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SHORT COMMUNICATION

QUASSINOIDS FROM *AESCHRION CRENATA**

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Abstract—From the bark of *Aeschrion crenata* Vell. (sin. *Picrasma crenata* (Vell.) Engl., Simaroubaceae) three new quassinoids, paraine (II), isoparaine (III), and 12-norquassine (IV), have been isolated. The last two compounds are already known as transformation products of other quassinoids.

INTRODUCTION

Aeschrion crenata Vell. (sin. *Picrasma crenata* (Vell.) Engl.) is a Simaroubaceae that grows in northeast Argentina, known to the guaraní indians as paraíh. From its wood, Polonsky and Lederer reported the isolation of 2,6-dimethoxybenzoquinone and quassine.[1] More recently two new β-carboline alkaloids, crenatine and crenatidine, were isolated from its bark.[2] From the non-basic fractions of the bark extract, three other quassinoids have now been isolated by chromatographic procedures.

RESULTS

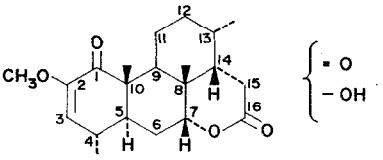
The structure of paraine (II), $C_{21}H_{28}O_6$, M^+ 376, m.p. 245–246°, $[\alpha]_D$ + 28·6° ($CHCl_3$), was established by spectroscopic methods and confirmed by a simple chemical procedure. Five of the six oxygen atoms were assigned on account of the following IR bands: 3400 cm^{-1} (broad), H-bonded OH group; 1720 cm^{-1}, six-membered ring ketone; 1735 cm^{-1} (sh), δ-lactone (confirmed by its solubility in alkali in spite of carboxy and phenol group absence); 1680 cm^{-1} and 1640 cm^{-1} (weak), α, β-unsaturated CO group. The UV spectrum shows a band at 270 nm, not displaced in alkaline medium, attributable to an alkylated diosphenol group.

A preliminary analysis of the NMR spectrum (Table 1) showed a similarity with that of quassine and indicated the presence of an olefinic proton (doublet at δ 5·46, J = 2·5 Hz, 1H), of a OMe group (singlet at δ 3·64, 3H), of two superimposed quaternary Me group signals at δ 1·55 (s, 6H), and of two tertiary Me groups (doublets at δ 1·06 and 1·15, J = 6·5 and 7·0 Hz respectively, 3H each).

All the above data could be accounted for by formula I, in which only the non-conjugated CO function and the OH group must be located. These could be placed by considering the chemical shift of the quaternary Me groups. In contrast to other quassinoids like quassine and the nigakilactones,[3] in whose NMR spectra they appear as two well separated singlets, the C-8 Me group at *ca.* δ 1·20 and the C-10 one at *ca.* δ 1·50, in the

* Part XXXIII in the series 'Studies on Argentine Plants'. For Part XXXII see C. MAMMARELLA and J. COMIN, *An. Asoc. Quím. Argent.* **59**, 239 (1971).

[1] J. POLONSKY and E. LEDERER, *Bull. Soc. Chim.* 1157 (1959).
[2] E. SÁNCHEZ and J. COMIN, *Phytochem.* **10**, 2155 (1971).
[3] T. MURAE, T. TSUYUKI, T. NISHIHAMA, S. MASUDA and T. TAKAHASI, *Tetrahedron Letters* 3013 (1969).



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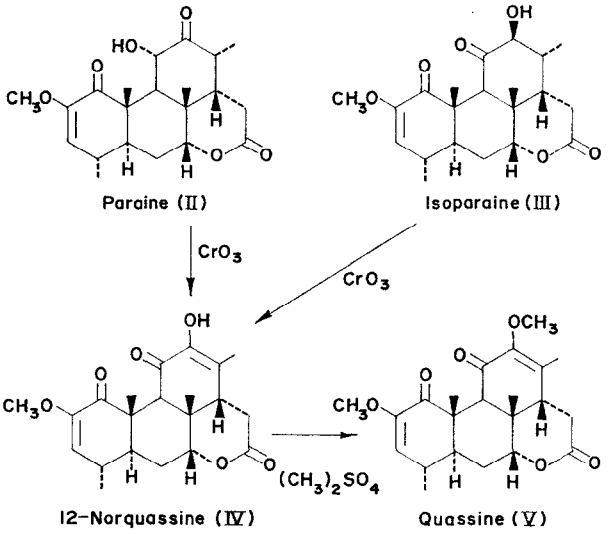

TABLE 1. NMR SPECTRAL DATA

Compound	CH_3-4	CH_3-13	CH_3-8	CH_3-10	CH_3O-2	H-3	H-7	H-11	H-12
Paraine (II)	1·06d J=6·5	1·15d J=7·0	1·55s	1·55s	3·64s	5·46d J=2·5	4·36m	—	—
Paraine acetate	1·05d J=6·5	1·10d J=7·0	1·53s	1·33s	3·54s	5·20d J=2·5	4·30m	5·29d J=12	—
Isoparaine (III)	1·14d J=6·5	1·18d J=6·5	1·12s	1·66s	3·58s	5·41d J=2·5	4·34m	—	—
Isoparaine acetate	1·06d J=6·5	1·12d J=6·5	1·19s	1·63s	3·58s	5·40d J=2·5	4·34m	—	5·20d J=12
12-Norquassine (IV)	1·12d J=6·5	1·88s	1·21s	1·50s	3·59s	5·32d J=2·5	4·26m	—	—
12-Norquassine acetate	1·11d J=6·5	1·83s	1·33s	1·50s	3·56s	5·30d J=2·5	4·31m	—	—
Quassine (V)	1·13d J=6·5	1·90s	1·21s	1·58s	3·71s	5·41d J=2·5	4·36m	—	—

Chemical shifts in δ units; s—singlet, d—doublet, m—multiplet. Coupling constants in Hz.

paraine spectrum both signals appear superimposed at δ 1·55, indicating a strong deshielding (*ca.* 0·3 ppm) of the C-8 Me group. This could be explained by placing the CO group at C-12. Zürcher tables[4] indicate for such a relative configuration a downfield shift of the Me group signal of 0·24 ppm. The OH group was therefore placed, by analogy with other quassinoids, at C-11.

The proposed structure was confirmed by oxidation of paraine (II) with chromic acid to 12-norquassine (IV), followed by methylation with Me_2SO_4 to quassine (V). In this way the configuration of all the assymetric centers except C-11 and C-13 was also established. The C-11 configuration was determined through its carbinolic proton signal in the NMR spectrum of paraine acetate, $C_{23}H_{30}O_7$, m.p. 142–145°, where it is clearly visible at δ 5·29 as a doublet ($J = 12$ Hz), indicating its axial character, coupled with the axial proton at C-9; the respective OH group is accordingly α-equatorial. The C-13 configuration was not established, but by analogy with the other known quassinoids, an α-equatorial configuration could be provisionally assigned to the Me group attached to that carbon atom.

Isoparaine (III), $C_{21}H_{28}O_6$, m.p. 258–261°, $[\alpha]_D$ − 35·1° ($CHCl_3$), has UV, IR, and NMR spectra very similar to those of paraine (II). In the NMR spectrum, the only significant difference is that the signals due to the quaternary Me groups are two well separated singlets at δ 1·12 and 1·66, i.e. the paramagnetic shift of the paraine C-8 Me group not being present in this case. This could be accounted for by changing the position of the CO group to C-11 and of the OH group to C-12, an arrangement in which no deshielding of the C-8 Me group is to be expected, and which also explains the sharper OH band in the IR spectrum (no H-bond to the C-1 CO group), and the 0·11 ppm downfield shift of the C-10 Me group signal; Zürcher tables[4] indicate for such a change a 0·10 ppm shift. The proposed structure was confirmed, like in the case of paraine, by oxidation of isoparaine with chromic acid, when 12-norquassine was obtained. Isoparaine is therefore identical with the 'α-ketol' obtained by oxidation of nigakilactone A, and its UV, IR, and NMR spectra agree with the published data.[3]

The NMR spectrum of isoparaine acetate, $C_{23}H_{30}O_7$, m.p. 250–253°, shows the carbinolic C-12 proton signal at δ 5·20 as a doublet $J = 12$ Hz, thus establishing the configuration of the OH group as β-equatorial, and of the C-13 Me group as α-equatorial. This product is identical with the 'keto-acetate' obtained by oxidation of nigakilactone A, and its UV, IR, and NMR spectra are coincident with the published data.[3]

12-Norquassine (IV), $C_{21}H_{26}O_6$, M^+ 374, m.p. 282–286° $[\alpha]_D$ + 122·5° ($CHCl_3$), has an NMR spectrum identical with the published one,[5] and was identified by comparison with a synthetic sample.

EXPERIMENTAL

M.ps are uncorrected. NMR spectra were determined at 60 MHz with TMS as internal standard. TLC on SiO_2 and $CHCl_3$–EtOH(95:5)(A) and *i*-Pr_2O–Me_2CO(5:2)(B) as solvents; R_f values are given relative to quassine (R_q).

Extraction and separation. The bark of *Aeschrion crenata*, collected near Puerto Iguazú, Misiones, Argentina, was dried and ground. A 2·5-kg sample was extracted first with light petroleum and then with MeOH. The MeOH extract was concentrated to 200 ml and poured on 1·5 l. of 1% HCl. A ppt formed that was filtered and dried (IA, 50 g). The filtrate was made alkaline with conc NH_3: an alkaloidal ppt formed that was filtered. The filtrate was extracted with $CHCl_3$, and this extract washed with 1% HCl, dried and concentrated, leaving a strongly bitter residue (NA, 3·5 g).

[4] R. F. Zürcher, *Helv. Chim. Acta* **46**, 2054 (1963), cited by N. Bhacca and D. Williams, *Applications of NMR Spectroscopy in Organic Chemistry*, Holden–Day, San Francisco (1964).

[5] C. G. Casinovi, G. Grandolini, G. B. Marini-Bettolo and V. Bellavita, *Ann. Chim.* **59**, 230 (1969).

The IA ppt was extracted with cold 2 N NaOH and the alkaline soln. acidified with conc HCl and extracted with $CHCl_3$. Drying and concentration of the extract yielded a residue (4·0 g) that was chromatographed on SiO_2. Elution with $CHCl_3$ containing increasing amounts of EtOH (up to 4%) yielded seven main fractions. Fraction A-3 weighed 1·010 g and showed two spots on TLC, R_q 1·03 and 0·75 (A). It was separated by a second chromatography on SiO_2, eluting with $CHCl_3$–EtOH(99:1). Two main crystalline fractions were obtained: B-3 (330 mg, R_q 1·03), and B-4 (620 mg, R_q 0·73).

The residue NA was chromatographed on SiO_2, eluting with $CHCl_3$–EtOH up to 96:4. The main crystalline fraction (C-3, 927 mg) gave one spot on TLC, R_q 0·73 (A).

Paraine (II). Fraction C-3 was recrystallized from MeOH, giving needles, m.p. 245–246°, $[\alpha]_D^{31}$ + 28·6° (c = 0·69, $CHCl_3$); λ_{max}^{EtOH} 270 nm (log ϵ 3·67); ν_{max}^{Nujol} 3400, 1735 (sh), 1720, 1680, 1640 cm^{-1}; NMR spectrum: Table 1; mass spectrum: *m/e* 376 (M^+), 359, 315, 165, 152, 121. R_q 0·59 (A). (Found: C, 67·04; H, 7·44; O, 25·57. $C_{21}H_{28}O_6$ requires: C, 67·00; H, 7·50; O, 25·50%).

Paraine acetate. A soln. of 100 mg of paraine in Ac_2O–pyridine (1:1) was left at room temp for 48 hr. After working up, 128 mg of crude product was obtained, that on recrystallization from EtOH melts at 142–145°; λ_{max}^{EtOH} 262 nm (log ϵ 3·67); ν_{max}^{Nujol} 1730, 1640 cm^{-1}; NMR spectrum: Table 1. R_q 0·92 (A). (Found: C, 65·83; H, 7·27. $C_{23}H_{30}O_7$ requires: C, 66·01; H, 7·23%.)

Isoparaine (III). Fraction B-4 on recrystallization from MeOH gives needles, m.p. 258–261°, $[\alpha]_D^{20}$ − 35·1° (c = 1·02, $CHCl_3$); λ_{max}^{EtOH} 261 nm (log ϵ 3·78); ν_{max}^{Nujol} 3400, 1730, 1690, 1630 cm^{-1}; NMR spectrum: Table 1. R_q 0·73 (A). (Found: C, 66·83; H, 7·48; O, 25·67. $C_{21}H_{28}O_6$ requires: C, 67·00; H, 7·50; O, 25·50%.)

Isoparaine acetate. A soln. of 50 mg of isoparaine in a 1:1 mixture of Ac_2O and pyridine was left at room temp. for 48 hr. Working up in the usual way, a residue was obtained (40 mg) that on recrystallization from EtOH melts at 250–253°, $[\alpha]_D^{16}$ − 7·7° (c = 0·5, $CHCl_3$); λ_{max}^{EtOH} 262 nm (log ϵ 3·77); ν_{max}^{Nujol} 1740, 1725, 1700, 1640 cm^{-1}. R_q 1·03 (A). (Found: C, 65·83; H, 7·27. $C_{23}H_{30}O_7$ requires: C, 66·01; H, 7·23%.)

12-*Norquassine* (IV). Fraction B-3, recrystallized from EtOH, melts at 282–286°, $[\alpha]_D^{15}$ + 122·5° (c = 0·93, $CHCl_3$); λ_{max}^{EtOH} 268 nm (log ϵ 3·85); λ_{max}^{EtOH} + NaOH 265, 317 nm (log ϵ 3·81, 3·65); ν_{max}^{Nujol} 3300, 1720, 1690, 1670, 1655, 1630 cm^{-1}, coincident with an authentic sample; NMR spectrum: Table 1; mass spectrum: *m/e* 374 (M^+), 359, 313, 193, 165. R_q 1·03 (A), coincident with an authentic sample. (Found: C, 67·41; H, 6·97; O, 25·47. $C_{21}H_{26}O_6$ requires: C, 67·36; H, 7·00; O, 25·64%.)

12-*Norquassine acetate.* A soln. of 40 mg of 12-norquassine in a 1:1 mixture of Ac_2O and pyridine was left at room temp. for 48 hr. A residue was obtained (41 mg) that on recrystallization from EtOH melts at 264–267°, $[\alpha]_D^{15}$ + 33·2° (c = 0·63, $CHCl_3$); λ_{max}^{EtOH} 243 nm (log ϵ 4·19); ν_{max}^{Nujol} 1760, 1740, 1690, 1655, 1640 cm^{-1}; NMR spectrum: Table 1. R_q 0·95 (A). (Found: C, 66·51; H, 6·78. $C_{23}H_{28}O_7$ requires: C, 66·33; H, 6·78%.)

Quassine (V). To a soln. of paraine (104 mg) or isoparaine (37 mg) in Me_2CO, a slight excess of Jones' reagent was slowly added. After 20 min at room temp. a few drops of MeOH were added, and the whole poured into water. The aq. soln. was brought to pH 7 with K_2CO_3 and extracted with $CHCl_3$. The extract was dried and concentrated, leaving a residue (82 and 36 mg respectively), that recrystallizes from EtOH, m.p. 273–276°; λ_{max}^{EtOH} 268 nm (log ϵ 3·85); ν_{max}^{Nujol} 3300, 1720, 1690, 1670, 1655, 1630 cm^{-1}, coincident with an authentic sample of 12-norquassine. R_q 1·03 (A), coincident with an authentic sample.

The above product (30 mg) was dissolved in 0·6 ml of 2 N NaOH and 0·15 ml of Me_2SO_4 added. After 10 min another 0·3 ml of 2 N NaOH added and the whole left at room temp. 4 hr. The soln. was then extracted with $CHCl_3$ and the extract dried and concentrated. The residue (28 mg) was recrystallized from aq. MeOH, m.p. 220–222° (lit.[6] 221–222°), no depression on admixture with an authentic sample; λ_{max}^{EtOH} 255 nm (log ϵ 4·13); ν_{max}^{Nujol} 1740, 1690, 1640 cm^{-1}, coincident with an authentic sample; NMR spectrum: Table 1; mass spectrum: *m/e* 388 (M^+), 373, 313, 165, 152, 127. R_f 0·61 (A), 0·23 (B), coincident with an authentic sample.

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[6] Z. VALENTA, S. PAPADOPOULOS and C. PODESVA, *Tetrahedron* **15**, 100 (1961).

Key Word Index—Aeschrion crenata; Simaroubaceae; quassinoids; paraine; isoparaine; 12-norquassine.