

An Efficient Synthesis of Biologically Active N-Aryl phthalimides Using DES

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ABSTRACT

The newer view of Deep Eutectic Solvent (DES) in chemistry has number of advantages and one of the promising greener alternatives. We are also report herein catalyst free synthesis of various N-aryl phthalimides compounds using K₂CO₃+Glycerol as DES.

Keywords: Green Chemistry, Deep Eutectic Solvent, Phthalimide, Arylation and Fungicide.

I. INTRODUCTION

Imide group especially phthalimide moiety containing compounds are distinguished by their potent fungicidal action [1-3] and their some well known products namely, captan [N-(trichloromethyl-thio) tetrahydrophthalimide], folpet [N-(trichloro methyl) phthalimide].

Phthalimides are important synthetic intermediates to prepare primary amines, agricultural pesticides and also used in preservatives, pigments and pharmaceuticals[4-6]. The phthaloyl group is a well-established protective group for primary amines[7] in various types of compounds, particularly peptides[8], aminoglycosides[9] and β -lactum antibiotics [10] and also number of way methods for preparation of phthaloylation of amines [11-20].

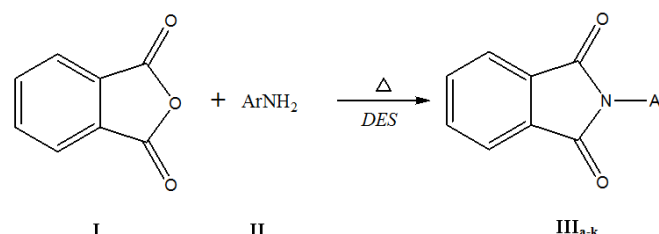
Considering an importance of phthalimides not only as fungicides but also equally as protective group for primary amines, H₂NR, we have reported herein a simple and greener method for the preparation of N-aryl phthalimides derivatives with higher purity and easy work up procedure.

II. Experimental Work

All chemicals and solvents were synthetic grade commercial products [s.d. fine chemicals, Qualigens etc], also solvents were distilled before use. The completion of reaction was check by Thin Layer Chromatography technique. The synthesized products

were also characterized by comparing their IR, ¹H NMR, MS and melting points with those reported in literature.

Synthesis of N-Aryl phthalimides



Where Ar-

- a) *o*-NO₂-C₆H₄
- b) *p*-COOH-C₆H₄
- c) C₆H₅-
- d) *p*-Cl-C₆H₄
- e) *p*-Br-C₆H₄
- f) α -C₁₀H₇
- g) *m*-OH-C₆H₄
- h) *m*-NO₂-C₆H₄
- i) *p*-CH₃-C₆H₄
- j) *p*-OH-C₆H₄
- k) *m,p*-dichloro-C₆H₃

Reaction Scheme

General procedure

A solution of aryl amine **IIc** (0.6283 gm, 0.006 mole) and phthalic anhydride **I** (1 gm, 0.0067 mole) was added to a solution of mixture K₂CO₃+Glycerol as *DES* molar ratio 1:5 (15 ml). Then the reaction mixture was refluxed at 60°C for 2.5 hrs. The completion of the

reaction was monitored by TLC [Solvent system, Pet. Ether: Methanol (9:1)]. After addition of water in the reaction mixture, obtained product was recrystallized with alcohol to afford the desired *N*-phenyl phthalimide compound **III_c**. [Reaction Scheme]

Similarly, the compounds **III_{a-k}** were synthesized by same way using different types of aryl amines. [Table-1]

Table – 1: Synthesized *N*-aryl phthalimides

Compounds	M.F.	Reaction time (Hrs.)	Percent Yield (%)	M.P. ^{21,22} (°C)
III _a	C ₁₄ H ₈ O ₄ N ₂	3.0	80	70
III _b	C ₁₅ H ₉ O ₂ N	1.5	76	282
III _c	C ₁₄ H ₉ O ₂ N	2.5	74	206
III _d	C ₁₄ H ₈ O ₂ NCl	2.0	75	185
III _e	C ₁₄ H ₈ O ₂ NBr	2.5	74	215
III _f	C ₁₄ H ₁₁ O ₂ N	2.0	70	178
III _g	C ₁₄ H ₉ O ₃ N	2.0	71	222
III _h	C ₁₄ H ₈ O ₄ N ₂	1.5	70	288
III _i	C ₁₅ H ₁₁ O ₂ N	3.0	70	236
III _j	C ₁₄ H ₉ O ₃ N	2.5	73	274-276
III _k	C ₁₄ H ₇ O ₂ NCl ₂	2.0	72	190

Characterization data: ¹H-NMR DATA

III_f: δ_{ppm} 7.4-7.8 (m, Ar-H), 7.9-8.02(m, Ar-H).

III_i: δ_{ppm} 4.09(s, 2H, -CH₂-), 7.35-7.45(m, 4H, Ar-H), 7.89-7.95(m, Ar-H)

III_j: δ_{ppm} 2.41 (s, 3H, -CH₃), 7.26 (d, 4H, Ar-H), 7.78 (dd, Ar-H), 7.95 (dd, Ar-H).

III. RESULTS AND DISCUSSION

Green chemistry pay attention to focused on development of clean, high yield and environmentally friendly chemical processes and technologies [23,24]. From last two decades, use of ionic liquids has attracted enormous attention from the scientific community for a

variety of applications including catalysis, CO₂ absorption, etc. [25]. But other sides of ionic liquids are of high price, poor biodegradability, biocompatibility, toxicity and environmental persistence [26,27]. The cost and availability as well as tuning of anions always represent problems for synthetic research. From this point of view, alternative solvent systems are being investigated. In this regards, deep eutectic solvents (DESs) have been considered as alternatives to ionic liquids (ILs) [28,29]. Generally, DESs are mixtures of a quaternary ammonium salt such as choline chloride with hydrogen-bond donors such as urea, carboxylic acid, glycerol and also K₂CO₃+Glycerol. DESs are environmentally benign, cheap, nontoxic, and biodegradable [30]. Their negligible vapor pressure, non flammability, non reactivity with water, and synthesis from readily available raw materials makes them promising alternatives to ionic liquids (ILs) [31-33].

We have successfully developed a catalyst-free protocol for clean synthesis of *N*-aryl phthalimides using K₂CO₃+Glycerol as nontoxic, low-cost and environmentally benign solvent. Such a mixture of K₂CO₃+Glycerol not only acts as solvents but it also provides basic condition to reaction media i.e. it doesn't require catalyst. Thus methodology offers benefits such as clean and mild reaction conditions, short reaction time and quantitative product yield.

Use of this inexpensive and biodegradable solvent makes this methodology a greener approach compared with other methods reported in literature.

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