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Studies on the Neutral Constituents of *Pachysandra terminalis* Sieb. *et* Zucc. VIII.[1] Methyl Migration in the Dehydration Reaction of Pachysonol and Pachysandiol-B Derivatives

Tohru Kikuchi,*,[a] Mineo Niwa,[b] Toshio Yokoi,[c] and Shigetoshi Kadota[a]

Research Institute for Wakan-Yaku (Oriental Medicines), Toyama Medical and Pharmaceutical University,[a] 2630 Sugitani, Toyama, 930-01, Japan, Central Research Laboratory, Fujisawa Pharmaceutical Co., Ltd.,[b] Kashima-2-chome, Yodogawa-ku, Osaka, 532, Japan, and Faculty of Pharmaceutical Sciences, Kobe-Gakuin University,[c] Ikawadani-cho, Tarumi-ku, Kobe, 673, Japan

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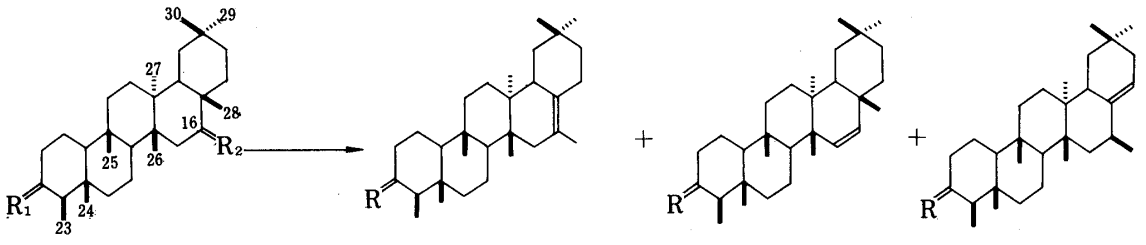
Rearrangements of the 28-methyl group of pachysonol and pachysandiol-B derivatives in the reaction with methanesulfonyl chloride were examined. It was found that two kinds of methyl-migrated products [(IIa, IIb, and VIIIa) and (IVa, IVb, and Xa)] were formed in addition to normally dehydrated products (IIIa, IIIb, and IX), and their structures were elucidated by chemical and spectroscopic methods.

Keywords——*Pachysandra terminalis*; pachysonol; pachysandiol-B; triterpene; dehydration; methyl migration; rearrangement; methanesulfonyl chloride

In a previous paper,[2] we reported that the reaction of pachysonol (Ia) with methanesulfonyl chloride (MsCl) in pyridine gave friedel-15-en-3-one (IIIa) and a rearranged product whose structure was tentatively assigned as IIa (see Chart 1). In this paper, we will discuss the structure of this rearranged product (IIa) and also those of the rearranged products of pachysandiol-B derivatives (Ib, Ic, VIc, and VIIc) in the same reaction.

Reexamination of the reaction of pachysonol (Ia) with MsCl revealed the formation of a small amount of another product (IVa) in addition to IIa and IIIa. However, the third product (IVa) could not be isolated at this stage; all attempts at separation gave only a mixture of IIa and IVa. After the Wolff–Kishner reduction of the mixture (IIa and IVa), the deoxo products could be separated by careful chromatography using silver nitrate ($AgNO_3$)-impregnated silica gel to give compounds IIb and IVb.

Then we examined the reaction of friedelan-16β-ol (Ib)[2] and its 16α-epimer (Ic).[2] Treatment of Ib with MsCl under the conditions used for pachysonol (Ia) gave a rearranged product



Ia : R_1=O, R_2= 

Ib : R_1=H_2, R_2= 

Ic : R_1=H_2, R_2= 

IIa : R=O
IIb : R=H_2

IIIa : R=O
IIIb : R=H_2

IVa : R=O
IVb : R=H_2

Chart 1

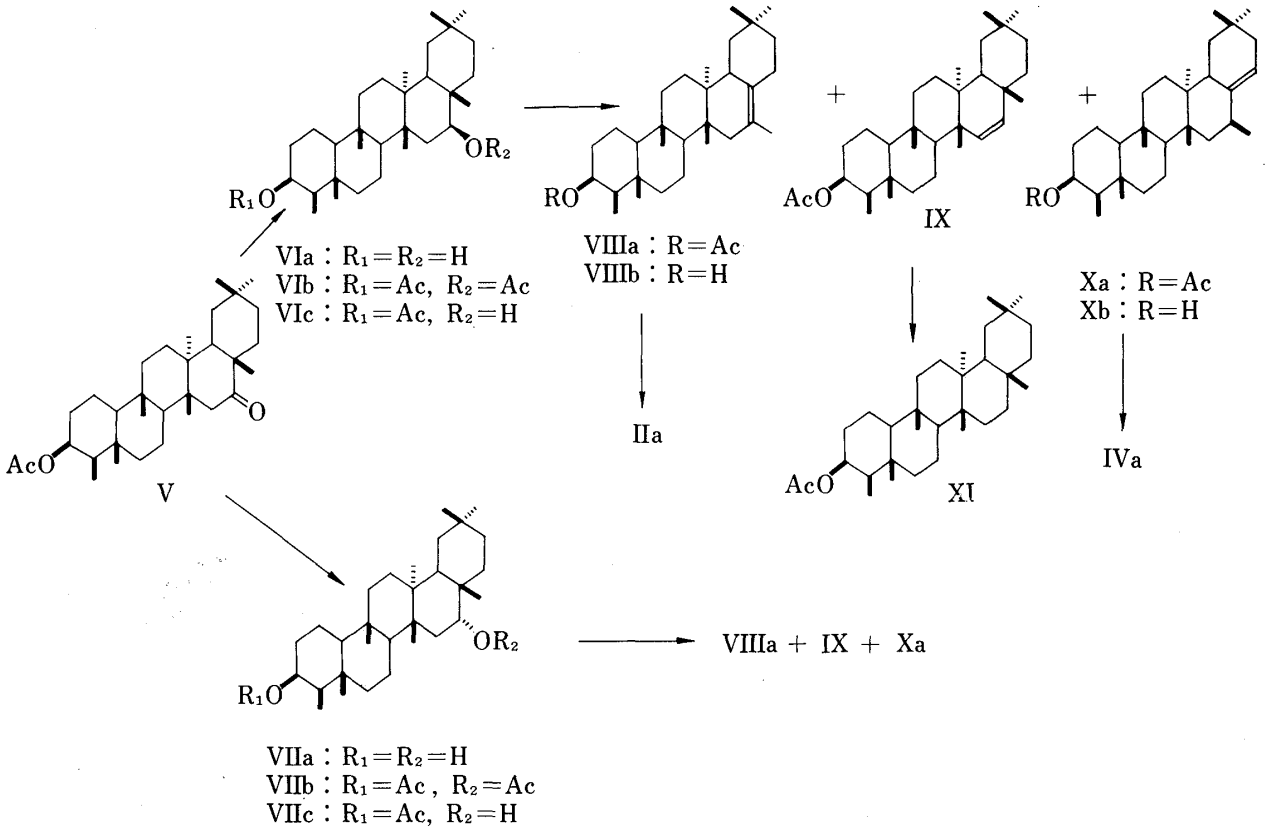


Chart 2

(IIb), $C_{30}H_{50}$, mp 225—226 °C, together with small amounts of two other products: IVb, $C_{30}H_{50}$, mp 210—213 °C, and IIIb, $C_{30}H_{50}$, mp 216—225 °C.

Among the above compounds, IIb and IVb were found to be identical with the deoxo compounds (IIb and IVb) derived from pachysonol (Ia), mentioned above.

The third product (IIIb) showed two olefinic proton signals at δ 5.23 and 5.75 (each doublet, J=10 Hz) in the 200 MHz nuclear magnetic resonance (NMR) spectrum, and it was identified as friedel-15-ene (IIIb) by gas chromatographic (GC) and NMR comparisons with a sample (IIIb) prepared by the Wolff-Kishner reduction of IIIa.

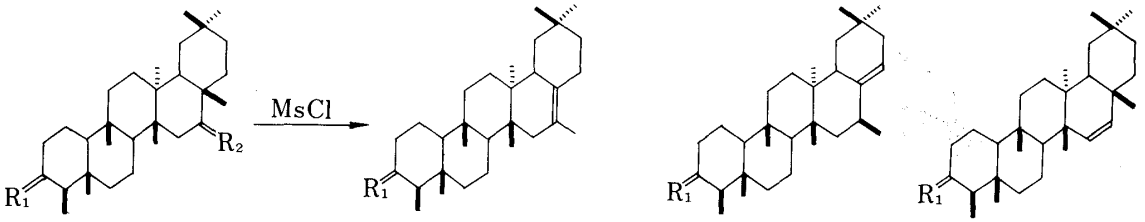
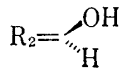
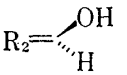
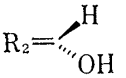
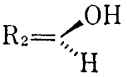
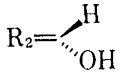
On the other hand, treatment of the 16α-epimer (Ic) with MsCl gave mainly the product IVb, mp 210—214 °C, along with IIb, mp 223—225 °C, and IIIb, mp 216—220 °C. The identities of these compounds were confirmed by GC and NMR comparisons with the corresponding samples (IVb, IIb, and IIIb) obtained from Ib.

Next, we examined the reaction of 3-O-acetyl-pachysandiol-B (VIc) and its C_{16}-epimer (VIIc). VIc and VIIc were prepared from a keto-acetate (V)[2] in the following way. Reaction of V with $LiAlH_4$ afforded a mixture of epimeric diols (VIa and VIIa) in a ratio of 1: 2 (judged from the NMR spectrum). Acetylation of this mixture followed by preparative thin-layer chromatography (TLC) gave pachysandiol-B diacetate (VIb) and its C_{16}-epimer (VIIb), mp 246—249 °C. The NMR spectrum of the latter (VIIb) exhibited two signals due to hydrogens geminal to the acetoxyl groups at δ 5.18 (dd, J=7.5, 8.5 Hz) and at δ 4.90 (br) and the acetyl methyl signal at δ 2.03 (6H, s).

Partial hydrolysis of VIb and VIIb with 5% KOH–MeOH at 50 °C gave VIc, amorphous powder, δ 4.90 (1H, br, $W^{1/2}$=6.5 Hz, C<u>H</u>–OAc), 4.00 (1H, t, J=9 Hz, C<u>H</u>–OH), 2.04 (3H, s, Ac), and VIIc, colorless needles, mp 237—239 °C, δ 5.00 (1H, br, $W^{1/2}$=6.5 Hz, C<u>H</u>–OAc), 3.93 (1H, dd, J=7.0, 11.0 Hz, C<u>H</u>–OH), 2.03 (3H, s, Ac), respectively.

Reaction of VIc with MsCl gave three products in an approximate ratio of 2:1:1 as shown in Table I. However, as in the case of pachysonol, attempts at chromatographic separation led only to the isolation of two products: a rearranged compound (VIIIa), $C_{32}H_{52}O_2$, mp 239—241 °C, and another compound (IX), $C_{32}H_{52}O_2$, mp 277—278 °C. The latter (IX) showed signals at δ 5.77, 5.23 (2H, ABq, J=10 Hz, -CH=CH-), 4.92 (1H, br, C<u>H</u>-OAc), 2.06 (3H, s, Ac), 1.19—0.90 (7×*tert*-CH_3), and 0.84 (3H, d, J=7 Hz, *sec*-CH_3) in the NMR spectrum, suggesting that the compound may be a normally dehydrated product. This was confirmed by the catalytic hydrogenation of IX to epifriedelanol acetate (XI). On the other hand, the former (VIIIa) was subjected to alkaline hydrolysis and subsequent CrO_3 oxidation to afford a ketone (IIa), mp 243—245 °C, which was identical with compound IIa obtained from pachysonol (Ia).

Table I. Approximate Product Ratios in the Dehydration (based on the Peak Areas in GC)

Starting Material	Products		
			
Pachysonol (Ia)			
R_1=O, R_2= 	55—60	15—20	20—25
3-O-Acetyl-pachysandiol-B (VIc)			
R_1=  , R_2= 	50—60	20—25	20—25
3-O-Acetyl-16-epi-pachysandiol-B (VIIc)			
R_1=  , R_2= 	33	60	7
Friedelan-16β-ol (Ib)			
R_1=H_2, R_2= 	50	25	25
Friedelan-16α-ol (Ic)			
R_1=H_2, R_2= 	37	56	7

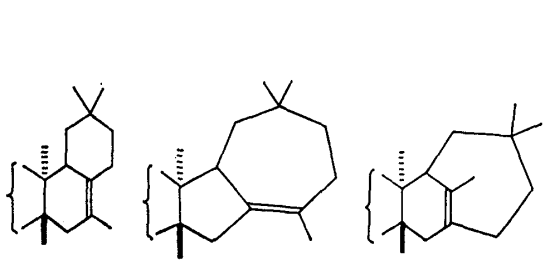
On the contrary, compound VIIc having the epimeric C_{16}-OH configuration afforded mainly a new product (Xa), $C_{32}H_{52}O_2$, mp 263—265 °C, along with VIIIa and IX in the same reaction (see Table I). Incidently, in GC and GC–MS experiments compound Xa was found to be identical with the third product (Xa) in the reaction of VIc, mentioned above.

Turning now to the structures of the above rearranged products (IIa, IIb, and VIIIa), the presence of a tetrasubstituted double bond was suggested by their NMR spectra, which showed no olefinic proton signal, but a signal ascribable to a vinyl methyl group at around δ 1.6 (br s). Thus, the partial structures **A** and **B** could be postulated for these compounds based on the Wagner–Meerwein type rearrangement.[3]

Then, in order to make a choice among these possibilities, we carried out the ozonolysis of IIa, and a triketone (XIIa), $C_{30}H_{48}O_3$, mp 188—189 °C, was obtained as the sole product.

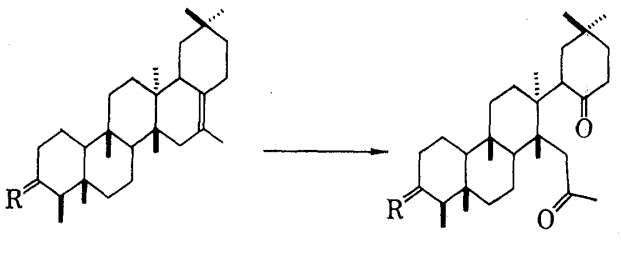
The IR spectrum of XIIa showed a strong carbonyl band at 1700 cm^{-1}, which corresponds to an open-chain and a six-membered or larger ring ketone. Its NMR spectrum exhibited signals for an isolated methylene at δ 3.02 and 2.36 (ABq, J=18 Hz) (confirmed by a double resonance experiment) and for an acetyl methyl group at δ 2.20 (3H, s). The mass spectrum of XIIa showed significant peaks at m/z 456 (M^+), 398 (*a*), 383 (*d*), 331 (*b*), 277 (*e*), 273 (*c*), and 219 (*f*), which were reasonably explained by the fragmentations shown in Chart 5.

Similarly, ozonolysis of VIIIa gave rise to a diketone (XIIb), $C_{32}H_{52}O_4$, mp 204—206 °C; ν: 1715 (sh) and 1700 cm^{-1}, δ: 4.90 (1H, br, $W^{1/2}$=6.5 Hz, C<u>H</u>–OAc), 2.92, 2.40 (2H, ABq, J= 18 Hz, $-CH_2CO-$), 2.17 (3H, s, CH_3CO), and 2.03 (3H, s, Ac). The mass spectrum of XIIb exhibited fragment ion peaks at m/z 500 (M^+), 442 (*a*), 427 (*d*), 375 (*b*), 367 (*d*-60), 321 (*e*), 317 (*c*), 263 (*f*) and 203 (*f*-60), which were also interpreted in the same way as above (see Chart 5).



A **B** **C**

Chart 3



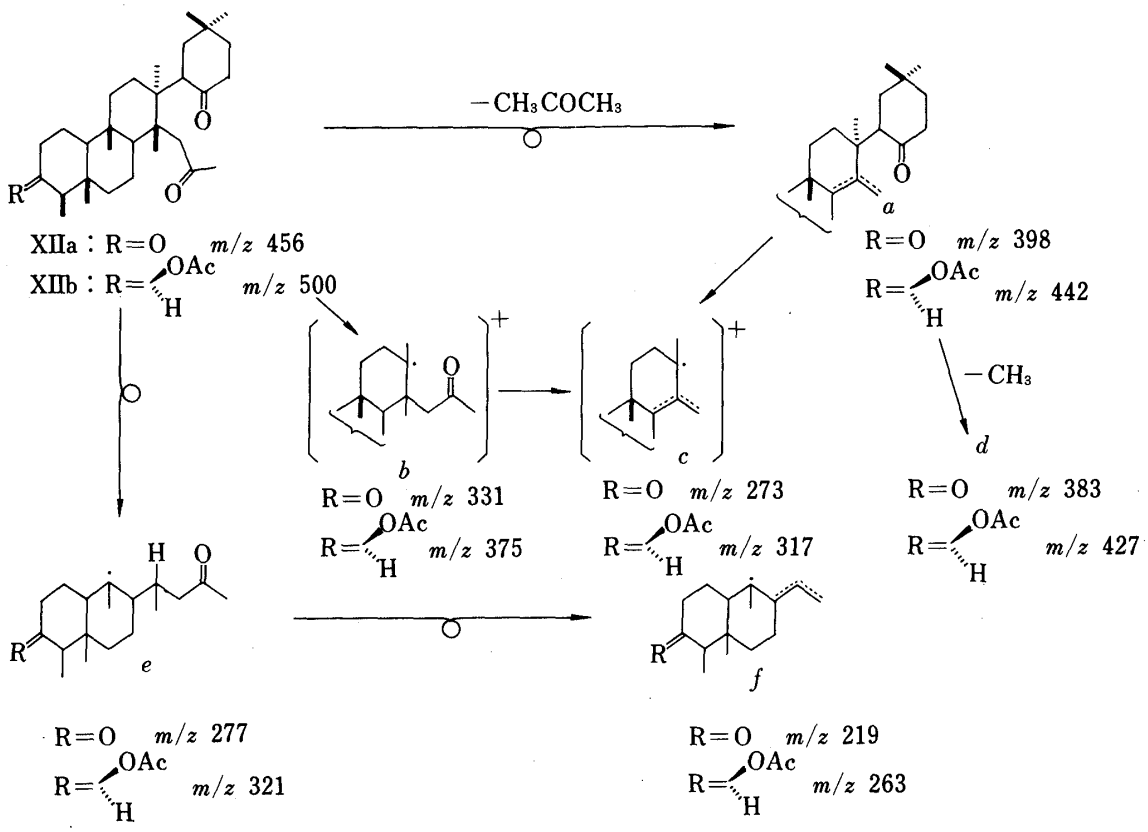
IIa : R=O

VIIIa : R=OAc

XIIa : R=O

XIIb : R=OAc

Chart 4



XIIa : R=O *m/z* 456

XIIb : R=OAc *m/z* 500

$-CH_3COCH_3$

a R=O *m/z* 398; R=OAc *m/z* 442

b R=O *m/z* 331; R=OAc *m/z* 375

c R=O *m/z* 273; R=OAc *m/z* 317

$-CH_3$

d R=O *m/z* 383; R=OAc *m/z* 427

e R=O *m/z* 277; R=OAc *m/z* 321

f R=O *m/z* 219; R=OAc *m/z* 263

Chart 5

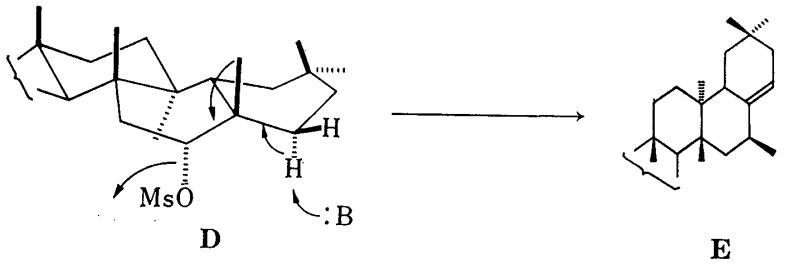
The above findings evidently supported the partial structure **A** and thus the structures of the rearranged products from pachysonol (Ia) and its derivatives (Ib, Ic, VIc, and VIIc) can be assigned as IIa, IIb, and VIIIa, respectively.

On the other hand, the other rearranged products IVb and Xa showed a broad signal for a newly introduced olefinic hydrogen at δ 5.35 and a new doublet signal (J=8 Hz) ascribable to a *sec*-methyl group at δ 1.19 in the NMR spectra. On irradiation of the allylic proton at around δ 2.4, this methyl signal changed to a singlet.

Alkaline hydrolysis of Xa, followed by chromium trioxide oxidation, gave a ketone (IVa), $C_{30}H_{48}O$, mp 244—247 °C, which was shown to be identical with the unidentified product (IVa) in the reaction of pachysonol (Ia) by GC and GC–MS comparisons. In the NMR spectrum, the ketone (IVa) also showed a broad signal for an olefinic proton (δ 5.35) and a doublet signal for a *sec*-methyl group (δ 1.19).

Based on the foregoing NMR data, the rearranged products of this series, obtained from pachysonol (Ia) and its derivatives (Ib or Ic and VIc or VIIc), could be represented by the structures IVa, IVb, and Xa, respectively. The configuration of the C_{16}-methyl group in these compounds must be β from mechanistic considerations.

The observed preferential formation of IVb and Xa in the reactions of 16α-alcohols (Ic and VIIc) might be ascribed to the participation of a concerted mechanism as shown in Chart 6.



D E

Chart 6

Experimental

All melting points were measured with a Kofler-type apparatus and are uncorrected. All specific rotations were measured in $CHCl_3$ solutions. Mass spectra (MS) were determined on a Hitachi RMU-6D (for low resolution MS) or a JEOL JMS-D300 (for high resolution MS) using a direct inlet system or a GC injection system. Infrared (IR) spectra were measured for solutions in $CHCl_3$, unless otherwise noted. NMR spectra were taken on Varian Associates A-60, HA-100D, and/or XL-200 spectrometers in $CDCl_3$ solutions using tetramethylsilane as an internal standard, and chemical shifts are recorded in δ-values. Gas chromatographic (GC) measurements were run on a Shimadzu GC-6AM gas chromatograph using a glass column (2 m×4 mm) packed with 2% OV-17 on Gas-Chrom Q (80—100 mesh): column temperature, 280°C; injection temperature, 300°C. Column chromatography was performed on Merck Kieselgel G 60 or Mallinckrodt silicic acid (100 mesh). For column chromatography on silica gel impregnated with $AgNO_3$, the adsorbent was prepared by extensive mixing of Mallinckrodt silicic acid and $AgNO_3$ (8: 2) with the aid of water followed by drying at 110°C for 24 h. Preparative thin layer chromatography (TLC) was performed on Merck Kieselgel GF_{254} with $CHCl_3$, and plates were examined under ultraviolet (UV) light (for UV-absorbing materials on GF_{254} plates). For the extraction of substances from the Kieselgel, methylene chloride was used as a solvent. TLC was carried out with Merck Kieselgel G acc. to Stahl. Coloring reagent: $Ce(SO_4)_2$ in 10% H_2SO_4. For drying organic solutions, anhydrous $MgSO_4$ was used.

Reaction of Pachysonol (Ia) with Methanesulfonyl Chloride——Methanesulfonyl chloride (MsCl) (0.5 ml) was added to a chilled (0°C) solution of pachysonol (Ia) (50 mg) in pyridine (2 ml) and the whole was kept overnight in a refrigerator. The reaction mixture was diluted with ice-water and extracted with ether. The ether solution was washed successively with 3% HCl and dil. Na_2CO_3, dried, and concentrated *in vacuo*. Crystallization of the residue from ether–MeOH gave a crystalline mass (35 mg), which was chromatographed on silica gel (4 g) and eluted with benzene–hexane (15: 85) to afford a rearranged product IIa (12 mg), mp 240—243°C (recrystallized from ether–MeOH). This product was identical with an authentic sample (IIa), previously obtained,[2] as judged by GC and IR (KBr) comparisons.

Further elution with benzene–hexane (3: 7) gave a mixture of three products (20 mg), which was again chromatographed on 20% $AgNO_3$–SiO_2 (20 g). Elution with benzene–hexane (15: 85) afforded a mixture

of IIa and IVa (10 mg, approximate ratio of 2: 1 based on GC; the identity of IVa was confirmed by GC–MS), and elution with benzene–hexane (3: 7) gave an anhydro compound (IIIa) (7 mg). The latter (IIIa) was recrystallized from ether–MeOH to give needles (4 mg), mp 237—240°C, which were identical with an authentic sample of IIIa, previously obtained,[2] as judged by GC and IR (KBr) comparisons.

Wolff-Kishner Reduction of the Mixture of IIa and IVa——A solution of the mixture of IIa and IVa (10 mg), mentioned above, and anhydrous hydrazine (0.2 ml) in dimethylsulfoxide (DMSO) (1 ml) was heated at 140°C in an oil bath for 2 h. Then, KOH pellets (*ca.* 200 mg) were added and the whole was heated at 200°C for 4 h. The reaction mixture was diluted with water and extracted with ether. The extract was washed with water, dried, and evaporated to leave a crystalline residue (10 mg), which was chromatographed on 20% $AgNO_3$–SiO_2 (11 g) using hexane. The first eluate (3 mg) was recrystallized from ether–acetone to give a deoxo compound (IVb), fine prisms (2 mg), mp 210—215°C. High resolution MS *m/z*: Found 410.3917. Calcd for $C_{30}H_{50}(M^+)=410.3912$. NMR (200 MHz) δ: 0.72 (3H, d, $J=6$ Hz, *sec*-CH_3), 0.76, 0.81, 0.84, 0.86, 0.93, 1.01 (each 3H, $6\times$*tert*-CH_3), 1.18 (3H, d, $J=8$ Hz, *sec*-CH_3), 5.35 (1H, br, C=CH). The next eluate (7 mg) was also recrystallized from ether–acetone to give another product (IIb), needles (5 mg), mp 223—225°C. High resolution MS *m/z*: Found 410.3869. Calcd for $C_{30}H_{50}(M^+)=410.3912$. NMR (200 MHz) δ: 0.74 (3H, d, $J=6$ Hz, *sec*-CH_3), 0.74, 0.77, 0.79, 0.83, 0.92, 0.94 (each 3H, $6\times$*tert*-CH_3), 1.58 (3H, s, vinyl CH_3).

Wolff-Kishner Reduction of the Anhydro Compound (IIIa)——A mixture of IIIa (3 mg), anhydrous hydrazine (0.2 ml), and DMSO (1 ml) was heated under argon gas at 140°C for 1 h. Then, KOH pellets (*ca.* 200 mg) were added to this mixture and the whole was heated at 200°C for 3 h. The reaction mixture was worked up in the same manner as above and the crude product (4 mg) was chromatographed on 20% $AgNO_3$–SiO_2 (4 g). Elution with hexane gave a small amount of crystalline substance[4] (0.5 mg). Subsequent elution with benzene–hexane (15: 85) afforded a deoxo compound (IIIb) (2 mg), which was recrystallized from ether–acetone to give needles (1.6 mg), mp 217—219°C. High resolution MS *m/z*: Found 410.3926. Calcd for $C_{30}H_{50}(M^+)=410.3912$. NMR (200 MHz) δ: 0.73 (3H, d, $J=6$ Hz, *sec*-CH_3), 0.78, 0.85, 0.90, 0.96, 1.01, 1.06, 1.17 (each 3H, $7\times$*tert*-CH_3), 5.23, 5.75 (each 1H, d, $J=10$ Hz, C<u>H</u>=C<u>H</u>).

Reaction of Friedelan-16β-ol (Ib) with MsCl——Friedelan-16β-ol (28 mg) was treated with MsCl (0.3 ml) in pyridine (1 ml) in the same manner as described for pachysonol (Ia). The product (22 mg) was chromatographed on 20% $AgNO_3$–SiO_2 (22 g) and eluted with hexane to give a rearranged product (IVb). Recrystallization of this product from ether–acetone gave prisms (3 mg), mp 210—213°C, which were identical with the sample (IVb) derived from pachysonol as judged by GC and NMR comparisons. Further elution with hexane gave another rearranged product (IIb) (10 mg), which was recrystallized from ether–acetone to show mp 225—226°C. This product was identical with the sample (IIb) derived from pachysonol as judged by GC and NMR comparisons. Subsequent elution with benzene–hexane (5: 95) afforded an anhydro compound (IIIb) (4 mg), which was recrystallized from ether–acetone, mp 216—225°C. This was found to be identical with the sample (IIIb), described above, as judged by GC and NMR comparisons.

Reaction of Friedelan-16α-ol (Ic) with MsCl——Friedelan-16α-ol (Ic) (29 mg) was treated with MsCl (0.3 ml) in the same manner as described above and the crude product (21 mg) was chromatographed on 20% $AgNO_3$–SiO_2 (24 g) to give compound IVb (9 mg), mp 210—214°C, compound IIb (8 mg), mp 223—225°C, and compound IIIb (2 mg), mp 216—220°C.

Lithium Aluminum Hydride Reduction of the Ketol Acetate (V) and Subsequent Acetylation——The ketol acetate (V) (260 mg) was treated with excess $LiAlH_4$ (600 mg) in boiling ether–tetrahydrofuran (THF) (each 10 ml) for 3 h. Usual work-up gave a mixture of diols (VIa and VIIa) (245 mg), which was treated with acetic anhydride–pyridine (each 2 ml) overnight at room temperature. The reaction mixture was worked up in the usual manner to afford a crystalline residue (260 mg), which was separated by preparative TLC into two fractions. The less polar fraction (96 mg) was recrystallized from CH_2Cl_2–MeOH to give 16-epi-pachysandiol-B diacetate (VIIb) as colorless needles, mp 246—249°C. $[\alpha]_D^{15}$ −3.7°C ($c=1.0$). *Anal.* Calcd for $C_{34}H_{56}O_4$: C, 77.22; H, 10.67. Found: C, 77.56; H, 10.76. IR ν_{max} cm^{-1}: 1716, 1250 (OAc). NMR δ: 5.18 (1H, dd, $J=7.5$, 8.5 Hz, C<u>H</u>–OAc), 4.90 (1H, br, $W^{1/2}=6.5$ Hz, C<u>H</u>–OAc), 2.03 (6H, s, $2\times$Ac), 1.18—0.88 ($7\times$*tert*-CH_3), 0.80 (3H, $J=6$ Hz, *sec*-CH_3). The more polar fraction (53 mg) was recrystallized from CH_2Cl_2–MeOH to afford colorless needles (VIb), mp 222—224°. This compound was identified as pachysandiol-B diacetate (VIb) by TLC and IR(KBr) comparisons with an authentic sample.

Partial Hydrolysis of Pachysandiol-B Diacetate (VIb)——A mixture of pachysandiol-B diacetate (VIb) (370 mg) and 5% KOH–MeOH (15 ml) was stirred at 50°C on a glycerol bath for 6 h. The mixture was diluted with water, extracted with $CHCl_3$, dried, and concentrated to leave a jelly-like residue (350 mg). This was chromatographed on silica gel (17.5 g) using benzene. The first eluate was the starting material (VIb) (30 mg) and the next eluate was a monoacetate (VIc) (288 mg), obtained as a colorless amorphous powder. *Anal.* Calcd for $C_{32}H_{54}O_3\cdot 1/2H_2O$: C, 77.55; H, 11.18. Found: C, 78.00; H, 10.89. MS *m/z*: 486 (M^+), 468 (M−18), 453 (M−18−15). IR ν_{max} cm^{-1}: 3600 (OH), 1720, 1260 (AcO). NMR δ: 4.90 (1H, br, $W^{1/2}=6.5$ Hz, C<u>H</u>–OAc), 4.00 (1H, t, $J=9$ Hz, C<u>H</u>–OH), 2.04 (3H, s, Ac), 1.19—0.88 ($7\times$*tert*-CH_3), 0.83 (3H, d, $J=6$ Hz, *sec*-CH_3).

Partial Hydrolysis of 16-epi-Pachysandiol-B Diacetate (VIIb)——A mixture of 16-epi-pachysandiol-B diacetate (VIIb) (68 mg) and 5% KOH–MeOH (10 ml) was stirred at 50°C for 5 h and the usual work-up

gave an oily residue (65 mg), which was chromatographed on silica gel (10 g). Elution with benzene gave first the starting material (VIIb) (20 mg) and next 3-O-acetyl-16-epi-pachysandiol-B (VIIc) (26 mg). The latter (VIIc) was recrystallized from CH_2Cl_2–MeOH to afford colorless needles (20 mg), mp 237—239°C. *Anal.* Calcd for $C_{32}H_{54}O_3$: C, 78.96; H, 11.18. Found: C, 79.14; H, 11.03. MS *m/z*: 486 (M^+), 468 (M−18), 453 (M−18−15). IR ν_{max} cm^{-1}: 3600 (OH), 1720, 1260 (OAc). NMR δ: 5.00 (1H, br, $W^{1/2}$=6.5 Hz, C<u>H</u>–OAc), 3.93 (1H, q, J=7, 11 Hz, C<u>H</u>–OH), 2.03 (3H, s, Ac), 1.17—0.75 (7×*tert*-CH_3), 0.80 (3H, d, J=6 Hz, *sec*-CH_3).

Reaction of 3-O-Acetyl-pachysandiol-B (VIc) with MsCl——MsCl (1 ml) was added to a chilled (0°C) solution of 3-O-acetyl-pachysandiol-B (VIc) (170 mg) in pyridine (2 ml) and the whole was left to stand at room temperature for 48 h. The reaction mixture was poured into ice-water and extracted with CH_2Cl_2. The CH_2Cl_2 solution was washed successively with 3% HCl and dil. Na_2CO_3, and dried. Removal of the solvent by evaporation *in vacuo* gave a brownish oily residue, which crystallized on addition of MeOH. The collected crystals (*ca.* 150 mg) were chromatographed on 20% $AgNO_3$–SiO_2 (30 g) and eluted with benzene-hexane (1: 9) to give a mixture of rearranged products VIIIa and Xa (*ca.* 60 mg, approximate ratio of 2: 1 based on GC; the identity of each component was confirmed by GC–MS). Further elution with the same solvent afforded a fairly pure substance (VIIIa) (40 mg), which was recrystallized from CH_2Cl_2–MeOH to afford a pure sample (VIIIa), colorless needles, mp 239—241°C. $[\alpha]_D^{25}$ +54.5°C (c=0.77). *Anal.* Calcd for $C_{32}H_{52}O_2$: C, 81.99; H, 11.18. Found: C, 82.21; H, 11.43. MS *m/z*: 468 (M^+). IR(KBr) ν_{max} cm^{-1}: 1730, 1250 (OAc). NMR δ: 4.90 (1H, br, $W^{1/2}$=6.5 Hz, C<u>H</u>–OAc), 2.04 (3H, s, Ac), 1.59 (3H, br s, C=C–CH_3), 0.94—0.75 (*sec*-CH_3 and 6×*tert*-CH_3).

Subsequent elution with benzene–hexane (3: 7) gave another product (IX) (9 mg). This compound (IX) was recrystallized from CH_2Cl_2–MeOH to afford colorless leaves (8 mg), mp 277—278°C. MS *m/z*: 468 (M^+). IR(KBr) ν_{max} cm^{-1}: 1730, 1245 (AcO). NMR δ: 5.77, 5.23 (each 1H, d, J=10 Hz, CH=CH), 4.92 (1H, br, $W^{1/2}$=6.5 Hz, C<u>H</u>–OAc), 2.06 (3H, s, Ac), 1.19—0.90 (7×*tert*-CH_3), 0.84 (3H, d, J=6 Hz, *sec*-CH_3).

Hydrolysis of the Rearranged Product VIIIa and Subsequent Oxidation with Chromium Trioxide——The compound VIIIa (60 mg) was treated with excess $LiAlH_4$ in boiling ether–THF (each 2 ml) for 1 h. Usual work-up gave a crude alcohol (VIIIb) which was repeatedly recrystallized from CH_2Cl_2–MeOH to afford colorless needles (50 mg), mp 251—252°C. $[\alpha]_D^{33}$ +41.1°C (c=0.95). IR ν_{max} cm^{-1}: 3500, 3300 (OH). *Anal.* Calcd for $C_{30}H_{50}O$: C, 84.44; H, 11.81. Found: C, 84.28; H, 11.91. MS *m/z*: 426 (M^+).

A suspension of chromium trioxide (40 mg) in pyridine (1.5 ml) was added to a solution of the above alcohol (VIIIb) (36 mg) in pyridine (1 ml) and the whole was stirred for 1 h at room temperature. The reaction mixture was diluted with water and extracted with CH_2Cl_2. The extract was washed with 3% HCl and dil. Na_2CO_3, dried, and concentrated. The residue (35 mg) was repeatedly recrystallized from ether–MeOH to give a ketone (IIa) (21 mg), colorless prisms, mp 238—241°C. $[\alpha]_D^{33}$ −1.7°C (c=1.21). *Anal.* Calcd for $C_{30}H_{48}O$: C, 84.84; H, 11.39. Found: C, 84.67; H, 11.75. IR ν_{max} cm^{-1}: 1710 (C=O). NMR δ: 1.61 (3H, br s, C=C–CH_3), 0.93—0.83 (7×CH_3). The IR(KBr) spectrum of this substance was superimposable upon that of the rearranged product (IIa) obtained from pachysonol (Ia).

Catalytic Hydrogenation of the Compound IX——The compound IX (3 mg), mentioned above, was hydrogenated over Pd–C (prepared with 1% $PdCl_2$ (1 ml) and charcoal (100 mg)) in ethyl acetate (4 ml) at room temperature for 24 h. The catalyst was filtered off and the filtrate was concentrated under reduced pressure. The crystalline residue was chromatographed on 20% $AgNO_3$–SiO_2 (15 g) and the eluate with benzene–hexane (1: 4) was recrystallized from CH_2Cl_2–MeOH to give colorless prisms (XI) (1 mg), mp 295—298°C. The IR(KBr) spectrum of this substance was identical with that of an authentic sample of epi-friedelanol acetate (XI).

Reaction of 3-O-Acetyl-16-epi-pachysandiol-B (VIIc) with MsCl——MsCl (0.4 ml) was added to a chilled solution of 3-O-acetyl-16-epi-pachysandiol-B (VIIc) (26 mg) in pyridine (1 ml) and the whole was kept for 24 h at room temperature. Usual work-up afforded a yellow crystalline mass (20 mg). This was carefully chromatographed on 20% $AgNO_3$–SiO_2 (25 g) and elution with benzene–hexane (1: 9) gave a rearranged product (Xa), which was recrystallized from ether–MeOH to give colorless prisms (6 mg), mp 259—261°C. High resolution MS *m/z*: Found: 468.3940. Calcd for $C_{32}H_{52}O_2$(M^+)=468.3965. IR ν_{max} cm^{-1}: 1735, 1250 (AcO). NMR δ: 5.35 (1H, br, olefinic H), 4.90 (1H, br, $W^{1/2}$=6.5 Hz, C<u>H</u>–OAc), 2.04 (3H, s, Ac), 1.19 (3H, d, J=8 Hz, *sec*-CH_3), 1.05—0.83 (6×*tert*-CH_3), 0.81 (3H, d, J=6 Hz, *sec*-CH_3). Subsequent elution afforded another rearranged product (VIIIa), which was recrystallized from CH_2Cl_2–MeOH to give colorless needles (2 mg), mp 226—229°C. The IR(KBr) spectrum of this substance was superimposable upon that of the rearranged product (VIIIa) obtained from 3-O-acetyl-pachysandiol-B (VIc).

Further elution with benzene–hexane (3: 7) gave rise to an anhydro compound (IX), which was recrystallized from CH_2Cl_2–MeOH to give colorless leaves (1 mg), mp 275—276°. The IR(KBr) spectrum of this substance was superimposable upon that of the anhydro compound (IX) obtained from 3-O-acetyl-pachysandiol-B (VIc).

Hydrolysis of the Rearranged Product Xa and Subsequent Oxidation with Chromium Trioxide——The compound Xa (10 mg) was refluxed with 10% KOH–MeOH (10 ml) for 8 h and the reaction mixture was worked up as usual. The product was recrystallized from CH_2Cl_2–MeOH to give an alcohol (Xb) as colorless

needles (5 mg), mp 197—199°C.

This alcohol (Xb) was oxidized with CrO_3 (20 mg) in pyridine (1.5 ml) at room temperature. Usual work-up gave a ketone (IVa) (4 mg), which was repeatedly recrystallized from ether–MeOH to afford fine prisms (2 mg), mp 244—247°. High resolution MS *m/z*: Found 424.3692. Calcd for $C_{30}H_{48}O(M^+)=424.3702$. IR ν_{max} cm^{-1}: 1700 (C=O). NMR (200 MHz) δ: 5.37 (1H, br, $W^{1/2}=11$ Hz, C=CH), 1.19 (3H, d, $J=7.5$ Hz, *sec*-CH_3), 1.03, 0.94, 0.89, 0.86, 0.85, 0.72 (each 3H, s, *tert*-CH_3), 0.88 (3H, d, $J=6$ Hz, *sec*-CH_3).

Ozonolysis of 28-Nor-16-methyl-friedel-16-en-3-one (IIa)——A solution of the rearranged product IIa (36 mg) in CH_2Cl_2 (20 ml) and pyridine (7 drops) was treated with ozone gas at −70°C (dry ice-acetone bath) for 2 h. The pale blue reaction mixture was added to a suspension of zinc powder (2 g) in acetic acid (10 ml) and the whole was stirred for 3 h in an ice bath. The zinc powder was filtered off and washed with $CHCl_3$. The filtrate and washings were combined, washed with water and dil. Na_2CO_3, dried, and concentrated to give an oily residue (48 mg). Purification of this residue by preparative TLC, followed by recrystallization from ether, afforded a triketone (XIIa) (25 mg) as colorless needles, mp 188—189°C. High resolution MS *m/z*: Found 456.3592, 398.3208, 383.2938, 331.2663, 277.2137, 273.2209, 219.1745. Calcd for $C_{30}H_{48}O_3$-$(M^+)=456.3602$, $C_{27}H_{42}O_2(a)=398.3185$, $C_{26}H_{39}O_2(d)=383.2948$, $C_{22}H_{35}O_2(b)=331.2637$, $C_{18}H_{29}O_2(e)=277.2164$, $C_{19}H_{29}O(c)=273.2218$, $C_{15}H_{23}O(f)=219.1746$. IR ν_{max} cm^{-1}: 1700 (C=O). NMR δ: 3.02, 2.96 (each 1H, ABq, $J=18$ Hz, $-CH_2-CO$), 2.20 (3H, s, $COCH_3$), 1.20—0.72 ($7\times CH_3$).

Ozonolysis of 3β-Acetoxy-28-nor-16-methyl-friedel-16-ene (VIIIa)——A solution of the rearranged product VIIIa (45 mg) in CH_2Cl_2 (20 ml) and pyridine (7 drops) was treated with ozone gas at −70°C for 2 h and the pale blue reaction mixture was treated with zinc powder (2 g) in acetic acid (10 ml) for 3 h in the same manner as above. The crude product (48 mg) was purified by preparative TLC to give a diketo-acetate (XIIb). This was recrystallized from ether–MeOH to afford colorless plates (40 mg), mp 204—206°C. High resolution MS *m/z*: Found 500.3889, 442.3489, 375.2917, 367.3005, 321.2447, 317.2502, 203.1789. Calcd for $C_{32}H_{52}O_4(M^+)=500.3866$, $C_{29}H_{46}O_3(a)=442.3447$, $C_{24}H_{39}O_3(b)=375.2899$, $C_{26}H_{39}O(d-60)=367.3000$, $C_{20}H_{33}O_3(e)=321.2430$, $C_{21}H_{33}O_2(c)=317.2480$, $C_{15}H_{23}(f-60)=203.1797$. IR ν_{max} cm^{-1}: 1715 (sh), 1700, 1255 (C=O and OAc). NMR δ: 4.90 (1H, br, $W^{1/2}=6.5$ Hz, CH–OAc), 2.92, 2.40 (each 1H, ABq, $J=18$ Hz, $-CH_2-CO$), 2.17 (3H, s, $COCH_3$), 1.19—0.83 ($6\times$ *tert*-CH_3), 0.83 (3H, d, $J=6$ Hz, *sec*-CH_3).

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References and Notes

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