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Isolation and Structure Determination of Two New Macrocyclic Biaryl Ethers from *Garuga gamblei*

Short Communication

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Two new macrocyclic biaryl ethers have been isolated from the bark of *Garuga gamblei* King (Burseraceae). The structure of the compounds has been established by NMR spectroscopy.

(Keywords: Garuga gamblei; Burseraceae; Garugamblin; Macrocyclic biaryl ether; Structure determination; NMR)

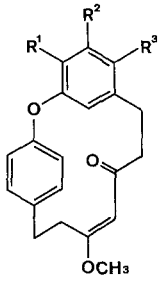
Isolierung und Strukturermittlung von zwei neuen makrocyclischen Biarylethern aus Garuga gamblei (Kurze Mitteilung)

Aus der Rinde von *Garuga gamblei* King (Burseraceae) wurden zwei neue makrocyclische Biarylether isoliert. Die Struktur der Verbindungen wurde mittels NMR-Spektroskopie bestimmt.

In recent years, various new compounds have been isolated from the leaves and the bark of *Garuga pinnata* Roxb., a member of the family of Burseraceae [1, 2]. Two of these substances, garuganin-I and garuganin-III, have been shown to contain a 15-membered macrocyclic biaryl ether backbone [2, 3]. We have isolated and characterized two more members of this class of compounds from the bark of *Garuga gamblei* King, a related species.

Extraction of the bark of *Garuga gamblei* K. and subsequent chromatography (cf. Exp. Part) yielded four crystalline substances. Two of them could be identified as β-sitosterol [4] and garuganin-I [2] (**1a**), respectively. The structures of the remaining two compounds for which

we suggest the names *garugamblin*-1 and *garugamblin*-2 are given in formulas **1 b** and **1 c**.



	R^1	R^2	R^3
1a	OCH_3	H	OCH_3
1b	OCH_3	H	H
1c	$O-CH_2-O$		H

From NMR spectroscopy it is evident that the structures of the new compounds differ only slightly from **1 a**. The seven-membered functionalized chain exhibits the same pattern both in ^{13}C and ^1H NMR spectroscopy for compounds **1 a–1 c**. In particular, the *E*-configuration of the double bond can clearly be established by the observation of an NOE-effect from the methyl group of the enol ether function to the olefinic proton in all cases. In addition, the signals of a *para*-substituted aromatic ring can be observed in all compounds under investigation. We therefore conclude that the structural differences between **1 a, 1 b** and **1 c** can only be located at the polysubstituted aromatic system which will be referred to as "ring A" in the following discussion.

In **1 b**, one methoxy NMR signal is lacking with respect to **1 a**. This fact, together with the molecular formula $C_{21}H_{22}O_4$ as established by NMR and MS, leads to a structure with only one methoxy group on ring A. Further support for this proposal is given by the multiplicities of the signals of the aromatic carbons in the ^{13}C NMR spectrum. The proton NMR spectrum of **1 b** indicates a 1,2,4 substitution pattern for the aromatic protons of ring A. Therefore, the remaining methoxy group cannot be located in a *meta* position both to the biaryl ether linkage and the aliphatic chain. No unambiguous decision could be made which of the two still possible sites is occupied by the OCH_3 substituent at the present state of investigation. However, spectral simulation using a ^{13}C NMR data base [5, 6] strongly suggests the structure shown in **1 b**. Moreover, this assumption is in accordance with the structures of macrocyclic biaryl ethers of similar biogenesis isolated from *Myrica gale* L. [7] and *Acer nikoense* M. [8].

The molecular formula of **1 c**, $C_{21}H_{20}O_5$, indicates an additional ring or double bond with respect to **1 b**. There is only one methoxy group left which can unambiguously be assigned to the enol ether function by NOE

difference spectroscopy. This, in combination with shift and multiplicity informations from the ^{13}C NMR spectrum, points to a structure as given for **1c**. The proposed structure is confirmed by ^{1}H NMR spectroscopy. As to the position of the dioxolane moiety, the same arguments apply as for the position of the aromatic methoxy group in **1b**.

As a consequence of the relatively crowded and, as can be shown by molecular models, somewhat strained structure, the compounds **1a–1c** exhibit unusual features in NMR spectroscopy. The study of these items as well as a complete assignment of the ^{1}H and ^{13}C NMR spectra are in progress and will be published elsewhere.

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Experimental Part

^{1}H and ^{13}C NMR spectra were measured in $CDCl_3$ on a Bruker WM 250 NMR spectrometer at 250 MHz and 62.5 MHz, respectively. Mass spectra were recorded on a Varian MAT-311 mass spectrometer. Melting points were measured in a sulfuric acid bath and are uncorrected. PTLC separations were performed on SiO_2 (0.25 mm). Spots were visualized by UV light, iodine, and H_2SO_4.

Plant material: *Garuga gamblei* King was collected in Assam, India, in September 1986.

Extraction and isolation: The bark of *Garuga gamblei* King was chipped into small pieces and dried on air at room temperature. A portion of 1.5 kg was extracted twice with 5 l of hot petroleum ether (60–80°) for 48 hours. The extract was evaporated to dryness and the residue (8 g) was chromatographed on silica using a benzene–ethyl acetate gradient for elution. The fraction containing **1b** and **1c** was subjected to PTLC (benzene : ethyl acetate = 19 : 1) to yield pure **1b** and **1c**.

Treatment of the remaining plant material from the petroleum ether extraction with 4 l of hot ethanol for 48 hours and subsequent evaporation of the extract yielded 25 g of a dark gummy material which gave 10 g of a dark coloured solid on trituration with dry ether. This residue was chromatographed on silica in the same manner as mentioned above. The fraction containing **1b**, **1c** and β-sitosterol was separated by PTLC to give more **1b** and **1c**. A further fraction yielded garuganin-I. β-sitosterol was identified by comparison with a reference sample, garuganin-I by NMR spectroscopy.

Garugamblin-1 (**1b**): $C_{21}H_{22}O_4$; 50 mg; colourless solid (benzene): m.p. 205–206°; MS: M^+ 338; R_f (SiO_2; C_6H_6 : *EtOAc* = 19 : 1) 0.38.

Garugamblin-2 (**1c**): $C_{21}H_{20}O_5$; 70 mg; colourless solid (benzene); m.p. 195–197°; MS: M^+ 352; R_f (SiO_2; C_6H_6 : *EtOAc* = 19 : 1) = 0.50.

^{1}H and ^{13}C NMR spectra are in accordance with the proposed structures.

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