were observed in the ^{13}C NMR spectrum of cyperenal as shown in Table 1 However, tentative assignments could be made by INEPT experiments and by comparing the chemical shifts with those of cyperenic acid (**5**), obtained from cyperenal by Jones' oxidation [3] There was no problem in the assignments of cyperenic acid. However, the assignments of C-2, C-3, C-6 and C-8 of cyperenal were interchangeable Therefore, the C-2, C-3, C-6 and C-8 carbons were finally assigned by using ^{1}H–^{1}H homonuclear and ^{1}H–^{13}C heteronuclear chemical shift correlation spectra Thus, the assignments of cyperene derivatives were established as shown in Table 1

EXPERIMENTAL

Extraction and isolation Procedures were similar to those described in the preceding paper [1]

Cyperenyl acetate (**3**) Oil, $[\alpha]_D$ −5 1° ($CHCl_3$, *c* 0 8), ^{1}H NMR (270 MHz, $CDCl_3$) δ0.76 (3H, *s*, H-12), 0 80 (3H, *d*, *J* = 6 Hz, H-15), 0.94 (3H, *s*, H-13), 2 02 (3H, *s*, H-17), 4 59 (2H, AB*q*, *J* = 12 8 Hz, H-14), ^{13}C NMR, Table 1, IR ν_{max}^{film} cm^{-1} 1725, 1240, 1020 and 960, EIMS *m/z* 262 (M^+ $C_{17}H_{26}O_2$)

Cyperenal (**4**) Oil, $[\alpha]_D$ 9.6° ($CHCl_3$, *c* 0.4), ^{1}H NMR ($CDCl_3$) δ0 82 (3H, *s*, H-12), 0 84 (3H, *d*, *J* = 6 Hz, H-15), 1 02 (3H, *s*, H-13), 9 84 (1H, *s*, H-14), ^{13}C NMR, Table 1, IR ν_{max}^{film} cm^{-1} 1670, EIMS *m/z* 218 (M^+ $C_{15}H_{22}O$)

Cyperenic acid (**5**) Obtained from cyperenal by Jones' oxidation Oil, $[\alpha]_D$ −13 7° ($CHCl_3$, *c* 0 3), ^{1}H NMR ($CDCl_3$) δ0 83 (3H, *s*, H-12), 0 86 (3H, *d*, *J* = 6 Hz, H-15), 1 00 (3H, *s*, H-13), ^{13}C NMR, Table 1, IR ν_{max}^{film} cm^{-1} 1700, EIMS *m/z* 234 (M^+ $C_{15}H_{22}O_2$)

REFERENCES

1 Takano, S and Kawaminami, S (1987) *Phytochemistry* **26**, 435
2 Teisseire, P, Maupetit, P, Corbier, B and Rouillier, P. (1974) *Recherches* (*RBD*) **19**, 36
3 Nerali, S B and Chakravarti, K K (1967) *Tetrahedron Letters*, 2447
4 Joseph-Nathan, P, Martinez E, Santillan, R L, Wesener, J. R and Gunther, H (1984) *Org Magn Reson* **22**, 308

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KANSHONES A AND B, SESQUITERPENOIDS OF *NARDOSTACHYS CHINENSIS**

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Key Word Index—*Nardostachys chinensis*, Valerianaceae, sesquiterpenoid, kanshones A and B

Abstract—Two new sesquiterpenoids, kanshones A and B, isolated from *Nardostachys chinensis* were fully characterized by chemical and spectroscopic means.

INTRODUCTION

Nardostachys chinensis Batalin (Japanese name: Kanshōkō), a valerianaceous plant, the roots and rhizomes of which have been used in Oriental medicine is a rich source of sesquiterpenoids [1–9]. As a continuation of our earlier work [10], we have now isolated two new sesquiterpenoids, kanshones A and B, in addition to the major constituent nardosinone (**3**), from the methylene chloride extract of this plant material The structures of these sesquiterpenoids were established on the basis of detailed spectral analysis and chemical transformations to compounds of known structure

RESULTS AND DISCUSSION

Kanshone A isolated as oil, $[\alpha]_D$ −147 8°, was analysed for $C_{15}H_{22}O_2$ on the basis of its mass ion peak at *m/z* 234 [M^+] and from its ^{13}C NMR spectrum which showed resonances for 15 carbon atoms. The UV absorption maximum at 248 nm and IR spectral bands at 3450 and 1665 cm^{-1} indicated that kanshone A bears a hydroxyl group and a conjugated carbonyl function. The ^{1}H NMR spectrum of kanshone A showed a signal assigned to a β-hydrogen of an enone system at δ 7.00 (1H, *d*, *J* = 4 0 Hz) as well as those due to three hydrogens of an ABX system at 2.62 (1H, *dd*, *J* = 7.1 and 1 0 Hz), 6.16 (1H, *dd*, *J* = 10.0 and 1.0 Hz) and 6.96 (1H, *dd*, *J* = 10 0 and 7 1 Hz) These data, along with the ^{13}C NMR signals at δ 128.9 (*d*), 137.2 (*d*), 141 6 (*s*), 151 1 (*d*) and 187.9 (*s*), revealed that the carbonyl group was flanked by two double bonds In addition to above, the ^{1}H NMR spect-

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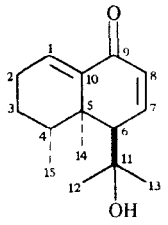

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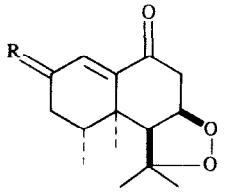

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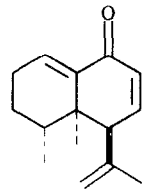
3 R = H_2



5

rum displayed signals at δ 1 02 (3H, *d*, *J* = 6 5 Hz), 1 08, 1 18 and 1 25 (3H, each *s*), pointing to the presence of one secondary and three tertiary methyl groups The resonance positions of the latter two tertiary methyl signals and the carbinyl carbon signal at δ 75 9 (*s*), suggested that kanshone A bears a hydroxyisopropyl group in its molecule and this was further substantiated by an ion peak at *m/z* 59 in the mass spectrum From these findings, together with the fact that nardosinone (**3**) was isolated from the same source, it was assumed that kanshone A has the same carbon skeleton as that of nardosinone (**3**) In order to confirm this point, kanshone A was dehydrated with phosphorus oxychloride in pyridine to afford a dienone which was identical with compound **5** prepared from hydrogenation of nardosinone (**3**) followed by dehydration [7] This established that kanshone A has the same carbon framework and stereochemistry as those of nardosinone (**3**) Thus, the structure of kanshone A was established as **1**

Kanshone B was obtained as needles, $[\alpha]_D$ +133 8 , and it had the molecular formula $C_{15}H_{22}O_4$ determined from its molecular ion peak at *m/z* 266 1539 (*m/z* 266 1519 calcd for $C_{15}H_{22}O_4$) and an analysis of its ^{13}C NMR spectrum In the ^1H NMR specturm of kanshone B, the signals due to four hydrogens at δ 2 72 (1H, *dd*, *J* = 18 6 and 2 0 Hz), 2 91 (1H, *dd*, *J* = 18 6 and 7 0 Hz), 4 91 (1H, *ddd*, *J* = 9 3, 7 0 and 2 0 Hz) and 2 95 (1H, *d*, *J* = 9 3 Hz) and one secondary and two tertiary methyl groups at δ 1 03 (3H, *d*, *J* = 6 6 Hz), 1 11 and 1 40 (3H, each *s*) appeared essentially at the same positions as the C-8, C-7, C-6, C-15, C-14 and C-13 hydrogens of nardosinone (**3**), suggesting that kanshone B is a congener of nardosinone (**3**) Besides these signals, kanshone B exhibited a ^1H NMR signal assigned to an olefinic hydrogen at δ 6 97 as a doublet (1H, *J* = 5 0 Hz), while nardosinone (**3**) displayed the corresponding signal at 7 03 as a double doublet (1H, *J* = 5 2 and 2 6 Hz) Furthermore, a carbinyl hydrogen signal at δ 4 34 (1H, *m*) coupled with an olefinic hydrogen signal was also discernible in kanshone B These observations, in conjunction with an IR spectral band at 3480 cm^{-1} and the fact that the molecular formula of kanshone B differs from that of nardosinone (**3**) only by the presence of an extra oxygen atom, revealed that kanshone B has a hydroxyl group at C-2 The orientation of this hydroxyl group was deduced to be spatially close to the C-4 hydrogen from the distinct downfield shift (Δδ 0 38 ppm) of the C-4 methine hydrogen signal at δ 2 33 (1H, *ddq*, *J* = 12 7, 4 5 and 6.6 Hz) and the significant upfield shift (Δδ 5 5 ppm) of the C-4 carbon signal at δ 27 5 (*d*) as compared to those of nardosinone (**3**) [δ 1 95 (1H, *ddq*, *J* = 12 8, 4 8 and 6 4 Hz) and δ 33 0 (*d*)]. The Cotton effects in the CD spectrum of kanshone B have identical signs to those of nardosinone (**3**), revealing that both compounds have the same absolute configurations Accordingly, the structure of kanshone B was deduced to be **2**, which was also confirmed by comparison of the ^{13}C NMR data with those of nardosinone (**3**), which were not reported earlier

Kanshones A and B were preliminarily examined for their possible biological activities and it was found that kanshone B, at the dose of 0 01 1 mg/ml in the culture medium, exerted a weak antihepatotoxic activity in the complement mediated cytotoxicity model system employing primary cultured mouse hepatocytes [11]

EXPERIMENTAL

Isolation of kanshones A and B Dried rhizomes and roots (1 5 kg) of *Nardostachys chinensis* were extracted with CH_2Cl_2 (2 l × 3) to afford brownish oil (50 g), which was chromatographed over silica gel (0 5 kg) The column was eluated with *n*-hexane and *n*-hexane–EtOAc mixtures of increasing polarity Rechromatography of the *n*-hexane–EtOAc (7 3) eluates (5 g) of the above column over silica gel (0 4 kg) using C_6H_6–EtOAc (17 3) as an eluating solvent furnished kanshone A (**1**) as an oil (0 05 g) and kanshone B (**2**) as colourless needles (0 04 g)

Kanshone A (**1**), colourless oil, $[\alpha]_D$ 147 8 ($CHCl_3$, *c* 0 35), EIMS (direct inlet) 70 eV, *m/z* 234 $[M]^+$, 216 $[M-H_2O]^+$, 201, 162, 160, 134, 59, UV λ_{max}^{MeOH} nm 248 (ε 5100), IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3450, 1665, 1612, 1460, 1380 1270, 1150 ^1H NMR (100 MHz, $CDCl_3$) δ 1 02 (3H, *d*, *J* = 6 5 Hz, H-15), 1 08, 1 18, 1 25 (3H, each *s*, H-14, H-12, H-13), 2 20 (1H, *m*, H-4), 2 62 (1H *dd J* = 7 1 and 1 0 Hz, H-6), 6 16 (1H, *dd*, *J* = 10 0 and 1 0 Hz H-8), 6 96 (1H *dd*, *J* = 10 0 and 7 1 Hz, H-7), 7 00 (1H *dd J* = 4 0 Hz, H-1), ^{13}C NMR (25 MHz, $CDCl_3$) δ 16 9 (*q*, C-15), 23 9 (*q* C-12) 24 4 (*q*, C-13), 26 2 (*t*, C-3), 26 4 (*t*, C-2), 32 3 (*q*, C-14), 33 2 (*d*, C-4), 42 0 (*s*, C-5), 54 4 (*d*, C-6), 75 9 (*s*, C-11), 128 9 (*d* C-8), 137 2 (*d*, C-1), 141 6 (*s*, C-10), 151 1 (*d*, C-7), 187 9 (*s*, C-9)

Kanshone B (**2**), colourless needles, mp 137 138 , $[\alpha]_D$ +133 8 ($CHCl_3$, *c* 1 10), CD (dioxane *c* 0 052) $[\theta]_{234}$ +15880, $[\theta]_{344}$ +870, HRMS *m/z* 266 1539 ($C_{15}H_{22}O_4$) $[M]^+$, 208 1090 ($C_{12}H_{16}O_3$), 193 0856 ($C_{11}H_{13}O_3$), 191 1066 ($C_{12}H_{15}O_2$), 166 0981 ($C_{10}H_{14}O_2$), 161 0920 ($C_{11}H_{13}O$), 151 0714 ($C_9H_{11}O_2$) 148 0873 ($C_{10}H_{12}O$) 137 0955 ($C_9H_{13}O$), 124 0879 ($C_8H_{12}O$), 122 0718 ($C_8H_{10}O$), 109 0638 (C_7H_9O) 107 0858 (C_7H_7O), UV λ_{max}^{MeOH} nm 244 (ε 7210), IR ν_{max}^{KBr} cm $^{-1}$ 3480, 1685, 1612, 1455, 1235, 1025, ^1H NMR (500 MHz, $CDCl_3$) δ 1 03 (3H, *d*, *J* = 6 6 Hz, H-15), 1 11, 1 22, 1 40 (3H, each *s*, H-14, H-12, H-13), 1 70 (2H, *m*, H-3), 2 33 (1H, *ddq*, *J* = 12 7, 4 5 and 6 6 Hz, H-4), 2 72 (1H, *dd J* = 18 6 and 2 0 Hz, H-8), 2 91 (1H, *dd*, *J* = 18 6 and 7 0 Hz, H-8), 2 95 (1H, *d*, *J* = 9 3 Hz, H-6), 4 36 (1H, *m*, H-2) 4 91 (1H, *ddd*, *J* = 9 3, 7 0 and 2 0 Hz H-7), 6 97 (1H, *d*, *J* = 5 0 Hz, H-1), ^{13}C NMR (25 MHz, $CDCl_3$) δ 15 1 (*q*, C-15), 21 7 (*q*, C-12), 22 6 (*q*, C-13), 26 8 (*q*, C-14), 27 5 (*d*, C-4), 34 3 (*t*,

C-3), 39 0 (s, C-5), 40 1 (t, C-8), 59 3 (d, C-6), 62 5 (d, C-2), 77 1 (d, C-7), 85 1 (s, C-11), 133 4 (d, C-1), 142 1 (s, C-10), 197 1 (s, C-9).

Dehydration of kanshone A with phosphorus oxychloride To a stirring soln of kanshone A (**1**) (10 mg) in pyridine (1 ml), $POCl_3$ (0 04 ml) was added and the reaction was continued for 30 min at room temp The reaction was arrested by addition of ice H_2O and the mixture extracted with *n*-hexane The *n*-hexane layer was washed with H_2O, dried and chromatographed over silica gel (10 g) Elution with C_6H_6 afforded **5** as an oil, $[\alpha]_D$ −217 8° ($CHCl_3$, *c* 0 12), EIMS (direct inlet) 70 eV, *m/z* 216 $[M]^+$, 201, 173, 161, 160, 134, 119, 93, 79, 77, ^1H NMR (100 MHz $CDCl_3$) δ 0 92 (3H, *d*, *J* = 6 4 Hz, H-15), 1 08 (3H, *s*, H-14), 1 54 (3H, *s*, H-13), 2 15 (1H, *m*, H-4), 3 15 (1H, *dd*, *J* = 6 6 and 1 0 Hz, H-6), 4 90 (2H, *m*, H-12), 6 15 (1H, *dd*, *J* = 10 0 and 1 0 Hz, H-8), 6 70 (1H, *dd*, *J* = 10 0 and 6 5 Hz, H-7), 6 88 (1H, *t*, *J* = 4 0 Hz, H-1).

Hydrogenation of nardosinone followed by dehydration with phosphorus oxychloride A soln of nardosinone (**3**) (50 mg) in MeOH (5 ml) was stirred at room temp in an atmosphere of H_2 and in the presence of $Pd/CaCO_3$ (10 mg) for 1 hr After usual work-up, it yielded nardosinone diol (**4**) (50 mg), $([\alpha]_D$-4 2° ($CHCl_3$, *c* 0 50), the ^1H NMR spectrum (100 MHz, $CDCl_3$) was identical to that of the reported nardosinone diol (**4**) [5]) Nardosinone diol (**4**) (20 mg) was dehydrated in the same manner as described above to afford **5**, $[\alpha]_D$ −355 4° ($CHCl_3$, *c* 0 44), whose mass and ^1H NMR spectra were superimposable on those of **5** prepared from kanshone A (**1**)

^{13}C *NMR* (25 *MHz*, $CDCl_3$) *of nardosinone* (**3**). δ 16 0 (*q*, C-15), 22 0 (*q*, C-12), 23 7 (*q*, C-13), 25 8 (*t*, C-2 and C-3), 26 8 (*q*, C-14), 33 0 (*d*, C-4), 39 9 (*t*, C-8), 39 9 (*s*, C-5), 59 6 (*d*, C-6), 77 9 (*d*, C-7), 85 0 (*s*, C-11), 137 6 (*d*, C-1), 140 0 (*s*, C-10), 196.3 (*s*, C-9)

REFERENCES

1 Schulte, K E , Rucker, G., Glauch, G (1967) *Planta Med* **15**, 274
2 Rucker, G (1968) *Liebigs Ann Chem* **717**, 221
3 Rucker, G (1969) *Chem Ber* **102**, 2691
4 Rucker, G (1969) *Chem Ber* **206**, 2697
5 Rucker, G (1970) *Chem Ber* **102**, 2707
6 Rucker, G (1970) *Planta Med* **19**, 16
7 Rucker, G (1970) *Liebigs Ann Chem* **733**, 152
8 Rucker, G , Kretzschmar, U (1971) *Liebigs Ann Chem.* **748**, 214
9 Hikino, H., Hikino, Y , Koakutsu, S , Takemoto, T (1972) *Phytochemistry* **20**, 2097
10. Bagchi, A , Oshima, Y , Hikino, H (1988) *Planta Med* (in press)
11 Kiso, Y , Kawakami, Y , Kikuchi, K , Hikino, H. (1987) *Planta Med* 241

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EUDESMANOLIDES FROM *PICRIS ACULEATA*

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Key Word Index—*Picris aculeata*, Compositae, Lactuceae; sesquiterpene lactones, eudesmanolides, scopoletin

Abstract—Extraction of the aerial parts of *Picris aculeata* afforded two new eudesmanolides, 1-epierivanin and 1-epialkhanol.

Previous studies of two representatives of the Old World genus *Picris* (Compositae, Lactuaceae) have furnished guaianolides such as lactucin, 8-deoxylactucin, jaquilenin and glycosides thereof [1, 2]. We now report the isolation from *Picris aculeata* Vahl [syn *Helminthia aculeata* (Vahl)DC], a plant of southern Italy and central Sicily, of two new eudesmanolides 1-epierivanin (**1**) and 1-epialkhanol (**2**). Scopoletin (**3**) was also found

The structures assigned to **1** and **2** are based on the ^1H NMR spectra and extensive decoupling experiments (Table 1) Thus in the case of **1**, irradiation at the frequency of the H-13 methyl doublet (δ 1 24) collapsed the *dq* of H-11 at δ2.35 to a doublet Irradiation at the latter frequency in turn identified a multiplet at δ1 65 as that due to H-7 Subsequent irradiation at the frequency of H-7 located H-6 as a triplet at δ4 07 and H-8α and H8β as a *dq* at δ. 1.90 and as a multiplet at δ1 50, while further irradiation at the frequencies of H-8α, β identified the signals of H-9α, β

Irradiation at the frequency of H-6 collapsed a broadened doublet at δ2 45 (H-5) to a broad singlet The broadening was shown to be due to allylic coupling to