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ASSAMICADINE, A NEW PYRROLIZIDINE ALKALOID FROM CROTALARIA ASSAMICA

D. CHENG, Y. LIU, T.T. CHU,

Institute of Organic Chemistry

Y. CUI, J. CHENG,

Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou, Gansu 730001, People's Republic of China

and E. ROEDER*

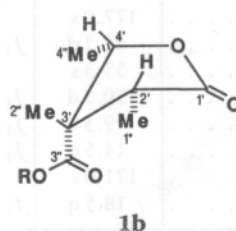
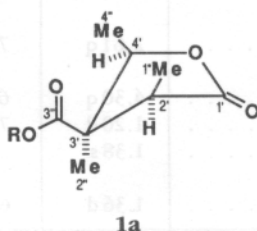
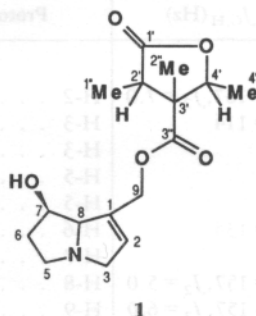
Institute of Pharmaceutical Chemistry, University of Bonn, An der Immenburg 4, D-5300 Bonn 1, FRG

ABSTRACT.—A minor alkaloid was isolated from *Crotalaria assamica*, and its structure was determined by spectroscopic methods as the 9-*O*-(γ -lactone) of (2',3'-dimethyl-4'-hydroxypentane-2',3'-dicarboxyl)-retronecine [**1**]. The new alkaloid was named assamicadine.

As we reported previously, monocrotaline has been isolated from *Crotalaria assamica* Benth. (Leguminosae), which occurs in the southern parts of China (1,2). The seeds of *C. assamica* yield about 3.5% of monocrotaline. During the further investigation of the seeds, another new pyrrolizidine alkaloid has been isolated which has been named assamicadine. This alkaloid occurs only in traces. Its structure **1** as the 9-*O*-(γ -lactone) of (2',3'-dimethyl-4'-hydroxypentane-2',3'-dicarboxyl)-retronecine was determined by its physical and spectroscopic properties.

The ir spectrum of **1** showed characteristic signals for a free hydroxyl group at 3373 cm^{-1} , a saturated ester at 1736 cm^{-1} , and a γ -lactone structure at 1778 cm^{-1} . The eims spectrum had a molecular ion peak $[\text{M}]^+$ of m/z 309 (4%), which can be correlated to the formula $\text{C}_{16}\text{H}_{23}\text{NO}_5$. Characteristic peaks appear at m/z 266, 265, 256, 211, 155, 139, 138, 137, 136, 111, 94, 93, 80.

This fragmentation indicated the presence of the necine, retronecine, or one of its isomers. Alkaline saponification yielded a necine, whose spectroscopic data verify the structure to be that of retronecine.



The characteristic intensities of the ms fragments at m/z 136, 137, and 138 support the presence of a C-9-mono-ester structure (3). The ^1H -nmr chemical shift of H-7 at 4.46 ppm is an indication for the presence of a free hydroxyl group in position 7.

The DEPT spectrum of **1** gave the signals of five CH, four CH_2 and three Me groups. The exact classification of the ^1H -nmr signals was made by the ^1H - ^1H -correlation spectrum. The 2D NOESY of assamicadine was used to determine the relative configuration of the molecule. The cross-signals in this spectrum showed an nOe effect indicating that H-2' is sterically near to the methylprotons of Me-1". The same is true for H-4' and Me-4". In addition, it was indicated that H-2' and Me-2" are on the same side of the ring plane of the lactone [**1a** and **1b**].

In the cd spectrum we observed a negative Cotton effect at 203 nm. The rule of Klyne and Beecham (5,6) concerning γ -lactones suggested that the β carbon lies under the ring plane of the γ lactone. The ester carbonyl group in po-

sition 3' is either pseudo-axial or pseudo-equatorial. H-2', H-4', and Me-2" are on the same side of the lactone ring system. The relative configuration of the lactone is either 2'S, 3'R, 4'R [**1a**] or 2'R, 3'S, 4'S [**1b**].

EXPERIMENTAL

APPARATUS.—The melting points have been determined on a Kofler apparatus and are uncorrected. Optical rotation and cd spectra: J-20C, JSPCO, Japan. Ms spectra: JMS-D300, 70 eV, 180° . ^1H - and ^{13}C -nmr spectra: AM-400 Bruker, (400.1 MHz for ^1H , 100.6 MHz for ^{13}C). The sample for all nmr experiments was 10 mg assamicadine in 0.4 ml CDCl_3 ; δ values are in ppm with TMS as internal standard. ^1H - ^1H -correlation: AM-400 Bruker, COSY 45, conditions 256 exp./16 scans/1K; Relax-Delay = 0.4 sec; NOESY mixing time = 1000 msec.

ISOLATION OF THE ALKALOIDS.—Powdered seeds of *C. assamica* (3 kg) taken from the Hubei Institute of Botany, Academia Sinica, were exhaustively extracted with 96% MeOH. (Voucher specimens have been deposited in the Wuhan Botanical Institute, Academia Sinica.) The solvent was evaporated in vacuum, and the residue was dissolved in 2.5% HCl. The neutral compounds were eliminated by liquid-liquid extraction with Et_2O and CH_2Cl_2 . The aqueous phase was basified with NH_3 and again extracted with CH_2Cl_2 . This purification procedure was re-

TABLE 1. ^1H - and ^{13}C -nmr Data of Assamicadine [**1**].

^{13}C			^1H		
Carbon	ppm	$J_{\text{C,H}}$ (Hz)	Proton	ppm	J (Hz)
C-1	132.3 s	$J_1 = 167, J_2 = 7.0$ $J_1 = 114$	H-2	5.88 brs	15.7
C-2	127.6 d		H-3	4.18 brd	
C-3	61.8 t		H-3	3.57 brs	
C-5	53.7 t	$J_1 = 134$	H-5	3.52 m	18.4, 9.7
C-6	36.4 t		H-5	2.91 dd	
C-7	78.1 d		H-6	2.10 m	
C-8	81.2 d	$J_1 = 157, J_2 = 5.0$ $J_1 = 157, J_2 = 6.0$	H-7	4.46 brs	14.8, 2.0
C-9	61.8 t		H-8	4.46 brs	
			H-9	4.89 dd	
			H-9	4.68 dd	14.8, 2.0
C-1'	177.0 s	$J_1 = 123, J_2 = 5.0$	H-2'	2.61 q	7.0
C-2'	46.1 d				
C-3'	55.3 s				
C-4'	70.5 d	$J_1 = 155, J_2 = 5.0$ $J_1 = 124, J_2 = 2.0$	H-4'	4.30 q	6.5
C-1"	9.3 q		H-1"	1.20 d	7.0
C-2"	14.5 q		H-2"	1.38 s	
C-3"	171.0 s	$J_1 = 157$			
C-4"	18.5 q		H-4"	1.36 d	6.5
		$J_1 = 150, J_2 = 1.0$			

peated and yielded 105 g of pure monocrotaline. Alkaloids in the mother liquor were separated by preparative tlc [Si gel plates, 0.5 mm; eluent CH_2Cl_2 -MeOH-NH₃ (25%) (85:14:1); detection Dragendorff reagent]. Removal of the Si gel and the extraction of the zone at R_f 0.32 with CH_2Cl_2 yielded monocrotaline, and the zone at R_f 0.22 yielded assamicadine. The purification procedure was repeated twice, and 13 mg of assamicadine was isolated.

IDENTIFICATION OF THE ALKALOIDS.—*Monocrotaline*.—Mp 200–201°; $[\alpha]^{25}_{\text{D}} -55.5^\circ$ ($c = 1$, CHCl_3) [lit. (4) 202–203°, $[\alpha]_{\text{D}} -55^\circ$ (CHCl_3); $R_f = 0.32$ (CH_2Cl_2 -MeOH-NH₃ (25%) (85:14:1)); ir (KBr, cm^{-1}) 3450 (-OH), 1735, 1710 (saturated and α,β -unsaturated ester). The ms, ^1H -nmr, and ^{13}C -nmr data corresponded with those of an authentic sample (1).

Assamicadine.—Colorless, viscous material: $[\alpha]^{19}_{\text{D}} -9.4^\circ$ ($c = 0.4$, MeOH); $\text{cd } \lambda_2 = 203 \text{ nm}$, $\Delta\epsilon_2 = -4.4$; $R_f = 0.22$; ir (KBr, cm^{-1}) 3373 (-OH), 1778 (γ -lactone), 1736 (saturated ester); eims $[\text{M}]^+$ 309 (4.0), 266 (2.0), 265 (5.5), 256 (1.0), 211 (2.4), 155 (8.0), 139 (2.0), 138 (24), 137 (20), 136 (10), 111 (20), 94 (24), 93 (100), 80 (42); exact mass calcd for $\text{C}_{16}\text{H}_{23}\text{NO}_5$, 309.1570, found 309.1568; ^1H and ^{13}C nmr see

Table 1.

ACKNOWLEDGMENTS

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