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Short Note

N-{4-[(2*E*)-3-(2*H*-1,3-Benzodioxol-5-yl)prop-2-enoyl]phenyl}quinoline-3-carboxamide

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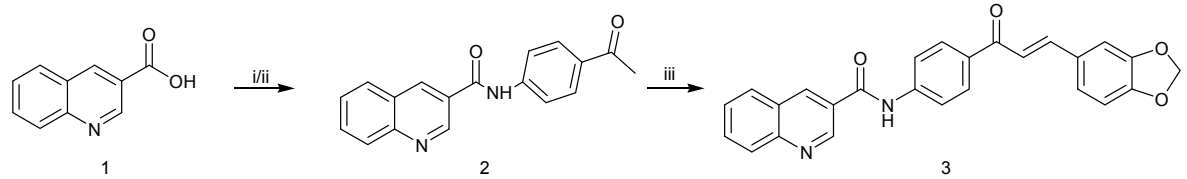
Abstract: An amide chalconehas been synthesized in a two-step reaction. First, *N*-(4-acetylphenyl) quinoline-3-carboxamide **2** was synthesized by the reaction of quinoline-3-carboxylic acid **1** and thionyl chloride ($SOCl_2$), following the addition of 4-aminoacetophenone. Then, a typical Claisen–Schmidtreactionwas made between **2** and piperonal using KOH solution as a catalystin ethanol, under ultrasonic irradiation. The structure of the target compound was established by FTIR (Fourier-transform infrared spectroscopy), HRMS, ^{1}H and ^{13}C-NMR.

Keywords: quinoline; amide; chalcone

1. Introduction

Chalcones, or 1,3-diaryl-2-propen-1-ones, are a class of polyphenolic compounds belonging to the flavonoid family which possess a wide range of pharmacological activities, including anti-cancer [1], anti-infective [2], anti-diabetic [3], and anti-oxidant [4] activities. These one compounds are obtained by means of the Claisen–Schmidt condensation reaction between aldehydes and ketones using basic or acidic catalysis [5]. On the other hand, Quinoline derivatives have a wide range of biological activity, depending mainly on the nature and position of the substituents. Antimalarial [6], antitumor [7], antibacterial [8], and anti-oxidant [9] properties are reported in theliterature. In continuation of our search for heterocycles with structural diversity, the fusion of both chemical nuclei may be of interest for later studies of bioactivity.

The synthesis of the compounds **2** and **3** was realized by a cascade reaction of quinoline-3-carboxylic acid **1** and thionyl chloride ($SOCl_2$), following the addition of 4-aminoacetophenone to give the compound **2**, and then a Claisen–Schmidt reaction was made between **2** and piperonal using KOH solution as a catalyst in ethanol, under ultrasonic irradiation to give the compound **3**, as presented in Scheme 1. The structure of compounds was confirmed by ^{1}H and ^{13}C-NMR, mass spectral data, IR spectra, and all data are in concordance with the assumed structure.



Scheme 1. The synthesis of *N*-{4-[(2*E*)-3-(2*H*-1,3-benzodioxol-5-yl)prop-2-enoyl]phenyl}quinoline-3-carboxamide.

Previously, Dehmel et al. [10] used the intermediary **2** for the construction of trithiocarbonates as HDAC (Histone deacetylase) Inhibitors.

2. Experimental Section

2.1. General Information

Chemical reactive for synthesis was obtained from Sigma-Aldrich, solvents were reagent grade and, in most cases, dried and distilled before use according to standard procedures. Reaction progress was monitored by TLC (thin-layer chromatography) on silica gel GF254 aluminum sheets (0.25 mm) using various developing systems. Spots were detected under UV light (λ 254 nm). ^{1}H and ^{13}C-NMR spectra (400 MHz for proton and 100 MHz for carbon) were recorded on an AM-400 spectrometer (Bruker, Rheinstetten, Germany); IR spectra (KBr pellets, 500–4000 cm^{-1}) were recorded on a NEXUS 670 FT-IR spectrophotometer (Thermo Nicolet, Madison, WI, USA).Melting points (uncorrected) were measured on a Electrothermal IA9100 melting point apparatus (Stone, Staffs, UK). High-resolution mass spectrometry ESI-MS and ESI-MS/MS analyses were conducted in a high-resolution hybrid quadrupole (Q) and orthogonal time-of-flight (TOF) mass spectrometer (Waters/Micromass Q-TOF micro, Manchester, UK) with a constant nebulizer temperature of 100 °C.

2.2. Synthesis of Compound 3: N-{4-[(2E)-3-(2H-1,3-Benzodioxol-5-yl)prop-2-enoyl]phenyl}quinoline-3-Carboxamide

A mixture of commercial carboxylic acid **1** in freshly distilled thionyl chloride was warmed to reflux for 3 h, then cooled to room temperature and evaporated under vacuum to dryness to afford quantitatively corresponding acid chlorides. This crude material might be used without further purification. A mixture of acid chloride (1.0 equiv) and 4-aminoacetophenone (1.0 equiv) in toluene (10 mL) was stirred at room temperature for 2 h and then treated with $NaHCO_3$ solution. The biphasic solution was vigorously stirred for 30 min, then decanted, and finally separated. The collected aqueous phase was extracted with EtOAc (2 × 10 mL). The combined organic layer was dried over Na_2SO_4 and evaporated. The solid was washed with cold water and crude material was crystallized into ethanol to afford the compound **2** (90%).

A mixture of *N*-(4-acetylphenyl)quinoline-3-carboxamide **2** (0.3 g, 1 mmol), piperonal (0.15 g, 1 mmol), 20% KOH aqueous solution (0.5 mL), and 96% EtOH (5 mL), was sonicated for 20 min in the water bath of an ultrasonic cleaner bath. The progress of the reaction was monitored by TLC using dichlorometane:ethyl acetate (9:1 *V*/*V*) as eluent. The reaction mixture was cooled in an ice-water bath. The formed precipitate was filtered, washed with cool water and purified by recrystallization from ethanol.The ultrasonic irradiation was performed by using a Branson ultrasonic cleaner bath, model 1510, 115 V, 1.9 L with a mechanical timer (60 min with continuous hold) and heater switch, 47 kHz. These procedures give the compound **3** (92%). Yelow solid; m.p. = 237–239 °C; IR (KBr) υ_{max} cm^{-1}: 3480 (NH), 1666 (C=O), 1597, 1242 (CO);^{1}H-NMR (400 MHz, $CDCl_3$) δ: 6.10 (s, 2H),6.99 (d, *J* = 8.0 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.66 (s, 1H), 7.69–7.72 (m, 2H), 7.83 (s, 1H), 7.88–7.90 (m, 1H), 8.01 (d, *J* = 8.0 Hz, 2H), 8.13 (dd, *J* = 8.0, 16.8 Hz, 2H), 8.21 (d, *J* = 8.0 Hz, 2H), 9.00 (s, 1H), 9.39 (s, 1H), 10.93 (bs, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$);102.0 (CH_2), 107.3 (CH), 108.9 (CH), 120.7 (CH), 121.7 (CH), 125.9 (CH), 127.3 (C), 127.4 (CH), 129.1 (CH × 2), 129.5 (CH × 2), 130.0 (CH × 2), 130.9 (CH), 135.9 (CH), 143.0 (CH), 148.5 (C), 148.6 (C), 149.7 (C), 150.8 (C), 165.9 (C), 187.4 (C); HRMS (ESI): $[M + H]^+$ calculated for $C_{26}H_{19}N_2O_4$ = 423.1345; found 423.1332.

Supplementary Materials: The following are available online at www.mdpi.com/1422-8599/2017/4/M960, ^{1}H and ^{13}C-NMR spectra for compounds **2** and **3** are available online.

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Conflicts of Interest: The authors declare no conflict of interest.

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