Synthesis of 7-Hydroxy-4-methyl Coumarin Under Microwave Irradiation

SHUJING LIU*, BIN ZHAO, QINGMEI JIANG and YANEN WANG

College of Science, Agriculture University of Hebei, Baoding 071000, P.R. China

*Corresponding author: Tel/Fax: +86 31 27528291; E-mail: liushujing66@126.com

Received: 24 September 2013;

Accepted: 25 January 2014;

Published online: 15 April 2014;

AJC-15049

The 1,3-benzenediol and ethyl acetoacetate as raw materials were used to synthesize 7-hydroxy-4-methyl coumarin under microwave irradiation with zirconium sulfate tetrahydrate as the catalyst. Experiment showed that the yield reached up to 87.5 %, when the reaction conditions were as follow: the molar ratio of phenolic and ester was 1.0:1.0, 0.4 g of $Zr(SO_4)_2 \cdot 4H_2O$, 10 mL of cyclohexane, the mixtures react 12 min under 500 W microwave radiation.

Keywords: 7-Hydroxy-4-methyl coumarin, Microwave irradiation, Zirconium sulfate tetrahydrate.

INTRODUCTION

7-Hydroxy-4-methyl coumarin is a white acicular crystal. It has many uses such as medicine, pesticide and as the important chemical intermediates¹⁻³. Sulfuric acid as catalyst used in the synthesis methods of coumarin in industry, but it corrode the equipment and pollution the environment seriously. In recent years, new type of catalysts appeared in the synthesis of coumarin, such as ion exchange resin, solid super acid and ionic liquids⁴⁻⁷. However, they present some issues *e.g.*, high cost, harsh reaction conditions and complex operation. Microwave technique is widely used in organic synthesis. It has many advantages such as the conventional conditions, shorter reaction time and higher yields compared with other organic reactions. In this paper, the 1,3-benzenediol and ethyl acetoacetate as raw materials $Zr(SO_4)_2 \cdot 4H_2O$ as catalyst by microwave radiation technology were used to synthesize 7-hydroxy-4-methyl coumarin. The results showed that the catalyst has good catalytic activity. Furthermore, the 7-hydroxyl-4-methyl coumarin reaction has the characters: simple operation, short reaction time and high yield under microwave radiation. The reaction principle is as follows:

EXPERIMENTAL

$Zr(SO_4)_2 \cdot 4H_2O$, 1,3-benzenediol, ethyl acetoacetate (Chemical pure, Sinopharm Chemical Reagent Co., Ltd.).

Method of synthesis of 7-hydroxy-4-methyl coumarin:

Mix 1,3-benzenediol (4.4 g, 0.04 mol), ethyl acetoacetate (5.6 mL, 0.04 mol) and $Zr(SO_4)_2 \cdot 4H_2O$ 0.4 g, then put into a three mouth bottle. The mixtures were stirred and heated in microwave oven under certain power radiation. Then stop heating, cool the reaction liquid to below 90 °C, add a small amount of anhydrous ethanol to reflux the mixed solution then filtering the recovered catalyst. Poured the left thermal liquid into the ice water and filtered to collect the crystalline, then recrystallized by 67 % alcohol. Finally, get a milky white acicular crystal. The fusion process was 188-192 °C, the theoretical value is 186-192 °C.

The products were dried, then grinded with potassium bromide and pressed into tablets, they were put into the Nicolet Impact-670 FTIR spectrometer to analysis of product structure.

RESULTS AND DISCUSSION

Fig. 1 showed that 3493 cm^{-1} is the characteristic absorption peak of -OH; 3121 cm^{-1} is the characteristic absorption peak of -CH₃; 1683 cm^{-1} , 1605 and 1450 cm^{-1} are the absorption peak of benzene skeleton vibration; 845 cm^{-1} is the bending vibration of C=C-H outside the phenyl ring.

Effect of microwave irradiation power on the yield:

Mix 1,3-benzenediol (4.4 g, 0.04 mol), ethyl acetoacetate (5.6 mL, 0.04 mol), 0.4 g $Zr(SO_4)_2 \cdot 4H_2O$ and 10 mL cyclohexane. The mixtures reacted 12 min. The effect of changing the microwave radiation power upon the yield was shown in Fig. 2. The yield was low within the specified time for reaction was not complete when microwave irradiation power was small. When the power was so large that reaction temperature was elevated

Fig 1. Infrared spectroscopy of 7-hydroxyl-4-methyl coumarin

Fig. 2. Effect of microwave irradiation power on the yield

too fast in the short time. It led to the reactant volatilization so the yield reduced. 500 W was appropriate.

Effect of microwave time on the yield: Mixed 4.4 g (0.04 mol) 1,3-benzenediol, 5.6 mL (5.74 g, 0.04 mol) ethyl acetoacetate, 0.4 g $\text{Zr}(\text{SO}_4)_2 \cdot 4\text{H}_2\text{O}$ and 10 mL cyclohexane. Investigate the effect of the microwave time on the yield when microwave irradiation power was 500 W. The yield increased with increasing the microwave irradiation time. As the reaction time was increased the product color changed from white to yellow. Under such condition, the yield decreased due to side reaction increased. Fig. 3 shows 12 min was the optimal microwave irradiation time.

Effect of catalyst quantity on the yield: Mix 4.4 g (0.04 mol) 1,3-benzenediol, 5.6 mL (5.74 g, 0.04 mol) ethyl acetoacetate and 10 mL cyclohexane. The mixtures reacted 12 min under 500 W microwave irradiation power. The catalyst quantities were changed. Fig. 4 shows 0.4 g is the optimal catalyst dosage. With the increase of catalyst dosage the yield increased significantly. But when it reached 0.4 g and then increased the dosage of catalyst, the yield basically unchanged, so the optimum amount of catalyst was 0.4 g.

Fig. 3. Effect of microwave irradiation time on the yield

Fig. 4. Effect of quantity of catalyst on the yield

Effect of molar ratio of phenolic and ester on the yield. Change the reactant molar ratio, the other reaction conditions were the same. Fig. 5 shows that when the molar ratio was 1:1, the yield was the maximum. But as increasing the proportion, this product further reacted with ethyl acetoacetate so the yield decreased.

Effect of different water retaining agent on yield: Mixed 4.4 g (0.04 mol) 1,3-benzenediol, 5.6 mL (5.74 g, 0.04 mol) ethyl acetoacetate, 0.4 g $\text{Zr}(\text{SO}_4)_2 \cdot 4\text{H}_2\text{O}$ and 10 mL dehydrating agent. The mixtures reacted 12 min under 500 W microwave irradiation power. Use different dehydrating agent the yield was significantly different. Table-1 showed it had the maximum yield when cyclohexane was as the dehydrating agent.

TABLE-1
EFFECT OF DIFFERENT WATER RETAINING
AGENT ON THE YIELD

Dehydrating agent	Yield (%)
—	40.5
Benzene	30.2
Toluene	24.3
Cyclohexane	87.5

Fig. 5. Effect of phenolic ester molar ratio on the yield

Compare microwave technology with general synthesis

method: Mix 4.4 g (0.04mol) 1,3-benzenediol, 5.6 mL (5.74 g, 0.04 mol) ethyl acetoacetate. The mixtures reacted with sulfuric acid and $\text{Zr}(\text{SO}_4)_2 \cdot 4\text{H}_2\text{O}$ as catalyst respectively under microwave irradiation and conventional heating method. Table-2 shows microwave irradiation heating method is better than the ordinary heating method with $\text{Zr}(\text{SO}_4)_2 \cdot 4\text{H}_2\text{O}$ as catalyst. Layered zirconium sulfate four water structure is stable. Crystal water and laminated zirconium sulfate has strong interactions, resulting form a stronger B acid catalytic activity center in the layer⁸. That is allowing the catalytic reaction to go on smoothly.

TABLE-2
COMPARISON MICROWAVE TECHNOLOGY
WITH GENERAL SYNTHESIS METHOD

Catalyst	Heating method	Reaction time	Yield (%)
H_2SO_4	Microwave radiation	24 min	57.80
	Ordinary heating	10 h	42.38
$\text{Zr}(\text{SO}_4)_2 \cdot 4\text{H}_2\text{O}$	Microwave radiation	12 min	87.57
	Ordinary heating	1.5 h	66.38

Conclusion

Experiment shows that $\text{Zr}(\text{SO}_4)_2 \cdot 4\text{H}_2\text{O}$ was a effective catalyst when the reaction conditions were as follow: The molar ratio of phenolic and ester was 1:1, the weight of $\text{Zr}(\text{SO}_4)_2 \cdot 4\text{H}_2\text{O}$ was 0.4 g, 10 mL cyclohexane, the reaction time was 12 min, microwave radiation power was 500 W, the yield reached up to 87.5 %. $\text{Zr}(\text{SO}_4)_2 \cdot 4\text{H}_2\text{O}$ as catalyst has many advantages under microwave irradiation.

ACKNOWLEDGEMENTS

This work was financially supported by the Science and Technology Research and Development Foundation of BaoDing (12ZF023).

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