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ALKALOIDS FROM CROTON SPECIES. XII[1]. GLUTARIMIDE PEPTIDES FROM C. HUMILIS L.

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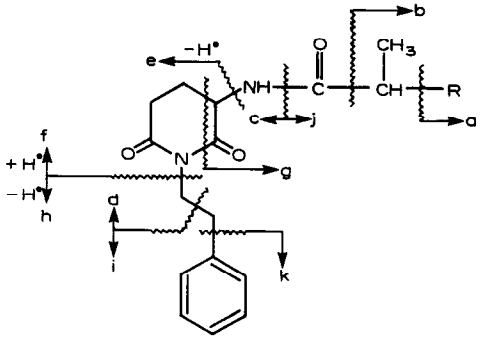
Recently[1] we reported the occurrence of N-[N-(2-methylpropanoyl)glutaminoyl]-2-phenylethylamine and N-[N-(2-methylbutanoyl)glutaminoyl]-2-phenylethylamine in C. humilis from the Long Mountain area in Jamaica. Extraction of C. humilis plants from Port Henderson not only yielded these two peptides but also a 1:1 crystalline mixture of new but related peptides, $C_{17}H_{22}N_2O_3$ and $C_{18}H_{24}N_2O_3$ for which the 2-[N-(2-methylpropanoyl)]-N-phenylethylglutarimide (I) and 2-[N-(2-methylbutanoyl)] -N-phenylethylglutarimide (II) structures have been established on the basis of spectral and chemical analysis. Repeated attempts to separate these components met with failure.

The glutarimide moiety in I and II was readily discernible from the characteristic[2] absorption bands at 1733 and 1667 cm^{-1}.

Detailed high resolution mass spectrometric investigations of the mixture can be summarized as indicated in the structures and in Table I.



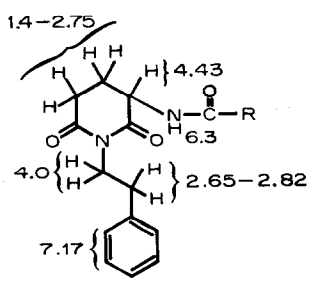
I, R = CH_3
II, R = CH_2CH_3

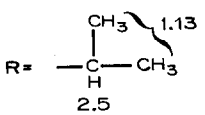
Table I. Mass Spectral Data on Peptidyl Compounds I and II.[a]

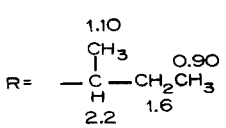
Ion	$C_{18}H_{24}N_2O_3$ (R = CH_2CH_3)		$C_{17}H_{22}N_2O_3$ (R = CH_3)	
	Found(m/e)	Formula	Found(m/e)	Formula
$M^{\cdot+}$	316.178	$C_{18}H_{24}N_2O_3$	302.162	$C_{17}H_{22}N_2O_3$
a	288		288	
b	259		259	
c	231.113	$C_{13}H_{15}N_2O_2$	231.113	$C_{13}H_{15}N_2O_2$
d	225.124	$C_{11}H_{17}N_2O_3$	---	
e	215		215	
f	212.116	$C_{10}H_{16}N_2O_3$	198	
g	141		127	
h	104.061	C_8H_8	104.061	C_8H_8
i	91.053	C_7H_7	91.053	C_7H_7
j	85.063	C_5H_9O	71.049	C_4H_7O
k	77.039	C_6H_5	77.039	C_6H_5

[a]Data obtained on Atlas CH4 and AEI MS-902 mass spectrometers at 70 eV.

Extensive double resonance n.m.r. experiments (in $CDCl_3$) and INDOR measurements[3] allowed firm assignments to all the protons present in these molecules. A summary of these assignments as expressed in ppm (δ values) is shown.







Chemical evidence in support of the above was obtained by acidic hydrolysis and analysis of the resultant products. For example, treatment of the mixture with 6 N hydrochloric acid at 105° for 24 hours yielded 2-phenylethylamine as established by comparison (i.r., t.l.c.) with an authentic sample, glutamic acid (automatic amino acid analyzer), 2-methylpropanoic and 2-methylbutanoic acids isolated as their p-bromophenacyl ester derivatives.

To the best of our knowledge this is the first report of a glutarimide type structure to be isolated from a higher plant. It is of interest to note that glutarimides have been found to possess pharmacological activity, as for example, the potent anticholinergic activity of benzetimide[4] and the strong hypotensive action of 2-phenyl-2-ethyl-N-(β-morpholinoethyl)glutarimide[5]. Because of this the biological evaluation of our compounds is being undertaken.

Acknowledgements

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