

Catalytic Acetylation of Aromatics with Metal Chlorides and Solid Acids – a Comparative Study

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Abstract

Evaluation of catalytic performances of selected metal chlorides such as AlCl_3 , SnCl_4 , ZnCl_2 , FeCl_3 , InCl_3 and GaCl_3 with solid acids such as sulfated zirconia, and zeolite beta was accomplished for acetylation of anisole, toluene and naphthalene. Presence of super acidity (Lewis or Bronsted acid) is found to be indispensable for activation of substrates towards acetylation reactions. In addition, presence of redox centers would further complement with the Lewis acid sites rendering catalytic stamina against deactivation. Strength of Lewis acid basically determines the activity of the metal chlorides towards acetylation. Among the Lewis acids investigated, FeCl_3 , InCl_3 and GaCl_3 exhibit their catalytic behaviour mostly through redox property as is evident from the conservation of Turn over number even after first cycle. Sulfated zirconia surpasses all the acid catalysts including metal chlorides and exhibits extended catalytic activity in acetylation of anisole. The pre-eminence of sulphated zirconia over other catalytic systems is owing to the synergistic effect of Lewis and Bronsted acidity.

Introduction

Synthesis of aromatic ketones possesses a high industrial significance, as it is a key intermediate in the synthesis of many of the pharmaceuticals [1] and this task is normally achieved through catalytic acylation route. Until now, Lewis acids such as FeCl_3 , AlCl_3 , BF_3 and Bronsted acids such as HF , H_2SO_4 having super acidity have been used in a homogenous catalytic fashion through Friedel-Crafts acylation and alkylation processes for this purpose, regardless of the generation of environmentally hazardous products [1,2]. The increase in demand for pharmaceutical and petrochemical products has driven the scientists around the world to look in for better catalytic routes to achieve acylation of various aromatic substrates. It is well known that higher acidic strength is required for the surface to catalyze acylation. It is claimed by Gillespie and Peel that a super acid with acid strength higher than that of 100% sulphuric acid is desired to execute alkylation and acylation reactions [3]. However, employing Lewis acids in stoichio-

metric quantities as "catalysts" raises an important question concerning the real catalytic properties of these metal chlorides. If Lewis acids provide only single turn over in forming aromatic ketones, then attempts to heterogenise them would be a highly ineffective task to achieve. Consequently, the attempts made in grafting the Lewis acids over high surface area supports such as silica encountered the problem of leaching under reaction conditions resulting in homogeneous catalytic reaction.

Owing to the emerging stringent environmental regulations around the world, the current interest in the industrial sector is pertaining to the development of novel catalytic materials, which are environmentally benign. As a result, recent developments in FC acylation reactions are directed towards solid acids such as zeolite beta [4], SAC 13 [5], clays [6], sulphated zirconia [7] and heteropoly acids [8,9]. In the recent past, Yadav and Nair have published an excellent review on catalytic potential of sulfated zirconia, which renders a comprehensive account of its catalytic performance.

Attempts are still under way to mimic the metal chlorides (liquid super acids) to develop novel cata-

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lytic protocols comprising either the solid version of it by grafting them over high surface area supports [10-12] or exchanging the counter ion (chlorides) with less coordinating triflamide anion [13]. In addition, Frost *et al.* as well as Wang *et al.* have reported on incorporating metals such as Fe, Ga or In over solid acids as redox centers to increase the catalytic performance towards acylation reactions [13, 14]. However, a comprehensive and comparative understanding on catalytic contributions of Lewis, Bronsted and redox centers towards acetylation reactions under normalized reaction conditions is lacking in the literature.

As a measure of addressing the issue of contributions of the Lewis, Bronsted acidity along with redox centers towards acylation, a systematic investigation of catalytic acetylation activity of metal chlorides, sulfated zirconia, and zeolite beta has been accomplished using turn over number as a measure of catalytic activity. The aromatics chosen in the present investigation can be classified as activated (anisole) electron rich (toluene) and bulkier (naphthalene) in nature.

Experimental

Anisole, (anhydrous, 99.7%), toluene, (anhydrous, 99.8%), naphthalene, (99%) dichlorobenzene (DCB) were all purchased from Aldrich and were stored in a closed container with granulated precalcined molecular sieve UOP 3A (Fluka) under moisture free conditions. Anhydrous metal chlorides (Aldrich) were stored in glove box. Sulfated zirconia, was prepared by pretreating the sulfated $Zr(OH)_2$ (containing 75% of Zirconia hydroxide and 25% of Zirconia oxide) as received from MEL[®] Chemicals (XZO-1077/01) at 873 K for 2 hours at a heating rate of 13°/min. Sulphur content of the pretreated sample was evaluated to be 2 wt.% (SEM).

Zeolite beta CP-806-HL-25 was purchased from PQ Corporation with the following specifications; Si/Al = 70 and surface area as 730 m²/g. Activation of zeolite beta was carried out at 823 K for 2 hours in the stream of air prior to catalytic study.

Acetylation reactions with Lewis acids were carried out typically in a magnetically stirred glass reactor (capacity 50 mL) equipped with a reflux condenser. Catalyst, aromatic substrate and solvent were charged under atmosphere of nitrogen in the glove-box. The concentration of substrate (anisole/toluene/naphthalene) in organic solvent was maintained be-

tween 12-14% by weight. Reaction mixture was heated in atmosphere of N₂. Subsequently, the reaction was initiated by drop wise addition of acetic anhydride to the reaction mixture, containing substrate, solvent and catalyst at 343 K for 30 minutes.

Similarly, acetylation with solid acids was performed in magnetically stirred mini-autoclave of capacity 40 mL, equipped with thermowell, sampling valve and heating jacket. Reagents, solvent and catalyst were also loaded in glove-box. Subsequently, autoclave was pressurized to 3 atm by N₂ and heated with out stirring to a temperature which is 10° lesser than the reaction temperature and the reaction was initiated by stirring. It was observed that reaction did not proceed in the absence of stirring.

Analysis of the products was done by withdrawing the reaction mixture at the end from the reactor. The sample was analysed by GC (Hewlett Packard 6890) using HP-5 column with decane as internal standard.

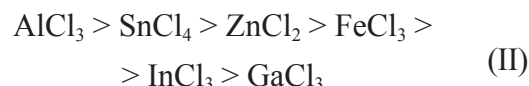
Lewis acids

Acetylation of anisole, toluene and naphthalene was carried out with metal chlorides according to Scheme 1 and the results are presented in Tables 1, 2 and 3 respectively. It can be realized that the activity of aromatics in acetylation decreases in the order:



In the case of toluene, the aromatic ring is much less activated than that of anisole $\sigma_p^+(\text{Me}) = -0.31$, $\sigma_p^+(\text{OMe}) = -0.78$ [15]. Consequently, its acetylation is more difficult to achieve.

Comparison of activity of metal chlorides in acetylation of anisole is presented in Fig. 1. It has to be taken into consideration that reaction time required for attaining 90% conversion of anisole has been selected as a measure of catalytic activity. Thus, the order of catalytic activity of metal chlorides towards acetylation of anisole in accordance with Fig. 1 is given below as:



In addition, virtually a same trend with an exception to FeCl₃, was observed in acetylation of naphthalene and toluene at constant reaction time (Tables 2, 3) resulting in comparable conversion levels. It can readily be comprehended that the activity in acetylation of aromatics correlates well with the

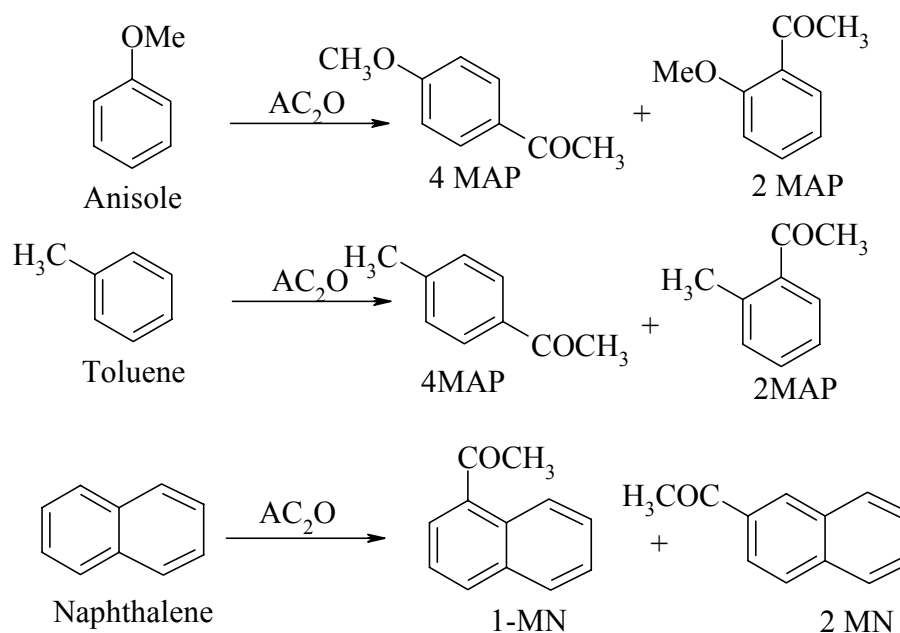


Table 1
Acetylation of anisole

Catalyst	Cycle I			Cycle II (Addition of new portion of anisole)		
	Conversion of Toluene	Selectivity of 4-MAP*	TON after first cycle	Conversion of Toluene	Selectivity of 4-MAP	TON after second cycle
AlCl ₃	9.1	51.9	0.9	0	0	0
SnCl ₄	54.8	84.0	5.5	0	0	0
ZnCl ₂	66.7	99.0	6.7	0	0	0
FeCl ₃	83.5	80.4	8.3	25.7	52	10.9
InCl ₃	85.2	81.0	8.5	29.1	62	11.3
GaCl ₃	90.0	77.7	9.0	31.7	61	12.7

*4-MAP – 4-methylacetophenone

Reaction conditions: temperature 90°C; Molar ratio = Cat:anisole:Ac₂O = 1:10:20; Reaction time 3 hrs; Solvent – dichlorobenzene

Table 2
Acetylation of toluene

Catalyst	Molar ratio Cat:Tol:Ac ₂ O	Conversion of Toluene	Yield 1+4 acetophenone	Selectivity of 4 methyl acetophenone	TON
AlCl ₃	1:1:2	89	81	91	0.9
	1:10:20	1.4	0.5	36	1.4
SnCl ₄	1:1:2	72	24	39	0.6
ZnCl ₂	1:1:2	54	21	39	0.5
GaCl ₃	1:1:2	51	22	43	0.5
FeCl ₃	1:1:2	48	32	67	0.5

Reaction conditions: temperature 90°C; Molar ratio = Cat:toluene:Ac₂O = 1:1:2; Reaction time 3 hrs; Solvent – dichlorobenzene

Table 3
Acetylation of naphthalene

Catalyst	Molar ratio Cat:Naph:Ac ₂ O	Conversion of Naphthalene	Yield 1+2 acetoneaphthone	Selectivity of 2 acetoneaphthone	TON
AlCl ₃	1:1:2	89	81	85	0.9
	1:10:20	12	83	78	1.2
SnCl ₄	1:1:2	70	55	50	0.7
	1:10:20	0.9	0.2	43	0.9
ZnCl ₂	1:1:2	26	1.8	40	0.3
InCl ₃	1:1:2	22	7.5	75	0.2
GaCl ₃	1:1:2	18	6.0	60	0.2
FeCl ₃	1:1:2	15	5	70	0.2

Reaction conditions: temperature 90°C; Molar ratio = Cat:naphthalene:Ac₂O = 1:1:2; Reaction time 3 hrs; Solvent – dichlorobenzene

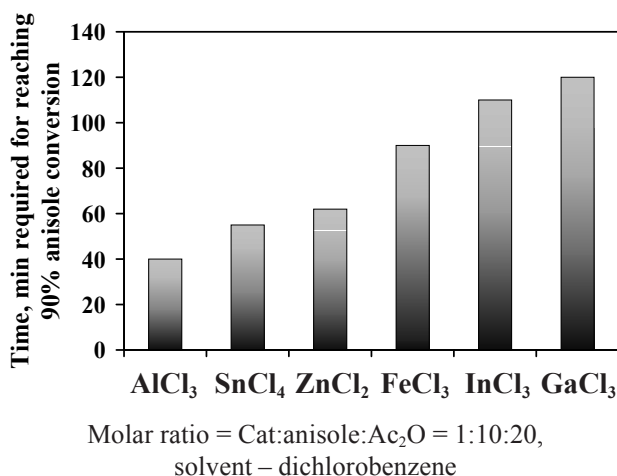
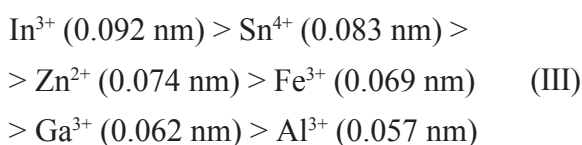


Fig. 1. Comparison of Lewis acid activity in anisole acetylation at 90°C.

Lewis acidity of these chlorides at equimolar ratio of aromatic substance and metal chloride and therefore such factor is selected as criterion for comparison of Lewis activity.

The order of strength of Lewis acid sites can be compared with the order of cationic size as follows:

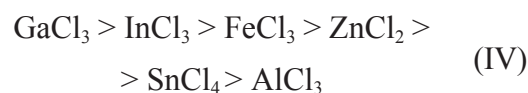


It is known that higher the cationic size lower is the strength of Lewis acid. From the above order it can also be realized that, though In³⁺ and Ga³⁺ differ in their ionic sizes they have similar redox potential (0.44 V) and similar activity towards acetylation of anisole. This supports the role of non-Lewis acidic

pathway in catalytic performance that could probably be associated with the redox property of the metal cations.

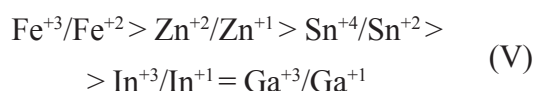
It is important to further comprehend the exact role played by the Lewis acidity of these metal chlorides in acetylation reactions. To achieve this, comparison of catalytic properties of the above metal chlorides in acetylation were made with three different substrates using turn over number (TON) as a measure. In these experiments ratio between aromatics and catalyst was increased up to 10:1. AlCl₃ though exhibited higher activity than other chlorides, did not work catalytically with all the three aromatics. The highest turn over numbers that were accomplished in acetylation of anisole, toluene and naphthalene were 0.9, 1.4 and 1.2 respectively along with the low aromatic conversion. Thus, it is obvious that equimolar quantities of AlCl₃ are required to achieve higher yields in all the three reactions. Whereas, the rest of the metal chlorides though were catalytically inactive in acetylation of toluene and naphthalene exhibited a significant increase of TON in acetylation of anisole. Thus, the above observation indicates that the strength of Lewis acidity basically determines the activity of metal chlorides in acetylation and ostensibly not responsible for catalytic properties.

On the other hand the above sequence (III) indicates exactly an opposite trend in the order of Lewis acidity from AlCl₃ to InCl₃ from the experimental results of acetylation of anisole (II).



It can be seen that moving from AlCl_3 to SnCl_4 results in 5 – fold increase of anisole conversion. Moreover, employing FeCl_3 , InCl_3 and GaCl_3 as catalysts brings about a conversion of more than 80% at molar ratio of anisole: metal chloride 10:1. Besides this, activity was retained even after adding a second portion of anisole- Ac_2O mixture in the second cycle leading to a total TON of about 11-12 in accordance with Table 1. These high values of TON prompt us to consider the weak Lewis acids such as In and Ga chlorides behaving as real catalysts in acetylation of anisole.

The diminished catalytic activity of other AlCl_3 after the first cycle as indicated by the turn over numbers can readily be explained by the established view of complexation of AlCl_3 with products, blocking and preventing them from further catalytic cycle. Moreover, the extended catalytic activity manifested by Fe, In and Ga chlorides compared to Al, Sn and Zn chlorides further supports the participation of non Lewis acid assisted catalytic pathway. Further, the profound promoting effect reported by Choudary *et al.* for Ga^{+3} , In^{+3} , Fe^{+3} and Zn^{+2} incorporated in cation-exchanged clays or montmorillonite K-10 in acylation of aromatic ethers, benzylation of benzene [16, 17] along with a sharp increase in TON of other Lewis acids in comparison with AlCl_3 evidences the likelihood of additional route for formation of products that proceeds in parallel with the traditional Lewis acidic pathway. Possibility of redox pathway has also been proposed Choudary *et al.* [16,17] for acid catalysed reactions using metal doped solid catalysts. Scheme 2 represents redox mechanism of anisole acetylation. This makes clear that carbocation intermediate can also be produced and stabilized through non-Lewis acidic pathway. However decrease of redox potentials as shown in (V) not exactly correlates with conversion of anisole and decrease of turn over numbers in acetylation:



1. $\text{mCH}_3\text{COOOCCH}_3 + \text{M}^{+n} \leftrightarrow \text{mCH}_3\text{COOOCCH}_3^+ + \text{M}^{(n-m)+}$
2. $\text{mCH}_3\text{COOOCCH}_3^+ \leftrightarrow \text{mCH}_3\text{CO}^+ + \text{mCH}_3\text{COO}^+$
3. $\text{mCH}_3\text{CO}^+ + \text{mMeOPh} \rightarrow \text{mMeOPhAc} + \text{mH}^+$
4. $\text{M}^{(n-m)+} + \text{mCH}_3\text{COO}^- \rightarrow \text{M}^{+n} + \text{mCH}_3\text{COO}^-$
5. $\text{mH}^+ + \text{mCH}_3\text{COO}^- \rightarrow \text{mCH}_3\text{COOH}$

Redox mechanism
Scheme 2

Thus, it can be deduced that the contribution of each mechanism in the formation of intermediate carbocation is strictly confined to the given metal chlorides.

The fact that the turn over numbers in acetylation of anisole with Fe, In and Ga chlorides are retained with the proportional reduction in conversion and selectivity after first cycle indicates that irrespective of the decline in number of active sites, the same performance (efficiency) is maintained due to the extended activity of redox centers towards activated aromatics. The reduction in conversion of anisole (Table 1) after first cycle from the range of 80-90% to 25-31% for Fe, In and Ga chlorides suggests that though the Lewis acidic sites were deactivated in the first cycle, the site efficiency remains the same. Therefore, it can be followed that the catalytic performance in the first cycle could essentially be attributed to the redox mode of activation rather than Lewis acidic pathway. At the same time, the non-catalytic participation of Lewis acid sites cannot be ruled out as is evident from the decrease in conversion and selectivity levels. Further, the fact that the order of activity of aromatics corresponds to the requirements of Friedel-Crafts reaction (*i.e.*, anisole > toluene > naphthalene) for all the metal chlorides suggests the participation of Lewis acidity in activation process cannot be excluded. Redox centers are playing a complementary role in the same. In addition, it can be followed that redox center in isolation can perform acetylation of anisole but acetylation of toluene or naphthalene basically requires the presence of super acidic sites for activation.

Solid acids

Acetylation of anisole, toluene and naphthalene has also been performed on solid acids such as sulfated zirconia and zeolite beta and the results are shown in Table 4. Higher turn over of 82 per mol of sulphur for acetylation of anisole observed with sulfated zirconia than zeolites (2.6 per Al) is due to the

combined action of Lewis and Bronsted acid sites over the former, wherein Bronsted acid sites initiate the formation of acetyl cation while Lewis acid sites triggers to accomplish electrophilic substitution [16]. It has also been established by Morterra *et al.* and Biro *et al.* that the calcined sulfated zirconia develops Bronsted acidity while cooling in desiccator due to the interconversion of part of Lewis acid sites to Bronsted acid sites [18,19]. On the contrary, acetylation of toluene with sulfated zirconia shows the

limited conversion with turn over of 20 per mol of sulphur and selectivity around 90% towards 4 MAP. Zeolite beta, provided only Bronsted acid sites [20] showed less activity for acetylation of toluene and no activity for naphthalene. Since these demanding organic transformations depend on total acidity, probably, higher amount of catalyst and higher reaction temperature would yield better results [20]. It implies the need for the presence of complementary centers for acetylation of activated aromatics.

Table 4
Acetylation of aromatics with solid acids

Catalyst	Cycle I			Cycle II (Addition of new portion of anisole)		
	Conversion	Selectivity*	TON** after first cycle	Conversion	Selectivity	TON after second cycle
Acetylation of anisole, 140°C*** and zeolite beta 70°C, 3 hrs, dichlorobenzene						
SO ₄ -ZrO ₂	36.9	92.1	82	43.8	86.2	97.3
Zeolite beta	20.2	90	2.6	41	88	5.3
Acetylation of toluene, 140°C*** and zeolite beta 70°C, 3 hrs, dichlorobenzene						
SO ₄ -ZrO ₂	5.3	90.0	20.2	–	–	–
Zeolite beta	1.5	64.1	5.6	–	–	–
Acetylation of naphthalene*** and zeolite beta 70°C, 3 hrs, dichlorobenzene						
SO ₄ -ZrO ₂	–	–	–	–	–	–
Zeolite beta	10	90	1.2	–	–	–

*Selectivity to 4-methoxy acetophenone, 4-methyl acetophenone and 2-aceto-naphthone accordingly

**TON is estimated as mol of converted aromatics/mol of S or Al for SO₄-ZrO₂ and Zeolite beta accordingly

***Optimal temperature for acetylation of anisole, toluene and naphthalene on solid catalysts

Conclusions

The facts deduced from the comparative evaluation of solid acids with metal chlorides as Lewis acids results in the following proposition that designing a solid acid containing, Lewis and Bronsted acid sites in particular ratio in conjunction with redox centers as promoters would be a catalyst of higher order performance for acetylation reactions. Employing Fe, In or Ga metals as redox promoters would be beneficial in offering extended catalytic activity.

In addition, enhancing the morphological properties of solid acids such as surface area and porosity by evolving a suitable synthetic strategy would further broaden its range of application to bulkier

substrates curtailing the diffusion limitations. Investigations are underway in our laboratory to develop a solid acid possessing above qualities to accomplish acetylation reaction in a greener fashion and with higher selectivity.

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