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A STILBENE DERIVATIVE FROM *ARTOCARPUS INCISUS*

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Key Word Index—*Artocarpus incisus*; Moraceae; heartwood; stilbene; dimethylchromene ring; artocarbene; tyrosinase inhibitor.

Abstract—A novel stilbene with dimethylchromene ring, 3,2′,4′-trihydroxy-6″,6″-dimethyl-pyrano(3″,2″:4,5)-*trans*-stilbene, named artocarbene, has been isolated from the heartwood of *Artocarpus incisus*. © 1997 Elsevier Science Ltd. All rights reserved

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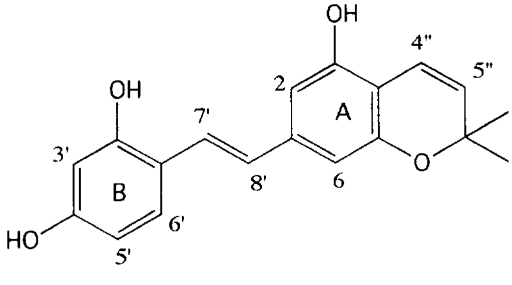
INTRODUCTION

Our search for biologically active natural products has been focused on Papua New Guinean woods, from which several active components have been isolated [1]. This work concerns the results obtained on chemical examination of the tyrosinase inhibitory extract of the heartwood of *Artocarpus incisus* [2]. *A. incisus* belongs to the Moraceae and is grown for its fruit (breadfruit). Examination of the ether extract led us to isolate a novel stilbene with dimethylchromene ring (**1**), to which we have given the trivial name artocarbene.



1

RESULTS AND DISCUSSION

The ^{13}C NMR spectrum of **1** revealed 19 carbon atoms (DEPT: 8 × C, 9 × CH and 2 × Me). The FAB mass spectral data ($[M+H]^+ = m/z$ 311) together with the ^{13}C NMR data suggested the molecular formula $C_{19}H_{18}O_4$. The ^1H NMR spectrum of **1** suggested the presence of a *trans* disubstituted double bond flanked by quaternary carbons based on the presence of two doublet olefinic proton resonances at δ 7.33 ($J = 16.36$ Hz) and 6.89 ($J = 16.36$ Hz). Two one-proton doublets at δ 6.60 ($J = 1.46$ Hz) and 6.47 ($J = 1.46$ Hz) in the ^1H NMR spectrum suggested that the A ring had a trisubstitution pattern. Three aromatic protons on the B ring revealed a clear ABX system [δ 6.38 (*dd*, $J = 8.54$, 2.44 Hz), δ 6.44 (*d*, $J = 2.44$ Hz) and δ 7.39 (*d*, $J = 8.55$ Hz)] typical of substitutions at the 2′- and 4′-positions on the B ring. The presence of a dimethylchromene ring [δ 5.60, 6.66 (*d*, $J = 9.76$ Hz) assigned to the *cis*-olefinic protons and 1.29 (2 × Me)] was indicated from the ^1H NMR spectrum. ^1H-^1H COSY relationships permitted the assignment of aromatic proton chemical shifts and also supported the substitution pattern. HMQC data were used to assign carbon resonances to their attached protons. In the HMBC spectrum, the olefinic carbon at δ 126 (C-8′) was correlated with the aromatic protons at δ 6.60 (H-2) and 6.47 (H-6). Moreover, the aromatic proton at δ 7.39 (H-6′) caused a cross-peak with the olefinic carbon at δ 125, identified as C-7′. In the NOESY spectrum, NOE enhancement between the 6″ (-Me) protons at δ 1.39 and the olefinic proton at δ 5.60 identified the latter as H-5″. Full proof of the skeleton of **1** was obtained by a combination of HMBC, DEPT, ^1H-^1H COSY, NOESY and HMQC experiments. Therefore, **1** was elucidated as 3,2′,4′-trihydroxy-6″,6″-dimethyl-pyrano (3″,2″:4,5)-*trans*-stilbene.

Stilbenes with a dimethylchromene ring are rare structures in plants. To the best of our knowledge, this is the first report of the occurrence of a stilbene with a dimethylchromene ring in the Moraceae. A similar structural type had been found in the Leguminosae [3]. Stilbenes are found in many plant genera, and some are considered to be phytoalexins [4]. They exhibit a variety of biological and pharmacological activities including protein tyrosine kin-

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ase (PTK) and protein kinase C (PKC) inhibitory effects [5]. The tyrosinase inhibitory effect of **1** will be reported in the near future.

EXPERIMENTAL

General. NMR: 400 MHz, Me$_2$CO-d_0. TMS as for int. std (^{1}H NMR) and deuterated solvents (for ^{13}C NMR).

Plant material. Heartwood of *A. incisus* was collected in Papua New Guinea and in Okinawa, Japan. A voucher specimen is deposited at the herbarium of Department of Forest Products, Kyushu University in Japan.

Extraction and isolation. Air-dried milled heartwood of *A. incisus* (37 kg) was extracted for 10 days with Et$_2$O at room temp. and the extract concd to dryness. The dry Et$_2$O extract (330 g) was crystallized successively from Et$_2$O–hexane and MeOH. The yellow solid deposited was collected and recrystallized from MeOH–H$_2$O yielding artocarpin [6]. After sepn of the mother liquor (89 g) by CC and MPLC on silica gel repeatedly using an EtOAc–hexane gradient as eluent, **1** (12 mg) was purified by prep. HPLC (Inertsil PREP-ODS: 20 mm i.d. × 250 mm) using H$_2$O–MeCN (1:1).

Artocarbene (**1**). Yellow powder. ^{1}H NMR (400 MHz, Me$_2$CO-d_6): δ 1.39 (6H, *s*, H-6″), 5.60 (1H, *d*,$J = 9.76$ Hz, H-5″), 6.38 (1H, *dd*, $J_{5',6'} = 8.54$ Hz, $J_{3',5'} = 2.44$ Hz, H-5′), 6.44 (1H, *d*, $J = 2.44$ Hz, H-3′), 6.47 (1H, *d*, $J = 1.46$ Hz, H-6), 6.60 (1H, *d*, $J = 1.46$ Hz, H-2), 6.66 (1H, *d*, $J = 9.76$ Hz, H-4″), 6.89 (1H, *d*, $J = 16.36$ Hz, H-8′), 7.33 (1H, *d*, $J = 16.36$ Hz, H-7′), 7.39 (1H, *d*, $J = 8.55$ Hz, H-6′); ^{13}C NMR (400 MHz, Me$_2$CO-d_6): δ 28 (C-6″(-Me)), 77 (C-6″), 104 (C-3′), 106 (C-6), 107 (C-2), 108 (C-5′), 109 (C-4), 117 (C-1′), 118 (C-4″), 125 (C-7′), 126 (C-8′), 128 (C-6′), 129 (C-5″), 141 (C-1), 154 (C-3), 155 (C-5), 157 (C-2′), 160 (C-4′); Positive ion FABMS: *m/z* 311.

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