

Boron Trifluoride Etherate-catalyzed Backbone Rearrangement of 5 α ,10 α -Epoxyalnan-3 β -yl Acetate and Partial Synthesis of Isomultiflorenol¹⁾

Masaki TAKAI, Motoo TORI, Takahiko TSUYUKI, Takeyoshi TAKAHASHI,* Akiko ITAI,[†] and Yoichi IITAKA[†]

Department of Chemistry, Faculty of Science, The University of Tokyo,

*[†]Faculty of Pharmaceutical Sciences, The University of Tokyo,
Hongo, Bunkyo-ku, Tokyo 113*

(Received July 23, 1984)

Epoxidation of alnus-5(10)-en-3 β -yl acetate with *m*-chloroperbenzoic acid gave a 5 α ,10 α -epoxide, treatment of which with boron trifluoride etherate afforded multiflora-5,8-dien-3 β -yl acetate. On hydrogenation and hydrolysis, the diene gave isomultiflorenol.

In the previous paper,²⁾ the boron trifluoride etherate (BF₃·OEt₂)-catalyzed backbone rearrangement of 5,6-epoxyalnan-3 β -yl acetate was reported. Further investigation on a behavior of carbonium ions generated on B-ring was attempted. This paper describes the epoxidation of alnus-5(10)-ene derivatives, the BF₃·OEt₂-catalyzed backbone rearrangement of a 5 α ,10 α -epoxy acetate, and also a preparation of isomultiflorenol (1)^{3–7)} from one of the rearranged products.

Alnus-5(10)-en-3 β -yl acetate (4),⁸⁾ prepared from dendropanoxide (5),⁹⁾ was subjected to the epoxidation with *m*-chloroperbenzoic acid (MCPBA) to afford a single epoxide (6) in a good yield. However, no information on the configuration of the epoxide ring could be obtained from any spectrum of 6 (See Experimental).

In order to determine the configuration of the epoxide (6), the following epoxidation reactions were examined. Alnus-5(10)-en-3 β -ol (7) and its benzoate (8) were epoxidized with MCPBA under the same conditions as above to afford single epoxides (9 and 10), respectively. On acetylation, the epoxide (9) yielded an epoxy acetate, which was identical with 6. Treatment of 10 with lithium aluminium hydride afforded an epoxy alcohol identical with 9. Therefore, the epoxide rings of 6, 9, and 10 are in all the same configurations.

Since the signals due to 3 α -protons of alnus-5(10)-en-3 β -ol (7), -3 β -yl acetate (4), and -3 β -yl benzoate (8) were observed as double doublets at δ 3.44 (*J*=10 and 4 Hz), δ 4.69 (*J*=10 and 4 Hz), and δ 4.94 (*J*=10 and 4 Hz), respectively, in the ¹H NMR spectra, the substituents at C-3 β exist in an equatorial orientation. From these facts, it could be understood why the 3 β -oxygen functions did not participate in these epoxidation reactions, hence the reagent attacked exclusively from the less hindered α -side of the molecule (4 β - and 9 β -methyl groups are perpendicular to the 5,10-double bond plane, while the 4 α -methyl group lies in the plane). Therefore, the epoxide rings of 6, 9, and 10 were considered to be in the α -configuration.

Then, epoxidation reactions of alnus-5(10)-en-3 α -O-

derivatives were examined. In the case of these 3 α -O-derivatives, since the substituents at C-3 α exist in an axial orientation, the bulky substituents block the α -side of the molecule and the attack of the epoxidizing reagent from the α -side was considered to be hindered. Epoxidation of alnus-5(10)-en-3 α -ol (11) and its acetate (12) under the same conditions as above gave single epoxides (13 and 14), respectively, while 3 α -benzoate (15), on epoxidation, gave two epoxides (16 and 17) in a ratio of 7:1. The relative configurations of the epoxide rings of 13, 14, and 16 were confirmed by the derivatization as in the case of the 3 β -O-derivatives, and proved to be in all the same. These substituent effects are explained by the steric hindrance due to 4 β - and 9 β -methyl groups and partly by the hydrogen bond formation between the reagent and the 3 α -axial hydroxyl group in the case of 11, resulting in the exclusive formation of the α -epoxide (13). In the case of the benzoate (15), the attack from the α -side of the molecule was sterically slightly hindered by the bulky benzoyloxyl group to afford the β -epoxide (17) as the minor product, while the acetoxy group was not large enough to prevent the attack from the α -side. Thus the configurations of the epoxide rings of 13, 14, and 16 are concluded to be α .

These assignments of the epoxide rings were further confirmed by the Sharpless epoxidation.¹⁰⁾ Epoxidation of alnus-5(10)-en-3 α -ol (11) with vanadyl acetylacetonate (VO(acac)₂) and *t*-butyl hydroperoxide afforded a single epoxide which was identical with 5 α ,10 α -epoxide (13) obtained by MCPBA. However epoxidation of alnus-5(10)-en-3 β -ol (7) with the same conditions gave a single epoxide, but it was different from the 5 α ,10 α -epoxide (9) obtained by MCPBA. From the spectral data and formation mechanism, it was concluded to be a 5 β ,10 β -epoxide (18).

The epoxy-3 β -ol (9), obtained by the reaction with MCPBA, was oxidized to give a keto epoxide (19) which was identical with that obtained by the oxidation of the epoxy-3 α -ol (13); thus the epoxide rings of the 3 β -O-derivatives (6, 9, and 10) and the 3 α -O-derivatives (13, 14, and 16) are the same.

From these facts, the epoxidation reaction of these 5(10)-ene derivatives was shown to occur from the α -side of the molecule exclusively except for 5(10)-en-3 α -yl benzoate (**15**). These results are opposite from those obtained for the epoxidation of alnus-5-en-3 β -ol and its derivatives.²⁾

The assignments of these epoxide rings were supported by the NMR spectral measurement (see Tables 1 and 2). The protons at C-3 of alnus-5(10)-en-3 β -ol (**7**) and -3 α -ol (**11**) resonated at nearly the same magnetic fields, while a remarkable difference in shift values due to the protons at C-3 was observed between 5 α ,10 α -epoxy-3 β -ol (**9**) and 5 α ,10 α -epoxy-3 α -ol (**13**); the 3 α -H of **9** is deshielded by 0.34 ppm relative to that of **13**. This observation is ascribed to an anisotropic effect of an

oxygen atom of the epoxide caused by a proximation of the 3 α -axial proton of **9** to the oxygen atom.

This anisotropic effect is also observed in the ^1H NMR spectra of the corresponding acetates (**6** *vs.* **14**) and benzoates (**10** *vs.* **16**).

The same observations were given in the ^1H NMR spectral examination of 5 β ,10 β -epoxides, although the differences are not so large, because the 3 β -protons exist in an equatorial orientation. The 3 β -protons of 5 β ,10 β -epoxy-3 α -ol (**20**), 5 β ,10 β -epoxy-3 α -yl acetate (**21**), and 5 β ,10 β -epoxy-3 α -yl benzoate (**17**) appeared at

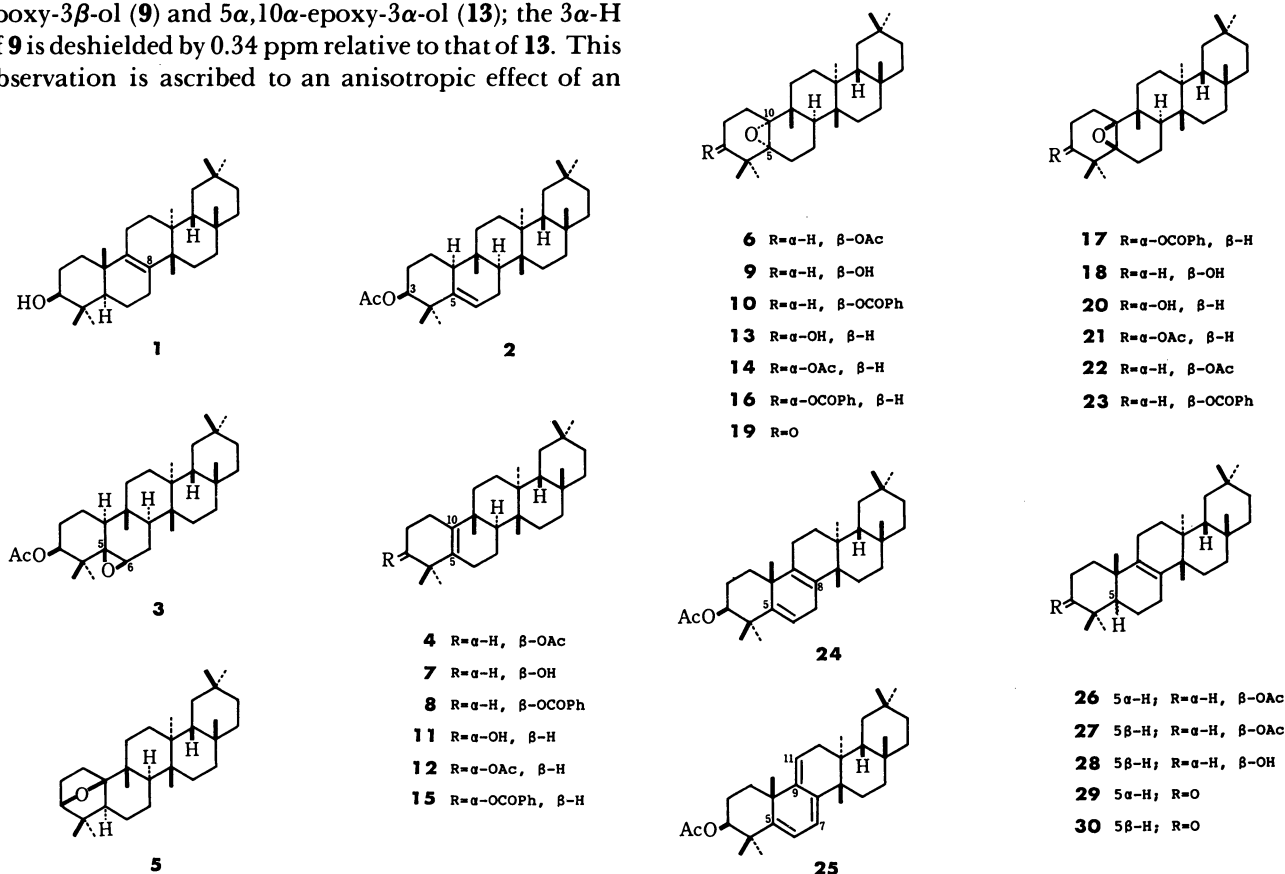


TABLE 1. THE δ VALUES OF C-3 PROTONS OF ALNUS-5(10)-ENE DERIVATIVES AND 5,10-EPOXYALNUSANE DERIVATIVES IN THE ^1H NMR SPECTRA

	δ -values	
	C-3 α protons of 3 β -O- derivatives	C-3 β protons of 3 α -O- derivatives
5(10)-en-3-ol	7 3.44 dd $J=10, 4$	11 3.45 t-like $J=4$
5 α ,10 α -epoxy-3-ol	9 3.58 dd $J=10, 5$	13 3.24 dt $J=11, 3$ 3.52 d $J=11$ (-OH)
5 β ,10 β -epoxy-3-ol	18 3.17 br s 2.71 br s (-OH)	20 3.41 dd $J=7, 3$
5(10)-en-3-yl acetate	4 4.69 dd $J=10, 5$	12 4.70 t $J=4$
5 α ,10 α -epoxy-3-yl acetate	6 4.77 dd $J=10, 4$	14 4.47 dd $J=7, 4$
5 β ,10 β -epoxy-3-yl acetate	22 4.36 dd $J=11, 4$	21 4.57 dd $J=7, 3$
5(10)-en-3-yl benzoate	8 4.94 dd $J=10, 4$	15 4.96 dd $J=5, 3$
5 α ,10 α -epoxy-3-yl benzoate	10 5.02 dd $J=11, 4$	16 4.72 dd $J=7, 3$
5 β ,10 β -epoxy-3-yl benzoate	23 4.62 dd $J=10, 5$	17 4.78 dd $J=5.5, 3$

TABLE 2. ^{13}C NMR SPECTRA OF ALNUS-5(10)-EN-3-OLS AND 5,10-EPOXYALNUSAN-3-OLS

7	11	9	13	18	20
18.6	18.6 t	16.7 t	16.7 t	15.6 t	15.9 t
18.8	18.8 q	17.2 q	18.4 q	18.1 q	18.0 q
20.5	19.0 t	18.3 q	18.6 q	18.9 q	18.9 q
20.7	20.5 q	18.7 q	19.5 t	19.9 q	19.7 t
21.0	21.2 q	19.9 q	19.8 q	20.6 t	21.1 q
23.2	23.1 q	20.6 q	21.4 q	21.0 q	21.1 q
24.7	25.9 t	23.5 t	24.1 t	24.7 t	22.6 q
27.0	27.0 t	24.4 t	24.2 t	25.4 q	24.5 t
27.7	28.0 q	26.1 t	25.5 q	28.1 s	28.1 s
28.2	28.2 s	28.1 s	28.2 s	29.0 t	29.5 t
30.1	30.1 t	29.0 t	28.8 t	29.9 s	30.0 s
31.0	31.0 s	30.0 s	30.1 s	31.6 q	31.7 q
31.6	31.8 t	30.2 t	30.2 t	31.8 t	31.8 s
31.8	31.8 q	31.9 q	32.0 q	32.2 t	32.2 t
32.2	32.2 q	32.1 q	32.1 q	32.2 q	32.2 q
32.3	32.4 t	32.4 t	32.4 t	32.7 t	32.6 t
32.9	32.9 t	32.9 t	32.9 t	32.9 t	32.8 t
35.1	35.1 q	34.9 q	34.9 q	35.1 q	35.2 q
35.5	35.5 t	35.3 t	35.3 t	35.5 t	35.5 t
36.1	36.1 t	36.0 t	36.0 t	35.9 t	36.0 t
37.5	37.6 s	36.9 s	36.9 s	37.6 s	37.7 s
38.3	38.3 s	37.9 s	37.1 s	37.8 s	37.8 s
39.4	38.8 s	38.6 s	37.9 s	38.8 s	38.8 s
39.4	39.4 t	* 38.8 d	* 38.7 d	39.4 t	39.4 t
39.5	39.5 s	39.2 t	39.2 t	39.4 s	39.5 s
42.8	42.8 d	39.3 s	39.3 s	42.6 d	42.7 d
* 47.9	* 47.8 d	42.9 d	42.9 d	* 49.6 d	* 49.7 d
** 76.2	** 75.5 d	71.0 s	71.4 s	71.8 s	69.7 s
131.7	130.0 s	71.9 s	73.3 s	73.6 s	** 72.7 d
137.3	137.4 s	** 72.2 d	** 76.5 d	** 76.5 d	72.8 s

* Assignable to C-8. ** Assignable to C-3.

lower fields than the 3 α -protons of the corresponding 3 β -alcohol (**18**), 3 β -acetate (**22**), and 3 β -benzoate (**23**), respectively.

In the ^1H NMR spectra of **13** and **18**, signals due to hydroxyl protons were observed at δ 3.52 and 2.71, respectively. Appearance of these signals is ascribed to the formation of hydrogen bond between the epoxide oxygen atom and the hydroxyl proton, resulting in the retardation of the exchange rate of the hydroxyl proton. This observation also supports the assignment of the epoxides, because the hydrogen bond could not be formed in 5 α ,10 α -epoxy-3 β -ol (**9**) nor 5 β ,10 β -epoxy-3 α -ol (**20**).

In the ^{13}C NMR spectrum of α -epoxy-3 β -ol (**9**), a signal due to C-3 atom to which the proton resonating in a low field (δ 3.58) was attached, was observed in a higher field by 3.3 ppm than that of C-3 atom of α -epoxy-3 α -ol (**13**). In the ^{13}C NMR spectra of β -epoxy alcohols, it was shown that C-3 atom of 3 α -alcohol (**20**) resonated in a higher field relative to that of 3 β -alcohol (**18**).

From the same reason, it is understood that C-8 atoms, bearing hydrogen atoms in α -orientation, of

α -epoxides (**9** and **13**) resonate in a higher field by ca. 9 ppm than those of 5(10)-en-3-ols (**7** and **11**), while C-8 atoms of β -epoxides (**18** and **20**) resonates at nearly the same magnetic field as 5(10)-en-3-ols.

These observations described above are strongly indicative of the correct assignment of the epoxide rings.

The unequivocal proof for the structure of 5 α ,10 α -epoxyalnusan-3 β -yl acetate (**6**) was provided by X-ray single crystal analysis. The crystals of **6** belong to a monoclinic space group C_2 , and the lattice parameters are $a=13.446(4)$, $b=6.739(2)$, $c=32.257(7)$ Å, and $\beta=103.71(3)^\circ$; $z=4$. Intensity data were measured on a Philips PW1100 automatic four-circle diffractometer using monochromated $\text{Cu K}\alpha$ radiation. A total of 2951 independent reflections with $F_o \geq 2.5\sigma(F_o)$ were obtained by $2\theta-\theta$ scanning mode. The structure was solved by the direct method using the MULTAN 80 program and was refined by the block-diagonal least squares method. All hydrogen atoms were located on a difference electron density map. The final R -value was 0.056 assuming the anisotropic temperature factors for the non-hydrogen atoms and the isotropic ones

for the hydrogen atoms. The final atomic coordinates are listed in Table 3 and bond lengths and bond angles are listed in Tables 4 and 5.¹¹⁾ Figure 1 is a computer-generated perspective drawing of the molecule of 5 α ,10 α -epoxyalnusan-3 β -yl acetate (**6**).

5 α ,10 α -Epoxyalnusan-3 β -yl acetate (**6**) was treated with BF₃·OEt₂ (1.2 equiv) in benzene to afford a reac-

tion mixture, which was shown to consist of a main product (**24**; *ca.* 80% yield) and more than seven minor components by HPLC examination. The reaction mixture was subjected to separation by column chromatography to give the pure main product (**24**), C₃₂H₅₀O₂ (determined by the high-resolution mass spectrum), showed no characteristic absorption maxi-

TABLE 3. ATOMIC POSITIONAL PARAMETERS ($\times 10^4$) AND ISOTROPIC TEMPERATURE FACTORS ($\times 10^3$) FOR NON-HYDROGEN ATOMS OF 5 α , 10 α -EPOXYALNUSAN-3 β -YL ACETATE (**6**) WITH ESTIMATED STANDARD DEVIATIONS IN PARENTHESES

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> _{eq} ^{a)}	Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> _{eq} ^{a)}
C(1)	3874 (2)	2605 (0)	1572 (1)	422 (6)	C(19)	6057 (3)	69 (7)	3862 (1)	460 (6)
C(2)	3564 (3)	3303 (6)	1111 (1)	395 (5)	C(20)	6432 (3)	-918 (8)	4300 (1)	523 (7)
C(3)	4317 (3)	4817 (5)	1017 (1)	361 (5)	C(21)	7585 (3)	-421 (10)	4482 (1)	633 (9)
C(4)	5408 (3)	4000 (6)	1075 (1)	377 (5)	C(22)	8037 (3)	880 (9)	4179 (1)	571 (7)
C(5)	5765 (2)	3210 (5)	1529 (1)	328 (4)	C(23)	6112 (3)	5711 (7)	1010 (1)	530 (7)
C(6)	6882 (3)	2618 (8)	1662 (1)	496 (7)	C(24)	5444 (3)	2326 (7)	753 (1)	531 (7)
C(7)	7142 (2)	1077 (7)	2018 (1)	439 (6)	C(25)	5128 (3)	-1072 (5)	1939 (1)	440 (6)
C(8)	6508 (2)	1412 (5)	2351 (1)	303 (4)	C(26)	6268 (3)	3116 (6)	3203 (1)	431 (6)
C(9)	5361 (2)	1012 (4)	2138 (1)	278 (4)	C(27)	7037 (3)	-1899 (6)	2723 (1)	457 (6)
C(10)	5018 (2)	2486 (5)	1768 (1)	289 (4)	C(28)	8459 (3)	-2047 (9)	3776 (1)	630 (8)
C(11)	4734 (2)	1340 (6)	2475 (1)	350 (5)	C(29)	6277 (4)	-3205 (10)	4262 (1)	704 (9)
C(12)	5163 (2)	259 (6)	2896 (1)	353 (5)	C(30)	5799 (4)	-68 (13)	4598 (1)	875 (14)
C(13)	6273 (2)	861 (5)	3108 (1)	297 (4)	C(31)	3496 (3)	7192 (6)	496 (1)	451 (6)
C(14)	6954 (2)	367 (5)	2788 (1)	323 (4)	C(32)	3252 (5)	7673 (9)	22 (1)	766 (10)
C(15)	8049 (2)	1158 (8)	2972 (1)	487 (6)	O(1)	5461 (2)	4458 (3)	1846 (1)	373 (3)
C(16)	8386 (3)	1346 (8)	3461 (1)	559 (7)	O(2)	3962 (2)	5451 (4)	573 (1)	447 (4)
C(17)	7874 (2)	-46 (7)	3726 (1)	428 (6)	O(3)	3298 (3)	8235 (6)	764 (1)	728 (7)
C(18)	6687 (2)	-328 (5)	3530 (1)	342 (5)					

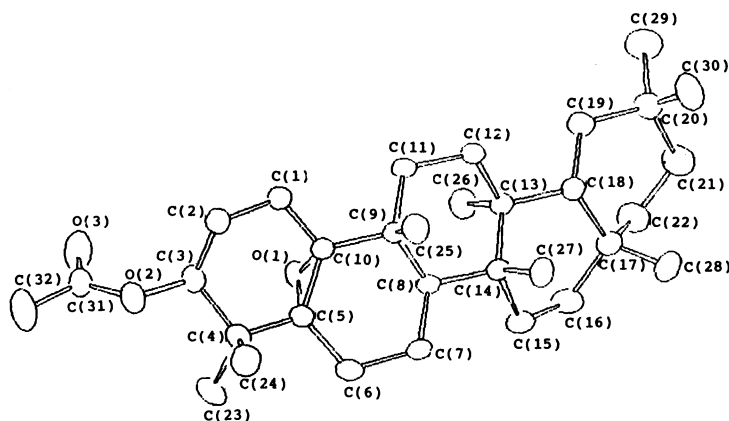
a) $B_{eq} = 8\pi(u_1^2 + u_2^2 + u_3^2)/3$.

TABLE 4. BOND LENGTHS (*l*/Å) OF 5 α ,10 α -EPOXYALNUSAN-3 β -YL ACETATE (**6**) WITH ESTIMATED STANDARD DEVIATIONS IN PARENTHESES

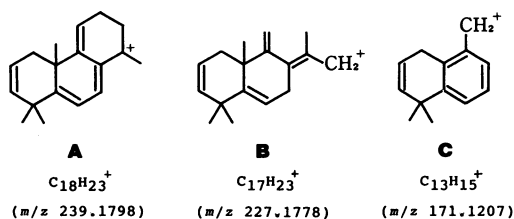
Bond length			Bond length		
Atom 1	Atom 2	(<i>l</i> /Å)	Atom 1	Atom 2	(<i>l</i> /Å)
C(1)	-C(2)	1.523 (5)	C(12)	-C(13)	1.542 (4)
C(1)	-C(10)	1.520 (4)	C(13)	-C(14)	1.569 (5)
C(2)	-C(3)	1.517 (5)	C(13)	-C(18)	1.563 (4)
C(3)	-C(4)	1.537 (5)	C(13)	-C(26)	1.550 (5)
C(3)	-O(2)	1.461 (4)	C(14)	-C(15)	1.546 (4)
C(4)	-C(5)	1.525 (4)	C(14)	-C(27)	1.549 (5)
C(4)	-C(23)	1.537 (6)	C(15)	-C(16)	1.539 (5)
C(4)	-C(24)	1.542 (6)	C(16)	-C(17)	1.537 (6)
C(5)	-C(6)	1.514 (5)	C(17)	-C(18)	1.582 (4)
C(5)	-C(10)	1.486 (5)	C(17)	-C(22)	1.557 (6)
C(5)	-O(1)	1.456 (4)	C(17)	-C(28)	1.550 (7)
C(6)	-C(7)	1.526 (6)	C(18)	-C(19)	1.538 (5)
C(7)	-C(8)	1.539 (5)	C(19)	-C(20)	1.535 (5)
C(8)	-C(9)	1.556 (4)	C(20)	-C(21)	1.558 (6)
C(8)	-C(14)	1.562 (4)	C(20)	-C(29)	1.555 (9)
C(9)	-C(10)	1.538 (4)	C(20)	-C(30)	1.539 (7)
C(9)	-C(11)	1.540 (5)	C(21)	-C(22)	1.539 (7)
C(9)	-C(25)	1.546 (5)	C(31)	-C(32)	1.520 (6)
C(10)	-O(1)	1.454 (4)	C(31)	-O(2)	1.326 (5)
C(11)	-C(12)	1.529 (4)	C(31)	-O(3)	1.193 (5)

TABLE 5. BOND ANGLES ($\phi/^\circ$) OF 5 α ,10 α -EPOXYALNUSAN-3 β -YL ACETATE (6) WITH ESTIMATED STANDARD DEVIATIONS IN PARENTHESES

Bond angle				Bond angle			
Atom 1	Atom 2	Atom 3	$\phi/^\circ$	Atom 1	Atom 2	Atom 3	$\phi/^\circ$
C(2)	-C(1)	-C(10)	116.0 (2)	C(14)	-C(13)	-C(18)	108.7 (2)
C(3)	-C(2)	-C(1)	111.2 (3)	C(14)	-C(13)	-C(26)	111.6 (3)
C(4)	-C(3)	-C(2)	113.4 (3)	C(12)	-C(13)	-C(18)	111.0 (3)
C(4)	-C(3)	-O(2)	107.7 (3)	C(12)	-C(13)	-C(26)	107.2 (3)
C(2)	-C(3)	-O(2)	108.3 (3)	C(18)	-C(13)	-C(26)	110.4 (3)
C(5)	-C(4)	-C(3)	108.3 (3)	C(15)	-C(14)	-C(8)	108.5 (3)
C(5)	-C(4)	-C(23)	109.2 (3)	C(15)	-C(14)	-C(13)	109.0 (3)
C(5)	-C(4)	-C(24)	109.8 (3)	C(15)	-C(14)	-C(27)	107.4 (3)
C(3)	-C(4)	-C(23)	108.4 (3)	C(8)	-C(14)	-C(13)	109.8 (2)
C(3)	-C(4)	-C(24)	111.2 (3)	C(8)	-C(14)	-C(27)	110.3 (3)
C(23)	-C(4)	-C(24)	109.9 (3)	C(13)	-C(14)	-C(27)	111.7 (3)
C(6)	-C(5)	-C(4)	115.3 (3)	C(16)	-C(15)	-C(14)	116.4 (3)
C(6)	-C(5)	-C(10)	120.9 (3)	C(17)	-C(16)	-C(15)	117.2 (4)
C(6)	-C(5)	-O(1)	112.2 (3)	C(18)	-C(17)	-C(16)	113.1 (3)
C(4)	-C(5)	-C(10)	121.1 (3)	C(18)	-C(17)	-C(22)	109.1 (3)
C(4)	-C(5)	-O(1)	113.4 (3)	C(18)	-C(17)	-C(28)	112.1 (3)
C(10)	-C(5)	-O(1)	59.2 (2)	C(16)	-C(17)	-C(22)	107.2 (3)
C(7)	-C(6)	-C(5)	115.3 (3)	C(16)	-C(17)	-C(28)	107.8 (3)
C(8)	-C(7)	-C(6)	111.1 (3)	C(22)	-C(17)	-C(28)	107.2 (3)
C(9)	-C(8)	-C(7)	108.7 (3)	C(19)	-C(18)	-C(13)	112.0 (3)
C(9)	-C(8)	-C(14)	116.6 (2)	C(19)	-C(18)	-C(17)	111.8 (3)
C(7)	-C(8)	-C(14)	114.0 (3)	C(13)	-C(18)	-C(17)	113.8 (3)
C(10)	-C(9)	-C(8)	108.3 (2)	C(20)	-C(19)	-C(18)	116.8 (3)
C(10)	-C(9)	-C(11)	109.9 (2)	C(21)	-C(20)	-C(19)	109.5 (4)
C(10)	-C(9)	-C(25)	105.6 (2)	C(21)	-C(20)	-C(29)	110.2 (4)
C(8)	-C(9)	-C(11)	108.4 (2)	C(21)	-C(20)	-C(30)	109.4 (4)
C(8)	-C(9)	-C(25)	115.0 (3)	C(19)	-C(20)	-C(29)	110.4 (4)
C(11)	-C(9)	-C(25)	109.5 (3)	C(19)	-C(20)	-C(30)	107.8 (4)
O(1)	-C(10)	-C(1)	110.9 (2)	C(29)	-C(20)	-C(30)	109.5 (4)
O(1)	-C(10)	-C(5)	59.4 (2)	C(22)	-C(21)	-C(20)	113.1 (4)
O(1)	-C(10)	-C(9)	114.9 (2)	C(17)	-C(22)	-C(21)	112.2 (4)
C(1)	-C(10)	-C(5)	120.6 (3)	C(32)	-C(31)	-O(2)	110.9 (4)
C(1)	-C(10)	-C(9)	116.4 (2)	C(32)	-C(31)	-O(3)	124.9 (4)
C(5)	-C(10)	-C(9)	120.0 (3)	O(2)	-C(31)	-O(3)	124.2 (4)
C(12)	-C(11)	-C(9)	113.8 (3)	C(3)	-O(2)	-C(31)	118.2 (3)
C(13)	-C(12)	-C(11)	113.0 (3)	C(5)	-O(1)	-C(10)	61.4 (2)
C(14)	-C(13)	-C(12)	107.9 (2)				

Fig. 1. Perspective view of 5 α ,10 α -epoxyalnusan-3 β -yl acetate (6).

imum above 210 nm, while the ^1H NMR spectrum revealed the presence of a doubly allylic methylene (δ 2.60, 2H; m) and an olefinic proton (δ 5.71, 1H; dd). The spectral data and mechanistic considerations lead to the structure, multiflora-5,8-dien-3 β -yl acetate for the main product (**24**). The proposed structure was supported by the mass spectral measurement; the appearance of the fragment peaks at m/z 239 (**A**), m/z 227 (**B**), and m/z 171 (**C**) indicates the presence of the 5,8-diene structure.



The seven minor products obtained by the $\text{BF}_3 \cdot \text{OEt}_2$ -catalyzed backbone rearrangement of **6** could not be identified, because of difficulty of the separation and a paucity of the material.

The diene (**24**) was treated with selenium dioxide¹² in boiling aqueous benzene to give a dehydrogenation product (**25**), the molecular formula, $\text{C}_{32}\text{H}_{48}\text{O}_2$, of which was given by the high-resolution mass spectrum. Since the ^1H NMR and UV spectra indicate the presence of a $\Delta^{5,7,9(11)}$ -triene moiety, the structure of the dehydrogenation product (**25**) is formulated as multiflora-5,7,9(11)-trien-3 β -yl acetate.

The backbone rearrangement of 5 α ,10 α -epoxyalnan-3 β -yl acetate (**6**) was shown to yield multiflora-5,8-dien-3 β -yl acetate (**24**) as the main rearranged product, no further rearranged product being obtained much enough to be characterized. Although it is not clear the reason why further migration did not occur efficiently, the following account could be proposed. On attack of $\text{BF}_3 \cdot \text{OEt}_2$, the 5 α ,10 α -epoxide ring would be cleaved to yield a carbonium ion on C-10 and a BF_3 -coordinated oxygen-function at C-5 α . A methyl group at C-9 β would migrate to C-10 and then a migration of $\text{C}_{8\alpha}\text{-H}$ to C-9 α would follow immediately to afford a carbonium ion on C-8. If the BF_3 -coordinated group is absent, it is expected to take place the further backbone rearrangement up to the C and D rings. However, since the BF_3 -coordinated group at C-5 α and the $\text{C}_{9\alpha}\text{-H}$ are located in a 1,3-diaxial relationship, the neighboring group participation could assist the abstraction of the $\text{C}_{9\alpha}\text{-H}$, while the competitive migration of $\text{C}_{14}\text{-Me}$ would be impeded, resulting in the interruption of the further backbone rearrangement.

The diene (**24**) in ethyl acetate was hydrogenated in the presence of 5% palladium on carbon for 3 d to give a hydrogenation product in 97% yield, which was shown to be a mixture of **26** and **27** in a ratio of 2:3 by GC examination. The mixture was subjected to

separation by repeating column chromatography on silica gel to afford isomultiflorenyl acetate (**26**) and its 5 β -H isomer (**27**). The spectral data of the former (**26**) were identical with those of literatures⁴) and two compounds (**26** and **27**) exhibited nearly the same mass spectra characteristic of multiflor-8-ene skeleton.¹³ Since the diene molecule (**24**) bends towards the α -side so much that the adsorption onto the surface of the catalyst was impeded, the hydrogenation from the α -side was hindered. On the other hand, the hydrogenation from the β -side was also hindered by the presence of 4 β - and 10 β -methyl groups. The fact that the hydrogenation had required a long reaction time could be explained by these two effects, which were estimated to be almost the same from the product ratio.

Isomultiflorenyl acetate (**26**) and its 5 β -H isomer (**27**) were hydrolyzed with alkali to give isomultiflorenol (**1**)^{6,14,15} and 5 β -isomultiflorenol (**28**), respectively.

Thus the conversion of dendropanoxide (**5**) into isomultiflorenol (**1**) was achieved in 18% overall yield (6 steps) through thermodynamically favorable pathways,¹⁶ which formally constitutes the total synthesis of isomultiflorenol (**1**).¹⁷

When the acetate mixture (**26** and **27**), obtained by the hydrogenation of the diene (**24**), was treated with 5% potassium hydroxide in methanol-tetrahydrofuran (5:1) at room temperature, the acetate (**26**) was easily hydrolyzed and afforded isomultiflorenol (**1**) within a half day, while most of the acetate (**27**) still remained intact; it required additional 4 d for completion of the hydrolysis of **27**.

Isomultiflorenol (**1**) and the 5 β -H isomer (**28**) were subjected to Collins oxidation to give isomultiflorenone (**29**) and the 5 β -H ketone (**30**), respectively. Isomultiflorenone (**29**)^{15,18} exhibits IR absorption band at 1710 cm^{-1} and the positive Cotton effect. 5 β -Isomultiflorenone (**30**) shows IR absorption band at 1715 cm^{-1} , intense fragment peaks at m/z 257 and m/z 245 characteristic of the multiflor-8-ene skeleton,¹³ and the negative Cotton effect.

Experimental¹⁹

Epoxidation of Alnus-5(10)-en-3 β -yl Acetate (4). Alnus-5(10)-en-3 β -ol (**7**), prepared from dendropanoxide (**5**), was acetylated with acetic anhydride in pyridine to give alnus-5(10)-en-3 β -yl acetate (**4**), mp 289–293 °C. The acetate (**4**; 224 mg) was dissolved in chloroform (20 ml) and treated with MCPBA (208 mg) and disodium hydrogenphosphate dodecahydrate ($\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$; ca. 5 mg) at 0 °C for 7 h. The usual work-up gave a residue (224 mg; 97% yield), which was purified by silica-gel (30 g) column chromatography. Elution with benzene afforded 5 α ,10 α -epoxyalnan-3 β -yl acetate (**6**), mp 272–273 °C (from $\text{CHCl}_3\text{-CH}_3\text{OH}$); IR (KBr) 1730, 1250, 1025, 990, and 980 cm^{-1} ; ^1H NMR (CDCl_3) δ =0.97 (3H, s), 0.99 (6H, s), 1.02 (6H, s), 1.03 (6H, s), 1.15 (3H, s), 2.00 (3H, s), and 4.77 (1H, dd, J =10

and 4 Hz); MS m/z (%) 484 (M^+ ; 5), 466 (14), 406 (100), 391 (42), 227 (22), 205 (32), and 202 (46); Found: m/z 484.3867. Calcd for $C_{32}H_{52}O_3$: M , 484.3914.

Epoxidation of Alnus-5(10)-en-3 β -ol (7). Alnus-5(10)-en-3 β -ol (**7**; 118 mg) in chloroform (10 ml) was treated with MCPBA (122 mg) and $Na_2HPO_4 \cdot 12H_2O$ (ca. 5 mg) at 0 °C for 4 h. The usual work-up afforded 5 α ,10 α -epoxyalnusan-3 β -ol (**9**; quantitative yield), mp 247–248 °C (from acetone) (decomp); IR (KBr) 3450, 1690, 1050, 1020, 1000, and 970 cm^{-1} ; 1H NMR ($CDCl_3$) δ =0.94 (6H, s), 1.00 (6H, s), 1.01 (3H, s), 1.03 (3H, s), 1.07 (3H, s), 1.15 (3H, s), and 3.58 (1H, dd, J =10 and 5 Hz); MS m/z (%) 442 (M^+ ; 3), 427 (7), 424 (47), 409 (14), 406 (9), 391 (36), 245 (25), 206 (100), 201 (32), 109 (50), and 95 (54).

5 α ,10 α -Epoxyalnusan-3 β -ol (**9**; 37 mg) was treated with acetic anhydride (1 ml) and pyridine (4 ml) at room temperature for 14 h to give **6** in 95% yield.

Epoxidation of Alnus-5(10)-en-3 β -yl Benzoate (8). Alnus-5(10)-en-3 β -ol (**7**; 33 mg) was benzoylated with benzoyl chloride (1 ml) and pyridine (5 ml) at room temperature for 1 h to give the benzoate (**8**; 36 mg), mp 273–274 °C (from $CHCl_3$ -acetone); IR (KBr) 1715, 1280, 1115, 705, and 685 cm^{-1} ; 1H NMR ($CDCl_3$) δ =0.96 (6H, s), 1.04 (12H, s), 1.14 and 1.18 (each 3H, s), 4.94 (1H, dd, J =10 and 4 Hz), and 7.35–8.14 (5H); MS m/z (%) 530 (M^+ ; 0.5), 515 (0.2), 408 (66), 393 (30), 365 (21), 205 (28), 203 (37), 190 (36), 189 (36), 187 (39), 175 (42), and 105 (100).

The benzoate (**8**; 33 mg) in chloroform (5 ml) was epoxidized with MCPBA (27 mg) and $Na_2HPO_4 \cdot 12H_2O$ (ca. 2 mg) at 0 °C for 3 h to afford 5 α ,10 α -epoxyalnusan-3 β -yl benzoate (**10**; 28 mg), mp 272–278 °C (from $CHCl_3$ - CH_3OH) (decomp); IR (KBr) 1715, 1275, 1115, and 710 cm^{-1} ; 1H NMR ($CDCl_3$) δ =0.95, 0.99, 1.02, 1.04, 1.06, 1.08 (each 3H, s), 1.19 (6H, s), 5.02 (1H, dd, J =11 and 4 Hz), and 7.37–8.13 (5H); MS m/z (%) 546 (M^+ ; 0.6), 528 (3), 406 (43), 391 (41), 274 (18), 259 (20), 205 (30), 201 (19), 187 (24), 185 (25), 171 (41), and 105 (100).

On treatment with lithium aluminium hydride, the epoxy benzoate (**10**; 24 mg) afforded 5 α ,10 α -epoxyalnusan-3 β -ol (**9**; 15 mg) identical with an authentic sample.

Epoxidation of Alnus-5(10)-en-3 α -ol (11). Alnus-5(10)-en-3 α -ol (**11**, 21 mg), mp 255–258 °C, was dissolved in chloroform (5 ml) and treated with MCPBA (22 mg) and $Na_2HPO_4 \cdot 12H_2O$ (ca. 2 mg) at 0 °C for 1.5 h. The usual work-up gave 5 α ,10 α -epoxyalnusan-3 α -ol (**13**; 20 mg), mp 272–276 °C (from C_6H_6 - CH_3OH) (decomp); IR (Nujol) 3480 cm^{-1} ; 1H NMR ($CDCl_3$) δ =0.95 (3H, s), 1.00 (9H, s), 1.02, 1.05 (each 3H, s), 1.17 (6H, s), 3.24 (1H, dt, J =11 and 3 Hz), and 3.52 (1H, d, J =11 Hz; disappeared on addition of D_2O); MS m/z (%) 442 (M^+ ; 0.8), 424 (79), 406 (17), 391 (46), 206 (100), 201 (48), 189 (38), 187 (35), 171 (35), 109 (65), and 95 (83).

5 α ,10 α -Epoxyalnusan-3 α -ol (**13**; 12 mg) was treated with acetic anhydride (3 ml) and pyridine (5 ml) at 120 °C for 4 h to give **14** in 53% yield.

Epoxidation of Alnus-5(10)-en-3 α -yl Acetate (12). Alnus-5(10)-en-3 α -yl acetate (**12**; 14 mg), mp 206–207 °C, in chloroform (3 ml) was epoxidized with MCPBA (21 mg) at 0 °C for 1.3 h to afford 5 α ,10 α -epoxyalnusan-3 α -yl acetate (**14**; 10 mg), mp 246–248 °C (from C_6H_6 - CH_3OH); IR (KBr) 1740, 1255, 1030, 995, and 925 cm^{-1} ; 1H NMR ($CDCl_3$) δ =0.93 (3H, s), 1.03 (18H, s), 1.15 (3H, s), 2.03 (3H, s), and 4.47 (1H, dd, J =7 and 4 Hz); MS m/z (%) 484 (M^+ ; 0.3), 409 (6), 406 (8),

391 (59), 248 (19), 227 (20), 205 (38), 201 (43), 189 (75), 187 (53), 137 (95), 109 (82), and 95 (100).

Epoxidation of Alnus-5(10)-en-3 α -yl Benzoate (15).

Alnus-5(10)-en-3 α -ol (**11**) was treated with benzoyl chloride and pyridine to afford the benzoate (**15**), mp 175–177 °C (from $CHCl_3$ - CH_3OH); IR (KBr) 1720, 1280, 1120, 755, and 710 cm^{-1} ; 1H NMR ($CDCl_3$) δ =0.96, 1.00, 1.01 (each 3H, s), 1.06, 1.09 (each 6H, s), 1.20 (3H, s), 4.96 (1H, dd, J =5 and 3 Hz), and 7.35–8.12 (5H); MS m/z (%) 530 (M^+ ; 4), 408 (93), 393 (36), 365 (33), 229 (21), 218 (24), 205 (39), 203 (37), 190 (39), 189 (45), 187 (40), 175 (39), and 105 (100).

Alnus-5(10)-en-3 α -yl benzoate (**15**; 302 mg) in chloroform (40 ml) was treated with MCPBA (246 mg) in the presence of $Na_2HPO_4 \cdot 12H_2O$ (ca. 10 mg) at 0 °C for 2 h. After the usual work-up, the reaction product was separated by column chromatography on silica gel (40 g) eluted with benzene to afford the major epoxide (**16**; 267 mg) and the minor epoxide (**17**; 35 mg). 5 α ,10 α -Epoxyalnusan-3 α -yl benzoate (**16**); mp 202–203 °C (from $CHCl_3$ - CH_3OH); IR (KBr) 1720, 1275, 1115, and 715 cm^{-1} ; 1H NMR ($CDCl_3$) δ =0.96, 1.00, 1.03, 1.06 (each 3H, s), 1.10 (6H, s), 1.15, 1.17 (each 3H, s), 4.72 (1H, dd, J =7 and 3 Hz), and 7.38–8.18 (5H); MS m/z (%) 546 (M^+ ; 2), 528 (19), 406 (32), 391 (64), 310 (16), 205 (26), 201 (26), 189 (37), 187 (31), 137 (40), and 105 (100). 5 β ,10 β -Epoxyalnusan-3 α -yl benzoate (**17**); mp 154–155 °C (from $CHCl_3$ - CH_3OH); IR (film) 1720, 1275, 1115, 1025, 940, and 710 cm^{-1} ; 1H NMR ($CDCl_3$) δ =0.97, 1.00, 1.02, 1.08 (each 3H, s), 1.09 (6H, s), 1.15, 1.20 (each 3H, s), 4.78 (1H, dd, J =5.5 and 3 Hz), and 7.33–8.18 (5H); MS m/z (%) 546 (M^+ ; 5), 424 (11), 406 (8), 391 (9), 288 (36), 274 (18), 273 (19), 219 (19), 218 (21), 205 (36), 189 (18), 185 (41), 137 (64), 109 (50), 105 (100), and 95 (61).

5 α ,10 α -Epoxyalnusan-3 α -yl benzoate (**16**; 22 mg) was treated with lithium aluminium hydride (5 mg) at room temperature for 30 min to give **13** in 68% yield.

5 β ,10 β -Epoxyalnusan-3 α -yl benzoate (**17**; 31 mg) was treated with a mixture of 5% potassium hydroxide (KOH) in methanol (6 ml) and tetrahydrofuran (THF) (2 ml) for 2 d to give 5 β ,10 β -epoxyalnusan-3 β -ol (**20**; 21 mg); mp 210–211 °C (from $CHCl_3$ - CH_3OH); IR (KBr) 3580, 1070, and 965 cm^{-1} ; 1H NMR ($CDCl_3$) δ =0.95 (6H, s), 1.02 (12H, s), 1.03, 1.17 (each 3H, s), and 3.41 (1H, dd, J =7 and 3 Hz); MS m/z (%) 442 (M^+ ; 10), 427 (12), 424 (70), 406 (10), 391 (12), 218 (24), 206 (100), 205 (40), 201 (50), 187 (25), 179 (31), 137 (41), 109 (54), and 95 (60).

5 β ,10 β -Epoxyalnusan-3 α -ol (**20**; 14 mg) was treated with acetic anhydride (1 ml) and pyridine (3 ml) at 100 °C for 4 h to give 5 β ,10 β -epoxyalnusan-3 α -yl acetate (**21**; 15 mg); mp 173–174 °C (from $CHCl_3$ - CH_3OH); IR (KBr) 1730, 1250, 1050, 1020, and 965 cm^{-1} ; 1H NMR ($CDCl_3$) δ =0.96 (6H, s), 0.98 (3H, s), 1.01 (9H, s), 1.05, 1.07, 2.03 (each 3H, s), and 4.57 (1H, dd, J =7 and 3 Hz); MS m/z (%) 484 (M^+ ; 41), 469 (16), 424 (19), 409 (18), 406 (17), 391 (12), 342 (11), 288 (98), 274 (62), 273 (60), 259 (21), 245 (28), 218 (79), 205 (91), 137 (100), 109 (59), and 95 (56).

Sharpless Epoxidation of Alnus-5(10)-en-3 α -ol (11) and -3 β -ol (7).

Alnus-5(10)-en-3 α -ol (**11**; 35 mg) was dissolved in benzene (7 ml) and treated with the benzene solution of *t*-butyl hydroperoxide (80 μ l; 2.35 mmol/ml)^{10a} and $VO(acac)_2$ (ca. 1 mg) at room temperature in nitrogen atmosphere for 4 h. The usual work-up afforded 5 α ,10 α -epoxyalnusan-3 α -ol (**13**; 32 mg), which was identical with that obtained by the MCPBA-epoxidation of **11**.

Alnus-5(10)-en-3 β -ol (**7**; 47 mg) was treated with the ben-

zene solution of *t*-butyl hydroperoxide (100 μ l) and VO(acac)₂ (ca. 1 mg) under the same conditions for 7 h to give 5 β ,10 β -epoxyalnanus-3 β -ol (**18**; 34 mg); mp 199–200 °C (from acetone); IR (film) 3380, 1055, 1030, 995, and 980 cm⁻¹; ¹H NMR (CDCl₃) δ =0.97 (6H, s), 1.03 (3H, s), 1.06 (9H, s), 1.10, 1.18 (each 3H, s), 2.71 (1H, br; disappeared on addition of D₂O), and 3.17 (1H, br; changed into a triplet (J =5 Hz) on addition of D₂O); MS m/z (%) 442 (M⁺; 2), 424 (91), 409 (18), 406 (30), 391 (100), 227 (49), 206 (87), 205 (47), 201 (55), 189 (76), 187 (62), 137 (65), 109 (84), and 95 (95); high resolution MS m/z 442.3797. Calcd for C₃₀H₅₀O₂: M, 442.3809.

5 β ,10 β -Epoxyalnanus-3 β -ol (**18**; 30 mg) was treated with acetic anhydride (1 ml) and pyridine (2 ml) at room temperature for 40 h to give 5 β ,10 β -epoxyalnanus-3 β -yl acetate (**22**; 25 mg); mp 258.5–259.5 °C (from CHCl₃-CH₃OH); IR (KBr) 1735, 1250, and 1025 cm⁻¹; ¹H NMR (CDCl₃) δ =0.96 (6H, s), 1.01 (9H, s), 1.04 (6H, s), 1.17 (3H, s), 2.03 (3H, s), and 4.36 (1H, dd, J =11 and 4 Hz); MS m/z (%) 484 (M⁺; 12), 469 (8), 466 (28), 451 (6), 424 (22), 409 (12), 406 (100), 391 (51), 342 (33), 288 (20), 274 (40), 259 (34), 218 (43), 205 (73), 137 (72), 109 (78), and 95 (83).

5 β ,10 β -Epoxyalnanus-3 β -ol (**18**; 31 mg) was benzoylated with benzoyl chloride (0.1 ml) and pyridine (2 ml) at room temperature for 1.5 h to give 5 β ,10 β -epoxyalnanus-3 β -yl benzoate (**23**; 23 mg); mp 245–246 °C (from CHCl₃-CH₃OH); IR (KBr) 1720, 1275, 1115, 1025, and 710 cm⁻¹; ¹H NMR (CDCl₃) δ =0.97, 1.03, 1.07, 1.20 (each 6H, s), 4.62 (1H, dd, J =10 and 5 Hz), and 7.38–8.12 (5H); MS m/z (%) 546 (M⁺; 12), 424 (49), 409 (22), 406 (34), 391 (16), 342 (18), 288 (26), 274 (20), 273 (22), 249 (17), 218 (35), 205 (53), 137 (85), 105 (100), and 95 (52).

Oxidation of 5 α ,10 α -Epoxyalnanus-3 β -ol (9) and 5 α ,10 α -Epoxyalnanus-3 α -ol (13). 5 α ,10 α -Epoxyalnanus-3 β -ol (**9**; 56 mg) and -3 α -ol (**13**; 22 mg) were oxidized with Collins reagent to give the same product, 5 α ,10 α -epoxyalnanus-3-one (**19**; 43 mg and 11 mg, respectively), mp 261–263 °C (from CHCl₃-CH₃OH) (decomp); IR (KBr) 1710 and 980 cm⁻¹; ¹H NMR (CDCl₃) δ =0.94, 0.99 (each 3H, s), 1.04 (6H, s), 1.11, 1.13, 1.15, 1.17 (each 3H, s), and 2.24 (2H, t, J =6 Hz); MS m/z (%) 440 (M⁺; 12), 425 (11), 422 (19), 407 (9), 205 (97), 204 (87), 177 (53), 137 (44), 123 (57), 109 (81), and 95 (100).

Backbone Rearrangement of 5 α ,10 α -Epoxyalnanus-3 β -yl Acetate (6). 5 α ,10 α -Epoxyalnanus-3 β -yl acetate (**6**; 121 mg) in benzene (30 ml) was treated with BF₃·OEt₂ (38 μ l; 1.1 equiv) at room temperature in nitrogen atmosphere for 30 min. The reaction product, after addition of a saturated sodium hydrogencarbonate solution, was worked up as usual to give a residue (117 mg). The residue showed eight peaks at 12.8, 16.5, 18.9 (a main peak; a ratio of the product was estimated at ca. 80% from the peak height), 21.1, 22.1, 23.9, 25.7, and 27.9 min on HPLC (column: μ PORASIL, solvent system; 1% ether-hexane, 1 ml/min). The residue was chromatographed on alumina (Alumina Woelm N, Akt I, 35 g; impregnated with 15% silver nitrate). Elution with 5–10% ethyl acetate-hexane afforded a mixture (ca. 24 mg) of the minor products and the product, multiflora-5,8-dien-3 β -yl acetate (**24**; 81.4 mg). The latter was purified by column chromatography on silica gel eluted with hexane-benzene to give pure **24**, mp 190–193 °C (from C₆H₆-CH₃OH); IR (KBr) 1735, 1250, 1035, 1020, and 990 cm⁻¹; ¹H NMR (CDCl₃) δ =0.98 (6H, s), 1.01 (3H, s), 1.10 (6H, s), 1.12, 1.14, 1.18, 2.04 (each 3H, s), 2.60 (2H, m), 4.50

(1H, dd, J =8 and 6 Hz), and 5.71 (1H, dd, J =5 and 3 Hz); ¹³C NMR (CDCl₃) δ =19.2, 21.1, 21.3, 24.1, 25.1, 25.2, 25.8, 27.1, 27.6, 28.3, 30.9, 31.1, 31.7, 33.1, 33.8, 34.2, 34.5, 34.5, 36.8, 36.8, 37.3, 38.4, 40.4, 40.7, 44.2, 79.1, 120.2, 131.1, 134.0, 146.4, and 170.7; MS m/z (%) 466 (M⁺; 5), 406 (15), 391 (100), 239 (13), 227 (28), 187 (18), 185 (20), and 171 (43); high resolution MS m/z 466.3791 (Calcd for C₃₂H₅₀O₂: M, 466.3809), m/z 239.1798 (Calcd for C₁₈H₂₃: 239.1798), m/z 227.1778 (Calcd for C₁₇H₂₃: 227.1798), and m/z 171.1207 (Calcd for C₁₃H₁₅: 171.1174).

Dehydrogenation of Multiflora-5,8-dien-3 β -yl Acetate (24).

The diene (**24**; 39 mg) was heated with selenium dioxide in a mixture of benzene (5 ml) and water (5 drops) under reflux for 38 h to give multiflora-5,7,9(11)-trien-3 β -yl acetate (**25**; 22 mg), mp 211–214 °C (from CHCl₃-CH₃OH); IR (KBr) 1740, 1250, 1035, 1005, 980, and 850 cm⁻¹; ¹H NMR (CDCl₃) δ =0.84, 0.96, 0.99, 1.02, 1.06, 1.09 (each 3H, s), 1.21 (6H, s), 2.07 (3H, s), 4.57 (1H, dd, J =6 and 5 Hz), 5.38 (1H, m), 5.57 (1H, d, J =6 Hz), and 5.89 (1H, d, J =6 Hz); UV λ (C₂H₅OH) 307 (ϵ 11600) and 317 nm (12200); MS m/z (%) 464 (M⁺; 7), 404 (100), 389 (21), 251 (26), 237 (26), and 225 (80); high resolution MS m/z 464.3649 (Calcd for C₃₂H₄₈O₂: M, 464.3654), m/z 237.1645 (Calcd for C₁₈H₂₁: 237.1643), and m/z 225.1661 (Calcd for C₁₇H₂₁: 225.1644).

Hydrogenation of Multiflora-5,8-dien-3 β -yl Acetate (24).

A solution of multiflora-5,8-dien-3 β -yl acetate (**24**; 103 mg) in ethyl acetate (70 ml) was hydrogenated in the presence of 5% palladium on carbon (470 mg) for 3 d to give hydrogenated products (101 mg), which showed two peaks at 16.3 and 21.4 min (peak height ratio 3:2) on GC examination (column: Dexsil 300 GC, 2%, 1.5 m) and two peaks at 20.2 and 22.2 min (peak height ratio 2:3) on HPLC examination. (column: μ PORASIL, solvent system: 0.8% ether-hexane, 1 ml/min). The mixture was separated by repeating column chromatography on silica gel to give isomultiflorenyl acetate (**26**; 40 mg) and 5 β -isomultiflorenyl acetate (**27**; 60 mg). Isomultiflorenyl acetate (**26**); mp 223–225 °C (from CH₂Cl₂-CH₃OH); IR (KBr) 1735, 1455, 1380, 1255, 1025, 1005, and 990 cm⁻¹; ¹H NMR (CDCl₃) δ =0.88, 0.96, 0.98 (each 6H, s), 1.06, 1.07, (each 3H, s), 2.03 (3H, s), and 4.48 (1H, dd, J =11 and 5 Hz); MS m/z (%) 468 (M⁺; 58), 453 (15), 408 (21), 393 (23), 301 (28), 289 (17), 241 (26), 229 (27), 218 (64), 205 (100), 203 (47), and 189 (23). 5 β -Isomultiflorenyl acetate (**27**); mp 151–152 °C (from CH₂Cl₂-CH₃OH); IR (film) 1730, 1245, and 1030 cm⁻¹; ¹H NMR (CDCl₃) δ =0.94 (3H, s), 0.97, 1.03 (each 6H, s), 1.06 (3H, s), 1.08 (6H, s), 2.04 (3H, s), and 4.54 (1H, t, J =3 Hz); MS m/z (%) 468 (M⁺; 74), 453 (58), 408 (21), 393 (62), 301 (57), 289 (29), 241 (100), 229 (93), 205 (94), 203 (49), and 189 (58); high resolution MS m/z 468.3960. Calcd for C₃₂H₅₂O₂: M, 468.3965.

Hydrolysis of Isomultiflorenyl Acetate (26) and Its 5 β -H Isomer (27).

Isomultiflorenyl acetate (**26**; 15 mg) was treated with a mixture of 5% KOH in methanol (50 ml) and THF (10 ml) at room temperature in nitrogen atmosphere for 1 d. The usual work-up gave isomultiflorenol (**1**; 13 mg); mp 182–183 °C (from CHCl₃-CH₃OH); IR (Nujol) 3350 and 1025 cm⁻¹; ¹H NMR (CDCl₃) δ =0.80 (3H, s), 0.97 (9H, s), 0.99, 1.00, 1.06, 1.07 (each 3H, s), and 3.23 (1H, dd, J =11 and 5 Hz); MS m/z (%) 426 (M⁺; 100), 411 (29), 408 (31), 393 (43), 259 (83), 247 (55), 241 (56), 229 (65), 218 (77), 205 (98), 204 (50), 191 (40), and 189 (44); high resolution MS m/z 426.3863. Calcd for C₃₀H₅₀O: M, 426.3862.

5 β -Isomultiflorenyl acetate (**27**; 25 mg) was treated with

5% KOH in methanol-THF (5:1, 40 ml) under the same conditions as above for 4 d to afford 5 β -isomultiflorenol (**28**; 20 mg); mp 159–159.5 °C (from ether-CH₃OH); IR (film) 3430, 1060, 950, and 935 cm⁻¹; ¹H NMR (CDCl₃) δ =0.98 (6H, s), 1.04 (12H, s), 1.09 (6H, s), and 3.33 (1H, t-like, J =3 Hz); MS m/z (%) 426 (M⁺; 32), 411 (92), 408 (19), 393 (63), 259 (87), 247 (38), 241 (100), 229 (85), 205 (65), 203 (37), 189 (87), 109 (90), and 95 (88); high resolution MS m/z 426.3907 (Calcd for C₃₀H₅₀O: M, 426.3862), m/z 259.2060 (Calcd for C₁₈H₂₇O: 259.2060), m/z 247.2065 (Calcd for C₁₇H₂₇O: 247.2062), m/z 241.1944 (Calcd for C₁₈H₂₅: 241.1955), and m/z 229.1967 (Calcd for C₁₇H₂₅: 229.1956).

Oxidation of Isomultiflorenol (1) and 5 β -Isomultiflorenol (28).

Isomultiflorenol (**1**; 17 mg) in dichloromethane (5 ml) was oxidized with Collins reagent (4 ml; 17 eq) at room temperature for 16 min to give isomultiflorenone (**29**; 16 mg); mp 189–193 °C (from CHCl₃-CH₃OH); IR (KBr) 1710 cm⁻¹; ¹H NMR (CDCl₃) δ =0.97 (6H, s), 0.99 (3H, s), 1.06 (6H, s), 1.10 (9H, s), and 2.40–2.62 (2H, m); MS m/z (%) 424 (M⁺; 16), 409 (7), 257 (48), 245 (39), 205 (100), 109 (38), and 95 (54); CD (c 0.016, CHCl₃, Amb. temp.) [θ]₂₉₁ +1580 and [θ]₃₂₃ -110.

5 β -Isomultiflorenol (**28**; 18 mg) was oxidized with Collins reagent (4 ml; 16 eq) under the same conditions as above to give 5 β -isomultiflorenone (**30**; 17 mg), mp 143–144 °C (from ether-CH₃OH); IR (KBr) 1715 cm⁻¹; ¹H NMR (CDCl₃) δ =0.97 (6H, s), 1.02 (3H, s), 1.10 (6H, s), 1.11, 1.14, 1.16 (each 3H, s) and 2.16–2.40 (2H, m); MS m/z (%) 424 (M⁺; 16), 409 (11), 257 (73), 245 (60), 205 (100), 109 (39), and 95 (56); CD (c 0.016, CHCl₃, Amb. temp) [θ]₃₁₄ -750, [θ]₃₀₅ -880, and [θ]₂₇₃ +120.

References

- 1) A preliminary account of this report: M. Takai, M. Tori, T. Tsuyuki, T. Takahashi, A. Itai, and Y. Iitaka, *Chem. Pharm. Bull.*, **32**, 2464 (1984).
- 2) M. Tori, M. Takai, Y. Matsumoto, Y. Moriyama, T. Tsuyuki, T. Takahashi, A. Itai, and Y. Iitaka, *Chem. Lett.*, **1983**, 527; M. Tori, M. Takai, Y. Matsumoto, Y. Moriyama, T. Tsuyuki, T. Takahashi, H. Ohnishi, A. Itai, and Y. Iitaka, *Bull. Chem. Soc. Jpn.*, **57**, 2490 (1984).
- 3) T. Itoh, T. Shigemoto, N. Shimizu, T. Tamura, and T. Matsumoto, *Phytochemistry*, **21**, 2414 (1982).
- 4) L. Cattel, G. Balliano, O. Caputo, and F. Viola, *Planta Med.*, **41**, 328 (1981).
- 5) J. Vaquette, J. L. Pousset, A. Cavé, P. Delaveau, and R. R. Paris, *Ann. Pharm. Fr.*, **31**, 49 (1973).
- 6) R. T. Aexel, R. B. Ramsey, and H. J. Nicholas, *Phytochemistry*, **11**, 2353 (1972).
- 7) H. N. Khastgir and P. Sengupta, *Chem. Ind. (London)*, **1961**, 1077.
- 8) H. R. Arthur and W. H. Hui, *J. Chem. Soc.*, **1961**, 551; J. H. Block and G. H. Constantine, Jr., *Phytochemistry*, **11**, 3279 (1972).
- 9) Dendropanoxide (**5**) was obtained from leaves of *Gilibertia triflidas* MAKINO, which were collected at the Botanical Gardens, Faculty of Science, the University of Tokyo. The authors would like to thank Mr. Eiichi Ishii for collection of leaves of the plant.
- 10) a) K. B. Sharpless and T. R. Verhoeven, *Aldrichimica Acta*, **12**, 63 (1979); b) K. B. Sharpless and R. C. Michaelson, *J. Am. Chem. Soc.*, **95**, 6136 (1973); c) S. Tanaka, H. Yamamoto, H. Nozaki, K. B. Sharpless, R. C. Michaelson, and J. D. Cutting, *J. Am. Chem. Soc.*, **96**, 5254 (1974).
- 11) The complete F_o - F_c data, anisotropic thermal parameters for non-hydrogen atoms, atomic positional parameters and isotropic thermal parameters for hydrogen atoms are deposited as Document No. 8505 at the Office of the Editor of Bull. Chem. Soc. Jpn.
- 12) A. C. Paton, F. S. Spring, and R. Stevenson, *J. Chem. Soc.*, **1958**, 2640.
- 13) H. Budzikiewicz, J. M. Wilson, and C. Djerassi, *J. Am. Chem. Soc.*, **85**, 3688 (1963).
- 14) S. H. Rizvi, A. Shueb, R. S. Kapil, and S. P. Popli, *Phytochemistry*, **19**, 2409 (1980).
- 15) P. Sengupta and H. N. Khastgir, *Tetrahedron*, **19**, 123 (1963).
- 16) Corey *et al.* reported a partial synthesis of multiflorenol from β -amyryn via energetically unfavorable pathways. I. Agata, E. J. Corey, A. G. Hortmann, J. Klein, S. Proskow, and J. J. Ursprung, *J. Org. Chem.*, **30**, 1698 (1965). On Hydrogenation in acetic acid in the presence of a platinum catalyst, multiflorenol is isomerized to isomultiflorenol (**1**).^{7,15)}
- 17) Conversion of friedelin into dendropanoxide (**5**): M. Tori, T. Torii, K. Tachibana, S. Yamada, T. Tsuyuki, and T. Takahashi, *Bull. Chem. Soc. Jpn.*, **50**, 469 (1977). Total synthesis of friedelin: R. E. Ireland and D. M. Walba, *Tetrahedron Lett.*, **1976**, 1071.
- 18) K. Seifert, H. Budzikiewicz, and K. Schreiber, *Pharmazie*, **31**, 816 (1976).
- 19) General procedures are the same as those described in lit.2.