Synthesis of Manool-Related Labdane Diterpenes as Platelet Aggregation Inhibitors

Ken YASUI, Kenji KAWADA,* Kiyomi KAGAWA, Katsuya TOKURA, Kengo KITADOKORO, and Yuji IKENISHI

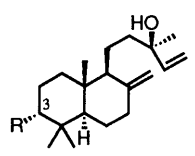
Shionogi Research Laboratories, Shionogi & Co., Ltd., Fukushima-ku, Osaka 553, Japan. Received February 10, 1993

Enantioselective total synthesis of the labdane diterpene (−)-1, was achieved starting from the *R*-(−)-enantiomer of the Wieland–Miescher ketone (3). The enantiomer (+)-1 was obtained by partial synthesis *via* microbial transformation of sclareol (24). These results established that the natural compound (+)-1, a platelet aggregation inhibitor, has a normal absolute stereochemistry like that of manool (2). The *B*-norlabdane-related compound 44 was also synthesized using a novel ring contraction reaction.

Keywords labdane; platelet aggregation inhibitor; ring contraction; enantioselective synthesis; microbial transformation; *trans*-hydrindan

Platelet activating factor (PAF) is a potent phospholipid mediator with the structure 1-*O*-alkyl-2-*O*-acetyl-*sn*-glycero-3-phosphocholine.[1] It is produced by a variety of stimulated cells and is known to be involved in a spectrum of pathological conditions including bronchial asthma, disseminated intravascular coagulation, endotoxin shock, inflammation, and acute allergy, though the mechanisms of its action in these diseases have not been clarified. PAF antagonists should be useful in studies to elucidate the role of PAF in disease and to provide a new class of therapeutic agents. However, although a number of PAF antagonists have been developed during studies aimed at obtaining higher potency, lower toxicity, and better bioavailability, no therapeutic agent has yet emerged. As plants are still the most important source of therapeutic agents,[2] various medicinal plants have been screened in these laboratories in order to find specific PAF antagonists as lead compounds.[3]

In the previous paper, the isolation and structure elucidation of labdane diterpenes from a Bhutanese medicinal plant, Shug Chher, were reported.[4] Among them, the manool-related compound (+)-**1** exhibited the most potent inhibitory effect on PAF-induced platelet aggregation (Fig. 1). Unfortunately, only meager supplies were available of the Bhutanese plant, and the absolute stereochemistry of (+)-**1** could not be established. In addition, due to the limited availability of the compounds from the natural source, their structure–activity relationships could not be fully established. With the recent increasing interest in chirality in pharmaceutical research,[5] we also wanted to clarify the relationship between the chirality and the biological activity for labdane diterpenes. Therefore, we decided to solve these problems by a synthetic approach.



(+)-**1**: R=OH
manool (**2**): R=H

Fig. 1

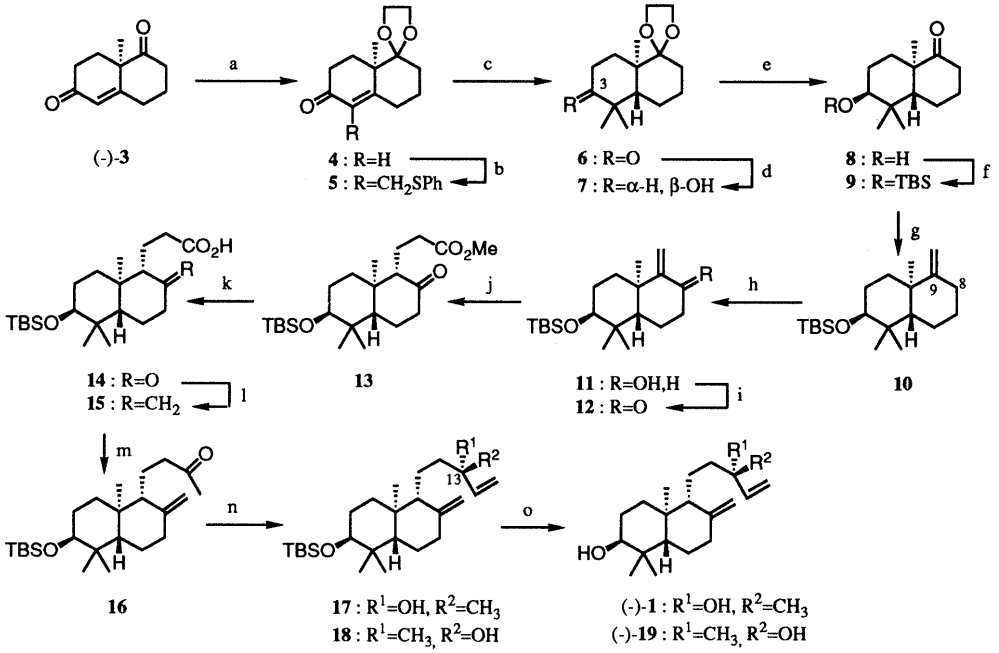
Results and Discussion

Since we planned to elucidate the absolute stereochemistry of the natural diterpene (+)-**1** and to clarify the relationship between the biological activity and structure (including chirality), we needed to synthesize both enantiomers (+)- and (−)-**1**. It was anticipated that the normal type of labdane diterpene **1** could be prepared from the readily available natural compound, sclareol (**24**). The *ent*-labdane type of **1** would be prepared by total synthesis, which we elected to pursue first. The starting material was the Wieland–Miescher ketone (**3**) chosen because of its availability as either enantiomer in high chemical yield and high enantiomeric excess (ee) using the Hajos–Parrish procedure.[6,7] With this starting material (−)-**3** available in 99% ee, we completed a straightforward synthesis of (−)-**1** through the sequence shown in Chart 1.

Among a variety of reported approaches for constructing a *trans*-decalone **6**,[8] we adopted a convenient method involving (phenylthio)methylation[9] of **4** and reductive alkylation of **5** developed by Smith and Mewshaw.[8b] One of the characteristic features of the diterpene **1** is the C-3 (labdane numbering) axial hydroxyl group. K-Selectride reduction selectively afforded the C-3 axial alcohol **7** which was identical to the compound reported by Hagiwara and Uda as a minor product of sodium borohydride reduction of **6**.[8c] Deprotection of the ketal group of **7**, protection of the C-3 hydroxyl group of **8** with *tert*-butyldimethylsilyl (TBS) chloride, and the Wittig reaction of the ketone **9** gave the C-9 exomethylene compound **10**.

Although several allylic oxidation procedures including Barton's method[10] failed to elevate the oxidation level at C-8, the oxidation with selenium dioxide and *tert*-butylhydroperoxide[11] secured the desired product as a mixture of the alcohol **11** and the enone **12**. Swern oxidation of the alcohol **11** gave the enone **12** in good yield, while the yield of pyridinium dichromate oxidation was relatively low.

We planned to introduce a chiral side chain **20**, which was derived from the optically active glycidol, into the enone **12** by a radical intermolecular addition,[12] but all attempts to obtain the adduct **21** were unsuccessful, as shown in Chart 2. Michael addition of methyl acetoacetate to the enone **12** gave the adduct **22** in Chart 3, and although decarbomethoxylation of **22** led to the tricyclic enone



(a) 2-ethyl-2-methyl-1,3-dioxolane, *p*-TsOH; (b) PhSH, HCHO, Et_3N; (c) Li, NH_3, MeI (Ref. 8*b* for steps a, b, c); (d) K-Selectride (99%); (e) HCl (96%); (f) TBSCl, imidazole (99%); (g) $Ph_3P{=}CH_2$ (95%); (h) SeO_2, *tert*-BuO_2H; (i) DMSO, $(CF_3CO)_2O$ followed by Et_3N (80% for steps h, i); (j) $CH_2{=}C(OMe)OTBS$, $TiCl_4$ (54%); (k) KOH; (l) $Ph_3P{=}CH_2$ (77% for steps k, l); (m) MeLi (73%); (n) $CH_2{=}CHMgBr$ (88%); (o) *n*-Bu_4NF (89%).

Chart 1

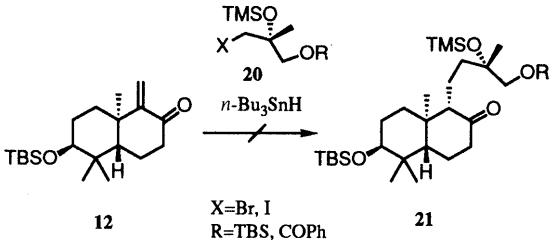
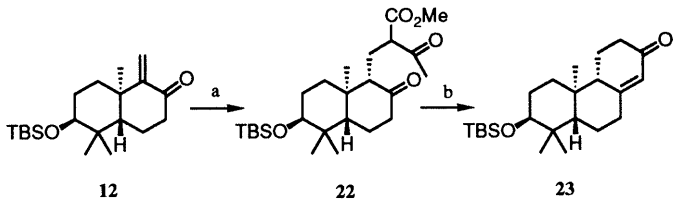


Chart 2



(a) $CH_3COCH_2CO_2CH_3$, NaOMe; (b) KOH (86% for steps a, b).

Chart 3

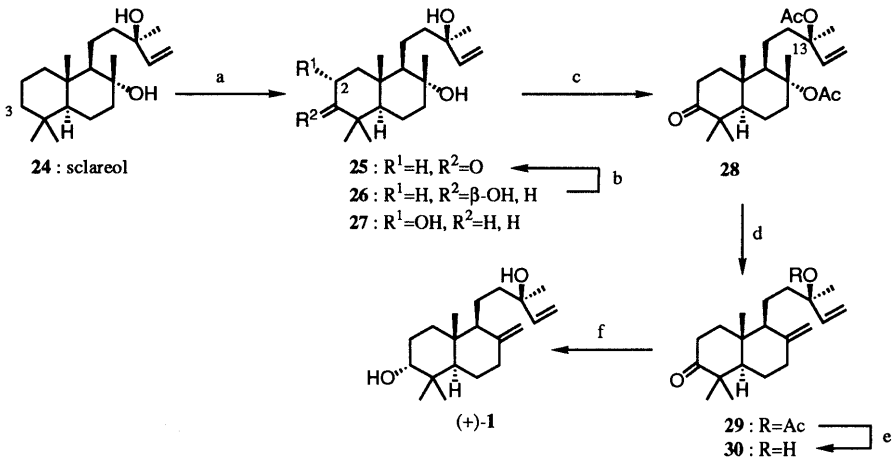
23,[13] we were unable to utilize it in a productive fashion. Consequently, a stepwise manipulation was employed to secure the labdane side chain.

Titanium(IV) chloride-promoted Michael addition[14] of the enone **12** with silyl enol ether was employed to acquire the methyl ester **13**. Saponification of the methyl ester **13** and the Wittig reaction of the ketone **14** provided the exomethylene compound **15**. Ethyl ester could not be used instead of methyl ester in this case because of the difficulty of hydrolysis. Addition of methyl lithium to the carboxylic acid **15** furnished the ketone **16**, which set the stage for the introduction of the last vinyl group.

Grignard reaction of **16** using vinylmagnesium bromide gave a 1 : 1.2 mixture of the 13*S* and 13*R* epimers **17** and **18**, respectively, which could be separated by silica gel chromatography either at this or at the last step. The C-13 stereochemical assignments were confirmed later by comparison with the natural diterpene **1**. The epimer **18** was also beneficial to the structure–activity studies as discussed later.

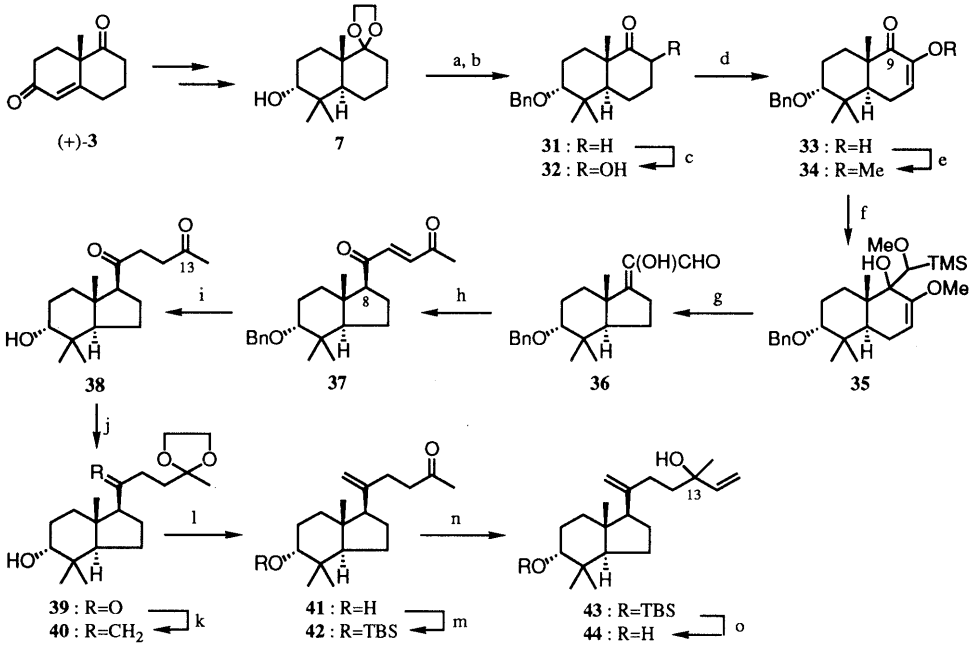
We completed the total synthesis of the *ent*-labdane type of **1** by deprotection of the TBS group using *n*-tetrabutylammonium fluoride. Spectroscopic data of the synthetic compound were identical to those of the natural diterpene isolated from Shug Chher. Its molecular rotation showed the opposite sign ($[\alpha]_D$ $-10.6°$) to that of the natural compound ($[\alpha]_D$ $+9.2°$).[4] These results established that the absolute stereochemistry of the natural diterpene (+)-**1** was as depicted in the formula in Fig. 1, being identical to that of manool.

Next, we undertook partial synthesis of the normal type of (+)-**1** from sclareol (**24**). We had to introduce a hydroxyl group at the chemically unreactive C-3 carbon. Oxidation of **24** by the "Gif system" was reported to give 3-keto-sclareol (**25**) in 0.7% yield.[15] However, recent interest in biological transformation has led to the availability of a variety of enzymes and microorganisms which promote such reactions.[16] Recently, Kouzi and McChesney[17] and Aranda *et al.*[18] reported this C-3 microbial oxidation using *Septomyxa affinis* and *Mucor plumbeus*, respectively. Following their procedures, we could acquire the C-3 ketone **25**, the C-3β alcohol **26**, and the C-2α alcohol **27** as shown in Chart 4. Although *Corynespora casiicola* and *Syncephalostrum racemosa* are reliable microorganisms for



(a) *Septomyxa affinis* (Ref. 17) or *Mucor plumbeus* (Ref. 18) ; (b) CrO_3,Py (Ref. 17); (c) AcCl, $PhNMe_2$ (87%); (d) heat (28%); (e) aqueous KOH,MeOH (85%); (f) K-Selectride (33%).

Chart 4



(a) BnBr, NaH (92%); (b) HCl (88%); (c) LHMDS, TMSCl followed by MCPBA followed by *n*-Bu_4NF (96%); (d) DMSO, TFAA followed by Et_3N (80%); (e) MeI, NaH (100%); (f) $TMSCH_2OMe$, *sec*-BuLi; (g) HF; (h) $Ph_3P{=}CHCOCH_3$ (51% for steps f, g, h); (i) H_2, Pd-C (78%); (j) 2-ethyl-2-methyl-1,3-dioxolane, *p*-TsOH (75%); (k) Zn, CH_2Br_2, $TiCl_4$ (80%); (l) HCl (90%); (m) TBSCl, imidazole (92%); (n) $CH_2{=}CHMgBr$ (93%); (o) *n*-Bu_4NF (90%).

Chart 5

oxidation of the unactivated carbon of various steroids[19] and terpenes,[20] their application to sclareol (**24**) or manool (**2**) was unsuccessful.[21] Conversion of the ketone **25** to the diacetate **28** and pyrolysis of **28** provided the exomethylene compound **29**.[22] Efforts to convert **25** directly to the exomethylene compound **30** by using phosphoryl chloride and pyridine,[23] Martin's method,[24] Swern oxidation,[25] or boron trifluoride etherate[26] were unrewarding. Subsequent saponification of the C-13 acetate of **29** and reduction of the ketone **30** with K-Selectride furnished the normal type of labdane diterpene **1**. Since the $[\alpha]_D$ value of this compound **1** showed the same sign ($[\alpha]_D$ +9.1°) as that of the natural compound ($[\alpha]_D$ +9.2°),[4] the absolute stereochemistry of the natural diterpene (+)-**1** was unambiguously established.

We also tried another approach which led to a novel ring contraction reaction that we then used to synthesize the *B*-norlabdane-related compound **44** for structure–activity studies (Chart 5). In this case, the hydroxyl group of **7**, which was derived from the *S*-(+)-enantiomer of the Wieland–Miescher ketone (**3**), was protected as the benzyl (Bn) ether **31** in order to be compatible with operations later in the synthesis. Conversion of the ketone **31** to the trimethylsilyl enol ether and peracid oxidation with

m-chloroperbenzoic acid followed by treatment with tetrabutylammonium fluoride in tetrahydrofuran[27] provided the α-ketol **32**. Swern oxidation of **32** by Watt's procedure[28] and protection of the hydroxyl group of the diosphenol **33** as the methyl ether furnished the *O*-methyldiosphenol **34**.

Methoxy(trimethylsilyl)methyllithium[29] was employed for nucleophilic attack at the electronically less reactive and sterically hindered C-9 position of **34**.[30] Treatment of the adduct **35** in ether saturated with 46% hydrogen fluoride[31] gave an unexpected ring-contracted aldehyde **36** in good yield, while using potassium hydride effected normal elimination of trimethylsilanol. As this aldehyde **36** was relatively unstable, it was used immediately in the next reaction. The structure of the aldehyde **36** was confirmed later in the synthesis by X-ray crystallographic analysis of **40** (Fig. 2). Although the precise mechanism was not clear, this ring contraction reaction seemed to be new.[32] Since the *trans*-hydrindan structure is found in many biologically important compounds such as steroids and vitamin D analogues, a number of reagents and procedures have been developed to date.[33] This reaction could provide an additional method for the construction of an optically active *trans*-hydrindan system.

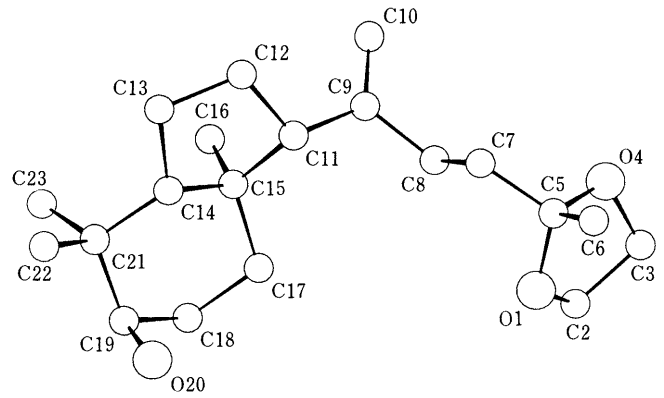


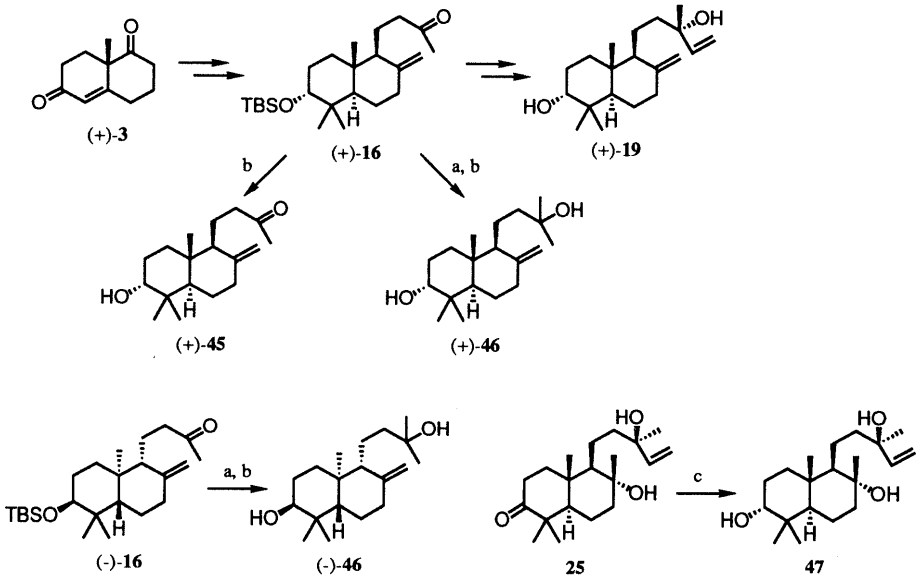
Fig. 2. Perspective View of the Molecule **40**

The Wittig reaction of the aldehyde **36** provided stereoselectively the compound **37** having the C-8β side chain. Selective hydrogenation of the double bond along with deprotection of the benzyl ether of **37**, selective ketalization of the sterically less hindered C-13 ketone of **38**, and methylenation of the ketone **39** by the methods of Nozaki *et al.* and Lombardo[34] afforded the olefin **40**. Deprotection of the ketal group of **40**, and re-protection of the hydroxyl group of **41** as the TBS ether furnished the ketone **42**. The Grignard reaction of **42** gave a 1 : 1 mixture of the C-13 epimers **43** as before. Since separation of a mixture of both epimers was rather difficult in this case, the *B*-norlabdane-related compound **44** obtained by deprotection of the TBS group was evaluated in biological screening as a 1 : 1 mixture of the C-13 epimers.

For the structure–activity studies, a few more labdane derivatives of the normal type, (+)-**19**, (+)-**45** and (+)-**46**, were synthesized starting from the *S*-(+)-enantiomer of the Wieland–Miescher ketone (**3**) using the same sequence as that in Chart 1. The alcohols (−)-**46** and **47** were also prepared as shown in Chart 6.

The compounds synthesized in this study were tested for *in vitro* inhibitory effect on platelet aggregation in rabbit platelet-rich plasma induced by PAF.[3] For the active compounds, the PAF-specific activity was confirmed by using arachidonic acid (AA), U 46619 (assumed to be a thromboxane A_2 agonist),[35] collagen, or adenosine diphosphate (ADP) as an inducer. These results are summarized in Table I.

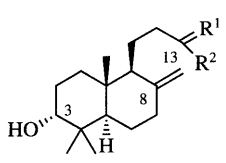
Compared to the natural compound (+)-**1**, the enantiomer (−)-**1** exhibited no significant inhibitory activity. The same observations were made with (+)-**19** *vs.* (−)-**19** and (+)-**46** *vs.* (−)-**46**. These results clearly showed an enantioselectivity in the biological activity for labdane diterpenes. As for the side chain, its modification seems to be possible, since (+)-**45** and (+)-**46** retained the biological activity.



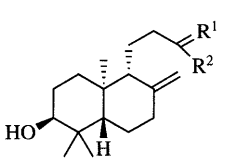
(a) MeLi (10 eq) (97%); (b) *n*-Bu_4NF (89%); (c) K-Selectride (Ref. 17).

Chart 6

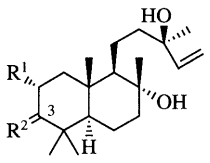
TABLE I. Rabbit Platelet Aggregation-Inhibitory Activity of Labdane-Related Compounds



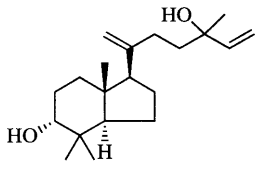
(+)-**1**, -**19**, -**45**, -**46**



(−)-**1**, -**19**, -**46**



24—**27**, **47**



44

Compound		IC_{50} (μM)				
		C-16PAF (20 μM)	AA (200 μM)	U 46619 (4 μM)	Collagen (5 μg/ml)	ADP (10 μM)
(+)-**1**	R^1=α-CH_3, β-OH, R^2=–CH=CH_2	60	—	—	—	—
(+)-**19**	R^1=α-OH, β-CH_3, R^2=–CH=CH_2	59.4	—	—	—	—
(+)-**45**	R^1=O, R^2=CH_3	89.4				
(+)-**46**	R^1=CH_3, CH_3, R^2=OH	149.4				
(−)-**1**	R^1=α-OH, β-CH_3, R^2=–CH=CH_2	—				
(−)-**19**	R^1=α-CH_3, β-OH, R^2=–CH=CH_2	—				
(−)-**46**	R^1=CH_3, CH_3, R^2=OH	—				
24 (sclareol)	R^1=H, R^2=H, H	—				
25	R^1=H, R^2=O	—				
26	R^1=H, R^2=α-H, β-OH	—				
27	R^1=OH, R^2=H, H	—				
47	R^1=H, R^2=α-OH, β-H	48.3	—	—	—	—
44		—				

—, negative at 200 μM.

The C-13 configuration made no difference (comparison of (+)-**1** *vs.* (+)-**19**). The exomethylene group at the C-8 position could also be replaced by the sclareol-type functionality as shown by **47**. On the other hand, the C-3α hydroxyl group seems to be a requisite functional group for the biological activity as shown by **24**—**27**. Furthermore, modification of the *trans*-decalin to the *trans*-hydrindan system diminished the activity as shown by **44**. These results suggest that the 3α-hydroxylabdane skeleton is essential for the platelet aggregation inhibitory activity.

Experimental

Melting points were determined with a Yanagimoto micro melting point apparatus and are uncorrected. Infrared (IR) spectra were determined on a JASCO A-702 infrared spectrometer. Nuclear magnetic resonance (NMR) spectra were determined on a Varian GEMINI-200 or Varian VXR-200 spectrometer. Mass spectra (MS) were determined on a Hitachi M-68 or Hitachi M-2000A mass spectrometer. Liquid secondary ion mass spectra (LSIMS) and high resolution (HR)-LSIMS were determined on a Hitachi M-90 mass spectrometer using *m*-nitrobenzyl alcohol as a matrix. Unless otherwise stated, all reactions were carried out under a nitrogen atmosphere with anhydrous solvents that had been dried over type 4A molecular sieves. Drying of an organic phase over anhydrous sodium sulfate is simply indicated by the word "dried." Column chromatography using Merck Silica gel 60 or a Merck Lobar column is referred to as "chromatography on silica gel."

(+)-(4a*R*,6*S*,8a*R*)-3,4,4a,5,6,7,8,8a-Octahydro-6-hydroxy-5,5,8a-trimethyl-1(2*H*)-naphthalenone 1-Ethylene Ketal (7) To a solution of 2.49 g (9.88 mmol) of (+)-(4a*R*,8a*R*)-3,4,4a,5,8,8a-hexahydro-5,5,8a-trimethyl-1,6(2*H*,7*H*)-naphthalenedione 1-ethylene ketal (**6**)[8b] in 50 ml of tetrahydrofuran was added 30 ml (30 mmol) of 1 M K-Selectride in tetrahydrofuran solution at −78 °C. The solution was stirred for 4 h at −78 °C, then 2.5 h at 25 °C. Then 15 ml of 10% aqueous sodium hydroxide solution and 15 ml of 30% aqueous hydrogen peroxide solution were added. The mixture was diluted with water, and extracted with ethyl acetate. The organic layer was washed with brine, dried, and concentrated. The crude product was chromatographed on silica gel using 1 : 4 ethyl acetate–hexane to afford 2.49 g (99%) of **7**, which gave spectral data identical with published values ($[\alpha]_D$ was not reported).[8c] **7**: $[\alpha]_D$ +32.0° (c=1.02, $CHCl_3$).

(+)-(4a*R*,6*S*,8a*R*)-3,4,4a,5,6,7,8,8a-Octahydro-6-hydroxy-5,5,8a-trimethyl-1(2*H*)-naphthalenone (8) To 6.97 g (27.4 mmol) of **7** in 120 ml of tetrahydrofuran was added 60 ml of 10% hydrochloric acid solution. The mixture was stirred for 3 h at 25°C, then diluted with ethyl acetate. The organic layer was washed with saturated sodium bicarbonate solution and brine, dried, and concentrated. The crude product was chromatographed on silica gel with 1 : 3 ethyl acetate–hexane to afford 5.54 g (96%) of **8**, mp 113—114 °C. $[\alpha]_D$ +58.1° (c=1.01, $CHCl_3$). IR ($CHCl_3$): 3610 and 3500 (OH), 1700 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.96, 0.99, and 1.16 (each 3H, each s, 5-CH_3×2, 8a-CH_3), 2.15—2.30 and 2.46—2.71 (each 1H, each m, 2-H_2), 3.40 (1H, dd, J=2.0, 3.2 Hz, 6-H). MS *m/z*: 210 (M^+), 192, 121. *Anal.* Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.02; H, 10.47.

(+)-(4a*R*,6*S*,8a*R*)-3,4,4a,5,6,7,8,8a-Octahydro-6-*tert*-butyldimethylsilyloxy-5,5,8a-trimethyl-1(2*H*)-naphthalenone (9) To a solution of 5.66 g (26.9 mmol) of **8** in 200 ml of *N*,*N*-dimethylformamide was added 9.34 g (137 mmol) of imidazole and 19.1 g (126 mmol) of *tert*-butyldimethylsilyl chloride. The mixture was stirred for 3 h at 90 °C, diluted with ethyl acetate, washed with brine, dried, and evaporated. The residue was chromatographed on silica gel using 1 : 49 ethyl acetate–hexane to afford 8.66 g (99%) of **9**, mp 90—92 °C. $[\alpha]_D$ +51.1° (c=1.01, $CHCl_3$). IR ($CHCl_3$): 1699 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.02 and 0.05 (each 3H, each s, $Si(CH_3)_2$), 0.88 (9H, s, $SiC(CH_3)_3$), 0.88, 0.92 and 1.14 (each 3H, each s, 5-CH_3×2, 8a-CH_3), 2.10—2.28 and 2.45—2.68 (each 1H, each m, 2-H_2), 3.36 (1H, dd, J=2.1, 2.7 Hz, 6-H). MS *m/z*: 324 (M^+), 309, 267, 175. *Anal.* Calcd for $C_{19}H_{36}O_2Si$: C, 70.31; H, 11.18. Found: C, 69.94; H, 11.16.

(+)-(2*S*,4a*R*,8a*R*)-Decahydro-2-*tert*-butyldimethylsilyloxy-1,1,4a-trimethyl-5-methylenenaphthalene (10) To a solution of the dimethyl anion, which was prepared using 2.42 g (61 mmol) of 60% sodium hydride and 50 ml of dimethyl sulfoxide, was added 21.87 g (61 mmol) of methyltriphenylphosphonium bromide in 50 ml of dimethyl sulfoxide. After being stirred for 15 min at 60 °C, the solution was added to **9** in 65 ml of dimethyl sulfoxide. The mixture was stirred for 6 h at 60 °C, diluted with water, and extracted with ethyl acetate. The organic layer was wahed with brine, dried, and concentrated. The crude product was chromatographed on silica gel using 1 : 99 ethyl acetate–hexane to give 7.45 g (95%) of **10**, mp 41—43 °C. $[\alpha]_D$ +78.6° (c=1.00, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.02 and 0.05 (each 3H, each s, $Si(CH_3)_2$), 0.82, 0.85 and 1.05 (each 3H, each s, 1-CH_3×2, 4a-CH_3), 0.90 (9H, s, $SiC(CH_3)_3$), 3.36 (1H, dd, J=1.6, 3.6 Hz, 2-H), 4.48 and 4.52 (each 1H, each br s, 5-CH_2). MS *m/z*: 321 ($M-H)^+$, 307, 265. *Anal.* Calcd for $C_{20}H_{38}OSi$: C, 74.46; H, 11.87.

Found: C, 74.06; H, 11.77.

(+)-(4a*R*,6*S*,8a*R*)-3,4,4a,5,6,7,8,8a-Octahydro-6-*tert*-butyldimethylsilyloxy-5,5,8a-trimethyl-1-methylene-2(1*H*)-naphthalenone (12) To a solution of 1.18 g (10.6 mmol) of selenium dioxide in dichloromethane was added 0.6 ml (43.9 mmol) of 70% *tert*-butyl hydroperoxide. The solution was stirred for 30 min at 25 °C followed by the addition of 6.82 g (21.2 mmol) of **10** in 70 ml of dichloromethane. This solution was stirred for 14 h at 25 °C, diluted with dichloromethane, washed with water and brine, then dried and concentrated. The crude product was chromatographed on silica gel using ethyl acetate–hexane to afford 2.31 g (34%) of **10**, 2.97 g (41%) of (2*R* and 2*S*,4a*R*,6*S*,8a*R*)-decahydro-6-*tert*-butyldimethylsilyloxy-5,5,8a-trimethyl-1-methylene-2-naphthalenol (**11**), and 1.11 g (16%) of **12**. This procedure was repeated two more times using the recovered starting material **10** to afford 4.48 g (62%) of **11** and 1.78 g (25%) of **12** in all. The alcohol **11** was used in the next reaction without separating the two diastereomers. **11**: mp 112—113 °C. IR ($CHCl_3$): 3600 (OH) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.02, 0.05, 0.06 and 0.07 (6H, each s, $Si(CH_3)_2$), 0.84, 0.86, 0.87, 0.90, 1.03 and 1.24 (9H, each s, 5-CH_3 × 2, 8a-CH_3), 0.89 (9H, s, $SiC(CH_3)_3$), 3.36—3.38 (1H, m, 6-H), 4.34 (1H, t, J=2.8 Hz, 2-H), 4.75, 4.81, 4.84 and 4.88 (2H, each d, J=1.5 Hz, 1-CH_2). MS *m/z*: 338 (M^+), 323, 305, 281, 263. *Anal.* Calcd for $C_{20}H_{38}O_2Si$: C, 70.94; H, 11.31. Found: C, 70.73; H, 11.19.

To a solution of 3.2 ml (45.1 mmol) of dimethyl sulfoxide in 60 ml of dichloromethane was added 4.5 ml (31.9 mmol) of trifluoroacetic anhydride at −78 °C. After 15 min, a solution of 4.31 g (12.7 mmol) of **11** in 20 ml of dichloromethane was added. The solution was stirred for 20 min at −78 °C, and then 13 ml (93.4 mmol) of triethylamine was added. The mixture was allowed to warm to 25 °C, stirred for 30 min, diluted with water, and extracted with ethyl acetate. The organic phase was washed with brine, dried and evaporated. The crude product was chromatographed on silica gel with 3 : 97 ethyl acetate–hexane to give 3.80 g (89%) of **12**, mp 54—56 °C. $[\alpha]_D$ +67.6° (c=1.03, $CHCl_3$). IR ($CHCl_3$): 1685 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.05 and 0.07 (each 3H, each s, $Si(CH_3)_2$), 0.90 (9H, s, $SiC(CH_3)_3$), 0.91, 0.94 and 1.02 (each 3H, each s, 5-CH_3 × 2, 8a-CH_3), 2.27—2.45 and 2.59—2.75 (each 1H, each m, 3-H_2), 3.42 (1H, t, J=2.4 Hz, 6-H), 5.04 and 5.55 (each 1H, each d, J=1.4 Hz, 1-CH_2). LSIMS *m/z*: 337 $(M+H)^+$. *Anal.* Calcd for $C_{20}H_{35}O_2Si$: C, 71.37; H, 10.78. Found: C, 71.15; H, 10.57.

(+)-(1*S*,4a*R*,6*S*,8a*R*)-3,4,4a,5,6,7,8,8a-Octahydro-6-*tert*-butyldimethylsilyloxy-5,5,8a-trimethyl-2(1*H*)-naphthalenone-1-propionic Acid Methyl Ester (13) To a solution of 2.06 g (6.13 mmol) of **12** in 25 ml of dichloromethane was added dropwise 0.76 ml (6.92 mmol) of titanium(IV) chloride in 10 ml of dichloromethane at −78 °C. After 20 min, a solution of *O*-methyl-*O*-*tert*-butyldimethylsilyl ketene acetal in 8 ml of dichloromethane was added. The solution was stirred for 3 h at −78 °C, allowed to warm to 25 °C, and stirred for 1 h at 25 °C. The mixture was added to 2.34 g (16.9 mmol) of potassium carbonate in 50 ml of water at 0 °C and filtered through a Celite pad. The aqueous layer was extracted with ethyl acetate, then the organic phase was washed with brine, dried, and evaporated. The crude product was chromatographed using 1 : 1 : 8 benzene–diethyl ether–hexane to give 1.35 g (54%) of **13**, mp 57—59 °C. $[\alpha]_D$ +47.0° (c=1.01, $CHCl_3$). IR ($CHCl_3$): 1729 (ester C=O), 1704 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.06 and 0.07 (each 3H, each s, $Si(CH_3)_2$), 0.73 and 0.84 (each 3H, each s, CH_3 × 2), 0.94 (12H, s, CH_3, $SiC(CH_3)_3$), 2.22—2.55 (3H, m, 1-H, 3-H_2), 3.40 (1H, dd, J=1.2, 2.4 Hz, 6-H), 3.65 (3H, s, OCH_3). MS *m/z*: 411 (M^+), 353, 135. *Anal.* Calcd for $C_{23}H_{42}O_4Si$: C, 67.27; H, 10.31. Found: C, 67.17; H, 10.24.

(−)-3β-*tert*-Butyldimethylsilyloxy-15,16-dinor-*ent*-labd-8(17)-en-13-one (16) A solution of 806 mg (1.96 mmol) of **13** in 8 ml of 5% aqueous potassium hydroxide, 8 ml of methanol, and 4 ml of ethanol was refluxed for 3.5 h, and after it had cooled, 10% hydrochloric acid solution was added to adjust the pH to 4. The mixture was extracted with ethyl acetate, and the organic phase was washed with brine, and dried. The solution was concentrated to afford 776 mg of (1*S*,4a*R*,6*S*,8a*R*)-3,4,4a,5,6,7,8,8a-octahydro-6-*tert*-butyldimethylsilyloxy-5,5,8a-trimethyl-2(1*H*)-naphthalenone-1-propionic acid (**14**), which was used for the next reaction without further purification. **14**: colorless oil. IR ($CHCl_3$): 2750—2350 (COOH), 1707 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.06 and 0.07 (each 3H, each s, $Si(CH_3)_2$), 0.73, 0.84 and 0.92 (each 3H, each s, 5-CH_3 × 2, 8a-CH_3), 0.94 (9H, s, $SiC(CH_3)_3$), 3.40 (1H, d-like, J=2.6 Hz, 6-H).

The procedure described for the preparation of **10** was repeated using the above product, 399 mg (9.97 mmol) of 60% sodium hydride, and 3.61 g (10.1 mmol) of methyl triphenylphosphonium bromide to afford, after chromatography on silica gel using 3 : 7 ethyl acetate–hexane, 689 mg (89%) of (1*S*,4a*R*,6*S*,8a*R*)-decahydro-6-*tert*-butyldimethylsilyloxy-5,5,8a-trimethyl-2-methylenenaphthalene-1-propionic acid (**15**) which was used for the next reaction without purification. **15**: colorless oil. IR ($CHCl_3$): 2750—2400 (COOH), 1706 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.03 and 0.05 (each 3H, each s, $Si(CH_3)_2$), 0.69, 0.79 and 0.85 (each 3H, each s, 5-CH_3 × 2, 8a-CH_3), 0.92 (9H, s, $SiC(CH_3)_3$), 3.35 (1H, t, J=2.4 Hz, 6-H), 4.49 and 4.84 (each 1H, each br s, 2-CH_2).

To a solution of 689 mg (1.75 mmol) of **15** in 15 ml of tetrahydrofuran was added 3.8 ml (5.32 mmol) of 1.4 M methyllithium in diethyl ether at 0 °C. The mixture was stirred for 3 h at the same temperature, then 3.8 ml (29.8 mmol) of chlorotrimethylsilane was added. After 15 min, the reaction mixture was diluted with saturated ammonium chloride solution, and extracted with ethyl acetate. The organic phase was washed with brine, dried, and evaporated. The residue was chromatographed on silica gel using 3 : 97 ethyl acetate–hexane to give 512 mg (75%) of **16** as a colorless oil. $[\alpha]_D$ −3.4° (c=0.95, $CHCl_3$). IR ($CHCl_3$): 1710 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.03 and 0.05 (each 3H, each s, $Si(CH_3)_2$), 0.68, 0.79 and 0.84 (each 3H, each s, 18-H_3, 19-H_3, 20-H_3), 0.92 (9H, s, $SiC(CH_3)_3$), 2.12 (3H, s, 14-H_3), 2.18—2.42 (2H, m, 12-H_2), 2.50—2.70 (1H, m, 7α-H), 3.34 (1H, t, J=2.4 Hz, 3-H), 4.42 and 4.82 (each 1H, each br s, 17-H_2). ^{13}C-NMR ($CDCl_3$) δ: 19.3, 22.5, 23.1, 27.0, 28.8, 30.9, 31.2, 34.4, 34.8, 36.7, 43.1, 43.3, 44.3, 48.1, 53.3, 61.0, 111.1, 153.3, 214.5. MS *m/z*: 392 (M^+), 377, 335, 321, 119. *Anal.* Calcd for $C_{24}H_{44}O_2Si$: C, 73.41; H, 11.29. Found: C, 73.37; H, 11.20.

(−)-3β-*tert*-Butyldimethylsilyloxy-13α-hydroxy-*ent*-labd-8(17),14-diene (17) and (−)-3β-*tert*-Butyldimethylsilyloxy-13β-hydroxy-*ent*-labd-8(17),14-diene (18) To 1.0 g (41.1 mmol) of magnesium and a trace of iodine in 5 ml of tetrahydrofuran was added dropwise 3.0 ml (42.6 mmol) of vinyl bromide in 16 ml of tetrahydrofuran at such a rate as to maintain gentle refluxing. The mixture was refluxed for an additional 30 min. This solution was added to 146 mg (0.372 mmol) of **16** in 5 ml of tetrahydrofuran at 0 °C. After being stirred for 1 h at 0 °C, the mixture was poured into saturated ammonium chloride solution, and extracted with ethyl acetate. The organic solution was washed with brine, dried, and concentrated. The crude product was chromatographed on silica gel using 3 : 97 ethyl acetate–hexane. **17**: colorless oil. $[\alpha]_D$ −1.1° (c=0.80, $CHCl_3$). IR ($CHCl_3$): 3590 and 3460 (OH) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.03 and 0.05 (each 3H, each s, $Si(CH_3)_2$), 0.66, 0.78 and 0.84 (each 3H, each s, 18-H_3, 19-H_3, 20-H_3), 0.92 (9H, s, $SiC(CH_3)_3$), 1.28 (3H, s, 16-H_3), 2.37 (1H, ddd, J=2.3, 4.2, 12.6 Hz, 7α-H), 3.34 (1H, t, J=3.0 Hz, 3-H), 4.46 and 4.79 (each 1H, each d, J=1.2 Hz, 17-H_2), 5.06 (1H, dd, J=1.3, 10.8 Hz, 15-H *cis* to 14-H), 5.21 (1H, dd, J=1.3, 17.5 Hz, 15-H *trans* to 14-H), 5.92 (1H, dd, J=10.8, 17.5 Hz, 14-H). MS *m/z*: 420 (M^+), 402, 363, 345, 135, 75. *Anal.* Calcd for $C_{26}H_{48}O_2Si$: C, 74.22; H, 11.50. Found: C, 73.99; H, 11.43. **18**: mp 63—64 °C. $[\alpha]_D$ −14.1° (c=1.25, $CHCl_3$). IR ($CHCl_3$) 3590 and 3460 (OH) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.04 and 0.05 (each 3H, each s, $Si(CH_3)_2$), 0.67, 0.79 and 0.85 (each 3H, each s, 18-H_3, 19-H_3, 20-H_3), 0.92 (9H, s, $SiC(CH_3)_3$), 1.28 (3H, s, 16-H_3), 2.32—2.42 (1H, m, 7α-H), 3.35 (1H, t, J=3.0 Hz, 3-H), 4.50 and 4.80 (each 1H, each d, J=1.2 Hz, 17-H_2), 5.05 (1H, dd, J=1.4, 10.8 Hz, 15-H *cis* to 14-H), 5.20 (1H, dd, J=1.4, 17.4 Hz, 15-H *trans* to 14-H), 5.93 (1H, dd, J=10.8, 17.4 Hz, 14-H). MS *m/z*: 420 (M^+), 402, 345, 75. *Anal.* Calcd for $C_{26}H_{48}O_2Si$: C, 74.23; H, 11.51. Found: C, 73.92; H, 11.40.

(−)-*ent*-Labd-8(17),14-diene-3β,13α-diol (1) To a solution of 33.0 mg (0.0796 mmol) of **17** in 2 ml of tetrahydrofuran was added 0.6 ml (0.6 mmol) of 1 M tetra-*n*-butylammonium fluoride in tetrahydrofuran. The solution was refluxed for 7.5 h, then diluted with ethyl acetate, washed with brine, dried, and concentrated. The crude product was chromatographed on silica gel using 1 : 3 ethyl acetate–hexane to afford 21.3 mg (89%) of **1**, of which the ^{1}H-NMR, ^{13}C-NMR, IR, MS, and TLC behavior were identical with those of the natural diterpene isolated from Shug Chher. Its molecular rotation showed the opposite sign ($[\alpha]_D$ −10.6° (c=1.45, $CHCl_3$)) to that of the natural compound ($[\alpha]_D$ +9.2° (c=0.4, $CHCl_3$)).[4]

(−)-*ent*-Labd-8(17),14-diene-3β,13β-diol (19) The procedure described for the preparation of (−)-**1** was repeated using 44.5 mg (0.106 mmol) of **18** and 0.8 ml (0.8 mmol) of 1 M tetra-*n*-butylammonium fluoride to afford, after chromatography on silica gel using 1 : 3 ethyl acetate–hexane, 28.8 mg (89%) of **19** as a colorless oil. $[\alpha]_D$ −26.0° (c=1.49, $CHCl_3$). IR ($CHCl_3$) 3594 and 3460 (OH) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.70, 0.83 and 0.96 (each 3H, each s, 18-H_3, 19-H_3, 20-H_3), 1.28 (3H, s, 16-H_3), 2.40 (1H, ddd, J=2.4, 4.4, 12.9 Hz, 7α-H), 3.43 (1H, t, J=2.9 Hz, 3-H), 4.53 and 4.83 (each 1H, each d, J=1.3 Hz, 17-H_2), 5.05 (1H, dd, J=1.2, 10.7 Hz, 15-H *cis* to 14-H), 5.20 (1H, dd, J=1.2, 17.3 Hz, 15-H *trans* to 14-H), 5.91 (1H, dd, J=10.7, 17.3 Hz, 14-H). ^{13}C-NMR ($CDCl_3$) δ: 14.3, 17.7, 22.2, 24.0, 25.9, 27.8, 28.5, 31.6, 37.8, 38.2, 39.5, 41.3, 48.5, 57.0, 73.6, 76.1,

106.6, 111.6, 145.2, 148.4. MS *m/z*: 306 (M^+), 288, 273, 255, 135. HR-LSIMS *m/z*: 329.2462 $(M+Na)^+$ (Calcd for $C_{20}H_{34}NaO_2$ *m/z*: 329.2455).

(−)-8α,13β-Diacetoxylabd-14-en-3-one (28) To a solution of 227 mg (0.705 mmol) of 8α,13β-dihydroxylabd-14-en-3-one (**25**)[17] in 0.5 ml (3.95 mmol) of *N,N*-dimethylaniline was added 0.25 ml (3.52 mmol) of acetyl chloride at 0 °C. The solution was stirred for 20 h at 25 °C, then 5% sulfuric acid solution and diethyl ether were added. The organic layer was washed with 20% sulfuric acid solution and brine, then dried and concentrated. The residue was chromatographed on silica gel using 3 : 17 ethyl acetate–hexane to afford 250 mg (87%) of **28** as a colorless oil. $[\alpha]_D$ −18.57° (*c*=1.14, $CHCl_3$). IR ($CHCl_3$): 1725 (ester C=O), 1705 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.97, 1.01 and 1.09 (each 3H, each s, 18-H_3, 19-H_3 20-H_3), 1.49 and 1.54 (each 3H, each s, 16-H_3, 17-H_3), 1.96 and 2.02 (each 3H, each s, 8-$OCOCH_3$, 13-$OCOCH_3$), 2.33—2.75 (3H, m, 2-H_2, 7β-H), 5.14 (1H, dd, *J*=0.8, 10.9 Hz, 15-H *cis* to 14-H), 5.17 (1H, dd, *J*=0.8, 17.6 Hz, 15-H, *trans* to 14-H), 5.95 (1H, dd, *J*=10.9, 17.6 Hz, 14-H). LSIMS *m/z*: 429 $(M+Na)^+$, 407 $(M+H)^+$, 405 $(M-H)^+$. *Anal.* Calcd for $C_{24}H_{38}O_5$: C, 70.90; H, 9.42. Found: C, 70.65; H, 9.41.

(+)-13β-Acetoxylabd-8(17),14-dien-3-one (29) Pyrolysis of 995 mg (0.072 mmol) of **28** at 145 °C under 2—3 Torr for 6 h afforded, after chromatography on silica gel using 1 : 9 ethyl acetate–hexane, 545 mg (55%) of starting material **28** and 237 mg (28%) of **29** as a colorless oil. $[\alpha]_D$ +15.76° (*c*=1.08, $CHCl_3$). IR ($CHCl_3$): 1725 (ester C=O), 1705 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.86, 1.02 and 1.09 (each 3H, each s, 18-H_3, 19-H_3, 20-H_3), 1.54 (3H, s, 16-H_3), 2.02 (3H, s, $OCOCH_3$), 2.34—2.74 (3H, m, 2-H_2 and 7β-H), 4.58 and 4.89 (each 1H, each d, *J*=1.1 Hz, 17-H_2), 5.13 (1H, dd, *J*=1.0, 11.0 Hz, 15-H *cis* to 14-H), 5.15 (1H, dd, *J*=1.0, 17.4 Hz, 15-H *trans* to 14-H), 5.95 (1H, dd, *J*=11.0, 17.4 Hz, 14-H). LSIMS *m/z*: 369 $(M+Na)^+$, 347 $(M+H)^+$. *Anal.* Calcd for $C_{22}H_{34}O_3$: C, 76.26; H, 9.89. Found: C, 76.07; H, 9.95.

(+)-13β-Hydroxylabd-8(17),14-dien-3-one (30) To a solution of 232 mg (0.671 mmol) of **29** in 3 ml of methanol was added 2.0 ml of 5% aqueous potassium hydroxide. The solution was refluxed for 2.5 h. The reaction mixture was extracted with ethyl acetate, and the organic solution was washed with brine, dried, and concentrated. The crude product was chromatographed on silica gel using 1 : 4 ethyl acetate–hexane to afford 173 mg (85%) of **30**, which had spectral data identical with published values (mp and $[\alpha]_D$ were not reported).[18] mp 63—65 °C, $[\alpha]_D$= +17.82° (*c*=1.01, $CHCl_3$).

(+)-3α-Hydroxymanool (Labd-8(17),14-diene-3α,13β-diol) (1) The procedure described for the preparation of **7** was repeated using 40.7 mg (0.134 mmol) of **30** and 0.8 ml (0.8 mmol) of 1 M K-Selectride in tetrahydrofuran solution to afford, after chromatography on silica gel using 1 : 3 ethyl acetate–hexane, 13.7 mg (33%) of **1** that was identical in all respects, including molecular rotation ($[\alpha]_D$ +9.1° (*c*=0.42, $CHCl_3$)), with the natural compound isolated from Shug Chher ($[\alpha]_D$ +9.2° (*c*=0.4, $CHCl_3$)).[4]

(−)-(4a*S*,6*R*,8a*S*)-3,4-4a,5,6,7,8,8a-Octahydro-6-benzyloxy-5,5,8a-trimethyl-1(2*H*)-naphthalenone (31) To a solution of 13.4 g (52.7 mmol) of (−)-(4a*S*,6*R*,8a*S*)-3,4,4a,5,6,7,8,8a-octahydro-6-hydroxy-5,5,8a-trimethyl-1(2*H*)-naphthalenone 1-ethylene ketal (**7**) in 120 ml of *N,N*-dimethylformamide was added 26 ml (219 mmol) of benzyl bromide. The mixture was cooled to 0 °C, and 3.91 g (163 mmol) of sodium hydride was added. The mixture was stirred for 5 h at 25 °C and then the reaction was quenched with methanol at 0 °C. The mixture was extracted with ethyl acetate, and the product solution was washed with brine, dried, and evaporated. The residue was chromatographed on silica gel using 1 : 19 ethyl acetate–hexane to give 16.8 g (92%) of (−)-(4a*S*,6*R*,8a*S*)-3,4,4a,5,6,7,8,8a-octahydro-6-benzyloxy-5,5,8a-trimethyl-1(2*H*)-naphthalenone 1-ethylene ketal, mp 57—58 °C. $[\alpha]_D$ −54.0° (*c*=1.01, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.84, 0.96 and 1.07 (each 3H, each s, 5-CH_3 × 2, 8a-CH_3), 3.02 (1H, br t, *J*=2.5 Hz, 6-H), 3.76—4.00 (4H, m, OCH_2CH_2O), 4.37 and 4.64 (2H, AB q, *J*=12.4 Hz, CH_2Ph), 7.20—7.43 (5H, m, aromatic H). MS *m/z*: 344 (M^+), 253, 99, 91. *Anal.* Calcd for $C_{22}H_{32}O_3$: C, 76.70; H, 9.36. Found: C, 76.71; H, 9.42.

The procedure described for the preparation of **8** was repeated using 16.8 g (49 mmol) of the above product, 300 ml of tetrahydrofuran, and 150 ml of 10% hydrochloric acid solution to afford, after chromatography on silica gel using 2 : 23 ethyl acetate–hexane, 12.8 g (88%) of **31**, mp 81—83 °C. $[\alpha]_D$ −87.3° (*c*=1.01, $CHCl_3$). IR ($CHCl_3$): 1697 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.95, 1.01 and 1.16 (each 3H, each s, 5-CH_3 × 2, 8a-CH_3), 2.11—2.27 (1H, m, 2-H), 2.47—2.64 (1H, m, 2-H), 3.07 (1H, br t, *J*=2.5 Hz, 6-H), 4.32 and 4.60 (2H, ABq, *J*=11.6 Hz, CH_2Ph), 7.23—7.39 (5H, m, aromatic H). MS *m/z*: 300 (M^+), 209, 91. *Anal.* Calcd for $C_{20}H_{28}O_2$: C, 79.96; H, 9.39. Found: C, 79.90; H, 9.63.

(−)-(4a*S*,6*R*,8a*S*)-4a,5,6,7,8,8a-Hexahydro-6-benzyloxy-2-hydroxy-5,5,8a-trimethyl-1(4*H*)-naphthalenone (33) To 91.8 ml (91.8 mmol) of 1 M lithium bis(trimethylsilyl)amide in tetrahydrofuran was added 6.92 g (23 mmol) of **31** in 33 ml of tetrahydrofuran at −78 °C. The solution was stirred for 1 h at −78 °C, then 13.1 ml (103 mmol) of chlorotrimethylsilane was added at −78 °C. After being stirred for 1 h at 25 °C, the reaction mixture was poured into saturated sodium bicarbonate solution at 0 °C. The mixture was extracted with pentane, and the organic solution was washed with brine, dried, and evaporated. The silyl enol ether was used immediately in the next reaction.

To a solution of the above product in 160 ml of dichloromethane were added 5.9 g (34.1 mmol) of *m*-chloroperbenzoic acid and 2.07 g (24.6 mmol) of sodium bicarbonate at 0 °C. The mixture was stirred for 1 h at 0 °C, then 65.6 ml (65.6 mmol) of 1 M tetra-*n*-butylammonium fluoride was added dropwise at 0 °C. The whole was stirred for 1 h at the same temperature, then the reaction was quenched with saturated sodium sulfite solution. The mixture was extracted with dichloromethane, and the organic solution was washed with brine, dried, and evaporated. The residue was chromatographed using 1 : 4 ethyl acetate–hexane to afford 6.97 g (96%) of (2*R* and 2*S*,4a*S*,6*R*,8a*S*)-3,4,4a,5,6,7,8,8a-octahydro-6-benzyloxy-2-hydroxy-5,5,8a-trimethyl-1(2*H*)-naphthalenone (**32**) as colorless needles. IR ($CHCl_3$): 3478 (OH), 1702 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.94 and 0.96 (3H, each s, 8a-CH_3), 1.02 and 1.18 (each 3H, each s, 5-CH_3 × 2), 3.04—3.13 (1H, m, 6-H), 3.42 and 3.62 (1H, each d, *J*=4.5 Hz, OH), 4.28—4.66 (3H, m, 2-H, CH_2Ph), 7.19—7.40 (5H, m, aromatic H). MS *m/z*: 316 (M^+), 298, 234, 207, 91. *Anal.* Calcd for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92. Found: C, 75.76; H, 8.95.

To a solution of 7.88 ml (55.7 mmol) of trifluoroacetic anhydride in 105 ml of dichloromethane was added 5.78 ml (81.4 mmol) of dimethyl sulfoxide at −78 °C. After 15 min, a solution of 6.97 g (22.1 mmol) of **32** in 26 ml of dichloromethane was added. The solution was stirred for 15 min at −78 °C, and 14.2 ml (102 mmol) of triethylamine was added. The mixture was allowed to warm to 25 °C, stirred for 1 h, diluted with dichloromethane, washed with brine, dried, and concentrated. The residue was chromatographed on silica gel using 7 : 93 ethyl acetate–hexane to afford 5.57 g (80%) of **33** as a colorless oil. $[\alpha]_D$ −57.6° (*c*=1.10, $CHCl_3$). IR ($CHCl_3$): 3452 (OH), 1674 and 1654 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.02, 1.03 and 1.13 (each 3H, each s, 5-CH_3 × 2, 8a-CH_3), 3.12 (1H, br t, *J*=2.5 Hz, 6-H), 4.33 and 4.60 (2H, ABq, *J*=13.0 Hz, CH_2Ph), 5.86 (1H, br s, OH), 6.08 (1H, dd, *J*=4.7, 5.1 Hz, 3-H), 7.23—7.40 (5H, m, aromatic H). MS *m/z*: 314 (M^+), 223, 205, 91. *Anal.* Calcd for $C_{20}H_{26}O_3$: C, 76.40; H, 8.34. Found: C, 76.40; H, 8.38.

(−)-(4a*S*,6*R*,8a*S*)-4a,5,6,7,8,8a-Hexahydro-6-benzyloxy-2-methoxy-5,5,8a-trimethyl-1(4*H*)-naphthalenone (34) To 4.02 g (12.8 mmol) of **33** in 63 ml of *N,N*-dimethylformamide was added 5 ml (80 mmol) of iodomethane. The solution was cooled to 0 °C, and 1.54 g (64 mmol) of sodium hydride was added. The mixture was stirred for 1.5 h at 25 °C and the reaction was quenched with methanol at 0 °C. The whole was extracted with ethyl acetate, and the product solution was washed with brine, dried, and concentrated. The residue was chromatographed using 3 : 17 ethyl acetate–hexane to afford 4.2 g (100%) of **34**, mp 118—120 °C. $[\alpha]_D$ −69.3° (*c*=1.01, $CHCl_3$). IR ($CHCl_3$): 1679 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.01, 1.03 and 1.12 (each 3H, each s, 5-CH_3 × 2, 8a-CH_3), 2.29—2.40 (2H, m, 4-H_2), 3.10 (1H, br t, *J*=2.5 Hz, 6-H), 3.57 (3H, s, 2-OCH_3), 4.32 and 4.59 (2H, ABq, *J*=13.0 Hz, CH_2Ph), 5.77 (1H, t, *J*=5.0 Hz, 3-H), 7.20—7.38 (5H, m, aromatic H). MS *m/z*: 328 (M^+), 237, 91. *Anal.* Calcd for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59. Found: C, 76.71; H, 8.71.

(+)-(1*S*,3a*S*,5*R*,7a*S*)-1′-(Octahydro-5-benzyloxy-4,4,7a-trimethyl-1*H*-inden-1-yl)-2′-pentene-1′,4′-dione (37) To a solution of 8.42 ml (54.2 mmol) of (methoxymethyl)trimethylsilane in 55 ml of tetrahydrofuran was added dropwise 41.4 ml (53.8 mmol) of 1.3 M *sec*-butyllithium in cyclohexane at −78 °C. The solution was allowed to warm to −25 °C for 1.5 h, then 2.93 g (8.93 mmol) of **34** in 18 ml of tetrahydrofuran was added. The mixture was allowed to warm to 0 °C for 1.5 h and poured into saturated ammonium chloride solution at 0 °C, the extracted with ethyl acetate. The organic layer was washed with brine, dried, and concentrated to afford (4a*S*,6*R*,8a*S*)-1,4,4a,5,6,7,8,8a-octahydro-1-hydroxy-6-benzyloxy-2-methoxy-1-methoxy(trimethylsilyl)methyl-5,5,8a-trimethylnaphthalene (**35**), which was used for the next reaction without further purification. **35**: colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 0.05 (9H, s, $Si(CH_3)_3$), 1.03, 1.06 and 1.15 (each 3H, each s, 5-CH_3 × 2, 8a-CH_3), 3.18 (1H, br t, *J*=2.5 Hz, 6-H), 3.36 (1H, s, OCHSi), 3.39 (1H, s, OCH_3), 3.51 (3H, s, 2-OCH_3), 4.42 and 4.67 (2H, ABq, *J*=11.6 Hz, CH_2Ph), 4.46 (1H, t, *J*=5.0 Hz, 3-H), 7.24—7.45 (5H, m, aromatic H).

A solution of the above product in 11 ml of diethyl ether saturated with 46% aqueous hydrogen fluoride was stirred for 1 h at 25 °C. The reaction mixture was poured into saturated sodium bicarbonate solution, and extracted with ethyl acetate. The organic layer was washed with brine, dried, and concentrated to afford (3a*S*,5*R*,7a*S*)-octahydro-5-benzyloxy-1-formyl(hydroxy)methylene-4,4,7a-trimethyl-1*H*-indene (**36**), which was used immediately for the next reaction. **36**: colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 0.94, 1.03 and 1.08 (each 3H, each s, 4-CH_3 × 2, 7a-CH_3), 3.14 (1H, t, J = 2.5 Hz, 5-H), 4.37 and 4.61 (2H, ABq, J = 11.6 Hz, CH_2Ph), 5.52 (1H, br s, OH), 7.19—7.41 (5H, m, aromatic H), 9.55 (1H, s, CHO).

To a solution of the above product in 110 ml of acetonitrile was added 5.49 g (17.3 mmol) of 1-triphenylphosphoranylidene-2-propanone. The mixture was stirred for 6 h at 25 °C, refluxed for 2 h, then concentrated and the residue was chromatographed on silica gel using 7:93 ethyl acetate–hexane to afford 1.69 g (51%) of **37** as a pale yellow oil. $[\alpha]_D$ +127.2° (c = 1.11, $CHCl_3$). IR ($CHCl_3$): 1675 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.68, 0.88 and 0.99 (each 3H, each s, 4-CH_3 × 2, 7a-CH_3), 2.35 (3H, s, 5′-H_3), 2.85 (1H, t, J = 8.9 Hz, 1-H), 3.14 (1H, br t, J = 2.5 Hz, 5-H), 4.40 and 4.63 (2H, ABq, J = 11.8 Hz, CH_2Ph), 6.80 (1H, d, J = 16.0 Hz, vinylic H), 6.91 (1H, d, J = 16.0 Hz, vinylic H), 7.22—7.41 (5H, m, aromatic H). MS m/z: 368 (M^+), 325, 278, 91. *Anal.* Calcd for $C_{24}H_{32}O_3$: C, 78.22; H, 8.75. Found: C, 78.05; H, 8.79.

(+)-(1*S*,3a*S*,5*R*,7a*S*)-1′-(Octahydro-5-hydroxy-4,4,7a-trimethyl-1*H*-inden-1-yl)-1′,4′-pentanedione (38) A mixture of 1.26 g (3.42 mmol) of **37** in 50 ml of ethanol was hydrogenated using 540 mg of 5% palladium on carbon for 15 min. The mixture was filtered, the filtrate was concentrated, and the residue was chromatographed on silica gel using 3:7 ethyl acetate–hexane to afford 745 mg (78%) of **38** as a colorless oil. $[\alpha]_D$ +104.6° (c = 1.25, $CHCl_3$). IR ($CHCl_3$): 3620 and 3500 (OH), 1699 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.69, 0.88 and 0.94 (each 3H, each s, 4-CH_3 × 2, 7a-CH_3), 2.20 (3H, s, 5′-H_3), 2.48—2.83 (5H, m, 1-H, 2′-H_2, 3′-H_2), 3.49 (1H, t, J = 2.5 Hz, 5-H). MS m/z: 262 ($M^+ - H_2O$), 244, 209, 43. HR-LSIMS m/z: 281.2115 ($M+H)^+$ (Calcd for $C_{17}H_{29}O_3$ m/z: 281.2115).

(+)-(1*S*,3a*S*,5*R*,7a*S*)-1′-(Octahydro-5-hydroxy-4,4,7a-trimethyl-1*H*-inden-1-yl)-1′,4′-pentanedione 4′-Ethylene Ketal (39) To 745 mg (2.66 mmol) of **38** in 1.96 g (16.8 mmol) of 2-ethyl-2-methyl-1,3-dioxolane were added 41 mg (0.21 mmol) of *p*-toluenesulfonic acid monohydrate and 40 mg (0.65 mmol) of ethylene glycol. The mixture was stirred for 3 h at 25 °C, then triethylamine was added. The crude mixture was diluted with ethyl acetate, washed with saturated sodium bicarbonate solution and brine, then dried and concentrated. The residue was chromatographed on silica gel using 3:7 ethyl acetate–hexane to afford 298 mg (40%) of **38** and 455 mg (53%) of **39**. This procedure was repeated two more times using the recovered starting material **38** to afford a total of 647 mg (75%) of **39**. **39**: colorless oil. $[\alpha]_D$ +81.6° (c = 0.93, $CHCl_3$). IR ($CHCl_3$): 3618 (OH), 1697 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.69, 0.88 and 0.94 (each 3H, each s, 4-CH_3 × 2, 7a-CH_3), 1.31 (3H, s, 5′-H_3), 2.38—2.64 (3H, m, 1-H, 2′-H), 3.47 (1H, br t, J = 2.8 Hz, 5-H), 3.86—3.97 (4H, m, OCH_2CH_2O). MS m/z: 324 (M^+), 309, 262, 87. HR-LSIMS m/z: 347.2189 ($M+Na)^+$ (Calcd for $C_{19}H_{32}NaO_3$ m/z: 347.2196).

(+)-(1*S*,3a*S*,5*R*,7a*S*)-5′-(Octahydro-5-hydroxy-4,4,7a-trimethyl-1*H*-inden-1-yl)-5′-hexen-2′-one 2′-Ethylene Ketal (40) To 2.89 g (44.1 mmol) of activated zinc powder in 25 ml of tetrahydrofuran was added 1.0 ml (14.3 mmol) of dibromomethane, then 1.15 ml (10.5 mmol) of titanium (IV) chloride was added at −40 °C. The suspension was stirred for 48 h at 5 °C. This suspension was added to a solution of 515 mg (1.59 mmol) of **39** in 45 ml of dichloromethane at 0 °C. The reaction mixture was stirred for 2 h at 25 °C, and diluted with pentane. The mixture was added dropwise to a mixture of 3 g of sodium bicarbonate and 1.5 g of water. The organic layer was separated, and the residue was washed with ether. The combined organic layers were dried and concentrated. The crude product was chromatographed on silica gel using 1:4 ethyl acetate–hexane to give 410 mg (80%) of **40**, mp 64—66 °C. $[\alpha]_D$ +3.3° (c = 1.09, $CHCl_3$). IR ($CHCl_3$): 3616 and 3478 (OH) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.66, 0.88 and 0.92 (each 3H, each s, 4-CH_3 × 2, 7a-CH_3), 1.32 (3H, s, 1′-H_3), 3.46 (1H, t, J = 2.8 Hz, 5-H), 3.84—3.98 (4H, m, OCH_2CH_2O), 4.75 and 4.90 (each 1H, each br s, 5′-CH_2). MS m/z: 322 (M^+), 260, 243, 227, 87. *Anal.* Calcd for $C_{20}H_{34}O_3$: C, 74.49; H, 10.63. Found: C, 74.17; H, 10.56.

(+)-(1*S*,3a*S*,5*R*,7a*S*)-5′-(Octahydro-5-hydroxy-4,4,7a-trimethyl-1*H*-inden-1-yl)-5′-hexen-2′-one (41) The procedure described for the preparation of **8** was repeated using 7.2 mg (0.022 mmol) of **40**, 0.6 ml of tetrahydrofuran, and 0.3 ml of 10% hydrochloric acid solution to afford, after chromatography on silica gel using 1:4 ethyl acetate–hexane, 5.6 mg (90%) of **41** as a colorless oil. $[\alpha]_D$ +0.84° (c = 1.17, $CHCl_3$). IR ($CHCl_3$) 3612 and 3478 (OH), 1706 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.66, 0.88 and 0.93 (each 3H, each s, 4-CH_3 × 2, 7a-CH_3), 2.15 (3H, s, 1′-H_3), 2.52—2.64 (2H, m, 3′-H_2), 3.47 (1H, t, J = 2.8 Hz, 5-H), 4.78 and 4.86 (each 1H, each br s, 5′-CH_2). MS m/z: 278 (M^+), 260, 243, 43. HR-LSIMS m/z: 301.2150 ($M+Na)^+$ (Calcd for $C_{18}H_{30}NaO_2$ m/z: 301.2142).

(−)-(1*S*,3a*S*,5*R*,7a*S*)-5′-(Octahydro-5-*tert*-butyldimethylsilyloxy-4,4,7a-trimethyl-1*H*-inden-1-yl)-5′-hexen-2′-one (42) The procedure described for the preparation of **9** was repeated using 203 mg (0.73 mmol) of **41**, 519 mg (3.44 mmol) of *tert*-butyldimethylsilyl chloride, and 255 mg (3.74 mmol) of imidazole to afford, after chromatography on silica gel using 7:93 ethyl acetate–hexane, 262 mg (92%) of **42** as a colorless oil. $[\alpha]_D$ −9.95° (c = 1.48, $CHCl_3$). IR ($CHCl_3$): 1709 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.03 and 0.04 (each 3H, each s, $Si(CH_3)_2$), 0.63, 0.82 and 0.83 (each 3H, each s, 4-CH_3 × 2, 7a-CH_3), 0.91 (9H, s, $SiC(CH_3)_3$), 2.15 (3H, s, 1′-H_3), 2.52—2.62 (2H, m, 3′-H_2), 3.38 (1H, t, J = 2.4 Hz, 5-H), 4.77 and 4.83 (each 1H, each br s, 5′-CH_2). MS m/z: 392 (M^+), 377, 335, 243. HR-LSIMS m/z: 415.2998 ($M+Na)^+$ (Calcd for $C_{24}H_{44}NaO_2Si$ m/z: 415.3006).

(1*S*,3a*S*,5*R*,7a*S*,3′*R* and 3′*S*)-6′-(Octahydro-5-*tert*-butyldimethylsilyloxy-4,4,7a-trimethyl-1*H*-inden-1-yl)-3′-methyl-1′,6′-hepten-3′-ol (43) The procedure described for the preparation of **17** and **18** was repeated using 45.2 mg (0.115 mmol) of **42**, 309 mg (12.7 mmol) of magnesium, and 0.93 ml (13.1 mmol) of vinyl bromide to give, after chromatography on silica gel using 2:23 ethyl acetate–hexane, 45 mg (93%) of **43** as a colorless oil. IR ($CHCl_3$): 3592 and 3460 (OH) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.03 and 0.05 (each 3H, each s, $Si(CH_3)_2$), 0.63, 0.81 and 0.83 (each 3H, each s, 4-CH_3 × 2, 7a-CH_3), 0.91 (9H, s, $SiC(CH_3)_3$), 1.28 and 1.29 (3H, each s, 3′-CH_3), 3.38 (1H, t, J = 2.4 Hz, 5-H), 4.74 and 4.91 (each 1H, each br s, 5′-CH_2), 5.05 and 5.06 (1H, each dd, J = 1.2, 10.8 Hz, 1′-H *cis* to 2′-H), 5.21 (1H, dd, J = 1.2, 17.4 Hz, 1′-H *trans* to 2′-H), 5.90 and 5.92 (1H, each dd, J = 10.8, 17.4 Hz, 2′-H). MS m/z: 420 (M^+), 402, 363, 345, 75. HR-LSIMS m/z: 443.3325 ($M+Na)^+$ (Calcd for $C_{26}H_{48}NaO_2Si$ m/z: 443.3319).

(1*S*,3a*S*,5*R*,7a*S*,3′*R* and 3′*S*)-6′-(Octahydro-5-hydroxy-4,4,7a-trimethyl-1*H*-inden-1-yl)-3′-methyl-1′,6′-hepten-3′-ol (44) The procedure described for the preparation of (−)-**1** was repeated using 10.8 mg (0.0257 mmol) of **43** and 0.3 ml (0.3 mmol) of 1 M tetra-*n*-butylammonium fluoride to give, after chromatography on silica gel using 1:3 ethyl acetate–hexane, 7.1 mg (90%) of **44** as a colorless oil. IR ($CHCl_3$): 3596 and 3460 (OH) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.65, 0.87 and 0.92 (each 3H, each s, 4-CH_3 × 2, 7a-CH_3), 1.28 and 1.29 (3H, each s, 3′-CH_3), 3.47 (1H, t, J = 2.7 Hz, 5-H), 4.76 and 4.92 (each 1H, each br s, 5′-CH_2), 5.06 (1H, dd, J = 1.5, 10.6 Hz, 1′-H *cis* to 2′-H), 5.20 (1H, dd, J = 1.5, 17.4 Hz, 1′-H *trans* to 2′-H), 5.90 and 5.91 (1H, each dd, J = 10.6, 17.4 Hz, 2′-H). MS m/z: 306 (M^+), 288, 271, 179, 135. HR-LSIMS m/z: 329.2462 ($M+Na)^+$ (Calcd for $C_{20}H_{34}NaO_2$ m/z: 329.2455).

(+)-3α-Hydroxy-15,16-dinorlabd-8(17)-en-13-one (45) The procedure described for the preparation of (−)-**1** was repeated using 4.7 mg (0.012 mmol) of (+)-**16** and 0.1 ml (0.1 mmol) of 1 M tetra-*n*-butylammonium fluoride in tetrahydrofuran to afford, after chromatography on silica gel using 1:3 ethyl acetate–hexane, 3.3 mg (100%) of (+)-**45** as a colorless oil. IR ($CHCl_3$): 3625 and 3500 (OH), 1711 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.71, 0.83 and 0.96 (each 3H, each s, 18-H_3, 19-H_3, 20-H_3), 2.11 (3H, s, 14-CH_3), 2.20—2.45 (2H, m, 12-H_2), 2.49—2.69 (1H, m, 7α-H), 3.43 (1H, t, J = 2.7 Hz, 3-H), 4.44 and 4.83 (each 1H, each br s, 17-H_2). MS m/z: 278 (M^+), 260, 245, 227, 202, 135, 31. HR-LSIMS m/z: 301.2149 ($M+Na)^+$ (Calcd for $C_{18}H_{30}NaO_2$ m/z: 301.2142).

(+)-15-Norlabd-8(17)-ene-3α,13-diol (46) To a solution of 5.6 mg (0.014 mmol) of (+)-**16** in 1 ml of tetrahydrofuran was added 0.1 ml (0.14 mmol) of 1.4 M methyllithium in diethyl ether at 0 °C. The solution was stirred for 3 h at 25 °C. The reaction mixture was diluted with saturated ammonium chloride solution, and extracted with ethyl acetate. The organic layer was washed with brine, dried, and evaporated. The crude product was chromatographed on silica gel using 7:93 ethyl acetate–hexane to afford 5.6 mg (97%) of (+)-3α-*tert*-butyldimethylsilyloxy-15-norlabd-8(17)-en-13-ol as a colorless oil. IR ($CHCl_3$): 3596 and 3450 (OH) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.03 and 0.05 (each 3H, each s, $Si(CH_3)_2$), 0.68, 0.79 and 0.85 (each 3H, each s, 18-H_3, 19-H_3, 20-H_3), 0.92 (9H, s, $SiC(CH_3)_3$), 1.22 (6H, s, 14-H_3 and 16-H_3), 2.38 (1H, ddd, J = 2.2, 4.2, 12.6 Hz, 7α-H), 3.35 (1H, t, J = 3.0 Hz, 3-H), 4.51 and 4.81 (each 1H, each d, J = 1.2 Hz, 17-H_2).

The procedure described for the preparation of (−)-**1** was repeated using 5.6 mg (0.014 mmol) of the above product and 0.1 ml (0.1 mmol) of 1 M tetra-*n*-butylammonium fluoride in tetrahydrofuran to afford, after chromatography on silica gel using 2:3 ethyl acetate–hexane, 3.6 mg

TABLE II. Atomic Coordinates for **40** with Their e.s.d.'s in Parentheses

Atom	x	y	z
O1	0.8662 (1)	0.7705 (1)	0.5244 (2)
C2	0.8166 (2)	0.7021 (1)	0.5600 (2)
C3	0.6732 (2)	0.7144 (1)	0.5692 (2)
O4	0.6669 (1)	0.7862 (1)	0.6170 (2)
C5	0.7745 (2)	0.8242 (1)	0.5597 (2)
C6	0.7360 (3)	0.8635 (1)	0.4308 (3)
C7	0.8276 (2)	0.8743 (1)	0.6672 (2)
C8	0.8787 (2)	0.8365 (1)	0.7931 (2)
C9	0.9235 (2)	0.8882 (1)	0.9014 (2)
C10	0.8493 (2)	0.9001 (2)	1.0091 (2)
C11	1.0542 (1)	0.9230 (1)	0.8794 (2)
C12	1.0726 (2)	0.9984 (1)	0.9404 (2)
C13	1.2192 (2)	1.0091 (1)	0.9603 (2)
C14	1.2791 (2)	0.9404 (1)	0.9040 (1)
C15	1.1773 (1)	0.8818 (1)	0.9294 (1)
C16	1.1578 (2)	0.8613 (1)	1.0794 (2)
C17	1.2170 (2)	0.8161 (1)	0.8459 (2)
C18	1.3582 (2)	0.7945 (1)	0.8758 (3)
C19	1.4549 (2)	0.8542 (1)	0.8537 (2)
O20	1.4611 (1)	0.8726 (1)	0.7130 (1)
C21	1.4224 (2)	0.9228 (1)	0.9334 (2)
C22	1.5066 (2)	0.9853 (1)	0.8828 (3)
C23	1.4547 (2)	0.9120 (2)	1.0844 (2)

e.s.d., estimated standard deviations.

TABLE III. Bond Distances (Å) of **40** with Their e.s.d.'s in Parentheses

Bond	Distance	Bond	Distance
O1–C2	1.422 (3)	C12–C13	1.538 (3)
O1–C5	1.423 (3)	C13–C14	1.530 (3)
C2–C3	1.499 (3)	C14–C15	1.538 (3)
C3–O4	1.425 (3)	C14–C21	1.542 (3)
O4–C5	1.434 (3)	C15–C16	1.545 (3)
C5–C6	1.524 (4)	C15–C17	1.536 (3)
C5–C7	1.519 (3)	C17–C18	1.540 (4)
C7–C8	1.525 (3)	C18–C19	1.513 (4)
C8–C9	1.515 (3)	C19–O20	1.434 (3)
C9–C10	1.330 (4)	C19–C21	1.542 (3)
C9–C11	1.512 (3)	C21–C22	1.539 (4)
C11–C12	1.545 (3)	C21–C23	1.543 (4)
C11–C15	1.565 (3)		

(89%) of (+)-**46** as a colorless oil. IR ($CHCl_3$): 3602 and 3450 (OH) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.71, 0.84 and 0.96 (each 3H, each s, 18-H_3, 19-H_3 and 20-H_3), 1.22 (6H, s, 14-H_3, 16-H_3), 2.34—2.46 (1H, m, 7α-H), 3.44 (1H, t, J = 3.0 Hz, 3-H), 4.53 and 4.83 (each 1H, each d, J = 1.2 Hz, 17-H_2). MS m/z: 294 (M^+), 276, 258, 243, 135. HR-LSIMS m/z: 317.2453 $(M+Na)^+$ (Calcd for $C_{19}H_{34}NaO_2$ m/z: 317.2452).

X-Ray Structure Analysis of 40 Crystal Data: $C_{20}H_{34}O_3$; M_r = 322.5; orthorhombic; $P2_12_12_1$; a = 10.313(1), b = 18.696(2), c = 9.887(1) Å; $\alpha=\beta=\gamma=90.0°$; V = 1906.3(2) Å^3; Z = 4; D_C = 1.123 g/cm^3; $F(000)$ = 178. Colorless plate crystals were grown from ether–hexane. The diffraction intensities were collected from a single crystal with dimensions of 0.5 × 0.3 × 0.3 mm on a Rigaku AFC-5R four-circle diffractometer using graphite-monochromated CuK_α radiation. A total of 1865 unique reflections were measured within the q range of 130°, of which 1820 with $F \geq 3\sigma$ (F_O) were considered as observed. The structure was solved by the direct method using MULTAN 84[36] and refined by the block-diagonal least-squares method. In the final refinement, anisotropic thermal parameters were used for non-hydrogen atoms. The final R value was 0.054. The final atomic coordinates and bond distances are given in Tables II and III, respectively.

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