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SESQUITERPENES FROM *CACALIA HASTATA*

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Key Word Index—*Cacalia hastata:* Compositae; yobusumaso; sesquiterpenes; cacalohastine; dehydrocacalohastine; chemotaxonomy.

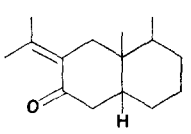
Abstract—From the roots of *Cacalia hastata* L. subsp. *orientalis* Kitamura 5 sesquiterpenes were isolated; fukinone (I), dehydrofukinone (II), bakkenolide *A* (III), cacalohastine (IV) and dehydrocacalohastine (V).

INTRODUCTION

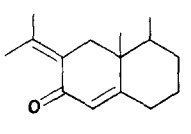
PREVIOUSLY, we reported the isolation of an alkaloid, integerrimine,[1] from *Cacalia hastata* L. subsp. *orientalis* Kitamura (Japanese name 'Yobusumaso'), which grow wild in northern Japan. The present paper reports the isolation of 5 sesquiterpenes from this plant.

RESULTS

The fresh roots were extracted with hot MeOH. After several procedures, fukinone[2] (I) and dehydrofukinone (II) were isolated as the major components and bakkenolide *A*[3] (III) as the minor. The structures of these sesquiterpenes were determined from the comparison of spectral data.



(I)



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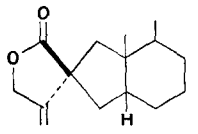

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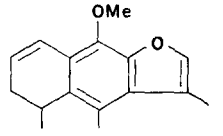
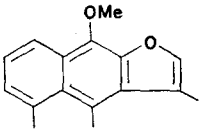
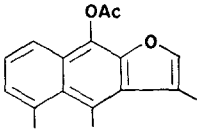


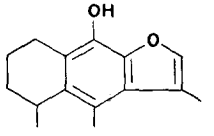
(IV)



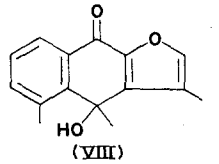
(V)



(VI)



(VII)



(VIII)

The other minor components IV and V were obtained as needles. NMR spectrum of IV exhibited a doublet (3H, *J* 7 Hz) at δ 1·02 for a secondary methyl group, a doublet (3H, *J* 1·2 Hz) at δ 2·30, and a singlet (3H), at δ 2·42 for two methyls on aromatic rings, and a singlet (3H) at 3·98 for a methoxyl group. The signal at δ 7·12 (1H, *q*, *J* 1·2 Hz) showed

[1] HAYASHI, K., NATORIGAWA, A. and MITSUHASHI, H. (1972) *Chem. Pharm. Bull. (Tokyo)* **20,** 201.
[2] NAYA, K., TAKAGI, I., KAWAGUCHI, Y. and ASADA, Y. (1968) *Tetrahedron* **24,** 5871.
[3] (a) SHIRAHATA, K., KATO, T., KITAHARA, Y. and ABE, N. (1969) *Tetrahedron* **25,** 3179. (b) KITAHARA, Y., ABE, N., KATO, T. and SHIRAHATA, K. (1969) *J. Chem. Soc. Japan Pure Chem. Sect.* **90,** 221.

allylic coupling with the methyl signal at δ 2·30. From these results and other spectral data, this compound was assumed to be a furano sesquiterpene having a structure formulated as IV. This sesquiterpene (IV) and the compound derived from decompostine by Romo *et al.*[4] agreed in their spectra, m. m.p. and $[\alpha]_D$ values (Romo's sample: +79·3°; *c* 0·605, MeOH). IV was named cacalohastine. The NMR spectrum of another substance (V), was similar to that of IV. Disappearance of the signal at δ 1·02 for a secondary methyl group in the NMR spectrum of IV and a singlet at δ 2·96 or 3·10 for a methyl group in the NMR spectrum of V suggested an aromatization of cacalohastine. Furthermore, a pattern of the UV spectrum of V was similar to that of VI converted from cacalol (VII) by Romo *et al.*[5] Though the structure of our compound was assumed to be V and named dehydrocacalohastine, further examination could not be made due to the small amount of the sample available. The substances obtained from the roots were also detected in the buds.

DISCUSSION

In 1970, Herout employed the bakkenane-type lactone as a chemotaxonomic marker for the Senecioneae, family Compositae,[6] and he suggested that possession of substances of the eremophilane type is an important character in this tribe.[7] Co-existence of both types of sesquiterpene is observed in a few species of the genus *Petasites*.[2,7,8] With regard to sesquiterpenes from the genus *Cacalia* belonging to the same tribe, Romo *et al.* isolated cacalane-type sesquiterpenes only from *Cacalia decomposita* A-Gray.[5,9] From the chemotaxonomic view, it is very interesting that the three types of sesquiterpenes were isolated from *Cacalia hastata* L. subsp. *orientalis* Kitamura.[10]

EXPERIMENTAL

M. ps were determined on a Kofler hot stage apparatus and are uncorrected. IR were measured on a 215 Hitachi grating IR Spectrophotometer, UV and NMR on a Hitachi EPS-3T spectrophotometer and a JEOLCO JNM-P S-100 or Hitachi H-60 spectrometer. For GLC a Shimadzu GC-4BPF was employed. MS were measured on a Hitachi RMU-6E instrument. Merck Kieselgel HF_{254} was used for TLC and preparative TLC. For column chromatography, silica gel (Merck Kieselgel, 0·05–0·20 mm or below 0·08 mm) was used.

Extraction. Fresh roots (10·8 kg) collected at Nishino, a suburb of Sapporo, in April 1971, were extracted with MeOH under reflux. The extract was concentrated *in vacuo*. The concentrated soln (4·3 l.) was extracted with $CHCl_3$ to give the extract (108 g).

Chromatography of $CHCl_3$ *extract.* The $CHCl_3$ extract (45 g) was chromatographed on silica gel (450 g) with C_6H_6; fract. 1–6, C_6H_6:acetone (9:1, fract. 7–12, and 3:2, fract. 13–15) and acetone, fract. 16–24 (each fraction: 1 l.). The corresponding fractions were rechromatographed by column or preparative TLC.

Isolation of fukinone (I). Repeated preparative TLC of the fraction 3 gave a colorless oil: b.p. 135°/4 mm; MS: M^+ ion, *m/e* 220, base peak *m/e* 109; IR ν_{max}^{film}: 1695, 1635 cm^{-1}; UV λ_{max}^{EtOH}: 251 nm (ε 4600), $[\alpha]_D$ + 69·1° (*c* 0·36, MeOH); NMR (CCl_4), σ 1·88 (*s*, 3H), 1·76 (*s*, 3H), 0·95 (*s*, 3H), 0·83 (*d*, 3H, *J* 6 Hz) The IR spectrum was superimposable with that of the authentic sample kindly sent by Prof. Naya of Kwansei

[4] ROMO, J. (1969) *Bol. Inst. Quim. Univ. Nacl. Auton. Mex.* **21,** 92.
[5] ROMO, J. and JOSEPH-NATHAN, P. (1964) *Tetrahedron* **20,** 2331.
[6] HEROUT, V. (1971) in *Pharmacognosy and Phytochemistry,* Springer, New York.
[7] NOVOTNY, L., KOTVA, K., TOMAN, J. and HEROUT, V. (1972) *Phytochemistry* **11,** 2795.
[8] (a) NAYA, K., TAKAGI, I., HAYASHI, M., NAKAMURA, S., KOBAYASHI, M. and KATSUMURA, S. (1968) *Chem. Ind. (London)* 318; (b) NAYA, K. and TAKAGI, I. (1968) *Tetrahedron Letters* 629; (c) NAYA, K., HAYASHI, M., TAKAGI, I., NAKAMURA, S. and KOBAYASHI, M. (1972) *Bull. Chem. Soc. Japan.* **45,** 3673.
[9] (a) JOSEPH-NATHAN, P., MORALES, J. J. and ROMO, J. (1966) *Tetrahedron* **22,** 301; (b) CORREA, J. and ROMO, J. (1966) *Tetrahedron* **22,** 685; (c) RODRIGUEZ-HAHN, L., GUZMAN, A. and ROMO, J. (1968) *Tetrahedron* **24,** 477.
[10] Recently, Dr. Kusano *et al.* isolated compound IV, V and VIII from *C. auriculata* var. *kamtschatica.* Compound V was correlated with IV and mentioned that compound VIII is probably artefact from compound V. KANESHIMA, M., KUSANO, G., AOTA, K. and TAKEMOTO, T. (1973) 93rd *Ann. Meet. Pharmac. Soc. Japan,* Vol. II, p. 219, Abstract Papers, Tokyo.

Gakuin University. The 2,4-dinitrophenylhydrazone of fukinone recrystallized from EtOH as deep red needles, m.p. 152–153° (Found: C, 63·13; H, 7·17; N, 13·75. Calc. for $C_{21}H_{28}O_4N_4$: C, 62·98; H, 7·05; N 13·99%). This was confirmed by direct comparison with an authentic sample.

Dehydrofukinone (II). Repeated preparative TLC of the fraction with fukinone (I) gave a colorless oil: MS: M^+ ion *m/e* 218, base peak *m/e* 161; IR ν_{max}^{film}: 3025, 1664, 1629, 1618 cm^{-1}; UV λ_{max}^{EtOH}: 274 nm (ε 7280), 249 (ε 11 400); $[\alpha]_D$ + 162° (*c* 1·85, MeOH); NMR (CCl_4) δ 5·57 (*t*, 1H, *J* 1Hz), 2·02 (*s*, 3H), 1·82 (*s*, 3H), 0·94 (*s*, 3H), 0·94 (*d*, 3H, *J* 6 Hz).

Separation of fraction 1. Repeated column chromatography and preparative TLC of fraction 1 gave bakkenolide-*A* (III) (12 mg), cacalohastin (IV) (85 mg), and dehydrocacalohastine (V) (16 mg).

Bakkenolide-A (III). Repeated chromatography and preparative TLC of fraction 1 gave a yellow oil, which recystrallized from hexane as prisms (12 mg): m.p. 80·0–80·5°; MS: M^+ ion *m/e* 234, base peak *m/e* 109; IR $\nu_{max}^{CHCl_3}$: 3100, 3050, 1780, 1675, 900 cm^{-1}; NMR ($CDCl_3$): δ 5·08 (*m*, 1H), 5·01 (*m*, 1H), 4·74 (*m*, 2H), 0·98 (*s*, 3H), 0·84 (*d*, 3H, *J* 6 Hz).

Cacalohastine (IV). Repeated chromatography of fraction 1 gave a crystalline mass (85 mg), which was purified by sublimation, m.p. 84·0–85·5°. MS: M^+ ion *m/e* 242, base peak *m/e* 227; IR $\nu_{max}^{CHCl_3}$: 2875, 1570–1640, 1340, 1120, 1000 cm^{-1}: UV λ_{max}^{EtOH}: 223 nm (ε 3880), 241 (ε 2920), 249 (ε 2800), 284 (ε 4340), 293 (ε 3690); $[\alpha]_D$ + 90·5° (*c* 0·54, MeOH); NMR (CCl_4) σ 7·12 (*q*, 1H, *J* 1·2 Hz), 6·82 (*m*, 1H), 5·84 (*m*, 1H), 3·98 (*s*, 3H), 3·15 (*m*, 1H), 2·42 (*m*, 1H), 2·42 (*s*, 3H), 2·30 (:, 3H, *J* 1·2 Hz), 2·16 (*m*, 1H), 1·02 (*d*, 3H, *J* 7 Hz), (Found: C, 79·42; H, 7·54, $C_{16}H_{18}O_2$ requires: C, 79·31, H; 7·49%). This was identified with Romo's sample by NMR, IR, UV and mixed fusion.

Dehydrocacalohastine (V). Fractions eluted after cacalohastine (IV) gave a crystalline mass (16 mg), which was recrystallized from H_2O-MeOH as needles: m.p. 71·0–77·5°; MS: M^+ ion *m/e* 250, base peak *m/e* 225; IR $\nu_{max}^{CHCl_3}$: 2870, 1640, 1600, 1370, 1110, 1000 cm^{-1}; UV λ_{max}^{EtOH}: 221, 253, 247, nm; NMR ($CDCl_3$) σ 8·18 (*d,d*, 1H, *J* 2 Hz, 4 Hz), 7·34 (*m*, 1H), 7·19 (*m*, 1H), 7·19 (*q*, 1H, *J* 1·2 Hz), 4·12 (*s*, 3H), 3·10 (*s*, 3H), 2·96 (*s*, 3H), 2.46 (*d*, 3H, *J* 1·2 Hz).

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