purified a neurotoxin named 'viperotoxin' from the venom of *Vipera palaestinae* which has a molecular weight of about 11,600. From the venom of the South-American rattlesnake *Crotalus durissus terrificus*, crotamine, a strongly basic polypeptide with a molecular weight of about 5,500[81] and crotoxin with a molecular weight of 30,000[82] were isolated. The latter possessing beside toxicity also phospholipase A activity was separated into 2 components, a non-toxic, acidic polypeptide and a basic phospholipase A with very wol toxicity[83,84]. Only a combination of both factors restores the full toxic activity.

It has to be noted that the so-called non-venomous snakes of the family *Colubridae*, and probably of other families too, produce toxic secretions in homologous glands. Thus, the venom of the colubrid snake, *Dispholidus typus*, is highly toxic and possesses marked coagulant and proteolytic properties[85], that of *Leptodeira annulata* has phospholipase A, phosphodiesterase and proteolytic activity[86]. However, further research in this field may give a more comprehensive picture of these snake venoms in future.

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SPECIALIA

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Alkaloids of Cranberries V

We have recently shown[1-3] that extracts of cranberry leaves contain N-methylindolic[1] and N-methylazatricyclo type alkaloids[2,3]. Many studies have shown that most cranberry extracts (especially European) have an application in 'naive' cancer therapy as well as in traditional folklore medicine. New Brunswick cranberry extracts were purified and a basic fraction separated[2], using column chromatography fractionation. Final purification was realised by thin-layer preparative chromatography, giving a minimum of 19 different basic products. We have succeeded in isolating and identifying the three principal constituents, and now report the configurational and conformational results of our work.

Method. Three products – cannivonines **1**, **2** and **3** – were isolated from 2.5 kg of dry material, with respective yields of 1.7, 5.3 and 1.4 mg[1,2].

Results and discussion. The mass peaks of the products studied by high resolution mass spectrometry (AEI

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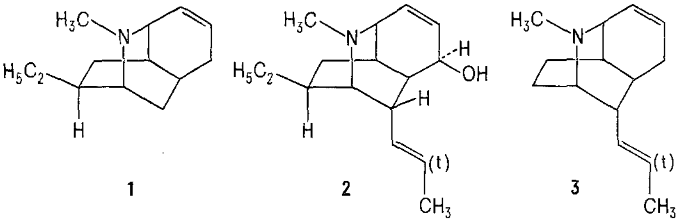
Table I. Cannivonine 2

Chemical shifts				Vicinal coupling Hz		
	δ	δSR[a]	J	HC ∅°	B ∅°	Observed[a]
OH	3.60	4.20	6.7	4.3 (45)	9.1 (0)	4.5
CH–OH	4.20	5.16	7.11	7.9 (20)	2.5 (100)	7.0
N–$\mathrm{CH_3}$	3.71	4.02	1.11	2.8 (55)	2.0 (60)	2.5
$\mathrm{CH_3}$–CH_2	1.65	1.85	7.8	1.3 (65)	5.1 (40)	1.0
$\mathrm{CH_2}$–CH_3	1.02	1.15	5.6	2.5 (80)	5.1 (40)	2.0
$\mathrm{CH_3}$–C=	2.3	2.84	4.5	—	—	10.2
H–11	2.0–2.3	2.53	3.4	5.1 (40)	7.2 (20)	4.5
H–5	5.5–5.6	6.03				
H–4		5.84	10.9 ax	7.2 (25)	7.2 (20)	7.0
H–3	2.0–2.3	2.6	10.9 eq	5.9 (145)	2.5 (100)	5.0
H–1		2.5	1.10	2.5 (80)	2.0 (60)	2.2
(CH=CH–C)–11	4.7	5.3 and 5.5				

[a] After addition of 0.1 m E-FOD. Varian HR 220 MHz.

Scheme 1



1 **2** **3**

MS-30) revealed by exact mass measurement cannivonine **1** → 191.1668 a.m.u., **2** → 247.1979 a.m.u., and **3** → 203.1699 a.m.u., which correspond to the respective formulas $C_{13}H_{21}N$ (191.1669), $C_{16}H_{25}NO$ (247.1930), and $C_{14}H_{21}N$ (203.1669).

Medium resolution mass spectrometry afforded a base peak at $C_{13}H_{17}N$, or M-59 a.m.u. for cannivonine **2**. The IR-spectrum showed OH absorption at 3217 and unsaturation absorption at 1632 and 1662 cm^{-1} and the UV-spectrum shows 2 olefinic absorptions (208 nm and 238 nm). The NMR-spectrum (VARIAN T-60) consisted of only a few signals, the majority of protons being located in the 1.7–3.3 ppm region (Table).

From these data, the tricyclic structur of 2-methyl-10-ethyl-11-prop-2-enyl azatricyclo $[5.3.1.0]^{3,8}$ undec-4-en-6-ol, isproposed for cannivonine **2** (Scheme). The two other Cannivonines, **1** and **3**, are likely to possess the structures presented in Scheme 1.

The assignment of hydroxyl, propenyl, and ethyl group, as well as double bond position on the skeleton was made using the NMR shift reagent technique. We are conscious of the fact that the coupling constants calculated for our product are not the true product coupling constants but the coupling constants of the resulting complex[4–6]. The best expansion of the spectrum was obtained using a Varian HR-220MHz NMR-spectrometer, together with the shift reagent E-FOD. The values of all coupling constants permitted the establishment of the stereochemistry of C(6), C(10) and C(11). Unfortunately, the molecule of cannivonine **2** is not as rigid as it would seem to be. The cylcohexene side of the molecule can adopt 2 conformations, half-chair (HC) or boat (B) which changes considerably the conformation of the whole molecule. Theoretical calculation of angles (using a Karplus type equation) permitted the elimination of the boat structure. The Table contains the average angle values for the 2 possible conformations of the cyclohexene ring. The differences between calculated values of vicinal coupling constants and observed values can be attributed to the presence of the shift reagent. However, they are in good agreement with the half-chair conformation values of a cylcohexene ring.

The nitrogen lone pair is pushed to the inside of the molecule, which is its more natural position (endo).

Some long-range coupling constants were also studied. The absence of a 'W' coupling between the N-CH_3 protons and the 1-C proton shows that the nitrogen doublet is endo orientated. The other long-range coupling constant – homoallylic, 1.7 Hz – between H-3 and H-6 proved that these protons are *cis*. Some known pseudoaxial, pseudoequatorial homoallylic coupling constants are of the same order[7–10].

Resumé. La séparation de trois nouveaux alcaloïdes de canneberges – cannivonines **1**, **2** et **3** – a été effectuée à l'aide de solvants appropriés et de la chromatographie sur couche mince préparative. Une identification des structures des trois alcaloïdes est proposée.

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New Utilizations of the Phenacyloxy Protecting Group in Peptide Synthesis

The reaction of 2-bromoacetophenone and its derivatives with phenolates[1] and carboxylates[2,3] to form the corresponding phenacyloxy (PAO) ethers and esters, is well known. The preparation of such derivatives is a simple procedure usually providing a crystalline product in good yield. As a consequence, this reaction became very useful for the systematic identification of carboxylic acids[2,3].

More recently, this group was introduced into peptide synthesis by STELAKATOS et al.[4] as carboxy protecting group. PAO ethers and esters are quite stable to acidic hydrolysis[5] and acidolysis[4]. Their reductive cleavage, however, can be carried out under mild conditions e.g. with zinc dust and acetic acid[5]. This approach has been suggested by TRUDELLE[6] for activation of the *o*-phenacyloxy-phenyl carboxy protecting group to obtain the active *o*-hydroxyphenyl esters.

In view of the cyanhydrine formation of acetophenone investigated a long time ago[7], it came to our attention

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