# NATIVE AMERICAN MEDICINAL PLANTS. FALCARINDIOL AND 3-*O*-METHYLFALCARINDIOL FROM *OSMORHIZA OCCIDENTALIS*

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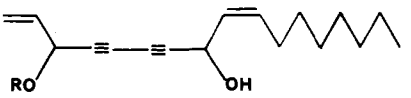
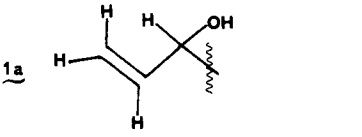
Umbelliferous plants are well represented in the pharmacopoeias of many native American cultures. Various species of *Osmorhiza*, for example, have been employed by the Flathead (1), Crow (2), Blackfoot (3) and Thompson (4) nations for the treatment of colds, pneumonia, sore throats, toothaches and stomach aches. Our investigation of *Osmorhiza occidentalis* (Mountain Sweet Cicely), a species common in southwestern Montana, has resulted in the isolation of falcarindiol, **1**, and the previously unknown 3-*O*-methylfalcarindiol, **2**, from extracts of the rhizomes.

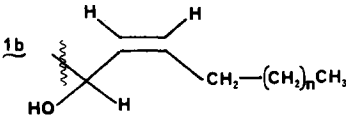


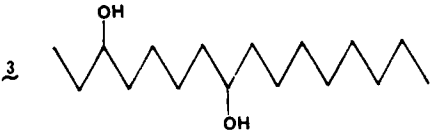

**1** R = H

**2** R = $CH_3$

Adsorption and gel permeation chromatography of the dichloromethane soluble extracts of rhizomes collected in late autumn yielded **1**, a major constituent (9.4%) of the extract. $^1H$ nmr decoupling experiments developed part structures **1a** and **1b**; the $^{13}C$ nmr spectrum (see table 1) exhibited signals for the four olefinic carbons, four acetylenic carbons, two methines bearing heteroatoms, six methylenes and one methyl group. Catalytic reduction of **1** yielded the dodecahydro-derivative **3** and **1** gave a diacetate upon treatment with acetic anhydride and pyridine. These data, together with the uv and ir spectra, matched those reported for falcarindiol, first prepared and characterized two decades ago by Bohlmann (5) and subsequently found in numerous umbellifers by various research groups (6).




From less polar chromatography fractions we isolated a related compound, also a colorless oil. The $^1H$-nmr spectrum revealed a few differences from **1**; the presence of a three proton singlet at $\delta$ 3.38 and a diamagnetic shift of the C–3 methine proton from $\delta$ 4.92 to $\delta$ 4.58 suggested structure **2** for this new compound. The $^{13}C$-nmr spectrum (see table 1) supported a molecular formula of $C_{18}H_{26}O_2$ and was very similar to that of **1**, with the exception of a signal at $\delta$ 55.6 for a methoxyl carbon and a substantial shift of the carbon at C–3 from $\delta$ 63.2 in **1** to $\delta$ 71.8. Although 3-acetoxyfalcarindiol is known (6b), this is the first report of an alkoxypolyacetylene from an umbelliferous plant.[1]

[1]That **2** is an artifact cannot, at this time, be ruled out. The extraction of the roots with methanol could have led to alcoholysis of a glycoside linkage to C–3 of falcarindiol. A C–10 rhamnoside of a related acetylenic alcohol from *Serratula gmelini* has been reported (8).

TABLE 1. $^{13}$C-nmr chemical shift assignments, falcarindiol and 3-*O*-methylfalcarindiol.

| Carbon No. | Falcarindiol (1) | 3-*O*-methylfalcarindiol (2) |
|---|---|---|
| 1 | 117.0, t | 118.5, t |
| 2 | 135.8, d | 133.9, d |
| 3 | 63.2, d | 71.8, d |
| 4 | 78.2, s[c] | 76.4, s[c] |
| 5 | 70.1, s[c] | 71.3, s[c] |
| 6 | 68.6, s[c] | 68.7, s[c] |
| 7 | 79.8, s[c] | 79.3, s[c] |
| 8 | 58.4, d | 58.5, d |
| 9 | 134.3, d | 134.5, d |
| 10 | 127.6, d | 127.8, d |
| 11 | 28.9, t[a] | 28.9, t[b] |
| 12 | 27.5, t[a] | 28.9, t[b] |
| 13 | 27.5, t[a] | 27.5, t[b] |
| 14 | 29.1, t[a] | 29.1, t[b] |
| 15 | 31.6, t | 31.6, t |
| 16 | 22.5, t | 22.4, t |
| 17 | 13.9, q | 13.9, q |
| 18 | — | 55.6, q |

[a]assignments interchangeable; [b]assignments interchangeable; [c]based on the assignments of Hearn (9).

The antifungal activity of falcarindiol has been documented by several groups (6d, 6e, 7); the elegant study by Garrod, Lewis and Coxon (6e) demonstrated a gradient distribution of **1** in the rhizomes of the carrot (*Daucus carota*), the heaviest concentrations residing in the outer tissue layers. We consistently found high concentrations of **1** in *O. occidentalis*, regardless of the season in which the plants were collected.[2] It is interesting to note that *O. chilensis* extracts yielded only 7 mg of **1** from 332 g of fresh rhizomes. This could be attributed to a simple difference between the species, but might just as well be due to greater populations of pathogenic microorganisms in the soil bearing the *O. occidentalis*.

## EXPERIMENTAL[3]

PLANT MATERIAL.—The roots of *Osmorhiza occidentalis* were collected from a ditch in the Gallatin National Forest, 3 miles north of Bozeman, Montana, U.S.A., in November 1980 and in June 1982. *Osmorhiza chilensis* was collected in July 1981 from the banks of a stream on the Montana State University Agricultural Experiment Station at Red Bluff, Montana, in July, 1981.

EXTRACTION, FALL COLLECTION.—The rhizomes (836 g, fresh weight) were ground in a Waring blender and steeped for 24 hours in methanol (x2). The methanolic extracts were removed by suction filtration and evaporated, *in vacuo*, to a brown syrup. The ground rhizomes were then steeped in dichloromethane for 24 hours (x2). The reduced methanolic extracts were suspended in 200 ml $H_2O$ and equilibrated with the dichloromethane extracts. The combined dichloromethane phase was evaporated, *in vacuo*, to a brown syrup, 18.6 g (2.2% of net weight).

ISOLATION OF FALCARINDIOL.—The crude dichloromethane extract (8.0 g) was chromatographed on Florisil (200g, 4.5 x 60 cm column). Elution commenced with hexane and proceeded through a series of solvent combinations of gradually increasing polarity (hexane-ethyl acetate-methanol); sixteen fractions were collected.

Fraction 4 (2.55g) was rechromatographed on silica gel (200g, 4.5 x 60 cm column) with cyclohexane-dichloromethane (1:4) as the eluent; four fractions were collected. Fraction 4 (1.66g) was permeated through Sephadex LH-20 (195 x 2.5 cm column) with dichloromethane-methanol (1:1) as the eluent. The seventh of seven fractions obtained was falcarindiol, **1**, 754 mg colorless oil, uv, ir and $^1$H-nmr spectra identical to those reported earlier (6b).

CATALYTIC HYDROGENATION OF FALCARINDIOL.—Falcarindiol (32 mg) was hydrogenated in 10 ml ethanol (5% Pd/C) for 45 minutes at 30 psi on a Parr hydrogenator. Filtration of the reaction mixture and

[2]To our knowledge, this is the highest known concentration (0.21% of fresh weight) of falcarindiol in an umbelliferous plant.

[3]Nmr spectra were obtained on a Bruker 250 MHz FT nmr spectrometer with $CDCl_3$ as solvent and internal standard. The ir spectra were measured on a Beckman ir 20 and uv spectra were recorded on a Cary 14 ultraviolet spectrophotometer. Combustion analyses were performed by Galbraith Laboratories. Melting points were determined with a Mel-Temp apparatus and are uncorrected.

evaporation of the solvent gave **3**, 30.5 mg white solid. Recrystallization from diethylether-hexane gave colorless crystals, mp 90–1°; $^1$H-nmr ($CDCl_3$), $\delta$0.8 (3H, t), 0.9 (3H, t), 1.2 (18H, m), 1.4 (8H, m), 2.35 (2H, br), 3.55 (2H, m); $^{13}$C-nmr ($CDCl_3$): $\delta$9.6 (q), 13.9 (t), 22.5 (t), 25.5 (t), 25.6 (t), 29.2 (t), 29.3 (t), 29.5 (3C,t), 30.0 (t), 31.7 (t), 36.7 (t), 37.3 (t), 37.4 (t), 71.8 (d), 73.1 (d). Analysis. Calculated for $C_{17}H_{36}O_2$: C, 74.94%; H, 13.32%. Found: C, 74.88%; H, 13.46%.

ISOLATION OF 3-*O*-METHYLFALCARINDIOL.—Fraction 3 (516 mg) from the Florisil chromatography was permeated through Sephadex LH-20 (195 x 2.5 cm column) with dichloromethane-methanol (1:1); ten fractions were collected. Fraction 7, 162 mg, was identified as 3-*O*-methylfalcarindiol, **2**, a nearly colorless oil, ir ($CHCl_3$): $\nu$max 3400, 2150 cm$^{-1}$; $^1$H-nmr: $\delta$ 5.80 (1H, ddd, $J$=17, 11.5, 7); 5.60 (1H, dt, $J$=11.5, 6); 5.50 (1H, dd, $J$=11.5, 8.5); 5.45 (1H, dd, $J$=17, 4); 5.30 (1H, dd, $J$=11.5, 4); 5.18 (1H, d, $J$=8.5); 4.58 (1H, d, $J$=7); 3.38 (3H, s); 2.10 (2H, m); 2.2 (O–H, br s); 1.25 (8H, br m); 0.85 (3H, br t, $J$=6.5).

## ACKNOWLEDGMENTS

We thank Mr. Patrick Plantenburg for his guidance in the collection and identification of the plant materials. Support of this work by Montana State University and Eli Lilly and Company is deeply appreciated.

*Received 22 December 1981*

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