When reduced with zinc and hydrochloric acid, nandazurine (I) afforded colorless needles, mp 150 ~153°, $C_{19}H_{19}O_4N$, which was proved to be completely identical with an authentic sample of dl-domesticine (III)[3] by IR ($CHCl_3$), NMR ($CDCl_3$) and TLC-comparisons. Therefore, it is proved that the hexahydronandazurine has structure II, and consequently nandazurine must have structure I.

Since it has been known[4,5] that 7-oxo-dibenzo[de, g]quinoline derivatives possessing a phenol group on C-1 or C-11 exhibit green color when they can assume a zwitterionic structure, the foregoing observations suggest that nandazurine possesses a mesomeric and zwitterionic structure (Ia) ↔ (Ib).

Zusammenfassung. Strukturaufklärung des grünen Farbstoffs Nandazurin, aus Rinden von *Nandina domestica* Thumb. extrahiert. Chemische Reaktion und Spektren weisen auf eine Zwitterstruktur hin (Formel Ia ↔ Ib).

J. Kunitomo, M. Ju-ichi, Y. Yoshikawa[6] and
H. Chikamatsu[7,8]

Faculty of Pharmaceutical Sciences, Mukogawa Women's University, Hyogo; and
Faculty of Engineering Science, Osaka University[7],
Osaka (Japan), 13 November 1972.

---

[3] J. Kunitomo, K. Morimoto, S. Tanaka and S. Hayata, J. pharm. Soc. Japan *92*, 207 (1972).

[4] V. Preininger, J. Hrbek, Z. Samek and F. Santavy, Arch. Pharm. Berl. *302*, 808 (1969).

[5] I. Ribas, J. Sueiras, L. Castedo, Tetrahedron Lett. *1971*, 3093.

[6] Address: 4–16 Edagawa-cho, Nishinomiya, Hyogo (Japan).

[7] Address: 1–1 Machikaneyama-cho, Toyonaka, Osaka (Japan).

[8] The authors are grateful to President M. Tomita, Kyoto College of Pharmacy, for his encouragement in this work.

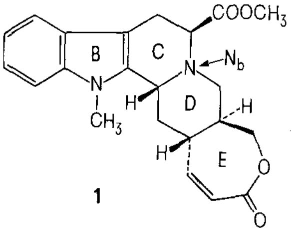
Alkaloids of Cranberries

Alkaloids separated up to date from cranberries are derivatives of two major chemical families, these being the indolic – cannagunine series – and the azatricyclic – cannivonine series – families[1–4]. All the alkaloids, each having a N-methyl function, probably participate as active ingredients in the physiologically active extracts of this plant. The study of 2 basic products isolated from cranberry extracts is now reported (Formulae).

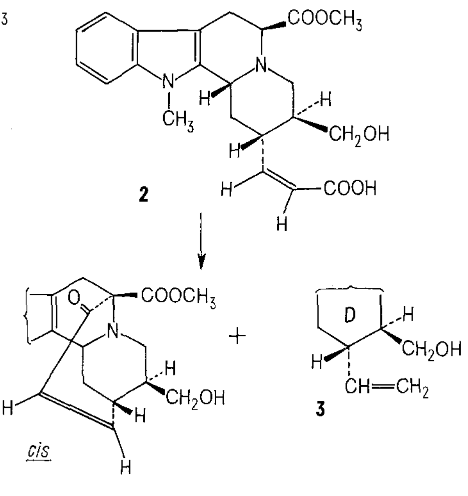
Results and discussion. The identification of the first alkaloid – Cannagunine B (**1**) was relatively easy because of the similarity in structure with the known product[1], the only difference being the carbomethoxy group α to the N_B atom. The NMR-spectra (Varian A-60, $CDCl_3$, TMS, δ, ppm) of Cannagunine[1] and Harmene type alkaloids[5] give the following results: $N–CH_3$ proton signal at 2.7 ppm, $COOCH_3$ proton signal at 3.6 ppm, 4 aromatic protons' signal at 2.2–2.6 ppm. The IR-spectrum showed an α, β-unsaturated, 7 membered, lactone ring system at 1718 cm^{-1}.

The first problem was determining the posision of substitution by the $COOCH_3$ group. The particular N–C*H*–$COOCH_3$ proton, its signal appearing at 3.70 ppm, having a common coupling constant with the protons of the tryptophane part of the skeleton[6], permitted the localisation of the carbomethoxy group in the indicated position. The exact mass measurement of the molecular weight peak gives 380.1740, which corresponds to $C_{22}H_{24}N_2O_4$. The base peak at 379 (M^+–1) corersponds to a loss of hydrogen and an intense M^+–15 fragment confirms our suppositions. The structure of the E ring is supported by two fragments, at M^+–44 and M^+–70 (–CO_2, –C_2H_4). Details of the fragmentation process were previously discussed[1].

The structure of the second alkaloid-Cannagunine C (**2**), exact mass measurement–398.1847–($C_{22}H_{26}N_2O_5$), was established through spectral analysis and basic hydrolysis of **1**. The possibility that **2** was formed during the isolation of **1** is improbable because the hydrolysis condi-



1



2 4 3

---

[1] K. Jankowski, I. Jankowska and J. Boudreau, Experientia *27*, 1141 (1971).

[2] K. Jankowski and I. Jankowska, Experientia *27*, 1383 (1971).

[3] K. Jankowski, Can. J. Chem. *50*, in press (1973).

[4] K. Jankowski, Science, in press (1973).

[5] L. D. Antonaccio, N. A. Pereira, B. Gilbert, H. Vorbrueggen, H. Budzikiewicz, J. M. Wilson, L. J. Durham and C. Djerassi, J. Am. chem. Soc. *84*, 2161 (1962). – G. Spiteller and M. Spiteller-Friedmann, Mh. Chem. *93*, 795 (1962). – H. Budzikiewicz, D. H. Williams and C. Djerassi, *Structure Elucidation of Natural Products by Mass Spectrometry* (Holden-Day, Inc., San Francisco 1964), vol. 1, p. 77.

[6] see Varian Analytical Instrument Division, High resolution NMR-spectra Catalog, Palo Alto, cif. (1962), vol. 2, p. 582.

tions are not present during the isolation process. It is possible however that both alkaloids exist as components, joined through the –COOR linkage, of larger molecules and that the isolated alkaloids are the result of the breakage of such links by methaonlysis.

The NMR-spectrum of **2** gave the following results: $N-CH_3$ proton signal at 2.7 ppm, $-CH_2O-$ proton signal at 4.45 ppm, $-COOCH_3$ proton signal at 3.5 ppm, olefinic proton signals at 5.4 ppm and 5.9 ppm, and 3 α to N protons signal at 2.2–2.6 ppm. The base peak in the mass spectrum of **2** was similar to that of the previous alkaloid, that is the $M^{+}-1$ fragment. Important ($> 60\%$) peaks occurred for the $M^{+}-15$, $M^{+}-44$, and m/e 31 fragments. This last fragment is the $^{+}CH_2 = OH$ ion, thus confirming the presence of a primary alcohol function (IR-absorption at 3,510 cm^{-1}). Here also we observed carbonyl absorption, for the ester group (1,745 cm^{-1}). and for the α,β-unsaturated acid group (1,710 cm^{-1}).

The structure and configuration of this alkaloid was further studied by NaH (in THF) condensation[7]. 2 products formed from the condensation are traces of decarboxylation product **3** (terminal $C=CH_2$, NMR-signal 4.20 ppm) and the compound **4**. This latter product was identified as being a Dieckmann type condensation product, formed between the $^{+}C-COOCH_3$ and COOH groups of a conjugated system. The formation of the keto-ester **4** is characterized by the disappearance of the N-*CH*-COOR and COO*H* proton signals in the NMR-spectrum of **2**.

The spectrum of **4** is similar to that of **2** with the exception of the D-ring allylic proton signals, which are shifted 0.5 ppm downfield.

The formation of **4** shows that the C- and D-ring junction must be *cis* (H, β-axial). The position of the $COOCH_3$ group, originally unknown, is shown to be β-equatorial, the α – axial position causing a 1,3-diaxial interaction. This is necessary to make the cyclisation easier. The *cis* configuration of the double bond was determined by the olefinic proton coupling constant (6.5 Hz). The CH_2OH and $C=C-COOH$ groups are *trans*-diequatorial and CH_2OH group is β-equatorial to avoid a 1,3-diaxial interaction, present if the CH_2OH group is α-axial[8].

Résumé. Une étude à l'aide de spectroscopie de masse et de spectroscopie r.m.n., ainsi que de dégradations, a permi l'identification de la structure de quelques bases isolées de feuilles de canneberges et leur classification parmi les alkaloids de la famille indolique.

K. JANKOWSKI

Département de Chimie, Université de Moncton, Moncton (Nouveau-Brunswick, Canada),
6 November 1972.

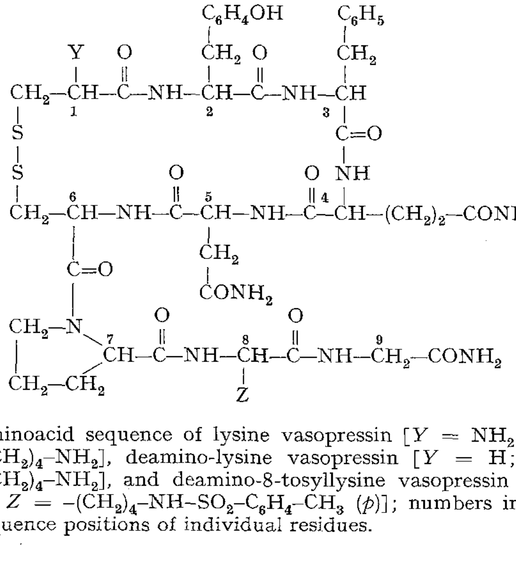
---

[7] L. J. DOLBY and Z. ESFANDIANI, J. org. Chem. *37*, 43 (1972). M. USKOKOVIC, H. BRUDERER, C. VON PLANTA, T. WILLIAMS and A. BROSSI, J. Am. chem. Soc. *86*, 3364 (1964). – J. D. HOBSON, J. RAINES and R. J. WHITEOAK, J. chem. Soc. *1963*, 3495.

[8] Author thanks Mr. G. G. ARSENAULT for the collaboration and NRC of Canada for the research grant.

Solid-Phase Synthesis of Lysine Vasopressin Analogs: [1-β-Mercaptopropionic Acid, 8- Lysine]-Vasopression and [1-β-Mercaptopropionic Acid, 8-(ε-N-p-Toluenesulfonyl)-Lysine]-Vasopressin[1,2]

The syntheses according to the general solid-phase procedure of MERRIFIELD[3] of [1-β-mercaptopropionic acid, 8-lysine]-vasopressin ([$\beta SP_p{}^1$, Lys^8]-Vpn) and [1-β-mercaptopropionic acid, 8-(ε-N-p-toluenesulfonyl)-lysine]-vasopressin ([$\beta SP\ ^1$, $TosLys^8$]-Vpn) are described (Figure). These peptides are analogs of the antidiuretic hormone lysine vasopressin([Lys^8]-Vpn) in which the potential centers for cationic charges have been progressively reduced. The conformational changes evoked by these stepwise modifications have been studied by proton magnetic resonance spectroscopy[4] and have been related to the proposed conformation of [Lys^8]-Vpn[5].



Aminoacid sequence of lysine vasopressin [$Y = NH_2$; $Z = -(CH_2)_4-NH_2$], deamino-lysine vasopressin [$Y = H$; $Z = -(CH_2)_4-NH_2$], and deamino-8-tosyllysine vasopressin [$Y = H$; $Z = -(CH_2)_4-NH-SO_2-C_6H_4-CH_3$ (p)]; numbers indicate sequence positions of individual residues.

In detail the syntheses of the protected octapeptide derivatives of [$\beta SP_p{}^1$, Lys^8]-Vpn and [$\beta SP_p{}^1$, $TosLys^8$]-Vpn followed our earlier synthesis of arginine vasopressin [Arg^8]-Vpn[6] and of radioactively-labelled oxytocin, [Lys^8]-Vpn and [Arg^8]-Vpn[7]. The tert. butyloxycarbonylglycine-resin (0.49 mmole of Gly per g of copolystyrene-2% divinylbenzene resin as determined by Volhard titration[3]) was deprotected and elongated stepwise with the appropriate protected amino acid active esters to yield the protected nonapeptide attached to the resin. Ammonolysis of this material, carried out as detailed by BAXTER et al.[8], gave 0.5 g of crude S-benzyl-β-mercaptopropionyl-

---

[1] Supported by USPHS Grants Nos. AM-13567 and AM-10080.

[2] Abbreviations follow the rules of the IUPAC-IUB Commission on Biochemical Nomenclature in Biochemistry *6*, 362 (1967).

[3] R. B. MERRIFIELD, J. Am. chem. Soc. *85*, 2149 (1963).

[4] J. D. GLICKSON, D. W. URRY, R. T. HAVRAN and R. WALTER, Proc. natn. Acad. Sci. USA *69*, 2136 (1972).

[5] R. WALTER, J. D. GLICKSON, I. L. SCHWARTZ, R. T. HAVRAN, J. MEIENHOFER and D. W. URRY, Proc. Acad. Sci. USA *69*, 1920 (1972).

[6] J. MEIENHOFER, A. TRZECIAK, R. T. HAVRAN and R. WALTER, J. Am. chem. Soc. *92*, 7199 (1970).

[7] R. WALTER and R. T. HAVRAN, Experientia *27*, 645 (1971).

[8] J. W. M. BAXTER, M. MANNING and W. H. SAWYER, Biochemistry *8*, 3592 (1969).