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Original Research Article

Microwave assested synthesis of phthalimide amino derivatives with their antioxidant potential

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ABSTRACT

Imide is the configuration of amide in which the nitrogen atom is affix to two carbonyl group. Imide mention to any compound which carry the divalent radical. Phthalimide possess a structural feature $C_8H_5NO_2$ and an imide ring which help them to be biologically active and pharmaceutically useful.Phthalimides have served as starting materials and intermediates for the synthesis of many types of alkaloids and pharmacophores.In view of broad biological activity of phthalimide, we herein plan to synthesize a series of new phthalimide derivatives by incorporating new pharmacophores at various positions with the hope to get therapeutically active compounds. The aim the study is to synthesize phthalimide derivatives by using microwave assisted synthesis method and compare the activity of the synthesized molecules. Thus, the current communication employed the technology gracefully for the synthesis, identification and characterization of some novel derivatives by the reaction of Phthalic anhydride with urea, glycine, aniline, sulphanilic acid to yield various Phthalimide derivatives using domestic microwave by getting percentage yield 70.7%, 76.65%, 80.21% and 73.78% of synthesized compound B_1, B_2, B_3 and B_4 respectively. The compound B_3(92.86%) showed higher percentage practical yield. All synthesized compound(s) were subjected to melting point determination, TLC analysis, column chromatography (for purification), ^{1}H-NMR and Mass Spectrometry. All synthesized derivatives were subjected for DDPH scavenging activity, in which compound $B_4$was found to have high anti-oxidant potential (69.56%) when ascorbic acid was taken as standard. All the chemicals used were of highly pure and procured from Central Drug House (New Delhi).

1. Introduction

Imide is the form of amide in which the nitrogen atom is affix to two carbonyl group. Imide mention to any compound which contains the divalent radical. These compounds are obtained from ammonia or primary amine, where two hydrogen atoms are replaced by a bivalent acid group or two monovalent acid groups, resulting in comprising of two carboxylic acid groups.[1]

Phthalimide possess a structural feature $C_8H_5NO_2$ and an imide ring which help them to be biologically active and pharmaceutically useful.[2] Among bicyclic non-aromatic nitrogen heterocycles, phthalimides are an interesting class of compounds. Phthalimides have served as starting materials and intermediates for the synthesis of many types of alkaloids and pharmacophores.[3] The structural diversity and biological importance of nitrogen containing heterocycles have prepared them important targets for synthesis over many years.[4] Phthalimide and some of its derivatives proved to have received awareness due to their antibacterial, antifungal, analgesic, antitumour, anxiolytic and anti-HIV-1 activities.When phthalimide is subjected to Mannich condensation, it may yield Mannich bases which may display more potent biological activities. The present research focuses on novel synthesized phthalimides having significant biological activities.[3] Amongstheterocyclic

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scaffolds, phthalimides are of particular biological interest and have been reported as herbicides, insecticides and anti-inflammatory agents. Phthalimide are an important class of drugs exhibiting anxiolytic, antimicrobial, antibacterial, antituberculosis, anticancer, hypolipidemic, analgesic, antiproliferative, acetylcholinesterase inhibitors and inhibitor of human neuronal nitric oxide synthase.[4] Chemically, oxidation is the removal of electrons and reduction is the gain of electrons, oxidation is always coupled with reduction. Many biological oxidation can takes place without the participation of molecular oxygen, e.g. dehydration.[5] "Antioxidants are reducing agents which are add up to the drug or other pharmaceuticals to avert their oxidation through oxidative process".[6] For convenience, antioxidants have been traditionally divided into two classes, primary or chain breaking antioxidants and secondary or preventative antioxidants. Secondary or preventative antioxidants are compounds that retard the rate of oxidation.[7] Many human diseases and degeneration process have been linked in some way to the action of free radicals.[6–8]

The aim of the present study is to synthesize Phthalimide derivatives by using microwave assisted synthesis method and compare the activity of the synthesized molecules.

2. Materials and Methods

Phthalic anhydride, Urea, Glycine, Sulphanilic acid, Aniline, Chloroform & DPPH were received from Central Drug House Ltd. New Delhi, India. Methanol, Ethyl acetate & n-Hexane were received from Himedia Pvt. Ltd.

2.1. Method and methodology

Thus, the present communication utilized the technology gracefully for the synthesis, identification and characterization of some novel derivatives by the reaction of Phthalic anhydride with urea, glycine, aniline, sulphanilic acid to yield various Phthalimide derivatives using domestic microwave by getting percentage yield 70.7%, 76.65%, 80.21% and 73.78% of synthesized compound B_1, B_2, B_3 and B_4 respectively. All synthesized compound(s) were subjected to melting point determination, TLC analysis, column chromatography (for purification), ^{1}H-NMR and Mass Spectrometry.

3. Result and Discussion

We developed new synthetic methodologies for the synthesis of Phthalimidederivatives. The starting material phthalic acid was reacted with amino acids to give phthalimide, the addition reaction was takes place:

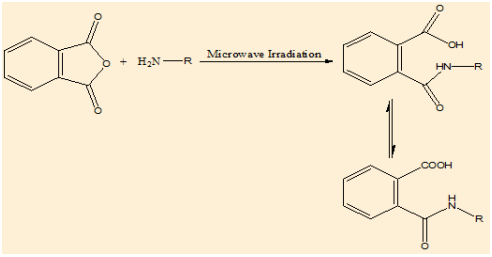

Fig. 1: General mechanism of phthalimide

3.1. Mechanism of synthesis(Figure 1)

3.1.1. For phthalimide derivatives

3.1.2. Percentage yield(Table 1)

Table 1: Percentage yield of phthalimide compounds

S.No.	Compounds	% yield
1.	B1	70.7
2.	B2	76.65
3.	B3	80.21
4.	B4	73.78

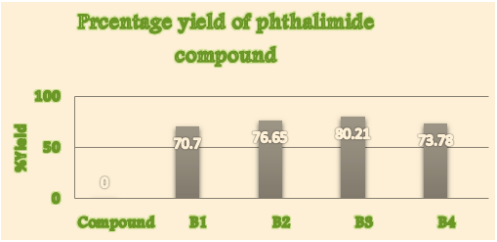

Fig. 2: Bar diagram of different Phthalimide derivatives

3.1.3. Physicochemical properties(Table 2)

Table 2: Physicochemical properties of various Phthalimide derivatives (B_1-B_4)

Compound	Molecular formula	Molecular weight	Appearance	Percentage yield (%)
B $_1$	$C_9H_6O_3N_2$	190.16	White crystals	70.70
B $_2$	$C_{10}H_7O_4N$	205.17	Brown powder	76.65
B $_3$	$C_{14}H_9O_2N$	223.23	Off White crystals	80.21
B $_4$	$C_{14}H_9O_5NS$	303.29	Off White crystals	73.78

Table 3: Melting Point of Phthalimide derivatives

S.No.	Compound	Melting Point Range (^{0} C)
1.	1, 3-dioxoisoindoline-2-carboxamide (B_1)	210±2
2.	2-(1,3-dioxoisoindoline-2-yl)acetic acid (B_2)	146±2
3.	2-phenylisoindoline-1,3-dione (B_3)	203±2
4.	4-(1,3-dioxoisoindoline-2-yl)benzenesulfonic acid (B_4)	230±2

Table 4: Solubility of Phthalimide derivatives

S.No.	Compound	Solubility
1.	1, 3-dioxoisoindoline-2-carboxamide (B_1)	Water, Methanol
2.	2-(1,3-dioxoisoindoline-2-yl)acetic acid (B_2)	Water, Ethanol
3.	2-phenylisoindoline-1,3-dione (B_3)	Water, Chloroform
4.	4-(1,3-dioxoisoindoline-2-yl)benzenesulfonic acid (B_4)	Water, Ethanol

Table 5: pH of Phthalimide compounds

S.No.	Compound	Observation
1.	1, 3-dioxoisoindoline-2-carboxamide (B_1)	7.88
2.	2-(1,3-dioxoisoindoline-2-yl)acetic acid (B_2)	11.53
3.	2-phenylisoindoline-1,3-dione (B_3)	8.78
4.	4-(1,3-dioxoisoindoline-2-yl)benzenesulfonic acid (B_4)	8.25

Table 6: Wavelength of phthalimide derivatives

S.No.	Compound	Solvent	Wavelength(nm)
1.	1, 3-dioxoisoindoline-2-carboxamide (B_1)	Water	281nm
2.	2-(1,3-dioxoisoindoline-2-yl)acetic acid (B_2)	Water	374nm
3.	2-phenylisoindoline-1,3-dione (B_3)	Water	298nm
4.	4-(1,3-dioxoisoindoline-2-yl)benzenesulfonic acid (B_4)	Water	245nm

3.1.4. Melting point(Table 3)

3.1.5. Solubility(Table 4)

3.1.6. PH(Table 5)

3.1.7. Ultraviolet spectroscopy(Table 6)

3.1.8. Thin layer chromatography(Figure 3)

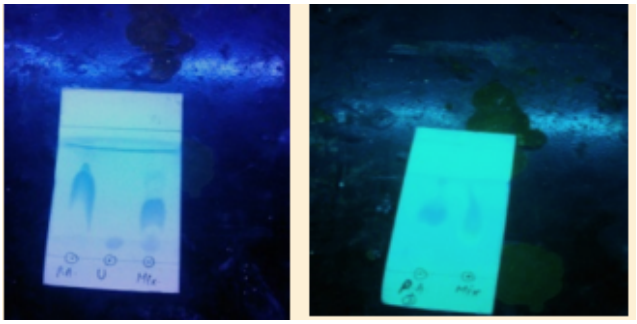

Fig. 3: Spots of derivatives of phthalimidevisualized in uv

Table 7: Retention factor of phthalimidecompounds

S.No	Compound	Rf value
1.	1, 3-dioxoisoindoline-2-carboxamide (B_1)	0.70
2.	2-(1,3-dioxoisoindoline-2-yl)acetic acid (B_2)	0.48
3.	2-phenylisoindoline-1,3-dione (B_3)	0.60
4.	4-(1,3-dioxoisoindoline-2-yl)benzenesulfonic acid(B_4)	0.52

3.1.9. The characteristic ^1H NMR data and interpretation of synthesized compounds

Table 8: ^{1}H NMRdata and interpretation of synthesized compounds

Compound No.	δ (ppm)	Group	No. of H
B $_1$	7.55-7.69	Ar-H	4
B $_2$	7.81- 7.94 4.32	Ar-H CH_2	4 2
B $_3$	7.41-7.54 7.88-7.97	Ar-H Ar-H	5 4
B $_4$	2.52-2.53 7.55-7.69 11.91	OH (Alcohol) Ar-H CH (Benzene)	1 4 1

3.1.10. Elemental analysis(Table 9)

3.1.11. Antioxidant activity(Table 10)

• In vito antioxidant activity by using DPPH scavenging method

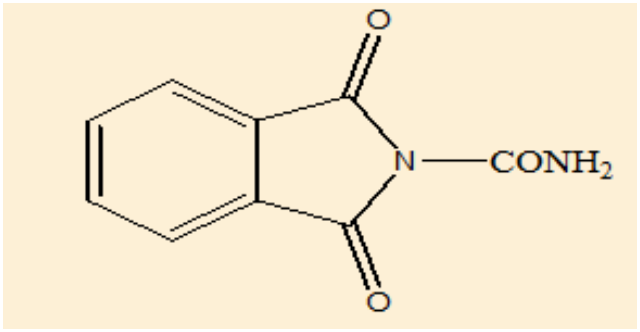

Fig. 4: Table 8+Compound structure (B_1)

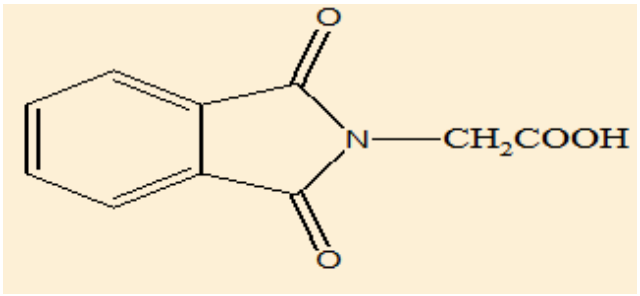

Fig. 5: Table 8+Compound structure (B_2)

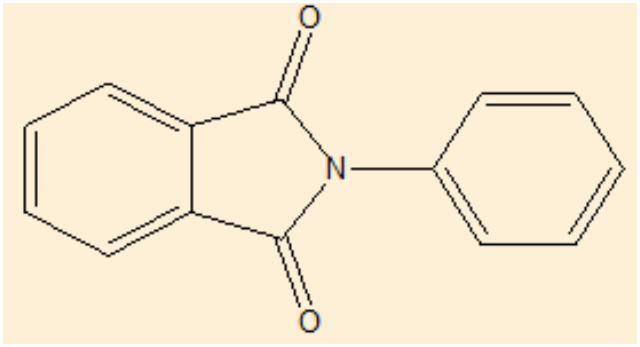

Fig. 6: Table 8+Compound structure (B_3)

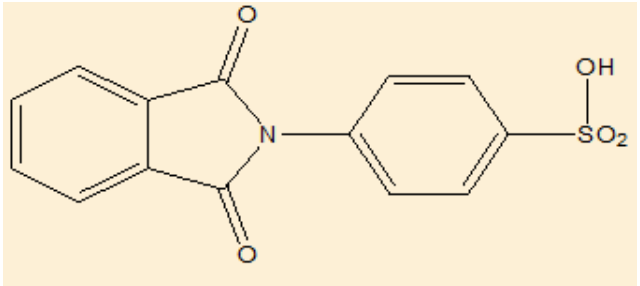

Fig. 7: Table 8+Compound structure (B_4)

Table 9: Elemental analysis of different Phthalimide compounds

Comp.	Mol. Formula	Mol. Weight	Compound- Name	Calculated % found			
				C%	H%	N%	O%	S
B_1	$C_9H_6O_3N_2$	190.16	1, 3-dioxoisoindoline-2-carboxamide (B_1)	56.85%	03.18%	14.73%	25.24%	–
B_2	$C_{10}H_7O_4N$	205.17	2-(1,3-dioxoisoindoline-2-yl)acetic acid (B_2)	58.54%	03.44%	06.83%	31.19%	–
B_3	$C_{14}H_9O_2N$	223.23	2-phenylisoindoline-1,3-dione (B_3)	75.33%	04.06%	06.27%	14.33%	–
B_4	$C_{14}H_9O_5NS$	303.29	4-(1,3-dioxoisoindoline-2-yl)benzenesulfonic acid (B_4)	49.52%	13.36%	04.12%	23.56%	09.44%

Table 10: DPPH scavenging activity of different Phthalimide derivatives

Concentration (mg/ml)	% inhibition				
	B_1	B_2	B_3	B_4	Ascorbic acid
0	0.0	0.0	0.0	0.0	0.0
0.02	13.35	31.23	16.88	65.72	84.02
0.04	17.51	44.95	21.26	67.43	86.35
0.06	18.88	53.93	24.37	69.09	86.57
0.08	20.92	55.72	24.77	69.52	86.92
0.10	25.22	59.79	25.59	69.56	98.42

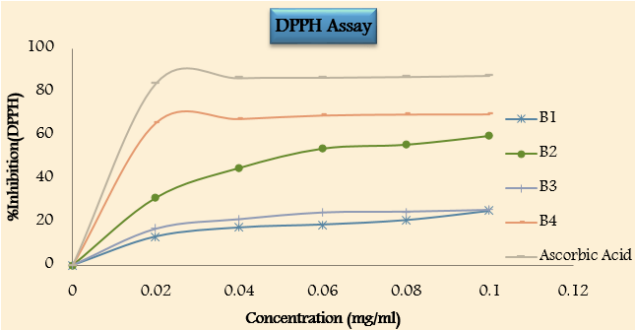

Fig. 8: Bar diagram of different Phthalimide derivatives

4. Conclusion

On the basis of the previous results, the study concluded that the synthesis of the designed compound has been successfully achieved. Purity and characterization of the synthesized compounds were confirmed by determination of physical properties (melting point, pH and R_f values), elemental analysis and 1H-NMR spectra. The compound B_3 of phthalimide shows higher percentage practical yield. The in-vitro antioxidant activity of all synthesized compound was tested by using DDPH scavenging activity. The compounds were concealed at distinct concentration from 0.02-0.10mg/ml in order to examine the percentage inhibition of compounds. From the result in table (10) compound B_4manifest highly significant activity against DPPH. The result shows that as the concentration of compound increase, the compound showed high remarkable activity against DPPH. The other complete tested compound showed low to moderate activity.Thus, the study could be concluded as the compounds have significant antioxidant activity. Thus, it may be concluded that the synthesized compound productively can be further used in the treatment of above-mentioned element.

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6. Source of Funding

None.

7. Conflict of Interest

None.

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