J = 2.5, 8 Hz, C-8), 7.33 (1 H, *s*, C-4), 7.46 (1 H, *d*, J = 2.5 Hz, C-10), 8.01 (1 H, *s*, C-1), 8.13 (1 H, *d*, J = 8 Hz, C-7). (Found: C, 66.15; H, 4.61. $C_{24}H_{20}O_8$ requires C, 66.05, H, 4.58%).

Synthesis of psoralidin oxide diacetate (**1a**). To a soln of psoralidin diacetate (**2a**) (50 mg) in 5 ml $CHCl_3$ was added a soln of *m*-chloroperbenzoic acid (22 mg) in 5 ml $CHCl_3$ and the mixture kept at 10° for 18 hr. The $CHCl_3$ soln was washed free of acid, first with 2% $NaHCO_3$ soln (10 ml) and then with H_2O, and dried (Na_2SO_4). The solvent was removed and the residue purified on a Si gel column and crystallized from EtOH to yield colourless needles (35 mg), mp 233–235°. It was found to be identical with natural psoralidin oxide diacetate (co-TLC, mmp, IR and ^{1}H NMR).

2′,3′-*Dihydro*-3,9,2′,3′-*tetraacetyl psoralidin* (**3b**). Compound **1a** (30 mg) was refluxed for 2 hr with Ac_2O–NaOAc. The reaction product was worked up as usual and found to be a mixture of two compounds by TLC (R_f 0.33, 0.17; C_6H_6–Me_2CO, 19:1). These were separated on a Si gel column by eluting with C_6H_6–EtOAc (with incresing polarity). The compound with higher R_f (0.33) on TLC was eluted first by C_6H_6–EtOAc (19:1) and crystallized as fine needles from Me_2CO–petrol (11 mg), mp 210–212°. This compound could not be characterized. Compound **3b** was eluted with C_6H_6–EtOAc (19:1) in later fractions and crystallized from EtOH as fine needles (11 mg), mp 244–246°, R_f (0.17). UV λ_{max}^{MeOH} nm: 208, 224 sh, 237 sh, 260 sh, 288 sh, 299, 328, 344. IR ν_{max}^{KBr} cm^{-1}: 1765, 1740, 1735, 1635, 1365. ^{1}H NMR (100 MHz, $CDCl_3$): δ 1.54 and 1.58 (3 H each, 2*s*, Me_2C–), 1.88 (3 H, *s*, *O*–Ac), 1.98 (3 H, *s*, O–Ac), 2.35 (3 H, *s*, O–Ac), 2.40 (3 H, *s*, *O*–Ac), 2.96 (2 H, *m*, Ar–CH_2 at C-1′), 5.40 (1 H, *m*, C-2′), 7.20 (1 H, *s*, C-4), 7.26 (1 H, *dd*, J = 2, 8 Hz, C-8), 7.48 (1 H, *d*, J = 2 Hz, C-10), 7.88 (1 H, *s*, C-1), 8.08 (1 H, *d*, J = 8 Hz, C-7).

2′,3′-*Dihydro*-2′-3′-*dihydroxy psoralidin* (**3a**). Compound **3b** (30 mg) was deacetylated in alcoholic KOH (4 g KOH in 50 ml EtOH, refluxed for 4 hr) and the reaction mixture separated on a Si gel column with C_6H_6–EtOAc (with increasing polarity). The C_6H_6–EtOAc (7:3) eluate gave **3a**, crystallized from EtOH as fine needles (9.5 mg), mp 261–263°, R_f 0.06 (C_6H_6–Me_2CO, 4:1). MS *m/e* 370, M^+, UV λ_{max}^{MeOH} nm: 207, 225 sh, 244, 266 sh, 293 sh, 305, 314 sh, 348, 362. IR ν_{max}^{KBr} cm^{-1}: 3320, 1708, 1630, 1392, 1378. ^{1}H NMR (220 MHz, DMSO-d_6): δ 1.10 and 1.13 (3 H each, 2*s*, Me_2C–), 3.0 (2 H, *d*, J = 13.2 Hz, –CH_2 at C-1′), 3.40 (1 H, *m*, C-2′), 6.88 (1 H, *d*, *C*-4), 6.92 (1 H, *dd*, J = 2.5, 10 Hz, C-8), 7.15 (1 H, *d*, J = 2.5 Hz, C-10), 7.65 (1 H, *d*, J = 10 Hz, C-7), 7.76 (1 H, *s*, C-1).

3,9-*Dibenzyloxy psoralidin* (**2b**). Psoralidin (200 mg) was benzylated ($C_6H_5CH_2Cl$, 1 ml; K_2CO_3, 1.5 gm; NaI, 0.3 g; Me_2CO, 10 ml; DMF, 10 ml; refluxed for 8 hr), 3,9-Dibenxyloxy psoralidin was crystallized from EtOH as needles, mp 147–148°, R_f 0.81 (C_6H_6–Me_2CO, 19:1). Yield 220 mg.

3,9-*Dibenzyloxy psoralidin* -2′,3′-*oxide* (**1b**). To a soln of compound **2b** (185 mg) in 5 ml $CHCl_3$ was added a soln of *m*-chloroperbenzoic acid (70 mg) in 5 ml $CHCl_3$ and the mixture kept at 10° for 48 hr. The reaction product processed as for **1a** and **1b** was crystallized from EtOH to yield colourless needles (120 mg), mp 159–161° R_f, 0.64 (C_6H_6–Me_2CO, 19:1). UV λ_{max}^{MeOH} nm: 210, 243, 265 sh, 292 sh, 304, 342, 360 sh. IR ν_{max}^{KBr} cm^{-1}: 1742, 1735, 1638, 1630, 1378, 1355, 1265, 955, 820. ^{1}H NMR (60 MHz, $CDCl_3$): δ 1.33 and 1.40 (3 H each, 2*s*, Me_2C–), 3.00 (3 H, *m*, AR–CH_2–$\underset{\diagdown O \diagup}{CH}$–$CMe_2$), 5.10 and 5.13 (2 H each, 2*s*, –*O*–CH_2–Ar), 6.90 (1 H, *s*, C-4), 7.13 (1 H, *dd*, J = 2.5, 8 Hz, C-8), 7.23 (1 H, *d*, J = 2.5 Hz, C-10), 7.41 (10 H, *s*, 2 × O-$CH_2C_6H_5$), 7.70 (1 H, *s*, C-1), 7.90 (1 H, *d*, J = 8 Hz, C-7).

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LAMPROLOBINE AND OTHER QUINOLIZIDINE DERIVATIVES FROM *LUPINUS HOLOSERICEUS*

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Key Word Index—*Lupinus holosericeus*; Leguminosae; quinolizidine alkaloids; anagyrine; α-isolupanine; lamprolobine; lupanine.

INTRODUCTION

Several species of the legume genus *Lupinus* are reported to be toxic to grazing animals in the Rocky Mountain region of the United States [1]. It is generally acknowledged that the quinolizidine alkaloids from these lupines are responsible for acute toxicoses and death in livestock [2, 3]. The Kellogg's spurred lupine, *L. caudatus* Kell., has caused cattle loss in Nevada and Utah [4] and a number of chemical studies [5–7] have shown this plant to contain anagyrine, α-isosparteine, α-isolupanine, lupanine, sparteine, and thermopsine. More recently, hydroxylupanine and three unidentified dehydrolupanine isomers have also been detected [8].

Presently, *L. holosericeus* Nutt. and *L. caudatus* are viewed as being taxonomically distinct ([9, 10]; D. B. Dunn, personal communication), although they have been

considered as being synonymous in the past [11]. Because of an apparent close relationship to the toxic *caudatus* species, the above-ground parts of the previously uninvestigated *L. holosericeus* were extracted and processed to give an alkaloid fraction. The major component of this mixture was the unusual quinolizidine base lamprolobine [1-(glutarimidomethyl-quinolizidine)]. Anagyrine, α-isolupanine, and lupanine were identified as the minor alkaloids.

RESULTS AND DISCUSSION

GC and TLC of the alkaloid extract suggested the presence of anagyrine, α-isolupanine, and lupanine. The preliminary finding of anagyrine and α-isolupanine was confirmed by GC–MS analysis. This analysis also suggested the major GC peak to be a mixture of lupanine and an unknown compound.

Preparative TLC of the alkaloid mixture gave two bands of interest. One band was shown (TLC, GC, MS) to be a binary mixture of lupanine and α-isolupanine. A chromatographic analysis (TLC, GC) of a MeOH extract of the other band revealed the presence of a component that was chromatographically identical with reference lamprolobine [1-(glutarimidomethyl-quinolizidine] and a substantial quantity of a compound not present in the original alkaloid extract. GC MS of this binary mixture indicated the presence of lamprolobine and suggested that the other constituent was the Me ester of lamprolobine, a known artefact [12]. Rechromatography (preparative TLC) of the mixture gave two bands, one of which was collected and extracted with EtOH. Since this EtOH band extract was homogeneous and identical with reference lamprolobine, the additional compound in the MeOH band extract was considered to be lamprolobine Me ester and an artefact. The optical activity and the mp of the picrate derivative of the compound in the EtOH band extract confirmed lamprolobine as the major alkaloidal component of *L. holosericeus*.

Lamprolobine has been isolated one other time from the Australian legume *Lamprolobium fruiticosum* Benth. [12], a member of the alkaloid-poor Galegeae tribe. It is of chemotaxonomic interest to find this alkaloid in a member of the Genisteae. Lamprolobine appears to arise biosynthetically from a pathway different from those proposed for the sparteine and matrine type alkaloids, a postulate that contributes to the chemotaxonomic aspect of this paper. The effects of the lamprolobine-rich *L. holosericeus* on grazing livestock are unknown.

EXPERIMENTAL

Plant material. L. holosericeus was collected 2 miles northwest of the Hailey city limits in Blaine County, Idaho, on 22 August 1977. The plant was identified by Dr. David B. Dunn and a voucher specimen (LL-77) is on deposit at the University of Missouri Herbarium, Columbia, MO 65201.

Extraction and fractionation. The dried, powdered (40 mesh) above-ground plant parts (60 g) were homogenized with EtOH and processed as usual [13] to give a crude alkaloid fraction.

Chromatography. All analytical TLC employed $CHCl_3$–MeOH–conc NH_4OH (100:10:1) as solvent while all prep. TLC involved developing 1 mm Si gel plates twice with cyclohexane–diethylamine (4:1). GC was carried out using 3% OV-17 on Gas Chrom Q with an initial temp. of 140° and programming to 265° at 4° per min. The same GC system was combined with MS and interfaced with a data reduction system.

Identification of alkaloids. Anagyrine, α-isolupanine, lamprolobine and lupanine were all identified by TLC, GC and MS comparisons with ref. standards. The optical activity of the isolated lamprolobine, $[\alpha]_D^{26}$ + 34° (MeOH, *c* 0.004), was consistent with lit. value [13]. Lamprolobine was further characterized by preparing the picrate derivative, mp 152–153° (lit. [13] mp 153–154°).

Quantitation of alkaloids. An int. standard (100 mg of *N,N*-dimethyl-3,4-dimethoxyphenethylamine hydrochloride) was added to 50 g of powdered plant material prior to homogenization with EtOH. The alkaloid fraction was produced and analysed using GC as described above. The peak area–wt ratio obtained from analysis of an int. standard soln of known concn was used to determine the efficiency of extraction (88%). Based on dry wt of the plant, the following amounts of alkaloid were found: lamprolobine, 0.40%; lupanine, 0.19%; α-isolupanine, 0.02%; and anagyrine, 0.02%. The relative conc of the four alkaloids in the plant were calculated to be: lamprolobine 64%, lupanine 30%, α-isolupanine 3% and anagyrine 3%.

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