Synthesis and Qualitative Analysis of Phthalimides in Presence of Montmorillonite –KSF as Catalyst

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ABSTRACT: The most important synthesis of phthalimides is the dehydrative condensation of phthalic anhydride at high temperatures with primary amines, when the amine is available. When the amine is not readily accessible, the direct N-alkylation of phthalimides with alcohols under Mitsunobu conditions Phthalimide derivatives synthesis were carried out by conventional methods where, montmorillonite-KSF was used as the reusable clay catalyst. Catalytic reactions are preferred in environmentally friendly green chemistry due to the reduced amount of waste generated as opposed to stoichiometric reactions in which all the reactants are consumed and more side products are formed. Research conducted to improve percentage yield and reduce reaction time by utilizing Montmorillonite as natural reusable catalyst.

Keywords: Phthalimides, Montmorillonite –KSF, Phthalic anhydride, amine

INTRODUCTION

Development of the simple and general synthetic routes for widely used organic compounds from the readily available reagents is one of the major challenges in organic synthesis. The area of reaction of phthalic acid and phthalic anhydride with nitrogen containing compounds is very large. The well-known reactions of phthalic acid anhydride are reactions with ammonia, urea, thiourea, hydroxylamine, methylamine, ethylamine and aniline[1].

Acylation of amines by phthalic anhydride[2, 3] produces phthalamic acid derivatives, which are organic herbicides. Further cyclization results into the formation of N-substituted imides, which exhibit various biological activities such as antimicrobial[4], anti-inflammatory[4] analgesic[5] and anxiolytic[6, 7].

Montmorillonite[8, 9]: Montmorillonite clays have been used as catalysts for number of organic reactions and offer several advantages over classical acids, e. g., the strong acidity, non-corrosive properties, cheapness, mild reaction conditions, high yields, selectivity and the ease of setting and working-up. Generally, heterogeneous solid acids are advantageous over conventional homogeneous acid catalysts as they can be easily recovered from the reaction mixture by filtration and can be reused after activation or without activation making the process economically viable. In many cases, heterogeneous catalysts can be recovered with only minor changes in activity and selectivity so that they can be used in continuous flow reactions. Clays are attractive because of their low cost, reusability, flexibility in their acid strength, ease of handling, environmental compatibility, nontoxicity and experimental simplicity[1].

Materials and Methods:

The chemicals required for the synthesis of phthalimides were purchased from Merck Specialities Pvt. Ltd., Spectrochem Laboratories, and Rankem Laboratories.

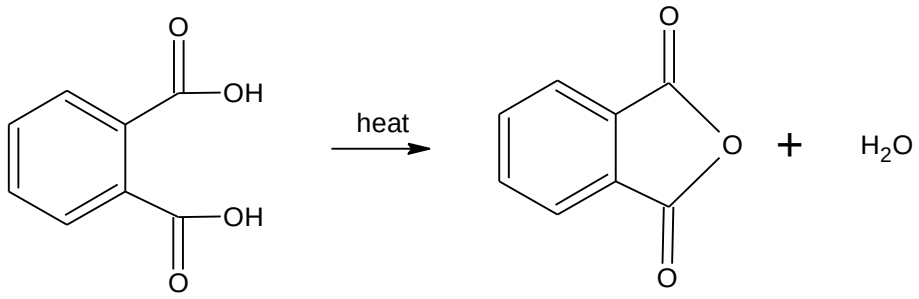
Synthesis of phthalimides:

A series of 15 phthalimides was synthesized by reacting different amines with phthalic anhydride in presence of montmorillonite –KSF as catalyst.

Scheme:

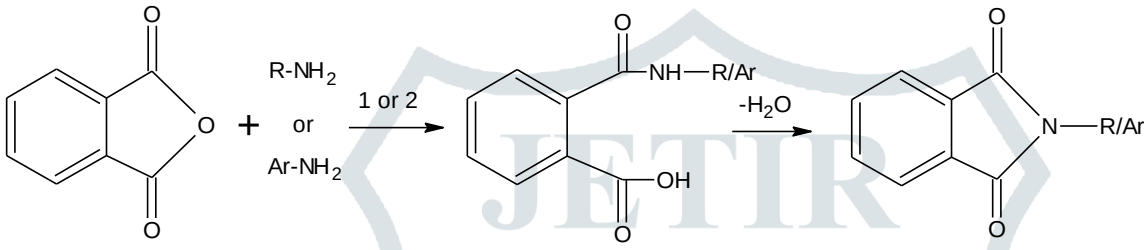
Synthesis of phthalimides was carried out into two steps.

Step-1: Synthesis of Phthalic anhydride



Phthalic acid **Phthalic anhydride**

Step-2: Synthesis of Phthalimides



Phthalic anhydride Primary amine Phthalamic acid derivatives Phthalimides

where,
1 /2= Montmorillonite - KSF, Reflux at 145-150 ºC for 50 min to 4 hr 20 min

Procedure:
Phthalic anhydride and montmorillonite-KSF were ground properly to a uniform mixture. This mixture was refluxed with an alkyl or an aryl amine using acetic acid as a solvent. Reaction was monitored by TLC. The reaction mixture was allowed to cool to room temperature and resulting product was extracted in CH_2Cl_2/ $CHCl_3$. Product was washed with dilute HCl and distilled water and recrystallized from a suitable solvent. In the conventional method, the reaction was carried out by refluxing the reaction mixture for 50 min to 4 hrs. Each reaction was carried out at least thrice to standardize the reaction conditions and yields.

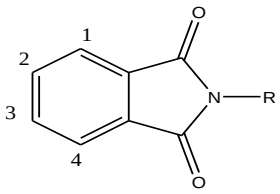
Qualitative analysis of the synthesized derivatives
The qualitative analysis of the synthesized derivatives was done by –

1. TLC
2. MP determination
3. IR spectroscopy
4. NMR spectroscopy

Melting points of all the synthesized compounds were determined in open glass capillaries on EXPO-HiTech melting point apparatus and were uncorrected. The purity of compounds was checked by thin layer chromatography (TLC). The structures of all the synthesized compounds were characterized from their IR spectra and confirmed from their ^{1}H-NMR spectra. The IR spectra were recorded on JASCO FTIR 5300 IR spectrometer using KBr pellet method in the range of 4000–400 cm^{-1}. The ^{1}H-NMR spectra were recorded on VNMRS-300 and BRUKER-av400 spectrometers, using TMS as an internal standard and carbon tetrachloride and DMSO as the solvents.

RESULT AND DISCUSSION:

Fifteen phthalimides were synthesized using low cost and easily available raw materials by conventional methods. Montmorillonite – KSF plays important role as natural catalysis for faster reaction. Qualitative analysis of synthesized compounds was summarized in following tables.



Phthalimide derivatives

Table 1

Comp. No.	Substituent (R)	Comp. No.	Substituent (R)	Comp. No.	Substituent (R)
1	2-Phenyl	6	2-Aminophenyl	11	4-Methoxyphenyl
2	2-Chlorophenyl	7	2-Methylphenyl	12	4-Nitrophenyl
3	Cyclohexyl	8	3-Methylphenyl	13	3-Nitrophenyl
4	1-Naphthyl	9	4-Methylphenyl	14	2-Nitrophenyl
5	Ethenamine	10	2-Methoxyphenyl	15	Amino

Table 1: Substituents on the synthesized phthalimide derivatives

Table 2:

Comp No.	IR Wave numbers (cm^{-1})	H^1NMR Chemical shift values (δ ppm)
1	1385, C-N str 1494, Ar,C=C str 1707, C=O str 3076, C-H str	7.26-7.54 (m, 5H, Ar- H_5, H_6, H_7, H_8, H_9) 7.81 (d, 2H, Ar-H_2, H_3) 7.98 (d, 2H, Ar-H_1, H_4)
2	715, C-Cl str 1381, C-N str 1487, Ar, C=C str 1718, C=O str	7.26-7.61 (m, 4H, Ar-H_5, H_6, H_7, H_8) 7.83 (d, 2H, Ar-H_2, H_3) 8.0 (d, 2H, Ar-H_1, H_4)
3	1392 C-N str 1602, Ar, C=C str 1705 C=O str	1.20-1.45 (m, 6H, Ar-H_7, H_8, H_9, H_{10}, H_{11}, H_{12}) 1.45-1.89 (t, 2H, Ar-H_{13}, H_{14}) 2.14-2.2 (t, 2H, Ar-H_5, H_6) 7.7 (d, 2H, Ar-H_2, H_3) 8.1 (d, 2H, Ar-H_1, H_4)
4	1373, C-N str 1464, Ar, C=C str 1714, C=O str	7.45-8.01 (m, 11H, Ar-H_1, H_2, H_3, H_4, H_5, H_6, H_7, H_8, H_9, H_{10}, H_{11})

	3057, C-H str	
5	1319, C-N str 1462, Ar, C=C str 1620, N-H ben 1712, C=O str 3454, N-H str	3.96 (d, 2H, NH_2) 4.32 (d, 2H, H_5, H_6) 7.75 (d, 2H, Ar-H_2, H_3) 7.8 (d, 2H, Ar-H_1, H_4)
6	1385, C-N str 1494, Ar, C=C str 1602, N-H ben 1707, C=O str 3400, N-H str 3076, C-H str	6.98-7.966 (m, 8H, Ar-H_1, H_2, H_3, H_4, H_5, H_6, H_7, H_8) 3.33 (s, 2H, NH_2)
7	1305, C-N str 1419, 1452, 1493, Ar, C=C str 1637, C=O str	2.21 (s, 3H, 1xCH_3) 7.1 (d, 1H, Ar-H_5) 7.31-7.39 (m, 3H, Ar-H_6, H_7, H_8) 7.81 (d, 2H, Ar-H_2, Ar-H_3) 7.97 (d, 2H, Ar-H_1, Ar-H_4)
8	1300, C-N str 1491, 1556, 1591, Ar, C=C str 1720, C=O str	2.42 (s, 3H, 1xCH_3) 7.21-7.26 (m, 3H, Ar-H_5, H_6, H_7) 7.40 (s, 1H, Ar-H_8) 7.79 (d, 2H, Ar-H_2, H_3) 7.96 (d, 2H, Ar-H_1, H_4)
9	1388, C-N str 1516, 1547, Ar, C=C str 1718, C=O str	2.41 (s, 3H, 1xCH_3) 7.26 (d, 2H, Ar-H_5, H_8) 7.31 (d, 2H, Ar-H_6, H_7) 7.79 (d, 2H, Ar-H_2, H_3) 7.96 (d, 2H, Ar-H_1, H_4)
10	597, C=O str 1344, C-N str 1464, 1489, 1527, 1597, Ar, C=C str	3.80 (s, 3H,1xOCH_3) 7.04 (d,1H, H_5) 7.08 (d, 1H, H_8) 7.26 (t, 1H, H_7) 7.44 (t, 1H, H_6) 7.78 (d, 2H, H_2, H_3) 7.95 (d, 2H, H_1, H_4)
11	1302, C-N str 1516, Ar, C=C str 1655, C=O str	3.85 (s, 3H,1xOCH_3) 7.03 (d, 2H, Ar-H_6, H_7) 7.73 (d, 2H, Ar-H_5, H_8) 7.79 (d, 2H, Ar-H_2, H_3) 7.95 (d, 2H, Ar-H_1, H_4)
12	1346, C-N str 1466, 1496, Ar, C=C str 1521, NO_2 str 1597, 1732, C=O str	7.77 (d, 2H, Ar-H_6, H_7) 7.86 (d, 2H, Ar-H_2, H_3) 8.01 (d, 2H, Ar-H_1, H_4) 8.38 (d, 2H, Ar-H_5, H_8)
13	1300, 1531,	7.70 (t,1H, Ar-H_6)

	-NO_2 str 1352, C-N str 1467, 1485, 1531, 1726, Ar, C=C str 1726, C=O str	7.85 (d, 2H, Ar-H_2, H_3) 7.87 (d, 1H, Ar-H_5) 8.01 (d, 2H, Ar-H_1, H_4) 8.26 (d, 1H, Ar-H_7) 8.44 (s, 1H, Ar-H_8)
14	1354, C-N str 1467, 1485, 1531, Ar, C=C str 1335, NO_2 str 1583,1726, C=O str 2918, C-H str	7.70 (t, 1H, Ar-H_6) 7.86 (d, 2H, Ar- H_2, H_3) 7.89 (d, 1H, Ar-H_5) 8.01 (d, 2H, Ar-H_1, H_4) 8.28 (d, 1H, Ar-H_8) 8.44 (t, 1H, Ar-H_7)
15	1329, 1348, C-N str 1493, 1556, Ar, C=C str 1601, C=O str 1660, N-H ben 2900, N-H str 2916, C-H str	7.89 (d, 2H, Ar-H_2, H_3) 8.06 (d, 2H, Ar-H_1, H_4) 11.52 (s, 2H, NH_2)

Table 2: Structural data of the synthesized derivatives is presented in.

Table 3

Comp. No.	Reaction Time	% yield MW	Melting point (°C)	Thin Layer Chromatography	
				R_f	Mobile phase
1	1.20	75.1	207-208	0.75	Benzene:Ethyl acetate (3:1)
2	1.50	91.1	140-143	0.57	Cyclohexane:Ethyl acetate (3:1)
3	2.30	60.4	164-168	0.84	Methanol:Benzene (3:1)
4	1.10	90.1	180-184	0.79	Benzene:Ethyl acetate (3:1)
5	3.50	51.6	89-90	0.71	Mthanol:Benzene (3:1)
6	3.15	50.4	150-154	0.63	Benzene:Acetone (2.5:1)
7	1.30	73.3	182-184	0.82	Benzene:Ethyl acetate (3:0.5)
8	1.15	86.0	175-177	0.80	Benzene:Ethyl acetate (2:0.5)
9	2.45	60.7	203-204	0.80	Hexane:Ethyl acetate (2:1.5)
10	3.45	85.3	158-160	0.81	Benzane:Ethyl acetate (3:0.5)
11	4.15	91.6	164-168	0.79	Hexane:Ethyl acetate (2:1)
12	1.25	73.1	264-266	0.82	Benzene:Acetone (2.5:0.5)
13	2.10	89.1	247-256	0.80	Benzene:Ethyl acetate (2.5:0.5)
14	4.20	51.1	245-246	0.62	Hexane:Ethyl acetate (4:1)
15	2.30	42.2	289-292	0.63	Hexane:Ethyl acetate (4:1)

Table 3: The reaction time and yield of phthalimides obtained by conventional methods with mp and TLC

CONCLUSIONS:

Synthesis of Phthalimides in Presence of Montmorillonite –KSF as Catalyst resulted in mild reaction conditions, high yields, selectivity and the ease of setting and work-up. Study of biological activity of synthesized compound will be future plan of research.

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