

Microwave Accelerated Synthesis of 4-Phenylethynylphthalic Anhydride

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An efficient method for the synthesis of 4-phenylethynylphthalic anhydride has been developed. The target compound was prepared through Sonogashira coupling in water under microwave condition, followed by dehydration of 4-phenylethynylphthalic acid under microwave condition as well, with overall yield of 83.8 %. The products were characterized by IR, ¹H NMR, ¹³C NMR, MS and elemental analysis, respectively.

Keywords: Polyimides, 4-Phenylethynylphthalic anhydride, Sonogashira coupling reaction, Aqueous medium, Microwave synthesis.

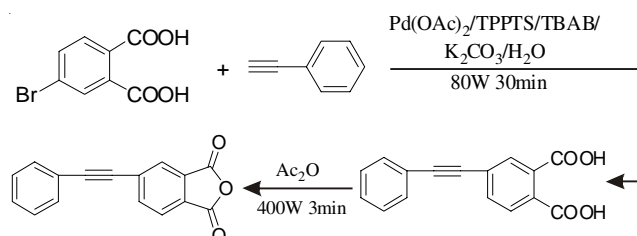
INTRODUCTION

Polyimides have been widely used in aerospace and microelectronics due to their excellent mechanical properties and thermo oxidative stability¹⁻³. However, most polyimides are difficult to process because of their narrow processing window, which restricts their wider applications^{4,5}. For this reason, there is a continuing effort for improving the processibility of polyimides and it was found that phenylethynyl end-capped polyimides have excellent thermal stability and could effectively improve the processibility^{6,7}.

4-Phenylethynylphthalic anhydride is one of the most important terminated agents of polyimides. The traditional two approaches for synthesis of 4-phenylethynylphthalic anhydride employed 4-bromophthalic anhydride⁸⁻¹⁰ or 4-bromodimethyl phthalate¹¹ as the substrates to react with phenylacetylene in coupling reaction. However, these substrates are not commercialized and usually prepared from 4-bromophthalic acid. In our previous study, we directly employed 4-bromophthalic acid as the substrate in coupling reaction for the purpose of shortening the reaction steps and decreasing the cost of the product¹². We also reported the improvement of this method for the following two aspects: (a) employed water instead of organic solvents as the reaction solvents¹³; (b) used the monosodium salt of 4-bromophthalic acid as the substrate¹⁴. However, all the reactions were undergoing in conventional heating condition, which required a long reaction time.

In recent years, the use of microwave energy has become an increasingly popular technique in the scientific community¹⁵⁻¹⁸. The synthesis of 2,2',3,3'-biphenyltetracarboxylic

dianhydride under microwave conditions has been reported and obtained satisfying result¹⁹. In this study, we try to synthesize 4-phenylethynylphthalic anhydride under microwave condition and our strategies are outlined in **Scheme-I**.



Scheme-I: Synthetic routes of 4-phenylethynylphthalic anhydride

EXPERIMENTAL

Melting points were determined on an XRC melting point apparatus. IR spectra were recorded on a PK1600 FTIR-type spectrophotometer using KBr pellets. ¹H NMR (400 MHz) and ¹³C NMR (100 MHz) spectra were measured on a Bruker AV II-400 instrument spectrometer with TMS as an internal standard. MS and Elemental analysis were recorded on Q-TOF-Premimer and Euro EA 3000 apparatus, respectively. TPPTS [*tris*-(3-sulfonatophenyl)phosphine, sodium salt] was synthesized as described in the literature²⁰. All the other reagents and chemicals were commercially available and were used without purification.

A three neck flask was charged with 4-bromophthalic acid (3 g, 12.20 mmol), K₂CO₃ (6.76 g, 48.80 mmol) and H₂O (30 mL) and the resulting solution was degassed *via* three freeze-

pump-thaw cycles. Phenylacetylene (1.50 g, 14.6 mmol), Pd(OAc)₂ (0.04 g, 0.18 mmol), TPPTS (0.45 g, 0.73 mmol) and tetrabutyl ammonium bromide (0.20 g, 0.61 mmol) was then added under an argon atmosphere. The mixture was subjected to microwave irradiation at 80 W for 0.5 h. The solution was cooled and then adjusted pH to 2-3 with concentrated HCl to give pale yellow precipitate. The precipitate was filtered, washed with water and recrystallized from ethanol/H₂O (v:v = 6:1) to afford 4-phenylethynyl phthalic acid as pale yellow solids (2.66 g, 84.6 %). m.p. 210-212 °C (lit.¹¹ m.p. 211.0-211.6 °C). IR (KBr, ν_{\max} , cm⁻¹): 3074 (aromatic C-H), 3012-2525 (COO-H), 2208 (C≡C), 1708 (C=O), 1280 (C-O). ¹H NMR (DMSO-*d*₆, 400 MHz) δ (ppm): 13.40 (s, 2H), 7.81 (s, 1H), 7.75 (s, 2H), 7.62 (dd, *J* = 3, 6.6 Hz, 2H), 7.47 (m, 3H). ¹³C NMR (DMSO-*d*₆, 100 MHz) δ (ppm): 168.40, 168.38, 134.2, 133.7, 132.6, 132.1, 131.4, 129.8, 129.6, 129.3, 125.3, 122.1, 92.3, 88.2; MS (ESI): *m/z* 266 (M-H)⁻¹. Anal. Calcd. for C₁₆H₁₀O₄: C, 72.16; H, 3.79. Found: C, 72.05; H, 3.80.

4-Phenylethynyl phthalic acid (2.60 g, 9.77 mmol) and acetic anhydride (8 mL) were placed in a three necked flask. After irradiate the reaction mixture for 3 min at 400 W, the solvent was removed and the residue was recrystallized from toluene/*n*-hexane (v:v = 1:1) to afford pale yellow crystals (2.40 g, 99 %). m.p. 152-153 °C (lit.⁸ 150-152 °C). IR (KBr, ν_{\max} , cm⁻¹): 3063 (aromatic C-H), 2205 (C≡C), 1843, 1772 (C=O), 1245 (C-O). ¹H NMR (CDCl₃, 400 MHz) δ (ppm): 8.11 (s, 1H), 7.99 (s, 2H), 7.58 (m, 2H), 7.40 (m, 3H). ¹³C NMR (CDCl₃, 100 MHz) δ (ppm): 162.2, 138.7, 132.04, 131.99, 131.7, 129.7, 129.6, 128.6, 128.2, 125.6, 121.6, 96, 86.9; MS (ESI): *m/z* 282 ([M-H]⁻¹Cl). Anal. Calcd. for C₁₆H₈O₃: C, 77.40; H, 3.25. Found: C, 77.30; H, 3.26.

RESULTS AND DISCUSSION

The application of microwave techniques for organic synthesis has attracted considerable interest in recent years, which can be ascribed to the reason that this technology can enhance the reactivity, increase the chemical yields and shorten the reaction time¹⁵⁻¹⁸. Base on this, we attempted to synthesize 4-phenylethynylphthalic anhydride under microwave conditions and satisfactory results have been obtained.

In previous report¹³, the Sonogashira coupling reaction for synthesis of 4-phenylethynyl phthalic acid was carried out in water in the presence of Pd(OAc)₂, TPPTS, K₂CO₃, tetrabutyl ammonium bromide. We now synthesize the target compound under microwave irradiation by use of these conditions for the initial study. It was found that the microwave assisted coupling reaction occurred very fast. The reaction time is shortened from 12 h to about 0.5 h and the product was obtained in moderate yield.

With these promising results, we sought to optimize the reaction conditions in order to obtain better results. Firstly, the effects of microwave irradiation power were investigated. It was found that the coupling yield increased from 40 to 73 % with the increasing of irradiation power from 50 to 80 W, but decreased with the continuous increasing of irradiation power. This might be due to the increase of by-products at higher power under heterogeneous conditions. Therefore, 80 W is

the best power for microwave assisted synthesis of 4-phenylethynyl phthalic acid. Secondly, we also optimized the amount of catalyst. The coupling yield increased dramatically with catalyst loading changing from 0.5 to 1.5 %. Even higher amount of catalyst did not lead to any further improvement of the coupling yield. It was found that the yield of microwave assisted coupling reaction was improved from 73.8 to 84.6 % without co-catalyst CuI as reported earlier¹⁹. At last, the amount of the ligand was studied. The coupling yield increased with the increase of the amount of the ligand and leveled off with further increasing the amount of ligand. The optimized amount of ligand was found to be 4 equiv. of catalyst loading. The optimum molar ratio of 4-bromophthalic acid to Pd(OAc)₂: TPPTS was 1:0.015:0.06 and the optimum yields was found to be 84.6 %.

In addition, we also carried out the dehydration reaction of 4-phenylethynylphthalic acid under microwave condition. The reaction time was shortened from several hours to only 3 min and the product was obtained in excellent yield (99 %) when the microwave irradiation power was at 600 W.

As expected, the reaction time under microwave conditions was greatly decreased, which reflected the intriguing advantages of microwave technique. The reaction time and relative reaction yields were summarized in Table-1. Under microwave conditions, the coupling reaction time was decreased to 0.5 h, 24 times shorter than that of under conventional heating conditions. Similarly, the reaction time of dehydration was also decreased from 1 h to 3 min under microwave conditions. It was worth noting that the overall yield was 5.3 % higher than that reported in the literature¹³.

TABLE-1
COMPARISON OF REACTION TIME AND REACTION YIELDS OF CONVENTIONAL HEATING (CH) AND MICROWAVE HEATING (MH)

Entry	Heating method	Time (min)	Isolated yield (%)
Step 1	CH	720 [Ref. 13]	82.6 [Ref. 13]
	MH	30	84.6
Step 2	CH	60 [Ref. 13]	95.0 [Ref. 13]
	MH	3	99.0
Overall	CH	780 [Ref. 13]	78.5 [Ref. 13]
	MH	33	83.8

Conclusion

In conclusion, a green and efficient approach to the synthesis of 4-phenylethynylphthalic anhydride under microwave conditions has been developed. The microwave technique was greatly shortening the reaction time and also improving the yields. In comparison to conventional heat methods, the microwave technique owns the advantages of more readily available raw materials, shorter reaction time, higher yield and a better prospect of application.

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