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BENZYLTETRAHYDROISOQUINOLINE ALKALOIDS FROM Nectandra membranacea (LAURACEAE)

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Chagas disease, which is caused by the protozoan *Trypanosoma cruzi*, affects millions of people worldwide, particularly in South and Central America. The available treatments, benznidazole and nifurtimox, have several adverse effects.[1] Therefore, it is necessary to search for new compounds with anti-*T. cruzi* activity, especially those based on the structures of natural products. In this context, the Brazilian floral biodiversity is an inexhaustible source of new bioactive compounds. Previous studies on *Nectandra membranacea* (Lauraceae) revealed alkyl γ-lactones with anti-*T. cruzi* activity. As a continuation of our studies on this plant, we subjected the MeOH extract from its branches to a chemically active procedure to afford an alkaloidal phase. This phase exhibited *in vitro* activity against *T. cruzi*, resulting in 100% death of trypomastigote forms of the parasite at 300 µg/mL. Thus, it underwent several chromatographic steps over silica gel and Sephadex LH-20, yielding alkaloids **1**–**4**. NMR analysis and comparison with literature data[2,3] identified **1** and **2** as the diastereomers (*R*)- and (*S*)-*O*,*O*-dimethylcoclaurine, while **3** was characterized as velucryptine. The NMR spectra of compound **4** showed, in addition to the signals attributed to benzene rings and methoxy groups, peaks at δ_H 8.35 (d, J = 5.5 Hz) / δ_C 138.6 and δ_H 7.52 (d, J = 5.5 Hz) / δ_C 119.5 assigned to hydrogens and carbons from positions 2 and 3, respectively. Additionally, these spectra showed also signals at δ_H 6.08 (s) / δ_C 72.5 attributed to an oxymethine carbon at α position. Therefore, the structure of compound **4** was elucidated as depicted on Figure 1. The discovery of alkaloids **1**–**4** expands the knowledge of the chemical diversity biosynthesized by *N. membranacea* and contributes to the chemosystematics of the genus *Nectandra* in addition to identifying new bioactive compounds against *T. cruzi* (CNPq, FAPESP, CAPES)

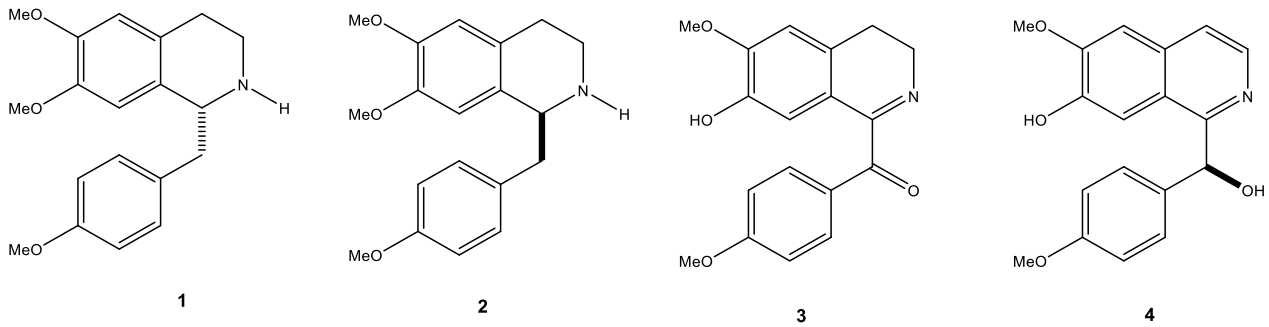

Figure 1. Structures of alkaloids **1** – **4** from *Nectandra membranacea.*

Keywords: *Nectandra membranacea;* alkaloids; benzylisoquinoline
References: [1]Pérez-Molina et al., *The Lancet* **2018**, *10115*, 82; [2]Werner et al., *Eur. J. Org. Chem*. **2007**, 3911; [3]Lebœuf et al., *J. Nat. Prod*. **1989**, *52*, 516.