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Studies on the Constituents of the Crude Drug "Fritillariae Bulbus." III.[1] On the Diterpenoid Constituents of Fresh Bulbs of *Fritillaria thunbergii* Miq.

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In addition to *trans*-communol and *trans*-communic acid (obtained in the form of the methyl ester), seven new diterpenoids were isolated as non basic constituents from fresh bulbs of *Fritillaria thunbergii* Miq. (Liliaceae). Their structures were determined to be isopimaran-19-ol (**3**), isopimaran-19-oic acid [obtained in the form of the methyl ester (**4**)], *ent*-kauran-16β,17-diol (**5**), *ent*-kauran-16α,17-diol (**6**), *ent*-16β,17-epoxy-kaurane (**7**), *ent*-16α-methoxy-kauran-17-ol (**8**), and *ent*-kaur-15-en-17-ol (**9**).

Keywords——*Fritillaria thunbergii* Miq.; isopimarane-type diterpenoid; *ent*-kaurane-type diterpenoid; ^{1}H-NMR; ^{13}C-NMR

Fritillaria thunbergii Miq. (Liliaceae) is a Chinese plant cultivated in Japan. The bulbs which are treated with lime then bleached in the sun are called "Bai-mo" in Japanese and are used as a principle in Chinese medicine.

As for the constituent alkaloids of fresh bulbs of *Fritillaria thunbergii* Miq. grown in Japan, Fukuda isolated verticine, verticinone, verticilline and an amorphous base.[2] Morimoto and Kimata obtained peimine (verticine), and its glucoside, peiminoside.[3] The structures of verticine and verticinone were determined by Ito *et al.*[4] Recently, Kaneko and Mitsuhashi isolated isoverticine (the 6-epimer of verticine)[5] and we identified a minor alkaloid, 11-deoxo-6-oxo-5α,6-dihydrojervine.[6] From the aerial parts of this plant, three glycosidal Solanum alkaloids (basic steroid saponins) were isolated and characterized together with minor amounts of two alkaloids, verticine and verticinone.[1] However, the non basic constituents have not been examined.

This paper describes the structure elucidation of diterpenoids isolated from the fresh bulbs of *Fritillaria thunbergii* Miq.

The sliced fresh bulbs (19.6 kg), cultivated in Nara prefecture, were collected in May and extracted with MeOH. The extractives were fractionated and purified according to the procedure shown in Chart 1 to give nine kinds of diterpenoids. Compounds (Compds.) II and IV were obtained as their methyl ester derivatives after methylation.

Compds. I[$C_{20}H_{32}O$, a colorless oil, $[\alpha]_D$ +14.5° ($CHCl_3$)] (**1**) and II [$C_{21}H_{32}O_2$, mp 104—105°C, $[\alpha]_D$ +48.0° ($CHCl_3$)] (**2**) were identified as *trans*-communol and *trans*-communic acid methyl ester from their physical and spectral data[7] (Chart 2).

Compds. III[$C_{20}H_{32}O$, mp 86°C, $[\alpha]_D$ −39.0° ($CHCl_3$)] (**3**) and IV [$C_{21}H_{32}O_2$, colorless oil, $[\alpha]_D$ +26.7° ($CHCl_3$) (**4**) showed the signals of three tertiary (*tert*) methy groups (excluding the signal of the methyl ester of **4**), one *exo*-methylene, and one tri-substituted double bond in the proton nuclear magnetic resonance (^{1}H-NMR) spectrum (Table I).

Compd. **3** was derived from **4** by treatment with $LiAlH_4$ in tetrahydrofuran (THF). Thus, **3** and **4** were considered to be a tricyclic diterpenoid alcohol and the corresponding acid methyl ester, respectively. Comparison of the ^{1}H-NMR spectral data of **3** with those of pimarinol (**11**),[8] isopimarinol (**12**)[9] and sandaracopimarinol (**13**),[10] which are representative diterpenoid monoalcohols, showed good similarity between **3** and **12**, except for the downfield shift of the 4-*methyl* (δ 0.97) and hydroxymethyl (δ 3.49 and 3.90, each doublet, J=11 Hz) groups (Chart 3). These results indicated the presence of axial hydroxymethyl. Thus, **3** and **4** were assumed

to be isopimarane-7,15-diene type diterpenoids bearing an O-function at C-19.[11]

The electron impact mass (EI-MS) spectrum of **4** lacked the ion peak at *m/z* 121, $[C_9H_{13}]^+$, which appeared as the base peak due to the C-ring in pimaric acid methyl ester (**14**) and sandaracopimaric acid methyl ester (**15**), both of which contain a double bond at C-8/C-14.[12]

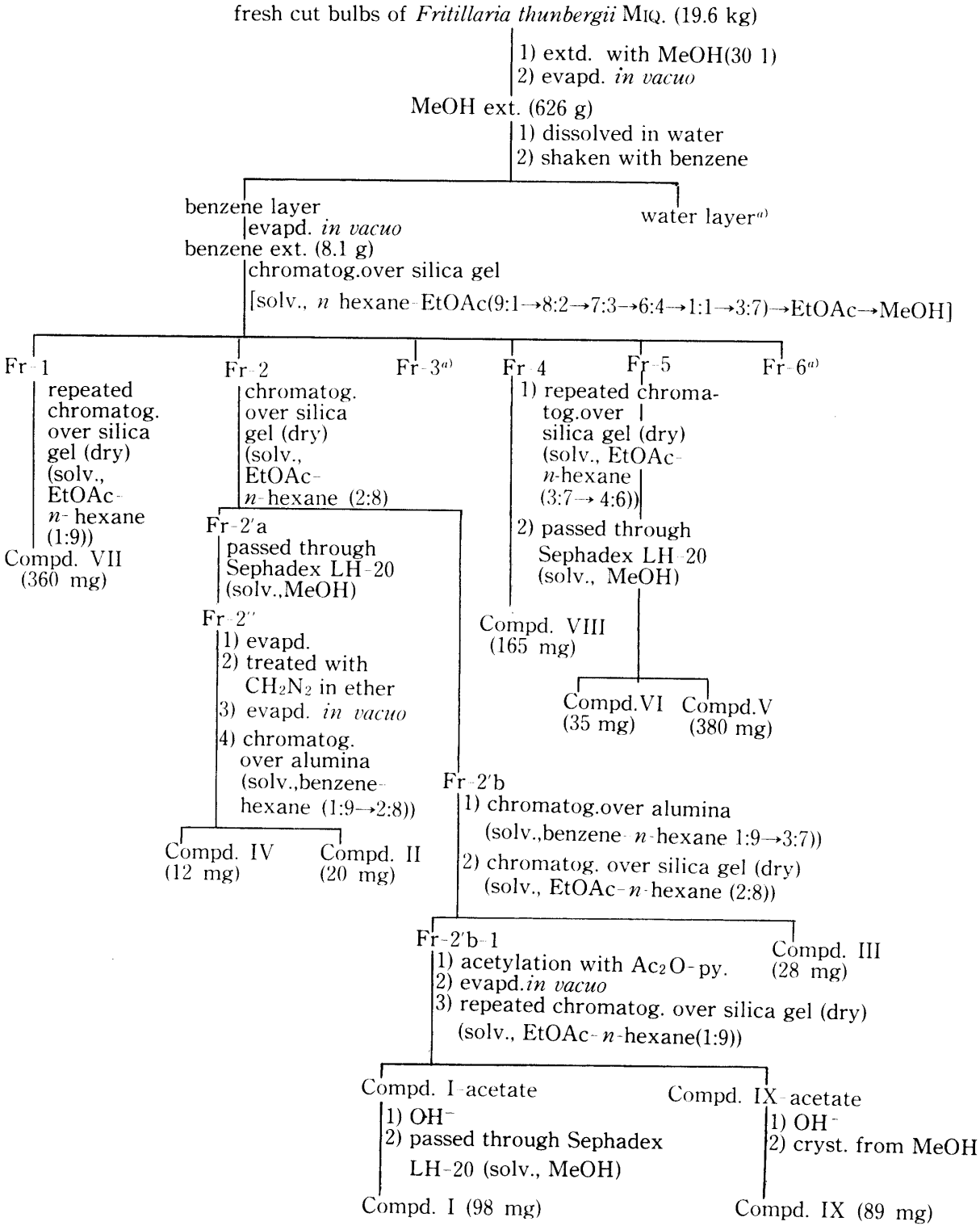
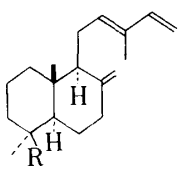
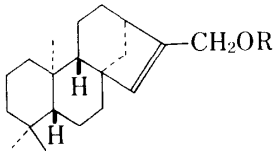


Chart 1. Isolation of Diterpenoids

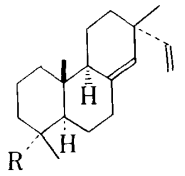
a) see Part VI of this series.



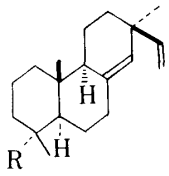
1 : R=CH_2OH
2 : R=$COOCH_3$



9 : R=H
10 : R=Ac

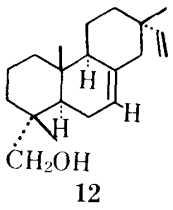


13 : R=CH_2OH
15 : R=$COOCH_3$



14 : R=$COOCH_3$

Chart 2



12

tert-CH_3	$H_2C=CH_2$
0.86	4.86
0.86	4.95
0.89	5.75
	(J=17 Hz, 10 Hz and 2 Hz)
$C=CH$	CH_2OH
5.28	3.08
	3.31
	(d, J=11 Hz)

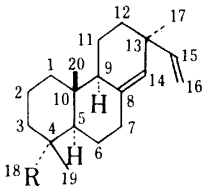
Chart 3. ^{1}H-NMR Spectral Data for **12**[9] (ppm)

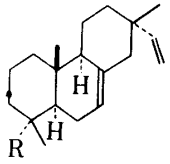
TABLE I. ^{1}H-NMR Spectral Data for **3** and **4**

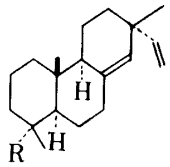
3 (ppm)		**4** (ppm)	
0.85 0.85 0.97	*tert*-CH_3	0.70 0.87 1.21	*tert*-CH_3
3.49 3.90	$-CH_2OH$	3.65	$-COOCH_3$
(each 1H, d, J=11 Hz)			
4.85 (C) 4.94 (B) 5.81 (A)	$H_2C=CH$	4.85 (C) 4.94 (B) 5.81 (A)	$H_2C=CH$
(each 1H, J_{AB}=17 Hz, J_{AC}=10 Hz, J_{BC}=2 Hz)		(each 1H, J_{AB}=17 Hz, J_{AC}=10 Hz, J_{BC}=2 Hz)	
5.36 (1H, t)		5.40 (1H, t)	

The carbon nuclear magnetic resonance (^{13}C-NMR) spectral data of **3** and **4** were very similar to those of **12**, isopimaric acid (**16**), and isopimara-7,15-dien (**17'**), except for the chemical shifts of C-18 and C-19 (Table II). Thus, it was confirmed that **3** and **4** are isopimarane type diterpenoids.

TABLE II. ^{13}C-NMR Spectral Data for 3 and 4[a,b]







11: R=CH_2OH **14′**: R=COOH **16**: R=COOH **16′**: R=COOH
17: R=CH_3 **17′**: R=CH_3

C	11	12	3	14′	16′	16	4	17	17′
1	38.3	39.6	39.7(t)	38.4	38.6	39.2	39.8(t)	39.7	40.1
2	18.5	18.5	18.4(t)	18.3	18.5	17.9	19.6(t)	19.4	19.0
3	35.5	35.8	35.2(t)	37.1	37.5	37.2	38.2(t)	42.5	42.5
4	37.9	37.6	37.7(s)	47.2	47.6	46.4	43.8(s)	33.5	33.1
5	47.5	43.7	45.9(d)	48.7	49.1	45.4	51.0(d)	55.2	50.5
6	22.5	23.5	22.9(t)	24.9	15.5	25.7	24.4(t)	22.9	23.5
7	33.5	121.5	121.3(d)	35.5	35.5	121.3	121.1(d)	36.3	121.5
8	138.1	135.3	135.2(s)	136.2	138.5	135.6	134.4(s)	138.8	135.2
9	51.5	52.0	52.0(d)	50.7	51.9	52.4	51.6(d)	51.8	52.2
10	38.8	35.4	35.2(s)	38.1	38.1	35.5	35.6(s)	38.8	35.6
11	19.3	20.5	20.3(t)	18.8	19.5	20.5	20.9(t)	19.1	20.3
12	36.0	36.5	36.0(t)	34.6	36.0	36.0	36.3(t)	36.3	36.4
13	39.0	36.9	36.8(s)	37.4	39.0	37.5	36.8(s)	38.8	37.0
14	128.1	46.4	45.9(t)	129.3	128.2	46.5	46.1(t)	128.1	46.3
15	147.0	150.0	149.9(d)	149.9	147.8	150.7	149.9(d)	147.7	149.9
16	113.1	109.5	108.9(t)	110.5	113.2	109.7	109.0(t)	112.9	109.5
17	29.8	21.8	21.4(q)	26.2	29.2	21.9	21.4(q)	29.8	21.8
18	71.7	71.9	26.9(q)	185.3	185.7	183.9	28.9(q)	34.5	33.9
19	18.3	18.5	64.7(t)	16.8	17.6	17.5	177.4(s)	22.5	22.6
20	15.6	15.9	16.1(q)	15.3	15.4	15.7	14.1(q)	14.9	15.2

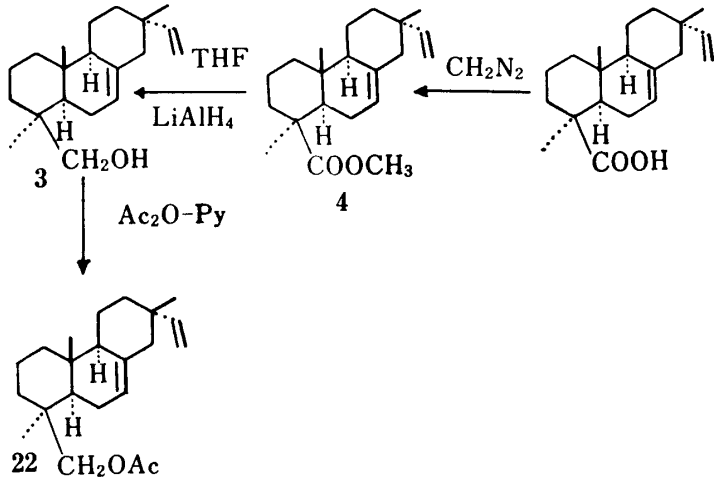
a) Reference substances :[13] **11**, **12**, pimaric acid (**14′**), sandaracopimaric acid (**16′**), **16**, pimara-8 (14),15-diene (**17**) and **17′**.
b) Solvent: **3**, **4**, **14′** and **16′** ($CDCl_3$), **11**, **12**, **16**, **17** and **17′** (CCl_4).

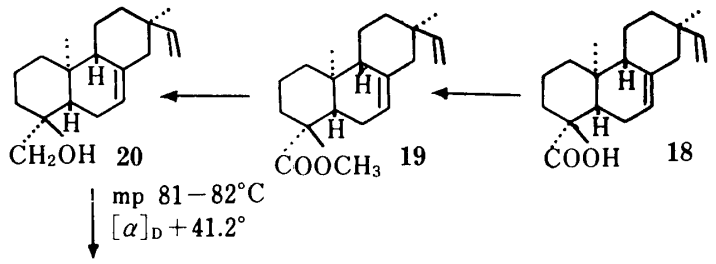
Aiyar and Seshadri obtained oblongifolic acid (**18**) from the Euphorbiaceous plant *Croton oblongifolium*, and determined the structure to be *ent*-isopimaran-19-oic acid.[14] They also obtained the methyl ester (**19**), monoalcohol (**20**) and monoacetate (**21**) of **18**, and the physical properties of **19** through **21** were identical with those of **4**, **3** and 3-acetate (**22**), respectively, except for optical rotations. Thus, **3** and **4** are isopimaran-19-ol and isopimaran-19-oilc acid methyl ester, respectively (Chart 4).

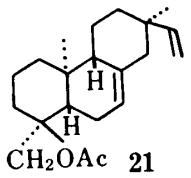
Compds. V [$C_{20}H_{34}O_2$, mp 188—189°C, $[\alpha]_D$ −47.0° ($CHCl_3$)] (**5**) and VI [$C_{20}H_{34}O_2$, mp 177°C, $[\alpha]_D$ −45.5° ($CHCl_3$)] (**6**) showed an infrared (IR) absorption band due to the hydroxy group, and their ^{1}H-NMR spectra showed signals due to three *tert* methyl and one hydroxymethyl groups. Thus, **5** and **6** were considered to be tetracyclic diterpenoids having two O-functions (Table III).

On acetylation with Ac_2O–pyridine at room temperature, **5** and **6** each yielded a monoacetate, **23** and **24**, and their IR spectra still showed the presence of a hydroxy group. Therefore, it was clarified that **5** and **6** each contain one secondary and one *tert* hydroxy group.

On treatment with HIO_4 in MeOH, **5** and **6** yielded the same product (**25**) [$C_{19}H_{30}O$, mp 117—118°C, $[\alpha]_D$ −29.0° ($CHCl_3$)], which was identified as *ent*-17-norkauran-16-one by comparison with an authentic sample.[15] Consequently, **5** and **6** are *ent*-kaurane type diterpenoids, which have hydroxy groups at C-16 and C-17 (Chart 5). The ^{13}C-NMR signals of C-1 through C-11, C-14, C-18, C-19 and C-20 of compounds **5** and **6** (Table IV) were similar to those of *ent*-







	tert-CH_3	$H_2C=CH_2$	$C=C$
	0.70	4.84	5.38
19:	0.87	4.89	
	1.20	5.83	
	0.87	4.87	5.38
20:	0.87	4.93	
	0.97	5.86	
	0.87	4.86	5.37
21:	0.87	4.91	
	0.95	5.85	
		(ppm)	

Chart 4

TABLE III. ^{1}H-NMR Spectral Data for **5**, **6**, **7**, **8**, and **9**

5 (ppm)		**6** (ppm)		**7** (ppm)	
0.80 0.84 1.02	*tert*-CH_3	0.80 0.84 1.03	*tert*-CH_3	0.83 0.87 1.05	*tert*-CH_3
3.65 3.80	$-CH_2OH$	3.37 3.51	$-CH_2OH$	2.79 2.84	$C(H)-C(H)-O$
(each 1H, d, $J=11$ Hz)		(each 1H, d, $J=12$ Hz)		(each 1H, d, $J=5$ Hz)	

8 (ppm)		9 (ppm)	
0.79 0.84 1.01	*tert*-CH_3	0.81 0.86 1.05	*tert*-CH_3
3.15	$-OCH_3$	4.17 4.18	$-CH_2OH$
3.70 3.72	$-CH_2OH$	(each 1H, s)	
(each 1H, m)		5.36 (1H, m)	

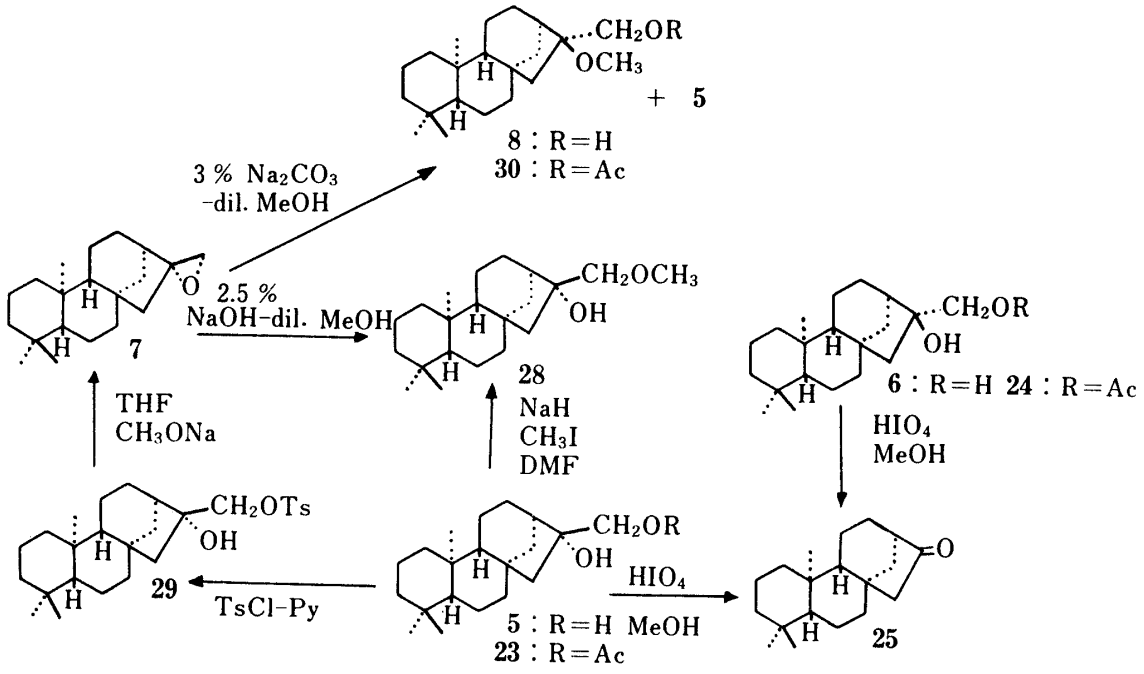


Chart 5

kaurane (**26**).[16] However, the chemical shifts of C-12, C-13, C-15, C-16 and C-17, which are influenced by the hydroxy groups, were found to be consistent with those of *ent*-kauran-16β,17-diol-19-oic acid (**27**).[17]

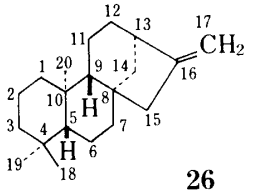
The melting point and optical rotation of **5** showed good agreement with those of *ent*-kauran-16β,17-diol, which was derived from **26**.[15] Thus, **5** and **6** are *ent*-kauran-16β,17-diol and *ent*-kauran-16α,17-diol, respectively.

Compd. VII [$C_{20}H_{32}O$, mp 114—116°C, $[\alpha]_D$ −18.5° ($CHCl_3$)] (**7**) showed an IR absorption band assignable to an epoxy group instead of the hydroxy group. Its ^{1}H-NMR spectrum showed signals of three *tert* methyl groups and the presence of a methylene group bearing an O-function (Table III). Therefore, **7** was considered to be a tetracyclic diterpenoid with one epoxy group.

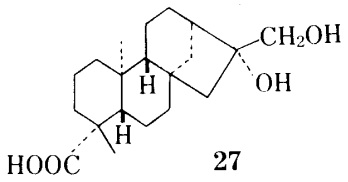
Comparison of the ^{13}C-NMR spectra of **5**, **6** and **7** showed that the chemical shifts of C-1 through C-12, C-14, C-18, C-19, and C-20 of **7** were in agreement with those of **5** and **6** (Table IV). Thus, **7** was considered to be *ent*-16,17-epoxy-kaurane.

Alkaline hydrolysis of **7** with 2.5% NaOH–dil. MeOH afforded a methoxy compound (**28**) [$C_{21}H_{36}O_2$, mp 174—176°C, $[\alpha]_D$ −33.0° ($CHCl_3$)], which was derived from **5** by application of the Kuhn method.[18] Compd. **7** could also be connected with **5** *via* epoxidation of **5**-tosylate (**29**) (see Chart 5). Thus, **7** was determined to be *ent*-16β,17-epoxy-kaurane.

TABLE IV. ^{13}C-NMR Spectral Data for **5**, **6**, **7**, **8**, **9**, **26** and **27**



26



27

C	5	6	7	8	9	27	26
1	42.0(t)	41.9(t)	40.0(t)	41.4(t)	42.0(t)	41.1	41.3
2	18.2(t)	18.7(t)	19.3(t)	18.5(t)	18.6(t)	19.8	18.7
3	42.0(t)	42.0(t)	41.9(t)	42.0(t)	43.8(t)	38.7	42.0
4	33.4(s)	33.2(s)	33.2(s)	33.1(s)	33.2(s)	43.9	33.3
5	56.1(d)	56.1(d)	55.8(d)	56.0(d)	48.3(d)	57.0	56.1
6	20.5(t)	20.0(t)	20.1(t)	20.4(t)	19.2(t)	22.9	20.3
7	37.2(t)	38.2(t)	38.5(t)	36.8(t)	39.2(t)	42.7	40.4
8	44.6(s)	43.5(s)	45.3(s)	44.3(s)	48.8(s)	44.9	44.2
9	56.7(d)	56.9(d)	56.1(d)	56.0(d)	55.8(d)	56.3	56.1
10	39.4(s)	39.3(s)	39.2(s)	39.2(s)	39.4(s)	40.0	39.3
11	18.3(t)	18.6(t)	18.6(t)	18.3(t)	18.6(t)	18.9	18.1
12	26.3(t)	26.7(t)	29.1(t)	25.9(t)	25.6(t)	26.8	33.3
13	45.5(d)	52.6(d)	42.6(d)	48.8(d)	41.1(d)	45.8	44.2
14	40.4(t)	40.4(t)	40.3(t)	40.2(t)	40.4(t)	37.8	39.9
15	53.4(t)	56.1(t)	48.8(t)	56.6(t)	135.7(d)	53.9	49.2
16	81.6(s)	79.7(s)	66.2(s)	86.7(s)	145.6(s)	81.6	156.0
17	66.2(t)	69.7(t)	50.2(t)	60.4(t)	61.1(t)	66.4	102.8
18	33.4(q)	33.6(q)	33.6(q)	33.5(q)	33.5(q)	29.3	33.7
19	21.5(q)	21.5(q)	21.5(q)	21.5(q)	21.5(q)	180.1	21.7
20	17.7(q)	17.6(q)	17.6(q)	17.7(q)	17.6(q)	16.0	17.6

Solv.: $CDCl_3$.

Compd. VIII [$C_{21}H_{36}O_2$, mp 171—173°C, $[\alpha]_D$ −45.6° ($CHCl_3$)] (**8**) showed the ^{1}H-NMR signals of one methoxy, three *tert* methyl, and one hydroxymethyl groups. The EI-MS spectrum of **8** lacked the M^+ ion peak, but elemental analysis of **8**, and the presence of a fragment ion at *m/z* 289 $(M-OCH_3]^+$ gave $C_{21}H_{36}O_2$ as the formula of **8** (Table III).

Compd. **8** showed a distinctive absorption due to the hydroxy group in its IR spectrum, and acetylation of **8** with Ac_2O–pyridine at room temp. yielded a monoacetate (**30**). Therefore, **8** was considered to be a tetracyclic diterpenoid bearing one methoxy and one hydroxymethyl groups.

Comparison of the ^{13}C-NMR spectra of **5**, **6** and **8** showed that the chemical shifts of C-1 through C-12, C-14, C-18, C-19, and C-20 of **8** were in accord with those of **5** and **6**. Therefore, **8** was considered to be *ent*-16-methoxy-kauran-17-ol (Table IV).

Hydrolysis of **7** with 3% Na_2CO_3–dil. MeOH yielded two compounds in a ratio of *ca.* 1 : 1, they were identified as **5** and **8**, respectively. It is known that the cleavage of the *exo*-epoxide ring, in neutral or basic media, proceeds in a usual S_N2 manner[19] (Chart 6). Therefore, the C-16 methoxy group of **8** must be β-oriented. From these results it is evident that **8** is *ent*-16α-methoxykauran-17-ol, which is probably formed during the isolation procedures.

Compd. IX [$C_{20}H_{32}O$, mp 134—136°C, $[\alpha]_D$ −26.1° ($CHCl_3$)] (**9**) showed an IR absorption band due to a hydroxy group, and ^{1}H-NMR spectral signals due to three *tert* methyl groups, one hydroxymethyl group, and one tri-substituted double bond (Table III). The ^{13}C-NMR spectrum of **9** was similar to those of **5**, **6**, and **7**, especially in the signals of C-1 through C-12, C-14, C-18, C-19, and C-20 (Table IV). Therefore, **9** was considered to be *ent*-kaur-15-en-17-ol,

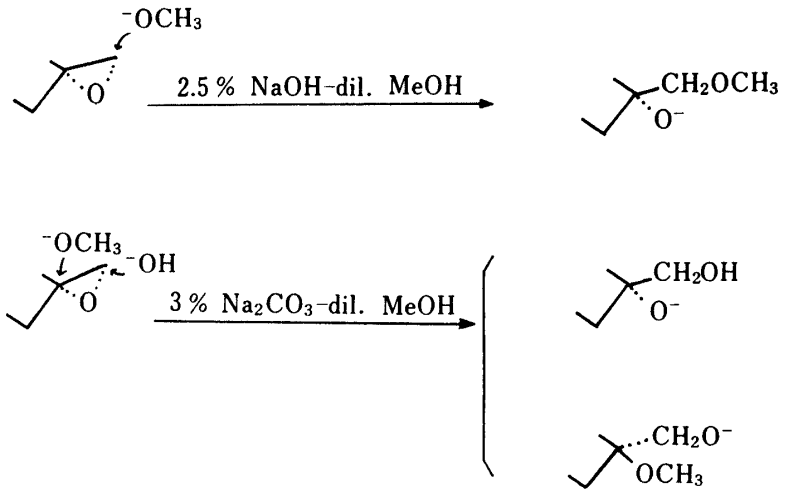


Chart 6

which has been derived from **26** by Briggs *et al.*. In fact, both compounds showed identical properties (melting point, ^{1}H-NMR spectrum and optical rotation[20]). The melting point of **9**-acetate (**10**) coincided with that reported for *ent*-kaur-15-en-17-ol monoacetate [lit.[20] mp 70°C]. Thus, **9** was determined to be *ent*-kaur-15-en-17-ol.

Experimental

Melting points are uncorrected. Optical rotations were taken with a JASCO DIP-SL automatic polarimeter at 17—27°C. IR spectra were obtained with a JASCO IR-G spectrometer. ^{13}C-NMR data were obtained in $CDCl_3$ solution on a JEOL-FX-100 spectrometer (25.05 MHz) under the following conditions: pulse width 5 μs, repetition time 1 s, and data points 8192. ^{1}H-NMR spectra were recorded at 100 MHz on a JEOL-PS-100 spectrometer: in the ^{13}C-NMR and ^{1}H-NMR studies, a 5 mmϕ sample tube was used. Chemical shifts are expressed in ppm from tetramethylsilane as an internal reference, and coupling constants (J) are given in Hz. Abbreviations used are: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet. EI-MS spectra were measured on a JEOL JMS-01SG double focusing mass spectrometer with direct insertion of the probe into the ion source. The spectra were recorded with an accelerating potential of 6.5—6.7 kV, an ionizing potential of 75 eV, and a sample temperature of 47—196°C. Thin layer chromatography (TLC) was performed on DC-Alufolien Kieselgel 60 F_{254} (Merck) using anisaldehyde reagent[21] and 10% H_2SO_4 as the detector. Column chromatography was carried out under TLC monitoring using Kieselgel (silica gel 0.063—0.2 mm, Merck), Silica Woelm TSC (silica gel for dry column (dry), Woelm Pharma.), Aluminiumoxide standardisiert (grade III, Merck), and Sephadex LH-20 (25—100 μ, Pharmacia Fine Chemicals) in an amount equivalent to fifty to two hundred fold excess over the material. Gas–liquid chromatography (GLC) was run on a JEOL JGC-1100 machine with a flame ionization detector using a glass column (1.5 m×7 mmϕ) packed with 10% SE-30 Chromosorb W (60—80 mesh).

Extraction and Isolation of Diterpenoids——The bulbs were collected in May from plants cultivated in Nara prefecture, and the isolation procedure is shown in Chart 1.

Compd. I——Colorless oil, $[\alpha]_D^{19.1}$ +14.5° (c=1.8, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 3300 (OH), 1645, 1605 (double bond), 888 (*exo*-methylene). ^{1}H-NMR ($CDCl_3$) δ: 0.71, 1.00, 1.77 (each 3H, s, *tert* CH_3), 3.40, 3.77 (each 1H, d, J=11 Hz, C_{19}–H_2), 4.46, 4.82 (each 1H, s, C_{17}–H_2), 4.82—5.32 (2H, m, C_{15}–H_2), 5.42 (1H, t, C_{12}–H), 6.35 (1H, q, J=17 Hz and 11 Hz, C_{14}–H). EI-MS m/z: 288 (M^+, base peak), 257, 81. 1-Acetate: colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 0.84, 0.98, 1.86 (each 3H, s, *tert* CH_3), 2.04 (3H, s, –OAc), 4.25, 4.16 (each 1H, d, J=11 Hz, C_{19}–H_2), 4.46, 4.82 (each 1H, s, C_{17}–H_2), 4.82—5.32 (2H, m, C_{15}–H_2), 5.41 (1H, t, C_{12}–H), 6.35 (1H, q, J=17 and 12 Hz, C_{14}–H). EI-MS m/z: 330 (M^+), 288, 257 (base peak), 81. GLC (column temp.: 210°C, N_2; 1.0 kg/cm^2, H_2; 1.5 kg/cm^2) t_R 10′49″.

Compd. II (**2**)——Needles (MeOH), mp 104—105°C, $[\alpha]_D^{19.0}$ −48.0° (c=1.0, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 1710 (C=O), 1642, 1605 (double bond), 895, 882 (*exo*-methylene). ^{1}H-NMR ($CDCl_3$) δ: 0.56, 1.77, 1.19 (each 3H, s, *tert* CH_3), 3.61 (3H, s, $COOCH_3$), 4.46, 4.82 (each 1H, s, C_{17}–H_2), 4.82—5.32 (2H, m, C_{15}–H_2), 5.42 (1H, t, C_{12}–H), 6.34 (1H, q, J=17 Hz and 11 Hz). EI-MS m/z: 316 (M^+, base peak), 257, 235, 181, 175, 121. *Anal.* Calcd for $C_{21}H_{32}O_2$: C, 79.70; H, 10.91. Found: C, 79.41; H, 10.91.

Compd. III (**3**)——Needles (MeOH), mp 86°C, $[\alpha]_D^{24.0}$ −39.0° (c=1.2, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 3350, 1028 (OH), 1640, 907 (*exo*-methylene). ^{1}H-NMR ($CDCl_3$) δ: see Table I. EI-MS m/z: 288 (M^+), 273, 270, 257

(base peak). ^{13}C-NMR ($CDCl_3$) δ: see Table II. *Anal.* Calcd for $C_{20}H_{32}O \cdot 1/4H_2O$: C, 81.99; H, 11.18. Found: C, 82.49; H, 11.13.

Compd. IV (**4**)——Colorless oil, $[\alpha]_D^{19.5}$ +26.7° (c=3.3, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1725 (C=O), 1640, 908 (*exo*-methylene). ^{1}H-NMR ($CDCl_3$) δ: see Table I. EI-MS m/z: 316 (M^+, base peak), 301, 287, 257, 241. ^{13}C-NMR ($CDCl_3$) δ: see Table II.

3-Monoacetate (**22**)——The conventional acetylation of **3** (20 mg) with Ac_2O–pyridine (1: 1 ml each) at room temperature overnight, and subsequent purification of the crude product by silica gel column chromatography (dry, 10 g, solv.: *n*-hexane–EtOAc=9: 1) gave **22**, colorless oil, $[\alpha]_D^{19.5}$ +30.0° (c=1.9, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1743 (OAc), 1640, 910 (*exo*-methylene). ^{1}H-NMR ($CDCl_3$) δ: 0.87 (6H, s, *tert* $CH_3 \times 2$), 0.94 (3H, s, *tert* CH_3), 2.05 (3H, s, OAc), 3.95, 4.35 (each 1H, d, J=11 Hz, C_{19}–H_2), 4.86$_{(C)}$, 4.95$_{(B)}$, 5.81$_{(A)}$ (each 1H, J_{AB}=17 Hz, J_{AC}=10 Hz, J_{BC}=2 Hz, C_{15}–H, C_{16}–H_2), 5.36 (1H, t, J=2 Hz, C_7–H).

$LiAlH_4$ Reduction of 4——A mixture of **4** (25 mg), THF (5 ml), and $LiAlH_4$ (15 mg) was stirred for 1 h at room temperature. After quenching of excess $LiAlH_4$ with MeOH (10 ml), the reaction mixture was poured into water and extracted with Et_2O. The organic layer was washed with dil. H_2SO_4 and water, and concentrated to give the residue, which was chromatographed on a silica gel column (dry, 10 g, solv.: *n*-hexane–EtOAc=4: 1) to give **3**, 6.5 mg of needles from MeOH.

Compd. V (**5**)——Needles (MeOH), mp 188—189°C. $[\alpha]_D^{20.0}$ −47.0° (c=2.1, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3350 (OH). ^{1}H-NMR ($CDCl_3$) δ: see Table III. EI-MS m/z: 306 (M^+), 288, 275 (base peak), 257, 123. ^{13}C-NMR ($CDCl_3$) δ: see Table IV. *Anal.* Calcd for $C_{20}H_{34}O_2 \cdot 1/2H_2O$: C, 76.14; H, 11.18. Found: C, 76.48; H, 11.24.

5-Monoacetate (**23**)——Acetylation of **5** (25 mg) with Ac_2O–pyridine (1: 1 ml each) at room temperature overnight gave **23**, 20.5 mg of needles from acetone. mp 159°C. IR ν_{max}^{Nujol} cm^{-1}: 3480 (OH), 1730 (OAc). ^{1}H-NMR ($CDCl_3$) δ: 0.79, 0.84, 1.03 (each 3H, s, *tert* CH_3), 2.10 (3H, s, OAc), 4.23 (2H, s, C_{17}–H_2). EI-MS m/z: 348 (M^+), 330, 315, 275 (base peak), 270 257, 123.

HIO_4 Oxidation of 5——A mixture of **5** (100 mg), MeOH (10 ml), and HIO_4 (50 mg) was stirred for 2 h at room temperature. The reaction mixture was poured into water and extracted with Et_2O. The organic layer was concentrated to give the residue, which was chromatographed on a silica gel column (dry, 30 g, solv.: *n*-hexane–EtOAc=9: 1) to afford **25** as prisms, 52 mg from MeOH. mp 117—118°C, $[\alpha]_D^{20.0}$ −29.0° (c=1.3, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 1742 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 0.83, 0.87, 1.08 (each 3H, s, *tert* CH_3). EI-MS m/z: 274 (M^+, base peak), 261.

Compd. VI (**6**)——Needles (MeOH), mp 177°C, $[\alpha]_D^{20.0}$ −45.5° (c=1.2, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3350 (OH). ^{1}H-NMR ($CDCl_3$) δ: see Table III. EI-MS m/z: 306 (M^+), 288, 275 (base peak), 257, 123. ^{13}C-NMR ($CDCl_3$) δ: see Table IV. *Anal.* Calcd for $C_{20}H_{34}O_2 \cdot 1/2H_2O$: C, 76.14; H, 11.18. Found: C, 76.38; H, 11.21.

6-Monoacetate (**24**)——Acetylation of **6** (25 mg) with Ac_2O–pyridine (1: 1 ml each) at room temperature overnight gave **24**, 20 mg of needles from acetone. mp 127—129°C. IR ν_{max}^{Nujol} cm^{-1}: 3480 (OH), 1730 (OAc). EI-MS m/z: 348 (M^+), 330, 315, 288, 275, (base peak), 270, 257, 123.

HIO_4 Oxidation of 6——A mixture of **6** (50 mg), MeOH (6 ml), and HIO_4 (30 mg) was stirred for 2 h at room temperature. After the usual work-up, the residue was purified by silica gel column chromatography (dry, 10 g, solv.: *n*-hexane–EtOAc=9: 1) to afford prisms **25**, 32 mg from MeOH.

Compd. VII (**7**)——Needles (MeOH), mp 114—116°C, $[\alpha]_D^{17.0}$ −18.5° (c=2.0, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 792 (epoxy). ^{1}H-NMR ($CDCl_3$) δ: see Table III. EI-MS m/z: 288 (M^+), 273 (base peak), ^{13}C-NMR ($CDCl_3$) δ: see Table IV. *Anal.* Calcd for $C_{20}H_{32}O$: C, 83.27; H, 11.18. Found: C, 83.02; H, 11.09.

Alkaline Hydrolysis of 7——**7** (30 mg) was refluxed in 2.5% NaOH–dil. MeOH (10 ml) on a hot water bath for 2 h, then the solution was poured into water and extracted with Et_2O. The organic layer was washed with water and concentrated to give a residue, which was chromatographed on silica gel (dry, 10 g, solv.: *n*-hexane–EtOAc=4: 1) to afford **28**, 25 mg of needles from MeOH. mp 174—176°C, $[\alpha]_D^{27.0}$ −33.0° (c=1.0, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3430 (OH). ^{1}H-NMR ($CDCl_3$) δ: 0.81, 0.85, 1.02 (each 3H, s, *tert* CH_3), 3.40 (3H, s, OCH_3), 3.40, 3.58 (each 1H, d, J=9 Hz, C_{17}–H_2). EI-MS m/z: 320 (M^+). 302, 289 (base peak), 257.

Methylation of 5——A mixture of NaH (35 mg), DMF (4 ml) and **5** (70 mg) was stirred for 10 min at room temperature, then CH_3I (2 ml) was added. After being stirred for 2 h, the reaction mixture was poured into water and extracted with Et_2O. The organic layer was washed with water and concentrated to give a residue, which was chromatographed on silica gel (dry, 15 g, solv.: *n*-hexane–EtOAc=9: 1) to afford **28**, 58 mg of needles from MeOH.

Preparation of *p*-Toluene Sulfonate (**29**)——A mixture of **5** (80 mg), pyridine (5 ml), and *p*-toluenesulfonyl chloride (150 mg) was stirred overnight at room temperature. The reaction mixture was poured into water and extracted with $CHCl_3$. The organic layer was taken up and concentrated to give a residue, which was chromatographed on a silica gel column (dry, 15 g, solv.: *n*-hexane–EtOAc=9: 1) to afford **29**, 57 mg of needles from MeOH. mp 142—143°C.

Epoxidation of 29——A mixture of **29** (30 mg), THF (5 ml), and CH_3ONa (3.5 mg) was refluxed on a hot water bath for 1 h, then the solution was poured into water and extracted with Et_2O. The organic layer was washed with water and concentrated to give a residue, which was chromatographed on a silica gel column (dry, 10 g, solv.: *n*-hexane–EtOAc=9: 1) to afford **7**, 14.5 mg of needles from MeOH.

Compd. VIII (**8**)——Needles (MeOH), mp 171—173°C, $[\alpha]_D^{17.0}$ −45.6° (c=1.1, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3400

(OH). ^{1}H-NMR ($CDCl_3$) δ: see Table III. EI-MS m/z: 289 $(M-OCH_3)^+$, 274 (base peak). ^{13}C-NMR ($CDCl_3$) δ: see Table IV. *Anal.* Calcd for $C_{21}H_{36}O_2$: C, 78.69; H, 11.32. Found: C, 78.07; H, 11.23.

8-Monoacetate (30)——Acetylation of **8** (20 mg) with Ac_2O–pyridine (each 1 ml) at room temperature overnight gave **30**, 18 mg of prisms from MeOH. mp 127—128°C. ^{1}H-NMR ($CDCl_3$) δ: 0.77, 0.83, 0.99 (each 3H, s, *tert* CH_3), 2.08 (3H, s, OAc), 3.12 (3H, s, OCH_3), 4.14, 4.37 (each 1H, d, $J=12$ Hz, C_{17}–H_2).

Alkaline Hydrolysis of 7——**7** (50 mg) was refluxed in 3% Na_2CO_3–dil. MeOH (10 ml) on a hot water bath for 4 h, then the solution was poured into water and extracted with Et_2O. The organic layer was washed with water and concentrated to give a residue, which was chromatographed on silica gel (dry, 10 g, solv.: *n*-hexane–EtOAc=3: 2) to afford **8**, 17 mg of needles from MeOH, and **5**, 16 mg of needles from MeOH. **5**, mp 188—189°C. IR ν_{max}^{KBr} cm^{-1}: 3350 (OH). **8**, mp 171—172°C, $[\alpha]_D^{19.0}$ −45.5° ($c=1.2$, $CHCl_3$).

Compd. IX (9)——Needles (MeOH), mp 134—136°C, $[\alpha]_D^{17.0}$ −26.1° ($c=3.3$, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3300 (OH). ^{1}H-NMR ($CDCl_3$) δ: see Table III. EI-MS m/z: 288 (M^+, base peak), 263, 163. ^{13}C-NMR ($CDCl_3$) δ: see Table IV. *Anal.* Calcd for $C_{20}H_{32}O$: C, 83.27; H, 11.18. Found: C, 83.39; H, 11.12.

9-Monoacetate (10)——Acetylation of **9** (30 mg) with Ac_2O–pyridine (each 1 ml) at room temperature overnight gave **10**, 26 mg of needles from MeOH. mp 69°C. EI-MS m/z: 330 (M^+). GLC: (column temp.: 210°C, N_2; 1.0 kg/cm^2, H_2; 1.5 kg/cm^2) t_R 10′43″.

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