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Application of Novel Clay catalyst for the Synthesis of bis-indole derivatives from 2-phenyl-1-H- indole

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Abstract

In this study, we report that the novel clay material was found to catalyze electrophilic substitution reaction of 2-phenyl-1-H-indoles with a variety of aromatic aldehydes to excellent yields of bis (indolyl) methanes at room temperature. The efficient synthesis of 2-phenyl-1-H-indoles was achieved by Fischer indole synthesis with addition of phenyl hydrazine and acetophenone.

Key words : Novel Clay, XRD, EDS, FESEM, 2-phenyl-1-H-indoles, substituted aromatic aldehydes, nanomaterial.

1. Introduction

The indoles ring system are ubiquitous heterocycles that represents an important structural component in many pharmacologically active compounds, agrochemistry, dyes, material science as well as in synthetic chemistry[1]. Derivatives of 2-phenyl-1-H-indoles were found to inhibit the growth of human breast cancer cells by different mechanisms depending on the type and position of the substituents[2]. Substituted methane with two units of indole is commonly known as bis (indolyl) methane (BIM) or diindolylmethane (DIM) is present in various natural products possessing anticancer activity. DIMs induce apoptosis in many cancer cells by signaling various proapoptotic genes and proteins[3]. Bis (indolyl) methanes (BIMs) isolated from marines or terrestrial matrices exhibit a wide range of pharmacological activities against various tumor cells. Naturally occurring BIMs such as vibrindoles are useful in the treatment of fibromyalgia, chronic fatigue and irritable bowel syndrome[4].

Indole and its derivatives have wide range of applications in biological and medicinal activities[5]. Bis-indole derivatives not only increase the natural metabolism of hormones in the body but also used as anticancer drug[6]. Such as antibacterial antitumor. Bis (indolyl) methane are members of promising new drug class these are diarylamidine derivatives that target DNA synthesis, providing a broad-spectrum antibacterial activity[7]. For the synthesis of bis indole from indole different catalyst are reported such as Ln $(OTf)_3$, I_2, PCl_5, PPA/SiO_2, silica sulphuric acid, Lewis acid, protic acid[8]. However, many of procedures have significant drawbacks such as required stoichiometric amount of catalyst, long reaction time, expensive catalyst, low yield and use of environmentally toxic reagents. But in the present work, we replaced this catalyst by low cost cheaply available clay.

2. Experimental Protocols

2.1. Chemistry :

All chemicals were purchased from major chemical suppliers of high or highest purity grade and used without further purification. As a part of our study of Chemistry indole [Biological active moiety] we have synthesized bis indole derivatives by using Novel Clay catalyst. TLC is run in N- hexane and ethyl acetate in required amount. FT-IR is recorded in KBr, HNMR in $CDCl_3$ from Central instrumentation facility (CIF), Savitribai Phule Pune University. X-Ray Powder diffraction (XRD) is recorded from department of Physics. Energy Dispersive X-Ray Spectroscopy (EDS) and Field Emission Scanning Electron Microscope (FESEM) by using instrument Nova Nano SEM 450 UOP were recorded from (CIF), Savitribai Phule Pune University, Maharashtra.

2.2. Preparation of catalyst :

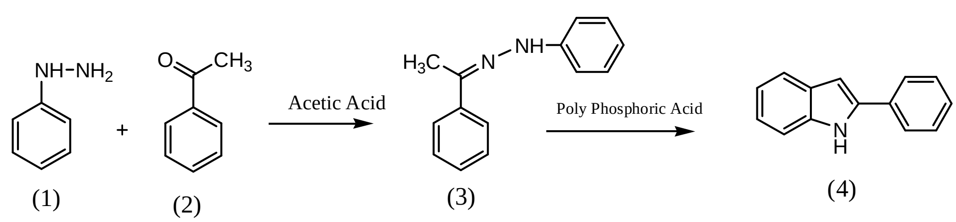
The Clay was obtained from the field of Bashir Farm (Jatadevala), Tq. Patahrdi, Dist. Ahmednagar, Maharashtra, India. The clay was crushed in a fine powder in mortar and pestle, wash with distilled water and soakedin (0.1 M) H_2SO_4 to remove organic particles for 24 hour then filtered with Whatman filter paper then again washed the catalyst with distilled water for several times to remove adsorbed acid particles, it was dried it at 110°C in oven then cooled and used it as a catalyst. This catalyst is characterized by using XRD, EDS and FESEM.

2.3. Synthesis of Indole :

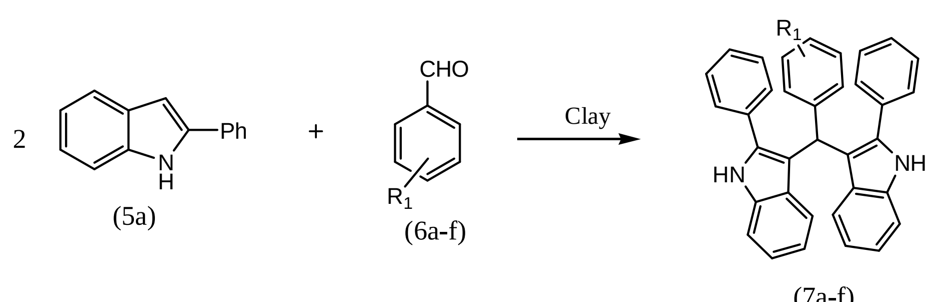
Acetophenone (1mole) and phenyl hydrazine (1mole) is taken in beaker, two to three drop of acetic acid is added to mixture, stirred well and heat reaction mixture in water bath for five minutes solid hydrazone product is separated recrystallize with ethanol. Take 5 ml poly phosphoric acid in beaker and add hydrazone prepared in last stage stir well heat this mixture in water bath for five minutes the then pour this reaction mixture in to ice cold water solid product is separated out filter it and dry and recrystallize with ethanol.

2.4. The synthesis of bis-indole derivatives :

Themixture of aldehyde (1 mole), 2-Phenyl-1H-indole (2 moles) and catalyst (0.10 mg) in ethyl acetate is grinded in mortar and pestle for specific period. The reaction was monitored by TLC. Reactions checked by TLC then add (10 ml) dichloromethane then reaction mixture was filtered. Catalyst is separated by filtration. This catalyst was reused. Then some amount of N-hexane is added in solvent. This mixture was kept in deep freezer pure crystals are separated. We have synthesized six bis-indole derivatives by this method. The general scheme is given below we also compare this reaction with stone powder as catalyst but the reactive gives moderate yield and require longer duration of time.



Scheme 1: Synthesis of 2-phenyl-1H-indole.



Scheme 2: Synthesis of Bis (indolyl) methane Derivatives.

3. Result and Discussion

The phenyl indole and aldehydes along with product is given true yield and time period. The reaction completes from in table 1 with10 to 35 minutes with quite good yield 75 to 96 %. The catalyst is characterized using EDS, FESEM and X-ray Diffraction.

3.1. Spectral Data:

7a) 3-((4-nitrophenyl)(2-phenyl-1H-indol-3-yl) methyl)-2-phenyl-1H-indole, IR: 3627, 3409, 3121, 3015, 2820, 2851, 1615, 1344, 1089, 731 cm^{-1}; Mass: 520, 519, 518, 500, 475, 408, 384, 255, 180,110, 77, 51; HNMR ($CDCl_3$): 6.0(S, 1H), 6.7(m, 2H), 6.8(m, 2H), 6.9(m, 2H), 7.0(m, 2H), 7.2(m, 6H),7.32(m, 4H),7.44(m, 2H), 8.1(d, 2H), 11.4(S, 2H).

7b) 3-((4-chlorophenyl)(2-phenyl-1H-indol-3-yl) methyl)-2-phenyl-1H-indole, IR: 3419, 3213, 3113, 3019, 2922, 2849, 1615, 1339, 1078, 741 cm^{-1};Mass: 511, 510, 509, 507, 483, 449, 445, 395, 312, 255, 155 HNMR: 5.9 (S,1H), 6.6(m, 2H), 6.7(m, 2H), 6.9(m, 2H), 7.0(d, 2H),7.12(m, 6H), 7.2(m, 4H), 7.3(m, 2H), 7.39(d, 2H), 11.38(S, 2H).

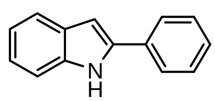
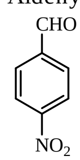
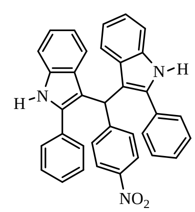
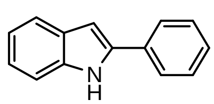
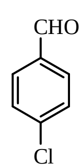
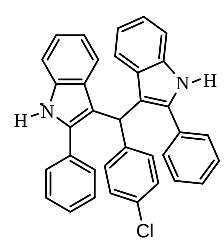
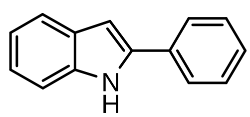
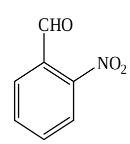
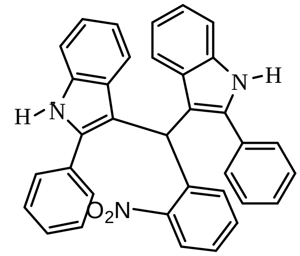
7c) 3-((2-nitrophenyl)(2-phenyl-1H-indol-3-yl) methyl)-2-phenyl-1H-indole, IR: 3529, 3413, 3113, 3019, 2922, 2849, 1615, 1339, 1078, 731 cm^{-1}; Mass: 511, 510, 509, 507, 483, 449, 445, 395, 312, 255, 155; HNMR: 6.0(S, 1H), 6.8(m, 2H), 7.0(m, 2H), 7.2(t, 2H),7.22(m, 4H),7.24(m, 4H), 7.3(dd, 2H), 7.5(d, 2H), 7.6(d, 2H), 8.1(d,2H), 10.9(S, 2H).

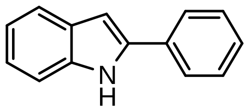
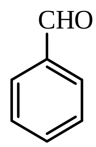
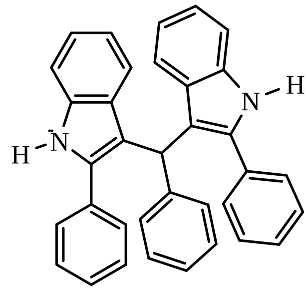
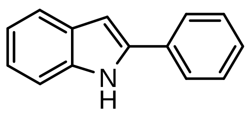
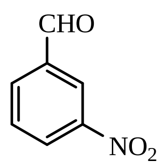
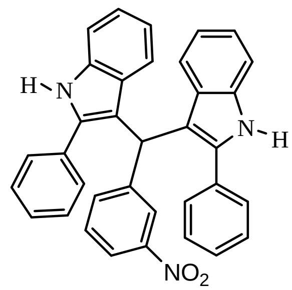
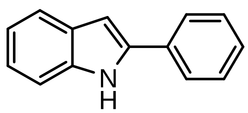
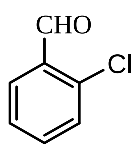
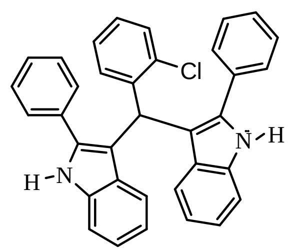
7d) 2-phenyl-3-(phenyl(2-phenyl-1H-indol-3-yl) methyl)-1H-indole, IR: 3425, 3113, 3019, 1599, 1499, 732; cm^{-1}; Mass: 485, 484, 483, 465, 440, 220; Mass: 476, 475, 474, 395, 312, 255, 155; HNMR: 5.8(S, 1H), 6.3(S, 1H), 6.8(m, 1H), 6.9(m, 1H), 7.0(m, 2H), 7.2(m, 4H), 7.22(m, 5H), 7.24(m, 4H), 7.3(m, 5H), 10.82(S, 2H).

7e)3-((3-nitrophenyl)(2-phenyl-1H-indol-3-yl) methyl)-2-phenyl-1H-indole, IR: 3625, 3413, 3113, 3019, 2920, 2850, 1615, 1340, 1088, 732; cm^{-1};Mass: 520, 519, 518, 500, 475, 408, 255; HNMR: 6.0(d,1H), 6.5(d,1H), 6.6(d, 2H), 7.0(m, 1H), 7.1(m,1H), 7.2(m, 1H),7.22(m, 4H), 7.24(m, 4H), 7.3(m, 2H), 7.4(m, 2H), 7.5(m, 2H), 7.6(m, 1H), 7.7(m,1H), 8.0(S,1H), 8.1(S,1H).

3.2. Table 1

Physico-chemical characteristics of 2-phenyl-3-(phenyl(2-phenyl-1H-indol-3-yl)methyl)-1H-indole 2/3/4-sustituted derivatives

Compound No.	Indole	Aldehyde	Product	Times (Min)	Yield (%)
7a				30	92
7b				35	83
7c				40	78

7d				35	78
7e				45	77
7f				40	80

3.3. Structure and size of clay nanoparticles:

The XRD pattern of the precursor is shown in below figure peak at 32 A^o and broad peak at 94 A^o indicates that clay used as a catalyst which contains nanoparticles.

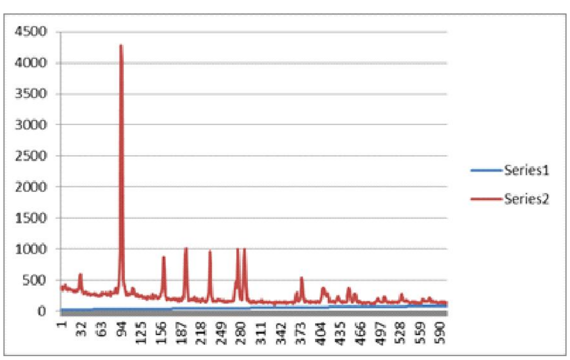
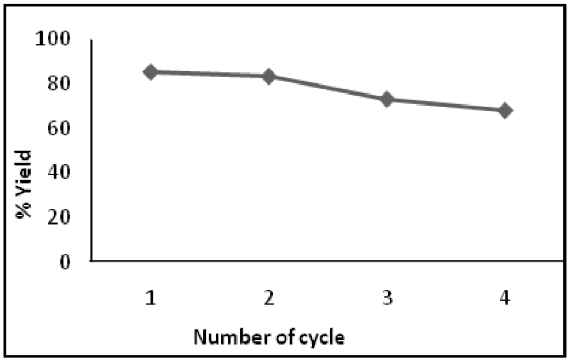


Figure: XRD graph of clay as a catalyst

3.4. Catalytic activity:

This catalyst can be recycling for several times. This gives good yield for three times. Indole show electrophilic substitution reaction at beta or three positions. When aldehydes react with indole in presence of clay as a catalyst in ethyl acetate as solvent, bis-indole ware obtained in good yield. The reaction is illustrated in scheme 1. As this is ecofriendly catalyst that's why it is easily separated and use as catalyst in same reaction we have used this catalyst in same reaction scheme in several times we get better yield and better catalytic activity but as number of cycle increases more than four cycle yield is poor percent of yield and number of cycles of reaction given below chart.



4. Conclusion

2-phenyl-1H-indole is more reactive towards electrophilic substitution reaction at beta position the effect of substituents in the aromatic ring of aldehyde was investigated. The yield of bis-indole derivatives in the presence of clay nanoparticles as a catalyst is summaries in the table 1. It is seen that Para nitro benzaldehyde gives very fast reaction high yield within thirty minutes at room temperature.

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