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Short Note

6-[1-Acetyl-5-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazole-3-yl]-2(3*H*)-benzoxazolone

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Abstract: The title compound, 6-[1-acetyl-5-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]-2(3*H*)-benzoxazolone, was synthesized by condensation of 6-[3-(4-methoxyphenyl)-2-propenoyl]-2(3*H*)-benzoxazolone (**1**) and hydrazine hydrate in acetic acid in 84% yield. The structure of the target compound was confirmed using ^{1}H-NMR, ^{13}C-NMR, IR, MS, and elemental analysis.

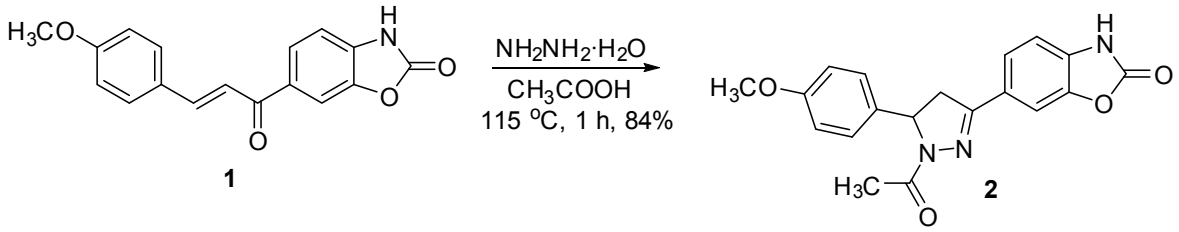
Keywords: chalcone; 2(3*H*)-benzoxazolone; pyrazole

1. Introduction

Chalcones are important compounds in medicinal chemistry, which exhibit diverse biological activities [1] and undergo a variety of chemical reactions that lead to several heterocyclic systems [2]. Pyrazole derivatives are also known to exhibit antimicrobial, antiviral, and anti-inflammatory activities [3–5]. In the present study we use a heterocyclic chalcone as an intermediate for the synthesis of a new compound with a pyrazole moiety.

2. Results

The synthesis of 6-[1-acetyl-5-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazole-3-yl]-2(3*H*)-benzoxazolone (**2**) (Scheme 1) was performed by reaction of 6-[3-(4-methoxyphenyl)-2-propenoyl]-2(3*H*)-benzoxazolone (**1**) with hydrazine hydrate. The reaction was carried out in acetic acid at 115 °C for 1 h and led to the formation of a single product in good yield.



Scheme 1. Synthesis of 6-[1-acetyl-5-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazole-3-yl]-2(3*H*)-benzoxazolone (**2**).

The structure of compound **2** was confirmed by ^{1}H and ^{13}C-NMR, IR, MS and elemental analysis and all data are in accordance with the proposed structure. The C=O stretching bands in IR spectra were seen at about 1610 cm^{-1} and 1780 cm^{-1}. In the ^{1}H-NMR spectrum the vinyl proton signals

characteristic of the starting chalcone **1** are replaced by three multiplets corresponding to the pyrazole protons in the range δ = 3.12–5.48 ppm. Aromatic protons are observed as doublets of doublets at δ = 6.87–7.68 ppm. Three singlet signals corresponding to the methyl, methoxy, and urethane groups are observed at 2.28, 3.71, and 11.9 ppm, respectively. The ^{13}C-NMR spectrum displays 17 signals corresponding to the total number of carbon atoms in compound **2**.

3. Experimental Section

3.1. General Information

All chemicals were purchased from Acros Organics (Geel, Belgium). 6-[3-(4-Methoxyphenyl)-2-propenoyl]-2(3*H*)-benzoxazolone (**1**) was synthesized as described previously [6,7]. Reactions and purity of the final compound were monitored by thin-layer chromatography (TLC) on silica gel plates (Kieselgel 60 F_{254}), using ethyl acetate/cyclohexane (3:2 *v*/*v*) as eluent.

Melting points were determined on a Boetius hot-stage microscope (Carl Zeiss Jena, Germany). IR spectrum (nujol) was recorded on a Specord 71 spectrometer (Carl Zeiss Jena, Germany). NMR spectra were recorded in DMSO-d_6 on a Bruker Avance III HD 500 (Bruker BioSpin GmbH, Rheinstetten, Germany), operating at 500 MHz for ^{1}H and at 125.8 MHz for ^{13}C. Chemical shifts are given in parts per million (δ) relative to the solvent peak. Coupling constants (*J*) were measured in hertz (Hz). Mass spectra were recorded on an Agilent 6890 system (Wilmington, DE, USA) with MSD 5973 (single quadrupol and electron ionization (EI) at 70 eV ionization), using a capillary column HP-5/MS (30 m × 0.250 mm × 0.25 μm). Carrier gas He was used at 0.8 mL/min. The temperature programmed mode was used (from 60 °C for 2 min, then with 10 °C/min to 300 °C for 10 min). The sample was introduced in splitless injection mode. The elemental analysis was carried on a "VARIO EL III Elemental analyzer" (Elementar Analysensysteme GmbH, Hanau, Germany) and the results for C, H, and N were within ±0.4% of the theoretical values.

3.2. Synthesis of 6-[1-Acetyl-5-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazole-3-yl]-2(3H)-benzoxazolone (**2**)

To a suspension of 6-[3-(4-methoxyphenyl)-2-propenoyl]-2(3*H*)-benzoxazolone (**1**, 295 mg, 1 mmol) in acetic acid (10 mL), hydrazine hydrate (200 mg, 4 mmol) was added. The reaction mixture was refluxed for 1 h, until the reaction was complete as monitored by TLC. The resulting yellow solution was poured on crushed ice. The crystalline product was filtered, washed with water, and dried.

Pale orange crystals. Yield: 84% (294 mg), m.p.: 275–277 °C (acetic acid). IR (nujol): 1610, 1780 (C=O) cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d_6): δ (ppm) 2.28 (s, 3H, CH_3), 3.12 (dd, 1H, pyrazoline, *J* = 18.0 Hz, *J* = 4.4 Hz), 3.71 (s, 3H, CH_3), 3.80 (dd, 1H, pyrazoline, *J* = 18.0 Hz, *J* = 12.0 Hz), 5.48 (dd, 1H, pyrazoline, *J* = 12.0 Hz, *J* = 4.3 Hz), 6.87 (d, 2H, arom. H, *J* = 8.7 Hz), 7.10 (d, 2H, arom. H, *J* = 8.7 Hz), 7.15 (d, 1H, arom. H, *J* = 8.1 Hz), 7.58 (dd, 1H, arom. H, *J* = 8.1 Hz, *J* = 1.5 Hz), 7.68 (d, 1H, arom. H, *J* = 1.3 Hz), 11.9 (brs, 1H, NH). ^{13}C-NMR (125.8 MHz, DMSO-d_6): δ (ppm) 21.8, 42.2, 55.1, 59.0, 107.4, 109.8, 114.0, 123.0, 125.3, 126.8, 132.3, 134.5, 143.6, 153.9, 154.4, 158.4, 167.2. Anal. calcd. for $C_{19}H_{17}N_3O_4$ (351.36): C, 64.95; H, 4.88; N 11.96. Found: C, 64.91; H, 4.79; N, 11.72. MS (EI): $[M]^+$ *m*/*z* = 351(56), $[M + 2]^+$ *m*/*z* = 353(3), 308(100), 294(8), 278(9), 264(6), 202(17), 191(12), 176(25), 161(4), 149(9), 134(15), 121(8).

Supplementary Materials: The following are available online, ^{1}H-, ^{13}C-NMR and MS spectra for compound **2**.

Author Contributions: O.P. and Y.I. designed the experiments; Y.I. and A.T. performed the experiments; O.P. and Y.I. analyzed the spectral data and wrote the manuscript; C.C. obtained the mass spectra. All authors read and approved the final manuscript.

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

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