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ICACENONE, A FURANODITERPENE WITH A PIMARANE SKELETON FROM *ICACINA MANNII*

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Key Word Index—*Icacina mannii*; Icacinaceae; roots; furane; lactonic diterpenes; pimarane skeleton; X-ray structure.

Abstract—Icacenone was isolated from the roots of *Icacina mannii*. This new diterpene has a furane ring fused to a pimarane skeleton. Its structure was established by X-ray diffraction analysis. Its spectroscopic properties are also discussed.

INTRODUCTION

Previous studies carried out on *Icacina guesfeldtii* and *I. claessensis* extracts [1–3] showed that novel diterpene lactone structures related to the pimarane skeleton occured in the genus *Icacina*. In support of these findings, a new diterpene has been isolated from *Icacina mannii* Oliv., a shrub endemic to different regions of Tropical Africa; the root decoctions are used in popular medicine around Kinshasa (Zaïre) for the treatment of fibrous tumours.

RESULTS AND DISCUSSION

Icacenone (**1**) crystals were very slightly soluble in most organic solvents and moderately soluble in chloroform–methanol mixtures and in pyridine.

The molecular formula of **1**, $C_{19}H_{20}O_7$ was deduced from high resolution mass spectrum measurements and further confirmed by ^{1}H and ^{13}C NMR data. The UV spectrum of **1** showed a maximum at 262 nm. Its IR spectrum contained absorption bands at 3500 (hydroxyl), 1770 (carbonyl), 1740 (lactone carbonyl) and 1660 cm^{-1} (double bond). Its ^{1}H NMR showed the presence of two olefinic protons (δ7.59, *d* and 6.87, *d*), one proton on a carbon bearing a hydroxyl (δ4.36, *dd*, moved downfield to 5.49 upon acetylation) and two methylene protons (δ4.65 and 3.65) suggesting the presence of a hemiacetalic function as found in icacine [1] and icacinol [3]. Its ^{13}C NMR (DEPT) spectrum indicated the presence of four methylenes among the 19C of the skeleton and confirmed the existence of two carbonyl groups (δ191.1 and 177.4).

Upon acetylation at room temperature, **1** afforded only a monoacetate derivative (**2**) (M^+ 402).

In order to determine unequivocally the structure of **1**, it was subjected to X-ray analysis. The stereoscopic view of the molecule is shown in Fig. 1 (relative configuration).

Interpretation of the ^{1}H NMR and ^{13}C NMR spectra of **1** was achieved on the basis of the X-ray results and previous spectroscopic data obtained from icacine and icacinol [1, 3] and is given in the Experimental section.

Pharmacological studies of **1** are in progress.

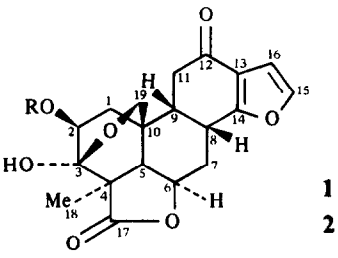
EXPERIMENTAL

Mp: uncorr.; ^{1}H NMR (250 MHz) and ^{13}C NMR (62.89 MHz): pyridine-d_5 using TMS as int. reference; MS: direct inlet, 70 eV.

Plant material. Roots of *Icacina mannii* were collected around Kinshasa (Zaïre). Plants were identified by Dr. H. Breyne (INERA Herbarium). A voucher specimen has been deposited in the INERA Herbarium, University of Kinshasa, Zaire.

Extraction and separation. Air dried powder (1.5 kg) of *I. mannii* roots was first defatted with petrol then extracted with EtOH (10 l). Evaporation of the EtOH soln afforded 350 g of a crude residue which was suspended in 500 ml 1% aq. HCl. The suspension was filtered and extracted several times with $CHCl_3$. Evaporation to dryness of the combined $CHCl_3$ extracts afforded a white yellow residue (58 g). This residue was stirred with Me_2CO and the yellow solvent discarded after decantation of the solid. Further purification was obtained by prep. TLC on silica gel 60F_{254} (toluene–Me_2CO–EtOH–NH_4OH, 40:40:8:3, R_f 0.15, detection under UV at 254 nm). Yield of icacenone (**1**): 0.2%.

Icacenone (**1**). White crystals from MeOH–$CHCl_3$ (1:3). Mp 278–280°, α_D^{20} 13.1° (*c* 0.3, C_5H_5N); UV λ_{max}^{EtOH} nm: 262; IR ν_{max}^{KBr} cm^{-1}: 3500, 1770, 1745, 1660; ^{1}H NMR (C_5D_5N): δ1.57



1 Icacenone R = H

2 2 – Acetylicacenone R = Ac

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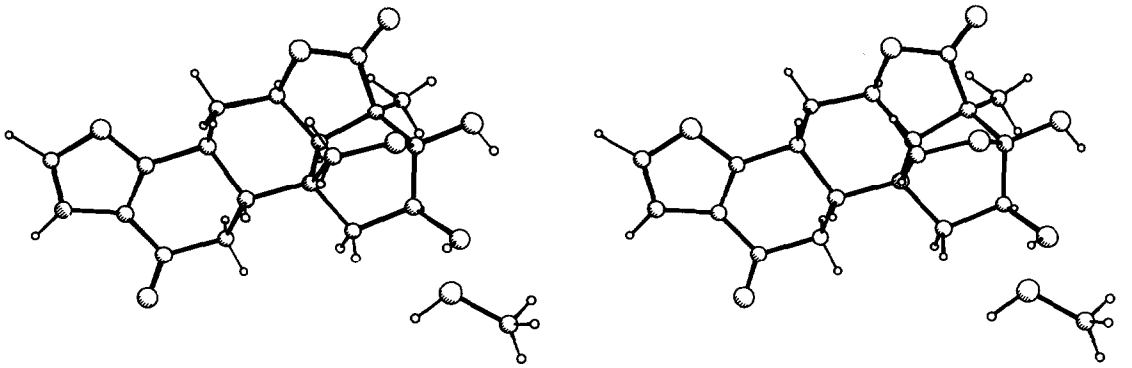

Fig. 1. Stereoscopic view of the molecule of icacenone {Me (Program PLUTO [4])}.

(3H, *s*, H-18), 2.32 (1H, *d* (*br*), J = 5.5, H-5), 3.75 (1H, *dd*, J_1 = 9.5, J_2 = 1.5, H-19), 4.36 (1H, *dd*, J_1 = 5.0, J_2 = 4.5, H-2), 4.65 (1H, *dd*, J_1 = 8.5, J_2 = 3.5, H-19'), 4.78 (1H, *m*, H-6), 6.87 (1H, *d*, J = 2, H-15), 7.59 (1H, *d*, J = 2.0, H-16); ^{13}C NMR (C_5D_5N): δ 17.5 (C-18), 27.4 (C-7), 27.6 (C-9), 33.4 (C-10), 34.8 (C-1), 38.3 (C-8), 41.5 (C-11), 44.5 (C-5), 51.2 (C-4), 66.6 (C-6), 72.8 (C-19), 73.5 (C-2), 97.9 (C-3), 106.8 (C-15), 120.4 (C-13), 144.1 (C-16), 170.4 (C-14), 177.9 (C-17), 191.9 (C-12); MS *m/z* (rel. abundance): 360.118900 (M^+, $C_{19}H_{20}O_7$ requires 360.120891), 344 (6), 342 (10), 263 (13), 257 (18), 199 (44), 198 (35), 147 (58), 135 (46), 121 (100), 115 (12), 107 (13), 105 (12), 98 (12), 95 (12), 93 (10), 91 (24), 81 (22), 79 (24), 78 (27), 77 (30), 69 (16), 67 (17), 65 (18), 55 (28), 53 (18), 44 (25), 42 (28). The crystal data of the complex between icacenone and MeOH were as follows: $C_{19}H_{20}O_7$. MeOH, monoclinic, space group $C2$ with a = 13.000 (7), b = 7.158 (3), c = 19.163 (19) Å, β = 94.06 (7)°; V = 1779 (2) Å^3. Four molecules per unit cell (Z = 4) give D_x = 1.47 g cm^{-3}. The intensity data were collected on a Syntex $P2_1$ diffractometer using graphite monochromatized Mo$K\alpha$ radiation (λ = 0.71069 Å). 1442 reflections were measured of which 1253 with $^{-}I \geqslant 2.5\sigma(I)$ were used in the structure determination. A misplaced fragment obtained by MULTAN 80 [5] was translated to the correct position by TRADIR procedure of DIRDIF 81 [6]. The complete molecule was then obtained by SHELX 84 [G. M. Sheldrich, personal communication]. Refinement was carried out by SHELX 76 program [7]. The final R value is 0.036. The list of atomic coordinates and molecular dimensions has been deposited with the Cambridge Crystallographic Data Centre.

2-Acetylicacenone (**2**). A soln of **1** (17 mg) in 2 ml C_5H_5N–Ac_2O (1:1) was allowed to stand overnight at room temp. After solvents evapn, the residue was purified by prep TLC on silica gel (toluene–Me_2CO–EtOH–NH_4OH, 40:40:8:3, R_f 0.55). MS *m/z*: 402 $[M]^+$, 360 $[M-\text{acetyl}]^+$.

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