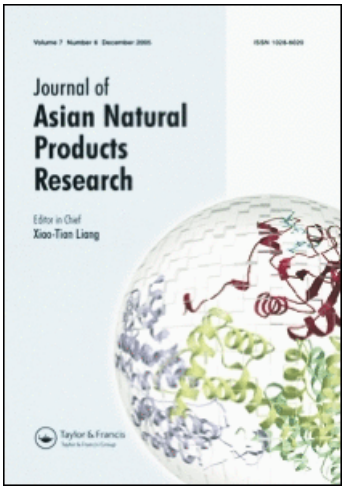

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Synthesis of Tetradecyl (E)-Ferulate, A Metabolite of *Jatropha gossypifolia*

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SYNTHESIS OF TETRADECYL (E)-FERULATE, A METABOLITE OF *JATROPHA GOSSYPIFOLIA*

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Tetradecyl (E)-ferulate (**1**) has been synthesized starting from vanillin in four steps with an overall yield of 48%.

Keywords: Tetradecyl (E)-ferulate; Phenylpropanoid; *Jatropha gossipifolia*

INTRODUCTION

Phenylpropanoids (C_6–C_3) are biosynthetic precursors for a variety of bioactive natural products, like flavonoids (C_6–C_3–C_6), lignans (C_6–C_3–C_3–C_6), coumarins (C_6–C_3), etc [1]. Phenylpropanoids also occur naturally and are reported to possess important biological activities like antioxidant [2,3], anthelmintic [4], plant growth inhibitor [5] etc. Tetradecyl (E)-ferulate (**1**) was isolated as one of the metabolites from the roots of *Jatropha gossypifolia* Linn. (Euphorbeaceae) [6]. Due to our interest on phenylpropanoids [7,8], we have synthesized **1**, and the results are reported in this note.

RESULTS AND DISCUSSION

Condensation of 3-methoxy-4-benzyloxybenzaldehyde (**3**) [9], obtained from vanillin (**2**), with malonic acid under Knoevenagel–Doebner conditions [10]

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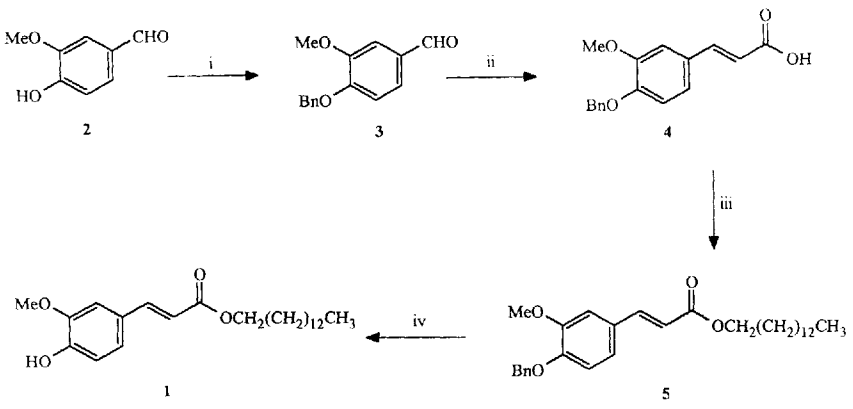

SCHEME 1 (i) BnBr, CH_3COCH_3, K_2CO_3, reflux, 4 h; 94%. (ii) $CH_2(COOH)_2$, pyridine, piperidine, Δ, 3 h; 94%. (iii) $SOCl_2$; 1-tetradecanol, Et_3N, DMAP; 80%. (iv) $AlCl_3$, N,N-dimethylaniline, 68%.

gave 3-methoxy-4-benzyloxycinnamic acid (**4**) in 94% yield. **4** was converted into the corresponding acid chloride with $SOCl_2$ and then esterified with 1-tetradecanol to give tetradecyl (E)-4-O-benzylferulate (**5**) in 80% yield. Debenzylation of **5** was carried out using $AlCl_3$ and N,N-dimethylaniline [11] to give the title compound **1** in 68% yield (Scheme 1). Thus, **1** was obtained starting from vanillin in four steps with an overall yield of 48%. The spectral data of synthetic **1** agree well with those reported for natural **1**.

EXPERIMENTAL SECTION

General Experimental Procedures

Melting points were determined 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 Varian Gemini 400 MHz or Jeol JNM EX 90 MHz NMR spectrometer and Mass Spectra on VG micromass 70-70H mass spectrometer. TLC was carried out on silica gel (ACME) layers. Petroleum ether is the fraction of b.p. 60–80°C.

3-Methoxy-4-benzyloxybenzaldehyde (**3**) A mixture of vanillin (**2**, 1.0 g, 6.5 mmol), benzyl bromide (1 ml, 8.4 mmol), potassium carbonate (1.8 g, 13.0 mmol) and acetone (15 ml) was heated under reflux for 4 h. After the completion of reaction, the solid was filtered off and the solvent was evaporated. The residue obtained was recrystallized from petroleum ether and ethyl acetate to give **3** (1.5 g, 94%), m.p. 60–62°C (Ref. [9] m.p. 60–62°C)

IR (KBr) ν_{max} 2839, 2761, 1675 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz): δ 3.95 (3H,s), 5.24 (2H,s), 6.92–7.59 (8H,m), 9.83 (1H,s).

3-Methoxy-4-benzyloxycinnamic acid (**4**) A mixture of **3** (1 g, 4.1 mmol), malonic acid (1.2 g, 11.5 mmol), pyridine (2.5 ml, 31 mmol) and piperidine (0.25 ml) was heated on a water bath for 3 h. The reaction mixture was poured into excess of dilute HCl (20 ml, 2.0 N). The precipitated solid was filtered and recrystallized from methanol to give **4**, (1.1 g, 94%), m.p.189–190°C (Ref. [9] m.p. 189–191°C). IR (KBr) ν_{max} 2939, 1672 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz): δ 3.94 (3H,s), 5.21 (2H,s), 6.33 (1H, d, $J = 15.8$ Hz), 6.78–7.90 (9H,m).

Tetradecyl (E)-4-O-benzylferulate (**5**) 3-Methoxy-4-benzyloxycinnamoyl chloride was prepared from **4** (0.5 g, 1.2 mmol) using thionyl chloride (0.2 ml, 2.5 mmol) by refluxing on a water bath for 30 min, and the excess thionyl chloride was removed under vacuum.

To a mixture of 1-tetradecanol (0.3 g, 1.2 mmol), triethylamine (1 ml, 7.2 mmol), and CH_2Cl_2 (10 ml) and a catalytic amount of DMAP at room temperature, was added the solution of 3-methoxy-4-benzyloxycinnamoyl chloride (0.36 g, 1.2 mmol) in CH_2Cl_2 (3 ml) dropwise for about 20 min under stirring. After two more hours, the reaction mixture was diluted with ethyl acetate (50 ml) and washed with saturated sodium bicarbonate solution, brine and water, successively and dried over Na_2SO_4. The residue obtained after removal of the solvent was purified further by column chromatography over silica gel using mixtures of petroleum ether and ethyl acetate (97 : 3) as eluant to give **5** (0.49 g, 80%), as a low melting solid, IR (KBr) ν_{max} 1739, 1470, 1194 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$): δ 0.90 (3H, t, $J = 6.1$ Hz), 1.06–1.85 (24H,m), 3.92 (3H,s), 4.21 (2H, t, $J = 7.2$ Hz), 5.23 (2H,s), 6.31 (1H, d, $J = 15.8$ Hz), 6.79–7.51 (8H,m), 7.63 (1H, d, $J = 15.8$ Hz).

Tetradecyl (E)-ferulate (**1**) To a solution of **5** (0.2 g, 0.42 mmol) in N,N-dimethylaniline (0.15 g, 1.2 mmol) and CH_2Cl_2 (10 ml), was added anhydrous aluminium chloride (0.16 g, 1.2 mmol) at 0°C and the reaction allowed to continue at the same temperature for further 30 min. The reaction mixture was then allowed to warm up to room temperature and continued for 2 h. After completion of the reaction, the reaction mixture was quenched with dilute HCl (5 ml, 1.0 N) and extracted with ethyl acetate (20 ml), the organic layer was washed with saturated sodium bicarbonate solution, brine and water successively, dried and the solvent was evaporated. The residue obtained was chromatographed over silica gel column using mixtures of petroleum ether and ethyl acetate (95 : 5) as eluant to give **1** (0.11 g, 68%), m.p. 65–66°C (Ref. [6] m.p. 65–66°C); IR (KBr) ν_{max} 3536, 1688, 1624,

1597 cm^{-1}; ^1H NMR ($CDCl_3$ 270 MHz): δ 0.87 (3H, t, $J = 6.6$ Hz), 1.20–1.50 (22H,m), 1.70 (2H,m), 3.92 (3H,s), 4.18 (2H, t, $J = 6.6$ Hz), 5.87 (1H,brs), 6.29 (1H, d, $J = 15.8$ Hz), δ 6.91 (1H, d, $J = 7.4$ Hz), 7.04 (1H, dd, $J = 7.4, 2$ Hz), 7.09 (1H, d, $J = 2$ Hz), 7.60 (1H, d, $J = 15.8$ Hz): ^{13}C NMR ($CDCl_3$, 67.8 Hz): δ 167.4, 147.9, 146.7, 144.6, 127.0, 123.0, 115.7, 114.7, 109.3, 64.6, 55.9, 31.9, 28.8–31.1 (9C), 26.0, 22.7, 14.1; EIMS *m/z* $[M]^+$ 390(75), 194(100), 177(46), 150(18), 137(12) and 43(20).

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