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Eupatriol, a New Monoterpene from *Eupatorium tashiroi* HAYATA

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An investigation of the constituents of the whole plant of *Eupatorium tashiroi* HAYATA (Compositae) afforded a new monoterpene, eupatriol. The structure of eupatriol was characterized as 2-(2-hydroxy-4-methylphenyl)propane-1,2-diol on the basis of spectral and chemical evidence.

Keywords——*Eupatorium tashiroi*; Compositae; eupatriol; monoterpene; ^{13}C-NMR

Introduction

Eupatorium tashiroi HAYATA (Compositae)[1] is a wild herb which has been used as a folk medicine for treating edema and hemoptysis in Taiwan.[2] The constituents of this plant have not previously been studied. We report here the isolation and characterization of a new aromatic monoterpene, eupatriol, as well as *p*-hydroquinone from the whole plant.

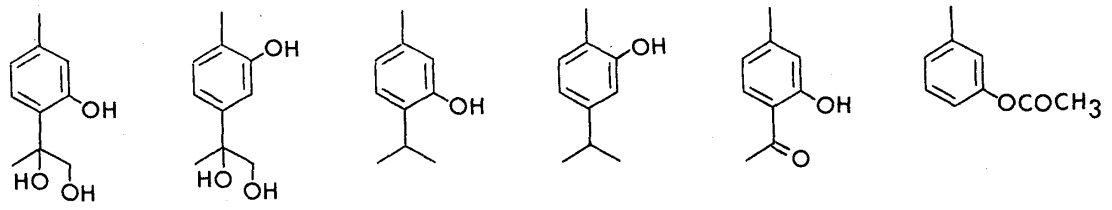
Results and Discussion

Eupatriol (**1**) was isolated as a colorless oil, having the molecular formula $C_{10}H_{14}O_3$ as determined by high-resolution mass spectroscopy. It exhibited ultraviolet (UV) absorption bands at 217 and 279 nm, which are characteristic of a benzenoid compound. The bands at 1630, 1575 and 1510 cm^{-1} in the infrared (IR) spectrum also indicated aromatic character. The 1,2,4-trisubstituted pattern of the benzene ring was deduced from the following signals and their splitting patterns in the proton nuclear magnetic resonance (^{1}H-NMR) spectrum: a doublet at δ 6.57 (1H, J=8 Hz), a singlet (overlapped with a doublet) at δ 6.60 (1H) and another doublet at δ 6.82 (1H, J=8 Hz). Two of the three substituents were easily characterized as a methyl group (δ_H 2.21 (3H, s) and δ_C 20.9 (q)) and a phenolic hydroxy group (δ_C 156.3 (s)). The third was confirmed to be an oxygenated isopropyl group on the basis of the mass, ^{1}H- and ^{13}C-NMR spectra, as follows. The presence of a primary alcohol was indicated by the fragment peak at m/z 151 ($M^+ - \cdot CH_2OH$), an A, B-type quartet at δ_H 3.46 and 3.81 (each 1H, J=12 Hz), and a triplet carbon signal at δ_C 69.2. The tertiary alcohol was shown by a singlet at δ_C 78.0 in addition to a singlet methyl peak at δ_H 1.52. Based on all the data mentioned above, the structure of eupatriol can be represented by **1** or **2**, analogous to thymol (**3**) and carvacrol (**4**), respectively, which seems to be biogenetically reasonable.

The oxidative cleavage of eupatriol (**1**) with sodium metaperiodate yielded an acetophenone derivative (**5**) whose ^{1}H-NMR spectrum showed signals due to an acetyl moiety and a hydroxy group chelated with the newly produced carbonyl moiety at δ 2.59 and 12.29, respectively. These results indicated that the hydroxy and acetyl groups were located at mutually *ortho* positions. Moreover, a strong acetyl-induced paramagnetic shift ($\Delta\delta$ 0.79 ppm)

of an aryl proton (**1**; δ 6.82, **5**; δ 7.61) suggested that only one proton existed *ortho* to the acetyl group. Therefore, the structure should be represented as 2-hydroxy-4-methylacetophenone (**5**); this product was confirmed to be identical with an authentic sample prepared by Fries rearrangement of *m*-cresyl acetate (**6**).[3] On the basis of these results, eupatriol is a thymol derivative, 2-(2-hydroxy-4-methylphenyl)propane-1,2-diol (**1**).

In addition, a known compound *p*-hydroquinone[4] was also isolated and characterized.



1 **2** **3** **4** **5** **6**

Experimental

^{1}H-NMR (100 MHz) and ^{13}C-NMR (25 MHz) spectra were recorded in $CDCl_3$. Chemical shifts are shown in ppm (δ) with tetramethylsilane (TMS) as an internal standard. Mass spectra (MS) were recorded using a direct-inlet system. UV spectra were obtained in MeOH. High-performance liquid chromatography (HPLC) conditions: (A) column, Fine pack SIL C-18, i.d. 4.6 × 250 mm (Nihon Bunko); solvent, MeOH : H_2O (75 : 25); flow rate, 0.5 ml/min; chart speed, 5 mm/min; detector, UV 254 nm; (B) column, Cosmosil $5C_8$ i.d. 4.6 × 150 mm (Nakarai Chemicals); solvent, MeOH : H_2O (75 : 25); flow rate, 0.5 ml/min; chart speed, 3 mm/min; detector, UV 254 nm.

Extraction and Separation——The EtOH extract of powdered whole herb (1 kg) of *Eupatorium tashiroi* HAYATA collected in Tainan Hsien, Taiwan, was partitioned between $CHCl_3$ and H_2O. The $CHCl_3$ portion was chromatographed on silica gel (500 g) by eluting successively with benzene, $CHCl_3$ and $CHCl_3$–acetone (9 : 1). The $CHCl_3$–acetone fraction was rechromatographed on silica gel and eluted with $CHCl_3$–acetone (19 : 1) to afford *p*-hydroquinone and eupatriol, successively.

Eupatriol (1)——Colorless oil $[\alpha]_D^{20}$ +0° (c=0.5, $CHCl_3$). Found: M^+ 182.0955; $C_{10}H_{14}O_3$ requires 182.0943. UV λ_{max} nm (log ε): 217 (4.88), 279 (3.79). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3320, 1630, 1575, 1510. ^{1}H-NMR δ: 1.52 (3H, s, CH_3), 2.21 (3H, s, 4′-CH_3), 3.46 and 3.81 (each 1H, d, J=12 Hz, 1-CH_2), 3.0—4.60 (2H, br s, 2 × OH), 6.57 (1H, d, J=8 Hz, 5′-H), 6.60 (1H, s, 3′-H), 6.82 (1H, d, J=8 Hz, 6′-H), 9.0 (1H, br s, 2′-OH). MS m/z (%): 182 (M^+, 3), 164 ($M^+ - H_2O$, 23), 151 (28), 135 (33), 121 (12), 105 (16), 91 (28), 83 (78), 55 (100), 43 (58). ^{13}C-NMR: 156.3 (s), 139.5 (s), 125.8 (d), 123.7 (s), 120.6 (d), 118.4 (d), 78.0 (s), 69.2 (t), 25.2 (q), 20.9 (q).

Oxidative Cleavage of Eupatriol with $NaIO_4$——A mixture of eupatriol (0.42 mg) and $NaIO_4$ (1 mg) in 75% MeOH (0.1 ml) was stirred for 30 min at room temperature. The mixture was diluted with saturated NaCl solution (0.4 ml) and extracted with ether. The ether layer was dried over Na_2SO_4 and evaporated to give an oily residue, which was purified by preparative thin layer chromatography (SiO_2, benzene) to afford a colorless oil, $C_9H_{10}O_2$. UV λ_{max} nm: 216, 260, 323. IR ν_{max}^{neat} cm^{-1}: 1630, 1570, 1505. ^{1}H-NMR δ: 2.35 (3H, s, CH_3), 2.59 (3H, s, CH_3), 6.71 (1H, dd, J=1, 8 Hz, 5′-H), 6.78 (1H, d, J=1 Hz, 3′-H), 7.61 (1H, d, J=8 Hz, 6′-H), 12.29 (1H, s, 2′-OH). MS m/z (%): 150 (M^+, 2), 135 (4), 77 (34), 63 (14), 53 (27), 52 (15), 51 (28), 50 (22), 43 (100), 39 (51). This compound was found to be identical with authentic 2-hydroxy-4-methyl-acetophenone (**5**) prepared from *m*-cresyl acetate (**6**)[3] by comparison of the ^{1}H-NMR, MS and IR spectra and HPLC behavior (room temp., condition (A), 12.8 min; condition (B), 8 min).

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