Isolation of a Hopane-Type Triterpenoid, Zeorin, from a Higher Plant, Tripterygium regelii

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Zeorin (1), a hopane-type pentacyclic triterpenoid lacking on oxygen function at C-3, was isolated from the roots of *Tripterygium regelii*.

Keywords zeorin; hopane-type compound; triterpenoid; Tripterygium regelii; Celastraceae; seed plant; phanerogam

Oleanane- and ursane-type triterpenoids such as wilforlide A, regelin and regelinol, together with regelidine, a nicotinoyl sesquiterpene alkaloid, have recently been isolated from *Tripterygium regelii* (東北雷公藤) (Calastraceae). In our continuing studies on the triterpenoid constituents of this plant, zeorin (1), mp 223—225 °C (221—223 °C³)), was obtained in a trace amount as crystals from the dried roots of *Tripterygium regelii* (see Experimental). Compound 1 has mostly been found in the cryptogams such as lichens and ferns. A literature survey showed that a typical hopane-type triterpenoid, zeorin, has been isolated from about forty kinds of lichens and four kinds of ferns. However, there is no precedent for finding zeorin in seed plants, except for one case: *Iris missouriensis*. Some of the plants containing 1 are listed in Table I.

$$\begin{array}{c} 1: R_{1} = R_{3} = H; \ R_{2} = OH; \ R = \neg \land OH \\ 2: R_{1} = OH; \ R_{2} = R_{3} = H; \ R = \neg \land OH \\ 3: R_{1} = R_{2} = R_{3} = OH; \ R = \neg \land OH \\ 4: R_{1} = OH; \ R_{2} = R_{3} = H; \ R = \neg \land OH \\ 5: 3 = CO; \ R_{2} = R_{3} = H; \ R = \neg \land OH \\ 9: R_{1} = R_{2} = R_{3} = H; \ R = \neg \land OH \\ 10: R_{1} = R_{2} = R_{3} = H; \ R = \neg \land OH \\ 11: R_{1} = H; \ R_{2} = R_{3} = H; \ R = \neg \land OH \\ 13: R_{1} = OH; \ R_{2} = R_{3} = H; \ R = \neg \land OH \\ 13: R_{1} = OH; \ R_{2} = R_{3} = H; \ 23 = COOH; \ R = \neg \land OH \\ \end{array}$$

TABLE I. Some Plants from Which Zeorin Has Been Isolated

Chart 1

Lichens Parmelia leucotyliza5) Anaptychia6 Lopadium leucoxanthum⁷ Solenospora candicans⁷⁾ Hypogymnia vittata8) Lecanora frustulosa9a) Lecanora muralis9b) Lecanora stenotropa9c) Lepraria spp. 9a,10) Nephroma cellulosum¹¹⁾ Pseudocyphellaria impressa S. LAT. 12) Ferns Doryopteris concolor¹³⁾ Lemmaphyllum microphyllum¹⁴⁾ Adiantum capillus-junois 14 Adiantum edgeworthii 14) Phanerogams Iris missouriensis4)

TABLE II. Hopanes and Migrated Hopanes Distributed in Phanerogams

Name (compound)	Species (family)
Moretenol (2)	Ficus macrophylla (Moraceae)
Mollugogenol A (3)	Mollugo hirta (Molluginaceae)
21αH-Hop-22(29)-en- 3β,30 diol (4)	Rhodomyrtus tomentosa (Myrtaceae)
Hydroxyhopanone (5)	Hopae spp. (Dipterocarpaceae)
Arundoin (6)	Imperata cylindrica (Gramineae)
Motiol (7)	Rhododendron linearifolium (Ericaceae)
Ferneol (8)	Artemisia vulgaris (Compositae)

TABLE III. Typical Hopanes and Migrated Hopanes Distributed in Cryptogams

Name (compound)	Distribution
Diploptene (9)	Microorganisms
Diplopterol (10)	Microorganisms
Zeorin (1)	Ubiquitous in lichens
Leucotylin (11)	Parmelia leucotirhiza
Diploptene (9)	Common in ferns
Fernene (12)	Common in ferns
Woodwardinic acid (13) ¹⁵⁾	Woodwardia orientalis

The isolation of zeorin (1) from *Tripterygium regelii* is very important from phytochemical and biosynthetic points of view because 1 lacks an oxygen function at C-3. All of the triterpenoids, with more than forty kinds of carbon skeletons, including the hopane and migrated hopane groups, hitherto reported from seed plants (Table II) have the oxygen function (such as hydroxyl or ketone) at C-3 arising from their well known biosynthetic course from squalene oxide, while most of the pentacyclic triterpenoids found in ferns, lichens and other cryptogams (Table III) lack the oxygen function at C-3 as a result of their biosynthesis from squalene itself.

Finally, it is of interest to note that zeorin was found in this flowering plant coexisting with oleanane- and ursanetype triterpenoids as mentioned above.

Experimental

The ethanol extract of the dried roots of *Tripterygium regelii* collected at Chang Bai Shan in Fusong prefecture, Jilin province, China was percolated successively with *n*-hexane and ethyl acetate. Consecutive column chromatography of the ethyl acetate fraction using silica gel with petroleum ether and chloroform followed by neutral alumina with petroleum ether and chloroform resulted in the isolation of a trace of zeorin (1) together with wilforlide A (0.0003%), regelin (0.002%), regelin (0.0002%), regelin (0.0001%) regelidine (0.00026%). All the available physicochemical and spectral data [proton nuclear magnetic resonance (H-NMR), infrared (IR) and electron impact-mass spectrum (EI-MS)] were consistent with those of the authentic sample. (13)

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References and Notes

- H. Hori, G.-M. Pang, K. Harimaya, Y. Iitaka, and S. Inayama, Chem. Pharm. Bull., 35, 2125 (1987).
- H. Hori, G.-M. Pang, K. Harimaya, Y. Iitaka, and S. Inayama, Chem. Pharm. Bull., 35, 4683 (1987).
- J. A. Elix, A. A. Whitton, and A. J. Jones, Aust. J. Chem., 35, 641 (1982).
- 4) S.-M. Wong, J. M. Pezzuto, H. H. S. Fong, and N. R. Farnsworth, *J. Pharm. Sci.*, **75**, 317 (1986).
- 5) Y. Asahina and H. Akagi, Ber. Dtsch. Chem. Ges., B 71, 980 (1983).
- 6) S. Rangaswani, Indian J. Pharm., 16, 173 (1954).

- 7) C. F. Culberson and W. L. Culberson, Bryologist, 72, 210 (1969).
- 8) T. Hirayama, F. Fujikawa, I. Yosioka, and I. Kitagawa, Chem. Pharm. Bull., 23, 693 (1975).
- a) S. Huneck and K. Schreiber, *Phytochemistry*, 13, 2315 (1974); b) S. Huneck, 11th IUPAC Int. Symp. Chem. Nat. Prod., Abstracts of Papers, Vol. 4 (part 1), 1978, p. 197; c) S. Huneck, *Phytochemistry*, 21, 2407 (1982).
- A. V. N. Apra Rao, P. S. Rao, and S. Huneck, Fitoterapia, 55, 242 (1984).
- B. Renner and E. Gerstner, Z. Naturforsch., C: Biosci., 33C, 340 (1978).
- 12) A. L. Wilkins and P. W. James, Lichenologist, 11, 271 (1979).
- H. Ageta, K. Masuda, and Y. Tanaka, Shoyakugaku Zasshi, 35, 259 (1981).
- 14) H. Ageta, K. Shiojima, and K. Masuda, unpublished data.
- 15) As an exception, woodwardic acid (13) found in Woodwardia orientalis (Komochi-Shida)¹⁶⁾ might be produced by a secondary oxidation in its A-ring.
- 16) T. Murakami and C.-M. Chen, Chem. Pharm. Bull., 19, 25 (1971).