[Chem. Pharm. Bull. 33(9)3852—3858(1985)]

Saponin Composition of Rhizomes of *Panax japonicus* Collected in South Kyushu, Japan, and Its Significance in Oriental Traditional Medicine

TOSHINOBU MORITA, OSAMU TANAKA* and HIROSHI KOHDA

Institute of Pharmaceutical Sciences, Hiroshima University, School of Medicine, Kasumi, Minami-ku, Hiroshima 734, Japan

(Received January 30, 1985)

It was found that dammarane-saponin composition of rhizomes of *Panax japonicus* C. A. MEYER collected in Miyazaki-ken, Kyushu (South-West Province of Japan) was remarkably different from that of specimens (Japanese name: Chikusetsu-ninjin) collected at other places in Japan. From rhizomes of this specimen (local name: "Satsuma-ninjin"), four biologically active major dammarane-saponins of Ginseng roots, ginsenosides-Rg_1 (**11**), -Re (**12**), -Rc (**16**) and -Rb_1 (**17**) and two dammarane-saponins of Sanchi-Ginseng, notoginsenosides-R1 (**13**) and -R2 (**9**) as well as gypenoside-XVII (**14**) were isolated together with the saponins of oleanolic acid (**1**), chikusetsusaponins-IV (**3**) and -V (**5**), both of which have already been isolated from Chikusetsu-ninjin. From Chikusetsu-ninjin, none of **9**, **11**, **12**, **13**, **14**, **16** and **17** has been isolated, while in "Satsuma-ninjin," chikusetsusaponins-Ia (**6**), -III (**7**), which are the characteristic dammarane-saponins of Chikusetsu-ninjin, were not identified.

The present isolation of the major dammarane-saponins of Ginseng roots from "Satsuma-ninjin" in relatively high yields is significant not only from the viewpoint of the geographical relation of Japanese *P. japonicus* with Chinese and Himalayan *Panax* spp. but also from the viewpoint of the pharmacological importance of this specimen in oriental traditional medicine.

Keywords——*Panax japonicus*; Araliaceae; Miyazaki-ken; Ginseng saponin; ginsenosides-Rg_1, -Re, -Rc, -Rb_1; notoginsenosides-R1, -R2; gypenoside-XVII; chikusetsusaponins-IV, -V; Satsuma-ninjin; Chikusetsu-ninjin

Introduction

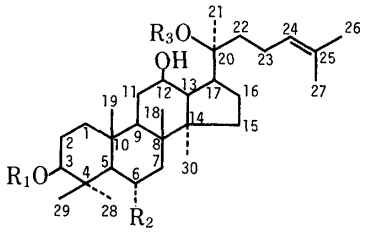
Panax japonicus C. A. MEYER (=*P. pseudo-ginseng* (WALL.) subsp. *japonicus* HARA,[1] Araliaceae), which grows wild throughout Japan, contains a long bamboo-like rhizome. The rhizome of this plant (Japanese name: Chikusetsu-ninjin) has long been known as an oriental traditional plant drug and from it, Shoji *et al.*[2] isolated four sapoins of oleanolic acid (**1**) named chikusetsusaponins-Ib (**2**), -IV (**3**), -IVa (**4**) and -V (**5**=ginsenoside-Ro, a minor saponin of the root of *P. ginseng* C. A. MEYER) along with the characteristic dammarane-saponins, chikusetsusaponins-Ia (**6**) and -III (**7**) as well as a small amount of ginsenoside-Rg_2 (**8**, a minor dammarane-saponin of Ginseng) (yields: see Table I).

Previously, Seo described the historical significance of *P. japonicus* growing wild in Miyazaki-ken, South Kyushu, Japan, the rhizome of which has been locally called "Satsuma-ninjin," being distinguished from the specimens collected at other places of Japan because of its superior medicinal quality[3]; Chin-chi Her, a Chinese physician who fled from his own country to Kyushu in 1646, discovered this plant therein and described its value as a medicine to the natives in this province. Seo mentioned that this might have been the first medicinal use of this plant in Japan. In our series of studies on the chemical constituents of *P. ginseng* and related plants,[4] we have now carried out the isolation and identification of saponins of this so-called "Satsuma-ninjin."

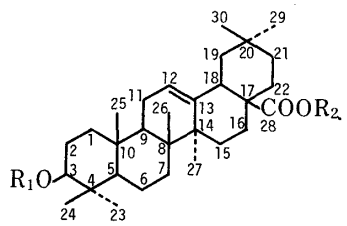
Results

No significant morphological difference was observed between "Satsuma-ninjin" and Chikusetsu-ninjin collected in other parts of Japan. However, the thin layer chromatogram (TLC) of the glycoside fraction of "Satsuma-ninjin" collected at several places in Miyazaki-ken was significantly different from those of Chikusetsu-ninjin collected at twenty-six other places in Japan (including Ohita-ken, North Kyushu), the TLC patterns of which all resembled each other (Fig. 1).

The methanolic extract of "Satsuma-ninjin" collected at Miyakonojou, Miyazaki-ken, was subjected to chromatographic separation, affording nine saponins tentatively named



	R_1	R_2	R_3
6:	-Glc-^{6}-Xyl	-H	-H
7:	-Glc-^{2}(Glc, ^{6}Xyl)	-H	-H
8:	-H	-O-Glc-^{2}-Rha	-H
9:	-H	-O-Glc-^{2}-Xyl	-H
10:	-H	-OH	-H
11:	-H	-O-Glc	-Glc
12:	-H	-O-Glc-^{2}-Rha	-Glc
13:	-H	-O-Glc-^{2}-Xyl	-Glc
14:	-Glc	-H	-Glc-^{6}-Glc
15:	-H	-H	-H
16:	-Glc-^{2}-Glc	-H	-Glc-^{6}-Ara
17:	-Glc-^{2}-Glc	-H	-Glc-^{6}-Glc
20:	-Glc-^{2}-Glc	-H	-Glc



	R_1	R_2
1:	-H	-H
2:	-GlcUA-^{4}(Ara, ^{6}Glc)	-H
3:	-GlcUA-^{4}-Ara	-Glc
4:	-GlcUA	-Glc
5:	-GlcUA-^{2}-Glc	-Glc
18:	-GlcUA-^{2}-Xyl	-Glc
19:	-GlcUA-^{2}-Xyl	-H

Glc; β-D-glucopyranosyl
Xyl; β-D-xylopyranosyl
Rha; α-L-rhamnopyranosyl
Ara; α-L-arabinofuranosyl
GlcUA; β-D-glucuronopyranosyl

Chart 1

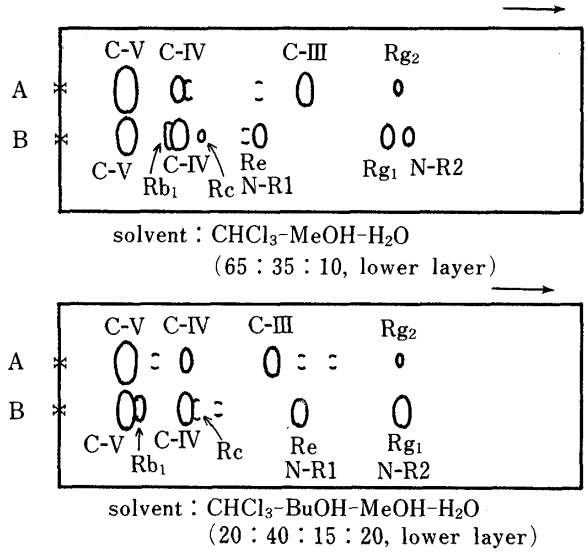


Fig. 1. Thin-Layer Chromatogram of Saponins from Rhizomes of *Panax japonicus*

Plates: Kieselgel $60F_{254}$. Color reagent: H_2SO_4.
C, chikusetsusaponin; N, notoginsenoside; Rb_1, Rc, Re, Rg_1, Rg_2, ginsenosides.
A: "Chikusetsu-ninjin"; Hokkaido (two specimens), Nagano-ken, Niigata-ken, Tokyo-to, Kyoto-fu, Nara-ken, Mie-ken (three specimens), Tottori-ken (three specimens), Shimane-ken, Hiroshima-ken (nine specimens), Ehime-ken, Fukuoka-ken, Ohita-ken.
B: "Satsuma-ninjin"; Miyazaki-ken (three specimens; collected at Miyakonojou, Mt. Futaishi and Shiiba).

TABLE I. Comparison of Saponins from Rhizomes of *Panax pseudo-ginseng*, *Panax japonicus* var. *major*, *Panax zingiberensis* and *Panax japonicus*

		Yield (%)							
		(A)[14] (Tzatogang)[a]	(A)[14] (Pari-la)[a]	(B)[15] (Yunnan)	(C)[16] (Yunnan)	(A)[17] (Khosa)[a]	(D)[18] (Yunnan)	(D)[b] (Miyazaki)	(D)[2] (Japan)
Oleanolic acid (**1**) saponins	C-IVa (**4**)	1.7	1.8	0.2	0.03	0.6	2.8	—	+
	C-IV (**3**)	—	—	—	0.3	0.3	3.4	1.4	0.4
	C-V (**5**)	0.4	0.1	1.0	2.1	7.3	3.1	2.2	5.4
	Z-R1	—	—	—	0.08	—	—	—	—
	Pro-C-V	—	0.02	—	—	—	—	—	—
	RT_1 (**18**)	1.5	5.0	—	—	—	—	—	—
	RP_1 (**19**)	0.07	0.1	—	—	—	—	—	—
	C-Ib (**2**)	—	—	—	—	—	—	—	+
Dammarane (**10**, **15**) saponins		Rb_1 (**17**, 0.3) Rd (**20**, 0.2) Rg_1 (**11**, 0.4) RT_3 (0.1)	Rb_1 (**17**, 0.05) Rd (**20**, 0.07) Re (**12**, 0.1) F_2 (0.02) Rg_1 (**11**, 1.2) Gy-XVII (**14**, 0.03) RT_3 (0.02)	Rd (**20**, 0.7) N-R2 (**9**, 0.03) 20glc-Rf (0.01)	Rg_1 (**11**, 0.6) Rh_1 (+)	Rb_1 (**17**, 1.1)	Rd (**20**, 0.04) Re (**12**, 0.1) Rg_1 (**11**, 0.2) Rg_2 (**8**, 0.05) N-R2 (**9**, 0.02)	Rb_1 (**17**, 0.7) Rc (**16**, 0.1) Re (**12**, 0.3) Rg_1 (**11**, 0.4) N-R1 (**13**, 0.05) N-R2 (**9**, 0.3) Gy-XVII (**14**, 0.02)	C-III (**7**, 1.2) Rg_2 (**8**, +) C-Ia (**6**, +)
Ocotillol saponins		F_{11} (0.07) RT_2 (0.09) RT_4 (0.08) RT_5 (0.07)	RT_4 (0.02)	M-R1 (0.07) M-R2 (0.1)			F_{11} (0.2)		

(A), *P. pseudo-ginseng* subsp. *himalaicus*; (B), *P. japonicus* var. *major*; (C), *P. zingiberensis*; (D), *P. japonicus*. *a*) Bhutan-Himalaya. *b*) Collected at Miyakonojou, Miyazaki-ken, Japan. C, chikusetsusaponin; Z, zingibroside; N, notoginsenoside; Gy, gypenoside; M, majonoside; Rb_1, Rc, Rd, Re, Rg_1, Rg_2, Rh_1, F_2, 20glc-Rf, ginsenosides; F_{11}, RP_1, RT_{1-5}, pseudo-ginsenosides; Pro-C-V, prosapogenin of C-V; +, very low yield.

saponins I—IX in decreasing order of the *Rf* values on TLC (Fig. 1). Saponin-I (0.3% yield) was identified as notoginsenoside-R2 (**9**; aglycone, 20 (*S*)-protopanaxatriol (**10**)) which was first isolated from Chinese Sanchi-Ginseng, the root of *P. notoginseng* (BURK.) F. H. CHEN, as one of the minor dammarane-saponins[5] and also from several other *Panax* species.

Saponins-II (0.4% yield) and -III (0.3% yield) were identified as ginsenosides-Rg_1 (**11**)[6] and -Re (**12**),[7] respectively, both of which are known as major dammarane-saponins (common aglycone, **10**) of Ginseng roots and many other *Panax* spp. Saponin-IV (0.05% yield) was identified as notoginsenoside-R1 (**13**), which was first isolated from Sanchi-Ginseng[5] and also from Ginseng roots.[8]

A minor saponin-V (0.02% yield) was identical with the dammarane-saponin, gypenoside-XVII (**14**; aglycone, 20(*S*)-protopanaxadiol (**15**)) previously isolated from *Gynostemma pentaphyllum* MAKINO[9] and also from Sanchi-Ginseng[10] and American Ginseng (*P. quinquefolium* L.).[11] Saponins-VI (0.1% yield) and -VIII (0.7% yield) were identified as ginsenosides-Rc (**16**) and -Rb_1 (**17**), respectively, both of which are known as major dammarane-saponins (common aglycone, **15**) of Ginseng roots[12] and have been identified in many other *Panax* spp. such as American Ginseng,[11,13] *etc.* It was surprising that these dammarane-saponins were not isolated from Chikusetsu-ninjin collected from any other place in Japan, while not even a trace of **7**, the characteristic major dammarane-saponin of Chikusetsu-ninjin, was identified in "Satsuma-ninjin."

Saponins-VII (1.4% yield) and -IX (2.2% yield) were identical with **3** and **5**, respectively, which are the major oleanane-saponins of Chikusetsu-ninjin[2] (Table I).

Discussion

A variety of wild *Panax* spp. which are morphologically related to each other, are distributed from Japan to the Eastern Himalayas through the South-Western Province of China (Yunnan, Szechwan and Tibet);[1,19] Japan, *P. japonicus*; China, *P. japonicus* (Zhao-shen, Zhujie-sanchi or Zhujie-shen), *P. japonicus* var. *major* (Zu-tzi-shen), *P. zingiberensis* C. Y. WU *et* K. M. FENG, *etc.*; Himalayas, *P. pseudo-ginseng* (WALL.) subsp. *himalaicus* HARA (Himalayan *Panax*) and its varieties. These *Panax* spp. (tentatively classified as group I) commonly have a large rhizome with a small round root in contrast to *P. ginseng*, Sanchi-Ginseng and American Ginseng (tentatively named group II) which have a large carrot-like root with a small rhizome.

We have conducted comparative studies on the saponin composition of *Panax* spp. in co-operation with Kunming Institute of Botany, Academia Sinica, and some of the results have been as follows. The saponin composition of roots of group II includes a large amount of various pharmacologically active dammarane-saponins (aglycones, **10** and **15**) either with a small amount of the oleanane-saponin, **5** (Ginseng and American Ginseng) or without it (Sanchi-Ginseng). It was also found that the small rhizome (a kind of corm)[10,20] of Ginseng and Sanchi-Ginseng contained the same dammarane-saponins as the roots. In contrast, saponins of the rhizomes of group I include a large amount of saponins of **1**, as summarized in Table I. It was noted that rhizomes of Himalayan *Panax* collected at relatively high altitude contained the characteristic saponins of **1**, pseudo-ginsenosides-RT_1 (**18**) and -RP_1 (**19**), but lacked **3** which is present in rhizomes of other plants of group I except for Zu-tzi-shen.[14]

With regard to dammarane-saponins of rhizomes of group I, it is significant that in Himalayan and Chinese specimens, the major dammarane-saponins of roots of group II, such as **11**, **12**, **16**, **17**, or ginsenoside-Rd (**20**), were identified in relatively high content (Table I), while from Japanese Chikusetsu-ninjin, as already mentioned, only a trace of the Ginseng minor saponin, **8** was isolated and the major dammarane-saponin is represented by **7**, which has not been identified in any other *Panax* spp., either of group I or group II (Table I). For

instance, Chinese Zhao-shen (*vide supra*) has been considered to be the same species as Japanese *P. japonicus*, showing no morphological difference from the Japanese specimen. However, our chemical studies revealed that the dammarane-saponin composition of the rhizome of Chinese Zhao-shen is remarkably different from that of Japanese Chikusetsu-ninjin, consisting of Ginseng dammarane-saponins, **8**, **11**, **12** and **20** as well as the dammarane-saponin of Sanchi-Ginseng, **9** (see Table I),[18] while not even a trace of **7** was isolated from rhizomes of Zhao-shen. These characteristic dammarane-saponin compositions seem to be evidence of a special botanical position of Japanese *P. japonicus* in group I.

Further, this remarkable difference in saponin composition between Ginseng roots and Chikusetsu-ninjin supports the argument that in oriental traditional medicine, Chikusetsu-ninjin should not be used as a substitute for Ginseng roots and unlike Ginseng roots, its efficacies center not on restorative action but on stomachic, expectorant and anti-pyretic properties. However, the present isolation of the major dammarane-saponins of Ginseng roots, **11**, **12**, **16** and **17** from "Satsuma-ninjin" in relatively high yields provides an exception to the above argument; "Satsuma-ninjin," may exceptionally be used as a substitute for Ginseng roots. The commercial "Satsuma-ninjin" available on the drug market in Japan shows the same saponin TLC pattern as the specimens of the present study. From the geographical point of view, it is also interesting that rhizomes of Japanese *P. japonicus* growing in South Kyushu, the province of Japan nearest to China, are similar to those of the related Chinese and Himalayan plants rather than to those of specimens from other places in Japan in respect to the contents of the common dammarane-saponins of Ginseng roots and other plants of group II. For the present study, specimens collected in Miyazaki-ken have been cultivated at the Experimental Station of Medicinal Plants of our institute.

Previously, we have reported that the saponin composition of the aerial parts of Japanese *P. japonicus*[21] is completely different from those of other *Panax* species, both groups I and II.[4,22] A study on saponins of the leaves of *P. japonicus* collected in Miyazaki-ken is in progress.

Experimental

General Procedures——Nuclear magnetic resonance (NMR) spectra were taken on JEOL FX-100 (^{1}H-NMR at 99.55 MHz and ^{13}C-NMR at 25.00 MHz) and JEOL GX-270 (^{1}H-NMR at 270 MHz and ^{13}C-NMR at 67.80 MHz) spectrometers in C_5D_5N with tetramethylsilane (TMS) as an internal standard.

Mass spectra (MS) were taken at 75 eV on a JEOL 01-SG-2 spectrometer by the direct inlet method; ionization current, 200 μA; accelerating voltage, 6—8 kV. Trimethylsilylation for MS: The methyl ester (1—2 mg) of each saponin prepared by treatment with CH_2N_2 was heated with *N*-trimethylsilylimidazole (5 drops) in a sealed micro-tube at 80 °C for 2 h. The reaction mixture was diluted with H_2O and then extracted with *n*-C_6H_{14}. The C_6H_{14} layer was washed with H_2O and concentrated to dryness by blowing N_2 gas over it at room temperature. The residue was subjected to MS. Acetylation for MS: A sample of saponin (1—2 mg) was heated with $(CH_3CO)_2O$ (2—3 drops) and C_5H_5N (5—6 drops) in a sealed micro-tube at 80 °C for 2—3 h. The reaction mixture was concentrated to dryness by blowing N_2 gas over it at room temperature and then the residue was subjected to MS.

Optical rotations were measured with a Union automatic digital polarimeter at 15—20 °C in MeOH or C_5H_5N.

High Performance Liquid Chromatography (HPLC) Equipment: HLC-802UR (Toyo Soda) or HLC 803D pump (Toyo Soda); detector, RI-8 differential refractometer (Toyo Soda).

Identification of the Known Saponins——Each known saponin was identified by TLC on Kieselgel 60F_{254} (Merck) with $CHCl_3$–MeOH–H_2O (65 : 35 : 10, lower layer), $CHCl_3$–MeOH–H_2O (6 : 4 : 1, homogeneous) and $CHCl_3$–BuOH–MeOH–H_2O (20 : 40 : 15 : 20, lower layer), and by reverse-phase TLC on silica gel plates (RP-8 and RP-18 F_{254} (Merck)) with 60—75% MeOH (detection: H_2SO_4), as well as by ^{1}H-NMR and ^{13}C-NMR spectroscopy, optical rotation measurement and MS (as the acetate or trimethylsilyl ether) in comparison with an authentic sample.

Extraction and Separation of Saponins——Dried and powdered rhizomes (200 g) of *Panax japonicus* (local name: Satsuma-ninjin) collected at Miyakonojou, Miyazaki-ken, Japan (Dec. 1983) were extracted with hot MeOH (500 ml × 5) and then with hot 50% MeOH (500 ml × 2) to give an MeOH extract (after concentration) in a yield of 36.5%. An aqueous solution of this MeOH extract was subjected to column chromatography on reverse-phase highly porous polymer (DIAION HP-20, Mitsubishi Chemical Ind., Ltd.); elution with H_2O (10 l), MeOH (10 l) and $CHCl_3$

(3 l) provided the H_2O eluate (47 g), MeOH eluate (crude saponin fraction) (25 g) and $CHCl_3$ eluate (400 mg). The MeOH eluate was separated into three fractions, Fr-1, Fr-2 and Fr-3 by column chromatography on silica gel (solvent: $CHCl_3$–MeOH–H_2O (30 : 10 : 1, 30 : 15 : 2.5 and then 30 : 20 : 5, all homogeneous)).

Fr-1 was chromatographed on silylated silica gel (LiChroprep RP-8 (Merck)) (solvent: 68% MeOH) to give crude **11** and **9** (0.3% yield), colorless prisms (from MeOH–H_2O), mp 185—187 °C, $[\alpha]_D^{17}$ +9.3° (c=1.09, MeOH). Crude **11** was further chromatographed on silica gel (solvent: $CHCl_3$–MeOH–H_2O (30 : 10 : 1, homogeneous)) to give **11** (0.4% yield), a white powder (MeOH–EtOAc), $[\alpha]_D^{17}$ +31.0° (c=1.40, MeOH).

Fr-2 was chromatographed on silica gel (solvent: $CHCl_3$–MeOH–H_2O (25 : 10 : 1, homogeneous)) to give a mixture of **12**, **13** and **14** and crude **16** (separation of **16**: see separation of Fr-3). The mixture of **12**, **13** and **14** was further chromatographed on silylated silica gel (*vide supra*) (solvent: 70% MeOH). The first fraction was subjected to preparative HPLC on a reverse-phase column of ODS-120A (Toyo Soda) (21.5 mm × 30 cm; mobile phase, 55% MeOH; flow rate, 8.2 ml/min; injection vol., 1 ml (990 mg/10 ml 55% MeOH); detector, RI-8) to give **13** (0.05% yield), colorless needles (from MeOH–H_2O), mp 211—213 °C, $[\alpha]_D^{17}$ +19.4° (c=1.09, MeOH) and **12** (0.3% yield), colorless needles (from 50% MeOH), mp 202—204 °C, $[\alpha]_D^{15}$ −2.2° (c=1.23, MeOH). The next fraction from the above chromatography was rechromatographed on silica gel (solvent: $CHCl_3$–MeOH–H_2O (30 : 10 : 1, homogeneous)) and then separated by preparative HPLC on a reverse-phase column of ODS-120A (*vide supra*) (21.5 mm × 30 cm; mobile phase, 75% MeOH; flow rate, 6.5 ml/min; injection vol., 1 ml (177 mg/2 ml 75% MeOH); detector, RI-8) to give **14** (0.02% yield), a white powder (MeOH–EtOAc), $[\alpha]_D^{20}$ +11.7° (c=0.95, MeOH).

Fr-3 was separated into three fractions, Fr-3a, Fr-3b and Fr-3c by column chromatography on silica gel (solvent: $CHCl_3$–MeOH–H_2O (30 : 15 : 2.5, homogeneous)). Fr-3a and crude **16** from Fr-2 (*vide supra*) were combined and chromatographed on silica gel (solvent: $CHCl_3$–MeOH–H_2O (6 : 4 : 1, homogeneous)) and then on silylated silica gel (*vide supra*) (solvent: 80% MeOH), and were finally purified by preparative HPLC on a reverse-phase column of ODS-120A (*vide supra*) (21.5 mm × 30 cm; mobile phase, 70% MeOH; flow rate, 7.5 ml/min; injection vol., 1 ml (410 mg/4 ml 70% MeOH); detector, RI-8) to give **16** (0.1% yield), a white powder (MeOH–EtOAc), $[\alpha]_D^{19}$ +1.5° (c= 1.15, MeOH). Fr-3b, after repeated column chromatography on silylated silica gel (*vide supra*) (solvent: 70 or 75% MeOH), followed by deionization with ion exchange resin (Amberlite MB-3), afforded **3** (1.4% yield), colorless prisms (from MeOH–H_2O), mp 217—219 °C (dec.), $[\alpha]_D^{19}$ −17.7° (c=1.23, C_5H_5N) and another fraction which was further separated by preparative HPLC on a reverse-phase column of ODS-120A (*vide supra*) (21.5 mm × 30 cm; mobile phase, 70% MeOH; flow rate, 7 ml/min; injection vol., 1 ml (1.4 g/14 ml 70% MeOH); detector, RI-8) to give **17** (0.7% yield), a white powder (MeOH–EtOAc), $[\alpha]_D^{20}$ +11.0° (c=1.82, MeOH). Fr-3c, after repeated column chromatography on silica gel (solvent: $CHCl_3$–MeOH–H_2O (6 : 4 : 1, homogeneous)), followed by deionization with ion exchange resin (Amberlite MB-3), afforded **5** (=ginsenoside Ro) (2.2% yield), a white powder (reprecipitated from MeOH–EtOAc), $[\alpha]_D^{19}$ +3.9° (c=1.58, MeOH).

Acknowledgement We are grateful to Mr. Akira Seo and Mr. Shoichiro Seo, Seo Pharmacy, Kagoshima, for their encouragement and valuable advice throughout this study. We are also grateful to Mr. Takahisa Sawada, National Institute of Kyushu Agricultural Experimental Station, Ministry of Agriculture, Forestry and Fisheries, Miyakonojou, for his kind co-operation in the collection of Satsuma-ninjin. Thanks are also due to Dr. Shoji Yahara, Kumamoto University, for his collection of Chikusetsu-ninjin, and to Dr. Hiromichi Matsuura, Wakunaga Pharmaceutical Co., Ltd., Hiroshima, for determination of NMR spectra on the JEOL GX-270 instrument.

References

1) H. Hara, *Journ. Jap. Bot.*, **45**, 197 (1970).
2) N. Kondo and J. Shoji, *Yakugaku Zasshi*, **88**, 325 (1968); N. Kondo, J. Shoji, N. Nagumo and N. Komatsu, *ibid.*, **89**, 846 (1969); N. Kondo, K. Aoki, H. Ogawa, R. Kasai and J. Shoji, *Chem. Pharm. Bull.*, **18**, 1558 (1970); N. Kondo, Y. Marumoto and J. Shoji, *ibid.*, **19**, 1103 (1971); T. D. Lin, N. Kondo and J. Shoji, *ibid.*, **24**, 253 (1976).
3) A. Seo, *Journal of the Japan Society for Oriental Medicine*, **27**, 193 (1977).
4) O. Tanaka and R. Kasai, "Fortschritte der Chemie Organisher Naturstoffe" Vol. 46, ed. by W. Herz, H. Grisebach, G. W. Kirby and Ch. Tamm, Springer-Verlag, Wien, New York, 1984, pp. 1—76.
5) J. Zhou, M.-Z. Wu, S. Taniyasu, H. Besso, O. Tanaka, Y. Saruwatari and T. Fuwa, *Chem. Pharm. Bull.*, **29**, 2844 (1981).
6) Y. Iida, O. Tanaka and S. Shibata, *Tetrahedron Lett.*, **52**, 5449 (1968); Y. Nagai, O. Tanaka and S. Shibata, *Tetrahedron*, **27**, 881 (1971).
7) S. Sanada, N. Kondo, J. Shoji, O. Tanaka and S. Shibata, *Chem. Pharm. Bull.*, **22**, 2407 (1974).
8) R. Kasai, H. Besso, O. Tanaka, Y. Saruwatari and T. Fuwa, *Chem. Pharm. Bull.*, **31**, 2120 (1983).
9) T. Takemoto, S. Arihara, T. Nakajima and M. Okuhira, *Yakugaku Zasshi*, **103**, 1015 (1983).
10) H. Matsuura, R. Kasai, O. Tanaka, Y. Saruwatari, T. Fuwa and J. Zhou, *Chem. Pharm. Bull.*, **31**, 2281 (1983).
11) H. Besso, R. Kasai, J. Wei, J.-F. Wang, Y. Saruwatari, T. Fuwa and O. Tanaka, *Chem. Pharm. Bull.*, **30**, 4534

(1982).
12) S. Sanada, N. Kondo, J. Shoji, O. Tanaka and S. Shibata, *Chem. Pharm. Bull.*, **22**, 421 (1974).
13) S. Sanada and J. Shoji, *Shoyakugaku Zasshi*, **32**, 96 (1978).
14) O. Tanaka, T. Morita, R. Kasai, J. Kinouchi, S. Sanada, Y. Ida and J. Shoji, *Chem. Pharm. Bull.*, **33**, 2323 (1985).
15) T. Morita, R. Kasai, O. Tanaka, J. Zhou, T.-R. Yang and J. Shoji, *Chem. Pharm. Bull.*, **30**, 4341 (1982).
16) T.-R. Yang, Z. D. Jiang, M. Z. Wu, J. Zhou and O. Tanaka, *Acta Pharm. Sinica*, **19**, 232 (1984).
17) N. Kondo, J. Shoji and O. Tanaka, *Chem. Pharm. Bull.*, **21**, 2702 (1973); N. Kondo and J. Shoji, *ibid.*, **23**, 3282 (1975).
18) T. Morita, R. Kasai, H. Kohda, O. Tanaka, J. Zhou and T.-R. Yang, *Chem. Pharm. Bull.*, **31**, 3205 (1983).
19) J. Zhou, W. Huang, M. Wu, T. Yang, G. Feng and C. Wu, *Acta Phytotaxonomica Sinica*, **13**, 29 (1975).
20) H. Otsuka, Y. Morita, Y. Ogihara and S. Shibata, *Planta Medica*, **32**, 9 (1977).
21) S. Yahara, R. Kasai and O. Tanaka, *Chem. Pharm. Bull.*, **25**, 2041 (1977); S. Yahara, O. Tanaka and I. Nishioka, *ibid.*, **26**, 3010 (1978).
22) *P. ginseng*: S. Yahara, O. Tanaka and T. Komori, *Chem. Pharm. Bull.*, **24**, 2204 (1976); S. Yahara, K. Matsuura, R. Kasai and O. Tanaka, *ibid.*, **24**, 3212 (1976); S. Yahara, K. Kaji (née Matsuura) and O. Tanaka, *ibid.*, **27**, 88 (1979); *P. quinquefolium*: S.-E. Chen and E. J. Staba, *Lloydia*, **41**, 361 (1978); J.-H. Lui and E. J. Staba, *J. Nat. Prod.*, **43**, 340 (1980); S.-E. Chen, E. J. Staba, S. Taniyasu, R. Kasai and O. Tanaka, *Planta Medica*, **42**, 406 (1981); *P. notoginseng*: S. Taniyasu, O. Tanaka, T.-R. Yang and J. Zhou, *Chem. Pharm. Bull.*, **44**, 124 (1982); T.-R. Yang, R. Kasai, J. Zhou and O. Tanaka, *Phytochemistry*, **22**, 1473 (1983); *P. pseudo-ginseng* subsp. *himalaicus*: O. Tanaka and S. Yahara, *Phytochemistry*, **17**, 1353 (1978); *P. japonicus* var. *major*: T.-R. Yang, M. Wu, J. Zhou, T. Morita, R. Kasai and O. Tanaka, *Acta Botanica Yunnanica*, **6**, 118 (1984).