

CHEMISTRY OF SAURURUS CERNUUS, VI:¹ THREE NEW NEOLIGNANS

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ABSTRACT.—From the relatively more lipophilic fraction of the extract of *Saururus cernuus*, seven neolignans were isolated of which three, named (–)-saururin, (–)-saururenin, and (+)-saururinone, are new and belong to the 1,4-diaryl-2,3-dimethylbutane group, with saururinone being a novel ketoneolignan. The remaining four were identified as (–)-austrobailignan 6, another member of the 1,4-diarylbutane group, and (–)-calopiptin, (–)-galbacin, and (+)-zuonin A, all three of which belong to the 2,5-diaryl-3,4-dimethyltetrahydrofuran group. Of these, zuonin A has the rarely seen stereochemistry for the tetrahydrofuran ring: 2/3 cis, 3/4 cis, and 4/5 trans.

Saururus cernuus L. (Saururaceae), an aquatic weed commonly found in the Eastern United States, is a rich source for a variety of neolignan structures. Isolation of manassantins A and B (which belong to a new class, the dineolignans) as the major neuroleptic active principles of the plant, along with a novel sesquieneolignan named saucerneol, has been reported earlier (1). Similarly, the occurrence of a new 2,5-diaryltetrahydrofuran, (+)-saucernein (2), and the related but known compound, (+)-veraguensin (3), together with the 1,4-diarylbutane, (–)-austrobailignan 5 (4), and the phenyltetralin, (+)-guaiacin (5), has also been described. Together, all these represent five different structural types of neolignans. The present communication describes the isolation of three new and four known neolignans from this plant.

The most abundant neolignan of *S. cernuus* is (–)-austrobailignan 5 [1] which has been obtained as a crystalline solid for the first time (6). Column chromatography of the concentrate from which most of 1 has been removed yielded a series of neolignans, which are described here.

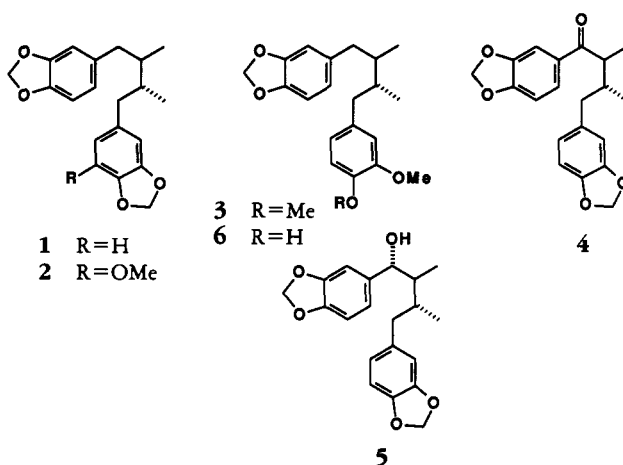
Compound 2, C₂₁H₂₄O₅, showed nmr spectral evidence for the presence of two CH-Me, two ArCH₂, OMe, two O-

CH₂-O, and five ArH, consistent with the structure of a 1,4-diaryl-2,3-dimethylbutane. The mass spectrum, [M]⁺ 356 and two prominent peaks *m/z* 193 (methoxy-methylenedioxyphenyl propyl) and *m/z* 135 (methylene dioxybenzyl) support the structure as 2. The compound is named (–)-saururin.

Compound 3, C₂₁H₂₆O₄, showed essentially the same nmr characteristics as 2, with the exception of two methoxyls and one methylenedioxy group. These, together with the mass spectral peaks, *m/z* 179 (dimethoxyphenylpropyl), 151 (dimethoxybenzyl, base peak) and 135 (methylenedioxybenzyl), point to the structure assigned. This compound is named (–)-saururenin and is the methyl ether of austrobailignan 6 (4).

Compound 4, C₂₀H₂₀O₅, showed uv spectral behavior somewhat different from that of 2, 3, and the other neolignans of this group, which generally show maxima at 220–230 nm and 275–285 nm. It showed instead, maxima at 228, 278, 292 (sh), and 320 nm, which indicated an aromatic methoxy ketone. The ir spectrum likewise showed an unusual carbonyl peak at 1680 cm⁻¹, also suggestive of such a group. The ¹H-nmr spectrum supported this view by showing two distinct signals for the CH-Me groups, δ 0.82 (d, 3H), 1.12 (d, 3H), 2.2 (m, 1H), and 3.25 (m, 1H), and the presence of only one Ar-CH₂ function. The rest of the spectrum showed signals

¹For Part V, see



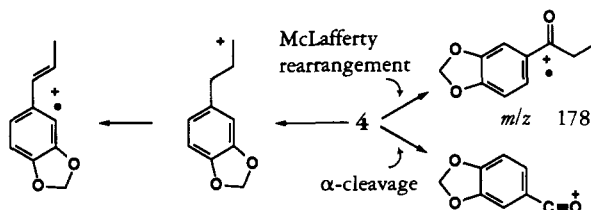
due to two methylenedioxy groups (δ 5.9, 6.0) and six aromatic protons, which appeared as two clearly separated multiplets at δ 6.7 (4H) and δ 7.3 (2H). All these suggested the structure of a 1,4-diaryl-2,3-dimethylbutane but with one of the benzylic groups oxidized to a ketone as shown in **4**. The mass spectrum confirmed this assignment with $[M]^+$ of 340 and fragments at m/z 178, 162, 149, and 135, the probable path of formation of which is shown in Scheme 1. The compound, named (+)-saururione, also readily underwent reduction with NaBH_4 to an alcohol **5**, identical with the compound prepared from **1** by the action of dichlorodicyanoquinone in HOAc, followed by hydrolysis (**6**).

Compound **6**, $\text{C}_{20}\text{H}_{24}\text{O}_4$, was phenolic, and the ^1H -nmr spectrum was in agreement with that of a 1,4-diarylbutane type neolignan with one methylene dioxy, one methoxy, and one hydroxyl group. These properties and rotation led to the assignment of the

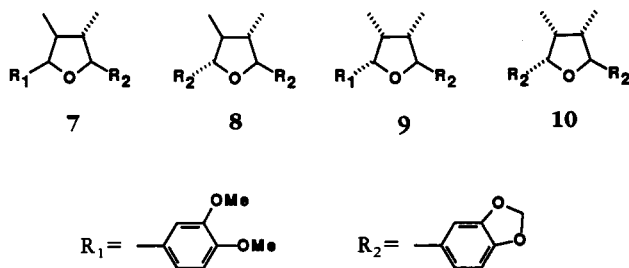
structure **6**, identical with that of atrobailignan **6** (**4**). A direct comparison was also made with a semisynthetic sample prepared from **1** by partial demethylenation (**7**).

Three other compounds isolated from the extract showed nmr spectral behavior consistent with that of a 2,5-diaryl-3,4-dimethyltetrahydrofuran system. Compound **7**, $\text{C}_{21}\text{H}_{24}\text{O}_5$, showed two distinct signals for the CH-Me, δ 0.67 (d, 3H), 1.05 (d, 3H), 1.8 (m, 1H), and 2.2 (m, 1H), and for the ArCH-O protons of the tetrahydrofuran ring, δ 4.38 (d, 1H), 5.11 (d, 1H). The chemical shifts of the ArCH-O protons suggested a 2/3 cis, 3/4 trans, 4/5 trans stereochemistry for the ring, as seen in the case of veraguensin (**3**). The presence of a methylenedioxy and two methoxyl groups as well as the identity of physical properties showed that the compound was (+)-caloptin [**7**] (**8**).

Compound **8**, $\text{C}_{20}\text{H}_{20}\text{O}_5$, showed a single signal for both the CH-Me groups and a single signal for the ArCH-O pro-



SCHEME 1



tons, thus suggesting a stereochemical similarity to the all-trans type such as (-)-galbacin [8] (9), with which it was found to be identical.

Compound **10**, $C_{20}H_{22}O_5$, isomeric with galbacin, showed the following nmr signals: δ 0.78 (d, 3H), 1.02 (d, 3H), 2.5 (m, 2H), 4.65 (d, 1H), 5.4 (d, 1H), 5.98 (s, 4H), 6.8 (m, 6H). Although this spectrum resembled generally that of (+)-calopiptin in that both showed two distinct signals for the Me and the ArCH-O groups, the chemical shifts were different. Also, while calopiptin showed two distinct multiplets for the CH-Me protons, **9** showed only one multiplet. These chemical shifts and characteristics agree with a tetrahydrofuran stereochemistry of 2/3 cis, 3/4 cis, and 4/5 trans, similar to what has been described for (-)-machilusin [9] (10). The nmr spectrum and the optical rotation agree with those described for a related compound with similar stereochemistry, zuonin A [10] (11).

Thus, the five diaryl tetrahydrofuranoid neolignans found in *S. cernuus* represent four of the six possible stereochemical arrangements for the tetrahydrofuran with identical substituents at 2, 5 and at 3, 4.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Mp's were obtained using Fisher-Johns apparatus and are uncorrected. The following instrumentation was used to record the spectra described: uv, Perkin-Elmer Lambda 3B, with MeOH as solvent; ir, Beckman Aculab III as KBr-pellets; nmr, Varian EM 390, 90 MHz instrument, $CDCl_3$ with TMS as internal standard; optical ro-

tations, Perkin-Elmer 141 polarimeter, 1% in $CHCl_3$; and eims, Kratos MS80RFA. Cc was performed using Si gel (Merck, 100–200 mesh) and tlc with Si gel (Merck H60-P254/360).

PLANT MATERIAL.—*S. cernuus* was collected during May–July 1989 and identified at the Herbarium of the University of Florida, where a voucher sample No. FLAS 170066 was deposited. The above-ground parts were sun-dried and ground through a coarse mesh.

EXTRACTION AND ISOLATION.—The plant material (10 kg) was extracted three times with MeOH at 20°, for 2 days each. The concentrated extract (1 liter) was extracted twice with $CHCl_3$ (1 liter each). The solvent layer was concentrated to a syrup which was partitioned between MeOH- H_2O (4:1) and ligroin (1 liter each). The ligroin layer was concentrated to an oil (100 g), which was subjected to chromatography in 25–30 g aliquots on Si gel (300 g) in ligroin. The solvent was incrementally changed with varying concentrations of C_6H_6 to reach pure C_6H_6 and then with increasing concentrations of Me_2CO up to 10%. The diarylbutanes were eluted with 50–75% C_6H_6 in ligroin and the diaryltetrahydrofurans with 1–2% Me_2CO in C_6H_6 . Fractions containing **1** were rechromatographed under similar conditions, and the purified **1** was crystallized from ligroin, yield 0.2%, mp 43–45°.

The filtrates from **1** were concentrated and rechromatographed using a slower rate of elution, and the various components were separated. Preparative tlc was carried out on Si gel for final purification using solvent systems such as 50–75% C_6H_6 in ligroin.

COMPOUND [2].—A colorless glass: yield 0.001%; uv λ max (log ϵ) 238 (4.70), 292 (4.37); ir 3000, 2900, 1630, 1490, 1430, 1310, 1240, 1190, 1130, 1080, 1040, 930, 800 cm^{-1} ; $[\alpha]_D -24.7^\circ$; 1H nmr δ 0.82 (d, $J = 7$ Hz, 2CH- CH_3), 1.3 (m, 2CH-Me), 2.42 (m, 2Ar- CH_2), 3.8 (s, 2OMe), 5.9 (s, O- CH_2 -O), 6.71 (m, 6ArH); ms 356.1805, calcd for $C_{21}H_{24}O_5$, 356.1799.

COMPOUND [3].—A colorless glass: yield 0.001%; uv λ max (log ϵ) 228 (4.95), 290 (4.62);

ir 3000, 1610, 1600, 1520, 1490, 1440, 1380, 1250, 1180, 1160, 1140, 1035, 935, 850, 810, 770 cm^{-1} ; $[\alpha]_D -34^\circ$; $^1\text{H nmr}$ 0.82 (d, $J=7$ Hz, 2CH- CH_3), 1.3 (m, 2CH-Me), 2.42 (m, 2Ar- CH_2), 3.8 (s, 2OMe), 5.9 (s, O- CH_2 -O), 6.72 (m, 6ArH); ms m/z (%) 342 (5), 341 (90), 206 (15), 152 (100), 150 (85), 135 (85). Hrms found 342.1828, calcd for $\text{C}_{21}\text{H}_{26}\text{O}_4$, 342.1832.

COMPOUND [4].—A colorless glass: yield 0.0005%; uv λ max (log ϵ) 228 (4.94), 278 (4.38), 292 (4.33), 320 (4.28); ir 3000, 2800, 1680, 1605, 1500, 1490, 1440, 1360, 1250, 1040, 930, 800 cm^{-1} ; $[\alpha]_D +139.6^\circ$; ms 340 (22), 306 (8), 178 (100), 162 (90), 149 (75), 135 (35). Hrms found 340.1316, calcd for $\text{C}_{20}\text{H}_{20}\text{O}_5$, 340.1311.

COMPOUND [6].—A colorless glass: yield 0.0005%; $[\alpha]_D -23.1^\circ$. Spectral properties were identical with those reported for austrobailignan 6 (7).

COMPOUND [7].—A colorless crystalline solid: yield 0.001%; mp 93–94°; $[\alpha]_D +35^\circ$. The physical and spectral properties were identical with those reported for (+)-calopiptin.

COMPOUND [8].—A colorless oil: yield 0.0005%; $[\alpha]_D -11.7^\circ$. The spectral properties were identical with those described for (–)-galbacin (9).

COMPOUND [10].—A colorless oil: yield

0.0006%; $[\alpha]_D -100.4$. The spectral properties were identical with those described for (–)-zuonin A (11).

ACKNOWLEDGMENTS

The authors express their grateful appreciation to the National Institute of Mental Health for the financial support through the grant no. 36039.

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Received 7 August 1989