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Research Article

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A green and efficient hydrolysis of methyl 5-chloropyrazine-2-carboxylate to 5-chloro- pyrazine-2-carboxylic acid

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ABSTRACT

an efficient and green procedure for the preparation of 5-chloropyrazine- 2-carboxylic acid from methyl 5-chloropyrazine-2-carboxylic acid ester using LiOH with the evident advantages of very easy operations, environmentally benign conditions and high yield of the product. It is a very green and easy transformation for no organic solvents were used during the whole reaction and separation procedure to obtain the high yield.

Keywords: 5-chloropyrazine-2-carboxylic acid, environmental, green chemistry, hydrolysis, environmental and toxicological

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INTRODUCTION

Hydrolysis of the ester is one of the most important reactions in organic chemistry for aromatic acid substituted phenol esters are very useful intermediates in organic synthesis . As a useful reaction, a review of the literatures indicates that several synthesis procedures have already existed. 5-chloropyrazine- 2-carboxylic acid (**2**) is an important building block in many pharmaceutically active agents. we have developed an efficient and green procedure for the preparation of 5-chloropyrazine-2-carboxylic acid (**2**) from methyl 5-chloropyrazine- 2 -carboxylic acid ester. It has advantage of very easy operations, environmentally benign conditions and high yield of the product.

EXPERIMENTAL SECTION

Starting materials were obtained from commercial suppliers and used without further purification. Mps are uncorrected. The purity of product was established on an Agilent 1100 HPLC. ^{1}H NMR spectra were recorded in $CDCl_3$ on a Bruker 400 (400 MHz) instrument with TMS as internal standard. All chemicals were reagent grade and available commercially. The elemental analysis was performed on a Flash EA1112 instrument.

5-Chloropyrazine-2-carboxylic Acid

In a 2 L round-bottomed flask, fitted with a mechanical stirrer and a thermometer, was placed 24.24 g (1.01 mol) of lithium hydroxide, and 1 L water. Methyl 5-chloropyrazine-2-carboxylic acid ester (172.5 g, 1.0 mol) was added in portions over 1.5 h while the reaction temperature was kept between 1-5°C *via* ice-water bath. When all the added methyl 5-chloropyrazine-2-carboxylic acid ester had dissolved, the reaction was nearly complete. The cold mixture (<5°C) was stirred for another 10 min and then poured into 1.01 L 1 M cold hydrochloric acid (1.01 mol) while the temperature was still kept below 5°C. The precipitated crystals were collected and dried *in vacuo* to afford 155.2 g

(98%) of the crude product as a colorless needles (HPLC >98.5%), mp. 151-152.5°C. ^{1}H NMR ($CDCl_3$)：δ4.17 (1 H, b), 8.69 (1 H, s), 9.19 (1 H, s). An analytical sample was prepared by recrystallization from water, mp.152.5-153°C (lit. mp.153°C).[2]

Anal. Calcd. for $C_5H_3Cl\ N_2O_2$: C, 37.88; H, 1.91; N, 17.67. Found: C, 37.77; H, 1.95; N, 17.74.

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[9] The hydrolysis reaction has been reported in the literature (ref. 2) using sodium hydroxide, but 5-hydroxypyrazine-2-carboxylic acid was reported as the only product in the literature.