Molbank **2015**, M852; doi:10.3390/M852

OPEN ACCESS

molbank

ISSN 1422-8599

www.mdpi.com/journal/molbank

Short Note

N-benzyl-(3*E*,5*E*)-3,5-bis(2-hydroxybenzylidene)-4-piperidone

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Academic Editor: Norbert Haider

Received: 23 February 2015 / Accepted: 31 March 2015 / Published: 2 April 2015

Abstract: A novel *N*-benzyl-(3*E*,5*E*)-3,5-bis(2-hydroxybenzylidene)-4-piperidone (**3**), was synthesized in good yield by a condensation reaction of 2-hydroxybenzaldehyde (**1**) and *N*-benzyl-4-piperidone (**2**) under microwave irradiation in the presence of 10% NaOH solution. The chemical structure was assigned on the basis of UV-visible, IR, ^{1}H-NMR, ^{13}C-NMR and mass spectral data.

Keywords: curcumin; *N*-benzyl-4-piperidone; *N*-benzyl-(3*E*,5*E*)-3,5-bis(2-hydroxybenzylidene)-4-piperidone

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Curcumin (diferuloylmethane) is an orange-yellow and dietary polyphenolic phytochemical in turmeric (*Curcuma longa*). In recent decades, curcumin has been shown to exhibit antioxidant [1], anti-inflammatory [2], antiviral [3], antibacterial [4] effects, and thus has potential use against various

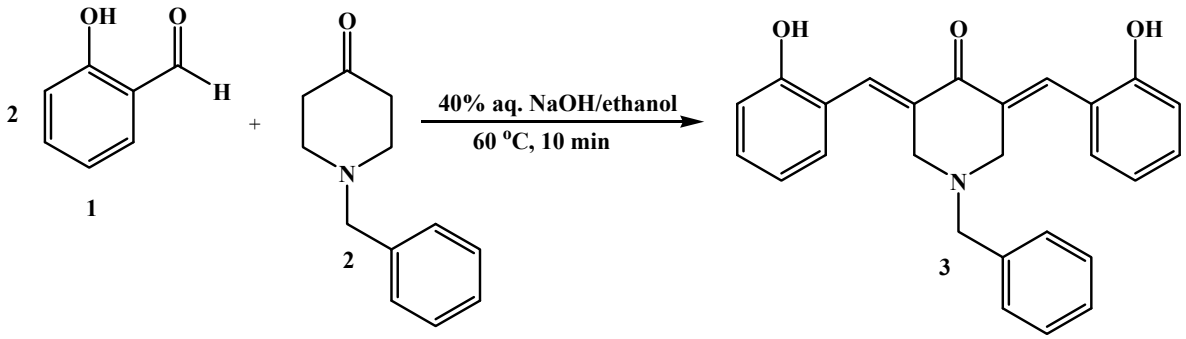
malignant cancers, diabetes, allergies, arthritis and other chronic illnesses [5–8]. For the purpose of finding novel derivatives with increased systemic bioavailability and enhanced pharmacological activity [9], chemical modifications as well as synthesis of curcumin analogues have been attempted by many research groups to find a better treatment for various diseases [9,10]. Analogous compounds to (*E*)-3,5-bis(benzylidene)-4-piperidones presented noteworthy cytotoxic activity against leukimia cell lines and colon cancer among others [11]. Different substituents with opposing electronic properties in the benzene rings were designed to investigate and discuss the structure–activity relationship [12]. During the course of our continuing search for novel curcumin analogues, we synthesized and characterized 3,4-bis(2-hydroxybenzylidene)-4-piperidone [13]. In this work, we prepared and characterized *N*-benzyl-(3*E*,5*E*)-3,5-bis(2-hydroxybenzylidene)-4-piperidone.

Experimental Section

Synthesis of N-Benzyl-(3E,5E)-3,5-bis(2-hydroxybenzylidene)-4-piperidone (**3**)

Melting points were determined on an Electrothermal melting point apparatus and are uncorrected. The UV spectra were obtained on a UV Ultraspec 3000 Pro spectrophotometer. The IR spectra were recorded on a Perkin-Elmer 1760X FT-IR (Waltham, MA, USA) in KBr. The mass spectra were recorded with a JEOL JMS-700 (Tokyo, Japan) and a SynaptG2 mass spectrometer (Waters, Milford, MA, USA). ^{1}H and ^{13}C-NMR spectra were recorded with an Agilent DD2 system (Santa Clara, CA, USA) operating at 500 (^{1}H) and 125 (^{13}C) MHz, using residual (δ_H 7.26) and deuterated solvent (δ_C 77.0) peaks of $CDCl_3$ as reference standards. For synthesis used Mas-II Sineo Microwave. Chromatographic separations were carried out on silica gel 60 (Merck, Darmstadt, Germany). TLC plates were precoated with silica GF_{254} (Merck, 0.25 mm) and detection was achieved by spraying with 10% H_2SO_4 in ethanol, followed by heating.

The title compound was synthesized by mixing the corresponding *N*-benzyl-4-piperidone (1.89 g, 0.01 mol), 2-hydroxybenzaldehyde (2.44 g, 0.02 mol), 40% aq. NaOH (0.7 mL) and 95% EtOH (5 mL) and was stirred at room temperature for 30 minutes, according to the partially modified procedure of a previous report [9], as shown in Scheme 1. The reaction mixture was subjected to microwave irradiation for 3 min at a power of 180 W and temperature of 60 °C. The reaction product was cooled and cold water was added. The precipitate formed was filtered and recrystallized from mixture of ethyl acetate–methanol to afford **3** (3.58 g, 90%) as an orange crystal, m.p: 143–144 °C. UV (MeOH) λ_{max}: 306 nm (ε 4,600) and 357 nm (ε 5,200).



Scheme 1. The synthesis of *N*-benzyl-(3*E*,5*E*)-3,5-bis(2-hydroxybenzylidene)-4-piperidone.

IR (KBr) ν_{max} cm^{-1}: 3235, 3064, 1706, 1661 and 1604.

^{1}H-NMR (Agilent DD2, 500 MHz, $CDCl_3$): δ (ppm) 8.90 (2H, s), 8.00 (2H, s), 7.40 (2H, d, *J* = 8.0 Hz), 6.90 (2H, d, *J* = 7.5 Hz), 6.80 (2H, d, *J* = 8.0 Hz), 6.70 (2H, d, *J* = 7.5 Hz), 3.83 (2H, s), 3.71 (4H, s).

^{13}C-NMR (125 MHz, $CDCl_3$): δ (ppm) 187.4, 157.6, 139.1, 134.0, 132.0, 131.3, 131.0, 129.8, 129.1, 127.9, 123.4, 120.1, 116.6, 62.1, 55.6.

HR-ESI-TOFMS: calculated for $C_{26}H_{24}NO_3$ *m/z* 398.1756, found $[M + H]^+$, *m/z* 398.1750.

Acknowledgments

This research was partially supported by Directorate General of Higher Education, Ministry of Educatioan and Culture, Indonesia (2012-2013, by YE).

Author Contributions

Unang Supratman and Adel Zamri designed the whole experiment and contributed to the manuscript. Yoshihito Shiono measured the NMR and HR-ESI-TOFMS spectra. Yum Eryanti and Tati Herlina synthesize a new curcumin analog and wrote the manuscript. Khalijah Awang and Siti Nadiah Abdul Halim analyzed the NMR and HR-ESI-TOFMS spectra. All authors read and approved the final manuscript.

Conflicts of Interest

The authors declare no conflict of interst.

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