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# An environmentally friendly acylation reaction of 2-methylnaphthalene in solvent-free condition in a micro-channel reactor

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**Abstract:** An efficient and solvent-free acylation of 2-methylnaphthalene (2-MN) is presented using acid chloride as both the acylating agent and solvent in a micro channel reactor. The effect of the catalyst, reactant ratio, mixing temperature, reaction temperature and reaction time on the product yield and selectivity was investigated. At room temperature with a reaction time of only 15 min, the target product, 2-methyl-6-propionynaphthalene (2,6-MPN), was obtained in 72.3% yield with 73.8% selectivity, and 2-methyl-6-acetylnaphthalene (2,6-MAN) was obtained in 54.1% yield with 55.4% selectivity. The route of synthesis provides a more environmentally friendly and efficient method to prepare 2,6-MPN with no other toxic solvents and efficient mass transfer and heat transfer.

**Keywords:** acylation; 2-methyl-6-propionynaphthalene; 2-methyl-6-acetylnaphthalene; solvent-free; micro channel reactor

## 1 Introduction

The Friedel-Crafts acylation of aromatic and heterocyclic compounds is an important reaction process used for the preparation of aromatic ketones [1-3]. In traditional organic synthesis, an organic solvent is the most commonly used reaction medium because it can dissolve organic matter and ensure uniform material distribution and heat exchange stability [4,5]. In addition, reaction processes

conventionally used homogeneous catalysts, including Lewis acids (such as metal halides) and Brønsted acids ( $\text{H}_2\text{SO}_4$ ,  $\text{HCl}$ ,  $\text{HF}$ ) [6,7]. However, in practical applications, the toxicity and difficulty of organic solvents and homogeneous catalysts are the main factors that lead to many problems concerning waste discharge, poor security, energy consumption, serious pollution and other shortcomings. Therefore, synthetic chemistry continues to develop various techniques to produce more green and safe chemicals.

Currently, the development of solvent-free organic synthetic methods has become an important and popular research area [8,9]. Researchers have begun to study organic reactions under solvent-free conditions, which has opened up a new field for the study of organic synthesis methods. There are many references on acylation reactions under solvent-free conditions, which can be attributed to two cases, those including the use of an ionic liquid as both the catalyst and solvent, and those using the acylating agent or raw material itself as the solvent. For instance, the acylation of maltodextrin using vinyl stearate or stearic acid can be carried out in 1-butyl-3-methylimidazolium dicyanamide. This work demonstrated that an ionic liquid can simultaneously act as the solvent and catalyst during the acylation reaction [10]. The acylation of salicylamide to 5-acetylsalicylamide can be carried in 1-butyl-3-methylimidazolium chloroaluminate or *N*-butylpyridinium chloroaluminate at low reaction temperatures, and the yield of the desired product can reach 81.3% and 89.2%, respectively. The Lewis acidic ionic liquid catalyst was not only used as the catalyst, but also as the reaction solvent to replace nitrobenzene in the reaction [11]. Shrinivas et al. studied the Friedel-Crafts acylation reaction under solvent-free conditions wherein acetyl chloride (AC) was used during the acylation of anisole or veratrole. Anisole and veratrole were used as both the substrate and solvent during this work [12]. 2-naphthol can be reacted with acetic anhydride in the presence of a sulphated zirconia catalyst with acetic anhydride acting as both the acylating agent and solvent [13]. In the acylation reaction of aromatic compounds using carboxylic acids, a mixture of graphite and *p*-toluenesulfonic acid was shown to be the best

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catalyst for the reaction. Carboxylic acids are not only used as a green acylating agent, but also as a solvent in this reaction [14]. The acylation of anisole with PC using  $\text{MoO}_4(\text{AlCl}_3)_2$  as the catalyst, in this reaction PC is the main reaction solvent [15].

In addition, the reaction rate observed in the absence of a solvent leads to more favorable reaction kinetics than those found in a solution, and the stereoselectivity and yield of the reaction may be improved because of the high concentration of the reactants. Now, traditional stirred reactors are commonly used as the reactor for most solvent-free reactions, which have low reaction efficiency, low selectivity, strong operation intensity and waste discharge [16-18]. Therefore, it is very important to find the suitable way to perform these reactions toward the development of green chemical processes for environmental protection and to reduce energy consumption. For example, the acylation reaction is one type of very fast exothermic reaction, and some acylation reactions can be carried out in a microchannel reactor [19-21]. Microchannel reactors can precisely control the reaction conditions, which offers the possibility for some solvent-free reactions [22]. A perfluoroalkoxy reactor was used to produce O-isopropyl propionylbenzene [23]. In this reaction, the main raw materials, isopropylbenzene and propionyl chloride (PC), were reacted under solvent-free conditions.

The possibility of using PC itself as the solvent was studied in our group. The complex formed between  $\text{AlCl}_3$  and PC was found to be stable for at least three days. Meanwhile, the acylation of 2-MN in different solvent was investigated [24]. The effects of the different

reaction solvents on the selectivity and yield of the target product were discussed, with nitrobenzene chosen as the optimal solvent. Under the optimal conditions, the target product, 2,6-MPN, was obtained in 85.8% yield with 87.5% selectivity. After the acylation of 2-MN using PC or AC, the target products, 2,6-MPN or 2,6-MAN, need to be separated from the nitrobenzene solvent, which consumes a lot energy. In addition, the nitrobenzene solvent is toxic.

Therefore, guided by the concept of green chemistry, we continue to study the acylation of 2-MN in a continuous micro-channel reactor with no solvent. The effects of the catalyst, and reaction processes and conditions on the results of the reaction are discussed, and the existing synthetic route to achieve green synthesis is optimized in this study.

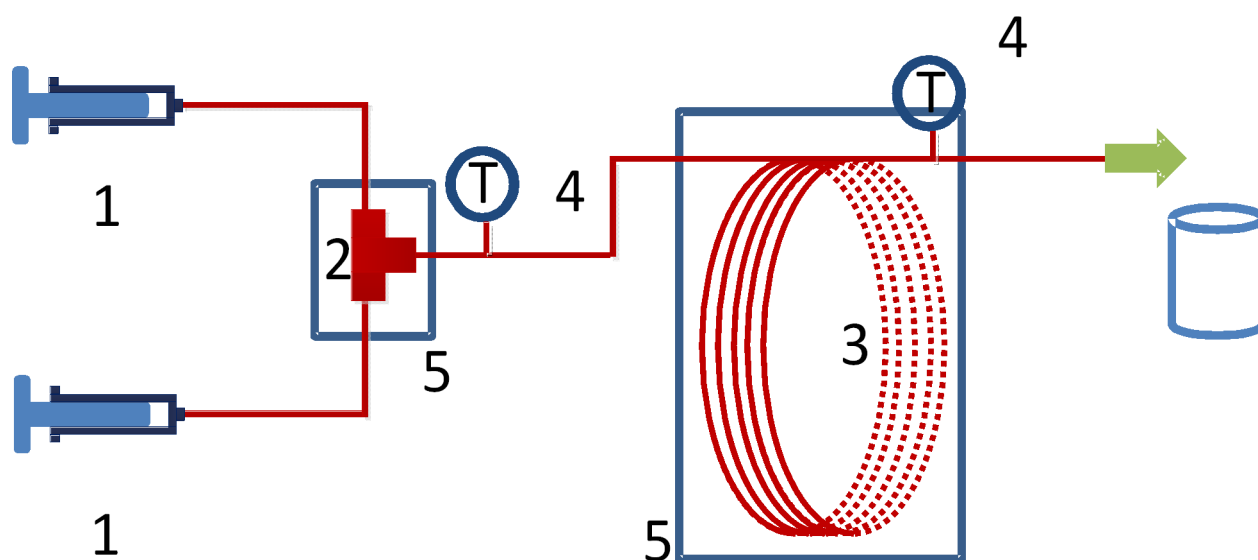
## 2 Experimental

### 2.1 Materials

2-Methylnaphthalene, propionyl chloride (98%), acetyl chloride (98%),  $\text{AlCl}_3$  (99%),  $\text{ZnCl}_2$  (99%) and  $\text{FeCl}_3$  (99%) were purchased from Shanghai Macklin Biochemical Co.

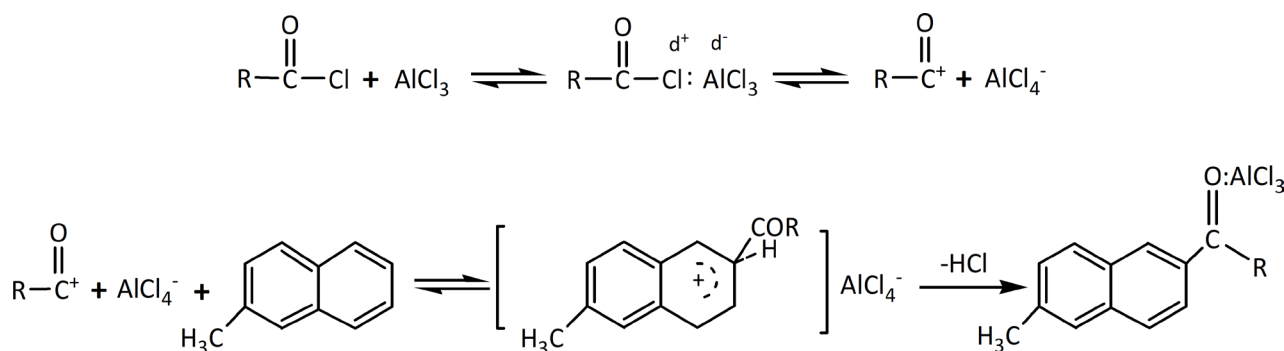
### 2.2 Methods and data treatment

The experimental set-up used for the present investigation is shown schematically in Figure 1, and the detailed experimental steps are as follows.



**Figure 1:** The experimental set-up.

(1 - Glass syringe, 2 - T-micromixer, 3 - Microchannel reactor, 4 - Thermocouple, 5 - Thermostatic bath)



**Figure 2:** Mechanism of the acylation reaction of 2-MN.

RCOCl: acetyl chloride (AC) or propionyl chloride (PC); Product: 2-methyl-6-acetylnaphthalene (2,6-MAN) or 2,6-MPN

- Preparation of the two acylating solutions: PC (AC) and  $\text{AlCl}_3$  were added to a glass-jacketed reactor with stirring and cooling in an ice bath, PC (AC) and 2-MN were also added to another glass-jacketed reactor with stirring and cooling in an ice bath. Stop stirring when the  $\text{AlCl}_3$  or 2-MN were completely dissolved in PC (AC).
- Mixing and Reaction: The two solutions were loaded into two glass syringes (20 mL, Bolivian Pigeons, China), which were attached to two syringe pumps, and mixed in a static T-micro mixer (inner diameter = 0.5 mm) with cooling in an ice bath. After mixing, the obtained solution entered the micro channel (inner diameter = 1 mm, length = 2 m) to react at a constant temperature.
- Distillation: After the reaction, the product was dissolved in the excess PC or AC, which can be separated by distillation and the distilled product washed in a beaker with stirring.

A sample of the reaction mixture was dissolved in acetone and analyzed using gas chromatography on a Shimadzu GC-2014 gas chromatograph equipped with a flame ionization detector and an HP-5 capillary column (50 m  $\times$  0.2 mm  $\times$  0.33  $\mu\text{m}$  film thickness). The yield (Y) and selectivity (X) of the target product were calculated as follows.

$$Y = \frac{W_3}{W_4} \times 100\% \quad (1)$$

$$X = \frac{W_1}{W_2} \times 100\% \quad (2)$$

where Y is the yield (% by mass) of 2,6-MPN, X is the selectivity (% by mass) of 2,6-MPN,  $W_1$  is the mass of 2,6-MPN,  $W_2$  is the mass of all the acylation products,  $W_3$  is the actual mass of 2,6-MPN and  $W_4$  is the theoretical mass of 2,6-MPN.

**Table 1:** The relationship between different catalysts and the results of the acylation reaction of 2-MN.

No.	Catalyst	Reaction Temperature ( $^{\circ}\text{C}$ )	Selectivity (wt%)	Yield (wt%)
1	$\text{AlCl}_3$	25	73.4	72.3
2	$\text{AlCl}_3$	40	70.0	68.8
3	$\text{FeCl}_3$	25	68.2	67.1
4	$\text{FeCl}_3$	40	67.3	66.2
5	$\text{ZnCl}_2$	25	30.2	29.3
6	$\text{ZnCl}_2$	40	29.8	29.1

Note: The molar ratio of 2-MN: $\text{AlCl}_3$ :PC = 0.15:0.17:1, mixing temperature =  $15^{\circ}\text{C}$  and reaction time = 15 min.

## 3 Results and discussion

### 3.1 The effect of the catalyst

Solid metal halides are commonly used a Lewis acid catalyst to catalyze an acylation reaction [25]. The acylation of 2-MN is generally performed using metal chlorides and acid chlorides as catalysts and acylating agents, respectively, via the mechanism shown in Figure 2.

In this study, the relationship between different catalysts ( $\text{AlCl}_3$ ,  $\text{FeCl}_3$  and  $\text{ZnCl}_2$ ) and the result of the acylation reaction of 2-MN was investigated as shown in Table 1.  $\text{AlCl}_3$  was found to be the optimal catalyst for the acylation of 2-MN using PC as the acylating agent. This was attributed to the electrophilicity of  $\text{Al}^{3+}$  being better than that of  $\text{Fe}^{3+}$  and  $\text{Zn}^{2+}$ . Thus,  $\text{AlCl}_3$  was found to be the optimal catalyst and was used in the subsequent experiments.

### 3.2 The effect of the molar ratio of reactants

The different molar ratios of the reactants have a significant effect on the acylation reaction when using nitrobenzene as

the reaction solvent [26]. Thus, the molar ratio of reactants had a significant effect on the product yield and selectivity under solvent-free conditions, and the best result was obtained using a molar ratio of 2-MN:AlCl<sub>3</sub>:PC = 0.15:0.17:1 (Table 2). The higher molar ratio of reactants used in this reaction system has a significant effect on the activity of the reaction, which will release a large amount of heat and affect the selectivity of the target product and the stability of the reaction. Therefore, at the higher molar ratios studied, the results of the reaction were poor and at the lower molar ratios, the output coefficient of PC was low.

3.3 The effect of the mixing temperature

When two different acylating solutions are mixed in the T-micro mixer, they quickly release a lot of heat and the mixing temperature increases. Therefore, the relationship between the mixing temperature and the results of the acylation reaction was investigated, and given in Table 3.

Table 2: The relationship between the molar ratio of the reactants and the results of the acylation reaction of 2-MN.

No.	n(2-MN)/n(AlCl <sub>3</sub> )/n(PC)	Selectivity (wt%)	Yield (wt%)
1	0.30:0.32:1	60.0	58.8
2	0.25:0.30:1	66.6	65.3
3	0.20:0.22:1	71.3	69.9
4	0.15:0.17:1	73.8	72.3
5	0.12:0.15:1	73.3	71.8
6	0.10:0.12:1	72.9	71.4
7	0.08:0.10:1	73.1	71.6

Note: The mixing temperature = 15°C, reaction temperature = 25°C and reaction time = 15 min.

The mixing temperature has a slight effect on the reaction. In order to better control the reaction temperature, the mixing temperature was lower than 25°C. However, the mixing temperature has a significant effect on the results of the acylation reaction using nitrobenzene as the reaction solvent [26]. The concentration of PC under solvent-free conditions is higher than that of PC dissolved in nitrobenzene. [C<sub>2</sub>H<sub>5</sub>CO]<sup>+</sup>[AlCl<sub>4</sub>]<sup>-</sup> is easily converted to [(C<sub>2</sub>H<sub>5</sub>CO)<sub>3</sub>CHCH<sub>3</sub>CO]<sup>+</sup>[AlCl<sub>4</sub>]<sup>-</sup> or other complexes, so the mixing temperature has a slight effect on the results [27].

3.4 The effect of the reaction temperature

The relationship between the reaction temperature and product selectivity is shown in Figure 3. With increasing the reaction temperature, the selectivity of 2,6-MPN and 2,6-MAN increases slowly. But they decrease in the reaction temperature over 25°C. The acylation reaction of 2-MN under solvent-free conditions was a very fast reaction.

Table 3: The relationship between temperature and the results of the acylation reaction of 2-MN.

NO.	Mixing Temperature (°C)	Reaction Temperature (°C)	Selectivity (wt%)	Yield (wt%)
1	-5	25	73.5	72.0
2	-5	15	71.2	69.8
3	5	25	73.6	72.1
4	5	15	70.9	69.5
5	15	25	73.8	72.3
6	15	15	71.6	70.2
7	25	25	72.1	70.7

Note: The molar of 2-MN:AlCl<sub>3</sub>:PC = 0.15:0.17:1, catalyst = AlCl<sub>3</sub>, acylating agent = PC and reaction time = 15 min.

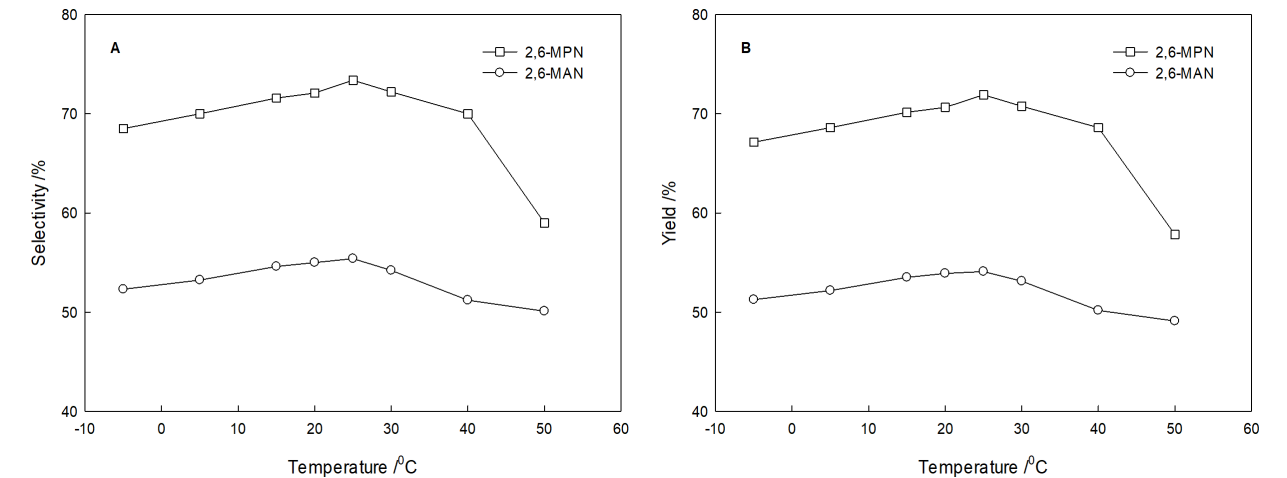


Figure 3: The relationship between the reaction temperature and the results of the acylation reaction of 2-MN. (2-MN:AlCl<sub>3</sub>:PC or AC = 0.15:0.17:1, AlCl<sub>3</sub>, PC or AC, 15 min)

In addition, increasing the temperature is beneficial to increasing the reaction rate and increasing the yield. On the other hand, increasing the temperature also accelerates the process of side reactions and increases the amount of additional monoacylated methylnaphthalene isomers in the product, which can reduce the purity of product. At 25°C, the selectivity and yield of the target product, 2,6-MPN, were 73.8% and 72.3%, respectively, and the selectivity and yield of the target product, 2,6-MAN, were 55.4% and 54.1%, respectively.

### 3.5 The effect of the reaction time

The relationship between the reaction time and the results of the acylation reaction is shown in Figure 4. In this reaction, the flow rate of the two syringe pumps was changed to control the reaction time. The conversion of 2-MN is 100% in 5 min. The selectivity of 2,6-MPN increased with time up to 15 min and that of 2,6-MAN will also increase with time up to 10 min. At the beginning, some 2-MN can generate unstable product isomers and some of these isomers converted into the target product. This acylation reaction under solvent-free conditions is a very fast reaction, and the selectivity has a significant effect on the yield. At 15 min, 2,6-MPN can be obtained in 72.3% yield and 73.8% selectivity, and 2,6-MAN can be obtained in 54.1% yield and 55.4% selectivity.

### 3.6 The effect of the acylating agent

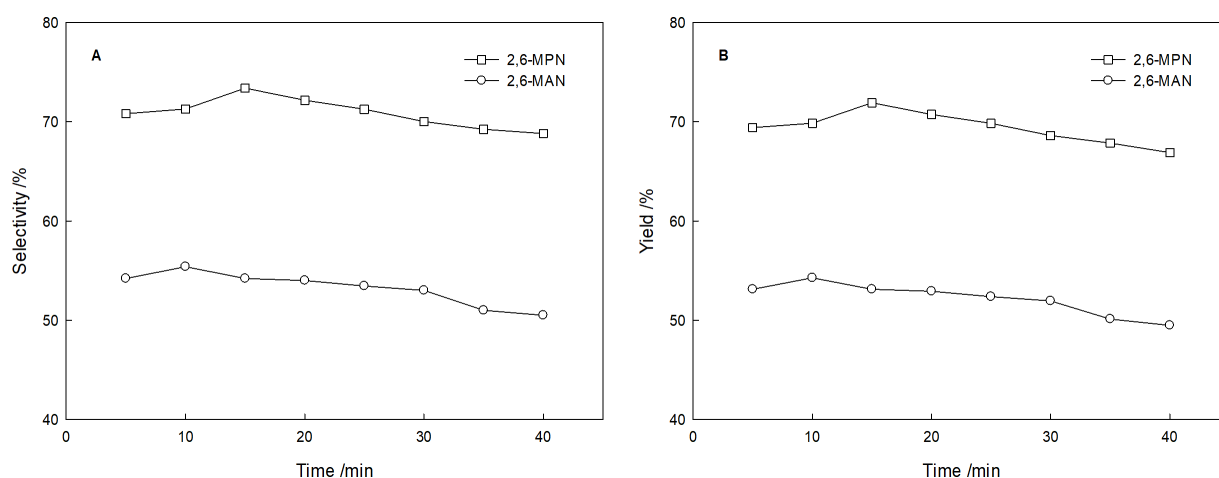
In order to examine the effect of the different acylating agents, propanoic anhydride (PA) was used as the

acylating agent for the acylation reaction of 2-MN.  $\text{AlCl}_3$  was the optimal catalyst for the acylation of 2-MN with PC, but a mixture of PA and  $\text{AlCl}_3$  will not be stable and produce a pale yellow gum. Therefore,  $\text{FeCl}_3$  was selected as the catalyst for the acylation of 2-MN with PA. The effects of the molar ratio of the reactants, mixing temperature, reaction temperature and reaction time on the acylation reaction were studied. When the mixing temperature was 30°C, the reaction temperature is 40°C, the molar ratio of 2-MN: $\text{FeCl}_3$ :PC was 0.28:0.3:1 and the reactants reacted for 30 min, the selectivity and yield of the target product were 69.5% and 43%, respectively.

## 4 Conclusions

Nitrobenzene is toxic and needs to be separated from the target product by vacuum distillation, which consumes a lot of energy. The acylation of 2-MN can be carried out under solvent-free conditions, which can result in a more efficient and environmentally friendly way to produce 2,6-MPN when compared with the acylation reaction conducted using nitrobenzene as the reaction solvent. In this acylation reaction, the reactant concentration is higher than the acylation carried out in the presence of a solvent, so the heat and mass transfer efficiency are high. When the mixing temperature is lower than 25°C, the reaction temperature is 25°C, the molar ratio of 2-MN: $\text{FeCl}_3$ :PC is 0.15:0.17:1 and the reactants reacted for 15 min, the selectivity and yield of target product were 73.8% and 72.3%, respectively.

A comparison of PA and PC shows that although PA can dissolve more 2-MN and catalyst, the yield of the product is lower because the catalytic activity of  $\text{FeCl}_3$  is minor than



**Figure 4:** The relationship between the reaction time and the results of the acylation reaction of 2-MN. (2-MN: $\text{AlCl}_3$ :PC or AC = 0.15:0.17:1,  $\text{AlCl}_3$ , PC or AC, 25°C)



that of  $\text{AlCl}_3$ , and the 2-MN conversion rate is less than 100%. Therefore, PC is the best acylating agent for the acylation of 2-MN conducted under solvent-free conditions.

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