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NEW ALKENE-ALKYNE-γ-LACTONES ISOLATED BY HPCCC AND CYTOTOXIC POTENTIAL FROM Sextonia rubra

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Sextonia rubra (Lauraceae) is known as raw material for the timber industry and is the only member of its genus found in northern Brazil. Research indicates that *S. rubra* has larvicidal, antioxidant, termiticidal, and fungicidal properties, mainly due to the biomarker compounds rubrenolide and rubrynolide. This study reports the isolation of two novel γ-lactones from the hexane extract of *S. rubra* bark by high-performance counter-current chromatography (HPCCC) and evaluates their cytotoxic properties. HPCCC is a reproducible method that avoids loss of samples by adsorption or denaturation and uses analytical-grade solvents. The fractions were analyzed using thin-layer chromatography and nuclear magnetic resonance. The hexane extract (600 mg) was fractioned by HPCCC, using the preparative column in a step-gradient normal phase elution mode. The solvent systems consisted of eight ratios about hexane-ethyl acetate-methanol-water (HEMWat, v/v/v/v) S28 (1:0:1:0), S26 (9/1/9/1), S24 (5/1/5/1), S22 (3/1/3/1), S20 (2/1/2/1), S18 (6/5/6/5), S16 (5/6/5/6) and S14 (1/2/1/2)[1]. The lower phase was employed as the stationary phase, while the upper phases served as mobile phases. The stationary phase retention (*Sf*) at the first step of the gradient was 86%. Fractions F76 (35.4 mg) and F77 (36.0 mg), rich in γ-lactones were purified by analytical column in a step-gradient, normal elution mode (HEMWat) S21 (5/2/5/2), S20, S19 (3/2/3/2) and S18, for both samples the *Sf* was 75%. This procedure yielded two main samples: **F76-16** (2.5 mg) and **F77-66** (3.8 mg). The NMR data analysis proposed two new lactones 9-acetyl-5-dec-18-ynyl-3-(7-hydroxybuthyl)oxolan-2-one (**1**) and 9-acetyl-5-dec-18-enyl-3-(7-hydroxybuthyl)oxolan-2-one (**2**).The compound (**1**) presented cytotoxic activity against prostate cancer, inhibiting 63 % of the cells with IC_{50} of 4.70 µg/mL and against promyelocytic leukemia cells a IC_{50} of 6.80 µg/mL. The isolation was performed in two steps, without the use of any adsorption chromatography procedure. Furthermore, **1** should be subject to further investigation into the mechanism of action.

[1] N. Sumner. Developing counter-current chromatography to meet the needs of pharmaceutical discovery. Journal of Chromatography v. 1218, n. 36, p. 6107-6113, 2011

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