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Euparone, a New Benzofuran from *Ruscus aculeatus* L.

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Abstract □ The structure of euparone, a new benzofuran from *Ruscus aculeatus*, as 2,5-diacetyl-6-hydroxybenzofuran was determined by spectral means and conversion to euparone methyl ether (*O*-methyleuparone).

Keyphrases □ *Ruscus aculeatus* L. constituents—structure determination of euparone □ Euparone (2,5-diacetyl-6-hydroxybenzofuran)—structure determination □ 2,5-Diacetyl-6-hydroxybenzofuran—structure determination □ Benzofurans—from *R. aculeatus*, structure determination

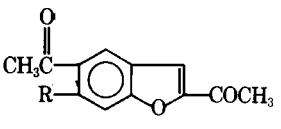
Ruscus aculeatus (Liliaceae), also known as Butcher's Broom or Knee-Holly, is a low evergreen shrub of southern and western Europe and southern United States (1). It has been used medicinally as a diuretic (2) and an anti-inflammatory (3) agent, as well as to treat hemorrhoids (4) and to prevent atherosclerosis (5) and circulatory insufficiency (6). Extracts of various *Ruscus* species have been shown to contain saponins (7) and flavonoids (8). This paper reports the isolation and structure determination of euparone, a new benzofuran.

DISCUSSION

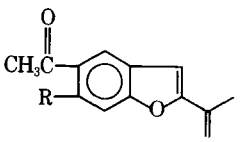
Euparone (I) was isolated as yellow rhomboid crystals from an ethanolic extract of the roots of *R. aculeatus*. Some pertinent data are: $C_{12}H_{10}O_4$; mp 143° ($CHCl_3$–C_2H_5OH); $[\alpha]_D$ 0° (c 1.0, $CHCl_3$); $\lambda_{max}(CH_3OH)$: 228 (sh) (log ϵ 4.19), 233 (4.21), 254 (4.37), 266 (sh) (4.35), 303 (4.11), and 348 (4.07) nm; λ_{max}(0.1 *N* methanolic KOH): 210 (log ϵ 4.32), 244 (4.00), 260 (sh) (3.82), 291 (3.66), 343 (3.78), and 403 (4.01) nm; ν_{max}(KBr): 3150 (bonded OH), 1667 (CO), and 1635 (CO) cm^{-1}; $\delta_{60\ MHz}(CDCl_3)$: 2.57 (s, 3H, $COCH_3$), 2.70 (s, 3H, $COCH_3$), 7.10 (s, 1H, Ar), 7.50 (s, 1H, Ar), 8.23 (s, 1H, Ar), and 12.66 (s, 1H, OH); mass spectroscopy M^+: *m/e* 218 (59%), 203 (100), and 43 (18). The spectral data were indicative of a phenolic 2,5,6-trisubstituted benzofuran containing two acetyl groups, one of which (1635 cm^{-1}) was *ortho* to a phenolic hydroxy (δ 12.66) group (9–12). Euparone gave a positive iodoform reaction characteristic of a methyl ketone. Treatment of euparone with acetic anhydride and pyridine afforded a monoacetate (II), $C_{14}H_{12}O_5$; mp 126° ($CHCl_3$–C_2H_5OH); $\lambda_{max}(CH_3OH)$: 227 (sh) (log ϵ 3.97), 249 (4.20), 287 (3.98), and 320 (sh) (3.68) nm; ν_{max}(KBr): 1765 (ArO-$COCH_3$) and 1665 (CO) cm^{-1}; $\delta_{60MHz}(CDCl_3)$: 2.36 (s, 3H, $COCH_3$), 2.58 (s, 6H, $2COCH_3$), 7.31 (s, 1H, Ar), 7.50 (s, 1H, Ar), and 8.15 (s, 1H, Ar); mass spectroscopy M^+: *m/e* 260 (2%), 218 (88), 203 (100), and 43 (30).

A further indication of the bonded nature of the hydroxy group of euparone was the failure of the compound to form a methyl ether on treatment with diazomethane. However, treatment of euparone with methyl iodide and silver oxide in refluxing chloroform afforded *O*-methyleuparone (euparone methyl ether) (III), $C_{13}H_{12}O_4$; mp 135–136° ($CHCl_3$–CH_3OH); $\lambda_{max}(CH_3OH)$: 232 (log ϵ 4.11), 245 (sh) (4.16), 251 (4.19), 299 (4.07), and 330 (4.11) nm; ν_{max}(KBr): 1685 (CO) and 1665 (CO) cm^{-1}; $\delta_{60\ MHz}(CDCl_3)$: 2.56 (s, 3H, $COCH_3$), 2.63 (s, 3H, $COCH_3$), 3.97 (s, 3H, OCH_3), 7.09 (s, 1H, Ar), 7.46 (s, 1H, Ar), and 8.05 (s, 1H, Ar); mass spectroscopy M^+: *m/e* 232 (48%), 217 (100), 202 (14), and 43 (28). This compound was identical with an authentic sample of euparone methyl ether by direct comparison (UV, IR, NMR, mass spectroscopy, melting point, and mixed melting point).

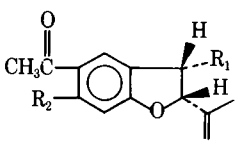
To the knowledge of the authors, this is the first reported isolation of euparone from nature. Euparone methyl ether (*O*-methyleuparone) (III), the first 2-acetylbenzofuran of nature, was first isolated from *Encelia californica* (Compositae) and was so named because of the obvious structural relationship to its probable 2-isopropenyl precursor, euparin (IV), also present in *E. californica* (13). Other 2,5-disubstituted benzofurans of nature include 2,5-diacetylbenzofuran (V) from *Aplopappus* species (14); tremetone (VI), dehydrotremetone (VII), and hydroxytremetone (VIII) (as a group formerly called tremetol) from *Eupatorium* (15, 16) and *Ap-*



I: R = OH
II: R = $OCOCH_3$
III: R = OCH_3
V: R = H



IV: R = OH
VII: R = H



VI: $R_1 = R_2 = H$
VIII: $R_1 = H, R_2 = OH$
IX: $R_1 = OH, R_2 = H$

lopappus species (16–18); and toxol (IX) from *Aplopappus heterophyllus* (18).

EXPERIMENTAL[1]

Isolation of Euparone—The detailed isolation procedure of euparone and other constituents of *R. aculeatus*[2] will be reported later.

Acetylation of Euparone—To euparone (30 mg) in pyridine (2 ml) was added acetic anhydride (2 ml). The mixture was stirred overnight at room temperature, poured into ice water (10 ml), neutralized with sodium bicarbonate, and extracted three times with chloroform (15 ml). The combined chloroform extracts were shaken with diluted H_2SO_4 (10%) (15 ml), washed with water (10 ml), dried (anhydrous sodium sulfate), filtered, and evaporated to leave *O*-acetyleuparone (II), which crystallized from chloroform–ethanol as pale-yellow plates (28 mg), mp 126°; $\lambda_{max}(CH_3OH)$: 227 (sh) (log ϵ 3.97), 249 (4.20), 287 (3.98), and 320 (sh) (3.68) nm; ν_{max}(KBr): 1765, 1685 (sh), 1665, 1610, 1555, 1420, 1350, 1305, 1285, 1240, 1190, 1135, 1070, 1035, 960, 915, 870, 845, and 620 cm^{-1}; $\delta_{60\ MHz}(CDCl_3)$: 2.36 (s, 3H), 2.58 (s, 6H), 7.31 (s, 1H), 7.50 (s, 1H), and 8.15 (s, 1H); mass spectroscopy M^+: *m/e* 260 (2%), 218 (88), 203 (100), and 43 (30).

Methylation of Euparone—To a solution of euparone (25 mg) in chloroform (3 ml) were added silver oxide (50 mg) and methyl iodide (2 ml). The mixture was refluxed for 4 hr, after which additional methyl iodide (2 ml) and silver oxide (50 mg) were added. Then the mixture was refluxed for 4 additional hr, the reaction mixture was filtered, and the filtrate was evaporated to dryness. Treatment of the residue with chloroform–methanol afforded euparone methyl ether (*O*-methyleuparone) (III) as yellowish rosettes (20 mg), mp 135–136°; $\lambda_{max}(CH_3OH)$: 232 (log ϵ 4.11), 245 (sh) (4.16), 251 (4.19), 299 (4.07), and 330 (4.11) nm; ν_{max}(KBr): 3120, 3090, 3020, 3000, 2955, 2930, 1685, 1665, 1620, 1585, 1560, 1475, 1450, 1425, 1410, 1352, 1310, 1293, 1245, 1235, 1192, 1175, 1150, 1075, 1040, 1025, 1003, 960, 920, 905, 855, 812, and 630 cm^{-1}; $\delta_{60\ MHz}(CDCl_3)$: 2.56 (s, 3H), 2.63 (s, 3H), 3.97 (s, 3H), 7.09 (s, 1H), 7.46 (s, 1H), and 8.05 (s, 1H); mass spectroscopy M^+: *m/e* 232 (48%), 217 (100), 202 (14), and 43 (28).

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[1] Melting points were taken on a Thomas-Hoover Uni-melt capillary apparatus and are corrected. The IR spectra were determined on a Perkin-Elmer model 257 or 137 spectrometer in KBr pellets. The UV spectra were obtained on a Perkin-Elmer model 202 recording spectrometer. Optical rotations were measured in a Rudolph polarimeter. Mass spectra were taken with a LKB-9000 mass spectrometer. The NMR spectra were obtained in $CDCl_3$, with tetramethylsilane as the internal standard, on a Hitachi Perkin-Elmer R-24 60-MHz high-resolution spectrometer.

[2] Lot BRC 926, S. B. Penick and Co., New York, N.Y.

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