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Chemical Papers 67 (11) 1474–1478 (2013)
DOI: 10.2478/s11696-013-0411-z

SHORT COMMUNICATION

Alternative two-step route to khellactone analogues using silica tungstic acid and sodium hydrogen phosphate

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Received 26 November 2012; Revised 15 February 2013; Accepted 16 February 2013

A series of coumarins was synthesised via the silica tungstic acid-catalysed Pechmann reaction; some of these were employed for known three-component reactions with aromatic aldehydes and malononitrile in the presence of sodium hydrogen phosphate (Na_2HPO_4) as a basic catalyst, affording a variety of potentially anti-HIV active khellactone analogues.

Keywords: anti-HIV, khellactone, coumarins, Pechmann condensation, silica tungstic acid, sodium hydrogen phosphate

Among heterocyclic compounds containing the oxygen atom, coumarins (benzo-2-pyrones) are well known due to their applications in the synthesis of pharmaceuticals, fragrances, agrochemicals, and insecticides (Oyamada et al., 2002).

In recent years, multi-component reactions (MCRs) have become valued tools for the generation of structurally diverse chemical libraries of drug-like heterocycles (Gladkov et al., 2007). Among MCRs, the three-component reactions have emerged as a useful method, because the combination of three-components to generate new products in a single step is extremely economical (Karami et al., 2012a; da Silva et al., 2012; Szakonyi et al., 2010; Shaabani & Maleki, 2007; Yavari & Beheshti, 2011). It is worth noting that the majority of polyheterocyclic compounds containing the oxygen atom exhibit biological activities. For example, 3′,4′-di-*O*-(*S*)-(−)-camphanoyl-(3′*R*,4′*R*)(+)-*cis*-khellactone (DCK) and 3′-*O*-acetyl-4′-*O*-isopentanoyl-(+)-*cis*-khellactone (suksdorfin; isolated from the fruit of *Lomatium suksdorfii*) have been found to show anti-HIV activity (Xie et al., 1999).

Some khellactone-type compounds are also used in preventing transmission of the HIV infection from an HIV-infected pregnant woman to a foetus and in preventing transmission of the HIV infection during sexual intercourse (Huang et al., 1994). Moreover, those compounds with fused pyran and coumarin rings are important as synthons for the synthesis of some pharmacological agents (El-Agrody et al., 2001). Following ongoing studies on the synthesis of dihydropyrano[*c*]chromene derivatives via MCRs by employing hydroxycoumarins (Mehrabi & Abusaidi, 2010), the synthesis of some 5-hydroxycoumarin derivatives via an eco-friendly method is described here. Subsequently, these coumarins were utilised in the one-pot synthesis of fused pyrano[2,3-*h*]coumarin derivatives as khellactone analogues.

All chemicals were purchased from Merck Co. (Germany) and Sigma–Aldrich Co. (USA). The silica chloride and silica tungstic acid were prepared as detailed in the previous paper (Karami et al., 2012b). The reactions were monitored by TLC (silica gel 60 F_{254}). IR spectra (in KBr discs) were recorded on a FTIR Shimadzu-470 spectrometer (Shimadzu, Japan) in the scanning range of 400–4000 cm^{-1} and the ^1H NMR spectra (400 MHz) were obtained on a Bruker DPX-400 Avance II instrument (Bruker, USA).

5,7-Dihydroxy-4-substituted coumarins (*III*) were prepared as in the published method (Karami et al., 2012a) by the reaction of *β*-ketoester (*I*) (1 mmol) and phloroglucinol (*II*) (1 mmol), using STA (0.25 g, 5 mole %) (Fig. 1) instead of 10 mole % of $ZrOCl_2 \cdot 8H_2O$

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