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Application of the Homonuclear Internuclear Double Resonance Technique in the Triterpene Field. II.[1] Assignments of Methyl Resonances of Triterpenes related to Friedelin

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The homonuclear internuclear double resonance (INDOR) technique in combination with the pseudo-contact shift method was applied to several triterpenes related to friedelin, and the methyl resonances of these triterpenes were assigned. The results suggest that rings D and E of friedelin in solution are in a boat form.

Keywords——NMR; homonuclear INDOR; triterpenes; friedelin; NMR shift reagent; methyl signal assignment; NOE

In the preceding paper,[1] we reported that the homonuclear internuclear double resonance (INDOR) technique in nuclear magnetic resonance (NMR) spectroscopy was quite effective for qualitative measurements of nuclear Overhauser effect (NOE) between methyl-methyl protons, and it was successfully applied for the assignment of the methyl resonances of β-amyrin and related triterpenes. As regards friedelin-type triterpenes, assignments of only the 23- and 24-methyl resonances have so far been reported by Takahashi,[3] while the others remain to be investigated. Methyl resonances of shionone and its derivatives, which are closely related to friedelin, have also been studied by Takahashi and co-workers[4] on the basis of substituent effects and pseudo-contact shifts. We recently examined the methyl resonances of triterpenes of these series by the INDOR method in conbination with the pseudo-contact shift, and the results are reported in the present paper.

Here we used tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionato)praseodymium ($Pr(FOD)_3$) as the NMR shift reagent instead of tris(dipivaloylmethanato)europium, since the former is more soluble and is more stable in deuteriochloroform than the latter. The compounds studied were as follows: friedelin (Ia), epifriedelanol acetate (IIa), friedelanol acetate (IIIa), 16β-acetoxyfriedelane (IV), 16α-acetoxyfriedelane (V), shionone (VI),[5] epishionol acetate (VII),[5] and shionol acetate (VIII).[5]

1) Friedelin (Ia), Epifriedelanol Acetate (IIa), and Friedelanol Acetate (IIIa)

The NMR spectra of friedelin (Ia), epifriedelanol acetate (IIa), and friedelanol acetate (IIIa) were measured in the presence of various amounts of $Pr(FOD)_3$ and the induced shifts of the methyl signals are shown graphically in Fig. 1. It is clear that each methyl signal suffers an upfield shift in the presence of the Pr ion, and that the 23-methyl signal is most markedly shifted to higher field.

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1) Part I: T. Kikuchi, T. Yokoi, M. Niwa, and T. Shingu, *Chem. Pharm. Bull.*, **25**, 2078 (1977).
2) Location: *a) 2630 Sugitani, Toyama, 930, Japan; b) Ikawadani-cho, Tarumi-ku, Kobe, 673, Japan; c) Kashima-2-chome, Yodogawa-ku, Osaka, 532, Japan.*
3) T. Takahashi, *Nippon Kagaku Zasshi*, **87**, 101 (1966).
4) Y. Tanahashi, Y. Moriyama, and T. Takahashi, *Bull. Soc. Chim. Fr.*, **1966**, 2374; T. Takahashi, Y. Tanahashi, Y. Moriyama, T. Tsuyuki, and T. Hirao, *Nippon Kagaku Zasshi*, **92**, 1040 (1971).
5) In this paper, the methyl groups of shionone and its derivatives are conveniently numbered as shown in Chart 1.

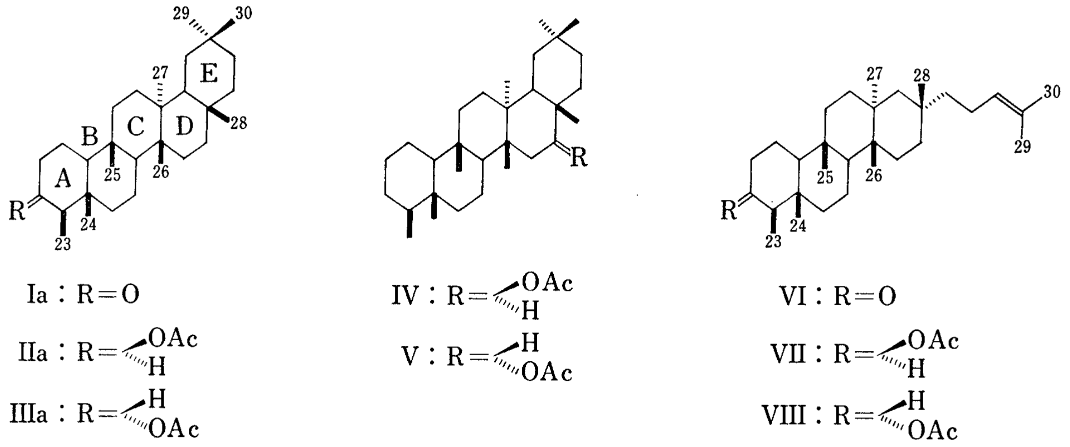

Chart 1

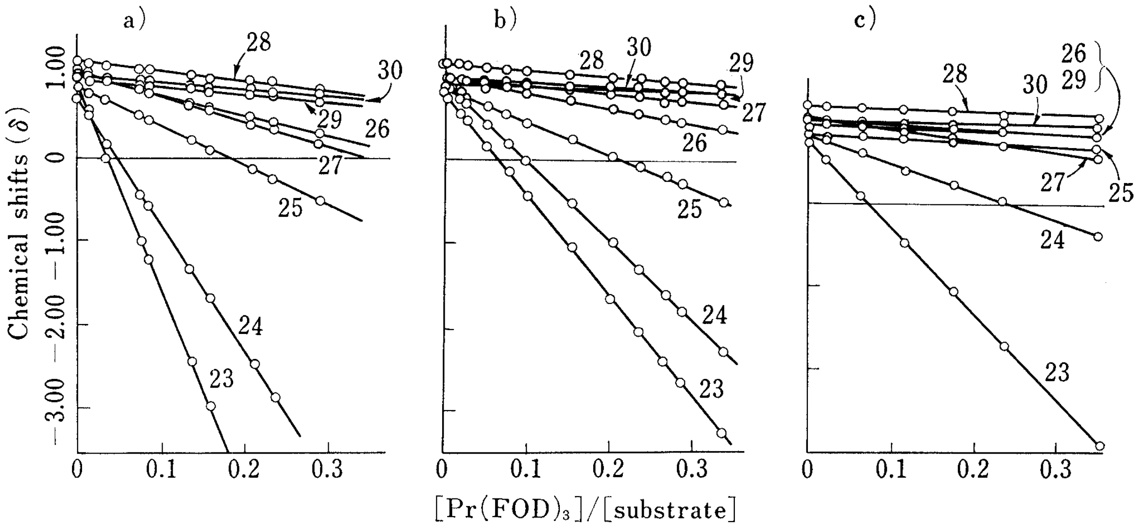

Fig. 1. Lanthanide-induced Shifts in the Methyl Signals of a) Friedelin (Ia), b) Epifriedelanol Acetate (IIa), and c) Friedelanol Acetate (IIIa), plotted against the molar Ratios of $Pr(FOD)_3$ to Substrate

According to Sanders *et al.*[6] and Shingu *et al.*,[7] the coordinating metal ion is thought to locate near the β-face of the molecule in the cases of friedelin (Ia) and friedelanol acetate (IIIa). With epifriedelanol acetate (IIa), the metal ion is also considered to be over the β-side of the molecule, since the acetoxyl group stands axially. Based on consideration of these conformations of the coordinate complexes and the McConnel–Robertson equation.[8] the 24- and 25-methyl signals are expected to show the next largest upfield shifts after the 23-methyl doublet. We next carried out INDOR experiments in order to obtain more detailed information.

The NMR spectrum of friedelin (Ia) in the presence of $Pr(FOD)_3$ (*ca.* 0.3 mol eq.) is reproduced in Fig. 2, where six methyl signals appear as singlets at δ −3.84, −0.53, 0.18, 0.27, 0.75, and 0.81; one of the tertiary methyl signals is hidden in the FOD signal at δ 0.7 and the 23-methyl signal is shifted outside the figure.

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[6] J.K.M. Sanders and D.H. Williams, *J. Am. Chem. Soc.*, **93**, 641 (1971).
[7] T. Shingu, T. Yokoi, M. Niwa, and T. Kikuchi, *Chem. Pharm. Bull.*, **21**, 2252 (1973).
[8] H.M. McConnel and R.E. Robertson, *J. Chem. Phys.*, **29**, 1361 (1958).

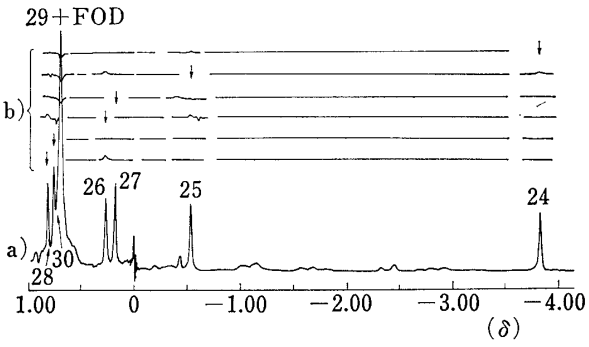

Fig. 2. INDOR Experiments with Friedelin (Ia)

a) 100 MHz NMR spectrum of Ia in the presence of $Pr(FOD)_3$.
b) INDOR spectra.

The INDOR experiment monitoring the singlet line at δ −3.84 gave a small peak at δ −0.53. In turn, when the singlet line at δ −0.53 was monitored, two small peaks were observed at δ −3.84 and 0.27. On monitoring at δ 0.27, two small peaks appeared at δ −0.53 and 0.81. These peaks are due to methyl-methyl NOE's and indicate that the methyl groups concerned are spatially close to one another. Therefore, the signals at δ −3.84, −0.53, and 0.27 should be assigned to the 24-, 25-, and 26-methyl groups, respectively. Similarly, an INDOR experiment monitoring at δ 0.81 afforded an NOE peak at δ 0.27, while monitoring at δ 0.18 or δ 0.75 gave no significant peak.

Here it is noteworthy that NOE was observed between the 26-methyl (δ 0.27) and the methyl signal at δ 0.81, which is one of the 27-, 28-, 29-, and 30-methyls. Among them, only the 28-methyl group can be sterically close to the 26-methyl group when ring D of friedelin (Ia) is in a boat conformation. Thus, the signal at δ 0.81 should be assigned to the 28-methyl protons.

The conformations of friedelin-type triterpenes were first studied by Corey *et al.*[9] who suggested on the basis of two-dimensional X-ray analysis that friedelin (Ia) has an all-chair conformation. On the other hand, Laing *et al.*[10] recently carried out an X-ray analysis of epifriedelanol (see Fig. 3) and concluded that all compounds with the friedelane skeleton have rings D and E in a boat-boat conformation. Our result mentioned above supports Laing's conclusion and also suggests that even in solution friedelin (Ia) has rings D and E in a boat-boat conformation.

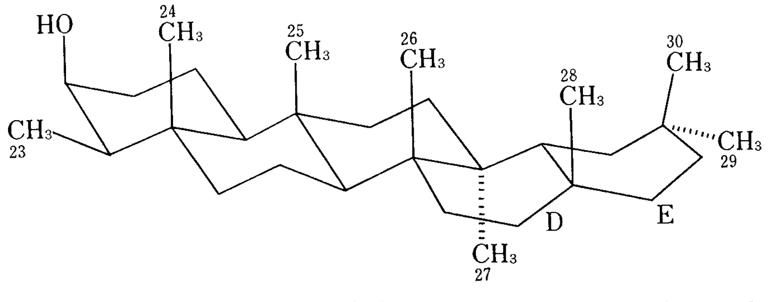

Fig. 3. Conformation of Epifriedelanol reported by Laing *et al.*

Furthermore, the assignment of the 28-methyl signal was confirmed by comparison of the NMR spectrum of Ia with that of friedelin-28,28-d_2 (Ib), as shown in Fig. 4. The latter compound (Ib) was synthesized from canophyllol (IX)[11] through the introduction of deuterium by means of Wolff-Kishner reduction (ND_2ND_2, DMSO-d_6, and NaOD), as shown in Chart. 2.

We also synthesized friedelin-29,29-d_2 (Ic) from methyl polpunonate (XIII)[12] in essentially the same manner as for the 28-deuterated analog (Ib) in order to assign the remaining three

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[9] E.J. Corey and J.J. Ursprung, *J. Am. Chem. Soc.*, **78**, 5041 (1956).

[10] M. Laing, M.E. Burke-Laing, R. Bartho, and C.M. Weeks, *Tetrahedron Lett.*, **1977**, 3839.

[11] T.R. Govindachari, N. Viswanathan, B.R. Pai, V. Ramadas Rao, and M. Srinivasan, *Tetrahedron*, **23**, 1901 (1967).

[12] F. Delle Monache, J.F. de Mello, G.B. Marini Bettolo, O. Goncalves de Lima, and I.L. d'Albuqurque, *Gazz. Chim. Ital.*, **102**, 636 (1972). It should be noted that there is some confusion regarding the numbering of the 20α-carboxyl carbon in polpunonic acid; see S.P. Gunasekera and M.U.S. Sultabawa, *J. Chem. Soc. Perkin I*, **1977**, 418.

methyl signals (δ 0.18, 0.75, and 0.7). As shown in Chart 3, compound XIII was transformed into the aldehyde (XVI), which on Wolff–Kishner reduction using deuterated hydrazine, followed by acid hydrolysis, gave the desired compound (Ic).

The NMR spectrum (Fig. 5b) and the lanthanide-induced shift pattern of friedelin-29,29-d_2 (Ic) indicated clearly that the signal at δ 0.7 (overlapping with the FOD signal) is due to the 29-methyl protons. The other two signals at δ 0.18 and 0.75 could be assigned to the 27- and 30-methyls, respectively, in the order of lanthanide-induced shift values, simply based on the distances from the coordinating metal ion.

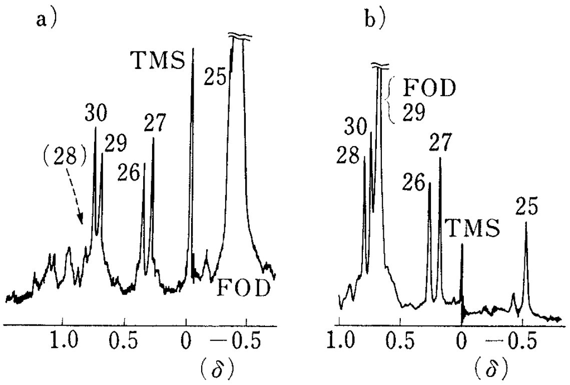

Fig. 4. 100 MHz NMR Spectra of a) Friedelin-28,28-d_2 (Ib) and b) Friedelin (Ia) in the Presence of $Pr(FOD)_3$

Final assignments of the methyl resonances in the absence of $Pr(FOD)_3$ are given in Table I.

Next, we applied the same method to epifriedelanol acetate (IIa) and friedelanol acetate (IIIa). The lanthanide-induced shifts of the methyl signals in these compounds are given in Fig. 1 and the NOE peaks observed in the INDOR experiments are shown in Fig. 6 and Fig. 7. It is noteworthy here that in the case of epifriedelanol acetate (IIa), monitoring the 24-methyl singlet at δ −2.28 afforded NOE peaks on each line of the 23-methyl doublet at δ −3.38 and *vice versa*, although no corresponding NOE peak was observed with friedelanol acetate (IIIa).[13]

Careful inspection of these NMR data and comparison with those of the 28- and 29-deuterated compounds (IIb, IIc, IIIb, and IIIc) (see Fig. 8 and Fig. 9) led to assignments of the methyl resonances of epifriedelanol acetate (IIa) and friedelanol acetate (IIIa) as shown in Table I.

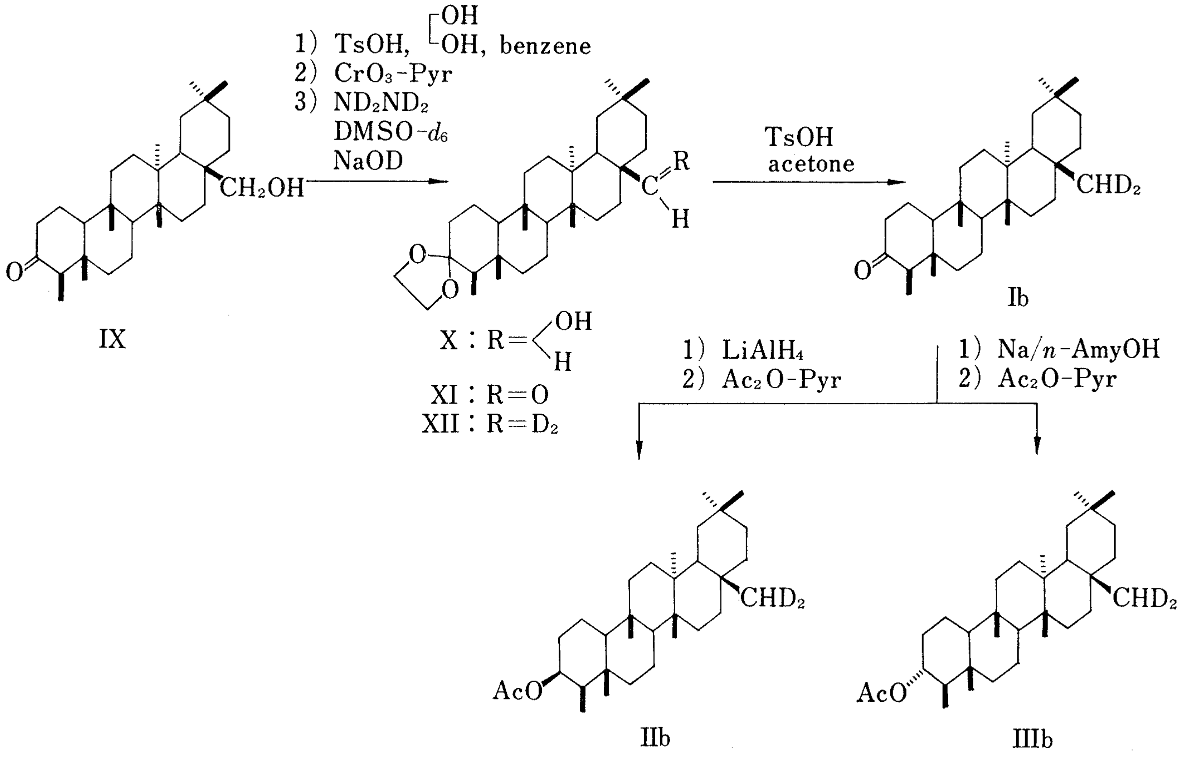

Chart 2

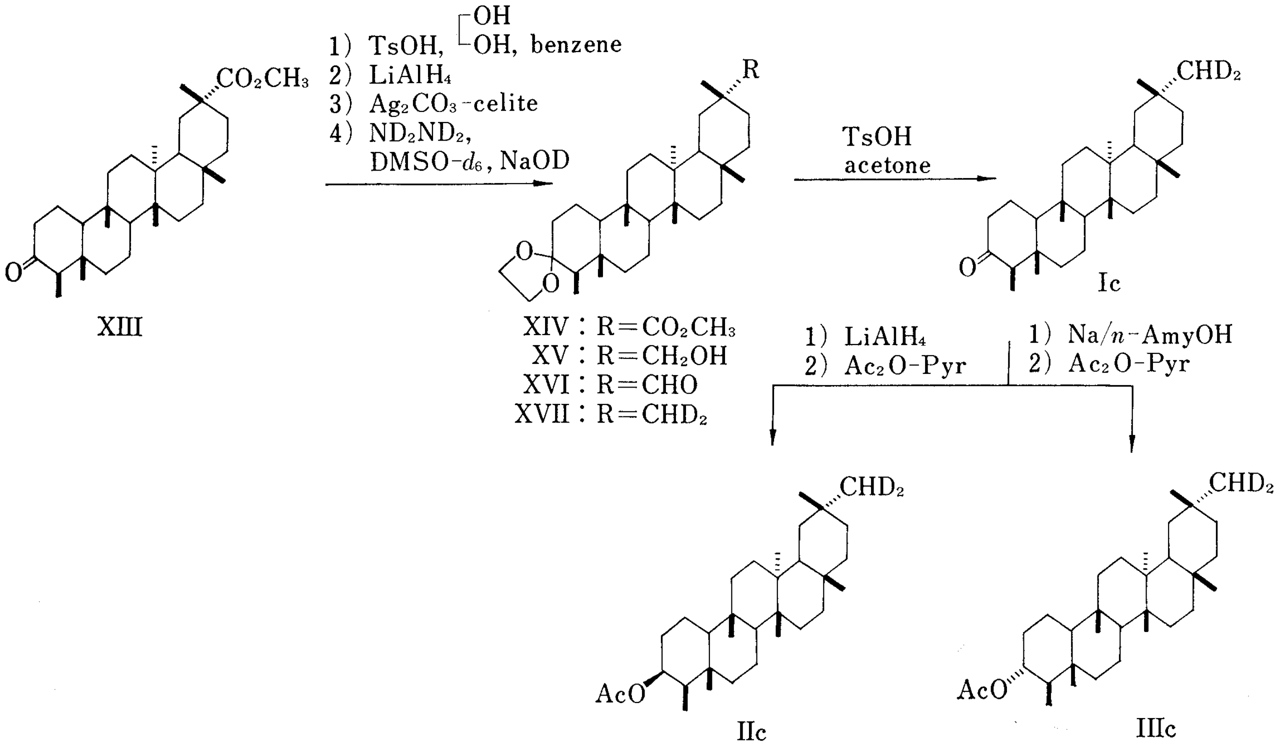

Chart 3

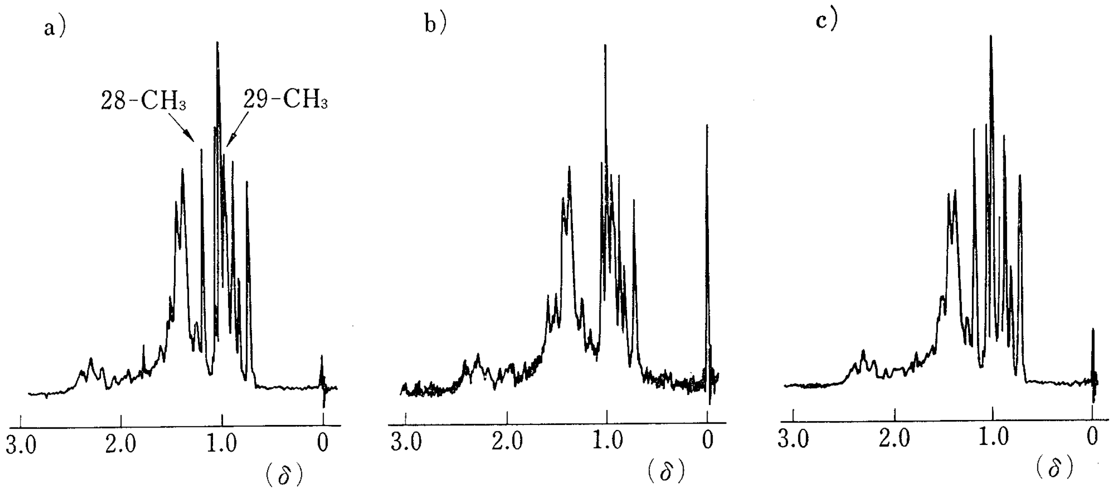

Fig. 5. 60 MHz NMR Spectra of a) Friedelin (Ia), b) Friedelin-28,28-d_2 (Ib), and c) Friedelin-29,29-d_2 (Ic)

TABLE I. Assignments of Methyl Resonances of Several Triterpenes related to Friedelin

		23	24	25	26	27	28	29	30
Friedelin (Ia)	δ	0.88	0.73	0.88	1.01	1.05	1.18	0.97	1.01
Epifriedelanol acetate (IIa)		0.81	0.93	0.86	1.00	1.00	1.17	0.94	1.00
Friedelanol acetate (IIIa)		0.75	0.83	0.83	0.99	1.01	1.17	0.94	0.99
16β-Acetoxyfriedelane (IV)		0.71	0.76	0.83	1.09	1.03	1.24	0.95[a]	1.01[a]
16α-Acetoxyfriedelane (V)		0.72	0.76	0.84	0.96	1.15	1.17	0.99	0.96
Shionone (VI)		0.87	0.72	0.92	0.90	1.14	0.90	(1.61	1.69)[b]
Epishionol acetate (VII)		0.81	0.93	0.93	0.87	1.09	0.89	(1.60	1.68)[b]
Shionol acetate (VIII)		0.75	0.81	0.87	0.87	1.09	0.89	(1.60	1.68)[b]

[a] Assignments may be reversed.
[b] Signals in parentheses were not assigned.

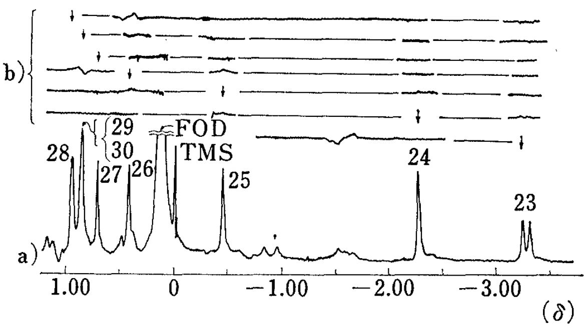

Fig. 6. INDOR Experiments with Epifriedelanol Acetate (IIa)

a) 100 MHz NMR spectrum of IIa in the presence of $Pr(FOD)_3$ (0.34 mol eq.).
b) INDOR spectra.

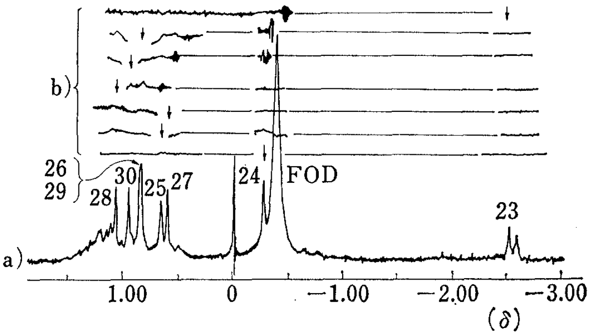

Fig. 7. INDOR Experiments with Friedelanol Acetate (IIIa)

a) 100 MHz NMR spectrum of IIIa in the presence of $Pr(FOD)_3$ (0.31 mol eq.).
b) INDOR spectra.

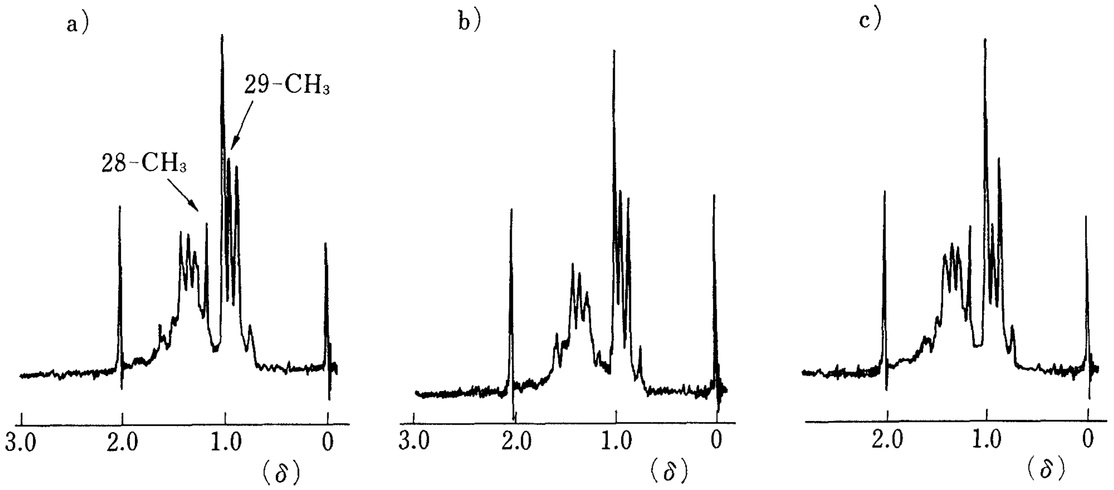

Fig. 8. 60 MHz NMR Spectra of a) Epifriedelanol Acetate (IIa), b) Epifriedelanol Acetate-28,28-d_2 (IIb), and c) Epifriedelanol Acetate-29,29-d_2 (IIc)

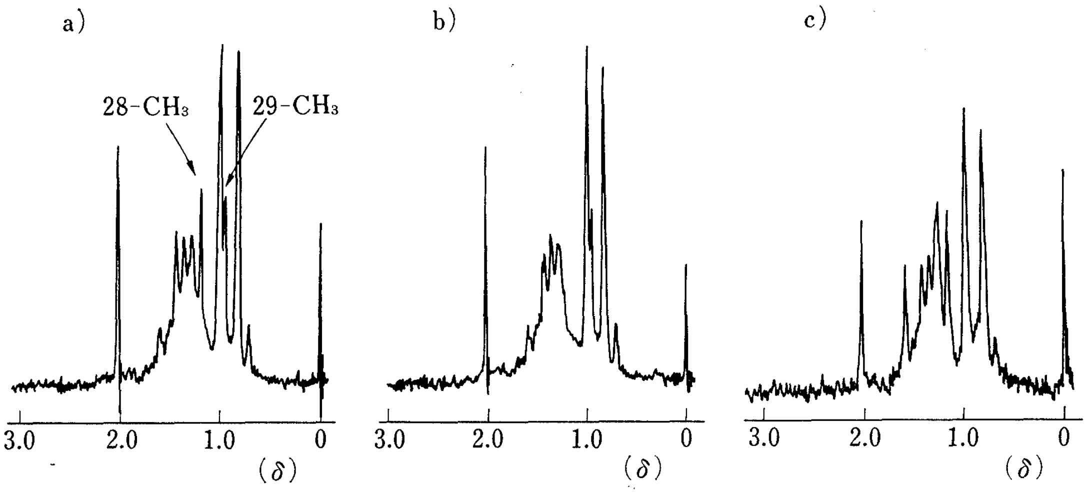

Fig. 9. 60 MHz NMR Spectra of a) Friedelanol Acetate (IIIa), b) Friedelanol Acetate-28,28-d_2 (IIIb), and c) Friedelanol Acetate (IIIc)

2) 16β- and 16α-Acetoxyfriedelanes (IV and V)

In an analogous manner, the methyl resonances of 16β- and 16α-acetoxyfriedelanes (IV and V)[14] were investigated. In these compounds, the 28-methyl signal is expected to be influenced most significantly by the added shift reagent, and the 26- or 27-methyl signal should be next most affected.

With the 16β-compound (IV) having ring D in a boat form,[14] the 28-, 26-, 25-, and 24-methyl signals were readily identified, as shown in Fig. 11a, b, on the basis of NOE peaks observed in INDOR experiments. Assignments of the other methyl signals were based on a consideration of their lanthanide-induced shift values (Fig. 10).

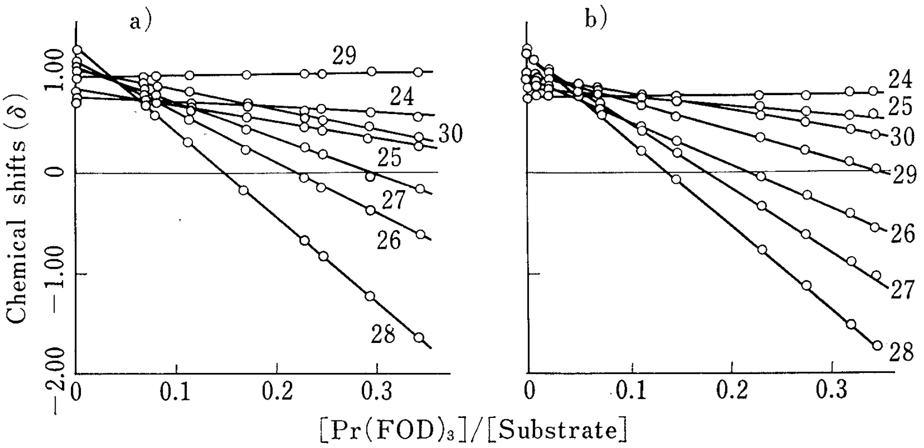

Fig. 10. Lanthanide-induced Shifts in the Methyl Signals of a) 16β-Acetoxyfriedelane (IV) and b) 16α-Acetoxyfriedelane (V), plotted against the molar Ratios of $Pr(FOD)_3$ to Substrate

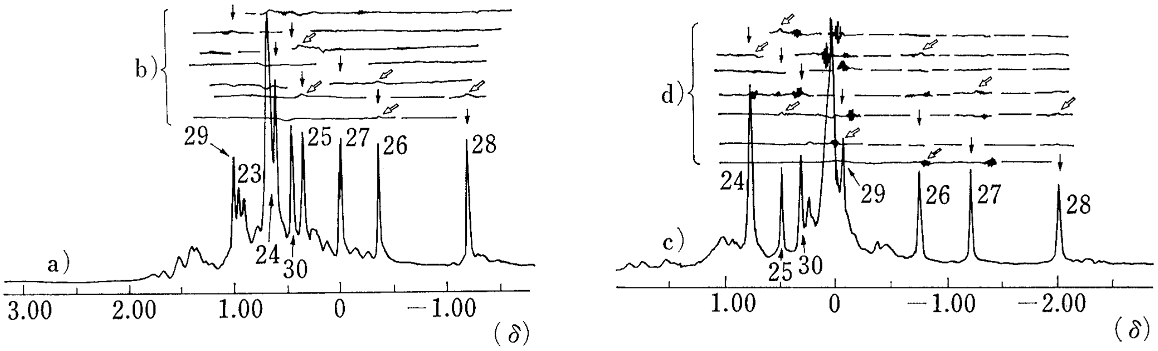

Fig. 11. INDOR Experiments with 16β- and 16α-Acetoxyfriedelanes (IV and V)

a), c): NMR spectra of IV and V in the presence of $Pr(FOD)_3$ (0.29 and 0.37 mol eq., respectively).
b), d): INDOR spectra (⇩: NOE peaks).

In contrast, the 16α-isomer (V) has ring D in a chair conformation and it showed an NOE between the 27- and 29-methyls besides NOE's between the 24-, 25-, and 26-methyl protons (Fig. 11c,d).[15]

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13) The reason is probably that the concentration of IIIa in $CDCl_3$ solution was not sufficient to provide optimum conditions for the INDOR experiment because of its low solubility.

14) T. Kikuchi, T. Shingu, M. Niwa, and T. Yokoi, *Chem. Pharm. Bull.*, **21**, 1396 (1973); N. Masaki, M. Niwa, and T. Kikuchi, *J. Chem. Soc. Perkin II*, **1975**, 610.

15) On monitoring the singlet at δ −0.77 (26-methyl), a very small peak was observed at the 28-methyl signal and *vice versa*. This might be ascribed to NOE, and suggests that ring D in V has a distorted chair conformation.

Assignments of the methyl resonances of IV and V in the absence of the shift reagent are listed in Table I.

3) Shionone (VI), Epishionol Acetate (VII), and Shionol Acetate (VIII)

The method described above was applied to shionone (VI), epishionol acetate (VII), and shionol acetate (VIII), which have the same partial structure as friedelin-type triterpenes with regard to rings A, B, and C. The lanthanide-induced shift properties of their methyl signals and the results of INDOR experiments are illustrated in Fig. 12 and Fig. 13.[16]

The NOE's observed between the 24-, 25-, and 26-methyls and a consideration of the shift pattern led us to assignments of the methyl resonances of VI, VII, and VIII as given in Table I.

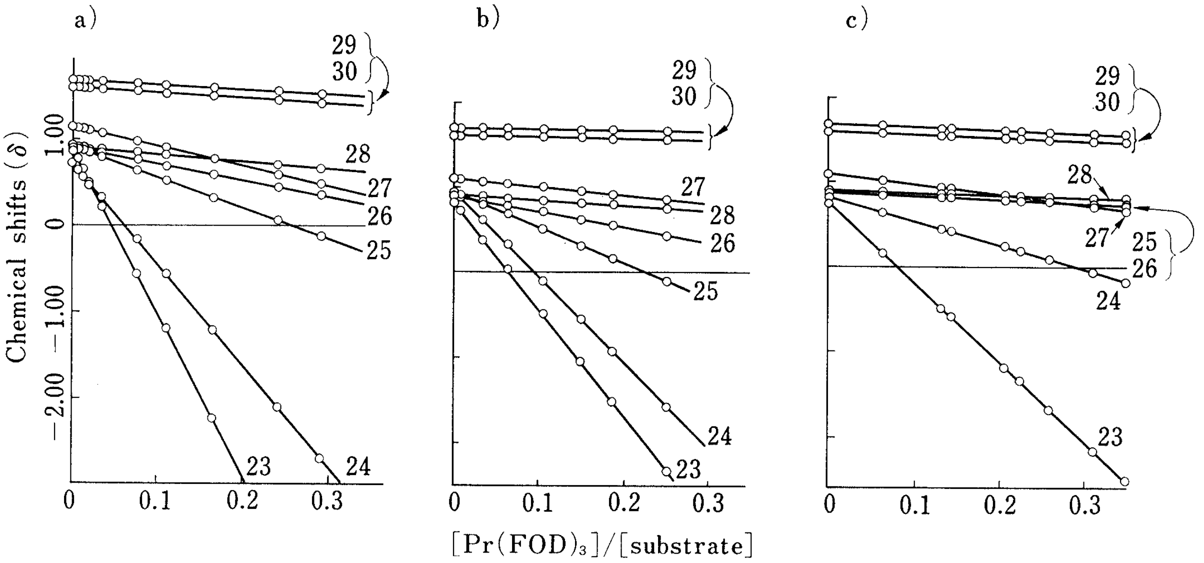

Fig. 12. Lanthanide-induced Shifts in the Methyl Signals of a) Shionone (VI), b) Epishionol Acetate (VII), and c) Shionol Acetate (VIII), plotted against the Molar Ratios of $Pr(FOD)_3$ to Substrate

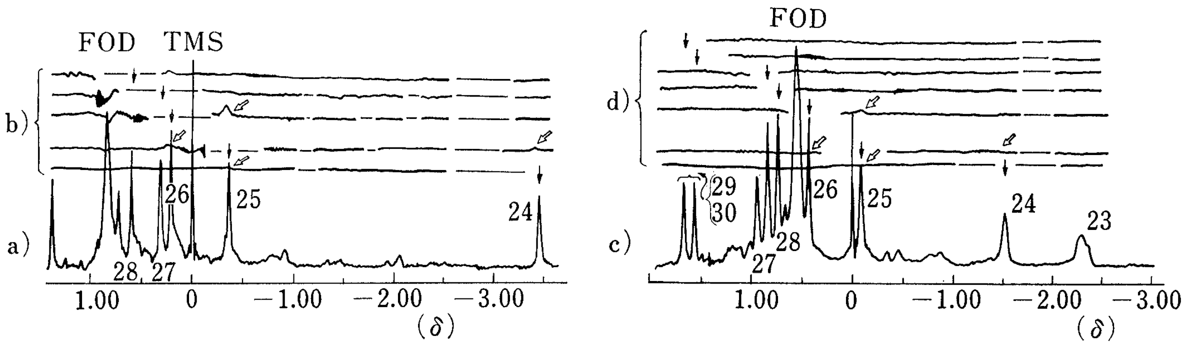

Fig. 13. INDOR Experiments with Shionone (VI) and Epishionol Acetate (VII)

a), c): NMR spectra of VI and VII in the presence of $Pr(FOD)_3$ (0.36 and 0.25 mol eq., respectively).
b), d): INDOR spectra (⇩: NOE peaks).

Experimental

All melting points were determined with a Kofler-type apparatus and are uncorrected. Mass spectral (MS) determinations were performed with a Hitachi RMU-6D mass spectrometer with a direct inlet system.

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[16] An INDOR experiment could not be carried out with shionol acetate (VIII) because the quantity of the sample available was too small.

Infrared (IR) spectra were measured on a Hitachi KPI spectrometer using chloroform solutions, unless otherwise noted. Usual measurements of NMR spectra were made in deuteriochloroform solutions using Varian A-60 and/or HA-100D spectrometers. Line positions of signals are given in the δ-scale with reference to tetramethylsilane as an internal standard. NMR measurements in the presence of NMR shift reagent were made after adding a weighed amount of the reagent to a solution of the substrate in $CDCl_3$. INDOR spectra were measured with a Varian HA-100D instrument modified for INDOR experiments. Preparative thin-layer chromatography (TLC) was performed on Merck Kieselgel GF_{254} or PF_{254} with chloroform or methanol-chloroform mixture, and plates were examined under ultra-violet light. For the extraction of substances from the Kieselgel, methylene chloride or methylene chloride-methanol mixture was used as a solvent. For drying organic solutions, anhydrous $MgSO_4$ was employed.

Canophyllal-3-ethylene Acetal (XI)——A mixture of canophyllol (IX) (270 mg), ethylene glycol (1 ml), *p*-toluenesulfonic acid (*p*-TsOH) (60 mg), and benzene (40 ml) was heated in a Dean-Stark apparatus for 12 hr. The reaction mixture was concentrated under reduced pressure and the residue was diluted with water, then extracted with CH_2Cl_2. The organic layer was washed with dil. Na_2CO_3, dried, and concentrated to leave a crystalline residue (250 mg). Recrystallization of this residue from $CHCl_3$–MeOH gave canophyllol ethylene acetal (X) (255 mg), colorless prisms, mp 331—333° (dec.). MS *m/e*: 486 (M^+, $C_{32}H_{54}O_3$).

A solution of canophyllol ethylene acetal (X) (250 mg) in pyridine (4 ml) was added to a mixture of CrO_3 (100 mg) and pyridine (3 ml), and the mixture was stirred for 3 hr under ice-cooling. The reaction mixture was poured into water and extracted with $CHCl_3$. The $CHCl_3$ solution was washed successively with 3% HCl, dil. Na_2CO_3, and water, and then dried. Removal of the solvent gave a crystalline residue (170 mg). Chromatography of this residue on alumina (10 g) using $CHCl_3$, followed by recrystallization from MeOH–$CHCl_3$, afforded canophyllal-3-ethylene acetal (XI) (155 mg), colorless needles, mp>300°. MS *m/e*: 484 (M^+, $C_{32}H_{52}O_3$). IR (KBr) ν_{max} cm^{-1}: 2700, 1725 (CHO), 1070 (C–O).

Friedelin-28,28-*d*$_2$ (Ib)——Canophyllal-3-ethylene acetal (XI) (153 mg) was added to a solution of ND_2ND_2 in DMSO-d_6 (freshly prepared by distilling a mixture of anhydrous $ND_2ND_2 \cdot D_2SO_4$ (5 g), anhydrous Na_2CO_3 (7 g), and DMSO-d_6 (10 ml)) and the mixture was heated at 120—130° for 4 hr. NaOD (1 g) was then added and the temperature was elevated to 180—190°; this was maintained for 28 hr. After cooling, water was added to the mixture and the mixture was extracted with $CHCl_3$. The combined extracts were washed with water, dried, and concentrated. The residue (172 mg) was chromatographed on alumina (8 g), eluting with benzene, to afford a crystalline substance (80 mg) which was recrystallized from $CHCl_3$–MeOH to give friedelin ethylene acetal-28,28-d_2 (XII) (73 mg), colorless needles, mp>300°. IR ν_{max} cm^{-1}: 2250 (C–D), 1070 (C–O).

A mixture of friedelin ethylene acetal-28,28-d_2 (XII) (73 mg), *p*-TsOH (70 mg), and acetone (45 ml) was heated on a steam bath for 7 hr. The reaction mixture was then concentrated *in vacuo*, diluted with water, and extracted with CH_2Cl_2. The organic layer was washed with water, dried, and concentrated. The residue was subjected to preparative TLC and then recrystallized from CH_2Cl_2–MeOH to afford friedelin-28,28-d_2 (Ib) (45 mg), colorless needles, mp 257—259°. MS *m/e*: 428 (M^+, $C_{30}H_{48}D_2O$). IR ν_{max} cm^{-1}: 2260 (C–D), 1700 (C=O). NMR δ: 1.06—0.72 (*sec*-CH_3+6×*tert*-CH_3).

Epifriedelanol Acetate-28,28-*d*$_2$ (IIb)——A mixture of friedelin-28,28-d_2 (Ib) (23 mg), dry tetrahydrofuran (THF) (3 ml), and dry ether (3 ml) was treated with $LiAlH_4$ (100 mg) and the whole was gently refluxed with stirring for 5 hr. The reaction mixture was then poured into water and the product was taken up in $CHCl_3$. The $CHCl_3$ solution was washed successively with 3% HCl, dil. Na_2CO_3, and water, then dried and concentrated to give a crystalline residue (13 mg). This residue was mixed with acetic anhydride-pyridine (each 0.5 ml) and left stand overnight at room temperature. The reaction mixture was worked up in the usual manner to give a crystalline residue, which was recrystallized from CH_2Cl_2–MeOH to afford epifriedelanol acetate-28,28-d_2 (IIb) (10 mg), colorless needles, mp 297—298°. MS *m/e*: 472 (M^+, $C_{32}H_{52}D_2O_2$). IR ν_{max} cm^{-1}: 2250 (C–D), 1720 (C=O). NMR δ: 4.90 (1H, m, C$\underline{H}$–OAc), 2.04 (3H, s, $COCH_3$), 1.00—0.75 (*sec*-CH_3+6×*tert*-CH_3).

Friedelanol Acetate-28,28-*d*$_2$ (IIIb)——Metallic sodium (100 mg) was added in small portions to a solution of friedelin-28,28-d_2 (Ib) (26 mg) in *n*-amyl alcohol (3 ml) and the mixture was heated with vigorous stirring at 90° for 1.5 hr. After concentration *in vacuo*, the mixture was diluted with water, extracted with ether, dried, and concentrated. The residue was subjected to preparative TLC to give a crystalline substance (8 mg), which was treated with acetic anhydride–pyridine (each 0.5 ml) at room temperature for 2 days. Usual work-up of the reaction mixture and subsequent recrystallization from CH_2Cl_2–MeOH afforded friedelanol acetate-28,28-d_2 (IIIb) (7 mg), colorless needles, mp>300°. MS *m/e*: 472 (M^+, $C_{32}H_{52}D_2O_2$). IR ν_{max} cm^{-1}: 2200 (C–D), 1720 (C=O), 1260 (C–O). NMR δ: 4.60 (1H, m, C$\underline{H}$–OAc), 2.02 (3H, s, $COCH_3$), 1.01—0.72 (*sec*-CH_3+6×*tert*-CH_3).

Acetal Ester (XIV)——A mixture of methyl polpunonate (XIII) (277 mg), ethylene glycol (1.5 ml), *p*-TsOH (110 mg), and benzene (90 ml) was heated in a Dean-Stark apparatus for 4 hr. The reaction mixture was washed with dil. Na_2CO_3, dried, and concentrated *in vacuo*. The crystalline residue (253 mg) was recrystallized from $CHCl_3$–MeOH to afford the acetal ester (XIV) (220 mg), colorless leaves, mp 304—305°. MS *m/e*: 514 (M^+, $C_{33}H_{54}O_4$). IR ν_{max} cm^{-1}: 1720 (–COO–), 1070 (C–O). NMR δ: 3.94 (4H, m, –O–C$\underline{H}_2$–C$\underline{H}_2$–O–), 3.65 (3H, s, $COOCH_3$), 1.28—0.84 (6×*tert*-CH_3), 0.77 (3H, d, J=7 Hz, *sec*-CH_3).

Acetal Aldehyde (XVI)——A solution of the acetal ester (XIV) (210 mg) in dry ether (5 ml) and dry THF (5 ml) was treated with $LiAlH_4$ (150 mg), and the whole was gently heated with stirring for 4 hr. After decomposition of the excess reagent with water, the mixture was extracted with ether and the combined ether extracts were washed successively with 3% HCl, dil. Na_2CO_3, and water, then dried and concentrated. Recrystallization of the residue (200 mg) from $CHCl_3$–MeOH afforded the acetal alcohol (XV) (187 mg), colorless prisms, mp>300°.

Silver carbonate-celite (8 g) (freshly prepared according to Fetizon *et al.*[17]) was added to a solution of the above acetal alcohol (XV) (187 mg) in benzene (80 ml) and the whole was heated at 80° with vigorous stirring for 4 hr in the dark. The reaction mixture was filtered by suction and the filtrate was concentrated *in vacuo* to leave a crystalline residue (126 mg). Further purification by preparative TLC and subsequent recrystallization from $CHCl_3$–MeOH gave the acetal aldehyde (XVI) (101 mg), colorless prisms, mp 254—256°. MS *m/e*: 484 (M^+, $C_{32}H_{52}O_3$). IR ν_{max} cm^{-1}: 2700, 1715 (CHO), 1070 (C–O). NMR δ: 9.40 (1H, s, –CHO), 3.90 (4H, m, $-O-C\underline{H}_2-C\underline{H}_2-O-$), 1.10—0.85 (6×*tert*-$CH_3$), 0.76 (3H, d, $J=7$ Hz, *sec*-CH_3).

Friedelin-29,29-*d*₂ (Ic)——The acetal aldehyde (XVI) (99 mg) was added to a solution of ND_2ND_2 in DMSO-d_6 (freshly prepared from $ND_2ND_2\cdot D_2SO_4$ (5 g), Na_2CO_3 (7 g), and DMSO-d_6 (10 ml)) and heated at 120—130° for 10 hr. NaOD (1 g) was then added to the above mixture in small portions and the whole was heated further at 180—190° for 36 hr. The reaction mixture was treated in the same manner as described for XII and the product was recrystallized from $CHCl_3$–MeOH to afford friedelin acetal-29,29-d_2 (XVII) (58 mg), colorless needles, mp 310°. MS *m/e*: 472 (M^+, $C_{32}H_{52}D_2O_2$). IR ν_{max} cm^{-1}: 2250 (C–D), 1070 (C–O).

A mixture of friedelin acetal-29,29-d_2 (XVII) (57 mg), *p*-TsOH (50 mg), and acetone (35 ml) was refluxed on a steam bath for 4 hr. The reaction mixture was concentrated *in vacuo*, then the residue was diluted with dil. Na_2CO_3 and extracted with $CHCl_3$. The extract was dried, and concentrated. The residue (53 mg) was recrystallized from CH_2Cl_2–MeOH to give friedelin-29,29-d_2 (Ic) (41 mg), colorless needles, mp 263—264°. MS *m/e*: 428 (M^+, $C_{30}H_{48}D_2O$). IR ν_{max} cm^{-1}: 2200 (C–D), 1700 (C=O). NMR δ: 1.17—0.73 (6×*tert*-CH_3), 0.87 (3H, d, $J=6.5$ Hz, *sec*-CH_3).

Epifriedelanol Acetate-29,29-*d*₂ (IIc)——A mixture of friedelin-29,29-d_2 (Ic) (12 mg), dry THF (2 ml), and dry ether (2 ml) was treated with $LiAlH_4$ (100 mg) for 6 hr at room temperature. Usual work-up furnished a crystalline residue (13 mg), which was purified by preparative TLC to give crystals (9 mg). A mixture of the crystals, acetic anhydride (0.5 ml), and pyridine (0.5 ml) was left to stand overnight at room temperature. Usual work-up of the reaction mixture gave epifriedelanol acetate-29,29-d_2 (IIc) (9 mg), colorless needles, mp 298—300°. MS *m/e*: 472 (M^+, $C_{32}H_{52}D_2O_2$). IR ν_{max} cm^{-1}: 2200 (C–D), 1725, 1260 (–O–CO–). NMR δ: 4.90 (1H, m, $C\underline{H}$–OAc), 2.03 (3H, s, $COCH_3$), 1.18—0.86 (6×*tert*-CH_3), 0.80 (3H, d, $J=7$ Hz, *sec*-CH_3).

Friedelanol Acetate-29,29-*d*₂ (IIIc)——Metallic sodium (150 mg) was added to a solution of friedelin-29,29-d_2 (Ic) (11 mg) in freshly distilled *n*-amyl alcohol (3 ml) and the whole was heated at 90° with stirring for 1.5 hr. Usual work-up gave a crystalline residue (7 mg), which was acetylated in the usual manner. The product was purified by preparative TLC and recrystallization from CH_2Cl_2–MeOH to yield friedelanol acetate-29,29-d_2 (IIIc) (3.5 mg), colorless needles, mp>300°. MS *m/e*: 472 (M^+, $C_{32}H_{52}D_2O_2$). IR ν_{max} cm^{-1}: 2200 (C–D), 1720, 1260 (–O–CO–). NMR δ: 4.60 (1H, m, $C\underline{H}$–OAc), 2.03 (3H, s, $COCH_3$), 1.18—0.81 (6×*tert*-CH_3), 0.74 (3H, d, $J=7$ Hz, *sec*-CH_3).

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