New quinolizidine and diaza-adamantane alkaloids from Acosmium dasycarpum (Vog.) Yakovlev—Fabaceae

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Aiming the isolation and identification of bioactive substances, we have isolated several alkaloids during the conventional chromatographic fractioning of the methanol crude extract from the root bark of A. dasycarpum. The alkaloids lupanine 1, acosmine 2, acosminine 3 and panacosmine 5 have been previously reported in Acosmium. However, the alkaloids lupanacosmine 4 and dasycarpumine 6 have been described for the first time herein. Acosmium dasycarpum aerial roots were collected at Chapada dos Guimarães, state of Mato Grosso, Brazil and identified by Dr. M. Macedo (Universidade Federal de Mato Grosso—UFMT). Voucher specimens numbered 24079 (01/02/2000) were deposited at UFMT Central Herbarium. The dried root barks (3.3 kg) were sequentially extracted with hexane (3 L) and methanol (5 L). A portion (55.0 g) of the crude methanol extract (EBMeOH) dissolved in methanol (50 mL) and alkalinized with 28% NH4OH (pH 8.5–9.0), afforded the alkaloids fraction FA-I (5.5 g; 9.98%). FA-I was submitted to column chromatography, affording compound 1 (11.5 mg; 0.02%). Compound 1 (3.3 mg; 0.006%) was obtained after HPLC purification. Another EBMeOH portion (150.0 g) was acidified with 10% acetic acid (pH 2.5–3.0), extracted with CHCl3 (50 mL) and alkalinized with NH4OH (pH 8.9–9.0), affording the alkaloids fraction FA-II (5.5 g; 9.98%). FA-II was submitted to column chromatography, affording compound 6 (11.5 mg; 0.02%). Compound 1 (3.3 mg; 0.006%) was obtained after HPLC purification. Another EBMeOH portion (150.0 g) was acidified with 5% HCl (pH 2.5–3.0), extracted with ethyl ether (4 × 50 mL) and alkalinized with 28% NH4OH (pH 8.5–9.0), affording the alkaloids fraction FA-II (3.8 g; 2.53%). Preparative thin-layer chromatography carried out on FA-II led to the isolation of 2 (15.3 mg; 0.01%), 3 (21.2 mg; 0.14%), 4 (56.4 mg; 0.04%), and 5 (8.1 mg; 0.01%). Compound 1 has shown, in its IR spectrum, typical amide absorption at 1620 cm⁻¹. This absorption is coherent with the 13C NMR signal at δ 172.0. These and the other spectral
data obtained for compound 1 were fully consistent with the literature description for the quinolizidine alkaloid lupanine.\textsuperscript{12,14,18} Mass spectra for compound 2 has shown an odd molecular ion [M\textsuperscript{+}] at 357, pointing out to the presence of an odd number of nitrogen atoms in its structure. The DEPT experiment has presented a methinic signal at \( \delta \) 70.9. Therefore in comparison with compound 1, compound 2 must have a substituent at C-10. The absence of an amide carbonyl group at C-2, as well as the evidences for the presence of the substituent at C-10, could be demonstrated from the HMBC data, correlating H-10 (\( \delta \) 2.36) to C-2 (\( \delta \) 52.9) C-8 (\( \delta \) 27.9), C-9 (\( \delta \) 37.3), C-11 (\( \delta \) 60.8), C-18 (\( \delta \) 117.4), C-19 (\( \delta \) 24.7), and C-23 (\( \delta \) 123.0) (Fig. 1A; Table 2). In the same experiment, the correlation of H-23 (\( \delta \) 6.67/7.27) to C-10 (\( \delta \) 70.9), C-19 (\( \delta \) 24.7) and C-21 (\( \delta \) 40.4) (Fig. 1B; Table 2) and the correlation of H-25 (\( \delta \) 2.20/2.15) to C-23 (\( \delta \) 123.0/122.0) and C-24 (\( \delta \) 168.0) (Table 2) has also been observed. The coupling of H-23 (\( \delta \) 6.67/2.15) to C-23 (\( \delta \) 123.0/122.0) has been shown by the COSY and HSQC experiments. HMBC experiments has shown that the methycyclo H-25 (\( \delta \) 2.20/7.27) correlates to C-24 (\( \delta \) 168.0) and C-23 (\( \delta \) 123.0/122.0), confirming the presence of an acetylamide portion at the substituent (Fig. 1B). Restricted rotation around C-N bond at the acetylamide moiety has caused the doubling of \( ^{13} \text{C} \) NMR signals at C-23 and C-25 (Table 2). The same has been observed in \( ^{1} \text{H} \) NMR spectra, at positions H-23 and H-25, as previously observed in the literature.\textsuperscript{11,14,16} The stereochemistry of the substituent at C-10 in compound 2 has been demonstrated to be equatorial, as it could be seen by the coupling of H-25ax with H-10ax in the COSY experiment (Table 2). These data are fully supportive of structure 2, previously reported by the literature.\textsuperscript{14} However, literature \( ^{13} \text{C} \) NMR spectral data have shown the following attribution to C-6 (\( \delta \) 57.9), C-7 (\( \delta \) 37.1), C-9 (\( \delta \) 44.8), C-11 (\( \delta \) 67.6), C-19 (\( \delta \) 33.3), and C-20 (\( \delta \) 25.7).\textsuperscript{14} These data are not consistent with the ones we have