Seneganolide, a Novel Antifeeding Mexicanolide from *Khaya senegalensis*

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Seneganolide, a new mexicanolide type rings B,D-seco limonoid was isolated as insect antifeedant together with a known methyl angolensate from the stem bark of *Khaya senegalensis* (Meliaceae). The structure was elucidated on the basis of spectroscopic means and the antifeedant activity was tested by a conventional leaf disk method.

Khaya senegalensis (Desr.) A. Juss. is one of the most popular medicinal plants in the African traditional remedies. The decoction of the bark is extensively used as febrifuge which could be associated with its use as an antimalarial drug.[1] This genus is the main source of African mahogany and is closely related to the South American genus *Swietenia*, which is one of the main source of rings B,D-seco limonoid mexicanolides,[2] which were biogenetically derived from 1,3-diketodiene lactones of the andirobin-type B,D-seco limonoids like methyl angolensate (**2**) by spontaneous Michael cyclization.[3] Some B,D-seco limonoids containing the mexicanolide have been also reported from *K. senegalensis*.[3–5] In a series of our experiments on Meliaceae plants, several types of limonoids were isolated as insect antifeedant from *Trichilia roka*,[6] *Melia azedarach*[7] and *M. toosendan*.[8] In view of our interest in the antifeedant activity of members of the family Meliaceae, we have studied the ether extract of the bark of *K. senegalensis*. Droplet countercurrent chromatography (DCCC) with descending mode of the extract, followed by reversed phase HPLC purification, resulted in the isolation of one novel limonoid belonging to the mexicanolide, named seneganolide (**1**), together with a known rings B,D-seco compound, methyl angolensate (**2**).[9] In this paper, we report the structure of **1** and its antifeedant activity against the larvae of a Japanese insect pest *Spodoptera littoralis* by a leaf disk method.[10]

Seneganolide (**1**) (5 mg),[11] mp 276–278 °C (decomp) and $[\alpha]_D$ –27° (*c* 0.11, MeOH), was obtained as white needles from acetone/hexane. Its molecular formula $C_{26}H_{30}O_8$ (12 unsaturations) was determined by HRFAB-MS (*m/z* 471.2021 $[M+1]^+$; Δ +0.2 mmu). The UV maximum at 210 nm (ε 5000) and IR absorption at 3580–3300, 1730, 1700, 1637 and 875 cm^{-1} showed the presence of carbon–carbon double bonds and hydroxyl and carbonyl (keto and ester) groups. From its ^1H and ^{13}C NMR data (Table 1) measured in $CDCl_3$ containing a small amount of CD_3OD owing to the poor solubility of **1** in $CDCl_3$, it was evident that five of the elements of unsaturation were present as double bonds: two carbon–carbon (as a furan ring), three CO (two as esters and one ketone). Therefore, the molecule is heptacyclic. The NMR data also revealed that compound **1** has three methyls, six methylenes, eight methines (three olefinic), nine quaternary carbons (one olefinic) and one proton due to OH group. Furthermore, the spectra showed the presence of a β-furyl moiety.

After assignment of all protons directly bonded with carbon atoms by the ^1H–^{13}C shift-correlated measurement (HMQC spectrum), it was possible to assume from the ^1H–^1H COSY spectrum, decouplings and HMBC spectrum (Figure 2) that **1** was a mexicanolide. The chemical shifts and couplings for protons attached to carbons—17, 5 and 6; 2 and 30; 9, 11 and 12; 14 and 15—also interpreted the presence of the carbon skeletone of **1**.

Especially, the presence of the hemiacetal linkage of C-1 to C-8 in **1** was confirmed from the chemical shifts of C-1 (δ 107.7, s) and C-8 (δ 80.8, s) and from a W-type long range coupling between 30α and 9α-H signals. The same acetal linkage of C-1 to C-8 has been observed in some mexicanolides,[12–14] in which the ring C is present in a skew boat form. A W-type long range coupling between 12β and 15β-H signals and NOEs (Figure 3) between 5β and 11β-H, 9α and 14α-H, 14α and 18-H (13α-Me), 15β and 30α-H, and 30α and 2-H signals also elucidated the relative configuration of four chiral centers at C-8, 9, 13 and 14.

The presence of three methyls at 4α (29), 4β (28) and 13α (18) and that the remaining methyl group (19) to be at C-10 in the basic mexicanolide skeleton was changed to a methylene group directly attached to an oxycarbonyl group was confirmed from the HMBC spectrum. Then, the relative stereochemical

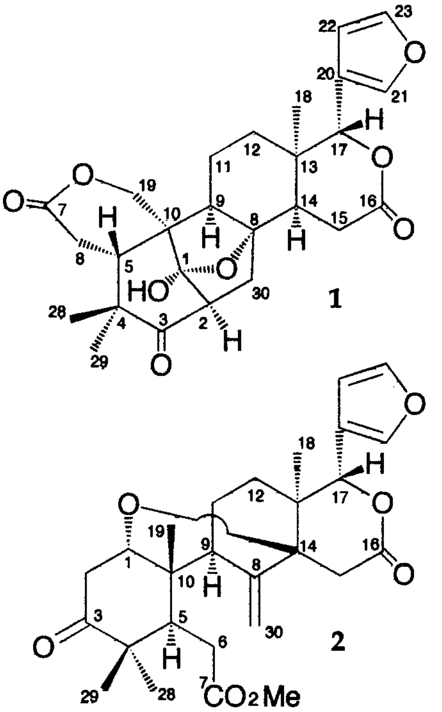

Figure 1. Structure of compounds **1** and **2**.

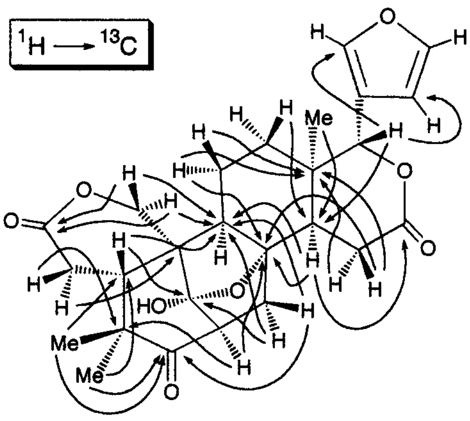

Figure 2. Significant HMBC correlations in **1**.

assignment of all of the protons in **1** was established from the NOESY experiment (Figure 3). Although many rings B,D-seco limonoids have been reported, this is, to the best of our knowledge, the first report of occurrence of C-19 oxygenated compound in mexicanolides.

The antifeedant activity of seneganolide (**1**) and methyl angolensate (**2**) was tested by a conventional leaf disk method against the third-instar larvae of a Japanese insect pest *Spodoptera littoralis* (Boisduval). Seneganolide (**1**) was active at 300 ppm, corresponding to a concentration of 6 μg/cm^2, and the compound **2** at 500 ppm. Their potent activities were comparable to those of trichilins[6] and azedarachins[7] from meliaceous plants.

Table 1. ^{13}C and ^{1}H NMR data for seneganolide (**1**)

atom	δ_C	δ_H	atom	δ_C	δ_H
1	107.7 s		15α	27.8 t	2.80 dd
2	53.8 d	2.86 dd			(19.8, 2.2)
		(13.2, 6.8)	β		2.85 dd
3	212.1 s				(19.8, 7.0)
4	44.9 s		16	170.6 s	
5	38.7 d	2.30 dd	17	78.3 d	5.26 s
		(11.0, 7.0)	18	22.6 q	1.03 s
6α	29.6 t	2.68 dd	19α	73.8 t	4.48 d
		(14.9, 11.0)			(11.7)
β		2.56 dd	β		4.21 d
		(14.9, 7.0)			(11.7)
7	173.3 s		20	120.7s	
8	80.8 s		21	140.9 d	7.38 br s
9	61.5 d	2.02 br d	22	109.7 d	6.31 br d
		(9.7)			(1.5)
10	46.9 s		23	143.2 d	7.40 t
11α	21.1 t	1.63 m			(1.5)
β		1.41 m	28	24.1 q	1.19 s
12α	35.1 t	1.43 br t			
		(12.2)	29	19.6 q	1.31 s
β		1.78 dd	30α	31.9 t	2.23 td
		(11.0, 2.7)			(13.2, 1.9)
13	35.5 s		β		1.85 dd
14	44.9 d	2.27 dd			(13.2, 6.8)
		(7.0, 2.1)	OH		1.88 br

Measured in $CDCl_3$ containing a small amount of CD_3OD at 40°C at 125 and 500 MHz. *J* values (in Hz) are presented in parentheses.

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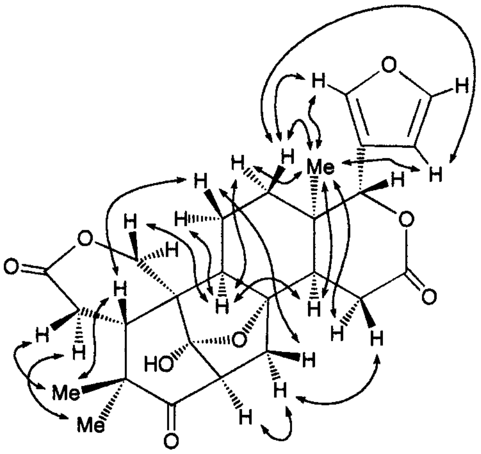

Figure 3. Selected NOE correlations in **1**.

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11 Compounds **1** (5 mg) and **2** (2.4 mg) were finally isolated by HPLC with 55 and 45% H_2O–MeOH solvent systems from the extract (3.9 g), respectively.

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