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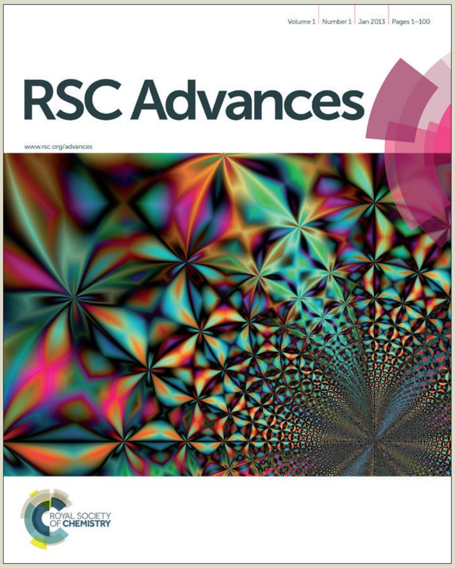

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Melamine trisulfonic acid (MTSA): An efficient and recyclable heterogeneous catalyst in green organic synthesis

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Abstract:

Melamine trisulfonic acid (MTSA) as a highly efficient heterogeneous solid acid catalyst catalyzes various organic transformations. The great efforts have been made by many scientists to utilize MTSA as a green catalyst for the preparations of N- and O-containing heterocyclic compounds, for the protections of alcohol, phenols, amines and aldehydes and ketones, for the acetylation of alcohols and phenols and for the *N*-formylation of amines. The superior advantage of this heterogeneous catalyst is that it can be recovered and reused several times without the loss of their efficiency. In this review, preparation and applications of MTSA in organic synthesis are investigated.

Keywords:

Melamine trisulfonic acid (MTSA), Heterogeneous, Recyclable, Green synthesis, Solid acid catalyst, Heterocyclic compounds

Content:

1) Introduction:

Catalysis have played a significant role in reducing pollution from the chemical processes in our environment. By utilizing catalysts, organic reactions can be more efficient and selective thereby eliminating large amounts of by-products and other waste compounds.[1] It is one of the fundamental pillars of green chemistry.[2] Homogeneous acid catalysts such as HF, HCl, CH_3COOH, HBr, CF_3COOH and H_2SO_4 are widely used in many important industrial processes, but they have some disadvantages in handling, corrosiveness, trouble work-up procedures and production of toxic waste.[3] Hence, in recent years, the search for environmentally benign chemical processes or methodologies has received much attention, and the development of heterogeneous catalysts for fine chemical synthesis has become a major area of research. The potential advantages of these materials over homogeneous systems are such as ease of handling, decreased reactor and plant corrosion problems, and more environmentally safe waste disposal procedures.[4-8] For this purpose various solid acids such as solid acid zeolite,[9] solid super acid sulfated zirconia,[10] silica sulfuric acid,[5] alumina sulfuric acid,[11] tungstate sulphuric acid,[12] molybdate sulfuric acid,[13] alum,[14] $ZrOCl_2.8H_2O$,[15] MCM-41-SO_3H,[16] PPA-SiO_2,[17] SiO_2-$HClO_4$,[18] SiO_2-$NaHSO_4$,[19] SiO_2-Pr-SO_3H,[20] Amberlyst-15,[21] heteropoly acids[22] and montmorillonite K-10[23] ware developed by many scientists and utilized in the synthesis of a wide range of organic compounds. Nowadays, the use of SO_3H-containing catalysts has received considerable interest in organic synthesis, because of their unique advantages such as efficiency, high reactivity, operational simplicity, environmental compatibility, non-toxicity, low cost, ease of isolation, green nature, easy availability of their starting materials, and ability to promote a wide range of reactions. [16, 20, 24-26] However, cellulose sulfuric acid, starch sulfuric acid and PEG-OSO3H were explored as biodegradable solid acids for the synthesis of various organic compounds, While other SO_3H-containing catalysts are metal base catalysts and are non-biodegradable. One of the attractive SO_3H-containing catalysts is melamine trisulfonic acid (MTSA), which is also used as a versatile catalyst, which makes organic processes convenient, more economic and environmentally benign. MTSA have been explored as powerful catalysts for the preparations of N- and O-containing heterocyclic compounds, for the protections of alcohol, phenols, amines and aldehydes and ketones, for the acetylation of alcohols and phenols and for the *N*-formylation of amines. Moreover, this catalyst can be recovered and reused several times without a decrease in activity as well as its efficiency. The present review is intended briefly in recent research progress concerning the various organic transformations catalyzed by MTSA as a heterogeneous and recyclable catalyst.

2) Preparation of melamine trisulfonic acid (MTSA)[27]

In 250 mL suction flask take 5 mL chlorosulfonic acid (75.2 mmol) was equipped with a gas inlet tube for conducting HCl gas over an adsorbing solution. Melamine (3.16 g, 25.07 mmol) was added in small portions over a period of 30 min at room temperature. HCl gas evolved from the reaction vessel immediately (**Figure 1**). After completion of the addition of melamine, the mixture was shaken for 30 min; meanwhile, the residual HCl was removed by suction. MTSA (7.7 g, 85 %) was obtained as a white solid, which was stored in a capped bottle. M.p.: 142-144 °C. It is hygroscopic in nature and possessing an acidic pH. It is soluble in water. It is insoluble in ethyl acetate, methanol, ethanol, dichloromethane, diethyl ether, *n*-hexane, chloroform and acetone.

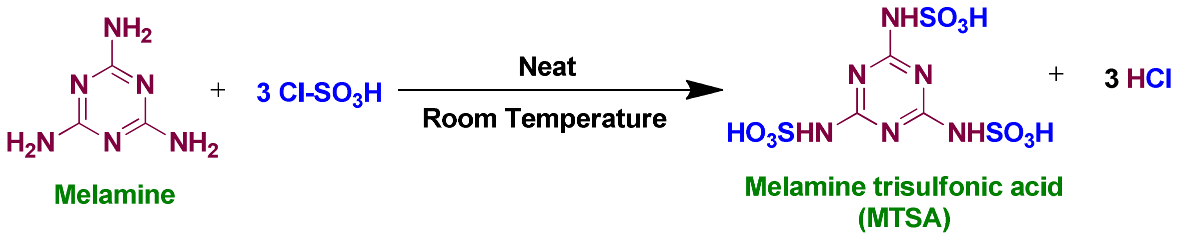


Figure 1. Synthesis of Melamine trisulfonic acid (MTSA)

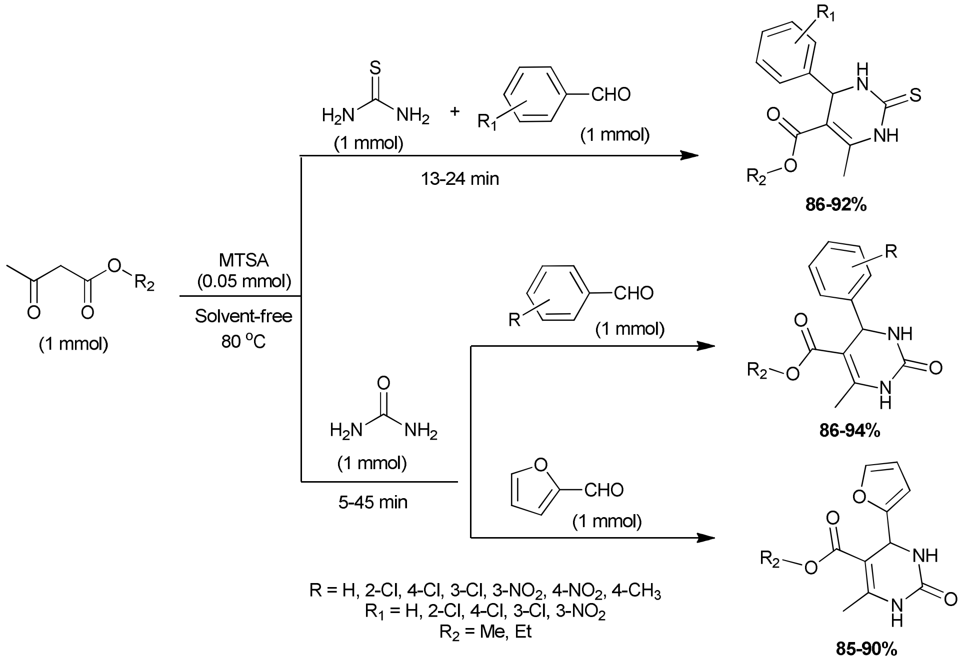
3) Melamine trisulfonic acid (MTSA) catalyzed various organic reactions

3.1) Solvent-free organic reactions catalyzed by MTSA

3.1.1) Preparations of N- and O-containing heterocyclic compounds

3.1.1.1) Synthesis of 3,4-dihydropyrimidin-2(1*H*)-one/thione derivatives

3,4-dihydropyrimidin-2(1*H*)-one/thione derivatives possesses a wide range of pharmaceutical activities such as antitumor, antiviral, anti-inflammatory and antibacterial.[28] Different catalysts such as $MgBr_2$,[29] PPh_3,[30] $ZrCl_4$,[31] $Bi(OTf)_3$,[32] CaF_2,[33] Silica triflate,[34] $FeCl_3$,[35] Sulfamic acid,[36] $Cu(OTf)_2$[37] and $Fe(HSO_4)_3$[38] have been reported for the preparation of these skeletons. However, high temperatures, expensive catalyst, long reaction times, lower product yields, tedious work-up process and the use of volatile organic solvents are limitations of these protocols. Therefore, Shirini and co-workers represented an environmentally friendly protocol for the preparation of 3,4-dihydropyrimidin-2(1H)-ones/thiones (DHPMs) via three component synthesis of aldehydes, β-ketoesters and urea/thiourea in the presence of melamine trisulfonic acid (MTSA) as green and recyclable catalyst **(Scheme 1)**.[39] This synthesis was carried out at the 80 °C under solvent-free conditions. An electronic and steric effect of the nature of the substituents on the aromatic ring does not show any obvious effect on this conversion. In addition, hetero aromatic aldehydes were also reacted efficiently to afford products in excellent yields. Compared to cellulose sulfuric acid (CSA), PEG-OSO_3H and starch sulfuric acid (SSA), MTSA shows excellent efficiency for this synthesis in terms of product yield, reaction temperature and catalyst loading.[24, 25] In addition, CSA catalyzed this reaction was completed within shorter period of time as compared to MTSA and SSA. The added advantage of this method is that the catalyst could be recycled and reused three times without significant loss of their efficiency.

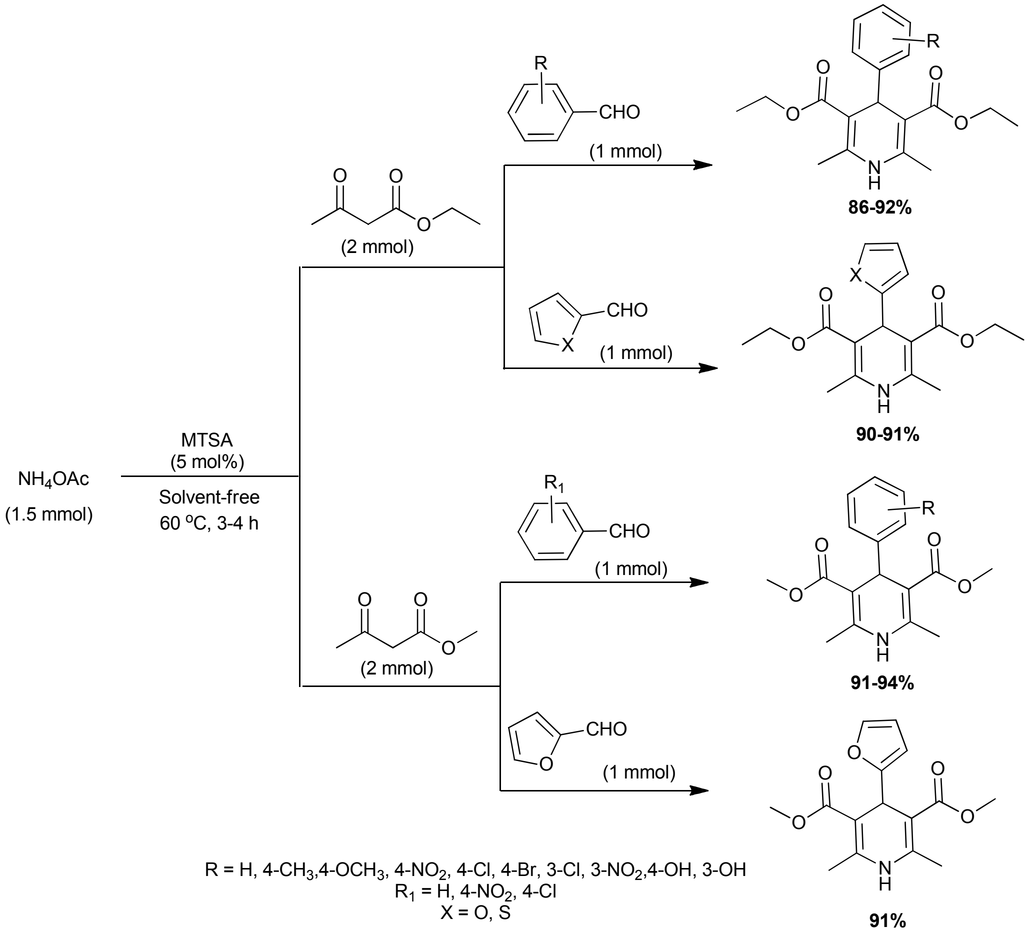


Scheme 1

3.1.1.2) Synthesis of 1,4-dihydropyridines (1,4-DHPs) derivatives

1,4-dihydropyridines possesses various biological activities such as glycoprotein inhibitors,[40] anticancer,[41] anticoagulant,[42] anti-inflammatory and anti-microbial agents[43] and neurotropic.[44] Mansoor and co-workers have reported a green method for the synthesis of 1,4-dihydropyridines (1,4-DHPs) through three component condensation reaction of ethyl acetoacetate or methyl acetoacetate, aldehydes and ammonium acetate catalysed by melamine trisulfonic acid (MTSA) as an efficient and eco-friendly catalyst **(Scheme 2)**.[45] This synthesis was performed under solvent-free condition at the 60 °C. Moreover, the catalyst could be recyclable and reused three times without significant loss of their efficiency. In this synthesis the authors have screened various solvents like methanol, THF, acetonitrile, ethanol, dichloromethane, cyclohexane, benzene as well as solvent-free conditions. However, the best result was obtained under solvent-free conditions in terms of product yields and reaction times. All the electron-rich and electron deficient aldehydes worked well leading to excellent yields of the products. The authors have demonstrated various Lewis acid catalysts such as $AlCl_3$, $ZnCl_2$, $FeCl_3$, $BiBr_3$, $BiCl_3$ and $Bi(OTf)_3$ for the comparative results with MTSA in this transformation. Although, the results presented that MTSA is a more efficient catalyst with respect to catalyst load, reaction temperature, product yield and reaction time than other catalysts. However, for this synthesis the

CSA shows higher efficiency in terms of reaction times, while MTSA shows greater efficiency in terms of product yield.[24]



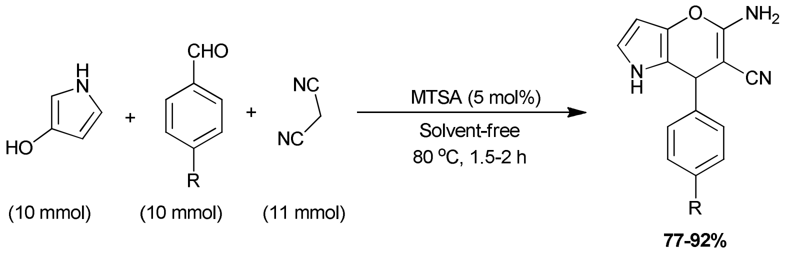
R = H, 4-CH_3,4-OCH_3, 4-NO_2, 4-Cl, 4-Br, 3-Cl, 3-NO_2,4-OH, 3-OH
R_1 = H, 4-NO_2, 4-Cl
X = O, S

Scheme 2

3.1.1.3) Synthesis of 5-amino-7-aryl-6-cyano-4*H*-pyrano[3,2-*b*]pyrroles derivatives

4*H*-Pyrans possess potent biological activities like antitumor,[46] antibacterial,[47], [48] antiviral,[49] spasmolytic[50] and antianaphylactic.[51] An environmentally friendly preparation of 5-amino-7-aryl-6-cyano-4*H*-pyrano[3,2-*b*]pyrroles via three component synthesis of malononitrile, 3-hydroxypyrrole and several aromatic aldehydes in the presence of melamine trisulfonic acid (MTSA), which was discovered by the Mansoor's group **(Scheme 3)**.[52] The authors have screened various solvents such as ethanol, benzene, acetonitrile, methanol, cyclohexane, toluene, dichloroethane as well as solvent-free conditions in this synthesis. However, solvent-free condition was proved to be the best for this transformation. Only, 5 mol% MTSA was sufficient to achieving products in excellent yield within shorter period of time. To find out the optimize reaction condition; the authors have established reaction at various temperatures from 50 °C to

100 °C. Finally, they have achieved 80 °C temperature as the optimum temperature for this transformation. The catalyst was tested for four runs. It was seen that the catalyst exhibited very good reusability efficiency.

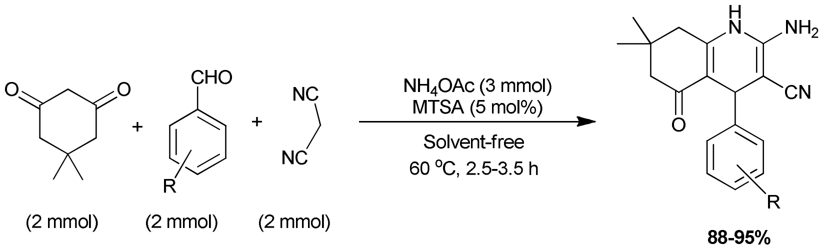


R = H, CH_3, OCH_3, F, Br, Cl, CN, OH, NO_2

Scheme 3

3.1.1.4) Synthesis of 2-amino-4-phenyl-3-cyano-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinolines

Aswin and associates have reported a green protocol for the synthesis of synthesis of 2-amino-4-phenyl-3-cyano-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinolines via three component synthesis of dimedone, aldehydes, malononitrile and ammonium acetate under solvent-free conditions **(Scheme 4)**.[53] The authors have examined various solvents like 1,4-dioxane, methanol, ethanol, acetonitrile, cyclohexane and toluene as well as solvent-free conditions in this synthesis. Although, the best result was obtained by using 5 mol% MTSA under solvent-free condition at 60 °C. Both an electron-withdrawing and an electron-donating substituents on aldehydes were reacted efficiently to afford corresponding products in high to excellent yield within a short period of times. The catalyst could be reused four times without substantial damage of its activity.

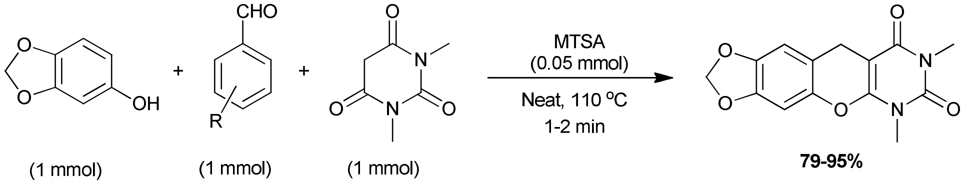


R = H, 4-CH_3, 4-OCH_3, 4-F, 4-Br, 3-Br, 4-Cl, 3-Cl, 3-OH, 4-OH, 4-NO_2, 3-NO_2

Scheme 4

3.1.1.5) Synthesis of 10-aryl-6,8-dimethyl-6,10-dihydro-5-oxa-6,8-diazaanthra[2,3-*d*][1,3]dioxole-7,9-dione derivatives

Li and co-workers have reported utilization of melamine trisulfonic acid (MTSA) as an efficient and recyclable catalyst for the one-pot synthesis of 10-aryl-6,8-dimethyl-6,10-dihydro-5-oxa-6,8-diazaanthra[2,3-*d*][1,3]dioxole-7,9-dione derivatives by condensation of 3,4-methylene dioxyphenol, aromatic aldehydes and 1,3-dimethylbarbituric acid under solvent-free conditions at the 110 °C **(Scheme 5)**.[54] Maximum yield was obtained with 5 mol% of the catalyst. Different types of aromatic aldehydes bearing electron releasing as well as electron accepting groups were used in the reaction and in all cases the products were obtained in good to excellent yields. An aliphatic aldehydes, such as phenyl acetaldehyde, propionaldehyde, *n*-butyl aldehyde and *n*-heptaldehyde, were not reacting efficiently with this protocol and the desired products were not found and obtained successfully. The catalyst could be successfully recovered and recycled at least for three runs without significant loss in activity. A tentative mechanism for this transformation was also proposed by the authors. The reaction likely proceeds *via* the initial formation of oxonium species**,** which then undergo dehydration to give olefin. Subsequent Michael-type addition of 3,4-methylenedioxyphenol to the olefin followed by cyclization and dehydration to afford the corresponding products in excellent yield.

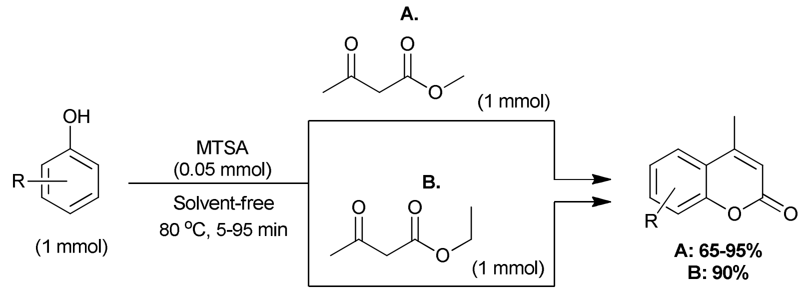


R = H, 4-Cl, 4-F, 4-CH$_3$, 4-NO$_2$, 3-NO$_2$, 2,4-diCl, 3,4-diCl, 2-Cl

Scheme 5

3.1.1.6) Synthesis of coumarins *via* Pechmann condensation

Coumarins and their derivatives are important classes of heterocyclic compounds, whose synthesis has been the focus of attention of many organic and medicinal chemists.[55] Generally, the Pechmann reaction is carried out using various catalysts such as H_2SO_4,[56] CF_3COOH,[57] $InCl_3$,[58] $Bi(NO_3)_3.5H_2O$,[59] silica triflate,[60] $ZrCl_4$[61] and $TiCl_4$.[62] The main disadvantages of the processes are, long reaction times, low yields, harsh reaction conditions, non-reusability of the catalyst and use of excess amounts of the reagent. Thus, Shirini et al. have discovered green synthesis of coumarins *via* Pechmann condensation of phenols and ethyl acetoacetate or methyl acetoacetate by utilizing melamine trisulfonic acid (MTSA) as a bio-degradable catalyst under solvent-free conditions at the 80 °C **(Scheme 6)**.[63] Only, 0.05 mmol of catalyst was sufficient for this transformation. Phenols with electron-donating groups are easily converted to their corresponding coumarins, while electron-withdrawing groups were not reacting under these conditions and starting materials remained intact even after prolonged heating. The catalyst could be reused several times without a considerable change in the reaction times and yields. Compared to MTSA, PEG-OSO$_3$H catalysed this synthesis afforded products within shorter period of time, while higher product yield was observed in case of MTSA.[25]

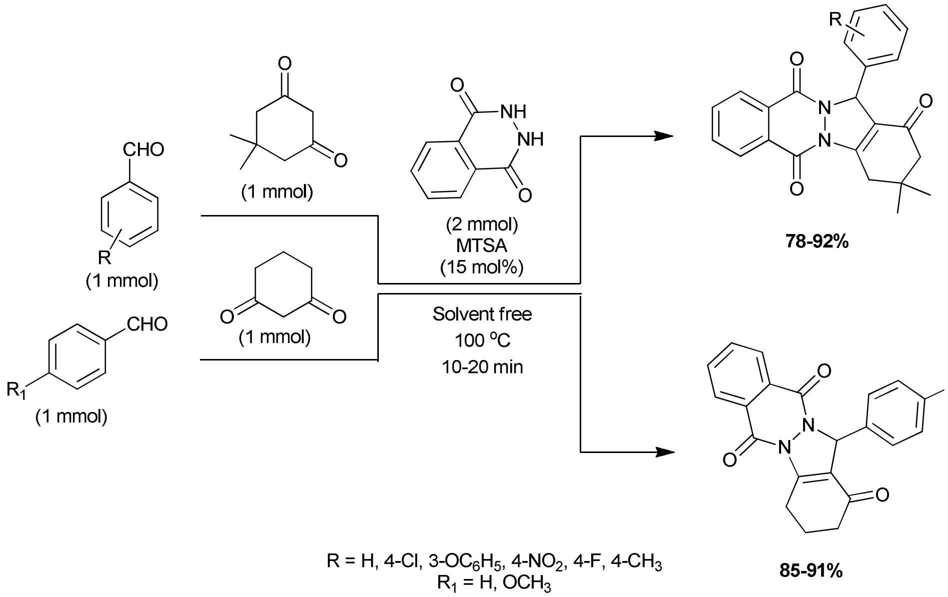


R = 3-OH, 4-OH, 2,3-diOH, 3,5-diOH, 3-OCH$_3$, 3-CH$_3$, 3-CH$_3$-5-OH,
2-CH$_3$-3-OH. 4-OCH$_3$

Scheme 6

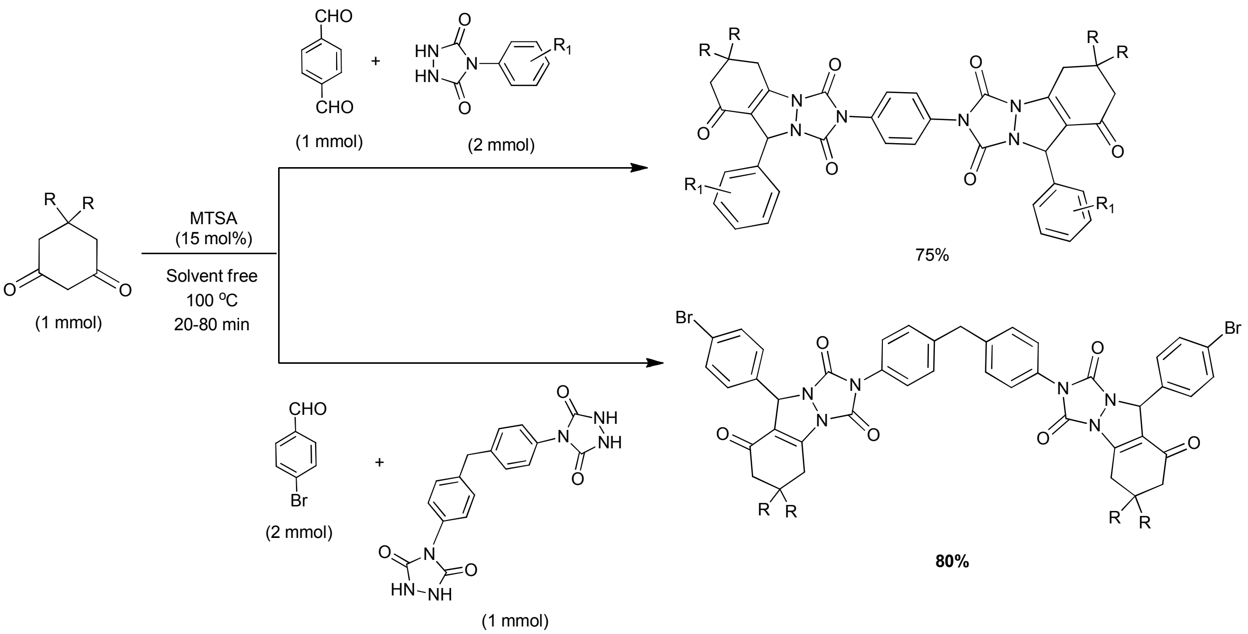
3.1.1.7) Preparation of triazolo[1,2-*a*]indazole-1,3,8-trione and 2*H*-indazolo[2,1-*b*]phthalazine-1,6,11-trione derivatives

Khazaei and associates discussed a sustainable synthetic method for the preparation of triazolo[1,2-*a*]indazole-1,3,8-trione and 2*H*-indazolo[2,1-*b*]phthalazine-1,6,11-trione derivatives by the three-component condensation reaction of urazoles or phthalhydrazide, dimedone or 1,3-cyclohexanedione and aldehydes using melamine trisulfonic acid (MTSA) as an efficient heterogeneous catalyst under solvent-free conditions **(Scheme 7a-c)**.[64] Only, 15 mol% was sufficient for the excellent yields of the products. The influence of electron-withdrawing and electron-donating substituents on the aromatic ring of aldehydes have no significant effect on the reaction yields. In the case of aliphatic aldehydes longer reaction time was observed for the completion of the reaction. Influence of different catalysts such as p-TSA,[65] silica sulfuric acid,[66] sulfuric acid[67] and *N*-halosulfonamides[68] on the reaction of benzaldehyde, dimedone and phthalhydrazide was also studied by the authors. However, they were not efficient as compared to MTSA in terms of product yields and reaction times. In this synthesis, PEG-OSO$_3$H shows greater activity in terms of product yield and reaction time as compared to MTSA.[25]



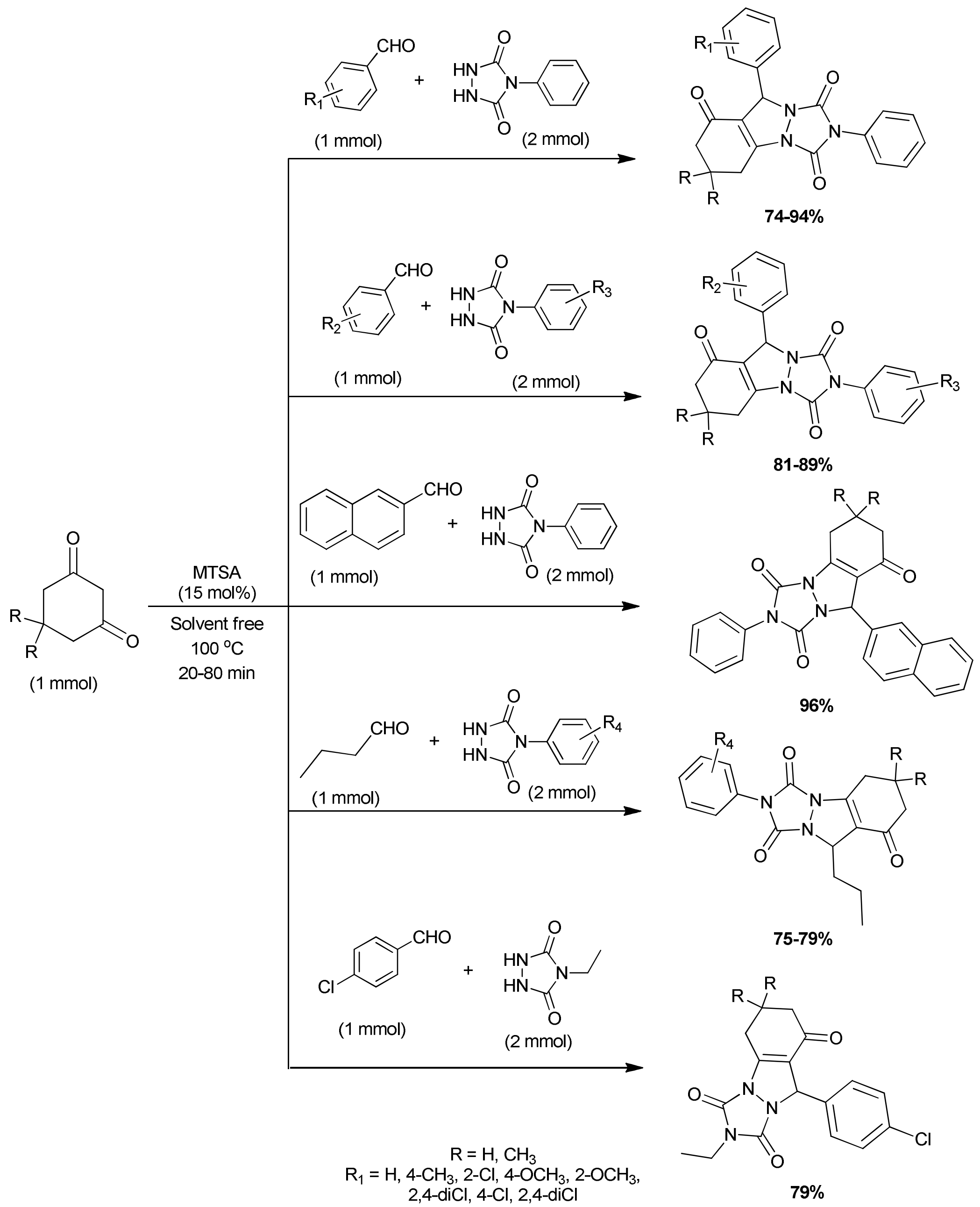
R = H, 4-Cl, 3-OC_6H_5, 4-NO_2, 4-F, 4-CH_3
R_1 = H, OCH_3

Scheme 7a



R = H, CH_3
R_1 = 4-Cl, 4-*tert*-But

Scheme 7b



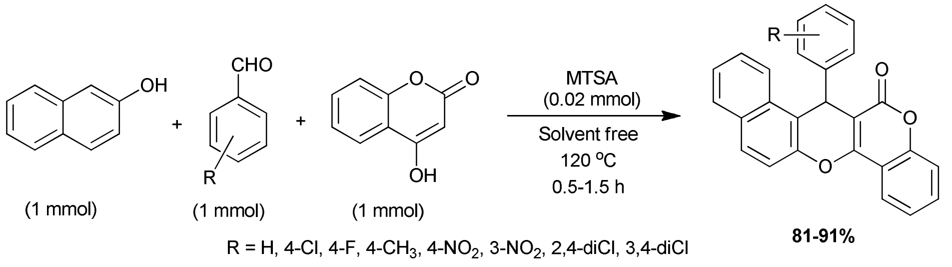
R = H, CH_3
R_1 = H, 4-CH_3, 2-Cl, 4-OCH_3, 2-OCH_3, 2,4-diCl, 4-Cl, 2,4-diCl
R_2 = 4-Cl, 2,4-diCl, 2-NO_2, 3-NO_2
R_3 = 4-Cl, 3,4-diCl, 4-tertBu
R_4 = H, 4-Cl

Scheme 7c

3.1.1.8) Preparation of 7-alkyl-6*H*,7*H*-naphtho-[10,20:5,6]pyrano[3,2-*c*]chromen-6-ones

Chromene derivatives possessing a wide range of pharmaceutical activities such as antirhinovirus,[69] antioxidant,[70] antimicrobial,[71] anticancer[72] and antihypertensive.[73] An efficient preparation of 7-alkyl-6*H*,7*H*-naphtho-[10,20:5,6]pyrano[3,2-*c*]chromen-6-one derivatives by three-component condensation reaction of *β*-naphthol, aromatic aldehydes and 4-

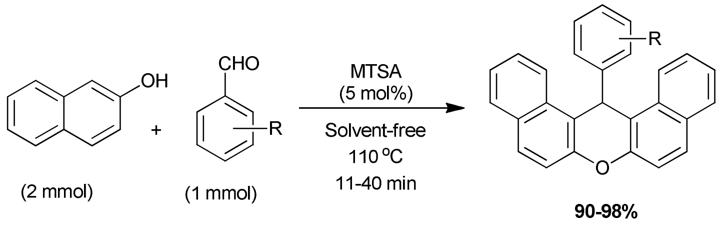
hydroxycoumarin catalyzed by melamine trisulfonic acid (MTSA) as a green and reusable catalyst under solvent-free conditions, which was developed by Ma's group **(Scheme 8).**[74] At 120 °C, the reaction proceeded smoothly to afforded excellent product yields within shorter period of time. In addition, maximum yield was obtained with 2 mol% of the MTSA. The authors have also suggested reaction mechanism, according to them the reaction likely proceeds via the initial formation of ortho-quinone methide. The oxonium species are then formed by reaction with 4-hydroxycoumarin, which then undergoes dehydration to afford the desired product in excellent yield. A variety of aryl aldehydes including those bearing electron-withdrawing and electron-donating groups reacted smoothly with this protocol to afford efficient product yields. For comparison the effect of different catalysts such as sulfuric acid, $NaHSO_3$, $NaHSO_4$, $AlCl_3$, I_2 and MTSA on this reaction was also examined by the authors. However, MTSA showed better results as compared to others.



Scheme 8

3.1.1.9) Synthesis of 14-aryl-14*H*-dibenzo[*a,j*]xanthene derivatives

Zare et al. have also reported catalytic application of a melamine trisulfonic acid (MTSA) in the synthesis of 14-aryl-14*H*-dibenzo[*a,j*]xanthene derivatives via condensation of 2-naphthol with arylaldehydes under solvent-free conditions **(Scheme 9).**[75] This reaction was performed under conventional thermal (110 °C) or microwave irradiation (540 W). Only, 2.5 mol% of the catalyst was sufficient to promote the reaction efficiently under thermal conditions, while under microwave irradiation 0.5 mol% of the catalyst was sufficient to promote the reaction in forward direction. In addition, lower catalyst loading and shorter reaction time was required in case of MTSA and CSA as compared to PEG-OSO_3H, while higher product yield was obtained in the case of MTSA as compared to PEG-OSO_3H and CSA.[24, 25] Moreover, the reaction under microwave irradiation was completed within shorter period of time as compared to the conventional thermal conditions. Both electro-releasing and electron-withdrawing substituents on aromatic aldehydes were efficiently converted into the products.

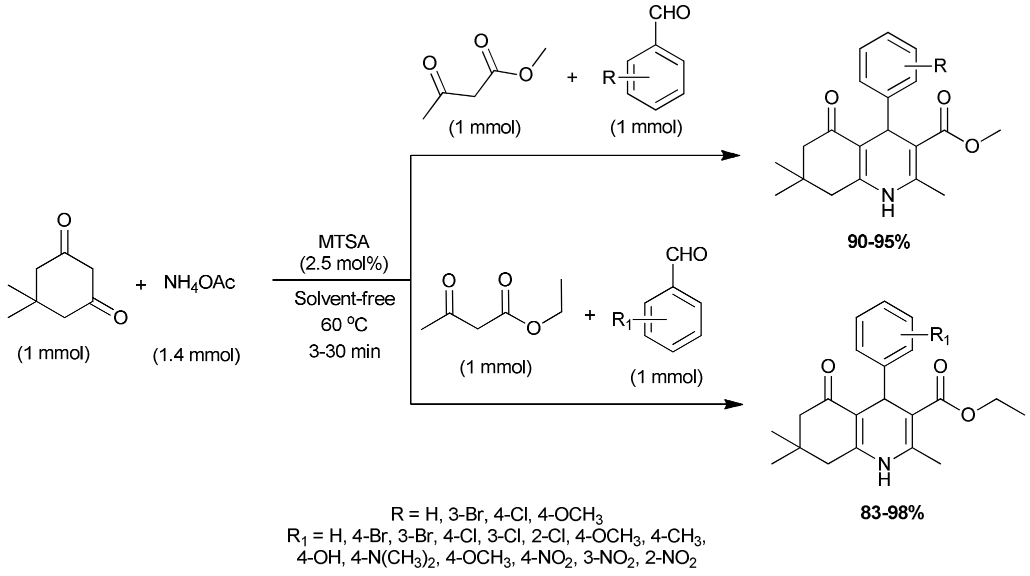


R = H, 4-NO_2, 3-NO_2,2-NO_2, 4-Cl, 3-Cl, 2-Cl,
3-Br, 4-Br, 4-F, 4-CH_3, 4-OCH_3, 3-OCH_3

Scheme 9

3.1.1.10) Synthesis of polyhydroquinolines

Quinolines and their derivatives have attracted much attention, because a large number of natural products and drugs possess this heterocyclic scaffold.[76] Zare and co-workers have reported an environmentally friendly and clean method for the synthesis of polyhydroquinolines via one-pot multi-component condensation reaction between aryl aldehydes, dimedone (5,5-dimethylcyclohexane-1,3-dione), β-ketoesters and ammonium acetate in the presence of melamine trisulfonic acid (MTSA) under solvent-free conditions at 60 °C **(Scheme 10)**.[77] Only, 2.5 mol% of the catalyst was sufficient to promote the reaction in forward direction efficiently. An electronic and steric effect of the nature of the substituents on the aromatic ring does not show any obvious effect on this conversion. The authors have suggested that at first dimedone is converted to its enol form using MTSA. On the other hand, the activated β-ketoester (by the catalyst) and ammonia (resulted from ammonium acetate) gives enamine. Afterward, the enol and enamine react with the activated aldehyde (by MTSA) to afford intermediate, which was tautomerized followed by an intramolecular nucleophilic attack of the NH_2 group to the activated carbonyl group and again tautomerized to form polyhydroquinonine in good yields. After completion of the reaction, the catalyst could be recovered and reused several times without loss in their activity.

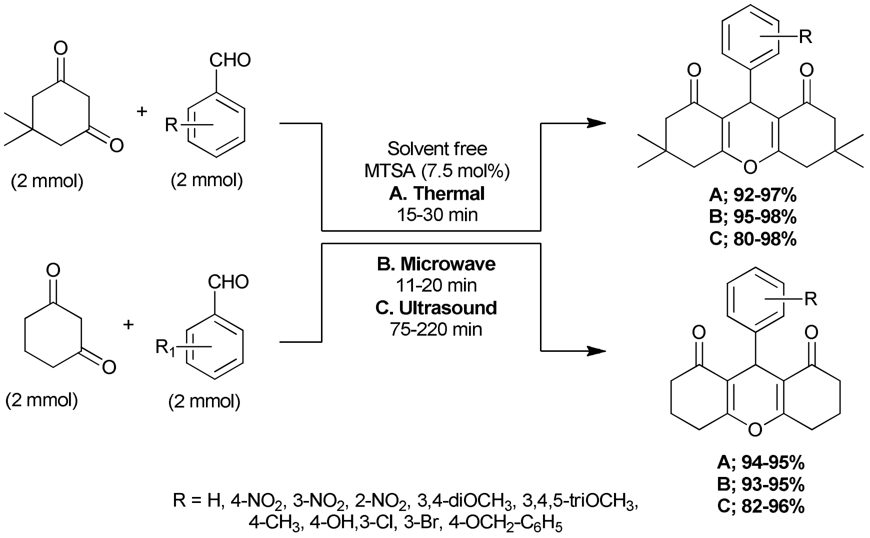


R = H, 3-Br, 4-Cl, 4-OCH$_3$
R$_1$ = H, 4-Br, 3-Br, 4-Cl, 3-Cl, 2-Cl, 4-OCH$_3$, 4-CH$_3$, 4-OH, 4-N(CH$_3$)$_2$, 4-OCH$_3$, 4-NO$_2$, 3-NO$_2$, 2-NO$_2$

Scheme 10

3.1.1.11) Synthesis of 9-aryl-1,8-dioxo-octahydroxanthene derivatives

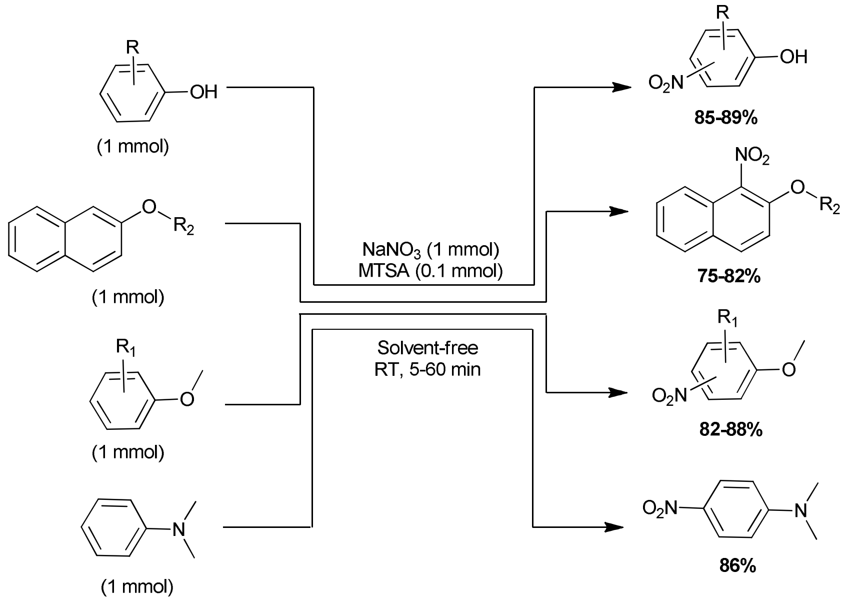
Xanthene derivatives are essential unit of a large number of naturally occurring as well as synthesized biological compounds.[78,79] Zare et al. have disclosed an efficient synthesis of 9- aryl-1,8-dioxo-octahydroxanthene derivatives from 1,3-cyclohexanediones and aryl aldehydes in the presence of catalytic amount of melamine trisulfonic acid (MSTA), which afforded products in excellent yields **(Scheme 11).**[80] This reaction was performed under thermal (solvent-free/80 °C), microwave (solvent-free/180 W/90 °C) and ultrasound (solvent/34-37 kHz/350 W/60 °C) conditions. A wide range of electro releasing as well as electron withdrawing groups bearing aldehydes was efficiently converted into the products makes this protocol have wide synthetic utility. Best results were obtained under microwave irradiation (MWI) as compared to thermal and ultrasound conditions in terms of products yield and reaction time. In addition, in ultrasound condition more time was needed to complete the reaction as compared to thermal and MWI.



Scheme 11

3.1.2) Mono-nitration of the phenolic compounds

The mono-nitration of the phenolic compounds is one the most difficult and challenging field for the organic chemist, because the nitration of phenols usually results in a complex mixture of mono and even di-nitrated products. It is especially to perform selective mono-nitration of phenols.[81] Albadi et al. disclosed an efficient synthetic protocol for the regioselective nitration of various phenols by utilizing sodium nitrate in the presence of melamine trisulfonic acid (MTSA) under solvent-free conditions at room temperature **(Scheme 12)**.[82] This protocol delivers the superior advantage like good selectivity between ortho and para positions of the phenols. Compounds containing the electron donating substituents on phenols were found to be more reactive and converted to the corresponding mono-nitrated products in shorter reaction times. This method afforded *para*-substituted products predominantly. Phenol offered mostly the *para*-nitrophenol as the predominant product. The authors have also demonstrated possible reaction mechanism, according to them in situ generation of nitronium ion was caused by the reaction of MTSA with sodium nitrate. This nitronium ion is powerful electrophile, and was reacted with aromatic compounds to form Nitro aromatic compounds.

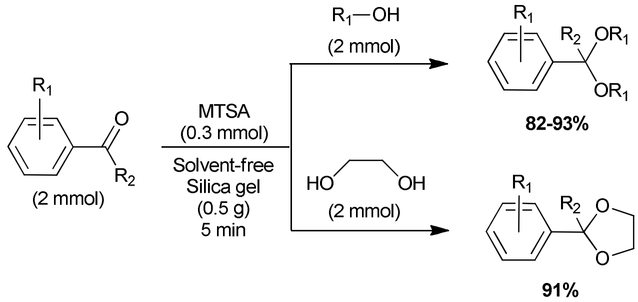


R = H, 2-Cl, 4-Cl, 2,4-diCl, 2,2'-diCH3, 2,4-diCH_3, 2-Cl-4-F, 2-CH_3-4-Cl,
2-NO_2, 4-CHO, 2-CHO-4-Br
R_1 = H, 4-CHO
R_2 = H, CH_3

Scheme 12

3.1.3) Acetalization of carbonyl compounds

During a synthetic sequence a carbonyl group may have to be protected against attack by various reagents such as nucleophiles, reducing agents; and some oxidants. The most useful protective groups are acetals or ketals.[83] Fallah-Mehrjardi et al. have disclosed the utilization of Melamine trisulfonic acid (MTSA) as an eco-friendly and recyclable catalyst for acetalization of carbonyl compounds with various alcohols **(Scheme 13)**.[84] Aldehydes and ketones are rapidly transformed into acetals and ketals at room temperature in high yields. Moreover, I_2,[85] sulfamic acid[86] and $Bi(NO_3)_3$[87] have been previously used as a catalyst in this transformation. However, they are not efficient as like MTSA in terms of the product yields and the reaction times. The catalyst could be reused 5 times without significant loss of their efficiency. The catalyst could be reused five times with no change in catalytic efficiency.

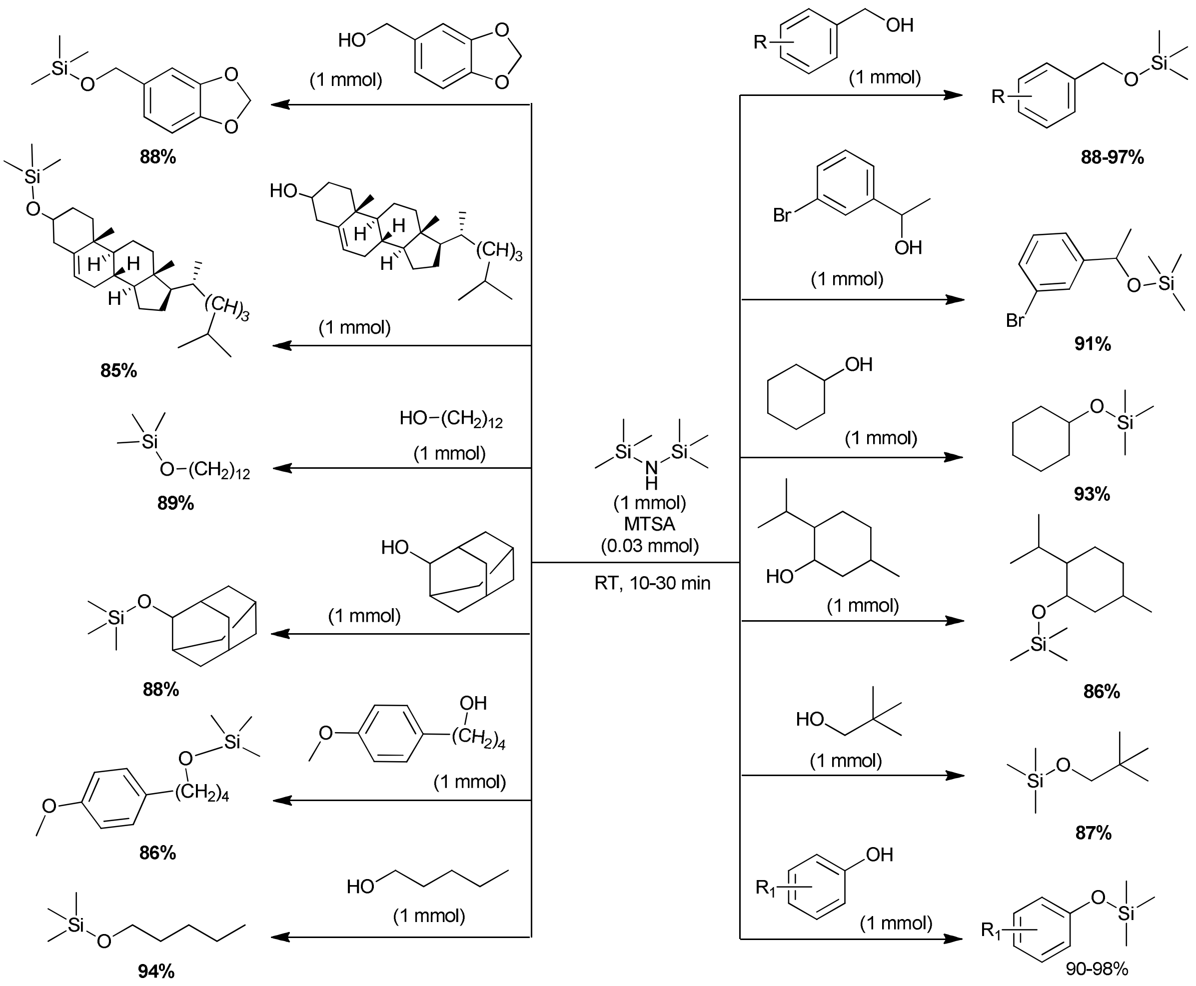


R = H, 4-NO_2, 4-CH_3, 3-Br, 2,4-diOCH_3, 2-OH-5-Br
R_1 = CH_3CH_2, $CH_3CH_2CH_2$, $(CH_3)_2CH$, $C_6H_5CH_2$

Scheme 13

3.1.4) Trimethylsilylation of alcohols and phenols

The protection of hydroxyl groups by the formation of silyl ethers has been extensively used in organic synthesis.[88] Wu's group has demonstrated a green method for the trimethylsilylation of alcohols and phenols via treatment by hexamethyldisilazane in the presence of melamine trisulfonic acid (MTSA) as a recyclable catalyst under solvent-free conditions at room temperature **(Scheme 14)**.[89] A wide variety of hydroxyl groups were selectively protected under this condition. There are a variety of catalysts such as ZnO,[90] $InBr_3$,[91] $LaCl_3$,[92] $Fe(HSO_4)_3$,[93] $ZrCl_4$,[94] NBS,[95] $CuSO_4$[96] and I_2[97] were previously utilized in this transformation, but they did not prove higher efficiency as compared to MTSA. Only, 3 mol% of catalyst was sufficient for this reaction. The catalyst was tested for 6 runs. It was seen that the catalyst displayed very good reusability and efficiency. For this synthesis higher catalysis loading of CSA was required as compared to MTSA.[24] In addition, the reaction was completed within shorter period of time in case of CSA as compared to MTSA.

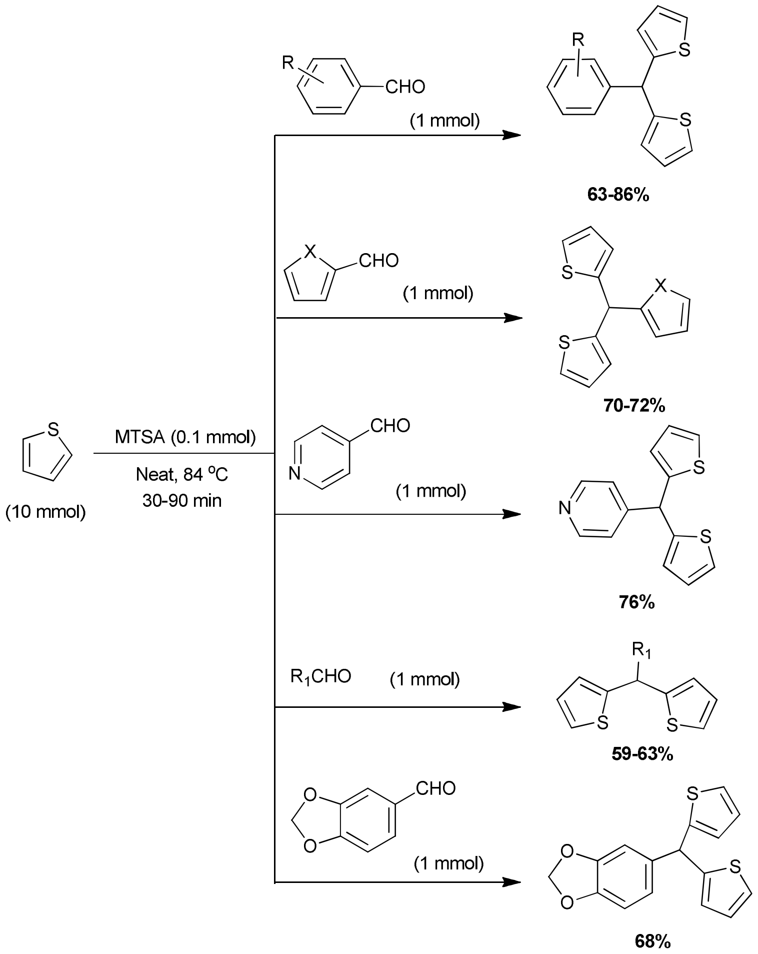


R = H, 4-Cl, 3-NO$_2$, 4-NO$_2$, 4-CH$_3$, 4-OCH$_3$, 2,4-diCl
R$_1$ = H, 4-Cl, 4-NO$_2$, 4-CH$_3$, 4-OCH$_3$

Scheme 14

3.1.5) Preparation of dithienylmethanes from aldehydes

Dithienylmethanes are widely used as important building blocks for the synthesis of a variety of functionalized porphyrins and porphyrin analogs.[98, 99] An efficient procedure for the preparation of dithienylmethanes via bisarylation of aldehydes with thiophene in the presence of melamine trisulfonic acid (MTSA) as a catalyst under solvent-free conditions at the 84 °C, which was described by the Wu's group **(Scheme 15).**[100] A wide range of aldehydes were efficiently converted into the desired products with higher yields. The authors have concluded that the aldehydes with electron-withdrawing groups reacted quickly as compared to electron-donating groups. The catalyst could sbe reused three times without significant loss of their efficiency.

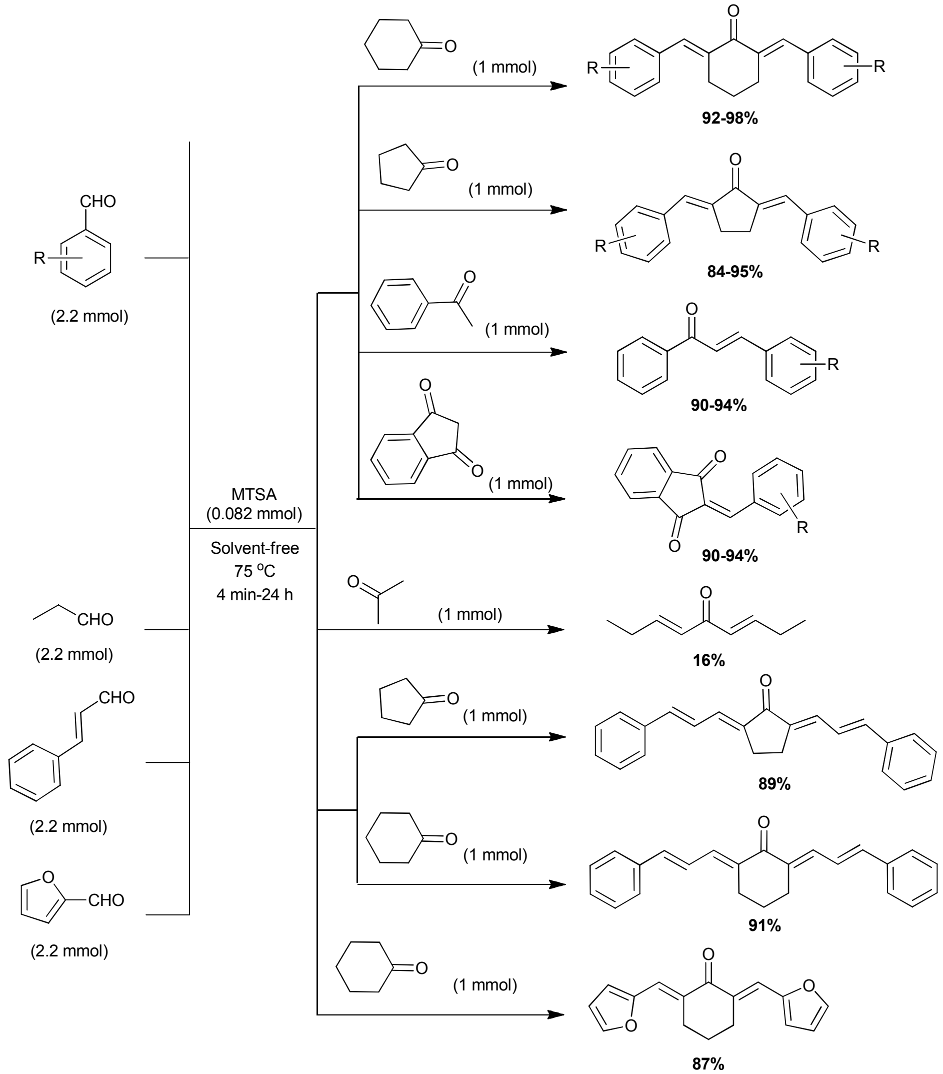


R = H, 4-Cl, 4-Br, 4-F, 4-NO$_2$, 3-NO$_2$, 4-OCH$_3$, 4-CH$_3$,
3-OH, 4-OH, 3-OCH3-4-OH, 4-OCH$_3$-3-OH
X = O,S
R$_1$ = H, CH$_3$, (CH$_3$)$_2$CH, (CH$_3$)$_3$C

Scheme 15

3.1.6) Crossed-Aldol condensation of aldehydes with ketones

Previously, Crossed-Aldol condensation was performed using various catalysts like RuCl$_3$,[101] SmI$_3$,[102] KF-Al$_2$O$_3$,[103] FeCl$_3$,[104] InCl$_3$,[105] LiClO$_4$,[106] I$_2$,[107] Yb(OTf)$_3$,[108] Mg(HSO$_4$)$_2$[109] and LiOH.H$_2$O.[110] However, high temperatures, expensive catalyst, long reaction times, lower product yields and use of volatile organic solvents are disadvantages of these methods. Therefore, Shirini et al. developed an efficient Crossed-Aldol condensation of various types of aldehydes with ketones in the presence of melamine trisulfonic acid (MTSA) under solvent-free conditions at the 75 °C **(Scheme 16)**.[111] Aromatic aldehydes having various substituents like electron-donating as well as electron withdrawing and cinnamaldehyde were efficiently converted to their corresponding *α,α'*-bis(substituted benzylidene) cycloalkanone derivatives in excellent yield. The authors have also demonstrated the reaction mechanism, and on the basis of this mechanism, MTSA catalyses the reaction by the nucleophilic activation of ketone to form an enol tautomer, the formation of enol is slow, and the reaction rate depends on this step. Then the condensation of enol with aldehyde gives aldol adduct, which then is dehydrated to give the final product. After completion of the reaction the catalyst could be recovered and reused for three times without any decrease in its catalytic activity. MTSA exhibited higher activity in terms of product yields and reaction times as compared to PEG-OSO_3H.[25]

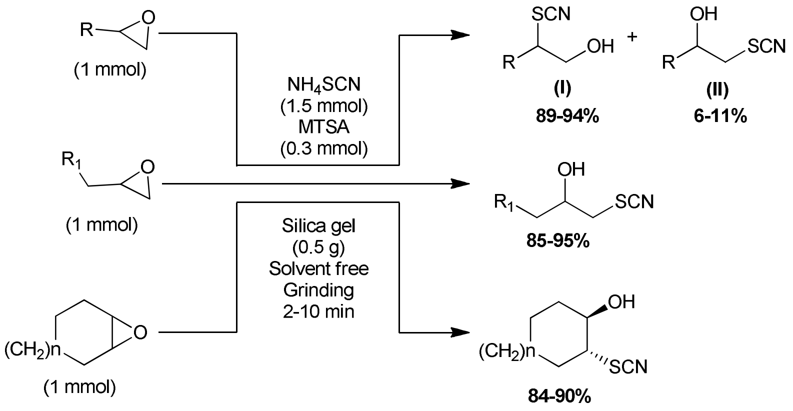


R = H, 4-Cl, 2-F, 4-F,3-Br, 4-NO_2, 3-NO_2

Scheme 16

3.1.7) Preparation of thiocyanohydrins via ring opening of epoxides

Kiasat et al. reported an efficient preparation of thiocyanohydrins via ring opening of epoxides catalyzed by melamine sulfonic acid (MTSA) as a solid acid catalyst under solvent-free conditions with good regioselectivity and very short reaction times **(Scheme 17)**.[112] Only, 0.3 mmol catalyst per 1 mmol of the reactant was sufficient for this reaction. This reaction was completed after 3 min and the corresponding thiocyanohydrin was obtained, whereas in the absence of a catalyst, this reaction was completed after 10 min and corresponding thiirane was obtained as the only product. This reaction was performed in different solvents like acetonitrile, dichloromethane, PEG and water. Although the best result was obtained under solvent-free condition. Here, styrene oxide and 1,2-butene oxide gave regioisomer (I) according to the more important electronic effect. Furthermore, cycloalkyl epoxides were reacted smoothly in an SN_2 fashion with NH_4SCN in the presence of a catalytic amount of MTSA to afford the corresponding β-hydroxy thiocyanates in excellent isolated yields. The authors have also demonstrated efficiency of MTSA by a comparison of other catalysts, such as silica sulfuric acid, Dowex, PEG-SO_3H, $B(HSO_4)_3$, $Mg(HSO_4)_2$, $Zn(HSO_4)_3$ and $Al(HSO_4)_3$. However, MTSA was proved to be the best catalyst for this transformation. The catalyst could be easily separated and reused three times without significant loss of their activity.

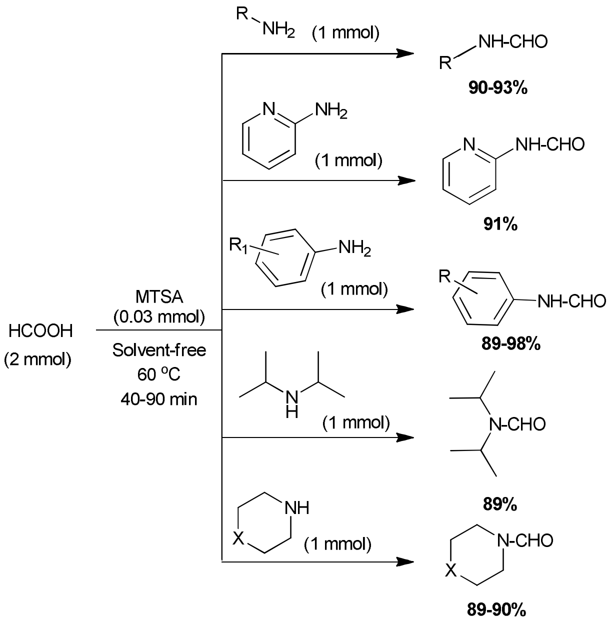


$R = C_6H_5, CH_2CH_3$
$R_1 = CH_2OC_6H_5, CH_2(OH)C(CH_3)_2, CH_2OCH_2CH_2CH_2CH_3CH_2OCH_2CH{=}CH_2,$
$CH_2OCOC({=}CH_2)CH_3, CH_2Cl$

Scheme 17

3.1.8) *N*-formylation of amines

Previously, the *N*-formylation of amines by using formic acid were carried out in the presence of various catalysts, such as Amberlite IR-120,[113] thiamine hydrochloride,[114] polyethylene glycol[115] and ZnO[116]. However, many of these procedures are associated with one or more disadvantages such as expensive reagents, longer reaction time, tedious work-up, lower product yields, low selectivity and large amount of catalysts. Thus, Yang and co-workers have discussed an efficient catalytic application of a melamine trisulfonic acid (MTSA) for the *N*-formylation of amines by utilizing formic acid under solvent-free conditions at the 60 °C **(Scheme 18)**.[117] The authors have also reported that anilines containing electron-withdrawing groups and electron-donating groups did not affect the reaction time and corresponding product yields. Moreover, aliphatic and secondary cyclic amines are also giving moderate yields of the product. The general reaction mechanism involves nucleophilic attack of amines on the protonation of the carbonyl group of formic acid, which leads to the formation of intermediates, which is transformed into the desired formylated product.



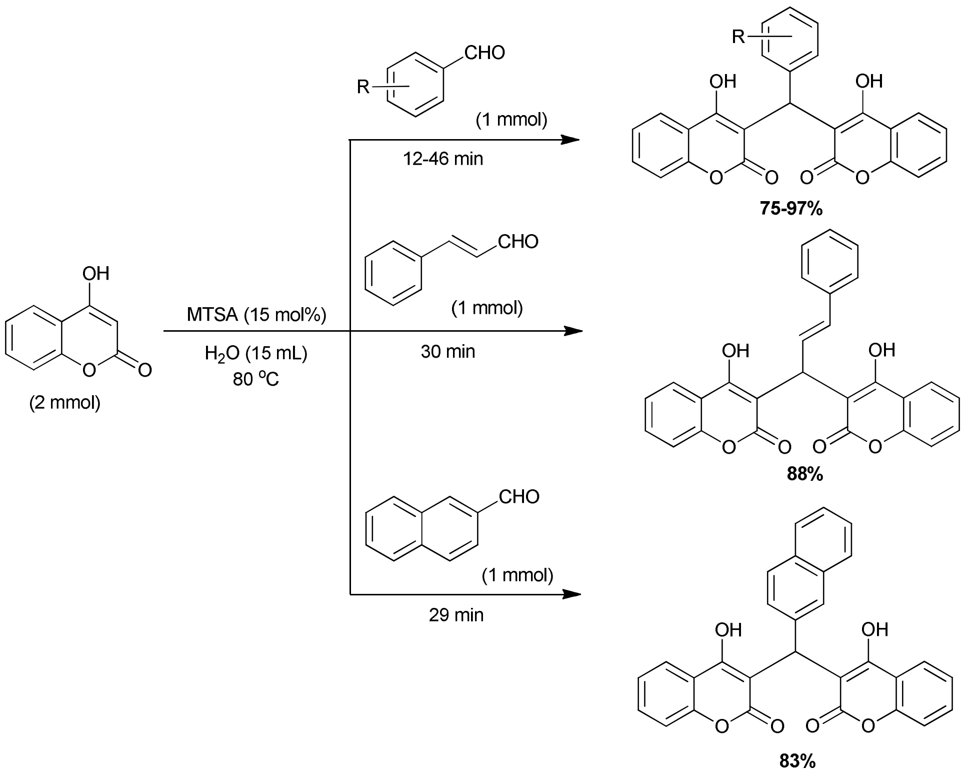
R = CH_2-C_6H_5, $CH_3CH_2CH_2$, $(CH_3)_2CH$
R_1 = H, 4-CH_3, 2-CH_3, 4-OCH_3, 4-OH,
2-OH, 2-Cl, 4-Cl, 4-Br, 3-NO_2, 4-NO_2
X = C, O

Scheme 18

3.2) Water mediated organic reactions catalyzed by MTSA

3.2.1) Preparation of 3,3'-(arylmethylene)-bis-(4-hydroxy-2*H*-chromene-2-one) derivatives

Iravani et al. have developed high yielding preparation of 3,3'-(arylmethylene)-bis-(4-hydroxy-2*H*-chromene-2-one) derivatives from the condensation reaction of two moles of 4-hydroxycoumarin and one mole of aromatic aldehydes, which catalyzed by melamine trisulfonic acid (MTSA) **(Scheme 19)**.[118] The reaction was carried out in the water at the 80 °C. The authors have also demonstrated various solvents in this synthesis for the comparative study. Although, water was demonstrated as the best solvent for this transformation as compared to others. The authors were unsuccessful to get the product in the case of aliphatic aldehydes. The reason behind this occurs due to enolization of the alkyl aldehydes during the reaction. Whereas, benzaldehydes with electron-donating or electron-withdrawing groups were condensed into the corresponding products in excellent yield. The proposed mechanism for the synthesis of biscoumarin was also discussed by the authors, according to them at first proton activates carbonyl group of aromatic aldehyde, which increases the electrophilicity carbonyl carbon of aldehyde. Then the nuleophilic addition of 4-hydroxycoumarin to the activated aldehyde to give an intermediate and followed by loss of water to afford final intermediate, which is further activated by proton. Same way another molecule of 4-hydroxycoumarin is added to a final intermediate to give biscoumarin. As compared to MTSA, lower SSA loading was required to complete the reaction within a short period of time. While, higher product yield was obtained in the case of MTSA as compared to SSA.[24] Furthermore, the catalyst could be recovered and reused seven times with only slight reduction in its catalytic efficiency. This sustainable protocol has numerous advantages such as clean reaction conditions, short reaction times and simple work-up process.

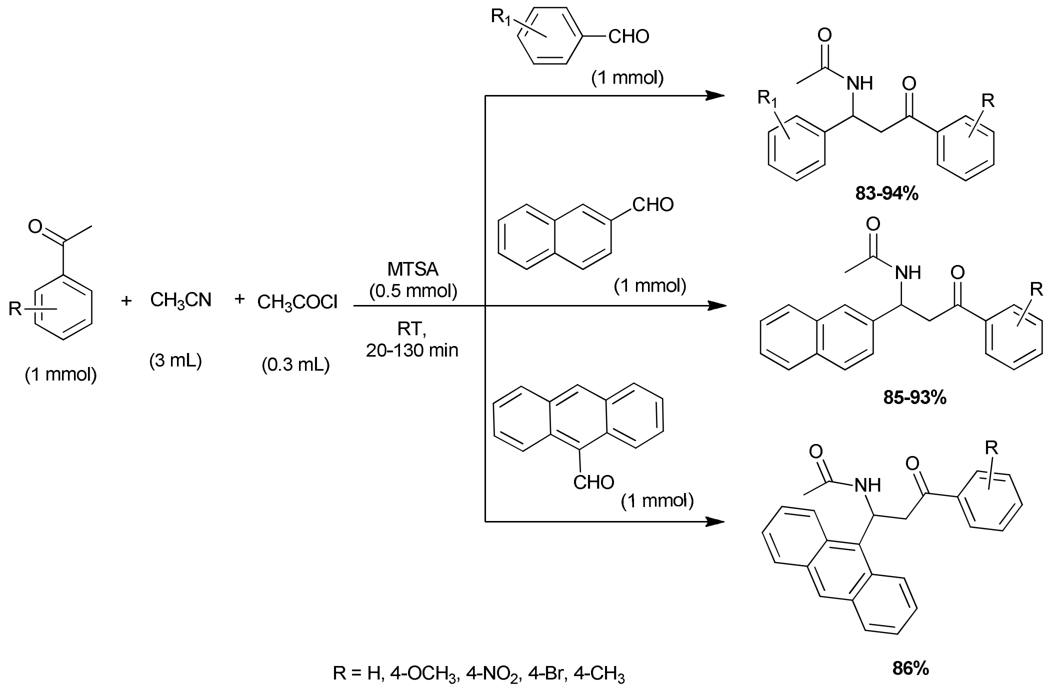


R = H, 4-CH_3, 4-Cl, 2-Cl, 2,4-diCl, 4-NO_2, 3-NO_2, 4-OH, 3-OH, 3,4-OCH_3, 4-CH_3S, 4-CN, 2-OH, 4-F, 4-iPr, 4-OCH_3, 2-Br, 4-Br, 4-$N(CH_3)_2$, 4-Cl-3-NO_2, 3,4,5-triOCH_3

Scheme 19

3.2.2) Preparation of β-acetamido ketones

β-Acetamido ketones are valuable organic intermediate for the preparation of highly important biologically important compounds.[119-122] Zare has disclosed one-pot condensation reaction of acetophenones, aromatic aldehydes, acetonitrile and acetyl chloride in the presence of melamine trisulfonic acid (MTSA) as an environmentally friendly catalyst at room temperature, which afforded β-acetamido ketone in excellent yields **(Scheme 20)**.[123] The reaction was completed within the shortest reaction time, when the reaction was performed using 5 mol% of the catalyst. Different acetophenones and aldehydes bearing electron-donating and electron-withdrawing groups were efficiently reacted in this protocol. The catalyst could be recovered three times without significant loss of its activity. Previously different catalysts like $Zr(HSO_4)_4$,[124] ZnO,[125] $ZrOCl_2.8H_2O$[126] and $CeCl_3.7H_2O$[127] were used in this reaction, but they were not efficient as compared to MTSA.

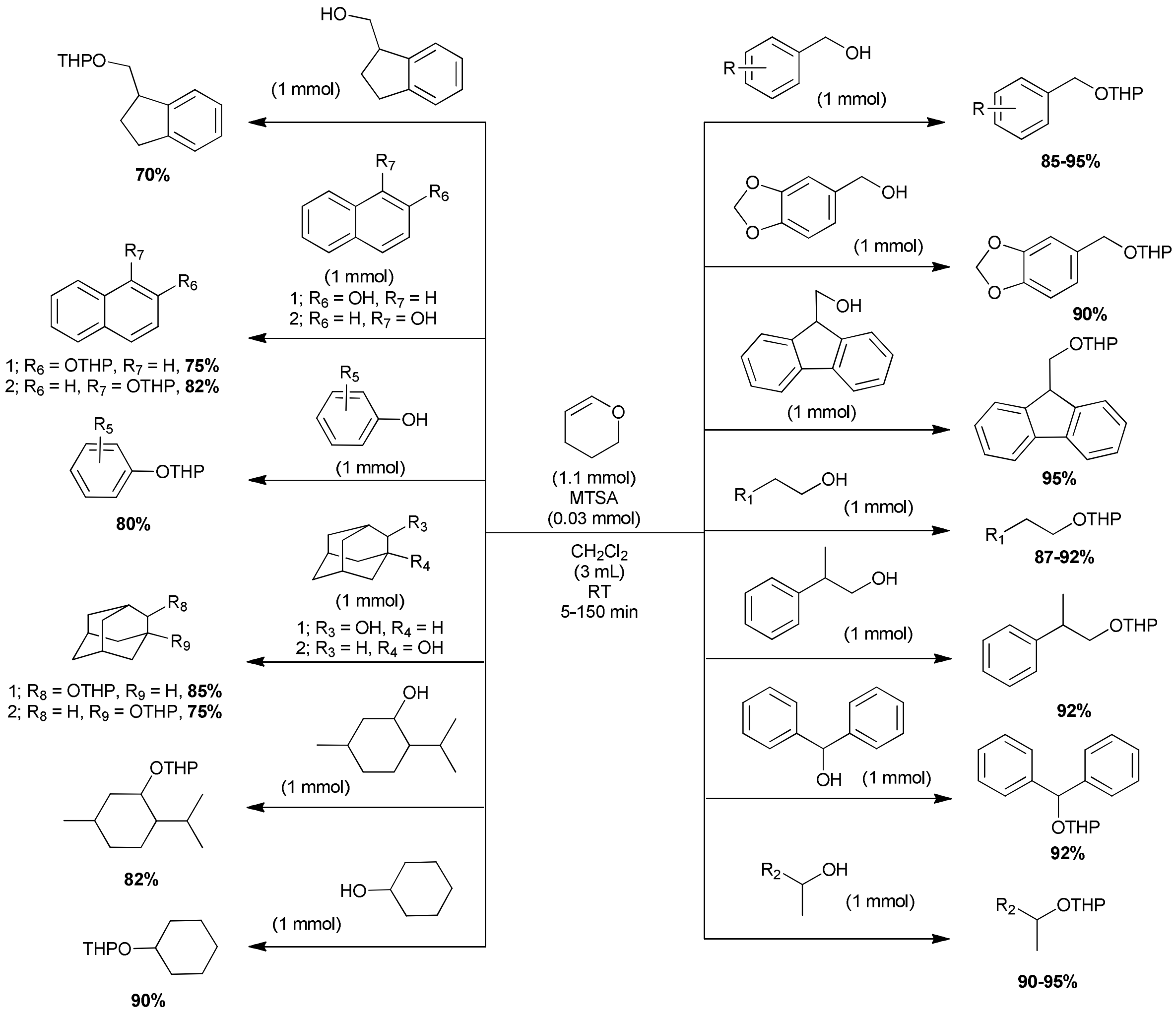


R = H, 4-OCH_3, 4-NO_2, 4-Br, 4-CH_3
R_1 = H, 4-OCH_3, 4-CH_3, 4-NO_2, 4-CHO, 4-Cl

Scheme 20

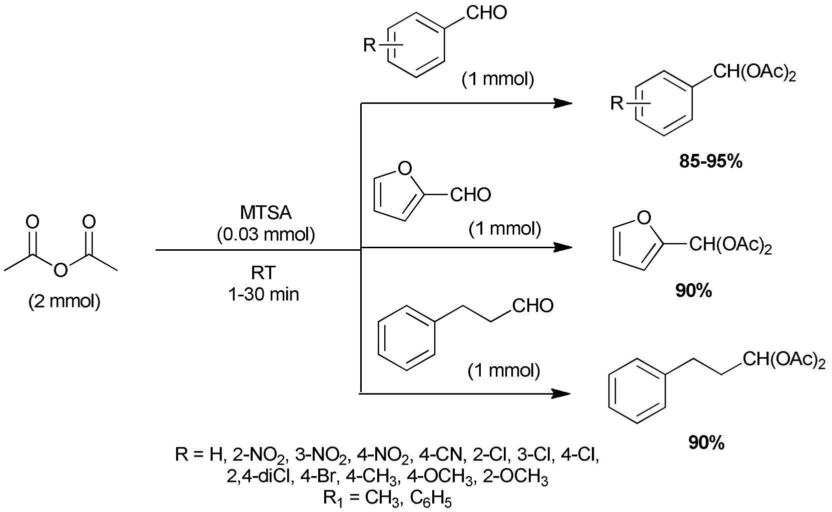
3.2.3) Tetrahydropyranylation of alcohols and phenols, acetylation of aldehydes and *N-Boc* protection of amines

The hydroxyl, formyl and amino groups are present in a number of compounds of biological and synthetic interest. Protection of these functional groups during multi-step synthesis are important processes. Shirini's group has presented an environmentally friendly methodology for the tetrahydropyranylation of alcohols and phenols, acetylation of aldehydes and *N-Boc* protection of amines, which was catalyzed by melamine trisulfonic acid (MTSA) **(Scheme 21a-c)**.[128] All reactions were performed at room temperature in good to excellent high yields of the products. Different types of benzylic alcohols having both electron-withdrawing and electron-donating groups were tetrahydropyranylated with DHP in the presence of catalytic amounts of MTSA in dichloromethane at room temperature in good to excellent yield. This method was found to be useful for the protection of hindered secondary and tertiary alcohols. This method was also useful for the protection of phenols to their corresponding tetrahydropyranyl ethers. The acetylation of aldehydes with acetic anhydride was performed in the presence of catalytic amounts of MTSA in the absence of solvent at room temperature, to produce the desired 1,1-diacetate in good to excellent yields. Aliphatic and aromatic aldehydes, were efficiently converted into the products with excellent yield. The authors have also performed the N-*Boc* protection of amines using $(Boc)_2O$. Different types of amines, including aliphatics and aromatics were efficiently N-*Boc* protected with this protocol. For the protection of aldehydes MTSA exhibited excellent activity in terms of catalyst loading and product yield as compared to PEG-OSO_3H.[25]



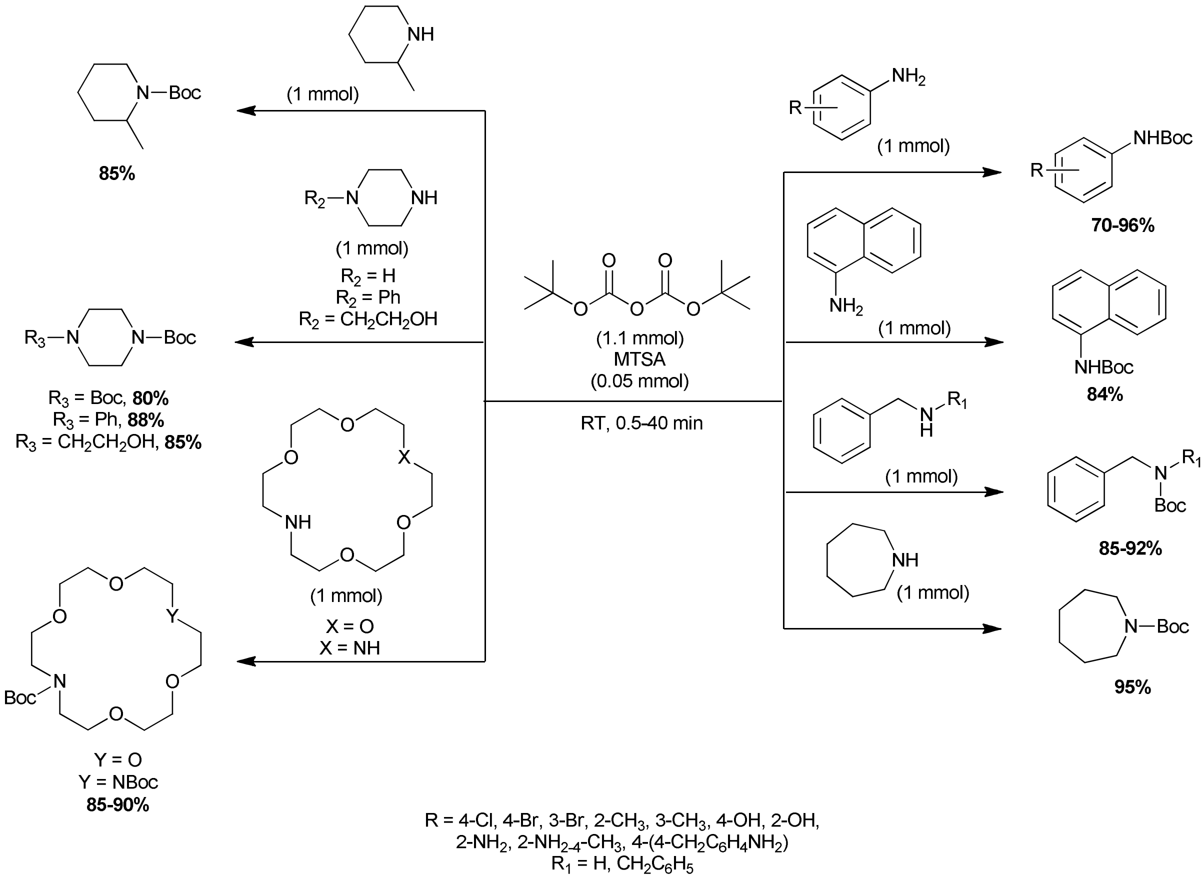
R = H, 4-Cl, 2-Cl, 2-Br, 2-NO_2, 3-NO_2, 4-NO_2, 2-CH_3,
4-$C(CH_3)_3$, 2-OCH_3, 3-OCH_3, 4-OCH_3
R_1 = C_6H_5, $CH_2CH_2C_6H_5$, CH_2CH_3
R_2 = C_5H_5, $CH_2C_6H_5$, CH_2CH_3
R_5 = 4-OCH_3, 4-Cl

Scheme 21a



R = H, 2-NO_2, 3-NO_2, 4-NO_2, 4-CN, 2-Cl, 3-Cl, 4-Cl,
2,4-diCl, 4-Br, 4-CH_3, 4-OCH_3, 2-OCH_3
R_1 = CH_3, C_6H_5

Scheme 21b



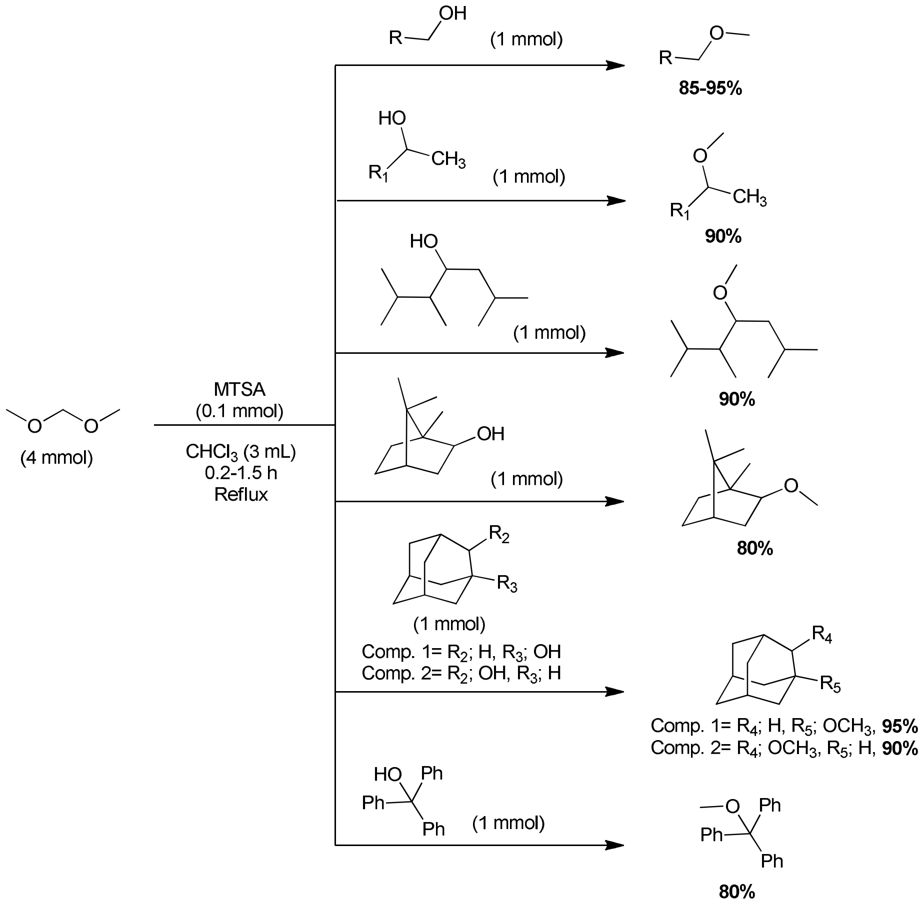
R = 4-Cl, 4-Br, 3-Br, 2-CH_3, 3-CH_3, 4-OH, 2-OH,
2-NH_2, 2-$NH_{2\text{-}4}$-CH_3, 4-(4-$CH_2C_6H_4NH_2$)
R_1 = H, $CH_2C_6H_5$

Scheme 21c

3.2.4) Chemoselective methoxymethylation of alcohols

Shirini's group presented melamine trisulfonic acid (MTSA) as an environmentally friendly and reusable catalyst for chemoselective methoxymethylation of alcohols with dimethoxymethane

(DMM) in chloroform under reflux conditions **(Scheme 22).**[129] However, Phenols could not be reacted under the same reaction conditions. A wide range of benzyl, alkyl and cyclo alkyl alcohols were efficiently undergoing methoxymethylation to afford corresponding products in excellent yields, which makes this protocol have wide synthetic utility.

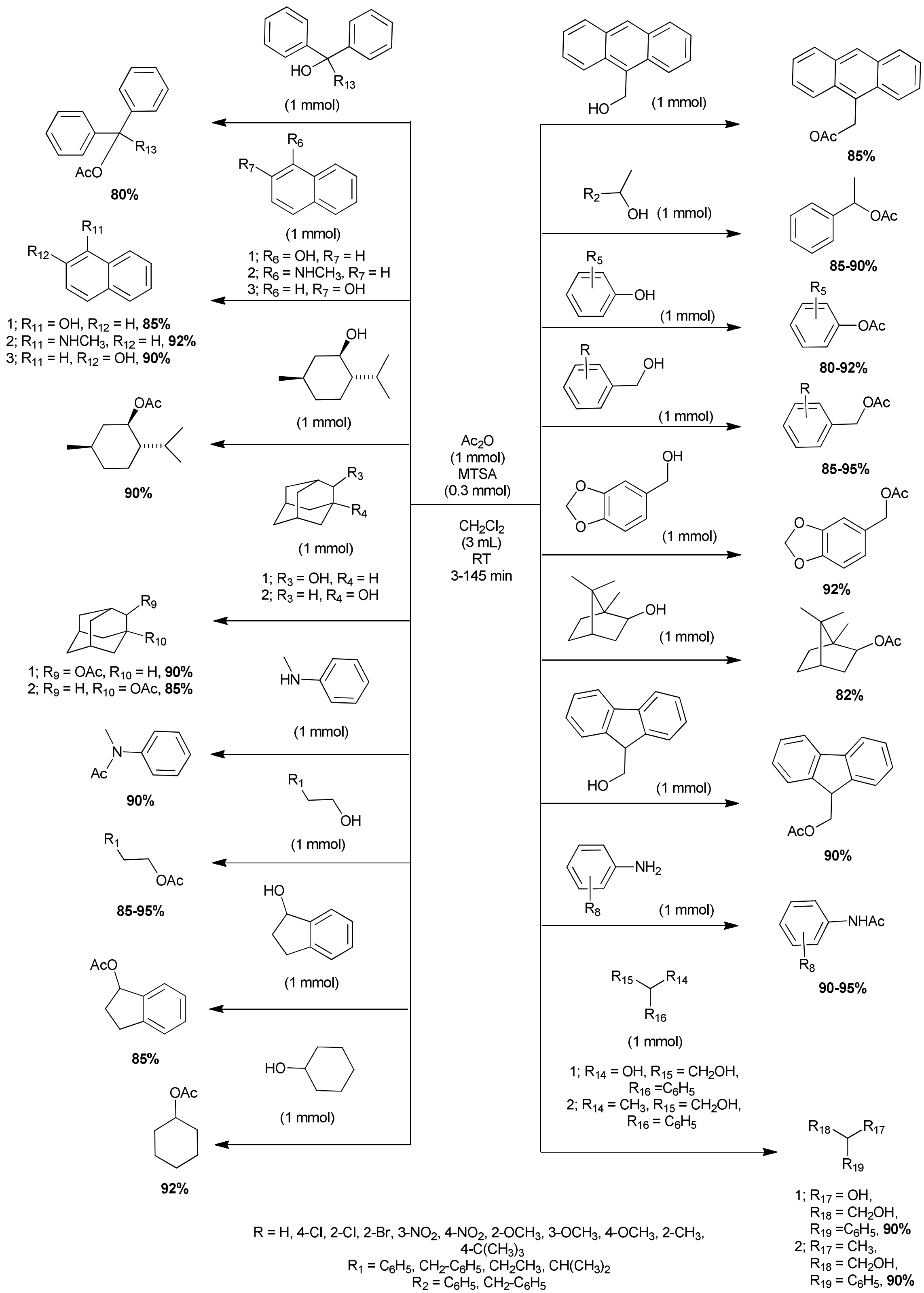


R = C_6H_4, 2-Br-C_6H_4, 4-Cl-C_6H_4, 4-OCH_3-C_6H_4, 4-NO_2-C_6H_4, C_6H_4-CH_2,
C_6H_4-CH_2CH_2, $CH_3CH_2CH_2$
R_1 = C_6H_4, CH_3CH_2

Scheme 22

3.2.5) Acetylation of alcohols, phenols and amines

The acetylation of alcohols with Ac_2O have been reported previously by using various catalysts such as including cerium(III) triflate,[130] $Zr(HSO_4)_4$,[131] $NaHSO_4.SiO_2$,[132] bismuth(III) salts,[133] silica sulfuric acid,[134] gadolinium triflate,[135] $Al(OTf)_3$[136] $Al(HSO_4)_3$.[137] However, these protocols have one or more of the following disadvantages such as lower product yield, high temperature, longer reaction times, difficult work-up procedure, thermal instability of the reagents and formation of undesirable or toxic by-products. Therefore, Shirini et al. have also demonstrated a sustainable methodology for the acetylation of alcohols, phenols and amines with acetic anhydride utilizing melamine trisulfonic acid (MTSA) as a reusable catalyst under mild and heterogeneous conditions **(Scheme 23)**.[138] These reactions were carried out in dichloromethane at room temperature. The authors have also concluded that the by-products resulting from the dimerization of diarylcarbinols, dehydration of tertiary alcohols, change in the configuration of optically active alcohols and Firese rearrangement of phenols were not observed with this methodology. After completion of the reaction, MTSA could be reused two times in subsequently two runs without significant loss in its activity. A wide range of alcohols, phenols and amines were efficiently converted into the products, which makes this protocol have wide synthetic utility.

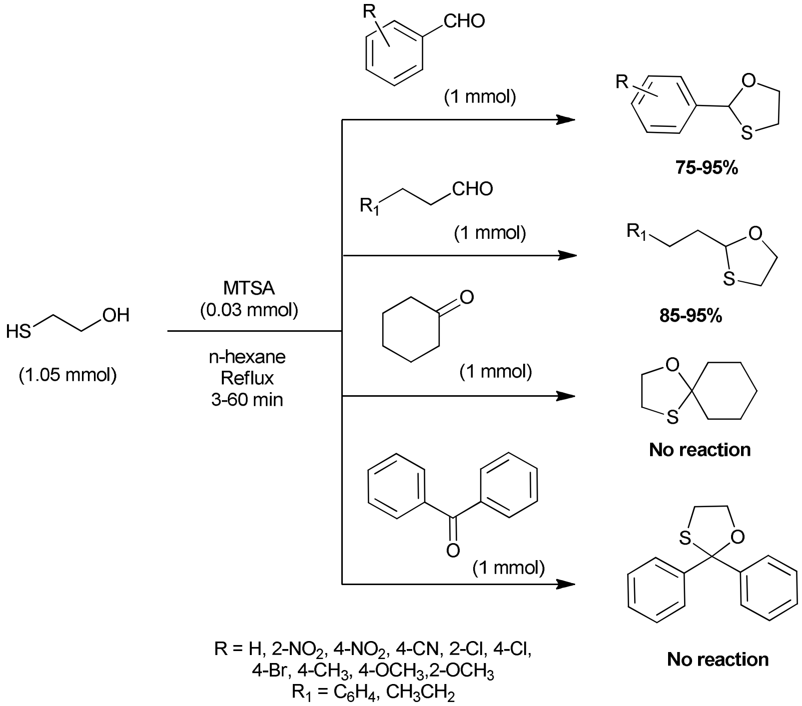


R = H, 4-Cl, 2-Cl, 2-Br, 3-NO$_2$, 4-NO$_2$, 2-OCH$_3$, 3-OCH$_3$, 4-OCH$_3$, 2-CH$_3$, 4-C(CH$_3$)$_3$
R$_1$ = C$_6$H$_5$, CH$_2$-C$_6$H$_5$, CH$_2$CH$_3$, CH(CH$_3$)$_2$
R$_2$ = C$_6$H$_5$, CH$_2$-C$_6$H$_5$
R$_5$ = 4-Cl, 2,4-diCl, 2-C$_6$H$_5$, 2,4-diNO$_2$, 4-OCH$_3$, 4-CH$_2$-C$_6$H$_5$, 2-OH, 4-OH, 4-C$_6$H$_4$-OH
R$_8$ = H, 4-CH$_3$, 2-CH$_3$, 3-CF$_3$
R$_{13}$ = H, C$_6$H$_5$

Scheme 23

3.2.6) Chemoselective oxathioacetalyzation of aldehydes

Shirini et al. have discovered a green procedure for the chemoselective oxathioacetalyzation of aldehydes with 2-mercaptoethanol catalyzed by melamine trisulfonic acid (MTSA) in n-Hexane under reflux conditions, which afforded products in excellent yield **(Scheme 24)**.[139] Previously, different catalysts such as HCl,[140] *p*-TSA,[141] $ZrCl_4$,[142] NBS,[143] TBAB,[144] alumina sulfuric acid[145] and $Bi(NO_3)_3$[60] were utilized in this transformation. Although they are not efficient as compared to MTSA in terms of product yields and reaction times. Aldehydes bearing electron-donating electron-withdrawing groups were efficiently converted to their corresponding 1,3-oxathiolane derivatives in good to high yields during relatively short reaction times. In addition, aliphatic aldehydes were also smoothly converted into the products efficiently. This method can be used for the chemoselective oxathioacetalyzation of aldehydes in the presence of ketones, because ketones were very stable in this reaction condition and can't be reacted. The MTSA could be recovered and reused three times without significant loss of their efficiency.

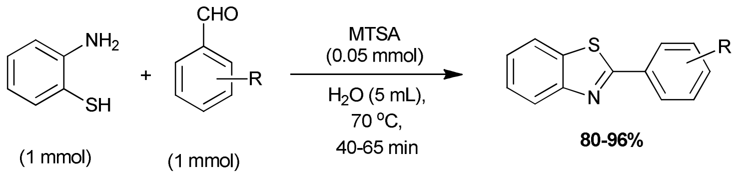


Scheme 24

3.2.7) Solvents mediated preparations of O- and N-containing heterocyclic compounds

3.2.7.1) Synthesis of 2-substituted benzothiazoles

The Mansoor's group has utilized melamine trisulfonic acid (MTSA) as an efficient and recyclable catalyst for the synthesis of 2-substituted benzothiazoles by condensation reaction of aromatic aldehydes and *o*-aminothiophenol in water at the 70 °C **(Scheme 25)**.[146] Various oxidative reagents and catalysts, such as CTAB, $FeCl_3$/Montmorillonite K-10, ZnO-beta zeolite, $KAl(SO_4)_2.12H_2O$, silica sulfuric acid, iodine, H_2O_2/CAN and H_2O_2/HCl have all been used in the reaction.[147] However, they do not give efficient results as compared to MTSA. The authors have examined various solvents such as methanol, ethanol, dichloromethane, 1,4-dioxane, THF, acetonitrile, DMF, ethyl acetate, chloroform and water. Although, the best conversion was obtained, when the reaction was performed in water. Only, 0.05 mmol of MTSA was sufficient for this conversion. The catalyst could be recycled and reused four times without any additional treatment or appreciable reduction in catalytic activity.

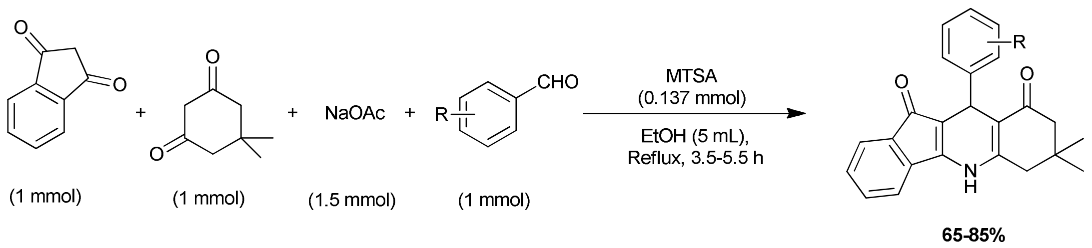


R = H, 4-Cl, 4-OH, 4-CH_3, 4-OCH_3, 4-NO_2, 4-$N(CH_3)_2$, 2-Cl, 2-OH, 2-OCH_3, 3-Cl, 3-NO_2

Scheme 25

3.2.7.2) Preparation of 7,8-dihydro-10-aryl-5*H*-indeno[1,2-*b*]quinoline-9,11-diones

Shirini and co-workers have demonstrated a green protocol for the preparation of 7,8-dihydro-10-aryl-5*H*-indeno[1,2-*b*]quinoline-9,11-diones via a one-pot four component condensation of aromatic aldehydes, dimedone, 1,3-indandione and ammonium acetate using melamine trisulfonic acid (MTSA) as a recyclable catalyst in ethanol **(Scheme 26)**.[148] A 50 mg loading of MTSA was found to be sufficient to promote the reaction in forward direction. Good yields were obtained using aromatic aldehydes with electron-donating or electron-withdrawing substituents. Aromatic aldehydes with electron-withdrawing groups yielded the products in a short time rather than electron-donating ones. The authors have also discussed this synthesis with mechanistic point of view, according to them in the first step Knoevenagel product was formed via condensation of aldehydes and active methylene compounds. The second key intermediate is enamine, produced by the condensation of dimedone with ammonia. Condensation of these two fragments gives the acyclic Michael adduct, which undergoes intermolecular cyclization with the participation of the amino function and one of the indanedione carbonyl groups to form the dihydroindenoquinoline in good yield. The catalyst could be recycled and reused three times without significant loss of activity.

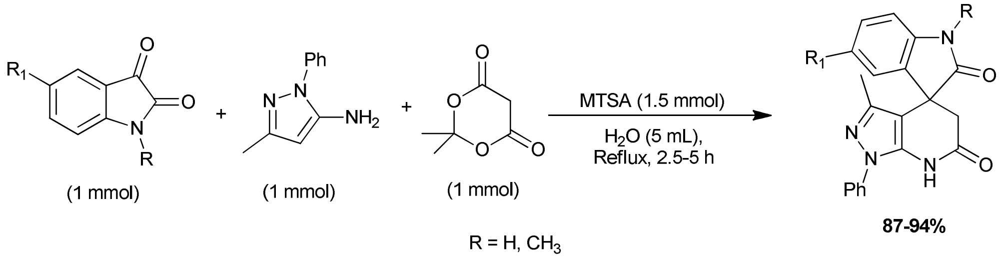


R = H, 4-Cl, 4-Br, 4-NO_2, 4-OH, 4-OCH_3, 2-Cl
R_1 = $CH_3CH_2CH_2$, $CH_3CH_2CH_2CH_2$

Scheme 26

3.2.7.3) Synthesis of spiro[pyrazolo[3,4-*b*]pyridine-4,3-indoline] derivatives

Yang et al. have discussed an efficient protocol for the synthesis of spiro[pyrazolo[3,4-*b*]pyridine-4,3-indoline] derivatives by the three component reaction of isatins, 3-methyl-1-phenyl-1*H*-pyrazol-5-amine and Meldrum's acid in the presence of a catalytic amount of melamine trisulfonic acid (MTSA) in water under reflux conditions **(Scheme 27)**.[149] The authors have demonstrated comparison study of various catalysts such as sulfuric acid, *p*-TSA, sulfamic acid and $FeCl_3$ with MTSA. Use of an inexpensive, non-toxic, reusable and an easily available catalyst makes this protocol green and clean.



R = H, CH_3
R_1 = H, Cl, CH_3, F, Br, H

Scheme 27

3.2.7.4) Synthesis of 4,4'-(Arylmethylene)-bis-(1*H*-pyrazol-5-ols)

Iravani and co-workers discussed catalytic application of a melamine trisulfunic acid (MTSA) as a recyclable catalyst for the condensation reaction of aromatic aldehydes with 3-methyl-l-phenyl-2-pyrazolin-5-one in ethanol under refluxing conditions, which afforded products in excellent yields **(Scheme 28)**.[150] Only, 15 mol% of catalyst was sufficient for this conversion. Different benzaldehydes with electron-donating or electron-withdrawing groups were smoothly reacted with this protocol to afforded products in excellent yields. The recycled catalyst could be reused five times without significant loss of their efficiency. As compared to CSA, MTSA shows good efficiency for this synthesis in terms of product yield and reaction time.[24]

R = H, 4-CH_3, 4-Cl, 2-Cl, 2,4-diCl, 4-NO_2, 3-NO_2, 4-OH, 3-OH, 3,4-diOCH_3, 4-CH_3S, 4-CN, 2-OH, 4-F, 4-$CH(CH_3)_2$, 4-OCH_3, 2-Br, 3-Br

Scheme 28

4) Conclusion:

In summary, we gave an overview on application of, melamine trisulfunic acid (MTSA) as an efficient, recyclable and heterogeneous catalyst in organic reactions. This catalyst with mild acidity, have shown excellent activity in various chemical reactions especially organic synthesis. Excellent accessibility, biodegradability, thermal stability and inexpensiveness are significant properties of this catalyst. The superior advantage of this heterogeneous catalyst is that it can be recovered and reused several times without the loss of their efficiency. A wide range of the reactions catalyzed by MTSA were carried out under solvent-free conditions, which makes those protocols green and clean. Here, MTSA proved to be a recyclable, green, and highly effective solid acid catalyst for a wide range of organic transformation and no doubt we will see large number of organic transformation catalyzed by MTSA.

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6) References:

1. M. Lancaster, *Green chemistry: an introductory text*, Royal Society of Chemistry, Cambridge, 2002.
2. P. T. Anastas and M. M. Kirchhoff, *Acc. Chem. Res.*, 2002, **35**, 686-694.
3. B. Karimi and M. Khalkhali, *J. Mol. Catal. A Chem.*, 2005, **232**, 113-117.
4. B. Karimi and D. Zareyee, *Org. Lett.*, 2008, **10**, 3989-3992.
5. P. Salehi, M. Ali Zolfigol, F. Shirini and M. Baghbanzadeh, *Curr. Org. Chem.*, 2006, **10**, 2171-2189.
6. K. Niknam and M. Zolfigol, *J. Iran. Chem. Soc.*, 2006, **3**, 59-63.

7. K. Niknam, B. Karami and M. A. Zolfigol, *Catal. Commun.*, 2007, **8**, 1427-1430.
8. K. Niknam, M. A. Zolfigol, G. Chehardoli and M. Dehghanian, *Chin. J. Catal.*, 2008, **29**, 901-906.
9. A. Corma and H. Garcia, *Chem. Rev.*, 2002, **102**, 3837-3892.
10. P. B. Venuto, *Microporous Mater.*, 1994, **2**, 297-411.
11. S. Besoluk, M. Kucukislamoglu, M. Nebioglu, M. Zengin and M. Arslan, *J. Iran. Chem. Soc.*, 2008, **5**, 62-66.
12. B. Karami, M. Montazerozohori and M. H. Habibi, *Phosphorus, Sulfur Silicon Relat. Elem.*, 2006, **181**, 2825-2831.
13. B. Karami, S. Khodabakhshi and M. Nikrooz, *Polycycl. Aromat. Comp.*, 2011, **31**, 97-109.
14. M. Dabiri, P. Salehi, S. Otokesh, M. Baghbanzadeh, G. Kozehgary and A. A. Mohammadi, *Tetrahedron Lett.*, 2005, **46**, 6123-6126.
15. H. Firouzabadi, N. Iranpoor, M. Jafarpour and A. Ghaderi, *J. Mol. Catal. A: Chem.*, 2006, **253**, 249-251.
16. S. Rostamizadeh, A. Amirahmadi, N. Shadjou and A. M. Amani, *J. Heterocycl. Chem.*, 2012, **49**, 111.
17. H. R. Shaterian, A. Hosseinian and M. Ghashang, *ARKIVOC*, 2009, **2**, 59-67.
18. P. K. Mandal and A. K. Misra, *Lett. Org. Chem.*, 2006, **3**, 848-853.
19. C. Ramesh, J. Banerjee, R. Pal and B. Das, *Adv. Synth. Catal.*, 2003, **345**, 557-559.
20. R. H. Vekariya and H. D. Patel, *Synth. Commun.*, 2014, **45**, 1031-1054.
21. S. Ko and C.-F. Yao, *Tetrahedron Lett.*, 2006, **47**, 8827-8829.
22. I. V. Kozhevnikov, *Chem. Rev.*, 1998, **98**, 171-198.
23. A.-X. Li, T.-S. Li and T.-H. Ding, *Chem. Commun.*, 1997, 1389-1390.
24. R. H. Vekariya and H. D. Patel, *ARKIVOC*, 2015, **1**, 136-159.
25. R. H. Vekariya and H. D. Patel, *RSC Adv.*, 2015, **5**, 49006-49030.
26. R. H. Vekariya and H. D. Patel, *ARKIVOC*, 2015, **1**, 70-96.
27. F. Shirini and J. Albadi, *Bull. Korean Chem. Soc*, 2010, **31**, 1119-1120.
28. C. O. Kappe, *Tetrahedron*, 1993, **49**, 6937-6963.
29. H. Salehi and Q. X. Guo, *Synth. Commun.*, 2004, **34**, 171-179.
30. A. Debache, M. Amimour, A. Belfaitah, S. Rhouati and B. Carboni, *Tetrahedron Lett.*, 2008, **49**, 6119-6121.

31. C. V. Reddy, M. Mahesh, P. Raju, T. R. Babu and V. N. Reddy, *Tetrahedron Lett.*, 2002, **43**, 2657-2659.
32. R. Varala, M. Mujahid Alam and S. R. Adapa, *Synlett*, 2003, 67-70.
33. S. Chitra and K. Pandiarajan, *Tetrahedron Lett.*, 2009, **50**, 2222-2224.
34. F. Shirini, K. Marjani and H. T. Nahzomi, *Arkivoc*, 2007, 51-57.
35. J. Lu and Y. Bai, *Synthesis*, 2002, 466-470.
36. P. M. Pihko, *Lett. Org. Chem.*, 2005, **2**, 398-403.
37. A. Paraskar, G. Dewkar and A. Sudalai, *Tetrahedron Lett.*, 2003, **44**, 3305-3308.
38. F. Shirini, M. Zolfigol and A.-R. Abri, *J. Iran. Chem. Soc.*, 2008, **5**, 96-99.
39. F. Shirini, M. A. Zolfigol and J. Albadi, *Chin. Chem. Lett.*, 2011, **22**, 318-321.
40. X.-f. Zhou, L. Zhang, E. Tseng, E. Scott-Ramsay, J. J. Schentag, R. A. Coburn and M. E. Morris, *Drug Metab. Dispos.*, 2005, **33**, 321-328.
41. T. Tsuruo, H. Iida, M. Nojiri, S. Tsukagoshi and Y. Sakurai, *Cancer Res.*, 1983, **43**, 2905-2910.
42. R. S. Kumar, A. Idhayadhulla, A. J. A. Nasser and J. Selvin, *Eur. J. Med. Chem.*, 2011, **46**, 804-810.
43. S. R. Kumar, A. Idhayadhulla, A. J. A. Nasser and J. Selvin, *J. Serb. Chem. Soc.*, 2011, **76**, 1-11.
44. A. Krauze, S. Ģērmane, O. Eberlin, I. Šturms, V. Klusā and G. Duburs, *Eur. J. Med. Chem.*, 1999, **34**, 301-310.
45. S. S. Mansoor, K. Aswin, K. Logaiya and S. Sudhan, *J. King Saud Univ. Sci.*, 2013, **25**, 191-199.
46. J.-L. Wang, D. Liu, Z.-J. Zhang, S. Shan, X. Han, S. M. Srinivasula, C. M. Croce, E. S. Alnemri and Z.Huang, *Proc. Natl. Acad. Sci.*, 2000, **97**, 7124-7129.
47. D. Kumar, V. B. Reddy, S. Sharad, U. Dube and S. Kapur, *Eur. J. Med. Chem.*, 2009, **44**, 3805-3809.
48. N. J. Thumar and M. P. Patel, *Arkivoc*, 2009, **13**, 363-380.
49. A. Martinez-Grau and J. Marco, *Bioorg. Med. Chem. Lett.*, 1997, **7**, 3165-3170.
50. H. Valizadeh and A. Azimi, *J. Iran. Chem. Soc.*, 2011, **8**, 123-130.
51. L. Bonsignore, G. Loy, D. Secci and A. Calignano, *Eur. J. Med. Chem.*, 1993, **28**, 517-520.

52. S. S. Mansoor, K. Aswin, K. Logaiya, S. Sudhan and H. Ramadoss, *J. Saudi Chem. Soc.*, 2013.
53. K. Aswin, K. Logaiya, P. N. Sudhan and S. S. Mansoor, *J. Taibah Univ. Sci.*, 2012, **6**, 1-9.
54. W. Li and Q. Luo, *J. Chem.*, 2011, **8**, 1972-1978.
55. R. H. Vekariya and H. D. Patel, *Synth. Commun.*, 2014, **44**, 2756-2788.
56. H. Von Pechmann and C. Duisberg, *Chem. Ber.*, 1884, **17**, 929-936.
57. L. L. Woods and J. Sapp, *J. Org. Chem.*, 1962, **27**, 3703-3705.
58. D. S. Bose, A. Rudradas and M. H. Babu, *Tetrahedron Lett.*, 2002, **43**, 9195-9197.
59. V. M. Alexander, R. P. Bhat and S. D. Samant, *Tetrahedron Lett.*, 2005, **46**, 6957-6959.
60. F. Shirini, K. Marjani, H. T. Nahzomi and M. A. Zolfigol, *Chin. Chem. Lett.*, 2007, **18**, 909-911.
61. G. Sharma, J. J. Reddy, P. S. Lakshmi and P. R. Krishna, *Tetrahedron Lett.*, 2005, **46**, 6119-6121.
62. H. Valizadeh and A. Shockravi, *Tetrahedron Lett.*, 2005, **46**, 3501-3503.
63. F. Shirini, M. Zolfigol and J. Albadi, *J. Iran. Chem. Soc.*, 2010, **7**, 895-899.
64. A. Khazaei, M. A. Zolfigol, T. Faal Rastegar, G. Chehardoli and S. Mallakpour, *Iran. J. Catal.*, 2013, **3**, 211-220.
65. M. Sayyafi, M. Seyyedhamzeh, H. R. Khavasi and A. Bazgir, *Tetrahedron*, 2008, **64**, 2375-2378.
66. H. R. Shaterian, M. Ghashang and M. Feyzi, *Appl. Catal. A: Gen.*, 2008, **345**, 128-133.
67. J. M. Khurana and D. Magoo, *Tetrahedron Lett.*, 2009, **50**, 7300-7303.
68. R. Ghorbani-Vaghei, R. Karimi-Nami, Z. Toghraei-Semiromi, M. Amiri and M. Ghavidel, *Tetrahedron*, 2011, **67**, 1930-1937.
69. C. Conti and N. Desideri, *Bioorg. Med. Chem.*, 2010, **18**, 6480-6488.
70. A. Foroumadi, G. Dehghan, A. Samzadeh-Kermani, F. Arabsorkhi, M. Sorkhi, A. Shafiee and M. Abdollahi, *Asian J. Chem.*, 2007, **19**, 1391-1396.
71. M. S. El-Gaby, M. A. Zahran, M. M. Ismail and Y. A. Ammar, *Il Farmaco*, 2000, **55**, 227-232.
72. H. Gourdeau, L. Leblond, B. Hamelin, C. Desputeau, K. Dong, I. Kianicka, D. Custeau, C. Boudreau, L. Geerts and S.-X. Cai, *Mol. Cancer Ther.*, 2004, **3**, 1375-1384.

73. F. Cassidy, J. M. Evans, M. S. Hadley, A. H. Haladij, P. E. Leach and G. Stemp, *J. Med. Chem.*, 1992, **35**, 1623-1627.
74. W. Ma, X. Wang, F. Yan, L. Wu and Y. Wang, *Monatsh. Chem.*, 2011, **142**, 163-167.
75. A. Zare and F. Monfared, *Iran. Chem. Commun.*, 2013, **2**, 1-17.
76. S. M. Prajapati, K. D. Patel, R. H. Vekariya, S. N. Panchal and H. D. Patel, *RSC Adv.*, 2014, **4**, 24463-24476.
77. A. Zare, M. Dashtizadeh and M. Merajoddin, *Iran. Chem. Commun.*, 2015, **3**, 208-217.
78. M. A. Pasha and V. P. Jayashankara, *Bioorg. Med. Chem. Lett.*, 2007, **17**, 621-623.
79. G. W. Rewcastle, G. J. Atwell, L. Zhuang, B. C. Baguley and W. A. Denny, *J. Med. Chem.*, 1991, **34**, 217-222.
80. A. Moosavi-Zare, M. Rezaei, M. Merajoddin, H. Hamidian, A. Zare and M. Kazem-Rostami, *Scientia Iranica*, 2014, **21**, 2049.
81. R. H. Vekariya and H. D. Patel, *Synth. Commun.*, 2014, **44**, 2313-2335.
82. J. Albadi, F. Shirini, B. Ghabezi and T. Seiadatnasab, *Arab. J. Chem.*, 2012, DOI:10.1016/j.arabjc.2012.1010.1011.
83. P. G. Wuts and T. W. Greene, *Greene's protective groups in organic synthesis*, John Wiley & Sons, New York, 2007.
84. M. Fallah-Mehrjardi and K. Ghanemi, *Jordan J. Chem.*, 2012, **7**, 393-399.
85. D. J. Kalita, R. Borah and J. C. Sarma, *Tetrahedron Lett.*, 1998, **39**, 4573-4574.
86. B. Wang, Y. Gu, G. Song, T. Yang, L. Yang and J. Suo, *J. Mol. Catal. A: Chem.*, 2005, **233**, 121-126.
87. N. Srivastava, S. K. Dasgupta and B. K. Banik, *Tetrahedron Lett.*, 2003, **44**, 1191-1193.
88. P. G. Wuts and T. W. Greene, *Greene's protective groups in organic synthesis*, John Wiley & Sons, New York, 2006.
89. L. Wu, P. Sun and F. Yan, *Phosphorus Sulfur Silicon Relat. Elem.*, 2011, **186**, 2055-2060.
90. H. R. Shaterian and M. Ghashang, *Phosphorus Sulfur Silicon Relat. Elem.*, 2007, **183**, 194-204.
91. J. Yadav, B. Reddy, A. Basak, G. Baishya and A. Venkat Narsaiah, *Synthesis*, 2006, 3831-3834.
92. A. V. Narsaiah, *J. Organomet. Chem.*, 2007, **692**, 3614-3618.
93. F. Shirini, M. A. Zolfigol and A.-R. Abri, *Monatsh. Chem.*, 2008, **139**, 17-20.

94. F. Shirini and E. Mollarazi, *Catal. Commun.*, 2007, **8**, 1393-1396.
95. H. R. Shaterian, R. Doostmohammadi and M. Ghashang, *Chin. J. Chem.*, 2008, **26**, 1709-1714.
96. B. Akhlaghinia and S. Tavakoli, *Synthesis*, 2005, 1775-1778.
97. I. Saxena, N. Deka, J. C. Sarma and S. Tsuboi, *Synth. Commun.*, 2003, **33**, 4185-4191.
98. W.-S. Cho and C.-H. Lee, *Bull. Korean Chem. Soc.*, 1998, **19**, 314-318.
99. F. Chevalier, G. R. Geier III and J. S. Lindsey, *J. Porphyrins Phthalocyanines*, 2002, **6**, 186-197.
100. L. Wu, Y. Yan and F. Yan, *Phosphorus Sulfur Silicon Relat. Elem.*, 2012, **187**, 149-154.
101. N. Iranpoor and F. Kazemi, *Tetrahedron*, 1998, **54**, 9475-9480.
102. W. Bao and Y. Zhang, *Chin. J. Org. Chem.*, 1998, **18**, 272-242.
103. J.-T. Li, W.-Z. Yang, G.-F. Chen and T.-S. Li, *Synth. Commun.*, 2003, **33**, 2619-2625.
104. X. Zhang, X. Fan, H. Niu and J. Wang, *Green Chem.*, 2003, **5**, 267-269.
105. G. Deng and T. Ren, *Synth. Commun.*, 2003, **33**, 2995-3001.
106. M. Abaee, M. Mojtahedi, R. Sharifi, M. Zahedi, H. Abbasi and K. Tabar-Heidar, *J. Iran. Chem. Soc.*, 2006, **3**, 293-296.
107. B. Das, P. Thirupathi, I. Mahender and K. R. Reddy, *J. Mol. Catal. A: Chem.*, 2006, **247**, 182-185.
108. L. Wang, J. Sheng, H. Tian, J. Han, Z. Fan and C. Qian, *Synthesis*, 2004, 3060-3064.
109. P. Salehi, M. M. Khodaei, M. A. Zolfigol and A. Keyvan, *Monatsh. Chem.*, 2002, **133**, 1291-1295.
110. S. Bhagat, R. Sharma and A. K. Chakraborti, *J. Mol. Catal. A: Chem.*, 2006, **260**, 235-240.
111. F. Shirini, S. Sarvi Beigbaghlou and S. V. Atghia, *Iran. J. Catal.*, 2012, **2**, 157-163.
112. A. R. Kiasat and M. Fallah-Mehrjardi, *Synth. Commun.*, 2010, **40**, 1551-1558.
113. M. R. M. Bhojegowd, A. Nizam and M. A. Pasha, *Chin. J. Catal.*, 2010, **31**, 518-520.
114. M. Lei, L. Ma and L. Hu, *Tetrahedron Lett.*, 2010, **51**, 4186-4188.
115. B. Das, M. Krishnaiah, P. Balasubramanyam, B. Veeranjaneyulu and D. N. Kumar, *TetrahedronLett.*, 2008, **49**, 2225-2227.
116. M. Hosseini-Sarvari and H. Sharghi, *J. Org. Chem.*, 2006, **71**, 6652-6654.
117. X. J. Yang and Y. S. Zhang, *Res. Chem. Intermed.*, 2013, **39**, 2843-2848.

118. N. Iravania, M. Keshavarzb, M. Mousavia and M. Baghernejadc, *Iran. J. Catal.*, 2015, **5**, 65-71.
119. D. Enders, M. Moser, G. Geibel and M. C. Laufer, *Synthesis*, 2004, 2040-2046.
120. B. Das, M. Krishnaiah, K. Laxminarayana and K. R. Reddy, *J. Mol. Catal. A: Chem.*, 2007, **270**, 284-288.
121. I. N. Rao, E. Prabhakaran, S. K. Das and J. Iqbal, *J. Org. Chem.*, 2003, **68**, 4079-4082.
122. A. K. Tiwari, R. M. Kumbhare, S. B. Agawane, A. Z. Ali and K. V. Kumar, *Bioorg. Med. Chem. Lett.*, 2008, **18**, 4130-4132.
123. A. Zare, *J. Chem.*, 2012, **9**, 2322-2331.
124. A. R. Momeni and M. Sadeghi, *Appl. Catal. A: Gen.*, 2009, **357**, 100-105.
125. M. T. Maghsoodlou, A. Hassankhani, H. R. Shaterian, S. M. Habibi-Khorasani and E. Mosaddegh, *Tetrahedron Lett.*, 2007, **48**, 1729-1734.
126. R. Ghosh, S. Maiti, A. Chakraborty, S. Chakraborty and A. K. Mukherjee, *Tetrahedron*, 2006, **62**, 4059-4064.
127. A. T. Khan, L. H. Choudhury, T. Parvin and M. A. Ali, *Tetrahedron Lett.*, 2006, **47**, 8137-8141.
128. F. Shirini, M. A. Zolfigol, J. Albadi and T. F. Rastegar, *Iran. J. Catal.*, 2011, **1**, 11-17.
129. F. Shirini, M. A. Zolfigol and J. Albadi, *Synth. Commun.*, 2010, **40**, 910-914.
130. R. Dalpozzo, A. De Nino, L. Maiuolo, A. Procopio, M. Nardi, G. Bartoli and R. Romeo, *Tetrahedron Lett.*, 2003, **44**, 5621-5624.
131. F. Shirini, M. Zolfigol and A. Safari, *Indian J. Chem. B*, 2005, **44**, 201.
132. B. Das and P. Thirupathi, *J. Mol. Catal. A: Chem.*, 2007, **269**, 12-16.
133. I. Mohammadpoor-Baltork, H. Aliyan and A. R. Khosropour, *Tetrahedron*, 2001, **57**, 5851-5854.
134. F. Shirini, M. A. Zolfigol and K. Mohammadi, *Bull. Korean Chem. Soc.*, 2004, **25**, 325-327.
135. R. Alleti, M. Perambuduru, S. Samantha and V. P. Reddy, *J. Mol. Catal. A: Chem.*, 2005, **226**, 57-59.
136. A. Kamal, M. N. A. Khan, K. S. Reddy, Y. Srikanth and T. Krishnaji, *Tetrahedron Lett.*, 2007, **48**, 3813-3818.
137. F. Shirini, M. A. Zolfigol and M. Abedini, *Monatsh. Chem.*, 2004, **135**, 279-282.

138. F. Shirini, M. A. Zolfigol, A.-R. Aliakbar and J. Albadi, *Synth. Commun.*, 2010, **40**, 1022-1028.
139. F. Shirini and J. Albadi, *Bull. Korean Chem. Soc.*, 2010, **31**, 1119-1120.
140. J. W. Ralls, R. Dodson and B. Riegel, *J. Am. Chem. Soc.*, 1949, **71**, 3320-3325.
141. C. Djerassi and M. Gorman, *J. Am. Chem. Soc.*, 1953, **75**, 3704-3708.
142. B. Karimi and H. Seradj, *Synlett*, 2000, 805-806.
143. A. Kamal, G. Chouhan and K. Ahmed, *Tetrahedron Lett.*, 2002, **43**, 6947-6951.
144. B. C. Ranu and A. Das, *Aus. J. Chem.*, 2004, **57**, 605-608.
145. H. R. Shaterian, A. Hosseinian and M. Ghashang, *Synth. Commun.*, 2008, **38**, 4097-4106.
146. S. S. Mansoor, K. Logaiya, S. Sudhan, K. Aswin, N. R. Ahmed and A. M. Hussain, *J. Indian Chem. Soc.*, 2014, **91**, 1-7.
147. N. P. Prajapati, R. H. Vekariya, M. A. Borad and H. D. Patel, *RSC Adv.*, 2014, **4**, 60176-60208.
148. F. Shirini, S. S. Beigbaghlou, S. V. Atghia and S. A.-R. Mousazadeh, *Dyes Pigm.*, 2013, **97**, 19-25.
149. L. M. Yang, P. L. Sun and L. Q. Wu, *J. Chin. Chem. Soc.*, 2012, **59**, 1500-1503.
150. N. Iravani, J. Albadi, H. Momtazan and M. Baghernejad, *J. Chin. Chem. Soc.*, 2013, **60**, 418-424.

Melamine trisulfonic acid (MTSA): An efficient and recyclable heterogeneous catalyst in green organic synthesis

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Graphical Abstract: