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4,13-α-EPOXYMUZIGADIAL, A SESQUITERPENE FROM *CANELLA WINTERANA*

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Key Word Index—*Canella winterana*; Canellaceae; muzigadial (canellal); sesquiterpene; NOESY; 4,13-α-epoxymuzigadial; antimicrobial; antifeedant.

Abstract—The leaves of *Canella winterana* yielded a new compound that was found to be 4,13-α-epoxymuzigadial. Epoxidation of muzigadial gave two epimers, one of which was identical with the isolated material. Stereochemical differentiation between the two epimers was mainly based on a comparison of their NOESY spectra.

INTRODUCTION

In an earlier report [1], the isolation and structure elucidation of muzigadial (canellal) (**1**) [2] from the bark of *Canella winterana* were described. Examination of the leaves of the same plant yielded, in addition to **1**, its epoxide **2** which was not detected in the bark. This note describes the structure and stereochemistry of this compound.

RESULTS AND DISCUSSION

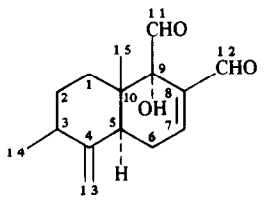
The hexane extract of the leaves of *C. winterana* yielded muzigadial (canellal) (**1**) and a more polar compound (**2**), mp 140–142° (after initial softening at 115–120°), $[\alpha]_D$ −240° ($CHCl_3$; *c* 0.5), $C_{15}H_{20}O_4$. The ^1H and ^{13}C NMR spectra of **2** were remarkably similar to those of **1** [1, 2], except for the absence of the signals due to an exocyclic methylene group [see Experimental]. Instead, the ^{13}C NMR spectrum revealed two oxygenated signals at δ 60.8 (*s*) and 44.9 (*t*), while the ^1H NMR exhibited two one-proton AB doublets at δ 2.79 and 2.73 ($J = 3.6$ Hz), suggesting an epoxide group at C_4–C_{13}.

To confirm the structure of **2**, muzigadial (**1**) was epoxidized with *m*-chloroperbenzoic acid to give a 4:1 mixture of **2** and **3**, respectively. The two compounds were separated by flash chromatography [3], and their spectral features (see Experimental) suggested that they were epimeric at C-4. Since **2** is the major product of epoxidation of **1**, and it has been established that the axial methyl group at C-10 preferentially induces an α-attack of the expoxidizing agent [4], the configuration of the epoxide group must be that depicted in **2**. This conclusion was further substantiated by a study of the NOESY spectra of both **2** and **3**. Here, the cross-relaxation effects in space between nuclei may be correlated in the form of signals in 2D plots, where cross peaks correspond to dipolar couplings through space. Only the NOESY spectrum of **2** showed a strong enhancement for H-13b and Me-15, thus confirming the stereochemistry at C-4.

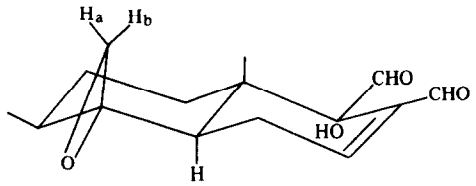
While muzigadial (**1**) was reported [1, 2] to have antimicrobial and insect antifeedant properties, the antimicrobial activity of **2** and **3** was only marginal in comparison. Both **2** and **3** are being evaluated against some plant pathogens and the results will be published in due course.

EXPERIMENTAL

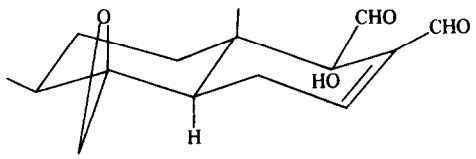
Mps: uncorr; IR; KBr; ^1H NMR and ^{13}C NMR 300 and 75 MHz (Varian VSR-300) respectively, $CDCl_3$, TMS as int. standard, standard pulse sequences were used for COSY [5], HETCOR [6], DEPTGL [7] and NOESY [8]. TLC was performed on silica gel plates using MeCN–CH_2Cl_2 (7:93) as solvent and visualized under short wavelength UV light or by spraying with



1



2



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anisaldehyde spray reagent [9]. HPLC was performed on a μ-Porasil column using MeCN CH_2Cl_2 (1:4) as solvent, with a UV detector set at 254 nm. The bark and leaves of *Canella winterana* were collected in the Florida Keys area, U.S.A. in the Spring of 1985. A voucher specimen was deposited in the herbarium of the School of Pharmacy, University of Mississippi, University 38677, U.S.A.

Isolation of muzigadial (**1**) *and 4,13-α-epoxymuzigadial* (**2**) *from* C. winterana *leaves.* The powdered leaves (1.05 kg) were exhaustively extracted with hexane in a Soxhlet. The solvent was removed and the residue (117 g) was partitioned between MeCN and hexane presaturated with each other. Evapn of the MeCN phase left 31 g of a greenish residue, which was subjected to flash chromatography [3] on silica gel, using $CHCl_3$ as solvent to give 0.379 g of muzigadial (**1**), indistinguishable from the material previously isolated from the bark [1] (mp, mmp, spec. rot. and superimposable IR and NMR spectra). 4,13-α-Epoxymuzigadial (**2**) (97 mg) was obtained from a subsequent fraction as colourless prisms from Me_2CO–Et_2O, mp 140–142° (after initial softening at 115–120°) $[\alpha]_D^{25} -240°$ ($CHCl_3$; *c* 0.5). UV: λ_{max}^{MeOH} 227 (ε = 1320); IR ν_{max}^{KBr} cm^{-1}: 3250 (OH), 1718 (CO), 1687 (CO) and 1648 (C=C); ^1H NMR ($CDCl_3$): δ 9.68 (1H, *d*, *J* = 1.5, H-11), 9.42 (1H, *s*, H-12), 7.17 (1H, *dd*, *J* = 4.8 and 2.7, H-7), 4.07 (1H, *d*, *J* = 1.2, exchangeable, OH), 2.79 (1H, *d*, *J* = 3.6, H-13a), 2.73 (1H, *d*, *J* = 3.6, H-13b), 1.01 (3H, *s*, Me-15) and 0.75 (3H, *d*, *J* = 6, Me-14); ^{13}C NMR ($CDCl_3$): δ 201.0 (*d*, C-11), 192.4 (*s*, C-12), 155.2 (*d*, C-7), 140.1 (*s*, C-8), 76.6 (*s*, C-9), 60.8 (*s*, C-4), 44.9 (*t*, C-13), 42.6 (*s*, C-10), 38.5 (*d*, C-5), 36.5 (*d*, C-3), 30.4, 29.2 and 23.9 (3*t*, C-1, C-3 and C-6, indistinguishable), 18.1 (*q*, C-14) and 14.1 (*q*, C-15); CI(NH_3)-MS (*m/z*): 282 $(M + NH_4)^+$ (Found: C, 68.23; H, 7.77. $C_{15}H_{20}O_4$ (264) requires: C, 68.16; H, 7.63%).

Epoxidation of muzigadial (**1**) *with m-chloroperbenzoic acid to* **2** *and* **3**. Muzigadial (**1**) (1.0 g) was dissolved in CH_2Cl_2 (40 ml) and 1.0 g of *m*-chloroperbenzoic acid was added to the soln. After 24 hr the mixture was worked-up [10] to provide 881 mg of an oil that crystallized from Et_2O to give 0.65 g of a mixture of **2** (R_t 4.12 min.) and **3** (R_t 3.95 min) in the ratio of 4:1, respectively, as determined by HPLC. Flash chromatography [3] on silica gel using MeCN–CH_2Cl_2 (1:24) as solvent provided 500 mg of **2**, identical with the natural material (mp, mmp and superimposable IR and NMR spectra), and 100 mg of **3**, mp 159–160°; $[\alpha]$-91° ($CHCl_3$; *c* 0.5); UV: λ_{max}^{MeOH} 228 (ε 920); IR ν_{max}^{KBr} cm^{-1}: 3228 (OH) 1710 (CO), 1678 (CO) and 1645 (C=3); ^1H NMR ($CDCl_3$): 9.68 (1H, *d*, *J* = 1.5, H-11), 9.41 (1H, *s*, H-12), 7.17 (1H, *dd*, *J* = 4.5 and 3.3, H-7), 4.08 (1H, *d*, *J* = 1.2, OH, exchangeable), 2.62 and 2.54 (1H each, *d*, *J* = 3.6, H-13a and H-13-b), 1.12 (3H, *s*, Me-15) and 0.75 (3H, *d*, *J* = 6.6, Me-14); ^{13}C NMR ($CDCl_3$): δ 201.5 (*d*, C-11), 192.3 (*d*, C-12), 155.9 (*d*, C-7), 140.1 (*s*, C-8), 76.6 (*s*, C-9), 59.9 (*s*, C-4), 43.1 (*t*, C-13), 42.0 (*s*, C-10), 36.6 (*d*, C-5), 34.6 (*d*, C-3), 30.8, 27.8 and 24.3 (*t* each, C-1, C-2 and C-6, indistinguishable), 16.4 (*q*, C-14) and 14.2 (*q*, C-15); EI(NH_3)-MS (*m/z*): 282 $(M + NH_4)^+$ (Found: C, 68.00; H, 7.39. $C_{15}H_{20}O_4$ (264) requires: C, 68.16; H, 7.63%).

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