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Silica-bonded *N*-propylpiperazine sodium *n*-propionate as an efficient recyclable catalyst for one-pot synthesis of 2-amino-4-aryl-4*H*,8*H*-6-methyl-8-oxo-pyrano[3,2-*b*]pyran derivatives

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Abstract An efficient and convenient method for synthesis of a series of 2-amino-4-aryl-4*H*,8*H*-6-methyl-8-oxo-pyrano[3,2-*b*]pyran derivatives by one-pot, three-component reaction of an aromatic aldehyde, malononitrile or a cyanoacetate, and 5-hydroxy-2-methyl-4*H*-pyran-4-one (allomaltol) in the presence of a catalytic amount of silica-bonded *N*-propylpiperazine sodium *n*-propionate (SBPPSP), in aqueous ethanol, is described. The method has the advantages of short reaction time, mild reaction conditions, high yields, and convenience.

Keywords 5-Hydroxy-2-methyl-4*H*-pyran-4-one (allomaltol) · Silica-bonded *N*-propylpiperazine sodium *n*-propionate · Pyrano[3,2-*b*]pyran · Malononitrile · Cyanoacetate

Introduction

Multicomponent reactions (MCRs) have attracted much attention in combinatorial and medicinal chemistry. MCRs have significant advantages over conventional linear-type syntheses by virtue of their convergence, productivity, facile execution, and high yield [1]. MCRs are valuable and efficient synthetic methods for construction of highly complex molecules and for introducing molecular diversity in a single step by use of simple building blocks [2]. With a small set of starting

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materials, very large compound libraries can be developed in a short time then used in research on medicinal chemistry. Because of these advantages, development of new, environmentally benign MCRs has been recognized as one of the most important topics of green chemistry [3].

The 5-hydroxy-2-methyl-4*H*-pyran-4-one (allomaltol) structure is important in many natural and synthetic compounds. A series of 3-hydroxy-6-methyl-2-((4-substituted piperazin-1-yl)methyl)-4*H*-pyran-4-one derivatives has been synthesized by reaction of allomaltol with suitable piperazine derivatives under Mannich reaction conditions. The antibacterial activity of the compounds was assessed in vitro by using broth dilution for determination of minimum inhibitory concentration (MIC) [4]. Their inhibitory effects on the enzyme DNA gyrase were evaluated by use of a DNA gyrase supercoiling assay. Allomaltol and its derivatives also have a variety of other interesting bioactivity, for example anticancer [5], anticonvulsant [6], antidiabetic [7], antimalarial [8], and antimicrobial [9].

Many pyrans and fused pyran derivatives also have a wide range of pharmacological and biological activity, for example antiviral [10], anti-tuberculosis [11], anti-HIV [12], anti-Alzheimer [13], calcium channel antagonist [14], anti-fungal [15], anti-leukemic [16], anticonvulsant [17], antiproliferative [18], and anti-diabetic [19]. Pyranopyranones, also, are known for their biological properties, including antioxidant and cytotoxic activity [20]. Synthesis of the pyranopyranone structure is, thus, of great importance.

Methods have recently been developed for synthesis of pyrano[4,3-*b*]pyran derivatives by one-pot reaction of aromatic aldehydes with malononitrile and 4-hydroxy-6-methylpyran-2-one using catalysts such as KF/Al_2O_3 [21], alum ($KAl(SO_4)_2{\cdot}12H_2O$) [22], mesoporous NH_2-MCM-41 [23], ammonium acetate under solvent-free conditions using the grinding method [24], nano-CaO based on eggshell waste [25], and $[BMIm]BF_4$-LiCl [26]. We have synthesized a series of pyrano[4,3-*b*]pyran derivatives by using thiourea dioxide (TUD) in water [27].

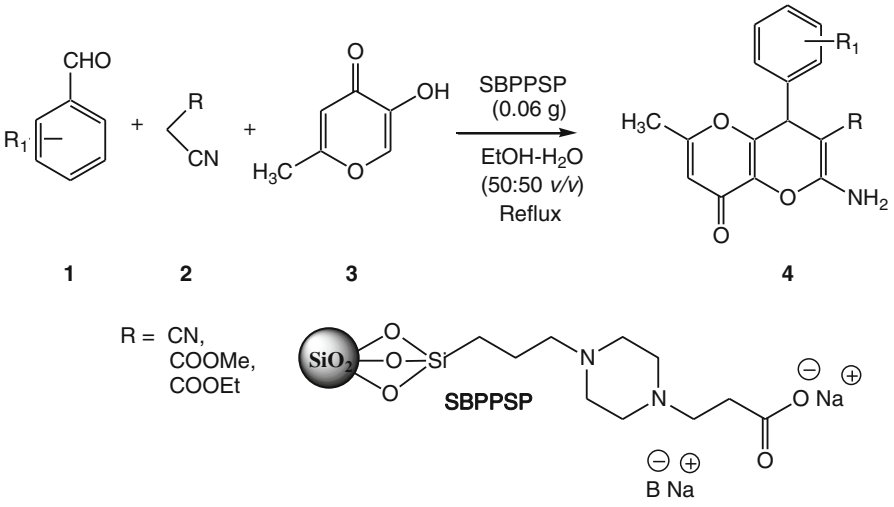
A survey of the literature revealed that few methods are available for synthesis of pyrano[3,2-*b*]pyran derivatives [28–30]. Li et al. [28] reported the synthesis of a series of 2-amino-4-aryl-4*H*,8*H*-6-methyl-8-oxo-pyrano[3,2-*b*]pyran derivatives from an aromatic aldehyde, malononitrile or a cyanoacetate, and allomaltol via a one-pot three-component reaction catalyzed by Et_3N in the ionic liquid $[bmim]BF_4$. Rahmati et al. [29] synthesized 2′-amino-6′-(hydroxymethyl)-8′*H*-spiro[indoline-3,4′-pyrano[3,2-*b*]pyran]-2,8′-diones by one-pot, three-component reaction of isatin, kojic acid, and an active methylene compound, for example ethyl cyanoacetate, methyl cyanoacetate, or malononitrile, in methanol, with a catalytic amount of 1,4-diazabicyclo[2.2.2]octane. Parthasarathy et al. [30] developed a $Cu(OTf)_2$-catalyzed efficient synthesis of spiropyrano[3,2-*b*]pyran-4(8*H*)-ones by one-pot, three component reaction of isatin, kojic acid, and an active methylene compound. Although these methods are useful, there is still a need to develop methods which proceed under mild reaction conditions.

The development of heterogeneous catalysts for organic synthesis has become a major topic of research. Economic and environmental concerns encourage use of heterogeneous catalysts for organic transformations. These catalysts are convenient to handle and easy to remove from the reaction mixture, making the experimental

procedure simple and eco-friendly [31]. Heterogeneous catalysts are known to suppress side reactions, resulting in better selectivity and product yield. Moreover, replacement of liquid acids and bases with the corresponding cleaner solid alternatives with such desirable characteristics as being non-stoichiometric, non-corrosive, and reusable is also attractive. Use of solid basic catalysts, for example hydrotalcites and basic zeolites has been studied in numerous reactions [32, 33]. Their use also avoids complex neutralization and separation steps, and the recovered catalysts can be readily regenerated for further use.

Silica-bonded *N*-propylpiperazine sodium *n*-propionate (SBPPSP) has recently received substantial attention as an efficient catalyst for construction of carbon–carbon and carbon–hetero atom bonds [34, 35], because of its eco-friendly nature, ease of handling, high reactivity, and easy work-up procedures. SBPPSP has been used as a recyclable heterogeneous solid-base catalyst for synthesis of 3,4-dihydropyrano[*c*]chromenes [34] and 4*H*-pyran derivatives [35]. An efficient heterogeneous palladium catalyst system has been developed by immobilization of Pd nanoparticles on SBPPSP. SBPPSP effectively stabilizes the Pd nanoparticles, improving their stability against aggregation. The catalytic activity of these catalysts has been investigated in the Sonogashira reaction [36].

In a continuation of our studies on the use of solid catalysts in organic transformations [37–41], we report an efficient method for synthesis of pyrano[3,2-*b*]pyran derivatives with SBPPSP as catalyst, by three-component condensation of an aromatic aldehyde, malononitrile or a cyanoacetate, and 5-hydroxy-2-methyl-4*H*-pyran-4-one in EtOH–H_2O (50:50 *v*/*v*) under reflux (Scheme 1).



Scheme 1 Preparation of 2-amino-4-aryl-4*H*,8*H*-6-methyl-8-oxo-pyrano[3,2-*b*]pyran derivatives from aromatic aldehydes, malononitrile/methyl cyanoacetate/ethyl cyanoacetate, and allomaltol, catalyzed by SBPPSP in EtOH–H_2O (50:50 *v*/*v*) under reflux

Experimental

Apparatus and analysis

Chemicals were purchased from Merck, Fluka, and Aldrich. All yields refer to isolated products unless otherwise stated. ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were obtained by use of a Bruker DRX-500 Avance at ambient temperature, with TMS as internal standard. FT-IR spectra were obtained as KBr discs on Shimadzu spectrometer. Mass spectra were obtained by use of a Varian Saturn 2000 GC–MS instrument. Elemental analysis were performed by use of a Perkin Elmer 2400 CHN elemental analyzer.

General procedure for synthesis of pyrano[3,2-*b*]pyran derivatives

A dry 50-mL flask was charged with a mixture of aromatic aldehyde **1** (1 mmol), malononitrile or cyanoacetate **2** (1 mmol), and allomaltol **3** (1 mmol) and the mixture was heated under reflux in EtOH–H_2O (50:50 *v*/*v*) containing SBPPSP (0.06 g, 5.2 mol%). After completion of the reaction, as indicated by thin-layer chromatography, the reaction mixture was filtered. The residue was washed with warm ethanol (3 × 30 mL) to separate the heterogeneous catalyst. The crude products precipitated on cooling of the filtrate and were purified by recrystallization from ethanol (95 %). The recovered catalyst was dried and reused for subsequent runs.

Spectral data for the synthesized compounds (**4a**–**z**)

*2-Amino-6-methyl-8-oxo-4-(4-chlorophenyl)-4H,8H-pyrano[3,2-b]pyran-3-carbonitrile (**4a**)*

IR (KBr, cm^{-1}): 3,450 and 3,370 (NH_2), 3,274 (Ar–H), 2,208 (CN), 1,707 (C=O); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.09 (s, 3H, CH_3), 4.67 (s, 1H, CH), 6.55 (s, 1H, =CH), 6.97 (s, 2H, NH_2), 7.22 (d, J = 8.0 Hz, 2H, Ar–H), 7.40 (d, J = 8.0 Hz, 2H, Ar–H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 21.3, 31.3, 54.9, 100.5, 111.1, 117.7, 126.2, 127.9, 129.1, 138.0, 143.9, 164.0, 168.5, 177.7 ppm; MS (ESI): *m*/*z* 315 $(M + H)^+$. Anal. Calcd. for $C_{16}H_{11}ClN_2O_3$ (%): C, 61.06; H, 3.52; N, 8.90. Found: C, 61.00; H, 3.47; N, 8.83.

*2-Amino-6-methyl-8-oxo-4-(3-methylphenyl)-4H,8H-pyrano[3,2-b]pyran-3-carbonitrile (**4b**)*

IR (KBr, cm^{-1}): 3,444 and 3,366 (NH_2), 3,282 (Ar–H), 2,217 (CN), 1,712 (C=O); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.09 (s, 3H, CH_3), 2.19 (s, 3H, CH_3), 4.71 (s, 1H, CH), 6.56 (s, 1H, =CH), 6.98 (s, 2H, NH_2), 7.33 (t, J = 8.0 Hz, 1H, ArH), 7.57 (tt, J = 8.2 Hz, J' = 1.3 Hz, 1H, Ar–H), 7.72 (t, J = 2.2 Hz, 1H, Ar–H), 7.83 (dd, dd, J = 8.2 Hz, J' = 2.2 Hz, J''= 1.3 Hz, 1H, Ar–H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 20.4, 21.5, 31.4, 55.5, 101.3, 111.3, 117.5, 126.4, 127.7, 129.3, 138.2,

143.8, 164.1, 168.7, 177.9 ppm; MS (ESI): *m/z* 295 $(M + H)^+$. Anal. Calcd. for $C_{17}H_{14}N_2O_3$ (%): C, 69.38; H, 4.79; N, 9.52. Found: C, 69.31; H, 4.73; N, 9.50.

*2-Amino-6-methyl-8-oxo-4-(2-fluorophenyl)-4H,8H-pyrano[3,2-b]pyran-3-carbonitrile (**4c**)*

IR (KBr, cm^{-1}): 3,439 and 3,384 (NH_2), 3,280 (Ar–H), 2,219 (CN), 1,711 (C=O); ^1H NMR (500 MHz, DMSO-d_6) δ: 2.10 (s, 3H, CH_3), 4.63 (s, 1H, CH), 6.55 (s, 1H, =CH), 6.93 (s, 2H, NH_2), 7.26–7.45 (m, 4H, Ar–H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 20.7, 31.6, 55.7, 100.9, 110.6, 117.4, 126.2, 128.2, 129.7, 138.1, 144.2, 163.7, 168.5, 178.2 ppm; MS (ESI): *m/z* 299 $(M + H)^+$. Anal. Calcd. for $C_{16}H_{11}FN_2O_3$ (%): C, 64.43; H, 3.72; N, 9.39. Found: C, 64.35; H, 3.70; N, 9.31.

*2-Amino-6-methyl-8-oxo-4-(4-nitrophenyl)-4H,8H-pyrano[3,2-b]pyran-3-carbonitrile (**4d**)*

IR (KBr, cm^{-1}): 3,452 and 3,382 (NH_2), 3,284 (Ar–H), 2,220 (CN), 1,705 (C=O); ^1H NMR (500 MHz, DMSO-d_6) δ: 2.12 (s, 3H, CH_3), 4.65 (s, 1H, CH), 6.57 (s, 1H, =CH), 6.88 (s, 2H, NH_2), 7.19 (d, $J = 8.2$ Hz, 2H, Ar–H), 7.39 (d, $J = 8.2$ Hz, 2H, Ar–H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 20.5, 30.8, 56.0, 100.8, 110.7, 118.2, 125.7, 128.3, 129.5, 137.6, 144.0, 163.6, 168.6, 178.3 ppm; MS (ESI): *m/z* 326 $(M + H)^+$. Anal. Calcd. for $C_{16}H_{11}N_3O_5$ (%): C, 59.08; H, 3.41; N, 12.92. Found: C, 59.00; H, 3.37; N, 12.88.

*2-Amino-6-methyl-8-oxo-4-(3-chlorophenyl)-4H,8H-pyrano[3,2-b]pyran-3-carbonitrile (**4e**)*

IR (KBr, cm^{-1}): 3,440 and 3,374 (NH_2), 3,283 (Ar–H), 2,210 (CN), 1,713 (C=O); ^1H NMR (500 MHz, DMSO-d_6) δ: 2.16 (s, 3H, CH_3), 4.64 (s, 1H, CH), 6.63 (s, 1H, =CH), 6.94 (s, 2H, NH_2), 7.20–7.38 (m, 4H, Ar–H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 21.0, 30.9, 56.3, 101.4, 110.6, 118.1, 125.9, 128.5, 129.2, 137.8, 144.1, 163.8, 169.3, 178.0 ppm; MS (ESI): *m/z* 315 $(M + H)^+$. Anal. Calcd. for $C_{16}H_{11}ClN_2O_3$(%): C, 61.06; H, 3.52; N, 8.90. Found: C, 61.02; H, 3.44; N, 8.87.

*2-Amino-6-methyl-8-oxo-4-(2-methoxyphenyl)-4H,8H-pyrano[3,2-b]pyran-3-carbonitrile (**4f**)*

IR (KBr, cm^{-1}): 3,443 and 3,373 (NH_2), 3,278 (Ar–H), 2,214 (CN), 1,710 (C=O); ^1H NMR (500 MHz, DMSO-d_6) δ: 2.12 (s, 3H, CH_3), 3.66 (s, 3H, OCH_3), 4.63 (s, 1H, CH), 6.63 (s, 1H, =CH), 6.92 (s, 2H, NH_2), 7.28–7.47 (m, 4H, Ar–H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 21.2, 30.6, 55.4, 56.2, 101.2, 110.8, 117.8, 126.3, 127.8, 129.2, 137.9, 144.5, 163.9, 169.0, 177.9 ppm; MS (ESI): *m/z* 311 $(M + H)^+$. Anal. Calcd. for $C_{17}H_{14}N_2O_4$ (%): C, 65.80; H, 4.55; N, 9.03. Found: C, 65.72; H, 4.50; N, 9.00.

*2-Amino-6-methyl-8-oxo-4-(2-methylphenyl)-4H,8H-pyrano[3,2-b]pyran-3-carbonitrile (**4g**)*

IR (KBr, cm^{-1}): 3,447 and 3,385 (NH_2), 3,277 (Ar–H), 2,213 (CN), 1,709 (C=O); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.08 (s, 3H, CH_3), (2.22 s, 3H, CH_3), 4.65 (s, 1H, CH), 6.58 (s, 1H, =CH), 6.89 (s, 2H, NH_2), 7.21–7.41 (m, 4H, Ar–H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 20.2, 21.4, 31.3, 54.7, 101.4, 111.2, 117.7, 126.5, 128.4, 130.2, 137.6, 143.7, 163.7, 169.2, 177.9 ppm; MS (ESI): *m*/*z* 295 $(M + H)^+$. Anal. Calcd. for $C_{17}H_{14}N_2O_3$ (%): C, 69.38; H, 4.79; N, 9.52. Found: C, 69.30; H, 4.77; N, 9.53.

*2-Amino-6-methyl-8-oxo-4-(4-fluorophenyl)-4H,8H-pyrano[3,2-b]pyran-3-carbonitrile (**4h**)*

IR (KBr, cm^{-1}): 3,441 and 3,384 (NH_2), 3,281 (Ar–H), 2,209 (CN), 1,712 (C=O); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.13 (s, 3H, CH_3), 4.64 (s, 1H, CH), 6.57 (s, 1H, =CH), 6.91 (s, 2H, NH_2), 7.23 (d, $J = 8.0$ Hz, 2H, Ar–H), 7.43 (d, $J = 8.0$ Hz, 2H, Ar–H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 20.8, 31.5, 55.3, 101.5, 110.4, 117.8, 125.7, 128.3, 130.3, 137.9, 143.8, 164.0, 169.0, 177.7 ppm; MS (ESI): *m*/*z* 299 $(M + H)^+$. Anal. Calcd. for $C_{16}H_{11}FN_2O_3$ (%): C, 64.43; H, 3.72; N, 9.39. Found: C, 64.32; H, 3.73; N, 9.35.

*2-Amino-6-methyl-8-oxo-4-(3-bromophenyl)-4H,8H-pyrano[3,2-b]pyran-3-carbonitrile (**4i**)*

IR (KBr, cm^{-1}): 3,449 and 3,373 (NH_2), 3,280 (Ar–H), 2,210 (CN), 1,714 (C=O); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.12 (s, 3H, CH_3), 4.67 (s, 1H, CH), 6.51 (s, 1H, =CH), 6.88 (s, 2H, NH_2), 7.23–7.45 (m, 4H, Ar–H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 21.3, 31.7, 55.7, 100.9, 111.0, 118.3, 125.8, 127.7, 130.4, 138.2, 143.9, 164.2, 168.7, 177.7 ppm; MS (ESI): *m*/*z* 361 $(M + H)^+$. Anal. Calcd. for $C_{16}H_{11}BrN_2O_3$ (%): C, 53.50; H, 3.09; N, 7.80. Found: C, 53.42; H, 3.02; N, 7.77.

*2-Amino-6-methyl-8-oxo-4-(3-nitrophenyl)-4H,8H-pyrano[3,2-b]pyran-3-carbonitrile (**4j**)*

IR (KBr, cm^{-1}): 3,436 and 3,372 (NH_2), 3,287 (Ar–H), 2,214 (CN), 1,708 (C=O); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.11 (s, 3H, CH_3), 4.70 (s, 1H, CH), 6.60 (s, 1H, =CH), 6.91 (s, 2H, NH_2), 7.32–7.50 (m, 4H, Ar–H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 20.7, 30.8, 56.0, 100.8, 111.2, 118.2, 126.3, 128.0, 130.0, 138.3, 143.8, 164.2, 168.9, 178.0 ppm; MS (ESI): *m*/*z* 326 $(M + H)^+$. Anal. Calcd. for $C_{16}H_{11}N_3O_5$ (%): C, 59.08; H, 3.41; N, 12.92. Found: C, 59.04; H, 3.42; N, 12.86.

*2-Amino-6-methyl-8-oxo-4-(3,4-dichlorophenyl)-4H,8H-pyrano[3,2-b]pyran-3-carbonitrile (**4k**)*

IR (KBr, cm^{-1}): 3,442 and 3,381 (NH_2), 3,284 (Ar–H), 2,216 (CN), 1,703 (C=O); ^1H NMR (500 MHz, DMSO-d_6) δ: 2.15 (s, 3H, CH_3), 4.68 (s, 1H, CH), 6.62 (s, 1H, =CH), 6.92 (s, 2H, NH_2), 7.17 (dd, 1H, $J = 8.7$ Hz, $J' = 2.0$ Hz, Ar–H), 7.30 (d, 1H, $J = 2.0$ Hz, Ar–H), 7.55 (d, 1H, $J = 8.7$ Hz, Ar–H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 20.6, 31.0, 56.1, 100.9, 110.6, 117.9, 126.2, 128.0, 129.5, 138.0, 143.7, 163.7, 168.8, 178.2 ppm; MS (ESI): *m/z* 350 $(M + H)^+$. Anal. Calcd. for $C_{16}H_{10}Cl_2N_2O_3$ (%): C, 55.04; H, 2.89; N, 8.02. Found: C, 54.95; H, 2.85; N, 8.03.

*2-Amino-6-methyl-8-oxo-4-(2,4-dichlorophenyl)-4H,8H-pyrano[3,2-b]pyran-3-carbonitrile (**4l**)*

IR (KBr, cm^{-1}): 3,447 and 3,384 (NH_2), 3,279 (Ar–H), 2,218 (CN), 1,711 (C=O); ^1H NMR (500 MHz, DMSO-d_6) δ: 2.11 (s, 3H, CH_3), 4.65 (s, 1H, CH), 6.55 (s, 1H, =CH), 6.90 (s, 2H, NH_2), 7.22 (d, 1H, $J = 8.3$ Hz, Ar–H), 7.41 (dd, 1H, $J = 8.3$ Hz, $J' = 2.4$ Hz, Ar–H), 7.58 (d, 1H, $J = 2.4$ Hz, Ar–H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 20.8, 31.1, 55.7, 100.7, 110.5, 117.6, 126.0, 128.4, 129.8, 138.1, 144.2, 163.7, 168.7, 178.1 ppm; MS (ESI): *m/z* 350 $(M + H)^+$. Anal. Calcd. for $C_{16}H_{10}Cl_2N_2O_3$ (%): C, 55.04; H, 2.89; N, 8.02. Found: C, 55.00; H, 2.87; N, 8.00.

*2-Amino-6-methyl-8-oxo-4-(4-chloro-3-nitrophenyl)-4H,8H-pyrano[3,2-b]pyran-3-carbonitrile (**4m**)*

IR (KBr, cm^{-1}): 3,453 and 3,378 (NH_2), 3,273 (Ar–H), 2,215 (CN), 1,715 (C=O); ^1H NMR (500 MHz, DMSO-d_6) δ: 2.13 (s, 3H, CH_3), 4.64 (s, 1H, CH), 6.52 (s, 1H, =CH), 6.93 (s, 2H, NH_2), 7.40 (d, 1H, $J = 2.0$ Hz, Ar–H), 7.53 (dd, 1H, $J = 8.6$ Hz, $J' = 2.0$ Hz, Ar–H), 7.82 (d, 1H, $J = 8.6$ Hz, Ar–H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 21.4, 31.3, 55.8, 101.3, 110.7, 117.6, 125.9, 128.3, 129.9, 137.5, 144.3, 163.9, 169.2, 178.0 ppm; MS (ESI): *m/z* 360.5 $(M + H)^+$. Anal. Calcd. for $C_{16}H_{10}ClN_3O_5$ (%): C, 53.42; H, 2.80; N, 11.68. Found: C, 53.35; H, 2.75; N, 11.64.

*2-Amino-6-methyl-8-oxo-4-(3-fluorophenyl)-4H,8H-pyrano[3,2-b]pyran-3-carbonitrile (**4n**)*

IR (KBr, cm^{-1}): 3,438 and 3,382 (NH_2), 3,281 (Ar–H), 2,216 (CN), 1,708 (C=O); ^1H NMR (500 MHz, DMSO-d_6) δ: 2.09 (s, 3H, CH_3), 4.63 (s, 1H, CH), 6.55 (s, 1H, =CH), 6.92 (s, 2H, NH_2), 7.26–7.44 (m, 4H, Ar–H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 21.0, 30.7, 55.5, 101.4, 111.3, 118.3, 125.7, 127.8, 130.1, 137.9, 144.0, 164.1, 169.0, 177.8 ppm; MS (ESI): *m/z* 299 $(M + H)^+$. Anal. Calcd. for $C_{16}H_{11}FN_2O_3$ (%): C, 64.43; H, 3.72; N, 9.39. Found: C, 64.41; H, 3.66; N, 9.38.

*Methyl 2-amino-6-methyl-8-oxo-4-(4-fluorophenyl)-4H,8H-pyrano[3,2-b]pyran-3-carboxylate (**4o**)*

IR (KBr, cm^{-1}): 3,428 and 3,360 (NH_2), 3,272 (Ar–H), 1,699 (C=O), 1,665 (C=O); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.21 (s, 3H, CH_3), 3.69 (s, 3H, CH_3), 4.72 (s, 1H, CH), 6.59 (s, 1H, =CH), 6.95 (s, 2H, NH_2), 7.32 (d, $J = 8.0$ Hz, 2H, Ar–H), 7.54 (d, $J = 8.0$ Hz, 2H, Ar–H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 19.5, 30.1, 53.3, 55.4, 102.6, 111.4, 126.0, 128.0, 128.5, 138.0, 143.4, 163.0, 166.6, 172.5, 176.2 ppm; MS (ESI): *m/z* 332 $(M + H)^+$. Anal. Calcd. for $C_{17}H_{14}FNO_5$ (%): C, 61.63; H, 4.26; N, 4.23. Found: C, 61.55; H, 4.21; N, 4.19.

*Methyl 2-amino-6-methyl-8-oxo-4-(3-nitrophenyl)-4H,8H-pyrano[3,2-b]pyran-3-carboxylate (**4p**)*

IR (KBr, cm^{-1}): 3,431 and 3,366 (NH_2), 3,277 (Ar–H), 1,707 (C=O), 1,671 (C=O); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.23 (s, 3H, CH_3), 3.60 (s, 3H, CH_3), 4.61 (s, 1H, CH), 6.55 (s, 1H, =CH), 6.93 (s, 2H, NH_2), 7.21-7.49 (m, 4H, Ar–H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 19.7, 30.6, 53.2, 55.5, 102.8, 111.5, 126.3, 127.8, 128.7, 138.1, 143.6, 163.5, 166.2, 172.6, 176.3 ppm; MS (ESI): *m/z* 359 $(M + H)^+$. Anal. Calcd. for $C_{17}H_{14}N_2O_7$ (%): C, 56.99; H, 3.94; N, 7.82. Found: C, 56.90; H, 3.89; N, 7.80.

*Methyl 2-amino-6-methyl-8-oxo-4-(2-chlorophenyl)-4H,8H-pyrano[3,2-b]pyran-3-carboxylate (**4q**)*

IR (KBr, cm^{-1}): 3,439 and 3,361 (NH_2), 3,273 (Ar–H), 1,701 (C=O), 1,673 (C=O); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.19 (s, 3H, CH_3), 3.63 (s, 3H, CH_3), 4.64 (s, 1H, CH), 6.57 (s, 1H, =CH), 6.87 (s, 2H, NH_2), 7.34-7.55 (m, 4H, Ar–H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 19.9, 30.3, 53.5, 55.3, 102.5, 111.0, 126.5, 127.7, 128.9, 137.5, 143.4, 163.3, 166.4, 172.7, 176.0 ppm; MS (ESI): *m/z* 348.5 $(M + H)^+$. Anal. Calcd. for $C_{17}H_{14}ClNO_5$ (%): C, 58.72; H, 4.06; N, 4.03. Found: C, 58.66; H, 4.02; N, 4.00.

*Methyl 2-amino-6-methyl-8-oxo-4-(3-bromophenyl)-4H,8H-pyrano[3,2-b]pyran-3-carboxylate (**4r**)*

IR (KBr, cm^{-1}): 3,444 and 3,372 (NH_2), 3,280 (Ar–H), 1,695 (C=O), 1,677 (C=O); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.16 (s, 3H, CH_3), 3.61 (s, 3H, CH_3), 4.70 (s, 1H, CH), 6.60 (s, 1H, =CH), 6.94 (s, 2H, NH_2), 7.24 (t, $J = 8.0$ Hz, 1H, ArH), 7.47 (tt, $J = 8.2$ Hz, $J' = 1.3$ Hz, 1H, Ar–H), 7.66 (t, $J = 2.2$ Hz, 1H, Ar–H), 7.76 (dd, dd, $J = 8.2$ Hz, $J' = 2.2$ Hz, $J'' = 1.3$ Hz, 1H, Ar–H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 20.2, 31.0, 53.6, 55.3, 102.6, 111.3, 126.4, 128.1, 128.8, 137.6, 143.3, 163.6, 166.3, 172.7, 176.5 ppm; MS (ESI): *m/z* 393 $(M + H)^+$. Anal. Calcd. for $C_{17}H_{14}BrNO_5$ (%): C, 52.06; H, 3.60; N, 3.57. Found: C, 52.01; H, 3.56; N, 3.53.

*Methyl 2-amino-6-methyl-8-oxo-4-(4-methylphenyl)-4H,8H-pyrano[3,2-b]pyran-3-carboxylate (**4s**)*

IR (KBr, cm^{-1}): 3,438 and 3,374 (NH_2), 3,274 (Ar–H), 1,703 (C=O), 1,669 (C=O); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.07 (s, 3H, CH_3), 2.15 (s, 3H, CH_3), 3.66 (s, 3H, CH_3), 4.63 (s, 1H, CH), 6.61 (s, 1H, =CH), 6.92 (s, 2H, NH_2), 7.23 (d, $J = 8.0$ Hz, 2H, Ar–H), 7.50 (d, $J = 8.0$ Hz, 2H, Ar–H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 20.0, 31.1, 53.3, 55.2, 102.7, 111.5, 126.2, 127.9, 128.7, 137.7, 143.4, 163.2, 166.7, 172.5, 176.4 ppm; MS (ESI): *m/z* 328 $(M + H)^+$. Anal. Calcd. for $C_{18}H_{17}NO_5$ (%): C, 66.05; H, 5.23; N, 4.28. Found: C, 65.97; H, 5.21; N, 4.24.

*Methyl 2-amino-6-methyl-8-oxo-4-(2-fluorophenyl)-4H,8H-pyrano[3,2-b]pyran-3-carboxylate (**4t**)*

IR (KBr, cm^{-1}): 3,442 and 3,370 (NH_2), 3,267 (Ar–H), 1,706 (C=O), 1,673 (C=O); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.14 (s, 3H, CH_3), 3.65 (s, 3H, CH_3), 4.69 (s, 1H, CH), 6.58 (s, 1H, =CH), 6.91 (s, 2H, NH_2), 7.16-7.35 (m, 4H, Ar–H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 19.7, 30.7, 53.2, 55.6, 102.4, 111.3, 126.3, 127.8, 128.5, 137.8, 143.5, 163.1, 166.3, 172.4, 176.2 ppm; MS (ESI): *m/z* 332 $(M + H)^+$. Anal. Calcd. for $C_{17}H_{14}FNO_5$ (%): C, 61.63; H, 4.26; N, 4.23. Found: C, 61.59; H, 4.23; N, 4.17.

*Ethyl 2-amino-6-methyl-8-oxo-4-(2,4-dichlorophenyl)-4H,8H-pyrano[3,2-b]pyran-3- carboxylate (**4u**)*

IR (KBr, cm^{-1}): 3,452 and 3,389 (NH_2), 3,289 (Ar–H), 1,712 (C=O), 1,670 (C=O); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.01 (t, 3H, $J = 7.0$ Hz, CH_3), 2.05 (s, 3H, CH_3), 3.77 (q, 2H, $J = 7.0$ Hz, CH_2), 4.67 (s, 1H, CH), 6.55 (s, 1H, =CH), 6.91 (s, 2H, NH_2), 7.16 (d, 1H, $J = 8.2$ Hz, Ar–H), 7.47 (dd, 1H, $J = 8.2$ Hz, $J' = 2.4$ Hz, Ar–H), 7.62 (d, 1H, $J = 2.4$ Hz, Ar–H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 14.5, 21.4, 31.6, 55.3, 58.3, 100.4, 110.3, 125.6, 128.2, 129.5, 135.2, 144.0, 164.2, 166.4, 172.1, 178.0 ppm; MS (ESI): *m/z* 397 $(M + H)^+$. Anal. Calcd. for $C_{18}H_{15}Cl_2NO_5$ (%): C, 54.56; H, 3.82; N, 3.54. Found: C, 54.50; H, 3.77; N, 3.50.

*Ethyl 2-amino-6-methyl-8-oxo-4-(3,4-dichlorophenyl)-4H,8H-pyrano[3,2-b]pyran-3-carboxylate (**4v**)*

IR (KBr, cm^{-1}): 3,449 and 3,390 (NH_2), 3,295 (Ar–H), 1,709 (C=O), 1,672 (C=O); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.03 (t, 3H, $J = 7.0$ Hz, CH_3), 2.11 (s, 3H, CH_3), 3.79 (q, 2H, $J = 7.0$ Hz, CH_2), 4.65 (s, 1H, CH), 6.54 (s, 1H, =CH), 6.91 (s, 2H, NH_2), 7.23 (dd, 1H, $J = 8.4$ Hz, $J' = 2.0$ Hz, Ar–H), 7.41 (d, 1H, $J = 2.0$ Hz, Ar–H), 7.57 (d, 1H, $J = 8.4$ Hz, Ar–H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 14.6, 21.6, 31.8, 55.7, 58.4, 100.6, 110.2, 125.5, 128.4, 129.6, 135.3, 143.7, 164.0, 166.3, 172.3, 178.2 ppm; MS (ESI): *m/z* 397 $(M + H)^+$. Anal. Calcd. for $C_{18}H_{15}Cl_2NO_5$ (%): C, 54.56; H, 3.82; N, 3.54. Found: C, 54.48; H, 3.79; N, 3.51.

*Ethyl 2-amino-6-methyl-8-oxo-4-(3-bromophenyl)-4H,8H-pyrano[3,2-b]pyran-3-carboxylate (**4w**)*

IR (KBr, cm^{-1}): 3,450 and 3,392 (NH_2), 3,293 (Ar–H), 1,710 (C=O), 1,675 (C=O); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.04 (t, 3H, $J = 7.0$ Hz, CH_3), 2.15 (s, 3H, CH_3), 3.83 (q, 2H, $J = 7.0$ Hz, CH_2), 4.63 (s, 1H, CH), 6.55 (s, 1H, =CH), 6.88 (s, 2H, NH_2), 7.20–7.48 (m, 4H, Ar–H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 14.7, 21.3, 31.5, 55.4, 58.6, 100.3, 110.3, 125.4, 128.2, 129.7, 135.4, 143.6, 164.4, 166.0, 172.5, 178.3 ppm; MS (ESI): *m/z* 407 $(M + H)^+$. Anal. Calcd. for $C_{18}H_{16}BrNO_5$ (%): C, 53.22; H, 3.97; N, 3.45. Found: C, 53.17; H, 3.95; N, 3.43.

*Ethyl 2-amino-6-methyl-8-oxo-4-(3-fluorophenyl)-4H,8H-pyrano[3,2-b]pyran-3-carboxylate (**4x**)*

IR (KBr, cm^{-1}): 3,457 and 3,387 (NH_2), 3,288 (Ar–H), 1,714 (C=O), 1,677 (C=O); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.07 (t, 3H, $J = 7.0$ Hz, CH_3), 2.14 (s, 3H, CH_3), 3.80 (q, 2H, $J = 7.0$ Hz, CH_2), 4.72 (s, 1H, CH), 6.53 (s, 1H, =CH), 6.93 (s, 2H, NH_2), 7.27–7.46 (m, 4H, Ar–H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 14.8, 21.5, 31.4, 55.6, 58.5, 100.5, 110.4, 125.3, 128.3, 129.8, 135.6, 143.5, 164.1, 166.2, 172.4, 178.4 ppm; MS (ESI): *m/z* 346 $(M + H)^+$. Anal. Calcd. for $C_{18}H_{16}FNO_5$ (%): C, 62.61; H, 4.67; N, 4.06. Found: C, 62.55; H, 4.62; N, 4.02.

*Ethyl 2-amino-6-methyl-8-oxo-4-(4-nitrophenyl)-4H,8H-pyrano[3,2-b]pyran-3-carboxylate (**4y**)*

IR (KBr, cm^{-1}): 3,455 and 3,377 (NH_2), 3,282 (Ar–H), 1,703 (C=O), 1,661 (C=O); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.00 (t, 3H, $J = 7.0$ Hz, CH_3), 2.09 (s, 3H, CH_3), 3.82 (q, 2H, $J = 7.0$ Hz, CH_2), 4.68 (s, 1H, CH), 6.52 (s, 1H, =CH), 6.92 (s, 2H, NH_2), 7.17 (d, $J = 8.2$ Hz, 2H, Ar–H), 7.40 (d, $J = 8.2$ Hz, 2H, Ar–H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 14.5, 21.4, 31.8, 55.7, 58.4, 100.7, 110.5, 125.4, 128.2, 129.5, 135.2, 143.8, 164.6, 166.6, 172.6, 178.3 ppm; MS (ESI): *m/z* 373 $(M + H)^+$. Anal. Calcd. for $C_{18}H_{16}N_2O_7$ (%): C, 58.06; H, 4.33; N, 7.52. Found: C, 58.00; H, 4.29; N, 7.48.

*Ethyl 2-amino-6-methyl-8-oxo-4-(4-methoxyphenyl)-4H,8H-pyrano[3,2-b]pyran-3-carboxylate (**4z**)*

IR (KBr, cm^{-1}): 3,446 and 3,380 (NH_2), 3,289 (Ar–H), 1,707 (C=O), 1,660 (C=O); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 1.02 (t, 3H, $J = 7.0$ Hz, CH_3), 2.06 (s, 3H, CH_3), 3.61 (s, 3H, OCH_3), 3.87 (q, 2H, $J = 7.0$ Hz, CH_2), 4.63 (s, 1H, CH), 6.58 (s, 1H, =CH), 6.93 (s, 2H, NH_2), 7.25 (d, $J = 8.1$ Hz, 2H, Ar–H), 7.43 (d, $J = 8.1$ Hz, 2H, Ar–H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 14.3, 21.5, 31.6, 55.6, 58.3, 100.9, 110.3, 125.6, 128.4, 129.7, 135.6, 143.5, 164.3, 166.2, 172.7, 178.7 ppm; MS (ESI): *m/z* 358 $(M + H)^+$. Anal. Calcd. for $C_{19}H_{19}NO_6$ (%): C, 63.86; H, 5.36; N, 3.92. Found: C, 63.78; H, 5.31; N, 3.88.

Results and discussion

We report herein an efficient and environmentally benign procedure for synthesis of 2-amino-4-phenyl-4*H*,8*H*-6-methyl-8-oxo-pyrano[3,2-*b*]pyran derivatives by three-component condensation of an aromatic aldehyde with malononitrile or a cyanoester and 5-hydroxy-2-methyl-4*H*-pyran-4-one catalyzed by SBPPSP in EtOH–H_2O (50:50 *v*/*v*) under reflux. SBPPSP was prepared as reported in the literature [34].

To determine the optimum conditions, we initially investigated reaction of 4-chlorobenzaldehyde (**1a**) with malononitrile and 5-hydroxy-2-methyl-4*H*-pyran-4-one in the solvents CH_3CN, $CHCl_3$, MeOH, EtOH, and H_2O under reflux, with SBPPSP (0.06 g) as catalyst, as model reaction. When an aprotic polar solvent, for example CH_3CN, was used the reaction afforded the corresponding pyrano[3,2-*b*]pyran **4a** in modest yield after reflux for 90 min (Table 1, entry 1). However, reactions in protic solvents, for example EtOH or H_2O, under reflux gave better yields (Table 1, entries 4 and 5). The model reaction was also examined under solvent-free conditions at 80 °C and gave **4a** in 55 % yield after 70 min (Table 1, entry 6). When the amount of catalyst was increased to 0.08 g and the temperature

Table 1 Optimization of reaction conditions for the synthesis of **4a**

Entry	Catalyst	Amount of catalyst	Solvent	Temperature (°C)	Time (min)	Yield (%)[a]
1	SBPPSP	0.06 g	CH_3CN	Reflux	90	43
2	SBPPSP	0.06 g	$CHCl_3$	Reflux	90	55
3	SBPPSP	0.06 g	MeOH	Reflux	30	81
4	SBPPSP	0.06 g	EtOH	Reflux	30	84
5	SBPPSP	0.06 g	H_2O	Reflux	30	77
6	SBPPSP	0.06 g	Solvent-free	80	70	55
7	SBPPSP	0.06 g	Solvent-free	100	70	81
8	SBPPSP	0.08 g	Solvent-free	80	70	77
9	SBPPSP	0.08 g	Solvent-free	100	70	84
10	SBPPSP	0.06 g	EtOH–H_2O (30:70 *v*/*v*)	Reflux	25	77
11	SBPPSP	0.06 g	EtOH–H_2O (50:50 *v*/*v*)	Reflux	15	94
12	SBPPSP	0.06 g	EtOH–H_2O (70:30 *v*/*v*)	Reflux	25	79
13	SBPPSP	0.04 g	EtOH–H_2O (50:50 *v*/*v*)	Reflux	20	80
14	SBPPSP	0.02 g	EtOH–H_2O (50:50 *v*/*v*)	Reflux	30	62
15	SBPPSP	0.08 g	EtOH–H_2O (50:50 *v*/*v*)	Reflux	15	94
16	PNPS	0.06 g	EtOH–H_2O (50:50 *v*/*v*)	Reflux	90	77
17	KH_2PO_4	10 mol%	EtOH–H_2O (50:50 *v*/*v*)	Reflux	60	61
18	NH_4OAc	10 mol%	EtOH–H_2O (50:50 *v*/*v*)	Reflux	60	55
19	TBAF	10 mol%	EtOH–H_2O (50:50 *v*/*v*)	Reflux	40	73
20	HMTA	10 mol%	EtOH–H_2O (50:50 *v*/*v*)	Reflux	60	74

Reaction conditions: 4-chlorobenzaldehyde (1 mmol), allomaltol (1 mmol), and malononitrile (1 mmol), solvent 5 mL, reflux

[a] Isolated yields

Table 2 Preparation of 2-amino-4-aryl-4*H*,8*H*-6-methyl-8-oxo-pyrano[3,2-*b*]pyran derivatives from aromatic aldehydes, malononitrile/methyl cyanoacetate/ethyl cyanoacetate, and allomaltol catalyzed by SBPPSP in EtOH–H_2O (50:50 *v*/*v*)

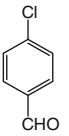
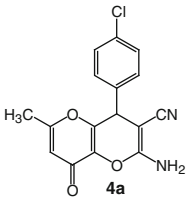
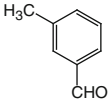
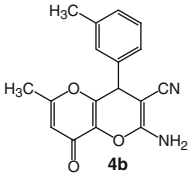
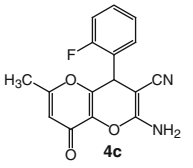
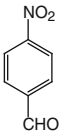
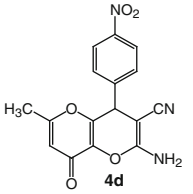
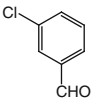
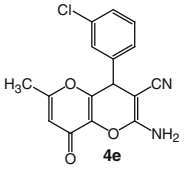
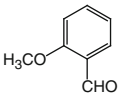
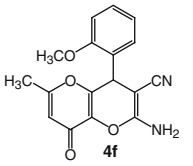
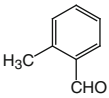
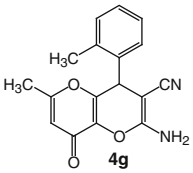
Entry	Aldehydes	R	Product	Time (min)	Yield (%)[a]
1		CN	 **4a**	15	94
2		CN	 **4b**	30	89
3		CN	 **4c**	12	95
4		CN	 **4d**	20	90
5		CN	 **4e**	15	92
6		CN	 **4f**	35	85
7		CN	 **4g**	30	86

Table 2 continued

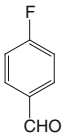
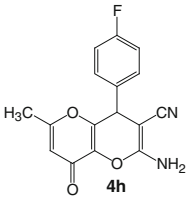
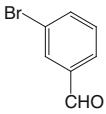
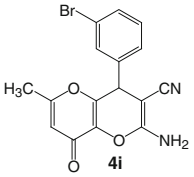
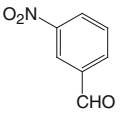
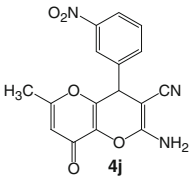
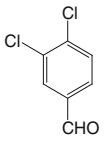
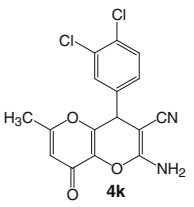
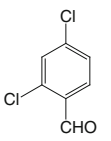
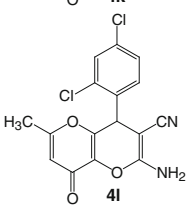
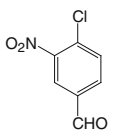
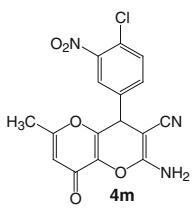
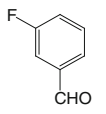
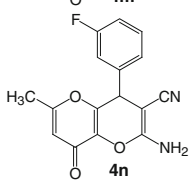
8		CN	 **4h**	20	85
9		CN	 **4i**	20	88
10		CN	 **4j**	20	91
11		CN	 **4k**	15	92
12		CN	 **4l**	15	93
13		CN	 **4m**	20	84
14		CN	 **4n**	18	93

Table 2 continued

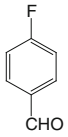
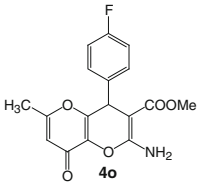
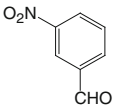
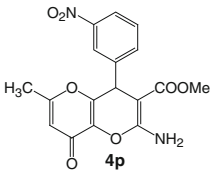
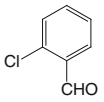
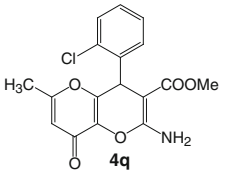
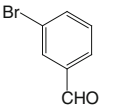
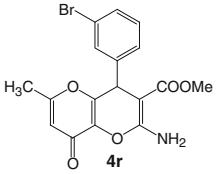
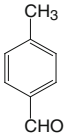
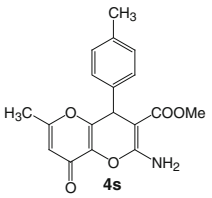
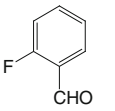
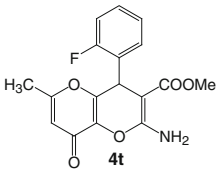
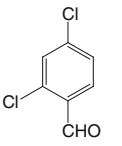
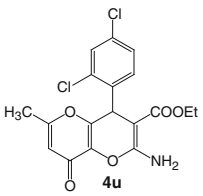
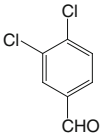
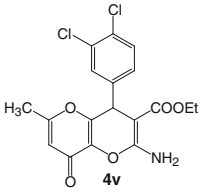
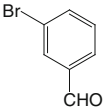
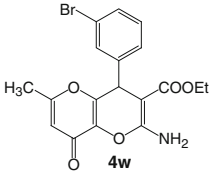
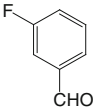
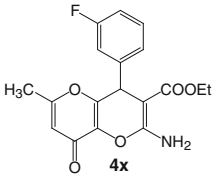
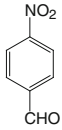
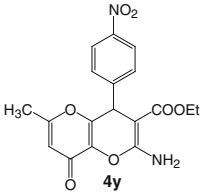
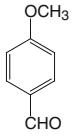
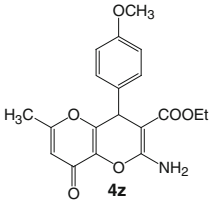
15		COOMe	 **4o**	20	87
16		COOMe	 **4p**	20	86
17		COOMe	 **4q**	15	92
18		COOMe	 **4r**	20	91
19		COOMe	 **4s**	30	85
20		COOMe	 **4t**	15	93
21		COOEt	 **4u**	15	89

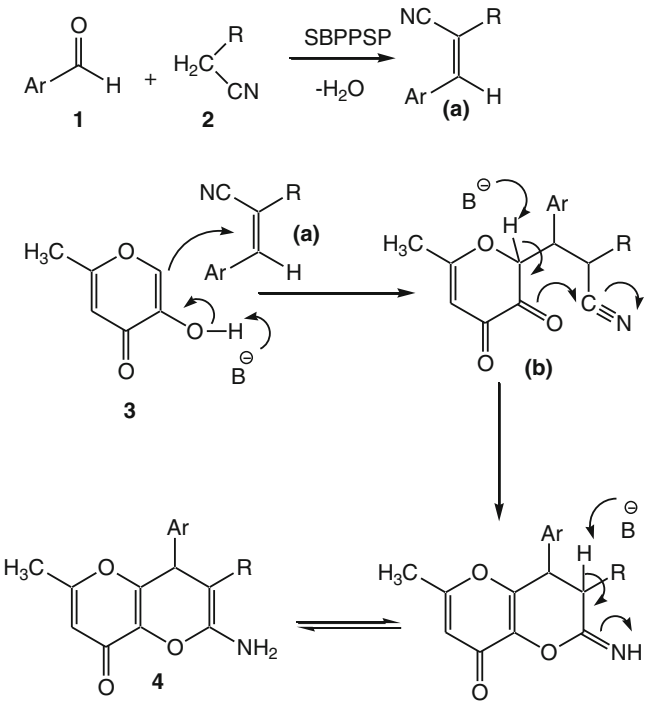
Table 2 continued

22		COOEt	 **4v**	15	88
23		COOEt	 **4w**	20	89
24		COOEt	 **4x**	20	91
25		COOEt	 **4y**	20	89
26		COOEt	 **4z**	35	85

Reaction conditions: arylaldehyde (1 mmol), malononitrile/methyl cyanoacetate/ethyl cyanoacetate (1 mmol), and allomaltol (1 mmol), EtOH–H_2O (50:50 *v*/*v*) 5 mL, reflux

[a] Isolated yields

to 100 °C, the yield of **4a** increased to 84 % (Table 1, entry 9). The model reaction was studied in different EtOH–H_2O mixtures. When the reaction was performed in EtOH–H_2O (30:70 *v*/*v*) and EtOH–H_2O (70:30 *v*/*v*) the yield was 77 and 79 %, respectively (Table 1, entries 10 and 12). EtOH–H_2O (50:50 *v*/*v*) was shown to be the most suitable solvent for this condensation in terms of yield and reaction time (Table 1, entry 11).



Scheme 2 Possible mechanism for formation of the pyrano[3,2-*b*]pyran derivatives

We next investigated the optimum amount of SBPPSP by varying the amount of catalyst. Maximum yield was obtained by use of 0.06 g (5.2 mol%) catalyst (Table 1, entry 11). When the amount of catalyst was reduced from 0.06 to 0.04 g and 0.02 g the yield decreased from 94 to 80 and 62 %, respectively (Table 1, entries 13 and 14). Increasing the amount of SBPPSP above 0.06 g had no significant effect on product yield (Table 1, entry 15).

When the model reaction was performed in the presence of silica-bonded *N*-propylpiperazine (PNPS) (3-piperazine-*N*-propylsilica) [42] in EtOH–H_2O (50:50 *v*/*v*) under reflux conditions the yield was 77 % (Table 1, entry 16). To show SBPPSP is an efficient catalyst, we performed the model reaction in the presence of other catalysts—potassium dihydrogen phosphate (KH_2PO_4), ammonium acetate (NH_4-OAc), tetrabutylammonium fluoride (TBAF), and hexamethylenetetramine (HMTA) (Table 1, entries 17–20). With these catalysts, yields were lower than with SBPPSP (Table 1, entry 11). Thus, EtOH–H_2O (50:50 *v*/*v*) and 0.06 g SBPPSP were chosen as the optimum conditions for investigation of the scope of the procedure.

Subsequent reaction of a variety of substituted aromatic aldehydes with malononitrile and 5-hydroxy-2-methyl-4*H*-pyran-4-one were attempted under similar conditions. The reactions proceeded smoothly, and equally well for

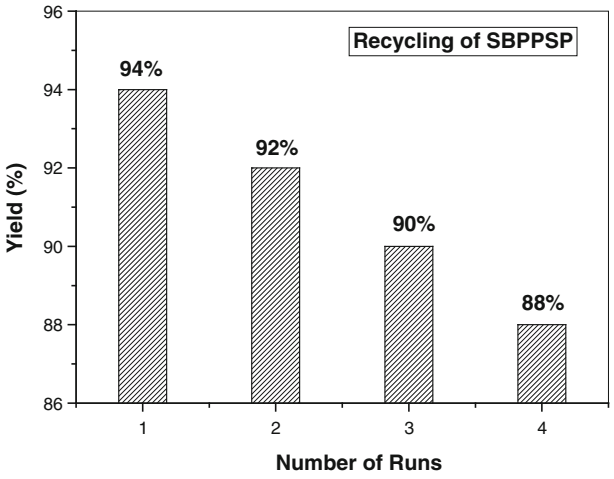


Fig. 1 Recycling of the SBPPSP catalyst in the preparation of 2-amino-6-methyl-8-oxo-4-(4-chlorophenyl)-4*H*,8*H*-pyrano[3,2-*b*]pyran-3-carbonitrile (**4a**)

aldehydes with electron-withdrawing or electron-donating substituents, affording the corresponding pyrano[3,2-*b*]pyrans in excellent yields (Scheme 1). We observed delicate electronic effects: aldehydes with electron-withdrawing groups reacted rapidly whereas electron-donating groups reduced the reactivity, so longer reaction times were required. The results are summarized in Table 2 (entries 1–14).

Encouraged by these results, we tried to extend the scope of the catalytic activity of SBPPSP to condensation of aromatic aldehydes and 5-hydroxy-2-methyl-4*H*-pyran-4-one with methyl cyanoacetate or ethyl cyanoacetate. Substituted aromatic aldehydes underwent condensation successfully under the same conditions and the corresponding pyrano[3,2-*b*]pyran derivatives were obtained in high yields (Table 2, entries 15–26). All the products were characterized by IR, ^{1}H NMR, ^{13}C NMR, and mass spectroscopy and elemental analysis.

On the basis of a previous report [35], a plausible mechanism for this reaction is depicted in Scheme 2. The first step is Knoevenagel condensation between aromatic aldehyde **1** and malononitrile or cyanoacetate **2** in the presence of the immobilized base to form intermediate **a**. Michael addition of allomaltol **3** to intermediate **a** then furnishes intermediate **b**. Finally, product **4** was obtained by intramolecular cyclization and tautomerism.

Recovery and reuse of the SBPPSP was studied by using preparation of **4a** as a model. On completion of the reaction the mixture was filtered and the solid residue was washed with hot ethanol, dried in air, and reused as the catalyst in the next reaction. As shown in Fig. 1, the solid base SBPPSP can be recycled at least four times without significant decrease in catalytic activity; yields ranged from 94 to 88 %.

Conclusion

We have developed a simple method for synthesis of pyrano[3,2-*b*]pyran derivatives by one-pot, three-component cyclocondensation of an aromatic aldehyde, malononitrile or a cyanoacetate, and 5-hydroxy-2-methyl-4*H*-pyran-4-one, in aqueous ethanol, in the presence of a catalytic amount of silica-bonded *N*-propylpiperazine sodium *n*-propionate (SBPPSP) as efficient, reusable, and green heterogeneous basic catalyst. Attractive features of the method are good yields, simple procedure, short reaction times, easy work-up, high catalytic activity, and recyclability and reusability of the catalyst. The catalyst can be used at least four times without substantial reduction of its catalytic activity.

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