Green and Simple method for the synthesis of Phenolic esters and their catalytic de-protection

Mr. Sagar Narayan Dakhane[a]

[1]Assistant Professor, MES Abasaheb Garware College, Pune-04 Affiliated to Savitribai pune university Pune Maharashtra, India,,

Dr. Bhavana Purushottam Khobragade[b]

**Assistant Professor, RDIK and NKD College Badnera, Maharashtra, India,*

Dr. Amrut Gunwantrao Gaddamwar[c]

[*]Assistant Professor, Amolkachand Mahavidyalaya Yavatmal, Affiliated to Sant Gadge Baba Amravati University Amravati, Maharashtra, India,

Dr. Tukaram P.Chavan[d]

[2]Associate Professor, Amolkachand Mahavidyalaya Yavatmal, Affiliated to Sant Gadge Baba Amravati University Amravati, Maharashtra, India.

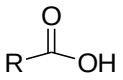
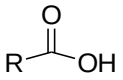
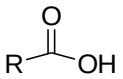
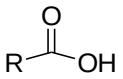
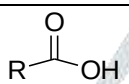
Abstract: *Phenolic Esters have been prepared by using different phenols and acetic anhydride without using any acidic/basic catalyst. This Esters preparation has been achieved by monitoring the temperature under solvent-free conditions. The synthesized esters are monitored by TLC and characterized by IR and NMR. The resultant phenolic esters are deprotected by greener method using metal catalyst loaded on MMT K-10. The metal catalysts supported on MMT-K10 (Fe-K10, Zn-K10) were synthesized using a simple wet impregnation method. These catalysts were characterized using various physicochemical techniques like PXRD, FTIR, BET-surface area. Among the synthesized catalysts, the 10% Zn-K10 exhibited high conversion up to 100% and high selectivity up to 100% towards phenolic ester at 100 °C in 3 hours. Further, the catalyst was used for the deprotection of several important esters to study the substrate scope. Metal supported Montmorillonite K10-catalyzed reactions of various substituted phenyl acetate are monitored by LCMS, IR, NMR, and product(s) are isolated, purified, and analyzed (IR, NMR). However, the catalyst is recyclable for three cycles without loss in catalytic activity.*

Keywords: **Phenolic esters, MMT-K-10, impregnation method, solvent-free condition.**

1. Introduction

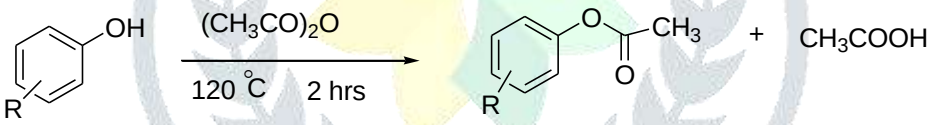
The carboxylic esters are fundamental organic compounds in organic synthesis and have been widely used in chemical and pharmaceutical industries, such as spices, daily chemical industries, foods, medicines, rubbers, coating materials, and so on[1]. Owing to the importance of esters, numerous chemical methods have been reported to accomplish this basic transformation [2, 3]. Esters are primarily prepared from the condensation of carboxylic acids with alcohols; generally, the most common methods for the preparation of ester proceed via carboxyl group activation and subsequent reaction with suitable alcohol [4]. Among them, acid halides were recognized as powerful esterifying agents because of their complete conversion and high yields; however, to the best of our knowledge, acid halides always generate highly acidic byproducts such as hydrochloric acid, which could result in decomposition of the initial materials; this method has almost no application in the synthesis of a natural product because of the greater possibility of reaction with some acid-sensitive functional groups [5] Moreover, acid chlorides are prone to hydrolysis under basic conditions through the standard ketene intermediate. Therefore, it is crucial to find a mild coupling system for the further development of chemistry. According to literature in the last 10 years, various methods for esterification are given in table 1

Table 1: Various esterification methods reported in literature

Sr. No.	Substrate 1	Substrate 2	Catalyst	Solvent	Time	Yield	Ref
1		R'OH	SO_2F_2	DCE	5 Hr	90%	[6]
2	R−OH	AcOH	Microporous Polymeric	Solvent free	12 hr	80%	[7]
3		MeOH	TCT/sonication PS-PPh_3	MeOH	30 min	80%	[8]
4		R'YH	o-NosylOXY	DCM	4 hr	70%	[9]
5		R'OH	Grapheme oxide	DCE	24 hr	70%	[10]
6		R'OH	$MgCl_2.6H2O$	Solvent free	72 hr	70%	[11]

Phenolic Esters are prepared by using different phenols and acetic anhydride without using any acidic/basic catalyst. This Esters preparation is achieved by monitoring the temperature under the solvent-free condition as a new greener methodology for ester synthesis

Scheme 1:

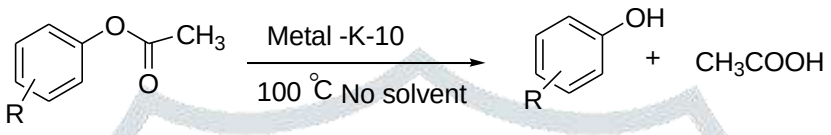


Nano clays have been one of the significant industrial minerals and with the recent development of nano clay technology. Montmorillonite, $\{[M_2(OH)_2(Si_4O_{10})]\cdot xH_2O\}$, M = Al and/or Mg is one of the most important nano clay minerals used in various organic reactions [12]. Montmorillonite has the capability to exchange various metal cations like Al^{3+}, Zn^{2+}, Mn^{2+}, Fe^{3+}, Cu^{2+}, Cr^{3+}, Ni^{2+}, etc. by the cations present in the interlayer of nano clay mineral [13]. The catalytic activity of nano clay minerals has been enhanced by manipulating the pore size, intercalating, and replacing interlayer cations and surface area [14]. Several acid-treated montmorillonite clays and high porosity silicas have previously been shown to be effective supports for $ZnCl_2$ and $FeCl_3$ used in many organic transformations. The catalytic activity of $ZnCl_2$, on these supports, is very much higher than that of the unsupported salt, and these catalysts are of some interest as possible replacements for homogeneous catalysts [15,16].

Phenolic esters, a type of aryl C-O electrophiles, are considered as notable functional groups or protecting groups in organic synthesis and can be found in various bioactive natural products, agrochemicals, pharmaceuticals, and functional polymers [17-19]. The ester hydrolysis is one of the most fundamental chemical transformations. Successful strategies for the preferential mono-hydrolysis of several different esters have been reported under often strong basic conditions [20-22], however, general applicability is limited by competing for elimination reactions under these conditions and chemoselectivity regarding a wide spectrum of multi ester compounds. No study has yet been reported for the selective deprotection of phenolic esters. Phenolic esters are an important class of precursors that give rise to

compounds with anti-infective, anti-inflammatory, and anti-cancer potencies [4–10], as well as in technical applications, such as in solar cells, where they are used as linkers for dyes [11] and hole transport materials [12], in metal-organic frameworks for gas storage [13], and as catalysts [14] in lithium-ion batteries [15] or rectification devices [16], in nanocomposite thin films for use in organic light-emitting diodes (OLED) [17], or even as material in HPLC columns for the isolation of aromatic compounds [18]. Chemoselective hydrolysis and subsequent functionalization of ester-based compounds, therefore, allow the generation of tailored molecules with increased potency and selectivity for their biological targets, improved bioavailability (absorption-distribution-metabolism-excretion-toxicity, ADMET) profiles, or unique magnetic or electronic properties. Metal catalyst loaded on MMT-K10 is proved as a greener catalyst. In this present work, phenolic esters are deprotected by various metal catalysts supported on montmorillonite clay in a solvent-free condition.

Scheme 2:



2. Materials and Methods

2.1 Preparation of catalyst

A known amount of K-10 (10 g) was stirred with 0.5M zinc chloride solution prepared in water (50 ml) at 80 ◦C overnight and then cooled to room temperature and the exchanged clay was separated by filtration. The above procedure was repeated once to ensure maximum zinc exchange. The residue obtained was filtered and washed twice with 100 ml of distilled water. This zinc-exchanged K-10 was dried at 120 ◦C for 12 h and then calcinated in a muffle furnace at 400 ◦C. The catalysts with varying concentrations of Zn in K-10 were prepared by taking different zinc chloride stock (0.01–0.5 M) solutions, by following the above procedure. Similarly, Fe/K-10 and Ba/K-10 catalysts were prepared by exchanging with the pre-decided stock solutions of the corresponding metal chlorides by following the above procedure. BET surface area of catalysts was determined by a surface area analyzer. The amount of exchanged metals on supports was determined by atomic absorption spectrophotometer. It was characterized by powder XRD and FT-IR.

2.2 Preparation of phenolic esters

In a 25 ml round bottom flask 2.0 ml (0.02 mol) of phenol, 2.0 ml (0.02 mol) of acetic anhydride were added and stirred in an oil bath at 1500C for 120 minutes. The reaction was monitored by TLC. After confirmation of phenol to phenylacetate conversion, the reaction mix was subjected to a work-up process. The whole reaction mixture was poured into ice-cold water in a separating funnel and extracted with hexane. The hexane fraction was evaporated to get product pure phenyl acetate the same procedure was applied to synthesize various substituted esters and characterized by H1 NMR and C 13 NMR.

2.3 Ester hydrolysis (Deprotection)

0.2 g of Zn-K10 was placed in a 25 ml round bottom flask. In this 1 ml of phenylacetate was taken and then stirred in an oil bath at 120˚C for 3 hours. This reaction was monitored by TLC. After 3 hours TLC of the reaction mixture was determined in 20% hexane-ethyl acetate. On the conformation of phenylacetate conversion to phenol, the reaction mixture was subjected to a work-up process. In the reaction flask, 3 ml cold distilled water and hexane was added. It was centrifuged and then filtered through Whatman filter paper-42. Such three pieces of washing (3ml water and 5 ml

hexane) were given to the reaction mixture. From the washings, the hexane layer is collected by distillation and evaporated under reduced pressure to get deprotected product i.e. phenol. The formation of free phenol was confirmed by a neutral FeCl3 test. The resultant phenol was separated 2N NaOH and reprecipitated concentration HCL. It was then dried and weighed. The TLC of this deprotected sample showed the presence of phenol as well as phenylacetate. On GC-MS and LCMS analysis this reaction showed 99% conversion. The same procedure was applied with various substituted phenylacetate. The compound showed analytical data according to those described in the literature.

3. Result and discussion

Esterification reaction between Phenols and acetic anhydride is known to be catalyzed by base sites. As per scheme:1 different substituted phenol on heating with acetic anhydride in solvent-free condition phenylacetate and its derivatives were obtained without using any acidic or basic catalyst. Temperature played a vital role in this conversion. The reaction was carried out at different time periods under the same experimental conditions. A series of reactions were conducted by refluxing phenol with acetic anhydride (1: 1 molar ratio) at different temperatures. The yield of the product increased as the increase in the reaction temperature from 25°C to 150°C and there was a decrease in yield beyond 120°C temperature. The conversion of phenol to phenylacetate was also monitored by GC using reaction mixture fractions at different temperatures. The structures of esters were confirmed by H1NMR and C13NMR. So, the optimum reaction period and temperature for the esterification of phenol was reported as 2 hours and 120°C respectively. The esterification was conducted using different substituted phenols and acetic anhydride at 120°C under the solvent-free condition and resultant products were confirmed by H1NMR and C13 NMR. It is given in table 2

Table 2: Physical properties of resultant esters

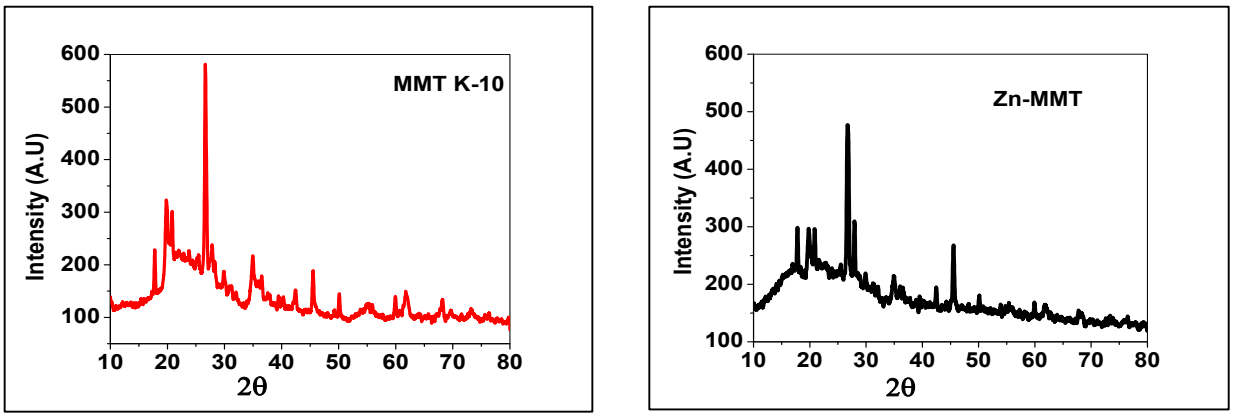
Entries	Esters	BP/MP	% yield(isolated)
1	Phenyl acetate	196	92
2	P-Cresyl acetate	208	95
3	m-Cresyl acetate	210	95
4	p-chlorophenyl acetate	230	90
5	m-Chlorophenyl acetate	197	85
6	p-nitrophenyl acetate	77	87
7	m-nitrophenyl acetate	56	90
8	β-naphthyl acetate	70	85

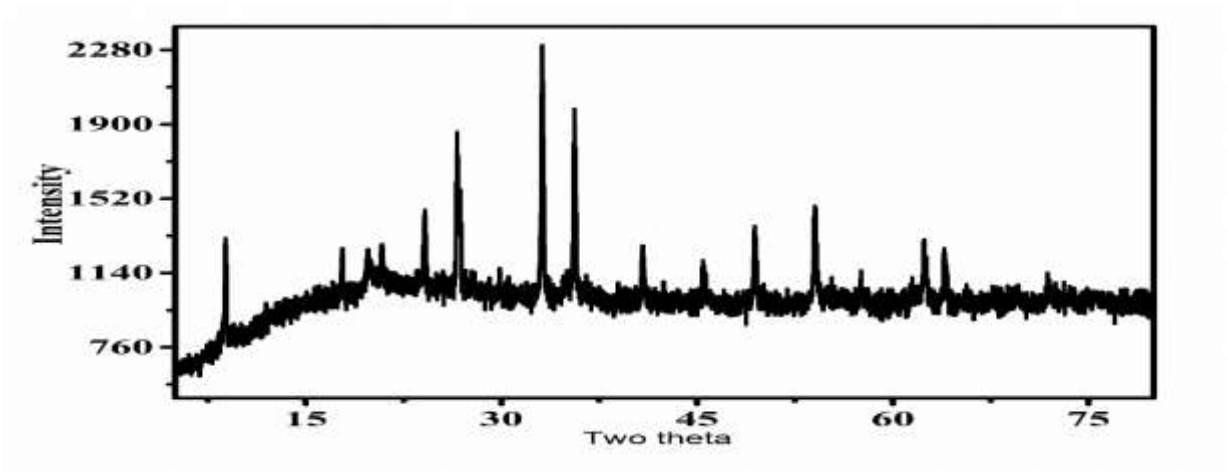
FTIR data of phenylacetate (cm−1): 3027, 2925, 1742, 1506, 1401, 1229, 1161, 908, 840, 618 and 495. IR peaks obtained at 1742 cm−1 are due to the C=O group (ester), a peak at 1506 cm−1 indicates C–O stretching, a peak at 2925 cm−1 represents C–H stretching and a peak at 495 cm−1 indicates benzene ring having substitution. 1HNMR data of phenyl acetate (δ =ppm): 2.33 (s, 3H), 3.85 (s, 2H), 6.92 (d, 2H), 7.15 (d, 2H) and 7.30–7.38 (m, 5H). 13C NMR data of phenyl acetate (δ =ppm) 170.0, 148.6, 135.3, 133.6, 129.8, 129.3, 128.7, 127.2, 121.1, 40.8, 20.7

The specific surface area of raw montmorillonite nano clay and amount of Zn was determined by BET methods using a Quantachrome NOVA 1000 surface area analyzer at liquid nitrogen temperature. The surface area of the raw montmorillonite nano clay was found to be 230 m_2 g^{-1} and that of Zn/K-10 was 23 m_2g^{-1} for 0.01 molar concentration of $ZnCl_2$ salt. Pyridine adsorption in situ FT-IR spectroscopy was performed for K-10 and Zn incorporated K-10 catalysts. And the spectra recorded after outgassing at 200 ◦C. Adsorption of pyridine on the parent K-10 clay resulted in

absorption bands at 1540 and 1450 cm−1, which can be assigned to pyridine molecules interacting with Bronsted and Lewis acid sites, respectively. Incorporation of zinc led to an increase in Lewis acidity and there is a decrease in the concentration of acid sites with an increase in zinc loading in the range of 0.1–0.6 mmol Zn per gram of K-10. It is seen that Zn/K-10 showed the highest activity with 90% conversion of phenylacetate to corresponding phenol in a solvent-free condition. The effect of Zn^{2+} concentration on the catalytic activity of the Zn/K-10was studied with Zn^{2+} concentrations ranging from 0.01 to 0.50 mmol/g. The conversion of PhAc increased linearly up to 0.22 mmol/g of zinc and a further increase has a marginal effect on the catalytic activity. Zn^{2+} is exchanged with interlayer cations as well as the Bronsted acid sites up to a concentration of 0.22 mmol/g. The higher loading results in the incorporation of zinc species as ZnO after calcination, which does not contribute to the catalytic activity.

Fig. 2 shows that XRD spectra of MMT-K10 Clay, Metal loaded MMT-K10





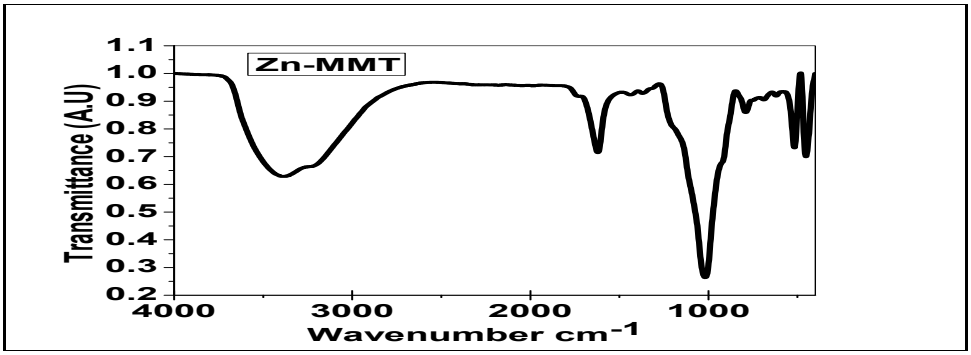
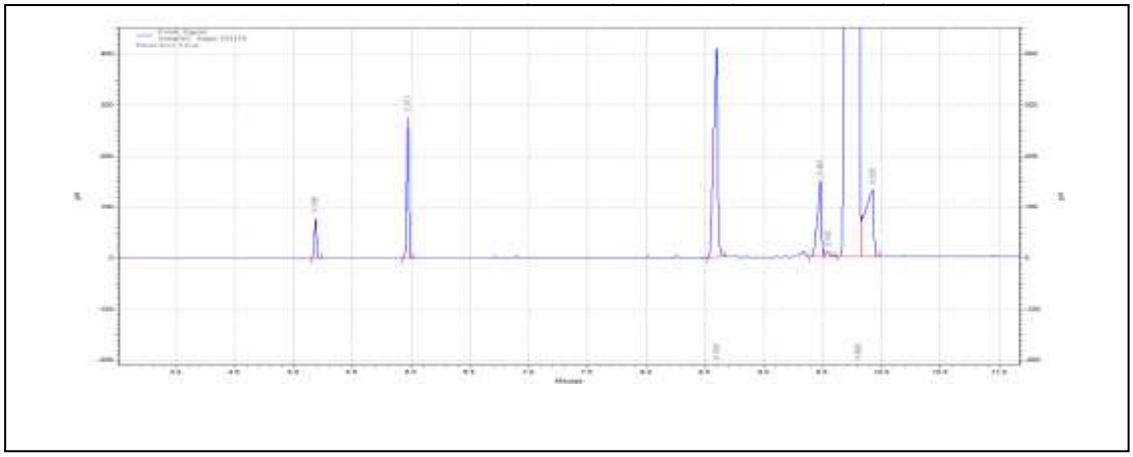


Fig4: GC showing conversion of phenol to phenyl acetate



4. Conclusion

Esterification of various substituted phenols using acetic anhydride has been accomplished by optimizing temperature only. In this scheme, 120 °C is the optimized temperature for esterification in solvent-free and catalyst-free conditions. The main advantage of this method is that no acidic or basic catalyst is required like regular conventional methods. Besides this, it is completed in a solvent-free condition.

Montmorillonite nano clay exchanged with different metal cations (Ba^{2+}, Zn^{2+}, Fe^{3+}) catalyzes the deprotection of substituted phenylacetate to their corresponding phenols. The percentage of yield obtained in this deprotection reaction indicated that using Zn^{2+}–mont-nano clay has better catalytic activity compared with other metal cation exchanged nano clays. The activity of the Zn^{2+} mont nano clay is nearly equal to the catalyst obtained commercially. The percentage yield obtained in ester hydrolysis using nano clay catalyst is nearly equal to the conventional methods. The catalyst used has strong Brønsted acid sites to catalyze ester hydrolytic reaction. The recyclability of these solid catalysts renders these processes economical. Other advantages of this method include operational simplicity, environmentally friendly, and reusable nature of the catalyst.

References

[1] *Otera J., "*Esterification: methods, reactions and applications". *Wiley-VCH., (2003).*
[2] *Tsakos M, Schaffert ES, Clement LL, Villadsen NL, Poulsen TB, "Ester coupling reactions-an enduring challenge in the chemical synthesis of bioactive natural products". Nat. Prod. Rep. vol. 32, (2015), pp. 605–632.*
[3] *Swamy KCK, Kumar NNB, Balaraman E, Kumar KVPP, "Mitsunobu and related reactions: advances and applications", Chem. Rev, vol. 109, (2009), pp. 2551–2651.*
[4] *Siengalewicz P, Mulzer J, Rinner U., "Org. Synth". II. 6, (2014). pp. 355–410.*
[5] *Fong-Kuang Chen synth.comm. (2013),43,19*
[6] *S.M. Wang, N. S. Alharbi, H.-L. Qin, Synthesis, (2019), 51, 3901-3907.*
[7] *M. Minakawa, H. Baek, Y. M. A. Yamada, J. W. Han, Org. Lett., (2013), 15, 5798-5801*
[8] *S. Jaita, W. Phakhodee, M. Pattarawarapan, Synlett, (2015), 26, 2006-2008.*
[9] *D. Dev, N. B. Palakurthy, K. Thalluri, J. Chandra, B. J. Org. Chem., (2014), 79, 5420-5431.*
[10] *Z. Chen, Y. Wen, Y. Fu, H. Chen, M. Ye, G. Luo, Synlett, (2017), 28, 981-985.*
[11] *G. Bartoli, M. Bosco, A. Carlone, R. Dalpozzo, E. Marcantoni, P. Melchiorre, L. Sambri, Synthesis, (2007), 3489-3496.*

[12] *Silva FC, de SouzaMCBV, Ferreira VF, Sabino SJ,Antunes OAC,. "Natural clays as efficient catalysts for obtaining chiral b-enamino esters", Catal. Commun, vol* ***5****, (2004), pp. 151–155*

[13] *Nazir MS, Mohamad Kassim MH, Mohapatra L, Gilani MA, Raza MR, Majeed K., "Characteristic properties of nanoclays and characterization of nanoparticulates and nanocomposites", In Nanoclay reinforced polymer composites (eds M Jawaid, A Qaiss, R Bouhfid), (2016), pp. 35–55.*

[14] *Singh B, Patial J, Sharma P, Agarwal SG, Qazi GN, Maity S., "Influence of acidity of montmorillonite and modified montmorillonite clay minerals for the conversion of longifolene to isolongifolene". J. Mol. Catal. A Chem., vol 266, (2007), pp. 215–220.*

[15] *Varma RS., "Clay and clay-supported reagents in organic synthesis", Tetrahedron, vol 58, (2002), pp. 1235–1255.*

[16] *Vogels RJMJ, Kloprogge JT, Geus JW., "Catalytic activity of synthetic saponite clays: effects of tetrahedral and octahedral composition" J. Catal, vol. 231, (2005), pp. 443–452.*

[17] *Li, Y.; Wang, L.; Yan, R.; Han, J.; Zhang, S., "Gold nanoparticles supported on Ce-Zr oxides for the oxidative esterification of aldehydes to esters", Catal. Sci. Technol., vol 5, (2015), pp. 3682–3692.*

[18] *Ghosh, K.; Iqubal, M.A.; Molla, R.A.; Mishra, A.; Islam, S.M., "Direct oxidative esterification of alcohols and hydration of nitriles catalyzed by a reusable silver nanoparticle grafted onto mesoporous polymelamine formaldehyde", Catal. Sci. Technol., vol 5, (2015), pp. 1606–1622.*