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Phosphomolybdic acid supported on silica gel as efficient and reusable catalyst for Amidation of esters

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ABSTRACT

A series of *N*-phenyl benzamide derivatives has been prepared from various aryl carboxylic esters and aniline under microwave irradiation conditions using catalytic amount of PMA-SiO₂ in 10 min. The catalyst reused several times.

Keywords: benzyl amine, Aryl carboxylic esters and PMA-SiO₂.

INTRUCTION

In modern chemistry, amide bond is one of the most significant functional group and most prolific moieties in modern pharmaceutical molecules [1]. Thus; efficient synthesis of amide is an important area in organic synthesis. Generally, amides are prepared from carboxylic acid derivatives (such as acids, anhydrides, acylchlorides, anhydrides, or esters) and amines, but there are some dis-advantages such as stoichiometric amount of wastes, poor atom efficiency, harsh reaction condition and diffucielty in purification [2]. Thus, the number of metal catalyst system has also been developed [3-4]. Among various methods, direct Amidation of ester with amines is a suitable method, because esters are usually economical and commercially. In this methods using catalysts (Zicornium (IV) alkoxide[5], iridium (III) complexes[6], Mg(OCH₃)₂[7], DBU[8], CaCl₂[6], K₃PO₄[9], NaOMe[10], Mg₂N₃[11], BEMP[12], Al(Me)₃[13], Ru-MaCHO [14], La(OTf)₃[15] and enzyme-catalysed transformation[16] have been reported. However, in these methods still suffer from some drawbacks, such as recycle of catalyst and longer reaction time.

In recent years, the use of microwave irradiation as a thermal source to accelerate organic reactions has gained popularity after Gedye's pioneering report. Due to shorter reaction times cleaner reactions, easy work up and minimization of thermal decomposition products of this technique are advantageous over conventional methods [17-18]. Therefore, to develop and efficient method for the synthesis of benzamide derivatives, using PMA-SiO₂ as catalyst and microwave sources.

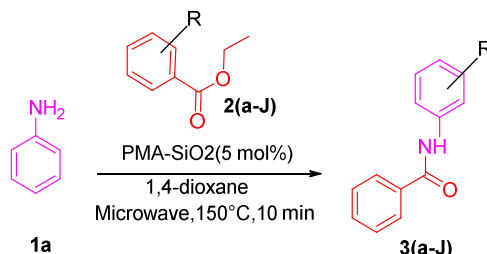
MATERIALS AND METHODS

General condition

All the reagents were obtained commercially (SD fine and Aldrich) and used with further purification. Melting points were determined by open capillary method. The IR spectra (in KBr pellets) were recorded on a Perkin-Elmer FTIR spectrophotometer. ¹H NMR (DMSO) 400 MHz and ¹³C NMR (DMSO-d₆, 100 MHz) were recorded on

spectrometer TMS as internal standard (chemical shifts and ppm). The purity of the compounds was checked by LCMS.

Scheme 1

**General procedure:**

A dry Pyrex tube fitted with an air-tight rubber cap was charged aniline (**1a**, 100 mg, 0.25 mmol), ethyl benzoate (**2a**, 35 mg, 0.25 mmol), PMA-SiO₂ (5 mol%) and 1,4-dioxane (3 mL) were added. The resulting mixture was placed in a CEM microwave reactor at 150°C for 10 min. Then the reaction mixture was cooled, filtered and the filtrate was transferred to a separatory funnel and diluted with ethyl acetate and water. The organic phase was separated and dried over anhydrous sodium sulfate. The organic solution was filtered and the filtrate concentrated prior to silica gel chromatography using hexane-ethyl acetate (1:1). The fractions were concentrated and dried in vacuum to get 113 mg (yield, 70%) of N-Phenylbenzamide. The used catalyst was reused several times.

N-Phenylbenzamide (3a): ¹H NMR (300 MHz, DMSO-d₆): δ (ppm) 7.15 (m, 1H), 7.32 (m, 2H), 7.51 (m, 3H), 7.80 (d, 2H), 7.96 (d, 2H), 10.20 (s, 1H); ¹³C NMR (75 MHz, DMSO-d₆): δ (ppm) 120.5, 123.6, 127.7, 128.5, 128.6, 131.2, 135.1, 139.1, 165.7.

N-p-Tolylbenzamide (3b): ¹H NMR (400 MHz, CDCl₃): δ (ppm) 2.31 (s, 3H), 7.12 (d, 2H, *J* = 8.0 Hz), 7.39-7.61 (m, 6H), 7.83 (d, 2H, *J* = 8.0 Hz); ¹³C NMR (100 MHz, CDCl₃): δ (ppm) 20.8, 120.4, 127.0, 128.3, 129.5, 130.1, 131.6, 133.6, 135.2, 171.8.

2-Methyl-N-phenylbenzamide (3c): ¹H NMR (400 MHz, d₆-DMSO): δ (ppm) 10.18 (s, 1H), 7.85 – 7.70 (m, 4H), 7.41 (m, 2H), 7.38 – 7.30 (m, 2H), 7.17 – 7.00 (m, 1H), 2.40 (s, 3H); ¹³C NMR (100 MHz, d₆-DMSO): δ (ppm) 165.4, 139.1, 137.2, 134.0, 132.5, 128.8, 128.6, 128.6, 124.9, 123.8, 120.4, 21.0;

3-Methyl-N-phenylbenzamide (3d): ¹H NMR (400 MHz, d₆-DMSO): δ (ppm) 10.28 (s, 1H), 7.72 (d, *J* = 7.9 Hz, 2H), 7.40 (d, *J* = 7.6 Hz, 1H), 7.42 – 7.25 (m, 5H), 7.17 (t, *J* = 7.4 Hz, 1H), 2.33 (s, 3H); ¹³C NMR (100 MHz, d₆-DMSO): δ (ppm) 167.5, 139.6, 137.9, 135.4, 130.1, 129.1, 128.9, 127.6, 125.9, 123.1, 119.9, 19.8

Phenylcinnamamide (3e): ¹H NMR (CDCl₃, 300 MHz) δ 9.70 (s, 1H, -NH), 7.53 (m, 10H, Ar-H), 7.55 (d, 1H, Hz), 6.70 (d, 1H, Hz). ¹³C NMR (300 MHz, CDCl₃): 163.7, 139.0, 140.20, 135.82, 128.40, 129.90, 128.4, 126.5, 122, 120.5.

4-nitro-N-phenylbenzamide (3f): ¹H NMR (400 MHz, d₆-DMSO): δ 10.47 (s, 1H), 8.26 (d, *J* = 8.9 Hz, 2H), 8.2 (d, *J* = 8.9 Hz, 2H), 7.76 (d, *J* = 7.6 Hz, 2H), 7.36 (t, *J* = 7.9 Hz, 2H), 7.17 (t, *J* = 7.4 Hz, 1H); ¹³C NMR (100 MHz, d₆-DMSO): δ (ppm) 163.9, 149.9, 141.9, 139.8, 129.3, 129.9, 124.3, 124.6, 121.9;

4-nitro-N-phenylbenzamide (3g): ¹H NMR (400 MHz, d₆-DMSO): δ (ppm) 10.7 (s, 1H), 8.4 (d, *J* = 8.9 Hz, 2H), 8.2 (d, *J* = 8.9 Hz, 2H), 7.8 (d, *J* = 7.6 Hz, 2H), 7.4 (t, *J* = 7.9 Hz, 2H), 7.17 (t, *J* = 7.4 Hz, 1H); ¹³C NMR (100 MHz, d₆-DMSO): δ (ppm) 164.9, 149.9, 141.8, 139.9, 129.2, 129.8, 124.2, 124.9, 121.8;

N-(4-Methoxy-phenyl)-benzamide (3h): ¹H NMR (400 MHz, d₆-DMSO): δ (ppm) 10.2 (s, 1H), 7.95 – 7.87 (m, 2H), 7.62 (d, *J* = 9.0 Hz, 2H), 7.60 – 7.40 (m, 3H), 6.96 – 6.80 (m, 2H), 3.72 (s, 3H); ¹³C NMR (100 MHz, d₆-DMSO): δ (ppm) 165.0, 155.4, 135.0, 131.2, 130.5, 127.4, 127.0, 121.2, 113.6, 53.9;

4-Fluoro-N-phenyl-benzamide (3i): ¹H NMR (400 MHz, d₆-DMSO): δ (ppm) 10.4 (s, 1H), 8.12 – 7.96 (m, 2H), 7.80 – 7.71 (m, 2H), 7.43 – 7.30 (m, 4H), 7.12 – 7.06 (m, 1H); ¹³C NMR (100 MHz, d₆-DMSO): δ (ppm) 166.8, 164.9, 163.3, 138.2, 131.9, 131.8, 131.2, 130.8, 129.2, 129.0, 124.6, 120.2, 114.9, 114.3.

N-phenyl-4-(trifluoromethyl) benzamide (3j): ¹H NMR (400 MHz, d₆-DMSO): δ (ppm) 10.38 (s, 1H), 8.14 (d, *J* = 8.1 Hz, 2H), 7.91 (d, *J* = 8.3 Hz, 2H), 7.77 (d, *J* = 7.6 Hz, 2H), 7.37 (m, 2H), 7.13 (t, *J* = 7.4 Hz, 1H); ¹³C NMR (100 MHz, d₆-DMSO): δ (ppm) 163.4, 138.2, 131.2, 130.9, 130.6, 128.2, 127.1, 126.8, 126.8, 125.8, 124.7, 123.5, 122.0, 120.1, 118.3;

RESULTS AND DISCUSSION

We first investigated the model reaction without catalyst in 1, 4-dioxane. The desired product (**3a**) 10 % was formed under microwave conditions (**Table 1**, entry 1). Under these conditions, when the reaction was performed using PMA-SiO₂ catalysts produce the desired products in good yields (**Table 1**, entries 1).

In order to investigate the recyclability and reusability of the catalyst, it was recovered by simple filtration, washing twice with 1,4 -dioxane (2mL) and dried in vacuum at 30 °C. Under similar reaction conditions, the dried catalyst was reused as such for subsequent experiments at least five consecutive cycles without much appreciable loss in its catalytic activity. This data demonstrate that high stability of the catalyst under the reaction conditions (**Figure 1**) under microwave irradiation conditions.

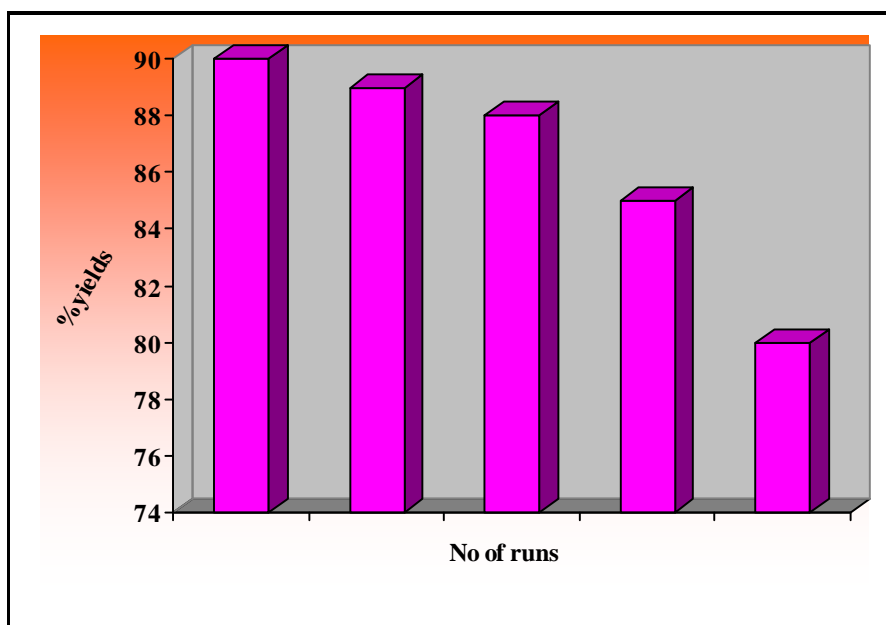
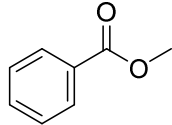
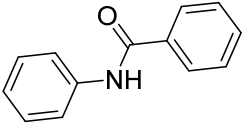
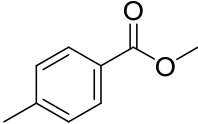
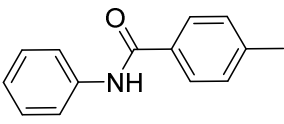
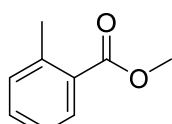
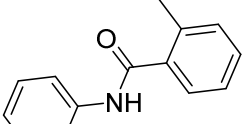
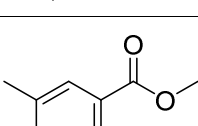
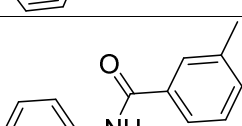
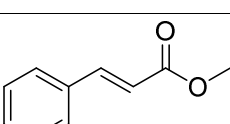
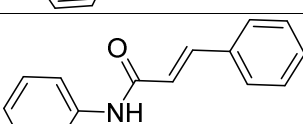
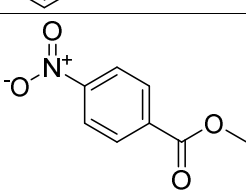
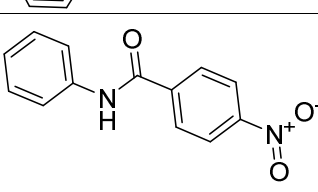
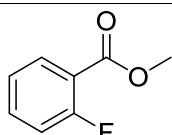
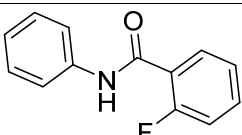
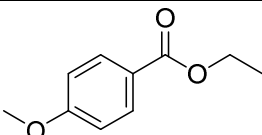
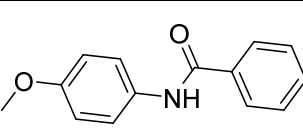
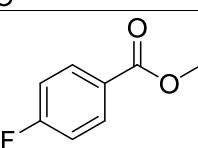
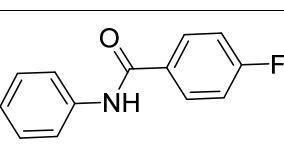
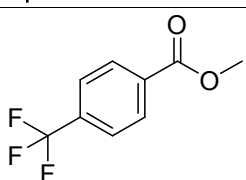
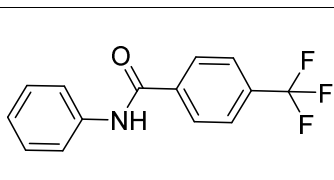


Figure 1: Reusability of the PMA-SiO₂ catalyst in Amide coupling

Finally optimized reaction conditions of various aryl carboxylic esters (**2a-j**) and aniline using 5 mol% PMA-SiO₂ to obtain the titled compounds (**3a-j**) with good to excellent product yields without formation of any side products under MWI with 100 W powers.

Table 2: Synthesis of N-phenyl benzamide derivatives

SNO	Esters	Products	Time(min)	yields
01			10	85
02			10	79
03			11	80
04			10	82
05			12	80
06			12	81
07			11	77
08			10	78
09			10	80
10			11	67

Reaction conditions: a. aniline (1a), ethyl benzoate (2a-j) and 5 mol% PMA-SiO₂ catalyst at 100 W power MWI for 10 min in 1, 4-Dioxane
b. isolated yields.

CONCLUSION

A series of N- phenyl benzamide derivatives were synthesized by one step procedure. The procedure exhibits several advantages, such as mild reaction conditions, simple protocol, and good yields. The Catalyst reused several times. Their structures were characterized by ¹H NMR, ¹³CNMR.

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