The Applications of Microwave Irradiation as Greener and Convenient Procedure in Organic Synthesis

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Abstract: This paper mainly described the new instruments of microwave-promoted organic synthesis which were appraised, and several microwave-assisted synthetic reactions, such as esterification reaction, orthogonal experimental design and fentanyl synthetic reactions. In comparison with traditional methods of organic synthesis, microwave-assisted chemistry could make high-speed processing of chemical transformation, to ensure short reactions times and allow for an optional-repro- ducibility, optimization process, optional power levels and the other optional reaction conditions. Our ongoing research work may lay foundation on investigating the mechanism of microwave-promoted organic synthetic reactions**.**

Keywords: microwave-assisted; organic synthesis; carfentanyl; stereospecific synthesis; combinatorial catalysis; ohmefentanyl

1 Instruction

The new kind of chemical revolution, green chemistry, play a vital role in environmental protection and social sustainability. The fundamental idea of green chemistry is that the designer of a chemical is responsible for considering what will happen to the world. Human should take on the responsibility of saving the environment and protecting nature in green cities[1,2]. The efficiency of microwave flash heating in accelerating organic transformations (reaction times reduced from days and hours to minutes and seconds) has recently been proven in several different fields of organic chemistry. The science of green chemistry was developed to meet the increasing demand for environmentally benign chemical processes. We believe the combination of techology and microwave heating will be of importance in the search for green laboratory-scale synthesis[3,4].

This paper mainly addressed the new instruments of microwave-promoted organic synthesis which were appraised, as shown in Figure 1, and several microwave-assisted synthetic reactions, such as esterification reaction, orthogonal experimental design and fentanyl synthetic reactions. In comparison with traditional methods of organic synthesis, microwave-assisted chemistry could make high-speed processing of chemical transformation, to ensure short reactions times and allow for an optional-reproducibility, optimization process, optional power levels and the other optional reaction conditions[5-7]. Our ongoing research work may lay foundation on investigating the mechanism of microwave-promoted organic synthetic reactions[8-10]**.**

2 Experimental

The design and synthesis of 9-xanthene carboxylic acid methyl usd microwave catalysis. Methyl 9-hydroxyl-9-xanthene carboxyate which is an important intermediate of xanthene anticholiergic drugs, was easily synthesized from methyl 9-xanthene carboxyate. Synthesis of methyl 9-xanthene carboxyate by using microwave catalysis was studied through orthogonal design, the effect of irradiation time, microwave power and the amount of catalyst were investigated. It was found that the effect of reaction time was notable.

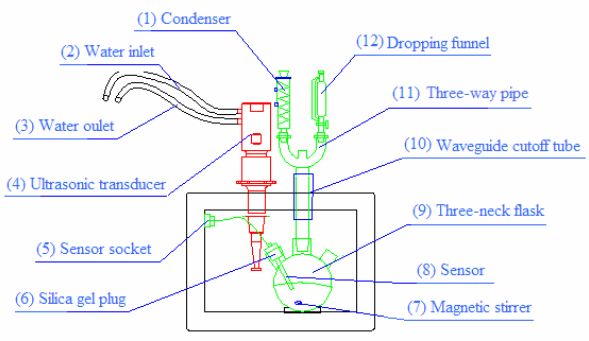

Figure 1 Microwave experimental device installation

According to Table 2 experimental data, the influence degree of irradiation time microwave power, catalyst amount, and their interactions to reaction degree were obtained by using variance analysis method, the results were shown in Table 3.

The reaction of carboxylic acid and alcohol generating to carboxylic ester is one of the classical reaction.Usually, heating and refluxing will cost long time, using microwave catalytic treatment may remarkably reduce reaction time. 9-xanthene carboxylic acid methyl is the main important intermediate of synthesis of xanthene type anticholinergic drug.Using and as materials, but the usual may cost 18 hours.The reaction time is too long. In order to further optimized the experimental systhetic to under microwave condition, investigate

catalyzed amount,microwave power and time to reation, influence, finding the optimal experimental condition.

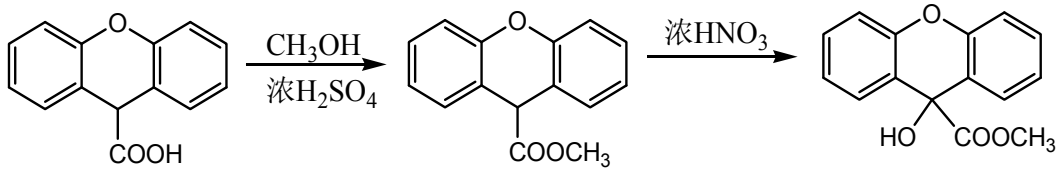

Figure 2 The synthesis of 9-hydroxy-xanthene carboxylic acid methyls

3 Results and Discussion

When using microwave method to synthesis 9-xanthene carboxylic acid methyl ,as shown in Figure 3, Figure4, the influence factors are many, including cataly amount, microwave power and time. In order to single factor prelimany study results, after we seclect inventory rating and catalytic agent , we seclect radiation time,microwave power and amount as the every factor seclet three levels, using L27(313) table arrange experiments synthesis.Through investigate reaction to study each factors and their interaction, influence on reaction results. Each factor of experiment and level were shown in Table 1. Experiment results were shown in Table 2. Variance analysis method were used to discuss each factor and their interactions.

As shown in Table 3, factor A(microwave radiation time)'s level changing had remarkable influence, as factor B(microwave power) and factor C(catalyst amount)'s had remarkable influence on reaction. Factor A select two levels, factors B seclect two levels, factors seclect two levels, synthesis may gain high reaction yield when synthsis 9-xanthene carboxylic acid methyl.

Our results showed that the radiation time may have great influence on esterification ratio, while the changing of catalyst amount and microwave power may had little influence on reaction yield. When the three factors interact with each other, the reaction time and power's interaction may have significant influence on reaction yield, but the other two factors may had weaker interaction effect with each other[11].

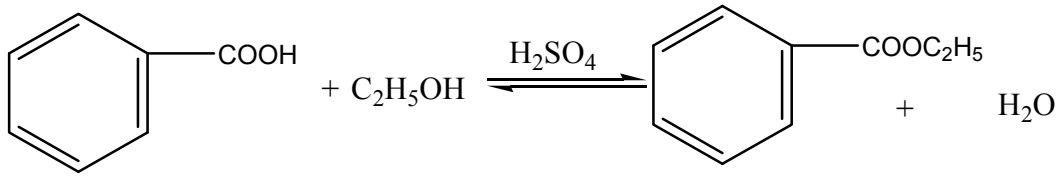

Figure 3 The synthesis of ethyl benzoate

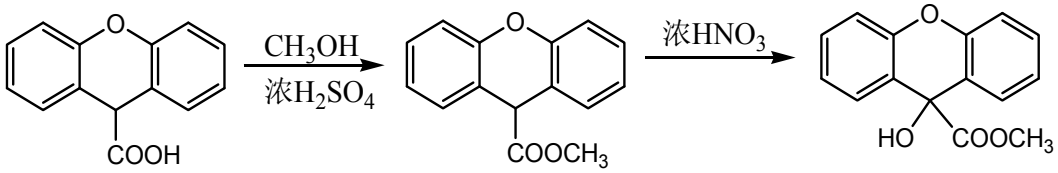

Figure 4 The synthesis of 9-hydroxy-xanthene carboxylic acid methyls

Table 1 Orthogonal text factors and levels

Factors	Level 1	Level 2	Level 3
A（Time/min）	15	30	60
B（Power/W）	400	500	600
C（catalyst amount/mL）	0.1	0.3	0.5

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Table 2 The experimental results of quadrature design

Number	Time（min）	Microwave Power（W）	Catalyst amount（mL）	Yield（%）
1	15	400	0.1	73.2
2	15	400	0.3	80.5
3	15	400	0.5	82.8
4	15	500	0.1	76.4
5	15	500	0.3	81.5
6	15	500	0.5	83.2
7	15	600	0.1	74.0
8	15	600	0.3	83.0
9	15	600	0.5	85.2
10	30	400	0.1	86.2
11	30	400	0.3	87.5
12	30	400	0.5	90.2
13	30	500	0.1	87.0
14	30	500	0.3	91.9
15	30	500	0.5	88.6
16	30	600	0.1	86.5
17	30	600	0.3	87.8
18	30	600	0.5	93.5
19	60	400	0.1	82.1
20	60	400	0.3	87.0
21	60	400	0.5	91.9
22	60	500	0.1	82.9
23	60	500	0.3	85.4
24	60	500	0.5	89.4
25	60	600	0.1	84.6
26	60	600	0.3	85.4
27	60	600	0.5	91.9

Table 3 The variance analysis of reaction yield

factors	Deviation sum of square	Degree of freedom	F ratio	significance
time	0.038	2	1.839	Relatively re-

				markable
power	0.001	2	0.048	
Catalyst	0.023	2	1.113	
A*B	0.016	4	2.000	Relatively remarkable
A*C	0.022	4	1.833	
B*C	0.007	4	0.001	
errors	0.07	6		

4 Conclusions

Ohmefentanyl is potential analgesics and selective μ-opioid receptor agonist. Due to its high analgesics activity and unique structure, it has been the typical anti-terrorism compound. Using microwave and ultrosonic wave combinatorial catalysis method, the synthesis rout of intermediate of Ohmefentanyl was improved and one compound was dealde with a simple method[12]. The optical isomer of intermediate of Ohmefentanyl was splited by chemistry method and the stereospecific synthesis of Ohmefentanyl had been accomplished.

The stereospecific synthesis of ohmefentanyl had been accomplished by using microwave and ultrasonic wave combinatorial catalysis method, the synthesis rout of intermediate of ohmefentanyl was improved and one compound was treated with a simple method[13]. The optical isomer of intermediate of ohmefentanyl was separated by chemistry method.The synthesis of carfentanil assisted by microwaves can reduce the reaction steps，shorten the reaction time and raise the product yield. This is a good method in synthesis of carfetanil.

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