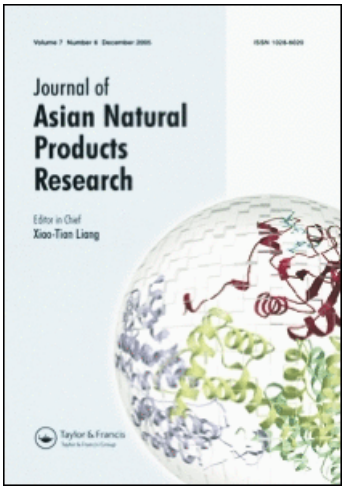

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ISOLATION AND STRUCTURE ELUCIDATION OF NOVEL γ-LACTONES FROM *SACCOPETALUM PROLIFICUM*

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Two novel γ-lactones, saccopetrin C (**1**) and saccopetrin D (**2**), were isolated from the roots of *Saccopetalum prolificum*. Their structures were established by spectroscopic and chemical methods.

Keywords: *Saccopetalum prolificum*; γ-Lactone; Saccopetrin C; Saccopetrin D

INTRODUCTION

In recent years, the phytochemical and pharmacological studies on Annonaceous species have been intensified due to the discovery of the Annonaceous acetogenins, a class of natural compounds with a wide variety of biological activities [1]. *Saccopetalum prolificum* (Chun *et* How) Tsiang (Annonaceae) is an evergreen tree distributed in Hainan Province, P.R. China. The ethanolic extract of the plant exhibits activity (20 μg/ml) against L1210 lymphocytic leukemia. In a previous paper [2], we reported two novel γ-lactones, saccopetrin A and saccopetrin B, obtained from *Saccopetalum prolificum*. Herein we describe further isolation of the γ-lactones, saccopetrin C and saccopetrin D, from the roots of *S. prolificum*.

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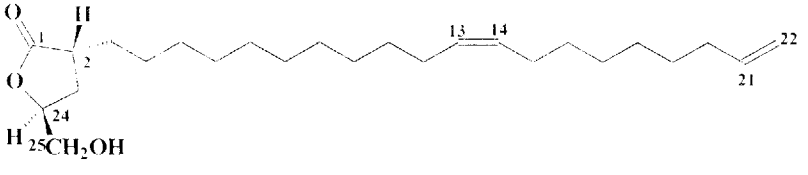
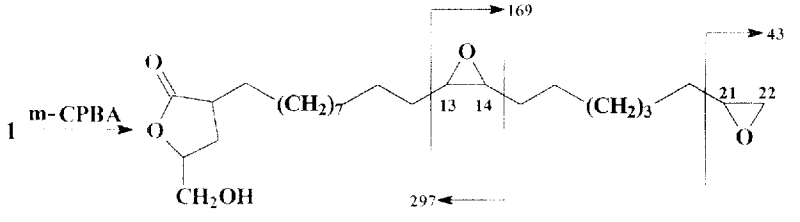
RESULTS AND DISCUSSION

Saccopetrin C (**1**) was isolated as waxy solid. It was shown to have a molecular formula of $C_{25}H_{44}O_3$ from the HRFABMS ($[MH]^+$ 393.3384, *calcd.* 393.3369). The IR spectrum showed characteristic absorption of γ-lactone (1768 cm^{-1}), hydroxy group (3483 cm^{-1}) and double bonds (3010, 1650, 949, 910 cm^{-1}). The ^{13}C NMR DEPT spectrum of **1** revealed 25 carbon signals, composed of 19 methylenes, 5 methines and 1 quaternary carbon. Two one proton multiplets at δ 4.59 (H-24) and 2.69 (H-2) coupled with δ 78.6 (C-24) and 39.5 (C-2) respectively in ^1H–^{13}C COSY spectrum, indicated that one methine was bearing an oxygen and the other was adjacent to the carbonyl. A hydroxymethyl group at δ 64.3 (C-25) in the ^{13}C NMR spectrum was characterised by the presence of two magnetic non-equivalent protons at δ 3.86 (1H, dd, $J = 12.3$, 3.3 Hz, H-25) and 3.65 (1H, dd, $J = 12.3$, 4.8 Hz, H-25) in the ^1H NMR spectrum. The olefinic proton signals at δ 5.81 (1H, m, H-21) and 4.95 (2H, m, H-22) in the ^1H NMR spectrum together with the olefinic carbons at δ 139.0 (C-21) and 114.0 (C-22) in the ^{13}C NMR spectrum indicated the presence of a terminal vinyl. A broad triplet in the ^1H NMR spectrum at δ 5.34 (2H, t, $J = 4.8$ Hz) and the methine carbon signal at δ 129.8 (d) in the ^{13}C NMR spectrum corresponded to an isolated double bond in **1**. Oxidation of **1** with *m*-CPBA afforded the epoxy derivative **1a** [3]. The position of the double bond at C-13,14 was deduced from analysis of the EIMS fragments of **1a** (Scheme 1). The HMQC spectrum of



1

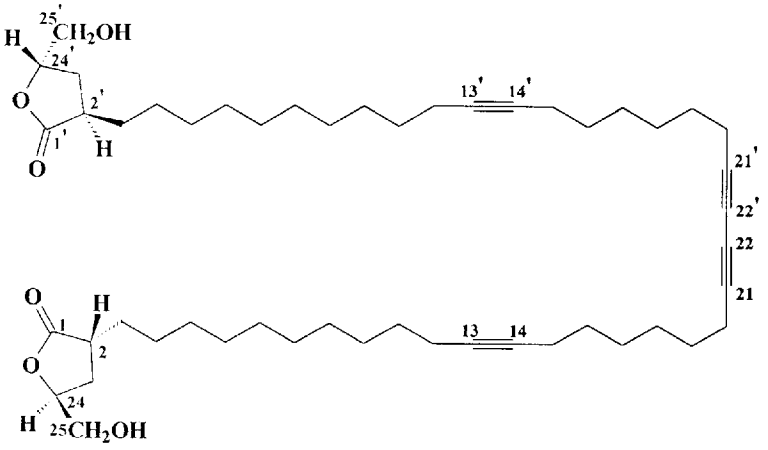


1a

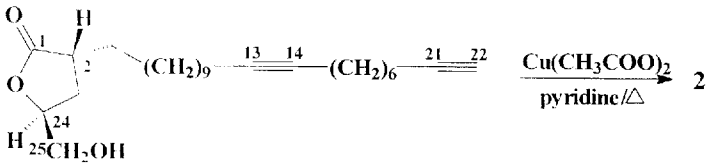
SCHEME 1 Oxidative reaction of **1**

1 showed that the proton resonances at δ 2.02 (H-12, H-15) correlated with the carbon resonances at δ 27.1 (C-12, C-15). The up-field nature of this allylic carbon resonance suggested a *Z*-geometry for the Δ^{13} disubstituted double bond [4], which was also in agreement with the absence of a strong, sharp band near 968 cm^{-1} in the IR spectrum [5]. The relative stereochemistry of **1** was solved by NOESY experiments. In the NOESY spectrum of **1**, a correlation between H-2 and H-25 was observed, which suggested that they were on the same side of the lactonic ring.

Saccopetrin D (**2**) was obtained as amorphous powder. The molecular formula of $C_{50}H_{78}O_6$ was established by HRFABMS which showed $[MH]^+$ at *m/z* 775.5887 (*calcd.* 775.5877). The existence of γ-lactone (1753 cm^{-1}), hydroxy group (3410 cm^{-1}) and triple bond (2350 cm^{-1}) was deduced from the IR spectrum. The ^1H NMR spectrum of **2** revealed signals at δ 4.58 (1H, m, H-24), 3.86 (1H, dd, $J = 12.3$, 2.7 Hz, H-25), 3.64 (1H, dd, $J = 12.3$, 4.5 Hz, H-25), 2.70 (1H, m, H-2), and a strong sharp signal at δ 1.30 due to a long methylene chain. The ^{13}C NMR spectrum of **2** displayed only 25 carbon resonances suggested that the molecule should have a symmetrical structure. The fact that only half of the expected resonances could be detected in the ^{13}C NMR spectrum implies the presence of two equivalent isolated triple bonds at δ 80.2 (s) and 79.8 (s) and two identical conjugated triple bonds at δ 77.1 (s) and 65.1 (s). The ^1H NMR spectrum of **2** was very similar to that of saccopetrin B except for the absence of the terminal ethynyl, thus it might be the dimer of saccopetrin B. This was confirmed by an oxidative coupling reaction of saccopetrin B (Scheme 2) [6]. After treatment of saccopetrin B with cupric acetate monohydrate in pyridine at 55°C, the reaction



2



Saccopetrin B

SCHEME 2 Oxidative coupling reaction of saccopetrin B.

product **2a** was isolated and its physical and spectral data were identical with those of saccopetrin D. So the structure of **2** was determined as described above. The relative stereochemistry of **2** was defined by means of NOESY experiments as **1**.

EXPERIMENTAL SECTION

General Experimental Procedures

Melting points were determined on a Reichert Nr-229 micromelting point apparatus and are uncorrected. The optical rotations were measured on a Perkin-Elmer 241 polarimeter. IR spectra were recorded on a Perkin-Elmer 683 infrared spectrometer. NMR spectra were run on Mercury 300 spectrometer with TMS as internal standard. MS were performed on VG-Autospec-3000 mass instrument.

Plant Material

The roots of *S. prolificum* were collected in August 1998 in Hainan Province, P.R. China. The plant material was identified by Professor Shi-Man Huang, Hainan University, Hainan Province, P.R. China. A voucher specimen (no. 276) is deposited in the herbarium of the Department of Medicinal Plants, Institute of Materia Medica, Chinese Academy of Medical Sciences, Beijing.

Extraction and Isolation

The dried and pulverized roots (10 kg) of *S. prolificum* were extracted with EtOH three times under reflux. The solvent was removed *in vacuo* to yield 1.0 kg of extract that was partitioned between H_2O and $CHCl_3$ (1 : 1).

The $CHCl_3$ fraction (505 g) was partitioned between petroleum ether and 90% MeOH. The MeOH fraction (350 g) was subjected to Si gel column chromatography with a gradient of petroleum ether–Me_2CO (10 : 1 → 4 : 1) system to give **1** (20 mg) and **2** (5 mg).

Saccopetrin C (**1**): waxy solid, m.p. 41–43°C, $[\alpha]_D^{20}$ − 7.5 (c 0.20, $CHCl_3$); IR (KBr) ν_{max} 3483, 3010, 2933, 2852, 1768, 1650, 1468, 1173, 1047, 949, 910 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.81 (1H, m, H-21), 5.33 (2H, t, J = 4.8 Hz, H-13, H-14), 4.95 (2H, m, H-22), 4.59 (1H, m, H-24), 3.86 (1H, dd, J = 12.3, 3.3 Hz, H-25), 3.65 (1H, dd, J = 12.3, 4.8 Hz, H-25), 2.69 (1H, m, H-2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.0 (C-1), 139.0 (C-21), 129.8 (C-13, C-14), 114.0 (C-22), 78.6 (C-24), 64.3 (C-25), 39.5 (C-2); FABMS *m/z* 393 $[MH]^+$; HRFABMS *m/z* 393.3384 $[MH]^+$ ($C_{25}H_{45}O_3$, *calcd.* 393.3369).

Epoxy Derivative (1a)

Compound **1** (5 mg, 0.013 mmol) was dissolved in $CHCl_3$ (1 ml) and *m*-CPBA (5 mg, 0.028 mmol) was added. The mixture was stirred at room temperature for 2 h, then washed with 1% $NaHCO_3$. The solvent was removed *in vacuo*. The ^1H NMR spectrum of the epoxy derivative **1a** was recorded without further purification. ^1H NMR (300 MHz, $CDCl_3$) δ 4.60 (1H, m, H-24), 3.87 (1H, dd, J = 12.3, 3.3 Hz, H-25), 3.65 (1H, dd, J = 12.3, 4.8 Hz, H-25), 2.90 (4 H, m, H-13, 14, 21, 22), 2.75 (1H, m, H-22), 2.70 (1H, m, H-2). EIMS *m/z*: 424 $[M]^+$, 393, 297, 169, 43.

Saccopetrin D (**2**): amorphous powder, m.p. 65–67°C, $[\alpha]_D^{20}$ − 21.6 (c 0.15, $CHCl_3$); IR (KBr) ν_{max} 3410, 2920, 2850, 2350, 1753, 1466, 1203, 1045 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.58 (1H, m, H-24), 3.86 (1H, dd, J = 12.3, 2.7 Hz, H-25), 3.64 (1H, dd, J = 12.3, 4.5 Hz, H-25), 2.70 (1H, m, H-2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.4 (C-1, C-1′), 80.2 (C-13, C-13′ or C-14, C-14′), 79.8 (C-13, C-13′ or C-14, C-14′), 78.2 (C-24, C-24′), 77.1 (C-21, C-21′), 65.1 (C-22, C-22′), 64.4 (C-25, C-25′); 39.4 (C-2, C-2′); FABMS *m/z* 775 $[MH]^+$; HRFABMS *m/z* 775.5887 $[MH]^+$ ($C_{50}H_{79}O_6$, *calcd.* 775.5877).

Oxidative Coupling Derivative (2a)

A solution of saccopetrin B (15 mg, 0.038 mmol) in 5 ml pyridine was added to a suspension of finely ground neutral cupric acetate monohydrate (225 mg, 1.13 mmol) in 15 ml pyridine. The mixture was heated to 55°C and stirred vigorously at this temperature under a reflux condenser for 3 h. After being cooled to room temperature, the mixture was filtered. The filtrate was

poured into dilute hydrochloric acid and extracted with ether. The combined organic layers were washed with saturated water solution of sodium chloride and dried with anhydrous sodium sulfate. The solvent was removed *in vacuo* at an outside temperature below 50°C. The crude product was chromatographed on an alumina column and eluted with petroleum ether : acetone (4 : 1) to afford **2a** (9 mg, 60%). Compound **2a**, m.p. 69–71°C, $[\alpha]_D^{20}$ – 20.7 (c 0.17, $CHCl_3$); IR (KBr) ν_{max} 3396, 2920, 2845, 2350, 1753, 1473, 1200, 1047 cm^{-1}; FABMS *m/z* 775 $[MH]^+$.

Acknowledgements

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References

[1] F.Q. Alali, X.X. Liu and J.L. McLaughlin. *J. Nat. Prod.* 1999, **62**, 504–540.
[2] M.L. Wang, R.Y. Chen, F.Z. Xie and D.Q. Yu. *J. Nat. Prod.*, submitted.
[3] E.L.M. Silva, F. Roblot, J. Mahuteau and A. Cave. *J. Nat. Prod.* 1996, **59**, 528–530.
[4] P.L. Mena, O. Pilet and C. Djerassi. *J. Org. Chem.* 1984, **49**, 3260–3264.
[5] A.D. Rodriguez and C. Ramirez. *J. Nat. Prod.* 1994, **57**, 339–347.
[6] F. Sondheimer and R. Wolovsky. *J. Am. Chem. Soc.* 1962, **84**, 260–262.