A short synthesis of trans-3-methoxy-4,5-methylenedioxyxycinnamaldehyde, a metabolite of Cassia grandis

Dodda Rajasekhar & Gottumukkala V Subbaraju* Department of Chemistry, School of Mathematical and Physical Sciences, Sri Venkateswara University, Tirupati 517502, India

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Claisen-Schmidt reaction of 3-methoxy-4,5-methylenedioxybenzaldehyde 2 with acetaldehyde affords the trans-3-methoxy-4,5-methylenedioxyxycinnamaldehyde 1, a metabolite of Cassia grandis, in 12% yield. Compound 2 could also be converted into 1, via the reaction with triethyl phosphonoacetate followed by reduction with LAH and oxidation with MnO₂ in 40% overall yield.

trans-3-Methoxy-4,5-methylenedioxyxycinnamaldehyde 1 has been reported recently¹ as a new natural product from Cassia grandis. Due to our interest in compounds having C₆-C₃ units², we report herein the synthesis of 1.

Condensation of 3-methoxy-4,5-methylenedioxybenzaldehyde 2 with freshly prepared acetaldehyde³ in the presence of aq. NaOH (10%) at 0°C afforded 1 (Scheme I) in 12% yield. The low yield of this reaction product is, perhaps, due to self-condensation of acetaldehyde.

In an alternative approach, 2 was condensed with triethyl phosphonoacetate and the resulting ethyl ester 3 reduced with LAH following the literature procedure⁴. The cinnamyl alcohol 4 so obtained was oxidised with MnO₂⁵ to give 1 in an overall yield of 40% starting from 2.

The spectral data of synthetic 1, obtained as above, were identical with those reported for natural 1.

Gonzalez et al.¹ have claimed 1 as a new compound, but, we have found during our literature survey that 1 was isolated earlier from the bark of Canella winterana by El-Feraly and Hoffstetter⁷. We have also found that the data reported⁶ for cis-3-methoxy-4,5-methylenedioxyxycinnamaldehyde 5, isolated from Piper auritum corroborates well with those of 1. The coupling constants (J=15 Hz) of the olefinic protons reported for 5 are untenable for a cis-isomer. Therefore, 5 may also be a trans-isomer and identical to 1.

It may be noted that 1 was prepared earlier by converting 2 into cinnamic acid followed by reaction with SOCl₂ and reduction with bis(triphenylphosphine)tetrabhydroborate copper (I)⁸.

Experimental Section

trans-3-Methoxy-4, 5-methylenedioxyxycinnamaldehyde 1: Method-I. To a mixture of 3-methoxy-4,5-methylenedioxybenzaldehyde 2 (90 mg, 0.5 mmole) and acetaldehyde (236 mg, 5.4 mmoles) at -10°C was added 0.3 mL of aq. NaOH (10%) dropwise and allowed the contents slowly to warm up to 0°C and continued the reaction for 30 hr. Thereafter the reaction mixture was diluted with water (5 mL) and extracted with chloroform. The chloroform layer was washed with water and solvent removed. The residue obtained was chromatographed over silica gel using mixtures of pet. ether (60-80°C) and ethyl acetate for elution to give 1 (12 mg, 11.6%) as a colourless solid, mp 136-137°C (Lit.⁷ 136-139°C); UV (MeOH): 241 and 335 nm; IR (KBr): 1695, 1678, 1639, 1069 and 815 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz): δ 3.94 (3H, s), 6.06
(2H, s), 6.57 (1H, dd, J=15.8, 7.7 Hz), 6.75 (1H, s), 6.78 (1H, s), 7.35 (1H, d, J=15.9 Hz) and 9.65 (1H, d, J=7.6 Hz); MS (%): m/z 206 (100.0, M⁺), 178 (57.5), 105 (34.0) and 77 (38.0).

Method-2. A mixture of 2 (180 mg, 1 mmole), triethyl phosphonoacetate (0.24 mL, 1.2 mmoles) and anhydrous K₂CO₃ (300 mg, 2.17 mmolcs) was treated with water (0.2 mL) dropwise at room temperature and then heated at 90 °C for 6 hr. Usual work-up followed by recrystallisation of the residue from n-hexane gave ethyl 3-methoxy-4,5-methyleneoxycinnamate 3 as a colourless solid (205 mg, 82%), mp 74-76 °C (Lit. 576 °C); ¹H NMR (CDCl₃, 300 MHz): δ 1.33 (3H, t, J=7.1 Hz), 3.92 (3H, s), 4.25 (2H, q, J=7.1 Hz), 6.02 (2H, s), 6.27 (1H, d, J=15.9 Hz), 6.70 (1H, s), 6.74 (1H, s) and 7.57 (1H, d, J=15.9 Hz).

A solution of 3 (120 mg, 0.48 mmole) in dry ether (10 mL) at -15 °C under nitrogen, was treated with LAII (60 mg, 1.6 mmoles) in portions over 30 min and continued the reaction for 3 hr. Usual work-up followed by recrystallisation from CCl₄ gave 3-methoxy-4, 5-methyleneoxycinnamyl alcohol 4 as a yellow solid (80 mg, 80%), mp 81-82°C (Lit. 3 77-81°C); ¹H NMR (CDCl₃, 300 MHz): δ 3.91 (3H, s), 4.30 (2H, dd, J=1.2, 5.9 Hz), 5.97 (2H, s), 6.22 (1H, dt, J=5.9, 15.7 Hz), 6.50 (1H, d, J=15.7 Hz), 6.54 (1H, bs) and 6.62 (1H, bs).

A solution of 4 (60 mg, 0.29 mmole) in dry pet. ether (40-60°C, 10 mL) was treated with MnO₂ (200 mg) at room temperature for 24 hr. The unreacted MnO₂ was filtered off, and the removal of solvent from the filtrate gave a residue which on chromatography over silica gel gave 1 (36 mg, 60%) as a colourless solid, mp 138-39°C.

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References