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Angustimaline, an unusual nitrogenous compound from *Alstonia angustifolia*

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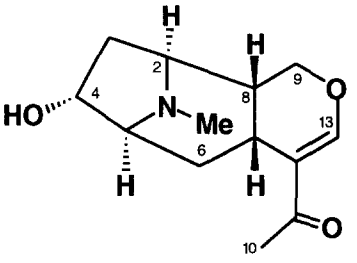
Abstract : An unusual nitrogenous compound probably derived from a macroline-type precursor was obtained from the stem-extract of *Alstonia angustifolia*. Copyright © 1996 Elsevier Science Ltd

Alstonia angustifolia is a tree widely distributed in Southeast Asia. Its alkaloidal content has been investigated previously and is known to provide a number of indole alkaloids including dimeric indoles[1]. A particularly notable feature of the alkaloidal composition of this plant is the preponderance of the macroline unit. We would like to report the isolation of an unusual C-13 nitrogenous compound, angustimaline, isolated from the stem-bark extract of this species[2].

Angustimaline **1** was obtained in amorphous form, $[\alpha]_D$ 115° ($CHCl_3$, *c* 0.1). The UV spectrum shows a maximum at 257 nm (log ε 4.11) while the IR spectrum showed bands for hydroxyl (3417 cm^{-1}), α,β-unsaturated carbonyl and enol ether (1614, 1644 cm^{-1}). The EIMS of **1** showed a molecular ion at *m/z* 237, the odd mass indicating the presence of a single nitrogen ($C_{13}H_{19}NO_3$). Other significant fragment peaks were observed at *m/z* 193 (M - CH_2=CHOH, base) and 150 (M - CH_2=CHOH - CH_3CO). The ^1H NMR spectral data (Table 1) showed the presence of a low field one H singlet at δ 7.52 attributable to a vinylic-H associated with a vinyl ether function, an *N*-methyl singlet at δ_H 2.49 and another methyl absorption due to an acetyl group at δ_H 2.16. The ^{13}C NMR spectrum (Table 1) indicated the presence of a ketonic carbonyl due to the acetyl group (δ_C 196.2), a two olefinic carbons associated with an enol ether function (δ_C 121.3 and 157.5) and an oxymethylene at δ_C 67.1. These, together with the two methine resonances at δ_C 23.4 and 37.4 are in good agreement with the E-ring of a typical type-B macroline[1] and suggested an early comparison with

macroline-type alkaloids such as alstophylline **2** which was also isolated from the plant. The ^{13}C NMR spectrum also indicated the presence of an oxymethine and full analysis of the NMR data employing COSY, HETCOR, HMBC and NOE-difference experiments furnished structure **1** for angustimaline. The connectivity is supported by the COSY spectrum which confirmed the H-coupling network of structure **1**. The stereochemistry of the 4-OH is deduced to be α since irradiation of H-4 resulted in enhancement of the H-7β signal. Other key NOE interactions (*N*Me-H2α/H5α; H6α-H5α/H9α) are consistent with the stereochemistry of the molecule as shown in **1**. The structure of angustimaline **1** shows that it retains all the features of the non-indole portion of a type-B macroline unit except for the presence of an additional, oxygenated carbon. It is probably derived from fragmentation of a macroline-type precursor, possibly alstophylline **2** (which also occurs in the plant) or its oxindole.



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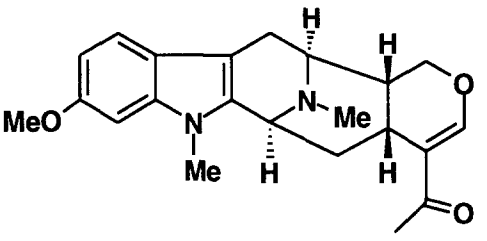

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Table 1. ^{1}H and ^{13}C NMR Spectral Data for **1**[a]

Position	δ_H	δ_C	Position	δ_H	δ_C
2	3.28 br d (6)	64.3	8	1.61 m	37.4
3α	2.28 ddd (14, 7, 3)	39.1	9β	4.06 ddd (12, 4, 1.5)	67.1
3β	2.12 dd (14, 7)	-	9α	4.28 t (12)	-
4	4.60 dd (7, 3)	76.4	10	2.16 s	25.0
5	3.02 m	71.1	11	-	196.2
6β	2.05 ddd (13, 7, 3)	33.6	12	-	121.3
6α	1.38 td (13, 3)	-	13	7.52 s	157.5
7	2.55 m	23.4	*N*Me	2.49 s	43.2

[a] $CDCl_3$, 270 MHz; assignments based on COSY, HETCOR, HMBC and NOE.

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References and Notes

1. Ghedira, K., Zeches-Hanrot, M., Richard, B., Massiot, G., Le Men-Olivier, L., Sevenet, T. and Goh, S. H. *Phytochemistry*, **1988**, *27*, 3955.
2. Other alkaloids found besides **1** were alstophylline, 19,20-dehydro-10-methoxytalcarpine, villalstonine, affinisine and normacusine-B. Isolation of alkaloids was carried out under mild conditions involving cold EtOH extraction, partitioning into dilute acid and SiO_2 chromatography.

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