Quassinoids and Other Constituents from *Picrasma crenata*

H. C. Krebs\(^a\), P. J. Schilling\(^a\), R. Wartchow\(^b\), and M. Bölte\(^c\)

\(^a\) Zentrum für Lebensmittelwissenschaften, ZA für Chemische Analytik und Endokrinologie, Haus 123, Tierärztliche Hochschule, Bispofsholer Damm 15, D-30173 Hannover, Germany
\(^b\) Institut für Anorganische Chemie, Universität Hannover, Callinstr. 9, D-30167 Hannover, Germany
\(^c\) Institut für Organische Chemie, J. W. Goethe-Universität, Marie Curie-Str. 11, D-60439 Frankfurt/Main, Germany

Reprint request to Prof. H. C. Krebs. Fax: +49-(0)511-8567690.
E-mail: Hans.Christoph.Krebs@tiho-hannover.de

Z. Naturforsch. 56b, 315–318 (2001); received September 1, 2000

*Picrasma crenata*, Simaroubaceae, Quassinoids

Two new, 16-\(\beta\)-O-methylneoquassin and 16-\(\beta\)-O-ethylneoquassin, and four known quassinoi
ds have been isolated together with coniferyl aldehyde, coniferin, cantin-6-one, 4,5-di- methoxyxan
tin-6-one and (+)-neo-olivil from the wood of *Picrasma crenata*. Their structures were
determined on basis of spectroscopic and X-ray analysis.

1. Introduction

*Picrasma crenata* (Simaroubaceae) is a Brazilian plant which is used in traditional medicine to treat Diabetes mellitus [1]. To this end, a decoction of ground wood is prepared. Plants of the family Simaroubaceae are well known to contain quassinoids and alkaloids. Some quassinoids have received attention due to their biological activity as potential antitumor [2–7] as well as antiulcer agents [8]. Polonsky and Lederer [9] isolated quassin from the plant which is used in traditional medicine to treat Diabetes mellitus [1]. To this end, a decoction of ground wood is prepared. Plants of the family Simaroubaceae are well known to contain quassinoids and alkaloids. Some quassinoids have received attention due to their biological activity as potential antitumor [2–7] as well as antiulcer agents [8]. Polonsky and Lederer [9] isolated quassin from the

2. Results and Discussion

Ground wood of *P. crenata* has been extracted with ethanol/water and the extract was separated between chloroform/water, butanol/water and by chromatography to yield six quassinoid compounds. Four of them showed identical spectra as described for quassin [11,12], neoquassin (1) [13], parain [10], and 11-dihydro-12-norneoquassin [12,14].

NMR spectra of neoquassin (1) were almost in accordance with literature [13]. Several proton and carbon nuclei gave rise to pairs of signals. It is therefore evident that both the 16\(\alpha\)- and 16\(\beta\)-OH hemiacetal forms are present. Integrals in the \(^1\)H NMR as well as peak heights in the \(^13\)C NMR spectrum showed that the ratio was 25% of \(\alpha\)-neoquassin (1a) and 75% of \(\beta\)-neoquassin (1b). NMR signals could be assigned unequivocally by two-dimensional experiments; as a result, the \(^13\)C chemical shifts of the 4- and 8-methyl groups as given by De Bellis and Lovati [13] have to be reversed. Preliminary results in a diabetes test showed positive reactions which will be published elsewhere.

NMR data of 2b were similar to the results reported for 16-\(\alpha\)-methylneoquassin (2a) by Barbetti \textit{et al.} [12]. HREIMS of 2b gave the same molecular formula, \(C_{23}H_{32}O_{16}\), as 2a. NMR data, the assignment of which were made by two-dimensional experiments, showed that there were three methoxy

---

OMe

\[ R^1 = H, R^2 = \text{Me} \]

\[ R^1 = \text{OH}, R^2 = \text{Me} \]

\[ R^1 = \text{H}, R^2 = \text{OCH}_3 \]

\[ R^1 = \text{OH}, R^2 = \text{H} \]

\[ 3: R^1 = \text{OC}_2\text{H}_5, R^2 = \text{H} \]
groups in the molecule. So it was obvious that \(2b\)
is an isomer of \(2a\). To determine the structural isomerism of \(2b\) a X-ray crystal structure analysis was performed which showed the structure to be \(16-\beta\)-O-methylneoquassin. The absolute configuration was determined, too, thus confirming the structures given in [15] and [16]. Lang’at \textit{et al.} have used a mixture of \(2a\) and \(2b\) as an intermediate in their synthesis of derivatives of quassin, but no \(13\)C NMR data were given and no crystal structure determination was performed [15]. Shing \textit{et al.} have used \(2b\) as an intermediate in their synthesis of quassin. They have determined the crystal structure of quassin, but not of \(2b\) [16]. The comparison of the two molecular structures shows a good congruence of the skeletons, except, of course, in the vicinity of C16.

Compound 3 has a molecular weight of 418, and from HREIMS the molecular formula could be deduced as \(C_{24}H_{34}O_{6}\). A peak in the MS at \(m/z = 373\) pointed to the loss of an ethoxy group. NMR spectra of 3 and 2b were similar. The absence of the peak for the 16-OMe group is characteristic; instead of it the \(13\)C NMR spectrum of 3 showed a peak for a methylene group at \(\delta = 63.6\) ppm and for a methyl group at 15.5 ppm. As the signal for C16 of 3 (\(\delta = 97.4\) ppm) agreed with that of 2b (\(\delta = 97.7\) ppm), the orientation of the ethoxy group in 3 was also determined as \(\beta\). Thus, 3 is the new compound 16-\(\beta\)-O-ethylneoquassin. Treatment of neoquassin (1) with methanol or ethanol under chromatographic conditions did not furnish the acetals 2 and 3, respectively.

In addition to the quassinoids the ethanol/water extract furnished coniferyl aldehyde [17], coniferin [18], cantin-6-one [19], 4,5-dimethoxycantin-6-one [20] and (+)-neo-olivil [21] after chromatography at silica gel, amberlite XAD 2 and sephadex LH 20. Spectroscopic data were in accordance with literature.

3. Experimental

3.1. General

NMR spectra (\(^1\)H: 300.13 MHz; \(^{13}\)C: 75.47 MHz) recorded in pyridine-\(D_5\) (1 and 2b) or methanol-\(D_4\) (3) soln with TMS as internal standard on a Bruker AM 300 instrument. Chemical shifts (\(\delta\)) are expressed in ppm. MS were measured by direct inlet with 70 eV ionization at 150 °C on Finnigan MAT 312 and MAT 95 spectrometers.

3.2. Plant material

Plant material was collected in September 1994 in southern Brazil, near the border to Argentina. Botanical identification was made by Prof. Dr. Walter B. Mors, Universidade Federal do Rio de Janeiro.

3.3. Extraction and isolation

3940 g wood without bark from \textit{Picrasma crenata} (Simaroubaceae) were ground and dried. 500 g portions were extracted at RT for 48 h each with 31 of petrolether (40–60 °C) followed by the same amount of ethyl acetate and ethanol/water (3:7). The ethanol/water extract was separated on amberlite XAD 2 by elution with water followed by methanol. The methanol eluate was partitioned between water and chloroform. After evaporation to dryness the chloroform fraction was chromatographed using Sephadex LH 20 with methanol, silica gel with a gradient starting from petrolether via diethyl ether and ethyl acetate to methanol, and silica gel with diethyl ether/ethyl acetate (9:1) to furnish 1 (131 mg), 2b (54 mg), and 3 (6 mg).

3.4. Neoquassin (1)

Compound 1 was isolated as a mixture of 25% of \(\alpha\)-neoquassin (1a) and 75% of \(\beta\)-neoquassin.
(1b) as deduced from NMR spectra. IR (KBr): ν = 3446, 2942, 2879, 1691, 1633, 1378, 1354, 1227, 1117, 1052 cm⁻¹. – 1H NMR (300.13 MHz, CD₂D₅N): δ = 0.95 (d, J = 5 Hz, 3-H), 1.05 (s, 8-Me 1a), 1.60 (s, 10-Me 1a), 1.61 (s, 10-Me 1b), 1.64-1.76 (m), 1.80 (s, 13-Me 1a), 1.83 (s, 13-Me 1b), 2.0-2.2 (m), 2.25-2.35 (m), 2.62-2.72 (m), 3.40 (m, 7-H 1b), 3.45 (s, 2-OME 1a + b), 3.56 (m, 14-H 1a + b), 3.68 (s, 12-OME 1b), 3.72 (s, 12-OME 1a), 4.14 (m, 7-H 1a), 5.08 (s, 16-Me 1b), 5.22 (d, J = 1 Hz, 3-H 1b), 5.26 (d, J = 1 Hz, 3-H 1a), 5.65 (m, 16-H 1a). – 13C NMR (75.47 MHz, CD₂D₅N): see Table 1. – MS (EI, 70 eV): m/z (%) = 404 (100) [M⁺], 372 (35), 357 (18), 328 (18), 312 (13), 301 (47), 152 (63), 127 (43), 91 (28), 69 (60).

3.5. 16-ß-O-Methylneouquassin (2b)

1H NMR (300.13 MHz, CD₂D₅N): δ = 0.95 (d, J = 5 Hz, 3-H), 1.02 (s, 3-H, 8-Me), 1.60 (s, 3-H, 10-Me), 1.62-1.96 (m, 4-H, 6-H + 15-H), 1.76 (s, 3-H, 13-Me), 1.96-2.10 (m, 1 H, 5-H), 2.25-2.42 (m, 2 H, 4-H + 14-H), 3.30 (s, 3 H, 16-OMe), 3.44 (s, 1 H, 9-H), 3.47 (s, 3 H, 2-OMe), 3.66 (m, 1 H, 7-H), 3.70 (s, 3 H, 12-OMe), 4.79 (m, 1 H, 16-H), 5.29 (d, J = 1 Hz, 1 H, 3-H). – 13C NMR (75.47 MHz, CD₂D₅N): see Table 1. – MS (EI, 70 eV): m/z (%) = 404 (100) [M⁺], 389 (28), 373 (15), 357 (13), 329 (22), 312 (21), 301 (27), 212 (39), 165 (26), 152 (84), 127 (38), 91 (25), 69 (54). – HREIMS m/z = 404.219299 (M⁺), calcld. 404.219889 for C₂₃H₂₅O₆.

Crystal structure analysis of 2b: C₂₃H₂₅O₆, M = 404.49 g/mol, recrystallized from acetone, colourless fragment of a plate (001), size 0.56 × 0.31 × 0.13 mm, orthorhombic, space group P₂₁₂₁, (No.19), a = 8.376(2), b = 13.278(2), c = 38.471(4) Å, α = 90.00, β = 90.00, γ = 90.00°, V = 4278.6(13) Å³, Z = 8, Dₓ = 1.256 g/cm³, T = 300(2) K; Stoe IPDS diffractometer, λ(Mo–Kα) = 0.71073 Å; Flack parameter x = 0.0553, wR(F²) = 0.0578. Full crystallographic details without structure factors have been deposited at CCDC, No. 153139 & 153140. Files of structure factors are available by R. W.

Table 1. 13C NMR spectroscopic data of quassinoids 1–3 (δ-values, TMS).

<table>
<thead>
<tr>
<th></th>
<th>1a</th>
<th>1b</th>
<th>2a</th>
</tr>
</thead>
<tbody>
<tr>
<td>C 1</td>
<td>198.7</td>
<td>198.3</td>
<td>198.9</td>
</tr>
<tr>
<td>C 2</td>
<td>148.5</td>
<td>148.5</td>
<td>148.0</td>
</tr>
<tr>
<td>C 3</td>
<td>116.4</td>
<td>116.4</td>
<td>116.3</td>
</tr>
<tr>
<td>CH</td>
<td>31.5</td>
<td>31.4</td>
<td>31.2</td>
</tr>
<tr>
<td>CH</td>
<td>44.3</td>
<td>44.3</td>
<td>43.6</td>
</tr>
<tr>
<td>CH</td>
<td>25.9</td>
<td>26.1</td>
<td>25.7</td>
</tr>
<tr>
<td>CH</td>
<td>38.8</td>
<td>38.3</td>
<td>38.4</td>
</tr>
<tr>
<td>CH</td>
<td>44.0</td>
<td>49.7</td>
<td>49.2</td>
</tr>
<tr>
<td>C</td>
<td>46.6</td>
<td>46.6</td>
<td>46.1</td>
</tr>
<tr>
<td>C</td>
<td>193.4</td>
<td>193.3</td>
<td>193.1</td>
</tr>
<tr>
<td>C</td>
<td>148.5</td>
<td>148.5</td>
<td>148.2</td>
</tr>
<tr>
<td>CH</td>
<td>46.3</td>
<td>47.0</td>
<td>45.8</td>
</tr>
<tr>
<td>CH₂</td>
<td>32.3</td>
<td>35.2</td>
<td>34.2</td>
</tr>
<tr>
<td>CH₂</td>
<td>90.6</td>
<td>96.2</td>
<td>90.7</td>
</tr>
<tr>
<td>CH₂</td>
<td>19.1</td>
<td>19.1</td>
<td>22.0</td>
</tr>
<tr>
<td>CH₂</td>
<td>20.0</td>
<td>21.4</td>
<td>19.4</td>
</tr>
<tr>
<td>CH₂</td>
<td>12.9</td>
<td>12.9</td>
<td>12.7</td>
</tr>
<tr>
<td>CH₂</td>
<td>15.1</td>
<td>15.0</td>
<td>15.2</td>
</tr>
<tr>
<td>CH₂</td>
<td>54.6</td>
<td>54.6</td>
<td>54.8</td>
</tr>
<tr>
<td>CH₂</td>
<td>59.1</td>
<td>59.1</td>
<td>59.1</td>
</tr>
<tr>
<td>CH₂</td>
<td>53.8</td>
<td>53.8</td>
<td>54.5</td>
</tr>
<tr>
<td>CH₂</td>
<td>63.6</td>
<td>63.6</td>
<td>63.6</td>
</tr>
<tr>
<td>CH₂</td>
<td>15.5</td>
<td>15.5</td>
<td>15.5</td>
</tr>
</tbody>
</table>

a De Bellis and Lovati [13]; b Barbetti et al. [12]; c may be reversed according to Barbetti et al. [12].
3.6. 16-ß-O-Ethylneoquassin (3)

$^1$H NMR (300.13 MHz, CD$_3$OD): δ = 1.10 (s, 3 H, 8-Me), 1.13 (d, J = 5 Hz, 3 H, 4-Me), 1.23 (t, J = 6 Hz, 3 H, CH$_3$ of 16-OEt), 1.52 (s, 3 H, 10-Me), 1.74–1.93 (m, 4 H, 6-H + 15-H), 1.88 (s, 3 H, 13-Me), 1.93–2.03 (m, 1 H, 5-H), 2.33–2.55 (m, 2 H, 4-H + 14-H), 3.20 (s, 1 H, 9-H), 3.42–3.53 (m, 1 H, 7-H), 3.56 (s, 3 H, 2-O Me), 3.58 (s, 3 H, 12-OMe), 3.64-3.80 (q, J = 6 Hz, 2 H, CH$_2$ of 16-OEt), 4.98 (m, 1 H, 16-H), 5.49 (d, J = 1 Hz, 1 H, 3-H). – $^{13}$C NMR (75.47 MHz, C$_5$D$_5$N): see Table 1. – MS (EI, 70 eV): m/z (%) = 418 (99) [M$^+$], 404 (35), 373 (23), 357 (12), 329 (34), 313 (32), 303 (46), 226 (42), 207 (31), 165 (34), 152 (100), 127 (41), 91 (30), 69 (51). – HREIMS m/z = 418.235168 ([M$^+$], calcd. 418.235539 for C$_{24}$H$_{34}$O$_6$).

Acknowledgements
We thank Prof. Dr. W. B. Mors, Universidade Federal do Rio de Janeiro, for supplying the plant material and for botanical identification.