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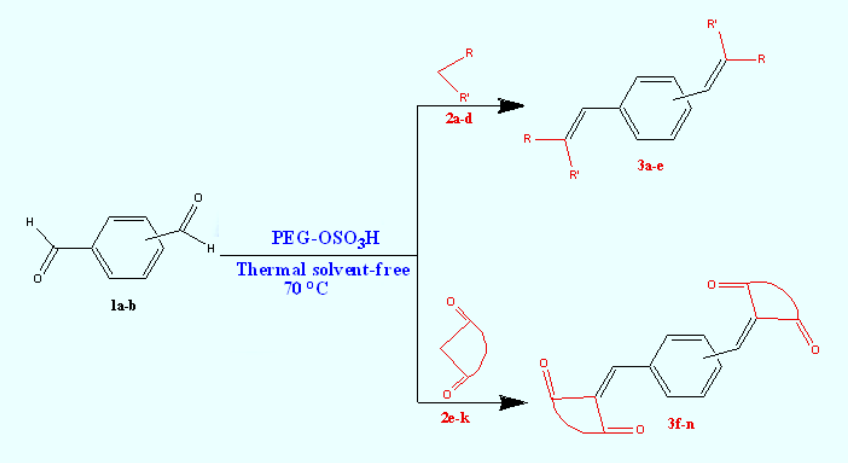
Graphical abstract



Sulfuric acid-modified PEG-6000 (PEG-OSO_3H): A biodegradable, reusable solid acid catalyst for highly efficient and eco-friendly synthesis of novel bis-Knoevenagel products under solvent-free conditions

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Abstract

Sulfuric acid-modified PEG-6000 (PEG-OSO_3H) is used as a highly efficient, biodegradable and reusable acid catalyst for the synthesis of novel acyclic and heterocyclic bis-Knoevenagel products under thermal solvent-free conditions. The remarkable features of this green, new methodology are high conversions, cleaner reaction profile, simple experimental and work-up procedure and economic viability. The catalyst is characterized for the first time by SEM-EDX and powder XRD. The catalyst can be reused several times without significant loss of its catalytic activity.

*Keywords:*PEG-OSO_3H, bis-Knoevenagel products, solvent-free condition.

Organic catalytic reactions have emerged as powerful synthetic tool for the synthesis of highly functionalized compounds.The eco-friendly and economically viable catalysts to make the organic transformations useful and are highly demanded by academic laboratories and industries.[1] In this respect, development of immobilized catalysts that allow simple work-up procedure and easy separation of products from reaction mixture is challenging and important.[2]

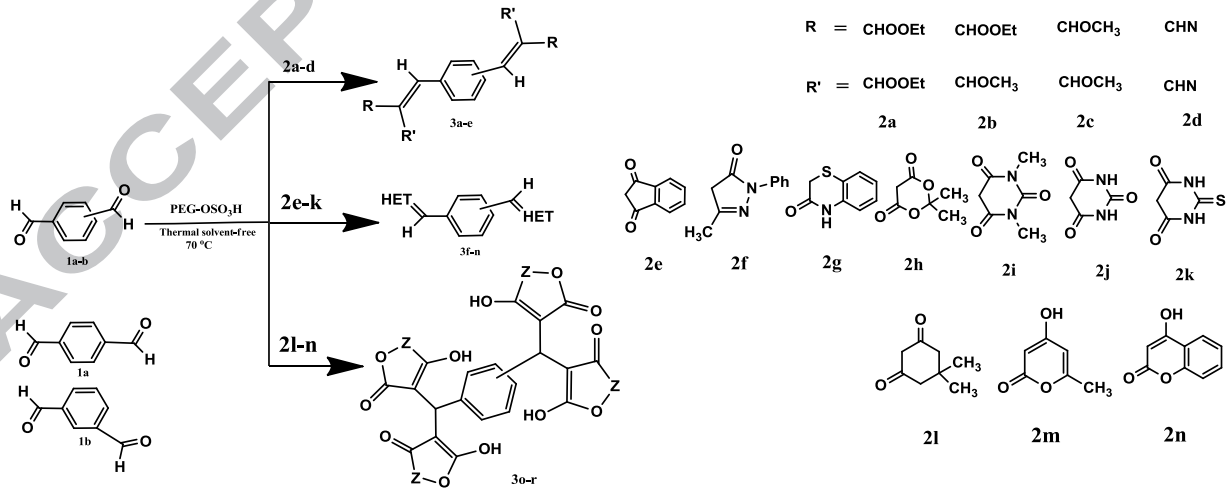
Knoevenagel condensation is a facile and versatile method for the formation of carbon-carbon bond,[3] with numerous applications in the synthesis of fine chemicals,[4] hetero-Diels–Alder reactions[5] and in the synthesis of carbocyclic as well as heterocycliccompoundsof biological significance.[6]Generally, the reaction is catalysed by bases,[7] ionic liquids,[8] amino acids,[9] basic MCM-41 silica,[10] Na-SBA-1,[11] Ni–SiO_2[12]and nanocrytalline ceria-zirconia.[13] Many of the reported methods involve refluxing in hazardous organic solvents for prolonged time, use of expensive and toxic catalysts, high temperature, low product yields and harsh conditions with non-recyclable catalysts.

Recently, much attention has been directed towards the use of polymer-supported catalysts from the economical point of view and in applications to industrial processes due to their unique properties such as low cost, high catalytic activity, easy work-up and separation of products and catalysts.[14]Among the different polymeric matrices employed in solid-phase chemistry, polyethylene glycol has emerged as a very convenient support for the synthesis of a variety of small organic molecules, ligands, and catalysts.[15]Sulfuric acid-modified PEG-6000 (PEG-OSO_3H) is an example of polyethylene glycol-supported catalyst which is functionalized by sulfonic acid groups. Itismild, biodegradable, recyclable, non-volatile and non-corrosive organic acid which has been used for the synthesis of several heterocyclic molecules.[15b,16]

Thus, based on the above findings and in continuation of our interest in the developmentof efficient, economical and new methodologies,[17] we herein report, for the first time, theuse of PEG-sulfuric acid (PEG-OSO_3H) as a biodegradable, environmentally benignand recyclable

solid acid catalyst, for the synthesis of novel acyclic and heterocyclic bis-Knoevenagel condensation products under solvent-free conditions in excellent yields.[18]The catalyst was recycled up to seven runs.The formation of PEG-OSO_3H system was detected by FT-IR, powder XRD and SEM-EDX analysis (Fig. 1, Fig. 2, Fig. 3 and Fig. 4,SI).

In our initial investigation to establish the optimum reaction conditions terephthaldehyde (**1**) (1.00 mmol, 0.134 g),diethyl malonate (**2a**)(2.00 mmol, 0.32 g) and PEG-OSO_3H (0.013 mmol, 0.08 g) under solvent-free conditions at 70 °C was chosen as a model reaction (Scheme 1). The controlled experiment demonstrated need of a catalyst, since the substrates did not react in the absence of the catalyst even after prolonged heating. Only 19% yield of the corresponding product was obtained in the presence of PEG-OSO_3H at room temperature (Table 1, entry 1), whereas by increasing the temperature to 60 °C and then 70 °C, a significant improvement was observed and yield of the product increased remarkably after 2 min (Table 1, entry 2, 3). Thus, 70 °C was chosen as reaction temperature in further investigations. Further, increase in temperature to 80 °C had no significant change in the yield of the product (Entry 4).



Scheme 1. Synthesis of **3(a-r)** under solvent-free conditions.

To compare the efficiency as well as capacity of the solvent-free conditions in comparison with solvent conditions, the model reaction was examined in the presence of PEG-OSO_3H in

different solvents (Table 1). When the reaction was performed in EtOH, MeOH, $(CH_3)_2CHOH$lower yield of the product (**3a**) was obtained after a longer time period (Table 1, entry 5,6, 7) whereas in H_2O, THF and CH_3CN, only trace amounts of the product was obtained (Table 1, entry 8, 9, 10). In AcOH relatively high yield of the product was obtained but reaction took longer time period for completion (Table 1, entry 11). When the reaction was carried out under solvent-free condition, it was completed within 2 min with considerable increase in yield of product **3a** (99%) (Table1, entry 3). Further in a comparative study using other green solvents, the model reaction was also performed in PEG-400, PEG-600 and $CH_2OH.CHOHCH_2OH$and was observed that the reaction completed relatively in shorter time but with mixture of products (entry 12-14). Thus, our study revealed that solvent-free condition is the best condition for PEG-OSO_3H catalyzed formation of bis-Knoevenagel products in terms of reduced reaction time and excellent yield of the products.

Table 1 Effect of various solvents versus the solvent-free on the model reaction.[a]

Entry	Solvent	Temperature	Time[b]	Yield (%)[c]
1	Solvent-free	25 °C	1.1 h	19
2	Solvent-free	60 °C	10 min	86
3	Solvent-free	70 °C	2 min	99
4	Solvent-free	80 °C	2 min	97
5	EtOH	Reflux	4.5 h	67
6	MeOH	Reflux	5 h	64
7	$(CH_3)_2CHOH$	Reflux	7 h	46
8	H_2O	Reflux	6 h	Trace
9	THF	Reflux	25 h	Trace
10	CH_3CN	Reflux	21 h	Trace
11	Acetic acid	Reflux	5.2 h	75
12	PEG-400	Reflux	3.2 h	61(mixture)
13	PEG-600	Reflux	4 h	47(mixture)
14	$CH_2OH.CHOHCH_2OH$	Reflux	3	63(mixture)

[a] Reaction conditions: terephthaldehyde (**1**, 1.00mmol, 0.134 g), diethyl malonate (**2a**, 2.00mmol, 0.32 g), catalyst (0.013 mmol, 0.08 g), thermal solvent-free condition, T=70°C.

[b]Reaction progress monitored by TLC.

[c]Isolated yields.

In order to establish superiority of the PEG-OSO_3H over other catalysts the model reaction was carried out under various sulfur analog acidic catalysts (Table 2). When the model reaction was examined inH_2SO_4-AcOH, p-toluene sulfonic acid (PTS), SiO_2-NH_2SO_3H, Xanthan-H_2SO_4, $NaHSO_4$-SiO_2,SiO_2-$H_2SO_4$and camphor-sulfonic acid (CSA), the reaction took longer time period for completion with lower to moderate yield of the product (entry 2-8). With $NH_2SO_3H$and $NH_2C_6H_4SO_3H$ the reaction was not successful (entry 9-10). Thus, PEG-OSO_3H is a more efficient and superior catalyst over other acidic catalysts in terms of time, yield and reaction conditions.

Table 2 Comparison of catalytic activity of different catalysts on the model reaction.[a]

Entry	Catalyst	Time[b]	Yield (%)[c]
1	PEG-OSO_3H	2 min	99
2	H_2SO_4-AcOH	2.6 h	59
3	PTS	1.5 h	68
4	SiO_2-NH_2SO_3H	2.2 h	69
5	Xanthan- H_2SO_4	1.4 h	70
6	$NaHSO_4$- SiO_2	1.3 h	71
7	SiO_2- H_2SO_4	1.8 h	70
8	CSA	20 min	81
9	NH_2SO_3H	-	Incomplete
10	$NH_2C_6H_4SO_3H$	-	Incomplete

[a] Reaction conditions: terephthaldehyde (**1**, 1.00 mmol, 0.134 g), diethyl malonate (**2a**, 2.00 mmol, 0.32 g), catalyst (0.013 mmol, 0.08 g), thermal solvent-free conditions, T=70°C.

[b]Reaction progress monitored by TLC.

[c]Isolated yields.

In order to establish the best reaction conditions, we performed an optimization study using model substrates (terephthaldehyde **1**, 1.00 mmol (0.134 g) and diethyl malonate **2a**, 2.00 mmol (0.32 g) in the presence of varying amounts of catalyst (Fig. 5). It was found that the optimum amount of catalyst turned out to be 0.013 mmol (0.08 g) in order to obtain best results.No significant improvement in the yield was observed on increasing the loading to

0.016 mmol (0.10 g), whereas the yield decreased due to decreasing the amount of catalyst to 0.01 mmol (0.06 g).

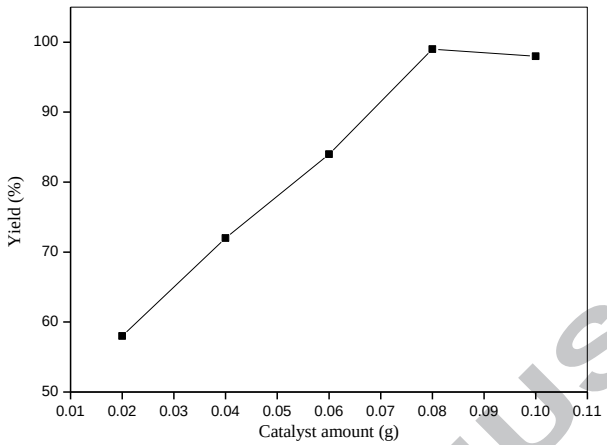
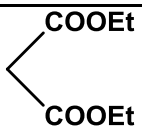
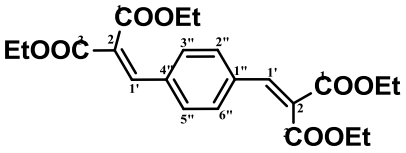
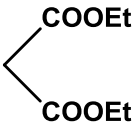
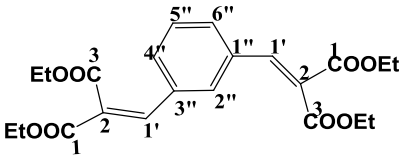
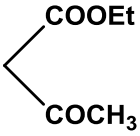
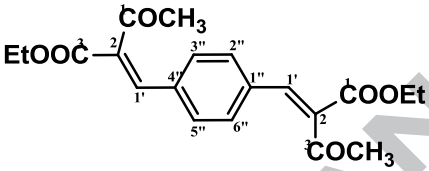
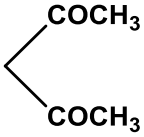
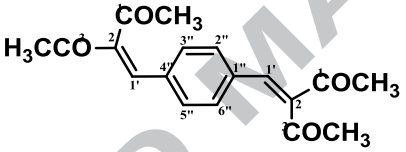
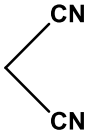
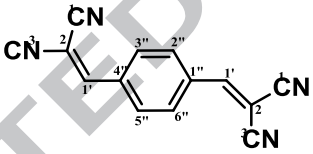
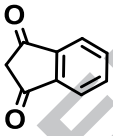
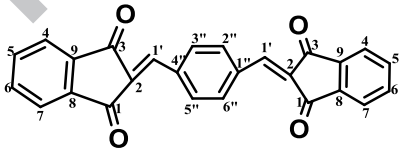
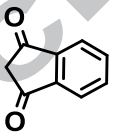
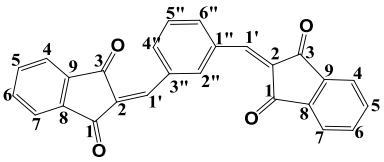
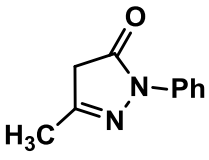
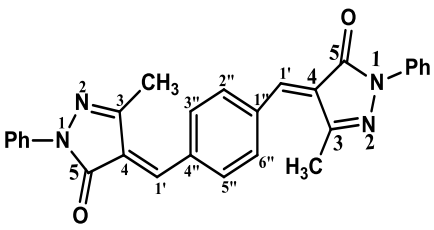
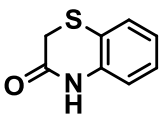
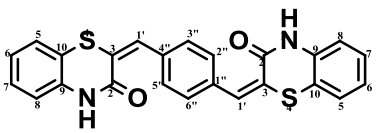


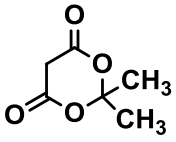
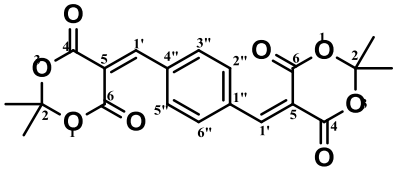
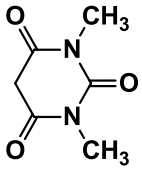
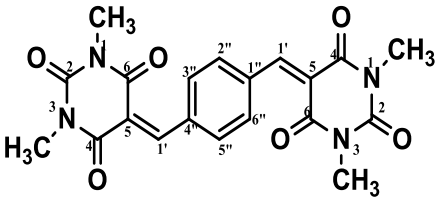
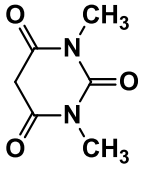
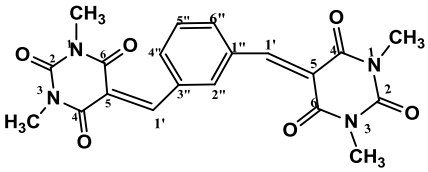
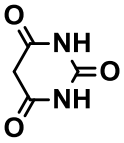
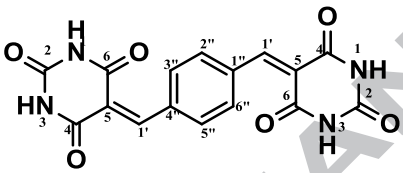
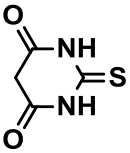
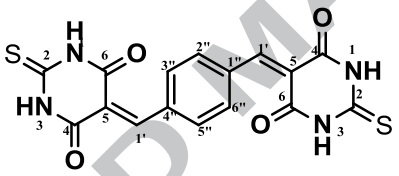
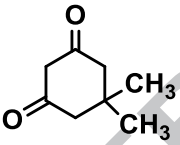
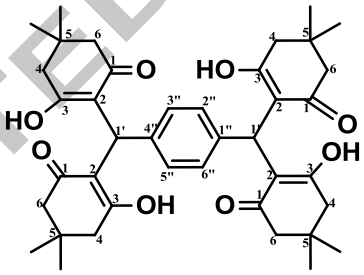
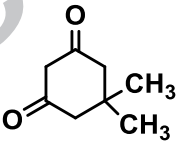
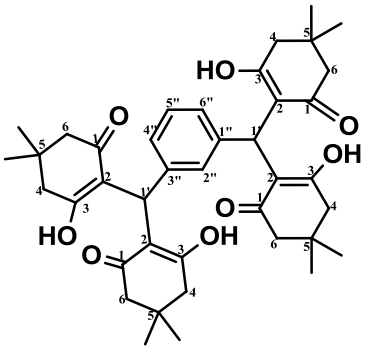
Fig 5. Effect of catalyst loading on the model reaction.

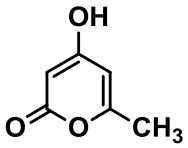
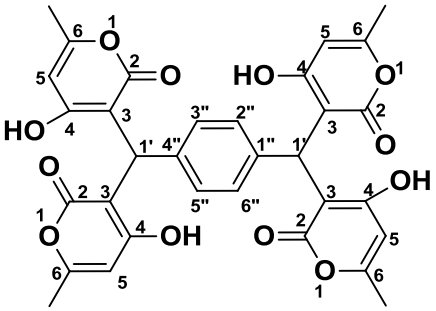
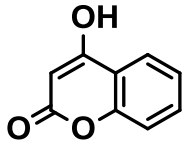
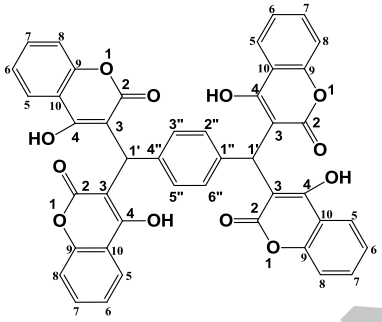
Recyclability of the catalyst was checked out under solvent-free conditions using model reaction of terephthaldehyde (**1**) with diethyl malonate(**2a**) in the presence of PEG-OSO_3H (0.013 mmol, 0.08 g). After completion of the reaction, the catalyst was recovered.The catalyst was then reused for sevenruns adopting the identical protocol without significant loss in product yield(Table 4)as can also be seen from XRD and SEM spectra (Fig. 2b and Fig. 6, SI). It is worth mentioning here that for every cycle the catalyst was tested for the reaction at microscale.

Under these optimized reaction conditions the scope and generality of the current protocol was further demonstrated by reaction of terephthaldehyde/isophthalaldehyde (**1a-b**) with different acyclic and cyclic active methylene compounds (**2a-n**) under solvent-free conditions. All the reactions proceeded smoothly and were completed within 2-8 min to afford the products in excellent yield (95-99%)(**3a-r**) (Table 5).

Table 5 Synthesis of bis-Knoevenagel condensation products (**3a-r**) under thermal solvent-free conditions.[a]

Entry	2a-n	Product	Time[b] (min)	Yield[c] (%)
3a			2	99
3b			3	97
3c			5	98
3d			7	96
3e			2	99
3f			4	95
3g			4	96
3h			3	99
3i			8	97

3j			5	95
3k			2	99
3l			2	98
3m			3	97
3n			6	95
3o			2	99
3p			4	95

3q			6	96
3r			4	98

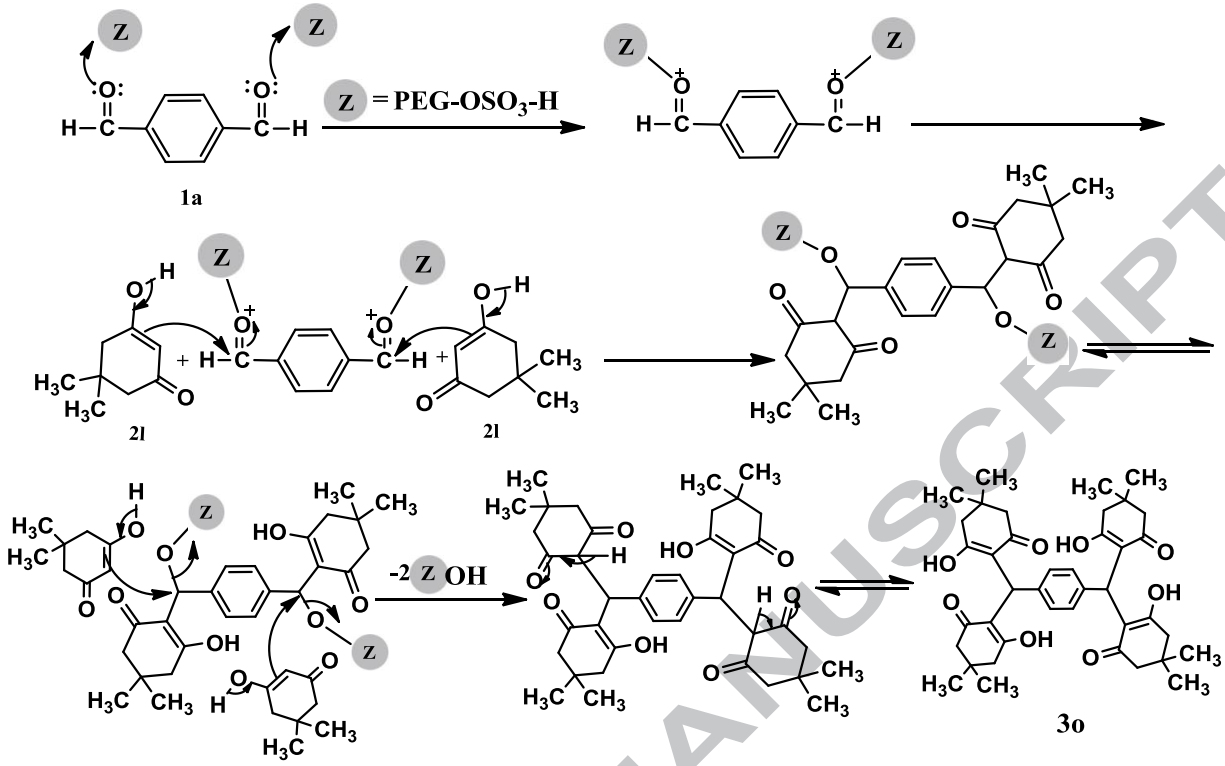
[a]Reaction conditions: terephthaldehyde/isophthalaldehyde(**1a-b**, 1.00 mmol, 0.134 g), different acyclic and cyclic active methylene compounds (**2a-n,** 2.00 mmol) and$PEG\text{-}OSO_3H$ (0.013 mmol, 0.08 g), thermal solvent-free condition, T=70°C.

[b]Reaction progress monitored by TLC.

[c] Isolated yields.

The structure of compounds (**3a-n**)was deduced on the basis of their spectral analysis**.** The IR spectrum of the newly synthesised compound**3a** showed sharp and strong absorption bands at 1628 and 1726 cm^{-1} for C=C and C=O of ester group. The proton nuclear magnetic resonance spectroscopy (^{1}H NMR) exhibitedmultiplets from δ 1.23-1.35 and δ 4.28-4.36 for CH_3 and CH_2 groups of diethyl malonate moiety. Four aromatic protons appeared as singlet at δ 7.46. The two olefinic protons were discernible as a singlet at δ 7.69. The ^{13}C NMR spectrum showed signals at δ 14.10 and δ 61.84 for CH_3 and CH_2 groups of diethyl malonate moieties whereas the aromatic carbons appeared in the range of δ 129.70-134.80. The olefinic carbons C-1′ and C-2 were present at *δ* 127.61 and δ 140.65 whereascarbonyl carbons of ester groups appeared at *δ* 163.6 and δ 166.29 respectively (SI). Further confirmation of the structure was provided by mass spectrometry which showed M^+at m/z 419.2 (M^++1 peak). The reaction of

terephthaldehyde/isophthalaldehyde**1a-b** with dimedone **2l,**triacetic acid lactone **2m**and 4-hydroxycoumarin **2n** did not give the expected Knoevenagel condensation products; instead, it afforded **3o**,**3p**,**3q** and **3r** in a very short period of time (Table 5). The IR spectrum of **3o** showed sharp and strong absorption bands at 1599 cm^{-1} and 3325 cm^{-1} for carbonyl and hydroxyl groups of dimedone moiety respectively. The ^{1}H NMR exhibited sharp singlets at δ 1.10 and δ 1.21 for CH_3 groups and a multiplet at δ 2.26-2.46for CH_2groups of dimedone moiety respectively. Another singlet integrating for two protons at δ 5.48 was assigned to methine proton. Four aromatic protons appeared as singlet at δ 7.01. The four hydroxyl protons were discernible as singlets at δ 11.35 and δ 11.83 respectively. The ^{13}C NMR spectrum showed signals at δ 27.95, 31.06 for CH_3 groups and C-5 carbons of dimedone moieties whereas methine, $CH_2$and C-2 carbons appeared at δ 46.40, 59.11 and 114.65 respectively. The aromatic carbons appeared in the range of δ 126.04-136.11 andsignals at *δ* 187.96 and δ 162.19were for hydroxyl and carbonyl group of dimedone moiety respectively. Further confirmation of the structure was provided by mass spectrometry which showed at m/z 659.3 (M^{+}+1 peak). A plausible mechanism for the formation of **3o** is depicted in Scheme 2.



Scheme 2. Plausible mechanism for the synthesis of **3o.**

In conclusion, we have reported a highly efficient andeco-friendly method for the synthesis of novel bis-Knoevenagel condensation products in excellent yieldusing PEG-OSO_3H as inexpensive, biodegradable and recyclable catalyst. Prominent advantages of this method are broad scope, operational simplicity, practicability, economic viability, excellent yield of the products in shorter reaction time, easy work-up, reusability of the catalyst. Moreover, the direct heating of the reaction mixture at lower temperature and solvent-free conditions have marked our work as a green and economically benign methodology. We believe that this method will be a more practical alternative to the other existing methods.

Acknowledgments

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Lucknow, Punjab University, Chandigarhfor providing spectral data.One of the authors (T.K.) would like to acknowledge the UGC, New Delhi, for the financial assistance in the form of Junior Research Fellowship [F. 17-43/08 (SA-I)].

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18.**General procedure for the synthesis of novel bis-Knoevenagel products under solvent-free conditions**

A mixture of terephthaldehyde/isophthalaldehyde**1a-b**(1.00mmol, 0.134 g), acyclic and cyclic active methylene compounds **2a–n** (2.00 mmol) and PEG-OSO_3H (0.013 mmol, 0.08 g) were mixed thoroughly using a mortar and pestle. The reaction mixture was then transferred to an open Pyrex 100 mL beaker and heated at 70 ˚C for the given time (Table 5).After completion of the reaction (monitored by TLC), the reaction mixture was cooled to room temperature and H_2O (5 mL) was added to it, and shaken for 3 min to dissolve PEG-OSO_3H. The crude product (insoluble in water) was filtered and recrystallized from hot ethanol (3 mL) to afford the pure product (**3a-r).** Inorder to recover the catalyst, the filtrate was dried under reduced pressure and recovered catalyst was washed with diethyl ether (2 mL) twice andreused after drying under reduced pressure.

Sulfuric acid-modified PEG-6000 (PEG-OSO_3H): A biodegradable, reusable solid acid catalyst for highly efficient and eco-friendly synthesis of novel bis-Knoevenagel products under thermal solvent-free conditions

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Supporting Information

Contents

General Information:

Melting points of all synthesized compounds were taken in a Riechert Thermover instrument and are uncorrected. The IR spectra (KBr) were recorded on Perkin Elmer RXI spectrometer.

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance II 400 spectrometer using tetramethylsilane (TMS) as an internal standard and DMSO-d_6/$CDCl_3$ as solvent. ESI-MS were recorded on a THERMO Finnigan LCQ Advantage max ion trap mass spectrometer having a ESI source. Elemental analyses (C, H and N) were conducted using the Elemental vario EL III elemental analyzer and their results were found to be in agreement with the calculated values. Chemicals were of commercial grade and used without further purification. The homogeneity of the compounds was checked by thin layer chromatography (TLC) on glass plates coated with silica gel G254 (E. Merck) using chloroform-methanol (3:1) mixture as mobile phase and visualized using iodine vapours. X-ray diffractograms (XRD) of the catalyst were recorded in the 2θ range of 10-70° with scan rate of 4°/ min on a Rigaku Minifax X- ray diffractometer with Ni-filtered Cu Kα radiation at a wavelength of 1.54060°A. The SEM-EDX characterization of the catalyst was performed on a JEOL JSM-6510 scanning electron microscope equipped with energy dispersive X-ray spectrometer operating at 20 kV.

Experimental:

Preparation of catalyst

At 0 °C, chlorosulfonic acid (10 mmol, 1.16 g) was added to a solution of PEG-6000 (1 mmol, 6.0 g) in CH_2Cl_2 (10 mL). Then the resulting solution was stirred at room temperature overnight, and the solution was concentrated under vacuum. Appropriate ether (50 mL) was added, and the precipitate filtered and washed with ether (30 mL) three times to afford the PEG-OSO_3H, according to the reported procedure.[1]

FT-IR spectrum of the catalyst

The FT-IR spectrum of the catalyst is shown in Fig. 1. A broad peak for OH absorption band was present at 3100-3600 cm^{-1}. The peaks at 2917, 2877 and at 1111 cm^{-1} represented CH_3, CH_2 stretching, and C-O-C symmetric stretching of the PEG unit, respectively.[2] The presence

of sulfonic acid functional group was established on the basis of a broad peak centred at 1162-1022 cm^{-1} as a result of merger of peaks at 1162, 1022 and 1111 cm^{-1} (C-O of PEG moiety), whereas the peak for S–O stretching mode is present at 662 cm^{-1}.

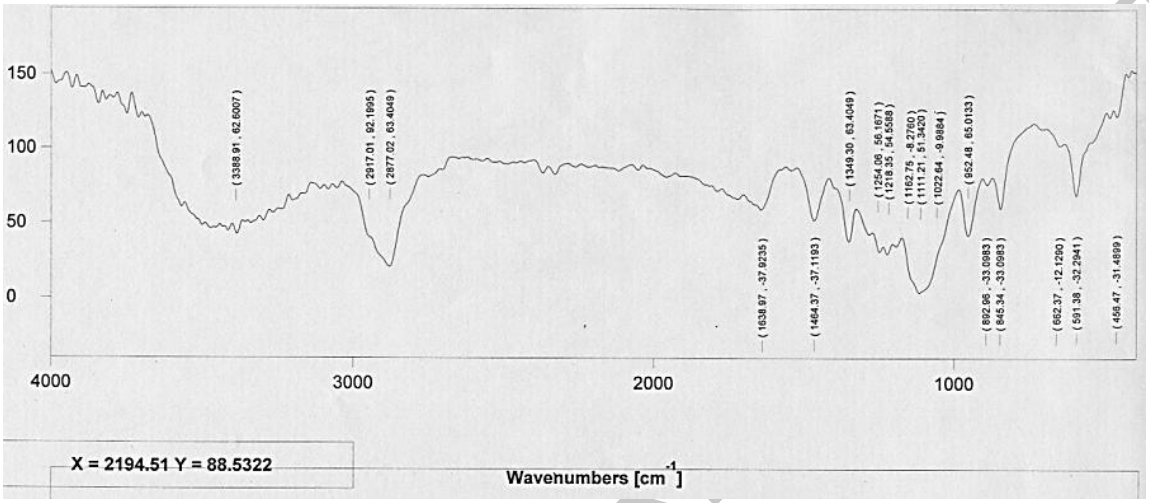

Fig. 1. FT-IR spectra of PEG-OSO3H

Powder X-ray diffraction (XRD) analysis of the catalyst

The structure of the prepared catalyst (PEG-OSO_3H) was identified by powder XRD. The XRD pattern of the matrix showed characteristic diffraction peaks for PEG moiety at 19.5, 23.6 and 24.5°.[2] The other characteristic peaks were due to SO_3 group.

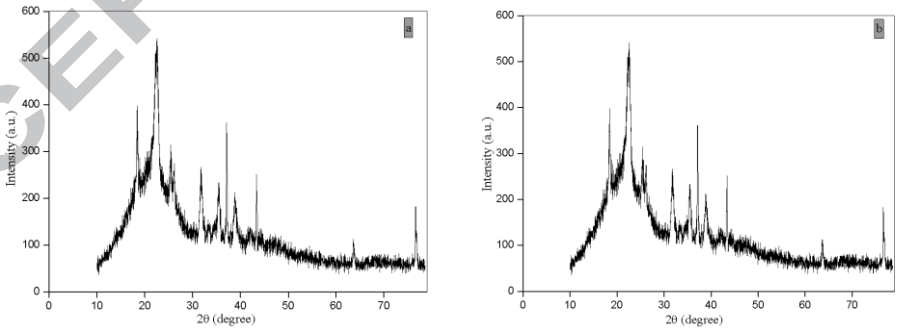

Fig. 2. Powder XRD of (**a**) fresh PEG-OSO_3H and (**b**) PEG-OSO_3H after seventh runs.

SEM-EDX analysis of the catalyst

To study the surface morphology of the catalyst, SEM micrographs of the catalyst was employed. The SEM images of the catalyst (Fig. 3) showed smooth, compact and homogeneous uniform surface.

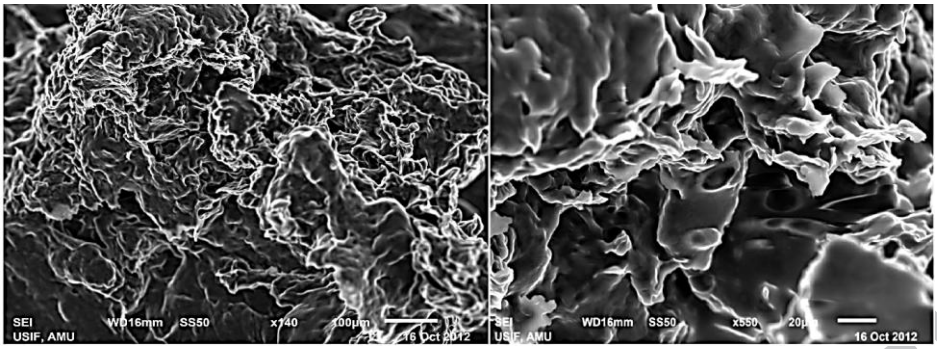

Fig. 3. SEM images of the catalyst (PEG-OSO_3H) at different magnifications.

EDX analysis (Fig. 4) of the catalyst showed the presence of C, O and S elements suggesting the formation of expected catalytic system.

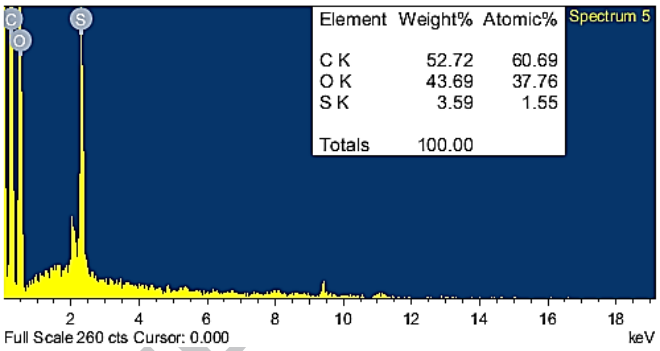

Fig. 4. EDX analysis of the catalyst (PEG-OSO_3H).

To the best of our knowledge there is no report on the characterization of the catalyst PEG-OSO_3H using XRD and SEM–EDX study.

The activity of different loadings of chlorosulfonic acid on PEG support was also investigated for the synthesis of (**3a)**, by using 5 mmol (0.58 g), 10 mmol (1.16 g) and 15 mmol (1.74 g) of chlorosulfonic acid supported on PEG 1 mmol (6.0 g) (Table 3). With 5 mmol PEG-OSO_3H lower yield of the product was obtained in longer time period possibly due to the lower ratio of chlorosulfonic acid to PEG (Table 3, entry 1) whereas with 15 mmol PEG-OSO_3H again yield was not satisfactory (Table 3, entry 3). The excellent yield of the product was obtained with 10 mmol PEG-OSO_3H (Table 3, entry 2).

Table 3 Effect of acid loading on the support for the synthesis of **3a** in thermal solvent-free conditions[a].

Entry	PEG-OSO_3H	Time (min)[b]	Yield (%)[c]
1	5 mmol	8	76
2	10 mmol	2	99
3	15 mmol	2	84

[a] Reaction conditions: terephthaldehyde (**1**, 1.00 mmol, 0.134 g), diethyl malonate (**2a**, 2.00 mmol, 0.32 g), catalyst (0.013 mmol, 0.08 g), thermal solvent-free condition, T=70°C.

[b] Reaction progress monitored by TLC.

[c] Isolated yields.

The reusability of the catalyst was checked out under solvent-free condition using model reaction of terephthaldehyde (**1**) with diethyl malonate (**2a**) in the presence of PEG-OSO_3H (0.013 mmol, 0.08 g). After completion of the reaction (monitored by TLC), the reaction mixture was cooled to room temperature, added H_2O (5 mL) and shaken for 3 min to dissolve PEG-OSO_3H. The crude product (insoluble in water) was filtered and recrystallized from hot ethanol (3 mL) to afford the pure product (**3a).** In order to recover the catalyst, the filtrate was evaporated under reduced pressure and recovered catalyst was washed with diethyl ether twice and dried. The recovered catalyst was reused for seven runs adopting the identical protocol without significant loss in product yield (Table 4). It is worth mentioning here that for every cycle the catalyst was tested for the reaction at microscale.

Table 4 Recycling data of the catalyst for the model reaction.[a]

Runs	Catalyst recycles	Time[b]	Yield[c]
1	0	2 min	99
2	1	2 min	99

3	2	2 min	99
4	3	2 min	98
5	4	4 min	96
6	5	4 min	96
7	6	4 min	95

[a] Reaction conditions: terephthaldehyde (**1**, 1.00 mmol, 0.134 g), Diethyl malonate (**2a**, 2.00 mmol, 0.32 g), catalyst (0.013 mmol, 0.08 g), thermal solvent-free condition, T=70°C.

[b] Reaction progress monitored by TLC.

[c] Isolated yields.

Identity of the recovered catalyst was checked by powder XRD (Fig. 2 b) and SEM (Fig. 6) analysis. It was found that peaks remained the same and there was no change in the morphology of the catalyst as compared to the fresh catalyst. These data established that PEG-OSO_3H is not damaged upon its reuse as a homogeneous catalyst.

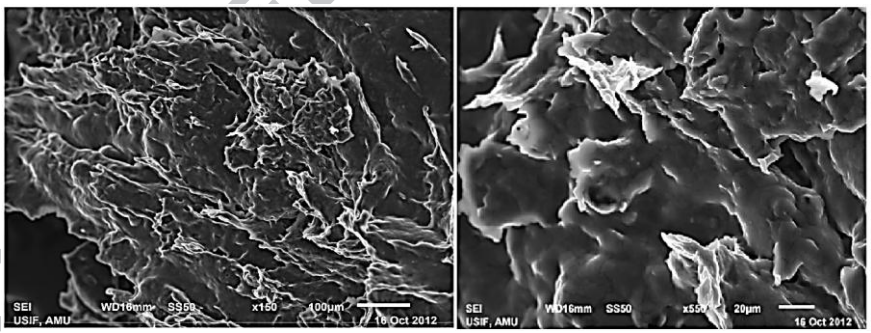

Fig. 6. SEM images of the recovered catalyst (PEG-OSO_3H) at different magnifications.

General procedure for the synthesis of bis-Knoevenagel products under solvent-free conditions

A mixture of terephthaldehyde/isophthalaldehyde **1a-b** (1.00 mmol, 0.134 g), acyclic and cyclic active methylene compounds **2a–n** (2.00 mmol) and PEG-OSO_3H (0.013 mmol, 0.08 g) were mixed thoroughly using a mortar and pestle. The reaction mixture was then transferred to an open Pyrex 100 mL beaker and heated at 70 ˚C for the given time (Table 5).

After completion of the reaction (monitored by TLC), the reaction mixture was cooled to room temperature, added H_2O (5 mL) and shaken for 3 min to dissolve PEG-OSO_3H. The crude product (insoluble in water) was filtered and recrystallized from hot ethanol (3 mL) to afford the pure product (**3a-r).** In order to recover the catalyst, the filtrate was evaporated under reduced pressure and recovered catalyst was washed with diethyl ether twice (2 mL) and reused after drying under reduced pressure.

Spectroscopy data of compounds:

Tetraethyl 2,2'-(1,4-phenylenebis(methanylylidene))dimalonate **(3a)**

Yellow solid; m.p. 125-127 °C; IR (KBr) cm^{-1}: 1628 (C=C), 1726 (COO). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.26-1.36 (12H, m, 4 x CH_3), 4.28-4.36 (8H, m, 4 x CH_2), 7.46 (4H, s, C_6H_4), 7.69 (2H, s, -CH=C). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.10 (2 x CH_3), 61.84 (2 x CH_2), 127.61 (2 x =C), 129.70, 134.80 (Ar-C), 140.65(2 x CH=), 163.62, 166.29 (4 x COO). ESI-MS: (*m/z*) 419.2 (M^+). Anal. Calcd. For $C_{22}H_{26}O_8$: C, 63.21; H, 6.22; found: C, 63.18; H, 6.26.

Tetraethyl 2,2'-(1,3-phenylenebis(methanylylidene))dimalonate **(3b)**

White solid; m.p. 121-123 °C; IR (KBr) cm^{-1}: 1611 (C=C), 1721 (COO). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.23-1.38 (12H, m, 4 x CH_3), 4.26-4.34 (8H, m, 4 x CH_2), 7.21-7.43 (3H, m, C_6H_4), 7.62 (1H, s, C_6H_4), 8.12 (2H, s, -CH=C). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.98 (2 x CH_3), 61.14 (2 x CH_2), 125.13 (2 x =C), 128.20, 133.0, 134.03 (Ar-C), 142.16(2 x CH=), 164.02, 165.19 (4 x COO). ESI-MS: (*m/z*) 419.1 (M^+). Anal. Calcd. For $C_{22}H_{26}O_8$: C, 63.21; H, 6.22; found: C, 63.18; H, 6.26.

(2E,2'E)-diethyl 2,2'-(1,4-phenylenebis(methanylylidene))bis(3-oxobutanoate) **(3c)**

Shining red solid; m.p. 131-133 °C; IR (KBr) cm^{-1}: 1603 (C=C), 1662 (CO), 1726 (COO). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.26 (6H, m, 2 x CH_3), 4.32 (4H, m, 2 x CH_2), 7.49 (4H, s, C_6H_4), 10.04 (2H, s, -CH=C). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.15 (2 x CH_3), 31.23 (2 x

CH_3), 61.91(2 x CH_2), 127.84, 130.0(Ar-C), 135.59 (2 x =C), 139.67(2 x CH=), 191.87 (2 x CO), 194.30 (2 x COO). ESI-MS: (*m/z*) 359.1 (M^+). Anal. Calcd. For $C_{20}H_{22}O_6$: C, 67.10; H, 6.15; found: C, 67.07; H, 6.12.

3,3'-(1,4-phenylenebis(methanylylidene))bis(pentane-2,4-dione) **(3d)**

Dark red crystals; m.p. >300 °C; IR (KBr) cm^{-1}: 1603 (C=C), 1698 (CO). ^1H NMR (400 MHz, $CDCl_3$): δ = 2.39 (12H, s, 4 x CH_3), 7.47 (4H, s, C_6H_4), 10.02 (2H, s, -CH=C). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 15.21 (4 x CH_3), 126.3, 128.0(Ar-C), 133.19 (2 x =C), 138.29(2 x CH=), 165.81 (4 x CO). ESI-MS: (*m/z*) 299.1 (M^+). Anal. Calcd. For $C_{18}H_{18}O_4$: C, 72.54; H, 6.04; found: C, 72.57; H, 6.07.

2.3.4. 2,2'-(1,4-phenylenebis(methanylylidene))dimalononitrile **(3e)**

White solid; m.p. 205-207 °C (lit. 206-208 °C)[3]; IR (KBr) cm^{-1}: 1635 (C=C), 2235 (CN). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.19 (4H, s, C_6H_4), 10.12 (2H, s, -CH=C). ^{13}C NMR (100 MHz, DMSO-d_6): *δ* = 110.21 (2 x =C), 114.6 (4 x CN), 129.83, 130.10 (Ar-C), 139.65 (2 x CH=). ESI-MS: (*m/z*) 231.1 (M^+). Anal. Calcd. For $C_{14}H_6N_4$: C, 73.11; H, 2.61; N, 24.34; found: C, 73.07; H, 2.64; N, 24.30.

2,2'-(1,4-phenylenebis(methanylylidene))bis(1H-indane-1,3(2H)-dione) **(3f)**

Green solid; m.p. 257–259 °C; IR (KBr) cm^{-1}: 1602 (C=C), 1693 (CO). ^1H NMR (400 MHz, DMSO-d_6): δ = 7.07-7.38 (8H, m, Ar-C), 7.45 (4H, s, C_6H_4), 8.10 (2H, s, -CH=C). ^{13}C NMR (100 MHz, DMSO-d_6): *δ* = 104.71 (2 x =C), 123.10, 126.72, 127.5, 131.91 (Ar-C), 137.91 (2 x CH=), 190.13 (4 x CO). ESI-MS: (*m/z*) 391.6 (M^+). Anal. Calcd. For $C_{26}H_{14}O_4$: C, 80.07; H, 3.59; found: C, 80.10; H, 3.57.

2,2'-(1,3-phenylenebis(methanylylidene))bis(1H-indane-1,3(2H)-dione) **(3g)**

Greenish yellow solid; m.p. >300 °C; IR (KBr) cm^{-1}: 1587 (C=C), 1690 (CO). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.32-7.67 (3H, m, C_6H_4), 7.94 (1H, s, C_6H_4), 8.18 (2H, s, -CH=C). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 103.27 (2 x =C), 124.15, 125.17, 127.5, 133.01 (Ar-C), 139.21

(2 x CH=), 191.23 (4 x CO). ESI-MS: (*m/z*) 391.1 (M^+). Anal. Calcd. For $C_{26}H_{14}O_4$: C, 80.07; H, 3.59; found: C, 80.10; H, 3.57.

4,4'-(1,4-phenylenebis(methanylylidene))bis(3-methyl-1-phenyl-1H-pyrazol-5(4H)-one **(3h)**

Reddish brown solid; m.p. >300 °C; IR (KBr) cm^{-1}: 1604 (C=C), 1684 (CO). ^1H NMR (400 MHz, $CDCl_3$): δ = 2.38 (6H, s, 2 x CH_3), 7.18-7.96 (14H, m, Ar-C, C_6H_4), 8.59 (2H, s, -CH=C). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.92 (2 x CH_3), 119.14 (2 x =C), 128.83, 129.0, 132.1, 133.50 (Ar-C), 139.10 (2 x CH=), 176.23 (2 x CO). ESI-MS: (*m/z*) 447.5 (M^+). Anal. Calcd. For $C_{28}H_{22}N_4O_2$: C, 75.40; H, 4.93; N, 12.55; found: C, 75.37; H, 4.96; N, 12.51.

2,2'-(1,4-phenylenebis(methanylylidene))bis(2H-benzo[b][1,4]thiazin-3(4H)-one) **(3i)**

Light yellow solid; m.p. 151 °C; IR (KBr) cm^{-1}: 1583 (C=C), 1662 (CO), 3202 (NH). ^1H NMR (400 MHz, DMSO-d_6): δ = 7.40 (4H, s, C_6H_4), 7.58-7.98 (8H, m, Ar-H,), 10.04 (2H, s, -CH=C), 10.57 (2H, s, NH). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 116.67 (2 x =C), 124.70, 129.33, 130.02, 132.50 (Ar-C), 139.31 (2 x CH=), 191.38 (2 x CO). ESI-MS: (*m/z*) 429.2 (M^+). Anal. Calcd. For $C_{24}H_{16}N_2O_4S_2$: C, 67.35; H, 3.74; N, 6.54; found: C, 67.37; H, 3.77; N, 6.57.

5,5'-(1,4-phenylenebis(methanylylidene))bis(2,2-dimethyl-1,3-dioxane-4,6-dione) **(3j)**

White soild ; m.p. 183–185 °C; IR (KBr) cm^{-1}: 1607 (C=C), 1722 (CO). ^1H NMR (400 MHz, DMSO-d_6): δ = 2.68 (12H, s, 4 x CH_3), 7.46 (4H, s, C_6H_4), 9.98 (2H, s, -CH=C). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 27.94 (4 x CH_3), 101.78 (2 x C2), 105.89 (2 x =C), 127.07, 129.87 (Ar-C), 137.09 (2 x CH=), 191.47 (4 x CO). ESI-MS: (*m/z*) 387.1 (M^+). Anal. Calcd. For $C_{20}H_{18}O_8$: C, 62.23; H, 4.66; found: C, 62.25; H, 4.64.

5,5'-(1,4-phenylenebis(methanylylidene))bis(1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione) **(3k)**

Light yellow powder; m.p. >300 °C; IR (KBr) cm^{-1}: 1578 (C=C), 1729 (CO). ^1H NMR (400 MHz, DMSO-d_6): δ = 1.24 (6H, s, 2 x CH_3), 2.11 (6H, s, 2 x CH_3), 7.48 (4H, s, C_6H_4), 8.11 (2H, s, -CH=C). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 29.4 (4 x CH_3), 119.40 (2 x =C),

129.5, 132.1 (Ar-C), 141.6 (2 x CH=), 150.7 (2 x C2), 172.3 (2 x C4, C6). ESI-MS: (*m/z*) 411.5 (M^+). Anal. Calcd. For $C_{20}H_{18}N_4O_6$: C, 58.59; H, 4.39; N, 13.65; found: C, 58.57; H, 4.34; N, 13.61.

5,5'-(1,3-phenylenebis(methanylylidene))bis(1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione) **(3l)**

Yellow powder; m.p. >300 °C; IR (KBr) cm^{-1}: 1579 (C=C), 1734 (CO). ^1H NMR (400 MHz, DMSO-d_6): δ = 2.10 (6H, s, 2 x CH_3), 3.14 (6H, s, 2 x CH_3), 8.15-8.17 (3H, m, C_6H_4), 8.41 (1H, s, C_6H_4), 8.48 (2H, s, -CH=C). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 30.1 (4 x CH_3), 120.24 (2 x =C), 128.1, 132.1, 133.6, 135.0 (Ar-C), 143.1 (2 x CH=), 149.3 (2 x C2), 174.2 (2 x C4, C6). ESI-MS: (*m/z*) 411.8 (M^+). Anal. Calcd. For $C_{20}H_{18}N_4O_6$: C, 58.59; H, 4.39; N, 13.65; found: C, 58.57; H, 4.34; N, 13.61.

5,5'-(1,4-phenylenebis(methanylylidene))bis(pyrimidine-2,4,6(1H,3H,5H)-trione)) **(3m)**

Light yellow powder; m.p. >300 °C; IR (KBr) cm^{-1}: 1570 (C=C), 1745 (CO), 3212 (NH). ^1H NMR (400 MHz, DMSO-d_6): δ = 8.06 (4H, s, C_6H_4), 8.32 (2H, s, -CH=C), 11.31 (2 x NH), 11.45 (2 x NH). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 121.10 (2 x CH=), 128.49, 135.64 (Ar-C), 137.16 (2 x =C), 153.4 (2 x C2), 164.3 (2 x C4, C6). ESI-MS: (*m/z*) 355.1 (M^+). Anal. Calcd. For $C_{16}H_{10}N_4O_6$: C, 54.28; H, 2.82; N, 15.82; found: C, 54.26; H, 2.84; N, 15.85.

5,5'-(1,4-phenylenebis(methanylylidene))bis(2-thioxodihydropyrimidine-4,6(1H,5H)-dione) **(3n)**

Orange powder; m.p. >300 °C; IR (KBr) cm^{-1}: 1574 (C=C), 1702 (CO), 3196 (NH). ^1H NMR (400 MHz, DMSO-d_6): δ = 8.12 (4H, s, C_6H_4), 8.33 (2H, s, -CH=C), 11.69 (2 x NH), 12.50 (2 x NH). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 122.2 (2 x CH=), 127.14, 133.16 (Ar-C), 138.13 (2 x =C), 166.9 (2 x C4, C6), 175.2 (2 x C2). ESI-MS: (*m/z*) 387.3 (M^+). Anal. Calcd. For $C_{16}H_{10}N_4O_4S_2$: C, 49.78; H, 2.59; N, 14.50; found: C, 49.75; H, 2.54; N, 14.53.

2,2',2'',2'''-(1,4-phenylenebis(methanetriyl))tetrakis(3-hydroxy-5,5-dimethylcyclohex-2-enone) **(3o)**

Shining white powder; m.p. 265 °C; IR (KBr) cm^{-1}: 1599 (CO), 3326 (OH). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.10 (12H, s, 4 x CH_3), 1.21 (12H, s, 4 x CH_3), 2.26-2.46 (16H, m, 8 x CH_2), 5.48 (2H, s, 2 x CH), 7.01 (4H, s, C_6H_4), 11.35 (2H, s, 2 x OH), 11.83 (2H, s, 2 x OH). ^{13}C NMR (100 MHz, DMSO-d_6): *δ* = 27.95 (8 x CH_3), 31.06 (4 x C5), 46.40 (2 x CH), 59.11(8 x CH_2), 114.65 (4 x C2), 126.04, 136.11(Ar-C), 162.19 (4 x C3), 187.96 (4 x C1). ESI-MS: (*m/z*) 659.3 (M^+). Anal. Calcd. For $C_{40}H_{50}O_8$: C, 73.01; H, 7.60; found: C, 73.04; H, 7.64.

2,2',2'',2'''-(1,3-phenylenebis(methanetriyl))tetrakis(3-hydroxy-5,5-dimethylcyclohex-2-enone) **(3p)**

White powder; m.p. 278 °C; IR (KBr) cm^{-1}: 1595 (CO), 3315 (OH). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.11 (12H, s, 4 x CH_3), 1.26 (12H, s, 4 x CH_3), 2.30-2.51 (16H, m, 8 x CH_2), 5.54 (2H, s, 2 x CH), 7.34-7.69 (3H, m, C_6H_4), 7.62 (1H, s, C_6H_4), 9.93 (2H, s, 2 x OH), 11.87 (2H, s, 2 x OH). ^{13}C NMR (100 MHz, DMSO-d_6): *δ* = 26.99 (8 x CH_3), 30.45 (4 x C5), 45.35 (2 x CH), 58.98 (8 x CH_2), 114.15 (4 x C2), 125.2, 126.04, 134.2, 136.11(Ar-C), 163.52 (4 x C3), 188.21 (4 x C1). ESI-MS: (*m/z*) 659.1 (M^+). Anal. Calcd. For $C_{40}H_{50}O_8$: C, 73.01; H, 7.60; found: C, 73.04; H, 7.64.

3,3',3'',3'''-(1,4-phenylenebis(methanetriyl))tetrakis(4-hydroxy-6-methyl-2H-pyran-2-one) **(3q)**

White powder; m.p. 253 °C; IR (KBr) cm^{-1}: 1705 (CO), 3421 (OH). ^1H NMR (400 MHz, DMSO-d_6): δ = 2.20 (12H, s, 4 x CH_3), 6.05 (4H, s, 4 x CH_5), 6.90 (2H, s, 2 x CH), 8.09 (4H, s, C_6H_4), 11.71 (4H, s, br, 4 x OH). ^{13}C NMR (100 MHz, DMSO-d_6): *δ* = 19.10 (4 x CH_3), 33.18 (2 x CH), 101.75 (4 x C3), 126.16, 129.79 (Ar-C), 160.66 (4 x C5), 166.59 (4 x C6), 168.18 (4 x C2), 192.20 (4 x C4). ESI-MS: (*m/z*) 603.6 (M^+). Anal. Calcd. For $C_{32}H_{26}O_{12}$: C, 63.84; H, 4.32; found: C, 63.87; H, 4.29.

3,3'-(1,4-phenylenebis((2-hydroxy-4-oxo-4H-chromen-3-yl)methylene))bis(4-hydroxy-2H-chromen-2-one) **(3r)**

Shining white powder; m.p. >300 °C; IR (KBr) cm^{-1}: 1719 (CO), 3380 (OH). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 6.44 (2H, s, 2 x CH), 7.15 (4H, s, C_6H_4), 7.34-7.96 (16H, m, Ar-H). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 35.18 (2 x CH), 99.48 (4 x C3), 123.74, 125.4, 128.3, 128.9, 132.13 (Ar-C), 167.23 (4 x C2), 183.12 (4 x C4). ESI-MS: (*m/z*) 747.2 (M^+). Anal. Calcd. For $C_{44}H_{26}O_{122}$: C, 70.84; H, 3.48; found: C, 70.87; H, 3.45.

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