The solvents acetone and chloroform produced a different and distinguishable precipitate. The sulfate dissolved at a moderate rate in acetone yielding, simultaneously, a light voluminous precipitate. In chloroform, the sulfate dissolved immediately followed by a slow but continuous precipitation. Isolation of the precipitate gave a 96% and 57% yield of lidocaine bisulfate in acetone and chloroform, respectively.

Thus over a 72-hr. period at room temperature a substantial disproportionation of lidocaine sulfate dihydrate to yield bisulfate and base was observed in acetone and chloroform.

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Occurrence of Bis-Noryangonin in *Gymnopilus spectabilis*

Keyphrases ☐ *Gymnopilus spectabilis*—analysis ☐ Bis-Noryangonin, occurrence—*Gymnopilus spectabilis*

Sir:

Gymnopilus spectabilis (Fr.) Singer has been reported to elicit hallucinogenic responses (1–3). Experimental pharmacologic data for confirmation or explanation of these reports are lacking for both the mushroom and known constituents of *Gymnopilus* species. However, bis-noryangonin [4-hydroxy-6-(4-hydroxystyryl)-2-pyrone], a styrylpyrone related to those occurring in kava root, has been isolated from *G. decurrens* Hesler (4), and the presence of indole derivatives other than psilocin and psilocybin has been suggested in *G. spectabilis* on the basis of thin-layer chromatographic examination (3).

Carpophores of *G. spectabilis* were collected near Tenino, Washington, on November 12, 1968, and freeze-dried. The powdered mushroom (50 g. of a 20-mesh powder) was extracted by shaking for 24 hr. at room temperature with 2 l. of ethyl acetate. TLC of the extract using a silica gel adsorbent and ethyl acetate–*n*-hexane–glacial acetic acid (5:3:1), chloroform–methanol (3:1), and 95% ethanol solvent systems revealed a constituent which was indistinguishable from bis-noryangonin. When the chromatograms were sprayed with 2% *p*-dimethylaminobenzaldehyde in acidic ethanol (concentrated HCl–95% ethanol, 1:3), this constituent formed a green chromophore which changed to purple with heat, a characteristic feature of bis-noryangonin.

The constituent suspected of being bis-noryangonin was isolated using the dry-column chromatographic procedures previously established for this compound (4). The IR spectrum (KBr pellet)[1] of the isolated material was consistent with this tentative identification showing characteristic peaks at 3200 cm.$^{-1}$ (OH); 1650 cm.$^{-1}$ (C=O of lactone ring); 1600, 1510 cm.$^{-1}$ (C=C). The UV spectrum[2] λ_{max}^{EtOH} 354 mμ (log ϵ 4.22) and 224 mμ (log ϵ 4.33) was also comparable to that observed with reference bis-noryangonin.

The methyl derivative of the isolated constituent was prepared by a proven method (4). No depression in the 156–157° m.p. of the derivative was noted upon admixing with known yangonin [4-methoxy-6-(4-methoxystyryl)-2-pyrone]. The mass spectrum[3] showed a parent and base ion peak at *m/e* 258.0892, both observed and calculated for $C_{15}H_{14}O_4$. The next most abundant peak was at *m/e* 230.0943 (28%), as anticipated from the known fragmentation pattern of yangonin (4, 5). The IR spectrum of the methyl derivative was identical in all respects with that of authentic yangonin, and the UV spectrum λ_{max}^{EtOH} 356 mμ (log ϵ 4.49) and 218 mμ (log ϵ 4.33) was in agreement.

The experimental observations establish the occurrence of bis-noryangonin in the fruiting bodies of *G. spectabilis*. No evidence of indole constituents was noted during the investigation, and it is presumed that the purple chomophore developing upon treatment of this styrylpyrone with *p*-dimethylaminobenzaldehyde explains the earlier suggestion of indole metabolites (3).

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[1] Beckman IR spectrophotometer, model IR-20, Beckman Instruments, Inc., Fullerton, Calif.

[2] Cary UV spectrophotometer, model 11-S, Cary Instruments—A Varian Subsidiary, Monrovia, Calif.

[3] Picker-AEI MS-9 mass spectrometer, Picker Nuclear Division, White Plains, N. Y.

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Further Applications of the 4-(Methylthio)-phenyl Ester in Peptide Chemistry

Keyphrases ☐ 4-(Methylthio)phenyl ester—peptide synthesis ☐ *N*-Carbobenzoxy-L-prolylglycylglycine ethyl ester—synthesis ☐ Optical rotation—identity

Sir:

The synthesis of proline containing peptides usually proceeds without complication, however, the alkaline hydrolysis of such sequences are frequently accompanied by side reactions. The hydrolysis of *N*-carbobenzoxy-glycyl-L-proline methyl ester with 1 *N* NaOH can be conducted with practically no cleavage of the peptide bond (1, 2). However, in the case of *N*-carbobenzoxy-L-prolylglycine methyl ester, hydrolysis causes cleavage to the extent of 70% yielding *N*-carbobenzoxy-L-proline and glycine (2). It is also difficult to hydrolyze higher peptides containing the sequence prolylglycyl in satisfactory yields (3).

In order to overcome this difficulty inherent in the synthesis of such sequences we have found that the 4-(methylthio)phenyl (MTP) protective ester (4–7) because of its facile conversion to the activated 4-(methylsulfonyl)phenyl (MSO_2P) ester, to be particularly useful for extending the peptide chain. For this purpose the synthesis of *N*-carbobenzoxy-L-prolylglycylglycine ethyl ester (Eq. 1) is described

Z-Pro-Gly-Gly-OEt (Eq. 1)

The synthesis commenced with the condensation of *N*-carbobenzoxy-L-proline and glycine 4(methylthio)-phenyl ester hydrochloride (4) using dicyclohexylcarbodiimide and triethylamine to give *N*-carbobenzoxy-L-prolylglycine 4-(methylthio)-phenyl ester, m.p. 92°, $[\alpha]_D$ −60° (c 3.23 in dimethylformamide).

In order to extend the peptide chain it was necessary to convert this protective MTP ester to its activated MSO_2P counterpart. This was achieved by the use of *m*-chloroperoxybenzoic acid in dioxane (7) for 4 hr., to yield *N*-carbobenzoxy-L-prolylglycine 4-(methylsulfonyl)phenyl ester, m.p. 117°, $[\alpha]_D$ −45°, (c 8.8 in dimethylformamide). The peptide chain was then extended through this MSO_2P activated ester by reaction of the dipeptide with glycine ethyl ester hydrochloride in the presence of triethylamine to give *N*-carbobenzoxy-L-prolylglycylglycine ethyl ester (8) (Eq. 1) m.p. 122°, $[\alpha]_D^{25}$ −23° (c 1 in ethanol).

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[1] The elemental analysis of all compounds were within experimental tolerance.