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Original article

Silica-bonded *N*-propyl sulfamic acid as an efficient recyclable catalyst for the synthesis of 3,4-dihydropyrimidin-2-(1*H*)-ones/thiones under heterogeneous conditions

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ABSTRACT

Silica-bonded *N*-propyl sulfamic acid (SBNPSA) catalyzed one-pot three component Biginelli condensation of different substituted aromatic aldehydes with ethyl acetoacetate and urea/thoiurea to the respective 3,4-dihydropyrimidin-2-(1*H*)-ones and thiones in environment friendly procedure is described. The facile reaction conditions, simple isolation and purification procedures of this method make it a good option for the synthesis of dihydropyrimidinones.

1. Introduction

Dihydropyrimidinones (DHPMs) and their derivatives have recently attracted great attention in synthetic organic chemistry due to their pharmacological and therapeutic properties, such as antibacterial and antihypertensive activity as well as behaving as calcium channel blockers, α-1a-antagonists [1] and neuropeptide Y (NPY) antagonists [2]. The biological activity of some alkaloids isolated recently has been attributed to a dihydropyrimidinone moiety [3]. The first synthesis of these compounds, reported by Biginelli [4] more than a century ago, makes use of the three components, one-pot condensation of a β-ketoester, an aldehyde and urea under strongly acidic conditions [5]. However, this method suffers from low yields in the case of substituted aromatic and aliphatic aldehydes [6]. Owing to the versatile biological activity of dihydropyrimidinones, development of an alternate synthetic methodology is of paramount importance.

In recent years, several synthetic procedures for the preparation of DHPMs have been reported including classical conditions with microwave irradiation [7] and by using Lewis acids, as well as protic acids and silica supported solid acids as promoters. Such promoters as conc. HCl [8], $BF_3{\cdot}OEt_2$ [9], PPE [10], KSF clay [11], $InCl_3$ [12], $LaCl_3$ [13,14], lanthanide triflate [15], H_2SO_4 [16], ceric ammonium nitrate (CAN) [17], $Mn(OAc)_3$ [18], ion-exchange resin [19], 1-*n*-butyl-3-methyl imidazolium tetrafluoroborate ($BMImBF_4$) [20], $BiCl_3$ [21], $LiClO_4$ [22], $InBr_3$ [23], $FeCl_3$ [24], $ZrCl_4$ [25], $Cu(OTf)_2$ [26], $Bi(OTf)_3$ [27], Silica gel-supported L-pyrrolidine-2-carboxylic acid-4-hydrogen sulfate [28], SBA-15 sulfonic acid [29], silica sulfuric acid [30], PEG–SO_3 [31], *p*-dodecylbenzenesulfonic acid (DBSA) [32], *etc.* have been found to be effective. Many of these methods involve expensive reagents, stoichiometric amounts of catalysts, strongly acidic conditions, long reaction times, unsatisfactory yields and incompatibility with other functional groups. Therefore, the development of a neutral alternative would extend the scope of the Biginelli reaction.

The heterogeneous catalysts, useful in making the organic transformations eco-friendly and economically viable, are now in high demand in academic laboratories and industries. Several heterogeneous catalysts are thus finding increasing applications in the field of catalysis [33]. Solid acid-based catalysts have offered simpler, more reactive and more benign alternatives than their homogeneous counterparts [34]. The expensive, organic polymer chain in traditional polymer supported catalysts has now been replaced by a silica chain having a covalently anchored organic spacer to create organic-inorganic hybrid (interphase) catalysts [35]. In these heterogeneous catalysts, the reactive centers are highly mobile similar to homogeneous catalysts and at the same time they can be recovered. Based on these concepts, various types

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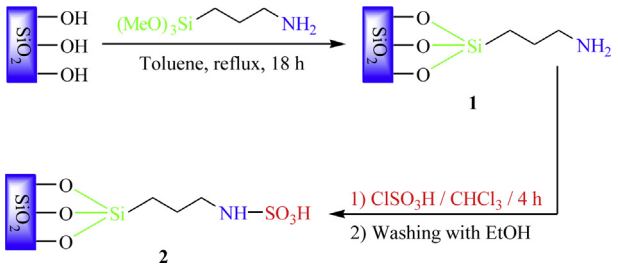


Scheme 1. Preparation of silica-bonded *N*-propyl sulfamic acid (2).

of functionalized, sulfonic acid silica, as Bronsted acid sites, have been considered in selectively catalyzing chemical transformations can be created [35,36].

The utility of heterogeneous catalysts can be improved by using high surface area materials, since the transport of the reactants to the active site on the particle surface can be enhanced by this method. Mesoporous silicas functionalized with sulfonic acid groups have been obtained by the condensation of alkoxy silanes and 3-mercapto propyl trimethoxy silanes, which are further oxidized to obtain their corresponding propyl sulfonic acid groups [37]. Shi *et al.* [38] had recently reported on a sulfonic acid-functionalized polypropylene fiber catalyst which was prepared by a simple process from inexpensive, readily available polypropylene fiber and the performance of the catalyst was tested in the successful completion of the Biginelli reaction. Excellent results, in terms of chemical yields, catalyst levels, work-up procedures and catalytic recyclability, are reported on the metal-free catalyzed, one-pot synthesis of a number of substituted 3,4-dihydropyrimidin-2-(1*H*)-ones/-thiones (DHPMs).

In this report, we describe a one-pot method for the Biginelli reaction using silica-bonded *N*-propyl sulfamic acid (SBNPSA) as a recyclable, heterogeneous, solid acid catalyst. The reaction involves the synthesis of a variety of 3,4-dihydropyrimidin-2(1*H*)-ones by the reaction of β-ketoester with urea (or thiourea) and various aromatic aldehydes in ethanol at reflux temperatures. The preparation procedure for catalyst **2** is outlined in Scheme 1 with slight modification than the previously reported method [35].

2. Experimental

2.1. Materials and methods

Reagents and solvents were of analytical grade or were purified by standard procedures prior to use. The ^{1}H NMR spectra were recorded on Varian FT-200 MHz (Gemini) in DMSO-d_6. Chemicals shifts are reported in parts per million (δ) relative to tetramethylsilane (δ 0.0) as an internal standard. Mass spectra were recorded under electron impact at 70 eV on Finnigan Mat 1020B mass spectrometer. Melting points were recorded on Buchi 535 and are uncorrected. Thin-layer chromatography was performed on Merck 60 F-254 silicagel gel plates. Products obtained are all known compounds and were identified by comparing their physical and spectral data with those reported in the literature.

2.2. Catalyst preparation

To a mixture of 3-aminopropylsilica **1** (5 g) in chloroform (20 mL), chlorosulfonic acid (1 g, 0.6 mL) was added dropwise at 0 °C over 2 h. After addition was complete, the mixture was stirred for 2 h until HCl gas evolution stopped. Then, the mixture was filtered and washed with ethanol (30 mL) and dried at room temperature to obtain silica-bonded *N*-propyl sulfamic acid (**2**) as a cream colored powder (5.13 g). The nitrogen content of 3-aminopropylsilica (**1**) and sulfur content of silica-bonded *N*-propyl sulfamic acid (**2**) determined by conventional elemental analysis were 5.13% and 9.29%, respectively.

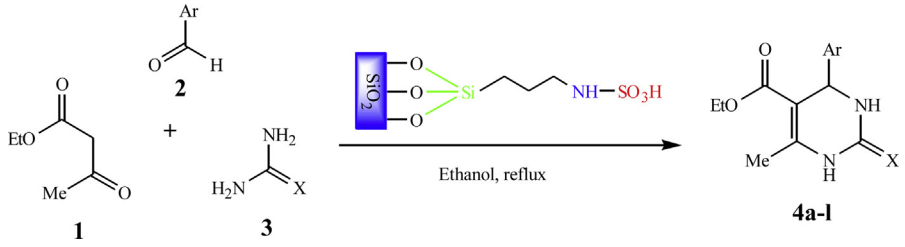
2.3. General procedure for the synthesis of 3,4-dihydropyrimidin-2(1H)-ones and -thiones ***4(a–n)*** using SBNPSA as catalyst

To a mixture of ethyl acetoacetate **1** (2.5 mmol), aromatic aldehyde **2** (2.5 mmol) and urea or thiourea **3** (2.5 mmol) in a round bottomed flask (100 mL), ethanol (15 mL) was added (Scheme 2). The reaction mixture was stirred at r.t. for 5 min and then catalyst **2** (0.2 g, 2.4 mol% of SO_3H) was added and the stirring was continued at 80 °C for an appropriate time. After completion of the reaction (monitored by TLC), the reaction mixture was filtered off. The product was obtained after removal of the solvent under reduced pressure followed by treatment with water and finally crystallization from EtOH. The residue was washed with warm ethanol, dried at 100 °C for 2 h and re-used for eight times without loss of significant activity.

5-(Ethoxycarbonyl)-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1*H*)-one (**4a**): ^{1}H NMR (DMSO-d_6): δ 1.09 (t, 3H, J = 7.1 Hz, OCH_2CH_3), 2.25 (s, 3H, CH_3), 3.97 (q, 2H, J = 7.1 Hz, OCH_2), 5.05 (d, 1H, J = 2.15 Hz, –CH), 7.28 (m, 5H, Ar–H), 7.75 (s, 1H, NH), 9.20 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 14.11, 17.94, 54.91, 60.05, 100.95, 112.85, 113.05, 125.15, 125.81, 129.05, 131.20, 150.16, 155.47, 163.81; IR (KBr, cm^{-1}): ν_{max} 3240, 1722, 1638; ESI-MS 261 (M + H); HRMS calcd. for $C_{14}H_{16}N_2O_3$: 260.1161, found: 260.1163.

5-(Ethoxycarbonyl)-4-(4-nitrophenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (**4b**): ^{1}H NMR (DMSO-d_6): δ 1.11 (t, 3H, J = 7.04 Hz, OCH_2CH_3), 2.32 (s, 3H, CH_3), 4.03 (q, 2H, J = 7.12 Hz, OCH_2CH_3), 5.78 (d, 1H, J = 2.28 Hz, –CH), 7.51 (d, 2H, J = 9.18 Hz, Ar–H), 7.69 (s, 1H, NH), 8.16 (d, 2H, J = 9.16 Hz, Ar–H), 9.05 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 14.22, 18.71, 55.81, 60.15, 101.60, 118.15, 130.37, 138.34, 152.26, 153.41, 159.15, 165.85; IR (KBr, cm^{-1}): ν_{max} 3235, 1740, 1631; ESI-MS 306 (M + H); HRMS calcd. for $C_{14}H_{15}N_3O_5$: 305.1012, found: 305.1010.

5-(Ethoxycarbonyl)-4-(3-chlorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (**4c**): ^{1}H NMR (DMSO-d_6): δ 1.10 (t, 3H, J = 7.14 Hz, OCH_2CH_3), 2.28 (s, 3H, CH_3), 3.88 (q, 2H, J = 7.16 Hz, OCH_2CH_3), 5.65 (d, 1H, J = 2.28 Hz, –CH), 7.25–7.41 (m, 4H,



Scheme 2. SBNPSA catalyzed synthesis of 3,4-dihydropyrimidin-2-(1*H*)-ones/thiones.

Ar–H), 7.61 (s, 1H, NH), 9.11 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 14.17, 18.60, 55.70, 60.20, 101.52, 126.312, 127.92, 128.42, 130.29, 135.51, 142.21, 153.23, 159.32, 165.75; IR (KBr, cm^{-1}): ν_{max} 3234, 1724, 1631; ESI-MS 295 (M + H); HRMS calcd. for $C_{14}H_{15}ClN_2O_3$: 294.0771, found: 294.0772.

5-(Ethoxycarbonyl)-4-(4-chlorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (**4d**): ^{1}H NMR (DMSO-d_6): δ 1.12 (t, 3H, *J* = 7.14 Hz, OCH_2CH_3), 2.30 (s, 3H, CH_3), 3.91 (q, 2H, *J* = 7.16 Hz, OCH_2CH_3), 5.70 (d, 1H, *J* = 2.28, –CH), 7.21 (d, 2H, *J* = 9.18, Ar–H), 7.69 (s, 1H, NH), 7.94 (d, 2H, *J* = 9.18, Ar–H), 9.16 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ: 14.18, 18.62, 55.72, 60.21, 101.55, 118.17, 130.32, 142.29, 152.31, 153.39, 159.17, 165.83; IR (KBr, cm^{-1}): ν_{max} 3225, 1720, 1615; ESI-MS 295 (M+H); HRMS calcd. for $C_{14}H_{15}ClN_2O_3$: 294.0771, found:294.0773.

5-(Ethoxycarbonyl)-4-(3-bromophenyl)-6-methyl-3, 4-dihydropyrimidin-2(1*H*)-one (**4e**): ^{1}H NMR (DMSO-d_6): δ 1.02 (t, 3H, *J* = 7.05 Hz, OCH_2CH_3), 2.30 (s, 3H, CH_3), 3.75 (q, 2H, *J* = 7.05 Hz, OCH_2CH_3), 5.41 (d, 1H, *J* = 2.25 Hz, –CH), 7.05–7.34 (m, 4H, Ar–H), 7.51 (s, 1H, NH), 9.05 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 14.16, 18.59, 55.74, 60.18, 101.57, 126.35, 127.82, 128.48, 130.32, 135.59, 143.94, 153.21, 159.30, 165.74; IR (KBr, cm^{-1}): ν_{max} 3212, 1731, 1620; ESI-MS 339 (M+H); HRMS calcd. for $C_{14}H_{15}BrN_2O_3$: 338.0266, found: 338.0268.

5-(Ethoxycarbonyl)-4-(4-methoxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (**4f**): ^{1}H NMR (DMSO-d_6) δ: 1.15 (t, 3H, *J* = 7.12 Hz, OCH_2CH_3), 2.33 (s, 3H, CH_3), 3.78 (s, 3H, –OCH_3), 4.06 (q, 2H, *J* = 7.12 Hz, OCH_2CH_3), 5.34 (d, 1H, *J* = 2.28 –CH), 6.82 (d, 2H, *J* = 8.60, Ar–H), 7.22 (d, 2H, *J* = 8.60, Ar–H), 7.76 (s, 1H, NH), 9.26 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ:14.32, 18.80, 55.23, 55.40, 60.17, 101.68, 114.06, 127.97, 136.22, 146.16, 153.59, 159.30, 165.87; IR (KBr, cm^{-1}): ν_{max} 3232, 1720, 1638; ESI-MS 291 (M+H); HRMS calcd. for $C_{15}H_{18}N_2O_4$: 290.1267, found: 290.1265.

5-(Ethoxycarbonyl)-4-(2,4-dichlorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (**4 g**): ^{1}H NMR (DMSO-d_6): δ 1.18 (t, 3H, *J* = 7.23 Hz, OCH_2CH_3), 2.64 (s, 3H, CH_3), 4.07 (q, 2H, *J* = 7.24 Hz, OCH_2CH_3), 5.92 (d, 1H, *J* = 2.30 Hz, –CH), 7.21–7.51 (m, 3H, Ar–H), 7.69 (s, 1H, NH), 9.16 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 14.20, 18.60, 55.75, 60.24, 101.56, 127.82, 128.91, 129.52, 131.29, 142.52, 143.25, 153.23, 159.32, 165.75; IR (KBr, cm^{-1}): ν_{max} 3255, 1731, 1651; ESI-MS 329 (M+H); HRMS calcd. for $C_{14}H_{14}C_{l2}N_2O_3$: 328.0381, found: 328.0379.

5-(Ethoxycarbonyl)-4-(3-nitrophenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (**4 h**): ^{1}H NMR (DMSO-d_6): δ 1.12 (t, 3H, *J* = 7.10 Hz, OCH_2CH_3), 2.25 (s, 3H, CH_3), 3.65 (q, 2H, *J* = 7.14 Hz, OCH_2CH_3), 5.71 (d, 1H, *J* = 2.20 Hz, –CH), 7.21–7.54 (m, 4H, Ar–H), 7.74 (s, 1H, NH), 9.26 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 14.16, 18.59, 55.74, 60.18, 101.57, 126.25, 127.45, 128.74, 130.56, 135.46, 144.81, 153.64, 159.45, 165.30; IR (KBr, cm^{-1}): ν_{max} 3229, 1724, 1630; ESI-MS 306 (M+H); HRMS calcd. for $C_{14}H_{15}N_3O_5$: 305.1012, found: 305.1013.

5-(Ethoxycarbonyl)-4-(4-flurophenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (**4i**): ^{1}H NMR (DMSO-d_6): δ 1.15 (t, 3H, *J* = 7.16 Hz, OCH_2CH_3), 2.41 (s, 3H, CH_3), 4.12 (q, 2H, *J* = 7.17 Hz, OCH_2CH_3), 5.88 (d, 1H, *J* = 2.25 Hz, –CH), 7.69 (s, 1H, NH), 7.81 (d, 2H, *J* = 8.5 Hz, Ar–H), 7.94 (d, 2H, *J* = 9.18 Hz, Ar–H), 9.16 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 14.18, 18.62, 55.72, 60.21, 101.55, 121.19, 132.42, 144.20, 153.39, 157.25, 159.17, 165.83; IR (KBr, cm^{-1}): ν_{max} 3250, 1741, 1654; ESIMS 279 (M+H); HRMS calcd. for $C_{14}H_{15}FN_2O_3$: 278.1067, found: 278.1069.

5-(Ethoxycarbonyl)-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1*H*)-thione (**4j**): ^{1}H NMR (DMSO-d_6): δ 1.11 (t, 3H, *J* = 7.21 Hz, OCH_2CH_3), 2.29 (s, 3H, CH_3), 4.12 (q, 2H, *J* = 7.24 Hz, OCH_2), 5.16 (d, 1H, *J* = 2.05 Hz, –CH), 7.51 (m, 5H, Ar–H), 7.81 (s, 1H, NH), 9.41 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 14.23, 17.91, 54.85, 60.15, 100.90, 112.84, 115.12, 125.15, 126.85, 129.64, 131.45, 150.27, 162.63, 180.25; IR (KBr, cm^{-1}): ν_{max} 3240, 1720, 1640, 1595, 1530; ESI-MS 277 (M+H); HRMS calcd. for $C_{14}H_{16}N_2O_2S$: 276.0932 found: 276.0932.

5-(Ethoxycarbonyl)-4-(4-methoxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-thione (**4k**): ^{1}H NMR (DMSO-d_6): δ 1.17 (t, 3H, *J* = 7.11 Hz, OCH_2CH_3), 2.37 (s, 3H, CH_3), 4.12 (s, 3H, –OCH_3), 4.15 (q, 2H, *J* = 7.10 Hz, OCH_2CH_3), 5.44 (d, 1H, *J* = 2.15 Hz, –CH), 7.11 (d, 2H, *J* = 8.15 Hz, Ar–H), 7.37 (d, 2H, *J* = 8.11 Hz, Ar–H), 7.84 (s, 1H, NH), 9.43 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 14.32, 18.05, 55.24, 55.49, 60.45, 101.84, 114.32, 127.74, 137.25, 147.15, 159.45, 165.62, 182.48; IR (KBr, cm^{-1}): ν_{max} 3240, 1725, 1635, 1574, 1540; ESI-MS 307 (M+H); HRMS calcd. for $C_{15}H_{18}N_2O_3S$: 306.1038, found: 306.1040.

5-(Ethoxycarbonyl)-4-(3-nitrophenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-thione (**4l**): ^{1}H NMR (DMSO-d_6): δ 1.15 (t, 3H, *J* = 7.14 Hz, OCH_2CH_3), 2.27 (s, 3H, CH_3), 4.02 (q, 2H, *J* = 7.11 Hz, OCH_2CH_3), 5.81 (d, 1H, *J* = 2.06 Hz, –CH), 7.23–7.37 (m, 4H, Ar–H), 7.78 (s, 1H, NH), 9.34 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 14.14, 18.60, 55.64, 60.21, 101.34, 126.25, 128.02, 129.32, 130.75, 135.65, 144.34, 160.40, 165.64, 182.65; IR (KBr, cm^{-1}): ν_{max} 3245, 1725, 1632, 1575, 1545; ESI-MS 322 (M+H); HRMS calcd. for $C_{14}H_{15}N_3O_4S$: 321.0783, found: 321.0781.

3. Results and discussion

In the FT-IR spectrum of catalyst (**2**), the major peaks for silica (SiO_2) are broad non-symmetric Si–O–Si stretching from 1300 cm^{-1} to 1010.6 cm^{-1} and symmetric Si–O–Si stretching near 880–852.5 cm^{-1}. For sulfuric acid functional group, the FT-IR absorption range of the O–S–O asymmetric and symmetric stretching modes lie in 1170 and 1060 cm^{-1}, respectively. FT-IR spectrum shows the overlap asymmetric and symmetric stretching bands of SO_2 with Si–O–Si stretching bands in the silica functionalized alkyl-sulfuric acid. The spectrum also shows a broad OH stretching absorption around 3600–2520 cm^{-1}.

The BET surface area and total pore volume of Silica-bonded *N*-propylsulfamic acid (2) were found to be 2.91 m^2 g^{-1} and 0.456 cm^3 g^{-1}, respectively.

In order to optimize the reaction conditions, the synthesis of compound **4f** was used as a model reaction. Therefore, a mixture of ethyl acetoacetate (2.5 mmol), 4-methoxybenzaldehyde (2.5 mmol), and urea (2.5 mmol) with different amounts of SBNPSA (Table 1) was selected. The efficiency of the reaction is mainly affected by the amount of the catalyst. No product could be detected in the absence of this catalyst even after 12 h (entry 1), while good results were obtained in the presence of SBNPSA. The optimal amount of the catalyst was 0.2 g (entry 5), whereas a higher amount of the catalyst did not increase the yield noticeably (entry 6).

As can be seen from (Table 2) compared to the classical Biginelli method, one additional important feature of the present protocol is the ability to tolerate variations in all three components

Table 1
Influence of the amount of SBNPSA on the synthesis of **4f** at reflux temperature.[a]

Entry	Catalyst	Amount of catalyst (g)	Time (h)	Yield (%)[b]
1	None	–	12	<10
2	SBNPSA	0.050	10	57
3	SBNPSA	0.1	8	71
4	SBNPSA	0.150	6	83
5	SBNPSA	0.2	4	94
6	SBNPSA	0.250	4	95

[a] The reaction conditions: ethyl acetoacetate **1** (2.5 mmol), 4-methoxybenzaldehyde **2** (2.5 mmol) and urea **3** (2.5 mmol) in ethanol (15 mL) under reflux temperature.
[b] Isolated yields.

Table 2
SBNPSA catalyzed synthesis of 3,4-dihydropyrimidin-2-(1*H*)-ones and thiones.

Entry	Ar	X	Product[a]	Yield (%)[b]	M.p (°C)	
					Found	Reported[c]
1	C_6H_5	O	**4a**	95	201–03	202–03
2	4-NO_2-C_6H_4	O	**4b**	92	209–10	208–10
3	3-Cl-C_6H_4	O	**4c**	90	192–93	191–93
4	4-Cl-C_6H_4	O	**4d**	91	214–15	215–16
5	3-Br-C_6H_4	O	**4e**	92	185–17	184–16
6	4-OCH_3-C_6H_4	O	**4f**	94	200–201	199–201
7	2,4-Cl-C_6H_3	O	**4g**	91	248–50	249–51
8	3-NO_2-C_6H_4	O	**4h**	93	227–28	227–29
9	4-F-C_6H_4	O	**4i**	93	183–85	185–86
10	C_6H_5	S	**4j**	95	209–10	208–10
11	4-OCH_3-C_6H_4	S	**4k**	94	151–52	150–52
12	3-NO_2-C_6H_4	S	**4l**	91	205–07	206–08

[a] All the products known, characterized by spectral analysis and by comparison of their physical properties with those of the authentic compounds.
[b] Isolated yields.
[c] Melting points of compounds are consistent with reported values [10,26,27,39].

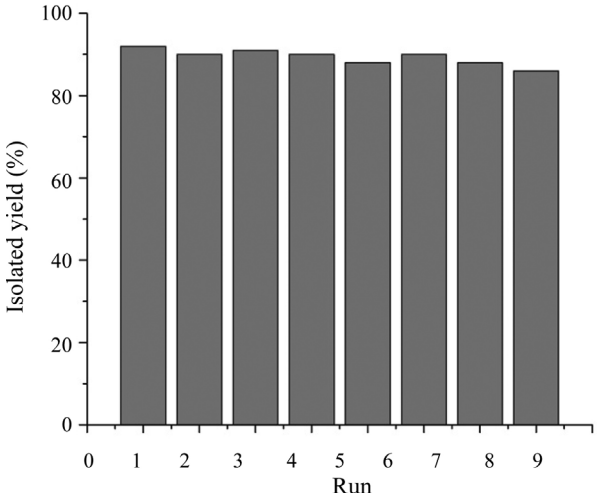


Fig. 1. Recycling of SBNPSA for model reaction.

Table 3
Comparison our results with results obtained by other groups.

Catalyst	Conditions	Yield (%)	Time (h)	Reference
Montmorillonit KSF	Solvent-free/130 °C	70–88	48	[12]
Yb(III)-resin	Solvent-free/120 °C	63–80	48	[20]
Ceric ammonium nitrate	Sonication/MeOH	84–92	5–7	[18]
$ZrCl_4$	Reflux EtOH	83–94	5–6	[26]
In(OTf)$_3$	Reflux EtOH/N_2	82–95	4–13.5	[40]
SBNPSA	Reflux EtOH	90–95	3–4	This work

simultaneously. Most importantly, many of the pharmacological relevant substitution patterns on the aromatic ring could be introduced without any reduction in efficiency. Aromatic aldehydes carrying either electron-donating or electron-withdrawing substituents afforded high yields of products in high purity. Thiourea has been used with similar success to provide the corresponding dihydropyrimidin-2(1*H*)-thiones (**4j–4l**), which are also of much interest with regard to biological activity. Thus, variation in all three components has been accomplished conveniently.

Table 3 summarizes our data (time, yield, reaction conditions) with results obtained by other groups. Based on this comparison, our method is simpler, more efficient for the synthesis of dihydropyrimidinone derivatives.

The recycling of the catalyst was also investigated. For this purpose, the same model reaction to synthesize the compound **4f** was again studied under the optimized conditions. After completion of the reaction, the catalyst was filtered, washed with warm ethanol, dried at 100 °C under vacuum for 2 h and reused for the same reaction process. As shown in Fig. 1, the catalyst could be reused for eight times with only slight reduction in the catalytic activity of the catalyst.

4. Conclusion

We have developed a simple, efficient, and green protocol for the synthesis of dihydropyrimidinones using silica-bonded *N*-propyl sulfamic acid catalyst under heterogeneous conditions. The short reaction times, simple work-up in the isolation of the products in high yields with high purity, mild reaction conditions, and recycability of supported catalyst are noteworthy features of this new procedure.

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