

## Efficient Synthesis of Symmetrical and Unsymmetrical Acyclic Imides Catalyzed by Reusable 12-Tungstophosphoric Acid under Thermal Conditions and Microwave Irradiation

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*(Received 7 February 2010, Accepted 28 May 2010)*

An efficient and environmentally friendly procedure has been developed for the synthesis of symmetrical and unsymmetrical acyclic imides by the reaction of nitriles with acyclic anhydrides in the presence of catalytic amounts of 12-tungstophosphoric acid ( $H_3PW_{12}O_{40}$ ) under thermal conditions and microwave irradiation. It was found that microwave improves the yields and significantly reduces the reaction times. Furthermore, the catalyst could be recovered and reused several times without decrease in its activity.

**Keywords:** Acyclic imides, 12-Tungstophosphoric acid, Acyclic anhydrides, Nitriles, Microwave irradiation

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### INTRODUCTION

The preparation of imides has received considerable attention during recent years. Imides are versatile intermediates in the synthesis of nitrogen-containing heterocycles [1,2]. The imide functionality is also an important component in many natural products that exhibit a broad range of activities including immunosuppressants [3], cytotoxic anticancer agents [4], antibiotics [5] and antifeedants [6]. Unlike cyclic imides, where much is known about their synthesis and reactivity [7], only few methods have been reported for the preparation of acyclic imides. A number of methods such as acylation of amides with acyl chlorides, anhydrides and carboxylic esters or acids [8-12], aminocarbonylation of aryl bromides [13], reaction of azalactones with oxygen and palladium [14], oxidation of amides with ruthenium tetroxide [15], reaction of deprotonated

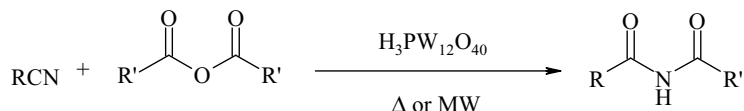
amides with pentafluorophenyl esters [16] reaction of amides with *N,N*-bis(trimethylsilyl)formamides [17],  $\alpha,\alpha,\alpha$ -trichloromethylcarbonyl compounds [18], diketene [19] or vinyl esters [20], and reaction of nitriles with acyclic anhydrides in the presence of silica sulfuric acid [21] have been reported for the preparation of acyclic imides. However, most of these methods suffer from drawbacks such as long reaction times, low yields, high temperature and producing side-products. Thus, development of a new and effective method for the synthesis of acyclic imides catalyzed by inexpensive and environmentally friendly reagent is in order.

Organic reactions assisted by microwave irradiation have attracted considerable attention in recent years [22-26]. The main benefits of the microwave reactions are much improved reaction rates, higher yields and formation of cleaner products. A noteworthy advantage of modern scientific microwave apparatus is the ability to control reaction parameters such as temperature, pressure and reaction times accurately.

One important class of solid catalysts is heteropoly acids (HPAs), having both redox and acid properties [27-29].

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*Scheme 1*

Among heteropoly acids, polytungstic acids are the most widely used catalysts due to their high acid strengths, thermal stability and low reducibility. Heteropoly acid catalysts have many advantages over the liquid acid catalysts. They are harmless to the environment with respect to corrosiveness, safety and quantity of waste. Solid heteropoly acids have attracted much attention in organic synthesis owing to easy work-up procedure, easy filtration and minimization of cost and waste generation due to their reusability and recyclability [30]. A variety of organic transformations catalyzed by heteropoly acids have been reported in the literature [31-38].

In continuation of our studies on the development of practical and environmentally benign methods for some important chemical transformations [39-44], we now report an efficient method for the one-pot synthesis of a wide variety of acyclic imides by the reaction of nitriles with aliphatic anhydrides catalyzed by  $\text{H}_3\text{PW}_{12}\text{O}_{40}$  under thermal conditions and microwave irradiation (Scheme 1).

## EXPERIMENTAL

The products were identified by comparison of their physical and spectral data with those of authentic samples. Melting points were determined using Stuart Scientific SMP2 apparatus.  $^1\text{H}$  NMR spectra were recorded in a  $\text{CDCl}_3$  solution on a Bruker-AC 500 MHz spectrometer. IR spectra were recorded on a Shimadzu IR-435 spectrophotometer. Gas chromatography experiments (GC) were performed on a Shimadzu GC-16A instrument using a 2 m column packed with silicon DC-200 or Carbowax 20m. GC-Mass analyses were carried out using Fisons TRO 1000 spectrometer. The microwave system used for these experiments included the following items: Micro-SYNTH labstation, complete with glass door, dual magnetron system with pyramid-shaped diffuser, 1000 W delivered power, exhaust system, magnetic

stirrer, "quality pressure" sensor for flammable organic solvents, and ATCFO fiber optic system for automatic temperature control.

### General Procedure for the Synthesis of Acyclic Imides by the Reaction of Liquid Aliphatic Nitriles with Aliphatic Anhydrides in the Presence of $\text{H}_3\text{PW}_{12}\text{O}_{40}$ under Thermal Conditions and MW Irradiation

A mixture of nitrile (20 mmol), aliphatic anhydride (1 mmol) and  $\text{H}_3\text{PW}_{12}\text{O}_{40}$  (0.055 mmol) was heated at 70 °C or irradiated under MW (800 W) at 40 °C (the total volume was less than 1 ml). The reaction progress was monitored by GC. After completion of the reaction, the mixture was cooled to room temperature and  $\text{Et}_2\text{O}$  (15 ml) was added. The catalyst was filtered and washed with  $\text{Et}_2\text{O}$  (10 ml). The filtrates were concentrated and the crude product was purified by chromatography on a short column of silica-gel (ethyl acetate: petroleum ether, 1:3) to obtain the pure product (Table 2).

### General Procedure for the Synthesis of Acyclic Imides by the Reaction of Liquid Aromatic Nitriles with Aliphatic Anhydrides in the Presence of $\text{H}_3\text{PW}_{12}\text{O}_{40}$ under Thermal Conditions and MW Irradiation

To a mixture of nitrile (5 mmol) and aliphatic anhydride (1 mmol) was added  $\text{H}_3\text{PW}_{12}\text{O}_{40}$  (0.055 mmol) and the mixture was heated at 70 °C or irradiated under MW (800 W) at 40 °C (the total volume was less than 1 ml). The reaction progress was monitored by TLC. After completion of the reaction, the mixture was cooled to room temperature and  $\text{Et}_2\text{O}$  (15 ml) was added. The catalyst was filtered and washed with  $\text{Et}_2\text{O}$  (10 ml). The filtrates were concentrated and the crude product was purified by chromatography on a short column of silica-gel (ethyl acetate:petroleum ether, 1:4) to afford the pure product (Table 3).

### General Procedure for the Synthesis of Acyclic Imides by the Reaction of Solid Aromatic Nitriles with Aliphatic Anhydrides in the Presence of $H_3PW_{12}O_{40}$ under Thermal Conditions and MW Irradiation

A mixture of nitrile (1 mmol), aliphatic anhydride (2 mmol) and  $H_3PW_{12}O_{40}$  (0.2 mmol) was heated at 80 °C or irradiated under MW (1000 W) at 40 °C. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was cooled to room temperature and  $Et_2O$  (15 ml) was added. The catalyst was filtered and washed with  $Et_2O$  (10 ml). The filtrates were evaporated and the crude product was purified by chromatography on a short column of silica-gel (ethyl acetate:petroleum ether, 1:6) to afford the pure imide (Table 5).

### Spectral Data

***N*-Acetylacetamide (Table 2, entry 1).** White solid, m.p.: 73 °C. IR (KBr)  $\nu_{max}$  3270, 3120, 2991, 1738, 1550, 1240  $cm^{-1}$ .  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  2.31 (6H, s, 2 $CH_3$ ), 8.63 (1H, br s, NH).

***N*-Acetyl-2-chloroacetamide (Table 2, entry 2).** White solid, m.p.: 113-114 °C. IR (KBr)  $\nu_{max}$  3254, 3180, 2998, 1740, 1545, 1225, 1160  $cm^{-1}$ .  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  2.42 (3H, s,  $CH_3$ ), 4.27 (2H, s,  $CH_2$ ), 8.63 (1H, br s, NH).

***N*-Acetylbutyramide (Table 2, entries 3 and 6).** White solid, m.p.: 56-57 °C. IR (KBr)  $\nu_{max}$  3260, 3175, 2984, 1740, 1540, 1240, 1160  $cm^{-1}$ .  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  0.99 (3H, t,  $J = 7.4$  Hz,  $CH_3$ ), 1.67-1.72 (2H, m,  $CH_2$ ), 2.36 (3H, s,  $CH_3$ ), 2.48 (2H, t,  $J = 7.35$  Hz,  $CH_2$ ), 7.83 (1H, br s, NH).

***N*-Acetylpropionamide (Table 2, entry 4).** White solid, m.p.: 84-85 °C. IR (KBr)  $\nu_{max}$  3265, 3236, 1727, 1538, 1510  $cm^{-1}$ .  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  1.18 (3H, t,  $J = 7.35$  Hz,  $CH_3$ ), 2.36 (3H, s,  $CH_3$ ), 2.55 (2H, q,  $J = 7.35$  Hz,  $CH_2$ ), 8.09 (1H, br s, NH).

***N*-Propionylbutyramide (Table 2, entry 5).** White solid, m.p.: 107-108 °C. IR (KBr)  $\nu_{max}$  3226, 3170, 2991, 1689, 1510, 1112  $cm^{-1}$ .  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  0.98 (3H, t,  $J = 7.35$  Hz,  $CH_3$ ), 1.16 (3H, t,  $J = 7.40$  Hz,  $CH_3$ ), 1.67-1.71 (2H, m,  $CH_2$ ), 2.56 (2H, t,  $J = 7.37$  Hz,  $CH_2$ ), 2.64 (2H, q,  $J = 7.35$  Hz,  $CH_2$ ), 8.37 (1H, br s, NH).

***N*-Butyrylbutyramide (Table 2, entry 7).** White solid, m.p.: 103-104 °C. IR (KBr)  $\nu_{max}$  3280, 3190, 2990, 1740,

1535, 1415, 1170, 780, 710  $cm^{-1}$ .  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  0.99 (6H, t,  $J = 7.40$  Hz, 2 $CH_3$ ), 1.67-1.73 (4H, m, 2 $CH_2$ ), 2.57 (4H, t,  $J = 7.4$  Hz, 2 $CH_2$ ), 7.81 (1H, br s, NH). MS (EI)  $m/z$ : 157.07 (6.43) [ $M^+$ ], 129.05 (18.29), 90.99 (47.66), 88.02 (88.24), 71.03 (100).

***N*-Acetyl-4-methylbenzamide (Table 3, entry 1).** White solid, m.p.: 111-113 °C. IR (KBr)  $\nu_{max}$  3291, 1742, 1675, 1597, 1482, 1240  $cm^{-1}$ .  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  2.43 (3H, s,  $CH_3$ ), 2.61 (3H, s,  $CH_3$ ), 7.30 (2H, d,  $J = 8.25$  Hz, ArH), 7.76 (2H, d,  $J = 8.25$  Hz, ArH), 8.72 (1H, br s, NH).

***N*-Acetyl-2-thiophenamide (Table 3, entry 2).** White solid, m.p.: 134-135 °C. IR (KBr)  $\nu_{max}$  3280, 3097, 2926, 1708, 1680, 1530, 1480, 1375, 1250, 1100, 840, 720  $cm^{-1}$ .  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  2.61 (3H, s,  $CH_3$ ), 7.16 (1H,  $J = 4.35$  Hz, CH), 7.67 (1H, d,  $J = 4.8$  Hz, CH), 7.83 (1H, d,  $J = 3.38$  Hz, CH), 9.32 (1H, br s, NH). MS (EI)  $m/z$ : 171.06 (3) [ $M+2$ ], 169.07 (57.40) [ $M^+$ ], 141.06 (16.42), 136.09 (37.87), 111.03 (100).

***N*-Acetylbenzamide (Table 3, entry 3).** White solid, m.p.: 109-110 °C. IR (KBr)  $\nu_{max}$  3290, 2940, 1725, 1680, 1600, 1520, 1220  $cm^{-1}$ .  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  2.63 (3H, s,  $CH_3$ ), 7.52 (2H, t,  $J = 7.8$  Hz, ArH), 7.62 (1H, t,  $J = 7.65$  Hz, ArH), 7.86 (2H, d,  $J = 7.8$  Hz, ArH), 8.63 (1H, br s, NH).

***N*-Propionyl-2-thiophenamide (Table 3, entry 4).** White solid, m.p.: 137-138 °C. IR (KBr)  $\nu_{max}$  3248, 3055, 2970, 1667, 1493, 1330, 1219, 1168, 950, 770  $cm^{-1}$ .  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  1.21 (3H, t,  $J = 7.30$  Hz,  $CH_3$ ), 3.02 (2H, q,  $J = 7.30$  Hz,  $CH_2$ ), 7.15 (1H, t,  $J = 4.65$  Hz, CH), 7.66 (1H, d,  $J = 4.50$  Hz, CH), 7.79 (1H, d,  $J = 3.80$  Hz, CH), 9.05 (1H, br s, NH). MS (EI)  $m/z$ : 185.11 (5.34) [ $M+2$ ], 183.11 (75.81) [ $M^+$ ], 155.14 (56.99), 150.16 (88.17), 128.13 (85.48), 111.13 (100), 83.13 (74.73).

***N*-Propionyl-4-methylbenzamide (Table 3, entry 5).** White solid, m.p.: 109-111 °C. IR (KBr)  $\nu_{max}$  3284, 3035, 2950, 1740, 1605, 1500, 1210, 1020, 840, 740  $cm^{-1}$ .  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  1.23 (3H, t,  $J = 7.35$  Hz,  $CH_3$ ), 2.44 (3H, s,  $CH_3$ ), 3.03 (2H, q,  $J = 7.35$  Hz,  $CH_2$ ), 7.31 (2H, d,  $J = 3.65$  Hz, ArH), 7.75 (2H, d,  $J = 6.65$  Hz, ArH), 8.57 (1H, br s, NH). MS (EI)  $m/z$ : 191.15 (19.91) [ $M^+$ ], 136.11 (13.27), 119.11 (100), 91.09 (78.40), 65.11 (35.80).

***N*-Acetyl-4-chlorobenzamide (Table 5, entry 1).** White solid, m.p.: 136-137 °C. IR (KBr)  $\nu_{max}$  3260, 1760, 1685, 1593, 1468  $cm^{-1}$ .  $^1H$  NMR (500 MHz,  $CDCl_3$ )  $\delta$  2.62 (3H, s,

CH<sub>3</sub>), 7.49-7.51 (2H, m, ArH), 7.81-7.83 (2H, m, ArH), 8.71 (1H, br s, NH).

**N-Acetyl-3-Nitrobenzamide (Table 5, entry 2).** White solid, m.p.: 195-196 °C. IR (KBr)  $\nu_{\max}$  3260, 3100, 2920, 1717, 1598, 1460, 1350 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  2.65 (3H, s, CH<sub>3</sub>), 7.75 (1H, t, *J* = 7.9 Hz, ArH), 8.22 (1H, d, *J* = 7.8 Hz, ArH), 8.47-8.49 (1H, m, ArH), 8.75 (1H, d, *J* = 1.75 Hz, ArH), 8.87 (1H, br s, NH).

**N-Acetyl-4-fluorobenzamide (Table 5, entry 3).** White solid, m.p.: 111-112 °C. IR (KBr)  $\nu_{\max}$  3295, 3090, 2990, 1690, 1600, 1585, 1465, 1395, 1265, 1190, 1020, 850, 750 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  2.62 (3H, s, CH<sub>3</sub>), 7.18-7.22 (2H, m, ArH), 7.88-7.91 (2H, m, ArH), 8.66 (1H, br s, NH). MS (EI) *m/z*: 181.14 (8.28) [M<sup>+</sup>], 123.13 (100), 95.14 (57.67), 75.14 (45.40).

**N-Acetyl-3-chlorobenzamide (Table 5, entry 4).** White solid, m.p.: 113-115 °C. IR (KBr)  $\nu_{\max}$  3420, 3270, 1718, 1685, 1580, 1260 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  2.62 (3H, s, CH<sub>3</sub>), 7.45 (1H, t, *J* = 7.4 Hz, ArH), 7.58-7.60 (1H, m, ArH), 7.69-7.71 (1H, m, ArH), 7.85 (1H, t, *J* = 1.85 Hz, ArH), 8.49 (1H, br s, NH).

**N-Propionyl-4-fluorobenzamide (Table 5, entry 5).** White solid, m.p.: 115 °C. IR (KBr)  $\nu_{\max}$  3250, 3100, 2920, 1720, 1685, 1605, 1480, 1370, 1260, 1190, 850, 750 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  1.22 (3H, t, *J* = 6.50 Hz, CH<sub>3</sub>), 3.03 (2H, q, *J* = 6.50 Hz, CH<sub>2</sub>), 7.18 (2H, t, *J* = 7.50 Hz, ArH), 7.94 (2H, s, ArH), 9.02 (1H, br s, NH). MS (EI) *m/z*: 195.15 (5.94) [M<sup>+</sup>], 123.13 (100), 95.11 (88.03), 75.12 (70.42).

**N-Propinyl-4-chlorobenzamide (Table 5, entry 6).** White solid, m.p.: 157-158 °C. IR (KBr)  $\nu_{\max}$  3320, 3100, 2940, 1720, 1680, 1595, 1260, 1220 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  1.23 (3H, t, *J* = 7.3 Hz, CH<sub>3</sub>), 3.03 (2H, q, *J* = 7.3 Hz, CH<sub>2</sub>), 7.47-7.49 (2H, m, ArH), 7.83-7.85 (2H, m, ArH), 8.86 (1H, br s, NH).

**N-Butyryl-4-fluorobenzamide (Table 5, entry 7).** White solid, m.p.: 108-109 °C. IR (KBr)  $\nu_{\max}$  3295, 3070, 1730, 1693, 1602, 1480, 1260, 1133, 810, 740 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  1.04 (3H, t, *J* = 7.40 Hz, CH<sub>3</sub>), 1.74-1.80 (2H, m, CH<sub>2</sub>), 2.96 (2H, t, *J* = 7.35 Hz, CH<sub>2</sub>), 7.17-7.20 (2H, m, ArH), 7.86-7.89 (2H, m, ArH), 8.45 (1H, br s, NH). MS (EI) *m/z*: 209.15 (2.29) [M<sup>+</sup>], 123.09 (100), 95.09 (64.94), 75.09 (40.75).

**N-Butyryl-3-chlorobenzamide (Table 5, entry 8).**

White solid, m.p.: 109-111 °C. IR (KBr)  $\nu_{\max}$  3420, 3185, 2920, 1710, 1555 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  1.03 (3H, t, *J* = 7.4 Hz, CH<sub>3</sub>), 1.73-1.79 (2H, m, CH<sub>2</sub>), 2.98 (2H, t, *J* = 7.35 Hz, CH<sub>2</sub>), 7.44 (1H, t, *J* = 7.9 Hz, ArH), 7.58 (1H, d, *J* = 7.9 Hz, ArH), 7.74 (1H, d, *J* = 7.75 Hz, ArH), 7.88 (1H, t, *J* = 1.7 Hz, ArH), 8.82 (1H, br s, NH).

**N-Butyryl-3-nitrobenzamide (Table 5, entry 9).** White solid, m.p.: 108-110 °C. IR (KBr)  $\nu_{\max}$  3312, 3097, 2980, 1713, 1690, 1535, 1460, 1350, 1230, 950, 820 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  1.04 (3H, t, *J* = 7.40 Hz, CH<sub>3</sub>), 1.74-1.80 (2H, m, CH<sub>2</sub>), 2.99 (2H, t, *J* = 7.35 Hz, CH<sub>2</sub>), 7.74 (1H, t, *J* = 8 Hz, ArH), 8.23-8.25 (1H, m, ArH), 8.46-8.48 (1H, m, ArH), 8.75 (1H, s, ArH), 9.03 (1H, br s, NH). MS (EI) *m/z*: 236.09 (2.40) [M<sup>+</sup>], 221.12 (9.45), 208.13 (22.36), 167.14 (56.10), 150.13 (85.37), 104.15 (61.79), 76.16 (100).

## RESULTS AND DISCUSSION

### Synthesis of Acyclic Imides by the Reaction of Liquid Aliphatic Nitriles with Aliphatic Anhydrides in the Presence of H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub> under Thermal Conditions and MW Irradiation

First, the amount of catalyst, reaction temperature and the amount of nitrile were optimized in the reaction of acetonitrile as a liquid aliphatic nitrile with acetic anhydride (1 mmol). As shown in Table 1, the best result was obtained with 20 mmol of acetonitrile in the presence of 0.055 mmol of the catalyst at 70 °C (entry 4). In the absence of the catalyst, only 8% of imide was produced (entry 17). The catalytic activity of other heteropoly acids such as H<sub>4</sub>SiW<sub>12</sub>O<sub>40</sub> and H<sub>3</sub>PMo<sub>12</sub>O<sub>40</sub> was also investigated in this reaction using the same amount of catalyst and the corresponding imide was obtained in 53% and 75% yields, respectively. These results showed that H<sub>4</sub>SiW<sub>12</sub>O<sub>40</sub> and H<sub>3</sub>PMo<sub>12</sub>O<sub>40</sub> were less efficient than H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub>. The reactions of liquid aliphatic nitriles (acetonitrile, chloroacetonitrile and butyronitrile) with aliphatic anhydrides (acetic, propionic and butyric anhydrides) were started under optimized conditions and the corresponding imides were obtained in good to excellent isolated yields (87-96%) (Table 2).

In order to investigate the effect of MW, the reaction of acetonitrile (20 mmol) with acetic anhydride (1 mmol) in the presence of the catalyst (0.055 mmol), as a model reaction,

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**Table 1.** Reaction of Acetonitrile with Acetic Anhydride (1 mmol) in the Presence of  $H_3PW_{12}O_{40}$  under Different Conditions

Entry	Catalyst (mmol)	Acetonitrile (mmol)	T (°C)	Conversion after 40 min (%) <sup>a</sup>
1	0.030	20	70	43
2	0.040	20	70	81
3	0.050	20	70	93
4	0.055	20	70	100
5	0.060	20	70	100
6	0.055	20	25	5
7	0.055	20	50	40
8	0.055	20	60	63
10	0.055	1	70	7
11	0.200	1	70	13
12	0.055	2	70	18
13	0.055	4	70	34
14	0.055	6	70	51
15	0.055	10	70	70
16	0.055	15	70	89
17	No catalyst	20	70	8

<sup>a</sup>GC yield.

**Table 2.** Synthesis of Acyclic Imides by the Reaction of Liquid Aliphatic Nitriles with Aliphatic Anhydrides Catalyzed by  $H_3PW_{12}O_{40}$  under Thermal Conditions and MW Irradiation<sup>a</sup>

Entry	Anhydride	Nitrile	Imide	Thermal		MW		Ref. <sup>c</sup>
				Time (min)	Yield (%) <sup>b</sup>	Time (s)	Yield (%) <sup>b</sup>	
1	$(CH_3CO)_2O$	$CH_3CN$		40	96	25	97	[21]
2	$(CH_3CO)_2O$	$ClCH_2CN$		30	91	30	93	[21]
3	$(CH_3CO)_2O$	$CH_3CH_2CH_2CN$		55	89	20	87	[45]
4	$(CH_3CH_2CO)_2O$	$CH_3CN$		50	94	25	93	[21]
5	$(CH_3CH_2CO)_2O$	$CH_3CH_2CH_2CN$		50	89	25	90	[21]
6	$(CH_3CH_2CH_2CO)_2O$	$CH_3CN$		50	89	40	89	[45]
7	$(CH_3CH_2CH_2CO)_2O$	$CH_3CH_2CH_2CN$		45	87	45	87	-

<sup>a</sup>Reaction conditions: nitrile (20 mmol), anhydride (1 mmol), catalyst (0.055 mmol), T (70 °C) for thermal conditions and T (40 °C) for MW irradiation at 800 W. <sup>b</sup>Isolated yield. <sup>c</sup>References of known compounds.

was performed at 500, 650 and 800 W and the product, *N*-acetylacetamide was obtained in 67, 88 and 97% yields, respectively. Therefore, 800 W and 40 °C were the best conditions. Blank control in the absence of the catalyst showed that only 14% of the product formed under the same reaction conditions. Then, the synthesis of acyclic imides by the reaction of liquid aliphatic nitriles with aliphatic anhydrides catalyzed by H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub> under MW irradiation was performed under these optimized conditions. The obtained results (Table 2) showed that the reaction times decreased to second and the corresponding imides were obtained in excellent yields (87-97%).

### Synthesis of Acyclic Imides by the Reaction of Liquid Aromatic Nitriles with Aliphatic Anhydrides in the Presence of H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub> under Thermal Conditions and MW Irradiation

In this part, liquid aromatic nitriles such as benzonitrile, 2-thiophenecarbonitrile and 4-methylbenzonitrile were used for the synthesis of imides. Due to the higher density and boiling point of these nitriles in comparison with aliphatic nitriles, it was difficult to remove the remaining nitrile at the end of the reaction. Therefore, the reactions were caused with 5 mmol of nitriles, 1 mmol of anhydride and 0.055 mmol of H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub>.

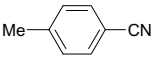
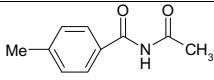
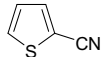
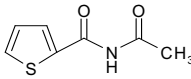
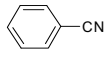
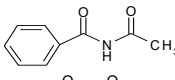
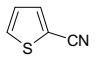
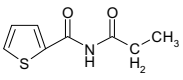
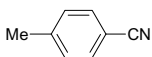
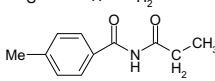
The results, which are summarized in Table 3, show that the corresponding imides were obtained in high isolated yields (73-85%) both under thermal conditions and MW irradiation. It is noteworthy that in the case of aryl nitriles, no corresponding amides were produced as side-products as reported previously [16].

### Synthesis of Acyclic Imides by the Reaction of Solid Aromatic Nitriles with Aliphatic Anhydrides in the Presence of H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub> under Thermal Conditions and MW Irradiation

First, we optimized the amount of catalyst in the synthesis of *N*-acetyl-3-chlorobenzamide by the reaction of 3-chlorobenzonitrile (1 mmol) with acetic anhydride (2 mmol) at 80 °C. The results showed that the highest yield of the product was obtained in the presence of 0.2 mmol of H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub> (Table 4, entry 4). Under these conditions, various substituted benzonitriles reacted with different aliphatic anhydrides and the corresponding imides were isolated in 76-93% yields (Table 5). However, 4-nitrobenzonitrile was less reactive in these reactions and the respective imide was obtained in 47-55% yields (Table 5, entries 2, 9).

The reaction of 3-chlorobenzonitrile (1 mmol) with acetic anhydride (2 mmol) was also investigated under microwave

**Table 3.** Synthesis of Acyclic Imides by the Reaction of Liquid Aromatic Nitriles with Aliphatic Anhydrides Catalyzed by H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub> under Thermal Conditions and MW Irradiation<sup>a</sup>

Entry	Anhydride	Nitrile	Imide	Thermal		MW		Ref. <sup>c</sup>
				Time (min)	Yield (%) <sup>b</sup>	Time (s)	Yield (%) <sup>b</sup>	
1	(CH <sub>3</sub> CO) <sub>2</sub> O			50	84	40	85	[21]
2	(CH <sub>3</sub> CO) <sub>2</sub> O			55	83	40	83	-
3	(CH <sub>3</sub> CO) <sub>2</sub> O			40	73	45	76	[21]
4	(CH <sub>3</sub> CH <sub>2</sub> CO) <sub>2</sub> O			45	80	45	85	-
5	(CH <sub>3</sub> CH <sub>2</sub> CO) <sub>2</sub> O			65	81	40	81	-

<sup>a</sup>Reaction conditions: nitrile (5 mmol), anhydride (1 mmol), catalyst (0.055 mmol), T (70 °C) for thermal conditions and T (40 °C) for MW irradiation at 800 W. <sup>b</sup>Isolated yield. <sup>c</sup>References of known compounds.

## Efficient Synthesis of Symmetrical and Unsymmetrical Acyclic Imides

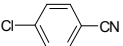
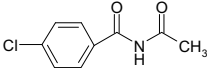
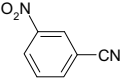
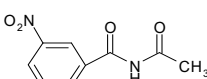
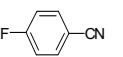
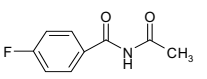
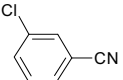
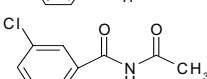
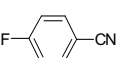
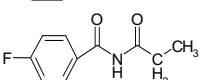
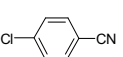
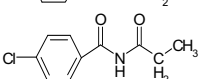
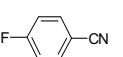
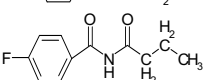
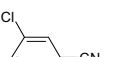
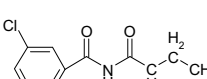
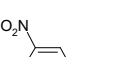
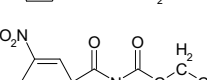
**Table 4.** Reaction of 3-Chlorobenzonitrile with Acetic Anhydride in the Presence of Different Amounts of  $H_3PW_{12}O_{40}$  under Thermal Conditions<sup>a</sup>

Entry	Catalyst (mmol)	Time (min)	Yield (%) <sup>b</sup>
1	0.055	95	62
2	0.10	95	67
3	0.15	95	75
4	0.20	95	85
5	0.25	95	85

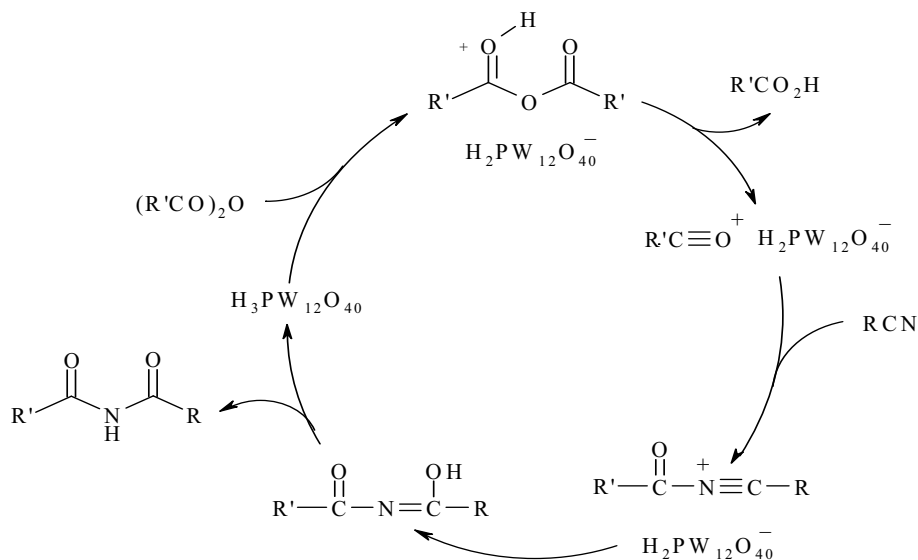
<sup>a</sup>Reaction conditions: 3-chlorobenzonitrile (1 mmol), acetic anhydride (1 mmol), catalyst, T (80 °C). <sup>b</sup>Isolated yield.

irradiation. For this purpose, the reaction occurred at 800, 900 and 1000 W and the corresponding imide was obtained in 75, 85 and 90% yields, respectively. Therefore, 1000 W and 40 °C were selected as the optimum power and temperature. Under these conditions, the reactions of solid aromatic nitriles with aliphatic anhydrides were triggered and the corresponding imides were obtained in good to high yields, except for 3-nitrobenzonitrile, in very short reaction times (Table 5). It is noteworthy that due to the advantages of solvent-free systems, all reactions took place under solvent-free conditions. A plausible mechanism for these reactions is proposed in Scheme 2.

**Table 5.** Synthesis of Acyclic Imides by the Reaction of Solid Aromatic Nitriles with Aliphatic Anhydrides Catalyzed by  $H_3PW_{12}O_{40}$  under Thermal Conditions and MW Irradiation<sup>a</sup>

Entry	Anhydride	Nitrile	Imide	Thermal		MW		Ref. <sup>c</sup>
				Time (min)	Yield (%) <sup>b</sup>	Time (s)	Yield (%) <sup>b</sup>	
1	$(CH_3CO)_2O$			85	86	50	90	[46]
2	$(CH_3CO)_2O$			120	55	70	55	[47]
3	$(CH_3CO)_2O$			70	93	40	93	-
4	$(CH_3CO)_2O$			95	85	60	90	[21]
5	$(CH_3CH_2CO)_2O$			75	91	40	94	-
6	$(CH_3CH_2CO)_2O$			80	81	40	87	[48]
7	$(CH_3CH_2CH_2CO)_2O$			75	83	40	90	-
8	$(CH_3CH_2CH_2CO)_2O$			90	76	60	83	[21]
9	$(CH_3CH_2CH_2CO)_2O$			140	47	90	51	-

<sup>a</sup>Reaction conditions: nitrile (1 mmol), anhydride (2 mmol), catalyst (0.2 mmol), T (80 °C) for thermal conditions and T (40 °C) for MW irradiation at 1000 W. <sup>b</sup>Isolated yield. <sup>c</sup>References of known compounds.



Scheme 2

**Table 6.** Recovery and Reuse of  $\text{H}_3\text{PW}_{12}\text{O}_{40}$  in the Reaction of Acetonitrile with Acetic Anhydride under Thermal Conditions and MW Irradiation<sup>a</sup>

Run	Thermal		MW	
	Time (min)	Yield (%) <sup>b</sup>	Time (s)	Yield (%) <sup>b</sup>
1	40	96	25	97
2	40	96	25	96
3	40	95	25	96
4	40	94	25	96
5	40	94	25	95
6	40	92	25	93

<sup>a</sup>Reaction conditions: nitrile (20 mmol), anhydride (2 mmol), catalyst (0.055 mmol), T (70 °C) for thermal conditions and T (40 °C) for MW irradiation at 800 W. <sup>b</sup>Isolated yield.

## CATALYST RECOVERY AND REUSE

The recovery and reusability of the catalyst were investigated using the acetonitrile as the model substrate in the reaction with acetic anhydride under both thermal conditions and MW irradiation. After completion of the reaction,  $\text{Et}_2\text{O}$  was added and the catalyst was separated by filtration. The

recovered catalyst was dried at 110 °C for 3 h and reused in the next run. The results show that the catalyst can be reused for six consecutive trials without loss of its activity (Table 6).

## CONCLUSIONS

In conclusion, we have reported a new, efficient and one-



pot synthesis of symmetrical and unsymmetrical acyclic imides from the commercially available starting materials. Simple and clean reaction, high yields, short reaction times, environmentally benign procedure and the use of a cheap, easily handled, relatively non-toxic and reusable catalyst are salient features of this methodology.

## ACKNOWLEDGEMENTS

We are grateful for the financial support of this work by the Center of Excellence of Chemistry and also the Research Council of the University of Isfahan.

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