Available online on 15.07.2019 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Research Article

An efficient and facile synthesis of the hybrid scaffold of Pyrazole-Triazole-Chromenes nucleus using PS-TBD as a green catalyst

Nileshkumar D. Vala*, Tapan H. Parekh, Mehulsinh R. Chhasatia

Shree P. M. Patel Institute of Post Graduate Studies & Research in applied Science, Sardar Patel University, Anand-388001, Gujarat, (INDIA)

ABSTRACT

A series of 16 derivatives of pyrazole-triazole-chromene moieties (4a-p) were synthesized via one-pot cyclocondensation reaction of pyrazole-triazole aldehyde (1a-d), 1, 3 diketone (3a-d) and malononitrile (2a) in presence of PS-TBD as catalyst. The reusability of PS-TBD (polystyrene supported 7-methyl-1, 5, 7-triazabicyclo [4.4.0] dec-5-ene) catalyst makes this reaction quick and efficient. On the basis of various trials and its results, best performance and reusability of catalyst was observed at 5 mol% concentration. The reusability of catalyst founds up to 5 runs. A synthesized compound was characterized by ^{1}HNMR, ^{13}CNMR, FT-IR and C, H, N elemental analysis and confirms theoretical chemical reaction.

Keywords: Chromenes, Pyrazole, Triazole, PS-TBD catalysis Chemistry

Article Info: Received 15 May 2019; Review Completed 21 June 2019; Accepted 24 June 2019; Available online 15 July 2019

Cite this article as:

Vala ND, Parekh TH, Chhasatia MR, An efficient and facile synthesis of the hybrid scaffold of Pyrazole-Triazole-Chromenes nucleus using PS-TBD as a green catalyst, Journal of Drug Delivery and Therapeutics. 2019; 9(4):222-226

http://dx.doi.org/10.22270/jddt.v9i4.3035

***Address for Correspondence:**

Nileshkumar D. Vala, Shree P. M. Patel Institute of Post Graduate Studies & Research in applied Science, Sardar Patel University, Anand-388001, Gujarat, (INDIA)

1. INTRODUCTION

Polymer-supported catalysts have an appeal much attention in recent decades due to their inherent advantages in green chemistry, for example, simplification of reaction procedures including the easy recovery of the catalyst by filtration, application to automated systems, and recycling of catalyst, In any polymer supported catalyst catalyzed a reaction, after the completion of reaction catalyst can be easy collected and reused catalyst.[1-4] Green chemistry emphasizes the development of environmentally benign chemical processes and technologies. So it will be equally beneficial for the environment as well as for the coast of green chemistry.[5] The Much Vantage of catalyst PS-TBD are reusability, cleanness and less harmful to the environment, makes the chemical reaction more eco-friendly, economic and environmental advantages.[6,] The PS-TBD is a polymer-supported organocatalyst consisting of a covalently linked guanidine TBD moiety to polystyrene which has been successfully used in a wide range of reactions, as epoxide ring opening, aldol-type condensation[7], Knoevenagel condensation[7], Michael additions[7] to α, β-unsaturated ketones, cyanosilylation of aldehydes, ketones, and imines[7], ring opening of aziridines and addition of dialkylphosphites to unsaturated systems. This series novel compounds softwood with polystyrene supported 7-methyl-1, 5, 7-triazabicyclo [4.4.0] dec-5-ene (PS-TBD).pyrano[4, 3-b]pyran and pyrano[3, 2-c]chromene compounds. In the continuation of our previous work we use PS-TBD (polystyrene supported 7-methyl-1, 5, 7-triazabicyclo[4.4.0]dec-5-ene) a catalyst for the one pot cyclocondesation reaction of triazole-pyrazole substituted aldehyde, various active methelene compounds, and malononitrile[8-12]. All synthesized compounds were characterized by various physicochemical methods.

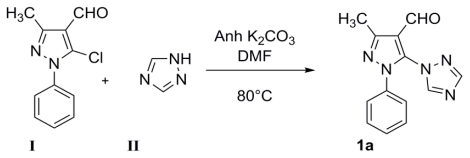
2. EXPERIMENTAL

All the reagents and solvents were obtained commercially and used without further purification. All melting points were taken in open capillaries and are uncorrected. For monitoring the progress of all reactions and purity of the synthesized compounds thin-layer chromatography (TLC, on aluminium plates precoated with silica gel ^{60}F254, Merck, Darmstadt, Germany) was used; eluent hexane: ethylacetate (1:1). UV radiation and/or iodine were used as the visualizing agents. The IR spectra were recorded Perkin-Elmer Spectrum GX FT-IR Spectrophotometer (Perkin-Elmer, USA), only the characteristic peaks are reported in cm^{-1}. Elemental analysis (% C, H, N) was carried out by Perkin-Elmer 2400 series-II elemental analyzer (Perkin-Elmer, USA); all compounds are within ±0.4% of theory specified. ^{1}H NMR and ^{13}C NMR spectra were recorded in DMSO-d_6 on a BrukerAvance 400F (MHz) spectrometer (Bruker Scientific Corporation Ltd., Switzerland) using solvent peak as internal standard at 400 MHz and 100 MHz respectively. Chemical shifts are reported in parts per million (ppm). Mass spectra were scanned on a Shimadzu LCMS 2010 spectrometer (Shimadzu, Tokyo, Japan).

2.1. General procedure for the synthesis of targeted compounds

2.1.1. Synthesis of 3-methyl-1-(4-substituted phenyl)-5-(1*H*-1, 2, 4-triazol-1-yl)-1*H*-pyrazole-4-carbaldehyde

Triazole substituted aldehyde (1a-d) was synthesized by heating previously prepared 0.05 mole substituted 5-chloro-3-methyl-1-(4-substituted phenyl)-1*H*-pyrazole-4-carbaldehyde [13-15] **(I)** and 0.05 mole 1*H*-1, 2, 4-triazole **(II)** and 0.075 mole of anhydrous Potassium carbonate (K_2CO_3) in dimethyl formamide at 80°C for 2 hr. After the completion of reaction monitoring by TLC, the reaction mass was poured into crushed ice. The product obtained was filtered, washed, dried and recrystalized from ethyl acetate.

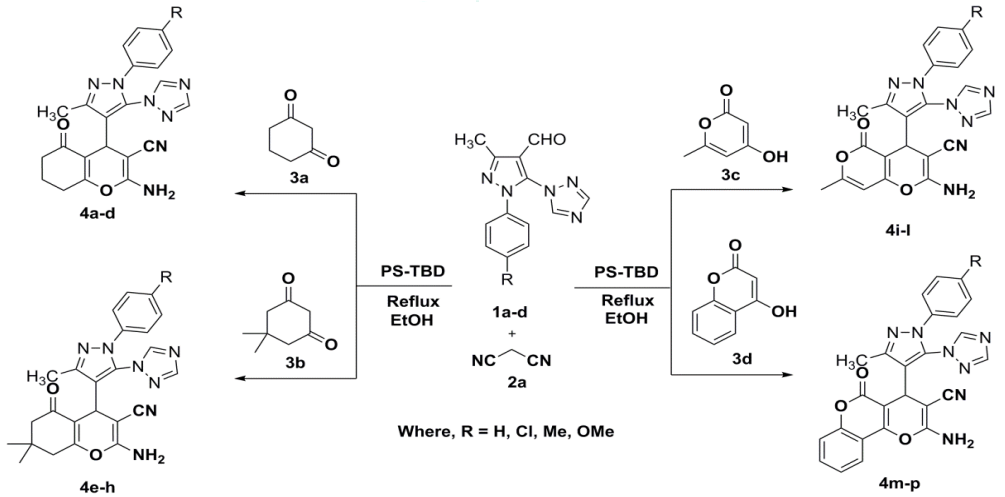


Scheme 1: Synthesis of 3-methyl-1-phenyl-5-(1*H*-1,2,4-triazol-1-yl)-1*H*-pyrazole-4 carbaldehyde

[Scheme 1]

2.1.2. General procedure for the synthesis of targeted compounds 4a-p

Mixture of appropriate 3-methyl-1-(4-substituted phenyl)-5-(1*H*-1, 2, 4-triazol-1-yl)-1*H*-pyrazole-4-carbaldehyde[7] (1a–d) (5 mmol), malononitrile (2a) (5 mmol), 1, 3-cyclohexanedione (3a) / dimedone[8] (3b) / 4-hydroxy-6-methyl-2*H*-pyran-2-one (3c) / 4-hydroxy-coumarin (3d) (5 mmol) and PS-TBD (5 mol %) in ethanol (5 ml) were charged in 100 ml round bottom flask equipped with condenser. The reaction mixture was stirred at reflux for 1.5 h. After completion of the reaction, as evidenced by TLC, the solid precipitated was dissolved by adding 15 ml chloroform: methanol (1:1). PS-PBD, which remained insoluble was collected by filtration and separately washed with 10 ml acetone and dried in oven to activate for the next batch. The filtrate was concentrated under vacuum to get solid and filtered (yield 86%–95%). The crude product was recrystallized from 50 ml chloroform: methanol (9:1) to get a pure solid sample. PS-TBD maintained its catalytic activity up to five runs.[16, 17]



[Scheme 2]

Table 1: Optimization of reaction condition for **4a**

Entry	Temperature (°C)	Time (h)	Mol % PS-TBD	%Yield [a]
1	RT	2	-	56
2	60	2	2	72
3	80	2	2	75
4	80	1.5	5	88
5	80	1.5	8	~88

[a] Isolated yield

3- Phenyl-5-(1H-1, 2, 4-triazol-1-yl)-1H-pyrazole-4-carbaldehyde**1a** (5 mmol), malononitrile **2**(5 mmol) and 4-hydroxy coumarin **6**(5 mmol)

Table 2: Activity of reused catalyst for synthesis of **4a**

Run	%Yield[a]
1st	88
2nd	85
3rd	81
4th	76
5th	73

[a] [a] Isolated yield

2-amino-4-(3-methyl-1-phenyl-5-(1*H*-1, 2, 4-triazol-1-yl)-1*H*-pyrazol-4-yl)-5-oxo-5, 6, 7, 8-tetrahydro-4*H*-chromene-3-carbonitrile (4a)

White solid(1.689g, 96%), mp223°C;IR(KBr):ν=3428, 3344, 2189, 1677, 1241cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 1.93 (3H)1.94 -2.92 (6H, m, 3×CH_2), 4.23 (1H, s, H_4), 7.58-8.54(8H, m, Ar-H+NH_2), 6.84(2H, s, NH) ppm; MS calcd. for $C_{22}H_{19}N_7O_2$ [M]$^+$ 413.16, found 413.44;Anal. calcd. C, 63.91; H, 4.63; N, 23.72; O, 7.74; Found: C, 64.19; H, 4.43; N, 23.40; O, 7.59 % ^{13}C NMR , 13.1, 21.3, 28.2, 29.0, 36.6, 58.3, 112.4, 118.9, 119.3, 199.4, 119.5, 125.7, 129.5, 129.9, 139.7, 147.5, 151.3, 152.4, 154.3, 155.4 , 159.5, 198.2.

2-amino-4-(1-(4-chlorophenyl)-3-methyl-5-(1*H*-1, 2, 4-triazol-1-yl)-1*H*-pyrazol-4-yl)-5-oxo-5, 6, 7, 8-tetrahydro-4*H*-chromene-3-carbonitrile (4b)

White solid (1.729 g, 96%), mp 225 °C; IR (KBr):ν =3416, 3356, 2195, 1673, 1241 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 1.92(3H), 1.93-2.93(6H m, 3×CH_2), 4.23 (1H, s, H_4), 7.58-8.26(8H, m, Ar-H+NH_2), 6.84(2H, s, NH) ppm; MS calcd. for $C_{22}H_{18}C_lN_7O_2$ [M]$^+$447.12, found447.88;Anal. calcd. C, C, 59.00; H, 4.05; Cl, 7.92; N, 21.89; O, 7.14; Found: C, 59.31; H, 4.17; Cl 7.52; N, 21.95; O, 6.93%; ^{13}C NMR 12.9, 21.5, 28.5, 28.9, 36.9, 58.4, 113.0 , 118.0, 118.2, 118.5, 118.8, 129.6, 130.3, 131.6, 137.9, 147.5, 151.5, 152.7, 154.6, 155.0, 158.2, 197.5.

2-amino-4-(3-methyl-1-(p-tolyl)-5-(1*H*-1, 2, 4-triazol-1-yl)-1*H*-pyrazol-4-yl)-5-oxo-5, 6, 7, 8-tetrahydro-4*H*-chromene-3-carbonitrile (4c)

White solid (1.619 g, 95%), mp 224 °C; IR (KBr):ν = 3399, 3365, 2195, 1673, 1255 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 1.94 (3H), 1.94-2.92 (6H, m, 3×CH_2), 4.32 (1H, s, H_4), 7.25-7.51(8H, m, Ar-H+NH_2), 6.80(1H, s, NH) ppm; MS calcd. for $C_{23}H_{21}N_7O_2$ [M]$^+$ 427.18, found 427.47;Anal. calcd. C, 64.63; H, 4.95; N, 22.94; O, 7.49; Found: C, 64.39; H, 5.13; N, 22.61; O, 7.12% ^{13}C NMR, 13.0, 21.6, 21.6, 28.6, 28.6, 36.7, 57.5, 113.2, 119.2, 119.6, 125.2, 125.5, 129.0, 129.1, 135.8, 136.9, 146.2, 151.3, 152.4, 154.1, 155.3, 159.4, 197.8.

2-amino-4-(1-(4-methoxyphenyl)-3-methyl-5-(1*H*-1, 2, 4-triazol-1-yl)-1*H*-pyrazol-4-yl)-5-oxo-5, 6, 7, 8-tetrahydro-4*H*-chromene-3-carbonitrile (4d)

White solid (1.889 g, 96%), mp 224 °C; IR (KBr):ν = 3374, 3295, 2208, 1677, 1275 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = (3H), 1.92-2.89(6H m, 3×CH_2), 4.11 (1H, s, H_4), 6.980-7.632 (8H, m, Ar-H+NH_2), 6.66(1H, s, NH) ppm; MS calcd. for $C_{23}H_{21}N_7O_3$ [M]$^+$ 443.17, found 443.47;Anal. calcd. C, 62.29; H, 4.77; N, 22.11; O, 10.82 Found: C, 62.41; H, 4.52; N, 21.86; O, 10.99 % ^{13}C NMR, 13.3, 20.7, 28.4, 28.5, 35.9, 55.5, 57.1, 111.9, 112.5, 113.0, 114.5, 114.9, 119.1, 119.4, 132.2, 147.4, 151.3, 152.5, 154.8, 155.4, 158.3, 159.5, 198.2.

2-amino-7, 7-dimethyl-4-(3-methyl-1-phenyl-5-(1*H*-1, 2, 4-triazol-1-yl)-1*H*-pyrazol-4-yl)-5-oxo-5, 6, 7, 8-tetrahydro-4*H*-chromene-3-carbonitrile (4e)

White solid (1.589 g, 96%), mp 222 °C; IR (KBr):ν = 3352, 3365, 2195, 1675, 1202 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 1.91 (3H), 1.01-2.32 (6Hm, 3×CH_2), 4.21 (1H, s, H_4), 7.49-8.26(8H, m, Ar-H+NH_2), 6.85(1H, s, NH) ppm; MS calcd. for $C_{24}H_{23}N_7O_2$ [M]$^+$ 441.19, found441.50;Anal. calcd. C, 65.29; H, 5.25; N, 22.21; O, 7.25; Found: C C, 65.44; H, 5.58; N, 22.37; O, 7.05 % ^{13}C NMR, 13.2, 20.5, 27.1, 28.0, 32.2, 38.3, 50.9, 57.8, 113.7, 118.6, 118.8, 119.3, 119.9, 126.5, 129.1, 129.6, 139.9 147.8, 151.7, 152.4, 154.9, 155.6, 159.4, 197.9.

2-amino-4-(1-(4-chlorophenyl)-3-methyl-5-(1*H*-1, 2, 4-triazol-1-yl)-1*H*-pyrazol-4-yl)-7, 7-dimethyl-5-oxo-5, 6, 7, 8-tetrahydro-4*H*-chromene-3-carbonitrile (4f)

White solid (1.569 g, 94%), mp218°C;IR(KBr):ν=3419, 3362, 2195, 1667, 1213cm^{-1};^{1}H NMR(400 MHz, DMSO-d_6)δ =1.93(3H), 1.12-2.30 (6H, m, 3×CH_2), 4.26 (1H, s, H_4), 7.31-7.56(8H, m, Ar-H+NH_2), 6.78(1H, s, NH) ppm; MS calcd. for $C_{24}H_{22}ClN_7O_2$ [M]$^+$ 475.15, found475.94;Anal. calcd. C, 60.57; H, 4.66; Cl, 7.45; N, 20.60; O, 6.72; Found: C, 60.23; H, 4.73; Cl, 7.67; N, 20.21; O, 6.45% ^{13}CNMR, 13.0, 27.4, 27.4, 28.2, 32.6, 38.7, 51.1, 58.0, 114.2, 119.0, 119.4, 119.7, 120.0, 129.1, 129.7, 131.9, 138.0, 146.8, 151.3, 152.5, 154.5, 155.3, 159.8, 198.4.

2-amino-7, 7-dimethyl-4-(3-methyl-1-(p-tolyl)-5-(1*H*-1, 2, 4-triazol-1-yl)-1*H*-pyrazol-4-yl)-5-oxo-5, 6, 7, 8-tetrahydro-4*H*-chromene-3-carbonitrile (4g)

White solid (1.489 g, 92%), mp 219 °C; IR (KBr):ν 3444, 3317, 2196, 1642, 1254 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ =1.93(3H), 1.81-2.78 (6H, m, 3×CH_2), 4.31 (1H, s, H_4), 7.27-7.57(8H, m, Ar-H+NH_2), 6.91(1H, s, NH) ppm; MS calcd. for $C_{25}H_{25}N_7O_2$ [M]$^+$ 455.21, found455.52;Anal. calcd. C, 65.92; H, 5.53; N, 21.52; O, 7.02; Found: C, 66.17; H, 5.76; N, 21.79; O, 7.56% ^{13}C NMR, 13.5, 21.5, 27.9, 26.7, 28.2, 32.5, 38.8, 51.7, 58.3, 113.5, 119.3, 119.6, 124.9, 125.3, 129.5, 129.9, 135.5, 136.5, 147.6, 151.9, 152.3, 154.6, 155.5, 159.7, 198.7.

2-amino-4-(1-(4-methoxyphenyl)-3-methyl-5-(1*H*-1, 2, 4-triazol-1-yl)-1*H*-pyrazol-4-yl)-7, 7-dimethyl-5-oxo-5, 6, 7, 8-tetrahydro-4*H*-chromene-3-carbonitrile (4h)

White solid (1.509 g, 95%), mp 220 °C; IR (KBr):ν 3449, 3373, 2203, 1672, 1214 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 1.94(3H), 1.81-2.50 (6H, m, 3×CH_2), 4.23 (1H, s, H_4), 7.31-7.66(8H, m, Ar-H+NH_2), 6.91(1H, s, NH) ppm; MS calcd. for $C_{25}H_{25}N_7O_3$ [M]$^+$471.20found471.52;Anal. calcd. C, 63.68; H, 5.34; N, 20.79; O, 10.18; Found: C, 63.99; H, 5.03; N, 20.47; 0, 10.58% ^{13}C NMR, 13.4, 27.1, 27.3, 28.2, 32.3, 38.7, 51.2, 54.9, 58.7, 112.6, 112.9, 113.5, 114.7, 115.0, 118.9, 119.3, 132.2, 147.5, 151.2, 152.6, 154.4, 155.2 , 158.5, 159.6, 199.2.

2-amino-7-methyl-4-(3-methyl-1-phenyl-5-(1*H*-1, 2, 4-triazol-1-yl)-1*H*-pyrazol-4-yl)-5-oxo-4*H*, 5*H*-pyrano [4, 3-b] pyran-3-carbonitrile (4i)

White solid (1.250 g, 91%), mp 221 °C; IR (KBr):ν = 3416, 3364, 2195, 1673, 1241 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ =1.91(3H), 2.21-6.42 (6H, m, 4×CH_2), 4.41 (1H, s, H_4), 7.25-8.56(8H, m, Ar-H+NH_2), 6.82(1H, s, NH) ppm; MS calcd. for $C_{22}H_{17}N_7O_3$ [M]$^+$ 427.14, found427.42;Anal. calcd. C, 61.82; H, 4.01; N, 22.94; O, 11.23; Found: C, 61.91; H, 3.88; N, 23.08; O, 11.51% ^{13}C NMR, 12.9, 21.1, 29.8, 58.1, 100.3, 100.5, 118.3, 118.9, 119.2, 119.4, 126.4, 129.2, 129.8, 139.1, 147.1, 151.1, 152.2, 154.5, 158.9, 162.1, 163.2, 175.5.

2-amino-4-(1-(4-chlorophenyl)-3-methyl-5-(1*H*-1, 2, 4-triazol-1-yl)-1*H*-pyrazol-4-yl)-7-methyl-5-oxo-4*H*, 5*H*-pyrano [4, 3-b] pyran-3-carbonitrile (4j)

White solid (1.189 g, 89%), mp 219 °C; IR (KBr):ν = 3419, 3335, 2194, 1673, 1249 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ =1.91(3H), 2.32-6.23 (6H, m, 4×CH_2), 4.43 (1H, s, H_4), 7.34-7.56(8H, m, Ar-H+NH_2), 6.67(1H, s, NH) ppm; MS calcd. for $C_{22}H_{16}ClN_7O_3$ [M]$^+$ 461.10, found461.87;Anal. calcd. C, 57.21; H, 3.49; Cl, 7.68; N, 21.23; O, 10.39; Found: C, 56.78; H, 3.88; Cl, 7.23; N, 21.76; O, 10.01%^{13}CNMR, 12.7, 21.0, 30.1, 58.3, 100.6, 100.7, 119.1, 119.8, 119.9, 120.8, 129.1, 129.6, 131.4, 136.6, 146.1, 151.3, 152.2, 154.6, 158.2, 161.6, 163.2, 175.1.

2-amino-7-methyl-4-(3-methyl-1-(p-tolyl)-5-(1*H*-1, 2, 4-triazol-1-yl)-1*H*-pyrazol-4-yl)-5-oxo-4*H*, 5*H*-pyrano [4, 3-b] pyran-3-carbonitrile (4k)

White solid (1.289 g, 90%), mp 223 °C; IR (KBr):ν = 3414, 3378, 2192, 1671, 1252 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 1.94(3H)2.43-6.43 (6H, m, 4×CH_2), 4.21 (1H, s, H_4), 7.27-7.58(8H, m, Ar-H+NH_2), 6.43(1H, s, NH) ppm; MS calcd. for $C_{23}H_{19}N_7O_3$ [M]$^+$ 441.15, found441.45;Anal. calcd. C, 62.58; H, 4.34; N, 22.21; O, 10.87; Found: C, 62.69; H, 3.67; N, 22.50; O,

11.21% ^{13}C NMR, 12.9, 19.8, 21.4, 30.5, 58.7, 100.3, 100.8, 119.0, 119.8, 125.1, 125.8, 129.6, 129.9, 134.7, 136.2, 147.4, 151.2, 152.8, 154.2, 160.1, 162.2, 163.6, 174.5.

2-amino-4-(1-(4-methoxyphenyl)-3-methyl-5-(1*H*-1, 2, 4-triazol-1-yl)-1*H*-pyrazol-4-yl)-7-methyl-5-oxo-4*H*, 5*H*-pyrano [4, 3-b] pyran-3-carbonitrile (4l)

White solid (1.342 g, 90%), mp 224 °C; IR (KBr):ν = 3375, 3385, 2192, 1665, 1252 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 1.93(3H)2.46-6.64 (8H, m, 4×CH_2), 4.36 (1H, s, H_4), 7.27-7.62(8H, m, Ar-H+NH_2), 6.55(1H, s, NH) ppm; MS calcd. for $C_{23}H_{19}N_7O_4$ [M]$^+$457.15, found457.45;Anal. calcd C, 60.39; H, 4.19; N, 21.43; O, 13.99; Found: C, 60.02; H, 4.53; N, 21.88; O, 13.25% ^{13}C NMR, 12.8, 20.7, 28.5, 55.1, 58.2, 100.4, 101.2, 112.0, 112.2, 113.9, 114.5, 119.0, 119.4, 132.2, 147.4, 151.2, 152.5, 154.7, 158.1, 158.8, 160.2, 162.4, 172.3.

2-amino-4-(3-methyl-1-phenyl-5-(1*H*-1, 2, 4-triazol-1-yl)-1*H*-pyrazol-4-yl)-5-oxo-4*H*, 5*H*-pyrano [3, 2-c] chromene-3-carbonitrile (4m)

White solid (1.328 g, 92%), mp 225 °C; IR (KBr):ν = 3416, 3356, 2195, 1673, 1241 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ =1.92(3H), 7.39-7.82 (8H, m, 4×CH_2), 4.41 (1H, s, H_4), 7.50-8.43(8H, m, Ar-H+NH_2), 6.91(1H, s, NH) ppm; MS calcd. for $C_{25}H_{17}N_7O_3$ [M]$^+$463.14, found463.46;Anal. calcd. C, 64.79; H, 3.70; N, 21.16; O, 10.36; Found: C, 64.21; H, 3.69; N, 21.35; O, 10.56% ^{13}C NMR, 12.9, 29.4, 57.7, 104.6, 115.3, 116.8, 118.8, 119.1, 119.5, 119.9, 123.3, 125.5, 126.6, 128.1, 129.2, 129.6, 139.1, 147.6, 151.2, 152.3, 153.2, 154.7, 159.2, 160.4, 162.3.

2-amino-4-(1-(4-chlorophenyl)-3-methyl-5-(1*H*-1, 2, 4-triazol-1-yl)-1*H*-pyrazol-4-yl)-5-oxo-4*H*, 5*H*-pyrano [3, 2-c] chromene-3-carbonitrile (4n)

White solid (1.502 g, 93%), mp 220 °C; IR (KBr):ν = 3426, 3366, 2195, 1673, 1249 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ =1.94(3H), 7.38-7.82 (8H, m, 4×CH_2), 4.43 (1H, s, H_4), 7.53-7.52(8H, m, Ar-H+NH_2), 6.92(1H, s, NH) ppm; MS calcd. for $C_{25}H_{16}ClN_7O_3$ [M]$^+$497.10, found 497.90; Anal. calcd. C, 60.31; H, 3.24; Cl, 7.12; N, 19.69; O, 9.64; Found: C, 60.63; H, 3.09; Cl, 6.69; N, 19.04; O, 9.14% ^{13}CNMR, 13.1, 29.2, 58.0, 104.2, 115.8, 116.5, 118.3, 119.1, 119.5, 119.8, 122.7, 125.4, 127.2, 129.1, 29.4, 131.4, 137.3, 147.2, 150.7, 152.5, 152.8, 154.2, 158.2, 160.1, 162.3.

2-amino-4-(3-methyl-1-(p-tolyl)-5-(1*H*-1,2, 4-triazol-1-yl)-1*H*-pyrazol-4-yl)-5-oxo-4*H*, 5*H*-pyrano [3, 2-c] chromene-3-carbonitrile (4o)

White solid (1.677 g, 95%), mp 219 °C; IR (KBr):ν = 3391, 3313, 2193, 1665, 1256 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 1.93(3H)7.41-7.86 (8H, m, 4×CH_2), 4.29 (1H, s, H_4), 7.14-7.56(8H, m, Ar-H+NH_2), 6.95(1H, s, NH) ppm; MS calcd. for $C_{26}H_{19}N_7O_3$ [M]$^+$ 477.15, found477.48;Anal. calcd. C, 65.40; H, 4.01; N, 20.53; O, 10.05; Found: C, 66.77; H, 4.45; N, 20.56; O, 10. 54% ^{13}C NMR 13.1, 21.7, 29.1, 57.9, 105.5, 115.0, 116.2, 119.0, 119.5, 123.3, 125.1, 125.3, 126.1, 128.3, 129.2, 129.8, 135.2, 136.1, 147.0, 151.2, 152.1, 152.5, 154.2, 159.5, 160.3, 161.4.

2-amino-4-(1-(4-methoxyphenyl)-3-methyl-5-(1*H*-1, 2, 4-triazol-1-yl)-1*H*-pyrazol-4-yl)-5-oxo-4*H*, 5*H*-pyrano [3, 2-c] chromene-3-carbonitrile (4p)

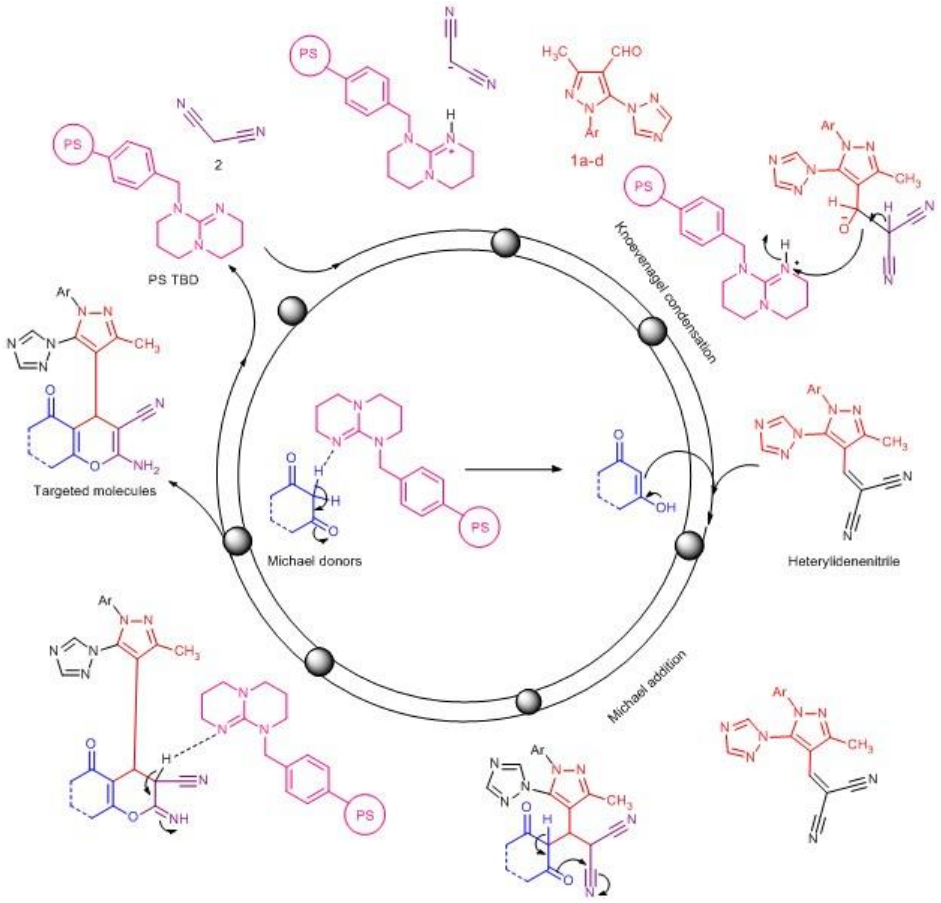
White solid (1.803 g, 97%), mp 223 °C; IR (KBr):ν =3392, 3318, 2193, 1664, 1253 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 1.90(3H)7.42-7.77 (8H, m, 4×CH_2), 4.42 (1H, s, H_4), 6.85-7.60(8H, m, Ar-H+NH_2), 6.98(1H, s, NH) ppm; MS calcd. for $C_{26}H_{19}N_7O_4$ [M]$^+$ 493.15, found493.48;Anal. calcd C, 63.28; H, 3.88; N, 19.87; O, 12.97; Found: C, 62.65; H, 4.11; N , 20.22; O, 12.54% ^{13}C NMR, 13.4, 29.4, 55.5, 58.5, 105.2, 112.1, 112.2, 114.9, 115.0, 115.2, 116.6, 119.5, 119.7, 123.1, 125.1, 127.9, 132.3, 147.4, 151.2, 152.1, 152.5, 154.1, 158.4, 159.1, 160.6, 161.5.

3. RESULTS AND DISCUSSION

3.1. Chemistry

A series of 16 compounds, 4*H*-chromene **4a–d** and **4e–h**, pyrano[4, 3-b]pyran **4i–l** and pyrano[3, 2-c]chromene **4m–p** were synthesized by the plausible reaction mechanism depicted in Scheme 2. The reaction was optimized by varying temperature, time and amount of catalyst (Table 1). We found that reaction of 3-methyl-1-(4-substituted phenyl)-5-(1*H*-1, 2, 4-triazol-1-yl)-1*H*-pyrazole-4-carbaldehyde **1a-d**, malononitrile (**2a)** and 4- hydroxy-coumarin **(3d)** with 5 mol% PS-TBD, in ethanol at 80°C for 1.5 h gave 95% yield of **4a**. Further increasing loading of catalyst didn't impact on yield. The catalytic activity of PS-TBD was investigated and it was found that PS-TBD maintained its efficiency up to five runs (Table 2). The newly synthesized compounds were characterized by ^{1}H NMR, ^{13}C NMR, FT-IR and elemental analysis. The molecular weight of compounds was confirmed by mass spectrometry. Physical, analytical and spectroscopic characterization data of all compounds are given in Supplementary material. ^{1}H NMR (DMSO-d_6) spectrum of 4a exhibited a singlet peak around 4.23 ppm stands for H4 proton. Amine and aromatic protons of 4a resonate as multiplets at around 7.58–8.54 ppm. ^{13}C NMR (DMSO- d_6) spectrum shows characteristic peak at 28.6 ppm for cyclized carbon, 58.3 ppm for C–CN, 119.3 ppm for C≡N, 152.4 ppm for C– NH_2 and 159.5 ppm for C=O, all these peaks support the structure of **4a**. The IR spectrum of compound **4a** exhibited characteristic absorption bands around 3428–3344 cm^{-1} and 2189 cm^{-1} stands for (asym. & sym. stretching) –NH_2 and –CN functional groups, respectively. The characteristic absorption band of C=O stretching and C–O–C ether stretching are observed around 1677 cm^{-1} and 1241 cm^{-1}.

The plausible reaction mechanism can be discussed as, in the first step, heterylidenenitrile forms by the Knoevenagel condensation of 3-methyl-1-(4-substituted phenyl)-5-(1*H*-1, 2, 4-triazol-1-yl)-1*H*-pyrazole-4-carbaldehyde **(4a–d)** and pre-activated malononitrile 2a in the presence of PS-TBD. The catalyst PS-TBD abstracts the acidic proton of malononitrile and makes it more nuclophilic towards a facial attack on the carbonyl carbon of aldehyde. In second step, Michael addition of activated (**3a-d)** on heterylidenenitrile results into targeted molecules (**4a–p)**. The catalyst is used in another cycle for synthesis of targeted molecules.



[Scheme 3]

4. CONCLUSION

In summary, use of PS-TBD as a reusable catalyst is proved to be very effective for the synthesis of titled compounds. 5 mol% PS-TBD showed good catalytic activity up to five runs with good yield of desired products in less time, that reduce economical cost and environmental pollution.

REFERENCES

1. Kristensen, T. E.; Hansen, T. Eur. J. *Org. Chem.* **2010**, 17, 3179–3204.
2. K. Chem. Rev. **2009**, 109, 322–359; (i) Ikegami, S.; Hamamoto, H. *Chem. Rev*. **2009**, 109, 583–593; (ii) Lu, J.; Toy, P. H. *Chem. Rev*. **2009**, 109, 815–838.
3. Huang, R.; Zhang, M.; Toy, P. H. *Chem. Eur. J*. **2007**, 13, 2369–2376.
4. Benaglia, M.; Puglisi, A.; Cozzi, F. *Chem. Rev*. **2003**
5. Elguero J 1996 In Comprehensive heterocyclic chemistry (eds) A R Katritzky, C W Rees, E F V Scriven (Oxford: Pergamon) Vol. 5.
6. Matsukawa, S.; and Fujikawa, S. *Tetrahedron Lett*. **2012**. 53(9). 1075-1077.
7. Bonollo, S.; Lanari, D.; et. al *J.Catal*., 285 (**2012**) 216; F. Fringuelli, F. Pizzo, C. Vittoriani, L. Vaccaro, Chem. Commun., (**2004**) 2756.
8. Vala, N.D.; H.H. Jardosh, and M.P. Patel, *Chin. Chem. Lett.*, **2016**. 27(1): 168-172.
9. Boisnard, S.; Chastanet, J.; and Zhu, J. *Tetrahedron Lett.***1999**. 40(42):7469-7472.
10. JohnBooth, R.; John C. Hodges. *J. Am. Chem. Soc.* **1997.** 119, 4882-4886.
11. Eswaran S, Adhikari AV, Shetty NS, *Eur J Med Chem,* **2009**, 44:4637–46477.
12. Suzuki, I., Suzumura, Y., Takeda, K., *Tetrahedron Lett.* **2006**. (47) 7861.
13. Chiara, J.L.; Encinas, L.; and Díaz, B. *Tetrahedron Lett*. **2005**. 46(14) 2445-244.
14. Diz, P.M.; et al. *Org. Lett.* **2013**. 78(13). 6540-6549.
15. Kolb, H.C., and Sharpless, K.B., *Drug Discov.* **2003**. 8(24) 1128-1137.
16. Bekhit, AA.; Ashour, HMA.; Ghany, YSA.; Bekhit, AEA.; Baraka, AM.; *Med Chem Res* **2008** 19(2):193–202.
17. Gulín, O.P.; Rabanal, F.; and Giralt, E. *Org. Lett.* **2006**. 8(23): 5385-538.