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Synthesis of Skeleton of Antitumor Quassinoid

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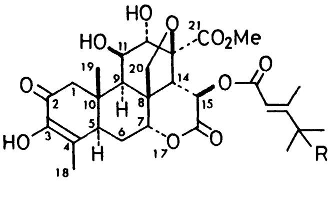
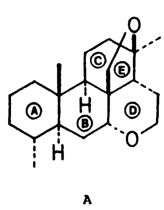
A compound having a skeleton of an antitumor quassinoid, bruceantin, was prepared according to the following strategy; 1) construction of ring ABC from ring AB by cyclization of a hindered 1,5-diketone; 2) construction of ring E (ether ring) by opening of a 12,13-epoxide ring followed by attack of oxygen at C-20 toward C-13; 3) formation of ring D (hemiacetal ring) by treatment of a 7α-hydroxy-16-al dimethyl acetal with PPTS.

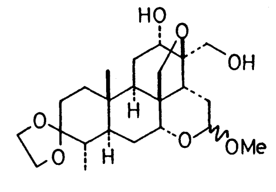
Quassinoids, highly degraded triterpenes which are isolated from Simaroubaceae plants specifically, have a wide spectrum of biological properties.[1] Among a large number of quassinoids,[1,2] bruceantin (**1**) and bruceantinol (**2**) which have a skeletal structure **A** exhibit remarkable antileukemic activity.[3] Although a large number of efforts for syntheses of antitumor quassinoids have been reported,[4] none of them accomplished the total synthesis. The first synthesis of a compound having the skeletal structure **A** has been achieved by the authors.[4] The synthetic plan was based on AB → ABC → ABCE → ABCDE ring strategy. The details of the synthesis of compound **3** which has the skeletal structure **A** bearing functional groups at suitable positions for syntheses of antitumor quassinoids are described in this paper.



1: R=H
2: R=OH



A



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The first problem of our strategy was the construction of ABC ring from AB ring. It has been reported by Snitman et al.[5] that on Robinson annulation the hindered 1,5-diketone **4** did not yield **5** giving the retro-Michael product as the principal one and the similar compound **6** afforded cyclized compound **7** in only 15% yield. It was eventually found that a 1,5-diketone bearing a conjugated diene system at C-3 through C-6[6] gave a cyclized product in better yield than that of **7** from **6**. Steric compression around the carbonyl group at C-9 may have been decreased by the introduction of the diene system. The conjugated double bond is also useful for further syntheses because the diene system is stable on treatments with acid and base and introduction of oxygen functional groups into suitable positions in rings **A** and **B** (C-3 and C-7) utilizing the diene system is possible.

The retro-Michael reaction occurs hardly when 1,5-diketones having a methyl group instead of the methoxycarbonyl group are used for the cyclization reaction. Therefore, reaction of 1,5-diketone **11** was examined first to check the feasibility of the cyclization reaction. The tricyclic compound **12** was smoothly obtained from **11** which was prepared by the following sequences. Reduction of the known monoacetal **8**[7] with sodium borohydride was followed by an acid treatment to yield a diene **9** in a quantitative yield. The diene **9** was monomethylated by the treatment with methyl iodide in the presence of lithium diisopropylamide (LDA) to give **10** in 85% yield. The Michael addition reaction of methyl vinyl ketone to **10** proceeded in the presence of 0.3 equivalent of sodium methoxide in methanol at room temperature to afford **11**. The cyclization of the adduct **11** was accomplished to give tricyclic compound **12** by heating at reflux in methanol with 1 equivalent of sodium methoxide. The reactions to obtain **12** from **10** were carried out in one pot and the yield was 89%.

As the cyclization reaction of the 1,5-diketone **11** proceeded in high yield, the 1,5-diketone **14** having a methoxycarbonyl group and the diene system was examined next. The 1,5-diketone **14** was prepared by addition of methyl vinyl ketone to the β-keto ester **13** which was obtained by the methoxycarbonylation of the ketone **9**. The diketone **14** gave retro-Michael reaction product as major one on heating with sodium methoxide in methanol or on heating with pyrrolidine in benzene. However, on treatment with the same reaction conditions (a combination of pyrrolidine and benzoic acid) as those with which **6** afforded the cyclization product **7** in 15% yield,[5] **14** yielded the cyclization product **15** in 52% yield.

Several combinations of benzoic acid derivatives and

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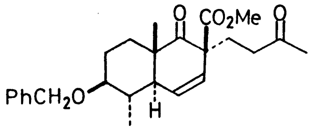
amines were examined to obtain **15** from **14** in better yield. Although couples of benzoic acid and secondary amines (pK_a) [pyrrolidine (11.3), piperidine (11.1), diethylamine (10.9), and morpholine (8.3)] did not show any remarkable change of the yield of **15**, couples of pyrrolidine and benzoic acid derivatives (pK_a) [*m*-toluic acid (4.94), *o*-toluic acid (4.79), benzoic acid (4.21), *m*-hydroxybenzoic acid (4.08), salicylic acid (3.00), and 3,5-dinitrobenzoic acid (2.82)] exhibited serious change of the yield of **15**. The weaker acid coupled with the amine gave **15** in the better yield. When salicylic and 3,5-dinitrobenzoic acids were used, only retro-Michael reaction occurred. The reason why the couple of pyrrolidine with the weaker benzoic acid gives **15** in better yield is not clear, but we consider that the weaker acid makes more tight complex with amines in benzene and suppresses base-catalyzed retro-Michael reaction.[8] It was also found that the use of excess amount of the acid made the yield better. And the treatment of **14** with 1.2 equivalent of *m*-toluic acid and 0.2 equivalent of pyrrolidine in benzene heated at reflux through Molecular Sieves 4A to remove water gave **15** in good yield (80—90%). By these reaction conditions, cyclization of **11** was accomplished in 6 h to give **12** in almost quantitative yield.



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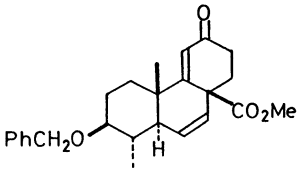

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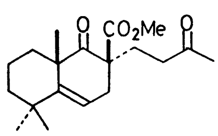

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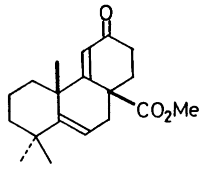

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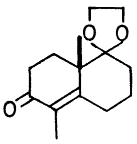

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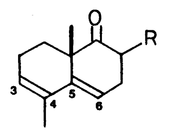
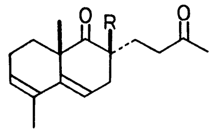
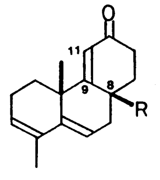


9: R=H
10: R=Me
13: R=CO$_2$Me



11: R=Me
14: R=CO$_2$Me

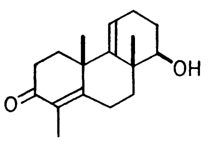


12: R=Me
15: R=CO$_2$Me

The stereochemistry of the methoxycarbonyl group of **15** was supposed to be β, because the Michael addition of methyl vinyl ketone to **13** was considered to proceed from less hindered opposite side to the angular methyl group. This was confirmed by conversion of the methoxycarbonyl group at C-8 of **15** into methyl group to give **12** and conversion of **12** into the α,β-unsaturated ketone **21**. The authentic specimen of **21** was derived from the known tricyclic compound **16**[9] via conjugated diene **17**, ketone **18**, tosylhydrazone **19**, and the enol thioether **20** according with the method developed by Nakai and Mimura.[10] The tricyclic compound **16** has been used for the construction of picrasane skeleton (skeletal structure **A** without ring E) by the authors.[9]

The UV absorption maximum at 302 nm indicates the presence of a conjugated enol thioether structure in **20**. This means that 1,3-shift of the proton at C-12 to C-14 occurred on the reaction of the tosylhydrazone **19** into the enol thioether **20**. Although hydrolysis of the enol thioether **20** using mercury(II) chloride gave the product in very poor yield and treatment of the thioether with titanium tetrachloride in acetic acid[11] afforded a complex mixture, on treatment with titanium tetrachloride in THF followed by addition of aqueous acetic acid **20** yielded the conjugated ketone **21** as a major product.

The transformations of **15** into **21** via **12** were carried out by the following reactions. Protection of the carbonyl group of **15** to give acetal **22**, whose methoxycarbonyl group was reduced with lithium alminium hydride (LAH) to yield alcohol **23**, which was oxidized with Collins' reagent to give aldehyde **24**. Wolff-Kishner reduction of **24** followed by treatment with



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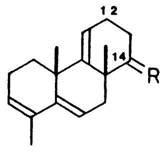
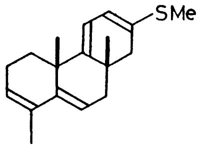


17: R=α-H,β-OH
18: R=O
19: R=NNHTs



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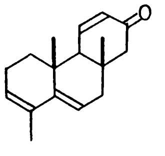

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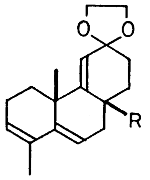
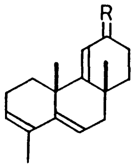


22: R=CO$_2$Me
23: R=CH$_2$OH
24: R=CHO

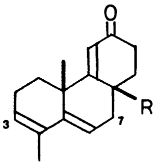


25: R=NNHTs

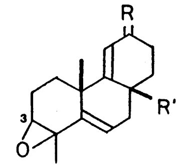
dilute hydrochloric acid gave the tricyclic compound **12**. The tricyclic compound **12** was converted into the conjugated ketone **21** via tosylhydrazone **25** and the enol thioether **20** using similar methods as those used for the conversion of **18** into **21**.

Although the diene system at C-3 through C-6 was very effective for the construction of the ring ABC, efficient methods for introduction of oxygen functions into C-3 and C-7 utilizing the diene system remained to be developed. A selective introduction of an oxygen function in a protected form into C-3 was desirable and it was performed by epoxidation with *m*-chloroperbenzoic acid (MCPBA) followed by a treatment under acetalization conditions. Hydrolysis of the acetal **23** gave ketone **26**, whose hydroxyl group was acetylated by the usual method to give acetate **27**. The acetate **27** afforded a 3 : 1 mixture of the α-epoxide **28α** and β-epoxide **28β** on epoxidation with MCPBA. The proton at C-3 was observed as a broad singlet ($W_{1/2}$=4.5 Hz) and a doublet (J=3.6 Hz) for **28α** and **28β**, respectively. Although **28α** afforded the acetal **29** in 90% yield by the treatment with ethylene glycol and boron trifluoride etherate ($BF_3 \cdot Et_2O$) in benzene at room temperature, **28β** gave a complex mixture by the same treatment. The fact suggests that the acetal at C-3 can be derived only from the α-epoxide and the use of a compound which gives α-epoxide in high selectivity is desirable.

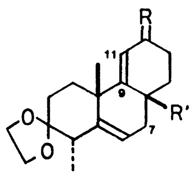
On epoxidation with MCPBA the monoacetal **22** afforded a 5 : 1 mixture of α- and β-epoxides (**30α** and **30β**). On treatment with ethylene glycol and $BF_3 \cdot Et_2O$ in benzene, the mixture yielded a 6 : 1 mixture of monoacetal **31** and diketone **32**. On acetalization under standard conditions the mixture of **31** and **32** afforded diacetal **33**. The overall yield of **33** from **22** was 64%. The diacetal **33** was obtainable from **15** by two steps (epoxidation and acetalization), but the ratio of the α- and β-epoxides (**34α** and **34β**) obtained by epoxidation of **15** with MCPBA was 2 : 1 and the final yield of **33** was low.



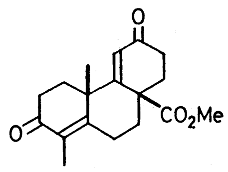
26: R=CH$_2$OH
27: R=CH$_2$OAc



28: R=O, R'=CH$_2$OAc
30: R=-O(CH$_2$)$_2$O-, R'=CO$_2$Me
34: R=O, R'=CO$_2$Me



29: R=O, R'=CH$_2$OAc
31: R=O, R'=CO$_2$Me
33: R=-O(CH$_2$)$_2$O-, R'=CO$_2$Me



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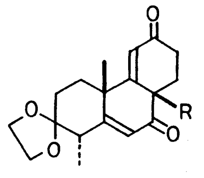


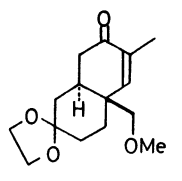
35: R=CO$_2$Me
36: R=CH$_2$OAc

Allylic oxidation of some tricyclic compounds obtained so far was tried to introduce an oxygen function into C-7. Oxidation of diacetal **33** yielded diketone **35**, but the yield (27%) was too low to continue the further syntheses. Oxidation of the acetate **29** afforded ketone **36** in poor yield. In our previous synthetic studies of quassinoids, it has been experienced that the yield of allylic oxidation at C-7 was seriously affected by the substituents of ring C. Therefore, we decided to examine the introduction of oxygen function into C-7 at the later stage.

Introduction of two carbon appendage into C-14 position through 1,4-addition was our strategy and so the presence of the double bond at C-9 (11) was undesirable. As introduction of oxygen function into the double bond at C-9 (11) was unsuccessful, reduction of the double bond was examined. Reduction of the double bond at C-9 (11) of the tetrahydropyranyl (THP) ether **38** derived from the α,β-unsaturated ketone **37** was tried by three methods. The saturated ketone **39** was given in 48%, 77%, and 99% yield on catalytic hydrogenation using 10% palladium on carbon, Birch reduction using lithium, and reduction with sodium hydrogentelluride (NaHTe),[12] respectively. The stereochemistry of the newly generated chiral center (C-9) of **39** was suggested to be α-H, because hydrogen attacks from less hindered α-side on catalytic hydrogenation. Although the protecting group of the hydroxyl group at C-20 was necessary to be removed without significant effect on the acetal at C-3, the selective removal of the THP group of **39** was hard. After several trials, it was found that 1-ethoxyethyl (EE) group was a satisfactory protecting group which could be removed selectively in almost quantitative yield. The EE ether **40** obtained by the treatment of **37** with ethyl vinyl ether and pyridinium *p*-toluenesulfonate (PPTS) was reduced with NaHTe to give ketone **41** in 98% yield.

Introduction of a double bond at C-13 was necessary prior to addition of two carbon unit to C-14. Regioselectivity of phenylselenylation of the EE ether **41** was poor, but a methoxycarbonyl group was regioselectively introduced into C-13 of **41** giving **42** (83% yield) by treatment with dimethyl carbonate and sodium hydride containing catalytic amount of potassium hydride.[13] When the reaction was carried out without potassium hydride, the yield of **42** was very low. The ratio of keto and enol forms of β-keto ester **42** produced is variable. Phenylselenylation of **42** and successive oxidative elimination of the phenylseleno group afforded α,β-unsaturated ester **43**.[14] Heathcock et al.[15] reported that addition of ketene acetal **44** to the "very reactive" Michael acceptor **45**, whose structure is very close to **43**, required 15 kbar for 24 h to do drive the reaction to completion. But a vinyl group was successfully introduced into the C-14 position of **43** to give **46** by conjugate addition of vinylmagnesium bromide catalyzed with a complex of copper(I) iodide and tributylphosphine[16] at −45 °C in 80% yield along with 1,2-addition product **47** (12% yield). The stereochemistry of the vinyl group of **46** was assumed to be α-axial, because the attack of the Grignard reagent was considered to occur from less hindered side. After our preliminary report it has been reported by Grieco et al.[17] that conjugate addition of C_2-unit to octalone **48** proceeded smoothly in ether at −78 °C, giving rise to **49** in 95% yield using an organocopper reagent derived from equimolar amounts of copper(I) iodide and vinyllithium and 2.6 equivalent of tributylphosphine. The compound **46** has all carbons contained in the skeletal structure **A** with desired stereochemistry.

Construction of ring E by attack of hydroxyl group at C-20 to C-13 was our selected strategy to be tried at first and introduction of a double bond at C-12 was necessary prior to the trial. Conversion of **46** into the α,β-unsaturated ester **51** via a mixture of stereoisomers of the alcohol **50** was carried out by the successive treatments with sodium borohydride in ethanol, methanesulfonyl chloride and triethylamine in dichloromethane, and then 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in refluxing benzene. The overall yield of **51** from **46** was 73%. The EE group of **51** was removed by treatment in ethanol containing catalytic amount of PPTS to give alcohol **52** in 81% yield. The tricyclic compound **52** is ready to form bruceantin skeleton **A**.



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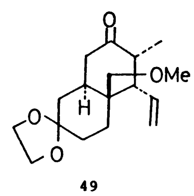

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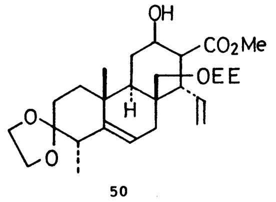

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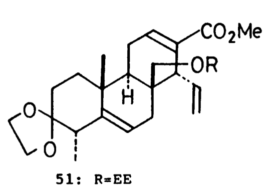
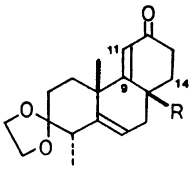
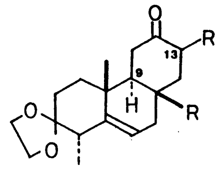


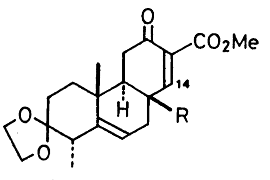
51: R=EE
52: R=H



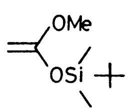
37: R=CH$_2$OH
38: R=CH$_2$OTHP
40: R=CH$_2$OEE
(EE: 1-ethoxyethyl)



39: R=CH$_2$OTHP, R'=H
41: R=CH$_2$OEE, R'=H
42: R=CH$_2$OEE, R'=CO$_2$Me
(THP: tetrahydropyranyl)



43: R=CH$_2$OEE
45: R=Me



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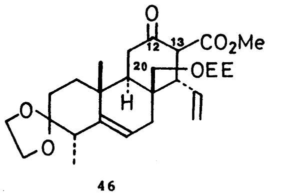

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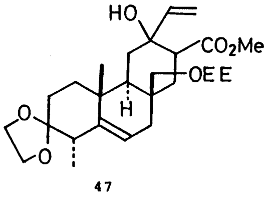

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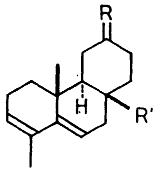
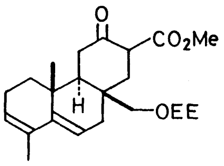
The modest yield we encountered when scaling up the synthesis of the diacetal **33** led us to search for another route for the synthesis of **51**. If the double bond at C-9(11) is reduced prior to the introduction of an oxygen function into C-3, the use of the unstable acetals such as **33** can be avoided. It was eventually found that the double bond of the α,β-unsaturated ketone of **15** could be reduced selectively to give ketone **53** in a quantitative yield with NaHTe in ethanol at room temperature (the conjugated diene system of **15** was reduced on Birch reduction and catalytic hydrogenation). The keto alcohol **55** was obtained by LAH reduction of acetal **54** and following acid treatment of the product. The yield of **55** from **53** was almost quantitative. The hydroxyl group of **55** was protected with EE to give **56** in 94% yield. The α,β-unsaturated ester **60** was synthesized from **56** via **57**, **58**, and **59** by the same methods used to obtain **51** from **41**, namely methoxycarbonylation to give **57**, phenylselenylation followed by oxidative elimination to afford **58**, conjugate addition reaction of vinylmagnesium bromide to yield **59**, reduction with sodium borohydride, mesylation, and treatment with DBU to give **60**. The overall yield of **60** from **56** was 58%.

Before introduction of an oxygen function into C-3, the EE group of **60** was replaced with an acetyl group to give **61** in 90% yield, because the EE group was affected with MCPBA giving a complex mixture. On oxidation with MCPBA the acetate **61** afforded epoxide **62**. No other product was detected in the ^{1}H NMR spectrum of the crude **62**. The signal of the proton at C-3 in the ^{1}H NMR was observed as a singlet ($W_{1/2}$= 4.5 Hz) suggesting the configuration of the epoxide to be α which is preferable stereochemistry for introduction of an acetal group into C-3 as shown in the case of **28**. The epoxide **62** yielded the acetal **63** on treatment with 2-ethyl-2-methyl-1,3-dioxolane and $BF_3 \cdot Et_2O$ in dichloromethane. The yield of **63** from **61** was 87%. The replacement of the acetyl group of **63** with EE group was accomplished in 93% yield to afford **51**. Thus the preparation of enough amount of the tricyclic compound **51** for further syntheses toward antitumor quassinoids has become possible.



53: R=O, R'=CO_2Me
54: R=-O$(CH_2)_2$O-, R'=CO_2Me
55: R=O, R'=CH_2OH
56: R=O, R'=CH_2OEE



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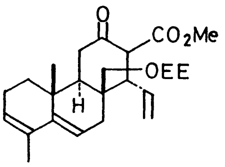

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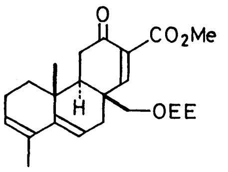

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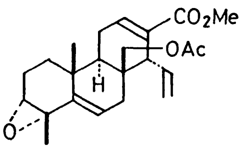

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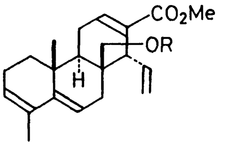
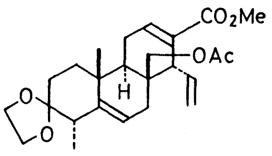


60: R=EE
61: R=Ac

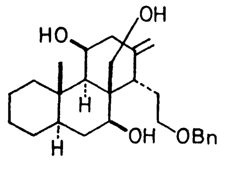


63

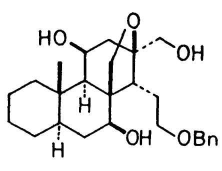
The next step in our strategy toward bruceantin skeleton was the construction of the epoxide ring E. The direct formation of tetracyclic triol **65** on MCPBA oxidation of triol **64** has been reported by Ziegler et al.[18] Therefore it was considered that the acid-catalyzed opening of 12,13-epoxide ring would provide a convenient access to ring E. For the regio- and stereospecific introduction of the epoxide into the C-12 double bond utilizing a hydroxyl group at C-21, the ester **51** was reduced to allylic alcohol **66** with DIBAL. The allylic alcohol **66** was oxidized with *t*-butyl hydroperoxide using titanium(IV) isopropoxide as a catalyst[19] to give epoxide **67** as a sole product in almost quantitative yield. The stereochemistry of the epoxide ring of **67** was hard to be determined by its NMR spectrum. On treatment with catalytic amount of PPTS in ethanol **67** afforded the diol **68** as nice crystalline compound in a quantitative yield. The similarity of the NMR spectra of **68** [^{1}H NMR signals for C-$20H_2$ (AB quartet at δ 3.33 and 4.36 with J=8 Hz) and C-12H (broad doublet at δ 4.05 with J=4 Hz) and ^{13}C NMR signals for C-12, C-13, C-20, and C-21] to those of the known compound **69**[20] suggested that the stereochemistry of the hydroxyl group at C-12 is α-axial. Therefore, the configuration of the epoxide ring of **67** was suggested to be α.

Even though the stereochemistry of the hydroxyl group at C-12 is axial, **68** gave diacetate **70** very easily. This facile acetylation of the axial hydroxyl group is compatible with acetylation of the primary hydroxyl group at C-21 followed by the migration of the acetyl group to the hydroxyl group at C-12 and successive acetylation of the regenerated primary hydroxyl group.

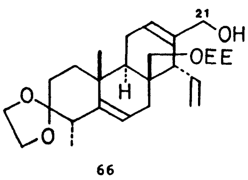
Migration of the protecting group of the hydroxyl group at C-21 to the hydroxyl group at C-12 was observed also for the *t*-butyldimethylsilyl (tBDMS) ether **71**. The acetate **72** derived from **71** showed the ^{1}H NMR signal of C-12H at δ ca. 5.0 suggesting the presence of the acetoxyl group at C-12. Although the silyl ether **71** was not affected by the treatment with chrolomethyl methyl ether (MOMCl) and *N*,*N*-diisopropylethylamine in refluxing dichloromethane, on treatment with MOMCl and potassium hydride in a mixed solvent of THF and *N*,*N*-dimethylformamide (DMF) **71** afforded methoxymethyl (MOM) ether **73**. On selective removal of the silyl protecting group with tetrabutylammonium fluoride followed by acetylation, **73** afforded the acetate **74** whose ^{1}H NMR spectrum suggested the presence of the acetoxyl group at C-12



64



65



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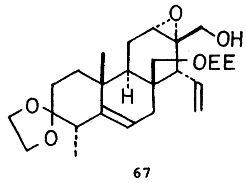
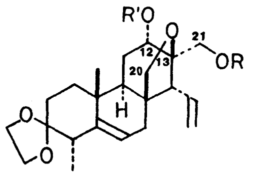
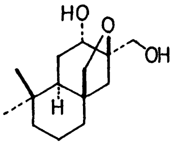


67



68: R=R'=H
70: R=R'=Ac
71: R=tBDMS, R'=H
72: R=tBDMS, R'=Ac
73: R=MOM, R'=tBDMS
74: R=MOM, R'=Ac
(tBDMS: t-butyldimethylsilyl)
(MOM: methoxymethyl)



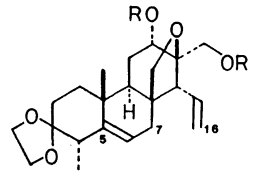
69

(C-12H: δ ca. 5.0). These observations indicate that the migration of the silyl group21) from the hydroxyl group at C-21 to that of at C-12 occurred during the reaction of **71** to **73**.

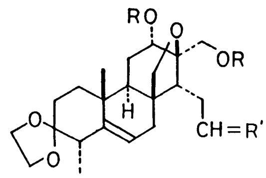
The final step for the synthesis of the bruceantin skeleton was the construction of ring D (lactone or hemiacetal ring). Oxidation at C-7 and C-16 and reduction of the double bond at C-5 were inevitable in order to construct the ring D. Protection of the hydroxyl groups at C-12 and C-21 was necessary prior to these reactions. Silyl groups were considered to be desirable for the protection. The monosilyl derivative **71** was treated with potassium hydride in the mixed solvent of THF and DMF and then the solution of tBDMSCl in THF was added to the reaction mixture to give the disilyl derivative **75** in 96% yield.

Selective introduction of a hydroxyl group into C-16 of **75** was carried out by hydroboration-oxidation using thexylborane to yield alcohol **76**. Simultaneous oxidation of the hydroxyl group and the allylic position (C-7) of **76** was hard, and so **76** was converted into aldehyde **77** by Collins' oxidation. Although protection of the formyl group of **77** using trimethyl orthoformate in methanol containing PPTS was inefficient because of concurring hydrolysis of the acetal group at C-3, dimethyl acetal **78** was obtained in 94% yield by the use of dichloromethane instead of methanol as the solvent in the above reaction conditions.

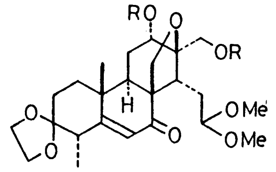
Allylic oxidation of the acetal **78** with the complexes of chromium trioxide and 3,5-dimethylpyrazole22) gave the α,β-unsaturated ketone **79** in 68% yield. The enhanced yield of allylic oxidation at C-7 of **78** compared with those of **29** and **33** is probably due to decrease of strain energy around the carbonyl at C-7 caused by saturation of the ring C and not due to simple change of steric hindrance around C-7. Birch reduction of **79** gave saturated ketone **80**. The stereo-



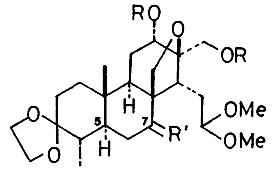
75: R=tBDMS



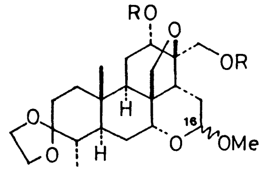
76: R=tBDMS, R'=H,OH
77: R=tBDMS, R'=O
78: R=tBDMS, R'=(OMe)$_2$



79: R=tBDMS



80: R=tBDMS, R'=O
81: R=tBDMS, R'=α-OH, β-H



82: R=tBDMS

Table 1. Isolated Isomer of **3**: Assignments, Chemical Shifts, and Coupling Constants from 270 MHz ^{1}H NMR in CDCl$_3$

Proton	Chemical shift (δ)	Signal type	J/Hz
$C_{(1)}$-αH	ca. 1.3a)		
$C_{(1)}$-βH	b)		
$C_{(2)}$-αH	b)		
$C_{(2)}$-βH	ca. 1.6a)		
$C_{(4)}$-H	1.72	m	$J_{4,5}=12$, $J_{4,\mathrm{Me}}=6$
$C_{(4)}$-Me	0.82	d	$J_{\mathrm{Me},4}=6$
$C_{(5)}$-H	1.92	dt	$J_{4,5}=12$, $J_{5,6\alpha}=3$, $J_{5,6\beta}=12$
$C_{(6)}$-αH	ca. 1.7a)	ddd	$J_{6\alpha,6\beta}=14$, $J_{6\alpha,5}=3$, $J_{6\alpha,7}=2$
$C_{(6)}$-βH	1.20	ddd	$J_{6\beta,6\alpha}=14$, $J_{6\beta,5}=12$, $J_{6\beta,7}=2$
$C_{(7)}$-H	3.73	t	$J_{7,6\alpha}=2$, $J_{7,6\beta}=2$
$C_{(9)}$-H	2.06	dd	$J_{9,11\alpha}=4$, $J_{9,11\beta}=14$
$C_{(10)}$-Me	0.93	s	
$C_{(11)}$-αH	ca. 1.6a)	dd	$J_{11\alpha,11\beta}=14$, $J_{11\alpha,9}=4$, $J_{11\alpha,12}=$ca. 0
$C_{(11)}$-βH	1.85	dt	$J_{11\beta,11\alpha}=14$, $J_{11\beta,9}=14$, $J_{11\beta,12}=4$
$C_{(12)}$-H	4.00	d	$J_{12,11\alpha}=0$, $J_{12,11\beta}=4$
$C_{(14)}$-H	2.02	dd	$J_{14,15\alpha}=14$, $J_{14,15\beta}=4$
$C_{(15)}$-αH	2.43	dt	$J_{15\alpha,14}=14$, $J_{15\alpha,15\beta}=14$, $J_{15\alpha,16}=3$
$C_{(15)}$-βH	1.71	dd	$J_{15\beta,14}=4$, $J_{15\beta,15\alpha}=14$, $J_{15\beta,16}=$ca. 0
$C_{(16)}$-H	4.80	d	$J_{16,15\alpha}=3$, $J_{16,15\beta}=0$
$C_{(20)}$-αH	3,31	d	$J_{20\alpha,20\beta}=8$
$C_{(20)}$-βH	4,23	d	$J_{20\beta,20\alpha}=8$
$C_{(21)}$-H_2	3.77	ABq	$J=11$, $\Delta\nu_{AB}=15$
Ethylenedioxy-H_4	3.93	m	

a) Determined by difference NOE. b) Undetermined because of overlapping with other signals.

chemistry at C-5 of **80** was supposed to be 5α-H, because the 5α-H compound is more stable than the 5β-H isomer.

For the completion of ring D, stereoselective reduction of the carbonyl group at C-7 into α hydroxyl group was necessary. Although bulky hydride reagents such as diisobutylaluminium hydride (DIBAL) were considered to give 7α-OH derivative selectively, 7β-OH derivative was obtained as the sole product on reduction of the ketone **80** with DIBAL and sodium borohydride. Chelation between the dimethyl acetal group and the hydride reagent may have controlled the stereochemistry of the reaction. On reduction with lithium triethylhydroborate the ketone **80** gave 7α-OH derivative **81** stereoselectively. The anomeric mixture at C-16 of the hemiacetal **82** was obtained smoothly by the treatment of **81** with catalytic amount of PPTS in MeOH at room temperature. The mixture could not be separated into each isomer, but an isomer of the anomeric mixture of the diol **3** obtained by the treatment of **82** with tetrabutylammonium fluoride could be separated.

Precise decoupling (Table 1) and difference NOE (Fig. 1) experiments using 270 MHz ^{1}H NMR confirmed the structure of the isolated isomer of **3** bearing 16β-methoxyl group to be that shown in Fig. 2. The stereochemistries of the epoxymethano bridge and the methyl group at C-4 are shown to be β-axial and α-equatorial, respectively, by the NOEs among $C_{(10)}$-Me, $C_{(20)}$-βH, and $C_{(4)}$-H (Fig. 1 A and B). The NOEs among $C_{(10)}$-Me, $C_{(20)}$-βH, and $C_{(11)}$-βH (Fig. 1 A and B) indicate that $C_{(11)}$-βH has axial conformation and the large coupling constant (14 Hz) between $C_{(9)}$-H and the $C_{(11)}$-βH suggests that the stereochemistry of the $C_{(9)}$-H is α-axial. The coupling constant (12 Hz) between $C_{(4)}$-H and $C_{(5)}$-H shows the α-axial nature of the $C_{(5)}$-H. The NOEs among $C_{(20)}$-αH, $C_{(14)}$-H, and $C_{(7)}$-H (Fig. 2 C, D, and E) indicate that these protons are located near place each other, therefore both of the protons at C-7 and C-14 have β-equatorial stereochemistry. This is also supported with the small coupling constants between the proton at C-7 and the protons at C-6. All of the NMR data of the isolated isomer of **3** are best compatible with the molecular structure (Fig. 3) having minimized steric energy (348.695 kJ mol^{-1}) given by MM2 force field calculation[23] for the 16β-methoxy isomer of **3** and unequivocally confirmed the stereochemical assignment.

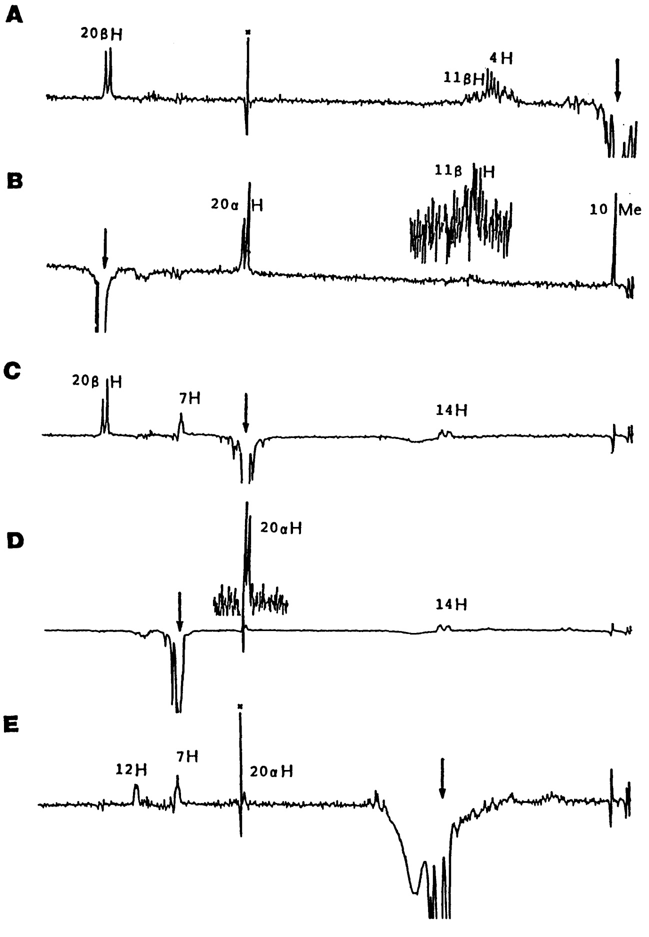


Fig. 1. Difference NOE spectra (270 MHz in $CDCl_3$) of 16β-methoxy isomer of **3**. ↓: Irradiated frequency. The NOE of 12H in E was induced by simultaneous irradiation on overlapping signal of 12-OH.

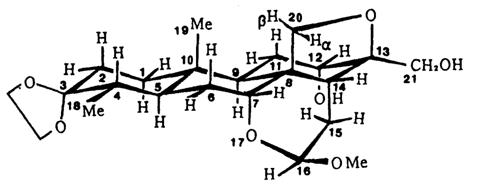


Fig. 2. Perspective drawing of the isolated isomer of **3**.

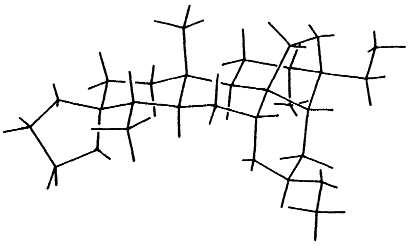


Fig. 3. Wire model generated by computer based on MM2 force field calculation for the 16β-methoxy isomer of **3** bearing minimum steric energy. Short lines from ether oxygen indicate lone pairs.

Experimental

General. All reactions were run under a nitrogen atmosphere with magnetic stirring unless otherwise noted. Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. Ether and tetrahydrofuran were distilled from lithium aluminium hydride immediately prior to use. Dichloromethane was distilled from P_2O_5. Absolute ethanol (EtOH) and methanol (MeOH) were distilled from magnesium. Hexane, benzene, toluene, pyridine, 1,2-dimethoxyethane (DME), acetonitrile, *N*,*N*-dimethylformamide (DMF), triethylamine, *N*,*N*-diisopropylethylamine, and dimethyl carbonate were distilled from calcium hydride. Chromium trioxide was dried overnight at reduced pressure and stored over P_2O_5. Liquid ammonia was distilled from sodium. Preparative chromatography was carried out on open column of silica gel (Wako, C-200). Thin-layer chromatography (TLC) was performed on E. Merck Kieselgel GF_{254} Art 7730.

Melting points were measured on Laboratory Devices Meltemp and are uncorrected.

^{1}H NMR spectra were determined with Varian EM 390 (90 MHz), JEOL FX 90Q (90 MHz), or Brucker WH 270 (270 MHz) spectrometers in $CDCl_3$ solutions with tetramethylsilane as internal standard. ^{13}C NMR spectra were recorded on JEOL FX 90Q spectrometer. ^{1}H NMR data are tabulated in order number of protons, multiplicity (s, singlet; brs, broad singlet; d, doublet; t, triplet; brt, broad triplet; q, quartet; m, multiplet), coupling constants in hertz. IR spectra were recorded on a Hitachi Model 260-30 grating infrared spectrometer. UV spectra were obtained on a Hitachi Model 340 instrument. Low- and high-resolution mass spectra were measured using JEOL JMS-D300 mass spectrometer equipped with JMA-2000 data analysis system.

3,7,8,8a-Tetrahydro-5,8a-dimethyl-1(2*H*)-naphthalenone (9): To a solution of monoacetal **8** (11.0 g, 46 mmol) in methanol (200 ml) was added sodium borohydride (3 g, 79 mmol) in portions under drying tube. The mixture was stirred at room temperature for 3 h. Acetic acid (200 ml) and 1 mol dm^{-3} HCl (100 ml) were added. After being set aside overnight, the solution was neutralized with 30% aqueous NaOH, extracted with ether, washed with water (×3) and then dried over $MgSO_4$. Removal of the solvent under reduced pressure and subsequent distillation afforded the diene **9** (6.1 g, 74%) as an oil: bp 83—94 °C (80.0 Pa); IR (oil) 1715 cm^{-1}; UV (EtOH) 237 nm (ε 16000); ^{1}H NMR δ=1.18 (3H, s, 10-CH_3), 1.81 (3H, brs, 4-CH_3), 5.50 (1H, m), and 5.75 (1H, brt, J=4 Hz); MS (70 eV) m/z (rel intensity) 176 (M^+, 36.5), 161 (13), and 118 (100); Found m/z 176.1217. Calcd for $C_{12}H_{16}O$: M, 176.1201.

3,7,8,8a-Tetrahydro-2α,5,8aβ-trimethyl-1(2*H*)-naphthalenone (10): To a solution of LDA (6.8 mmol) in THF (20 ml) was added a solution of **9** (1.11 g, 6.29 mmol) in THF (20 ml) dropwise with stirring at −78 °C. The mixture was stirred at room temperature for 30 min and to the solution was added MeI (0.8 ml, 13 mmol) which was passed through a neutral alumina column prior to use. After stirring at room temperature for 30 min the reaction was quenched by the addition of brine. The reaction mixture was acidified with dil HCl and extracted with ether. The ether solution was washed with brine and then dried (Na_2SO_4). Concentration in vacuo gave a residue that was chromatographed on silica gel (eluent: benzene) to give methylated compound **10** (1.02 g, 85%) which afforded colorless needles on crystallization from aqueous methanol: mp 47.0—48.8 °C; IR (oil) 1712 cm^{-1}; ^{1}H NMR δ=1.02 (3H, d, J=6 Hz, 8-CH_3), 1.16 (3H, s, 10-CH_3), 1.74 (3H, brs, 4-CH_3), 5.34 (1H, m), and 5.38 (1H, brt, J=4 Hz); MS (70 eV) m/z (rel intensity) 190 (M^+, 30), 175 (11), 134 (41), and 119 (100): Found: m/z 190.1357. Calcd for $C_{13}H_{18}O$: M, 190.1357.

1,4b,5,6,10,10a-Hexahydro-4bβ,8,10aβ-trimethyl-3(2*H*)-phenanthrenone (12): To a solution of 0.5 mol dm^{-3} NaOMe in MeOH (2.5 ml) was added **10** (0.70 g, 3.7 mmol) and then methyl vinyl ketone (0.65 ml). The mixture was stirred at room temperature for 20 h. (Michael adduct **11** could be obtained from the reaction mixture by usual work up.) To the reaction mixture was added 1 mol dm^{-3} NaOMe (2.5 ml) and the mixture was heated at reflux for 4 d. Brine was added into the mixture, which was extracted with ether and dried over Na_2SO_4. Evaporation of the solvent gave a residue which was purified by silica-gel column chromatography (50 g; eluent: 2% acetone in benzene) to give tricyclic compound **12** as a colorless oil (0.79g, 89%): IR (oil) 1672 and 1603 cm^{-1}; ^{1}H NMR δ=1.23 (3H, s), 1.42 (3H, s), 1.83 (3H, brs, 4-CH_3), 5.51 (1H, m), 5.66 (1H, brt, J=4 Hz), and 6.01 (1H, s, 11-CH); MS (70 eV) m/z (rel intensity) 242 (M^+, 100), and 227 (59); Found m/z 242.1689. Calcd for $C_{17}H_{22}O$: M, 242.1670.

3,7,8,8a-Tetrahydro-2-methoxycarbonyl-5,8a-dimethyl-1(2*H*)-naphthalenone (13): To a suspension of NaH (60 g, 1.5 mol 60% oil dispersion) and KH (1 g, 12 mmol, 50% oil dispersion) and dimethyl carbonate (110 ml) in DME was added **9** (200 g, 1.1 mol) in DME (250 ml) with stirring in an ice bath and releasing the hydrogen evolved by the reaction through mercury valve. The mixture was stirred in an ice bath until practical finish of evolution of hydrogen and then heated at reflux for 1 h. The reaction mixture was poured into saturated aqueous NH_4Cl and extracted with ether (1l×1, 0.5 l×2). The ether solution was washed with saturated aqueous NH_4Cl (100 ml) and then brine (100 ml×2). Drying over Na_2SO_4 and evaporation of the solvent gave an orange oil, which crystallized upon standing. An analytical sample of **13**, mp 51.8—53 °C, was obtained as colorless plates (colored slightly yellow on exposure to air) by crystallization from methanol: IR (KBr) 1663, 1640, and 1618 cm^{-1}; UV (EtOH) 232 (ε 30000) and 238 nm (sh 25000); ^{1}H NMR δ=1.17 (3H, s, 10-CH_3), 1.76 (3H, brs, 4-CH_3), 2.92 (2H, brd 7-CH_2), 3.70 (3H, s, CO_2CH_3), and 5.30—5.65 (2H, m); MS (70 eV) m/z (rel intensity) 234 (M^+, 32), 219 (69), and 187 (100); Found m/z 234.1268. Calcd for $C_{14}H_{18}O_3$: M, 234.1256.

3,7,8,8a-Tetrahydro-2β-methoxycarbonyl-5,8aβ-dimethyl-2α-(3-oxobutyl)-1(2*H*)-naphthalenone (14): To a solution of **13** (4.24 g, 18 mmol) in MeOH (50 ml) was added 0.5 mol dm^{-3} NaOMe in MeOH (3.0 ml) and methyl vinyl ketone (4.0 ml). The mixture was stirred at 40 °C for 3 h. The solvent was distilled off under reduced pressure. The residue was dissolved in ether and brine. The ether solution was washed with brine and dried (Na_2SO_4). Evaporation of the solvent gave 5.50 g (100%) of crude **14** pure enough for further use. An analytical sample of **14**, mp 78.5—80 °C, was obtained by crystallization from hexane as colorless needles: IR (KBr) 1742, 1715, and 1708 cm^{-1}; UV (EtOH) 240 nm (ε 19000); ^{1}H NMR δ=1.17 (3H, s, 10-CH_3), 1.83 (3H, brs, 4-CH_3), 2.09 (3H, s, $COCH_3$), 3.70 (3H, s, CO_2CH_3), 5.60 (1H, m), and 5.72 (1H, dd, J=7 and 3 Hz); MS (70 eV) m/z (rel intensity) 304 (M^+, 5.8), 286 (5), 257 (9.2), 233 (94), and 201 (100); Found: C, 70.87; H, 7.82%. Calcd for $C_{18}H_{24}O_4$: C, 71.03; H, 7.95%.

1,4b,5,6,10,10a-Hexahydro-10aβ-methoxycarbonyl-4bβ,8-dimethyl-3(2*H*)-phenanthrenone (15): To a solution of diketone **14** (30.4 g, 0.1 mol) and *m*-toluic acid (16.3 g, 0.12 mol) in benzene (750 ml) was added pyrrolidine (1.7 ml, 0.02 mol) and the mixture was refluxed for 14 h passing through Molecular Sieves 4A. The cooled mixture was washed with 5% aqueous potassium hydroxide (100 ml×3) and the combined aqueous layers were extracted with ether (100 ml×3). The combined organic extracts were washed with 2 mol dm^{-3} HCl (100 ml×3) and the combined aqueous layers were extracted with ether (100 ml×2). The combined organic extracts were washed with brine (100 ml), dried (Na_2SO_4-$MgSO_4$), filtered through a silica-gel column (70 g in benzene) and evaporated. The brown residue was chromatographed on silica-gel column (150 g in hexane, eluent: 2% AcOEt in hexane) to afford enone **15** (22.86 g, 80%) as a pale yellow solid. An analytical sample was obtained as colorless plates by recrystallization from ether-hexane: mp 80—82 °C; IR (Nujol) 1731, 1675, and 1608 cm^{-1}; UV (EtOH) 236.5 nm (ε 26000); ^1H NMR δ=1.05 (3H, s, 10-CH_3), 1.79 (3H, s, 4-CH_3), 3.72 (3H, s, CO_2CH_3), 5.53 (1H, m), 5.61 (1H, dd, J=7 and 3 Hz), and 6.18 (1H, s, 11-CH); ^{13}C NMR δ=198.67, 173.62, 166.44, 138.92, 130.30, 124.69, 123.75, 117.06, 51.88, 44.94, 38.82, 36.46, 35.59, 33.48, 31.45, 23.84, 22.13, and 19.56; MS (70 eV) m/z (rel intensity) 286 (M^+, 58) and 227 (100); Found: C, 75.46; H, 7.61%. Calcd for $C_{18}H_{22}O_3$: C, 75.49; H, 7.74%.

1,2,3,4b,5,6,10,10a-Octahydro-4bβ,8,10aβ-trimethyl-1-phenanthrenol (17): To a solution of **16** (6.0 g) in MeOH (180 ml) was added $NaBH_4$ (1.2 g) in portions with stirring in ice bath. After stirring at room temperature for 1 h, to the reaction mixture was added acetic acid (10 ml) and then 2 mol dm^{-3} hydrochloric acid (60 ml). After stirring for 1 h at room temperature, the reaction mixture was cooled in ice bath and was added 10% aqueous NaOH (120 ml). The reaction mixture was concentrated to ca. 150 ml with rotary evaporator and extracted with ether (100 ml×3). The combined ether extracts were washed with brine (100 ml×1) and dried over $MgSO_4$. Evaporation of the solvent afforded the alcohol **17** (5.88 g): IR (Nujol) 3400 and 1642 cm^{-1}; UV (MeOH) 239 nm (ε 10510) and 232 nm (ε 9716); ^1H NMR δ= 1.17 (3H, s), 1.20 (3H, s), 1.78 (3H, m, 4-CH_3), 3.50 (1H, dd, J=7 and 9 Hz, 14-CH), and 5.31—5.71 (3H, m); MS (70 eV) m/z (rel intensity) 244 (M^+, 89), 229 (69), 226 (26), and 211 (100); Found: m/z 244.1824. Calcd for $C_{17}H_{24}O$: M, 244.1825.

3,4b,5,6,10,10a-Hexahydro-4bβ,8,10aβ-trimethyl-1(2*H*)-phenanthrenone (18): To a solution of the alcohol **17** in CH_2Cl_2 (175 ml) was added pyridinium chlorochromate (13.0 g) and the mixture was stirred at room temperature for 1 h. The reaction mixture was decanted and the residue was washed with ether. The combined solution was passed through a florisil column and the solvent was evaporated to give a residue, which was chromatographed on a silica-gel column (50 g, eluent: benzene) to give the ketone **18** (3.4 g): IR (Nujol) 1720 cm^{-1}; UV (MeOH) 238 nm (ε 18660) and 232 nm (ε 17270); ^1H NMR δ=1.21 (3H, s), 1.43 (3H, s), 1.78 (3H, m, 4-CH_3), and 5.32—5.88 (3H, m); MS (70 eV) m/z (rel intensity) 242 (M^+, 64), 227 (20), 209 (77), and 184 (100); Found: m/z 242.1671. Calcd for $C_{17}H_{22}O$: M, 242.1671.

3,4b,5,6,10,10a-Hexahydro-4bβ,8,10aβ-trimethyl-1(2*H*)-phenanthrenone Tosylhydrazone (19): To a solution of the ketone **18** (3.4 g) in hot 95% EtOH (10 ml) was added a solution of tosylhydrazine (3.0 g) in hot 95% EtOH (6 ml) and the mixture was stirred for 10 min and then stood at room temperature for 12 h. Washing with 50% aqueous EtOH and crystallization from ether afforded the tosylhydrazone **19** as colorless crystals: mp 173—175 °C; IR (Nujol) 3215, 1602, and 1176 cm^{-1}; ^1H NMR δ=1.15 (3H, s), 1.30 (3H, s), 1.75 (3H, m, 4-CH_3), 2.37 (3H, s), 5.37—5.85 (3H, m), 7.28 (2H, d, J=8 Hz), and 7.86 (2H, d, J=8 Hz); MS (70 eV) m/z (rel intensity) 410 (M^+, 15), 395 (13), and 225 (100); Found: m/z 410.2071. Calcd for $C_{24}H_{30}N_2O_2S$: M, 410.2029.

1,4b,5,6,10,10a-Hexahydro-4bβ,8,10aβ-trimethyl-2-methylthiophenanthrene (20): To a solution of the tosylhydrazone **19** (869 mg) in THF (10 ml) and TMEDA (10 ml) was added 2 equiv of butyllithium in hexane dropwise with stirring at −78 °C and the mixture was stirred for 30 min at the temperature. After addition of dimethyl disulfide (0.22 ml, 1.1 equiv) dropwise at −78 °C, the reaction mixture was stirred at −30 °C for 1 h. *n*-Butyllithium (1.3 equiv) in hexane was added into the reaction mixture with stirring at −50 °C. The mixture was warmed to room temperature over 1 h and stirred at the temperature for 6 h. The reaction mixture was poured into saturated aqueous NH_4Cl (50 ml) and extracted with ether (50 ml×3). The combined extracts were washed with brine (20 ml×2) and dried over Na_2SO_4. The residue obtained by evaporation of the solvent was chromatographed on a silica-gel column (eluent: hexane) to give the enol thioether **20** (pale yellow viscous oil): IR (oil) 1620 and 1565 cm^{-1}; UV (MeOH) 302 nm (ε 8440), 238 nm (ε 16990), and 232 nm (ε 16780); ^1H NMR δ=1.13 (3H, s), 1.19 (3H, s), 1.77 (3H, m, 4-CH_3), 2.28 (3H, s, S-CH_3), 5.32—5.70 (3H, m), and 5.78 (1H, a part of ABq, J=6 Hz); MS (70 eV) m/z (rel intensity) 272 (M^+, 100) and 257 (74); Found: m/z 272.1594. Calcd for $C_{18}H_{24}S$: M, 272.1597.

4a,4b,5,6,10,10a-Hexahydro-4bβ,8,10aβ-trimethyl-2(1*H*)-phenanthrenone (21): To a solution of the enol thioether **20** (690 mg) in THF (6 ml) was added $TiCl_4$ (600 mg) in THF (20 ml) and the mixture was stirred at room temperature for 1 h. To the reaction mixture was added 80% aqueous acetic acid, stirred at room temperature for 4 d, poured into brine (20 ml), and then extracted with ether (40 ml×3). The combined ether layer was washed with brine (20 ml), saturated aqueous $NaHCO_3$ (50 ml×2), and then brine (20 ml) and dried over Na_2SO_4. The residue obtained by evaporation of the solvent was chromatographed on a silica-gel column (eluent: benzene) to give the α,β-unsaturated ketone **21** (410 mg) as colorless prisms (ether-hexane): mp 98—99.5 °C; IR (Nujol) 1680 cm^{-1}; UV (MeOH) 232 nm (ε 19000); ^1H NMR δ=0.99 (3H, s), 1.07 (3H, s), 1.80 (3H, m, 4-CH_3), 5.35—5.70 (2H, m), 6.11 (1H, dd, J=10 and 3.5 Hz, 12-CH), and 6.92 (1H, dd, J=10 and 2 Hz, 11-CH); MS (70 eV) m/z (rel intensity) 242 (M^+, 100) and 227 (50); Found: m/z 242.1665. Calcd for $C_{17}H_{22}O$: M, 242.1670.

1,4b,5,6,10,10a-Hexahydro-10aβ-methoxycarbonyl-4bβ,8-dimethyl-3(2*H*)-phenanthrenone 3-(Ethylene Acetal) (22): A mixture of enone **15** (2.162 g, 7.56 mmol), ethylene glycol (11.55 ml), and *p*-toluenesulfonic acid monohydrate (222 mg) in benzene (85 ml) was refluxed under Dean-Stark water separator for 9.5 h. The mixture was cooled to room temperature and the benzene layer was separated, and passed through an alumina column (eluent: benzene) to give monoacetal **22** (2.3661 g, 95%) as pale yellow crystals. An analytical sample was prepared by recrystallization from hexane to give colorless prisms: mp 121—122 °C; IR (Nujol) 1787 cm^{-1}; ^1H NMR δ=0.96 (3H, s, 10-CH_3), 1.78 (3H, brs, 4-CH_3), 3.66 (3H, s, CO_2CH_3), 3.96 (4H, m, acetal), 5.43 (1H, m), 5.57 (1H, dd, J=3 and 7 Hz), and 5.66 (1H, s, 11-CH); MS (70 eV) m/z (rel intensity) 330 (M^+, 35) and 271 (100); Found: C, 72.46; H, 7.74%. Calcd for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93%.

Conversion of 15 into 12: A solution of the acetal **22** (2.88 g) in DME (5 ml) was added into a refluxing solution of LAH (230 mg) in ether (5 ml) dropwise. After refluxing for 10 min ethyl acetate (1 ml) was added into the reaction mixture. Ether and water were added into the mixture and then the mixture was filtered through a celite column. The filtrate was extracted with ether and the extract was dried over

Na_2SO_4. The residue obtained by evaporation of the solvent was purified by florisil column chromatography (eluent: benzene-acetone) to give 2.1 g of the alcohol **23**: ^{1}H NMR δ=1.10 (3H, s, 10-CH_3), 1.77 (3H, brs, 4-CH_3), 3.62 (2H, s, 20-CH_2), 3.92 (4H, s, acetal), 5.26—5.60 (2H, m), and 5.62 (lH, s, 11-CH).

The alcohol **23** (122 mg) in CH_2Cl_2 (0.5 ml) was added into the Collins' reagent prepared from CrO_3 (244 mg) and pyridine (0.39 ml) in CH_2Cl_2 (5 ml). After stirring for 15 min at room temperature the reaction mixture was decanted and the residue was washed with ether. The CH_2Cl_2 solution was combined with ether washes and the combined solution was washed with 5% aqueous NaOH (15 ml×3) and then water (10 ml×4) and dried over Na_2SO_4. Removal of the solvent gave a residue (84.5 mg) which was chromatographed on florisil (eluent: benzene-acetone) to give the aldehyde **24** (57.8 mg): IR (Nujol) 1718 cm^{-1}.

A mixture of **24** (50 mg), diethylene glycol (2 ml), 80% hydrazine hydrate (0.4 ml), and KOH (0.1 g) was heated under reflux at 160—180 °C for 3 h. After heating at 85—90 °C for 1 h under reduced pressure using rotary evaporator, the residual mixture was heated at 170 °C for 6 h. Water was added into cooled reaction mixture and the mixture was extracted with ether. The ether layer was washed three times with dil HCl and dried over Na_2SO_4. The residue (32 mg) given by evaporation of the solvent was chromatographed on preparative TLC to afford the major product which was identified with **12**.

Conversion of 12 into 21: A mixture of **12** (0.94 g) and tosylhydrazine (1.0 g) in EtOH (4.5 ml) was stirred for 10 min and set aside overnight. Evaporation of the solvent, silica-gel column chromatography of the residue and crystallization from ether gave tosylhydrazone **25** as colorless crystals (0.75 g): mp 160—165 °C; IR (Nujol) 3210 and 1170 cm^{-1}; ^{1}H NMR δ=1.14 (3H, s), 1.23 (3H, s), 1.79 (3H, brs, 4-CH_3), 2.43 (3H, s, $-SO_2C_6H_4-\underline{CH_3}$), 5.50 (1H, m), 5.60 (1H, m), 6.08 (1H, s, 11-CH), 7.29 (2H, d), and 7.88 (2H, d).

To a solution of the tosylhydrazone **25** (250 mg, 0.61 mmol) in a mixed solvent of THF (2.1 ml) and *N*,*N*,*N'*,*N'*-tetramethylethylenediamine (TMEDA) (2.1 ml) was added 2.5 equiv of butyllithium in hexane and then dimethyl disulfide (0.1 ml, 1.5 equiv) with stirring at −78 °C. The mixture was stirred at −30 °C for 30 min. Hexane solution of butyllithium (1.7 equiv) was added to the reaction mixture at −78 °C to give deep red solution and the solution was warmed to room temperature over one hour and stirred at the temperature overnight. To the reaction mixture was added 15% aqueous ammonium chloride (50 ml) and extracted with hexane twice and with ether twice. The combined extracts were dried over $MgSO_4$ and the residue given on evaporation of the solvent was chromatographed on a silica-gel column (eluent: hexane–ether) to give a enol thioether (30 mg) whose spectra were identical with those of the enol thioether **20** derived from **16**.

To the enol thioether (30 mg) in THF (0.4 ml) was added a solution of $TiCl_4$ (30 mg) in THF (1 ml) and the mixture was stirred at room temperature for 90 min. Acetic acid (0.4 ml) and water (0.14 ml) were added into the reaction mixture and the mixture was stirred at room temperature for 4 d. The reaction mixture was cooled in ice bath and added NaOH (0.3 g) in water (2 ml). Extraction with ether, drying with Na_2SO_4, evaporation of the solvent and purification of the residue with preparative TLC gave an α,β-unsaturated ketone (13 mg), whose spectra were identical with those of the conjugated ketone **21** derived from **16**.

1,4b,5,6,10,10a-Hexahydro-10aβ-hydroxymethyl-4bβ,8-dimethyl-3(2*H*)-phenanthrenone (26): To a solution of LAH (230 mg, 6.06 mmol) in ether (5 ml) was added **22** (2.88 g, 8.73 mmol) in DME (5 ml) dropwise. The mixture was heated at reflux for 10 min and then AcOEt (1 ml) was added. Ether (50 ml) and water (20 ml) were added into the reaction mixture and the mixture was filtered through a column of celite. Aqueous 1 mol dm^{-3} HCl (30 ml) was added into the filtrate and stirred vigorously at room temperature for 30 min. The aqueous layer was extracted with ether, and combined organic layer was washed with brine and dried (Na_2SO_4). Removal of the solvent afforded keto alcohol **26** (2.25 g, 100%): IR (Nujol) 1655 and 1600 cm^{-1}; UV (EtOH) 237.5 nm (ε 24000); ^{1}H NMR δ=1.14 (3H, s, 10-CH_3), 1.80 (3H, brs, 4-CH_3), 3.74 (2H, ABq, J=13.5 Hz, $\Delta\nu_{AB}$=8.5 Hz, 20-CH_2), 5.48 (1H, m), 5.63 (1H, t, J=4 Hz), and 6.12 (1H, s, 11-CH); MS (70 eV) m/z (rel intensity) 258 (M^+, 69) and 227 (100); Found: m/z 258.1612. Calcd for $C_{17}H_{22}O_2$: M, 258.1620.

1,4b,5,6,10,10a-Hexahydro-10aβ-acetoxymethyl-4bβ,8-dimethyl-3(2*H*)-phenanthrenone (27): A solution of 209 mg (0.81 mmol) of alcohol **26** in 1 ml of pyridine and 0.5 ml of acetic anhydride was stirred at room temperature overnight. The reaction mixture was quenched by the addition of methanol. The solvent was evaporated in vacuo and the residue was chromatographed on a silica-gel column (10 g in hexane, eluent: ethyl acetate-hexane (1 : 2)) to afford 184 mg (76%) of acetate **27** as a colorless oil. An analytical sample was obtained by crystallization from ether-hexane as colorless prisms: mp 81—82.5 °C; IR (oil) 1740 and 1670 cm^{-1}; ^{1}H NMR δ=1.18 (3H, s, 10-CH_3), 1.82 (3H, brs, 4-CH_3), 2.10 (3H, s, $OCOCH_3$), 4.23 (2H, s, 20-CH_2), 5.50 (1H, m), 5.62 (1H, m), and 6.15 (1H, s, 11-CH); MS (70 eV) m/z (rel intensity) 300 (M^+, 23), 240 (43), and 227 (100); Found: C, 75.87; H, 7.93%. Calcd for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05%.

1,4b,5,6,7,8,10,10a-Octahydro-10aβ-acetoxmethyl-7,8-epoxy-4bβ,8-dimethyl-3(2*H*)-phenanthrenone (28): To a cold (−15 °C) solution of **27** (208 mg, 0.69 mmol) in CH_2Cl_2 (4 ml) was added 80% MCPBA (165 mg, 0.76 mmol) in portions under drying tube. The mixture was stirred at −15 °C for 30 min and then at room temperature for 1 h. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (2 ml) containing KI (ca. 20 mg). The mixture was taken up in ether, washed with aqueous Na_2SO_3, saturated aqueous $NaHCO_3$, and brine. Drying ($MgSO_4$) and evaporation of the solvent gave a mixture of α- and β-epoxide **28** (220 mg) in a 3 : 1 ratio (the ratio being determined by the ^{1}H NMR), which were separated by silica-gel column chromatography (5g in hexane, 20% to 50% ether–hexane) to afford α-epoxide **28α** (80 mg, more polar) and β-epoxide **28β** (48 mg, less polar) as colorless oil, respectively. **28α**: IR (oil) 1735 and 1665 cm^{-1}; ^{1}H NMR δ=1.13 (3H, s, 10-CH_3), 1.50 (3H, s, 4-CH_3), 2.28 (3H, s, $OCOCH_3$), 3.10 (1H, brs, $W_{1/2}$=4.5 Hz, 3-CH), 4.37 (2H, s, 20-CH_2), 6.05 (1H, m, 6-CH), and 6.32 (1H, s, 11-CH); MS (70 eV) m/z (rel intensity) 316 (M^+, 100), 256 (26), and 91 (86); Found: m/z 316.1705. Calcd for $C_{19}H_{24}O_4$: M, 316.1664. **28β**: IR (oil) 1740 and 1665 cm^{-1}; ^{1}H NMR δ=1.26 (3H, s, 10-CH_3), 1.52 (3H, m, 4-CH_3), 2.10 (3H, s, $OCOCH_3$), 3.60 (1H, d, J=3.6 Hz, 3-CH), 4.10 (2H, ABq, J=11 Hz, $\Delta\nu_{AB}$=7 Hz, 20-CH_2), 5.80 (1H, m, 6-CH), and 5.90 (1H, s, 11-CH); MS (70 eV) m/z (rel intensity) 316 (M^+, 56) and 91 (100); Found: m/z 316.1663. Calcd for $C_{19}H_{24}O_4$: M, 316.1664.

1,3,4,4a,7,8,8a,9-Octahydro-8a*β*-acetoxymethyl-1*α*,4a*β*-dimethyl-2,6-phenanthrenedione 2-(Ethylene Acetal) (29): To a solution of *α*-epoxide **28** (80 mg, 0.25 mmol) and ethylene glycol (0.5 ml) in benzene (2 ml) was added 2 drops of boron trifluoride etherate. The mixture was stirred at room temperature overnight and poured into saturated aqueous $NaHCO_3$ (5 ml), extracted with ether (10 ml), washed with saturated aqueous $NaHCO_3$ (5 ml) and brine (5 ml). The aqueous layer was reextracted twice with ether and washed as above. The combined ether layers were dried ($MgSO_4$) and concentrated in vacuo to afford 85.7 mg (94%) of **29** pure enough for further use: IR (oil) 1745 and 1675 cm^{-1}; ^1H NMR $\delta=1.00$ (3H, d, $J=6.6$ Hz, 4-CH_3), 1.28 (3H, s, 10-CH_3), 2.06 (3H, s, $OCOCH_3$), 3.90 (4H, m, acetal), 4.34 (2H, brs, 20-CH_2), 5.40 (1H, m, 6-CH), and 6.34 (1H, s, 11-CH); MS (70 eV) m/z (rel intensity) 360 (M^+, 0.7) and 99 (100); Found: m/z 360.1931. Calcd for $C_{21}H_{28}O_5$: M, 360.1936.

1,3,4,4a,7,8,8a,9-Octahydro-8a*β*-methoxycarbonyl-1*α*,4a*β*-dimethyl-2,6-phenanthrenedione 2,6-Bis(ethylene acetal) (33): To a cold solution (-10 °C) of acetal **22** (135 mg, 0.409 mmol) in 1 ml of CH_2Cl_2 was added 97.1 mg (0.45 mmol) of 80% MCPBA in 1 ml of CH_2Cl_2 under drying tube. After being stirred at the same temperature for 30 min, the mixture was poured into saturated aqueous $NaHCO_3$ containing KI and extracted with ether. The organic layer was washed with saturated aqueous $NaHCO_3$ containing a small amount of sodium hydrogensulfide and then with brine, dried (Na_2SO_4) and concentrated in vacuo to afford a mixture of *α*-epoxide and *β*-epoxide (**30*α*** and **30*β***) in a 5 : 1 ratio (the ratio being determined by the ^1H NMR) as colorless solids (150.9 mg), which were used directly in the next step. For analytical purposes, the pure *α*-epoxide **30*α*** was separated by crystallization from ether–hexane: mp 116.2—118.0 °C; IR (Nujol) 1620, 1246, 1102, 1020, 1010, and 922 cm^{-1}; ^1H NMR $\delta=0.98$ (3H, s, 4-CH_3), 1.41 (3H, s, 10-CH_3), 1.95 (1H, dd, $J=3$ and 18 Hz, 7-CH), 2.99 (1H, dd, $J=6$ and 18 Hz, 7-CH), 3.04 (1H, brs, 3-CH), 3.66 (3H, s, CO_2CH_3), 4.00 (4H, m, acetal), 5.63 (1H, s, 11-CH), and 6.04 (1H, dd, $J=3$ and 6 Hz); MS (70 eV) m/z (rel intensity) 346 (M^+, 58), 287 (100), 269 (28), 243 (32), and 231 (16).

To a solution of the above mixture of epoxides **30** (150.9 mg) in benzene (8 ml) was added six drops of boron trifluoride etherate with vigorous stirring. After being stirred at room temperature for 15 min, the reaction was quenched with saturated aqueous $NaHCO_3$. The benzene layer was separated and washed with saturated aqueous $NaHCO_3$ and then brine. The combined aqueous layers were extracted with ether and the ether solution was washed with saturated aqueous $NaHCO_3$ and then brine. The combined organic extracts were dried (Na_2SO_4) and concentrated in vacuo to give a pale yellow solid which contained monoacetal **31** as a major component along with a small amount of diketone **32**.

A mixture of the above crude residue, ethylene glycol (1.5 ml), and a catalytic amount of *p*-toluenesulfonic acid monohydrate in benzene (15 ml) was refluxed under Dean-Stark water separator for 4.5 h. To the cooled mixture was added saturated aqueous $NaHCO_3$ and the aqueous layer was extracted with ether. Combined organic layer was washed with brine, dried (Na_2SO_4) and concentrated in vacuo. The residue was chromatographed on a silica-gel column (5 g in benzene, eluent: 10% to 30% ether–benzene) to afford diacetal **33** (94.8 mg, 64% overall from **22** in 3 steps) as a colorless oil: IR (KBr) 1736 and 1652 cm^{-1}; ^1H NMR $\delta=0.98$ (3H, d, $J=7$ Hz, 4-CH_3), 1.20 (3H, s, 10-CH_3), 2.6 (1H, m, 4-CH), 2.82 (1H, dd, $J=6$ and 18 Hz, 7-CH), 3.63 (3H, s, CO_2CH_3), 3.9 (8H, m, acetal), 5.46 (1H, ddd, $J=6$, 1.5, and 1.5 Hz, 6-CH), and 5.63 (1H, s, 11-CH); MS (70 eV) m/z (rel intensity) 390 (M^+, 2), 346 (2.4), 331 (1), 302 (3.2), and 99 (100); Found: m/z 390.2096. Calcd for $C_{22}H_{30}O_6$: M, 390.2041.

3,4,4a,7,8,8a-Hexahydro-8a*β*-methoxycarbonyl-1*α*,4a*β*-dimethyl-2,6,9(1*H*)-phenanthrenetrione 2-(Ethylene Acetal) (35): To a solution of diacetal **33** (422 mg, 1.08 mmol) in CH_2Cl_2 (8 ml) was added a solution of $CrO_3 \cdot 2Pyr$ complex in CH_2Cl_2 (0.4 mol dm^{-3}, 40 ml) with vigorous stirring. The mixture was stirred at room temperature for 40 h and then quenched with $NaHSO_3$. The supernatant was filtered through a short column of florisil and the tarry solid in the flask was rinsed thoroughly with ether and the washings were filtered through a florisil column. The combined organic solutions were evaporated to give a residue, which was chromatographed on a silica-gel column (20 g in benzene, eluent: 10% to 40% ether–benzene) to afford 102.1 mg (27%) of **35** as a pale yellow oil and 170.5 mg (45%) of **31**. **35**: IR (oil) 1732, 1680, and 1668 cm^{-1}; ^1H NMR $\delta=1.12$ (3H, d, $J=7$ Hz, 4-CH_3), 1.43 (3H, s, 10-CH_3), 3.73 (3H, s, CO_2CH_3), 3.95 (4H, m, acetal), 6.07 (1H, brs, 6-CH), and 6.23 (1H, s, 11-CH); MS (70 eV) m/z (rel intensity) 360 (M^+, 1.4), 301 (0.8), 99 (94), and 57 (100); Found: m/z 360.1567. Calcd for $C_{20}H_{24}O_6$: M, 360.1572.

1,3,4,4a,7,8,8a,9-Octahydro-8a*β*-hydroxymethyl-1*α*,4a*β*-dimethyl-2,6-phenanthrenedione 2-(Ethylene Acetal) (37): To a solution of diacetal **33** (10.1 g, 25.6 mmol) in THF (200 ml) was added LAH (1 g, 26.3 mmol). The mixture was stirred at room temperature for 1 h. To the reaction mixture was added AcOEt (5 ml) and then saturated aqueous NH_4Cl (20 ml). The mixture was filtered and the solid was washed with THF. The filtrate and washings were combined and washed with brine and then dried (Na_2SO_4). Removal of the solvent afforded a residue which was dissolved in acetone (50 ml). Pyridinium *p*-toluenesulfonate (PPTS, 0.1 g) was added to the solution and stirred at room temperature for 1 h. To the reaction mixture were added $NaHCO_3$ (1 g) and benzene (100 ml). The mixture was condensed to ca. 70 ml under reduced pressure. Ether (100 ml) was added to the condensed mixture and the organic layer was washed with half-saturated aqueous NaCl (100 ml×2) and dried (Na_2SO_4). Evaporation of the solvent gave a residue which was purified with silica-gel chromatography (100 g, eluent: 2% acetone in benzene) to give **37**. An analytical sample of **37** was obtained by recrystallization from acetone–hexane as colorless prisms: mp 184—184.5 °C; IR (Nujol) 3420 and 1650 cm^{-1}; ^1H NMR $\delta=1.02$ (3H, d, $J=7$ Hz, 4-CH_3), 1.30 (3H, s, 10-CH_3), 3.68 (2H, brs, 20-CH_2), 3.90 (4H, m, acetal), 5.45 (1H, m, 6-CH), and 6.13 (1H, s, 11-CH); MS (70 eV) m/z (rel intensity) 318 (M^+, 4) and 99 (100); Found: m/z 318.1982. Calcd for $C_{23}H_{26}O_4$: M, 318.1982.

1,3,4,4a,7,8,8a,9-Octahydro-1*α*,4a*β*-dimethyl-8a*β*-[(tetrahydro-2-pyranyloxy)methyl]-2,6-phenanthrenedione 2-(Ethylene Acetal) (38): To a solution of **37** (706.9 mg, 2.22 mmol) in CH_2Cl_2 (30 ml) was added 55 mg of PPTS and 0.5 ml of dihydropyran. The mixture was stirred at room temperature for 5 h. The mixture was diluted with ether, washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on a silica-gel column (15 g in benzene, eluent: ether–benzene) to afford 904.5 mg (100%) of **38** as a pale yellow oil: IR (oil) 1672 cm^{-1}; ^1H NMR $\delta=1.02$

(3H, d, J=7 Hz, 4-CH_3), 1.26 and 1.36 (1.5H each, s, 10-CH_3), 3.2—4.3 (8H, m), 4.53 (1H, m), 5.45 (1H, ddd, J=6, 2, and 2 Hz, 6-CH), and 6.13 (1H, s, 11-CH); MS (70 eV) m/z (rel intensity) 402 (M^+, 16), 318 (12), 99 (over), and 85 (100); Found: m/z 402.2423. Calcd for $C_{24}H_{14}O_5$: M, 402.2406.

1,3,4,4a,4b,5,7,8,8a,9-Decahydro-1α,4aβ-dimethyl-8aβ-[(tetrahydro-2-pyranyloxy)methyl]-2,6-phenanthrenedione 2-(Ethylene Acetal) (39): (a) Hydrogenation: A mixture of **38** (408 mg, 1.02 mmol) and palladium on carbon (10%, 45 mg) in 20 ml of ethanol was stirred at room temperature under an atmosphere of hydrogen for 45 h. The catalyst was removed by filtration and washed with ethanol, and the filtrate was evaporated. The residue was chromatographed on a silica-gel column (5 g in benzene, eluent: ether-benzene) to afford 195 mg (48%) of **39** as colorless oil: IR (oil) 1706 cm^{-1}; ^1H NMR δ=0.98 (3H, d, J=7 Hz, 4-CH_3), 1.04 (3H, s, 10-CH_3), 4.54 (1H, m), and 5.37 (1H, ddd, J=6, 2, and 2 Hz, 6-CH); MS (70 eV) m/z (rel intensity) 404 (M^+, 2.3), 320 (2.3), and 99 (100); Found: m/z 404.2569. Calcd for $C_{24}H_{36}O_5$: M, 404.2536. (b) Birch reduction: Lithium metal (150 mg, 21 mmol) was dissolved in 40 ml of liquid ammonia. To this solution was added **38** (905 mg, 2.25 mmol) in THF (10 ml). The mixture was stirred at −33 °C for 30 min and then quenched by the addition of NH_4Cl (5 g). The ammonia was allowed to evaporate to afford a residue, which was extracted with CH_2Cl_2 and washed with brine. Drying ($MgSO_4$) and evaporation of the solvent gave a residue, which was chromatographed on a silica-gel column to afford 705 mg (77.5%) of **39**. (c) Reduction with NaHTe: A mixture of tellurium powder (3.49 g, 27 mmol) and $NaBH_4$ (2.44 g, 64 mmol) in EtOH (80 ml, deoxygenated with argon) was heated to reflux under argon. After refluxing for 15 min, the resulting dark purple solution was cooled to −20 °C and a deoxygenated solution of acetic acid (1.4 ml) in EtOH (5.6 ml) was added to the mixture. After 5 min, to the above mixture was added **38** (4.31 g, 10 mmol) in EtOH (55 ml) and the resulting solution was stirred at 70 °C for 4.5 h followed by reflux for 3.5 h. The cooled mixture was filtered through a column of Celite with CH_2Cl_2. The solvent was evaporated to give a residue, which was extracted with ether, washed with brine, and dried ($MgSO_4$). Removal of the solvent gave 4.29 g (99%) of crude **39** pure enough for further use.

1,3,4,4a,7,8,8a,9-Octahydro-8aβ-[(1-ethoxyethoxy)methyl]-1α,4aβ-dimethyl-2,6-phenanthrenedione 2-(Ethylene Acetal) (40): A solution of **37** (132 mg, 0.41 mmol) and ethyl vinyl ether (0.3 ml, 3.14 mmol) in CH_2Cl_2 (5 ml) containing PPTS (13 mg) was stirred at room temperature for 1 h. The solution was diluted with CH_2Cl_2 (30 ml) and washed with brine (10 ml). The aqueous layer was extracted with CH_2Cl_2 (20 ml) and the combined organic extracts were dried ($MgSO_4$). Removal of the solvent in vacuo gave pure **40** (173 mg, 100%) as a pale yellow oil: IR (oil) 1670 cm^{-1}; ^1H NMR δ=1.02 (3H, d, J=7 Hz, 4-CH_3), 1.08—1.40 (9H, 3×CH_3), 3.2—3.8 (4H, m), 3.8—4.1 (4H, m, acetal), 4.65 (1H, m), 5.5 (1H, m, 6-CH), and 6.12 (1H, s, 11-CH); MS (70 eV) m/z (rel intensity) 390 (M^+, 5.7), 345 (3.6), 318 (2.7), 288 (6), 99 (over), and 73 (100); Found: m/z 390.2395. Calcd for $C_{23}H_{34}O_5$: M, 390.2404.

1,3,4,4a,4b,5,7,8,8a,9-Decahydro-8aβ-[(1-ethoxyethoxy)-methyl]-1α,4aβ-dimethyl-2,6-phenanthrenedione 2-(Ethylene Acetal) (41): A mixture of tellurium powder (16.58 g, 0.13 mol) and sodium borohydride (10.78 g, 0.29 mol) in EtOH (200 ml, deoxygenated with argon) was cautiously heated to reflux under argon. After refluxing for several min, the resulting dark brown solution was cooled to −20 °C and acetic acid (6.7 ml) in EtOH (28.3 ml) was added. The mixture was warmed to room temperature. To the mixture was added **40** (18.81 g, 0.048 mol) in EtOH (220 ml) and the reaction mixture was heated to reflux for 17 h. The cooled mixture was filtered through a pad of Celite using CH_2Cl_2, AcOEt, and acetone. The solvent was evaporated to give a residue, which was partitioned between CH_2Cl_2 (500 ml) and brine (300 ml). The aqueous layer was extracted with CH_2Cl_2 (200 ml×2). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was chromatographed on a silica-gel column (200 g in benzene, eluent: 10% to 40% ether-benzene) to give 18.39 g (98%) of **41** as a pale yellow oil: IR (oil) 1705 cm^{-1}; ^1H NMR δ=0.9—1.4 (12H, 4×CH_3), 3.92 (4H, m, acetal), 4.67 (1H, m), and 5.39 (1H, m, 6-CH); MS (70 eV) m/z (rel intensity) 392 (M^+, 1.2), 346 (12), 320 (8), 302 (8), 99 (over), and 73 (100).

1,3,4,4a,4b,5,7,8,8a,9-Decahydro-8aβ-[(1-ethoxyethoxy)-methyl]-7-methoxycarbonyl-1α,4aβ-dimethyl-2,6-phenanthrenedione 2-(Ethylene Acetal) (42): To a suspension of sodium hydride (5.03 g, 12.5 mmol, 60% oil dispersion), potassium hydride (1 g, 8.7 mmol, 35% oil dispersion), and dimethyl carbonate (10 ml) in DME (150 ml) was added dropwise a solution of ketone **41** (18.39 g) in DME (270 ml) over 15 min. The mixture was refluxed for 2 h and then cooled to room temperature, poured into saturated aqueous NH_4Cl (200 ml), extracted with ether (500 ml, 300 ml×3) and dried ($MgSO_4$). Removal of the solvent gave an oily residue, which was chromatographed on a silica-gel column (200 g in benzene, eluent: 5% to 10% ether-benzene) to afford keto ester **42** (17.61 g, 83%) as a pale yellow oil: IR (oil) 1745, 1710, 1660, and 1620 cm^{-1}, ^1H NMR δ=0.9—1.3 (12H, 4×CH_3), 3.74 (3H, s, CO_2CH_3), 3.8—4.0 (4H, m, acetal), 4.65 (1H, m), 5.37 (1H, m, 6-CH), and 12.05 (0.5H, s, enol-OH); MS (70 eV) m/z (rel intensity) 450 (M^+, 3), 404 (22), 377 (20), 360 (14), 99 (over), and 73 (100); Found: m/z 450.2612. Calcd for $C_{25}H_{38}O_7$: M, 450.2615.

1,3,4,4a,4b,5,8a,9-Octahydro-8aβ-[(1-ethoxyethoxy)-methyl]-7-methoxycarbonyl-1α,4aβ-dimethyl-2,6-phenanthrenedione 2-(Ethylene Acetal) (43): To a cold (0 °C) suspension of sodium hydride (1.95 g, 48.75 mmol, 60% oil dispersion) in THF was added a solution of keto ester **42** (10.87 g, 24.15 mmol) in THF (70 ml) over 15 min. The mixture was stirred at room temperature for 15 min and then cooled to 0 °C. A solution of benzeneselenenyl chloride (6.97 g, 35.3 mmol) in THF was added rapidly, and the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (50 ml), extracted with ether (500 ml) and washed with brine. The aqueous layer was saturated with NaCl and extracted with ether (200 ml). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated in vacuo. To the crude product in 120 ml of CH_2Cl_2 was added 30% hydrogen peroxide (10 ml, 88 mmol) in 10 ml of water over 5 min at 0 °C. After being stirred at 0 °C for 30 min, the reaction mixture was diluted with CH_2Cl_2 (400 ml) and washed with saturated aqueous $NaHCO_3$ (200 ml). The aqueous layer was extracted with CH_2Cl_2 (200 ml) and the combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed on a silica-gel column (100 g in benzene, eluent: 5% to 50% ether-benzene) to afford **43** (7.37 g, 67%) as a pale yellow oil: IR (oil) 1740, 1710, 1680, and 1620 cm^{-1}; ^1H NMR δ=0.9—1.3 (12H, 4×CH_3), 3.82 (3H, s, CO_2CH_3), 3.83—4.03 (4H, m, acetal), 4.58 (1H, m), 5.36 (1H, m, 6-CH), and 7.35 and 7.37 (1H, each s, 14-CH); MS (70 eV) *m/z* (rel intensity) 448 (M^+, 0.4), 404 (0.5), 403 (0.8), 377 (0.4), 347 (2), 314 (0.8), and 99 (100); Found: *m/z* 448.2460. Calcd for $C_{25}H_{46}O_7$: M, 448.2459.

1,3,4,4a,4b,5,7,8,8a,9-Decahydro-8aβ-[(1-ethoxyethoxy)-methyl]-7-methoxycarbonyl-1α,4aβ-dimethyl-8α-vinyl-2,6-phenanthrenedione 2-(Ethylene Acetal) (46) and 3,4,4a,4b,5,6,8a,9-Octahydro-8aβ-[(1-ethoxyethoxy)methyl]-6-hydroxy-7-methoxycarbonyl-1α,4aβ-dimethyl-6-vinyl-2(1*H*)-phenanthrenone 2-(Ethylene Acetal) (47): To a solution of $(Bu_3P\cdot CuI)_4$ complex (2.03 g) in THF (30 ml) was added vinylmagnesium bromide (from magnesium (700 mg, 29 mmol) and vinyl bromide (3 ml, 42 mmol)) in THF (50 ml) at −45 °C dropwise over a period of 15 min. The resulting solution was stirred at −45 °C for 15 min, and then keto ester **43** (6.54 g, 14.6 mmol) in THF (70 ml) was added over a period of 15 min. The solution was stirred for 2 h, during which time the temperature of the bath came to −20 °C. Saturated aqueous NH_4Cl (50 ml) was added and the mixture was extracted with ether (400 ml) and washed with brine. The aqueous layer was extracted with ether (100 ml×3) and the combined organic layers were dried ($MgSO_4$). Evaporation of the solvent gave a residue which was chromatographed on a silica-gel column (100 g in benzene, eluent: 5% to 50% ether-benzene) to afford 1,4-adduct **46** (5.81 g, 80%) and 1,2-adduct **47** (0.87 g, 12%). **46**: IR (oil) 1650 and 1615 cm^{-1}; ^1H NMR δ=0.93—1.30 (12H, 4×CH_3), 3.71 (3H, s, CO_2CH_3), 3.8—4.1 (4H, m, acetal), 4.54 (1H, m), 4.8—5.1 (2H, m, 16-CH_2), 5.2—5.9 (2H, m, 6-CH and 15-CH), and 12.28 and 12.30 (1H, each s, enol-OH); MS (70 eV) *m/z* (rel intensity) 476 (M^+, 0.6), 430 (22), 403 (4), 371 (6), 99 (over), and 73 (100); Found: *m/z* 430.2361. Calcd for $C_{25}H_{34}O_6$: M−EtOH, 430.2356. **47**: IR (oil) 3500, 1740, 1700, and 1650 cm^{-1}; ^1H NMR δ=0.9—1.3 (12H, 4×CH_3), 3.77 (3H, s, CO_2CH_3), 3.92 (4H, m, acetal), 4.61 (1H, m), 4.89 (1H, d, *J*=17 Hz), 5.02 (1H, d, *J*=11 Hz), 5.35 (1H, m, 6-CH), 5.96 (1H, dd, *J*=17 and 11 Hz), and 7.06 (1H, s, 14-CH); MS (70 eV) *m/z* (rel intensity) 476 (M^+, 1), 450 (1.3), 430 (10), 404 (6), 386 (7), 356 (42), 99 (over), and 73 (100).

3,4,4a,4b,5,8,8a,9-Octahydro-8aβ-[(1-ethoxyethoxy)methyl]-7-methoxycarbonyl-1α,4aβ-dimethyl-8α-vinyl-2(1*H*)-phenanthrenone 2-(Ethylene Acetal) (51): To a solution of keto ester **46** (9.48 g, 19.9 mmol) in EtOH (300 ml) was added sodium borohydride (0.91 g, 24 mmol) at 0 °C. The mixture was stirred at 0 °C overnight. Acetone (50 ml) was added to the reaction mixture and the solvent was evaporated to afford a residue, which was partitioned between ether (500 ml) and saturated aqueous NH_4Cl (100 ml). The aqueous layer was extracted with $CHCl_3$ (200 ml×2) and the combined organic extracts were dried ($MgSO_4$). Evaporation of the solvent gave a mixture of stereoisomers of the alcohol **50** which was used for further reaction without any purification. To a stirred solution of the above mixture of alcohols and triethylamine (20 ml, 0.14 mol) in CH_2Cl_2 (200 ml) was added methanesulfonyl chloride (6.5 ml, 84 mmol) over a period of 15 min at 0 °C. After being stirred at 0 °C for 1 h and at room temperature for 3 h, the mixture was diluted with water (100 ml) and extracted with $CHCl_3$, and the extract was dried ($MgSO_4$). Removal of the solvent gave a crude mesylate, which was dissolved in benzene (400 ml) and DBU (40 ml). The mixture was heated to reflux for 5 h. The cooled mixture was diluted with saturated aqueous NH_4Cl and extracted with ether (300 ml×3). The combined organic extracts were dried ($MgSO_4$) and evaporated to afford a residue which was chromatographed on silica-gel column (300 g dry, eluent: 5% to 20% ether-benzene) to give conjugated ester **51** (6.71 g, 73% yield from **46**). Recrystallization from ether-hexane gave colorless prisms: mp 116—118 °C; IR (Nujol) 1720 and 1660 cm^{-1}; ^1H NMR δ=0.9—1.3 (12H, 4×CH_3), 3.69 (3H, s, CO_2CH_3), 3.91 (4H, m, acetal), 4.56 (1H, m), 4.86—5.20 (2H, m, 16-CH_2), 5.26—6.00 (2H, m, 6-CH and 15-CH), and 7.04 (1H, t, *J*=3.6 Hz, 12-CH); MS (70 eV) *m/z* (rel intensity) 460 (M^+, 0.6), 429 (1.1), 414 (21), 370 (40), 99 (over), and 73 (100); Found: *m/z* 460.2841. Calcd for $C_{27}H_{40}O_6$: M, 460.2826; Found: C, 70.67; H, 8.77%. Calcd for $C_{27}H_{40}O_6$: C, 70.41; H, 8.75%.

1,4,4a,4b,5,6,10,10a-Octahydro-10aβ-methoxycarbonyl-4bβ,8-dimethyl-3(2*H*)-phenanthrenone (53): Reactions were carried out under argon atmosphere and the solvent was deoxygenated with argon prior to use. A mixture of tellurium powder (20.58 g, 0.16 mol) and sodium borohydride (12.17 g, 0.32 mol) in EtOH (500 ml) was stirred at room temperature. After the finish of evolution of hydrogen, the mixture was heated to reflux for 30 min. The resulting solution was cooled to 0 °C and acetic acid (10 ml) was added to the mixture. To the above solution of NaHTe was added **15** (22.86 g, 80 mmol) in EtOH (600 ml) and the reaction mixture was stirred at room temperature for 48 h. As TLC monitoring showed that the conversion was not complete, additional NaHTe solution (2.5 g (20 mmol) of tellurium, 1.5 g (40 mmol) of $NaBH_4$, and 1.2 ml of acetic acid in 80 ml of EtOH) was added to the reaction mixture. The starting material was consumed on stirring at room temperature for 18 h. Then the reaction mixture was stirred for 3 h under open air. The resulting black precipitate was filtered and the filtrate was evaporated to give a residue, which was taken up in ether (300 ml) and water (300 ml). The aqueous layer was extracted with ether (200 ml×2), and the combined organic extracts were washed with brine (100 ml). After drying (Na_2SO_4), the solvent was evaporated to give 22.81 g (99%) of **53** as colorless crystals pure enough for further use. An analytical sample was obtained by recrystallization from ether-hexane as colorless needles: mp 107—109 °C; IR (KBr) 1720 and 1215 cm^{-1}; ^1H NMR δ=0.78 (3H, s, 10-CH_3), 1.80 (3H, brs, 4-CH_3), 3.72 (3H, s, CO_2CH_3), 5.43 (1H, m), and 5.61 (1H, m); MS (70 eV) *m/z* (rel intensity) 288 (M^+, 14), 228 (40), and 161 (100); Found: *m/z* 288.1713. Calcd for $C_{18}H_{24}O_3$: M, 288.1725; Found: C, 74.68; H, 8.33%. Calcd for $C_{18}H_{24}O_3$: C, 74.97; H, 8.39%.

1,4,4a,4b,5,6,10,10a-Octahydro-10aβ-methoxycarbonyl-4bβ,8-dimethyl-3(2*H*)-phenanthrenone 3-(Ethylene Acetal) (54): A solution of **53** (22.81 g, 79.2 mmol), *p*-toluenesulfonic acid (1.3 g), and ethylene glycol (80 ml) in benzene (500 ml) was refluxed under Dean-Stark water separator for 1.5 h. The mixture was cooled to room temperature, quenched by the addition of $NaHCO_3$ (3 g), and the ethylene glycol layer was separated and extracted with benzene (200 ml×2). The combined benzene layers were washed with saturated aqueous $NaHCO_3$ (100 ml) and brine (100 ml), dried (Na_2SO_4), and evaporated to give a residue (27.82 g), which afforded crystalline **54** on standing. The crystals were pure enough for further use. An analytical sample was obtained by recrystallization from ether-hexane as colorless needles: mp 101.5—102.5 °C; IR (KBr) 1730 cm^{-1}; ^1H NMR δ=0.72 (3H, s, 10-CH_3), 1.78 (3H, brs, 4-CH_3), 3.66 (3H, s, CO_2CH_3), 3.96 (4H, brs, acetal), 5.39 (1H, m), and 5.58 (1H, m); MS (70 eV) *m*/*z* (rel intensity) 332 (M^+, 100), 272 (66), and 99 (53); Found: C, 72.22; H, 8.28%. Calcd for $C_{20}H_{28}O_4$: C, 72.26; H, 8.49%.

1,4,4a,4b,5,6,10,10a-Octahydro-10a*β*-hydroxymethyl-4b*β*,8-dimethyl-3(2*H*)-phenanthrenone (55): To a solution of **54** (27.82 g) in THF (300 ml) was added $LiAlH_4$ (3 g) in portions. After being stirred at room temperature for 1 h, to the reaction mixture was added ethyl acetate (15 ml) and then saturated aqueous NH_4Cl (25 ml). The mixture was stirred for 30 min. The resulting precipitate was filtered, dissolved in 4 mol dm^{-3} HCl (200 ml), and extracted with ether (100 ml×2). The above filtrate, the washings, and the ether extracts were combined and evaporated. The residue was dissolved in 600 ml of 10% aqueous acetone containing *p*-toluenesulfonic acid (3 g). The mixture was stirred at room temperature for 20 h and then $NaHCO_3$ (3 g) was added. Removal of the solvent gave a yellow residue, which was taken up in 200 ml of water, filtered and washed with water (100 ml). The filtrate and the washings were combined, extracted with ether (200 ml×2). The above solid was dissolved in ether (500 ml) and combined with the ether extract and dried (Na_2SO_4). Evaporation of the solvent gave a crude residue, which was crystallized from ether-hexane to afford **55** (15.31 g). Chromatography on a silica-gel column (eluent: 5% acetone in benzene) followed by crystallization afforded 3.45 g of **55** from the mother liquor. The yield of the crystals of **55** was 90% overall from **15**. An analytical sample was obtained by recrystallization from ether as colorless prisms: mp 124—126 °C; IR (KBr) 3450 and 1715 cm^{-1}; ^{1}H NMR δ=0.93 (3H, s, 10-CH_3), 1.82 (3H, brs, 4-CH_3), 3.93 (2H, brs, 20-CH_2), and 5.50 (2H, m, 3-CH and 6-CH); MS (70 eV) *m*/*z* (rel intensity) 260 (M^+, 100) and 242 (27); Found: C, 78.43; H, 9.02%. Calcd for $C_{17}H_{24}O_2$: C, 78.42; H, 9.29%.

1,4,4a,4b,5,6,10,10a-Octahydro-10a*β*-[(1-ethoxyethoxy)-methyl]-4b*β*,8-dimethyl-3(2*H*)-phenanthrenone (56): To a solution of **55** (13.21 g, 50.8 mmol) in CH_2Cl_2 (250 ml) was added PPTS (3.4 g) and ethyl vinyl ether (10 ml). After being stirred at room temperature for 1 h, the mixture was washed with saturated aqueous $NaHCO_3$ (50 ml), dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed on a silica-gel column (eluent: 20% ether in hexane) to afford 15.83 g (94%) of **56** as a pale yellow oil: IR (oil) 1710 cm^{-1}; ^{1}H NMR δ=0.95 (3H, s, 10-CH_3), 1.1—1.4 (6H, 2×CH_3), 1.74 (3H, brs, 4-CH_3), 4.70 (1H, q, *J*=5 Hz), and 5.4—5.6 (2H, m, 3-CH and 6-CH); MS (70 eV) *m*/*z* (rel intensity) 332 (M^+, 1.6), 286 (76), 260 (26), and 73 (100); Found: *m*/*z* 286.1932. Calcd for $C_{19}H_{26}O_2$: M−EtOH, 286.1932.

1,4,4a,4b,5,6,10,10a-Octahydro-10a*β*-[(1-ethoxyethoxy)-methyl]-2-methoxycarbonyl-4b*β*,8-dimethyl-3(2*H*)-phenanthrenone (57): To a suspension of NaH (5.85 g, 0.146 mol, 60% oil dispersion), KH (550 mg, 4.8 mmol, 35% oil dispersion), and dimethyl carbonate (15 ml) in DME (300 ml) was added **56** (15.83 g, 47.7 mmol) in DME (180 ml). The mixture was refluxed for 1 h, cooled to 0 °C, and quenched with the addition of saturated aqueous NH_4Cl (100 ml). The organic layer was separated, washed with brine, and dried (Na_2SO_4). Removal of the solvent gave a residue, which was chromatographed on a silica-gel column (150 g in hexane, eluent: 10% ether in hexane) to afford 17.84 g (96%) of **57** as a pale yellow oil: IR (oil) 1750, 1720, 1665, and 1625 cm^{-1}; ^{1}H NMR δ=0.94 (3H, s, 10-CH_3), 1.05—1.40 (6H, 2×CH_3), 1.77 (3H, brs, 4-CH_3), 3.73 (3H, s, CO_2CH_3), 4.58 (1H, m), and 5.3—5.6 (2H, m, 3-CH and 6-CH); MS (70 eV) *m*/*z* (rel intensity) 344 (M^+−EtOH, 2.6), 300 (14.6), and 73 (100); Found: *m*/*z* 344.2005. Calcd for $C_{21}H_{28}O_4$: M−EtOH, 344.1987.

4a,4b,5,6,10,10a-Hexahydro-10a*β*-[(1-ethoxyethoxy)methyl]-2-methoxycarbonyl-4b*β*,8-dimethyl-3(4*H*)-phenanthrenone (58): To a cold (0 °C) suspension of NaH (3.96 g, 99 mmol, 60% oil dispersion) in THF (200 ml) was added **57** (17.84 g, 46 mmol) in THF (170 ml) dropwise with stirring. The mixture was stirred at room temperature for 1 h and cooled to 0 °C. A solution of benzeneselenenyl chloride (10.80 g, 56 mmol) in THF (70 ml) was added rapidly to the mixture. After 5 min, saturated aqueous NH_4Cl (100 ml) was added to the reaction mixture and the mixture was extracted with ether. The extract was washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (200 ml) and cooled to 0 °C. Hydrogen peroxide (30%, 5.5 ml) was added and the mixture was stirred at 0 °C for 1.5 h. The mixture was washed with brine (100 ml), dried over $MgSO_4$, and concentrated in vacuo to give a residue, which was chromatographed on a silica-gel column (150 g in hexane, eluent: 30% ether in hexane) to afford 12.98 g (73%) of **58** as a yellow oil. IR (oil) 1745, 1720, and 1685 cm^{-1}; ^{1}H NMR δ=0.9—1.3 (9H, 3×CH_3), 1.80 (3H, brs, 4-CH_3), 3.83 (3H, s, CO_2CH_3), 4.60 (1H, q, *J*=5.4 Hz), 5.50 (2H, m, 3-CH and 6-CH), and 7.38 and 7.39 (1H, each s, 14-CH); MS (70 eV) *m*/*z* (rel intensity) 388 (M^+, 2), 342 (9), 316 (13), 298 (14), 285 (28), 254 (23), 253 (22), and 73 (100); Found: *m*/*z* 388.2246. Calcd for $C_{23}H_{32}O_5$: M, 388.2249.

1,4,4a,4b,5,6,10,10a-Octahydro-10a*β*-[(1-ethoxyethoxy)-methyl]-2-methoxycarbonyl-4b*β*,8-dimethyl-1*α*-vinyl-3(2*H*)-phenanthrenone (59): To a cold (−45 °C) solution of $(Bu_3P \cdot CuI)_4$ complex (3.2 g) in THF (50 ml) under nitrogen was added vinylmagnesium bromide (from 190 mg (32.5 mmol) of magnesium and 4.3 ml (61 mmol) of vinyl bromide) in THF (50 ml) dropwise. The resulting mixture was stirred at −45 °C for 20 min, and **58** (10.48 g, 27.01 mmol) in dry THF (100 ml) was added over a period of 30 min. After being stirred at −45 °C for 1.5 h, the mixture was washed with saturated aqueous NH_4Cl (100 ml) and then with brine (100 ml). Drying ($MgSO_4$) followed by evaporation of the solvent gave a residue, which was chromatographed on a silica-gel column (150 g in hexane, eluent: 5% to 10% ether–hexane) to afford 9.78 g (87%) of **59** as a colorless oil: IR (oil) 1655 and 1620 cm^{-1}; ^{1}H NMR δ=0.9—1.3 (3×CH_3), 1.78 (3H, brs, 4-CH_3), 3.73 (3H, s, CO_2CH_3), 4.57 (1H, m), 4.85—5.15 (2H, m, 16-CH_2), 5.3—5.9 (3H, m, 3-CH, 6-CH, and 15-CH), and 12.30 and 12.32 (0.8H, each s, enol-OH); MS (70 eV) *m*/*z* (rel intensity) 370 (M^+−EtOH, 16), 326 (19), 294 (10), 171 (48), and 73 (100); Found: *m*/*z* 370.2145. Calcd for $C_{23}H_{30}O_4$: M−EtOH, 370.2140.

1,4,4a,4b,5,6,10,10a-Octahydro-10a*β*-[(1-ethoxyethoxy)-methyl]-2-methoxycarbonyl-4b*β*,8-dimethyl-1*α*-vinylphenanthrene (60): To a cold (0 °C) solution of **59** (6.55 g, 15.7 mmol) in EtOH (150 ml) was added $NaBH_4$ (0.71 g, 18.7 mmol) in portions. The mixture was stirred at 0 °C overnight. Acetone was added to the mixture and the solvent was evaporated to afford a residue, which was partitioned between CH_2Cl_2 (200 ml) and saturated aqueous NH_4Cl (50 ml). The aqueous layer was extracted with CH_2Cl_2 (200 ml×2) and the combined organic extracts were dried ($MgSO_4$). Removal of the solvent gave a residue, which was dissolved in CH_2Cl_2 (100 ml) containing triethylamine (10 ml, 71 mmol). To the above cold (0 °C) mixture was added methanesulfonyl chloride (3 ml, 39 mmol) dropwise over 10 min. After being stirred at 0 °C for 3.5 h, additional triethylamine (5 ml, 36 mmol) and methanesulfonyl chloride (2 ml, 26 mmol) was added to the mixture. The mixture was diluted with ether (300 ml) and washed with saturated aqueous NH_4Cl and then with brine. The aqueous layer was extracted with ether (100 ml×2) and the combined organic extracts were dried over $MgSO_4$. Removal of the solvent gave a residue, which was dissolved in benzene (100 ml) and DBU (20 ml). The mixture was refluxed until the mesylate was consumed. The cooling mixture was diluted with ether (300 ml) and washed with saturated aqueous NH_4Cl (100 ml). The aqueous layer was extracted with ether (100 ml×2) and the combined organic extracts were washed with water (100 ml) and brine (100 ml) and dried ($MgSO_4$). Removal of the solvent gave a residue which was chromatographed on a silica-gel column (60 g in hexane, eluent: 20% ether–hexane) to afford 4.82 g (76.5%) of **60** as a colorless oil: IR (oil) 1725 cm^{-1}; ^1H NMR δ=0.98 (3H, s, 10-CH_3), 1.09—1.39 (6H, 2×CH_3), 1.80 (3H, brs, 4-CH_3), 3.72 (3H, s, CO_2CH_3), 4.61 (1H, m), 4.89—5.24 (2H, m, 16-CH_2), 5.3—6.0 (1H, m, 15-CH), and 7.07 (1H, m, 12-CH); MS (70 eV) *m/z* (rel intensity) 368 (M^+−MeOH, 10), 354 (36), 310 (51), 295 (68), and 73 (100); Found: *m/z* 368.2359. Calcd for $C_{24}H_{32}O_3$: M−MeOH, 368.2351.

1,4,4a,4b,5,6,10,10a-Octahydro-10aβ-acetoxymethyl-2-methoxycarbonyl-4bβ,8-dimethyl-1α-vinylphenanthrene (61): A mixture of **60** (5.40 g, 13.5 mmol) and *p*-toluenesulfonic acid (0.5 g) in EtOH (100 ml) was stirred at room temperature for 30 min. The solvent was evaporated and the residue was diluted with ether (200 ml), washed with saturated aqueous $NaHCO_3$ (50 ml), and dried ($MgSO_4$). Removal of the solvent gave a residue, which was dissolved in pyridine (50 ml) and acetic anhydride (5 ml). The mixture was stirred at room temperature overnight. Excess acetic anhydride was decomposed by the addition of MeOH (10 ml) at 0 °C and the solvent was evaporated under reduced pressure. The residue was chromatographed on a silica-gel column (100 g in hexane, eluent: 20% to 40% ether–hexane) to afford 4.50 g (90%) of **61** as colorless crystals. An analytical sample of **61**, mp 108—108.5 °C, was obtained as colorless prisms by crystallization from ether–hexane: IR (KBr) 1740, 1715, and 1660 cm^{-1}; ^1H NMR δ=0.99 (3H, s, 10-CH_3), 1.78 (3H, brs, 4-CH_3), 2.06 (3H, s, $OCOCH_3$), 3.71(3H, s, CO_2CH_3), 3.96 and 4.17 (2H, ABq, *J*=10 Hz, 20-CH_2), 4.9—5.2 (2H, m, 16-CH_2), 5.3—5.9 (3H, m, 3-CH, 6-CH, and 15-CH), and 7.03 (1H, t, *J*=4 Hz, 12-CH); MS (70 eV) *m/z* (rel intensity) 370 (M^+, 1.6), 310 (100), and 171 (96); Found: *m/z* 370.2158. Calcd for $C_{23}H_{30}O_4$: M, 370.2144. Found: C, 74.35; H, 8.22%. Calcd for $C_{23}H_{30}O_4$: C, 74.56; H, 8.16%.

3,4,4a,4b,5,8,8a,9-Octahydro-8aβ-acetoxymethyl-7-methoxycarbonyl-1α,4aβ-dimethyl-8α-vinyl-2(1*H*)-phenanthrenone 2-(Ethylene Acetal) (63): To a cold (0 °C) solution of **61** (5.34 g, 14.4 mmol) in CH_2Cl_2 (100 ml) was added MCPBA (80%, 3.27 g, 15.1 mmol). After being stirred at 0 °C for 30 min under drying tube, the reaction mixture was poured into aqueous saturated Na_2SO_3 and extracted with ether (500 ml). The organic layer was washed with aqueous saturated $NaHCO_3$ (100 ml×2) and brine (60 ml), dried ($MgSO_4$) and concentrated in vacuo to afford the crude epoxide **62** (^1H NMR δ=0.97 (3H, s, 10-CH_3), 1.47 (3H, s, 4-CH_3), 2.09 (3H, s, $OCOCH_3$), 3.08 (1H, brs, $W_{1/2}$=4.5 Hz, 3-CH), 3.72 (3H, s, CO_2CH_3), 4.00 (2H, ABq, *J*=10 Hz, $\Delta\nu_{AB}$=5 Hz, 20-CH_2), 4.9—5.2 (2H, m, 16-CH_2), 5.4—5.9 (1H, m, 15-CH), 5.97 (1H, dd, *J*=5 and 3.5 Hz, 6-CH), and 7.00 (1H, *t*-like, 12-CH)), which was dried over P_2O_5 under reduced pressure for several hours. To a cold (0 °C) solution of the above epoxide and 2-ethyl-2-methyl-1,3-dioxolane (10 ml) in CH_2Cl_2 (100 ml) under argon was added boron trifluoride etherate (0.09 ml, 0.6 mmol) dropwise. The mixture was stirred at 0 °C for 1 h and additional $BF_3 \cdot Et_2O$ (0.04 ml, 0.3 mmol) was added. After being stirred at 0 °C for 30 min, the mixture was poured into saturated aqueous $NaHCO_3$ (100 ml), extracted with CH_2Cl_2 (200 ml×3), dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed on a silica-gel column (eluent: ether–hexane) to afford **63** (5.39 g, 87% from **61**) as colorless crystals. An analytical sample was recrystallized from ether–hexane: mp 173—174 °C; IR (KBr) 1735, 1715, and 1655 cm^{-1}; ^1H NMR δ=1.00 (3H, d, *J*=7 Hz, 4-CH_3), 1.13 (3H, s, 10-CH_3), 2.06 (3H, s, $OCOCH_3$), 3.72 (3H, s, CO_2CH_3), 3.93 (4H, m, acetal), 4.9—5.2 (2H, m, 16-CH_2), 5.3—5.9 (2H, m, 6-CH and 15-CH), and 7.01 (1H, m, 12-CH); MS (70 eV) *m/z* (rel intensity) 430 (M^+, 0.8), 386 (0.8), 370 (3.2), and 99 (100); Found: *m/z* 430.2335. Calcd for $C_{25}H_{34}O_6$: M, 430.2355. Found: C, 69.60; H, 8.02%. Calcd for $C_{25}H_{34}O_6$: C, 69.74; H, 7.96%.

Conversion of Acetate 63 into 1-Ethoxyethyl Ether 51: A solution of **63** (2.22 g, 5.16 mmol) in MeOH (50 ml) was mixed with a solution of K_2CO_3 (0.5 g, 3.6 mmol) in water (10 ml). The mixture was stirred at room temperature overnight. The solvent was evaporated and the residue was taken up in saturated aqueous NH_4Cl (50 ml) and extracted with ether (100 ml×4). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo to afford crude alcohol **52**, which was dissolved in 50 ml of CH_2Cl_2. To this solution was added PPTS (350 mg) and ethyl vinyl ether (2 ml). The mixture was stirred at room temperature for 1 h. The solution was washed with saturated aqueous $NaHCO_3$ (30 ml), dried ($MgSO_4$) and evaporated. The residue was chromatographed on a silica-gel column (20 g in hexane, eluent: 30% ether–hexane) to afford 2.20 g (93%) of **51**.

3,4,4a,4b,5,8,8a,9-Octahydro-8aβ-[(1-ethoxyethoxy)methyl]-7-hydroxymethyl-1α,4aβ-dimethyl-8α-vinyl-2(1*H*)-phenanthrenone 2-(Ethylene Acetal) (66): To a cold (−78 °C) solution of conjugated ester **51** (2.35 g, 5.11 mmol) in toluene (50 ml) was added dropwise 16 ml of a ca. 1 mol dm^{-3} solution of diisobutylaluminium hydride (DIBAL) in hexane. After 1.5 h at this temperature, the mixture was quenched by the addition of methanol (25 ml) and stirred at room temperature for 30 min. The resulting precipitate was filtered and washed thoroughly with methanol. The combined filtrates were evaporated to give a residue, which was chromatographed on a silica-gel column (50 g in $CHCl_3$, eluent: 1% to 3% MeOH–$CHCl_3$) to afford allylic alcohol **66** (2.23 g, quant.) as a colorless oil: IR (oil) 3470 cm^{-1}; ^1H NMR δ=0.9—1.3 (12H, 4×CH_3), 3.8—4.0 (6H), 4.53 (1H, m), 4.85—5.20 (2H, m, 16-CH_2), 5.37 (1H, m, 6-CH), 5.74 (1H, m, 12-CH), and 5.3—5.9 (1H, m, 15-CH); MS (70 eV) *m/z* (rel intensity) 432 (M^+, 0.1), 414 (0.4), 386 (7), 342 (19), 99 (over), and 73 (100); Found: *m/z* 386.2426. Calcd for $C_{24}H_{34}O_4$: M−EtOH, 386.2458.

1,2,3,4,4a,4b,5,6,8,10-Decahydro-3α-hydroxy-2α-hydroxymethyl-4bβ,8α-dimethyl-1α-vinyl-7*H*-2β,10aβ-(epoxymethano)-phenanthren-7-one 7-(Ethylene Acetal) (68): To a cold (−20 °C) solution of allylic alcohol **66** (1.19 g, 2.75 mmol) in CH_2Cl_2 (30 ml) was added dropwise titanium(IV) isopropoxide (4 ml, 13.44 mmol). After 15 min, an anhydrous solution of *t*-butyl hydroperoxide (5.9 M in 1,2-dichloroethane, 3.5 ml, 20.65 mmol) was added and the mixture was stirred at −20 °C for 3.5 h. Dimethyl sulfide (3 ml) and aqueous saturated sodium fluoride (5 ml) was added to the mixture at −20 °C and the mixture was stirred at room temperature for 1 h to result in white emulsion, which was filtered through a pad of Celite. The filtrate was extracted with $CHCl_3$ (100 ml×3), dried over $MgSO_4$, and concentrated in vacuo. The crude epoxy alcohol **67** without purification was dissolved in ethanol (100 ml) and treated with PPTS (70 mg, 0.28 mmol). The mixture was stirred at 40—50 °C for 30 min. Removal of the solvent gave a residue, which was chromatographed on a silica-gel column (40 g in $CHCl_3$, eluent: 1% to 3% MeOH–$CHCl_3$) to provide diol **68** (1.10 g, quant.) as colorless crystals. An analytical sample was obtained by recrystallization from acetone as colorless needles: mp 213—214 °C; IR (KBr) 3430, 1645, 1090, and 1045 cm^{-1}; ^1H NMR δ=0.99 (3H, d, *J*=6 Hz, 4-CH_3), 1.19 (3H, s, 10-CH_3), 3.33 (1H, d, *J*=8 Hz, 20-CH), 3.74 (2H, brs, 21-CH_2), 3.93 (4H, m, acetal), 4.05 (1H, brd, *J*=4 Hz, 12-CH), 4.36 (1H, d, *J*=8 Hz, 20-CH), 4.96—5.25 (2H, m, 16-CH_2), 5.36 (1H, m, 6-CH), and 6.1—6.6 (1H, m, 15-CH); ^{13}C NMR δ=9.89 (q), 19.72 (q), 29.88 (t), 30.82 (t), 31.07 (t), 36.81 (s), 37.08 (t), 40.47 (d), 40.90 (d), 44.04 (s), 58.29 (d), 64.79 (t), 64.95 (t), 65.22 (t), 70.64 (d), 76.38 (t), 84.51 (s), 111.14 (s), 117.99 (d), 118.86 (t), 134.99 (d), and 142.67 (s); MS (70 eV) *m/z* (rel intensity) 376 (M^+, 16), 358 (3), 292 (4), 100 (100), and 99 (over); Found: *m/z* 376.2226. Calcd for $C_{22}H_{32}O_5$: M, 376.2251.

1,2,3,4,4a,4b,5,6,8,10-Decahydro-3α-acetoxy-2α-acetoxymethyl-4bβ,8α-dimethyl-1α-vinyl-7*H*-2β,10aβ-(epoxymethano)phenanthren-7-one 7-(Ethylene Acetal) (70): A mixture of diol **68** (8.5 mg, 0.022 mmol), a catalytic amount of 4-dimethylaminopyridine (DMAP), acetic anhydride (0.3 ml), and pyridine (0.5 ml) was stirred at room temperature overnight. An excess acetic anhydride was decomposed by the addition of methanol and the volatiles were removed in vacuo. The residue was chromatographed on a silica-gel column (3 g in $CHCl_3$, eluent: 1% to 3% MeOH–$CHCl_3$) to afford diacetate **70** (7.9 mg, 76%): IR (oil) 1745 cm^{-1}; ^1H NMR δ=1.00 (3H, d, *J*=6 Hz, 4-CH_3), 1.16 (3H, s, 10-CH_3), 2.01 (3H, s, $OCOCH_3$), 2.08 (3H, s, $OCOCH_3$), 3.43 (1H, d, *J*=8 Hz, 20-CH), 3.83 (1H, d, *J*=12 Hz, 21-CH), 3.93 (4H, m, acetal), 4.38 (1H, d, *J*=12 Hz, 21-CH), 4.44 (1H, d, *J*=8 Hz, 20-CH), 4.83—5.35 (3H, m, 12-CH and 16-CH_2), 5.36 (1H, m, 6-CH), and 5.8—6.5 (1H, m, 15-CH); MS (70 eV) *m/z* (rel intensity) 460 (M^+, 1.6) and 99 (100); Found: *m/z* 460.2476. Calcd for $C_{26}H_{36}O_7$: M, 460.2462.

1,2,3,4,4a,4b,5,6,8,10-Decahydro-2α-(*t*-butyldimethylsiloxymethyl)-3α-hydroxy-4bβ,8α-dimethyl-1α-vinyl-7*H*-2β,10aβ-(epoxymethano)phenanthren-7-one 7-(Ethylene Acetal) (71): To a cold (0 °C) solution of diol **68** (1.4321 g, 3.81 mmol) and imidazole (0.549 g, 8.06 mmol) in DMF (15ml) was added *t*-buthyldimethylchlorosilane (tBDMSCl, 0.8625 g, 5.72 mmol). After being stirred at room temperature for 2 h, additional imidazole (0.39 g, 5.73 mmol) and tBDMSCl (0.57 g, 3.78 mmol) was added. After another 1 h, the mixture was poured into water (100 ml) and extracted with ether (100 ml×4). Drying ($MgSO_4$) and evaporation of the solvent gave a residue, which was chromatographed on a silica-gel column (40 g in hexane) with ether–hexane (1 : 2 to 1 : 1) to afford monosilyl ether **71** (1.8298 g, 98 %) as a colorless oil, which crystallized upon standing. An analytical sample was obtained by recrystallization from hexane as colorless prisms: mp 98—99 °C; IR (oil) 3500 cm^{-1}; ^1H NMR δ=0.90 (9H, s, *t*-Bu), 0.97 (3H, d, *J*=7 Hz, 4-CH_3), 1.15 (3H, s, 10-CH_3), 3.29 (1H, d, *J*=8 Hz, 20-CH), 3.77 (2H, ABq, *J*=10 Hz, $\Delta\nu_{AB}$=10 Hz, 21-CH_2), 3.91 (4H, m, acetal), 4.08 (1H, m, 12-CH), 4.32 (1H, d, *J*=8 Hz, 20-CH), 4.9—5.2 (2H, m, 16-CH_2), 5.33 (1H, m, 6-CH), and 6.2—6.7 (1H, m, 15-CH); MS (70 eV) *m/z* (rel intensity) 490 (M^+, 3), 433 (50), 415 (8), 99 (over), and 75 (100); Found: *m/z* 490.3107. Calcd for $C_{28}H_{46}O_5Si$: M, 490.3148. Found: C, 68.76; H, 9.68%. Calcd for $C_{28}H_{46}O_5Si$: C, 68.53, H, 9.45%.

1,2,3,4,4a,4b,5,6,8,10-Decahydro-3α-acetoxy-2α-(*t*-butyldimethylsiloxymethyl)-4bβ,8α-dimethyl-1α-vinyl-7*H*-2β,10aβ-(epoxymethano)phenanthren-7-one 7-(Ethylene Acetal) (72): A mixture of monosilyl ether **71** (12 mg), a catalytic amount of DMAP, acetic anhydride (0.5 ml), and pyridine (1 ml) was stirred at room temperature for 2.5 h. After the addition of methanol, the volatiles were removed in vacuo to give a residue. Chromatography on a silica-gel column (3 g in hexane) with ethyl acetate–hexane (1 : 5) afforded acetate **72** (11 mg, 84 %): IR (oil) 1745 cm^{-1}; ^1H NMR δ=0.90 (9H, s, *t*-Bu), 0.99 (3H, d, *J*=6 Hz, 4-CH_3), 1.15 (3H, s, 10-CH_3), 1.99 (3H, s, $OCOCH_3$), 3.33 (1H, d, *J*=8 Hz, 20-CH), 3.48 and 3.68 (2H, ABq, *J*=11 Hz, 21-CH_2), 3.92 (4H, m, acetal), 4.37 (1H, d, *J*=8 Hz, 20-CH), 4.95—5.25 (3H, m, 12-CH and 16-CH_2), 5.35 (1H, m, 6-CH), and 5.8—6.4 (1H, m, 15-CH); MS (70 eV) *m/z* (rel intensity) 532 (M^+, 0.1), 475 (3), 415 (8), and 99 (100); Found: *m/z* 475.2513. Calcd for $C_{26}H_{39}O_6Si$: M, 475.2517.

1,2,3,4,4a,4b,5,6,8,10-Decahydro-3α-(*t*-butyldimethylsiloxy)-2α-(methoxymethoxymethyl)-4bβ,8α-dimethyl-1α-vinyl-7*H*-2β,10aβ-(epoxymethano)phenanthren-7-one 7-(Ethylene Acetal) (73): Potassium hydride (1 g, 8.75 mmol, 35% oil dispersion) was washed with hexane (6 ml). To a suspension of the potassium hydride in a mixture of THF (20 ml) and DMF (10 ml) was added dropwise a solution of monosilyl ether **71** (1.00 g, 2.04 mmol) in THF (20 ml) at 0 °C. After 15 min, chloromethyl methyl ether (0.7 ml, 9.22 mmol) was added dropwise and the resulting mixture was stirred at room temperature for 80 min. The mixture was poured into saturated aqueous $NaHCO_3$ (60 ml), extracted with $CHCl_3$ (100 ml×1, 70 ml×2), and dried over $MgSO_4$. Removal of the solvent gave a residue, which was chromatographed on a silica-gel column (30 g in $CHCl_3$, eluent: 1% to 3% MeOH–$CHCl_3$) to afford methoxymethyl ether **73** (0.96 g, 88%) as a colorless viscous oil: IR (oil) no absorption due to hydroxyl group; ^1H NMR δ=0.90 (9H, s, *t*-Bu), 0.97 (3H, d, *J*=7 Hz, 4-CH_3), 1.15 (3H, s, 10-CH_3), 3.36 (3H, s, OCH_3), 3.37 (1H, 20-CH: broad signal due to overlapping with other signal), 3.57 (2H, brs, 21-CH_2), 3.92 (4H, m, acetal), 4.02 (1H, m, 12-CH), 4.34 (1H, d, *J*=8 Hz, 20-CH), 4.64 (2H, s, OCH_2O), 4.85—5.15 (2H, m, 16-CH_2), 5.34 (1H, m, 6-CH), and 6.1—6.6 (1H, m, 15-CH); MS (70 eV) *m/z* (rel intensity) 534 (M^+, 2), 503 (5), 477 (95), 445 (29), 415 (29), 99 (over), and 73 (100); Found: *m/z* 477.2673. Calcd for $C_{26}H_{41}O_6Si$: M, 477.2674.

1,2,3,4,4a,4b,5,6,8,10-Decahydro-3α-acetoxy-2α-(methoxymethoxymethyl)-4bβ,8α-dimethyl-1α-vinyl-7*H*-2β,10aβ-(epoxymethano)phenanthren-7-one 7-(Ethylene Acetal) (74): To a solution of **73** (25.8 mg, 0.048 mmol) in THF (1 ml) was added tetrabutylammonium fluoride (65 mg, 0.25 mmol) in THF (2 ml). The mixture was stirred at 50 °C for 23 h. The solvent was evaporated in vacuo to give a brown residue, which was filtered through florisil short column with ethyl acetate. The resulting crude alcohol was dissolved in pyridine (1 ml) and acetic anhydride (0.3 ml) containing a catalytic amount of DMAP, and the mixture was stirred at room temperature for 95 min. After the addition of methanol, the volatiles were evaporated in vacuo to give a residue, which was chromatographed on a silica-gel column (5 g in hexane) with ether-hexane (1 : 1) to afford acetate **74** (21.1 mg, 94%) as colorless crystals. An analytical sample was obtained by recrystallization from ether-hexane as colorless prisms: mp 158—159 °C; IR (KBr) 1745, 1380, and 1250 cm^{-1}; ^1H NMR δ=0.99 (3H, d, *J*=6 Hz, 4-CH_3), 1.17 (3H, s, 10-CH_3), 2.03 (3H, s, $OCOCH_3$), 3.35 (3H, s, OCH_3), 3.36 (1H, d, *J*=8 Hz, 20-CH), 3.41 and 3.63 (2H, ABq, *J*=10 Hz, 21-CH_2), 3.92 (4H, m, acetal), 4.39 (1H, d, *J*=8 Hz, 20-CH), 4.60 (2H, brs, OCH_2O), 4.9—5.3 (3H, m, 12-CH and 16-CH_2), 5.35 (1H, m, 6-CH), and 5.9—6.4 (1H, m, 15-CH); MS (70 eV) *m/z* (rel intensity) 462 (M^+, 1), 431 (0.4), 402 (1.1), and 99 (100); Found: *m/z* 462.2622. Calcd for $C_{26}H_{38}O_7$: M, 462.2617.

1,2,3,4,4a,4b,5,6,8,10-Decahydro-3α-(*t*-butyldimethylsiloxy)-2α-(*t*-butyldimethylsiloxymethyl)-4bβ,8α-dimethyl-1α-vinyl-7*H*-2β,10aβ-(epoxymethano)phenanthren-7-one 7-(Ethylene Acetal) (75): To a cold (0 °C) suspension of potassium hydride (3.13 g, 27.4 mmol, 35% oil dispersion) in a mixture of THF (40 ml) and DMF (20 ml) was added dropwise a solution of **71** (2.76 g, 5.63 mmol) in THF (40 ml) over the period of 15 min. After 15 min, a solution of tBDMSCl (2.6 g, 17.2 mmol) in THF (5 ml) was added to the solution. The mixture was stirred at room temperature for 1 h, poured into brine (100 ml), and extracted with ether (150 ml×4). Drying ($MgSO_4$) and evaporation of the solvent gave a residue, which was chromatographed on a silica-gel column (60 g in hexane) with ether-hexane (1 : 4) to afford disilyl ether **75** (3.26 g, 96%) as a colorless viscous oil: IR (oil) no absorption due to hydroxyl group; ^1H NMR δ=0.04 (12H, s, 2×$Si(CH_3)_2$), 0.86 (9H, s, *t*-Bu), 0.90 (9H, s, *t*-Bu), 0.91 (3H, d, *J*=7 Hz, 4-CH_3), 1.12 (3H, s, 10-CH_3), 3.25 (1H, d, *J*=8 Hz, 20-CH), 3.60 (2H, s, 21-CH_2), 3.90 (4H, m, acetal), 4.29 (1H, d, *J*=8 Hz, 20-CH), 4.8—5.2 (2H, m, 16-CH_2), 5.33 (1H, m, 6-CH), and 6.0—6.6 (1H, m, 15-CH); MS (70 eV) *m/z* (rel intensity) 604 (M^+, 0.2), 547 (28), 503 (6), 415 (7), and 99 (100); Found: *m/z* 604.3997. Calcd for $C_{34}H_{60}O_5Si_2$: M, 604.3981.

1,2,3,4,4a,4b,5,6,8,10-Decahydro-3α-(*t*-butyldimethylsiloxy)-2α-(*t*-butyldimethylsiloxymethyl)-1α-(2-hydroxyethyl)-4bβ,8α-dimethyl-7*H*-2β,10aβ-(epoxymethano)phenanthren-7-one 7-(Ethylene Acetal) (76): In a 200 ml three-necked flask was placed ca. 2 mol dm^{-3} borane-THF solution (9.5 ml) and THF (50 ml) under argon atmosphere. To the solution was added dropwise 2,3-dimethyl-2-butene (6.5 ml, 54 mmol) at 0 °C and this solution was stirred at 0 °C for 2h. To this solution was added disilyl ether **75** (3.26 g, 5.40 mmol) in THF (40 ml) and the mixture was stirred at 0 °C for 3 h, then at room temperature for 1 h. The solution was cooled to 0 °C, quenched by the careful addition of water (6 ml), followed by 3 M NaOH solution (17 ml) and 30% H_2O_2 (17 ml). After being stirred at ca. 50 °C for 1.5 h, the mixture was cooled to room temperature and the aqueous layer was saturated with NaCl, extracted with ether (150 ml×3), and dried over $MgSO_4$. Evaporation of the solvent gave a residue, which was chromatographed on a silica-gel column (60 g in hexane) with ether-hexane (1 : 4 to 1 : 1) to afford alcohol **76** (2.71 g, 81%) as a colorless oil. An analytical sample was obtained by crystallization from ether-hexane as colorless prisms: mp 145—146 °C; IR (oil) 3500cm^{-1}; ^1H NMR δ=0.02 and 0.04 (12H, each s, 2×$Si(CH_3)_2$), 0.87 (9H, s, *t*-Bu), 0.93 (9H, s, *t*-Bu), 0.99 (3H, d, *J*=6 Hz, 4-CH_3), 1.12 (3H, s, 10-CH_3), 3.26 (1H, d, *J*=8 Hz, 20-CH), 3.95 (4H, m, acetal), 4.24 (1H, d, *J*=8 Hz, 20-CH), and 5.40 (1H, m, 6-CH); MS (70 eV) *m/z* (rel intensity) 622 (M^+, 1.8), 565 (6), 490 (15), 433 (26), and 99 (100); Found: *m/z* 622.4077. Calcd for $C_{34}H_{62}O_6Si_2$: M, 622.4087.

1,2,3,4,4a,4b,5,6,8,10-Decahydro-3α-(*t*-butyldimethylsiloxy)-2α-(*t*-butyldimethylsiloxymethyl)-1α-(2-oxoethyl)-4bβ,8α-dimethyl-7*H*-2β,10aβ-(epoxymethano)phenanthren-7-one 7-(Ethylene Acetal) (77): To a Collins' reagent, prepared from chromium trioxide (2 g, 20 mmol) and pyridine (5 ml, 62 mmol) in CH_2Cl_2 (50 ml), was added alcohol **76** (1.95 g, 3.10 mmol) in CH_2Cl_2 (35 ml). The mixture was stirred at room temperature for 1 h, then diluted with ether. The supernatant was filtered through florisil column and washed thoroughly with ether and ethyl acetate. The dark brown residue was dissolved in saturated $NaHCO_3$ solution (70 ml) and extracted with ether (150 ml), washed with aqueous $NaHSO_3$, saturated aqueous $NaHCO_3$, and brine, dried over $MgSO_4$. The combined filtrate and organic extract were concentrated in vacuo to give a residue, which was chromatographed on a silica-gel column (40 g in hexane) with ether-hexane (1 : 2) to afford aldehyde **77** (1.81 g, 93%) as a colorless amorphous solid: IR (oil) 2720 and 1725 cm^{-1}; ^1H NMR δ=0.90 (18H, s, 2×*t*-Bu), 0.98 (3H, d, *J*=6 Hz, 4-CH_3), 1.13 (3H, s, 10-CH_3), 3.33 (1H, d, *J*=8 Hz, 20-CH), 3.64 (2H, s, 21-CH_2), 3.7—4.0 (5H, m, 12-CH and acetal), 4.35 (1H, d, *J*=8 Hz, 20-CH), 5.34 (1H, m, 6-CH), and 9.73 (1H, *t*-like, 16-CH); MS (70 eV) *m/z* (rel intensity) 620 (M^+, 2), 563 (7), 519 (2), 431 (14), and 99 (100); Found: *m/z* 620.3906. Calcd for $C_{34}H_{60}O_6Si_2$: M, 620.3930.

1,2,3,4,4a,4b,5,6,8,10-Decahydro-3α-(*t*-butyldimethylsiloxy)-2α-(*t*-butyldimethylsiloxymethyl)-1α-(2,2-dimethoxyethyl)-4bβ,8α-dimethyl-7*H*-2β,10aβ-(epoxymethano)phenanthren-7-one 7-(Ethylene Acetal) (78): A mixture of aldehyde **77** (1.2125 g, 1.95 mmol), PPTS (60 mg, 0.24 mmol), and trimethyl orthoformate (5 ml) in CH_2Cl_2 (35 ml) was stirred at room temperature for 2 days. The reaction mixture was poured into saturated $NaHCO_3$ solution (30 ml), and extracted with $CHCl_3$ (100 ml×3), dried over $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on a silica-gel column (25 g in hexane) with ether-hexane (1 : 3) to afford dimethyl acetal **78** (1.2196 g, 94%) as a pale yellow viscous oil: IR (oil) no absorption due to carbonyl group; ^1H NMR δ=0.06 and 0.08 (12H, each s, 2×$Si(CH_3)_2$), 0.91 (9H, s, *t*-Bu), 0.93 (9H, s, *t*-Bu), 0.99 (3H, d, *J*=6 Hz, 4-CH_3), 1.08 (3H, s, 10-CH_3), 3.26 (3H, s, OCH_3), 3.27 (1H, d, *J*=8 Hz, 20-CH), 3.28 (3H, s, OCH_3), 3.72 (2H, s, 21-CH_2), 3.8—4.1 (5H, m, 12-CH and acetal), 4.21 (1H, d, *J*=8 Hz, 20-CH), 4.4 (1H, m, 16-CH), and 5.38 (1H, m, 6-CH); MS (70 eV) *m/z* (rel intensity) 666 (M^+, 0.1), 651 (0.25), 634 (2), 609 (5), 577 (80), 499 (36), 445 (30), 99 (over), and 73 (100); Found: *m/z* 577.3390. Calcd for $C_{31}H_{53}O_6Si_2$: M−*t*-Bu−MeOH, 577.3382.

1,2,3,4,4a,4b,5,6-Octahydro-3α-(*t*-butyldimethylsiloxy)-2α-(*t*-butyldimethylsiloxymethyl)-1α-(2,2-dimethoxyethyl)-4bβ,8α-dimethyl-7*H*-2β,10aβ-(epoxymethano)phenanthrene-7,10(8*H*)-dione 7-(Ethylene Acetal) (79): To a cold (−20 °C) suspension of chromium trioxide (409 mg, 4.09 mmol) in CH_2Cl_2 (5 ml) was added 3,5-dimethylpyrazole (390 mg, 4.06 mmol) in one portion. The mixture was stirred at −20 °C for 20 min, and a solution of acetal **78** (135 mg, 0.20 mmol) in CH_2Cl_2 (10 ml) was added dropwise. After stirring at −20 °C for 4 h, 3M NaOH solution (3 ml) was added and the mixture was stirred at 0 °C for 30 min. The solution was diluted with brine (20 ml), extracted with ether (50 ml×3), dried over $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on a silica-gel column (10 g in benzene, eluent: 10% to 20% ether-benzene) to afford enone **79** (93.8 mg, 68%) as a pale yellow viscous oil: IR (oil) 1660 cm^{-1}; ^1H NMR δ=0.09 (12H, s, 2×$Si(CH_3)_2$), 0.91 (9H, s, *t*-Bu), 0.93 (9H, s, *t*-Bu), 1.08 (3H, d, *J*=7 Hz, 4-CH_3), 1.23 (3H, s, 10-CH_3), 3.13 (3H, s, OCH_3) 3.26 (3H, s, OCH_3), 3.95 (4H, m, acetal), and 5.95 (1H, d, *J*=2 Hz, 6-CH); MS (70 eV) *m/z* (rel intensity) 680 (M^+, 0.8), 649 (2), 623 (35), 591 (28), 459 (35), 99 (over), 75 (95), and 73 (100); Found: *m/z* 623.3412. Calcd for $C_{33}H_{55}O_8Si_2$: M−*t*-Bu, 623.3437.

1,2,3,4,4a,4b,5,6,8,8a-Decahydro-3α-(*t*-butyldimethylsiloxy)-2α-(*t*-butyldimethylsiloxymethyl)-1α-(2,2-dimethoxyethyl)-4bβ,8α-dimethyl-7*H*-2β,10aβ-(epoxymethano)-phenanthrene-7,10(9*H*)-dione 7-(Ethylene Acetal) (80): To a solution of lithium (ca. 20 mg, 2.9 mmol) in 30 ml of liquid ammonia at −78 °C was added a solution of enone **79** (93.8 mg, 0.14 mmol) in THF (5 ml) containing *t*-butyl alcohol (0.01 ml). The mixture was stirred at −78 °C for 20 min, warmed to −33 °C, and stirred for 20 min, then quenched by the addition of methanol (2 ml). After the ammonia was allowed to evaporate, saturated aqueous NH_4Cl was added and the mixture was extracted with $CHCl_3$ (30 ml×3). Drying ($MgSO_4$) and evaporation of the solvent gave a residue, which was chromatographed on a silica-gel column (5 g in hexane, eluent: 25% to 50% ether-hexane) to afford ketone **80** (66.5 mg, 70%) as colorless crystals. An analytical sample was obtained by recrystallization from hexane as colorless needles: mp 154.5—155.5 °C; IR (oil) 1700 cm^{-1}; ^1H NMR δ=0.8—1.0 (24H, 8×CH_3), 3.12 (3H, s, OCH_3), 3.24 (3H, s, OCH_3), 3.48 (1H, d, *J*=7.5 Hz, 20-CH), 3.58 (2H, s, 21-CH_2), 3.80 (1H, m, 12-CH), 3.95 (4H, m, acetal), 4.10 (1H, dd, *J*=8, 2 Hz, 16-CH), and 4.14 (1H, d, *J*=7.5 Hz, 20-CH); MS (70 eV) *m/z* (rel intensity) 682 (M^+, 0.4), 667 (1.2), 651 (3.6), 625 (80), 593 (34), 461 (72), and 99 (100); Found: *m/z* 625.3572. Calcd for $C_{32}H_{57}O_8Si_2$: M−*t*-Bu, 625.3594.

12α,21-Bis(*t*-butyldimethylsiloxy)-13,20-epoxy-16-methoxy-3-picrasanone 3-(Ethylene Acetal) (82): To a cold (−78 °C) solution of ketone **80** (195.5 mg, 0.287 mmol) in THF (6 ml) was added lithium triethylhydroborate (1 mol dm^{-3} solution in THF, 2.5 ml) and the mixture was stirred at −78 °C, then allowed to warm to room temperature overnight. The mixture was quenched by the addition of water, followed by 3 mol dm^{-3} aqueous NaOH (2 ml) and 30% H_2O_2 solution (2 ml), and stirred at room temperature for 2 h. The solution was poured into brine and extracted with $CHCl_3$ (70 ml×3), dried over $MgSO_4$, and concentrated in vacuo to give a crude alcohol **81**, which without purification was dissolved in methanol (10 ml) and treated with a catalytic amount of PPTS. The reaction mixture was stirred at room temperature for 1 h and the solvent was evaporated in vacuo. The residue was chromatographed on a silica-gel column (15 g in hexane, eluent: 50% ether-hexane) to afford methylated hemiacetal **82** (168.3 mg, 90%) as an inseparable 1 : 1 (by NMR) mixture of diastereomers at C-16: IR (oil) no absorption due to hydroxyl and carbonyl group: ^1H NMR δ=−0.1—0.1 (12H, 2×$Si(CH_3)_2$), 0.8—1.0 (24H, 4-CH_3, 10-CH_3, and 2×*t*-Bu), 3.26 and 3.42 (3H, each s, OCH_3), and 3.93 (4H, m, acetal); MS (70 eV) *m/z* (rel intensity) 652 (M^+, 0.1), 637 (1), 595 (79), 563 (35), and 99 (100).

13,20-Epoxy-12α,21-dihydroxy-16-methoxy-3-picrasanone 3-(Ethylene Acetal) (3): To a cold (0 °C) solution of methylated hemiacetal **82** (187.5 mg, 0.287 mmol) in THF (6 ml) was added tetrabutylammonium fluoride (380 mg, 1.45 mmol) in THF (3 ml). After being stirred at room temperature for 18 h, the mixture was poured into saturated $NaHCO_3$ solution and extracted with $CHCl_3$ (50 ml×3). Drying ($MgSO_4$) and evaporation of the solvent gave a residue, which was chromatographed on a silica-gel column (15 g dry, eluent: 0% to 6% MeOH-$CHCl_3$) to afford 85.6 mg (70%) of a mixture of diastereomers **3** and 36.1 mg (30%) of a pure diastereomer (more polar, $C_{(16)}$ β-OMe isomer of **3**). An analytical sample of the more polar isomer of **3** was obtained by recrystallization from acetone-hexane as colorless needles: mp 213—216 °C; IR (KBr) 3420 cm^{-1}: ^1H NMR Table 1; MS (70 eV) *m/z* (rel intensity) 424 (M^+, 3), 374 (20), 361 (8), 100 (100), and 99 (over); Found: *m/z* 424.2446. Calcd for $C_{23}H_{36}O_7$, 424.2462.

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