(+)-ACACIALACTAM, A NEW SEVEN-MEMBERED LACTAM FROM THE SEEDS OF *ACACIA CONCINNA*

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A new seven-membered lactam, (+)-acacialactam (1), was isolated from the viable seeds of *Acacia concinna* DC. Its structure is 3,7-dimethyl-7-vinyl-2,5,6,7-tetrahydro-1*H*-azepin-2-one (1), as determined by spectroscopic analysis.

KEYWORDS *Acacia concinna*; Leguminosae; seed; isolation; seven-membered lactam; (+)-acacialactam; 3,7-dimethyl-7-vinyl-2,5,6,7-tetrahydro-1*H*-azepin-2-one; azepine; azepinone; caprolactam

In searching for new biologically active natural products from medicinal plants, we recently isolated the anti-inflammatory constituents, entadamides A, B and C, from *Entada phaseoloides* Merr.[1-4] Continuing our chemical investigation of crude drugs used in Thailand, we isolated a new seven-membered lactam, (+)-acacialactam (1) from the viable seeds of *Acacia concinna* DC. (Leguminosae). These seeds are used as a source of folk medicine for skin diseases in Thailand and the tropical countries. The constituents previously isolated from this plant are several saponins[5-8] and a flavonoid.[6] However, there are no reports on the constituents of the basic fraction in the seeds. This communication deals with the isolation and structure determination of 1 from the basic fraction in the seeds of *A. concinna* DC.

The seeds were collected in the northern parts of Thailand. From the 75% EtOH extract of the viable seeds (200 g), the basic fraction was obtained in a yield of 0.63% of fresh wt., as reported previously.[1] The basic fraction was subjected to silica gel column chromatography by gradient elution, starting with CH_2Cl_2-MeOH-c.NH_4OH (90:1:0.2, v/v) then increasing the amounts of MeOH and c.NH_4OH to CH_2Cl_2-MeOH-c.NH_4OH (90:20:1). Compound 1-rich fractions were combined and subjected to prep. TLC (silica gel) using EtOAc-MeOH-c.NH_4OH (150:9:1, Rf 0.35) as an eluent to yield pure 1 (32mg, 0.016% / fresh wt.). Compound 1 was visualized by heating after spraying with 50% H_2SO_4 or by exposure to I_2 vapor. It was not positive to Dragendorff's reagent or I_2-platinate reagent.

Compound 1 is a colorless oil, $[\alpha]_D$ +4.3° (c=0.16, MeOH), showing the molecular ion *m/z* 165.1146 corresponding to the formula $C_{10}H_{15}NO$ by high resolution mass spectrum.[9] It showed an absorption maximum at 210 nm (ε 15700, MeOH) in the ultraviolet spectrum. In the infrared spectrum, peaks at 1670 and 1600 cm^{-1} showed the presence of an amide carbonyl and a conjugated double bond, respectively. The proton nuclear magnetic resonance (^{1}H-NMR) spectrum[10] showed a typical ABX system due to an isolated vinyl group (δ 5.91, 5.24, 5.10, each 1H, dd), one additional olefinic proton (δ 6.43, 1H, ddq), two methylene groups (δ 2.25, 1.65, each 2H, m), and two *tert*-methyl groups (δ 1.31, 3H, s; 1.85, 3H, dd). The ^{13}C nuclear magnetic resonance (^{13}C-NMR) spectrum of 1 exhibited signals due to two C-C double bonds, a carbonyl, a quaternary carbon, two methylene and two methyl groups (Table I). Homonuclear proton decoupling examination indicated that two methylene protons were coupled with each other and that a C_4-H proton was also coupled with one of the methylene protons. In addition, there were long range couplings between the methyl protons of C-10 (δ 1.85, 3H, dd) and the methylene protons (C_5-H) at 2.25 ppm, and also between the same methyl protons and C_4-H. From these observations,

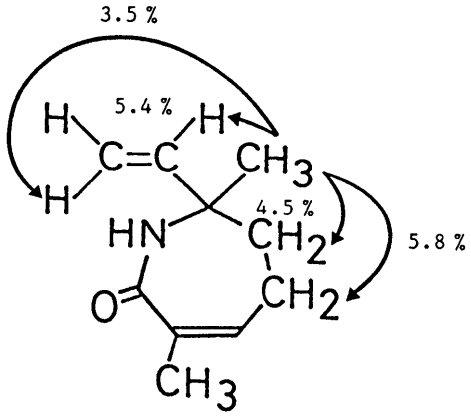

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Chart 1

Table I. ^{13}C-NMR Spectral Data of (+)-Acacialactam (1)

Assignment	Chemical shift	Multiplicity
C-2	171.5	s
C-4	144.6	d
C-8	137.7	d
C-3	129.9	s
C-9	112.2	t
C-7	73.0	s
C-5	40.8	t
C-10	28.0	q
C-6	23.2	t
C-11	12.7	q

Measured in $CDCl_3$, TMS as internal standard, 67.8MHz.

a structure for (+)-acacialactam is proposed to be 1 as shown in Chart 1, which also shows the results of the nuclear Overhauser effect (NOE) examination. NOEs were observed between the methyl protons of C-11 (δ 1.31) and two olefinic protons at 5.91 ppm (5.4%) and at 5.24 ppm (3.5%). There were additional NOEs between the same methyl protons and two methylene protons at 2.25 ppm (5.8%) and at 1.65 ppm (4.5%). From these results, the structure for (+)-acacialactam was finally determined to be 3,7-dimethyl-7-vinyl-2,5,6,7-tetrahydro-1H-azepin-2-one (1). Investigation of the biological activity and the absolute configuration of 1 is in progress.

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9) EI-MS m/z (rel. int.) :
165 [M^+](20), 121 (35), 113 (37), 110 (20), 102 (68), 71 (100), 69 (47), 43 (74).
10) ^{1}H-NMR ($CDCl_3$, 400MHz) : 1.31 (3H, s, C_{11}-H), 1.65 (2H, m, C_6-H), 1.85 (3H, dd, J=2.2, 1.0 Hz, C_{10}-H), 2.25 (2H, m, C_5-H), 5.10 (1H, dd, J=10.7, 1.0 Hz, C_9-Hcis), 5.24 (1H, dd, J=17.4, 1.0 Hz, C_9-Htrans), 5.56 (1H, br, disappears on addition of D_2O, NH), 5.91 (1H, dd, J=17.4, 10.7 Hz, C_8-H), 6.43 (1H, ddq, J=7.3, 7.3, 1.3 Hz, C_4-H).

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