Microwave assisted acylation of indole over green, heterogeneous & recyclable catalyst H-ZSM-5.

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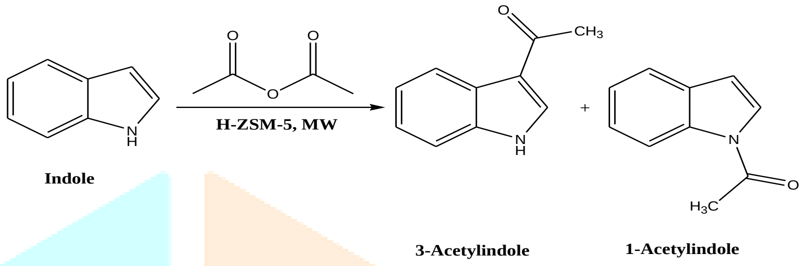
Abstract

Acylation of indole has been carried out over heterogeneous and recyclable H-ZSM-5 zeolite under microwave condition to obtain 3-acetyl indole. H-ZSM-5 zeolite shown the better catalytic activity compared to other zeolites due to increased accessible acidic sites, found to be more efficient and easily recyclable.



Scheme

Keywords: Heterogeneous, recyclable, microwave, H-ZSM-5, Zeolite, acetyl indole

1. Introduction

Synthesis of 3-substituted acetylindoles attracted much attention because they are essential intermediate, chiral auxiliaries in many reactions and shows the diverse applications in biological area such as in anticonvulsant [1, 2], platelet activating factor receptor (PAFR) antagonists for septic shock [3], anticancer, antifungal, antibacterial, antibiotic etc. activities[1]. Several well-known methodologies have been reported such as Vilsmeier-Haack reaction, Friedel-Crafts acylation, Grignard reaction [4], Green methodologies have been reported in recent years by using clay, ionic resins using heteropolyacids, zeolites, mesoporous silica, heteropolyacid supported zeolites such as 2-methoxynapthelene, 2-butylbenzene over various kinds of zeolites[5-7], Friedel-Crafts acylation of anisole using acetic anhydride over Hβ zeolite[8], regioselective synthesis of 3-acylindoles using $SnCl_2$ with nitrobenzene and acetyl chloride as co-solvent & acylating agent respectively[9] and tungstophosphoric acid-modified Hβ zeolite[10] have been reported. Recently, G.R. Wilson & Amit Dubey reported the acylation of indole over trichloroisocyanouric acid functionalised mesoporous silica nanocomposite (SBA/TCCA) [11]. These methods either toxic or not cost effective which have been enhanced the great attention towards the development of the green, easily recyclable for environmental and economic concerns.

Therefore, in the present work, we report the acylation of indole using acetic anhydride over H-ZSM-5 for the first time. In the light of the synthetic conditions and the abundant protons present in the high surface area aluminosilicate framework, we investigated how H-ZSM-5 (Si/Al = 30) is capable of supporting acid catalysed reactions[12]. We examined the shape selective catalysis by carrying out the nitration of toluene with n-propyl nitrate as a test reaction. The acidic nature of the catalyst formed nitronium ions from n-propyl nitrate required for nitration reaction. The reaction over this particular catalyst yielded only the *para*-isomer[13].

Last year, we have been reported the quinoxaline, methyl 2-(acetamido(phenyl) methyl)-3-oxobutanoate, ethyl 4-(2-aminophenylamino)-2,5-dihydro-5-oxo-2-phenylfuran-3-carboxylate, pyrimidine derivatives synthesis via MCRs over H-ZSM-5[12]. However, based on the accessibility of acidic sites, we investigated whether H-ZSM-5 with (Si/Al ratio=30) is capable of supporting the acylation of indole.

2. Experimental

2.1 Preparation of H-ZSM-5

H-ZSM-5 has been prepared from the reported method by us using wheat husk as silica source as given below:

(a) The wheat husk ash at first boiled in 1M HCl at 363 K and then washed with distilled water, slowly subjected to thermogravimetric decomposition and calcined around 823K for at least 6-7 hours in muffle furnace. Then, the silica thus extracted used for the preparation of ZSM-5.

(b) Extracted Silica & NaOH dissolved in distilled water at 353 K and it was charged with TPABr solution in distilled water at 323 K.

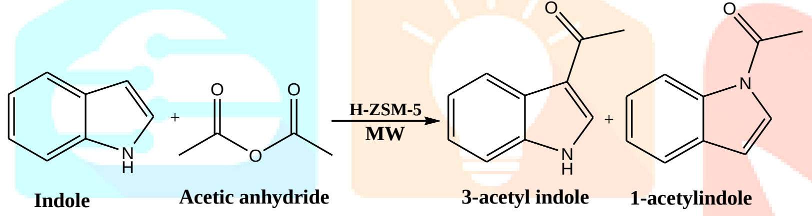
(c) Few drops of n-propyl amine to it stirred for 10 minutes and the aluminium sulfate solution in conc. H_2SO_4 and poured to the above prepared solution at pH 11.

(d) The pH of the mother liquor was maintained in the range of 11 to 12. The reactants were then subjected to hydrothermal crystallization in Teflon-lined stainless steel autoclaves for one week at around 423K.

(e) Then, the solid obtained was filtered, washed at least five times with deionized water and dried overnight at 383K and calcined in dry air at 823K for 5 h in furnace to decompose the organic amine template.

(f) The obtained Na-ZSM-5 impregnated with the solution of 1mol/L NH4Cl solution at 363K to give NH4 + form of ZSM-5 and calcined to obtain H- ZSM-5 at 773K overnight.

2.2 Catalytic study



Scheme-1

The round bottom flask containing 1mmol of indole charged with 1mmol acetic anhydride in suitable solvent. Then (50-100 mg) of H-ZSM-5 mixed in reaction mixture and subjected to microwave oven at 150 MW & 100^{o}C.The product formation was checked by TLC. After completion of the reaction, the catalyst was filtered out and solvent was evaporated. The obtained mass purified by column chromatography.

3. Result and Discussion

3.1 Catalyst Selection

From the literature review, it was found that 1,3-diacylated material as the major product, due to the rapid N-acylation of the 3-acylated intermediate[15] in Friedel–Crafts acylation of indole, so the selection of a suitable catalyst is crucial to the mono acylation of indole. Therefore, we first chose several different kinds of catalysts and to investigate their catalytic activities in this reaction and the results are listed in Table 1. Among the studied, H-ZSM-5 was found to manifest the best catalytic performance and the noticeable change in rate of reaction increased significantly in the presence of microwave radiation in comparison with compared with conventional heating. With the combination of microwave radiation and SBA/TCCA, the conversion of indole can achieve 88% and the selectivity to 3-acetylindole is 80%, but still below our expectation. Considering the benefits of acid modification, acid modified Hβ zeolites were prepared and investigated under the same reaction conditions (Table 1). As can be seen, some acid modified zeolites, especially a H-ZSM-5, exhibited higher activities than parent Hβ zeolite. Particularly, the conversion of indole and the selectivity to 3-acetylindole are 100% and 95% over the H-ZSM-5 under microwave radiation at 150 W.

We observed that microwave radiation promote the formation of 3-acetylindole by reducing side reactions, it results in shortening the reaction time. In comparison, the conversion of indole to and the selectivity for 3-acetylindole are only 76.2% and 73.4% over under microwave radiation. So there must be some synergistic effect of H-ZSM-5 to cause the highest activity in this reaction. Thus, H-ZSM-5 was chosen as the suitable catalyst for further investigation and microwave radiation was selected as the best heating method for this reaction.

It was found that the regenerated catalyst showed stable catalytic activity in three subsequent cycles. The conversion of indole remained above 90% and the selectivity to 3-acetylindole was up to 95% during the whole test. Thus, H-ZSM-5 was proven to have good stability in this reaction.

3.2 *Catalytic activity study*

The observations in our study may be attributed to its high acidic sites, (Si/Al = 30) ratio and heterogenic nature having large surface area of H-ZSM-5. Lesser conversion and the selectivity for 3-acetylindole was observed with some polymerised product in conventional heating in comparison to microwave heating. The data obtained depicted high activity of the total product and also high selectivity for 3-acetylindole (95%) over H-ZSM-5 but SBA/TCCA, Hβ- Zeolite, Al_2O_3 and SiO_2 showed lesser conversion and the selectivity for 3-acetylindole as compared.

Table: Variation of the different catalyst on conversion and selectivity of the product.

Sr. No.	**Catalyst**	**Mode of Heating**	**Conversion (%)**	**Selectivity**	
				1-acetyl indole	**3-acetyl indole**
1	H-ZSM-5	MW	100	05	95
		Δ	89	14	86
2	SBA/TCCA	MW	88	20	80
		Δ	77	25	75
3	MCM-41	MW	45	28	72
		Δ	40	30	65
4	Hβ- Zeolite	MW	80	18	80
		Δ	74	22	75
5	Al_2O_3	MW	70	28	72
		Δ	65	31	64
6	ZSM-5	MW	72	27	73
		Δ	64	32	66

Reaction Condition: Indole (1mmol), Ac_2O (1mmol), Temp. = 100°C & 150W, MW: Microwave heating
Δ: Conventional heating.

3.3 *Catalytic weight study*

On screening the transformation at different amount of catalyst, all the transformations with different amount of catalyst showed near about same conversion and high selectivity the selectivity for the 3-acetylindole in microwave heating as compared to conventional heating. Therefore, the optimum amount of catalyst required to convert 1mmol of indole into product is 50 mg. The credit of it may be attributed to its high acidic sites, (Si/Al = 30) and heterogenic nature having large surface area p of it. The optimum amount of catalyst showed that the H-ZSM-5 is potentially applicable in large scale conversion.

Table 2: Effect of amount of catalyst on conversion and selectivity of the product over H-ZSM-5.

Sr. No.	Catalyst Weight(mg)	Conversion (%)	Selectivity	
			1-Acetylindole	3-acetylindole
1	50	95	10	90
2	100	94	10	90
3	200	95	09	91
4	300	96	07	93
5	400	96	09	91
6	500	95	08	92

Reaction Condition: Indole (1mmol), Ac_2O (1mmol), H-ZSM-5 (50mg), Temperature: 100°C,
MW heating: 150MW

3.4 *Recyclability*

The catalyst used in the first cycle is collected and washed with methanol, water, acetone and oven dried. This fried H-ZSM-5 used up to the third cycle, slight decrease in conversion but no change in the selectivity of 3-acetylindole was observed.

4. Conclusion

In conclusion, series of different catalysts are tested for the synthesis of 3-acetylindole but the H-ZSM-5 manifested best performance under microwave condition which gives excellent yield. Particularly, the reaction rate of this microwave-assisted method is 65 to 80 times faster than that of the conventional heating method using $AlCl_3$ as a catalyst[15]. Thus, due to its good activity, thermal as well as chemical stability, this green process involving H-ZSM-5 is potentially applicable to industrial scale synthesis of 3-acetylindole. The catalyst could be recycled with negligible loss and reused three times, providing excellent yield.

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