* compounds.

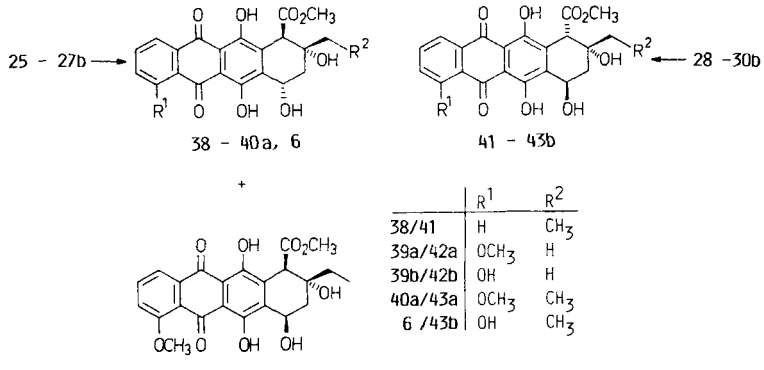
Microorganisms are capable of enantioselective cyclization of prochiral keto esters like aklanoic acid (**5**). It would be interesting to see if chiral bases are also capable of asymmetric induction. In preliminary experiments with lithium salts of (*S*)-(+)-2-(methoxymethyl)pyrrolidine as catalysts (see Table 1) we were not able to determine the exact enantiomeric excess due to uncertainties in the optical rotation measurements of anthracyclins[25]. In order to establish a much more reliable NMR method we prepared the (−)-menthyl ester **35** by transesterification from **16a**. Cyclization of this chiral ester with Triton B produced almost quantitatively the two diastereomeric *trans* esters **36** and **37** which could be separated

chromatographically. The ^{1}H NMR spectra of **36** and **37** differed not only in the signals of the phenolic protons but also in the chemical shifts of the three methyl groups of the menthol residue (see Experimental). The enantiomeric excess can thus be determined by a single NMR measurement without addition of any chiral shift reagents. We are now engaged in systematic studies on the asymmetric induction of various bases.



35 36: R = (-)-menthyl 37

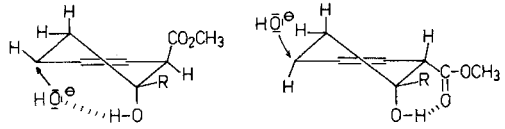
The 4-deoxy compound ξ-rhodomycinone (**27b**), obtained in racemic form, is a naturally occurring anthracyclinone. However, most anthracyclinones have an additional hydroxy group at C-4, where the biologically important sugar moiety of the molecule is attached. We have previously observed that this hydroxy group can be introduced directly by conducting the cyclization step in the presence of oxygen and a trace of water[6]. The reaction required prolonged reaction times, and partial decomposition of the reaction products led to decreased yields. The usual bromination/solvolysis procedure first introduced in the daunomycinone series by *Wong* et al.[26] was therefore also applied to the *trans*-hydroxy esters **25**–**27b** as well as to the *cis* compounds **28**–**30b**. The unstable products of the homolytic bromination (Br_2, light) were immediately treated with a solution of diluted sodium hydrogen carbonate to afford the C-4 alkohols **38**–**43b** in 72–83% reproducible yields. The stereoselectivity in both the *trans*-1,2-hydroxy esters **25**–**27b** and the *cis* compounds **28**–**30b** is remarkable: the *cis*-2,4-diols are formed almost exclusively in the first case and the *trans*-2,4-diols in the latter. In most reactions only trace amounts of the corresponding epimers could be detected by TLC. In one case the *trans*-2,4-diol **44** derived from the *trans*-hydroxy ester **27a** could be isolated in 4% yield.



	R^1	R^2
38/41	H	CH_3
39a/42a	OCH_3	H
39b/42b	OH	H
40a/43a	OCH_3	CH_3
6 /43b	OH	CH_3

The reason for the high stereoselectivity can be seen either in the bromination or in the subsequent displacement reaction. ^{1}H NMR studies confirm the predominant conformations of the *trans* and *cis* esters as shown in **III** and **IV** (R = CH_3, C_2H_5), the major difference being the orientation of the ester group. We believe that the selectivity can be better explained assuming an elimination-addition pathway *via* intermediate *ortho*-quinodimethanes as discussed for aklavinone[27] rather than by direction of the relatively remote ester at C-1. The existance of similar quinone methides has been proved spectroscopically[15]. Hydrogen bonding of the entering hydroxy group with the axial hydroxy group at C-2 favors the formation of *cis* diols whereas the chelated hydroxy group in the *cis*-hydroxy esters hinders the attack from the same side by 1,3-steric interaction.

Scheme 3



III IV

The configuration of the *cis*-2-4- and *trans*-2,4-diols can be determined by the ^{1}H NMR spectra. The most characteristic signal is derived from the proton at C-4: coupling constants of 6.0–6.5 Hz are typical for the *cis*-2,4-diols **38**–**40a** and **6** (equatorial 4-H) and 10–12 Hz for the *trans*-2,4-diols **41**–**43b** (axial 4-H). The proton of 4-OH always couples with the neighboring 4-H whereas the tertiary 2-OH appears as a sharp singlet. The chemical shift of the signal for 2-OH in **41**–**43b** (δ = 2.56–2.69) differs little from that of the precursors **28**–**30b** (δ = 2.45–2.46), whereas the signals in the corresponding *cis* diols **38**–**40a** and **6** (δ = 3.87–4.16) are shifted considerably downfield in comparison to the *trans*-hydroxy esters **24**–**26b** (δ = 1.54–1.65). This clearly reflects the intramolecular hydrogen bonding of 2-OH with the *cis* oriented 4-OH.

The spectroscopic data (IR, UV, NMR, and MS) of the racemic products **6**, **27b**, and **39b** are in agreement with those of the corresponding natural products ε-rhodomycinone[3,28], ξ-rhodomycinone[3,28], and δ-rhodomycinone Ist 299[4].

W. P. thanks the *Konrad-Adenauer Foundation* for a scholarship.

Experimental

For instrumentation and general remarks see ref.[13]. Elemental analyses were perfomed at the Institut für Pharmazeutische Chemie, D-3300 Braunschweig. – The hydroxylated anthraquinone derivatives crystallize as red and often microcrystalline needels.

2-[2-(2-Ethyl-1,3-dioxolan-2-yl)ethyl]-1,4-dihydroxy-9,10-anthraquinone (**12**): A solution of 2.20 g (6.81 mmol) of **9b**[29] in 200 ml of hot benzene was treated with 6.2 g (0.1 mol) of ethylene glycol, 5 ml of methyl orthoformate, and 50 ml of *p*-toluenesulfonic acid. The mixture was heated and vigorously stirred at 55 °C under reduced pressure in such a way,

that the solvent just did not boil (continous removal of methyl formate). Every hour an additional amount of 50 mg of *p*-toluenesulfonic acid was added. After 3–4 h the mixture was shaken twice with a solution of sodium carbonate, dried with Na_2SO_4, filtered, evaporated at reduced pressure, and the residue crystallized from ether/petroleum ether to afford 2.35 g (95%) of red crystalls; m. p. 119°C. – IR: 2900–2885 (CH), 1619 (quinone), 1586 cm^{-1}. – UV: λ_{max} (lg ε) = 209 (4.16), 235 (4.31), 249 (4.59), 254 (4.54), 285 (4.00), 311 (3.56), 461 (3.96), 483 (4.01), 498 (3.89), 514 nm (3.82). – ^1H NMR (300 MHz): δ = 0.97 (t, J_{vic} = 7.5 Hz; 3H, CH_3), 1.73 (q, J_{vic} = 7.5 Hz; 2H, CH_2), 1.99 und 2.82 (2 × quint; 2 × 2H, 2 × CH_2), 4.01 (s; 4H, OCH_2CH_2O), 7.17 (s; 1H, 3-H), 7.82 (m; 2H, 6- and 7-H), 8.33 (m; 2H, 5- and 8-H), 12.97 and 14.30 (2 × s; 2 × 1H, 2 × OH). – MS (140°C): *m/z* = 368 (71%, M^+), 350 (20, $M^+ - H_2O$), 339 (92, $M^+ - C_2H_5$), 324 (15), 306 (76), 295 (82), 277 (70), 267 (75), 254 (85), 240 (90), 225 (61), 219 (19), 197 (32).

$C_{21}H_{20}O_6$ (368.4) Calc. C 68.47 H 5.47 Found C 68.69 H 5.40

1,4-Dihydroxy-8-methoxy-2-[2-(methyl-1,3-dioxolan-2-yl)ethyl]-9,10-anthraquinone (**13**): 5.11 g (15.0 mmol) of **10b**[13] was treated as described for **12** to afford 5.56 g (97%) of **13**; m. p. 162°C. – IR: 1618 (quinone), 1575 cm^{-1}. – UV: λ_{max} (lg ε) = 231 (4.88), 249 (4.66), 282 (4.25), 390 sh, 477 (4.35), 493 (4.36), 521 (4.11), 560 nm sh. – ^1H NMR (400 MHz): δ = 1.43 (s; 3H, CH_3), 2.03 (quint; 2H, CH_2), 2.86 (quint; 2H, CH_2), 3.99 (s; 4H, OCH_2CH_2O), 4.09 (s; 3H, OCH_3), 7.14 (s; 1H, 3-H), 7.38 (dd, $J_{6,7}$ = 8.5 Hz, $J_{6,8}$ = 0.9 Hz; 1H, 7-H), 7.76 (t; 1H, 6-H), 8.02 (dd, $J_{5,7}$ = 7.5 Hz, $J_{5,6}$ = 0.9 Hz; 1H, 5-H), 12.97 and 13.75 (2 × s; 2 × 1H, 2 × OH). – MS (220°C): *m/z* = 384 (70%, M^+), 340 (38), 322 (100), 297 (65), 255 (34).

$C_{21}H_{20}O_7$ (384.4) Calc. C 65.62 H 5.24 Found C 65.36 H 5.10

2-[2-(2-Ethyl-1,3-dioxolan-2-yl)]-1,4-dihydroxy-8-methoxy-9,10-anthraquinone (**14**): 5.00 g (14.1 mmol) of **11b**[13] was treated as described for **12** to afford 5.08 g (91%) of **14**; m. p. 167°C. – IR and UV see **13**. – ^1H NMR (400 MHz): δ = 0.98 (t, J_{vic} = 7.0 Hz; 3H, CH_3), 1.76 (q, J_{vic} = 7.0 Hz; 2H, CH_2), 2.00 and 2.84 (2 × quint; 2 × 2H, 2 × CH_2), 4.01 (mc; 4H, OCH_2CH_2O), 4.09 (s; 8-OCH_3), 7.15 (s; 1H, 3-H), 7.38 (dd, $J_{7,6}$ = 8.4 Hz, $J_{7,5}$ = 1.0 Hz; 1H, 7-H), 7.89 (t; 1H, 6-H), 8.04 (dd, $J_{5,6}$ = 7.5 Hz, $J_{5,7}$ = 1.0 Hz; 1H, 5-H), 12.97 and 13.73 (2 × s; 2 × 1H, 2 × OH). – MS (160°C): *m/z* = 398 (79%, M^+), 380 (13, $M^+ - H_2O$), 369 (61, $M^+ - C_2H_5$), 353 (19), 336 (100), 325 (80), 309 (45), 279 (74), 283 (78), 268 (24), 255 (43), 240 (26), 225 (25), 212 (21).

$C_{22}H_{22}O_7$ (398.4) Calc. C 66.32 H 5.57 Found C 66.09 H 5.68

Methyl [9,10-dihydro-1,4-dihydroxy-9,10-dioxo-3-(3-oxopentyl)-2-anthracenyl]acetate (**15**): A solution of 1.01 g (2.76 mmol) of **12** in 300 ml of methanol and 40 ml of THF was treated at 90°C under N_2 with 80 ml of 1 N NaOH and 6.49 g (70 mmol) of glyoxylic acid hydrate. A 0.5 M solution of sodium dithionite was added in portions, whereby the color of the solution changes from deep red violett to brown. The mixture was boiled for 2–3 h (TLC control) with continous addition of the dithionite solution (altogether 30 ml; 2.58 g of $Na_2S_2O_4$) to maintain the brown color. Air was bubbled through the cold solution (15°C) for reoxidation (about 0.5–1 h, TLC control for disappearance of yellow compounds), and the mixture was acidified with hydrochloric acid. The products were isolated by repeated extraction with CH_2Cl_2, and the organic phase was washed three times with 150 ml of a diluted solution of sodium hydrogen carbonate to extract acidic products. The aqueous phase was acidified with hydrochloric acid and extracted three times with each 100 ml of CH_2Cl_2. The solution was evaporated, and the residue was suspended in 100 ml of CH_2Cl_2 and treated with an etheral solution of diazomethane. The solution was evaporated, the residue dissolved in a mixture of 50 ml of acetone and 1 ml of conc. HCl to cleave the acetal.

The solution was again evaporated to dryness and the residue crystallized from CH_2Cl_2/ether to afford 540 mg of **15**. Chromatography of the mother liquor gave another 130 mg of **15** (61%); m. p. 188°C. – IR: 2976–2835 (CH), 1730 (C=O, ester), 1709 (C=O), 1625 (quinone), 1588 cm^{-1} (aromate). – UV: λ_{max} (lg ε) = 208 (4.19), 250 (4.63), 256 (4.61), 284 (4.15), 315 sh, 475 (3.97), 483 (3.99), 517 (3.78), 560 nm sh. – ^1H NMR (300 MHz): δ = 1.07 (t, J_{vic} = 7.4 Hz; 3H, $COCH_2CH_3$), 2.46 (q, J_{vic} = 7.4 Hz; 2H, $COCH_2CH_3$), 2.80 and 3.07 (2 × t; 2 × 2H, 2 CH_2), 3.74 (s; 3H, $COOCH_3$), 3.97 (s; 2H, $CH_2CO_2CH_3$), 7.84 (m; 2H, 6- and 7-H), 8.35 (m; 2H, 5- and 8-H), 13.52 and 13.54 (2 × s; 2 × 1H, 2 × OH). – MS (120°C): *m/z* = 396 (100%, M^+), 378 (42, $M^+ - H_2O$), 365 (44, $M^+ - OCH_3$), 346 (22, 378 – CH_3OH), 340 (76), 318 (62), 307 (91), 293 (59), 279 (90), 266 (51), 251 (24).

$C_{22}H_{20}O_7$ (396.4) Calc. C 66.66 H 5.09 Found C 67.14 H 5.10

Methyl [9,10-dihydro-1,4-dihydroxy-5-methoxy-9,10-dioxo-3-(3-oxobutyl)-2-anthracenyl]-acetate (**16a**): 1.00 g (2.60 mmol) of **13** was treated as described for **15** to afford 664 mg of **16a**; m. p. 203°C. – IR: 2980–2843 (CH), 1740 (C=O, ester), 1705 (C=O), 1614 (quinone), 1573 cm^{-1} (aromate). – UV: λ_{max} (lg ε) = 220 (4.33), 234 (4.54), 246 (4.47), 288 (3.96), 425 sh, 455 sh, 479 (4.04), 497 (4.04), 531 nm (3.80). – ^1H NMR (400 MHz): δ = 2.17 (s; 3H, CH_3), 2.81 (t, *J* = 7.9 Hz; 2H, CH_2), 3.04 (t, *J* = 7.5 Hz; 2H, CH_2), 3.74 (s; 3H, CO_2CH_3), 3.94 (s; $CH_2CO_2CH_3$), 4.08 (s; 3H, OCH_3), 7.38 (dd, $J_{6,7}$ = 8.2 Hz, $J_{6,8}$ = 0.9 Hz; 1H, 6-H), 7.76 (t; 1H, 7-H), 8.03 (dd, $J_{7,8}$ = 7.5 Hz, $J_{6,8}$ = 0.9 Hz; 1H, 8-H), 13.50 and 13.86 (2 × s; 2 × 1H, 2 × OH). – MS (180°C): *m/z* = 412 (90%, M^+), 394 (34, $M^+ - H_2O$), 380 (59, $M^+ - CH_3OH$), 370 (45, $M^+ - CH_2CO$), 362 (42), 352 (55), 337 (85), 322 (56), 309 (100), 297 (85), 282 (56), 267 (38).

$C_{22}H_{20}O_8$ (412.4) Calc. C 64.08 H 4.89 Found C 63.87 H 4.59

Methyl [1,4-dihydro-10-hydroxy-5-methoxy-1,4-dioxo-3-(3-oxobutyl)-2-anthracenyl]acetate (**18**) *and methyl [1,4-dihydro-9-hydroxy-5-methoxy-1,4-dioxo-3-(3-oxobutyl)-2-anthracenyl]acetate* (**19**): The reaction of 1.00 g (2.60 mmol) of **13** was conducted as described for **15** but heated for 5 h instead of 2 h to afford after thin-layer chromatography on silica gel with decreasing polarity 310 mg (29%) of **16a**, 8 mg (0.7%) of **18** and 340 mg (33%) of **19**.

18: M. p. 178°C. – IR: 1738 (C=O, ester), 1707 (C=O), 1653 (quinone), 1629 (quinone), 1593 and 1567 cm^{-1} (aromate). – UV: λ_{max} (lg ε) = 214 (3.88), 245 (4.52), 280 (3.80), 326 sh 510 nm (3.76). – ^1H NMR (300 MHz): δ = 2.18 (s; 3H, CH_3), 2.78 and 2.92 (2 × m; 2 × 2H, 2 CH_2), 3.72 (s; 3H, CO_2CH_3), 3.80 (s; 2H, $CH_2CO_2CH_3$), 4.07 (s; 3H, 5-OCH_3), 7.08 (dd, $J_{6,7}$ = 8.0 Hz, $J_{6,8}$ = 1.0 Hz; 1H, 6-H), 7.50 (dd, $J_{8,9}$ = 7.6 Hz, $J_{8,6}$ = 1 Hz; 1H, 8-H), 7.63 (t; 1H, 7-H), 8.01 (s; 1H, 9-H), 15.11 (s; 1H, 10-OH). – MS (160°C): *m/z* = 396 (100%, M^+), 366 (46, $M^+ - CH_2O$), 396 (52), 323 (71), 308 (36), 293 (87), 279 (57). –

19: M. p. 142°C. – IR: 1723 (C=O, ester), 1708 (C=O), 1654 (quinone), 1625 (quinone), 1597, 1573 and 1500 cm^{-1}. – UV: λ_{max} (lg ε) = 207 (4.15), 244 (4.70), 269 (4.05), 325 sh, 492 (3.97), 603 nm sh. – ^1H NMR (400 MHz): δ = 2.17 (s; 3H, CH_3), 2.76 (t; *J* = 7.5 Hz; 2H, CH_2), 2.89 (t; *J* = 7.5 Hz; 2H, CH_2), 3.75 (s; 3H, CO_2CH_3), 3.84 (s; 2H, $CH_2CO_2CH_3$), 4.03 (s; 3H, 5-OCH_3), 7.07 (dd, $J_{6,7}$ = 7.8 Hz, $J_{6,8}$ = 1.0 Hz; 1H, 6-H), 7.60 (t; 1H, 7-H), 8.00 (dd, $J_{7,8}$ = 8.10 Hz, $J_{6,8}$ = 1.0 Hz; 1H, 8-H), 8.54 (d, $J_{8,10}$ = 1.0 Hz; 1H, 10-H), 13.74 (s; 1H, 9-OH). – MS (190°C): *m/z* = 396 (100%, M^+), 380 (30), 378 (27, $M^+ - H_2O$), 364 (86, $M^+ - CH_3OH$), 354 (32, M – CH_2CO), 348 (25).

$C_{22}H_{20}O_7$ (396.4) Calc. C 66.66 H 5.09
19: Found C 66.85 H 5.15
18: Found C 66.79 H 5.02

10-Hydroxy-8-methoxy-2-(3-oxobutyl)-1,4-anthraquinone (**22**): The organic phase from the extraction with sodium hydrogen carbonate (see **15**), which contains the nonacidic products, was separated by thin-layer chromatography to afford 10 mg (1%) of **22**; m. p. 164°C. – IR and UV see **23**. – ^{1}H NMR (300 MHz): δ = 2.17 (s; 3H, CH_3), 2.79–2.89 (m; 4H, 2 × CH_2), 4.03 (s; 3H, 8-OCH_3), 6.85 (s; 1H, 3-H), 7.05 (dd; 1H, 7-H), 7.60 (t; 1H, 6-H), 7.99 (dd; 1H, 5-H), 8.54 (s; 1H, 9-H), 13.73 (s; 1H, 10-OH). – MS (200°C): *m/z* = 324 (58%, M^+), 295 (10), 282 (100), 281 (60), 267 (17), 253 (17), 239 (8).

$C_{19}H_{16}O_5$ (324.3) Calc. C 70.36 H 4.97 Found C 69.89 H 4.99

Methyl [9,10-dihydro-1,4-dihydroxy-5-methoxy-9,10-dioxo-3-(3-oxopentyl)-2-anthracenyl]-acetate (**17a**), *methyl [1,4-dihydro-10-hydroxy-5-methoxy-1,4-dioxo-3-(3-oxopentyl)-2-anthracenyl]acetate* (**20**), *methyl [1,4-dihydro-9-hydroxy-5-methoxy-1,4-dioxo-3-(3-oxopentyl)-2-anthracenyl]acetate* (**21**), *and 10-Hydroxy-8-methoxy-2-(3-oxopentyl)-1,4-anthraquinone* (**23**): 1.10 g (2.76 mmol) of **14** was treated as described for **15** to afford after thin-layer chromatography on silica gel 563 mg of **17a** (48%), 32 mg (2.8%) of **20**; 158 mg (14%) of **21**, and 6 mg (0.6%) of **23**.

17a: M. p. 208°C (CH_2Cl_2/ether). – IR and UV see **16a**. – ^{1}H NMR (400 MHz): δ = 1.07 (t; J_{vic} = 7.0 Hz; 3H, $COCH_2CH_3$), 2.45 (q, J_{vic} = 7.0 Hz; 2H, $COCH_2CH_3$), 2.78 and 3.05 (2 × t; 2 × 2H, 2 CH_2), 3.73 (s; 3H, CO_2CH_3), 3.96 (s; 2H, $CH_2CO_2CH_3$), 4.10 (s; 3H, 5-OCH_3), 7.39 (dd, $J_{6,7}$ = 8.0 Hz, $J_{6,8}$ = 0.9 Hz; 1H, 6-H), 7.76 (t; 1H, 7-H), 8.05 (dd, $J_{8,7}$ = 7.6 Hz, $J_{8,6}$ = 0.9 Hz; 1H, 8-H), 13.52 and 13.88 (2 × s; 2 × 1H, 2 × OH). – MS (180°C): *m/z* = 426 (98%, M^+), 410 (22), 394 (29, $M^+ - CH_3OH$), 376 (19, $M^+ - H_2O - CH_3OH$), 366 (35), 348 (36), 377 (90), 322 (40), 309 (100), 294 (67), 281 (30), 267 (27), 253 (24), 237 (21), 217 (58), 203 (37).

$C_{23}H_{22}O_8$ (426.4) Calc. C 64.78 H 5.20 Found C 64.58 H 4.94

20: M. p. 170°C. – IR and UV see **18**. – ^{1}H NMR (400 MHz): δ = 1.09 (t, J_{vic} = 7.4 Hz; 3H, $COCH_2CH_3$), 2.46 (q, J_{vic} = 7.4 Hz; 2H, $COCH_2CH_3$), 2.76 and 2.93 (2 × t, J_{vic} = 7.5 Hz; 2H, 2 × CH_2), 3.73 (s; 3H, CO_2CH_3), 2.83 (s; 2H, $CH_2CO_2CH_3$), 4.07 (s; 3H, 5-OCH_3), 7.08 (dd, $J_{6,7}$ = 8.0 Hz, $J_{6,8}$ = 1.0 Hz; 1H, 6-H), 7.52 (dd, $J_{8,7}$ = 8.0 Hz, $J_{8,6}$ = 1.0 Hz; 1H, 8-H), 7.64 (t; 1H, 7-H), 8.05 (s; 1H, 9-H), 15.11 (s; 1H, 10-OH). – MS (160°C): *m/z* = 410 (100%, M^+), 392 (12, $M^+ - H_2O$), 379 (20, $M^+ - OCH_3$), 366 (12), 353 (34 $M^+ - C_2H_5CO$), 337 (27), 322 (55), 309 (29), 294 (67), 279 (41), 265 (25), 251 (23).

$C_{23}H_{22}O_7$ (410.4) Calc. C 67.31 H 5.40 Found C 67.09 H 5.46

21: M. p. 142–143°C. – IR and UV see **19**. – ^{1}H NMR (400 MHz): δ = 1.09 (t; J_{vic} = 7.3 Hz; 3H, $COCH_2CH_3$), 245 (q; J_{vic} = 7.3 Hz; 2H, $COCH_2CH_3$), 2.73 and 2.92 (2 × t; 2 × 2H, 2 × CH_2), 3.75 (s; 3H, CO_2CH_3), 3.85 (s; 2H, $CH_2CO_2CH_3$), 4.05 (s; 3H, 5-OCH_3), 7.08 (dd, $J_{6,7}$ = 7.6 Hz, $J_{6,8}$ = 2.1 Hz; 1H, 6-H), 7.60 (t; 1H, 7-H), 8.03 (dd, $J_{8,7}$ = 8.4 Hz, $J_{8,6}$ = 1.0 Hz; 1H, 8-H), 8.57 (s; 1H, 10-H), 13.75 (s; 1H, 9-OH). – MS (140°C): *m/z* = 410 (97%, M^+), 398 (41), 379 (28, $M^+ - OCH_3$), 367 (14), 350 (49, $M^+ - HCOCH_3$), 338 (90), 322 (72), 307 (52), 294 (86), 282 (100), 267 (50), 253 (69), 239 (35), 225 (24).

$C_{23}H_{22}O_7$ (410.4) Calc. C 67.31 H 5.40 Found C 67.46 H 5.37

23: M. p. 159°C. – IR and UV see **22**. – ^{1}H NMR (400 MHz): δ = 1.08 (t; J_{vic} = 7.3 Hz; 3H, CH_3), 2.47 (q; J_{vic} = 7.3 Hz; 2H, CH_2), 2.77 and 2.87 (2 × t; 2 × 2H, 2 × CH_2), 4.03 (s; 3H, 8-OCH_3), 6.85 (s; 1H, 3-H), 7.06 (dd, $J_{7,6}$ = 8.0 Hz, $J_{7,5}$ = 1.0 Hz; 1H, 7-H), 7.59 (t; 1H, 6-H), 8.00 (dd, $J_{5,6}$ = 8.4 Hz; $J_{5,7}$ = 1.0 Hz; 1H, 5-H), 8.54 (s; 1H, 9-H), 13.73 (s; 1H, 10-OH). – MS: *m/z* = 338 (5%, M^+), 309 (2), 291 (8), 282 (14), 256 (100), 224 (20), 192 (83).

Methyl [9,10-dihydro-1,4,5-trihydroxy-9,10-dioxo-3-(3-oxobutyl)-2-anthracenyl]acetate (**16b**): 1.00 g (2.60 mmol) of **13** was treated as described for **15**. However, prior to esterifi-

cation with diazomethane the CH_2Cl_2 solution of the acidic reaction products was treated with 2.64 g (20 mmol) of $AlCl_3$ for 8 h (TLC control) to cleave the methyl ether. The reaction mixture was hydrolyzed with 100 ml of cold water, and 10 ml of 10 N NaOH was added to destroy the aluminium complex. The solution was acidified with HCl, extracted three times with 100 ml of CH_2Cl_2, and the products were esterified with diazomethane and worked up as described for **15** to afford 579 mg (56%) of red crystalls; m. p. 213°C. – IR and UV see **17b**. – ^{1}H NMR (90 MHz): δ = 2.16 (s; 3H, CH_3), 2.76–2.82 (m; 4H, CH_2), 3.70 (s; 3H, CO_2CH_3), 3.94 (s; 2H, $CH_2CO_2CH_3$), 7.27 (dd; $J_{6,7}$ = 8.0 Hz, $J_{6,8}$ = 1.0 Hz; 1H, 6-H), 7.66 (t; 1H, 7-H), 7.85 (dd, $J_{7,8}$ = 8.0 Hz, $J_{6,8}$ = 1.0 Hz; 1H, 8-H), 12.16, 12.81, and 13.62 (3 × s; 3 × 1H, 3 × OH). – MS (150°C): *m/z* = 398 (87%, M^+), 380 (35, $M^+ - H_2O$), 367 (26, $M^+ - OCH_3$), 356 (22, $M^+ - CH_2CO$), 348 (29), 338 (23), 323 (99), 307 (30), 295 (100), 251 (25), 225 (16), 203 (63).

$C_{21}H_{18}O_8$ (398.4) Calc. C 63.32 H 4.55 Found C 63.35 H 4.50

Methyl [9,10-dihydro-1,4,5-trihydroxy-9,10-dioxo-3-(3-oxopentyl)-2-anthracenyl]acetate (**17b**): 1.80 g (4.52 mmol) of **14** was treated as described for **16b** to afford 1.26 g (68%) of red crystalls; m. p. 178°C. – IR: 2970–2845 (CH), 1734 (C=O, ester), 1712 (C=O), 1606 (quinone), 1577 (aromate), 715 cm^{-1}. – UV: λ_{max} (lg ε) = 207 (4.21), 235 (4.51), 252 (4.41), 293 (3.94), 472 (3.99), 485 sh, 493 (4.05), 510 sh, 528 (3.88), 568 nm sh. – ^{1}H NMR (400 MHz): δ = 1.08 (t; J_{vic} = 7.1 Hz; 3H, CH_3), 2.45 (q; J_{vic} = 7.1 Hz; 2H, CH_2), 2.78 and 3.05 (2 × t; 2 × 2H, 2 × CH_2), 3.74 (s; 3H, CO_2CH_3), 3.98 (s; 2H, $CH_2CO_2CH_3$), 7.32 (dd, $J_{6,7}$ = 8.1 Hz, $J_{6,8}$ = 1.0 Hz; 1H, 6-H), 7.70 (t; 1H, 7-H), 7.89 (dd; $J_{8,7}$ = 7.4 Hz, $J_{8,6}$ = 1.0 Hz; 1H, 8-H), 12.20, 12.87, and 13.67 (3 × s; 3 × 1H, 3 × OH). – MS (150°C): *m/z* = 412 (85%, M^+), 394 (42, $M^+ - H_2O$), 381 (29, $M^+ - OCH_3$), 362 (24, 394 – CH_3OH), 356 (46), 342 (35), 323 (100), 295 (98), 282 (76), 267 (29), 255 (40), 239 (26), 225 (35), 203 (77).

$C_{22}H_{20}O_8$ (412.4) Calc. C 64.08 H 4.89 Found C 63.98 H 4.85

Methyl (1RS,2RS)-2-ethyl-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-6,11-dioxo-1-naphthacenecarboxylate [(±)-4-deoxy-ξ-rhodomycinone] (**25**): A solution of 104 mg (0.26 mmol) of **15** in 20 ml of dry pyridine was treated under N_2 at –10°C with 100 mg of Triton B (as methoxide, without solvent). After 15 min the mixture was poured into cold diluted HCl and extracted three times with each 50 ml of CH_2Cl_2. The organic phase was washed first with diluted HCl and then with water, dried with Na_2SO_4 and evaporated at reduced pressure. The residue was separated by thin-layer chromatography on silica gel (1 mm, CH_2Cl_2/2% CH_3OH, 2–3 developments). Crystallization of the less polar fraction afforded 64.4 mg (62%) of **25**; m. p. 225°C (ether). – IR: 3555 and 3500 (OH), 2980–2860 (CH), 1731 (C=O, ester), 1620 (quinone), 1582 and 1565 cm^{-1}. – UV: λ_{max} (lg ε) = 209 (4.24), 228 (4.23), 251 (4.66), 254 (4.65), 288 (3.98), 325 sh, 455 (3.99), 480 (4.05), 495 (3.92), 514 nm (3.87). – ^{1}H NMR (400 MHz): δ = 1.15 (t; J_{vic} = 7.5 Hz; 3H, CH_3), 1.54 (s; 1H, OH), 1.61 and 1.78 (2 × sext, J_{gem} = 15.0 Hz, J_{vic} = 7.5 Hz; 2 × 1H, CH_2), 1.96 (ddt; $J_{3e,3a}$ = 14.0 Hz, $J_{3e,4a}$ = 7.0 Hz, $J_{3e,4e}$ = $J_{3e,1e}$ = 2.0 Hz; 1H, 3*e*-H), 2.03 (ddd, $J_{3a,3e}$ = 14.0 Hz, $J_{3a,4a}$ = 11.5 Hz, $J_{3a,4e}$ = 6.1 Hz; 1H, 3*a*-H), 2.88 (ddd; $J_{4a,4e}$ = 19.1 Hz, $J_{4a,3a}$ = 11.5 Hz; $J_{4a,3e}$ = 7.0 Hz; 1H, 4*a*-H), 3.12 (ddd; $J_{4e,4a}$ = 19.1 Hz, $J_{4e,3a}$ = 6.1 Hz; $J_{4e,3e}$ = 2.0 Hz; 1H, 4*e*-H), 3.75 (s; 3H, CO_2CH_3), 4.12 (d, $J_{1e,3e}$ = 2.0 Hz; 1H, 1*e*-H), 7.83 (m; 2H, 8- and 9-H), 8.35 (m; 2H, 7- and 10-H), 13.44 and 13.55 (2 × s; 2 × 1H, 2 × OH). – MS (200°C): *m/z* = 396 (100%, M^+), 378 (14, $M^+ - H_2O$), 364 (28, $M^+ - CH_3OH$), 346 (26, 378 – CH_3OH), 336 (70), 319 (91, 336), 307 (98, 336 – C_2H_5), 292 (40), 279 (78, 307 – CO), 265 (25), 233 (19), 205 (19).

$C_{22}H_{20}O_7$ (396.4) Calc. C 66.66 H 5.09 Found C 66.42 H 5.05

Methyl (1RS,2SR)-2-ethyl-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-6,11-dioxo-1-naphthacenecarboxylate [(±)-10-epi-4-deoxy-ξ-rhodomycinone] (**28**): From the polar fraction of the chromatography (see **25**) 7.6 mg (7%) of **28** crystallized from ether; m. p. 218 °C. Alternatively the cyclization of **15** can be conducted in 10 ml of DMF at 20 °C for 15 min using 20 mg of NaH (60% in oil) as base. Workup and separation were performed as described for **25** to afford 32 mg (37%) of **28** and 10.4 mg (12%) of **25** starting from 86 mg of **15**. Cyclization of 43 mg of **15** with (*S*)-(+)-1-lithio-2-(methoxymethyl)pyrrolidine[30] (see **29a**) gave 9 mg (21%) of **28**; m. p. 224 °C. – IR: 3950 and 3450 (OH), 2975–2880 (CH), 1733 (C=O, ester), 1622 (quinone), 1583 cm^{-1}. – UV: see **25**. – ^1H NMR (300 MHz): δ = 1.03 (t, J_{vic} = 7.5 Hz; 3H, CH_3), 1.59 and 1.61 (2 × sext, J_{gem} = 15.0 Hz, J_{vic} = 7.5 Hz; 2H, CH_2), 1.86 (dt, $J_{3e,3a}$ = 13.5 Hz, $J_{3e,4a}$ = $J_{3e,4e}$ = 6.0 Hz; 1H, 3*e*-H), 2.14 (ddd, $J_{3a,3e}$ = 13.5 Hz, $J_{3a,4a}$ = 9.0 Hz, $J_{3a,4e}$ = 6.0 Hz; 1H, 3*a*-H), 2.46 (s; 1H, 2-OH), 2.74 (ddd, $J_{4a,4e}$ = 19.0 Hz, $J_{4a,3a}$ = 6.0 Hz; 1H, 4*a*-H), 3.16 (dt, $J_{4e,4a}$ = 19.0 Hz, $J_{4e,3a}$ = $J_{4e,3e}$ = 6.0 Hz; 1H, 4*e*-H), 3.78 (s; 3H, CO_2CH_3), 4.04 (s; 1H, 1*a*-H), 7.84 (m; 2H, 8- and 9-H), 8.35 (m; 2H, 7- and 10-H), 13.40 and 13.59 (2 × s; 2 × 1H, 2 × OH). – MS (200 °C): *m/z* = 396 (65%, M^+), 378 (17, $M^+ - H_2O$), 364 (28, $M^+ - CH_3OH$), 346 (27), 336 (35), 319 (100, 336 – OH), 307 (82, 336 – C_2H_5), 303 (38), 292 (45), 279 (66, 307 – CO), 264 (27), 249 (13), 233 (18).

Methyl (1RS,2RS)-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-2-methyl-6,11-dioxo-1-naphthacenecarboxylate (**26a**): 104 mg of **16a** was treated as described for **25** to afford 79 mg (80%) of **26a** from the less polar fraction of the thin-layer chromatotraphy; m. p. 231–233 °C (ether). – IR: 3505 (OH), 1714 (C=O), 1615 (quinone), 1577 cm^{-1} (aromate). – UV: λ_{max} (lg ε) = 218 (4.32), 234 (4.50), 251 (4.44), 289 (3.91), 378 sh, 475 (4.05), 492 (4.07), 528 (3.86), 575 nm sh. – ^1H NMR (400 MHz): δ = 1.48 (s; 3H, 2-CH_3), 1.70 (s; 2*a*-OH), 1.91 (dddd, $J_{3e,3a}$ = 14.0 Hz, $J_{3e,4a}$ = 6.1 Hz, $J_{3e,4e}$ = 2.5 Hz, $J_{3e,1e}$ = 1.5 Hz; 1H, 3*e*-H), 2.10 (ddd, $J_{3a,3e}$ = 14.0 Hz, $J_{3a,4a}$ = 11.0 Hz, $J_{3a,4e}$ = 6.1 Hz; 1H, 3*a*-H), 2.89 (ddd, $J_{4a,4e}$ = 19.3 Hz, $J_{4a,3a}$ = 11.0 Hz, $J_{4a,3e}$ = 6.1 Hz; 1H, 4*a*-H), 3.12 (ddd, $J_{4e,4a}$ = 19.3 Hz, $J_{4e,3a}$ = 6.1 Hz, $J_{4e,3e}$ = 2.5 Hz; 1H, 4*e*-H), 3.77 (s; 3H, CO_2CH_3), 4.05 (d, $J_{1e,3e}$ = 1.5 Hz; 1H, 1*e*-H), 4.11 (s; 3H, OCH_3), 7.38 (dd, $J_{8,9}$ = 8.5 Hz, $J_{8,10}$ = 1.0 Hz, 1H, 8-H), 7.76 (t, 1H, 9-H), 8.02 (dd, $J_{9,10}$ = 7.5 Hz, $J_{8,10}$ = 1.0 Hz, 1H, 10-H), 13.49 (s; 1H, 5-OH), 13.80 (s; 1H, 12-OH). – MS (210 °C): *m/z* = 412 (87%, M^+), 394 (17, $M^+ - H_2O$), 380 (27, $M^+ - CH_3OH$), 362 (35, $M^+ - CH_3OH - H_2O$), 352 (76), 337 (100), 335 (94), 322 (51), 309 (84), 294 (42), 277 (21), 265 (20), 263 (20), 249 (20), 237 (19), 217 (48).

$C_{22}H_{20}O_8$ (412.4) Calc. C 64.08 H 4.89 Found C 64.45 H 4.88

Methyl (1RS,2RS)-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-2-methyl-6,11-dioxo-1-naphthacenecarboxylate (**29a**): From the polar fraction of the chromatography (see **26a**) 7.5 mg (7%) of **29a** was isolated. Cyclization of 86 mg of **16a** in DMF with NaH (see **28**) gave 32 mg of **29a** (37%) and 16.5 mg (19%) of **26a**. Alternatively the cyclization of **16a** could be conducted with lithium amides in THF at –78 °C. Thus, a solution of (*S*)-(+)-1-lithio-2-(methoxymethyl)pyrrolidine[30] was prepared by treating a solution of 517 mg (4.5 mmol) of (*S*)-(+)-2-(methoxymethyl)pyrrolidine[30] in 15 ml of dry THF with 2.2 ml of a 1.9 N solution of *n*-butyllithium in hexane at –78 °C. A solution of 50 mg (0.12 mmol) of **16a** in 15 ml of dry THF was added, and the solution was stirred for 3 h at –78 °C. Workup proceeded as described for **25** to afford 14 mg (28%) of **29a**; m. p. 227 °C. The racemic mixture of **29a** melted at 212–214 °C. – UV and MS see **26a**. – IR: 3450 (OH), 3000–2838 (CH), 1722 (C=O), 1618 (quinone), 1588 cm^{-1} (aromate). – ^1H NMR (400 MHz): δ = 1.48 (s; 3H, CH_3), 1.80 (dt, $J_{3e,3a}$ = 13.0 Hz, *J* = 6.5 Hz; 1H, 3*e*-H), 2.20 (ddd, $J_{3a,3e}$ = 13.0 Hz, $J_{3a,4a}$ = 8.5 Hz, $J_{3a,4e}$ = 6.5 Hz; 1H, 3*a*-H), 2.58 (s; 1H, 2*e*-OH), 2.82 (ddd, $J_{4a,4e}$ = 19.5 Hz, $J_{4a,3a}$ = 8.5 Hz, $J_{4a,3e}$ = 6.0 Hz, $J_{4a,1e}$ = 1.0 Hz; 4*a*-H), 3.17 (dt, $J_{4e,4a}$ = 19.5 Hz, *J* =

6.0 Hz; 1 H, 4*e*-H), 3.79 (s; 3 H, CO_2CH_3), 3.98 (d, $J_{1e,3e}$ = 1.0 Hz; 1 H, 1*e*-H), 4.12 (s; 3 H, OCH_3), 7.38 (dd, $J_{8,9}$ = 8.2 Hz, $J_{8,10}$ = 1.0 Hz; 1 H, 8-H), 7.77 (t; 1 H, 9-H), 8.05 (dd, $J_{9,10}$ = 7.7 Hz, $J_{8,10}$ = 1.0 Hz; 1 H, 10-H), 13.08 (s; 1 H, 5-OH), 13.29 (s; 1 H, 12-OH).

$C_{22}H_{20}O_8$ (412.4) Calc. C 64.08 H 4.89 Found C 63.68 H 5.07

Methyl (1RS,2RS)-1,2,3,4,6,11-hexahydro-2,5,7,12-tetrahydroxy-2-methyl-6,11-dioxo-1-naphthacenecarboxyxlate (**26b**): 102 mg (0.26 mmol) of **16b** was treated as described for **25** to afford 78.4 mg (76%) of **26b** from the less polar fraction of the chromatography; m. p. 250–251 °C (ether). – IR: 3540 (OH), 1715 (C=O), 1598 (quinone), 1573 cm^{-1} (aromate). – UV: λ_{max} (lg ε) = 218 (4.50), 235 (4.76), 253 (4.72), 293 (4.12), 463 (4.27), 470 (4.30), 489 (4.40), 510 (4.26), 525 (4.28), 573 nm (3.60). – ^{1}H NMR (400 MHz): δ = 1.45 (s; 3 H, CH_3), 1.91 (ddd, $J_{3e,3a}$ = 14.0 Hz, $J_{3e,4a}$ = 6.5 Hz, $J_{3e,4e}$ = 2.5 Hz, $J_{3e,1e}$ = 1.5 Hz; 1 H, 3*e*-H), 2.08 (ddd, $J_{3a,3e}$ = 14.0 Hz, $J_{3a,4a}$ = 11.5 Hz, $J_{3a,4e}$ = 6.5 Hz; 1 H, 3*a*-H), 2.88 (dddd, $J_{4a,4e}$ = 19.0 Hz, $J_{4a,3a}$ = 11.5 Hz, $J_{4a,3e}$ = 6.5 Hz, $J_{4a,1e}$ = 0.9 Hz; 1 H, 4*a*-H), 3.08 (ddd, $J_{4e,4a}$ = 19.0 Hz, $J_{4e,3a}$ = 6.5 Hz, $J_{4e,3e}$ = 2.5 Hz; 1 H, 4*e*-H), 3.74 (s; 3 H, CO_2CH_3), 4.04 (dd, $J_{1e,3e}$ = 1.5 Hz, $J_{1e,4a}$ = 0.9 Hz; 1 H, 1*e*-H), 7.30 (dd, $J_{8,9}$ = 8.5 Hz, $J_{8,10}$ = 1.0 Hz; 1 H, 8-H), 7.68 (t; 1 H, 9-H), 7.86 (dd, $J_{9,10}$ = 7.5 Hz, $J_{8,10}$ = 1.0 Hz; 1 H, 10-H), 12.36 (s; 1 H, 7-OH), 12.78 (s; 1 H, 5-OH), 13.65 (s; 1 H, 12-OH). – MS (190 °C): *m/z* = 398 (64%, M^+), 380 (17, $M^+ - H_2O$), 366 (34, $M^+ - CH_3OH$), 348 (39, $M^+ - CH_3OH - H_2O$), 346 (23), 338 (58), 323 (100, 338 – CH_3), 321 (98, 338 – OH), 308 (47), 295 (75, 323 – CO), 281 (28), 267(15), 249 (21), 237 (14), 221 (20), 213 (15), 203 (55).

$C_{21}H_{18}O_8$ (398.4) Calc. C 63.32 H 4.55 Found C 62.73 H 4.53

Methyl (1RS,2SR)-1,2,3,4,6,11-hexahydro-2,5,7,12-tetrahydroxy-2-methyl-6,11-dioxo-1-naphthacenecarboxylate (**29b**): From the polar fraction of the chromatography (see **26b**) 9.2 mg (7%) of **26b** of m. p. 225–226 °C was isolated. Cyclization of 42 mg of **16b** in DMF/NaH gave 5.3 mg (13%) of **29b** and 6.7 mg (16%) of **26b**. – IR: 3410 (OH), 2960–2850 (CH), 1720 (C=O), 1592 (quinone), 1573 cm^{-1} (aromate). – UV and MS see **26b**. – ^{1}H NMR: δ = 1.38 (s; 3 H, CH_3), 1.72 (ddd, J_{gem} = 13.1, $J_{3e,4a}$ = 5.9, $J_{3e,4e}$ = 6.3 Hz; 1 H, 3*e*-H), 2.19 (ddd, J_{gem} = 13.1, $J_{3a,4a}$ = 8.3, $J_{3a,4e}$ = 6.2 Hz; 1 H, 3*a*-H), 2.56 (s; 1 H, 2-OH), 2.81 (ddd, J_{gem} = 19.5 Hz; 1 H, 4*a*-H), 3.15 (dt; 1 H, 4*e*-H), 3.79 (s; 3 H, CO_2CH_3), 3.98 (broad s; 1 H, 1-H), 7.31 (dd, $J_{8,10}$ = 1.1, $J_{8,9}$ = 8.4 Hz; 1 H, 8-H), 7.69 (t; 1 H, 9-H), 7.88 (dd, $J_{8,10}$ = 1.1, $J_{9,10}$ = 7.5 Hz; 1 H, 10-H), 12.22 (s; 1 H, 7-OH), 12.76 (s; 1 H, 5-OH), 13.72 (s; 1 H, 12-OH).

$C_{21}H_{18}O_8$ Calc. 398.1002 Found 398.0987 (MS)

Methyl (1RS,2RS)-2-ethyl-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-1-naphthacenecarboxylate (**27a**): 102 mg (0.24 mmol) of **17a** was treated as described for **25** to afford 80.2 mg (78%) of **27a** from the less polar fraction of the chromatography; m. p. 268–269 °C (CH_2Cl_2/ether). – IR and UV see **26a**. – ^{1}H NMR (400 MHz): δ = 1.14 (t, J_{vic} = 7.0 Hz; 3 H, CH_3), 1.54 (s; 1 H, 2*a*-OH), 1.61 and 1.77 (2 × sext, J_{gem} = 14.0 Hz, J_{vic} = 7.0 Hz; 2 × 1 H, CH_2), 1.95 (ddd, $J_{3e,3a}$ = 14.0 Hz, $J_{3e,4a}$ = 7.0 Hz, $J_{3e,1e}$ = 2.0 Hz; 1 H, 3*e*-H), 2.03 (ddd, $J_{3a,3e}$ = 14.0 Hz, $J_{3a,4a}$ = 10.5 Hz, $J_{3a,4e}$ = 6.0 Hz; 1 H, 3*a*-H), 2.89 (dddd, $J_{4a,4e}$ = 19.4 Hz, $J_{4a,3a}$ = 10.5 Hz, $J_{4a,3e}$ = 7.0 Hz, $J_{4a,1e}$ = 1.0 Hz; 1 H, 4-H), 3.09 (ddd, $J_{4e,4a}$ = 19.5 Hz, $J_{4e,3a}$ = 6.0 Hz, $J_{4e,3e}$ = 2.0 Hz; 1 H, 4*e*-H), 3.73 (s; 3 H, CO_2CH_3), 4.08 (s; 3 H, OCH_3), 4.11 (d; 1 H, 1*e*-H), 7.38 (dd, $J_{8,9}$ = 8.0 Hz, $J_{8,10}$ = 1.0 Hz; 1 H, 8-H), 7.76 (t; 1 H, 9-H), 8.03 (dd, $J_{10,9}$ = 8.0 Hz, $J_{10,8}$ = 1.0 Hz; 1 H, 10-H), 13.52 and 13.80 (2 × s; 2 × 1 H, 2 × OH). – MS (210 °C): *m/z* = 426 (100%, M^+), 408 (10, $M^+ - H_2O$), 394 (17, $M^+ - CH_3OH$), 376 (20, 409 – CH_3OH), 366 (75), 349 (86, 366 – OH), 337 (91, 366 – C_2H_5), 322 (45), 309 (84), 294 (32), 281 (15).

$C_{23}H_{22}O_8$ (426.4) Calc. C 64.78 H 5.20 Found C 64.73 H 5.12

Methyl (1RS,2SR)-2-ethyl-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-1-naphthacenecarboxylate (**30a**): From the polar fraction of the chromatography (see **27a**) 5.2 mg (5%) of **30a** was isolated; m. p. 246°C (CH_2Cl_2/ether). Cyclization of 43 mg of **17a** in DMF/NaH (see **28**) gave 11.2 mg (26%) of **30a** and 6.6 mg (15%) of **27a**. – UV and MS see **27a**. – IR: 3470 (OH), 2980–2843 (CH), 1730 (C=O), 1616 (quinone), 1580 cm^{-1} (aromate). – ^1H NMR (400 MHz): δ = 1.02 (t, J_{vic} = 7.5 Hz; 3H, CH_3), 1.59 and 1.61 (2 × sext, J_{gem} = 15.0 Hz, J_{vic} = 7.5 Hz; 2 × 1H, CH_2), 1.87 (dt, $J_{3e,3a}$ = 13.5 Hz, $J_{3e,4a}$ = $J_{3e,4e}$ = 6.0 Hz; 1H, 3*e*-H), 2.14 (ddd, $J_{3a,3e}$ = 13.5 Hz, $J_{3a,4a}$ = 9.0 Hz, $J_{3a,4e}$ = 6.0 Hz; 1H, 3*a*-H), 2.45 (s; 1H, OH), 2.76 (ddd, $J_{4a,4e}$ = 19.4 Hz, $J_{4a,3a}$ = 9.0 Hz, $J_{4a,3e}$ = 6.0 Hz; 1H, 4*a*-H), 3.13 (dt, $J_{4e,4a}$ = 19.4 Hz, $J_{4e,3a}$ = $J_{4e,3e}$ = 6.0 Hz; 1H, 4*e*-H), 3.79 (s; 3H, CO_2CH_3), 4.03 (s; 1H, 1*a*-H), 4.09 (s; 3H, OCH_3), 7.39 (dd, $J_{8,9}$ = 8.0 Hz, $J_{8,10}$ = 1.0 Hz; 1H, 8-H), 7.77 (t, $J_{8,9}$ = $J_{9,10}$ = 8.0 Hz; 1H, 9-H), 8.04 (dd, $J_{10,9}$ = 8.0 Hz, $J_{10,8}$ = 1.0 Hz; 1H, 10-H), 13.57 and 13.83 (2 × s; 2 × 1H, 2 × OH).

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

Methyl (1RS,2RS)-2-ethyl-1,2,3,4,6,11-hexahydro-2,5,7,12-tetrahydroxy-6,11-dioxo-1-naphthacenecarboxylate [(±)-ξ-rhodomycinonc] (**27b**): 100 mg (0.24 mmol) of **17b** was treated as described for **25** to afford 75.6 mg (76%) of **27b** from the less polar fraction of the chromatography; m. p. 267°C (ether). – IR and UV see **26b**. – ^1H NMR (300 MHz): δ = 1.14 (t, J_{vic} = 7.0 Hz; 3H, CH_3), 1.59 and 1.77 (2 × sext, J_{gem} = 14.0 Hz, J_{vic} = 7.0 Hz; 2 × 1H, CH_2), 2.00 (m; 2H, 3*a*- and 3*e*-H), 2.87 (ddd, $J_{4a,4e}$ = 19.5 Hz, $J_{4a,3a}$ = 11.0 Hz, $J_{4a,3e}$ = 7.0 Hz; 1H, 4*a*-H), 3.10 (ddd $J_{4e,4a}$ = 19.5 Hz, $J_{4e,3a}$ = 6.0 Hz, $J_{4e,3e}$ = 2.0 Hz; 1H, 4*e*-H), 3.74 (s; 3H, CO_2CH_3), 4.11 (d, $J_{1e,3e}$ = 2.0 Hz; 1H, 1*e*-H), 7.30 (dd, $J_{8,9}$ = 8.4 Hz, $J_{8,10}$ = 1.0 Hz; 1H, 8-H), 7.69 (t; 1H, 9-H), 7.89 (dd, $J_{10,9}$ = 7.5 Hz, $J_{10,8}$ = 1.0 Hz; 1H, 10-H), 12.26, 12.79, and 13.68 (3 × s; 3 × 1H, 3 × OH). – MS (200°C): *m/z* = 412 (100%, M^+), 394 (14, $M^+ - H_2O$), 380 (32, $M^+ - CH_3OH$), 362 (24, 394 – CH_3OH), 352 (61), 355 (88), 323 (98, 352 – C_2H_5), 308 (39), 295 (74, 323 – CO), 281 (21), 249 (15).

Methyl (1RS,2SR)-2-ethyl-1,2,3,4,6,11-hexahydro-2,5,7,12-tetrahydroxy-6,11-dioxo-1-naphthacenecarboxylate [(±)-10-epi-ξ-rhodomycinone] (**30b**): From the polar fraction of the chromatography (see **27b**) 8.8 mg (9%) of **30b** was isolated; m. p. 252°C. – UV see **26b**, MS see **27b**. – IR: 3470 (OH), 2980–2845 (CH), 1741 (C=O), 1608 (quinone), 1590 cm^{-1} (aromate). – ^1H NMR (400 MHz): δ = 1.04 (t, J_{vic} = 7.5 Hz; 3H, CH_3), 1.59 (m; 2H, CH_2), 1.88 (dt, $J_{3e,3a}$ = 13.0 Hz, $J_{3e,4a}$ = $J_{3e,4e}$ = 6.0 Hz; 1H, 3*e*-H), 2.15 (ddd, $J_{3a,3e}$ = 13.0 Hz, $J_{3a,4a}$ = 9.0 Hz, $J_{3a,4e}$ = 6.0 Hz; 1H, 3*a*-H), 2.46 (s; 1H, 2*a*-OH), 2.74 (ddd, $J_{4a,4e}$ = 19.0 Hz, $J_{4a,3a}$ = 9.0 Hz, $J_{4a,3e}$ = 6.0 Hz; 1H, 4*a*-H), 3.14 (dt, $J_{4e,4a}$ = 19.0 Hz, $J_{4e,3a}$ = $J_{4e,3e}$ = 6.0 Hz; 1H, 4*e*-H), 3.80 (s; 3H, CO_2CH_3), 4.04 (s; 1H, 1*a*-H), 7.32 (dd, $J_{8,9}$ = 8.0 Hz, $J_{8,10}$ = 1.0 Hz; 1H, 8-H), 7.70 (t; 1H, 9-H), 7.88 (dd, $J_{10,9}$ = 7.0 Hz, $J_{10,8}$ = 1.0 Hz; 1H, 10-H), 12.33, 12.75, and 13.72 (3 × s; 3 × 1H, 3 × OH). – MS (200°C): *m/z* = 412 (80%, M^+), 394 (16, $M^+ - H_2O$), 380 (28, $M^+ - CH_3OH$), 362 (22, 394 – CH_3OH), 352 (36), 335 (100, 352 – OH), 323 (94, 352 – C_2H_5), 308 (31), 295 (68, 323 – CO), 281 (19).

$C_{22}H_{20}O_8$ (412.4) Calc. C 64.08 H 4.89
27b: Found C 63.38 H 4.85
30b: Found C 63.37 H 4.84

Methyl (1RS,2RS)-1,2,3,4,5,12-hexahydro-2,11-dihydroxy-7-methoxy-2-methyl-5,12-dioxo-1-naphthacenecarboxylate (**31**): 100 mg (0.24 mmol) of **19** was treated as described for **25** to afford 70.2 mg (70%) of **31** from the less polar fraction of the chromatography; m. p. 219–220°C (ether). – IR: 3430 (OH), 2990–2840 (CH), 1738 (C=O), 1656 (quinone), 1630 (quinone), 1602, 1572 cm^{-1} (aromate). – UV: λ_{max} (lg ε) = 209 (3.87), 244 (4.52), 275 (3.89),

285 (3.89), 322 sh, 485 nm (3.74). – ^{1}H NMR (400 MHz): δ = 1.44 (s; 3H, CH_3), 1.88 (dddd, $J_{3e,3a}$ = 14.0 Hz, $J_{3e,4a}$ = 6.5 Hz, $J_{3e,4e}$ = 3.0 Hz, $J_{3e,1e}$ = 2.0 Hz; 1H, 3*e*-H), 1.98 (ddd, $J_{3a,3e}$ = 14.0 Hz, $J_{3a,4a}$ = 10.5 Hz, $J_{3a,4e}$ = 6.5 Hz; 1H, 3*a*-H), 2.78 (dddd, $J_{4a,4e}$ = 20.5 Hz, $J_{4a,3a}$ = 10.5 Hz, $J_{4a,3e}$ = 6.5 Hz, $J_{4a,1e}$ = 2.0 Hz; 1H, 4*a*-H), 2.94 (dddd, $J_{4e,4a}$ = 20.5 Hz, $J_{4e,3a}$ = 6.5 Hz, $J_{4e,3e}$ = 3.0 Hz, $J_{4e,1e}$ = 1.0 Hz; 1H, 4*e*-H), 3.79 (s; 3H, CO_2CH_3), 3.89 (s; 1H, 1*e*-H), 4.03 (s; 3H, OCH_3), 7.04 (dd, $J_{8,9}$ = 8.0 Hz, $J_{8,10}$ = 1.0 Hz; 1H, 8-H), 7.58 (t; 1H, 9-H), 7.98 (dd, $J_{9,10}$ = 8.5 Hz, $J_{8,10}$ = 1.0 Hz; 1H, 10-H), 8.55 (d, J = 1.0 Hz; 1H, 6-H), 13.60 (s; 1H, 11-OH). – MS (200°C): m/z = 396 (63%, M^+), 376 (34), 364 (23, M^+ – CH_3OH), 344 (68), 336 (58), 329 (35), 319 (100, 336 – OH), 304 (29), 293 (64).

$C_{22}H_{20}O_7$ (396.4) Calc. C 66.66 H 5.09
31: Found C 66.49 H 4.99
33: Found C 66.23 H 5.01

Methyl (1RS,2SR)-1,2,3,4,5,12-hexahydro-2,11-dihydroxy-7-methoxy-2-methyl-5,12-dioxo-1-naphthacenecarboxylate (**33**): 23 mg (23%) of **33** was isolated from the polar fraction of the chromatography (see **31**); m. p. 209–210°C (ether). – UV and MS see **31**. – IR: 3375 (OH), 2990–2835 (CH), 1724 (C=O), 1654 (quinone), 1620 (quinone), 1610, 1598, 1500 cm^{-1} (aromate). – ^{1}H NMR (400 MHz): δ = 1.41 (s; 3H, CH_3), 1.62 (dd, J_{gem} = 13.5 Hz, J = 6.5 Hz; 1H, 3*e*-H), 2.10 (dd, J_{gem} = 13.5 Hz, J = 6.5 Hz; 1H, 3*a*-H), 2.59 (s; 1H, 2*e*-OH), 2.72 (ddd, J_{gem} = 20.5 Hz, J = 6.5 Hz, $J_{4a,1e}$ = 2.0 Hz; 1H, 4*a*-H), 2.98 (ddd, J_{gem} = 20.5 Hz, J = 6.5 Hz, $J_{4e,1e}$ = 2.0 Hz; 1H, 4*e*-H), 3.82 (d; 1H, 1*e*-H), 3.84 (s; 3H, CO_2CH_3), 4.03 (s; 3H, OCH_3), 7.07 (dd, $J_{8,9}$ = 7.5 Hz, $J_{8,10}$ = 0.7 Hz; 1H, 8-H), 7.60 (t; 1H, 9-H), 8.01 (dd, $J_{9,10}$ = 8.5 Hz, $J_{8,10}$ = 0.7 Hz; 1H, 10-H), 8.58 (d, J = 0.7 Hz; 1H, 6-H), 13.62 (s; 1H, 11-OH).

Methyl (1RS,2RS)-2-ethyl-1,2,3,4,5,12-hexahydro-2,11-dihydroxy-7-methoxy-5,12-dioxo-1-naphthacenecarboxylate (**32**): 90 mg (0.22 mmol) of **21** was treated as described for **25** to afford 70 mg (78%) from the less polar fraction of the chromatography; m. p. 249°C (ether). – IR and UV see **31**. – ^{1}H NMR (400 MHz): δ = 1.14 (t, J_{vic} = 7.4 Hz; 3H, CH_3), 1.58 and 1.74 (2 × sext, J_{gem} = 14.8 Hz, J_{vic} = 7.4 Hz; 2 × 1H, CH_2), 1.65 (s; 1H, 2*a*-OH), 1.92 (m; 2H, 3*a*- and 3*e*-H), 2.73 (dddd, $J_{4a,4e}$ = 20.0 Hz, $J_{4a,3a}$ = 10.0 Hz, $J_{4a,3e}$ = 7.5 Hz, $J_{4a,1e}$ = 2.0 Hz; 1H, 4*a*-H), 2.95 (ddd, $J_{4e,4a}$ = 20.0 Hz, $J_{4e,3a}$ = 5.8 Hz, $J_{4e,3e}$ = 3.0 Hz; 1H, 4*e*-H), 3.76 (s; 3H, CO_2CH_3), 3.96 (s; 1H, 1*e*-H), 4.05 (s; 3H, 7-OCH_3), 7.07 (dd, $J_{8,9}$ = 7.8 Hz, $J_{8,10}$ = 1.9 Hz; 1H, 8-H), 7.59 (t; 1H, 9-H), 8.00 (dd, $J_{10,9}$ = 8.0 Hz, $J_{10,7}$ = 1.8 Hz; 1H, 10-H), 8.55 (s; 1H, 6-H), 13.61 (s; 1H, 11-OH). – MS (190°C): m/z = 410 (95%, M^+), 392 (14, M^+ – H_2O), 378 (24, M^+ – CH_3OH), 360 (22, 392 – CH_3OH), 350 (76, M^+ – $HCOOCH_3$), 333 (100, 350 – OH), 321 (81, 350 – C_2H_5), 307 (40), 294 (71), 276 (36), 263 (19), 251 (19), 235 (18).

Methyl (1RS,2SR)-2-ethyl-1,2,3,4,5,12-hexahydro-2,11-dihydroxy-7-methoxy-5,12-dioxo-1-naphthacenecarboxylate (**34**): From the polar fraction of the chromatography (see **32**) 7.4 mg (8%) of **34** was isolated; m. p. 236°C. – UV see **31**, MS see **32**. – IR: 3590 and 3525 (OH), 3000–2848 (CH), 1738 (C=O), 1654 (quinone), 1632, 1600 (quinone), 1574, 1502 cm^{-1} (aromate). – ^{1}H NMR (400 MHz): δ = 1.02 (t, J_{vic} = 7.5 Hz; 3H, CH_3), 1.63 (q, J_{vic} = 7.5 Hz; 2H, CH_2), 1.78 (dt, $J_{3e,3a}$ = 13.0 Hz, $J_{3e,4a}$ = $J_{3e,4e}$ = 6.0 Hz; 1H, 3*e*-H), 2.06 (ddd, $J_{3a,3e}$ = 13.0 Hz, $J_{3a,4a}$ = 8.0 Hz, $J_{3a,4e}$ = 5.0 Hz; 1H, 3*a*-H), 2.46 (s; 1H, 2*a*-OH), 2.65 (dddd, $J_{4a,4e}$ = 20.0 Hz, $J_{4a,3a}$ = 8.0 Hz, $J_{4a,3e}$ = 6.0 Hz, $J_{4a,1a}$ = 2.0 Hz; 1H, 4*a*-H), 2.98 (ddt, $J_{4e,4a}$ = 20.0 Hz, $J_{4e,3a}$ = $J_{4e,3e}$ = 6.0 Hz, $J_{4e,1a}$ = 2.0 Hz; 1H, 4*e*-H), 3.82 (s; 3H, CO_2CH_3), 3.88 (s; 1H, 1*a*-H), 4.04 (s; 3H, OCH_3), 7.07 (dd, $J_{8,9}$ = 7.5 Hz, $J_{8,10}$ = 1.6 Hz;

1 H, 8-H), 7.60 (t; 1 H, 9-H), 8.02 (dd, $J_{10,9}$ = 8.0 Hz, $J_{10,8}$ = 1.5 Hz; 1 H, 10-H), 8.57 (d, J = 0.9 Hz; 1 H, 6-H), 13.63 (s; 1 H, 11-OH).

$C_{23}H_{22}O_7$ (410.4) Calc. C 67.31 H 5.40
32: Found C 66.97 H 5.28
34: Found C 66.94 H 5.24

(−)-m-Menth-4-yl [9,10-dihydro-1,4-dihydroxy-5-methoxy-9,10-dioxo-3-(3-oxobutyl)-2-anthracenyl]acetate (**35**): A solution of 100 mg (0.23 mmol) of **17a**, 500 mg of *p*-toluenesulfonic acid, and 1.56 g (10 mmol) of (−)-*m*-menthol in 100 ml of dry benzene was destilled with continuous addition of benzene (200 ml) for 12 h. The solution was washed with $NaHCO_3$ solution, dried (Na_2SO_4) and evaporated to dryness. The residue was crystallized three times from CH_2Cl_2/petroleum ether to afford 52 mg (41%) of **35**: m. p. 234 °C. – UV see **26a**. – IR: 2955–2850 (CH), 1734 (C=O), 1718 (C=O), 1619 (quinone), 1684 cm^{-1} (aromate). – ^1H NMR (400 MHz): δ = 0.74 (d, J_{vic} = 7.0 Hz; 3 H, CH_3), 0.86 and 0.90 (2 × d, J_{vic} = 7.0 Hz 2 × 3 H, 2 × CH_3), 1.00 (ddd, J = 14.0 Hz, J = J = 11.0 Hz; 1 H), 1.05 (dt, J = 14.0 Hz, J = J = 4.4 Hz; 1 H), 1.36 (dtd, J = 14.0 Hz, J = J = 7.0 Hz, J = 3.0 Hz; 1 H), 1.43–1.53 (m; 2 H), 1.66 (m; 2 H), 1.87 (dtd, J = 14.0 Hz, J = J = 7.0 Hz, J = 3.0 Hz; 1 H), 2.01 (m; 1 H), 2.16 (s; 3 H, CH_3), 2.79 and 3.03 (2 × t; 2 × 2 H, 2 CH_2), 3.88 (d; 2 H, CH_2CO_2R), 4.08 (s; 3 H, OCH_3), 4.69 (td, J = 11.0 Hz, J = 4.4 Hz; 1 H), 7.37 (dd, $J_{6,7}$ = 8.4, $J_{6,8}$ = 1.0 Hz; 1 H, 6-H), 7.76 (t; 1 H, 7-H), 8.03 (dd, $J_{8,7}$ = 7.7 Hz, $J_{8,6}$ = 1.0 Hz; 1 H, 8-H), 13.46 and 13.87 (2 × s; 2 × 1 H, 2 × OH). – MS (210 °C): m/z = 536 (12%, M^+), 398 (20, $M^+ - C_{10}H_{18}$), 380 (14, 398 − H_2O), 362 (11), 352 (11), 338 (100, 380 − CH_2CO), 320 (11), 310 (71), 296 (53), 278 (27).

$C_{31}H_{36}O_8$ (536.6) Calc. C 69.39 H 6.76 Found C 69.11 H 6.63

(−)-m-Menth-4-yl (1R,2R)-2-ethyl-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-1-naphthacenecarboxylate (**36**) *or* **37** (see below): 30 mg of **35** was cyclized as described for **25** to afford after repeated thin-layer chromatography 7 mg of nonpolar ester with m. p. 176 °C. – IR: 3510 (OH), 2955–2860 (CH), 1726, 1706 (C=O), 1620 (quinone), 1590 cm^{-1} (aromate). – ^1H NMR (300 MHz): δ = 0.76 (d, J_{vic} = 7.0 Hz; 3 H, CH_3), 0.90 and 0.96 (2 × d, J_{vic} = 7.0 Hz; 2 × 3 H, 2 × CH_3), 1.00–1.15 (m, 2 H), 1.49 (s; 3 H, CH_3), 1.89 (dtd, $J_{3e,3a}$ = 14.0 Hz, $J_{3e,4a}$ = 6.5 Hz, $J_{3e,4e}$ = $J_{3e,1e}$ = 2.0 Hz; 1 H, 3*e*-H), 2.01 (m; 2 H), 2.11 (ddd, $J_{3a,3e}$ = 14.0 Hz, $J_{3a,4a}$ = 11.0 Hz, $J_{3a,4e}$ = 6.0 Hz; 1 H, 3*a*-H), 2.13 (dtd, J = 14.0 Hz, J = 7.0 Hz, J = 2.5 Hz; 1 H), 2.88 (ddd, $J_{4a,4e}$ = 19.0 Hz, $J_{4a,3a}$ = 11.0 Hz, $J_{4a,3e}$ = 6.5 Hz; 1 H, 4*a*-H), 3.09 (ddd, $J_{4e,4a}$ = 19.0 Hz, $J_{4e,3a}$ = 6.0 Hz; 1 H, 4*e*-H), 3.99 (d, $J_{1e,3e}$ = 2.0 Hz; 1 H, 1*e*-H), 4.07 (s; 3 H, OCH_3), 4.70 (td, J = 11.0 Hz, J = 4.0 Hz; 1 H), 7.33 (dd, $J_{8,9}$ = 8.0 Hz, $J_{8,10}$ = 1.0 Hz; 1 H, 8-H), 7.72 (t; 1 H, 9-H), 7.96 (dd, $J_{8,10}$ = 8.0 Hz, $J_{9,10}$ = 1.0 Hz; 1 H, 10-H), 13.41 and 13.78 (2 × s; 2 × 1 H, 2 × OH). – MS (180 °C): m/z = 536 (22%, M^+), 398 (100, $M^+ - C_{10}H_{18}$), 330 (28, 398 − H_2O), 352 (89, 380 − CO), 337 (66, 380 − CH_3CO), 309 (59).

(−)-m-Menth-4-yl (1S,2S)-2-ethyl-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-1-naphthacenecarboxylate (**37**) or **36** (see above): From the polar fraction of the thin-layer chromatography (see **36**) 6 mg of ester with m. p. 174 °C was isolated. – MS see **36**. – IR: 3530 (OH), 2980–2860 (CH), 1722, 1702 (C=O), 1620 (quinone), 1588 cm^{-1} (aromate). – ^1H NMR (300 MHz): δ = 0.65 and 0.70 (2 × d, J_{vic} = 7.0 Hz, 2 × 3 H, 2 × CH_3), 0.89 (d, J_{vic} = 7.0 Hz; 3 H, CH_3), 0.91–1.08 (m; 2 H), 1.50 (s; 3 H, CH_3), 1.91 (dtd, $J_{3e,3a}$ = 13.0 Hz, $J_{3e,4a}$ = 6.5 Hz, $J_{3e,4e}$ = $J_{3e,1e}$ = 2.0 Hz; 1 H, 3*e*-H), 2.03 (m; 2 H), 2.10 (dtd, $J_{3a,3e}$ = 13.0 Hz, $J_{3a,4a}$ = 11.0 Hz, $J_{3a,4e}$ = 6.5 Hz; 1 H, 3*a*-H), 2.21–2.38 (m; 2 H), 2.89 (ddd, $J_{4a,4e}$ = 19.0 Hz, $J_{4a,3a}$ = 11.0 Hz, $J_{4a,3e}$ = 6.5 Hz; 1 H, 4*a*-H), 3.10 (ddd, $J_{4e,3a}$ = 6.5 Hz,

$J_{4e,3e}$ = 2.0 Hz; 1 H, 4*e*-H), 3.99 (d, $J_{1e,3e}$ = 2.0 Hz; 1 H, 1*e*-H), 4.09 (s; 3 H, OCH_3), 3.61 (td, J = 11.0 Hz, J = 4.0 Hz; 1 H), 7.37 (dd, $J_{8,9}$ = 8.6 Hz, $J_{8,10}$ = 1.0 Hz; 1 H, 8-H), 7.76 (t; 1 H, 9-H), 8.02 (dd, $J_{9,10}$ = 7.5 Hz, $J_{8,10}$ = 1.0 Hz; 1 H, 10-H), 13.45 and 13.82 (2 × s; 2 × 1 H, 2 × OH).

Methyl (1RS,2RS,4SR)-2-ethyl-1,2,3,4,6,11-hexahydro-2,4,5,12-tetrahydroxy-6,11-dioxo-1-naphthacenecarboxylate [(±)-4-deoxy-ε-rhodomycinone] (**38**): A solution of 50 mg (0.12 mmol) of **25** in 70 ml of dry CCl_4 was treated at 30 °C under N_2 with 38 mg of Br_2 (as a solution in CCl_4) and irradiated for 10–25 min (300 Watt, TLC control for disappearance of starting material). The solvent and the excess of bromine were removed at reduced pressure, and the residue was dissolved in 30 ml of THF. The solution was cooled to −10 °C and treated with 30 ml of a 0.1 N solution of $NaHCO_3$ for 15 min. The mixture was acidified with diluted HCl and extracted three times with CH_2Cl_2 (100 ml). The organic phase was dried (Na_2SO_4), evaporated to dryness at reduced pressure, dissolved in CH_2Cl_2 and filtered through a short column of silica gel (1 × 3 cm, CH_2Cl_2/10% ether) to remove some nonpolar aromatization products and polar material. Crystallization of the fraction of intermediate polarity afforded 40 mg (81%) of **38**; m. p. 186–187 °C (ether). – IR: 3454 (OH), 2970–2855 (CH), 1722 (C=O), 1621 (quinone), 1582 cm^{-1} (aromate). – UV: λ_{max} (lg ε) = 209 (4.16), 238 (4.34), 250 (4.59), 254 (4.54), 285 (3.96), 327 sh, 456 (3.94), 481 (3.98), 500 (3.85), 511 nm (3.77). – ^{1}H NMR (400 MHz): δ = 1.17 (t, J_{vic} = 7.2 Hz; 3 H, CH_3), 1.55 and 1.81 (2 × sext, J_{gem} = 14.5 Hz, J_{vic} = 7.2 Hz; 2 × 1 H, CH_2), 2.30 (m; 2 H, 3*a*- and 3*e*-H), 3.52 (d, $J_{4a\text{-}OH,4e}$ = 3.5 Hz; 1 H, 4*a*-OH), 3.74 (s; 3 H, CO_2CH_3), 3.87 (s; 1 H, 2*a*-OH), 4.30 (s; 1 H, 1*e*-H), 5.39 (td, $J_{4e,4a\text{-}OH}$ = $J_{4e,3a}$ = 4.5 Hz, $J_{4e,3e}$ = 2.5 Hz; 1 H, 4*e*-H; H/D exchange: dd), 7.86 (m; 2 H, 8- and 9-H), 8.37 (m; 2 H, 7- and 10-H), 13.34 and 13.60 (2 × s; 2 × 1 H, 2 × OH). – MS (180 °C): *m/z* = 412 (100%, M^+), 394 (17, $M^+ - H_2O$), 376 (29, $M^+ - 2\,H_2O$), 360 (23), 352 (46), 335 (32, 352 − OH), 323 (83, 352 − C_2H_5), 317 (52, 335 − H_2O), 306 (60), 278 (56).

$C_{22}H_{20}O_8$ (412.4) Calc. C 64.08 H 4.89 Found C 64.00 H 4.89

Methyl (1RS,2RS,4SR)-1,2,3,4,6,11-hexahydro-2,4,5,12-tetrahydroxy-7-methoxy-2-methyl-6,11-dioxo-1-naphthacenecarboxylate [(±)-4-*O*-methyl-δ-rhodomycinone Ist 299] (**39a**): 40 mg of **26a** was treated as described for **38** to afford 33 mg (77%) of **39a**; m. p. 234–235 °C. – IR and UV see **40a**. – ^{1}H NMR (400 MHz): δ = 1.46 (s; 3 H, CH_3), 2.24 (dt, $J_{3e,3a}$ = 15.0 Hz, $J_{3e,4e}$ = $J_{3e,1e}$ = 1.5 Hz; 1 H, 3*e*-H), 2.36 (dd, $J_{3a,3e}$ = 15.0 Hz, $J_{3a,4e}$ = 5.0 Hz; 1 H, 3*a*-H), 3.50 (s; 1 H, 2*a*-OH), 3.74 (s; 3 H, CH_3), 4.10 (s; 3 H, OCH_3), 4.17 (s; 1 H, 4*a*-OH), 4.22 (d, $J_{1e,3e}$ = 1.5 Hz; 1 H, 1*e*-H), 5.36 (dd, $J_{4e,3a}$ = 5.0 Hz, $J_{4e,3e}$ = 1.5 Hz; 1 H, 4*e*-H), 7.40 (dd, $J_{8,9}$ = 8.2 Hz, $J_{8,10}$ = 1.0 Hz; 1 H, 8-H), 7.79 (t; 1 H, 9-H), 8.05 (dd, $J_{9,10}$ = 8.0 Hz, $J_{8,10}$ = 1.0 Hz; 1 H, 10-H), 13.26 and 13.95 (2 × s; 2 × 1 H, 2 × OH). – MS (170 °C): *m/z* = 428 (95%, M^+), 414 (53), 392 (52, $M^+ - 2\,H_2O$), 378 (56, $M^+ - CH_3OH - H_2O$), 368 (100), 353 (82), 342 (62), 233 (94), 319 (67), 308 (65), 295 (60).

$C_{22}H_{20}O_9$ (428.4) Calc. C 61.68 H 4.71 Found C 61.32 H 4.73

Methyl (1RS,2RS,4SR)-1,2,3,4,6,11-hexahydro-2,4,5,7,12-pentahydroxy-2-methyl-6,11-dioxo-1-naphthacenecarboxylate [(±)-δ-rhodomycinone Ist 299] (**39b**): 50 mg of **26b** was treated as described for **38** to afford 40.2 mg (81%) of **39b**; m. p. 248 °C. – IR: 3480 and 3419 (OH), 2980–2850 (CH), 1721 (C=O), 1605 (quinone), 1595 and 1570 cm^{-1} (aromate). – UV: λ_{max} (lg ε) = 210 (4.19), 234 (4.62), 253 (4.42), 291 (3.94), 463 (4.08), 479 (4.14), 491 (4.18), 508 (4.06), 526 nm (4.00). – ^{1}H NMR (300 MHz): δ = 1.49 (s; 3 H, CH_3), 2.25 (dt, $J_{3e,3a}$ = 15.0 Hz, $J_{3e,4e}$ = $J_{3e,1e}$ = 1.5 Hz; 1 H, 3*e*-H), 2.37 (ddd, $J_{3a,3e}$ = 15.0 Hz, $J_{3a,4e}$ = 5.0 Hz, $J_{3a,4a\text{-}OH}$ = 2.0 Hz; 1 H, 3*a*-H; H/D exchange: dd) 3.50 (dd, $J_{4a\text{-}OH,4e}$ = 3.5 Hz, $J_{4a\text{-}OH,3a}$ = 2.0 Hz; 1 H, 4*a*-OH), 3.74 (s; 3 H, CO_2CH_3), 4.00 (s; 1 H, 2*a*-OH), 4.24 (d, $J_{1e,3e}$ =

1.5 Hz; 1H, 1*e*-H), 5.35 (ddd, $J_{4e,3a}$ = 5.0 Hz, $J_{4e,4a\text{-OH}}$ = 3.5 Hz, $J_{4e,3e}$ = 1.5 Hz; 1H, 4*e*-H; H/D exchange: dd), 7.34 (dd, $J_{8,9}$ = 8.5 Hz, $J_{8,10}$ = 1.0 Hz; 1H, 8-H), 7.72 (t; 1H, 9-H), 7.89 (dd, $J_{10,9}$ = 7.2 Hz, $J_{10,8}$ = 1.0 Hz; 1H, 10-H), 12.11, 12.92, and 13.44 (3 × s; 3 × 1H, 3 × OH). – MS (180°C): *m/z* = 414 (100%, M^+), 396 (18, $M^+ - H_2O$), 378 (41, $M^+ - 2\,H_2O$), 364 (17, 396 – CH_3OH), 354 (71), 319 (79, 354 – H_2O – OH), 294 (63), 283 (17), 268 (18).

$C_{21}H_{18}O_9$ (414.4) Calc. C 60.87 H 4.38 Found C 60.58 H 4.31

Methyl (1RS,2RS,4SR)-2-ethyl-1,2,3,4,6,11-hexahydro-2,4,5,12-tetrahydroxy-7-methoxy-6,11-dioxo-1-naphthacenecarboxylate [(±)-4-*O*-methyl-ε-rhodomycinone] (**40a**): 105 mg of **27a** was hydroxylated as described for **38** to afford 83.2 mg (78%) from the less polar fraction of the chromatography; m. p. 230°C (ether). – IR: 3534 and 3470 (OH), 2990–2840 (CH), 1731 (C=O), 1618 (quinone), 1583 cm^{-1} (aromate). – UV: λ_{max} (lg ε) = 209 (4.22), 233 (4.57), 250 (4.36), 263 sh, 288 (3.91), 377 (3.93), 475 (4.06), 494 (4.05), 530 nm (3.77). – ^1H NMR (400 MHz): δ = 1.16 (t, J_{vic} = 7.0 Hz; 3H, CH_3), 1.56 and 1.80 (2 × sext, J_{gem} = 14.0 Hz, J_{vic} = 7.0 Hz; 2 × 1H, CH_2), 2.29 (m; 2H, 3*a*- and 3*e*-H), 3.54 (dd, $J_{4a\text{-OH},4e}$ = 3.0 Hz; $J_{4a\text{-OH},3a}$ = 1.2 Hz; 1H, 4*a*-OH), 3.74 (s; 3H, CO_2CH_3), 4.00 (s; 1H, 2*a*-OH), 4.10 (s; 3H, OCH_3), 4.28 (s; 1H, 1*e*-H), 5.38 (ddd, $J_{4e,3a}$ = 4.0 Hz, $J_{4e,4a\text{-OH}}$ = 3.0 Hz, $J_{4e,3e}$ = 2.5 Hz; 1H, 4*e*-H; H/D exchange: dd), 7.41 (dd, $J_{8,9}$ = 8.0 Hz, $J_{8,10}$ = 1.0 Hz; 1H, 8-H), 7.79 (t, $J_{8,9}$ = $J_{9,10}$ = 8.0 Hz; 1H, 9-H), 8.04 (dd, $J_{10,9}$ = 8.0 Hz, $J_{10,8}$ = 1.0 Hz; 1H, 10-H), 13.29 and 13.98 (2 × s; 2 × 1H, 2 × OH). – MS (180°C): *m/z* = 442 (89%, M^+), 424 (18, $M^+ - H_2O$), 406 (24, $M^+ - 2\,H_2O$), 395 (17, 424 – C_2H_5), 382 (57), 374 (29, 406 – CH_3OH), 365 (43, 382 – OH), 353 (100, 382 – C_2H_5), 347 (68), 335 (58), 318 (23), 308 (36).

$C_{23}H_{22}O_9$ (442.4) Calc. C 62.44 H 5.01 Found C 62.29 H 4.94

Methyl (1RS,2RS,4RS)-2-ethyl-1,2,3,4,6,11-hexahydro-2,4,5,12-tetrahydroxy-7-methoxy-6,11-dioxo-1-naphthacenecarboxylate (**44**): From the polar fraction of the chromatography (see **40a**) 4.1 g (4%) of **44** was isolated; m.p. 239°C. – UV see **40a**. – IR: 3460 (OH), 2980–2845 (CH), 1740 (C=O), 1612 (quinone), 1571 (aromate), 803 cm^{-1}. – ^1H NMR (300 MHz); δ = 1.03 (t, J_{vic} = 7.5 Hz; 3H, CH_3), 1.65 and 1.75 (2 × 1H, CH_2), 1.96 (dd, $J_{3a,3e}$ = 14.0 Hz, $J_{3a,4a}$ = 5.5 Hz; 1H, 3*a*-H), 2.40 (dd, $J_{3e,3a}$ = 14.0 Hz, $J_{3e,4a}$ = 4.5 Hz; 1H, 3*e*-H), 3.73 (s; 1H, 2*a*-OH), 3.80 (s; 3H, 1*a*-CO_2CH_3), 3.93 (s; 1H, 1*e*-H), 4.05 (d, $J_{4e\text{-OH},4a}$ = 5.5 Hz; 1H, 4*e*-OH), 4.09 (s; 3H, OCH_3), 5.23 (td, $J_{4a,3a}$ = $J_{4a,4e\text{-OH}}$ = 5.5 Hz, $J_{4a,3e}$ = 4.5 Hz; 1H, 4a-H; H/D exchange; dd), 7.40 (dd, $J_{8,9}$ = 8.5 Hz, $J_{8,10}$ = 1.0 Hz; 1H, 8-H), 7.78 (t; 1H, 9-H), 8.03 (dd, $J_{10,9}$ = 7.7 Hz, $J_{10,8}$ = 1.2 Hz; 1H, 10-H), 13.48 and 13.98 (2 × s; 2 × 1H, 2 × OH). – MS (210°C): *m/z* = 442 (17%, M^+), 426 (14), 422 (16), 406 (49, $M^+ - 2\,H_2O$), 390 (27, 422 – CH_3OH), 382 (3), 374, 365 (21, 382 – OH), 356 (68), 349 (43), 347 (43), 337 (29), 309 (100), 294 (26).

Methyl (1RS,2RS,4SR)-2-ethyl-1,2,3,4,6,11-hexahydro-2,4,5,7,12-pentahydroxy-6,11-dioxo-1-naphthacenecarboxylate [(±)-ε-rhodomycinone] (**6**): 60 mg (0.15 mmol) of **27b** was hydroxylated as described for **38** to afford 47.1 mg (76%) of **6**; m.p. 247°C. – UV see **39b**. – IR: 3490 and 3428 (OH), 2990–2855 (CH), 1722 (C=O), 1609 (quinone), 1577 cm^{-1} (aromate). – UV: λ_{max} (lg ε) = 212 (4.19), 233 (4.60), 253 (4.40), 291 (3.91), 414 sh, 464 (4.06), 478 (4.11), 492 (4.16), 508 (4.04), 526 nm (3.98). – ^1H NMR (400 MHz); δ = 1.16 (t, J_{vic} = 7.0 Hz, 3H, CH_3), 1.56 and 1.81 (2 × sext, J_{gem} = 14.0 Hz, J_{vic} = 7.0 Hz; 2 × 1H, CH_2), 2.29 (m; 2H, 3*a*- and 3*e*-H), 3.51 (d, $J_{4a\text{-OH},4e}$ = 4.0 Hz; 1H, 4*a*-OH), 3.74 (s; 3H, CO_2CH_3), 3.82 (s; 1H, 2*a*-OH), 4.30 (d, $J_{1e,3e}$ = 1.0 Hz; 1H, 1*e*-H), 5.36 (td, $J_{4e,4a\text{-OH}}$ = $J_{4e,3a}$ = 4.0 Hz, $J_{4e,3e}$ = 2.0 Hz; 1H, 4*e*-H; H/D exchange: dd), 7.35 (dd, $J_{8,9}$ = 8.5 Hz, $J_{8,10}$ = 2.0 Hz; 1H, 8-H), 7.73 (t; 1H, 9-H), 7.90 (dd, $J_{10,9}$ = 7.0 Hz, $J_{10,8}$ = 1.0 Hz; 1H, 10-H), 12.12, 12.94, and 13.47 (3 × s; 3 × 1H, 3 × OH). – MS (200°C): *m/z* = 428 (100%, M^+), 410 (18, M^+ –

H_2O), 392 (43, $M^+ - 2\,H_2O$), 376 (18, 410 − CH_3OH − H_2), 368 (52, $M^+ - HCO_2CH_3$), 360 (85, 392 − CH_3OH), 351 (35, 368 − OH), 339 (72, 368 − C_2H_5), 333 (61), 322 (73), 305 (23).

$C_{22}H_{20}O_9$ (428.4) Calc. C 61.68 H 4.71 Found C 61.27 H 4.52

Methyl (1RS,2SR,4SR)-2-ethyl-1,2,3,4,6,11-hexahydro-2,4,5,12-tetrahydroxy-6,11-dioxo-1-naphthacenecarboxylate (**41**): 50 mg (0.12 mmol) of **28** was hydroxylated as described for **38** to afford 43 mg (83%) of **41**; m.p. 203°C. − UV see **38**. − IR: 3560 and 3454 (OH), 2990−2850 (CH), 1732 (C=O), 1623 (quinone), 1585 cm^{-1} (aromate). − ^1H NMR (400 MHz): δ = 1.06 (t, J_{vic} = 7.5 Hz; 3H, CH_3), 1.72 and 1.77 (2 × sext, J_{gem} = 15.0 Hz, J_{vic} = 7.5 Hz; 2 × 1H, CH_2), 2.00 (dd, $J_{3e,3a}$ = 14.0 Hz, $J_{3e,4a}$ = 5.0 Hz; 1H, 3*e*-H), 2.48 (dd, $J_{3a,3e}$ = 14.0 Hz, $J_{3a,4a}$ = 6.5 Hz; 1H, 3*a*-H), 2.59 (s; 1H, 2*a*-OH), 3.75 (d, $J_{4e\text{-}OH,4a}$ = 6.5 Hz; 1H, 4*e*-OH), 3.81 (s; 3H, CO_2CH_3), 4.10 (s; 1H, 1*a*-H), 5.39 (dd, $J_{4a,3a}$ = 6.5 Hz, $J_{4a,3e}$ = 5.0 Hz; $J_{4a,4e\text{-}OH}$ = 2.5 Hz; 1H, 4*a*-H), 7.86 (m; 2H, 8- and 9-H), 8.37 (m; 2H, 7- and 10-H), 13.49 and 13.74 (2 × s; 2 × 1H, 2 × OH). − MS (200°C): *m/z* = 412 (37%, M^+), 394 (21, $M^+ - H_2O$), 376 (19, $M^+ - 2\,H_2O$), 365 (30, 394 − C_2H_5), 352 (41), 344 (30, 376 − CH_3OH), 335 (100, 352 − OH), 323 (65, 352 − C_2H_5), 306 (54, 335 − C_2H_5), 295 (20), 278 (45).

$C_{22}H_{20}O_8$ (412.4) Calc. C 64.08 H 4.89 Found C 64.40 H 4.90

Methyl (1RS,2SR,4SR)-1,2,3,4,6,11-hexahydro-2,4,5,12-tetrahydroxy-7-methoxy-2-methyl-6,11-dioxo-1-naphthacenecarboxylate (**42a**): 25 mg (0.06 mmol) of **29a** was hydroxylated as described for **38** to afford 18.5 mg (72%) of **42a**; m.p. 217°C. − UV see **40a**. − IR: 3520 (OH), 2995−2840 (CH), 1721 (C=O), 1613 (quinone), 1577 and 1568 cm^{-1} (aromate). − ^1H NMR (300 MHz): δ = 1.50 (s; 3H, CH_3), 1.97 (dd, $J_{3e,3a}$ = 14.0 Hz, $J_{3e,4a}$ = 5.5 Hz; 1H, 3*e*-H), 2.55 (dd, $J_{3a,e}$ = 14.0 Hz, $J_{3a,4a}$ = 6.5 Hz; 1H, 3*a*-H), 2.69 (s; 1H, 2*a*-OH), 3.81 (s; 3H, CO_2CH_3), 3.84 (d, $J_{4e\text{-}OH,4a}$ = 2.5 Hz; 1H, 4*e*-OH), 4.02 (s; 1H, 1*a*-H), 4.12 (s; 3H, OCH_3), 5.40 (ddd, $J_{4a,3a}$ = 6.5 Hz, $J_{4a,3e}$ = 5.5 Hz, $J_{4a,4e\text{-}OH}$ = 2.5 Hz; 1H, 4*a*-H; H/D exchange: dd), 7.42 (dd, $J_{8,9}$ = 8.0 Hz, $J_{8,10}$ = 1.0 Hz; 1H, 8-H), 7.81 (t, $J_{8,9} = J_{9,10}$ = 8.0 Hz; 1H, 9-H), 8.05 (dd, $J_{10,9}$ = 8.0 Hz, $J_{10,8}$ = 1.0 Hz; 1H, 10-H), 13.45 and 14.15 (2 × s; 2 × 1H, 2 × OH). − MS (190°C): *m/z* = 428 (35%, M^+), 408 (35, $M^+ - H_2O - H_2$), 392 (56, $M^+ - 2\,H_2O$), 376 (52, 408 − CH_3OH), 368 (56), 360 (67, 392 − CH_3OH), 351 (100, 368 − OH), 342 (88), 333 (58), 309 (37).

$C_{22}H_{20}O_9$ (428.4) Calc. C 61.68 H 4.71 Found C 61.33 H 4.45

Methyl (1RS,2SR,4SR)-1,2,3,4,6,11-hexahydro-2,4,5,7,12-pentahydroxy-2-methyl-6,11-dioxo-1-naphthacenecarboxylate [(±)-7,10-diepi-δ-rhodomycinone Ist 299] (**42b**): 44 mg (0.1 mmol) of **29b** was hydroxylated as described for **38** to afford 34 mg (77%) of **42b**; m.p. 260°C. − UV see **39b**. − IR: 3584 and 3420 (OH), 2982−2850 (CH), 1720 (C=O), 1602 (quinone), 1588 and 1570 cm^{-1} (aromate). − ^1H NMR (400 MHz): δ = 1.51 (s; 3H, CH_3), 1.98 (dd, $J_{3e,3a}$ = 14.0 Hz, $J_{3e,4a}$ = 5.0 Hz; 1H, 3*e*-H), 2.55 (dd, $J_{3a,3e}$ = 14.0 Hz, $J_{4a,4a}$ = 6.0 Hz; 1H, 3*a*-H), 2.65 (s; 1H, 2*a*-OH), 3.66 (d, $J_{4e\text{-}OH,4a}$ = 3.0 Hz; 1H, 4*e*-OH), 3.81 (s; 3H, CO_2CH_3), 4.02 (s; 1H, 1*a*-H), 5.40 (dd, $J_{4a,3a}$ = 6.0 Hz, $J_{4a,3e}$ = 5.0 Hz, $J_{4a,4e\text{-}OH}$ = 3.0 Hz; 1H, 4*a*-H; H/D-exchange: dd), 7.35 (dd, $J_{8,9}$ = 8.2 Hz, $J_{8,10}$ = 1.0 Hz; 1H, 8-H), 7.72 (t; 1H, 9-H), 7.92 (dd, $J_{10,9}$ = 7.0 Hz, $J_{10,8}$ = 1.0 Hz; 1H, 10-H), 12.10, 13.09, and 13.62 (3 × s; 3 × 1H, 3 × OH). − MS (180°C): *m/z* = 414 (65%, M^+), 396 (22, $M^+ - H_2O$), 378 (22, $M^+ - 2\,H_2O$), 362 (20, 396 − CH_3OH − H_2), 354 (64), 346 (34, 378 − CH_3OH), 337 (100, 354 − OH), 322 (48), 311 (23), 294 (47).

$C_{21}H_{18}O_9$ (414.4) Calc. C 60.87 H 4.38 Found C 60.44 H 4.28

Methyl (1RS,2SR,4SR)-2-ethyl-1,2,3,4,6,11-hexahydro-2,4,5,12-tetrahydroxy-7-methoxy-6,11-dioxo-1-naphthacenecarboxylate (**43a**): 25 mg of **30a** was hydroxylated as described for

38 to afford 21.5 mg (81%) of **43a**; m.p. 250°C. – UV see **40a**. – IR: 3530 (OH), 2990–2840 (CH), 1728 (C=O), 1615 (quinone), 1580 and 1570 cm^{-1} (aromate). – ^1H NMR (300 MHz): δ = 1.05 (t, J_{vic} = 7.5 Hz; 3H, CH_3), 1.70 and 1.73 (2 × sext, J_{gem} = 15.0 Hz, J_{vic} = 7.5 Hz; 2 × 1H, CH_2), 1.98 (dd, $J_{3e,3a}$ = 14.0 Hz, $J_{3e,4a}$ = 5.5 Hz; 1H, 3*e*-H), 2.47 (dd, $J_{3a,3e}$ = 14.0 Hz, $J_{3a,4a}$ = 6.5 Hz; 1H, 3*a*-H), 2.59 (s; 1H, 2*a*-OH), 3.80 (s; 3H, CO_2CH_3), 3.84 (d, $J_{4e\text{-}OH,4a}$ = 2.5 Hz; 1H, 4*e*-OH), 4.08 (s; 1H, 1*a*-H), 4.11 (s; 3H, OCH_3), 5.38 (ddd, $J_{4a,3a}$ = 6.5 Hz, $J_{4a,3e}$ = 5.5 Hz, $J_{4a,4e\text{-}OH}$ = 2.5 Hz; 1H, 4*a*-H; H/D exchange; dd), 7.42 (dd, $J_{8,9}$ = 8.0 Hz, $J_{8,10}$ = 1.0 Hz; 1H, 8-H), 7.80 (t, 1H, 9-H), 8.05 (dd, $J_{10,9}$ = 8.0 Hz, $J_{10,8}$ = 1.0 Hz; 1H, 10-H), 13.45 and 14.15 (2 × s; 2 × 1H, 2 × OH). – MS (220°C): *m/z* · 442 (72%, M^+), 424 (26, $M^+ - H_2O$), 406 (21, $M^+ - 2\ H_2O$), 395 (33, 424 – C_2H_5), 390 (36, $M^+ - CH_3OH - H_2O - H_2$), 382 (53), 374 (30, 406 – CH_3OH), 365 (100, 382 – OH), 353 (81, 382 – C_2H_5), 374 (59), 325 (20, 353 – CO), 318 (25), 309 (45), 293 (22).

$C_{23}H_{22}O_9$ (442.4) Calc. C 62.44 H 5.01 Found C 62.36 H 4.92

Methyl (1RS,2SR,4SR)-2-ethyl-1,2,3,4,6,11-hexahydro-2,4,5,7,12-pentahydroxy-6,11-dioxo-1-naphthacenecarboxylate [(±)-7,10-diepi-ε-rhodomycinone] (**43b**): 57.4 mg (0.14 mmol) of **30b** was hydroxylated as described for **38** to afford 45 mg (75%) of **43b**; m.p. 245°C. – UV see **6**. – IR: 3950 and 3442 (OH), 2982–2850 (CH), 1730 (C=O), 1605 (quinone), 1593 and 1572 cm^{-1} (aromate). – ^1H NMR (400 MHz): δ = 1.05 (t, J_{vic} = 7.5 Hz; 3H, CH_3), 1.69 and 1.78 (2 × sext, J_{gem} = 15.0 Hz, J_{vic} = 7.5 Hz; 2 × 1H, CH_2), 2.00 (dd, $J_{3e,3a}$ = 14.0 Hz, $J_{3e,4a}$ = 5.5 Hz; 1H, 3*e*-H), 2.46 (dd, $J_{3a,3e}$ = 14.0 Hz, $J_{3a,4a}$ = 6.5 Hz; 1H, 3*a*-H), 2.56 (s; 1H, 2*a*-OH), 3.67 (d, $J_{4e\text{-}OH,4a}$ = 2.5 Hz; 1H, 4*e*-OH), 3.81 (s; 3H, CO_2CH_3), 4.10 (s; 1H, 1*a*-H), 5.38 (ddd, $J_{4a,3a}$ = 6.5 Hz, $J_{4a,3e}$ = 5.5 Hz, $J_{4a,4e\text{-}OH}$ = 2.5 Hz; 1H, 4*a*-H; H/D exchange: dd), 7.34 (dd, $J_{8,9}$ = 8.4 Hz, $J_{8,10}$ = 1.0 Hz; 1H, 8-H), 7.69 (t; 1H, 9-H), 7.88 (dd, $J_{10,9}$ = 7.2 Hz, $J_{10,8}$ = 1.2 Hz; 1H, 10-H), 12.09, 13.08, and 13.61 (3 × s; 3 × 1H, 3 × OH). – MS (190°C): *m/z* = 428 (50%, M^+), 410 (23, $M^+ - H_2O$), 392 (22, $M^+ - 2\ H_2O$), 381 (22, 410 – C_2H_5), 376 (24, 410 – $CH_3OH - H_2$), 368 (38), 360 (31, 392 – CH_3OH), 351 (100, 368 – OH), 339 (53, 368 – C_2H_5), 351 (36), 322 (52).

$C_{22}H_{20}O_9$ (428.4) Calc. C 61.68 H 4.71 Found C 61.95 H 4.93

CAS Registry Numbers

6: 103301-86-6 / **9b**: 72817-84-6 / **10b**: 95384-68-2 / **11b**: 75963-97-2 / **12**: 103201-41-8 / **13**: 103201-42-9 / **14**: 80255-03-4 / **15**: 103201-43-0 / **16a**: 103201-44-1 / **16b**: 103201-51-0 / **17a**: 103201-48-5 / **17b**: 80255-05-6 / **18**: 103201-45-2 / **19**: 103201-46-3 / **20**: 103201-45-2 / **21**: 103201-49-6 / **22**: 103201-47-4 / **23**: 103201-50-9 / **25**: 103201-52-1 / **26a**: 103201-54-3 / **26b**: 103301-80-0 / **27a**: 103201-56-5 / **27b**: 103301-82-2 / **28**: 103201-53-2 / **29a**: 103201-55-4 / **29b**: 103301-81-1 / **30a**: 103201-57-6 / **30b**: 103302-74-5 / **31**: 103201-58-0 / **32**: 103201-60-1 / **33**: 103201-59-8 / **34**: 103201-61-2 / **35**: 103201-62-3 / **36**: 103201-63-4 / **37**: 103301-83-3 / **38**: 103301-84-4 / **39a**: 103201-64-5 / **39b**: 103301-85-5 / **40a**: 103201-65-6 / **41**: 103301-87-7 / **42a**: 103201-67-8 / **42b**: 103301-88-8 / **43a**: 103201-68-9 / **43b**: 103301-89-9 / **44**: 103201-66-7 / glyoxylic acid hydrate: 563-96-2 / (–)-menthol: 2216-51-5

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