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SYNTHESES OF (±)-AKLAVINONES

APPLICATION OF THE STEREOCONTROLLED "ZIPPER" BICYCLO-CYCLIZATION REACTION

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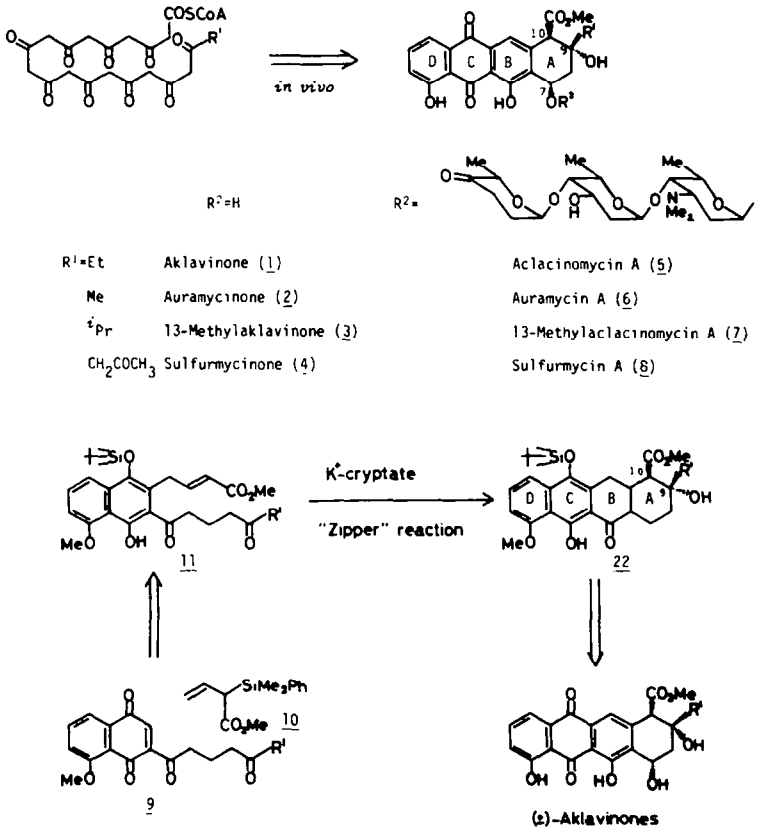
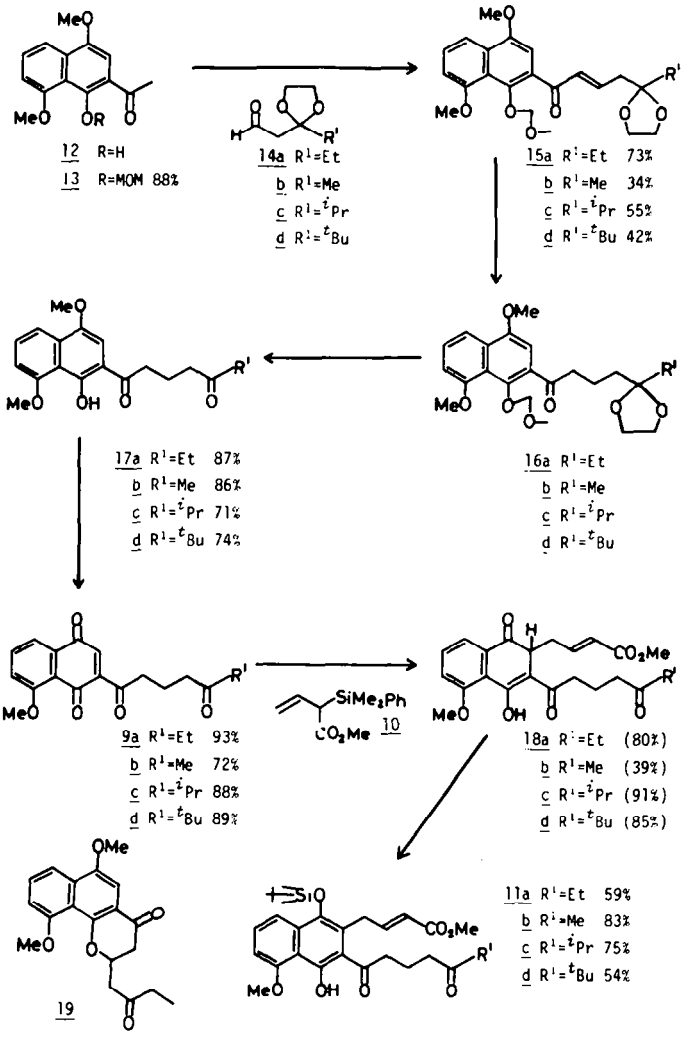
Abstract—Efficient syntheses of (±)-aklavinones; (±)-aklavinone (**1**), (±)-auramycinone (**2**), and (±)-13-methylaklavinone (**3**), are described. A key process of the tetracyclic ring construction in these syntheses is a stereocontrolled "zipper" bicyclo-cyclization using a KH-Kryptofix 222 (4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane) cryptate as a base. The reaction mechanism is discussed, too.

Aclacinomycin A (**5**),[1] which was originally isolated from *Streptomyces galilaeus* in 1975, is one of the most efficacious antitumor agents because of its reduced cardiac toxicity, compared to other anthracycline antibiotics such as daunomycin and adriamycin.[2] Much attention has been concentrated to search for related anthracyclines which might have more clinical efficiency and many kinds of new anthracyclines have been reported. Disregarding the glycosides, auramycinone (**2**),[3] 13-methylaklavinone (**3**),[4] and sulfurmycinone (**4**)[3] are very similar to aklavinone (**1**),[5] i.e. the aglycon of aclacinomycin A (**5**), differing in the 9-alkyl group. The anthracyclinones are thought to be synthesized *in vivo* from decaketides constructed of several carbonyl units of different origin; the units being from acetate, isobutyrate, and n-butyrate (or oxobutyrate). The biosynthetic pathway of anthracyclinones is of a latitudinal construction of decaketides, while almost all of the reported syntheses consist of a longitudinal combination of the ring systems.

In our preliminary report,[6] we discussed our success in the total synthesis of (±)-aklavinone (**1**) using base-promoted "zipper" bicyclo-cyclization of the related tricarbonylnaphthalene (**11a**) in the tetracyclization step. In that reaction, potassium cryptate [$K^+ \subset (2.2.2)$] played a very important role in the



Scheme 1.



Scheme 2.

stereoselective cyclization. Application of our method; the stereoselective "zipper" bicyclo-cyclization, was extended in the syntheses of (±)-auramycinone (**2**) and (±)-13-methylaklavinone (**3**).

RESULTS AND DISCUSSION

Preparation of key intermediates. We first focussed our attention on obtaining 5-oxoheptanoylquinone **9a**, to which the methyl butenoate unit could be introduced efficiently by using methyl 2 - dimethylphenylsilyl - 3 - butenoate (**10**).[7]

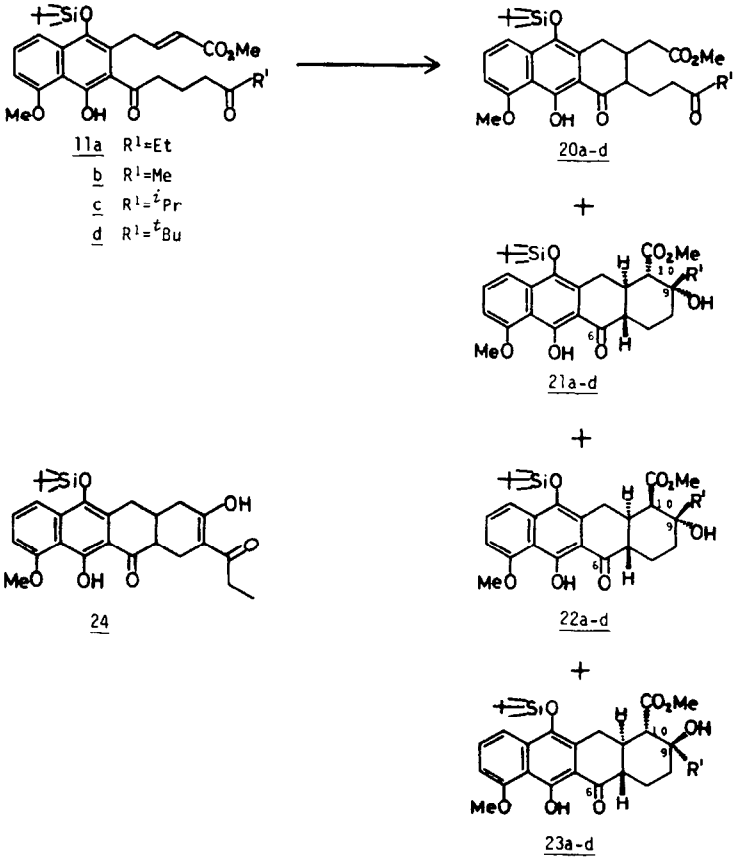
We selected 3 - acetyl - 1,5 - dimethoxy - 4 - naphthol (**12**)[8] as a starting material. The phenolic hydroxyl group of acetylnaphthol **12** was protected by methoxymethyl ether (chlorodimethyl ether (MOMCl), NaH, DMF/THF, 88%). Side chain elongation was achieved by aldol condensation of a lithium enolate of acetylnaphthalene **13** (LDA, THF) with 3,3-ethylenedioxypentanal (**14a**)[9] to give enone **15a** in a 73% yield. Hydrogenation of enone **15a** in methanol (10% Pd/C, H_2) gave 5-oxoheptanoylnaphthol **17a** (64%) and γ-dihydropyrone **19** (~ 10%). The latter may be produced by intramolecular addition of the phenolic hydroxyl group generated by solvolysis before hydrogenation to the enone moiety. On the contrary, in THF enone **15a** was hydrogenated quantitatively to afford ketone **16a**, which was refluxed in aqueous acetone in the presence of a catalytic amount of *p*-toluenesulfonic acid to yield naphthol **17a** (87% from **15a**). Oxidation of naphthol **17a** with ceric ammonium nitrate (CAN) gave naphthoquinone **9a** as yellow needles (m.p. 94–98.5°) recrystallized from ether–hexane in a 93% yield. In spite of the quinone **9a** having many reactive centers for a nucleophile, the methyl butenoate unit was introduced regioselectively to the quinone nucleus in a quantitative yield by Lewis acid mediated reaction of methyl 2-dimethylphenylsilyl-3-butenoate (**10**).[7,12] Dihydronaphthalene **17a** including all carbon units necessary for aklavinone (**1**) was obtained in an 80% yield. Aromatization and simultaneous phenolic hydroxyl protection were carried out by treating **18a** with *t*-butyldimethylsilyl chloride and imidazole in DMF[13] thereby preventing unfavorable dihydrofuran formation. *Mono*silyl ether **11a**: a key intermediate for our aklavione synthesis, was obtained in a 59% yield from **9a**.

Thus, the key intermediate of aklavinone was prepared from the starting acetylnaphthol **12** in an overall yield of 31%. Similarly, other key intermediates

11b, **11c**, and **11d** were obtained in the respective yields of 15%, 15%, and 13% from **12**.

Base promoted "Zipper" cyclization. In our initial experiment (Table 1, entry 3), the key intermediate **11a** (R^1 = Et) was treated with potassium *t*-butoxide (large excess, ~ 50 equiv.) in THF to give a fine yellow fluorescent mixture which consisted of octahydronaphthacene **21a** (72%, m.p. 199–205°) and diastereomeric tetrahydroanthracenes **20a** (27%, 2:1 mixture). 400 MHz NMR analysis of the octahydronaphthacene **21a** (Fig. 1, A) revealed that proton H^{6a} appeared as a doublet of triplets at δ = 2.24. As its coupling constant with proton H^{10a} was 8.9 Hz, the AB-ring junction was assigned *trans*. It was concluded that the 9-hydroxyl and 10-methoxycarbonyl groups had a *cis* relationship which was established by B-ring aromatization. A problem which still remained was whether there was an *anti* or *syn* relationship between positions 10 and 10a. By X-ray analysis, the octahydronaphthacene **21a** was finally confirmed to have a *trans-anti-cis* configuration (Fig. 3). Unfortunately, the relative stereochemistry of **21a** is opposite to that of the natural aklavinone.

We therefore aimed to attain stereocontrol of the reaction. Previously several groups have reported that intramolecular aldol condensation to form the A-ring in protic media led to good results.[5] In our trials, however, only Michael addition occurred and no aldol condensation proceeded; the diastereomeric tetrahydroanthracens **20a** were formed in good yields (Table 1, entries 1,2). Using [2.2.2]-KH cryptate as a base we at last succeeded in obtaining the desired 9,10-*trans* tetracyclic compound **22a** in a 53% yield (Table 1, entry 8), whose relative stereochemistry at the 9,10-positions was acertained by B-ring aromatization. In this reaction, the corresponding *trans-anti-cis* compound **21a** was also obtained in a 25% yield along with a small amount (< 5%) of another tetracyclic compound **23a**. From diagnosis by means of 400 MHz NMR including decoupling of the *trans* compound **22a** (Fig. 1, B), the following was confirmed. The proton H^{10a} appeared in double doublets of a triplet at δ = 2.45. The coupling constant between H^{10a} and H^{10} was 4.9 Hz and that between H^{10a} and H^{6a} was 12.5 Hz. Therefore, two protons, H^{10a} and H^{6a} are axial and the proton H^{10} is equatorial. Consequently, this compound has a *trans-syn-trans* relationship in the four chiral carbon centres. Rather low chemical shifts of the axial protons (H^{8ax} at δ = 2.13 and H^{6a} at δ = 2.98) can be explained by taking into consideration a deshielding effect of the axial methoxycarbonyl group at position 10. The NMR spectrum of **23a** (Fig. 1, C) showed that the coupling constant between H^{10} and H^{10a} was 10.4 Hz, but no other information for H—H coupling was obtained. Fortunately, its methyl analogue **23b** allowed us to analyze the configuration. The proton H^{10a} of **23b** appeared as doublets of a quartet at δ = 2.17 and the coupling constant between H^{10a} and H^{10} was 11.2 Hz and that between H^{10a} and H^{6a} was *ca* 11 Hz. Accordingly, it may be concluded that the three protons are all axial. After aromatizing the B-ring, the 9-hydroxyl and 10-methoxycarbonyl groups showed



Scheme 3.

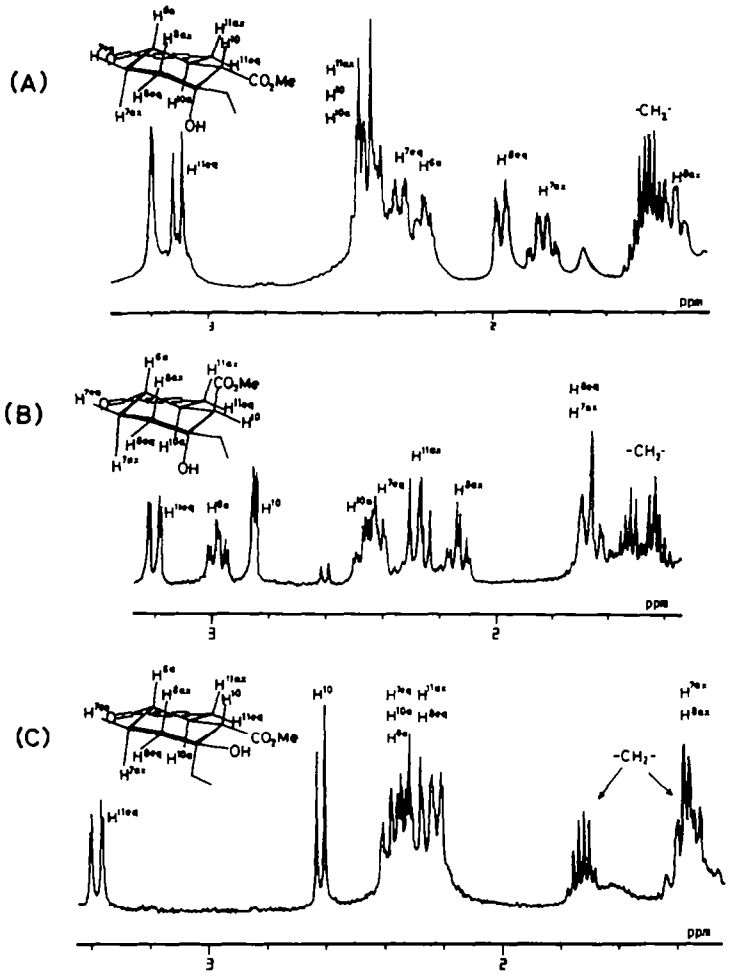


Fig. 1. 400 MHz NMR spectra of tetracyclic compounds: **21a** (A), **22a** (B) and **23a** (C).

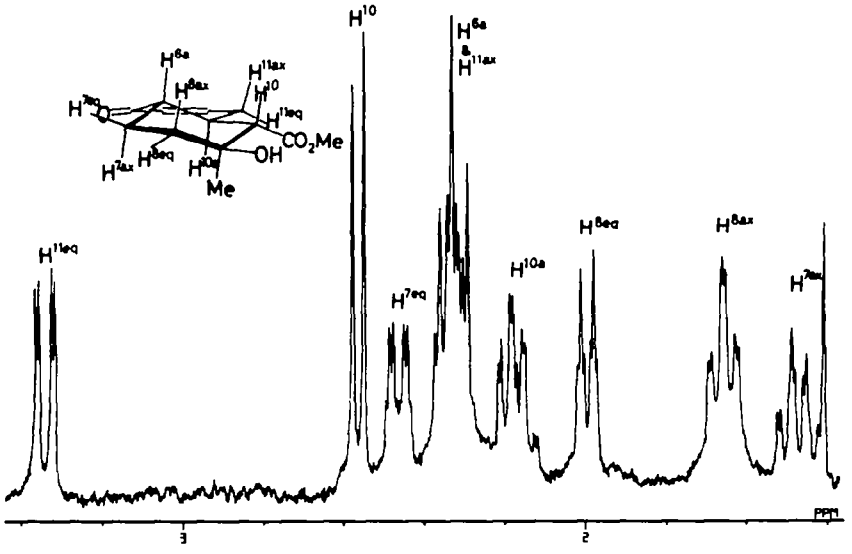


Fig. 2. 400 MHz NMR spectrum of **23b**.

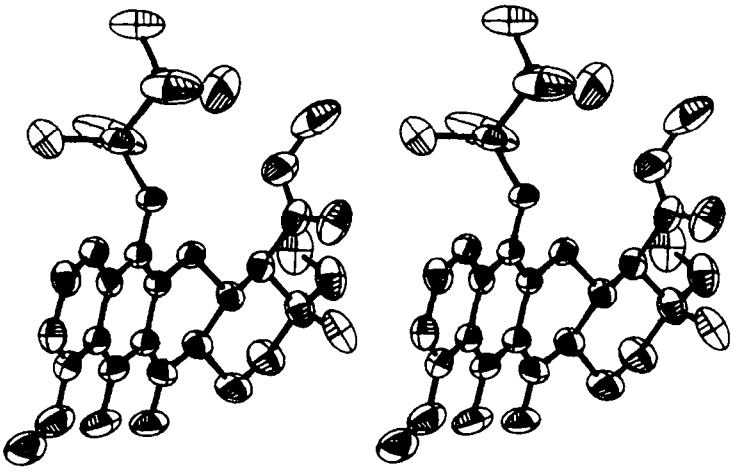


Fig. 3. Ortep drawing of **21a**. Protons are abbreviated.

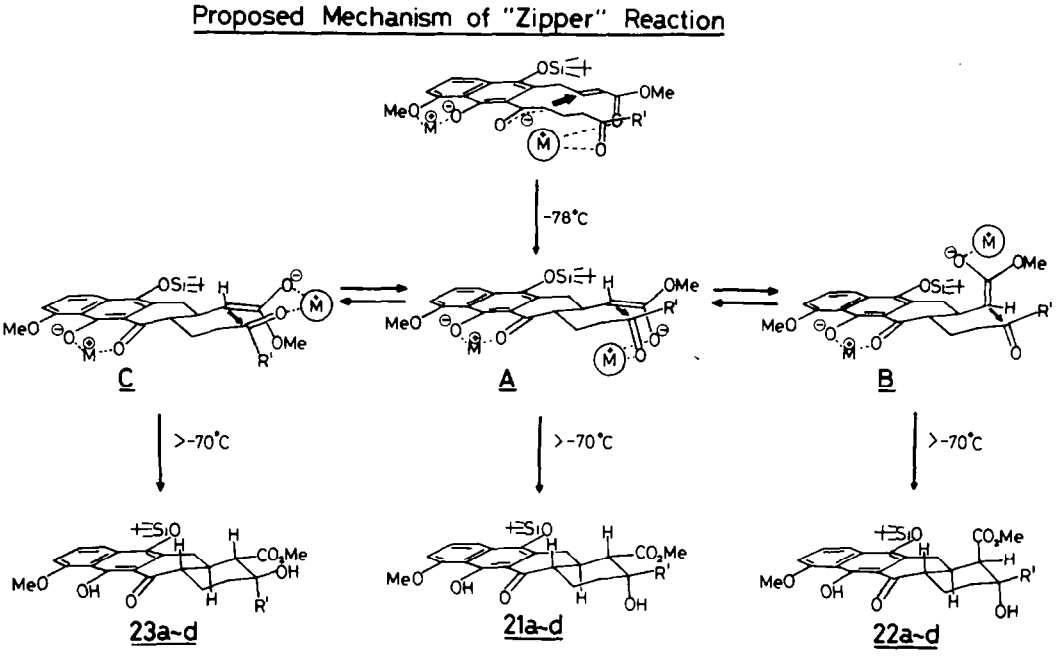
trans orientation (Fig. 2). Hence, **23b** is of the configuration of *trans-anti-trans* octahydronaphthacene. On the basis of the results described above we can deduce that the configuration of **23a** is *trans-anti-trans*, too. Instead of [2.2.2]-KH cryptate other cryptates such as [2.2.2]-NaH, [2.2.1]-NaH, and [2.1.1]-LiH were tried in our bicyclo-cyclization reaction, but better results could not be obtained. To synthesize auramycinone and 13-methylaklavinone we extended further the "zipper" bicyclo–cyclization reaction for other key intermediates using conditions similar to those given in Table 1, entry 9. In the synthesis of auramycinone, the reaction of **11b** (entry 16) gave *trans-anti-cis* **21b**, *trans-syn-trans* **22b**, and *trans-anti-trans* **23b** which were isolated by column chromatography in the respective yields of 48%, 35%, and 13%, while the reaction of 13-methylaklavinone precursor **11c** gave only two of the bicyclo–cyclization products: *trans-anti-cis* **21c** (14%) and *trans-syn-trans* **22c** (62%). In the reaction of *t*-butyl analogue **11d** the second aldol reaction to produce octahydronaphthacene derivatives was extremely retarded probably because of the steric hinderance of the *t*-butyl group.

Now, we turn our attention to the stereochemical

Table 1. Base promoted "zipper" cyclization

			Conditions				Isolated yield/%[a]			
Entry	**11**	Base	Additives	Solvent	Temperature	Time/hr	**20**	**21**	**22**	**23**
1	**a** (Et)	K_2CO_3	none	MeOH	r.t.	2	62	—	—	—
2	**a**	NaOMe	none	MeOH	−78° → r.t.	2	97	—	—	—
3	**a**	KO^{t}Bu	none	THF	−78° → −50°	2	27	72	—	—
4	**a**	NaH	none	DMF/THF	0°	2	—	89[b]	—	—
5	**a**	DBU	none	THF	−78° → r.t.	4.5	(100)[c]	—	—	—
6	**a**	Al_2O_3	none	THF	r.t.	19	(72)[c]	(28)	—	—
7	**a**	KH	18-croun-6	THF	−78° → 0°	2	—	(100)	—	—
8	**a**	LiH	HMPA	THF	−78° → r.t.	21	—	77	—	13
9	**a**	KH	K222,[d] HMPA	THF	−78° → −50°	3	—	25	53	trace
10	**a**	KH	K222,[d] HMPA	THF	−78° → −60°	12	17 (18)[e]	16 (24)	50 (54)	—
11	**a**	KH	K222,[d] HMPA	THF	−78°	9	(33)[e,f]	—	—	—
12	**a**	NaH	K222,[d] HMPA	THF	−78° → 0°	4.5	—	(46)	(41)	—
13	**a**	NaH	K221,[g] HMPA	THF	−78° → 0°	2	—	(60)	(40)	—
14	**a**	LiH	K211,[h] HMPA	THF	−78° → r.t.	7.5	—	(91)	(9)	—
15	**b** (Me)	KH	none	THF	−78° → 0°	2	—	82	—	—
16	**b**	KH	K222,[d] HMPA	THF	−78° → −50°	3	—	48 (49)	35 (38)	13 (13)
17	**c** (^{i}Pr)	KH	none	THF	−78° → −10°	3	—	80	—	—
18	**c**	KH	K222,[d] HMPA	THF	−78° → −50°	3	—	14 (27)	62 (37)	—
19	**d** (^{t}Bu)	KH	none	THF	−78° → −10°	3	—	54	—	—
20	**d**	KH	K222,[d] HMPA	THF	−78° → −30	3.5	(63)[e]	(10)	(26)	—

[a] Yields in the parentheses are estimated by NMR analyses of the reaction mixtures.
[b] Diekmann type compound **24** was obtained in a 10% yield.
[c] Diastereomeric mixture (about 2 : 1).
[d] Kryptofix 222.
[e] One diastereomer (trans).
[f] Starting material still remained in a 67% amount.
[g] Kryptofix 222.
[h] Kryptofix 211.



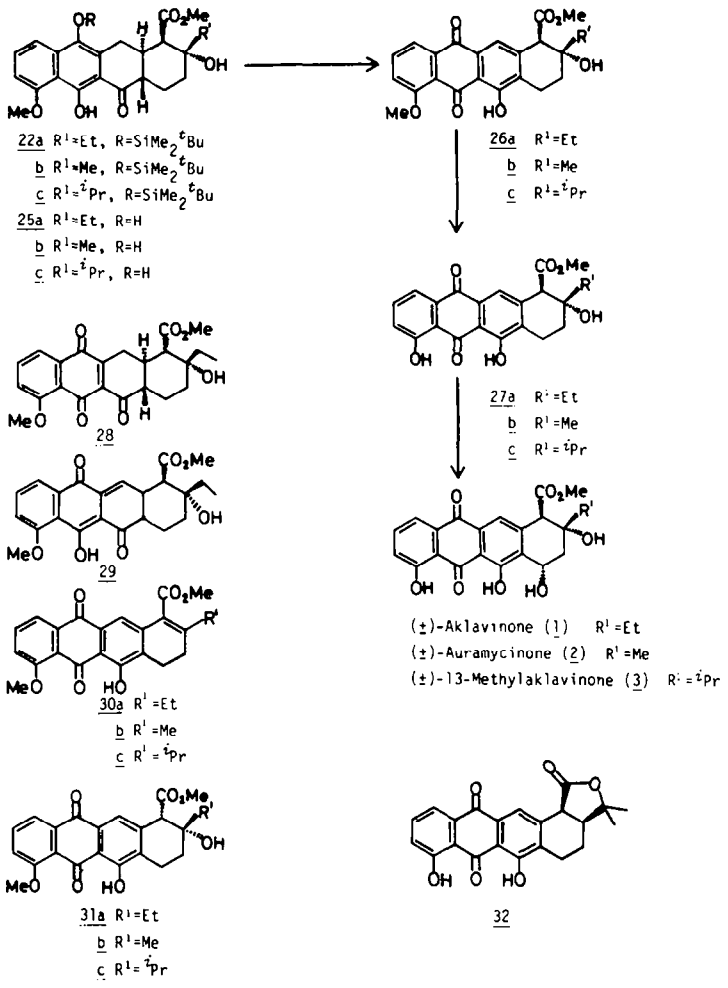
Scheme 4. Proposed mechanism of the "Zipper" reaction.

course of the "zipper" bicyclo–cyclization reaction. Since there is no isomerization among the three octahydronaphthacene derivatives under our conditions, the mechanism for the bicyclo–cyclization could be figured out as follows. First of all, as soon as the dianion of **11** would be generated, intramolecular Michael addition could start even about −78° to release the charge repulsive force of the dianion resulting in the formation of *trans* tricyclic ester enolate (zusammen enolate). Actually, in the presence of a conjugate acid which has a low pKa value (entries 1, 2, 3, 5, and 6), the ester enolate is partially or entirely quenched by proton to afford *trans* tricyclic deviative **20a**. Then thermodynamic equilibrium in the presence of a base causes the isomerization to give a diastereomeric mixture. In the absence of proton sources, the naked alkali metal enolate brings about the intramolecular aldol condensation smoothly via a cyclic transition state from conformer **A** (Scheme 4), while in the presence of HMPA, the product **23** from conformer **C** can be obtained via the isomerization of the enol moeity. A cryptate as a counter cation of the enolate would promote equilibration of conformers **A**, **B**, and **C**, even at a low temperature because of the retarded aldol condensation for which weak chelation of potassium cryptate to the carbonyl group in the side chain might be responsible. The reaction route via an acyclic conformer **B** may be more favorable because the steric repulsion and the dipole interaction will exceed the chelating effect of the large soft cryptate cation. In actuality, the larger the alkyl group (R^1, **11a–d**) was, the more the *trans-syn-trans* derivative **22a–d** was obtained except for R^1 = *t*-Bu. This can be explained by taking into account steric interactions among the equilibrated conformers **A**, **B**, and **C** in the reaction course.

Synthesis of (±)-*aklavinone*, (±)-*auramycinone*, *and* (±)-13-*methylaklavinone*

The *trans-syn-trans* octahydronaphthacenes **22a–c** were successfully converted to (±)-aklavionones; (±)-aklavionone (**1**), (±)-auramycinone (**2**), and (±)-13-methylaklavinone (**3**), as follows (Scheme 5). Desilylative oxidation of **22a** with CAN was performed to give quinone **28**. It was treated with aqueous sodium hydrosulfite to yield hydroquinone **25a** without isolation since quinone **28** easily isomerized to quinomethide **27**[13] by catalysis of a trace amount of acid or by exposure to silica gel. In order to aromatize the B-ring, we first employed homolytic bromination followed by dehydrobromination,[15] and this method proved to be the most efficient one. Bromine dissolved in carbon tetrachloride was added into a refluxed solution of the hydroquinone **25a** in the presence of azoisobutyronitrile. The resulting crude bromide without structural confirmation was treated with triethylamine (0°, 0.5 hr) and with subsequent air oxidation gave tetrahydronaphthacenequinone **26a** in a 76% yield. Under these conditions, we realized no isomerization of **26a** to **31a**. According to the reported method[16] air oxidation of the hydroquinone **25a** did not give any good result. Epimerization of the 10-methoxycarbonyl group was caused by heating it in DMF to afford a mixture of the tetrahydronaphthacenes; **26a**, **31a** (58%, **26a**:**31a** = 7:3), and dihydronaphthacenequinone **30a** (23%). Methyl ether cleavage of **26a** was accomplished to give (±)-galirubinone D (**27a**)[5d] in a 72% yield by using an excess amount of aluminum trichloride in dichloromethane at room temp. Stereoselective introduction of a hydroxyl group at position 7 was carried out to give (±)-aklavinone (**1**) (m.p. 199–203 and 223–228°, double m.ps) in a 94% yield.[5d]

After desilyation, the precursor of auramycinone **22b** was converted to **26b** in an 85% yield by using bromination followed by dehydrobromination, while air oxidation of **25b** in DMF gave a mixture of tetrahydronaphthacenes **26b** (50%), **31b** (21%), and the dehydration product **30b** (24%). Treatment of **26b** with an excess amount of $AlCl_3$ gave **27b** in a 59% yield (86% based upon the consumed **26b**). Hydroxylation of **27b**



Scheme 5.

gave (±)-auramycinone (**2**) as yellow powder (m.p. 183–186 and 266–270°, double m.ps) in an 86% yield. The substance showed identical spectroscopic data (^{1}H-NMR, ^{13}C-NMR, and IR) with natural one[3a] except for the m.p. (lit[3a]: m.p. 153.5°).

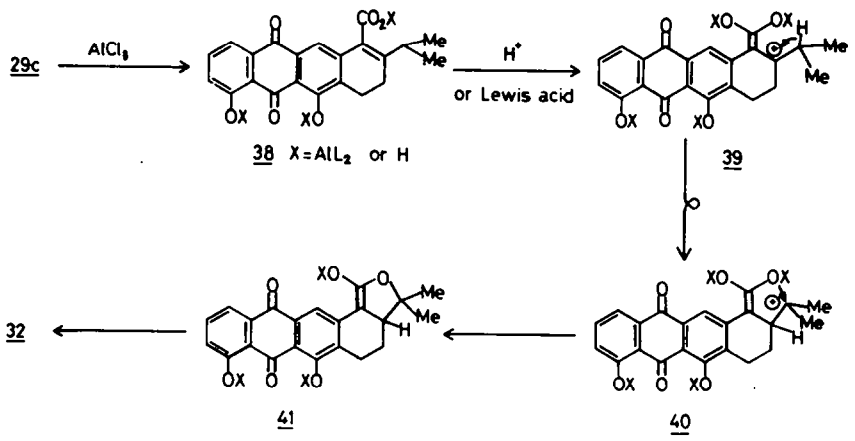
Similarly, **26c** was obtained in a 78% yield by using the bromination–dehydrobromination method. Air oxidation in DMF gave **26c** (64%) accompanied with **31c** (11%) and **30c** (12%). Demethylation of **26c** with $AlCl_3$ (CH_2Cl_2, r.t., overnight) gave the desired product **28c** (36%) from which (±)-13-methylaklavinone (**3**) was obtained in a 75% yield in a way similar to that mentioned above. Accompanying **28c** the demethylation gave unexpectedly lactone **32** (41%). The lactone formation could be explained as follows (Scheme 6).[17] Demethylation of both the ether and ester groups would be followed by dehydration under catalysis with $AlCl_3$ to give dihydronaphthacenecarboxylic acid derivative **38**. Carbocation **39** generated by protonation of (or by ligation with $AlCl_3$) the carbonyl group could isomerize to **40**, which traps the carboxylic oxygen atom intrameolecularly to form γ-lactone **41**.

Based on the successful procedure given above we tried to synthesize the isomer of (±)-aklavinone from the *trans-anti-cis* octahydronaphthacene **21a** (Scheme 7).

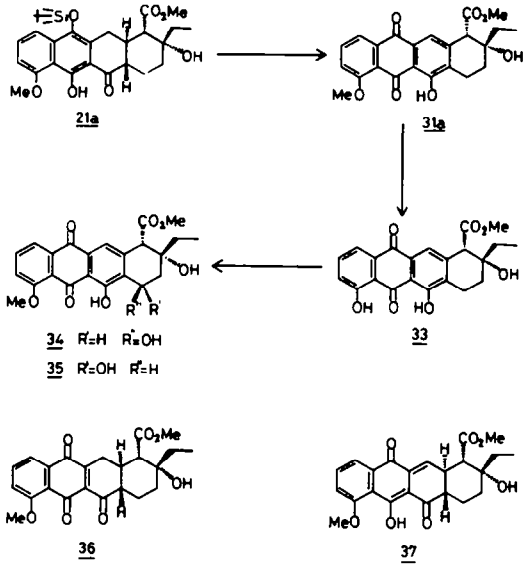
Oxidation of **21a** with CAN gave quinone **36**. Although the quinone **36** was obtained as orange crystals in a 55% yield, it was used for subsequent reaction usually without isolation because of its easy isomerization to the corresponding quinomethide **37**. After reduction of the quinone **36** with aqueous sodium hydrosulfite, aromatization of B-ring was performed to give tetrahydronaphthacene **31a** either by homolytic bromination–dehydrobromination method in a 73% yield or by auto-oxidation in a 75% yield (THF, under oxygen, 5 days). Demethylation of **31a** with $AlCl_3$ afforded **33** in an 85% yield. Hydroxylation of **33** (Br_2, AIBN, CCl_4, ref.; aq-THF) proved to occur at position 7 mainly from the side opposite to the 9-hydroxyl group, though we reported the converse result in the preliminary paper.[6] Thus, (±)-9-epiaklavionone **34** was obtained in a 73% yield successfully by our procedure.

Another route toward (±)-*aklavinone*. We explored the method to transform the tetrahydroanthracenes **20a** to (±)-aklavinone (**1**) *via* the anthraquinone **43** which was believed to be an *in vivo* precursor[18] (Scheme 8).

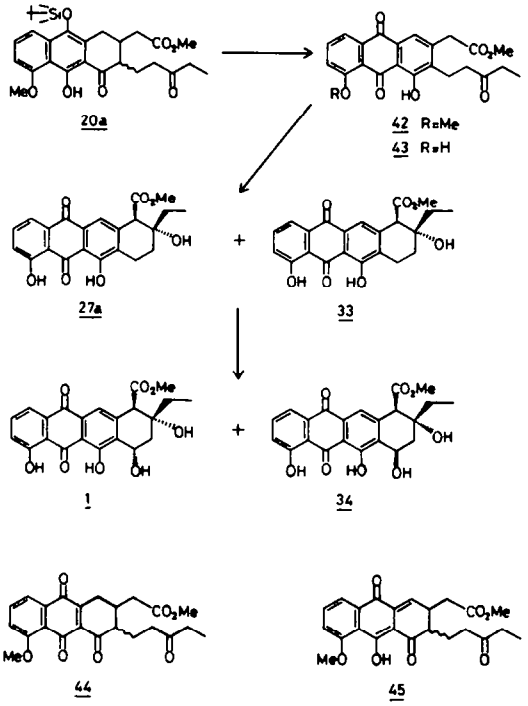
Oxidation of **20a** (2:1 diastereomeric mixture) with CAN gave the corresponding quinone **45** which was then treated with 4-dimethylaminopyridine under air (dichloromethane, overnight) to afford anthraquinone **42** in an overall yield of 66% from **20a**.[19] At an initial



Scheme 6.



Scheme 7.



Scheme 8.

stage of the aromatization the quinone **44** isomerizes to quinomethide **45** and base-catalyzed enolization of the two carbonyl groups followed by air oxidation of the hydroanthraquinone could give **42**. The precursor **43**[18] was obtained by treating anthraquinone **42** with $AlCl_3$ in a 91% yield. Intramolecular aldol reaction of **43** was carried out (Triton B, MeOH, r.t., 4 hr) to give a diastereomeric mixture of (±)-galirubinone D **27a** and (±)-7-deoxyepiaklavinone **33** (**27a** : **33** = *ca* 1 : 1) in a combined yield of 99%. The diastereomeric mixture was hydroxylated to afford a mixture of (±)-aklavinone (**1**) and (±)-9-epiaklavinone **35** in the respective yields of 48% and 46%.

CONCLUSION

We have achieved the total syntheses of (±)-aklavinone, (±)-auramycinone, and (±)-13-methylaklavinone in the respective overall yields of 8.1%, 2.3%, and 3.0% by using the biomimetic "zipper" bicyclo–cyclization reaction as the key ring construction step of anthracyclinone syntheses. In the "zipper" reaction, use of the potassium cryptate [$K^+ \subset (2.2.2)$] as a counter cation led us to a triumph in the battle of the stereocontrol. In addition to the synthesis of the other anthracyclinones, a wider applicability of the "zipper" cyclization reaction is being investigated in our laboratory.

EXPERIMENTAL

General. All m.ps were measured with a Yanagimoto micromelting point apparatus and are uncorrected. PMR spectra were observed with JEOL-PS-100, JNM-MH-100, and JEOL-GX-400 spectrometers with TMS as an internal standard and chemical shifts are reported in δ values. ^{13}C-NMR spectra were observed with a JEOL-GX-400 spectrometer. IR spectra were measured with a JASCO IRA-1 spectrometer. Mass spectra were measured with ESCO EMD-

05A and JEOL JMS-DX300 mass spectrometers. Column chromatography was performed using Wako-gel C-200. Microanalyses were performed by the Microanalytical Laboratory of Kyoto university.

3-*Acetyl*-1,5-*dimethoxy*-4-*methoxymethoxynaphthalene* (**13**)

To a suspension of NaH (360 mg, 15 mmol) in dry DMF (50 ml) was added a soln of **12**[8] (2.956 g, 12 mmol) dissolved in dry THF (20 ml) at 0° under a N_2 atmosphere. The mixture became an orange yellow colored suspension. After stirring for 1 hr at room temp, chlorodimethyl ether (MOMCl; 1.15 ml) was added and stirred for an additional 3 hr. The mixture was poured into ice-water and extracted with CH_2Cl_2. The organic phase was washed with water, $NaHCO_3$ aq, and brine, and dried over $MgSO_4$. After evaporation, the crude material was purified by column chromatography on silica gel (eluted by MeOH-free CH_2Cl_2) to give 3.075 g (88%) of **13**: pale yellow crystals recrystallized from ether–hexane, m.p. 57.5–59°; NMR(100 MHz, $CDCl_3$) δ 2.75 (3H, s), 3.38 (3H, s), 3.94 (6H, s), 4.98 (2H, s), 6.90 (1H, s; 1H, d, J = 8 Hz), 7.38 (1H, t, J = 8 Hz), 7.81 (1H, d, J = 8 Hz); IR(KBr) 1665, 1590, 1450, 1160 cm^{-1}; MS *m/e* 290 (M^+, 56), 248 (59), 246 (59), 230 (62), 215 (100). (Found: C, 66.45; H, 6.49. Calc for $C_{16}H_{18}O_5$: C, 66.20; H, 6.25%).

3-(5,5-*Ethylenedioxy*-2-*heptenoyl*)-1,5-*dimethoxy*-4-*methoxymethoxynaphthalene* (**15a**)

A dry THF (30 ml) soln of **13** (2.61 g, 9 mmol) was added dropwise to a lithium diisopropylamide (LDA, 10 mmol; THF, 10 ml) soln at −78° under a N_2 atm. The soln was warmed to −20° during 1 hr and stirred for an additional 30 min at the temp. After cooling to −78° again, **14a**; (1.543 g, 10.2 mmol, THF, 5 ml) was added to the soln. The mixture was allowed to warm to room temp and stirred for an additional 30 min. The mixture was poured into ice-water and extracted with CH_2Cl_2. The organic phase was washed with water and brine, and dried over Na_2SO_4. After evaporating the solvent, the residue was chromatographed on silica gel to give 2.754 g (73%) of **15a**: pale yellow plates recrystallized from ether–hexane; m.p. 92–93°; NMR(100 MHz, $CDCl_3$) δ 0.91 (3H, t, J = 7 Hz), 1.64 (2H, quartet, J = 7 Hz), 2.58 (2H, m), 3.40 (3H, s), 3.8–4.0 (10H, m), 4.92 (2H, s), 6.86 (4H, m), 7.36 (1H, t, J = 8 Hz), 7.79 (1H, d, J = 8 Hz); IR(KBr) 1680, 1620, 1600, 1575, 1380, 1270, 1150, 1065 cm^{-1}; MS *m/e* 417 (M^+ + 1, 30), 416 (M^+, 100), 316 (44), 310 (51), 302 (25), 301 (100), 271 (43), 257 (62). (Found: C, 66.03; H, 6.74. Calc for $C_{23}H_{28}O_7$: C, 66.33; H, 6.78%).

3-(5,5-*Ethylenedioxy*-2-*hexenoyl*)-1.5-*dimethoxy*-4-*methoxymethoxynaphthalene* (**15b**)

The reaction of **13** (7.83 g, 27 mmol) with **14b** (3.717 g) was performed according to the procedure for preparation of **15a** to give 3.644 g (34%) of **15b**: pale yellow plates recrystallized from ether–hexane; m.p. 107–111°; NMR(100 MHz, $CDCl_3$) δ 1.73 (3H, s), 2.64 (2H, m), 3.45 (3H, s), 3.97 (3H, s), 4.01 (7H, m), 5.01 (2H, s), 6.92–7.08 (4H, m), 7.50 (1H, t, J = 8 Hz), 7.94 (1H, d, J = 8 Hz); IR(KBr) 1675, 1620, 1600, 1570, 1365, 1265, 1150, 1060 cm^{-1}; MS *m/e* 403 (M^+ + 1, 24), 402 (M^+, 95), 316 (27), 301 (100), 296 (31), 271 (36), 257 (58). (Found: C, 65.39; H, 6.61. Calc for $C_{22}H_{26}O_7$: C, 65.66; H, 6.51%).

3-(5,5-*Ethylenedioxy*-6-*methyl*-2-*heptenoyl*)-1,5-*dimethoxy*-4-*methoxymethoxynaphthalene* (**15c**)

According to the preparation of **15a**, the reaction of **13** (1.76 g, 6 mmol) with **14c**; (1.086 g) was carried out to give 1.433 g (55%) of **15c**; pale yellow plates recrystallized from ether–hexane; m.p. 84–85°; NMR (100 MHz, $CDCl_3$) δ 0.94 (6H, d, J = 7 Hz), 1.92 (1H, m), 2.62 (2H, m), 3.22 (3H, s), 3.94 (3H, s), 3.98 (7H, m), 4.95 (2H, s), 6.82–7.00 (4H, m), 7.41 (1H, t, J = 8 Hz), 7.85 (1H, d, J = 8 Hz); IR(KBr) 1670, 1615, 1600, 1570, 1370, 1270, 1150, 1080, 1060 cm^{-1}; MS *m/e* 432 (M^+ + 2, 5), 431 (M^+ + 1, 28), 430 (M^+, 100), 387 (16), 324 (16), 316 (18), 302 (16), 301 (89). (Found: C, 66.82; H, 7.24. Calc for $C_{24}H_{30}O_7$: C, 66.96; H, 7.02%).

3-(5,5-*Ethylenedioxy*-6,6-*dimethyl*-2-*heptenoyl*)-1,5-*dimethoxy*-4-*methoxymethoxynaphthalene* (**15d**)

According to the preparation of **15a**, the reaction of **13** (4.64 g, 16 mmol) with **14d** (2.65 g, 15.4 mmol) was performed to afford 2.979 g (42%) of **15d**: pale yellow crystals recrystallized from ether–hexane; m.p. 110–112°; NMR(100 MHz, $CDCl_3$) δ 0.98 (9H, s), 2.69 (2H, m), 3.43 (3H, s), 3.96 (10H, m), 4.94 (2H, s), 6.8–7.0 (4H, m), 7.40 (1H, t, J = 8 Hz), 7.83 (1H, d, J = 8 Hz); IR(KBr) 1670, 1620, 1600, 1575, 1370, 1270, 1160, 1065 cm^{-1}; MS *m/e* 445 (M^+ + 1, 33), 444 (M^+, 100), 388 (23), 387 (95), 355 (24), 338 (67), 301 (72), 275 (84), 231 (66). (Found: C, 67.40; H, 7.30. Calc for $C_{25}H_{32}O_7$: C, 67.55; H, 7.26%).

1,5-*Dimethoxy*-3-(5-*oxoheptanoyl*)-4-*naphthol* (**17a**)

To a suspension of 10% Pd/C (280 mg) in THF (5 ml) was added a soln (THF, 20 ml) of **15a** (2.686 g, 6.45 mmol) under atmospheric H_2- pressure. After completion of H_2 absorption (1 equiv) the mixture was filtered through a $MgSO_4$ column which was washed with acetone. The solvent was evaporated to give crude 3-(5,5-*ethylenedioxyheptanoyl*)-1,5-*dimethoxy*-4-*methoxymethoxynaphthalene* (**16a**): pale yellow plates recrystallized from ether–MeOH; m.p. 60–62°; NMR(100 MHz, $CDCl_3$) δ 0.91 (3H, t, J = 7 Hz), 1.52–1.90 (6H, m), 3.22 (2H, t, J = 6 Hz), 3.44 (3H, s), 3.93 (3H, s), 4.00 (7H, m), 5.03 (2H, s), 6.86 (1H, s), 6.98 (1H, d, J = 8 Hz), 7.46 (1H, t, J = 8 Hz), 7.89 (1H, d, J = 8 Hz); IR(KBr) 1695, 1600, 1575, 1415, 1380, 1270, 1155, 1065 cm^{-1}; MS *m/e* 419 (M^+ + 1, 5), 418 (M^+, 22), 389 (9), 313 (22), 312 (100), 258 (27), 246 (19), 231 (23). (Found: C, 66.01; H, 7.23. Calc for $C_{23}H_{30}O_7$: C, 65.71; H, 7.31%).

Crude **16a** was refluxed in aqueous acetone (50 ml) in the presence of a catalytic amount of *p*-toluenesulfonic acid (10 mg) for about 4 hr. After the disappearance of **16a** as checked by TLC, the acetone was evaporated *in vacuo*. The resulting suspension was extracted with CH_2Cl_2 and the organic phase was washed with water and brine, and dried over Na_2SO_4. After evaporating the solvent, the residue was purified by column chromatography on silica gel (MeOH-free CH_2Cl_2 as eluent) to afford 1.859 g (87%) of **17a**: yellow needles recrystallized from MeOH, yellow fluorescence in soln; m.p. 128–130°; NMR (100 MHz, $CDCl_3$), δ 1.05 (3H, t, J = 7 Hz), 2.04 (2H, quintet, J = 7 Hz), 2.23 (2H, quartet, J = 7 Hz), 2.55 (2H, t, J = 7 Hz), 3.06 (2H, t, J = 7 Hz), 3.96 (3H, s), 4.02 (3H, s), 6.90 (1H, d, J = 8 Hz), 7.01 (1H, s), 7.46 (1H, t, J = 8 Hz), 7.75 (1H, d, J = 8 Hz), 13.37 (1H, s); IR(KBr) 1690, 1610, 1400, 1380, 1070 cm^{-1}; MS *m/e* 330 (M^+, 36), 312 (22), 258 (26), 245 (56), 230 (100). (Found: C, 69.06; H, 6.83. Calc for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71%).

6,10-*Dimethoxy*-2-(2-*oxobutyl*)-4-*benzo*[*h*]*chromanone* (**19**): pale yellow crystals recrystallized from benzene; m.p. 145–148°; NMR(100 MHz, $CDCl_3$) δ 1.11 (3H, t, J = 7 Hz), 2.62 (2H, quartet, J = 7 Hz), 2.75 (1H, m), 2.76 (2H, d, J = 8 Hz), 3.10 (1H, dd, J = 15, 8 Hz), 3.86 (3H, s), 3.93 (3H, s), 4.98 (1H, m), 6.84 (1H, d, J = 8 Hz), 7.10 (1H, s), 7.41 (1H, t, J = 8 Hz), 7.72 (1H, d, J = 8 Hz); IR(KBr) 1720, 1665, 1575, 1420, 1400, 1270, 1075 cm^{-1}; MS *m/e* 329 (M^+ + 1, 24), 328 (100), 257 (14), 231 (55), 187 (32). (Found: C, 69.41; H, 6.09. Calc for $C_{19}H_{20}O_5$: C, 69.50; H, 6.16%).

1,5-*Dimethoxy*-3-(5-*oxohexanoyl*)-4-*naphthol* (**17b**)

According to the method for preparing **17a**, 395 mg (96%) of **17b** was obtained from 588 mg (1.46 mmol) of **15b**.

3-(5,5-*Ethylenedioxyhexanoyl*)-1,5-*dimethoxy*-4-*methoxymethoxynaphthalene* (**16b**): pale yellow crystals recrystallized from ether–hexane; m.p. 65–67°; NMR (100 MHz, $CDCl_3$) δ 1.34 (3H, s), 1.6–2.0 (4H, m), 3.21 (2H, t, J = 7 Hz), 3.43 (3H, s), 3.93 (3H, s), 4.00 (7H, m), 5.02 (2H, s), 6.88 (1H, s), 6.99 (1H, d, J = 8 Hz), 7.47 (1H, t, J = 8 Hz), 7.90 (1H, d, J = 8 Hz); IR(KBr) 1690, 1600, 1575, 1510, 1410, 1380, 1270, 1155, 1060 cm^{-1}; MS *m/e* 405 (M^+ + 1, 6), 404 (M^+, 26), 386 (21), 298 (100), 258 (33). (Found: C, 65.36; H, 7.00. Calc for $C_{22}H_{28}O_7$: C, 65.33; H, 6.98%).

Compound **17b**: yellow needles recrystallized from MeOH, yellow fluorescence in soln; m.p. 117.5–118°; NMR (100 MHz, $CDCl_3$) δ 2.10 (2H, quintet, J = 7 Hz), 2.19 (3H, s) 2.64 (2H, t, J

= 7 Hz), 3.12 (2H, t, J = 7 Hz), 4.05 (3H, s), 4.11 (3H, s), 7.06 (1H, d, J = 8 Hz), 7.19 (1H, s), 7.65 (1H, t, J = 8 Hz), 7.95 (1H, d, J = 8 Hz), 13.41 (1H, s); IR(KBr) 1710, 1625, 1600, 1575, 1390, 1070 cm^{-1}; MS *m/e* 317 (M^+ + 1, 19), 316 (M^+, 95), 298 (9), 259 (17), 231 (100). (Found: C, 68.13; H, 6.38. Calc for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37%).

1,5-Dimethoxy-3-(6-methyl-5-oxoheptanoyl)-4-naphthol (**17c**)

From 1.413 g of **15c**, 804 mg (71%) of **17c** was obtained in a similar manner.

3 - (5,5 - *Ethylenedioxy* - 6 - *methylheptanoyl*) - 1,5 - *dimethoxy* - 4 - *methoxymethoxynaphthalene* (**16c**): pale yellow oil; NMR (100 MHz, $CDCl_3$) δ 0.92 (6H, d, J = 7 Hz), 1.6–2.1 (5H, m), 3.20 (2H, t, J = 7 Hz), 3.44 (3H, s), 3.95 (3H, s), 4.71 (7H, m), 5.03 (2H, s), 6.88 (1H, s), 6.99 (1H, d, J = 8 Hz), 7.47 (1H, t, J = 8 Hz), 7.91 (1H, d, J = 8 Hz); IR (neat) 1675, 1615, 1600, 1575, 1415, 1370, 1265, 1070 cm^{-1}; MS *m/e* 433 (M^+ + 1, 7), 432 (M^+, 26), 389 (28), 327 (24), 326 (100), 358 (32), 246 (51). (Found: 432.2146. Calc for $C_{24}H_{32}O_7$: 432.2147).

Compund **17c**: yellow needles recrystallized from MeOH, yellow fluorescence in soln; m.p. 83–84°; NMR(100 MHz, $CDCl_3$) δ 1.09 (6H, d, J = 7 Hz), 2.06 (2H, quintet, J = 7 Hz), 2.62 (3H, m), 3.08 (2H, t, J = 7 Hz), 4.00 (3H, s), 4.06 (3H, s), 6.97 (1H, d, J = 8 Hz), 7.08 (1H, s), 7.55 (1H, t, J = 8 Hz), 7.83 (1H, d, J = 8 Hz), 13.50 (1H, s); IR(KBr) 1710, 1620, 1605, 1580, 1390, 1080 cm^{-1}; MS *m/e* 345 (M^+ + 1, 22), 344 (M^+, 97), 259 (30), 246 (65), 231 (100). (Found: C, 69.85; H, 7.01. Calc for $C_{20}H_{24}O_5$: C, 69.75; H, 7.02%).

1,5-Dimethoxy-3-(6,6-dimethyl-5-oxoheptanoyl)-4-naphthol (**17d**)

From 2.835 g (6.38 mmol) of **15d**, 1.694 g (74%) of **17d** was obtained in a similar way.

Compound **17d**: yellow needles recrystallized from MeOH, yellow fluorescence in soln; m.p. 118–119°; NMR(100 MHz, $CDCl_3$) δ 1.14 (9H, s), 2.02 (2H, quintet, J = 7 Hz), 2.64 (2H, t, J = 7 Hz), 3.05 (2H, t, J = 7 Hz), 3.96 (3H, s). 4.01 (3H, s), 6.91 (1H, d, J = 8 Hz), 7.03 (1H, s), 7.46 (1H, t, J = 8 Hz), 7.76 (1H, d, J = 8 Hz), 13.50 (1H, s); IR(KBr) 1700, 1620, 1600, 1575, 1390, 1075 cm^{-1}; MS *m/e* 359 (M^+ + 1, 24), 358 (M^+, 100), 259 (30), 246 (60), 231 (97). (Found: C, 70.16; H, 7.44. Calc for $C_{21}H_{26}O_5$: C, 70.37; H, 7.31%).

5-Methoxy-3-(5-oxoheptanoyl-1,4-naphthoquinone (**9a**)

To a soln (CH_3CN, 150 ml) of **17a** (1.923 g, 5.83 mmol) was added an aqueous soln of CAN (7.916 g) at room temp. After stirring for 10 min, the mixture was extracted with CH_2Cl_2. The organic phase was washed with brine and dried over Na_2SO_4. The soln was passed through a short silica gel column. The solvent was evaporated to give 1.702 g (93%) of quinone **9a**: yellow needles recrystallized from ether–hexane; m.p. 94–98.5°; NMR(100 MHz, $CDCl_3$) δ 1.04 (3H, t, J = 7 Hz), 1.94 (2H, quintet, J = 7 Hz), 2.43 (2H, quartet, J = 7 Hz), 2.51 (2H, t, J = 7 Hz), 2.92 (2H, t, J = 7 Hz), 3.99 (3H, s), 6.85 (1H, s), 7.30 (1H, m), 7.55–7.75 (2H, m); IR(KBr) 1695, 1660, 1620, 1580, 1295, 1275, 1215, 1040 cm^{-1}; MS *m/e* 314 (M^+, 78), 296 (50), 285 (16), 258 (45), 243 (100), 242 (69). (Found: C, 68.59; H, 5.77. Calc for $C_{18}H_{18}O_5$: C, 68.78; H, 5.77%).

5-Methoxy-3-(5-oxohexanoyl)-1,4-naphthoquinone (**9b**)

To a soln (CH_3CN, 150 ml) of **17b** (1.649 g, 5.22 mmol) was added an aqueous soln of CAN (2.089 g) and the mixture was stirred for 10 min. After the work-up described above, quinone **9b** (1.128 g, 72%) was obtained. Yellow needles recrystallized from ether–hexane; m.p. 117.5–118°; NMR(100 MHz, $CDCl_3$) δ 1.94 (2H, quintet, J = 7 Hz), 2.15 (3H, s), 2.54 (2H, t, J = 7 Hz), 2.93 (2H, t, J = 7 Hz), 4.00 (3H, s), 6.91 (1H, s), 7.30 (1H, m), 7.66 (2H, m); IR(KBr) 1705, 1660, 1585, 1295, 1280, 1215 cm^{-1}; MS *m/e* 301 (M^+ + 1, 18), 300 (M^+, 92), 282 (36), 257 (38), 243 (85), 242 (72), 230 (52), 217 (96), 215 (95), 187 (100). (Found: C, 67.90; H, 5.22. Calc for $C_{17}H_{16}O_5$: C, 67.99; H, 5.73%).

5-Methoxy-3-(6-methyl-5-oxoheptanoyl)-1,4-naphthoquinone (**9c**)

To a soln (CH_3CN, 70 ml) of **17c** (745 mg, 2.17 mmol) was added an aqueous soln of CAN (2.947 g) at room temp and the mixture was stirred for 10 min. After the usual work-up, quinone **9c** (627 mg, 88%) was obtained as yellow needles recrystallized from ether–hexane; m.p. 100–108°; NMR (100 MHz, $CDCl_3$) δ 1.07 (6H, d, J = 7 Hz), 1.93 (2H, quintet, J = 7 Hz), 2.55 (3H, m), 2.92 (2H, t, J = 7 Hz), 3.99 (3H, s), 6.89 (1H, s), 7.28 (1H, m), 7.66 (2H, m); IR(KBr) 1700, 1665, 1585, 1470, 1300, 1275, 1220 cm^{-1}; MS *m/e* 329 (M^+ + 1, 20), 328 (M^+, 92), 310 (20), 385 (78), 257 (92), 243 (66), 242 (35), 217 (52), 215 (100). (Found: C, 69.29; H, 6.15. Calc for $C_{19}H_{20}O_5$: C, 69.50; H, 6.14%).

5-Methoxy-3-(6,6-dimethyl-5-oxoheptanoyl)-1,4-naphthoquinone (**9d**)

To a soln (CH_3CN, 60 ml) of **17d** (1.446 g, 4.04 mmol) was added an aqueous soln of CAN (5.486 g) at room temp and the mixture was stirred for 10 min. After the usual work-up, **9d** (1.228 g, 89%) was obtained as yellow needles recrystallized from ether–hexane; m.p. 71–74°; NMR(100 MHz, $CDCl_3$) δ 1.12 (9H, s), 1.92 (2H, quintet, J = 7 Hz), 2.59 (2H, t, J = 7 Hz), 2.93 (2H, t, J = 7 Hz), 4.00 (3H, s), 6.91 (1H, s), 7.30 (1H, m), 7.68 (2H, m); IR(KBr) 1700, 1660, 1585, 1470, 1300, 1280, 1230 cm^{-1}; MS *m/e* 343 (M^+ + 1, 3), 342 (M^+, 13), 286 (100), 285 (51), 258 (54), 241 (48), 215 (35). (Found: C, 70.02; H, 6.48. Calc for $C_{20}H_{22}O_5$: C, 70.16; H, 6.47%).

General procedure for the preparation of **11** *from* **9**

To a CH_2Cl_2 soln (20 ml/1 mmol) of **9** and **10**, (1.2 equiv to quinone **9**) was added $SnCl_4$ (1.2 equiv) at −78° with stirring and the color of the soln turned to deep purple. After addition was completed, the mixture was gradually warmed up to −20° during about 2 hr. The mixture was quenched at the temp by adding NH_4Cl aq and a small amount of ether. The organic layer was separated and the aqueous phase was extracted with CH_2Cl_2 several times. The combined organic phase was washed with brine and dried over Na_2SO_4. The solvent was evaporated to give a brown oil, which was again dissolved in a small amount of ether. To this ethereal soln was added an amount of n-hexane carefully until the soln became slightly cloudy. The soln was allowed to stand in a freezer overnight. A brownish yellow ppt formed. After the supernatant soln was removed by decantation, the ppt was rinsed with n-hexane several times. Although the ppt could be purified by recrystallizing from ether–hexane to yield **18**, *mono*silylation was carried out without further purification. The crude material, t-butyldimethylsilyl chloride (200 mg/1 mmol), and imidazole (200 mg/1 mmol) were placed in a vessel which was purged with N_2. DMF (1 ml/1 mmol) was added to the vessel and the mixture was stirred at room temp. During the course of the reaction, the brown soln turned to pale orange. After stirring for 4 hr, the mixture was quenched with NH_4Cl aq and CH_2Cl_2. Prolonged reaction time caused unfavorable disilylation. The organic layer was separated and the aqueous phase was extracted with CH_2Cl_2 several times. The combined organic phase was washed with brine. The organic phase was passed through a drying column (Na_2SO_4 and $MgSO_4$) and subsequently through a short silica gel column in order to remove imidazole. The solvent was evaporated to give a brown oil which was purified by column chromatography on silica gel using methanol-free CH_2Cl_2–ether (0 → 5%) as eluent to give pure **11**. Further purification was performed by recrystallization from ether–hexane.

Methyl 4-(1'-t-butyldimethylsilyloxy-4'-hydroxy-5'-methoxy-3'-(5"-oxoheptanoyl)-naphth-2'-yl)-2-butenoate (**11a**)

The reaction of **9a** (1.760 g, 5.60 mmol) with **10** was carried out according to the general procedure. *Methyl* 4 - (4' - *hydroxy* - 5' - *methoxy* - 1' - *oxo* - 3' - (5" - *oxoheptanoyl*) - 1',2' - dihydronapth - 2' - *yl*) - 2 - *butenoate* (**18a**) (1.855 g, 4.48 mmol, 80%) was obtained. Dihydronaphthylbutenoate **18a** was

monosilyated to give 1.743 g (53% from **9a**) of **11a**: pale yellow crystals; m.p. 109–111°; NMR (100 MHz, $CDCl_3$) δ 0.13 (6H, s), 1.06 (9H, s; 3H, t, J = 7 Hz), 2.44 (2H, quartet, J = 7 Hz), 2.52 (2H, t, J = 7 Hz), 2.94 (2H, t, J = 7 Hz), 3.67 (3H, s; 2H, d, J = 6 Hz), 4.03 (3H, s), 5.64 (1H, d, J = 16 Hz), 6.86 (1H, d, J = 8 Hz), 6.96 (1H, dt, J = 16, 6 Hz), 7.36 (1H, t, J = 8 Hz), 7.65 (1H, d, J = 8 Hz), 9.35 (1H, s); IR(KBr) 3360, 1715, 1675, 1645, 1610, 1590, 1410, 1370, 1260, 1165, 1050 cm^{-1}; MS *m/e* 528 (M^+, 100), 510 (44), 444 (22), 402 (15). (Found: C, 65.67; H, 7.58. Calc for $C_{29}H_{40}O_7Si$: C, 65.88; H, 7.63%).

Compound **18a**: pale yellow crystals; m.p. 95–103°; NMR (100 MHz, $CDCl_3$) δ 1.05 (3H, t, J = 7 Hz), 1.96 (2H, quintet, J = 7 Hz), 2.3–2.7 (8H, m), 3.70 (3H, s; 1H, t, J = 6 Hz), 4.02 (3H, s), 5.71 (1H, d, J = 16 Hz), 6.76 (1H, dt, J = 16, 8 Hz), 7.31 (1H, dd, J = 8, 2 Hz), 7.45–7.75 (2H, m), 17.40 (1H, s); IR(KBr) 1705, 1680, 1650, 1580, 1290, 1260, 1205 cm^{-1}; MS *m/e* 415 ($M^+ + 1$, 26), 414 (M^+, 100), 396 (11), 315 (14), 269 (22), 256 (17), 255 (17). (Found: C, 66.54; H, 6.28. Calc for $C_{23}H_{26}O_7$: C, 66.65; H, 6.32%).

Methyl 4-(1′-*t-butyldimethylsilyoxy-4′-hydroxy-5′-methoxy-3′-(5″-oxohexanoyl)naphth-2′-yl)-2-butenoate* (**11b**)

According to the general procedure, the reaction of **9b** (1.128 g, 3.76 mmol) with **10** was performed to give *methyl* 4-(4′-*hydroxy*-5′-*methoxy*-1′-*oxo*-3′-(5″-*oxohexanoyl*)-1′,2′-*dihydronaphth*-2′-*yl*)-2-*butenoate* (**18b**) and subsequent treatment with t-$BuMe_2SiCl$ and imidazole gave 1.620 g (60% from **9b**) of butenoate **11b**: pale yellow crystals; m.p. 129–130°; NMR (100 MHz, $CDCl_3$) δ 0.13 (6H, s), 1.06 (9H, s), 1.97 (2H, quintet, J = 7 Hz), 2.14 (3H, s), 2.54 (2H, t, J = 7 Hz), 2.94 (2H, t, J = 7 Hz), 3.66 (2H, m), 3.68 (3H, s), 4.05 (3H, s), 5.63 (1H, d, J = 16 Hz), 6.85 (1H, d, J = 8 Hz), 6.96 (1H, dt, J = 16, 6 Hz), 7.36 (1H, t, J = 8 Hz), 7.65 (1H, d, J = 8 Hz), 9.35 (1H, s); IR(KBr) 3320, 1720, 1660, 1650, 1610, 1590, 1430, 1375, 1255, 1210 cm^{-1}; MS *m/e* 516 ($M^+ + 2$, 11), 515 ($M^+ + 1$, 37), 514 (M^+, 100), 496 (14), 383 (17), 371 (22), 370 (20). (Found: C, 65.59; H, 7.59. Calc for $C_{28}H_{38}O_7Si$: C, 65.34; H, 7.44%).

Compound **18b**: pale yellow crystals; m.p. 70–80°; NMR (100 MHz, $CDCl_3$) δ 1.98 (2H, quintet, J = 7 Hz), 1.17 (3H, s), 2.4–2.7 (6H, m), 3.69 (3H, s; 1H, m), 4.01 (3H, m), 5.70 (1H, d, J = 16 Hz), 6.74 (1H, dt, J = 16, 8 Hz), 7.33 (1H, dd, J = 8, 2 Hz), 7.58 (2H, m), 17.05 (1H, s); IR(KBr) 1720, 1690, 1660, 1600, 1560, 1430, 1310, 1270, 1210 cm^{-1}; MS *m/e* 401 ($M^+ + 1$, 25), 400 (M^+, 100), 315 (15), 269 (23), 256 (26), 255 (20). (Found: C, 66.26; H, 6.07. Calc for $C_{22}H_{24}O_7$: C, 65.99; H, 6.04%).

Methyl 4-(1′-*t-butyldimethylsilyloxy-4′-hydroxy-5′-methoxy-(6″-methyl-5″-oxoheptanoyl)naphth-2′-yl*)-2-*butenoate* (**11c**)

According to the general procedure, the reaction of **9c** (728 mg, 2.22 mmol) with **10** was carried out to give *methyl* 4-(4′-*hydroxy*-5′-*methoxy*-3-(6″-*methyl*-5″-*oxoheptanoyl*)-1′-*oxo*-1′,2′-*dihydronaphth*-2′-*yl*)-2-*butenoate* **18c** (902 mg, 95%) and subsequent treatment with t-$BuMe_2SiCl$ and imidazole afforded 900 mg (75% from **9c**) of **11c**: pale yellow crystals; m.p. 89–90°; NMR (100 MHz, $CDCl_3$) δ 0.13 (6H, s), 1.97 (9H, s), 1.09 (6H, d, J = 7 Hz), 1.93 (2H, quintet, J = 7 Hz), 2.56 (3H, m), 2.91 (2H, t, J = 7 Hz), 3.61 (2H, m), 3.65 (3H, s), 4.02 (3H, s), 5.60 (1H, d, J = 16 Hz), 6.79 (1H, d, J = 8 Hz), 6.89 (1H, dt, J = 16, 6 Hz), 7.28 (1H, t, J = 8 Hz), 7.58 (1H, d, J = 8 Hz), 9.27 (1H, s); IR(KBr) 3400, 1720, 1690, 1650, 1615, 1595, 1580, 1380, 1270 cm^{-1}; MS *m/e* 544 ($M^+ + 2$, 12), 543 ($M^+ + 1$, 40), 542 (M^+, 100), 524 (20), 444 (14), 383 (24), 371 (33), 370 (26). (Found: C, 66.20; H, 7.91. Calc for $C_{30}H_{42}O_7Si$: C, 66.39; H, 7.80%).

Compound **18c**: pale yellow crystals; m.p. 81–84°; NMR (100 MHz, $CDCl_3$) δ 1.09 (6H, d, J = 7 Hz), 1.96 (3H, m), 2.3–2.8 (6H, m), 3.66 (3H, s; 1H, m), 3.98 (3H, s), 5.67 (1H, d, J = 16 Hz), 6.69 (1H, dt, J = 16, 8 Hz), 7.2–7.7 (3H, m), 17.03 (1H, s); IR (KBr) 1720, 1690, 1655, 1600, 1590, 1295, 1270, 1210 cm^{-1}; MS *m/e* 429 ($M^+ + 1$, 27), 428 (M^+, 100), 410 (8), 400 (11), 315 (16), 288 (13), 269 (24), 256 (20), 255 (19). (Found: 428.1841. Calc for $C_{24}H_{28}O_7$: 428.1835).

Methyl 4-(1′-*t-butyldimethylsilyloxy-4′-hydroxy-5′-methoxy-3′-(6″,6″-dimethyl-5″-oxoheptanoyl)naphth-2′-yl*)-2-*butenoate* (**11d**)

According to the general procedure, the reaction of **9d** (1.004 g, 2.936 mmol) with **10** was carried out to give 1.107 g (85%) of *methyl* 4-(4′-*hydroxy*-5′-*methoxy*-3′-(6″,6″-*dimethyl*-5″-*oxoheptanoyl*-1′-*oxo*-1′,2-*dihydronaphth*-2′-*yl*)-2-*butenoate* (**18d**) and subsequent treatment of **18d** (1.068 g, 2.42 mmol) with t-$BuMe_2SiCl$ and imidazole afforded 855 mg (64%: 54% calc from **9d**) of **11d**: pale orange crystals; m.p. 105–106°; NMR (100 MHz, $CDCl_3$) δ 0.12 (6H, s), 1.06 (9H, s), 1.13 (9H, s), 1.91 (2H, quintet, J = 7 Hz), 2.58 (2H, t, J = 7 Hz), 2.90 (2H, t, J = 7 Hz), 3.60 (2H, m), 3.64 (3H, s), 4.02 (3H, s), 5.59 (1H, d, J = 16 Hz), 6.79 (1H, d, J = 8 Hz), 6.89 (1H, dt, J = 16, 6 Hz), 7.48 (1H, t, J = 8 Hz), 7.58 (1H, d, J = 8 Hz), 9.26 (1H, s); IR(KBr) 3400, 1720, 1700, 1690, 1650, 1615, 1595, 1385, 1280 cm^{-1}; MS *m/e* 558 ($M^+ + 2$, 13), 557 ($M^+ + 1$, 41), 556 (M^+, 100), 538 (40), 444 (29), 429 (12), 402 (17), 383 (24), 372 (18), 361 (61), 339 (46). (Found: C, 66.59; H, 8.25. Calc for $C_{31}H_{44}O_7Si$: C, 66.87; H, 7.97%).

Compound **18d**: pale yellow crystals; m.p. 110–112°; NMR (100 MHz, $CDCl_3$) δ 1.15 (9H, s), 1.94 (2H, quartet, J = 7 Hz), 2.4–2.7 (6H, m), 3.68 (3H, s; 1H, m), 4.00 (3H, s), 5.69 (1H, d, J = 16 Hz), 6.75 (1H, dt, J = 16, 8 Hz), 7.28 (1H, dd, J = 8, 2 Hz), 7.53 (2H, m), 17.15 (1H, s); IR(KBr) 1715, 1700, 1690, 1655, 1600, 1585, 1310, 1290, 1265, 1205 cm^{-1}; MS *m/e* 443 ($M^+ + 1$, 29), 442 (M^+, 100), 330 (16), 315 (15), 288 (14), 269 (21), 257 (23), 256 (19), 255 (18). (Found: C, 67.99; H, 7.05. Calc for $C_{25}H_{30}O_7$: C, 67.86; H, 6.83%).

"Zipper" cyclization

Entry 1. To a soln (dry MeOH, 50 ml) of K_2CO_3 (276 mg, 2 mmol) was added a soln of **11a** (320 mg, 0.61 mmol) in THF (5 ml) at room temp under a N_2. After stirring for 2 hr, the mixture was quenched with NH_4Cl aq and extracted with CH_2Cl_2. The organic phase was washed with brine and dried over Na_2SO_4. After evaporating the solvent, the residue was purified by column chromatography on silica gel (MeOH-free CH_2Cl_2 as eluent) to give 198 mg (62%) of diastereomeric **20a** (*trans*: *cis* = 2:1): orange yellow viscous oil, yellow fluorescence in soln; NMR (100 MHz, $CDCl_3$) δ 0.14 (6H), 1.0 (3H), 1.08 (9H), 2.25 (2H), 1.6–3.4 (10H), 3.66 (3H of *trans* isomer; s), 3.68 (3H of *cis* isomer; s), 4.02 (3H), 6.86 (1H, dd, J = 8, 2 Hz), 7.54 (2H), 14.90 (1H of *cis* isomer; s), 15.04 (1H of *trans* isomer; s); IR(neat) 2920, 1715, 1705, 1605, 1255, 1050 cm^{-1}; MS *m/e* 528 (M^+, 100), 526 (51), 510 (8), 456 (8). (Found: 528.2525. Calc for $C_{29}H_{40}O_7Si$: 528.2543).

Entry 2. To a dry MeOH soln (10 ml) of NaOMe (54 mg) was added a dry THF soln (5 ml) of **11a** (30 mg) at −78° under a N_2. The mixture was allowed to warm to room temp. After stirring for 2 hr, the mixture was quenched with NH_4Cl aq and extracted with CH_2Cl_2. The extract was washed with brine and dried over Na_2SO_4. After evaporating the solvent, the residue was purified by column chromatography on silica gel to give 29 mg of diastereomeric **20a** (*trans*: *cis* = 2:1).

Entry 3. To a dry THF soln (100 ml) of KO′Bu was added a dry THF soln (100 ml) of **11a** (528 mg, 1 mmol) at −78° under a N_2. The mixture was gradually warmed to −50° and stirred for 2 hr. An NH_4Cl aq was added to the mixture at the temp to quench the reaction. The mixture was allowed to warm to room temp and extracted with CH_2Cl_2. The organic phase was washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave yellow solids. Recrystallization of the solids from ether–hexane afforded 206 mg of *methyl* (6a-SR,9-RS,10-SR,10a-RS)-9-*ethyl*-12-*t*-*butyldimethylsilyloxy*-5,9-*dihydroxy*-4-*methoxy*-6-*oxo*-6,6a,7,8,9,10,10a,11-*octahydronaphthacene*-10-*carboxylate* (**21a**): yellow needles, yellow fluorescence in soln; m.p. 199–205°; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.09 (3H, s), 0.13 (3H, s), 0.95 (3H, t, J = 7 Hz), 1.08 (9H, s) 1.35 (1H, m, J = 13.0, 10.0, 2.4 Hz), 1.42 (1H, d-quartet, J = 15.3, 7.3 Hz), 1.48 (1H, d-quartet, J = 15.3, 7.3 Hz), 1.82 (1H, m, J = 13.4, 11.0, 3.7 Hz), 2.37–2.50 (3H, m), 3.11 (1H, d, J = 12.2 Hz), 3.20 (1H, s), 6.84 (1H, m), 7.45–7.56 (2H, m), 15,04 (1H, s); ^{13}C-NMR ($CDCl_3$) δ 203.8, 175.5, 160.9,

159.7, 138.0, 135.0, 130.0, 123.0, 115.5, 115.0, 110.1, 105.9, 71.1, 56.7, 51.8, 49.7, 36.1, 34.7, 33.0, 30.2, 25.9, 20.3, 18.5, 7.7, −3.0, −3.5; IR(KBr) 3510, 2950, 1700, 1605, 1250, 1065 cm^{-1}; MS *m/e* 530 (M^+ + 2, 11), 529 (M^+ + 1, 36), 528 (M^+, 100), 499 (2), 382 (2), 325 (3), 267 (3), 259 (6). (Found: C, 65.93; H, 7.65. Calc for $C_{29}H_{40}O_7Si$: C, 65.88; H, 7.63%). The mother liquor was chromatographed on silica gel (MeOH-free CH_2Cl_2 as eluent) to give 172 mg (combined 378 mg, 72%) and 144 mg (27%) of **20a** (*trans*:*cis* = 2:1).

Entry 4. To a suspension of NaH (240 mg, 10 mmol; dry DMF/THF = 10 ml/10 ml) was added a soln of **11a** (528 mg, 1 mmol; dry THF, 10 ml) at 0° under a N_2. After stirring for 2 hr, the mixture was quenched with NH_4Cl aq and extracted with CH_2Cl_2. The organic phase was washed with brine and dried over Na_2SO_4. After evaporating the solvent, the residue was chromatographed on silica gel (methanol free CH_2Cl_2 as eluent) to give 53 mg (10%) of 12-*t*-*butyldimethylsilyloxy*-5,9-*dihydroxy*-4-*methoxy*-6-*oxo*-8-*propionyl*-6,6a,7,10,10a,11-*hexahydronaphthacene* (**24**): less polar fraction; NMR (100 MHz, $CDCl_3$) δ 0.10 (3H, s), 0.18 (3H, s), 1.10 (9H, s), 1.13 (3H, t, J = 7 Hz), 1.9–2.8 (7H, m), 2.8–3.2 (2H, m), 3.40 (1H, m), 4.03 (3H, s), 6.90 (1H, m), 7.80 (2H, m), 14.95 (1H, s), 15.67 (1H, s); and 468 mg (89%) of **21a**.

Entry 5. To a dry THF soln (3 ml) of diazabicycloundecene (DBU; 0.15 ml) was added a dry THF (5 ml) soln of **11a** (47 mg) at −78° under a N_2. The mixture was then allowed to warm to room temp. After stirring for 4.5 hr, the mixture was quenched with an NH_4Cl aq and extracted with CH_2Cl_2. The organic phase was washed with brine and dried over Na_2SO_4. The solvent was evaporated to give 47 mg of a crude material which consisted of a mixture of diastereomeric **20a** (*trans*:*cis* = *ca* 2:1) by its NMR analysis.

Entry 6. To a dry THF suspension (3 ml) of activated alumina (2 g, Woelm super I) was added a dry THF soln (5 ml) of **11a** at room temp under a N_2. After stirring for 19 hr, water (5 ml) was added to the suspension. Alumina was filtered and washed with THF and MeOH. The filtrate was concentrated to give a brownish yellow oil which consisted of a mixture of **20a** (72%) and **21a** (28%) estimated by its NMR analysis. Preparative TLC of the mixture gave 35 mg (66%) of **20a** and 4 mg (8%) of **21a**.

Entry 7. To a dry THF suspension (10 ml) of KH (160 mg, 4 mmol) and 18-crown-6 (264 mg, 1 mmol) was added a dry THF soln (10 ml) of **11a** (71 mg, 0.134 mmol) at −78° under a N_2. The mixture was gradually warmed up to 0° during 2 hr. The reaction was quenched with an NH_4Cl aq and extracted with CH_2Cl_2. The organic phase was washed with brine and dried over Na_2SO_4. The solvent was evaporated to give a yellow solid which consisted only of **21a**.

Entry 8. To a dry THF suspension (5 ml) of LiH (20 mg) was added a dry THF (5 ml) soln of **11a** (141 mg, 0.267 mg) and hexamethylphosphoric triamide (HMPA, 0.2 ml) at room temp. After stirring for 17 hr, the mixture was quenched with an NH_4Cl aq and extracted with CH_2Cl_2. The organic phase was washed with brine and dried over Na_2SO_4. After evaporating the solvent, the residue was developed on preparative TLC. From the upper yellow fluorescent band, 108 mg (77%) of **21a** was obtained. From the lower yellow fluorescent band, 18 mg (13%) of **23a** was obtained. *Methyl* (6a-SR,9-SR,10-SR,10a-RS)-9-*ethyl*-12-*t*-*butyldimethylsilyloxy*-5,9-*dihydroxy*-4-*methoxy*-6-*oxo*-6,6a,7,8,9,10,10a,11-*octahydronaphthacene*-10-*carboxylate* (**23a**): yellow crystals recrystallized from ether–hexane; yellow fluorescence in soln; m.p. 205–210°; NMR (400 MHz, $CDCl_3$) δ 0.14 (6H, s), 0.90 (3H, t, J = 7.3 Hz), 1.07 (9H, s), 1.25–1.45 (3H, m), 1.73 (1H, sextet, J = 14.6, 7.3 Hz), 2.20–2.41 (5H, m), 2.62 (1H, d, J = 10.4 Hz), 3.38 (1H, dd, J = 15.2, 2.4 Hz), 3.78 (3H, s), 4.02 (3H, s), 6.84 (1H, d, J = 7.7 Hz), 7.49 (1H, t, J = 8.2 Hz), 7.55 (1H, d, J = 8.3 Hz), 14.83 (1H, s); IR(KBr) 3400, 1700, 1610, 1570, 1380, 1250 cm^{-1}.

General procedure for cryptate controlled "Zipper" cyclization

An excess amount of KH and additives: Kryptofix 222 (1 equiv E. Merck, Jpn) and HMPA (1 equiv), were suspended in dry THF (30 ml/1 mmol) under N_2. After stirring for 1 hr at room temp, the suspension was cooled down to −78°. To the suspension was added a dry THF soln (50 ml/1 mmol) of **11**. The reaction was performed under the conditions listed in Table 1. The reaction mixture was quenched with an NH_4Cl aq and extracted with CH_2Cl_2 several times. The organic phase was washed with brine and dried over Na_2SO_4. After evaporating the solvent, the residue was chromatographed (preparative TLC or column chromatography on silica gel).

Entry 9. According the the general procedure, the reaction of **11a** (53 mg) was carried out at the temp from −78° to −50° for 3 hr. Separation of the mixture by preparative TLC gave 12 mg (23%) of **21a** and 28 mg (53%) of *methyl* (6a-SR, 9-RS,10-RS,10a-RS)-9-*ethyl*-12-*t*-*butyldimethylsilyloxy*-5,9-*dihydroxy*-4-*methoxy*-6-*oxo*-6,6a,7,8,9,10,10a,11-*octahydronaphthacence*-10-*carboxylate* (**22a**): orange yellow crystals recrystallized from ether–hexane, yellow fluorescence in solution; m.p. 97–101°; NMR (400 MHz, $CDCl_3$) δ 0.10 (3H, s), 0.14 (3H, s), 0.97 (3H, t, J = 7.3 Hz), 1.10 (9H, s), 1.44 (1H, d-quartet, J = 14.1, 7.3 Hz), 1.52 (1H, d-quartet, J = 14.1, 7.3 Hz), 1.58–1.62 (2H, m), 2.13 (1H, dt, J = 13.6, 4.4 Hz), 2.26 (1H, dd, J = 15.9, 13.5 Hz), 2.43 (1H, m), 2.45 (1H, m), 2.85 (1H, d, J = 4.9 Hz), 2.98 (1H, dt, J = 12.8, 4.1 Hz), 3.20 (1H, dd, J = 16.4, 2.9 Hz), 3.71 (3H, s), 4.01 (3H, s), 6.82 (1H, d, J = 7.8 Hz), 7.48 (1H, t, J = 8 Hz), 7.55 (1H, d, J = 8.3 Hz), 15.15 (1H, s); IR(KBr) 3460, 2900, 1720, 1600, 1240, 1060 cm^{-1}; MS *m/e* 528 (M^+, 100), 334 (8), 326 (5). (Found: 528.2491. Calc for $C_{29}H_{40}O_7Si$: 528.2543).

Entry 10. According to the general procedure, the reaction of **11a** (528 mg, 1 mmol) was carried out at the temp from −78° to −60° for 12 hr. The NMR spectrum of the mixture showed the ratio of **20a**:**21a**:**22a** to 18:24:54. Separation of the mixture by column chromatography on silical gel (MeOH-free CH_2Cl_2 as eluent) and preparative TLC gave 87 mg (17%) of *trans* isomer of **20a**, 83 mg (16%) of **21a**, and 264 mg (50%) of **22a**.

Entry 11. According to the general procedure, the reaction of **11a** (53 mg, 0.1 ml) was carried out at −78° for 9 hr. The NMR spectrum of the mixture showed the presence of starting material (67%) and the *trans* isomer of **20a** (33%).

Entry 12. According to the general procedure except for using NaH instead of KH, the reaction of **11a** (53 mg, 0.1 mmol) was carried out under 0° for 4.5 hr. The mixture consisted of **21a** (46%) and **22a** (41%) by NMR analysis.

Entry 13. According to the general procedure except for using NaH and Kryptofix 221 instead of KH and Kryptofix 222, the reaction of **11a** (53 mg, 0.1 mmol) was carried out under 0° for 2 hr. The reaction mixture consisted of **21a** (40%) and **22a** (60%) by the NMR analysis.

Entry 14. According to the general procedure except for using LiH and Kryptofix 211 instead of KH and Kryptofix 222, the reaction of **11a** (53 mg, 0.1 mmol) was carried out at room temp for 7.5 hr. The reaction mixture consisted of **21a** (91%) and **22a** (9%) by the NMR analysis.

Entry 15. To a dry THF suspension (3 ml) of KH (20 mg) was added a dry THF soln (5 ml) of **11b** (51 mg, 0.1 mmol) at −78° under a N_2. The mixture was allowed to warm to 0°. After stirring for 2 hr, the mixture was quenched with an NH_4Cl aq and extracted with CH_2Cl_2 several times. After evaporating the solvent, the residue was chromatographed on silica gel (MeOH-free CH_2Cl_2 as eluent) to give 42 mg (82%) of *methyl* (6a-SR,9-RS,10-SR,10a-RS)-12-*t*-*butyldimethylsilyloxy*-5,9-*dihydroxy*-4-*methoxy*-9-*methyl*-6-*oxo*-6,6a,7,8,9,10,10a,11-*octahydronapthacene*-10-*carboxylate* (**21b**): yellow needles recrystallized from ether–hexane, yellow fluorescence in soln; m.p. 224–227°; NMR (400 MHz, $CDCl_3$) δ 0.10 (3H, s), 0.16 (3H, s), 1.08 (9H, s), 1.22 (3H, s), 1.41 (1H, t), 1.84 (1H, d-quartet), 1.99 (1H, td, J = 14.1 Hz), 2.20–2.33 (2H, m), 2.33–2.45 (3H, m), 3.12 (1H, d, J = 12.7 Hz), 3.36 (1H, OH), 3.82 (3H, s), 4.01 (3H, s), 6.84 (1H, d, J = 7.8 Hz), 7.49 (1H, m), 7.54 (1H, m', 15.03 (1H, s); IR(KBr) 3400, 1730, 1610, 1575, 1380, 1250 cm^{-1}; MS *m/e* 516 (M^+ + 2, 11), 515 (M^+ + 1, 37), 514 (M^+, 100), 456 (2), 383 (3), 382 (4), 333 (4). (Found: C, 65.34; H, 7.65. Calc for $C_{28}H_{38}O_7Si$: C, 65.34; H, 7.44%).

Entry 16. According to the general procedure, the reaction

of **11b** (357 mg, 0.695 mmol) was carried out at the temp from −78° to −50° for 3 hr. Separation of the mixture by column chromatography and preparative TLC (silica gel, MeOH-free CH_2Cl_2 as eluent) gave 173 mg (48%) of **21b**, 124 mg (35%) of *methyl* (6a - SR,9 - RS,10 - RS,10a - RS) - 12 - *t-butyldimethylsilyloxy* - 5,9 - *dihydroxy* - 4 - *methoxy* - 9 - *methyl* - 6 - *oxo* - 6,6a,7,8,9,10,10a,11 - *octahydronaphthacene* - 10 - *carboxylate* (**22b**): yellow needles recrystallized from ether–hexane, yellow fluorescence in soln; m.p. 162–166°; NMR (400 MHz, $CDCl_3$) δ 0.09 (3H, s), 0.13 (3H, s), 1.09 (9H, s), 1.25 (3H, s), 1.62 (1H, t, J = 10.7 Hz), 2.21 (1H, dt, J = 15.5, 4.6 Hz), 2.28 (1H, dd, J = 15.1, 13.2 Hz), 2.35–2.50 (2H, m), 2.80 (1H, d, J = 3.9 Hz), 2.95 (1H, dt, J = 11.7, 4.5 Hz), 3.18 (1H, dd, J = 16.3, 3.1 Hz), 3.71 (3H, s), 4.00 (3H, s), 6.82 (1H, d, J = 7.8 Hz), 7.47 (1H, t, J = 8.0 Hz), 7.54 (1H, d, J = 8.3 Hz), 15.12 (1H, s); IR(KBr) 3520, 3440, 1720, 1610, 1575, 1380, 1250 cm^{-1}; MS *m/e* 516 (M^+ + 2, 12), 515 (M^+ + 1, 38), 514 (M^+, 100), 456 (3), 325 (6). (Found: 514.2433. Calc for $C_{28}H_{38}O_7Si$: 514.2387), and 48 mg (13%) of *methyl* (6a - SR,9-SR,10 - SR,10a - RS) - 12 - *t-butyldimethylsilyloxy* - 5,9 - *dihydroxy* - 4 - *methoxy* - 9 - *methyl* - 6 - *oxo* - 6,6a,7,8,9,10,10a,11 - *octahydronaphthacene* - 10 - *carboxylate* (**23b**): yellow crystals recrystallized from ether–hexane, yellow fluorescence in soln; m.p. 155–160°; NMR (400 MHz, $CDCl_3$) δ 0.13 (3H, s), 0.14 (3H, s), 1.07 (9H, s), 1.25 (3H, s), 1.47 (1H, d-quartet, J = 14.2, 3.0 Hz), 1.65 (1H, dt, J = 13.1, 2.9 Hz), 2.00 (1H, td, J = 12.7, 3.2 Hz), 2.17 (1H, d-quartet, J = 11.7, 3.0 Hz), 2.27–2.40 (2H, m), 2.46 (1H, quartet-d, J = 14.2, 3.9 Hz), 2.56 (1H, d, J = 11.2 Hz), 3.34 (1H, dd, J = 15.8, 3.2 Hz), 3.79 (3H, s), 4.02 (3H, s), 6.84 (1H, d, J = 7.3 Hz), 7.50 (1H, t, J = 8.0 Hz), 7.55 (1H, d, J = 7.8 Hz), 14.88 (1H, s); IR(KBr) 3460. 1725, 1615, 1580, 1390, 1255, 1165, 1060 cm^{-1}; MS *m/e* 516 (M^+ + 2, 12), 515 (M^+ + 1, 39), 514 (M^+, 100), 382 (6), 333 (7), 319 (8). (Found: 514.2400. Calc for $C_{28}H_{38}O_7Si$: 514.2387).

Entry 17. According to the procedure described in the case of entry 15 except that the reaction was quenched at −10° after stirring for 3 hr, the reaction of **11c** (54 mg, 0.1 mmol) gave 43 mg (80%) of *methyl* (6a - SR,9 - SR,10 - SR,10a - RS) - 12 - *t-butyldimethylsilyloxy* - 5,9 - *dihydroxy* - 4 - *methoxy* - 6 - *oxo* - 9 - (2 - *propyl*) - 6,6a,7,8,9,10,10a,11 - *octahydronaphthacene* - 10 - *carboxylate* (**21c**): yellow needles recrystallized from ether–hexane, yellow fluorescence in soln; m.p. 217–226°; NMR (400 MHz, $CDCl_3$) δ 0.07 (3H, s), 0.15 (3H, s), 0.94 (3H, d, J = 6.9 Hz), 0.98 (3H, d, J = 7.3 Hz), 1.07 (9H, s), 1.34 (1H, t, J = 13 Hz), 1.54 (1H, m), 1.80 (1H, m), 1.85 (1H, tt, J = 13.3 Hz), 2.21 (1H, dt, J = 11.5, 3.9 Hz), 2.25–2.50 (3H, m), 2.67 (1H, d, J = 10.7 Hz), 3.08 (1H, d, J = 12.7 Hz), 3.13 (1H, OH), 3.79 (3H, s), 4.01 (3H, s), 6.82 (1H, d, J = 7.8 Hz), 7.48 (1H, t, J = 8 Hz), 7.53 (1H, d, J = 8 Hz), 7.53 (1H, d, J = 8 Hz), 15.03 (1H, s); IR(KBr) 3510, 3420, 1710, 1610, 1575, 1390, 1260, 1070 cm^{-1}; MS *m/e* 544 (M^+ + 2, 12), 543 (M^+ + 1, 40), 542 (M^+, 100), 499 (5), 467 (4). (Found: C, 66.47; H, 8.05. Calc for $C_{30}H_{42}O_7Si$: C, 66.39; H, 7.80%).

Entry 18. According to the general procedure, the reaction of **11c** (109 mg, 0.2 mmol) was carried out at the temp from −78° to −50° for 3 hr. The NMR analysis of the mixture showed the presence of **21c** (27%) and *methyl* (6a - SR,9 - SR, 10 - SR,10a,RS) - 12 - *t-butyldimethylsilyloxy* - 5,9 - *dihydroxy* - 4 - *methoxy* - 6 - *oxo* - 9 - (2 - *propyl*) - 6,6a,7,8,9,10,10a, 11 - *octahydronaphthacene* - 10 - *carboxylate* (**22c**; 63%). Separation of the mixture by column chromatography gave 15 mg (14%) of **21c** and 68 mg (62%) of **22c**: yellow needles recrystallized from ether–hexane yellow fluorescence in soln; m.p. 155–160°; NMR (400 MHz, $CDCl_3$) δ 0.08 (3H, s), 0.13 (3H, s), 0.91 (3H, d, J = 6.8 Hz), 0.98 (3H, d, J = 6.8 Hz), 1.09 (9H, s), 1.55–1.65 (2H, m), 1.82 (1H, broad d, J = 14.1 Hz), 2.10 (1H, dt, J = 14.2, 4.4 Hz), 2.22 (1H, dd, J = 15.6, 13.2 Hz), 2.42 (2H, m), 2.91 (1H, dt, J = 12, 4.4 Hz), 2.97 (1H, d, J = 3.4 Hz), 3.19 (1H, dd, J = 15.6, 2.9 Hz), 3.71 (3H, s), 4.00 (3H, s), 6.82 (1H, d, J = 7.3 Hz), 7.47 (1H, t, J = 8 Hz), 7.55 (1H, d, J = 7.3 Hz), 15.14 (1H, s); IR(KBr) 3565, 1720, 1615, 1575, 1380, 1260, 1240 cm^{-1}; MS *m/e* 544 (M^+ + 2, 9), 543 (M^+ + 1, 40), 542 (M^+, 100), 326 (2), 325 (8). (Found: C, 66.37; H, 8.01. Calc for $C_{30}H_{42}O_7Si$: C, 66.39; H, 7.80%).

Entry 19. According to the procedure of entry 17, the reaction of **11d** (56 mg, 0.1 mmol) gave 30 mg (54%) of *methyl* (6a - SR,9 - SR,10 - SR,10a - RS) - 9 - *t-butyldimethylsilyloxy* - 5,9 - *dihydroxy* - 4 - *methoxy* - 6 - *oxo* - 6,6a,7,8,9,10,10a,11 - *octahydronaphthacene* - 10 - *carboxylate* (**21d**): yellow needles recrystallized from ether–hexane, yellow fluorescence in soln; m.p. 202–204°; NMR (100 MHz, $CDCl_3$) δ 0.07 (3H, s), 0.18 (3H, s), 0.96 (9H, s), 1.09 (9H, s), 1.3–3.2 (10H, m), 3.87 (3H, s), 3.99 (3H, s), 6.81 (1H, m), 7.40–7.60 (2H, m), 14.95 (1H, s); IR(KBr) 3520, 3440, 2960, 1710, 1615, 1575, 1390, 1260, 1170, 1070 cm^{-1}; MS *m/e* 558 (M^+ + 2, 13), 557 (M^+ + 1, 41), 556 (M^+, 100), 449 (11), 467 (12). (Found: 556.2880. Calc for $C_{31}H_{44}O_7Si$: 556.2857).

Entry 20. According to the general procedure, the reaction of **11d** (56 mg, 0.1 mmol) was carried out at the temp from −78° to −30° for 3.5 hr. The NMR analysis of the mixture showed the presence of **20d** (64%), **21d** (10%), and **22d** (26%).

Isomerization test of **22a**

According to the general procedure, the reaction of **22a** (61 mg, 0.115 mmol) was carried out at the temp from −55° to −40° for 3 hr. None of its isomers could be found in the NMR spectrum of the reaction mixture. Starting **22a** was recovered in an 82% yield (50 mg) by column chromatography on silica gel.

Isomerization test of **21a**

According to the general procedure, the reaction of **21a** (53 mg, 0.1 mmol) was carried out at −20° for 1 hr. Any other isomers could not be found by the NMR analysis of the mixture. Starting **21a** was recovered in a 57% yield (30 mg) by column chromatography on silica gel.

B-RING AROMATIZATION OF 22a

Method A

To an CH_3CN soln (50 ml) of **22a** (264 mg, 0.502 mmol) was added an aqueous soln of CAN (843 mg, 1.54 mmol) at room temp. After stirring for 10 min, CH_2Cl_2 (50 ml) and water (50 ml) was added and the organic phase was separated. The aqueous phase was extracted with ether. The combined organic phase was washed twice with brine. Then the organic phase was shaken with $Na_2S_2O_4$ aq. The orange yellow soln turned to a fine yellow fluorescent soln. After being dried over Na_2SO_4, the solvent was evaporated to give a brownish orange solid which consisted of **25a**. The crude **25a** was dissolved in $CHCl_3$ (20 ml) and CCl_4 (50 ml). The soln was refluxed and a CCl_4 soln of Br_2 (120 mg) containing a catalytic amount of AIBN was added to the refluxed soln. After refluxing for 1 hr, the solvent was evaporated *in vacuo*. The residue was again dissolved in CH_2Cl_2 (10 ml) and Et_3N (0.2 ml) was added at 0°. After stirring for 30 min under air, dilute HCl (*ca* 1%) was added and stirred for additional 5 min. The mixture was separated and the aqueous phase was extracted with CH_2Cl_2. The combined organic phase was washed with brine and dried over Na_2SO_4. After evaporating the solvent, the residue was chromatographed on silica gel (CH_2Cl_2 as eluent) to give 157 mg (76%) of (±) - 4 - O - *methyl* - 7 - *deoxyaklavinone* (**26a**): orange powder recrystallized from CH_2Cl_2-MeOH; m.p. > 230° (dec); NMR (400 MHz, $CDCl_3$) δ 1.07 (3H, t, J = 7.5 Hz), 1.58 (1H, s, OH), 1.60 (1H, d-quartet, J = 14.9, 7.5 Hz), 1.68 (1H, d-quartet, J = 14.9, 7.5 Hz), 1.91 (1H, ddd, J = 13.9, 7.0, 2.4 Hz), 2.29 (1H, ddd, J = 13.9, 10.3, 6.8 Hz), 2.83 (1H, ddd, J = 19.3, 10.3, 7.0 Hz), 3.05 (1H, ddd, J = 19.3, 6.8, 2.4 Hz), 3.70 (3H, s), 3.92 (1H, s), 4.06 (3H, s), 7.33 (1H, d, J = 8.4 Hz), 7.56 (1H, s), 7.71 (1H, t, J = 8.1 Hz), 7.92 (1H, d, J = 7.7 Hz), 13.38 (1H, s); IR(KBr) 3400, 1720, 1700, 1660, 1620, 1580, 1380, 1275, 1245 cm^{-1}; MS *m/e* 410 (M^+, 42), 392 (45), 354 (63), 333 (100), 321 (55), 292 (92). (Found: 410.1366. Calc for $C_{23}H_{22}O_7$: 410.1366).

Methyl (6a - SR,9 - RS,10 - RS,10a - RS) - 9 - *ethyl* - 9 - *hydoxy* - 4 - *methoxy* - 5,6,12 - *trioxo* - 5,6,6a,7,8,9,10,10a,11,12 - *decahydronaphthacene* - 10 - *carboxylate* (**28**): NMR (100

MHz, $CDCl_3$) δ 0.97 (3H, t, J = 7 Hz), 1.2–3.2 (12H, m), 3.75 (3H, s), 3.96 (3H, s), 7.31 (1H, m), 7.63 (2H, m).

Methyl (6a - SR,9 - RS,10 - RS,10 - RS) - 9 - *ethyl* - 5,9,12 - *trihydroxy* - 4 - *methoxy* - 6 - *oxo* - 6,6a,7,8,9,10,10a,11 - *octahydronaphthacene* (**25a**): NMR (100 MHz, $CDCl_3$) δ 0.95 (3H, t, J = 7 Hz), 1.2–3.2 (12H, m), 3.68 (3H, s), 6.82 (1H, m), 7.3–7.7 (3H, m), 15.00 (1H, s).

Quinomethide **29**: yellow fluorescence in soln; typical NMR signals ($CDCl_3$) at δ = 7.00 (1H, m), 15.92 (1H, s).

Method B

By the procedure described in Method A, hydroquinone **25a** was prepared from **24a** (61 mg, 0.16 mmol). A soln of **25a** in DMF (5 ml) was heated at 100° under O_2. After stirring at 100° for an hour, solvent was evaporated *in vacuo*. The residue was chromatographed on silica gel (MeOH-free CH_2Cl_2 as eluent) to give 11 mg (23%) of *methyl* 9 - *ethyl* - 6 - *hydroxy* - 4 - *methoxy* - 5,12 - *dioxo* - 5,7,8,12 - *tetrahydronaphthacene* - 10 - *carboxylate* (**30a**): orange needles recrystallized from $CHCl_3$-MeOH; m.p. 222–224°; NMR (100 MHz, $CDCl_3$) δ 1.15 (3H, t, J = 7 Hz), 2.40 (4H, m), 2.96 (2H, t, J = 8 Hz), 3.94 (3H, s), 4.07 (3H, s), 7.36 (1H, d, J = 8 Hz), 7.52 (1H, s), 7.73 (1H, t, J = 8 Hz), 7.96 (1H, d, J = 8 Hz), 13.30 (1H, s); IR(KBr) 1720, 1665, 1620, 1585, 1280, 1260 cm^{-1}; MS *m/e* 393 (M^+ + 1, 26), 392 (M^+, 77), 363 (35), 361 (37), 360 (100), 333 (23). (Found: 392.1270. Calc for $C_{23}H_{20}O_6$: 392.1260), and 29 mg (58%) of a mixture of **26a** (70 parts) and *methyl* (9 - RS,10 - SR) - 9 - *ethyl* - 6,9 - *dihydroxy* - 4 - *methoxy* - 5,12 - *dioxo* - 5,7,8,9,10,12 - *hexahydronaphthacene* - 10 - *carboxylate* (**31a**; 30 parts): yellow needles recrystallized from MeOH; m.p. 173–177°; NMR (400 MHz, $CDCl_3$) δ 1.00 (3H, t, J = 7.5 Hz), 1.57 (2H, quartet, J = 7.5 Hz), 1.81 (1H, dt, J = 18.9, 6.7 Hz), 2.28 (1H, dt, J = 18.9, 6.7 Hz), 2.76 (1H, dt, J = 13.7, 6.7 Hz), 3.06 (1H, dt, J = 13.7, 6.7 Hz), 3.04 (1H, s, OH), 3.84 (3H, s), 3.88 (1H, s), 4.03 (3H, s), 7.30 (1H, d, J = 8.5 Hz), 7.45 (1H, s), 7.68 (1H, t, J = 8.0 Hz), 7.87 (1H, d, J = 7.3 Hz), 13.42 (1H, s); IR(KBr) 3440, 1725, 1660, 1620, 1580, 1280, 1250 cm^{-1}; MS *m/e* 410 (M^+, 6), 392 (16), 354 (13), 333 (100). (Found: 410.1386. Calc for $C_{23}H_{22}O_7$: 410.1366).

Method C

By the procedure described in Method A, quinone **28** was prepared from 54 mg (0.102 mmol) of **27a**. The crude **28** was dissolved in THF and dilute HCl (5%, 5 drops) was added. The mixture was stirred at room temp for three days under air. After water was added, the mixture was extracted with CH_2Cl_2. The organic phase was washed with brine and dried over Na_2SO_4. After evaporating the solvent, the residue was chromatographed on silica gel (methanol-free CH_2Cl_2 as eluent) to give 24 mg (57%) of **26a**.

Demethylation of **26a**; *Preparation of* (±)-*galirubinone D*

To a CH_2Cl_2 soln (50 ml) of **26a** (146 mg, 0.356 mmol) was added $AlCl_3$ (400 mg) at room temp under a N_2. After complete consumption of **26a** (about 4 hr), the mixture was poured into ice-water with stirring. A mixture of NaCl and 5% dilute HCl (5 ml) was added to the resulting mixture and stirring was continued for 15 min. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2. The combined organic phase was washed with brine and dried over Na_2SO_4. After evaporating the solvent, crude material was chromatographed on silica gel (CH_2Cl_2 as eluent) to give 102 mg (72%) of (±)-*galirubinone D* (**27a**): orange powder recrystallized from MeOH; m.p. > 198° (dec); NMR (100 MHz, $CDCl_3$) δ 1.08 (3H, t, J = 7 Hz), 1.2–3.3 (7H, m), 3.73 (3H, s), 3.93 (1H, s), 7.25 (1H, m), 7.5–7.9 (3H, m), 12.02 (1H, s), 12.40 (1H, s); IR(KBr) 3400, 1720, 1660, 1610, 1280 cm^{-1}; MS *m/e* 396 (M^+, 36), 388 (46), 367 (25), 364 (28), 340 (57), 319 (94), 278 (100). (Found: 396.1212. Calc for $C_{22}H_{20}O_7$: 396.1210).

7-*Hydroxylation of* **27a**: *Preparation of* (±)-*aklavinone* (**1**)

Hydroxylation of the anthracyclinone at position 7 was carried out according to the reported method.[5] To a refluxed CCl_4 soln of **27a** (71 mg, 0.178 mmol) was added a CCl_4 soln of Br_2 (83 mg) containing a catalytic amount of azobisisobutyronitrile. After refluxing for 1 hr, the solvent was evaporated *in vacuo*. The residue was dissolved in THF (10 ml) and water (10 ml) was added. After stirring for 30 min at room temp, the reaction mixture was extracted with CH_2Cl_2. The extract was washed with brine and dried over Na_2SO_4. After evaporation of solvent crude material was purified by preparative TLC developed with CH_2Cl_2 to give 69 mg (94%) of (±)-*aklavinone* (**1**): orange yellow crystals recrystallized from $CHCl_3$ methanol; m.p. 199–203 and 223–228° (double m.ps); NMR (400 MHz, $CDCl_3$) δ 1.11 (3H, t, J = 7.6 Hz), 1.57 (1H, d-quartet, J = 14.1, 7.6 Hz), 1.72 (1H, d-quartet, J = 14.1, 7.6 Hz), 2.27 (1H, dt, J = 15.1, 1.4 Hz), 2.54 (1H, dd, J = 15.1 5.4 Hz), 3.70 (3H, s), 4.09 (1H, d, J = 1 Hz), 5.38 (1H, d, J = 4.4 Hz), 7.31 (1H, dd, J = 8.5, 1.2 Hz), 7.70 (1H, s; 1H, t, J = 8.1 Hz), 7.82 (1H, dd, J = 7.6, 1.2 Hz), 11.94 (1H, s), 12.71 (1H, s); IR(KBr) 3400, 1725, 1665, 1620, 1275 cm^{-1}; MS *m/e* 412 (M^+, 46), 394 (46), 376 (71), 365 (58), 335 (100), 333 (49). (Found: 412.1131. Calc for $C_{22}H_{20}O_8$: 412.1157). This substance was identical with natural aklavinone and synthesized aklavinone[5] in all respects.

B-RING AROMATIZATION OF **22b**

Method A

According to the procedure described in the B-ring aromatization of **22a** (Method A), the reaction of **22b** (32 mg, 0.062 mmol) was carried out to give 21 mg (85%) of *methyl* 6 - *hydroxy* - 4 - *methoxy* - 9 - *oxo* - 5,7,8,12 - *tetrahydronaphthacene* - 10 - *carboxylate* (**30b**): orange yellow needles recrystallized from $CHCl_3$-MeOH; m.p. 235–255° (decomp); NMR (100 MHz, $CDCl_3$) δ 2.10 (3H, s), 2.41 (2H, t, J = 8 Hz), 2.97 (2H, t, J = 8 Hz), 3.93 (3H, s), 4.08 (3H, s), 7.37 (1H, d, J = 8 Hz), 7.53 (1H, s), 7.73 (1H, t, J = 8 Hz), 7.96 (1H, d, J = 8 Hz), 13.29 (1H, s); IR(KBr) 3400, 1720, 1670, 1630, 1590, 1280, 1265 cm^{-1}; MS *m/e* 379 (M^+ + 1, 24), 378 (M^+, 100), 363 (25), 347 (14), 346 (15), 319 (51), 301 (26). (Found: 378.1099. Calc for $C_{22}H_{18}O_6$; 378.1095), and 111 mg (71%) of a diastereomeric mixture: **26b** and *methyl* (9 - RS,10 - SR) - 6,9 - *dihydroxy* - 4 - *methoxy* - 9 - *methyl* - 5,12 - *dioxo* - 5,7,8,9,10,12 - *hexahydronaphthacene* - 10 - *carboxylate* (**31b**): orange yellow crystals recrystallized from $CHCl_3$-MeOH; m.p. 192–197°; NMR (100 MHz, $CDCl_3$) δ 1.36 (3H, s), 1.77 (1H, dt, J = 14, 7 Hz), 2.30 (1H, dt, J = 14, 7 Hz), 2.6–3.2 (2H, m), 3.27 (1H, broad s, OH), 3.86 (4H, m), 4.03 (3H, s), 7.32 (1H, d, J = 8 Hz), 7.44 (1H, s), 7.68 (1H, t, J = 8 Hz), 7.87 (1H, d, J = 8 Hz), 13.35 (1H, s); IR(KBr) 3590, 3400, 1735, 1670, 1620, 1585, 1385, 1280, 1250 cm^{-1}; MS *m/e* 396 (M^+, 22), 378 (15), 354 (20), 353 (10), 319 (100). (Found: 396.1205. Calc for $C_{22}H_{20}O_7$: 396.1209).

Demethylation of **26b**

According to the procedure described in the demethylation of **26a**, the reaction of **26b** (42 mg, 0.106 mmol) was carried out to give 24 mg (59%) of (±)-7-*deoxyauramycinone* (**27b**): yellow powder recrystallized from $CHCl_3$-MeOH; m.p. 214–217°; NMR (100 MHz, $CDCl_3$) δ 1.41 (3H, s), 1.6–2.2 (2H, m), 2.8–3.2 (2H, m), 3.76 (3H, s), 3.92 (1H, s), 7.30 (1H, m), 7.55–7.90 (3H, m),

12.07 (1H, s), 12.46 (1H, s); IR(KBr) 3550, 3450, 1720, 1665, 1620, 1280, 1245 cm^{-1}; MS *m/e* 383 (M^+ + 1, 5), 382 (M^+, 24), 364 (18), 308 (11), 307 (41), 306 (24), 305 (100), 304 (22), 279 (29). (Found: 382.1060. Calc for $C_{21}H_{18}O_7$: 382.1053), and 13 mg (31%) of recovered starting material **26b**.

7-Hydroxylation of **27b**: *Preparation of* (±)-*auramycinone* (**2**)

According to the procedure described in the preparation of (±)-**1**, the reaction of **27b** (19 mg, 0.0497 mmol) was carried out to give 17 mg (86%) of (±)-*auramycinone* (**2**): yellow crystals recrystallized from $CHCl_3$-MeOH; m.p. 183–186 and 266–270° (double m.ps); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.43 (3H, s), 2.23 (1H, d, J = 15.2 Hz), 2.62 (1H, dd, J = 14.6, 5.4 Hz), 3.38 (1H, broad s, OH), 3.72 (3H, s), 4.04 (1H, broad s, OH), 4.06 (1H, s), 5.39 (1H, d, J = 4.9 Hz), 7.32 (1H, d, J = 8.8 Hz), 7.70 (1H, s; 1H, t, J = 7.8 Hz), 7.84 (1H, d, J = 7.4 Hz), 11.96 (1H, s), 12.74 (1H, s); ^{13}C-NMR ($CDCl_3$) δ 192.5, 181.0, 171.1, 162.4, 160.9, 142.2, 137.4, 133.3, 132.5, 132.4, 124.7, 121.1, 120.1, 115.5, 114.5, 69.7, 62.5, 57.8, 52.4, 36.8, 27.4; IR (KBr) 3440, 1730, 1665, 1620, 1470, 1450, 1390, 1290, 1255 cm^{-1}; MS *m/e* 398 (M^+, 33), 380 (46), 362 (13), 322 (23), 321 (100). (Found: 398.1007. Calc for $C_{21}H_{18}O_8$: 398.1002). These spectroscopic data (^{13}C-NMR, IR, and MS) are identical with ones of natural auramycinone[3] except for the m.p. (lit[3] m.p. for (+)-**2**: 153.5°).

B-RING AROMATIZATION OF 22c

Method A

According to the procedure applied to the preparation of **26a** (Method A), the reaction of **22c** (167 mg, 0.308 mmol) was carried out to give 102 mg (78%) of (±)-4-*O*-*methyl*-7-*deoxy*-13-*methylaklavinone* (**26c**): orange yellow crystals recrystalized from CH_2Cl_2-MeOH; m.p. 215–217°; NMR (400 MHz, $CDCl_3$) δ 1.04 (3H, d, J = 7.0 Hz), 1.11 (3H, d, J = 7.0 Hz), 1.37 (1H, s, OH), 1.80 (1H, septet, J = 7 Hz), 2.10 (1H, dd, J = 14.1, 7.5 Hz), 2.30 (1H, ddd, J = 14.3, 11.4, 7.3 Hz), 2.82 (1H, ddd, J = 19.4, 11.3, 8 Hz), 3.12 (1H, dd, J = 19.4, 6.2 Hz), 3.69 (3H, s), 4.04 (1H, s), 4.07 (3H, s), 7.34 (1H, d, J = 8.8 Hz), 7.61 (1H, s), 7.72 (1H, t, J = 8.3 Hz), 7.93 (1H, dd, J = 7.5, 1 Hz), 13.47 (1H, s); IR(KBr) 3440, 1735, 1665, 1630, 1590, 1370, 1260 cm^{-1}; MS *m/e* 424 (M^+, 76), 406 (30), 392 (25), 354 (58), 349 (39), 347 (51), 321 (64), 307 (57), 293 (100). (Found: 424.1527. Calc for $C_{24}H_{24}O_7$: 424.1522).

Accompanying **26c**, the reaction gave 12 mg (10%) of *methyl* 6-*hydroxy*-4-*methoxy*-5,12-*dioxo*-9-(2-*propyl*)-5,7,8,12-*tetrahydronaphthacene*-10-*carboxylate* (**30c**): orange yellow needles recrystallized from CH_2Cl_2-MeOH; m.p. 228–229°; NMR (400 MHz, $CDCl_3$) δ 1.13 (6H, d, J = 6.8 Hz), 2.34 (2H, t, J = 8.3 Hz), 2.85–2.95 (3H, m), 7.36 (1H, d, J = 8 Hz), 7.49 (1H, s), 7.73 (1H, t, J = 8 Hz), 7.95 (1H, d, J = 8 Hz), 13.28 (1H, s); IR(KBr) 3440, 1720, 1665, 1625, 1585, 1280, 1260 cm^{-1}; MS *m/e* 407 (M^+ + 1, 20), 406 (M^+, 100), 391 (11), 375 (15), 374 (30), 363 (15), 347 (24). (Found: 406.1414. Calc for $C_{24}H_{22}O_6$: 406.1415).

Method B

According to the procedure described in the preparation of **26a** (Method B), the reaction of **22c** (158 mg, 0.292 mmol) was performed to give 14 mg (12%) of **30c**, and 93 mg (75%) of a diastereomeric mixture; **26c** (64%) and **31c** (11%).

Methyl (9-SR,10-SR)-6,9-*dihydroxy*-4-*methoxy*-5,12-*dioxo*-9-(2-*propyl*)-5,7,8,9,10,12-*hexahydronaphthacene*-10-*carboxylate* (**31c**): orange yellow needles recrystallized from $CHCl_3$-MeOH; m.p. 187–189°; NMR (400 MHz, $CDCl_3$) δ 1.00 (3H, d, J = 7.0 Hz), 1.03 (3H, d, J = 7.0 Hz), 1.72 (1H, septet, J = 7.0 Hz), 1.83 (1H, dt, J = 13.2, 6.6 Hz), 2.19 (1H, dt, J = 13.8, 6.6 Hz), 2.84 (1H, dt, J = 19.4, 6.3 Hz), 3.00–3.10 (2H, m), 3.85 (3H, s), 4.08 (3H, s), 4.13 (1H, s), 7.35 (1H, d, J = 8.4 Hz), 7.49 (1H, s), 7.74 (1H, t, J = 8 Hz), 7.95 (1H, dd, J = 7.7, 1 Hz), 13.45 (1H, s); IR(KBr) 3460, 1720, 1665, 1625, 1585, 1280, 1240 cm^{-1}; MS *m/e* 424 (M^+, 25), 406 (46), 381 (21), 363 (36), 354 (100), 347 (91), 321 (39), 293 (71). (Found: 424.1524. Calc for $C_{24}H_{24}O_7$: 424.1522).

Demethylation of **26c**

According to the procedure described in the demethylation of **26a**, the reaction of **26c** (58 mg, 0.137 mmol) was carried out to give 20 mg (36%) of (±)-7-*deoxy*-13-*methylaklavinone* (**27c**): yellow powder recrystallized from CH_2Cl_2-MeOH; m.p. 238–241°; NMR (100 MHz, $CDCl_3$) δ 1.05 (3H, d, J = 7 Hz), 1.14 (3H, d, J = 7 Hz), 1.5–2.0 (2H, m), 2.0–2.4 (1H, m), 2.75–3.30 (2H, m), 3.71 (3H, s), 4.05 (1H, s), 7.24 (1H, m), 7.4–7.9 (3H, m), 12.10 (1H, s), 12.45 (1H, s); IR(KBr) 3440, 1765, 1665, 1625, 1585, 1390, 1280 cm^{-1}; MS *m/e* 411 (M^+ + 1, 11), 410 (M^+, 50), 392 (85), 378 (22), 367 (53), 349 (29), 340 (55), 333 (65), 307 (100), 305 (99). (Found: 410.1362. Calc for $C_{23}H_{22}O_7$: 410.1365), and 21 mg (41%) of (3a-SR,13b-SR)-6,8-*dihydroxy*-3,3-*dimethyl*-7,12-*oxo*-3,3a,4,5,7,12,13b-*octahydronaphthaceno*[1,2-c]*furan* (**32**): orange plates recrystallized from $CHCl_3$-MeOH; m.p. 267–270°; NMR (400 MHz, $CDCl_3$) δ 1.43 (1H, m, J = 12.7, 4.4 Hz), 1.51 (3H, s), 1.56 (3H, s), 2.17 (1H, m), 2.43 (1H, m), 2.49 (1H, m), 3.25 (1H, m), 4.10 (1H, d, J = 6.8 Hz), 7.29 (1H, d, J = 8.3 Hz), 7.68 (1H, t, J = 7.8 Hz), 7.84 (1H, d, J = 7.8 Hz), 8.01 (1H, s), 12.08 (1H, s), 12.50 (1H, s); IR(KBr) 3440, 1770, 1675, 1620, 1450, 1390, 1280 cm^{-1}; MS *m/e* 378 (M^+, 42), 334 (47), 319 (67), 291 (100). (Found: 378.1101. Calc for $C_{22}H_{18}O_6$: 378.1102).

7-Hydroxylation of **27c**: *preparation of* (±)-13-*methylaklavinone* (**3**)

According to the procedure described in the preparation of **1**, the reaction of **27a** (10.3 mg, 0.0251 mmol) was carried out to give 8 mg (75%) of (±)-13-*methylaklavinone* (**3**): yellow powder recrystallized from CH_2Cl_2-MeOH; m.p. 207–211° (lit.[4] m.p. 216°); NMR (400 MHz, $CDCl_3$) δ 1.07 (3H, d, J = 6.4 Hz), 1.12 (3H, d, J = 6.8 Hz), 1.71 (1H, septet, J = 6.6 Hz), 2.40 (1H, d, J = 15.1 Hz), 2.57 (1H, dd, J = 15, 5.5 Hz), 3.38 (1H, broad s, OH), 3.63 (1H, broad s, OH), 3.69 (3H, s), 4.24 (1H, s), 5.38 (1H, m), 7.31 (1H, d, J = 8.3 Hz), 7.70 (1H, t, J = 7.7 Hz), 7.74 (1H, s), 7.83 (1H, d, J = 7.8 Hz), 11.96 (1H, s), 12.72 (1H, s); IR(KBr) 3450, 1730, 1670, 1620, 1470, 1450, 1390, 1285 cm^{-1}; MS *m/e* 426 (M^+, 26), 408 (9), 390 (11), 366 (23), 365 (100), 349 (22). (Found: 426.1313. Calc for $C_{23}H_{22}O_8$: 426.1314). These spectroscopic data are identical with the reported data.[4]

B-RING AROMATIZATION OF 21a

Method A

According to the procedure described in the aromatization of **22a** (Method A), the reaction of **21a** (505 mg, 0.956 mmol) was carried out to give 287 mg (73%) of **31a**.

Methyl (6a-SR,9-RS,10-SR,10a-RS)-9-*ethyl*-9-*hydroxy*-4-*methyl*-5,6,12-*trioxo*-5,6,6a,7,8,9,10,10a,11,12-*decahydronaphthacene*-10-*carboxylate* (**36**): orange crystals recrystallized from CH_2Cl_2-ether–hexane; m.p. 114–120°; NMR (400 MHz, $CDCl_3$) δ 0.94 (3H, m), 1.30 (3H, m), 1.45 (2H, m), 1.82–2.00 (2H, m), 2.05 (2H, m), 2.18 (1H, dt, J = 12, 4 Hz), 2.60 (1H, dd, J = 19.2, 11 Hz), 2.47 (1H, d, J = 11 Hz), 2.54 (1H, dt, J = 12, 4 Hz), 2.81 (1H, dd, J = 19.2, 4.0 Hz), 3.84 (3H, s), 3.96 (3H, s), 7.29 (1H, m), 7.62–7.65 (2H, m); IR(KBr) 3400, 1710, 1660, 1580, 1270 cm^{-1}; MS *m/e* 414 (M^+ + 2, 34), 412 (M^+, 17), 410 (M^+ − 2, 13), 394 (35), 392 (34), 354 (35), 333 (100). (Found: 412.1528. Calc for $C_{23}H_{24}O_7$: 412.15222).

Quinomethide **37**: yellow fluorescence in soln; NMR (400 MHz, $CDCl_3$) δ 0.95 (3H, t, J = 7.7 Hz), 1.30 (1H, dt, J = 13, 4 Hz), 1.49 (2H, m), 1.87 (1H, m), 1.96 (1H, td, J = 14.1, 3 Hz), 2.24 (1H, m), 2.30 (1H, dt, J = 12.8, 3.0 Hz), 2.62 (1H, d, J = 12.0 Hz), 3.12 (1H, broad s, OH), 3.19 (1H, dt, J = 12.8, 3 Hz), 3.87 (3H, s), 4.00 (3H, s), 6.76 (1H, d, J = 2.5 Hz), 7.28 (1H, d, J = 8.1 Hz), 7.59 (1H, t, J = 8.1 Hz), 7.93 (1H, d, J = 7.7 Hz), 15.80 (1H, s); MS *m/e* 410 (M^+, 28), 392 (55), 354 (26), 335 (37), 334 (72), 333 (100).

Method B

According to the Method A described above, desilylation of **21a** (83 mg, 0.157 mmol) was performed to give the corresponding hydroquinone. The crude hydroquinone was dissolved in THF (40 ml) and oxygen gas was bubbled through

the soln. After stirring at room temp for five days under an oxygen atmosphere, the solvent was evaporated and the residue was chromatographed on silica gel (CH_2Cl_2 as eluent) to give 48 mg (75%) of **31a**.

Demethylation of **31a**

According to the procedure described in demethylation of **26a**, the reaction of **31a** (197 mg, 0.480 mmol) was carried out to give 161 mg (85%) of *methyl* (9 - RS,10 - SR) - 9 - *ethyl* - 4,6,9 - *trihydroxy* - 5,12 - *dioxo* - 5,7,8,9,10,12 - *hexahydronaphthacene* - 10 - *carboxylate* (**33**): orange yellow needles recrystallized from CH_2Cl_2-MeOH; m.p. 203–206°; NMR (100 MHz, $CDCl_3$) δ 1.00 (3H, t, J = 7 Hz), 1.56 (2H, quartet, J = 7 Hz), 1.80 (1H, m), 2.29 (1H, m), 2.7–3.3 (3H, m), 3.87 (3H, s), 3.92 (1H, s), 7.30 (1H, m), 7.59 (1H, s), 7.64–7.95 (2H, m), 12.08 (1H, s), 12.46 (1H, s); IR(KBr) 3440, 3200, 1720, 1660, 1600, 1440, 1410, 1375, 1250 cm^{-1}; MS *m/e* 396 (M^+, 4), 378 (19), 367 (6), 364 (8), 348 (10), 340 (15), 315 (100). (Found: 396.1185. Calc for $C_{22}H_{20}O_7$: 396.1209).

Hydroxylation of **33**

According to the procedure described in the preparation of (±)-aklavinone, the reaction of **33** (33 mg, 0.080 mmol) was carried out to give 24 mg (73%) of (±)-*9-epiaklavinone* (**35**): orange yellow crystals recrystallized from CH_2Cl_2-MeOH; m.p. 204–210°; NMR (400 MHz, $CDCl_3$) δ 1.04 (3H, t, J = 7.6 Hz), 1.69 (2H, quartet, J = 7.6 Hz), 1.86 (1H, dd, J = 13.9, 7.0 Hz), 2.59 (1H, dd, J = 13.9, 7.0 Hz), 3.89 (3H, s), 4.00 (1H, s), 5.40 (1H, t, J = 7.0 Hz), 7.30 (1H, dd, J = 8.5, 1.2 Hz), 7.53 (1H, s), 7.69 (1H, t, J = 8.0 Hz), 7.79 (1H, dd, J = 7.5, 1.2 Hz), 11.91 (1H, s), 12.82 (1H, s); IR(KBr) 3400, 1715, 1655, 1610, 1440, 1260 cm^{-1}; MS *m/e* 412 (M^+, 11), 394 (40), 376 (23), 365 (50), 335 (100), 319 (34). (Found: C, 64.11; H, 5.00. Calc for $C_{22}H_{20}O_8$: C, 64.07; H, 4.89%).

B-ring aromatization of **20a**

To an acetonitrile soln (30 ml) of **20a** (132 mg, 0.25 mmol) was added an aqueous soln of CAN (340 mg) at room temp. After stirring for 10 min, CH_2Cl_2 and water were added and the organic phase was separated. The aqueous phase was extracted with CH_2Cl_2. The combined organic phase was washed with brine and dried over Na_2SO_4. After evaporating the solvent, the residue was again dissolved in CH_2Cl_2 (30 ml). To the soln was added 4-dimethylaminopyridine (37 mg, 0.3 mmol) at room temp under air. After stirring overnight, diluted aqueous HCl (*ca* 1%) was added. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2. The combined organic phase was washed with brine and dried over Na_2SO_4. After evaporating the solvent, the residue was chromatographed on silica gel (CH_2Cl_2 as eluent) to give 68 mg (66%) of *methyl* 4 - *hydroxy* - 6 - *methoxy* - 5,10 - *dioxo* - 3 - (3 - *oxopentyl*) - 5,10 - *dihydroanthr* - 2 - *yl acetate* (**42**): yellow needles recrystallized from MeOH; m.p. 181–182°; NMR (100 MHz, $CDCl_3$) δ 1.06 (3H, t, J = 7 Hz), 2.48 (2H, quartet, J = 7 Hz), 2.7–3.1 (4H, m), 3.72 (3H, s), 3.87 (2H, s), 4.04 (3H, s), 7.37 (1H, d, J = 8 Hz), 7.61 (1H, s), 7.73 (1H, t, J = 8 Hz), 7.92 (1H, d, J = 8 Hz), 13.44 (1H, s); IR(KBr) 3400, 1715, 1700, 1660, 1620, 1580, 1375, 1275, 1240, 1175 cm^{-1}; MS *m/e* 410 (M^+, 53), 392 (23), 355 (53), 354 (100), 352 (69). (Found: C, 67.53; H, 5.40. Calc for $C_{23}H_{22}O_7$: C, 67.31; H, 5.40%).

Quinone **44**: diastereomeric mixture; brown oil; NMR (100 MHz, $CDCl_3$) δ 1.04 (3H, t, J = 7 Hz), 1.6–3.2 (12H, m), 3.78 (3H, s), 4.02 (3H, s), 7.20–7.45 (1H, m), 7.55–7.80 (1H, m).

Quinomethide **45**: diastereomeric mixture; brown oil, yellow fluorescence in solution; NMR (100 MHz, $CDCl_3$) δ 1.04 (3H, t, J = 7 Hz), 1.7–3.3 (11H, m), 3.70 (3H), 4.01 (3H), 7.04 (1H, d, J = 6 Hz), 7.27 (1H, d, J = 8 Hz), 7.60 (1H, t, J = 8 Hz), 7.96 (1H, d, J = 8 Hz), 16.04 (1H, s).

Demethylation of **42**

According to the procedure described in the demethylation of **26a**, the reaction of **42** (41 mg, 0.1 mmol) was carried out to give 36 mg (91%) of *methyl* 3,5 - *dihydroxy* - 5,10 - *dioxo* - 3 - (3 - *oxopentyl*) - 5,10 - *dihydroanthr* - 2 - *ylacetate* (**43**): yellow needles recrystallized from MeOH; m.p. 181–183° (lit.[17] m.p. 182°); NMR (100 MHz, $CDCl_3$) δ 1.06 (3H, t, J = 7 Hz), 2.24 (2H, quartet, J = 7 Hz), 2.6–3.1 (4H, m), 3.72 (3H, s), 3.88 (2H, s), 7.22 (2H, dd, J = 8, 2 Hz), 7.5–7.8 (3H, m), 11.93 (1H, s), 12.40 (1H, s); IR(KBr) 3400, 1710, 1700, 1665, 1615, 1590, 1290, 1260 cm^{-1}; MS *m/e* 396 (M^+, 48), 378 (26), 349 (28), 340 (100). (Found: C, 66.39; H, 5.03. Calc for $C_{22}H_{20}O_7$: C, 66.66; H, 5.09%).

Intramolecular aldol condensation of **43**

To an ice cooled soln (THF/MeOH = 4 m/1 ml) of **43** (24 mg, 0.059 mmol) was added a methanolic soln of Triton B (30%, 0.1 ml). After stirring for 5 hr, HCl aq (*ca* 1%) was added. The mixture was extracted with CH_2Cl_2. The extract was washed with brine and dried over Na_2SO_4. After evaporating the solvent, the residue was chromatographed on silica gel (CH_2Cl_2 as eluent) to give 23 mg (96%) of a mixture (**27a** : **33** = *ca* 1 : 1).

Hydroxylation of the mixture of **27a** *and* **33**

According to the procedure described in the preparation of **1**, the reaction of the mixture (63 mg, **27a** : **33** = *ca* 1 : 1) was carried out to give 32 mg (49%) of (±)-(**1**) and 30 mg (46%) of (±)-(**35**).

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