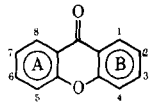
**Table I—Selective Demethylation of Polymethoxyxanthones**



| Compound | Substituents | Demethylation Substituents | Yield, % |
|---|---|---|---|
| I | 1,3-$(OCH_3)_2$ | 1-OH-3-$OCH_3$ | 44 |
| | | 1,3-$(OH)_2$ | 11 |
| II | 1-OH-3-$OCH_3$ | 1,3-$(OH)_2$ | 65 |
| III | 1,3,5-$(OCH_3)_3$ | 1-OH-3,5-$(OCH_3)_2$ | 40 |
| | | 1,3-$(OH)_2$-5-$OCH_3$ | 8 |
| IV | 1,3,7-$(OCH_3)_3$ | 1-OH-3,7-$(OCH_3)_2$ | 45 |
| | | 1,3-$(OH)_2$-7-$OCH_3$ | 10 |
| V | 2,3,4-$(OCH_3)_3$ | 2,4-$(OCH_3)_2$-3-OH | 52 |
| VI | 1,2,3-$(OCH_3)_3$ | 1,3-$(OCH_3)_2$-2-OH | 55 |
| | | 1-$OCH_3$-2,3-$(OH)_2$ | 5 |
| VII | 1,2,3,4,7-$(OCH_3)_5$ | 1,4,7-$(OCH_3)_3$-2,3-$(OH)_2$ | 38 |
| VIII | 1,3,5,6,7-$(OCH_3)_5$ | 1,6-$(OH)_2$-3,5,7-$(OCH_3)_3$ | 22 |
| | | 1,3,6-$(OH)_3$-5,7-$(OCH_3)_2$ | 36 |

The ease of *O*-demethylation is a function of resonance and steric factors. In compounds that are sterically less strained (I–IV), preferential demethylation occurs at C-1, followed by C-3 (and C-6), as could have been predicted on the basis of resonance factors (IX). Furthermore, since C-1 is more hindered than C-3 and C-6, the former should demethylate more readily. The selective demethylation at C-3 in V is caused by the relief of steric strain. However, this reaction can be explained as well in terms of simple resonance. In compounds having substitution at three or four adjacent carbon atoms, as in VI–VIII, the relief of steric strain is so important that it takes precedence over resonance effects, and one observes *O*-demethylation at C-2, C-3, and C-6, with C-2 demethylation being caused by the relief of steric strain.

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# South American Plants III: Isolation of Fulvoplumierin from *Himatanthus sucuuba* (M. Arg.) Woodson (Apocynaceae)


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Received October 3, 1977, from *Natural Products Advocates, Rockville, MD 20852.* Accepted for publication January 4, 1978. *Present address: School of Pharmacy, University of Maryland, Baltimore, MD 21201.



**Abstract** □ The bark of *Himatanthus sucuuba* was screened for pharmacological and anticancer activities. The lactone, fulvoplumierin ($C_{14}H_{12}O_4$), was isolated from the *n*-hexane fraction. The identity was proven by elemental analysis and IR, mass spectral, and melting-point determinations. Reference samples were used for comparison.



**Keyphrases** □ Fulvoplumierin—isolated from *Himatanthus sucuuba* bark, evaluated for pharmacological and anticancer activity □ *Himatanthus sucuuba*—fulvoplumierin isolated from bark, evaluated for pharmacological and anticancer activity □ Antineoplastic activity—fulvoplumierin isolated from *Himatanthus sucuuba* bark, evaluated


In the search for new drugs from plants growing in the Upper Amazon Valley in Peru, several hundred species were evaluated for antitumor[1] and other pharmacological activities[2]. Plants with known medicinal folk uses received priority.

One plant, "bellaco caspi," *Himatanthus sucuuba* (M. Arg.) Woodson (Apocynaceae)[3], has several uses. Infusions, decoctions, and poultices prepared from the stem bark are used as a vermifuge and laxative and for treating arthritis, "tumors," boils, hernias, and swellings. A 50% ethanol–water extract of the stem bark showed anti-inflammatory activity in the carrageenan-induced edema method and was marginally active against the human epidermoid carcinoma of the nasopharynx (KB) test system. Frac-

[1] Tests were performed at the Drug Evaluation Branch, Drug Research and Development Division of the Cancer Treatment, National Cancer Institute, National Institutes of Health, Bethesda, MD 20014.

[2] All tests were performed at the Natural Products Research Laboratories, Rockville, MD 20851.

[3] The plant was collected in Peru in April 1968. Identification was made by Dr. J. J. Wurdak, Smithsonian Institution, Washington, D.C. A herbarium specimen was deposited at the Smithsonian Institution.




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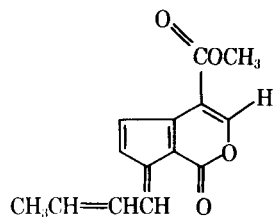


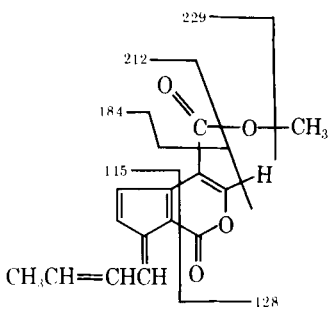
I

tionation of the stem bark was undertaken to isolate the active agent(s).

## EXPERIMENTAL[4]

The coarsely ground stem bark (2 kg) of *H. sucuuba* was extracted continuously for 24 hr using a soxhlet apparatus with *n*-hexane. The *n*-hexane extract was concentrated *in vacuo* and refrigerated. Two additional *n*-hexane extracts were similarly prepared from the marc. The combined extracts were concentrated *in vacuo* and refrigerated.

A yellow-orange compound (500 mg), which separated out on standing, was removed by filtration and dried. This compound was dissolved in hot *n*-hexane, and the undissolved portion was dissolved in chloroform and reduced *in vacuo*. Orange crystals (150 mg) formed and were recrystallized from hot ethanol. They proved to be the known compound fulvoplumierin (I), mp 149–150° [lit. (1–3) mp 151–152°].



II

Further evidence for the assigned structure of I was derived from mass spectrometric analysis. The parent ion (*m/e* 224) was also the base peak in the mass spectrum. The remaining major ions were accounted for by commonly encountered fragmentation pathways and rearrangements to II (Table I).

*Anal.*—Calc. for $C_{14}H_{12}O_4$: C, 68.85; H, 4.95. Found: C, 68.64; H, 4.98.

An IR spectrum was superimposable with that of an authentic reference sample of fulvoplumierin[5].

**Table I—Fragmentation Ions of Fulvoplumierin**

| *m/e* | Relative Intensity, % | Postulated Fragmentation Pattern |
|---|---|---|
| 244 | 100 | $M^+$ |
| 243 | 60 | M − 1 |
| 229 | 20 | M − $CH_3$ |
| 212 | 70 | M − $CH_3OH$ |
| 184 | 40 | *m/e* 212 − CO |
| 156 | 50 | *m/e* 184 − CO |
| 128 | 75 | — |
| 115 | 25 | Loss of pyrone ring |

## DISCUSSION

Fulvoplumierin, a lactone previously isolated from the root bark of *Plumeria acutifolia* L. (1, 2) and the stem bark of *P. rubra* L., was isolated from *H. sucuuba*. It was devoid of pharmacological activities. The present investigation establishes the first occurrence of this compound in this genus.

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[4] Elemental analysis was performed by Geller Laboratories, Saddle River, N.J. Melting points were taken on a Mel-Temp apparatus and are uncorrected. IR and mass spectra were determined using a Beckman IR-8 and an LKB-9000 mass spectrophotometer, respectively.

[5] Supplied by Prof. Dr. H. Schmid, Universitat Zurich, and E. Venkata Rao, Andhra University, Waltair, India.

# Synthesis and Antimicrobial Properties of 3-Substituted 1,2-Benzisothiazole 1,1-Dioxides


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Received October 21, 1977, from the *Monsanto Company, St. Louis, MO 63166.* Accepted for publication December 28, 1977.



**Abstract** □ Twenty aromatic alcohols and thiols were derivatized by reaction with 3-chloro-1,2-benzisothiazole 1,1-dioxide. The resulting 3-substituted 1,2-benzisothiazole 1,1-dioxides were tested against *Staphylococcus aureus, Salmonella typhosa,* and *Aspergillus niger,* and their activities were compared with the activities of the precursors.



**Keyphrases** □ 1,2-Benzisothiazole 1,1-dioxides, 3-substituted—synthesized, evaluated for antibacterial and antifungal activity □ Antibacterial activity—various 3-substituted 1,2-benzisothiazole 1,1-dioxides evaluated □ Antifungal activity—various 3-substituted 1,2-benzisothiazole 1,1-dioxides evaluated □ Structure–activity relationships—various 3-substituted 1,2-benzisothiazole 1,1-dioxides evaluated for antibacterial and antifungal activity


The herbicidal and fungicidal activities of some 3-substituted 1,2-benzisothiazole 1,1-dioxides were reported previously (1, 2). This paper is concerned with the preparation and antimicrobial activity of a series of these


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