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Studies on the Neutral Constituents of *Pachysandra terminalis* Sieb. et Zucc. V.[1] Structures of Pachysandiol-B and Pachysonol, New Friedelin Type Triterpenes[2]

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The structures of pachysandiol-B and pachysonol, new friedelin type triterpenes isolated from the neutral fraction of *Pachysandra terminalis* Sieb. et Zucc. (Buxaceae), were investigated and assigned to the formulae Ia and IIa, respectively, on the basis of chemical and spectroscopic evidences.

In a previous paper[4] we reported the isolation and characterization of new triterpenes, pachysandiol-B and pachysonol, from the neutral fraction of *Pachysandra terminalis* Sieb. et Zucc. (Japanese name: Fukki-so) along with other several triterpenes and sterols. This paper deals with the full detail of structure elucidation of these compounds.

Pachysandiol-B (Ia) was first isolated as its diacetate (Ib), mp 223—225°, and the pure diol (Ia), mp 280—282°, $[\alpha]_D$ +11°, was obtained by lithium aluminium hydride reduction of the latter (Ib). Microanalysis data of Ia agree with the molecular formula $C_{30}H_{52}O_2$. It shows a strong hydroxyl absorption in the infrared (IR) spectrum and the presence of two hydroxyl groups was indicated by the nuclear magnetic resonance (NMR) spectrum of its diacetate (Ib) which exhibits signals at τ 7.96 and 8.00 for two acetoxyl groups and at τ 4.80 (t, J=9 Hz) and 5.10 (br, $W^{1/2}$=6.5 Hz) for two hydrogens on the acetoxyl-bearing carbons (Fig. 1).

Pachysonol (IIa) was also isolated as its acetate (IIb), mp 234—237°, and the alkaline hydrolysis of the latter (IIb) gave a pure sample (IIa), $C_{30}H_{50}O_2$, mp 278—280°, $[\alpha]_D$ +7.0°. The IR spectrum of IIa demonstrates a carbonyl band at 1703 cm^{-1} and a hydroxyl band at 3400 cm^{-1} and the NMR spectrum of IIb reveals a signal at τ 8.00 for an acetoxyl group and a signal at τ 4.80 (t., J=9 Hz) for a hydrogen geminal to the acetoxyl group (Fig. 2), indicating the presence of a carbonyl and a hydroxyl group in IIa. In addition, NMR spectra of both Ib and IIb exhibit signals arising from one secondary methyl and seven tertiary methyl groups. These observations suggest that Ia and IIa might be pentacyclic triterpenes.

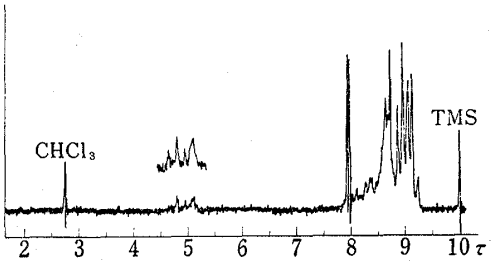


Fig. 1. NMR Spectrum of Pachysandiol-B Diacetate (Ib)

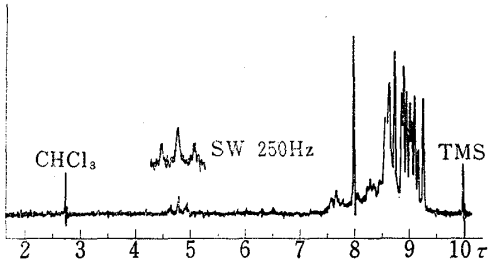


Fig. 2. NMR Spectrum of Pachysonol Acetate (IIb)

1) Part IV: N. Masaki, M. Niwa, and T. Kikuchi, *J. Chem. Soc.* (Perkin II), submitted.
2) Preliminary accounts of this work appeared in *Tetrahedron Letters*, **1971**, 1535.
3) Location: *Yoshida-shimoadachi-cho, Sakyo-ku, Kyoto.*
4) T. Kikuchi, T. Toyoda, M. Arimoto, M. Takayama, and M. Yamano, *Yakugaku Zasshi*, **89**, 1358 (1969).

Close relationship between pachysandiol-B (Ia) and pachysonol (IIa) was revealed by the following experiments. Chromium trioxide oxidation of Ia and of IIa gave the same diketone (III), $C_{30}H_{48}O_2$, mp 299—301°, which shows carbonyl absorption bands at 1703 and 1680 cm^{-1} in the IR spectrum. On the other hand, partial acetylation of Ia yielded a monoacetate (Ic), mp 256—259°, τ 4.80 (1H, t, J=9 Hz, C<u>H</u>-OAc), 6.26 (1H, br, $W^{1/2}$=6 Hz, C<u>H</u>-OH), and 8.01 (3H, Ac). Oxidation of the latter (Ic) with chromium trioxide led to a ketoacetate (IIb), which was found to be identical with pachysonol acetate (IIb) by mixed fusion and IR comparison (in KBr).

Furthermore, reaction of IIb with NBS under infrared light[5] gave rise to an oily bromoketone (IV), whose IR absorption of the ketone group shifted slightly toward higher frequency (1710 cm^{-1}). The NMR spectrum of this compound was characterized by the disappearance of the secondary methyl signal and the appearance of a newly formed tertiary methyl signal at τ 8.30. On the other hand, reaction of IIb with bromine in the presence of HBr afforded an isomeric bromoketone (V).[5] The IR spectrum of the latter (V) demonstrates a ketone band at 1710 cm^{-1} and the NMR spectrum gives a triplet (J=3 Hz) assignable to a hydrogen on the brominated carbon at τ 5.61 and a quartet (J=6.5 Hz) due to a hydrogen geminal to the secondary methyl group at τ 6.87. The chemical shift of the latter signal may be reflecting the 1,3-diaxial relationship between this hydrogen and the bromine atom.[6]

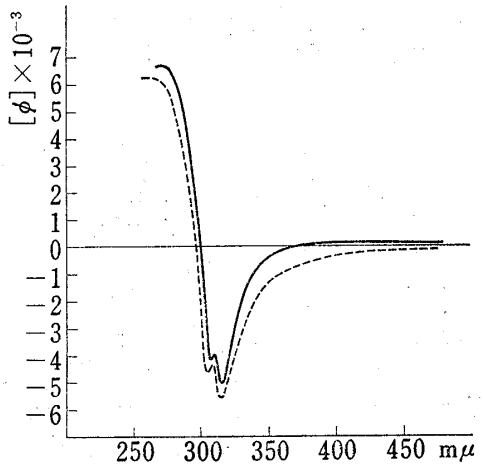


Fig. 3. ORD Curves of Pachysonol Acetate (IIb) (——) and Friedelin (XIII) (------)

These observations strongly suggest the presence of a partial structure -CH_2-CH_2-CO-$CH(CH_3)$-$\dot{C}$- in IIb and that the compound Ia and IIa may be members of friedelin type triterpenes. In support of this, the optical rotatory dispersion (ORD) curve (in dioxane) of pachysonol acetate (IIb) shows a negative Cotton effect (trough: $[\phi]_{314}$ -5600, peak: $[\phi]_{273}$ +6750) which is very similar to that of friedelin (Fig. 3).

Additional support was provided by the following experiment. Treatment of the diketone (III) with $NaBH_4$ reduced only one carbonyl group to yield a ketol (VIa), mp 273—278°, τ 6.26 (1H, br, $W^{1/2}$=7 Hz, C<u>H</u>-OH) and a small amount of an epimeric ketol (VIc), mp 299—300°, τ 6.70 (1H, br, $W^{1/2}$=17 Hz, C<u>H</u>-OH). Upon oxidation with chromium trioxide both VIa and VIc regenerated the original diketone (III) and in the IR spectra they show a carbonyl band at 1680 cm^{-1} and hydroxyl bands at 3550 and 3400 cm^{-1}. Reaction of VIa with phosphorous oxychloride in pyridine gave a dehydrated ketone (VII), mp 270—274°, whose NMR spectrum reveals a broad signal for a newly introduced olefinic proton at τ 4.84 and a singlet for a vinyl methyl group at τ 8.40.

In order to clarify the skeletal structure we next attempted the Wolff–Kishner reduction of the diketone (III), whereby obtained a monoketone (VIII), mp 282—285°, as the sole product. In the IR spectrum of this compound (VIII) the carbonyl absorption at 1680 cm^{-1} was retained unaffected. This monoketone (VIII) resisted further reduction even under vigorous conditions such as Nagata's modification[7] or Barton's modification.[8] Attempted

5) V.V. Kane and R. Stevenson, *Tetrahedron*, **15**, 224 (1961).
6) N.S. Bhacca and D.H. Williams, "Application of NMR Spectroscopy in Organic Chemistry," Holden-Day, Inc., San Francisco, 1964, p. 31.
7) W. Nagata and H. Itazaki, *Chem. Ind.* (London), **1964**, 1194.
8) D.H.R. Barton, D.A.J. Ives, and B.R. Thomas, *J. Chem. Soc.*, **1955**, 2056.

Clemmensen reduction and thioketalization resulted also in recovery of the starting material (VIII).

Lithium aluminium hydride reduction of VIII gave an unseparable mixture of epimeric alcohols (IXa and Xa). Acetylation of this mixture followed by preparative thin-layer chromatographic separation gave an acetate (A, IXb), mp 216—217°, and its epimer (B, Xb), mp 182—183°, in about 1:1 ratio. In the NMR spectra, the signal of hydrogen geminal to the acetoxyl group appears at τ 4.78 as a triplet with J=9 Hz in IXb and at τ 4.81 as a quartet with J=7.5 and 8.5 Hz in Xb, indicating that the acetoxyl group has the equatorial orientation in both compounds. Of these two acetates, IXb was also obtained by the direct Wolff–Kishner reduction of pachysonol (IIa) followed by acetylation (The configuration of acetoxyl group in IXb and Xb will be mentioned later.).

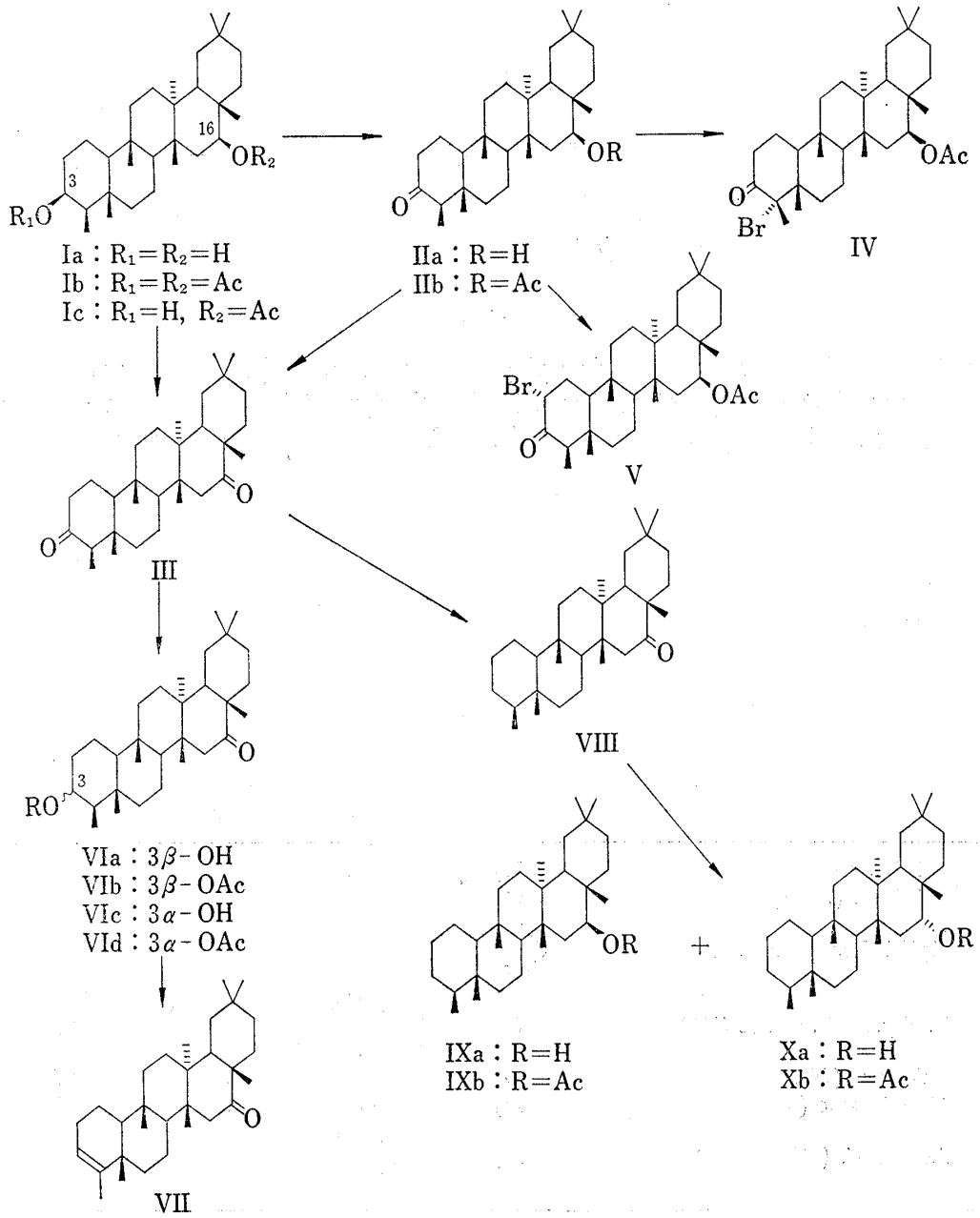
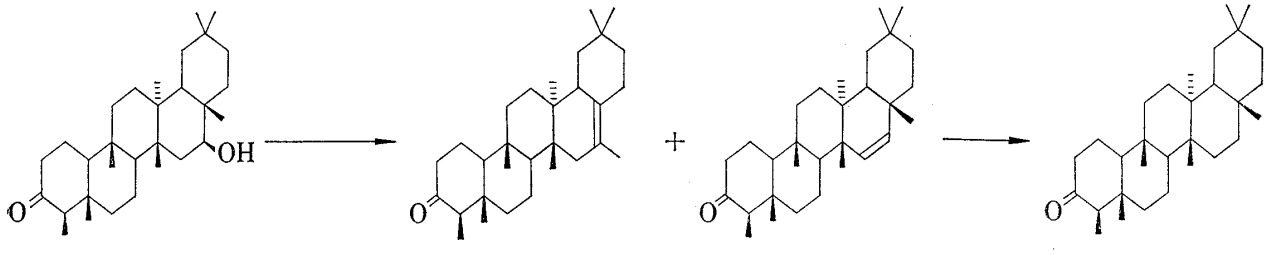


Chart 1

Treatment of IXa and Xa, obtained by alkaline hydrolysis of IXb and Xb, respectively, with methanesulfonyl chloride in pyridine failed to give the corresponding mesylates, but

gave a mixture of dehydrated products with rearranged skeleton. Similarly, reaction of pachysonol (IIa) with methanesulfonyl chloride led to an unstable oily mesylate, ν: 1340 and 1170 cm^{-1} ($-OSO_2CH_3$), which upon standing in ether–methanol solution eliminated methanesulfonic acid spontaneously to give a crystalline mass. Repeated chromatography of this substance over silica gel and 28% $AgNO_3$–silica gel[9] gave a rearranged product, mp 243—245°, whose structure was tentatively assigned to XI,[10] and a very small amount of another compound (XII), mp 238—241°, which exhibits a characteristic IR absorption for a cis disubstituted olefin at 730 cm^{-1} and NMR signals of two olefinic hydrogens at τ 4.26 and 4.77 (ABq, J=10 Hz).

Catalytic hydrogenation of XII over Pd-C gave rise to a saturated ketone (XIII), mp 264—265°, which was found to be identical with friedelin (XIII) in every respect. Thus the friedelin skeleton and the disposition of an oxygen function at C_3 in Ia and IIa were proved.

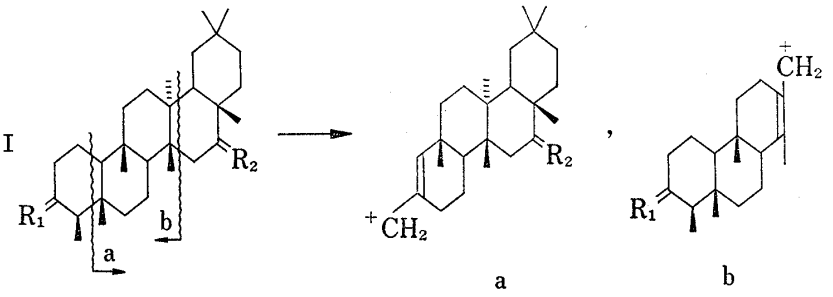


IIa XI XII XIII

Chart 2

Next, the position of another hydroxyl group common to Ia and IIa was investigated. It is well known that upon electron impact friedelin type triterpenes cleave preferentially at A and D ring to give fragment ions a and b[11] (Table I). In the mass spectra of various

TABLE I



a b

	R_1	R_2	a	b
Friedelane	H_2	H_2		259
Friedelin (XIII)	O	H_2	341	273
Epifriedelanol acetate	OAc, H	H_2		317
Pachysonol acetate (IIb)	O	OAc, H		273
Diketone (III)	O	O	355	273
Monoketone (VIII)	H_2	O	355	259
Acetate-A (IXb)	H_2	OAc, H		259

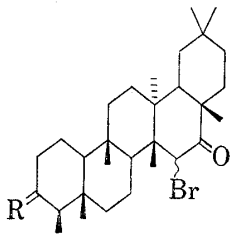
9) T. Norin and L. Westfelt, *Acta. Chem. Scand.*, **17**, 1828 (1963).
10) Structure determination of this rearranged product will be presented in a forthcoming paper.
11) H. Budzikiewicz, J.M. Wilson, and C. Djerassi, *J. Am. Chem. Soc.*, **85**, 3688 (1963).

derivatives of Ia and IIa there appeared the corresponding ions as summarized in Table I, suggesting that the hydroxyl group must locate on D or E ring.

Furthermore, NMR spectra of the ketoacetates, VIb and VId, and the monoketone (VIII) show a sharp AB quartet (J=19 Hz) which could be ascribed to methylene hydrogens neighbouring to the ketone group. Bromination of VIb and VIII afforded bromoketones XIVa and XIVb, respectively, each of which has a sharp singlet assignable to the hydrogen on the brominated carbon atom (at τ 5.88 and 5.86, respectively). These findings coupled with the fact that the NMR signal of the hydrogen geminal to the acetoxyl group common in Ia and IIb forms a triplet (J=9 Hz) as mentioned before, suggest a partial structure -Ç-CH_2-CH(OH)-Ç- to be present in the parent compounds. Therefore the possible position of this hydroxyl group is restricted to C_{15}, C_{16}, C_{21}, and C_{22}.

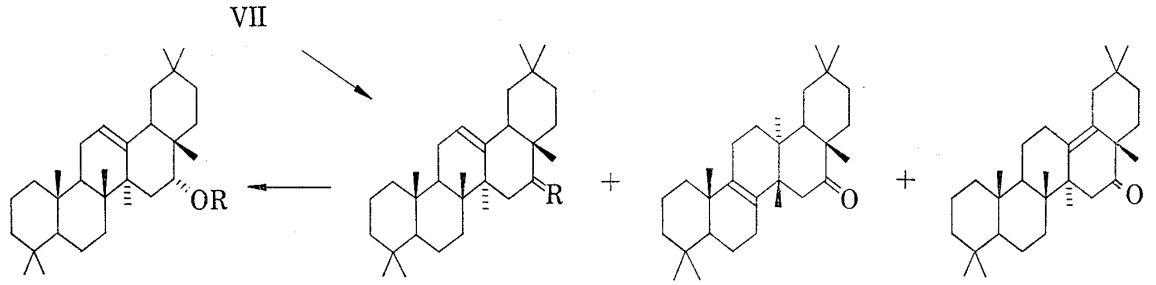
The acid-induced rearrangement of friedel-3-ene is well known to give several oleanene derivatives.[12] We applied this reaction to the keto-3-ene (VII).

Treatment of VII with zinc chloride in acetic acid gave a rearranged product (XVa), mp 192—193°, ν: 1690 cm^{-1}, and a mixture of two other products (XVI and XVII).[13] Wolff-Kishner reduction of XVa yielded an unsaturated hydrocarbon (XVb), mp 165—166°, which was identified with 18αH-olean-12-ene (XVb) by direct comparison with an authentic sample kindly provided by Prof. Barton.



XIVa : R=⟨OAc H⟩
XIVb : R=H_2
Chart 3

The mass spectrum of the above ketone (XVa) reveals the base peak at *m/e* 232 which could be assigned to the fragment c produced by the familiar retro Diels–Alder fragmentation at the ring C.[11] Now the possibility of C_{15}-disposition of the ketone group can be excluded, since in such case the most abundant fragment is reported to be the ion d which is formed by the McLafferty rearrangement[11] as shown in Chart 5.



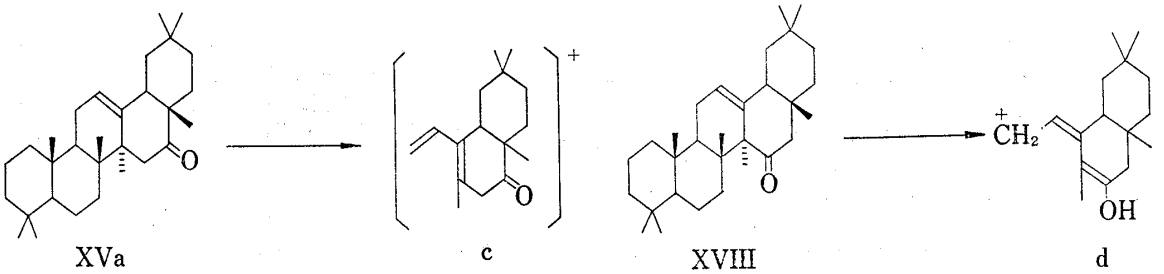
XIXa : R=H
XIXb : R=Ac

XVa : R=O
XVb : R=H_2

XVI

XVII

Chart 4



XVa c XVIII d

Chart 5

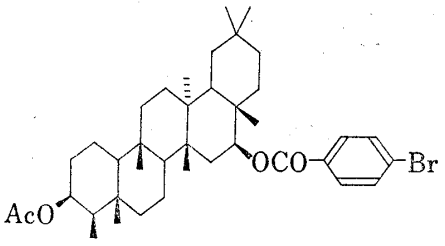
12) J.L. Courtney, R.M. Gascoigne, and A.Z. Szumer, *J. Chem. Soc.*, **1958**, 881; G. Brownile, M.B.E. Fayez, F.S. Spring, R. Stevenson, and W.S. Strachan, *J. Chem. Soc.*, **1956**, 1377.

13) Separation and structure determination of these rearrangement products (XVI and XVII) will be reported in succeeding paper.

NMR spectra of oleanane type triterpenes were examined thoroughly by Tursch, *et al.*[14] and Itō, *et al.*[15] and the characteristic methyl signal at the lowest field was assigned to the 27-methyl group. With the compound XVa, the signal at τ 8.85 may be assigned to the 27-methyl group (Table II). Upon $NaBH_4$ reduction, XVa gave solely an axial alcohol (XIXa), mp 187—189°, as indicated by the NMR spectrum which shows a broad signal with $W^{1/2}=$ 9 Hz at τ 6.30 due to the hydrogen at the foot of newly formed hydroxyl group. The signal of 27-methyl group in XIXa shifted to lower field by 15 Hz (τ 8.60) and that in the acetate (XIXb), mp 222—223°, shifted slightly toward higher field by 7 Hz (τ 8.32). This behavior is indicative of the 1,3-diaxial relationship of the 27-methyl group and the hydroxyl group[16]: hence the presence of 16α-hydroxyl in XIXa.

Table II

Me	23	24	25	26	27	28	29, 30
Olean-12-ene (XVb)	53	51	57	59	69	51	53, 53
(XVa)	53	50	58	63	69	74	53, 53
Alcohol (XIXa)	53	50	56	56	84	53	56, 47
Acetate (XIXb)	52	49	57	57	77	55	57, 52



XX

Chart 6

On the basis of chemical and spectroscopic evidences so far described the structures of pachy sandiol-B and pachysonol should be represented by the formulae Ia and IIa, respectively, except for the configuration of 16-hydroxyl group.

At this stage we carried out the X-ray analysis of 16-O-*p*-bromobenzoyl-3-O-acetylpachysandiol-B (XX) and confirmed the 16β-configuration.[1,17]

It is pertinent to note here that the ring D in a series of compounds (Ib, IIb, and IXb) having 16β-configuration has the boat conformation, while that in the 16-epimer (Xb) has the chair form.[17]

Experimental[18]

Pachysandiol-B (Ia)——To a solution of pachysandiol-B diacetate (Ib) (245 mg) in ether (15 ml) was added excess $LiAlH_4$ (160 mg). The mixture was stirred at room temperature for 3 hr and then refluxed for 30 min. After the excess reagent was decomposed with water, the reaction mixture was acidified with

14) B. Tursch, R. Savoir, R. Ottinger, and G. Chiurdoglu, *Tetrahedron Letters*, **1967**, 539.
15) S. Itō, M. Kodama, M. Sunagawa, T. Oda, and H. Hikino, *Tetrahedron Letters*, **1969**, 2905.
16) Y. Kawazoe, Y. Sato, M. Natsume, H. Hasegawa, T. Okamoto, and K. Tsuda, *Chem. Pharm. Bull.* (Tokyo), **10**, 338 (1962); Y. Kawazoe, Y. Sato, T. Okamoto, and K. Tsuda, *ibid.*, **11**, 328 (1963); T. Okamoto and Y. Kawazoe, *ibid.*, **11**, 648 (1963).
17) T. Kikuchi, M. Niwa, and N. Masaki, *Tetrahedron Letters*, **1972**, 5249.
18) All the melting points were measured with a Kofler-type apparatus and are uncorrected. All the specific rotations were measured in chloroform solutions. IR spectra were measured for solutions in chloroform, unless otherwise stated. NMR spectra were taken on a Varian Associates A-60 NMR Spectrometer in deuterated chloroform solutions using tetramethylsilane as the internal reference and chemical shifts are recorded in τ values. Preparative thin-layer chromatography (TLC) was performed on Merck Kieselgel GF_{254} with chloroform or benzene–chloroform or benzene, and plates were examined under UV light (for UV-absorption materials on GF_{254} plates). For extraction of substances from the Kieselgel methylene chloride was used as solvent. Thin-layer chromatography (TLC) was carried out by use of Merck Kieselgel G acc. to Stahl. Coloring reagent: $Ce(SO_4)_2$ in 10% H_2SO_4.

dil. HCl and extracted with CH_2Cl_2. The organic layer was washed with 10% NaOH, dried (K_2CO_3), and evaporated. Repeated recrystallizations of the residue (230 mg) from CH_2Cl_2–MeOH gave pachysandiol-B (Ia) (57 mg), colorless needles, mp 280—282°. $[\alpha]_D^{30}$ +11.0° (c=0.57). *Anal.* Calcd. for $C_{30}H_{52}O_2 \cdot 1/2H_2O$: C, 79.54; H, 12.02. Found: C, 79.80; H, 11.84.

Pachysonol (IIa)——Refluxing of pachysonol acetate (IIb) (370 mg) with 5% KOH–MeOH for 5 hr and the usual working up afforded pachysonol (IIa) (350 mg). Repeated recrystallizations from CH_2Cl_2–MeOH gave colorless prisms (53 mg), mp 278—280°. $[\alpha]_D^{32}$ +7.0° (c=0.5). IR ν_{max}^{KBr} cm^{-1}: 3400, 1703. *Anal.* Calcd. for $C_{30}H_{50}O_2 \cdot 1/2H_2O$: C, 79.76; H, 11.38. Found: C, 79.69; H, 11.76.

Chromium Trioxide Oxidation of Pachysandiol-B (Ia)——To a stirred solution of pachysandiol-B (Ia) (300 mg) in $CHCl_3$ (8 ml) and AcOH (7 ml) was added gradually a solution of CrO_3 (100 mg) in AcOH–H_2O (6: 1, 3.5 ml) at room temperature and the reaction continued until no starting material could be detected by TLC (about 2 hr). The reaction mixture was diluted with water and extracted with CH_2Cl_2. The extract was washed with dil. Na_2CO_3, dried (K_2CO_3), and evaporated. The residue (290 mg) was chromatographed over alumina (1.2×4 cm) from benzene and then recrystallized from CH_2Cl_2–MeOH to give a diketone (III) as colorless prisms (240 mg), mp 299—301°. $[\alpha]_D^{28}$ −38° (c=1.0). IR ν_{max} cm^{-1}: 1703, 1680. NMR τ: 8.71—9.21 (7×*tert*-CH_3), 9.13 (3H, d, J=7 Hz, *sec*-CH_3). *Anal.* Calcd. for $C_{30}H_{48}O_2$: C, 81.76; H, 10.98. Found: C, 81.46; H, 10.93.

Chromium Trioxide Oxidation of Pachysonol (IIa)——Pachysonol (IIa) (26 mg) was treated with CrO_3 (14 mg) in the same manner as above to give a diketone (III) (19 mg), mp 298°, which was identified with the above diketone (III) in all respects.

Partial Acetylation of Pachysandiol-B (Ia)——A mixture of pachysandiol-B (Ia) (300 mg), acetic anhydride (2 ml), and pyridine (5 ml) was allowed to stand overnight in a refrigerator. The reaction mixture was treated in the usual manner and the crude product (300 mg) was separated by preparative TLC to give a diacetate (Ib) (55 mg), a monoacetate (Ic) (150 mg), and the starting material (Ia) (31 mg). Recrystallization of the monoacetate (Ic) from CH_2Cl_2–MeOH afforded a pure sample as colorless needles, mp 256—259°. $[\alpha]_D^{25}$ +47° (c=1.0). IR ν_{max} cm^{-1}: 3600, 1720, 1260. NMR τ: 4.80 (1H, t, J=9 Hz, C<u>H</u>–OAc), 6.26 (1H, br, $W^{1/2}$= 6.5 Hz, C<u>H</u>–OH), 8.01 (3H, Ac), 8.76—9.13 (8×CH_3). *Anal.* Calcd. for $C_{32}H_{54}O_3$: C, 78.96; H, 11.18. Found: C, 79.19; H, 11.25.

Chromium Trioxide Oxidation of Pachysandiol-B Monoacetate (Ic)——To a solution of pachysandiol-B monoacetate (Ic) (43 mg) in pyridine (4 ml) was added a suspension of chromium trioxide (130 mg) in pyridine (3 ml) and the mixture was stirred for 13 hr at room temperature. The reaction mixture was diluted with water and extracted with CH_2Cl_2. The extract was washed with 3% HCl and 5% NaOH, dried ($MgSO_4$), and evaporated. The residue (50 mg) was chromatographed over alumina (0.7×3 cm) from benzene and the eluate was recrystallized from CH_2Cl_2–MeOH to give a ketoacetate (IIb) (22 mg), colorless needles, mp 233—235°. $[\alpha]_D^{22}$ +6° (c=1.0). This compound was found to be identical with pachysonol acetate (IIb) by IR (KBr) comparison.

4α-Bromopachysonol Acetate (IV)——N-Bromosuccimide (150 mg) was added to a solution of pachysonol acetate (IIb) (50 mg) in carbon tetrachloride (20 ml) and the mixture was heated under reflux by means of infrared lamp. After about 13 min an orange color appeared, followed by decolorization over 30 sec. After a reaction time of 50 min, the mixture was cooled, filtered and the solvent removed by evaporation *in vacuo*. The residue (70 mg) was chromatographed over silica gel and eluted with benzene–hexane (1: 1) and benzene to give 4-bromo compound (IV) as a pale yellow oil (IV) (38 mg). TLC: single spot. IR ν_{max} cm^{-1}: 1725, 1710, 1265. NMR τ: 4.80 (1H, t, J=9 Hz, C<u>H</u>–OAc), 8.00 (3H, Ac), 8.30 (3H, s, CBr–CH_3), 8.76—9.10 (7×*tert*-CH_3).

2α-Bromopachysonol Acetate (V)——A mixture of conc. HBr (one drop) and $CHCl_3$ (7 ml) was added dropwise under stirring to a solution of pachysonol acetate (IIb) (47 mg) in $CHCl_3$ (2.5 ml), followed by a solution of bromine (two drops) in $CHCl_3$. After stirred for 1 hr, the reaction mixture was diluted with water and extracted with CH_2Cl_2. The extract was washed with dil. Na_2CO_3, dried (K_2CO_3), and evaporated. The residue (55 mg) was purified by preparative TLC to give an oily bromoketone (V) (45 mg). IR ν_{max} cm^{-1}: 1725, 1710, 1265. NMR τ: 4.79 (1H, t, J=9 Hz, C<u>H</u>–OAc), 5.61 (1H, t, J=3 Hz, C<u>H</u>–Br), 6.87 (1H, q, J=6.5 Hz, C<u>H</u>–CH_3), 8.00 (3H, Ac), 8.75—9.27 (7×*tert*-CH_3), 9.10 (3H, d, J=6.5 Hz, *sec*-CH_3).

Sodium Borohydride Reduction of Diketone (III)——To a stirred solution of diketone (III) (410 mg) in MeOH (15 ml) and CH_2Cl_2 (15 ml) was added $NaBH_4$ (300 mg) in small portions and the mixture was gently refluxed for 3 hr. The reaction mixture was diluted with water and the product was taken up in CH_2Cl_2, dried (K_2CO_3), and evaporated. The residue (409 mg) was chromatographed over alumina (2.5×30 cm) and the eluate (360 mg) with benzene was recrystallized from CH_2Cl_2–MeOH to afford a ketol (VIa) (355 mg) as colorless plates, mp 275—277°. $[\alpha]_D^{23}$ +10° (c=0.83). IR ν_{max} cm^{-1}: 3550, 3400, 1680. NMR τ: 6.26 (1H, br, $W^{1/2}$=7 Hz, C<u>H</u>–OH), 7.56, 8.02 (2H, ABq, J=19 Hz, C<u>H</u>$_2$–CO), 8.72—9.16 (8×CH_3). *Anal.* Calcd. for $C_{30}H_{50}O_2$: C, 81.39; H, 11.38. Found: C, 81.22; H, 11.45. Subsequent elution with ether–benzene (1: 3 and 1: 1) gave an epimeric ketol (VIc) (30 mg), which was recrystallized from CH_2Cl_2–MeOH to give colorless prisms (VIc) (17 mg), mp 299—300°. $[\alpha]_D^{22}$ −5° (c=0.79). IR ν_{max} cm^{-1}: 3550, 3430, 1680. NMR τ: 6.70 (1H, br, $W^{1/2}$=17 Hz, C<u>H</u>–OH), 7.56, 8.02 (2H, ABq, J=19 Hz, C<u>H</u>$_2$–CO), 8.72—9.21 (8×CH_3). *Anal.* Calcd. for $C_{30}H_{50}O_2$: C, 81.39; H, 11.38. Found: C, 81.59; H, 11.51.

Acetylation of Ketol (VIa) and the Epimeric Ketol (VIc)——a) A mixture of the ketol (VIa) (80 mg), acetic anhydride (4 ml), and dry pyridine (4 ml) was kept at room temperature for two days and then worked up as usual. Recrystallization of the product (80 mg) from CH_2Cl_2–MeOH gave the ketol acetate (VIb) (60 mg), colorless needles, mp 285—287°. $[\alpha]_D^{21}$ +27° (c=1.0). IR ν_{max} cm^{-1}: 1725, 1680, 1250. NMR τ: 5.10 (1H, br, $W^{1/2}$=7 Hz, C<u>H</u>–OAc), 7.63, 7.92 (2H, ABq, J=19 Hz, C<u>H</u>$_2$–CO), 7.96 (3H, Ac), 8.70—9.14 (7×*tert*-CH_3), 9.18 (3H, d, J=7 Hz, *sec*-CH_3). *Anal.* Calcd. for $C_{32}H_{52}O_3$: C, 79.28; H, 10.81. Found: C, 79.25; H, 10.68.

b) Acetylation of VIc (33 mg) was performed in the same manner as run for VIa. The product (38 mg) was recrystallized from hexane to give colorless needles (VId) (33 mg), mp>305°. $[\alpha]_D^{24}$ +22.4° (c=1.03). IR ν_{max} cm^{-1}: 1720, 1680, 1260. NMR τ: 5.37 (1H, br, $W^{1/2}$=17 Hz, C<u>H</u>–OAc), 7.56, 8.02 (2H, ABq, J=19 Hz, C<u>H</u>$_2$–CO), 7.98 (3H, Ac), 8.72—9.14 (7×*tert*-CH_3), 9.24 (3H, d, J=7 Hz, *sec*-CH_3). *Anal.* Calcd. for $C_{32}H_{52}O_3$: C, 79.28; H, 10.81. Found: C, 79.10; H, 10.63.

Chromium Trioxide Oxidation of the Ketol (VIc)——The above ketol (VIc) (5 mg) in AcOH (1 ml) was treated with excess CrO_3 at room temperature for 2 hr. The product (2 mg), isolated in the usual way, was recrystallized from ether–MeOH to give colorless prisms (III), mp 298—302°, which was identified with the above diketone (III) by TLC, IR ($CHCl_3$) comparison and, mixed mp determination.

Reaction of Ketol (VIa) with Phosphorus Oxychloride——To a chilled solution of VIa (180 mg) in pyridine (6 ml) was added $POCl_3$ (0.3 ml) and the mixture was kept overnight at room temperature. The reaction mixture was diluted with water and extracted with ether. The extract was washed successively with 3% HCl and dil. Na_2CO_3, dried (K_2CO_3), and evaporated. Recrystallization of the residue (165 mg) afforded a dehydrated ketone (VII) (150 mg), colorless leaves, mp 279—280°. IR ν_{max} cm^{-1}: 1680. NMR τ: 4.84 (1H, br, olefinic H), 8.40 (3H, s, C=C–CH_3), 7.56, 8.02 (2H, ABq, J=19 Hz, C<u>H</u>$_2$–CO), 8.71—9.15 (7×*tert*-CH_3). *Anal.* Calcd. for $C_{30}H_{48}O$: C, 84.84; H, 11.39. Found: C, 84.62; H, 11.23.

Wolff-Kishner Reduction of Diketone (III)——A solution of the diketone (III) (210 mg) and anhydrous hydrazine (0.3 ml) in abs. DMSO (12 ml) was heated at 170° on an oil bath for 12 hr. Then KOH pellets (*ca.* 500 mg) were added and the mixture was heated for additional 4 hr. Thereafter the reaction mixture was diluted with water, and washed with 3% HCl and dil. Na_2CO_3, dried (K_2CO_3), and evaporated. The residue (220 mg) was chromatographed over alumina (15 g). Recrystallization of the hexane–benzene (3: 1) eluate (149 mg) from CH_2Cl_2–MeOH afforded a monoketone (VIII) (130 mg), colorless prisms, mp 282—285°. $[\alpha]_D^{30}$ +12° (c=1.0). IR ν_{max} cm^{-1}: 1680. NMR τ: 7.56, 8.02 (2H, ABq, J=19 Hz, C<u>H</u>$_2$–CO), 8.72—9.22 (8×CH_3). *Anal.* Calcd. for $C_{30}H_{50}O$: C, 84.44; H, 11.81. Found: C, 84.21; H, 11.93. Mass Spectrum m/e: 426 (M^+) ($C_{30}H_{50}O$).

Lithium Aluminium Hydride Reduction of Monoketone (VIII) and Subsequent Acetylation——The monoketone (VIII) (95 mg) was treated with excess $LiAlH_4$ (100 mg) in boiling mixture of ether (3 ml) and tetrahydrofuran (3 ml) for 6 hr. Usual working up gave a crude product (80 mg) which was chromatographed over alumina (5 g). The elution with benzene–hexane (1: 3) and benzene gave a mixture of mono-ols (IXa and Xa) (65 mg). This was acetylated with acetic anhydride–pyridine (1 ml each) in the usual manner and the product mixture (72 mg) obtained was separated by preparative TLC into two fractions. The less polar fraction gave an acetate (A, IXb) (28 mg) which was recrystallized from ether–MeOH to give colorless needles (18 mg), mp 216—217°. $[\alpha]_D^{19}$ +57° (c=0.77). IR ν_{max} cm^{-1}: 1720, 1265. NMR τ: 4.78 (1H, t, J=9 Hz, C<u>H</u>–OAc), 8.00 (3H, Ac), 8.76—9.24 (8×CH_3). *Anal.* Calcd. for $C_{32}H_{54}O_2$: C, 81.64; H, 11.56. Found: C, 81.45; H, 11.72. The polar fraction gave the epimeric acetate (B, Xb) (26 mg) which was recrystallized from ether–MeOH to give colorless needles (13 mg), mp 182—183°. $[\alpha]_D^{23}$ −23.5° (c=0.85). IR ν_{max} cm^{-1}: 1720, 1260. NMR τ: 4.81 (1H, q, J=7.5, 8.5 Hz, C<u>H</u>–OAc), 7.94 (3H, Ac), 8.81—9.23 (8×CH_3). *Anal.* Calcd. for $C_{32}H_{51}O_2$: C, 81.64; H, 11.56. Found: C, 81.77; H, 11.45.

Wolff-Kishner Reduction of Pachysonol Acetate (IIb) and Subsequent Acetylation——A solution of IIb (40 mg) and anhydrous hydrazine (0.2 ml) in abs. DMSO (2.5 ml) was heated at 120° on an oil bath for 3 hr. To this solution was added NaH (110 mg) and the mixture was heated at 190° for 12 hr. Usual working up followed by alumina (7 g) chromatography from benzene and CH_2Cl_2 gave a crude alcohol (IXa). Acetylation of this alcohol was performed in the usual manner. The product was recrystallized from hexane to afford a deoxo-acetate (IXb) (26 mg) as colorless needles, mp 215—218°. This material was identified with the acetate-A (IXb) described above by TLC, IR ($CHCl_3$), and NMR comparison.

Reaction of Pachysonol (IIa) with Methanesulfonyl Chloride——To a chilled solution of pachysonol (IIa) (110 mg) in pyridine (4 ml) was added methanesulfonyl chloride (1 ml) and the mixture was kept for 48 hr at room temperature. The reaction mixture was diluted with water and extracted with ether. The etherial solution was washed successively with 3% HCl and dil. Na_2CO_3, and dried ($MgSO_4$). Evaporation of the solvent *in vacuo* gave a yellow oily residue (105 mg), IR ν_{max} cm^{-1}: 1340, 1170. This residue was dissolved in a small amount of ether–MeOH mixture and allowed to stand for several days to deposit a crystalline mass (85 mg). This was chromatographed over silica gel (12 g, 1.5×22 cm) and elution with benzene–hexane (1: 4) gave a rearranged compound (XI) (45 mg). Subsequent elution with benzene–hexane (1: 4) gave a mixture (28 mg) which was again chromatographed over 28% $AgNO_3$–SiO_2 (1.3×19 cm). Elution with benzene–hexane (1: 5) gave an additional crop of XI (20 mg) and with benzene–hexane (1: 3) gave another product (XII) (6 mg). Recrystallizations of the compound (XI) (65 mg) from CH_2Cl_2–MeOH afforded

colorless fine prisms (58 mg), mp 243—245°. $[\alpha]_D^{32}$ +7° (c=1.43). IR ν_{max} cm^{-1}: 1705. NMR τ: 8.40 (3H, br. s., C=C-CH$_3$), 9.07—9.30 (7×CH$_3$). *Anal.* Calcd. for $C_{30}H_{48}O$: C, 84.84; H, 11.39. Found: C, 84.78; H, 11.26. Mass Spectrum *m/e*: 424 (M^+) ($C_{30}H_{48}O$). The compound XII (6 mg) was recrystallized from CH_2Cl_2–MeOH to give colorless needles (5 mg), mp 238—241°. $[\alpha]_D^{30}$ −6.4° (c=0.77). IR ν_{max} cm^{-1}: 1705, 730. NMR τ: 4.26, 4.77 (2H, ABq, J=10 Hz, C<u>H</u>=C<u>H</u>), 8.83—9.24 (8×CH$_3$). Mass Spectrum *m/e*: 424 (M^+) ($C_{30}H_{48}O$).

Catalytic Hydrogenation of the Compound XII——The compound XII (5 mg) was hydrogenated in AcOEt (3 ml) over Pd-C (prepared with 1% $PdCl_2$ (1 ml) and charcoal (100 mg)) at room temperature and atmospheric pressure for 20 hr. The catalyst was filtered off and the filtrate was evaporated under reduced pressure. The residue (4.8 mg) was chromatographed over alumina (0.7×7 cm) and the elution with benzene–hexane (1: 10) gave a dihydro compound (XIII) (3.2 mg), which was recrystallized from CH_2Cl_2–MeOH to give needles, mp 264—265°. The IR (KBr) spectrum of this substance was superimposable upon that of an authentic sample of friedelin (XIII) and their mixture showed no melting point depression.

Bromination of Ketol Acetate (VIb)——To a solution of VIb (36 mg) in AcOH (1.5 ml) was added 30% HBr–AcOH (one drop) and 0.1 mole. Br_2–AcOH (1 ml). The mixture was stirred at room temperature for 15 hr and then diluted with water and extracted with CH_2Cl_2. The extract was washed with 3.5% $Na_2S_2O_3$ and water, dried ($MgSO_4$), and evaporated. Purification of the residue (50 mg) by preparative TLC, followed by recrystallization from CH_2Cl_2–MeOH, afforded small plates (XIVa) (11 mg), mp 268—269°. IR ν_{max} cm^{-1}: 1725, 1695, 1255. NMR τ: 5.10 (1H, br, $W^{1/2}$=6.5 Hz, C<u>H</u>–OAc), 5.88 (1H, s, C<u>H</u>–Br), 7.97 (3H, Ac), 8.42—9.15 (7×*tert*-CH$_3$), 9.20 (3H, d, J=7 Hz, *sec*-CH$_3$). Mass Spectrum *m/e*: 563 (M^+) ($C_{32}H_{51}O_3Br$).

Bromination of Monoketone (VIII)——Bromination of VIII (45 mg) was performed in the same manner as described above. The product (XIVb) (30 mg) was recrystallized in colorless prisms from CH_2Cl_2–MeOH and showed mp 273—274°. IR ν_{max} cm^{-1}: 1690, NMR τ: 5.86 (1H, s, C<u>H</u>–Br), 8.42—9.22 (8×CH$_3$).

Treatment of Keto-3-ene (VII) with Zinc Chloride in Acetic Acid——To a solution of VII (220 mg) in AcOH (10 ml) was added crushed fused zinc chloride (6.3 g) and the mixture was heated at 90° under vigorous stirring for 20 min. The reaction mixture was then diluted with water, extracted with ether. The etherial extract was washed with dil. Na_2CO_3, dried (K_2CO_3), and evaporated. The residue (210 mg) was separated by preparative TLC into two fractions. The less polar fraction (65 mg) was recrystallized from CH_2Cl_2–MeOH to give a rearranged compound (XVa) as colorless plates (60 mg), mp 192—193°. $[\alpha]_D^{25}$ +28° (c=1.06). IR ν_{max} cm^{-1}: 1690. UV $\lambda_{max}^{dioxane}$ mμ: 298 (ε 34.5). NMR τ: 4.53 (1H, q, J=2.7, 3.7 Hz, CH$_2$–C<u>H</u>=C), 7.25, 8.17 (2H, ABq, J=15.5 Hz, C<u>H</u>$_2$–CO), 8.77—9.16 (8×*tert*-CH$_3$). ORD (−) Cotton effect ($[\Phi]_{320}$ −5940, $[\Phi]_{313}$ −3160, $[\Phi]_{390}$ −3920, $[\Phi]_{278}$ +9470). Mass Spectrum *m/e*: 424 (M^+) ($C_{30}H_{48}O$). *Anal.* Calcd. for $C_{30}H_{48}O$: C, 84.84; H, 11.39. Found: C, 85.12; H, 11.24. The polar fraction (122 mg) was a mixture of two other products (XVI and XVII).[13]

Wolff-Kishner Reduction of the Compound XVa——To a solution of XVa (22 mg) in abs. DMSO (3 ml) was added anhydrous hydrazine (0.1 ml) and heated in an oil bath at 120° for 4 hr. Then KOH pellets (200 mg) was added, and the mixture was heated for additional 5 hr. Usual working up gave a crude product (16 mg), which was chromatographed over silica gel (1.5 g). The eluate (10 mg) with hexane was repeatedly recrystallized from CH_2Cl_2–MeOH to give colorless plates (XIVb) (6 mg), mp 165—166°. $[\alpha]_D^{23}$ +97° (c=0.81). IR ν_{max}^{KBr} cm^{-1}: 819, 809. Mass Spectrum *m/e*: 410 (M^+) ($C_{30}H_{50}$). The IR (KBr) spectrum of this product was superimposable upon that of an authentic sample of 18αH-olean-12-ene (XVb), provided by Professor Barton.

Sodium Borohydride Reduction of the Compound XVa——To a solution of XVa (12 mg) in MeOH (2 ml) and CH_2Cl_2 (1 ml) was added $NaBH_4$ (30 mg) and the mixture was refluxed under stirring for 5 hr. Usual working up afforded a crystalline residue (12 mg). Purification by preparative TLC gave an alcohol (XIXa) (6 mg) which was recrystallized from CH_2Cl_2–MeOH to afford colorless leaves, mp 187—189°. $[\alpha]_D^{23}$ +59.1° (c=1.17). IR ν_{max} cm^{-1}: 3600. NMR τ: 4.60 (1H, q, J=2.7, 3.7 Hz, CH$_2$–C<u>H</u>=C), 6.30 (1H, br, $W^{1/2}$=8 Hz, C<u>H</u>–OH), 8.60—9.22 (8×*tert*-CH$_3$). Mass Spectrum *m/e*: 426 (M^+) ($C_{30}H_{50}O$).

Acetylation of Alcohol (XIXa)——A mixture of the above alcohol (XIXa) (15 mg), acetic anhydride (1 ml), and pyridine (1 ml) was warmed on a water bath for 16 hr, and then worked up in the usual manner. Purification by alumina chromatography (0.6×13 cm) gave an acetate (XIXb) (14.5 mg), which was repeatedly recrystallized from ether–MeOH to afford colorless prisms (13 mg), mp 222—223°. $[\alpha]_D^{21}$ +18.6° (c=0.97). IR ν_{max} cm^{-1}: 1720, 1250. NMR τ: 4.64 (1H, t, J=3 Hz, CH$_2$–C<u>H</u>=C), 5.13 (1H, br, $W^{1/2}$=8 Hz, C<u>H</u>–OAc), 7.94 (3H, Ac), 8.70—9.17 (8×*tert*-CH$_3$). *Anal.* Calcd. for $C_{32}H_{52}O_2$: C, 81.99; H, 11.18. Found: C, 81.70; H, 11.25.

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