'Townsville Prickly Orange' is not a pest taxon and has been found to be non-toxic in feeding trials. It is the only taxon in which C(24)-hydroxylated triterpenes have been found. Although lantadene A and lantadene B are present they are minor constituents, while oleanonic acid and 3-oxours-12-en-28-oic acid predominate. This taxon also contains icterogenin (**9**), previously obtained from *Lippia rehmanni*[6], and a new triterpene acid (methyl ester, $C_{31}H_{48}O_4$, m.p. 212–214°, $[\alpha]_D$ + 108° in $CHCl_3$) shown to be 24-hydroxy-3-oxoolean-12-en-28-oic acid (**10**). The methyl ester of this acid undergoes elimination of formaldehyde in a retroaldol reaction with dilute methanolic sodium hydroxide solution to give the known methyl hedragonate, and it is thereby shown to be the C(4) epimer of methyl 23-hydroxy-3-oxoolean-12-en-28-oate which has also been converted into methyl hedragonate[6].

Although it is not known to what extent the differences in toxicity between the taxa depend on the nature of the triterpenes and on their overall yields, these observations provide a basis for explaining the results of feeding trials. Lantadene A administered intraruminally as a single dose of 80 mg/kg body weight to sheep produces the characteristic toxicity previously shown to occur after feeding the whole *Lantana* plant[7,8]. From a study[9] of biliary secretion in the rabbit it had been concluded that when icterogenin, lantadene A and lantadene B were administered as fine aqueous suspensions into the peritoneal cavity, only icterogenin was active, and that any activity shown by samples of lantadene A was due to trace quantities of the toxic 3β-alcohol that would also be present with it. It was further suggested[10] that since lantadene A was non-toxic to the rabbit in these studies, the toxicity previously attributed by LOUW[11] and SEAWRIGHT[7] to lantadene A in oral dosing experiments in sheep was due to the unsuspected presence of small amounts of the 3β-alcohol. When the latter is dosed intraruminally to sheep at 3 mg/kg body weight, the amount estimated to be present in an effective dose of toxic *Lantana* leaf, however, no poisoning results. The present studies thus support the original observation by LOUW[11] that the toxicity to sheep of the crystalline isolate from *Lantana* leaves was due to the presence of the lantadene A itself, and further that the 3β-alcohol, in the amount likely to be present, is not sufficiently toxic when taken by this route for it to contribute significantly to the toxicity of the plant in the field.

Lantadene B in intraruminal doses of 200 to 300 mg/kg body weight was found also to be icterogenic for sheep and caused toxicity equivalent in severity to that produced by 80 mg/kg of lantadene A and 40 mg/kg of the 3β-alcohol from lantadene A. LOUW[11] found that when 2 g doses of lantadene A and lantadene B respectively were administered orally to adult sheep, lantadene A was toxic while lantadene B was not. As lantadene B differs from lantadene A only in the esterifying acid at C(22) it was accordingly concluded[9] that the angeloyloxy group at C(22) was a necessary structural requirement for icterogenicity. The present studies suggest that the dose rates of lantadene B used formerly[10,11] were too low to produce a toxic effect in those animal experiments. Lantadene B is however often a major constituent of *Lantana* leaves, and could thus contribute significantly to the overall toxicity of the plant.

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Synthesis of Ovulation-Inhibiting Compounds; Structure-Activity Relationship

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Summary. We describe the synthesis of some new derivatives of benzo(4,5)cyclohepta(1,2-b)thiophene which inhibit ovulation and the secretion of luteinizing hormone (LH) in the rat. We also describe the relationship between the structure and activity of these compounds.

In connection with a study on the ovulation and LH-inhibiting effects in rats of a particular benzocycloheptathiophene derivative: compound 26–921[1], we wish to report the preparation of 10-substituted benzo(4,5)cyclohepta(1,2-b)thiophenes from type **3**.

In another report[2], we describe the synthesis of 10-keto derivatives from type **1**. Reaction of **1** with phenyl magnesium bromide in anhydrous tetrahydrofuran or better phenyl lithium in anhydrous ether at room temperature for 1 h and at reflux for 1 additional h, followed by dehydration of the obtained hydroxycompounds **2** in a mixture of hydrochloric acid and isopropanol gave **3** (9,10: double bond; R′ = phenyl, R = alkyl, e.g. methyl).

On the other hand, **1** failed to react with alkyl magnesium halogenides, and when the reaction with methyl lithium was carried out at −20°, a very small yield of the desired alcohol **2** was obtained.

The second approach involved the condensation of the alkyl 2-thienyl ketones **5** with the diethyl *o*-cyanobenzylphosphonate in N,N-dimethylformamide at 20–100° for 2–5 h, to produce the compounds **6**, which were hydrogenated in ethanol with palladium on charcoal at 100° and 20 at. and hydrolyzed with potassium hydroxide in methyl diglykol at 150–180°. The obtained benzoic acid derivatives **7** were cyclized with polyphosphoric acid at 80–100° for 10–30 min to the ketones **8** (9,10: single bond; R′ = alkyl).

In the preparation of the final compounds listed partially in the Table, the attachment of the side chains in 4 position of the tricyclic intermediates and the following

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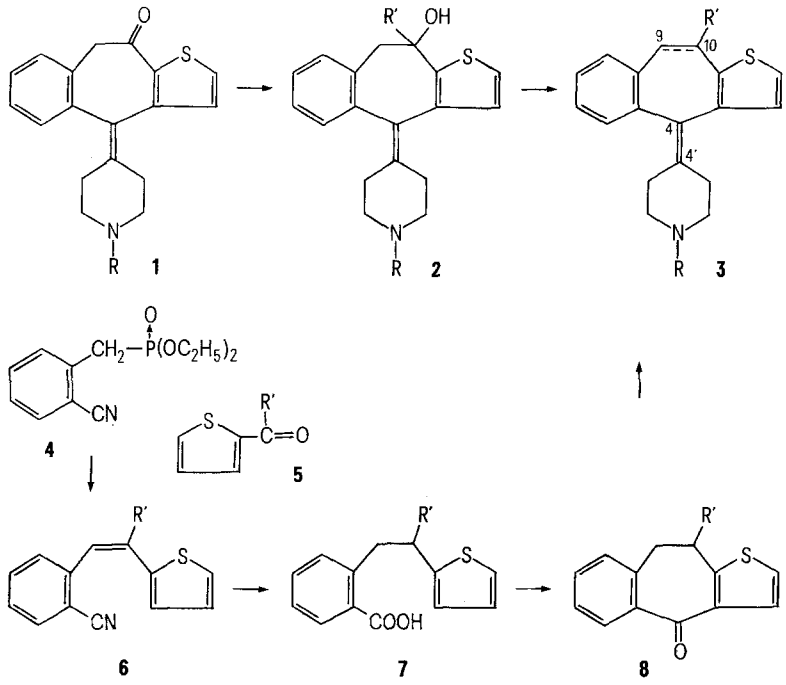
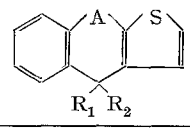
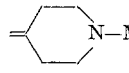
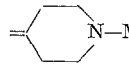
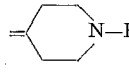
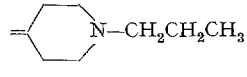
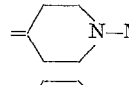
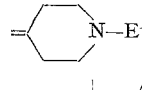
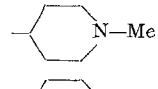
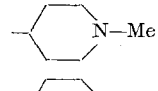
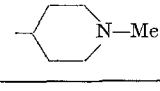




Compound	A	R_1	R_2	Salt form	Mp (°C)	Ovul. inhibition activity (%) Dose: 0.5 mg/kg s.c.
9 = 26-921	—CH_2—CH(Me)—	=O		Hydrogenmalate	190–91	100
10	—CH_2—CH(Et)—	=O		Hydrogenfumarate	220–21	80
11	—CH_2—CH(Me)—	=O		Free base	125–26	80
12	—CH_2—CH(Me)—	=O		Free base	115–17	80
13	—CH=C(Ph)—	=O		Hydrochloride	278–80	75
14	—CH_2—CH(Et)—	=O		Hydrogenmalate	154–56	40
15	—CH_2—CH(Me)—	—OH		Free base	177–78	0
16, isomer α	—CH_2—CH(Me)—	—H		Hydrogenfumarate	220–21	0
16, isomer β	—CH_2—CH(Me)—	—H		Hydrogenfumarate	210	0

Me, methyl; Et, ethyl; Ph, phenyl.

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

[1] The authors are grateful to Dr. R. Foltz, Battelle's Columbus Laboratories, and Mr. E. Fairchild of our laboratories for the mass spectral data, to Mr. Ruey-Ping Leu for the microbiological data, and to the NIH for grant No. AI-09846 in partial support of this work.

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