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SAPRIOLACTONE, A CYTOTOXIC NORDITERPENE FROM *SALVIA PRIONITIS*

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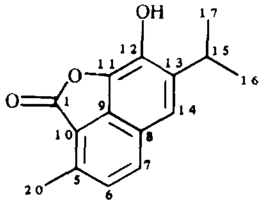
Key Word Index—*Salvia prionitis*; Labiateae; sapriolactone; diterpenoid; cytotoxicity.

Abstract—From the roots of *Salvia prionitis* a new norditerpene, sapriolactone was isolated and its structure elucidated on the basis of its ^{1}H NMR spectrum and NOE experiments. Sapriolactone showed cytotoxic activity against both P388 and KB cells *in vitro*.

INTRODUCTION

In previous investigations of *Salvia prionitis* Hance (Labiateae), a plant native to the Southern Provinces of China and used in traditional Chinese medicine as an antibacterial, antitubercular and antiphlogistic drug, we have reported the isolation and structure elucidation of several new diterpenoids [1–6]. In this report, we wish to present the isolation and structure elucidation of sapriolactone (**1**), a norditerpene of a new skeletal type.



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RESULT AND DISCUSSION

Sapriolactone (**1**), $C_{15}H_{14}O_3$ by HRMS, was obtained from the roots of *Salvia prionitis* (0.00006%, yield), and crystallized from acetone as yellowish needles, mp 123–124°. Intense absorptions in the UV spectrum were observed at 254, 344 and 370 nm, suggesting a highly conjugated naphthalene system, and the hyperchromic shift of 65 nm with base indicated the presence of a phenolic hydroxy group *ortho* to an oxygen function. In the IR spectrum absorptions for hydroxyl (3270 cm^{-1}), carbonyl (1750 cm^{-1}) and conjugated naphthalene (1640, 1505 and 1485 cm^{-1}) units were observed. The ^{1}H NMR spectrum demonstrated the presence of an aromatic isopropyl group (δ1.34, *d*, $J = 6.9$ Hz, 6H; 3.38, *septet*, $J = 6.6$ Hz, 1H), an aromatic methyl (δ2.79), three aromatic protons (δ7.78, *d*, $J = 8.2$ Hz; 7.90, *d*, $J = 8.2$ Hz; 7.46, *s*), two of which were *ortho*-related, and a hydroxyl group (δ5.96, *s*, D_2O exchangeable).

An NOE difference study was crucial in establishing the respective placement of the substituents on the naphthalene ring system. Thus, 12% NOE enhancement was observed between H-14 (δ7.46, *s*) and the isopropyl methyl resonances (δ1.34), and a 5% NOE was noted between the isopropyl methyls and the hydroxy group, demonstrating that the isopropyl group should be at the C-13 position, and the hydroxy group at C-12. The observation of a 5% NOE enhancement between H-14 and H-7 (δ7.90, *d*), and a 6% NOE enhancement between H-6 (δ7.38, *d*) and the methyl group (δ2.79) led to the conclusion that the aromatic methyl group must be at C-5 and a lactone at C-10; the latter formed between a C-10 carbonyl and a C-11 hydroxyl. Insufficient material was available for ^{13}C NMR analysis. Compound **1** showed cytotoxic activity against the P388 and KB test systems *in vitro* with ED_{50} values of 2.80 and 1.68 μg/ml, respectively (Yang, J.-L. and Xian, K.-X. unpublished results).

Biogenetically, sapriolactone (**1**) might be derived from the corresponding quinone methide diterpenoid through acid-catalysed migration of the C-10 methyl group to C-5 accompanied by fission of ring A [7], followed by oxidative cleavage of the C-1/C-2 bond and cyclization to a lactone with the C-11 hydroxy group.

EXPERIMENTAL

General. Mps. ^{1}H NMR spectra were obtained in $CDCl_3$ at 400 MHz. Chemical shifts (δ) are reported in ppm downfield of TMS. The TLC chromatograms were performed on silica gel F-254 plates (0.25 mm thickness for TLC and 0.5 mm thickness for preparative TLC).

Plant material. The plant material was collected in Jiang-Xi Province, China, in June, 1986, and voucher samples have been deposited in the herbarium of the Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai, China.

Isolation of sapriolactone (**1**). The powdered roots (11 kg) of *Salvia prionitis* were percolated with EtOH at room temp., and the EtOH extract conc *in vacuo* at 50° to afford a thick dark syrup, which was distributed between $CHCl_3$ and H_2O. The

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organic layer was subjected to CC on silica gel eluting with $CHCl_3$. Fractions containing **1** were subjected to repeated preparative TLC using cyclohexane–CH_2Cl_2 (1:4) to afford yellow needles of **1** (5 mg, 0.00006%), mp 205–206°; UV λ_{max}^{MeOH} nm (log ε): 215 (4.42), 230sh (4.16), 254 (4.38), 344 (3.66) and 370sh (3.63) nm; UV $\lambda_{max}^{MeOH+OH^-}$ nm (log ε): 204 (4.68), 225 (4.37), 240sh (4.18), 272 (4.29), 344 (3.51) and 435 (3.75); IR ν_{max}^{KBr} cm^{-1}: 3270, 1750, 1640, 1505 and 1485; ^{1}H NMR ($CDCl_3$, 400 MHz), (TMS): δ7.90 (*d*, $J = 8.2$ Hz, 1H, H-7), 7.38 (*d*, $J = 8.2$ Hz, 1H, H-6), 5.96 (*s*, 1H, OH, D_2O exch, C-12 OH), 3.47 (*sept*, $J = 6.9$ Hz, 1H, H-15), 2.79 (*s*, 3H, H-20) and 1.34 (*d*, $J = 6.9$ Hz, 6H, H-16 and H-17); MS (electron impact, 70 eV) *m/z* (rel. int.): 242 $[M]^+$ (96), 227 (100), 213 (27), 199 (9), 184 (6), 171 (12), 171 (12), 155 (9), 141 (21), 129 (38) and 115 (30); HRMS 242.0938 for $C_{15}H_{14}O_3$, cal. 242.0932.

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PHLOROACYLPHENONES IN THE ESSENTIAL OIL OF *THRYPTOMENE SAXICOLA*

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Key Word Index—*Thryptomene saxicola*; Myrtaceae; essential oil; phloroacylphenones; *O*-isobaeckeol.

Abstract—The essential oil of *Thryptomene saxicola* is shown to contain α-pinene, 1,8-cineole, α-terpineol, globulol, *O*-isobaeckeol and its homologue.

INTRODUCTION

The genus *Thryptomene* is endemic to Australia and consists of *ca* 25 species [1] most of which are restricted to the south-west and Eremean provinces of Western Australia [2]. Previous work on Thryptomene had been restricted to the detection and isolation of sesquiterpenes. Thus the essential oil of *T. kochi* has been shown to contain aromadendrene and globulol [3, 4]. The presence of the latter in *T. australis* Endl and *T. stenocalyx* F.v.M. has also been established [4]. As part of a screening programme of essential oils from Western Australian plants, we had the opportunity of analysing the essential oil of a sample of *T. saxicola* (A. Cunn.) Schau which from preliminary examination appeared to contain two aromatic compounds. These have been characterized as *O*-isobaeckeol (**1**) and its homologue (**2**).

RESULTS AND DISCUSSION

Steam distillation of the leaves and terminal branches of the plant yielded a yellow oil (1.5%) which on distillation afforded fractions of α-pinene (57%), a mixture (12%) of α-pinene, cineole, α-terpineol and five unidentified sesquiterpene hydrocarbons. A third fraction (20%) contained three compounds. Separation by chromatography on basic alumina gave globulol and another compound to which the structure of *O*-isobaeckeol (**1**) was assigned on the following evidence.

Interpretation of the spectral data indicated that the compound ($[M]^+$ 238) contained a pentasubstituted benzene with two methoxyls, a methyl, a hydrogen bonded hydroxyl (δ_H 13.14) and an isobutanoyl group as substituents. These features are consistent with the compound being baeckeol (**3**). However, comparison of their