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Research Article

Selective and facile Synthesis of 2-Aminothiophenes Using $Na_2CaP_2O_7$ as base Nano-Catalyst

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ABSTRACT

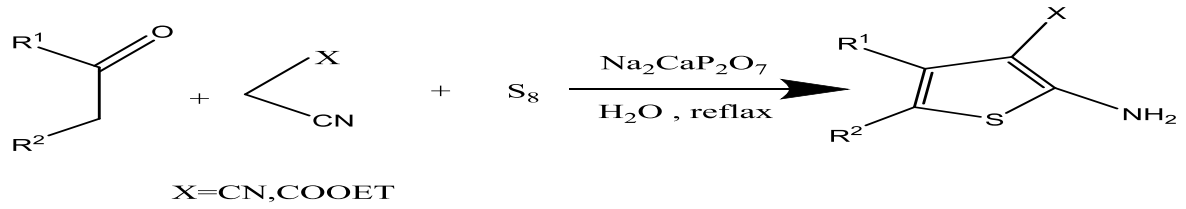
In the study we reported synthesis of 2-aminothiophene derivatives in pure water using nano-structured $Na_2CaP_2O_7$. Our results indicated that this heterogeneous catalyst performed good selectivity and catalytic activity in the synthesis of substituted 2- aminothiophene through Gewald reaction in water. The noticeable benefits of this procedure rely on several factors including: a simple method, mildness conditions, short time of reaction, operational simplicity and low cost.

Keywords:2-Aminothiophenes; Gewald reaction; nanocatalyst; $Na_2CaP_2O_7$

1. Introduction

The straightforward protocols development for the synthesis of molecules is typic of current organic chemists [1]. Development of three-component reactions is of importance [2]. 2-aminothiophenes derivatives are important precursor in organic synthesis to synthesize conductivity-based sensors, dyes and agrochemicals [3]. Furthermore, the thiophene ring is

synthetic biologically active molecules [4]. Therefore, 2-aminothiophenes derivatives synthesis has attracted attention. Many methods have been explained for 2-aminothiophenes synthesized [5]. Among the reported methods, Gewald reaction (Scheme 1) has obtained attention in the research process, which was components assembly of a ketone or aldehyde, a elemental S and an active nitrile [6]. Many organic compounds, such as 1,1,3,3-tetramethylguanidine lactate, morpholine, triethylamine, diethylamine, and imidazole were demonstrated to be achievable catalysts for this reaction[7].



Scheme 1. Synthetic route of 2-aminothiophene derivatives catalyzed by heterogeneous base catalysts, $Na_2CaP_2O_7$.

However, the recognized reactions based on the uses of these homogeneous as catalysts are often inundated by many problems including the generation of waste, the reactor corrosion and recycling catalyst difficult. Furthermore, these reactions are often associated with the use of hazardous polar solvents [8] which has a detrimental effect on the environment. Therefore, great efforts have been paid to developing an efficient and environmental-friendly heterogeneous catalyst system to synthesize the title compounds [9]. However, in many cases, the use of volatile organic solvent is still mandatory, which defeated to some extent the purpose of developing an coefficient system with a heterogonous catalyst. Therefore, it appealingly needs to develop a solid catalyst that is able to allow us to perform the reaction under a green solvent condition. Although the use of solid catalysts in organic reaction allowed us to take their advantages, such as environmental compatibility, reusability, operational simplicity, non-toxicity, non-corrosiveness, the preparation of heterogeneous

catalysts frequently associates with a tedious procedure, which includes generally consecutive steps of precipitation, aging, drying and calcination. This defeated thoroughly the purpose of employing a solid catalyst [10]. In addition, the catalytic activity of a man-made solid catalyst is often affected by many factors, such as precursor, conditions of preparation and pretreatment. This often resulted in a difficulty of reproducing the catalytic properties. It is conceivable that all these drawbacks can be avoided if the heterogeneous catalyst was a commercially available chemical. To this end, we have initiated a research program concerning the use of bulky and easily available chemicals as solid catalysts for organic reactions. $Na_2CaP_2O_7$ is a significant commercial inorganic chemical owing to its applicable versatility. However, $Na_2CaP_2O_7$has been seldom applied as a catalyst of synthetic reaction. The great potential of $Na_2CaP_2O_7$ as a catalyst has been identified by us and others quite recently [11]. However, up to now, it has been used intrans esterification reaction. In view of the fact that its slight basicity and good availability, more application examples of $Na_2CaP_2O_7$ as heterogeneous base catalyst are predictable in the future. In continuation of our study to explore eco-efficient transformations under environmentally kind conditions, in this work, for the first time, we studied $Na_2CaP_2O_7$ as a heterogeneous base catalyst to synthesized the thiophene derivatives through Gewald reaction. The established system is not only efficient for the produce of target compounds but also endowed by notable features of Na_2CaP_2O7 like cost-effective, environmental benign solvent and easy isolation of product.

2. Experimental

2.1. Materials and physical measurements

All experiments were carried out in air. All reagent were purchased commercially and used without further purification. Infrared spectra (4000-400 cm^{-1}) were recorded from KBr disks with a BOMEN MB102 FT-IR spectrometer. The size and morphology of composite was

determined by TEM using a Philips CM10-HT 100KV microscope. The SEM images of nano-structured $Na_2CaP_2O_7$ were gained by a Hitachi Japan S4160 scanning electron microscope.

2.2. Typical procedure for catalytic reaction.

The Nano-structured $Na_2CaP_2O_7$ was prepared by literature method [12].The Gewald reaction was implemented in a typical reaction, elemental S (1.1 mmol), ketone (or aldehyde) (1 mmol), and nitrile (1 mmol) were mixed. Then, $Na_2CaP_2O_7$ (0. 2g) and water (1.0 mL) were added. The mixture was then heated to 100^{o}C under stirring and reflux. After reaction, the solid catalyst was separated by a simple decantation after centrifugation. The reaction mixture was extracted with chloroform .The obtained product was recrystallized by ethanol. All products were identified by IR and ^{1}H NMR.

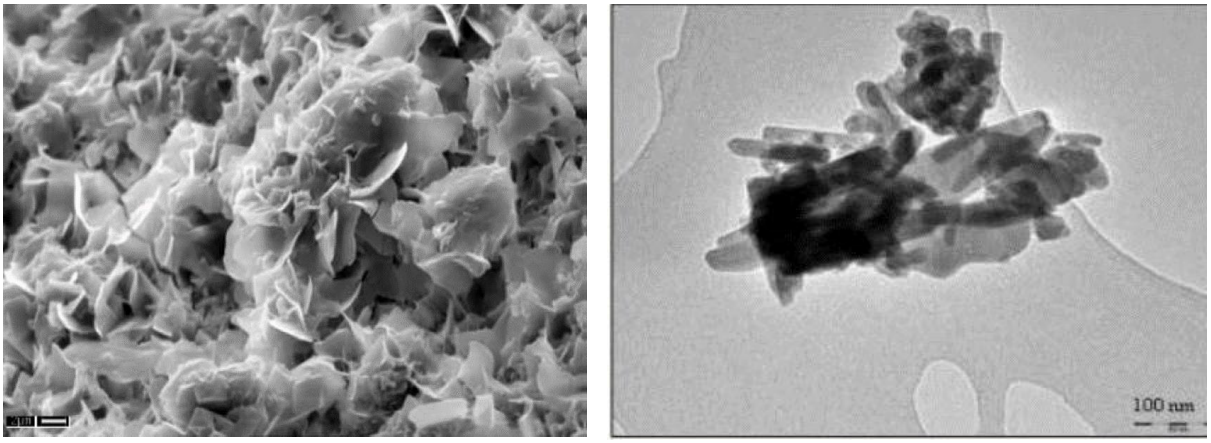
3. Results and discussion

3.1. Synthesis and spectroscopic characterization

The Nano-structured $Na_2CaP_2O_7$ synthesis in this report was prepared and characterized according to the procedures described in the previous literature [12]. The specific surface area of the $Na_2CaP_2O_7$ measured by using BET method from the adsorption-desorption isotherm was found to be 2.4 m^2g^{-1}.

SEM image was used to study the morphology of the surface of the Nano-structured $Na_2CaP_2O_7$ (Fig. **1a**). The micrographs revealed a condensed heterogeneous nanostructure where the particles were dispersed uniformly with a clear surface roughness. This can be described by a heterogeneous growth of the crystallites caused by the implemented method of synthesis, consequently affecting the morphology and also porosity. TEM image confirmed the multilayers structure of this nanostructured catalyst (Fig. **1b**). Based on the results above, which confirm the incorporation of

Nano-structured $Na_2CaP_2O_7$ in the porosity, we further investigated the potential use of this Nano-structured as an organized porous nan catalyst for green and efficient multicomponents synthesis of 2-aminothiophenes derivatives .Initially, malononitrile and Ethyl cyanoacetate was selected as a model substrate to react with elemental S and a variety of ketones.



(a) (b)

Fig1. The SEM image (a) and TEM image (b) of nano-structured $Na_2CaP_2O_7$.

3.2. Investigation of the influence of reaction conditions

The reaction of cyclohexanone, ethyl cyanoacetate and S_8 was chosen as a model reaction to study the influence of amount of $Na_2CaP_2O_7$ as catalyst on the synthesis of 2-aminothiophene

and the results were collected in Table 1.In the absence of $Na_2CaP_2O_7$, only a trace amount of desired product was obtained after 6 hours of reaction[18]. The yield of 2-aminothiophenes was significantly improved by putting catalytic amount of $Na_2CaP_2O_7$ into the substrates .The systematic investigation about the catalyst amount on the synthesis revealed that the reaction yield and time evidently depended on the dosage of the $Na_2CaP_2O_7$. Therefore, we selected 0.2g of catalyst for the next experiments. The best result was obtained when the reaction done

in the presence of 0.2 mg of Nano-structured $Na_2CaP_2O_7$ and water as solvent under reflux conditions.

Table 1. Optimization of the amount of the Nano-structured $Na_2CaP_2O_7$ as catalysts, temperature and solvent for the

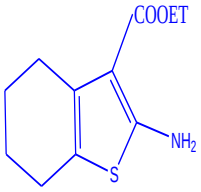
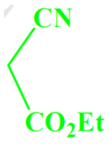
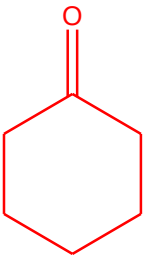
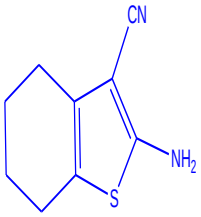
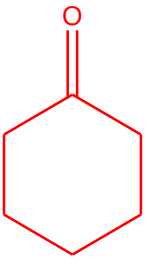
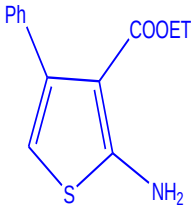
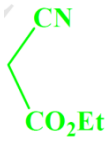
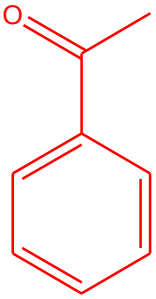
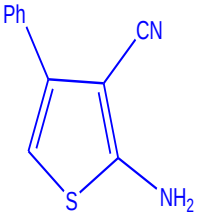
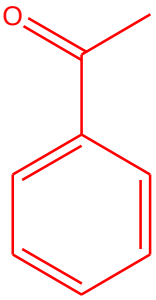
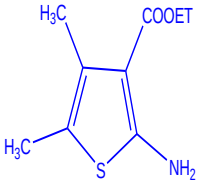
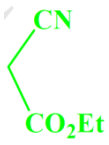
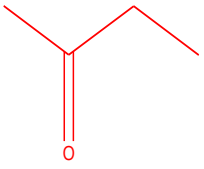
Entry	Catalyst(g)	Solvent	Temperature	Time(min)	Yield (%)
1	0.2	H_2O	reflux	17	91
2	0.3	H_2O	reflux	48	75
3	0.4	H_2O	reflux	45	80
4	0.1	H_2O	reflux	48	78
5	0.01	H_2O	reflux	40	85
6	0.05	H_2O	reflux	35	68
8	0.2	EtOH	reflux	30	88
9	0.2	EtOH	Room temperature	4320	86

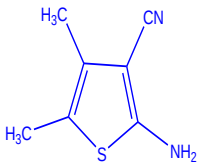
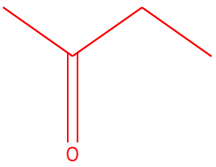
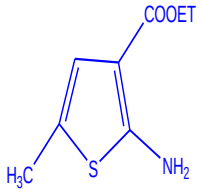
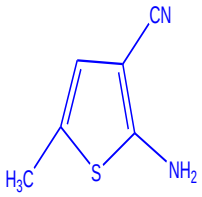
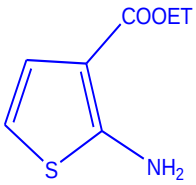
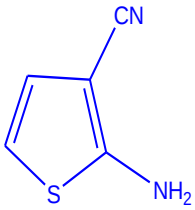
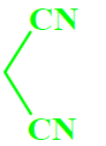
synthesis of 2-aminothiophene derivatives.

3.3. Synthesis of 2-aminothiophenes derivatives catalyzed by $Na_2CaP_2O_7$.

The reaction was performed in a 1:1:2 molar ratio as a water under reflux using $Na_2CaP_2O_7$ as catalyst, and the results were listed in Table 2. as you can see, all the successfully produced the expected thiophene derivatives in high yields. ethyl cyanoacetateunder gave lower yield than that of malononitrile the identical conditions (entries 2,4,6,8 and 10). Remarkably, when the former two were used, the yields of the desired 2-aminothiophenes reached over 80%. It demonstrated that the efficiency of the Gewald three-component reaction was significantly affected by the structure of components. Furthermore, cyclic Ketones to liner ketones improved the yield. On other hand, all have investigated Gewald synthesis of 2-aminothiophenes by using aldehydes as substrates. And they also found that the yield of 2-aminothiophene increased with the aldehydes.

Table2. Preparation of various 2-aminothiophene derivatives.

Entry	Product	mp (°C) (Reported) [13]	mp (°C) (Found)	Yield% (Reaction time, min)	amine	Ketone or aldehyde
1		117	114	91 (30)		
2		146	141	97 (15)		
3		98	96	89(30)		
4		140	141	90(18)		
5		91	88	85(45)		

6		141	138	89(16)		
7		44	44	80(40)		
8		105	98	87(19)		
9		122	120	86(40)		
10		104	98	92(21)		

3.4. Activity comparison of Nano-structured $Na_2CaP_2O_7$ with other catalysts.

The reaction yield of malononitrile, cyclohexanone and S_8 was compared with that reported in the literature, and the data are compiled in Table 3. All the solid bases are able to produce the desired product in reasonable yields under mild conditions. The catalytic ability of $Na_2CaP_2O_7$ is much better than that of other catalyst and comparable to a homogeneous catalyst, L-proline, which however has to be used in combination with DMF solvent. From the comparison with all the other heterogeneous catalyst, it is easy to identify that $Na_2CaP_2O_7$ is indeed an advantageous solid catalyst for Gewald reaction [13].

Table 3. Activity comparison of $Na_2CaP_2O_7$ with other catalysts.

Catalyst	Solvent	Temperature (^oC)	Time/min	Yield (%)
Diethylamine	EtOH	70	240	82
KF-alumina	EtOH	70	210	89
L-Proline	DMF	60	1440	84
Ethylenediamine diacetate	Ionic liquids	50	240	84
$Na_2CaP_2O_7$	H_2O	100	15	91

4. Conclusions

In conclusion, a base porous $Na_2CaP_2O_7$, was successfully synthesized and characterized. The catalytic activity of this nanostructured $Na_2CaP_2O_7$ has been successfully applied for the synthesis of Substituted 2-aminothiophenes under reflux condition. Compared to solvent, water can speed up the reaction and is more efficient and convenient.

Reusability, easy work-up, short reaction times, ecofriendly, and inexpensive are advantages of this new nano catalyst.

ASSOCIATED CONTENT

Supporting information Material and apparatus, characterization (NMR and IR) spectra data and spectra off Compounds, and product analysis.

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