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A CYCLOPENTENE AMIDE FROM *LINDACKERIA DENTATA*

SIMON GIBBONS,* ALEXANDER I. GRAY† and PETER G. WATERMAN†

Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Kuwait University, P.O. Box 24923, Safat 13110, Kuwait; †Phytochemistry Research Laboratories, Department of Pharmaceutical Sciences, University of Strathclyde, Glasgow G1 1XW, Scotland, U.K.

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Key Word Index—*Lindackeria dentata*; Flacourtiaceae; cyclopentenes; lindackeriamide; gynocardin; *rel*-1(ξ),4(*R*),5(*S*)-trihydroxy-2-cyclopentene-1-amide; HMBC NMR Spectroscopy.

Abstract—A novel cyclopentene amide has been isolated from the bark of the Cameroonian rainforest tree *Lindackeria dentata*. The structure elucidation of this metabolite was carried out by data comparison with the known cyclopentene nitrile glycoside gynocardin and by extensive one and two dimensional NMR studies.

INTRODUCTION

The Flacourtiaceae are a rich source of structurally diverse natural products with many recent examples of clerodane diterpenes [1, 2] and phenolic glucosides [3] being published. As part of a continuing chemotaxonomic investigation of this family we have investigated the aerial parts of the Cameroonian rainforest tree *Lindackeria dentata* Oliver (Flacourtiaceae) from which we have isolated the novel cyclopentenamide (**1**).

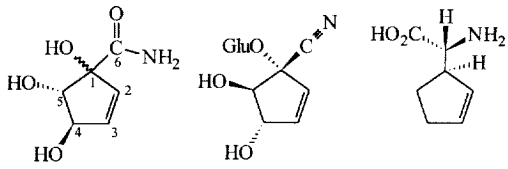
Structure elucidation of this natural product was achieved by 1D and 2D NMR, with particular emphasis on Heteronuclear Multiple Bond Coherence (HMBC) spectroscopy [4].

RESULTS AND DISCUSSION

By VLC [5] and recrystallisation from methanol, compound **1** was isolated as colourless cubes. By HR-EIMS, the highest ion fragment solved for $C_6H_7NO_3$. The ^{13}C NMR spectrum (Table 1) showed resonances for an amidic carbonyl, two methine carbons of an olefin, two oxymethine carbons and an oxygen-bearing aliphatic quaternary carbon. The ^1H NMR spectrum (Table 1) exhibited signals for two N-H protons, two olefinic protons and three hydroxyl protons, two of which appeared as doublets and one as a singlet. Further signals of two triplets for the protons associated with the oxymethine carbons completed resonances for the ^1H NMR spectrum. The carbon and proton spectra suggested the presence of four oxygens and nine hydrogens and consequently compound **1** must undergo the elimination of the elements of water in the HR-EI mass spectrum. The true molecular formula for **1** must therefore be $C_6H_9NO_4$.

A one bond H–C correlation experiment provided proof of connectivity for the above signals and a COSY-45 spectrum indicated a coupling system X–CH=CH–CH(O)–CH(O)–X with a block at either end of this spin system. This block took the form of the oxygen-bearing quaternary carbon, which bore a hydroxyl and an amide group. This arrangement indicated an unsaturated cyclopentane ring where each of the sp^3 carbons must bear a hydroxyl group. This oxygenation pattern is similar to that of the aglycone portion of the cyclopentene glucoside gynocardin (**2**). Analysis of the HMBC spectrum supported the COSY-45 and H-C direct correlation experiments. The final problem concerned the assignment of stereochemistry at positions C-4 and C-5. The magnitude of the coupling constant between the two oxymethine protons, H-4 and H-5, (δ 4.42, δ 3.78) was relatively large (J = 5.8 Hz) and indicated that, as in the case of gynocardin (**2**), they possess a *trans*-configuration [6, 7]. Unfortunately, it was not possible to define the stereochemistry at position C-1. Compound **1** is therefore assigned as *rel*-1(ξ),4(*R*),5(*S*)-trihydroxy-2-cyclopentene-1-amide.

*Author to whom correspondence should be addressed.



(1) (2) (3)

This cyclopentene amide may have been derived from the corresponding cyclopentene nitrile glycoside which, through mild hydrolysis, would yield the corresponding aglycone amide. Compound **1** may also be derived from the non-protein amino acid cyclopentenylglycine (**3**) which is the biosynthetic precursor for many of the cyclopentenyl fatty acids which are common within the Flacourtiaceae [8]. Decarboxylation and oxidation of **3** followed by hydroxylations at positions C-1, C-4 and C-5 could yield natural product (**1**).

EXPERIMENTAL

NMR spectra of **1** were recorded in DMSO-d_6. Spectra were run using a Bruker AMX-400 spectrometer. The HMBC experiment was set up using the Bruker pulse program inv4lplrnd set for d6 ($1/2J$) approximately equal to 7 Hz (Table 2). Direct correlation was established using a variant of H-C COSY (HCCOBI) and the experiment gave information for direct C-H connectivity with an optimum value of J_{CH} in the order of 135 Hz. Electron impact mass spectra were recorded on an AEIMS 902 double-focusing instrument at 70 eV using a direct insertion probe.

Plant material

Bark of *Lindackeria dentata* was collected from the area of the Tourist Camp, Korup National Park in May 1990. A voucher specimen has been deposited at the Centre for the Study of Medicinal Plants in Yaounde, Cameroon.

Extraction and isolation of compounds

The ground bark (500 g) was extracted in a Soxhlet with petrol ether (bp 60–80°), $CHCl_3$ and then MeOH. On concentration of the MeOH extract, a residue of 10.0 g of solid was obtained and this was fractionated by VLC over silica gel. The fraction eluted with 100% MeOH was recrystallised from MeOH to afford **1** (70 mg) as colourless cubes.

rel-1(ξ),4(R),5(S)-Trihydroxy-2-cyclopentene-1-amide; (**1**) *cubes*

Mp 208–210°; $[\alpha]_D$ −10 (MeOH, *c* 0.1); Found: 141.0419 $[M-H_2O]^+$, $C_6H_7NO_3$ requires 141.0426; IR υ_{max} (KBr disc): 3200–3600 (broad, OH), 2938, 1696, 1593, 1444, 1366, 1222, 1169, 1109, 1040, 1008, 977, 636 cm^{-1}. EIMS *m/z* (rel. int.): 141 $[M-H_2O]^+$ (9), 130 (34), 115 (79), 112 (19), 110 (58), 97 (100), 80 (16), 75 (38), 69 (37), 55 (33).

Table 1. ^1H and ^{13}C NMR data for compound **1**

Carbon	δ_H	δ_C
1	—	85.8
2	5.79 *dd* (1.5, 6.1)	137.0
3	5.50 *dd* (1.4, 6.1)	132.8
4	4.42 *t* (5.8)	78.4
5	3.78 *t* (6.1)	90.2
6	—	173.9
OH-1	5.69 *s*	—
OH-4	5.01 *d* (6.0)	—
OH-5	4.97 *d* (6.6)	—
NH_2	6.95 *s*, 7.10 *s*	—

Coupling constants are in Hz. All spectra are recorded in DMSO-d_6.

Table 2. HMBC data for compound **1**

Hydrogen	^2J	^3J
2	85.8, 132.8	78.4, 90.2
3	78.4, 137.0	85.8, 90.2
4	90.2, 132.8	85.8, 137.0
15	78.4, 85.8	132.8, 137.0
OH-1	85.8	173.9
OH-4	78.4	90.2
OH-5	90.3	78.4
NH_2	—	85.8

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