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ORIGINAL PAPER

Synthesis and keto–enol tautomerism of ethyl 4-oxo-3,4-dihydro-1*H*-pyrano[3,4-*b*]quinoline-3-carboxylate

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An efficient method has been developed for the synthesis of a novel β-keto ester-containing pyranoquinoline compound, i.e., ethyl 4-oxo-3,4-dihydro-1*H*-pyrano[3,4-*b*]quinoline-3-carboxylate. The method entails a two-step synthesis. The first step involves the Williamson-type reaction of ethyl 2-bromomethyl-3-quinoline-3-carboxylate with ethyl hydroxyacetate in anhydrous benzene to afford the intermediate ethyl 2-[(2-ethoxy-2-oxoethoxy)methyl]quinoline-3-carboxylate. The second step includes the Dieckmann condensation reaction of the resulting intermediate in the presence of sodium ethoxide in anhydrous toluene to afford the desired pyranoquinoline containing β-keto ester moiety. Keto–enol tautomerism of the compound thus obtained was investigated by spectroscopic methods.

Keywords: pyranoquinoline, β-keto ester, Williamson-type reaction, ethyl hydroxyacetate, Dieckmann condensation, keto–enol tautomerism

Introduction

Heterocyclic systems containing a quinoline nucleus represent an important group of compounds in medicinal chemistry; they are ubiquitous substructures associated with biologically active natural products (Witherup et al., 1995; Cimanga et al., 1997; Jonckers et al., 2002; Balamurugan et al., 2010). Some quinoline compounds, especially those with a pyranoquinoline core, constitute the basic skeleton of a number of alkaloids, such as flindersine, oricine, and verprisine. They have demonstrated a significant range of biological activities such as anti-allergic, psychotropic, anti-inflammatory, and anti-bacterial activities (Faber et al., 1984; Ramesh et al., 1984; Gould et al., 1988; Yamada et al., 1992; Mohmed, 1994; Chen et al., 1997; Magesh et al., 2004). As a consequence, the synthesis of novel pyranoquinoline derivatives still attracts much interest from medicinal chemists, even if many methods for the synthesis of pyranoquinolines have already been described (Kalita et al., 2006; Zhang et al., 2007; Singh et al., 2007; Chandra et al., 2009; Majumdar et al., 2010; Singh et al., 2011).

β-Keto esters are multi-coupling reagents containing both electrophilic carbonyl and nucleophilic carbon, the combination of which makes them valuable intermediates for the synthesis of complex molecules (Xue et al., 2005; Mordant et al., 2007; Kuninobu et al., 2009; Ghosh et al., 2010; Cui et al., 2010; Adepu et al., 2012). In addition, the chemistry of β-keto ester compounds has been a topic of constant interest, particularly in the study of their keto–enol tautomerism, the structures of both diketo and keto–enol forms and the intramolecular OH···O hydrogen bond formed by the enol tautomer (Jios & Duddeck, 2000; Allegretti et al., 2001; Iglesias, 2004). Keto–enol tautomerism plays a crucial role in compounds possessing a carbonyl group. Investigations of the keto–enol tautomerism in carbonyl compounds are very important in order to explain their biological activity and to understand the biochemical processes in which they take part (Nawrot-Modranka et al., 2006; Temperini et al., 2009). Chemically, this class of compounds has elicited a significant amount of interest, as demonstrated by

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