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Silica bonded n-propyl-1,3,5-triazine-2,4,6-triamine as a basic catalyst for synthesis of arylmethylenemalononitrile and pyran annulated heterocyclic compounds

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Abstract

In the present research, silica bonded n-propyl-1,3,5-triazine-2,4,6-triamine (SPTT) was synthesized by direct incorporation of chloropropyl groups through co-condensation of tetraethyl orthosilicate (TEOS) and 3-chloropropyl trimethoxysilane (CPTMS) and, subsequently, grafting the melamine onto the propyl groups *via* simple nucleophilic substitution reaction. The catalyst has been characterized by fourier transform infrared spectroscopy (FT-IR) and thermogravimetric analysis (TGA). The catalytic activity of catalyst was probed through synthesis of arylmethylenemalononitrile and pyran annulated heterocyclic compounds.

Keywords: Melamine; arylmethylenemalononitrile compounds; pyran heterocyclic compounds; functionalized silica catalyst.

Introduction

The immobilization of precursors on solid supports is one of the important routes for developing the novel heterogeneous catalysts. In recent years, silica supported catalysts have increasingly attracted attention [1]. Perhaps no class of inorganic support has widely been studied for catalytic applications more than silica.

Silica has abundant surface silanol groups, high surface area and good thermal stability. These advantageous characteristics has made silica as an attractive solid support in the field of functional materials.

Two general processes for organic functionalization of silica are direct synthesis and post-grafting synthesis methods [2-4]. 3-chloropropyltrialkoxysilane functionalized silica is one of the most important functionalized silica materials which has been used as a precursor for synthesis of many supported catalysts [5-7].

Homogeneous catalysts generally require special processing in the form of neutralization, which involves energy-inefficient catalyst separation from products [8]. Immobilization of homogeneous catalysts on solid supports and their conversion to insoluble polymeric derivatives has been suggested as alternative ways of getting around the problems [5]. Using these strategies, simplifies both the isolation of the reaction products and reagent recycling [7].

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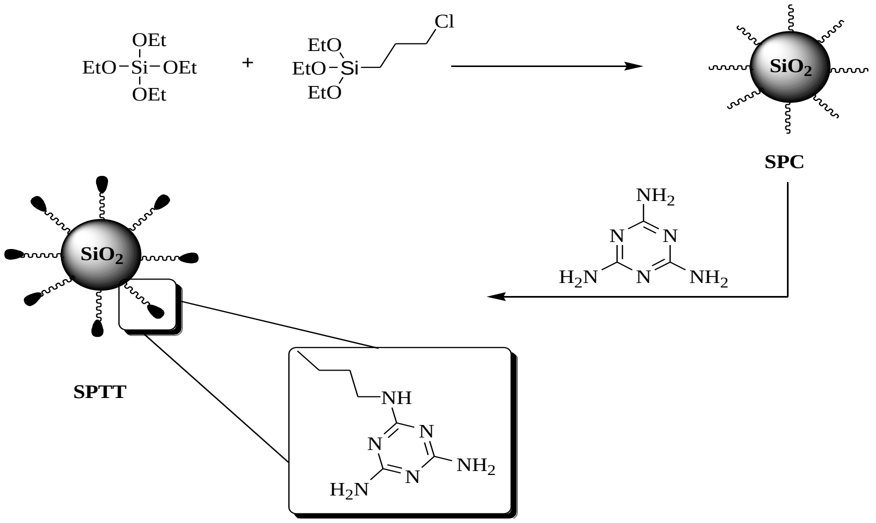
In contrast to the solid acid catalysts, solid basic catalysts have not been extensively studied [9-11]. Herein, 1,3,5-Triazine-2,4,6-triamine (melamine) is an organic base which has been used as a basic catalyst in organic transformations [12]. However, the major disadvantage of catalysts based on melamine is their separation from the products which needs solid-liquid or liquid-liquid techniques in many reactions. Thus, search for finding a heterogeneous, recoverable and reusable derivative of melamine is very desirable.

The Knoevenagel condensation of aldehydes with compounds containing activated methylene groups is a very useful reaction and has been widely employed for carbon-carbon bond formation in organic synthesis [13-15]. Conventionally, this reaction is catalyzed by weak bases like primary, secondary, and tertiary amines under homogeneous conditions. Over the last decades, various solid-supported catalysts have been applied to this reaction such as aminoalkylsilane functionalized silica. Additionally, Knoevenagel reactions catalyzed by Lewis acids have also been reported [16,17].

Moreover, in recent years, the synthesis of benzopyran compounds has attracted immense interests in the area of synthesizing the various drugs due to their pharmacological and biological activities [18,19]. Substituted 2-amino-4H-pyrans have a special importance among the 6-membered oxygen-containing heterocycles as they have been used as anticancer, antimicrobial agents [20], and photoactive materials [21] and also utilized in the synthesis of blood anticoagulant warfarin [22] and tacrine analogs (cholinesterase inhibitors) [23].

Considering these facts, we attempted to design an inorganic-organic hybrid basic catalyst by supporting melamine. The catalytic ability of this heterogeneous basic organocatalyst is studied for the one-pot synthesis of arylmethylenemalononitrile and pyran annulated heterocyclic compounds.



Scheme 1. Synthesis of SPTT

Experimental

Synthesis of chloropropyl grafted silica (SPC)

For preparation of chloropropyl grafted silica (SPC), initially, 8.41 g of tetraethyl orthosilicate (TEOS) was added in 100 mL of 1.0 M HCl solution at 40 °C for prehydrolysis, and then 3-chloropropyl trimethoxysilane (CPTMS) (2.3 g) was slowly added into the solution. The resulting mixture was stirred at 40 °C for 20 h and reacted at 95 °C under static condition for 24 h. The solid product was recovered by filtration and dried at 50 °C.

Preparation of silica bonded n-propyl-1,3,5-triazine-2,4,6-triamine (SPTT)

SPC (5 g) was added to a flask containing 50 mL of anhydrous acetone and an excess of melamine (10 mmol, 1.25 g). The reaction mixture was refluxed with stirring for 24 h. Then, the reaction mixture was cooled to room temperature, transferred to a vacuum glass filter, and washed with acetone. Finally, silica bonded n-propyl-1,3,5-triazine-2,4,6-triamine was dried at 50 ^{o}C for 8 h.

Typical procedure for the preparation of arylmethylenemalononitrile compounds

A mixture of aromatic aldehyde (1 mmol), malononitrile (1 mmol) and SPTT (0.05 g) was heated with stirring at 80 °C for appropriate time. After satisfactory completion of the reaction and cooling, the crude product was extracted by ethanol. The organic solvent was removed by simple evaporation and finally crude product recrystallized from EtOH/H_2O to afford pure corresponding arylmethylenemalononitrile derivatives in high yields.

Typical procedure for the preparation of pyran annulated heterocyclic compounds

A mixture of dimedone (1 mmol), malononitrile (1 mmol), aldehyde (1 mmol) and SPTT (0.05 g) was heated in ethanol at reflux condition. After complete consumption of aromatic aldehyde as judged by TLC (using n-hexane-ethylacetate as eluent), the reaction mixture was filtered for separation of the catalyst. Finally, the product was purified by recrystallization in hot EtOH. The desired pure product(s) was characterized by comparison of their physical data with those of known pyran annulated heterocyclic compounds.

Selected Spectral data

2-Amino-4-phenyl-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (Table 4, entry 1): ^{1}H-NMR (DMSO-d_6, 400 MHz) δ= 0.97 (3H, s), 1.04 (3H, s), 2.15 (2H, dd, J=16 Hz), 2.38 (2H, s), 4.33 (1H, s), 4.47 (2H, s), 7.23-7.10 (5H, m). ^{13}C-NMR (DMSO-d_6, 100.6 MHz): δ= 27.6, 28.8, 32.2, 35.5, 40.6, 50.6, 63.5, 114.0, 118.6, 127.1, 127.5, 128.5, 143.1, 157.4, 161.5, 195.8. IR (KBr) (υ_{max}, cm^{-1}): 518, 760, 1240, 1613, 1659, 2196, 3371, 3428.

2-Amino-4-(2-methoxy phenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (Table 4, entry 2): ^{1}H-NMR (DMSO-d_6, 400 MHz) δ= 0.97 (3H, s), 1.03 (3H, s), 2.10 (2H, dd, J=16 Hz), 2.16 (2H, dd, J=16 Hz), 3.75 (3H, s), 4.41 (2H, s), 4.63 (1H, s), 6.77-7.19 (4H, m). ^{13}C-NMR (DMSO-d_6, 100.6 MHz): δ= 27.3, 29.0, 30.6, 32.0, 40.6, 50.5, 55.5, 111.1, 112.9, 118.9, 120.6, 128.3, 129.0, 130.0, 157.1, 157.9, 162.2, 195.8. IR (KBr) (υ_{max}, cm^{-1}): 512, 758, 1212, 1371, 1605, 1654, 1686, 2138, 2445, 3219, 3229, 3395.

2-Amino-4-(4-nitro phenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (Table 4, entry 6): ^{1}H-NMR (DMSO-d_6, 400 MHz) δ= 0.95 (3H, s), 1.05 (3H, s), 2.14 (2H, dd, J=16 Hz), 2.44 (2H, dd, J=16 Hz), 4.38 (1H, s), 6.31 (2H, s), 7.37 (2H, d, J=8.4), 8.07 (2H, d, J=8.4 Hz). IR (KBr) (υ_{max}, cm^{-1}): 533, 782, 1243, 1600, 1668, 2195, 2450, 3330, 3401.

Benzylidene malononitrile (Table 2, entry 1): ^{1}H-NMR (DMSO-d_6, 400 MHz) δ= 7.28-7.52 (1H, m), 7.59-7.66 (2H, m), 7.80 (1H, s), 7.89 (2H, d, J=7.2 Hz).^{13}C-NMR (DMSO-d_6, 100.6 MHz): δ= 83.0, 113.1, 113.8, 129.8, 130.8, 131.0, 134.8, 160.1. IR (KBr) (υ_{max}, cm^{-1}): 1090, 1220, 1270, 1610, 1725, 2227, 2985, 3432.

4-Nitrobenzylidene malononitrile (Table 2, entry 6): ^{1}H-NMR (DMSO-d_6, 400 MHz) δ= 7.82 (1H, s), 8.02 (2H, d, J=9.4 Hz), 8.32 (2H, d, J=8.8 Hz). ^{13}C-NMR (DMSO-d_6, 100.6 MHz): δ= 87.7, 111.8, 112.4, 124.8, 131.5, 135.7, 150.6, 156.9. IR (KBr) (υ_{max}, cm^{-1}): 937, 1350, 1525, 1582, 2225, 2930.

Results and discussion

The FT-IR spectra of SiO_2-propylchloride (SPC) and silica bonded n-propyl-1,3,5-triazine-2,4,6-triamine (SPTT) samples are shown in Figure 1. The strong peak at 1075 cm-^{1} is due to the asymmetric stretching vibration of the structural silicone bond, Si-O-Si. The bands at 815 cm^{-1} and 465 cm^{-1} is due to the deformation of Si-O bond. The characteristic peaks around 1568 cm^{-1} and 1644 cm^{-1} could be clearly observed, which were attributed to C=C, C=N stretching vibrations of the melamine ring, respectively, and also the presence of peaks at 3335-3470 cm^{-1} is most probably due to the NH and NH_2 groups.

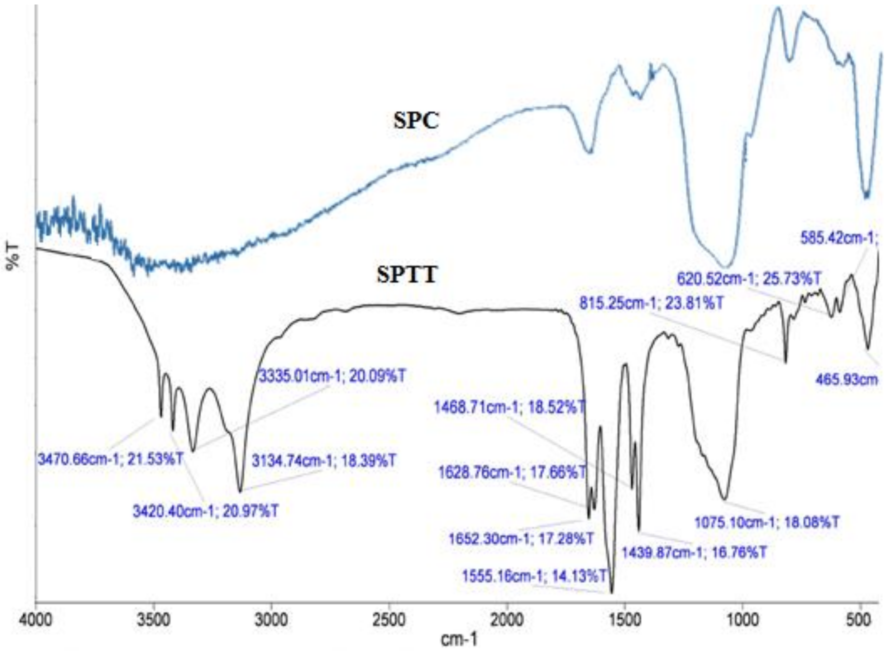


Figure 1. FT-IR spectra of SPC and SPTT

Thermal stability of the catalyst was investigated by thermal gravimetric analysis (TGA) in which the observed weight loss was associated with the loss of the organic components attached to the silica gel. TGA curve was shown in Figure 2. The sample shows three distinct steps of weight loss. The curve shows that the first weight loss occurs before 200 ^{o}C, which can be attributed completely to the loss of adsorbed water molecules. TGA of the catalyst demonstrated high thermal stability~~,~~ with decomposition starting at around 300 ^{o}C under a nitrogen atmosphere. The secondary weight loss at about 450 ^{o}C comes from the decomposition of organic substances in catalyst composite. The decomposition is complete at about 630 ^{o}C to form the constituent inorganic oxides.

Figure 2. Thermal gravimetric analysis (TGA) of SPTT

Scanning electron microscopy (SEM) is a useful tool for determining the size distribution. It has been a primary tool for characterizing the surface morphology and fundamental physical properties of the surface. Figure 3 shows SEM images of SPC and SPTT. According to the SEM images, the amorphous nature of micro-silica patrticles is evident. Furthermore, before and after functionalization, no significant change happened to micro-silica particles.

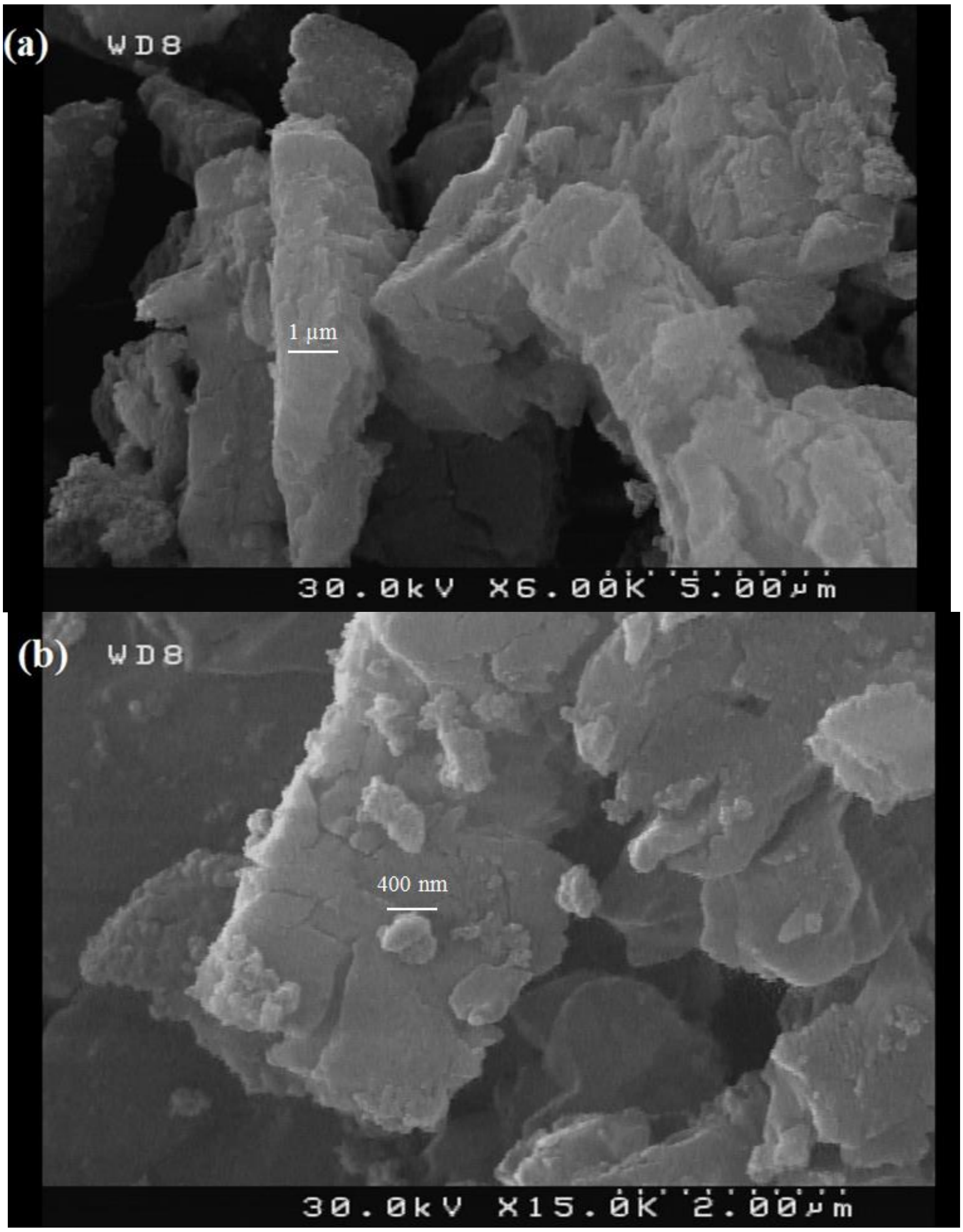
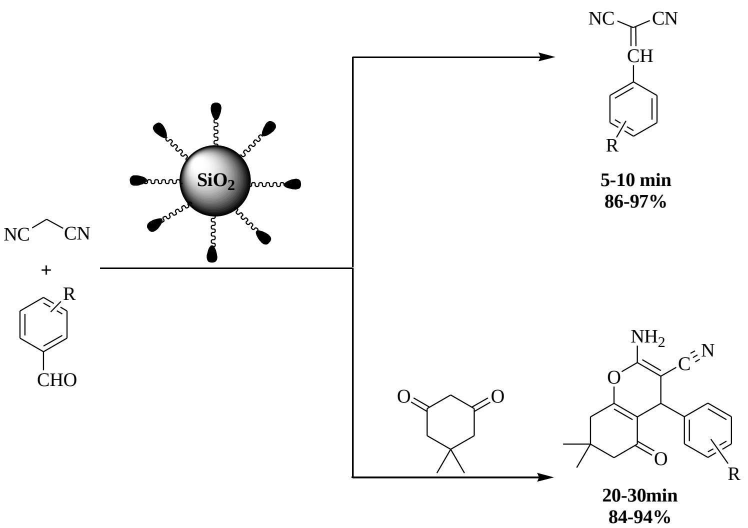


Figure 3. SEM image of SPC (a) and SPTT (b)

In continuation of our previous research to develop green chemistry by using heterogeneous catalysts [6,7], herein we report the synthetic applicability of SPTT as a basic catalyst for rapid and efficient preparation of arylmethylenemalononitrile and pyran annulated heterocyclic compounds (Scheme 2).



Scheme 2. Applicability of SPTT as a basic catalyst for rapid and efficient preparation of arylmethylenemalononitrile and pyran annulated heterocyclic compounds

In the preliminary stage of investigation, we focused on systematic evaluation of different conditions for the coupling of benzaldehyde and malononitrile. Various solvents and temperature, were screened to test the efficiency of the catalyst and the results are summarized in Table 1. Excellent yield of coupling product was obtained under the optimized conditions using 0.05 g of catalyst under solvent-free conditions at 80 °C in 5 min (Scheme 3).

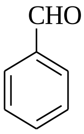
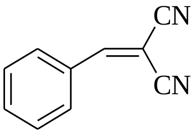
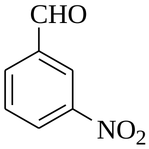
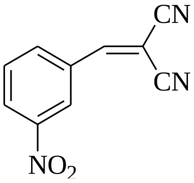
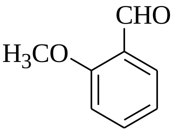
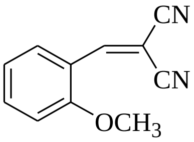
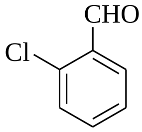
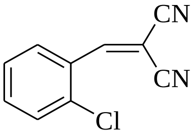
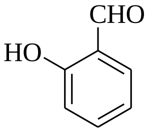
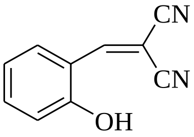
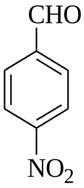
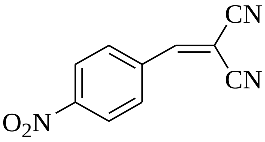
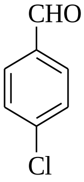
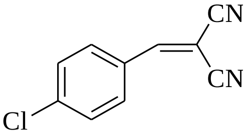
Scheme 3. The reaction of benzaldehyde and malononitrile in the presence of SPTT

Table 1. The reaction of benzaldehyde and malononitrile in the presence of SPTT

Entry	Solvent	Catalyst (g)	T (°C)	Time (min)	Yield (%)
1	H_2O	0.05	50	30	70
2	EtOH	0.05	50	30	82
3	CH_2Cl_2	0.05	40	30	78
4	CH_3CN	0.05	40	30	74
5	Solvent-free	0.05	40	15	86
6	Solvent-free	0.05	80	5	96
7	Solvent-free	1	80	15	96
8	Solvent-free	0.025	80	15	90

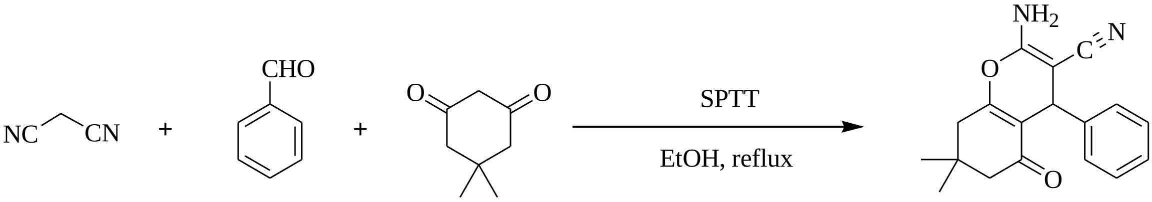
Different substituted arylmethylenemalononitriles were prepared changing the aromatic aldehyde substituents. Generally, the reactions that employed aromatic aldehydes bearing electron-withdrawing or electron-donating functional groups at different positions produced the corresponding products in good to excellent yields. Both of the aromatic aldehydes with electron-withdrawing and electron-donating functionalities were found to be compatible under the optimized reaction condition (Table 2). The structures of products were determined from their analytical and spectral (IR, ^1H & ^{13}C NMR) data and by direct comparison with authentic samples. Formation of the products was also confirmed by the comparison of their melting points with the products prepared by reporting methods.

Table 2. The reaction of aldehyde and malononitrile in the presence of SPTT

Entry	Aldehyde	Product	Time (min)	Yield (%)	m.pt (ºC)
1			5	96	82-85 [24]
2			5	96	105-107 [25]
3			7	88	-
4			7	92	94-97 [25]
5			10	86	101-103 [25]
6			5	97	158-160 [24]
7			5	95	157-159 [24]

After successfully synthesizing a series of arylmethylenemalononitrile in excellent yields, we turned our attention towards preparation of pyran annulated heterocyclic compounds through a multicomponent reaction.

To investigate the catalytic activity of SPTT in the one-pot multicomponent synthesis of pyran annulated heterocyclic compounds, we focused on systematic evaluation of different conditions for the model of three-component couplings of benzaldehyde, malononitrile and dimedone. After some experiments (Table 3), it was found that the use of benzaldehyde (1 mmol), malononitrile (1 mmol) and dimedone (1 mmol) in the presence of SPTT (0.05 g) under reflux condition in ethanol were the best condition. In order to elucidate the role of catalyst, a control reaction was set up in the absence of catalyst. It was found that, in the absence of catalyst, only %20 of the desired product was observed on the TLC plate even after 1h of heating.



25 min
92%

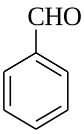
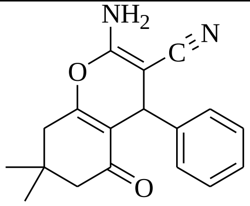
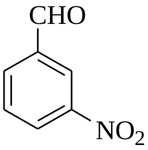
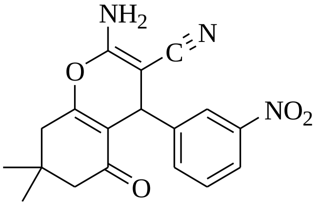
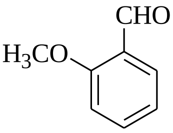
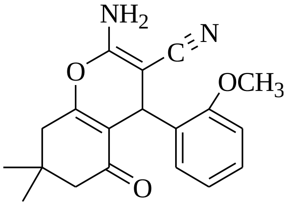
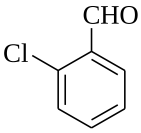
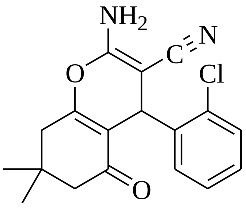
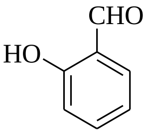
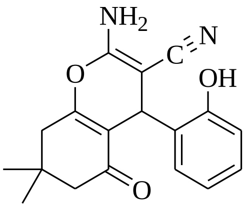
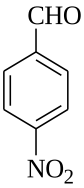
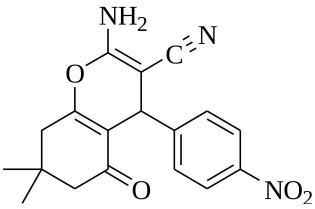
Scheme 4. The one-pot three component reaction of benzaldehyde, malononitrile and dimedone in the presence of SPTT

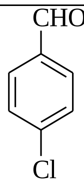
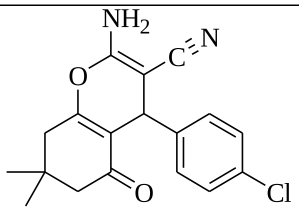
Table 3. The one-pot three component reaction of benzaldehyde, malononitrile and dimedone in the presence of SPTT

Entry	Solvent	Catalyst (g)	T (^{o}C)	Time (min)	Yield (%)
1	H_2O	0.05	50	60	68
2	EtOH	0.05	50	60	80
3	CH_2Cl_2	0.05	40	60	64
4	CH_3CN	0.05	40	60	63
5	Solvent free	0.05	40	60	70
6	EtOH	0.05	reflux	25	92
7	EtOH	1	reflux	25	92
8	EtOH	0.025	reflux	25	80
9	EtOH	-	reflux	60	20

When the reaction was performed in the presence of SPTT, it proceeded rapidly to give the desired product. Subsequently, with the optimal conditions in hand, to study the scope and limitations of the protocol, different substituted pyran heterocyclic compounds were prepared by changing the aromatic aldehyde substituents (Scheme 2). Generally, the reactions that employed aromatic aldehydes bearing electron-withdrawing or electron-donating functional groups at different positions produced the corresponding products in good to excellent yields. Both of the aromatic aldehydes with electron-withdrawing and electron-donating functionalities was found to be compatible under the optimized reaction condition (Table 2), because the desired products were obtained in high yields in relatively short reaction times.

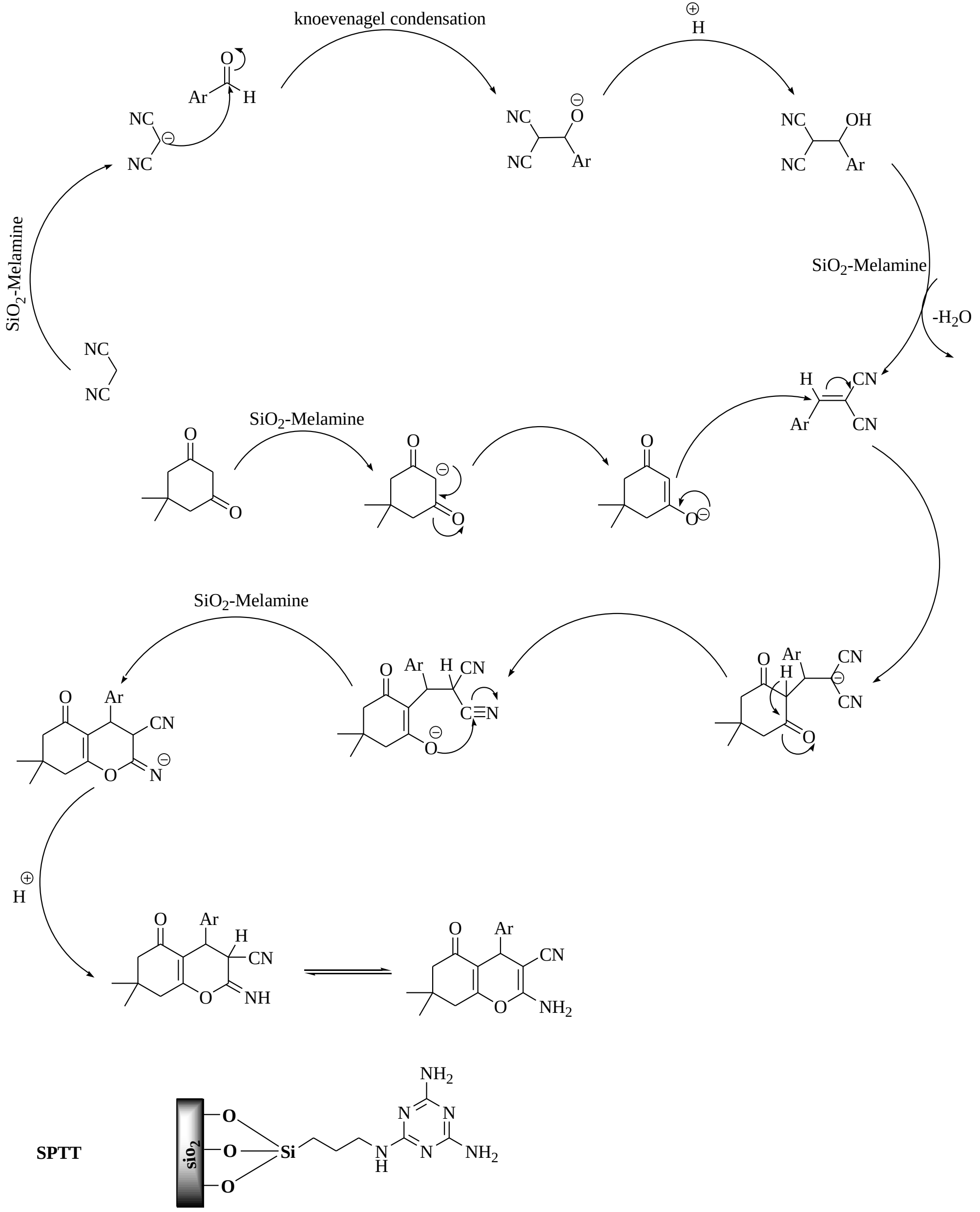
Table 4. The one-pot three component reaction of aldehyde, malononitrile and dimedone in the presence of SPTT under reflux condition in EtOH

Entry	**Aldehyde**	**Product**	**Time (min)**	**Yield (%)**	**m.pt (ºC)**
1			25	92	228-230 [26]
2			25	92	203-205 [26]
3			30	87	197-200 [27]
4			30	88	192-194 [26]
5			30	84	-
6			20	94	174-177 [26]

7			25	91	236-239 [26]

The structures of products were determined from their analytical and spectral (IR, ^{1}H & ^{13}C-NMR) data and by direct comparison with authentic samples. Formation of the products was also confirmed by the comparison of their melting points with the products prepared by reporting methods.

Scheme 5 shows a plausible mechanism that indicates the role of catalyst in the formation of the final product.



Scheme 5. Plausible mechanism for the synthesis of pyran heterocyclic compounds

In order to show the merit of the presented protocol in pyran heterocyclic compounds synthesis, we have compared the results of SPTT catalyst with some of those reported in the literatures. The model reaction of benzaldehyde, dimedone and malononitrile was considered as a representative example (Table 5).

Table 5. The comparison of the efficacy of SPTT catalyst with some of those reported in the literature

Entry	**Catalyst**	**Catalyst loading (g or wt. %)**	**Time (min)**	**Yield (%)**	**Ref**
1	SPTT	0.05 g	25	92	This work
2	SB-DABCO	6%	35	96	[9]
3	Pd (0)	6%	300	87	[27]
4	Amberlyst A21	0.03 g	60	87	[28]
5	MNPs-Guanidine	0.03 g	15	95	[26]
6	Fe_3O_4@SiO_2/DABCO	0.05 g	25	90	[29]

Conclusion

In conclusion, we report the synthesis of silica bonded n-propyl-1,3,5-triazine-2,4,6-triamine (SPTT) as a heterogeneous basic catalyst. The catalyst is easily synthesized and can catalyze the synthesis of arylmethylenemalononitrile and pyran annulated heterocyclic compounds.

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