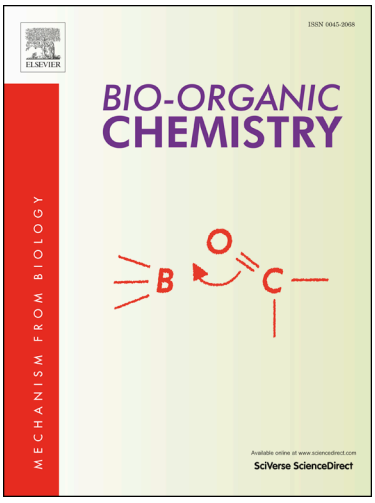

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Promiscuous Enzyme-catalyzed Cascade Reaction: Synthesis of Xanthone Derivatives

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Abstract

Based on the screening of biocatalysts and reaction conditions including organic solvent, water content, lipase loading, reaction temperature and time, lipase TLIM exhibited the prominent promiscuity for the Knoevenagel-Michael cascade reactions of 1, 3-diketones with aromatic aldehydes to synthesize xanthone derivatives. This procedure provides satisfactory advantages such as environmental begin, simple work-up, generality, obtaining in excellent yields (80-97%), and potential for recycling of biocatalyst.

Keywords lipase, Knoevenagel condensation, aromatic aldehyde, xanthone, catalysis

1 Introduction

Xanthone derivatives comprise key structural unit in a variety of natural products and are found to possess significant pharmacological and biological activities[1-3]. Besides, these compounds can be applied in the field of pH sensitive fluorescent material[4], laser technology[5] and dyestuff[6]. Owing to its important contributions in different areas, these compounds are getting an upsurge of interest in recent years. Xanthones are generally obtained from Knoevenagel condensation and Michael addition of 1, 3-diketones with aromatic aldehydes. Various catalysts for synthesizing xanthones have been reported such as phase transfer catalysts TEBA[7], CsF[8], urea under ultrasound[9], nano zeolites Fe/NaY[10], supercritical diethyl ether[11], natural phosphates NP[12], taurine[13], acidic ionic liquids under microwave irradiation[14], magnetic nanoparticles $CuFe_2O_4$@SiO_2- OP_2O_5H[15], MCM-41@Schiff Base-$Mn(OAc)_2$[16], and Oleylamine[17]. However, these methods are usually restricted by volatile toxic organic solvents needed, expensive and non reusable catalysts reused, impractical for large scale production, and sometimes only moderate yields obtained.

In recent years, enzymes have gained a wide interest of researchers for their increasingly important role in organic synthesis due to their high efficiency and environmental friendliness[18, 19]. It is well reported that enzymes play an important catalytic role in various C-C bond forming reactions such as Aldol condensation, Mannich reaction, Henry reaction, Knoevenagel condensation, Michael addition, Baylis-Hillman reaction and so on[20, 21]. Ye *et al*[22] reported the use of "Amano"