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CONSTITUENTS OF *CNEORIDIUM DUMOSUM* (NUTT.) HOOK. F.[1]

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Abstract—Osthol, imperatorin, isoimperatorin, bergapten, isopimpinellin, xanthotoxin, justicidin A and marmesin have been isolated from *Cneoridium dumosum* (Nutt.) Hook. f. (Rutaceae).

THE ISOLATION of bergapten from the monotypic genus, *Cneoridium dumosum* (Nutt.) Hook. f. (Rutaceae), was described in Part I of this series.[2] *C. dumosum* botanically stands somewhat isolated from the other members of the subtribe, *Rutinae*.[3] Among the other members of this subtribe, the genera *Boenninghausenia*, *Psilopeganum* and *Thamnosma* are closely related.[3] The constituents of *Thamnosma montana* Torr. and Frem. have been the subject of previous chemical studies in this program.[4] In view of the relationship between these genera within the subtribe it was of special interest to explore the constituents of *C. dumosum* in somewhat more detail.

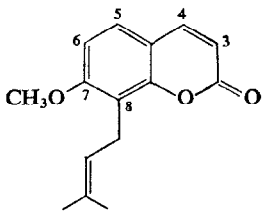
Chromatography of the plant extracts on alumina gave eight compounds, eluted in the following order: osthol (1), imperatorin (2), isoimperatorin (3), bergapten (4), isopimpinellin (5), xanthotoxin (6), justicidin A (diphyllin methyl ether) (7) and marmesin (8). All of these compounds have been previously reported occurring in plants of the Rutaceae with the exception of the lignan, justicidin A. This analyzed for $C_{22}H_{18}O_7$, was optically inactive and showed an intense blue fluorescence. The i.r. spectrum showed no hydroxy adsorption but had a carbonyl band at 1776 cm^{-1} indicating the presence of a γ-lactone group and a relatively strong band at 934 cm^{-1} suggesting the presence of a methylenedioxy group. The u.v. spectrum was very similar to that of related lignans,[5] for example, dehydroanhydropicropodophyllin, dehydro-β-peltatin methyl ether and dehydroanhydrosikkimotoxin. The NMR spectrum showed the appropriate resonances[6,7] for the presence of a methylenedioxy group and three methoxy groups, and comparison of the isolated compound with an authentic sample of justicidin A showed complete identity.

Justicidin A has previously been found in *Justicia hayatii* var. *decumbens* (Acanthaceae)[8]

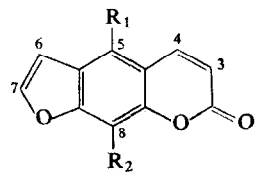
[1] "Chemotaxonomy of the Rutaceae"—VI. Part V, D. L. DREYER, *Phytochem.*, in press **8**, 1013 (1969).
[2] D. L. DREYER, *Phytochem.* **5**, 367 (1966).
[3] A. ENGLER and K. PRANTL, *Die Naturlichen Pflanzenfamilien*, 2nd edition, Vol. 19a, p. 202, Englemann, Leipzig (1931).
[4] D. L. DREYER, *Tetrahedron* **22** 2923 (1966); J. P. KUTNEY, T. INABA and D. L. DREYER, *J. Am. Chem. Soc.* **90**, 813 (1968).
[5] A. W. SCHRECKER and J. L. HARTWELL, *J. Am. Chem. Soc.* **75**, 5924 (1953); E. SCHREIER, *Helv. Chim. Acta* **46**, 75 (1963); H. KOFOD and C. JORGENSEN, *Acta Chem. Scand.* **8**, 1294 (1954).
[6] T. R. GOVINDACHARI, S. S. SATHE, N. VISWANATHAN, B. P. PAI and M. SRINIVASAN, *Tetrahedron Letters* 3517 (1967).
[7] Z. HORII, K. OHKAWA, S. KIM and T. MOMOSE, *Chem. Commun.* 653 (1968).
[8] K. MUNAKATA, S. MARUMO and Y. L. CHEN, *Tetrahedron Letters* 4167 (1965).

and its demethyl derivative, diphyllin (9) in *Cleistanthus collinus* (Roxb.) Benth. and Hook. f. (Euphorbiaceae)[6] and *Diphylleia grayi* (Berberidaceae).[9] Both of these plants are known for their fish-killing properties which is ascribed to the presence of justicidin A and derivatives.

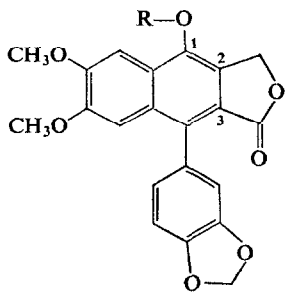
This is the first report of a compound of this type in the Rutaceae. Another striking feature is that in contast to *T. montana* which produces coumarins as well as the alkaloids, skimmianine, γ-fagarine and N-methylacridone,[4] *Cneoridium dumosum* lacks typical rutaceous alkaloids.[10]



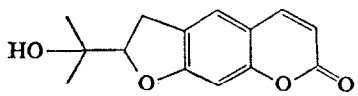
(1)



(2) $R_1 = H$, $R_2 = —O—CH_2CH=C(CH_3)_2$
(3) $R_1 = —O—CH_2CH=C(CH_3)_2$, $R_2 = H$
(4) $R_1 = —OCH_3$, $R_2 = H$
(5) $R_1 = R_2 = —O—CH_3$
(6) $R_1 = H$, $R_2 = —O—CH_3$



(7) $R = CH_3—$
(9) $R = H$



(8)

EXPERIMENTAL[11]

Isolation

The whole aerial part of the plant, collected in January 1966, 8 miles east of Mission San Luis Rey near Oceanside, California, was dried, ground and extracted with acetone. Solvent was removed from the extracts and the residue chromatographed on Al_2O_3. The content of the fractions from the column was checked by TLC on SiO_2 using a 1:1 $CHCl_3$:ethyl acetate solvent system. Elution of the column with hexane removed much wax, carotenoids and chlorophyll. Further elution with 1:1 benzene:hexane gave fractions containing osthol (1), m.p. 82–83° (ethyl acetate–hexane); NMR δ 7·58 (d) $J = 10$, H-4, 7·30 (d) $J = 8$ H-5, 6·82 (d) $J = 8$

[9] T. MARAKAMI and S. MATSUSHIMA, *J. Pharm. Soc. Japan* **81**, 1596 (1961).
[10] J. R. PRICE, in *Chemical Plant Taxonomy* (edited by T. SWAIN), Ch. 15, p. 429, Academic Press, London (1963).
[11] NMR spectra were taken at 60 MHz. The relative areas of the peaks were consistent with their assignments.

H-6, 6·25 (d) $J=10$ H-3, 5·24 (t) $J=7$ vinyl, 3·90 (s) methoxy, 3·52 (d) $J=7$ benzylic methylene, 1·84, 1·67 C-methyls ($CDCl_3$).

Further workup of the mother liquors gave imperatorin (2). m.p. 99–100° (ethyl acetate–hexane)[12] and isoimperatorin (3), m.p. 97·5–98·5° (ethyl acetate–hexane); NMR δ 8·14 (d) $J=10$ H-4, 7·56 (d) $J=2$ H-6, 7·11 (s) H-8, 6·95 (d) $J=2$ H-7, 6·24 (d) $J=10$ H-3, 5·57 (t) $J=7$ vinyl, 4·88 (d) $J=7$ allylic methylene, 1·80, 1·72 C-methyls ($CDCl_3$).

Elution of the column with benzene gave fractions containing bergapten (4), m.p. 172–176°, followed by isopimpinellin (5) from ethyl acetate–hexane.[13] Further workup of the mother liquors after removal of the bergapten and isoimpinellin gave xanthotoxin (6).

Elution of the column with 1:1 benzene–$CHCl_3$ and $CHCl_3$ gave justicidin A (7), m.p. 250–255°, from ethyl acetate–$CHCl_3$; ν 1776, 1621, 1591, 934 cm^{-1} (Nujol); λ_{max}^{EtOH} 259 (23, 300), 296 (5, 200), 309 (5, 300), 345 (2, 300) nm; NMR δ 7·55 (s) H-5, 7·06 (s) H-8, 6·89 (s) H-5′, 6·81 (s) H-2′, and H-6′, 6·12, 5·96 (AB doublet) $J=1$ methylenedioxy, 5·50 (s) γ-lactone methylene, 4·12 1-methoxy, 4·08 6-methoxy, 3·80 7-methoxy ($CDCl_3$). (Found: C, 66·9; H, 4·55. $C_{22}H_{18}O_7$ required: C, 67·00; H, 4·60 per cent.) Justicidin A was recovered unchanged after heating at 100° with 20% HCl in dioxan for 1·5 hr.

Elution of the column with 10% acetone in $CHCl_3$ yielded fractions which, after workup, gave marmesin, m.p. 180–188° (benzene–hexane); ν 1712, 1631, 1568 cm^{-1} (Nujol); NMR δ 7·60 (d) $J=9$ H-4, 7·24 (s) H-5, 6·74 (s) H-8, 6·12 (d) $J=9$ H-3, 4·85 (t) H-7, 3·23 (d) H-6, 1·38, 1·25 C-methyls ($CDCl_3$). Marmesin showed a plain positive ORD curve down to 370 nm; ORD in EtOH at 25° (*c* 0·126): $[\alpha]_{600}$ +17°, $[\alpha]_{372}$ +520° (last reading).

Acknowledgement—The authors are indebted to Dr. N. Viswanathan for an authentic sample of justicidin A.

[12] For NMR data, see D. L. DREYER, *J. Org. Chem.* **30**, 749 (1965).

[13] For NMR data see Ref. 2.