substitution on the nitrogen atom (for example to compounds **11** and **12**) or reduction of the double bond in position 4,4′ (to compounds **16**α, β) could be achieved by methods which were well developped for the other benzo-(4,5)cyclohepta(1,2-b)thiophene derivatives[3]. To test in rats the specificity of the ovulation-inhibiting activity of compound **9** (research number: 26–921), an attempt was made to clarify the structure-activity relationship within the substance group. Methodological and experimental conditions are described elsewhere[1]. The ovulation-inhibiting activity for each compound after 0.5 mg/kg s.c. dose is presented in the Table.

The following relationship was observed: 1. it seems that the methyl-radical in the piperidin ring and in the tricyclic part of the molecule favour the activity. 2. without the double-bond between piperidin-ring and the tricyclic part (position 4), the molecule is not active at all.

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Solacasine, a New Steroidal Alkaloid from *Solanum pseudocapsicum* Possessing Antimicrobial Activity

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Summary. Systematic fractionation of alcohol extracts of *Solanum pseudocapsicum* showed that solacasine is the main antibacterial constituent. Based on physiochemical studies, a structure is proposed.

Some years ago *Solanum pseudocapsicum* L., commonly called Jerusalem cherry or Christmas cherry, was reported to possess in vitro bioactivity against *Mycobacterium tuberculosis*[3,4] and solanocapsine was isolated and described as the active agent. No mention was made of other active constituents. Chemical studies eventually led to structure **1** for solanocapsine[5–11].

In our hands, column and thin layer chromatographic examination of the alkaloidal portions derived from ethanolic extracts of the dried flowering tops of plants grown in the Ohio State University medicinal plant garden revealed the presence of solanocapsine and additional antimicrobially active agents. We present here evidence that the best characterized of these, solacasine, isolated in 0.006% yield after extensive chromatography, most likely possesses structure **3**. Solacasine, $C_{28}H_{46}N_2O_2$, m.p. 215–220° d.; $[\alpha]_D$ +29° (Methanol); ν_{max}^{KBr} 3400, 1660 (C=N), 1600 cm^{-1}, etc.; λ_{max}^{EtOH} end absorption only; EIMS[12] M^+ 442 (38%), 427(22%), 410(M^+-MeOH, 10%), 130(14%), 189(8%), 169(10%), 115(100%), 95(10%), 93(10%), 83(10%), 82(16%), 73(22%),69(12%), 57(10%), 56(28%) and 55(23%); CIMS[12] (*i*-BuH) MH^+ 443(100%) and *m/e* 411 (MH^+-MeOH, 30%) (no other peaks of

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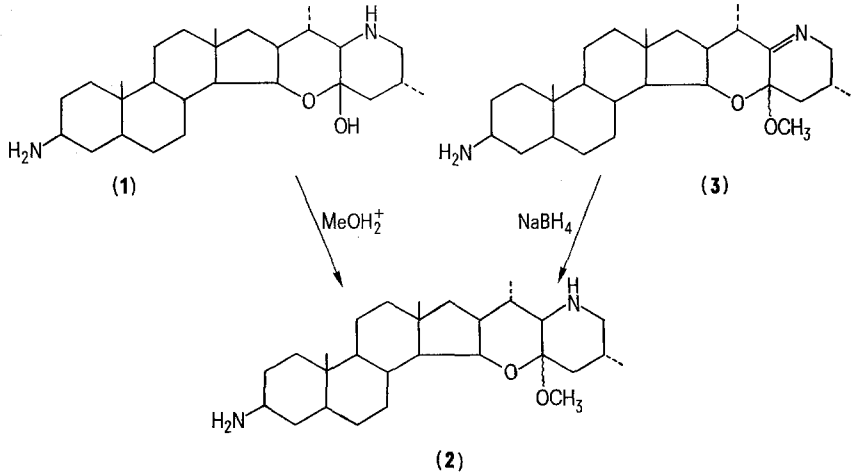
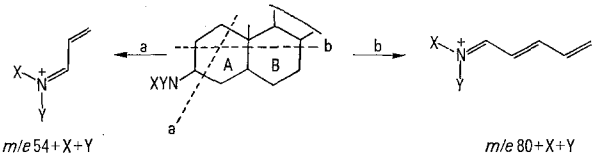
[12] EIMS = Electron Impact Mass Spectrometry; CIMS = Chemical Ionization Mass Spectrometry.



significent intensity), forms a diacetate, $C_{32}H_{50}N_2O_4$, m.p. 186–189°, ν_{max}^{ChF} 3440, 1720, 1660, 1510 and 1440 cm^{-1}, δ_{max}^{Chf} 1.95 (s), EIMS M^+ 526, when reacted with Ac_2O/pyridine for 18 h at 65°, followed by chromatography. When treated with sodium borohydride/formaldehyde in the modern version of the Eschweiler-Clark reaction[13], solacasine was converted to a tri-N-methyl dihydro analog **4**, $C_{31}H_{54}N_2O_2$, (EIMS[12], M^+ 486(5%), 471(12%), 454(M^+-CH_3OH, 53%), etc.) Reaction of solacasine with $NaBH_4$ alone led to a dihydro derivative **2**, $C_{28}H_{48}N_2O_2$, EIMS[12] M^+ 444(9%), 429(22%), 412(M^+-MeOH, 64%), 343(10%), 171(100%), 144(11%), 139(18%), 112(21%), 111(24%), 82(20%), 70(46%), 56(25%), etc., picrate salt, m.p. 178–182°. The common loss of methanol from the molecular ion in the mass spectra of these derivatives, coupled with an analogous loss of water by solanocapsine in its EIMS[12] (M^+ 430 (7%), 412 (M^+-HOH, 100%)) and CIMS[12] (*i*-BuH) MH^+ 431 (100%), 413 (MH^+-HOH 20%) no other significant peaks), the general similarity in spectra and properties suggested structure **3** as most likely for solacasine. Further support can be found in the fragmentation patterns. The mass spectra of steroidal alkamines are complex[14], but the presence or absence of certain fragments has diagnostic value. In particular cleavages a) and b) reveal a great deal about the structure of rings A and B. In this context, the presence of signi-



ficant ions at *m/e* 56 and 82 in the EIMS of **1**, **2** and **3**, and the lack of pairs of ions at *m/e* 70 and 96 in the same, argue that the 'extra' methyl group of **3** is unlikely to be attached to a carbon of either ring A or B and that the point of unsaturation must also be elsewhere. Ions *m/e* 84(55%) and 110(20%) in the EIMS of the Eschweiler-Clark product are consistent with that view as are their relative intensities (2:1)[14].

These inferences received strong support when solacasine and solanocapsine were converted to a common intermediate (**2**). Solanocapsine (**1**) was dissolved in cold, dry methanol and a slow stream of dry HCl gas was introduced intermittantly over 22 h at which time no more **1** was present upon TLC examination. Two main products were separated by sephadex LH-20 and silica gel chromatography. The more major of these two had identical TLC mobility in mixed spot experiments in 5 systems, an identical mass spectrum (EIMS), and formed an identical picrate salt (m.p. and IR-spectrum) when compared with **2** prepared by hydride reduction of **3**. The remaining point of uncertainly in the structure is the stereochemistry of the ketal moiety in **3**, but otherwise these experiments are rationalized by this formulation for solacasine.

The in vitro antimicrobial activity of these materials, using an agar-dilution streak assay[15], is as follows:

Microorganism	Compound 1	2	3	4
Staphylococcus aureus (6538P)[a]	100[b]	100	12.5	100
Mycobacterium smegmatis (607B)	100	100	5.0	100
Candida albicans (10231)	100	50	2.5	50

[a] American type culture collection number. [b] μg/ml.

The relatively small structural difference between **1** and **3** is nonetheless accompanied by a large difference in antibacterial potency. In vivo evaluation of **3** is in progress. The other agents are not potent enough to warrant further study.

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(−)-8β-Hydroxymethyl-Δ^1-Tetrahydrocannabinol: A Novel Physiologically Active Analog of Δ^1-Tetrahydrocannabinol[1]

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Summary. (−)-8β-Hydroxymethyl-Δ^1-tetrahydrocannabinol (THC) **1**, a novel analog of Δ^1, is shown to be as active as Δ^1-THC and twice as active as $\Delta^{1(6)}$-THC in the dog ataxia test.

We have recently reported[3] the synthesis of (−)-8β-hydroxymethyl-Δ^1-tetrahydrocannabinol (THC) (**1**), a novel analog of Δ^1-THC. In that paper, we stated that compound **1** exhibited THC-like overt central nervous systems (CNS) symptomatology in rodents at 1.0 mg/kg (i.v.). In the present communication, we confirm these results and compare the activity of **1** with Δ^1- and $\Delta^{1(6)}$-THC's in mice and dogs, and show that, in the latter, compound **1** is at least as active as Δ^1-THC and twice as active as $\Delta^{1(6)}$-THC. This is the first example of a modification in the geminal methyl part of the molecule of Δ^1-THC, although a few examples have been reported in the $\Delta^{3,4}$-THC series. The activity of **1** is noteworthy, since in the $\Delta^{3,4}$-THC's it has been shown that the geminal methyl group affords optimum activity[4–6]. However, no similar hydroxymethyl derivative is known in the $\Delta^{3,4}$- series for a direct comparison with **1**.

Δ^1-THC and other cannabinoids produce a characteristic effect in dogs, which includes static and dynamic ataxia, hyperflexia and decreased activity. This dog