Supporting Information

An Efficient and Mild Synthesis of Tetrahydro-4H-indol-4-one Derivatives via a Domino reaction in Water

Furen Zhang, Chunmei Li, Chenze Qi *

Zhejiang Key Laboratory of Alternative Technologies for Fine Chemicals Process, Shaoxing University, Shaoxing, Zhejiang Province 312000, China

E-mail: qichenze@usx.edu.cn

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General experimental methods

All reagents were commercial products without further purification, unless otherwise stated. Analytical thin layer chromatography (TLC) was performed using Merck silica gel GF254 plates. Flash column chromatography was performed on silica gel (200–300 mesh). Melting points were measured on an X-4 melting point apparatus. IR spectra were recorded with a Nicolet Nexus 670 FT-IR spectrometer. $^1$HNMR spectra were recorded on a 400 MHz instrument (Bruker Avance 400 Spectrometer). Chemical shifts ($\delta$) are given in ppm relative to TMS as the internal reference, with coupling constants ($J$) in Hz. $^{13}$C NMR spectra were recorded at 100 MHz. Chemical shift were reported in ppm with the internal chloroform signal at 77.0 ppm as a standard. Elemental analysis was carried out on EuroEA elemental analyzer. ESI-MS was determined by using the LCQ Fleet HPLC/MS instrument (Thermo Finnigan). HRMS (ESI) was measured with a Bruker Daltonics APEXII instrument.

General procedure for synthesis tetrahydro-4H-indol-4-ones 9: In a 10-mL reaction vial, nitroolefin (0.5 mmol), cyclohexane-1,3-dione (0.5 mmol), amine (0.5 mmol), L-proline (10 mol%) and water (3.0 mL) were mixed and then capped. The mixture was stirred for a given time (Table 2) at 60 °C. Upon completion as shown by TLC monitoring, the reaction mixture was cooled to room temperature and extracted with ethyl acetate (5 mL x 3). The resulting residue was purified by column chromatography on silica gel with the eluent (ethyl acetate/petroleum ether = 1:20~1:5) to give the pure product.

Synthesis of intermediate D: In a 10-mL reaction vial, nitroolefin (0.5 mmol), 5,5’-dimethylcyclohexane-1,3-dione (0.5 mmol), aniline (0.5 mmol), L-proline (10 mol%) and water (3.0 mL) were mixed and then capped. The mixture was stirred for 12 h at 45 °C. Upon completion as shown by TLC monitoring, the reaction mixture was cooled to room temperature and extracted with ethyl acetate (5 mL x 3). The resulting residue was purified by column chromatography on silica gel with the eluent (ethyl acetate/petroleum ether = 1:10) to give the pure product.
Copies of $^1$H and $^{13}$C NMR-spectra

9a

ppm (δ)

9a

ppm (δ)

S3