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STRYSPINOLACTONE, AN UNUSUAL MONOTERPENE LACTONE FROM *STRYCHNOS SPINOSA*

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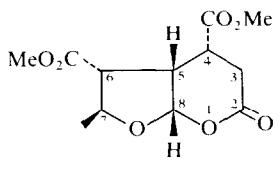
Key Word Index—*Strychnos spinosa*; Loganiaceae; lignan; lirioresinol B; stryspinolactone.

Abstract—The structure of stryspinolactone, an unusual lactone from *Strychnos spinosa*, was determined from spectroscopic data.

The plant *Strychnos spinosa* is reputed to be a versatile medicinal remedy against many diseases, the seeds are said to possess emetic action and are used in some parts of Africa as an antidote against snake bite [1].

The methanol extract of petrol-defatted seeds of *S. spinosa* after concentration was partitioned between chloroform and dilute acid and the chloroform extract fractionated by column chromatography. Two compounds were isolated; one was identified as the lignan lirioresinol B on the basis of its physical, chemical and spectroscopic properties, the other which crystallized as white plates from methanol was a new compound for which we propose the name stryspinolactone.

Structure **1** (minus stereochemistry) is proposed for stryspinolactone on the basis of the following analytical and spectroscopic evidence. Elemental analysis and MS establish the molecular formula as $C_{12}H_{16}O_7$. The IR absorptions at 1725 and 1733 cm^{-1} are assigned to the two methoxycarbonyls and that at 1765 to the δ-alkoxy-δ-lactone. The 220 MHz ^1H NMR spectrum of stryspinolactone shows two methoxy singlets at δ 3.70 and 3.78 due to the two $-CO_2Me$ groups and one secondary methyl as a doublet centred at δ 1.28 which is coupled to H-7 at δ 4.40. A one-proton narrow doublet at δ 5.86 is assigned to the acetal hydrogen H-8. A very confused one-proton double doublet centred at δ 3.10 attributed to H-4, a very complex pattern of signals between δ 2.55 and 2.85 attributed to H-3α, H-3β, H-5 and H-6, and the relationship of the methine and methylene protons were clarified by decoupling experiments. Irradiation of the methyl protons at 277 Hz resulted in the collapse of the quartet at 965 Hz (H-7) into a singlet. However, two sets of protons were affected on reverse irradiation, the doublet of the methyl protons collapsed into a singlet while a narrow double doublet at 603 Hz (H-6) became a doublet. When the doublet at 1286 Hz (H-8) was irradiated only the double doublet at 618 Hz (H-5) was transformed into a doublet. Triple irradiation experiments with simultaneous irradiations at 965 Hz and 674 Hz (H-4) reduced the narrow double doublets at 603 (H-6) to a broad singlet, the double doublets at 618 into a broader singlet and the pair of double doublets at 597 and 568 Hz (methylene protons) into a pair of doublets. It is therefore concluded that H-7 is coupled to the methyl group at C-7 and H-6; H-6 is further coupled to H-5 and H-4; H-5 is coupled to H-8 and H-4, while H-4 is further coupled to the methylene protons which are geminally coupled to each other.



1

The structure assigned to stryspinolactone is supported by ^{13}C NMR. The proton noise-decoupled spectrum shows 12 lines, one for each of the 12 carbon atoms while the off-resonance decoupled spectrum in conjunction with chemical shifts arguments are employed to assign the carbon atoms. Three low-field quarternary carbons at δ 170.70, 169.56 and 169.15 are due to the carbonyl carbons of the lactone and the two esters. Three quartets centred at 21.28, 52.04 and 52.80 are discernible, the first signal is the methyl carbon on C-7 and the other two are the methyl groups of the esters. The only triplet at δ 35.40 is assigned to the methylene carbon C-3. The remaining signals are doublets which absorb upfield of δ 100 and are therefore aliphatic methine carbons. Those at δ 96.91 and 67.10 are assigned to the ketal carbon C-8 and the ether-type carbon C-7, respectively. The nature and position of the ring substituents (Me and CO_2Me) are used to assign the remaining methine carbons at δ 49.47, 45.71 and 30.34 to C-6, C-4 and C-5, respectively. It is interesting to note that C-4 shows some broadening effect in the off-resonance decoupled spectrum in exactly the same way as the analogous carbon in oxysporone [2].

The detailed coupling constants in the ^1H NMR are given in the Experimental section. Using the Dreiding model, the dihedral angle between H-5 and H-8 that is consistent with the small coupling constant of 1.5 Hz a *cis* fusion of the two rings with the tetrahydro-2-pyrone ring assuming a chair conformation and the tetrahydrofuran the envelope or half-chair conformation. Following similar arguments for the other coupling constants the only structure that is consistent with all the data has the spatial arrangements as shown in structure **1**. The structure and relative stereochemistry of stryspinolactone are therefore proposed as **1**.

A large class of monoterpenes known as iridoids are widespread in the Loganiaceae family. We suggest that stryspinolactone is a monoterpene with an irregular isoprenoid skeleton. It is conceivable that oxidative bond cleavage between C-7 and C-8 took place at some stage after two isoprene units had joined in a normal head to tail fashion.

EXPERIMENTAL

Isolation of lirioresinol B and stryspinolactone. Ripe fruits of *S. spinosa* were collected in January from Borgu Games Reserve, Kwara State. The plant was identified by the Federal Department of Forestry Research, Ibadan, with whom a herbarium specimen No. FHI 94093 is filed. The fruits were split open and allowed to undergo aerobic fermentation for a few days to allow for easy separation of the seeds from the pulp. The dry seeds (4.3 kg) were too tough to be ground in the usual way and had to be frozen in liquid N_2 and ground cold. The ground seeds were defatted with petrol, followed by extraction with MeOH over 16 hr. The MeOH extract was concentrated and partitioned between $CHCl_3$ and dil. HCl. The $CHCl_3$ extract was chromatographed on a Si gel column.

Et_2O–petrol (1:1) eluted stryspinolactone (31 mg) which crystallised as white plates (MeOH), mp 108–110°. MS *m/z*: 272 $[M]^+$, 241, 236, 198, 153, 149, 127, 99, 95, 59, 41; IR ν_{max}^{KBr} cm^{-1}: 1725 (CO_2Me), 1733 (CO_2Me), 1765 (δ-lactone); ^1H NMR (220 MHz, $CDCl_3$, TMS): δ 1.28 (3 H, *d*, $J = 6$ Hz, C-Me), 2.60 (1 H, *dd*, $J_{3\alpha-3\beta} = 17$, $J_{3\alpha \text{ or } 3\beta-4} = 8$ Hz, H-3α or 3β), 2.70 (1 H, *dd*, $J_{3\alpha\ 3\beta} = 17$, $J_{3\alpha \text{or } 3\beta-4} = 7$ Hz, H-3α or 3β), 2.75 (1 H, *ddd*, $J_{6-7} = 0.5$, $J_{5-6} = 1$, $J_{4-6} = 3$ Hz, H-6), 2.80 (1 H, *ddd*, $J_{5-8} = 1.5$ $J_{5-6} = 1$, $J_{4-5} = 7$ Hz, H-5), 3.10 (1 H, *dddd*, $J_{4-3\alpha \text{or } 3\beta} = 8$ Hz, $J_{4-3\beta \text{ or } 3\alpha} = 7$ Hz, $J_{4-6} = 3$ Hz, H-4), 3.70 (3 H, *s*, CO_2Me), 3.78 (3 H, *s*, CO_2Me), 4.40 (1 H, *dq*, $J_{7-Me} = 6$, $J_{6-7} = 0.5$ Hz, H-7), 5.86 (1 H, *d*, $J_{5-8} = 1.5$ Hz, H-8); ^{13}C NMR (25 MHz, $CDCl_3$, TMS): δ 21.28 (*q*, C-$\underline{C}H_3$), 30.34 (*d*, C-5), 35.40 (*t*, C-3), 45.71 (*d*, C-4), 49.47 (*d*, C-6), 52.04 (*q*, $CO_2\underline{C}H_3$), 52.80 (*q*, $CO_2\underline{C}H_3$), 67.10 (*d*, C-7), 96.91 (*d*, C-8), 169.15 (*s*, $\underline{C}O_2Me$), 169.56 (*s*, $\underline{C}O_2Me$), 170.70. (*s*, C-2). (The last three assignments are interchangeable.)

Et_2O eluted lirioresinol B as a dense white solid (625 mg) which cryst. from MeOH, mp 169.5–171°, $[\alpha_D]$ +60° ($CHCl_3$) (lit: mp 172–177°, $[\alpha_D]$ +62° ($CHCl_3$) [3]), deep violet colour with $FeCl_3$. IR ν_{max}^{nujol} cm^{-1}: 3450 (—OH), 1615 and 1520; UV λ_{max}^{MeOH} nm (ε): 217 (16 450), 237 (11 240 shoulder), 273 (2090); ^1H NMR (220 MHz, $CDCl_3$, TMS): δ 6.60 (4 H, *s*, arom.), 5.62 (2 H, *s*, lost with D_2O, 2-OH), 4.75 (2 H, *d*, *br*), 4.2 (4 H, *m*, *br*), 3.85 (12 H, *s*, 4-OMe), 3.05 (2 H, *br*); MS *m/z*: 418 $[M]^+$, 389, 193, 181, 167, 123, 77. Diacetate, mp 179–181°, M^+ 502.

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