



## Green Synthesis of N-Substituted imides

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### Abstract:

An improved synthesis of N-substituted imides can be achieved from the reaction of anhydrides (phthalic, maleic & succinic.) with pre-melted anilines by grinding at room temperature in the absence of solvents. The advantages of this method are good yields, shorter reaction times, low cost and matching with green chemistry protocols.

**Keywords:** Phthalic anhydride, Maleic anhydride, Succinic anhydride and anilines.

### Introduction:

Phthalic anhydride is an important petrochemical producing a variety of commercially vital products/intermediates [1-2]. Its most predominant reaction is with nucleophiles. Phthalic anhydride reacts with a variety of nucleophiles, such as nitrogen nucleophiles [3-6], oxygen [7], carbon nucleophiles [8] etc. Although the reaction of phthalic anhydride with amines has been widely studied [3-4], there seems to be hardly any information [9] on reactions of phthalic anhydride with nucleophiles under green conditions. Interest in solid state reactions has increased in recent years, though the reactions in solutions are much more common. This is due to the fact that, in many cases, organic reactants when ground together in solid state, react more effectively than in solution phase where probably more complex interactions with solvent are present. Furthermore, the solid-state reactions have many advantages [10-12] over the solution-phase technique like less time, less vigorous conditions for reactions to occur, ease of processing, freedom from pollution-causing-solvent, removal of toxic solvents after completion of reactions etc. For instance, in many cases [10-12], simple solid-state reactions do yield desired products in excellent yields. We now wish to report a facile synthesis of imides under green conditions, specifically under solid-phase conditions.

### Materials and methods:

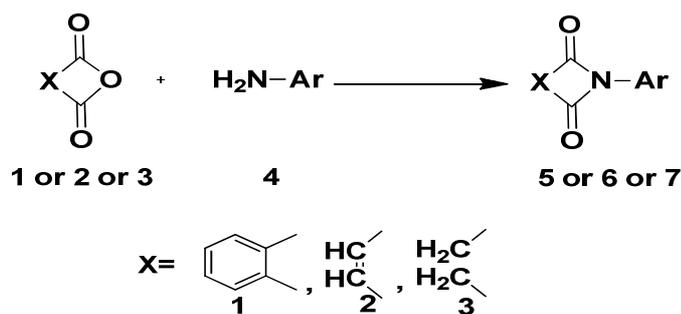
Melting points are uncorrected and were determined in open capillary tubes in sulphuric acid bath. TLC were run on silica gel-G and visualization was done using iodine or UV light. IR spectra were recorded using Perkin-Elmer 1000 instrument in KBr pellets. <sup>1</sup>H NMR spectra were recorded in CDCl<sub>3</sub>/DMSO-d<sub>6</sub> using TMS as internal standard with 400 MHz spectrometer. Mass spectra were recorded on Agilent-LCMS instrument.

### General procedure for the preparation of 3/6/10.

A mixture of the anhydride **1/2/3** (1 mM) and pre-melted anilines **4** (1 mM) were ground together in a mortar with a pestle for 5-10 minutes. The completion of the reaction was checked by Thin Layer Chromatography. Then ice-cold water was added to the reaction mixture, the solid that separated out was filtered, washed with water and dried. The product was recrystallised from ethanol to obtain **5/6/7**.

### Results and Discussion:

The reported general methods for the synthesis of N-Arylphthalimides need long time reflux & classical heating [13]. The results show solid phase synthesis can enhance the reaction rate when compared to classical heating, the reaction time were improved (**Table 1**). Simple physical grinding of a mixture of **1a** and aniline **4a** in a mortar and pestle at RT for about 5-10 min resulted in the formation of N-phenylphthaimide **5a**. Structure of the product has been established by comparison with authentic sample which was prepared [9] by direct reaction of phthalic anhydride with aniline in acetic acid at RT.



## SCHEME

This reaction has been found to be general one and has been extended to different pre-melted anilines **4** and the products thus obtained were assigned structure **5** by comparison with authentic samples [9].

(Scheme 1)(Table 1).

Similarly, simple physical grinding of a mixture of **2/3** and pre-melted aniline **4** in a mortar and pestle at RT for about 5-10 min resulted in the formation of N-phenylmaleimide **6/7**. Structure of the product has been established by comparison with authentic sample which was prepared [9] in solution phase.

**Table 1** Characterization data, reaction time and yields of **5/6/7**.

Entry	Starting Material	Reagent <b>4</b> (Ar)	Time (Min)	Product	Yield %	M.P( <sup>0</sup> C) (Ref.)
1	<b>1</b>	-C <sub>6</sub> H <sub>5</sub>	<b>5</b>	<b>5a</b>	<b>80</b>	202-203[9]
2	<b>1</b>	-C <sub>6</sub> H <sub>4</sub> -CH <sub>3</sub> -(p)	<b>5</b>	<b>5b</b>	<b>80</b>	198-200[9]
3	<b>1</b>	-C <sub>6</sub> H <sub>4</sub> -CH <sub>3</sub> -(o)	<b>5</b>	<b>5c</b>	<b>75</b>	181-182[9]
4	<b>1</b>	-C <sub>6</sub> H <sub>4</sub> -Cl-(p)	<b>7</b>	<b>5d</b>	<b>75</b>	191-192[9]
5	<b>1</b>	-C <sub>6</sub> H <sub>4</sub> -OCH <sub>3</sub> -(p)	<b>5</b>	<b>5e</b>	<b>75</b>	161-163[9]
6	<b>1</b>	-C <sub>6</sub> H <sub>4</sub> -Br-(p)	<b>10</b>	<b>5f</b>	<b>80</b>	203-204[9]
7	<b>1</b>	-C <sub>6</sub> H <sub>5</sub>	<b>6</b>	<b>6a</b>	<b>80</b>	>220[9]
8	<b>2</b>	-C <sub>6</sub> H <sub>4</sub> -CH <sub>3</sub> -(p)	<b>6</b>	<b>6b</b>	<b>75</b>	150-152[9]
9	<b>2</b>	-C <sub>6</sub> H <sub>4</sub> -CH <sub>3</sub> -(o)	<b>6</b>	<b>6c</b>	<b>75</b>	145-146[9]
10	<b>2</b>	-C <sub>6</sub> H <sub>4</sub> -Cl-(p)	<b>10</b>	<b>6d</b>	<b>80</b>	>220[9]
11	<b>2</b>	-C <sub>6</sub> H <sub>4</sub> -OCH <sub>3</sub> -(p)	<b>7</b>	<b>6e</b>	<b>75</b>	153-154[9]
12	<b>2</b>	-C <sub>6</sub> H <sub>4</sub> -Br-(p)	<b>10</b>	<b>6f</b>	<b>70</b>	>220[9]
13	<b>3</b>	-C <sub>6</sub> H <sub>5</sub>	<b>6</b>	<b>7a</b>	<b>70</b>	111-112[9]

14	3	$^-C_6H_4-CH_3-(p)$	6	7b	80	193-196[9]
15	3	$-C_6H_4-CH_3-(o)$	6	7c	80	146-147[9]
16	3	$-C_6H_4-Cl-(p)$	10	7d	80	141-143[9]
17	3	$-C_6H_4-OCH_3-(p)$	6	7e	75	161-162[9]
18	3	$-C_6H_4-Br-(p)$	10	7f	75	146-147[9]

\*Refers to yields of crude products only.

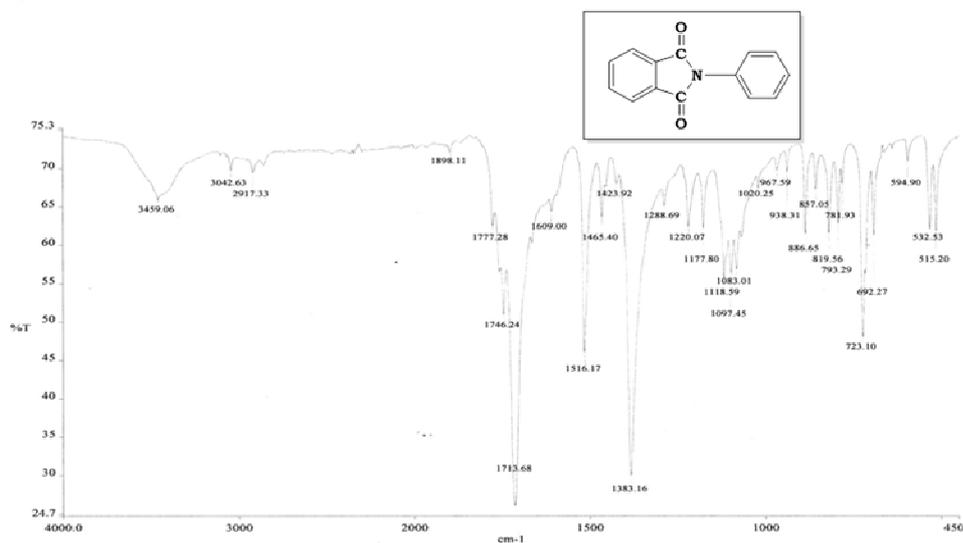
### Conclusion:

In conclusion, we have developed N-substituted imides by simple physical grinding. This method was green and efficient nature of preparation, short reaction time and good yields are notable advantages of this method. The present synthesis has many obvious advantages over the solution-phase technique like less time, less vigorous conditions for reactions to occur, ease of processing, freedom from pollution-causing-solvent, removal of toxic solvents after completion of reactions etc, compared to those reported in literature, including simplicity of the methodology and being environmentally benign.

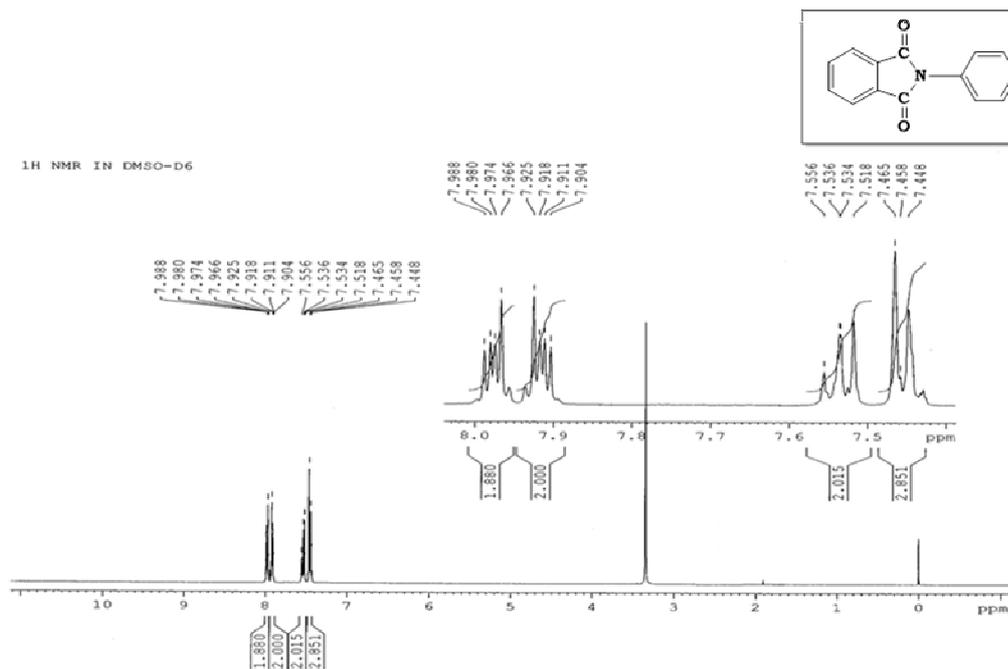
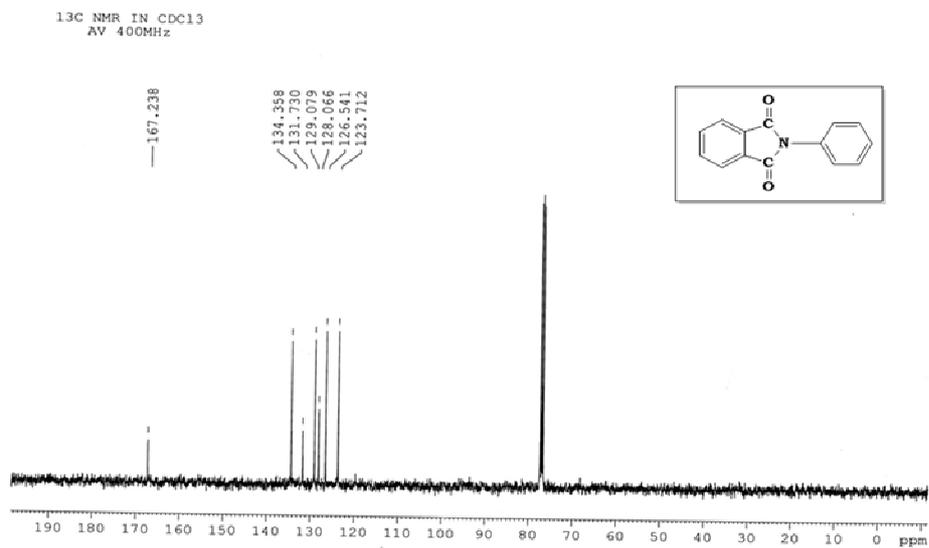
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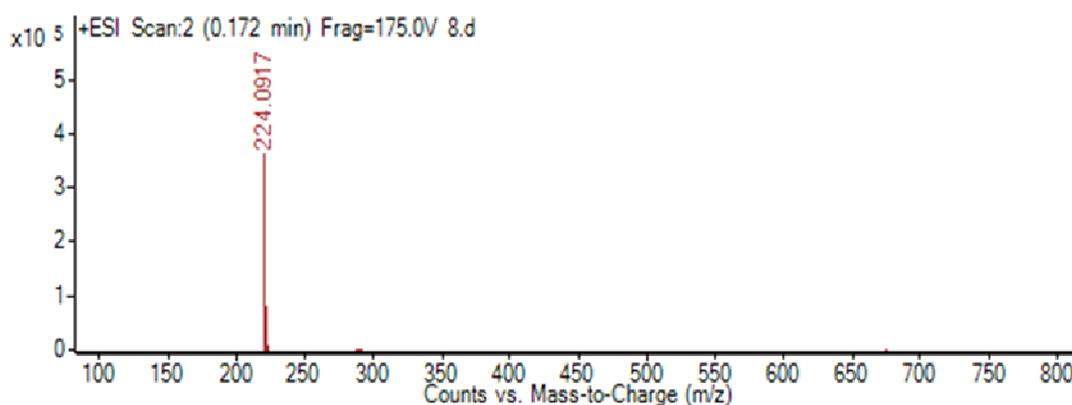
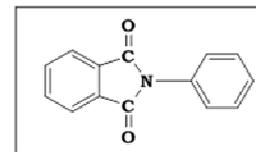
### Electronic Supporting Information



**Fig. 1: FT-IR spectrum of compound 5a**

**Fig. 2 <sup>1</sup>H NMR spectrum of compound 5a****Fig. 3 : <sup>13</sup>C NMR spectrum of compound 5a**

<b>Data Filename</b>		<b>Sample Name</b>	8
<b>Sample Type</b>	Sample	<b>Position</b>	P1-C8
<b>Instrument Name</b>	Instrument 1	<b>User Name</b>	
<b>Acq Method</b>	mass-sk.m	<b>Acquired Time</b>	
<b>IRM Calibration Status</b>	Success	<b>DA Method</b>	Default.m
<b>Comment</b>			



**Fig. 4: Mass spectrum of compound 5a**

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