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SHORT COMMUNICATION

PHYTOCHEMICAL STUDIES—VII[1].

ASSIGNMENT OF THE DOUBLE BOND CONFIGURATION IN HIBALACTONE AND ISOHIBALACTONE

Kung-Tsung Wang, Kyohei Yamashita and Boris Weinstein

Department of Chemistry, National Taiwan University, Taipei, Taiwan, Republic of China;
Department of Agricultural Chemistry, The University of Tokyo, Tokyo, Japan; and,
Department of Chemistry, Stanford University, Stanford, California, U.S.A.

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Abstract—The lignan hibalactone (α-piperonylidene-β-piperonyl-γ-butyrolactone) is shown to possess a *trans* double bond configuration; this result is correlated with other compounds containing a similar ring system.

INTRODUCTION

Hibalactone or savinin or Taiwanin B (I) is a lignan, which has been found in *Juniperus sabina*,[2] *J. communis*,[3] *J. thurifera*,[3] and *J. horizontalis*,[4] as well as in *Chamaecyparis obtusa* var. *breviramera*,[5] *C. obtusa*,[6] and *C. pisifera*,[6] and in the rare *Taiwania cryptomerioides*.[7,8] The structure of hibalactone was elucidated some years ago and the single asymmetrical carbon atom in this compound was found to be of the same configuration as the C_3 of (−)-hinokinin, since hibalactone forms (+)-isohinokinin upon hydrogenation.[9] The stereochemistry about the double bond in hibalactone remains uncertain; the sole suggestion in the literature is dependent on an ultraviolet comparison with the maxima at 264 and 273 mμ possessed by *cis*- and *trans*-cinnamic acid, respectively.[5] On this basis, a *trans* assignment was attributed to the substituents on the olefinic bond.[10] The racemic substance has been synthesized by several routes, some of which involve a Stobbe condensation, followed by partial reduction and cyclization.[11–14] The material is of economic importance, since it can be used as a natural synergist in insecticide formulations.[15–17]

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[1] For the previous paper in this series, see: K.- T. Wang and B. Weinstein, *Tetrahedron Letters* In press.

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[4] N. Narasimhachari and E. von Rudloff, *Can. J. Chem.* **39**, 2572 (1961).

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[10] For the purpose of definition, the use of *cis* and *trans* here refers to the analogous placement existing in the isomeric cinnamic acids.

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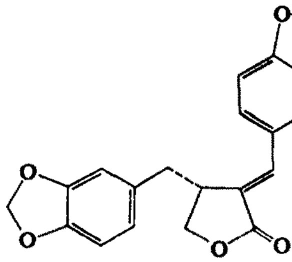
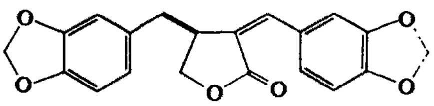


(I) Hibalactone



(II) Isohibalactone

RESULTS AND DISCUSSION

In earlier work, the structural elucidation[18] and the assignment of the geometrical configuration for the two olefinic bonds[19] of Taiwanin A (α, α′-dipiperonylidene-γ-butyrolactone) or dehydrohibalactone was materially assisted by use of various spectroscopic techniques. In view of the close relationship—both botanical and chemical—between hibalactone and Taiwanin A, a similar effort would allow the deduction of the spatial relationship at the single double bond in hibalactone. Fortunately, an isohibalactone II is available,[20] which differs from hibalactone only in the placement of substituents on this bond, and therefore can be used for comparison purposes. The alternative endocyclic α, β-unsaturated-γ-butyrolactone structure for isohibalactone is excluded on the basis of a variety of spectral and chemical evidence.

The u.v. spectra of hibalactone and isohibalactone are almost identical, with the exception that the absorptivity at 333 mμ (ε 15,100) for hibalactone is slightly higher than the related maximum at 339 mμ (ε 13,250) for isohibalactone. As *trans*-cinnamoyl chromophores have more intense maxima than *cis*-cinnamoyl groups,[21] it is tentatively believed that hibalactone has a *trans* configuration around the olefinic bond. For example, the somewhat related substances *trans*(?)-α-(*o*-methoxybenzylidene)- and *trans*(?)-α-benzylidene-γ-butyrolactone show principal maxima at 326 mμ (ε 15,000) and 283 nm (ε 18,000), respectively.[22,23] However, the structural assignment for hibalactone is not secure in view of the closeness of the observed data and the lack of precise, comparable models.

Alternative i.r. measurements reveal that the carbonyl and conjugated double bond absorptions are higher in frequency for hibalactone (1735 and 1640 cm^{-1}), in comparison to isohibalactone (1713 and 1585 cm^{-1}). The data here can be correlated with a possible *cis* olefin arrangement in hibalactone, for the *trans* form has a linear, extended dipole system that would shift these absorptions to a lower value. This particular point is uncertain due to possible association effects between the carbonyl group and the salt medium. One casual example is cited at this point, which would tend to favor the opposite assignment—the simple analog *trans*(?)-α-benzylidene-γ-butyrolactone absorbs at 1742 cm^{-1} (Nujol).[24] The absence

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[22] H. ZIMMER, D. C. ARMBUSTER and L. J. TRAUTH, *J. Heterocyclic Chem.* 2, 171 (1965).

[23] A compound considered to be *cis*(?)-α-benzylidene-γ-butyrolactone has an u.v. maximum at 280 mμ and a lower extinction coefficient; H. Zimmer, personal communication, May 19, 1966.

[24] A. R. PINDER, *J. Chem. Soc.* 2236 (1952).

of a series of measurements on related isomers does not permit these observations to be fully evaluated in a rigorous manner, and as a result, the i.r. measurements are considered to be inadequate here.

Fortunately, a comparison of the NMR spectra does furnish sufficient evidence to establish the olefinic configuration in hibalactone. Recent work has shown that for geometrical isomers, similar to those under discussion here, both a vinyl proton as well as an aromatic ring will be shifted downfield due to deshielding effects.[25, 26] Isohibalactone gives signals from aromatic protons at 7·8, 7·3, and 7·0–6·7 δ, two methylenedioxy groups at 6·1 and 6·0 δ, the ring methylene protons at 4·4–3·9 δ, a methine proton at 3·5 δ, and the benzyl protons at 3·0–2·4 δ. The signal from the vinyl proton is buried in the aromatic absorption between 7·0–6·7 δ, and cannot be seen here. Hibalactone contains a vinyl proton giving a signal at 7·3 δ, aromatic protons at 7·2, 7·1, 7·0, and 6·7–6·6 δ, methylenedioxy groups at 6·1 and 5·9 δ, methylene protons at 4·3–4·1 δ, a methine proton at 4·0 δ, and the benzyl protons at 2·8–2·4 δ. The displaced signal of the vinyl proton, which must be located geometrically near the carbonyl group, was shown to be coupled to that of the methine proton ($J = 1·65$ c/s) by irradiation experiments. In turn, the upfield shift of the signals of one of the methylenedioxy groups and the methine hydrogen is related to increased shielding effects.

The above information leads to the conclusion that the arrangement of the various substituents around the double bond in hibalactone is *trans*, as depicted in I; isohibalactone must therefore have the *cis* configuration, as in II. In view of the fact that Taiwanin A, hibalactone and hinokinin form a related group of lignan derivatives, then the dissimilar stereochemistry established here is possible evidence for a branched phytochemical interrelationship in this particular series.[27–29] It is felt that the *trans* structure may be favored on purely steric grounds, as molecular models (Dreiding) show pronounced rotational and electrostatic interactions in isohibalactone and an appreciable lessening of these restrictions in hibalactone.

EXPERIMENTAL

The u.v. spectra were obtained in alcohol solution, the i.r. spectra were determined in potassium bromide wafers, and the NMR spectra were recorded in deuterodimethylsulfoxide at 60 and 100 Mc/sec.

Isohibalactone; λ_{max} 237 sh., 293, and 337 mμ (ϵ 13,320, 9,430, and 13,250); ν_{max} 2875 (C—H), 1713 (C═O), 1615 (Ph), 1585 (C═C), 915 (O—CH_2—O) and 791 ($>$C═CH-) cm^{-1}; 7·8 (aromatic CH, area 1, singlet), 7·3 and 7·2 (aromatic CH, area 1, doublet), 7·0–6·7 (aromatic and vinyl CH, area 5, multiplet), 6·1 and 6·0 (methylenedioxy CH_2, area 4, singlets), 4·4–3·9 (ring methylene CH, area 2, heptet), 3·5 (ring methine CH, area 1, singlet), and 3·0–2·4 δ (benzyl methylene CH_2, area 2, complex doublet).

Hibalactone; λ_{max} 237, 293 and 333 mμ (ϵ 12,800, 11,200 and 15,100); ν_{max} 2910 (C—H), 1735 (C═O), 1640 (C═C), 1615 (Ph), 921 (O—CH_2—O) and 800 ($>$C═CH—) cm^{-1}; 7·3 (vinyl CH, area 1, doublet), 7·2 and 7·1 (aromatic CH, area 2, doublet), 7·0 and 6·9 (aromatic CH,

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[29] M. S. Adjaneba, *Bull. Soc. Chim. France* 2344 (1963).

area 1, doublet), 6·7–6·6 (aromatic CH, area 3, multiplet), 6·1 and 5·9 (methylenedioxy CH_2, area 4, singlets), 4·3–4·1 (ring methylene, area 2), 4·0 (ring methine CH, area 1, broad), and 2·8–2·4 (benzyl methylene CH_2, area 2, complex doublets).

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