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$SnCl_2$/Montmorillonite KSF is an highly efficient heterogeneous reusable catalyst for the selective alkylation of indoles with α, β unsaturated carbonyl compounds under solvent free conditions

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ABSTRACT

$SnCl_2$/ Montmorillonite KSF, a composite heterogeneous catalyst found to be recyclable and efficient for the selective alkylation of indole at 3-position with α, β unsaturated carbonyl compounds at room temperature under solvent free conditions. The montmorillonite catalyst was prepared and characterized using XRD. Obtained 3-substituted indoles products were purified with column chromatography and crystallization and all products were characterized by ^1H NMR and mass spectral data

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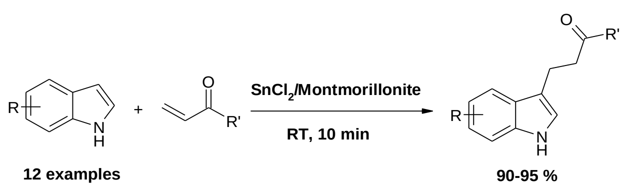
Introduction

The indole ring system is the most common heterocycle moiety in the preparation of many biologically and pharmacologically active compounds.[1] Among them the 3-substituted indoles are the building blocks for the preparation of such compounds. In the recent years many methods have been employed for the synthesis of 3- substituted and various other indole derivatives.[2] Friedel crafts reaction is the one of the effective transformation for the formation of C-C bonds by using Lewis acids as promoters. In the earlier reports several Lewis acids like $GaCl_3$, $InBr_3$, $InCl_3$, $ZnCl_2$, $CeCl_3.6H_2O$, $BiCl_3$, $FeCl_3$, $AlCl_3$, $ZrCl_2$, SmI_2, Cu and Sc salts were found to catalyse the conjugate addition of indoles to electron deficient olefins for the preparation of 3-substituted indoles derivatives. But the main limitation of these synthetic processes is there environmental incompatibility because many of the procedures involve expensive salts, low yields,[3] low selectivity, non-reusable catalysts and solvent feasible reactions that disturb the ecological balance. To ovecome these problems zeolites and clays[4] are used as efficient heterogeneous catalysts in various organic reactions.[5-12] In the present investigation we have studied the indole alkylation over zeolites, clays and metal modified clays. Among those $SnCl_2$/montmorillonite[13] KSF clay is highly acidic, from our experiments it is clearly observed that $SnCl_2$ itself is an highly effective Lewis acid catalyst for the alkylation of indoles, but the major disadvantage in using this catalyst is, $SnCl_2$ is a homogeneous catalyst and thus separation of the catalyst from the mixture requires lot of organic solvent that are expensive and hazardous for the environment, and it is a time taking process. In order to overcome these major disadvantages and to develop more efficient and environmentally benign methods in organic synthesis we have prepared $SnCl_2$/Montmorillonite supported catalyst which is highly efficient, heterogeneous reusable and selective catalyst for the alkylation of indoles at 3-position in solvent free condition at room temperature, side reactions like dimerizations and trimerizations are not absorved which indicates that catalyst is highly selective.



Scheme 1.

Preparation of catalysts

Different $SnCl_2$/Montmorillonite catalysts with varying the amount of $SnCl_2$ (5, 10, 15 and 20 wt.%) were prepared by solid state dispersion method (SSD). Required amount of $SnCl_2$ is dissolved in ethylalcohol followed by the addition of monntmorillonite KSF clay, the mixture is well mixed in the mortar pestle till the solvent get completely evaporated. The solid material obtained is dried overnight in the oven at 150˚C.

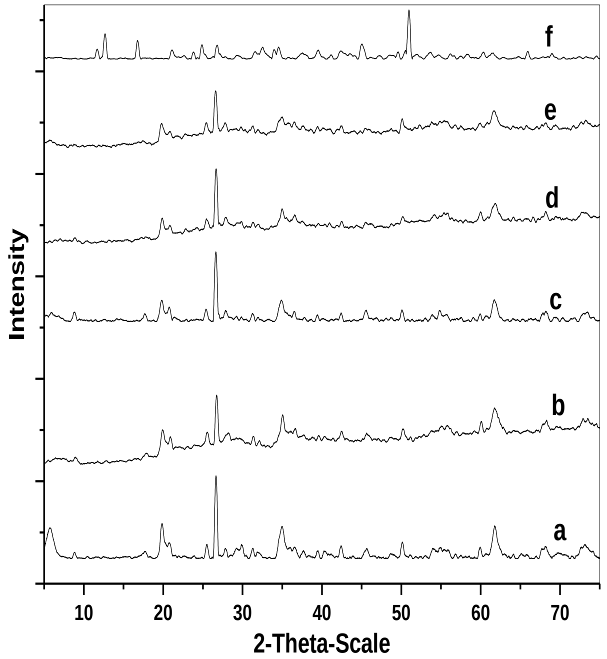


Figure 1.
XRD patterns of (a) montmorillonite KSF and $SnCl_2$ wt. % loaded on montmorillonite KSF (b) 5, (c) 10, (d) 15, (e) 20 and (f) $SnCl_2$

Table 1: Optimization of reaction conditions

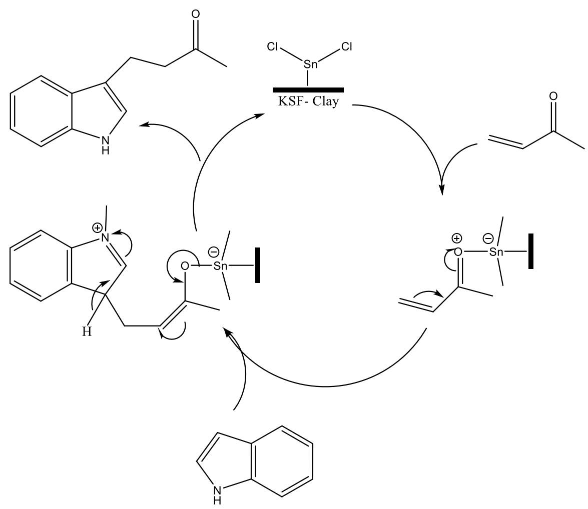
S. No	Catalysts	Time (h and min.)	Yield (%)
1	HZSM-5	3h	30
2	HY	3 h	45
3	H β	3 h	68
4	Montmorillonite KSF	3 h	75
5	$SnCl_2$. 9 H_2O	20 min	90
6	$SnCl_2$ /Montmorillonite KSF	10 min	95

General procedure for the alkylation of indoles

Indole (1mm), α β Unsaturated carbonyl compounds (1 mm) and 100 mg of $SnCl_2$/Montmorillonite catalyst were mixed under room temperature gave corresponding products. The formed product structure is analysed by ^{1}H NMR and yields are calculated by G.C analysis.

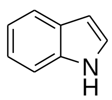
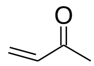
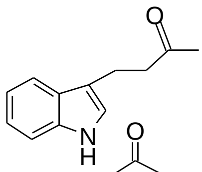
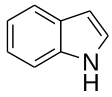
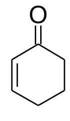
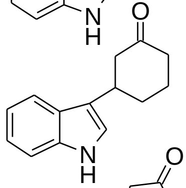
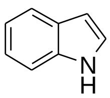
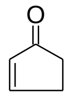
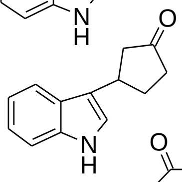
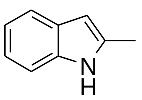
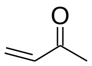
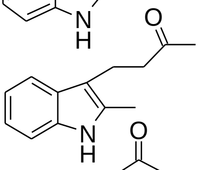
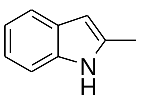
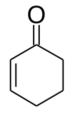
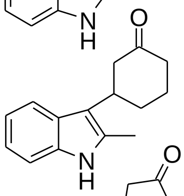
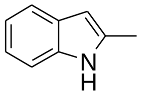
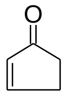
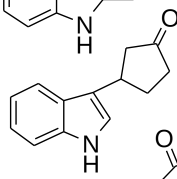
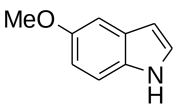
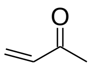
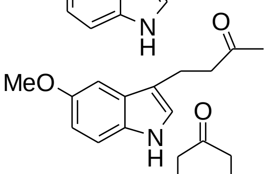
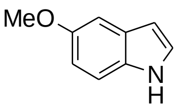
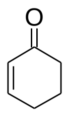
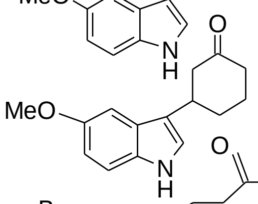
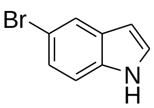
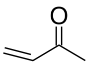
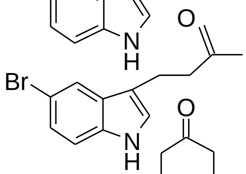
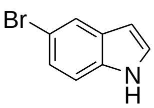
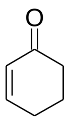
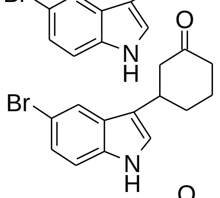
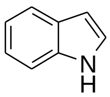
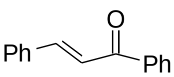
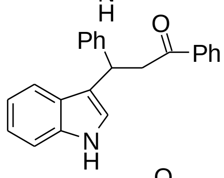
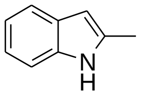
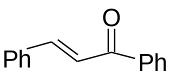
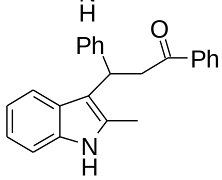
Results and Discussion

The XRD patterns of $SnCl_2$/montmorillonite catalysts are shown in Fig.1. Only a slight decrease in the intensity of typical diffraction peaks of montmorillonite is observed indicating that $SnCl_2$ does not change the basic structure of the solid support. Furthermore it should be noted that the phases of $SnCl_2$ is not detected even at higher **loadings** also. From this observation it is understood that $SnCl_2$ is highly dispersed on the surface of the support in amorphous form. Friedel crafts reaction usually requires lewis acid sites to create an electron deficient centre in the alkylating agent. Zeolites are the porous materials of high surface area with Lewis and a Bronsted acid site attracts the organic substrates on its surface and acts as a catalyst in alkylation reactions, first we compared the activity of the HY, Hβ, HZSM-5, and Montmorillonite KSF for Friedel alkylation of indole with methyl vinyl ketone at RT in solvent free conditions (Table 2). The activity of the catalysts is in the order of Montmorillonite KSF> Hβ> HY >HZSM-5. Since KSF is a strong acidic zeolite compared to other zeolites it makes the olefin more electron deficient for the nuleophile attack of indole facilitating the alkylation reaction, 75% of indole conversion is occured in 3 h. Since the reaction requires longer time and give lesser yields we carried out the same reaction under similar conditions in the presence of catalytic amounts of $SnCl_2$ where in the 95 % of 3-alkylated indole is obtained within 20 min (Table 1), but $SnCl_2$ is soluble in reaction mixture and forms homogeneous solution which is environmentally undesirable process. In this view on combining small amounts of $SnCl_2$ (with diff wt. %) with KSF



Scheme 2. Plausible Mechanism of alkylation of indoles with α, β unsaturated carbonyl compounds over $SnCl_2$/ montmorillonite showing catalyst recyclability

Table 2. Optimization selective alkylation of indoles with α, β unsaturated carbonyl compounds under solvent free conditions

Entry	Nucleophile	Electrophile	Product	Time (min)	Yield (%)
1.				30	95
2.				20	90
3.				20	80
4.				18	95
5.				20	90
6.				20	80
7.				15	95
8.				20	91
9.				15	89
10.				20	85
11				30	80
12.				30	82

[a]The reaction was conducted in solvent free conditions.
[b]The yields are calculated after purification and all products were characterized by ^{1}H NMR and mass spectral data.

clay an effective heterogeneous catalyst is prepared and the experimental results indicated that 15 wt. % $SnCl_2$/montmorillonite was an effective catalyst for the selective alkylation of indoles. The induced acidic sites of

$SnCl_2$/montmorillonite resulted in the synergistic activity wherein the alkylated products are formed in high yields in short time periods. Various α, β unsaturated compounds were reacted with indole, 2-methyl indole, 5-methoxy indole, 5-bromo indole to give corresponding 3-alkylated products in high yields the results are summarized in Table 2. The reactions were clean without formation of any side products such as an N-alkylation products or dimers or trimers. All products were characterized by ^{1}H NMR and mass spectral data. The catalyst is reusable and no considerable decrease in the efficiency of the catalysts were observed even after four cycles of the operation, only a slight reduction in the yields are observed. Catalyst is simply filtered and washed with solvent followed by drying in oven at 150˚C, Further no leaching of metal is observed during the reaction which is observed by our AAS results and activity of recyclable catalysts. A plausible mechanism occurring on the catalyst surface is depicted in scheme 2.

Conclusions

Solid acid catalyst such has clays/zeolites are found to be an alternative catalyst to conventional homogenous catalysts because these are environmentally benign which can work under solvent free conditions and reusable for several times. Various solid acids are studied for indole alkylation, among them montmorillonite KSF clay is found to be active than zeolites because of its high acidity. We also compared the activity of the clay with metal modified clay. Metal modified clays with additional Lewis acids are found to be highly active than the unmodified clay. Therefore metal modified solid acid catalyst can be a highly efficient heterogeneous catalyst for the alkyation reactions**.**

Acknowledgments

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