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[2-(Sulfooxy) ethyl]sulfamic acid: efficient and recyclable catalyst for one-pot synthesis of dihydropyrimidinone derivatives in biginelli condensation

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A mild, eco-friendly and efficient methods has been developed for the preparation of dihydropyrimidinone derivatives in high yields via condensation of aromatic aldehyde, 1, 3-dicarbonyl compounds and urea or thiourea in the presence of [2-(sulfooxy) ethyl] sulfamic acid as a difunctional Bronsted Acid, recyclable and organocatalyst under solvent-free, reflux conditions and microwave irradiation that reaction times were shortened and yields were generally higher.

Keywords: Biginelli reaction, [2-(sulfooxy) ethyl] sulfamic acid, dihydropyrimidinones, green chemistry

INTRODUCTION

Green chemistry has a significant impact on various synthetic methods using less toxic solvents, environmental- friendly chemicals, decrease the stages of the synthetic routes and minimize waste as far as actually possible [1- 3]. In recent years, solvent –free and one-pot reactions using either organic or inorganic solid supports have attracted much attention of researchers [4]. Microwave irradiation provides an alternative to the conventional methods, for heating or introducing energy into the system. In addition, solvent free microwave irradiation processes are also clean, fast and efficient. These techniques have many advantages due to reduced pollution, low cost, shorter reaction times, easier workup, economic and eco-friendly and rapid optimisation of chemical reactions [5, 6].

The Biginelli reaction is a well-known multicomponent reaction involving a one-pot cyclocondensation [7,8] that italian chemist Pietro reported this reaction for the first time in 1893, which is one of the most important reactions for the synthesis of dihydropyrimidinones (DHPMs) based on acid-catalyzed condensation of ethyl acetoacetate, benzaldehyde, and urea in ethanol by refluxing the mixture and on cooling he obtained a solid crystalline product 3,4-dihydropyrimidin-2(1*H*)-one which often have low yields [9]. Then using microwave technique in Biginelli reaction was reported by Gupta and co-workers [10].

Dihydropyrimidinones show a varied range of remedial properties and pharmacological activities such as antimitotic, analgesic, antiviral, antihypertensive, antiproliferative, antitumor, anti-inflammatory, antibacterial, antifungal and antitubercular, anti HIV activity [11-13], hepatitis B replication inhibitors [14], and inhibitors of the fatty acid transporters [15].

Although varied catalysts in presence of techniques under reflux [16- 18] or solvent free conditions [19-21] and microwave [22-24] or ultrasonic irradiation [25,26] have been presented in accelerating this reaction, but also development these reactions with the use of newer reagents is important in higher efficiency and milder reaction condition.

[2-(Sulfooxy) ethyl] sulfamic acid (SESA) can be easily prepared from commercially available materials. Recently it has been used for the synthesis of quinoxaline derivatives [27], xanthene derivatives [28] and thiocyanation reactions [29]. Here, we report silica supported [2-(sulfooxy) ethyl] sulfamic acid as an alternative, efficient and recyclable catalyst for the Biginelli reaction under solvent-free, reflux conditions and microwave irradiation (Scheme 1).

EXPERIMENTAL

Melting points were measured on the Electro thermal 9100 apparatus and are uncorrected. Elemental analyses were performed using a Costech ECS 4010 CHNS-O analyzer at analytical laboratory of Science and Researchs Unite of Islamic Azad University. IR spectra were recorded on a Perkin-Elmer FT-IR Spectrum BX. Mass spectra were recorded on a FINNIGAN-MAT 8430 mass spectrometer operating at an ionization potential of 70 eV. NMR spectra were obtained on a Bruker 400 MHz FT spectrometer (^{1}H NMR at 400 Hz, ^{13}C NMR at 100 Hz) in DMSO-d6 using TMS as internal standard. Microwave reactions

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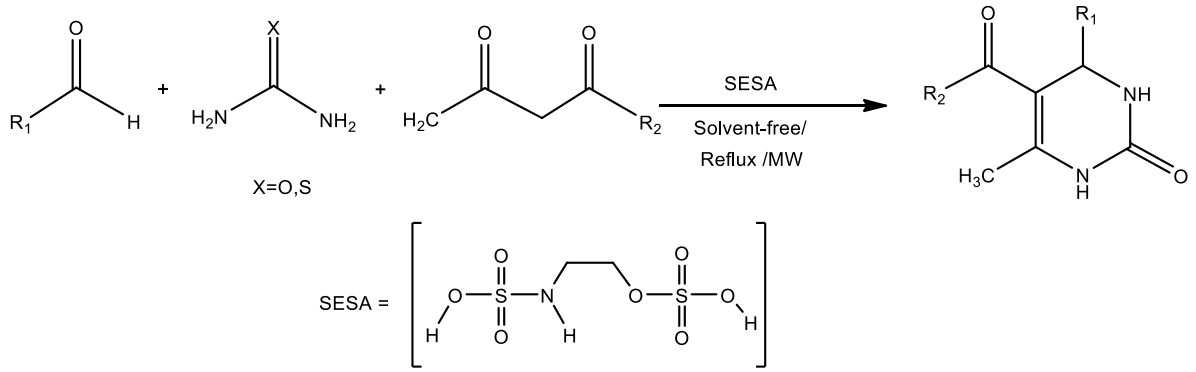
were carried out in microwave oven (2500 W power; Micro- Synth, Milestone). The chemicals used in this work purchased from Fluka (Buchs, Switzerland) and were used without further purification. The compound [2-(sulfooxy) ethyl] sulfamic acid was synthesized according to previous reported [27].



Scheme 1. Biginelli reaction catalyzed by SESA

Synthesis of dihydropyrimidinone: *general procedure*

(i) Conventional heating method: In a round-bottomed flask (10 mL), a mixture of an aromatic aldehyde (1 mmol), 1, 3-dicarbonyl compounds (1 mmol), urea/thiourea (1.3 mmol) and SESA (15 mol %) in H_2O (10 mL) was heated to reflux ($80^{\circ C}$) for the time indicated in (Table 2). The progress of the reaction was monitored by TLC. After cooling to room temperature, the reaction mixture was poured onto crushed ice (40 g) and stirred for 5–10min until free from organic material, The precipitate was filtered under suction, washed with H_2O (20 mL), then the solid was dissolved in hot ethanol and filtered to remove the catalyst and purified by recrystallization from ethanol to afford the desired dihydropyrimidinones.

(ii) Solvent-Free Conditions method: In a round-bottomed flask (10 mL), a mixture of an aromatic aldehyde (1 mmol), 1, 3-dicarbonyl compounds (1 mmol), urea/thiourea (1.3 mmol) and SESA (15 mol %) was heated to under solvent-free conditions at $80^{\circ C}$ for the time indicated in (Table 2). The progress of the reaction was monitored by TLC. After cooling to room temperature, the reaction mixture was poured onto crushed ice (40 g) and stirred for 5–10min until free from organic material, The precipitate was filtered under suction, washed with H_2O (20 mL), then the solid was dissolved in hot ethanol and filtered to remove the catalyst and purified by recrystallization from ethanol to afford the desired dihydropyrimidinones

(iii) Microwave irradiation method: A mixture of an aromatic aldehyde (1 mmol), 1, 3-dicarbonyl compounds (1 mmol), urea/thiourea (1.3 mmol) and SESA (15 mol %) in absence of solvent was placed in a screw capped Teflon vessel. Microwave irradiation was applied for 3 min at 90 °C (400 W). After the completion of reaction by TLC, the residue was washed was poured onto crushed ice (40 g) and stirred for 5–10min until free from organic material, The precipitate was filtered under suction, washed with H_2O (20 mL), then the solid was dissolved in hot ethanol and filtered to remove the catalyst and purified by recrystallization from ethanol to give pure product in high yield.

SELECTED CHARACTERIZATION DATA:

Ethyl-6-methyl-2-oxo-4-phenyl-1, 2, 3, 4-tetrahydropyrimidine-5-carboxylate **(Entry 1)**

White powder, IR (ν_{max}, cm^{-1}):3244, 3118, 2982, 2925, 1727, 1700, 1646, 1456, 1315, 1284, 1215, 1089; ^{1}H NMR (400 MHz, DMSO-d6): 1.10 (t, 3H, J= 7.0, CH_3CH_2O), 2.25 (s, 3H, CH_3), 3.99 (q, 2H, J=7.0 , CH_3CH_2O), 5.15 (d, 1H, J=3, CH), 7.32-7.23 (m, 5H, Ar-H), 7.73 (s, 1H, NH), 9.18 (s, 1H, NH) ppm; ^{13}C NMR (100 MHz, DMSO-d6): 14.04, 17.74, 53.93, 59.14, 99.23, 126.21, 127.22, 128.35, 144.83, 148.31, 152.09, 165.30 ppm; Anal. Calcd. For $C_{14}H_{16}N_2O_3$: C, 64.60; H, 6.20; N, 10.76; Found: C, 64.52; H, 6.17; N, 10.72%.

Ethyl-4-(4-methoxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate **(Entry 2)** White powder, IR (ν_{max}, cm^{-1}): 3247, 3115, 2955, 2832, 1724, 1703, 1649, 1507, 1456, 1275, 1221, 1089; ^{1}H NMR (400 MHz, DMSO-d6): 1.16 (t, 3H, J= 7.0, CH_3CH_2O), 2.30 (s, 3H, CH_3), 3.78 (s, 3H, OCH_3), 4.04 (q, 2H, J=7.0 , CH_3CH_2O), 5.15 (d, 1H, J=3.1, CH), 6.93 (d, 2H, J=8.6, Ar-H), 7.21 (d, 2H, J=8.6, Ar-H), 7.72 (s, 1H, NH), 9.20 (s, 1H, NH) ppm; ^{13}C NMR (100 MHz, DMSO-d6): 14.07, 17.71, 53.30, 55.02, 59.10, 99.54, 113.67, 127.35, 137.02, 147.96, 152.11, 158.41, 165.34 ppm; Anal. Calcd. For $C_{14}H_{16}N_2O_4$: C, 60.86; H, 5.84; N, 10.14; Found: C, 60.75; H, 5.94; N, 10.22%.

Ethyl-4-(2-chlorophenyl)-6-methyl-2-oxo-1, 2, 3, 4-tetrahydropyrimidine-5-carboxylate **(Entry 4)**

White powder, IR (ν_{max}, cm^{-1}): 3241, 3100, 2958, 1703, 1643, 1573, 1468, 1218, 1077; ^1H NMR (400 MHz, DMSO-d6): 0.99 (t, 3H, J= 7.0, CH_3CH_2O), 2.31 (s, 3H, CH_3), 3.90 (q, 2H, J=7.0 , CH_3CH_2O), 5.65 (d, 1H, J=2.76, CH), 7.41-7.27 (m, 4H, Ar-H), 7.71 (d, 1H, J=2.4, NH), 9.28 (s, 1H, NH) ppm; ^{13}C NMR (100 MHz, DMSO-d6): 13.85, 17.62, 51.47, 59.03, 97.88, 127.69, 128.74, 129.02, 129.31, 131.66, 141,68, 149.24, 151.33, 164.92 ppm; Anal. Calcd. For $C_{14}H_{15}ClN_2O_3$: C, 57.05; H, 5.13; N, 9.50; Found: C, 56.75; H, 5.15; N, 9.55%.

Ethyl- 4-(3, 5-dimethylphenyl)-6-methyl-2-oxo-1, 2, 3, 4-tetrahydropyrimidine-5-carboxylate **(Entry 6)**

White solid, IR (ν_{max}, cm^{-1}): 3301, 3244, 2925, 1700, 1652, 1613, 1537, 1447, 1227, 1086.; ^1H NMR (400 MHz, DMSO-d6): 1.11 (t, 3H, J=7.0, CH_3CH_2O), 2.23 (s, 6H, $2CH_3$), 2.24 (s, 3H, CH_3), 3.99 (q, 2H, J=7.0, CH_3CH_2O), 5.09 (d, 1H, J=3.2, CH), 6.84-6.94 (s, 3H, Ar-H), 7.67 (s, 1H, NH), 9.15 (d, 1H, J=1.2, NH) ppm; ^{13}C NMR (100 MHz, DMSO-d6): 14.04, 17.76, 20.99, 53.93, 59.11, 99.29, 123.99, 128.61, 137.18, 144.85, 148.04, 152.13, 165.33 ppm; Anal. Calcd. For $C_{16}H_{20}N_2O_3$: C, 66.65; H, 6.99; N, 9.72; Found: C, 66.78; H, 6.85; N, 9.80%.

Ethyl-6-methyl-2-oxo-4-(2-thienyl)-1, 2, 3, 4-tetrahydro-5- pyrimidinecarboxylate (**Entry 7**)

White solid, IR (ν_{max}, cm^{-1}): 3334, 3247, 3118, 2982, 1700, 1643, 1456, 1366, 1315, 1230, 1095; ^1H NMR (400 MHz, DMSO-d6): 1.25 (t, 3H J=7.0, CH_3CH_2O), 2.30 (s, 3H, CH_3), 4.15 (q, 2H J=7.0, CH_3CH_2O), 5.50 (d, 1H, J=3.4, CH), 6.97-7.44 (m, 3H, Ar-H), 7.99 (s, 1H, NH), 9.40 (s, 1H, NH) ppm; ^{13}C NMR (100 MHz, DMSO-d6): 14.12 , 17.64 , 49.31, 59.32, 99.73, 123.47, 124.60, 126.63, 148.62, 148.75 , 152.20 , 164.98 ppm; Anal. Calcd. For $C_{12}H_{14}N_2O_3S$: C, 54.12; H, 5.30; N, 10.52; S, 12.04; Found: C, 55.10; H, 5.15; N, 10.45; S, 11.98%.

Methyl -6-methyl-4-phenyl-2-thioxo-1, 2, 3, 4-tetrahydropyrimidine-5-carboxylate **(Entry 14)**

White solid, IR (ν_{max}, cm^{-1}): 3319, 3184, 2994, 1706, 1667, 1643, 1582, 1450, 1348, 1173; ^1H NMR (400 MHz, DMSO-d6): 2.37 (s, 3H, CH_3), 3.64 (s, 3H, OCH_3), 5.26 (d, 1H, J=3.6, CH), 7.38 (m, 5H, Ar-H), 9.75 (d, 1H, NH), 10.44 (s, 1H, NH) ppm; ^{13}C NMR (100 MHz, DMSO-d6): 17.18 , 51.08 , 53.85 , 100.39, 126.28, 127.68, 128.60, 143.26, 145.29 , 165.60 , 174.23 ppm; Anal. Calcd. For $C_{13}H_{14}N_2O_2S$: C, 59.52; H, 5.38; N, 10.68; S, 12.22; Found: C, 59.61; H, 5.25; N, 10.75; S, 12.18%.

5-Acetyl-6-methyl-4-phenyl-3, 4-dihydropyrimidin-2(1H)-one **(Entry 15)**

White powder, IR (ν_{max}, cm^{-1}): 3259, 3124, 2925, 1715, 1700, 1676, 1601, 1453, 1239, 1134; ^1H NMR (400 MHz, DMSO-d6): 2.17 (s, 3H, CH_3), 2.36 (s, 3H, CH_3), 5.33 (d, 1H, J=3.3, CH), 7.39-7.31 (m, 5H, Ar-H), 7.89 (s, 1H, NH), 9.24 (s, 1H, NH) ppm; ^{13}C NMR (100 MHz, DMSO-d6): 18.87, 30.27, 53.78, 109.55, 126.39, 127.30, 128.48, 144.21, 148.07, 152.09, 194.22 ppm; Anal. Calcd. For $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.17; Found: C, 67.85; H, 6.05; N, 12.15%.

5-Acetyl-4-(4-methoxyphenyl)-6-methyl-3, 4-dihydropyrimidin-2(1H)-one (**Entry 16**)

Yellow solid, IR (ν_{max}, cm^{-1}): 3343, 3274, 2955, 1715, 1682, 1594, 1456, 1384, 1236; ^1H NMR (400 MHz, DMSO-d6): 2.10 (s, 3H, CH_3), 2.28 (s, 3H, CH_3), 3.72 (s, 3H, CH_3O), 5.22 (d, 1H, J=3.2, CH), 6.81 (m, 4H, Ar-H), 7.79 (s, 1H, NH), 9.16 (s, 1H, NH) ppm; ^{13}C NMR (100 MHz, DMSO-d6): 18.82 , 30.23 , 53.64 , 54.93 , 109.36, 118.37, 129.62, 145.68, 148.13, 159.31, 152.14 , 194.27 ppm; Anal. Calcd. For $C_{14}H_{16}N_2O_3$: C, 64.60; H, 6.20; N, 10.76; Found: C, 64.65; H, 6.25; N, 10.72%.

5-Acetyl-4-(2-hydroxy-3-methoxyphenyl)-6-methyl-3, 4-dihydropyrimidin-2(1H)-one **(Entry 17)**

Cream powder, IR (ν_{max}, cm^{-1}): 3232, 3109, 2934, 2838, 1715, 1697, 1584, 1438, 1363, 1266, 1080 ^1H NMR (400 MHz, DMSO-d6): 1.66 (s, 3H, CH_3), 2.28 (s, 3H, CH_3), 3.73 (s, 3H, OCH_3), 4.62 (d, 1H, J=1.9, CH), 5.28 (s, 1H, OH), 6.87-6,79 (m, 3H, Ar-H), 7.11 (d, 1H, J=4.2, NH), 7.47 (s, 1H, NH) ppm; ^{13}C NMR (100 MHz, DMSO-d6): 23.56, 28.92, 46.79, 49.68, 55.38, 83.17, 111.51, 120.04, 120.29, 126.43, 140.09, 148.08, 154.65, 203.96 ppm; Anal. Calcd. For $C_{14}H_{16}N_2O_4$: C, 60.86; H, 5.84; N, 10.14; Found: C, 60.84; H, 5.90; N, 10.12%.

1-(6-Methyl-4-phenyl-2-thioxo-1, 2, 3, 4-tetrahydro-5-pyrimidinyl) ethanone (**Entry 18**): Yellow powder FT-IR (KBr, cm^{-1}): 3289, 3181, 2997, 1619, 1576, 1462, 1366, 1185. ^1H NMR (400 MHz, DMSO-d_6): δ = 2.24 (s, 3H), 2.41 (s, 3H), 5.37 (d, J = 3.7 Hz, 1H), 7.37 (m, 5H), 9.83 (d, 1H, NH), 10.36 (s, 1H, NH) ppm; ^{13}CNMR (100 MHz, DMSO-d_6): δ = 18.22, 30.40, 53.73, 110.43, 126.52, 127.67, 128.61, 142.88, 144.54, 174.04, 194.75 ppm. Anal. Calcd for $C_{13}H_{14}N_2OS$: C, 63.39; H, 5.73; N, 11.37; S, 13.02 %. Found: C, 63.45; H, 5.65; N, 11.42; S, 12.95 %.

RESULTS AND DISCUSSION

The syntheses of dihydropyrimidinones were performed in three different conditions conventional heating, solvent free and microwave irradiation using [2-(Sulfooxy) ethyl] sulfamic acid as a reusable eco-friendly catalyst. In all reactions it was found that the use of reflux, solvent free conditions and MW irradiation leads to a higher yield. To optimize the reaction conditions, the reaction of benzaldehyde, ethylacetoacetate and urea was used as a model reaction. Reactions at different conditions and various molar ratios of catalyst revealed that the best conditions to preparation the dihydroprymidinones compared to conventional heating were solvent-free at 80°C and microwave irradiation (400W) using catalytic amounts (15 mol %) of [2-(Sulfooxy) ethyl] sulfamic acid (Table 1). In the absence of the catalyst, the reaction was not completed even after 12 hours. The results are compared with conventional heating in Table 1. It seen that yields using microwave heating and solvent-free are generally higher than conventional heating and, importantly, reaction times are reduced from 5 h to under an hour.

Then, after optimization of the catalyst, the effect of varying the solvents and temperatures of reaction in presence of SESA catalyst and comparison the features of the previously reported procedure with those of the present methodology for the synthesis dihydropyrimidinones and thioderivatives on the model reaction of ethyl acetoacetate, benzaldehyde, and urea were evaluated. The results are exhibited in Table 2. At room temperature reaction in the presence and in the absence of solvent was sluggish **(**entry 8, 9, 10**),** the use of DMF or CH_2Cl_2 orC_2H_5OH as solvents at reflux, gave only low yields of product **(**entry 11**)**. Among the examined solvents H_2O at reflux **(**entry 12**)** obtained relatively good yields. Eventually microwave irradiation **(**entry 14**)** and 80°C **(**entry 16**)** under solvent-free conditions was the best choice among the conditions screened.

Table 1. Optimization of reaction conditions using of SESA for the synthesis of dihydropyrimidinones

Mol % of SESA	Conventional heating		Solvent-free		MWI	
	Time(h) Yield%[a]		Time(min) Yield%[a]		Time(min) Yield%[a]	
0	5	10	20	25	4	15
5	5	30	20	50	4	55
10	5	60	20	80	4	78
15	5	87	20	95	4	93
20	5	88	20	95	4	93

[a]Isolated yields.

The same model reaction, aromatic aldehydes substituted with electron-donating group or electron-withdrawing group proceeded successfully with urea or thiourea and 1, 3-dicarbonyl compounds (ketones /esters) and gave the dihydropyrimidinones in moderate to high yields using of SESA catalyst.

Table 2. Reaction of benzaldehyde , ethyl acetoacetate and urea under various reaction conditions and comparison for different catalyst used in synthesis of 5-(Ethoxycarbonyl)-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-ones.

Entry	Catalyst used	Time(h)	Solvent	Temp.	Yield %[a]	Ref.
1	$[Al(H_2O)_6](BF_4)_3$	20	CH_3CN	reflux	81	35
2	$SbCl_3$	18	CH_3CN	reflux	90	39
3	Ph_3p	10	-	100°C	70	37
4	Kaolin	2.5	AcOH	reflux	82	32
5	$TiCl_4$-$MgCl_2$	3	-	100°C	90	38
6	P_2O_5	10(min)	-	MWI	90	39
7	ASA	1	-	r.t	86	40
8	SESA	2.5	-	r.t	30	-
9	SESA	2.5	H_2O	r.t	25	-
10	SESA	2.5	DMF or CH_2Cl_2 or C_2H_5OH	r.t	25	-
11	SESA	5	DMF or CH_2Cl_2 orC_2H_5OH	reflux	55	-
12	SESA	5	H_2O	reflux	87	-
13	SESA	3(min)	H_2O	MWI	65	-
14	SESA	3(min)	-	MWI	96	-
15	SESA	20(min)	H_2O	80°C	60	-
16	SESA	20(min)	-	80°C	97,96,94,91,91[b]	-

[a]Isolated yields. [b]The same catalyst was used for each of five runs.

Under the optimized reaction conditions a mixture of variety of aldehydes whit 1, 3-dicarbonyl compounds (ethyl acetoacetate, methyl acetoacetate, acetyl acetone) and urea or thiourea in

the presence of SESA (15mol %), prepared a range of dihydropyrimidinones in excellent yields (Table 3). Also, the condensation reaction of isobutyraldehyde with ethyl acetoacetate and urea in presence of SESA presented lower yield and longer reaction time compared with aromatic aldehydes, which was due to the analysis or polymerization of aliphatic aldehydes under acidic conditions. We also tried to use benzoylacetone instead of ethyl acetoacetate in the model reaction. Unfortunately, our attempts to carry out the reaction in the presence of these reagents failed. These compounds (entry 10, 14, 18) have significant biological activity [28-41].

Table 3. Synthesis of different dihydropyrimidinones[a] in presence of 15% mol of SESA as a catalyst under different experimental conditions.

Entry	R_1	X	R_2	Conventional heating[b]		Solvent-free[c]		MWI[d]		M.p(°C)
				Time(h)	Yield%[e]	Time(min)	Yield%[e]	Time(min)	Yield%[e]	Found [ref]
1	C_6H_5	O	EtO	5	87	20	97	3	96	202-204[30]
2	4-$CH_3OC_6H_4$	O	EtO	5	82	20	93	3	95	202-203[30]
3	4-F C_6H_4	O	EtO	5	81	20	90	3	91	183-185[31]
4	2-Cl C_6H_4	O	EtO	5	75	20	85	3	90	215-217[30]
6	3,5- $(CH_3)_2$ C_6H_3	O	EtO	5	80	20	92	3	89	207-209[f]
7	2-Thienyl	O	EtO	5	70	20	95	3	90	211-213[33]
8	3-O_2N C_6H_4	O	EtO	5	75	20	86	3	89	226-227[30]
9	4-Cl C_6H_4	O	EtO	5	87	20	97	3	95	209-210[31]
10	C_6H_5	S	EtO	5	75	20	95	5	96	206-207[30]
11	C_6H_5	O	MeO	6	80	30	92	5	95	211-212[30]
12	4-$CH_3OC_6H_4$	O	MeO	6	81	30	93	5	96	204-205[30]
13	3-O_2N C_6H_4	O	MeO	6	75	30	92	5	94	280-283[30]
14	C_6H_5	S	MeO	6	70	30	95	5	92	226-228[30]
15	C_6H_5	O	Me	6	85	35	95	5	97	236-238[32]
16	4-$CH_3OC_6H_4$	O	Me	6	80	35	92	5	95	252-254[30]
17	2-HO,3-CH_3O- C_6H_3	O	Me	6	85	35	90	5	85	221-223[f]
18	C_6H_5	S	Me	6	85	35	95	5	93	220-221[30]

[a]Reaction conditions: aldehyde (1 mmol); urea or thiourea (1.3 mmol); 1,3- dicarbonyl compound (1 mmol); in water; [b]Refluxing at 80°C ; [c]Heating at 80°C. [d]Microwave irradiation (400 W, reaction time 3-5 min). [e]Isolated yields.[f]New compounds.

REUSABILITY OF THE CATALYST

The reusability of a catalyst is one of its most important benefits and makes it useful for commercial application. Thus, when optimizing the reaction conditions, the recycling of [2-(Sulfooxy) ethyl] sulfamic acid catalyst in the reaction of ethylacetoacetate, benzaldehyde with urea was investigated. After completion of the reaction to separate the catalyst from the product, the mixture was treated with hot ethanol and filtered. The residue, being the catalyst, was dried and reused. The catalyst can be used for 4 cycles without loss of its activity (Table 2)

CONCLUSION

In conclusion, we have developed very simple and efficient methods for the high-yielding synthesis of Biginelli Condensation by one-pot three-component coupling 1, 3-dicarbonyl compounds (ketones /esters), various aromatic aldehydes, and urea or thiourea using green recyclable SESA catalyst under solvent free conditions and MW irradiation. The simple

experimental procedure, Time minimizing, simple work-up and excellent yields of medicinally important nitrogen heterocycles are the advantages of the present method. These methods offered that the catalyst was highly active, stable, and recyclable from the reaction mixture and the lowest cost for its preparation was needed.

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