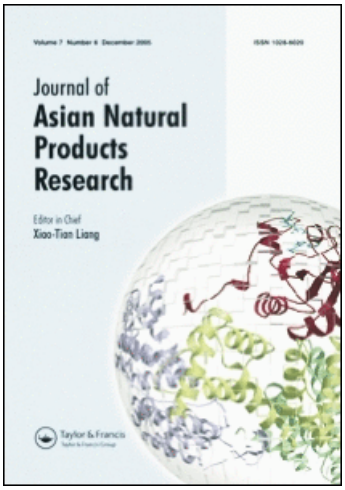

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Note

SYNTHESIS OF (+)-LARICIRESINOL 3a-ACETATE, A LIGNAN FROM *AGLAIA ELAEAGNOIDEA*

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(+)-Lariciresinol 3a-acetate {(+)-(3S)-acetyloxymethyl-(2S)-(4-hydroxy-3-methoxyphenyl)-(4R)-[(4-hydroxy-3-methoxyphenyl)methyl]tetrahydrofuran} (**1**), a metabolite of *A. elaeagnoidea* was synthesized starting from (+)-lariciresinol (**2**) in three steps with an overall yield of 66%.

Keywords: Lariciresinol 3a-acetate; Lariciresinol; *Aglaia elaeagnoidea*; Lignan

INTRODUCTION

Lariciresinol (**2**) and its derivatives have been reported to be cytotoxic [1–3] and insect antifeedant [4]. (+)-Lariciresinol 3a-acetate was isolated as a major component from *Aglaia elaeagnoidea*, recently [5]. During our phytochemical studies on *Justicia* species, we have isolated (+)-lariciresinol (**2**) [6,7], which could be converted into lariciresinol 3a-acetate (**1**) by a simple synthetic sequence (Scheme 1). Details of this semisynthesis are presented in this note.

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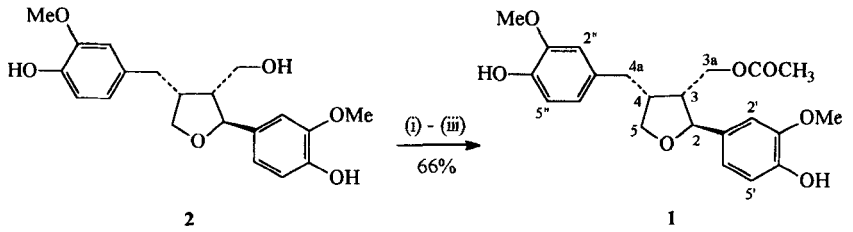

2 1

SCHEME 1 (i) $PhCH_2Br$, K_2CO_3, acetone, reflux, 6 h, 93%; (ii) Ac_2O/Py, rt, 12 h, 83%; (iii) Pd–C (10%), $HCOONH_4$, acetone, reflux, 2 h, 86%.

RESULTS AND DISCUSSION

Phenolic hydroxyls of (+)-lariciresinol (**2**) were selectively derivatized using benzyl bromide/K_2CO_3 [8] to give (+)-4′,4″-O-dibenzyllariciresinol (**3**), in 93% yield. Acetylation of **3** with Ac_2O/Py afforded (+)-4′,4″-O-dibenzyllariciresinol 3a-acetate (**4**) in 83% yield. Debenzylation of **4** was carried out using Pd–C (10%)/$HCOONH_4$ [9] to give the title compound **1** in 86% yield. Thus, **1** was obtained in 66% overall yield starting from **2** in three steps (Scheme 1). The spectral data of synthetic **1** agree well with those reported for natural **1** [5].

EXPERIMENTAL SECTION

General Experimental Procedures

Melting points were recorded on a MEL Temp apparatus and are uncorrected. IR spectra were measured on a Perkin-Elmer 1600 FT-IR spectrometer. ^{1}H NMR spectra were recorded on a Bruker 400 MHz NMR spectrometer and Mass spectra on VG micromass 70-70H spectrometer. Optical rotations were measured on a Jasco DIP-370 polarimeter. TLC was carried out on silica gel (ACME) layers.

(+)-*4′,4″-O-Dibenzyllariciresinol* (**3**) A mixture of (+)-lariciresinol (**2**) (50 mg, 0.14 mmol), benzyl bromide (100 mg, 0.58 mmol), potassium carbonate (100 mg, 0.72 mmol) and acetone (3 ml) was heated under reflux for 6 h. After the completion of reaction, K_2CO_3 was filtered off and the solvent was evaporated. The residue obtained was recrystallized from petroleum ether and ethyl acetate to give **3** (70 mg, 93%), m.p. 78–80°C; $[\alpha]_D^{25}$: +23.4

(c 0.35, $CHCl_3$); IR (KBr) ν_{max} 3437, 1606, 1514, 1262 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 2.30–2.92 (4H, m), 3.65–3.78 (3H, m), 3.83 (3H, s), 3.86 (3H, s), 3.97–4.06 (1H, m), 4.74 (1H, d, $J = 8.0$ Hz), 5.07 (2H, s), 5.10 (2H, s), 6.60–6.86 (6H, m), 7.25–7.43 (10H, m).

(+)-*4′,4″-O-Dibenzyllariciresinol 3a-acetate* (**4**) A mixture of **3** (60 mg, 0.11 mmol), acetic anhydride (0.4 mL) and pyridine (0.4 mL) was stirred at room temperature for 12 h. The reaction mixture was then quenched with cold water (10 mL) and extracted with ethyl acetate. The organic layer was washed with brine and water, successively and dried over anhydrous Na_2SO_4. The residue obtained after the removal of the solvent was purified by column chromatography over silica gel using mixtures of petroleum ether and ethyl acetate (95 : 5) as eluent to give **4** (54 mg, 83%), m.p. 86–88°C; $[\alpha]_D^{25}$: +11.5 (c 0.33, $CHCl_3$); IR (KBr) ν_{max} 1736, 1509, 1245 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.99 (3H, s, 3a-$OCOCH_3$), 2.50–2.57 (2H, m, H-3, H_A-4a), 2.73 (1H, m, H-4), 2.83 (1H, dd, $J = 13.4$, 4.9 Hz, H_B-4a), 3.73 (1H, dd, $J = 7.7$ Hz, H_A-5), 3.88 and 3.90 (each 3H, s, 3′,3″-OCH_3), 4.06 (1H, dd, $J = 8.5$, 6.7 Hz, H_B-5), 4.18 (1H, dd, $J = 11.2$, 7.2 Hz, H_A-3a), 4.34 (1H, dd, $J = 11.2$, 7.2 Hz, H_B-3a), 4.77 (1H, d, $J = 6.4$ Hz, H-2), 5.13 and 5.15 (each 2H, s, 4′,4″-$OC\underline{H}_2Ph$), 6.65 (1H, m, H-6″), 6.71 (1H, d, $J = 1.4$ Hz, H-2″), 6.78 (1H, m, H-6′), 6.81 (1H, d, $J = 8.2$ Hz, H-5″), 6.84 (1H, d, $J = 8.3$ Hz, H-5′), 6.89 (1H, d, $J = 1.4$ Hz, H-2′), 7.29–7.45 (10H, m, 4,4″-$OCH_2C_6\underline{H}_5$).

(+)-*Lariciresinol 3a-acetate* (**1**) To a stirred solution of **4** (50 mg, 0.086 mmol) in dry acetone (10 mL) were added ammonium formate (100 mg) and Pd–C (10%, 100 mg). The contents were refluxed for 2 h. The catalyst was filtered off and the solvent was evaporated. The residue obtained was purified by column chromatography over silica gel using mixtures of petroleum ether and ethyl acetate (99 : 5) to give **1** (30 mg, 86%) as liquid, $[\alpha]_D^{25}$: +45.6 (c 0.05, $CHCl_3$); IR (KBr) ν_{max} 3421, 1732, 1515, 1240 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.01 (3H, s, 3a-$OCOCH_3$), 2.52 (1H, dd, $J = 13.4$, 2.4 Hz, H_A-4a), 2.56 (1H m, H-3), 2.71 (1H, m, H-4), 2.83 (1H, dd, $J = 13.4$, 5.0 Hz, H_B-4a), 3.73 (1H, dd, $J = 8.5$, 6.8 Hz, H_A-5), 3.88 and 3.89 (each 3H, s, 3′,3″-OCH_3), 4.06 (1H, dd, $J = 8.5$, 6.8 Hz, H_B-5), 4.18 (1H, dd, $J = 11.2$, 7.2 Hz, H_A-3a), 4.35 (1H, dd, $J = 11.2$, 7.2 Hz, H_B-3a), 4.76 (1H, dd, $J = 6.4$ Hz, H-2), 5.53 and 5.61 (each 1H, brs, 4′,4″-OH), 6.66 (1H, brs, H-2″), 6.68 (1H, m, H-6″), 6.80 (1H, m, H-6′), 6.84 (1H, d, $J = 8.2$ Hz, H-5″), 6.85 (1H, d, $J = 1.5$ Hz, H-2′), 6.88 (1H, d, $J = 8.1$ Hz, H-5′); EIMS *m/z* (%) [M^+] 402 (34), 342 (3), 219 (7), 205 (16), 151 (38), 137 (87), 94 (9), 83 (42), 43 (100).

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