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Studies on the Constituents of the Crude Drug "Fritillariae Bulbus." IV.[1] On the Diterpenoid Constituents of the Crude Drug "Fritillariae Bulbus"

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Three new diterpenoids, in addition to *trans*-communol (**1**), *trans*-communic acid [obtained in the form of the methyl ester (**2**)], isomimaran-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**) and *ent*-17-norkauran-16-one (**7**), were isolated as non basic constituents of the crude drug "Fritillariae Bulbus" prepared from the bulbs of *Fritillaria thunbergii* Miq. by treatment with lime followed by bleaching in the sun.

These three diterpenoids were determined to be *ent*-15β,16-epoxy-kauran-17-ol (**8**), *ent*-16β-hydroxy-kauran-17-yl *ent*-kaur-15-en-17-oate (**9**) and *ent*-(16*S*)-atisan-13,17-oxide (**10**).

Keywords——*Fritillaria thunbergii* Miq.; crude drug Fritillariae Bulbus; *ent*-kauran-type diterpenoid; *ent*-atisan-type diterpenoid; ^{1}H-NMR; ^{13}C-NMR; X-ray analysis

The crude drug "Fritillariae Bulbus" ("Bai-mo" in Japanese) prepared from the bulbs of Chinese plants *Fritillaria thunbergii* Miq. (Liliaceae) by treatment with lime followed by bleaching in the sun is a principal clinical compound in Chinese traditional medicine. With regard to the constituent alkaloids of this crude drug, we have already reported the presence of verticine, verticinone and their *N*-oxides, 12,13-epoxy-11-deoxo-6-oxo-5α,6-dihydrojervine, and 12,13-epoxy-22*S*,25*S*,5α-varatranine-3β,17,23β-triol-6-one.[2] As for the non basic constituents of fresh bulbs of *Fritillaria thunbergii* Miq., we isolated nine diterpenoids and determined their structures as *trans*-communol (**1**), *trans*-communic acid [obtained in the form of the methyl ester (**2**)], 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-kauran (**11**), *ent*-16α-methoxy-kauran-17-ol (**12**), and *ent*-kaur-15-en-17-ol (**13**).[1] Because the non basic constituents of this crude drug have not previously been reported, we investigated the diterpenoid constituents to determine whether or not they are the same as those of the fresh bulbs (Chart 2).

The powdered crude drug "Bai-mo" (20 kg) prepared in Nara prefecture was extracted with MeOH and the extractives were fractionated and purified according to the procedure shown in Chart 1, to give ten kinds of diterpenoids. Compounds (Compds.) II and IV were methylated to obtain their methyl ester derivatives.

Compd. I [colorless oil, $[\alpha]_D$ +15.0° ($CHCl_3$)] **1**, Compd. II [mp 104—105°C, $[\alpha]_D$ +48.0° ($CHCl_3$)] **2**, Compd. III [mp 86°C, $[\alpha]_D$ −39.0° ($CHCl_3$)] **3**, Compd. IV [colorless oil, $[\alpha]_D$ +25.0° ($CHCl_3$)] **4**, Compd. V [mp 188—189°C, $[\alpha]_D$ −47.0° ($CHCl_3$)] **5**, and Compd. VI [mp 177—178°C, $[\alpha]_D$ −45.5° ($CHCl_3$)] **6** were identified as *trans*-communol, *trans*-communic acid methyl ester, isopimaran-19-ol, isopimaran-19-oic acid methyl ester, *ent*-kauran-16β,17-diol, and *ent*-kauran-16α,17-diol, respectively, by direct comparison with authentic samples isolated from bulbs of *Fritillaria thunbergii* Miq.[1]

Compd. VII [$C_{19}H_{30}O$, mp 117—118°C, $[\alpha]_D$ −29.0° ($CHCl_3$)] (**7**) showed distinctive absorptions in its infrared (IR) spectrum due to a carbonyl group, and its proton nuclear magnetic resonance (^{1}H-NMR) spectrum showed the presence of three tertiary (*tert*) methyl groups (Table I). Thus, **7** was considered to be a tetracyclic norditerpenoid having one carbonyl

group, and was found to be identical with *ent*-17-norkauran-16-one (**17**)[1] derived from **5** by treatment with HIO_4 in MeOH.

Compd. VIII [$C_{20}H_{32}O_2$, mp 160°C, $[\alpha]_D$ +9.4° ($CHCl_3$)] (**8**), showed distinctive absorptions in its IR spectrum due to a hydroxy group and its ^{1}H-NMR spectrum showed the presence of three *tert* methyl groups, one hydroxymethyl, and the ether ring (Table I). Acetylation of **8** with Ac_2O–pyridine at room temp. yielded **8**-monoacetate (**14**), whose IR spectrum lacked absorption bands due to a hydroxy group. In carbon nuclear magnetic resonance (^{13}C-NMR) studies of **8** using the off-resonance decoupling technique, the signals due to C-1 through C-8, C-10 through C-12, and C-18 through C-20 were shown to be in accord with those of **5** and **6**

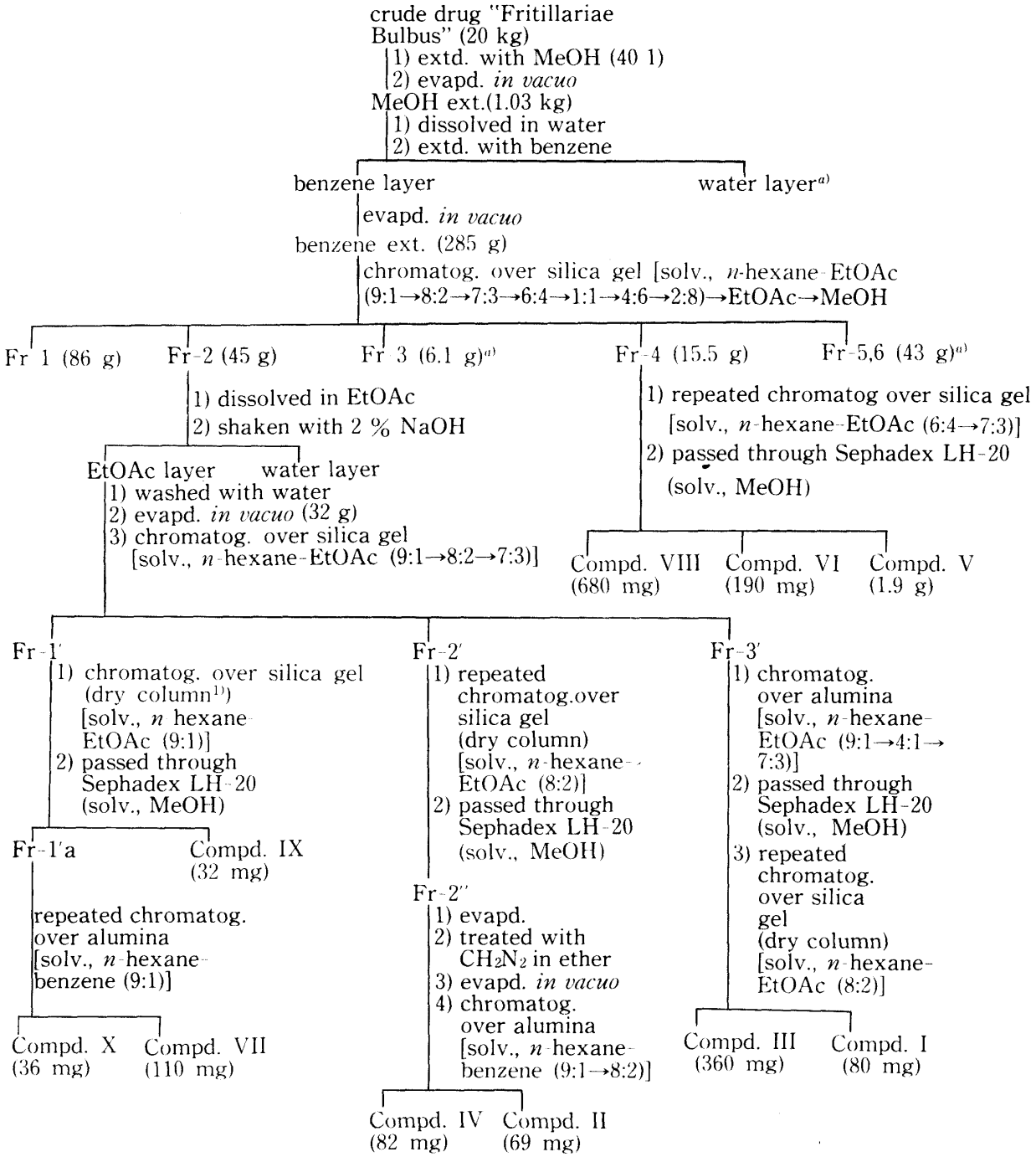


Chart 1. Isolation of Diterpenoids

a) See Part VI of this series.

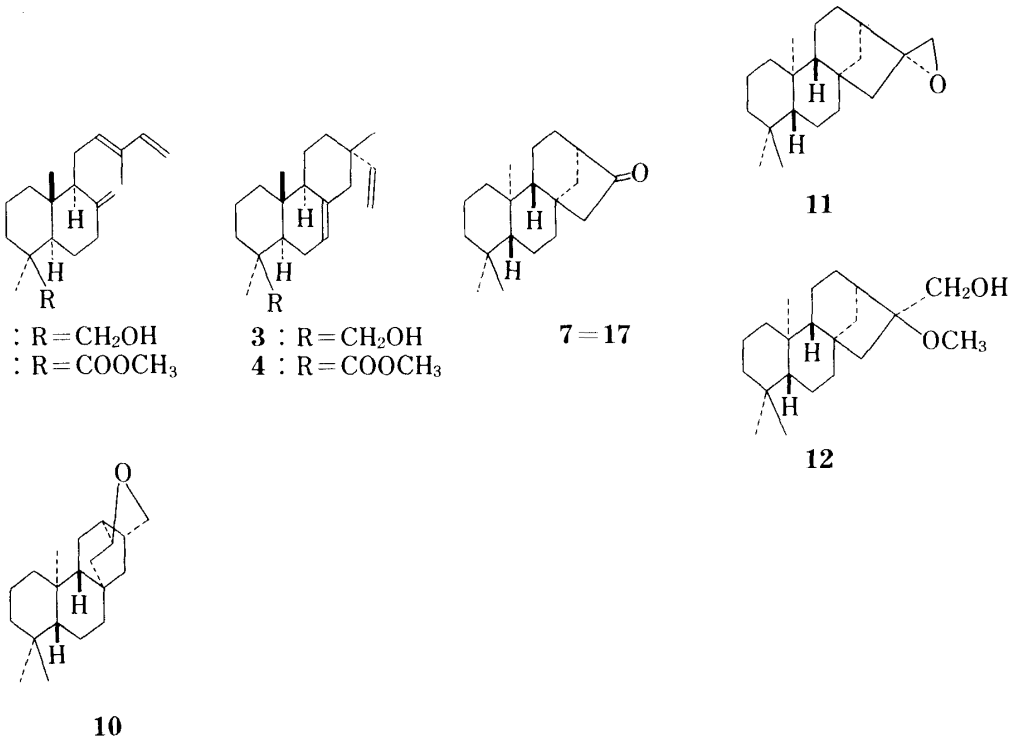


Chart 2

Table I. ^{1}H-NMR Spectral Data for **7** and **8**

8 (ppm)		**7** (ppm)	
0.81, 0.87, 1.00	*tert*-CH_3	0.83, 0.87, 1.08	*tert*-CH_3
2.53, 2.95 (1H, s)	-OH		
3.75, 4.05 (each 1H, d, J=12 Hz)	-CH_2OH		

(see Table II). Thus, **8** was assumed to be *ent*-15,16-epoxy-kauran-17-ol.

In order to determine the structure of **8**, we tried to convert **8** into **5** or **6** by treatment with $LiAlH_4$. However, all our attempts failed. Thus, **8** was treated with pyridine-*p*-toluenesulfonyl chloride to yield **8**-tosylate (**15**), which was converted to **16**, $C_{20}H_{32}O$, mp 116—118°C, $[\alpha]_D$ −8.5° ($CHCl_3$), by treatment with $LiAlH_4$ in tetrahydrofuran (THF). Compd. **16** was identified as *ent*-15β,16-epoxy-kaurane by comparison with an authentic sample,[3] and thus **8** was determined to be *ent*-15β,16-epoxy-kauran-17-ol (Chart 3).

Compd. IX [$C_{40}H_{63}O_3$, mp 251—254°C, $[\alpha]_D$ −49.2° ($CHCl_3$)] (**9**) showed distinctive absorptions in its IR spectrum due to a hydroxy group and a conjugated enone system (1682, 1620 cm^{-1}). The electron impact mass (EI-MS) spectrum showed a weak M^+ ion peak and a strong fragment peak at m/z 572 $[M-H_2O]^+$.

Alkaline hydrolysis of **9** yielded two compounds, and one of them was identical with **5** as determined by thin-layer chromatography (TLC) using several solvents. Therefore, **9** was considered to be a dimer derived from **5** and a diterpenoid mono-acid.

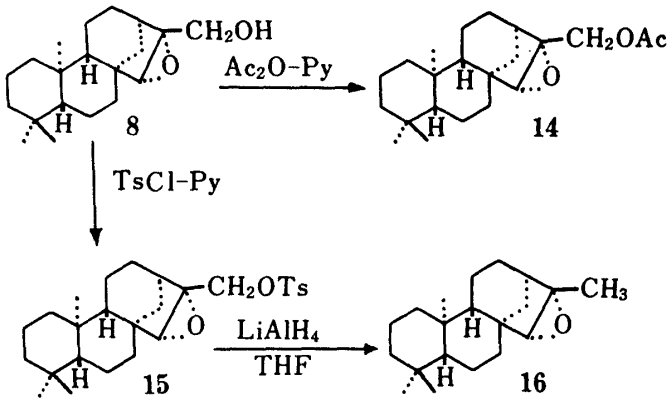
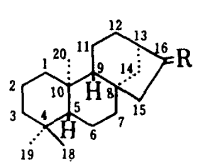
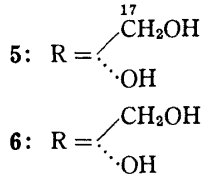


Chart 3

TABLE II. ^{13}C-NMR Spectral Data for **5**, **6**, and **8**





C	5	6	8
1	42.0(t)	41.9(t)	40.4(t)
2	18.2(t)	18.7(t)	18.7(t)
3	42.0(t)	42.0(t)	42.1(t)
4	33.4(s)	33.2(s)	33.3(s)
5	56.1(d)	56.1(d)	55.9(d)
6	20.5(t)	20.0(t)	19.3(t)
7	37.2(t)	38.2(t)	32.5(t)
8	44.6(s)	43.5(s)	43.4(s)
9	56.7(d)	56.9(d)	50.8(d)
10	39.4(s)	39.3(s)	39.2(s)
11	18.3(t)	18.6(t)	18.2(t)
12	26.3(t)	26.7(t)	27.0(t)
13	45.5(d)	52.6(d)	36.0(d)
14	40.4(t)	40.4(t)	36.0(t)
15	53.4(t)	56.1(t)	65.7(d)
16	81.6(s)	79.7(s)	69.5(s)
17	66.2(t)	69.1(t)	59.9(t)
18	33.4(q)	33.6(q)	33.6(q)
19	21.5(q)	21.5(q)	21.6(q)
20	17.7(q)	17.6(q)	17.5(q)

δ (ppm), solv.: $CDCl_3$.

The ^{1}H-NMR spectrum of **9** showed signals due to six *tert* methyl groups, one oxymethylene group (δ 4.27) which is shifted downfield by the presence of the ester bond, and one olefinic proton (δ 6.51) which suffers a downfield shift owing to the conjugation with a carbonyl group (Table III). As shown in Table III, the chemical shifts of the signals at 0.80, 0.84, and 1.00 ppm, were similar to those of *tert* methyl groups in the molecule of **5**, and the chemical shifts of the signals at 0.80, 0.85, and 1.05 ppm, were in accord with those of *tert* methyl groups of **13** isolated from fresh bulbs.

The ^{13}C-NMR spectrum of **9** showed 40 signals. Comparison of the ^{13}C-NMR spectrum of **9** with those of **5** and **13** led us to consider that **9** is the ester of **5** and *ent*-kaur-15-en-17-oic acid

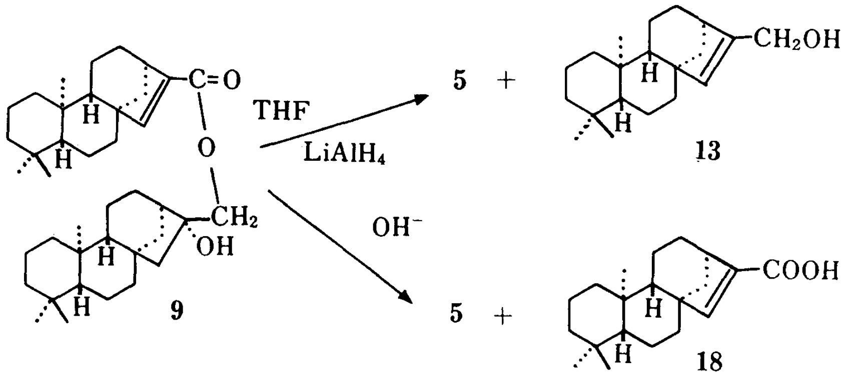


Chart 4

Table III. [1]H-NMR Spectral Data for **9**

9 (ppm)		**5** (ppm)		**13** (ppm)	
0.80 0.80 0.84 0.85 1.00 1.05	*tert*-CH_3	0.80 0.84 1.02	*tert*-CH_3	0.81 0.86 1.05	*tert*-CH_3
2.90	$\rangle\underset{\mathrm{H}}{\mathrm{C}}-\mathrm{C}\langle$				
4.27	$-\underset{\|}{\mathrm{C}}-\underset{\mathrm{H_2}}{\mathrm{C}}-\mathrm{O}-\overset{\mathrm{R}}{\underset{\mathrm{O}}{\mathrm{C}}}$	3.37 3.51 (each 1H, d, $J=11$ Hz)	$-CH_2OH$	4.17 4.18 (each 1H, s)	$-CH_2OH$
6.51				5.36	

Table IV. [13]C-NMR Spectral Data for **9**

C	**5**	**9**	**13**	C	**5**	**9**	**13**
1	42.0	41.8		1′		41.8	42.0
2	18.2	18.8		2′		18.5	18.6
3	42.0	42.0		3′		43.1	43.8
4	33.4	33.2		4′		33.2	33.2
5	56.1	56.1		5′		55.8	55.8
6	20.5	20.5		6′		20.5	19.2
7	37.2	37.1		7′		38.3	39.2
8	44.6	44.8		8′		50.5	48.8
9	56.7	56.5		9′		46.7	48.3
10	39.4	39.3		10′		39.4	39.4
11	18.3	18.2		11′		18.4	18.6
12	26.3	26.3		12′		25.6	25.6
13	45.5	46.2		13′		40.3	41.1
14	40.4	40.7		14′		40.3	40.4
15	53.4	53.0		15′		137.5	135.7
16	81.6	80.1		16′		153.8	145.6
17	66.2	68.1		17′		165.1	61.1
18	33.4	33.5		18′		33.5	35.5
19	21.5	21.5		19′		21.5	21.5
20	17.7	17.7		20′		17.7	17.6

δ (ppm), solv.: $CDCl_3$.

(**18**) (Table IV). Thus, **9** was treated with $LiAlH_4$ in THF to give two compounds, which were identified as **5** and **13**, respectively (Chart 4). Therefore, **9** is *ent*-16β-hydroxy-kauran-17-yl *ent*-kaur-15-en-17-oate.

Compd. X [$C_{20}H_{32}O$, mp 124—125°C, $[\alpha]_D$ −71.0° ($CHCl_3$)] (**10**) showed no absorptions due to the hydroxy group in its IR spectrum. The ^{1}H-NMR spectrum of **10** showed the presence of three *tert* methyl groups and an ether ring. The above data suggest that **10** is a pentacyclic diterpenoid with an ether ring. The ^{13}C-NMR spectrum of **10** showed the presence of three quaternary (*quat*) carbons, five *tert* carbons (the peak at 76.2 ppm is assignable to the carbon atom bearing the O-function), nine secondary (*sec*) carbons (the peak at 75.1 ppm is assignable to a carbon bearing the O-function), and three primary carbon atoms, as shown in Table V.

From these results and the optical rotation of **10**, **10** was considered to be an *ent*-kaurane or *ent*-atisane type diterpenoid having an ether ring at C-17.

Due to the small amount of the material available and the difficulty of structure determination by the chemical method, the structure of **10** was determined by direct single crystal X-ray

Table V. ^{1}H-NMR and ^{13}C-NMR Spectral Data for **10**

^{1}H-NMR δ (ppm)	0.80, 0.85, 0.85 *tert*-CH_3 3.46 (1H, d, J=7 Hz) 3.77 (1H, dd, J=4.5 Hz, 7 Hz) 3.99 (1H, dd, J=4.5 Hz, 7 Hz)			-C(H)-O-C(H)-	
^{13}C-NMR δ (ppm)	29.2, 32.9, 37.7 *quat* C (>C=)	35.0, 36.2, 51.3, 56.2, 76.2 *tert* C (-C(H)-)	18.0, 18.7, 19.1, 39.4, 39.4, 39.9, 42.1, 48.0, 75.1 *sec* C (-CH_2-)	14.9, 21.6, 33.3 -CH_3	

Table VI. Final Positional Parameters and Anisotropic Temperature Factors of **10** with Their Estimated Standard Deviations in Parentheses

Atom	X	Y	Z	B_{11}	B_{22}
C (1)	0.5360(3)	0.4413(8)	0.4300(12)	0.0014(1)	0.0105(8)
C (2)	0.5069(3)	0.5647(8)	0.4056(14)	0.0019(2)	0.0129(9)
C (3)	0.5475(4)	0.6611(7)	0.3300(14)	0.0032(2)	0.0096(9)
C (4)	0.5979(3)	0.6790(7)	0.4682(13)	0.0026(2)	0.0071(7)
C (5)	0.6252(3)	0.5494(6)	0.5034(11)	0.0020(2)	0.0075(7)
C (6)	0.6776(3)	0.5511(7)	0.6368(13)	0.0018(2)	0.0075(7)
C (7)	0.7094(3)	0.4318(7)	0.6021(13)	0.0014(1)	0.0092(7)
C (8)	0.6752(3)	0.3171(7)	0.6570(12)	0.0013(1)	0.0083(7)
C (9)	0.6179(3)	0.3233(6)	0.5531(10)	0.0016(1)	0.0069(6)
C (10)	0.5851(3)	0.4463(6)	0.5812(10)	0.0015(1)	0.0064(6)
C (11)	0.5854(3)	0.2079(6)	0.6138(12)	0.0016(1)	0.0083(7)
C (12)	0.6204(3)	0.1160(7)	0.7337(13)	0.0022(2)	0.0064(6)
C (13)	0.6444(3)	0.1664(7)	0.9457(13)	0.0027(2)	0.0076(7)
C (14)	0.6719(3)	0.2939(7)	0.9014(11)	0.0020(2)	0.0089(7)
C (15)	0.7042(3)	0.2012(6)	0.5582(13)	0.0017(2)	0.0101(8)
C (16)	0.6740(3)	0.0831(6)	0.6236(13)	0.0022(2)	0.0061(7)
C (17)	0.7039(4)	0.0180(7)	0.8083(17)	0.0028(2)	0.0095(8)
C (18)	0.5828(4)	0.7469(7)	0.6781(14)	0.0031(2)	0.0096(8)
C (19)	0.6386(4)	0.7589(7)	0.3424(16)	0.0032(3)	0.0085(8)
C (20)	0.5646(3)	0.4645(7)	0.8128(12)	0.0017(2)	0.0100(8)
C (21)	0.6871(3)	0.0802(5)	0.9993(10)	0.0034(2)	0.0115(6)

Atom	B_{33}	B_{12}	B_{13}	B_{23}
C (1)	0.0258(22)	−0.0005(3)	−0.0004(5)	−0.0022(13)
C (2)	0.0326(28)	0.0018(3)	−0.0026(6)	−0.0007(16)
C (3)	0.0283(27)	0.0024(4)	0.0004(7)	0.0002(14)
C (4)	0.0303(26)	0.0012(3)	−0.0001(6)	−0.0000(13)
C (5)	0.0181(18)	0.0004(3)	0.0010(5)	−0.0003(11)
C (6)	0.0291(23)	−0.0002(3)	−0.0003(6)	−0.0010(12)
C (7)	0.0337(27)	−0.0068(3)	−0.0004(5)	−0.0012(14)
C (8)	0.0243(21)	0.0001(3)	−0.0005(5)	−0.0001(12)
C (9)	0.0140(16)	−0.0003(3)	−0.0011(4)	−0.0026(9)
C (10)	0.0170(18)	−0.0000(3)	0.0001(4)	−0.0021(10)
C (11)	0.0271(23)	−0.0007(3)	−0.0011(5)	−0.0000(12)
C (12)	0.0298(25)	−0.0002(3)	−0.0002(6)	−0.0010(11)
C (13)	0.0271(24)	0.0009(3)	−0.0006(6)	0.0003(12)
C (14)	0.0212(20)	−0.0004(3)	−0.0015(5)	−0.0021(11)
C (15)	0.0269(23)	0.0009(3)	−0.0012(5)	−0.0017(13)
C (16)	0.0335(26)	0.0005(3)	0.0006(6)	−0.0031(12)
C (17)	0.0497(37)	0.0015(4)	−0.0027(8)	0.0003(17)
C (18)	0.0335(30)	0.0020(4)	−0.0006(8)	−0.0067(15)
C (19)	0.0397(30)	0.0000(4)	0.0021(8)	0.0027(15)
C (20)	0.0183(20)	0.0007(3)	0.0014(5)	−0.0017(12)
C (21)	0.0345(19)	0.0010(3)	−0.0031(5)	0.0017(11)

Anisotropic thermal parameters are in the form $\exp[-(h^2B_{11}+k^2B_{22}\times l^2B_{33}+2hkB_{12}+2hlB_{13}+2klB_{23})]$

TABLE VII. Bond Distances (Å) and Bond Angles (Degrees) of **10** with Estimated Standard Deviations (ESD)

	Dist. (ESD)		Dist. (ESD)		Dist. (ESD)
C (1)-C (2)	1.532(12)	C (1)-C (10)	1.526(11)	C (2)-C (3)	1.520(13)
C (3)-C (4)	1.514(12)	C (4)-C (5)	1.581(11)	C (4)-C (18)	1.549(12)
C (4)-C (19)	1.537(13)	C (5)-C (6)	1.526(11)	C (5)-C (10)	1.569(10)
C (6)-C (7)	1.534(11)	C (7)-C (8)	1.544(11)	C (8)-C (9)	1.542(10)
C (8)-C (14)	1.547(10)	C (8)-C (15)	1.577(11)	C (9)-C (10)	1.575(9)
C (9)-C (11)	1.537(10)	C (10)-C (20)	1.541(10)	C (11)-C (12)	1.516(11)
C (12)-C (13)	1.547(12)	C (12)-C (16)	1.519(12)	C (13)-C (14)	1.572(11)
C (13)-O (21)	1.445(10)	C (15)-C (16)	1.543(12)	C (16)-C (17)	1.538(14)
C (17)- O (21)	1.431(12)				
	Angle (ESD)		Angle (ESD)		Angle (ESD)
C (2)-C (1)- C (10)	113.2(7)	C (1)-C (2)- C (3)	109.9(7)	C (2)-C (3)-C (4)	116.3(7)
C (3)-C (4)-C (5)	107.7(7)	C (3)-C (4)-C (18)	110.5(7)	C (3)-C (4)-C (19)	107.9(7)
C (5)- C (4)-C (18)	114.3(7)	C (5)-C (4)-C (19)	108.0(7)	C (18)-C (4)-C (19)	108.2(7)
C (4)-C (5)-C (6)	114.7(6)	C (4)-C (5)-C (10)	115.2(6)	C (6)-C (5)-C (10)	111.3(6)
C (5)-C (6)-C (7)	109.7(6)	C (6)-C (7)-C (8)	112.7(7)	C (7)-C (8)-C (9)	111.2(6)
C (7)-C (8)-C (14)	112.3(6)	C (7)-C (8)-C (15)	108.9(6)	C (9)-C (8)-C (14)	111.9(6)
C (9)-C (8)-C (15)	106.1(6)	C (14)-C (8)-C (15)	106.0(6)	C (8)-C (9)-C (10)	116.8(6)
C (8)-C (9)- C (11)	109.2(6)	C (10)-C (9)-C (11)	114.3(6)	C (1)-C (10)-C (5)	108.9(6)
C (1)-C (10)- C (9)	107.5(6)	C (1)-C (10)-C (20)	109.2(6)	C (5)-C (10)-C (9)	105.3(5)
C (5)-C (10)-C (20)	113.5(6)	C (9)-C (10)-C (20)	112.3(6)	C (9)-C (11)-C (12)	112.1(6)
C (11)-C (12)-C (13)	113.4(7)	C (11)-C (12)-C (16)	114.7(7)	C (13)-C (12)-C (16)	98.4(6)
C (12)- C (13)-C (14)	109.1(6)	C (12)-C (13)-O (21)	113.7(6)	C (14)-C (13)-O (21)	108.2(6)
C (8)-C (14)-C (13)	109.9(6)	C (8)-C (15)-C (16)	110.8(6)	C (12)-C (16)-C (15)	109.4(7)
C (12)-C (16)-C (17)	100.3(7)	C (15)-C (16)-C (17)	111.0(7)	C (16)-C (17)-O (21)	105.5(8)
C (13)-O (21)-C (17)	108.9(7)				

analysis. An ORTEP drawing of the molecular structure is shown in Chart 5. The positional and thermal parameters with their standard deviations are listed in Table VI. The bond lengths and bond angles are given in Table VII. Consequently, the structure of **10** is *ent*-(16*S*)-atisan-13,17-oxide.

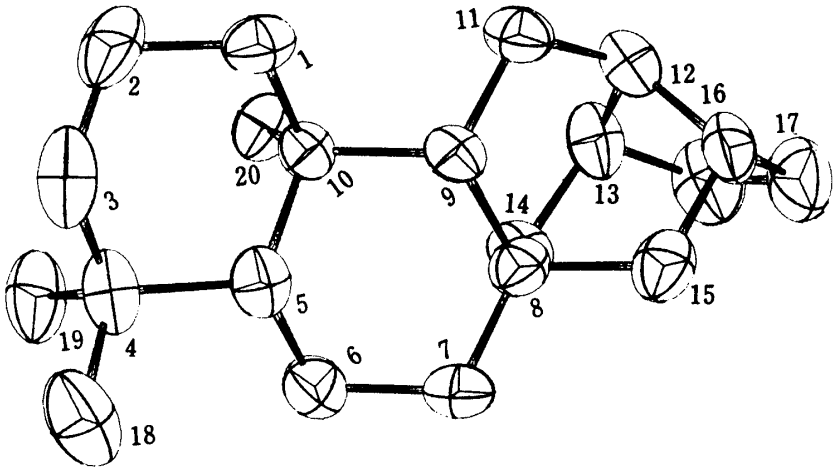


Chart 5. Drawing of the Structure of **10**

As for the diterpenoid constituents of the crude drug "Bai-mo", **1**—**5** and **6** were also isolated from fresh bulbs of *Fritillaria thunbergii* Miq., while **7**—**9** and **10** were not detectable in the fresh bulbs, even by TLC.

ent-16β,17-Epoxy-kaurane and *ent*-kaur-15-en-17-ol are apparently not components of the crude drug, but **8** was obtained as one of the main diterpenoid constituents. The diterpenoids isolated from the fresh bulbs were mostly oxidized by the treatment with lime followed by bleaching in the sun during the preparation of the crude drug.

Experimental

The instruments used and the experimental conditions for obtaining spectral data and for chromatography were the same as in the preceding paper.[1]

Extraction and Isolation of Diterpenoids——The procedure is shown in Chart 1.

Compd. I (**1**)——Colorless oil, $[\alpha]_D^{19.0}$ +15.0° (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, J=6 Hz, C_{12}–H), 6.35 (1H, dd, J=17 and 11 Hz, C_{14}–H). EI-MS m/z: 288 (M^+, base peak), 257, 81.

Compd. II (**2**)——Needles (MeOH), mp 104—105°C, $[\alpha]_D^{19.0}$ −48.0° (c=1.8, $CHCl_3$). 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, 1.19, 1.77 (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, J=6 Hz, C_{12}–H), 6.34 (1H, dd, J=17 and 11 Hz). EI-MS m/z: 316 (M^+, base peak), 257, 235, 181, 175, and 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, $[\alpha]_D^{19.0}$ −39.0° (c=1.0, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 3350, 1028 (OH), 1640, 907 (*exo*-methylene). ^{1}H-NMR ($CDCl_3$) δ: 0.85 (6H, s, *tert* $CH_3\times2$), 0.97 (3H, s, *tert* CH_3), 3.49, 3.90 (each 1H, d, J=11 Hz, C_{19}–H_2), $4.85_{(C)}$, $4.94_{(B)}$, $5.81_{(A)}$ (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). EI-MS m/z: 288 (M^+), 273, 270, 257 (base peak), 109. *Anal.* Calcd for $C_{20}H_{30}O\cdot1/4H_2O$: C, 81.99; H, 11.18. Found: C, 82.49; H, 11.13.

Compd. IV (**4**)——Colorless oil, $[\alpha]_D^{19.0}$ +25.0° (c=1.0, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1725 (C=O), 1640, 908 (*exo*-methylene). ^{1}H-NMR ($CDCl_3$) δ: 0.70, 0.87, 1.21 (each 3H, s, *tert* CH_3), 3.65 (3H, s, $COOCH_3$), $4.85_{(C)}$, $4.94_{(B)}$, $5.81_{(A)}$ (each 1H, J_{AB}=17 Hz, J_{AC}=10 Hz, J_{BC}=2 Hz, C_{15}–H, C_{16}–H_2), 5.40 (1H, t, J=2 Hz, C_7–H). EI-MS m/z: 316 (M^+, base peak), 301, 287, 257, 241.

Compd. V (**5**)——Needles (MeOH), mp 188—189°C, $[\alpha]_D^{19.0}$ −47.0° (c=1.0, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3350 (OH). ^{1}H-NMR ($CDCl_3$) δ: 0.80, 0.84, 1.02 (each 3H, s, *tert* CH_3), 3.65, 3.80 (each 1H, d, J=11 Hz, C_{17}–H_2). EI-MS m/z: 306 (M^+), 288, 275 (base peak), 257, 123. ^{13}C-NMR ($CDCl_3$) δ: see Table II. *Anal.* Calcd for $C_{20}H_{34}O_2\cdot1/2H_2O$: C, 76.14; H, 11.18. Found: C, 76.48; H, 11.24.

Compd. VI (**6**)——Needles (MeOH), mp 177—178°C, $[\alpha]_D^{19.0}$ −45.5° (c=1.0, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3350 (OH). ^{1}H-NMR ($CDCl_3$) δ: 0.80, 0.84, 1.03 (each 3H, s, *tert* CH_3), 3.37, 3.51 (each 1H, d, J=12 Hz, C_{17}–H_2). EI-MS m/z: 306 (M^+), 288, 275 (base peak), 257, 123. ^{13}C-NMR ($CDCl_3$) δ: see Table II. *Anal.* Calcd for $C_{20}H_{34}O_2\cdot1/2H_2O$: C, 76.14; H, 11.18. Found: C, 76.38; H, 11.21.

Compd. VII (**7**)——Prisms (MeOH), mp 117—118°C, $[\alpha]_D^{20.0}$ −29.0° (c=1.8, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 1742 (C=O). ^{1}H-NMR ($CDCl_3$) δ: see Table I. EI-MS m/z: 274 (M^+, base peak), 261. *Anal.* Calcd for $C_{19}H_{32}O \cdot 1/4H_2O$: C, 81.81; H, 11.02. Found: C, 82.16; H, 10.98.

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 a residue, which was chromatographed on a silica gel column (dry, 30 mg, solv.: *n*-hexane–EtOAc=9: 1) to afford prisms of **7**, 52 mg from MeOH.

Compd. VIII (**8**)——Needles (MeOH), mp 160°C, $[\alpha]_D^{20.0}$ +9.4° (c=1.5, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3490 (OH). ^{1}H-NMR ($CDCl_3$) δ: see Table I. EI-MS m/z: 304 (M^+), 289, 286 (base peak), 273, and 271. ^{13}C-NMR ($CDCl_3$) δ: see Table II. *Anal.* Calcd for $C_{20}H_{32}O_2$: C, 78.89; H, 10.59. Found: C, 78.65; H, 10.59.

8-Monoacetate 14——The conventional acetylation of **8** (25 mg) with Ac_2O–pyridine (each 1 ml) at room temperature overnight, followed by purification on a silica gel column (dry, 10 g, solv.: *n*-hexane–EtOAc=4: 1), gave **14**, 19.5 mg of prisms from acetone. mp 78—79°C. IR ν_{max}^{Nujol} cm^{-1}: 1745 (OAc). ^{1}H-NMR ($CDCl_3$) δ: 0.80, 0.87, 1.01 (each 3H, s, *tert* CH_3), 2.11 (3H, s, OAc), 2.88 (1H, s, C_{15}–H), 4.07, 4.68 (each 1H, s, C_{12}–H_2).

Tosylation of 8——A mixture of **8** (40 mg), pyridine (3 ml), and *p*-toluenesulfonyl chloride (100 mg) was allowed to stand overnight at room temperature. The reaction mixture was poured into water and extracted with Et_2O. The organic layer was chromatographed on a silica gel column (dry, 10 g, solv.: *n*-hexane–EtOAc=9: 1) to give **15**, 30 mg of needles from MeOH. mp 143—145°C. ^{1}H-NMR ($CDCl_3$) δ: 0.81, 0.87, 0.99 (each 3H, s, *tert* CH_3), 2.48 (3H, s, $-CH_3$), 4.05, 4.61 (each 1H, d, J=12 Hz, C_{17}–H_2), 7.34, 7.81 (each 2H, d, J=7 Hz, aromatic protons).

$LiAlH_4$ Reduction of 15——A mixture of **15** (25 mg), THF (5 ml), and $LiAlH_4$ (20 mg) was stirred for 6 h at room temperature. After being quenched 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, then concentrated to give a residue, which was chromatographed on a silica gel column (dry, 10 g, solv.: *n*-hexane–EtOAc=19: 1) to give **16**, 13 mg of needles from acetone. mp 116—118°C, $[\alpha]_D^{20.0}$ −8.5° (c=0.4, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.82, 0.87, 1.01, 1.14 (each 3H, s, *tert* CH_3), 2.68 (1H, s, C_{15}–H). EI-MS m/z: 288 (M^+, base peak).

Compd. IX (**9**)——Needles (*n*-hexane), mp 251—254°C, $[\alpha]_D^{19.5}$ −49.2° (c=1.4, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3480 (OH), 1682, 1620 (enone). ^{1}H-NMR ($CDCl_3$) δ: see Table III. EI-MS m/z: 590 (M^+), 572, 301 (base peak), 287, 285, 273, 271, 123. ^{3}C-NMR ($CDCl_3$) δ: see Table IV. *Anal.* Calcd for $C_{40}H_{62}O_3 \cdot 1/4H_2O$: C, 80.69; H, 10.58. Found: C, 80.53; H, 10.55.

Alkaline Hydrolysis of 9——**9** (3 mg) was refluxed in 5% NaOH–MeOH–THF (each 1 ml) on a hot water bath for 3 h. The reaction mixture was monitored by TLC (solv.: *n*-hexane–EtOAc=3: 2), and contained two compounds (*Rf* 0.07, the same as that of **5**, and *Rf* 0.24).

$LiAlH_4$ Reduction of 9——A mixture of **9** (25 mg), THF (4 ml) and $LiAlH_4$ (10 mg) was stirred for 1 h at room temperature. The usual work-up afforded the alcohols **13** (7 mg) and **5** (8 mg) as needles from MeOH. Compd. **13**: mp 134—136°C, $[\alpha]_D^{17.0}$ −25.5° (c=0.5, $CHCl_3$). 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).

Compd. X (**10**)——Needles (MeOH), mp 124—125°C, $[\alpha]_D^{20.0}$ −71.0° (c=1.1, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: no OH. ^{1}H-NMR ($CDCl_3$) δ: see Table V. EI-MS m/z: 288 (M^+, base peak), 275, 273 and 123. ^{13}C-NMR ($CDCl_3$) δ: see Table V. *Anal.* Calcd for $C_{20}H_{32}O \cdot 1/4H_2O$: C, 81.99; H, 11.18. Found: C, 82.28; H, 11.14.

Crystallographic Analysis of 10——A prismatic crystal of **10** was artificially formed into a sphere (0.3 mm in diameter). The cell parameters and intensities of this crystal were measured on a Syntex $P\bar{1}$ automated diffractometer with graphite-monochromated Mo $K\alpha$ radiation (λ=0.71069 Å). The cell parameters were determined by the auto-indexing and least-squares program for 15 reflections. The crystal data were: $C_{20}H_{32}O$ (M.W.=288.46), orthorhombic, a=24.392(7), b=10.937(3), c=6.234(1) Å, V=1663.14(76) Å^3, Dm=1.151 g/cm^3 (flotation method in aqueous KI solution), Dc=1.151 g/cm^3, z=4, space group $P2_12_12_1$. Intensities were collected by the θ—2θ scan technique with a variable scan rate of 4.0 to 24.0°/min. Three standard reflections were monitored every 100 reflections and their intensities showed good stability. A than 2.06σ(I) were used for the structure analysis. They were corrected for Lorenz and polarization effects, total of 2550 independent reflections with 2θ<55° were collected. The I values of 1098 reflectins greater but no correction was made for absorption. The structure of **10** was solved by the direct method using the MULTAN[4] series of programs and the UNICS-II[5] system. From the E map calculated with a set of phases which gave a figure of merit of 1.033, all 21 nonhydrogen atoms (R=0.30) in the molecule of **10** were located. Subsequent block-diagonal least-squares refinement with isotropic and then anisotropic thermal factors reduced the R factor value to 0.086. An ORTEP drawing of the structure, the final atomic parameters, the bond lengths and the bond angles for nonhydrogen atoms are shown in Chart 4, Table VI and Table VII, respectively. All the calculations were performed on a FACOM M-190 computer at the Computer Center of Kyushu University.

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