

RHAMNOFOLANE DERIVATIVES FROM *JATROPHA GROSSIDENTATA*

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Abstract—From the root bark of *Jatropha grossidentata* two pairs of epimeric rhamnofolane derivatives were isolated. The structures are elucidated by high field NMR spectroscopy.

INTRODUCTION

Jatropha grossidentata Pax et Hoffm. (Euphorbiaceae), named Canioja by the Indians, is used in folk medicine. So far nothing was known about its constituents. Therefore we have studied a sample of the root bark from Paraguayan Chaco as many of the ca 150 species of the genus contain interesting biologically active compounds [1].

RESULTS AND DISCUSSION

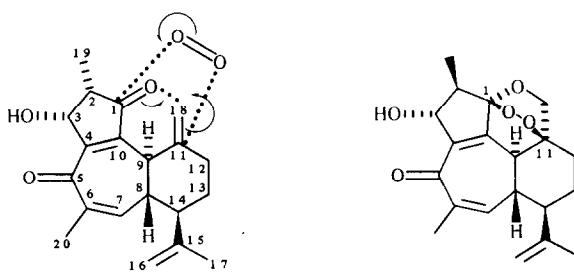
The ethanolic extract gave by column and thin layer chromatography two mixtures which finally by HPLC yielded four compounds, the diterpenes **1-4**. The main compound was the endoperoxide **3**. The structure was deduced from the spectral data, especially from detailed NMR studies. In the ¹H NMR spectrum (Table 1) all signals could be assigned by spin decoupling. The resulting sequences led to partial structures which allowed the connection of the carbons C-5 to C-17 and C-20. As a homoallylic coupling between H-3 and H-9 was present the remaining carbons except for C-18, could be connected with the main part of the molecule. Accordingly, the presence of the rare rhamnofolane carbon skeleton was very likely. However, this skeleton is closely related to the more common tigliane skeleton [1]. The stereochemistry was assigned by the observed NOE's. Clear effects were obtained between H-7, H-8, H-9, H-14, H-16', H-17 and

H-20, between H-18 and H-9, between H-8, H-16' and H-17, between H-9, H-14 and H-18', between H-14, H-9 and H-16' as well as between H-19 and H-3. The presence of an endoperoxide followed from the molecular formula (C₂₀H₂₄O₅) and the observed elimination of oxygen (m/z 312) and of CH₂O (m/z 314). This assumption was further supported by the ¹³C NMR spectrum (see Experimental). In addition to the C-3 doublet at δ 80.4, singlets at δ 104.9 and δ 75.7 and a triplet at δ 73.4 were visible which nicely agreed with the expected signals for the oxygen bearing carbons. Furthermore, the required signals for the six

Table 1. ¹H NMR spectral data of compounds **1-4** (400 MHz, CDCl₃, δ-values)

H	1	2	3	4
2	2.61 dq	2.41 dq	2.30 dq	2.23 dq
3	5.33 br d	4.88 br ddd	4.70 ddd	4.66 dd
7	5.89 dq	5.91 dq	6.37 dq	6.30 dq
8	2.58 dddq	2.58 dddq	2.94 dddq	2.68 dddq
9	3.21 br d	3.18 br d	2.81 dd	3.04 ddd
12	2.42 ddd	2.43 ddd	1.87 ddd	1.70 ddd
12'	2.27 br ddd	2.28 br ddd	1.60 m	1.61 ddd
13	1.89 dddd	1.89 dddd	1.60 m	1.86 ddd
13'	1.46 dddd	1.47 dddd	1.48 m	1.38 ddd
14	2.35 ddd	2.35 ddd	2.07 br ddd	2.17 br ddd
16	4.85 dq	4.85 dq	4.92 dq	4.97 dq
16'	4.82 br s	4.82 br s	4.86 br s	4.88 br s
17	1.59 br s	1.59 br s	1.65 br s	1.67 br s
18	4.75 br s	4.76 br s	4.30 d	4.22 d
18'	4.11 br s	4.10 br s	3.93 d	4.17 dd
19	1.21 d	1.32 d	1.20 d	1.23 d
20	1.85 dd	1.85 dd	1.91 dd	1.92 dd
OH		2.87 br s	3.85 br s	3.76 br s

J(Hz): Compounds **1** and **2**: 2,19 = 7; 7,8 = 5; 7,20 = 8,20 = 1.5; 8,9 = 8,14 = 12,12' = 12',13' = 13,13' = 13', 14 = 12; 12,13 = 3; 12,13' = 5; 12',13 = 13,14 = 4; 16,16' = 16,17 = 1.5; (compound **1**: 2,3 = 7; compound **2**: 2,3 = 3.9 = 3, OH = 2); compounds **3** and **4**: 2,3 = 5.5; 2,19 = 7; 3,9 = 2.5; 7,8 = 3; 7,20 = 8,20 = 1.5; 8,9 = 14; 8,14 = 13',14 = 12; 12,12' = 12',13' = 13,13' = 13.5; 12,13 = 12,13' = 12',13 = 13,14 = 3.5; 16,16' = 16,17 = 1.5; 18,18' = 9.5; (compound **3**: 3, OH = 1; compound **4**: 9,18 = 1).



1 **2** 2αH

3 **4** 1,11 bis epi

olefinic carbons were visible and the multiplicities of all signals agreed with the expected ones. We have given the name caniojane to compound **3**.

The ¹H NMR spectrum of **4** (Table 1) was similar to that of compound **3**. However, most chemical shifts differed while the splittings of the signals were nearly identical in both spectra. A clear *W*-coupling between H-18' and H-9 indicated a changed configuration at C-11. This was established by the observed NOE between H-8 and H-18. Further NOEs showed that the configurations at all the other centres were the same as in ketone **3**. Thus clear effects were observed between H-14 and H-9, between H-19 and H-3 as well as between H-8, H-7, H-17 and H-18.

The ¹H NMR spectra of compounds **1** and **2** (Table 1) were also similar. Again all signals could be assigned by spin decoupling. The spectra differed mainly in the shifts of H-2, H-8 and H-19 and in the couplings of H-3. Comparison of the spectra with those of **3** and **4** indicated that compounds **1** and **2** were closely related to the former ketones. Obviously, as already follows from the molecular formulae, in compounds **1** and **2** the endoperoxide bridge was missing. Additional low field broadened singlets between δ 4.1 and 4.8 and a down field shift of H-9 showed that the endoperoxide bridge was replaced by an exomethylene and a keto group. Accordingly, the epimeric diketones **1** and **2** were present. However, the question had to be solved whether the compounds were epimeric at C-2 or C-3. This could be determined by the observed Eu(fod)₃ shifts. As followed from a strong down field shift of H-9 the 1-keto group was, together with the hydroxy group, more complexed than the 5-keto group. As H-19 was more shifted in compound **1** (Δ 0.64) than in compound **2** (Δ 0.46) the only logical conclusion was the presence of a 2 α -methyl group in diketone **1**. We have given the name jatrogrossidione to diketone **1**.

Most likely **3** and **4** are formed by a cycloaddition of oxygen to **2** from the α - and β -side (see Scheme 1). Such a reaction is not very common but probably due to the rigid arrangement of the corresponding double bonds this addition is highly favoured. This arrangement also leads to a strong shielding of H-18' in compounds **1** and **2** by the carbonyl anisotropy.

EXPERIMENTAL

The root bark (465 g, collected in Campo Loro, Paraguayan Chaco, in August 1987, identified by A. Schinini, Instituto de Botanica de Nordeste, Corrientes, Argentina) was extracted with 1500 ml EtOH. After evapn and acidification with citric acid the residue was extracted with CHCl₃. This extract (3 g) was separated by CC (silica gel) yielding with CHCl₃-MeOH (9:1) a mixture which gave by repeated TLC (silica gel, PF 254, C₆H₆-CH₂Cl₂-Et₂O, 4:4:1) 10 mg **3** and a mixture of **1**-**4** which gave by TLC (C₆H₆-CHCl₃, 1:1, three developments) a mixture of **4** and **3** (A) as well as a mixture of **1** and **2** (B). HPLC of A (RP 8, MeOH-H₂O, 3:1) gave 3 mg **4** and 10 mg **3**. TLC of fraction B (CHCl₃-C₆H₆, 1:1, three developments) gave 5 mg **2** (*R*_f 0.6) and 2 mg **1** (*R*_f 0.5).

Jatrogrossidione (**1**). Colourless gum; IR ν _{max}^{CHCl₃}, cm⁻¹: 3560, 1720, 1650, 1620; MS *m/z* (rel. int.): 312.173 [M]⁺ (14) (calc. for C₂₀H₂₄O₅: 312.173), 284 [M-CO]⁺ (27), 269 [284-Me]⁺ (12), 241 [269-CO]⁺ (16), 69 (74), 55 (100).

2-Epijatrogrossidione (**2**). Colourless gum; IR ν _{max}^{CHCl₃}, cm⁻¹: 3570, 1720, 1650, 1620; MS *m/z* (rel. int.): 312.173 [M]⁺ (41) (calc. for C₂₀H₂₄O₅: 312.173), 284 (44), 269 (12), 241 (10), 69 (72), 55 (100).

Caniojane (**3**). Colourless crystals, mp 167-168°; IR ν _{max}^{CHCl₃}, cm⁻¹: 3580, 1680, 1620, 1605; MS *m/z* (rel. int.): 344.163 [M]⁺ (11) (calc. for C₂₀H₂₄O₅: 344.162), 314 [M-CH₂O]⁺ (31), 312 [M-O₂]⁺ (22), 296 [314-H₂O]⁺ (60), 187 (100); ¹³C NMR (CDCl₃, C-1-C-20): 104.9, 47.7, 80.4, 138.3, 192.1, 135.6, 141.4, 37.2, 43.4, 151.4, 75.7, 28.8, 25.6, 49.0, 145.8, 114.1, 20.4, 73.4, 19.0, 9.0; $[\alpha]_D^{24} = 348$ (CHCl₃; c 0.13).

1,11-Bisepicaniojane (**4**). Colourless gum; IR ν _{max}^{CHCl₃}, cm⁻¹: 3580, 1670, 1620, 1605; MS *m/z* (rel. int.): 344.163 [M]⁺ (8) (calc. for C₂₀H₂₄O₅: 344.162), 314 (27), 312 (19), 55 (100).

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