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Short Note

(*E*)-1-(2-Hydroxy-4,6-dimethoxyphenyl)-3-[4-methoxy-3-(3-methylbut-2-en-1-yl)phenyl]prop-2-en-1-one

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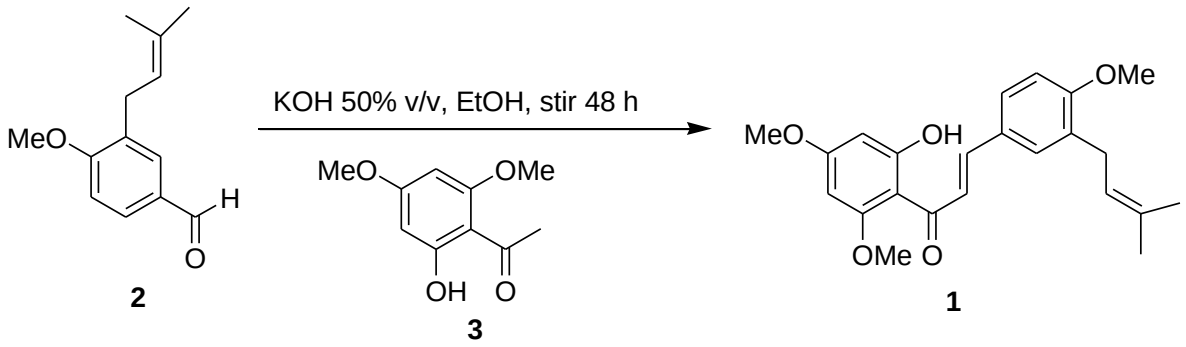
Abstract: A novel prenylated chalcone, (*E*)-1-(2-hydroxy-4,6-dimethoxyphenyl)-3-[4-methoxy-3-(3-methylbut-2-en-1-yl)phenyl]prop-2-en-1-one was synthesized and the structure of the title compound was established by ^{1}H and ^{13}C nuclear magnetic resonance (NMR), mass spectrometry (MS) and Fourier transform infrared (FT-IR) spectroscopy.

Keywords: chalcone; Claisen-Schmidt condensation; prenyl

1. Introduction

Prenylated chalcones are associated with a variety of biological activities such as anti-malarial [1], antidiabetic [2], antifungal [3], antibacterial [4], antitumor [5], antioxidative [6] and anti-inflammatory [7] activities. Most of the above activities are influenced by the substitution of the flavonoid ring system with prenyl groups which increases the lipophilicity and confers the molecule a strong affinity to biological membranes [8]. These findings have prompted interest in the synthesis of naturally and non-naturally occurring prenylated flavonoids.

As part of our ongoing program on the studies of prenylated flavanoids [9], we report herein a facile synthetic approach in the synthesis of (*E*)-1-(2-hydroxy-4,6-dimethoxyphenyl)-3-[4-methoxy-3-(3-methylbut-2-en-1-yl)phenyl]prop-2-en-1-one **(1)**. This prenylated chalcone is synthetically new and has not yet been isolated or reported elsewhere.



2. Synthesis

The starting material, 4-methoxy-3-(3-methylbut-2-enyl)benzaldehyde **(2),** was prepared according to the reported method [10]. Claisen-Schmidt condensation reaction of 4-methoxy-3-(3-methylbut-2-enyl)benzaldehyde **(2)** with compound **(3)** in aqueous/ethanolic solution by the action of potassium hydroxide-water-ethanolic [11] gave the desired chalcone in good yield (52.2%) with a melting point of 120–122 ℃ as a yellow crystalline solid. The structure of the compound was confirmed by IR, NMR (^{1}H and ^{13}C) and MS.

3. Experimental

Melting points were recorded on a Leica Galen III Kofler micro melting point apparatus and are uncorrected. Infrared (IR) spectra were recorded on a Perkin-Elmer series 1600 spectrometer as thin film (NaCl windows) for liquid samples or KBr pellet for solid samples. Mass spectral data were recorded on a Thermo Scientific LTQ Orbitrap Discovery LCMS. The ^{1}H and ^{13}C NMR spectra (300 and 75 MHz, respectively) were recorded on a Bruker Avance 300 spectrometer using $CDCl_3$ and acetone-d_6 as solvent. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.2 mm Merck pre-coated silica gel plates (60 F_{254}).

3.1. (E)-1-(2-Hydroxy-4,6-dimethoxyphenyl)-3-[4-methoxy-3-(3-methylbut-2-en-1-yl)phenyl]prop-2-en-1-one **(1)**

To a solution of 2-hydroxy-4,6-dimethoxyacetophenone **(3)** (100 mg, 0.39 mmol) and 4-methoxy-3-(3-methylbut-2-enyl)benzaldehyde **(2)** (100 mg, 0.43 mmol) in ethanol (10 mL) was added a 50% v/v aq. solution of KOH (0.8 mL). The mixture was then stirred at rt for 48 h. The mixture was poured into ice-water, acidified to pH ~5 with HCl (10%) (5 mL), and extracted with dichloromethane. The organic layer was washed with water and brine, dried over anhydrous $MgSO_4$, and evaporated under reduced pressure. The residual orange syrup was chromatographed on a silica gel column (PE:EtOAc, 9:1) to afford the title compound **(1)** (195 mg, 52.2%) as a yellow crystalline solid; R_f 0.52 (PE:EtOAc, 4:1).

m.p. 120–122 ℃

IR ν_{max} (KBr) cm^{-1}: 1619 (C=O), 1581 & 1440 (C=C aromatic), 1158 (C-O)

^{1}H NMR (acetone-d_6) δ_H ppm: 1.76 (3H, s, H-4"), 1.77 (3H, s, H-5"), 3.35 (2H, d, *J* = 7.5 Hz, H-1"), 3.88 (3H, s, OCH_3), 3.92 (3H, s, OCH_3), 4.0 (3H, s, OCH_3), 5.36 (1H, m, H-2″), 6.10 (1H, d, *J* = 2.4 Hz, H-3'), 6.13 (1H, d, *J* = 2.4 Hz, H-5'), 7.04 (1H, d, *J* = 8.4 Hz, H-5), 7.55–7.58 (2H, m, with unresolved couplings due to overlapping, H-2 and H-6), 7.77 (1H, d, *J* = 15.6 Hz, H-α), 7.91 (1H, d, *J* = 15.6 Hz, H-β), 14.40 (1H, s, OH)

^{13}C NMR (acetone-d_6) δ_C ppm: 17.33 (C-5", CH_3), 25.46 (C-4", CH_3), 28.5 (C-1", CH_2), 55.51 (OCH_3), 55.57 (OCH_3), 55.97 (OCH_3), 90.51 (C-1', C-4 ٩), 91.31 (C-5', C-H), 94.13 (C-3', C-H), 111.03 (C-5, C-H), 122.43 (C-2", C-H), 125.07 (C-α, C-H), 128.12 (C-3, C-4 ٩), 129.06 (C-6, C-H), 129.27 (C-2, C-H), 130.79 (C-1, C-4 ٩), 132. 83 (C-3", C-4 ٩), 143.21 (C-β, C-H), 159.91 (C-2', C-4 ٩), 163.14 (C-4, C-4 ٩), 166. 80 (C-6', C-4 ٩), 168.66 (C-4', C-4 ٩), 192.78 (C=O, C-4 ٩)

ESI-FTMS: *m/z* 383.25687 $[M+H]^+$, $C_{23}H_{27}O_5$ requires 383.18585

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