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Short Note

1,4-Dihydro-4-(nitromethyl)-2-phenyl-1-tosylquinoline-3-carbaldehyde

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Academic Editor: Norbert Haider

Received: 26 October 2016; Accepted: 22 November 2016; Published: 30 November 2016

Abstract: An aza-Michael/Michael cascade reaction of 2-((*E*)-2-nitrovinyl)-*N*-tosylbenzenamine with 3-phenylpropiolaldehyde catalyzed by pyrrolidine has produced a new compound, 1,4-dihydro-4-(nitromethyl)-2-phenyl-1-tosylquinoline-3-carbaldehyde. The structure of the newly synthesized compound was determined using ^{1}H, ^{13}C-NMR, IR, and mass spectral data.

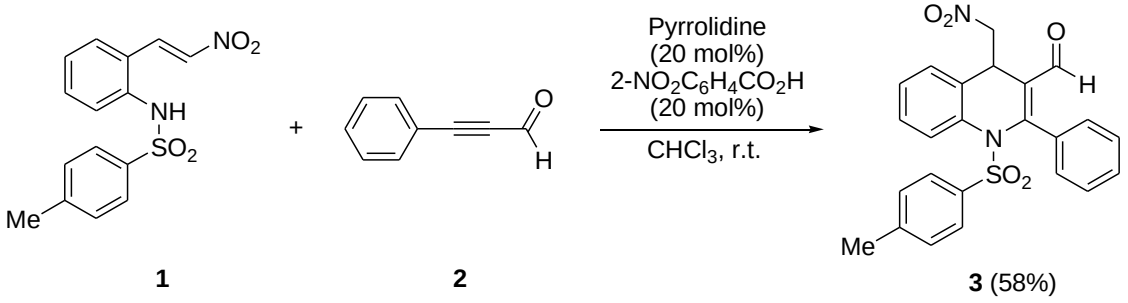
Keywords: dihydroquinoline; Michael addition; cascade reaction

1. Introduction

Hydroquinoline is structurally essential unit in biologically active natural products [1,2]. The hydroquinoline is widely used as a pharmacophore in drug discovery and exhibits a broad range of biological activities such as anti-HIV, antibacterial, antifungal, antimalarial, antitumor, and cardiovascular effects [3–5]. In view of the significance of the hydroquinoline structure in medicinal and organic chemistry, numerous synthetic methods for hydroquinline scaffolds have been developed [6]. Based on our previous results of the cascade reaction for the synthesis of hydroquinoline compounds [7–10], we have successfully obtained a novel compound: 1,4-dihydro-4-(nitromethyl)-2-phenyl-1-tosylquinoline-3-carbaldehyde.

2. Results

The synthesis of 1,4-dihydro-4-(nitromethyl)-2-phenyl-1-tosylquinoline-3-carbaldehyde (**3**) was achieved in one step, as presented in Scheme 1, which was performed via an aza-Michael/Michael cascade reaction of 2-((*E*)-2-nitrovinyl)-*N*-tosylbenzenamine (**1**) with 3-phenylpropiolaldehyde (**2**). The reaction was carried out in toluene in the presence of 20 mol % pyrrolidine as a catalyst and 20 mol % 2-nitrobenzoic acid as an additive. The desired product **3** was obtained in moderate yield via an aza-Michael/Michael cascade reaction. The structure of compound **3** was confirmed via ^{1}H- and ^{13}C-NMR, IR, and mass spectral data, and all data are in accordance with the proposed structure.



1 **2** **3** (58%)

Scheme 1. Synthesis of 1,4-dihydro-4-(nitromethyl)-2-phenyl-1-tosylquinoline-3-carbaldehyde (**3**).

3. Experimental Section

3.1. General Information

All reagents were used as received without further purification. Organic solutions were concentrated under reduced pressure using a Büchi rotary evaporator. Chromatographic purification of the title compound **3** was accomplished using forced-flow chromatography on ICN 60 32–64 mesh silica gel 63. Thin-layer chromatography (TLC) was performed on EM Reagents 0.25 mm silica gel 60-F plates. Developed chromatograms were visualized by fluorescence quenching and anisaldehyde staining. ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker Avance 400 spectrometer (Bruker BioSpin GmbH, Karlsruhe, Germany) in $CDCl_3$. Chemical shifts are internally referenced to residual protio solvent signals (δ 7.26 ppm for ^{1}H; δ77.16 ppm for ^{13}C). Data for ^{1}H-NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, m = multiplet), integration, coupling constant (Hz), and assignment. Data for ^{13}C-NMR are reported in terms of chemical shift. IR spectra were recorded on an ALPHA FT-IR spectrometer (Bruker Optics GmbH, Ettlingen, Germany) and reported in terms of frequency of absorption (cm^{-1}). High-resolution mass spectrometry data was recorded on a JEOL JMS-700 MStation mass spectrometer (JEOL, Tokyo, Japan).

3.2. Syntheis of 1,4-Dihydro-4-(nitromethyl)-2-phenyl-1-tosylquinoline-3-carbaldehyde (**3**)

2-((*E*)-2-Nitrovinyl)-*N*-tosylbenzenamine (**1**) (63 mg, 0.2 mmol) was added to a solution of pyrrolidine (3.4 μL, 0.04 mmol) and 2-nitrobenzoic acid (6.7 mg, 0.04 mmol) in $CHCl_3$ (0.7 mL) at room temperature. The solution was stirred for 5 min before the addition of 3-phenylpropiolaldehyde (**2**) (30 μL, 0.24 mmol). The resulting mixture was stirred for 48 h until complete consumption of 2-((*E*)-2-nitrovinyl)-*N*-tosylbenzenamine (**1**) was observed as determined by TLC. The resulting mixture was directly purified by flash silica gel column chromatography using EtOAc/hexane (1/10) as eluent to afford the desired title compound **3** (58%, 52 mg).

White solid; m.p. 215–217 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.31 (s, 1H), 8.06–7.95 (m, 1H), 7.64–7.42 (m, 6H), 7.33 (ddd, *J* = 10.5, 8.6, 4.7 Hz, 3H), 7.29–7.19 (m, 3H), 4.72 (dd, *J* = 9.7, 5.8 Hz, 1H), 3.91 (dd, *J* = 11.8, 5.8 Hz, 1H), 3.15 (dd, *J* = 11.8, 9.7 Hz, 1H), 2.40 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 190.37, 157.50, 145.87, 136.36, 134.81, 133.12, 131.22, 130.94, 130.42, 130.10, 129.27, 128.37, 128.35, 127.92, 127.82, 125.18, 124.83, 78.46, 34.56, 21.64; IR (film) 3235, 2863, 1714, 1592, 1512, 1440, 1398, 1318, 1185, 1125, 1084 cm^{-1}; HRMS (EI) *m/z* calcd for $[M]^+$ $C_{24}H_{20}N_2O_5S$: 448.1093 Found: 448.1084.

Supplementary Materials: ^{1}H- and ^{13}C-NMR spectra for compound **3** are available online at www.mdpi.com/1422-8599/2016/4/M918.

Acknowledgments: This work was supported by Kyonggi University's Graduate Research Assistantship 2015.

Author Contributions: Both authors contributed equally to this work.

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

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