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SUCCINIMIDE-*N*-SULFONIC ACID AS AN EFFICIENT RECYCLABLE CATALYST FOR THE SYNTHESIS OF SOME FUSED INDOLO PYRANO PYRIMIDINONE DERIVATIVES

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ABSTRACT. A new, simple, thermally efficient and solvent-free condensation of 2-amino-4,5-dihydro-4-phenylpyrano[3,2-b]indole-3-carbonitrile derivatives with coumarin-3-carboxylic acid employing succinimide-*N*-sulfonic acid (SuSA) as catalyst for the synthesis of a series of 5,6-dihydro-2-(2-oxo-2*H*-chromen-3-yl)-5-phenyl-indolo[2',3':5,6]pyrano[2,3-*d*]pyrimidin-4(3*H*)-one derivatives is described. This method has the advantages of high yield, simple methodology, and short reaction time, as well as being green in terms of avoiding the use of toxic catalysts and solvents. Furthermore, the catalyst could be recycled and reused four times without significant loss of activity. Thiourea dioxide (TUD) catalyzed efficient three-component coupling reactions of aromatic aldehydes, 3-hydroxyindole and malononitrile in water at 70 ºC was described as the preparation of 2-amino-4,5-dihydro-4-phenylpyrano[3,2-b]indole-3-carbonitrile derivatives.

KEY WORDS: Succinimide-*N*-sulfonic acid, Thiourea dioxide, Coumarin-3-carboxylic acid, Indolo pyrano pyrimidineone derivatives

INTRODUCTION

Coumarins are secondary heterocyclic metabolites composed of fused benzene and α-pyrone rings, and they occur widely in different parts of plants, such as roots, seeds, nuts, flowers and fruits [1]. The pharmacological and biochemical properties and therapeutic applications of coumarins depend upon the pattern of substitution and have attracted intense interest in recent years because of their diverse pharmacological properties [2]. The coumarin derivatives have demonstrated significant potential for use in a wide range of biological applications such as antioxidant [3], anticancer [4, 5], anti-proliferative [6], anti-tuberculosis [7] and antimicrobial activities [8]. Some novel coumarin-3-carboxamide derivatives linked to *N*-benzylpiperidine scaffold were synthesized and evaluated as acetylcholinesterase (AChE) and butyryl-cholinesterase (BuChE) inhibitors [9]. Osteoporosis is a progressive skeletal disorder, due to the unequal coupling between osteoclast mediated bone resorption and osteoblast mediated bone formation [10, 11]. Anti-osteoporotic effects of the newly synthesized coumarine pyridine hybrids were evaluated in primary cultures of rat calvarial osteoblasts *in vitro* [12]. The observed interesting biological properties of this class of compounds impelled us to synthesize new examples.

In view of the pharmaceutical importance of heterocyclic compounds containing coumarin moiety, various approaches toward the synthesis of this class of compounds have been explored [13-17]. Although these methods are quite satisfactory, most of these methods suffer from extended reaction times, low yields, use of costly reagents, vigorous reaction conditions and also requirement of tedious work-up procedures. Therefore, development of a simple, efficient, inexpensive and environment friendly process for the synthesis of coumarins is highly desirable.

The principles of green chemistry have been introduced to eliminate or reduce the use of hazardous materials [18]. Solvent-free organic reactions have attracted much interest particularly from the viewpoint of green chemistry. Implementation of organic transformations under solvent-free reaction conditions have gained in popularity in recent years because of their

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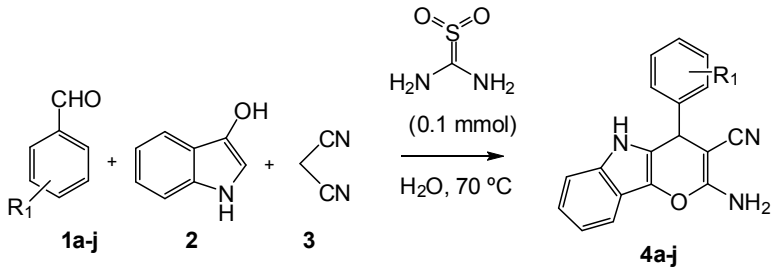
simple workup procedure, high efficiency, mild conditions, environmental friendliness, cleanliness, low cost, handling, and economical friendliness [19, 20]. In addition the growing concern for the influence of the chemical reagents on the environment as well as on human body, recovery and reusability of the chemical reagents has attracted the attention of synthetic organic chemists. More importantly pharmaceutical industry has given more importance towards recovery and reuse of chemical reagents to reduce the cost of a product as well as the environmental burden.

Recently, succinimide-*N*-sulfonic acid (SuSA) has been used as a catalyst for chemoselective trimethylsilylation of alcohols and phenols with hexamethyldisilazane (HMDS) [21], chemoselective conversion of amines to their corresponding *N*-Boc protected derivatives with $(Boc)_2O$ [22] and also for the acetylation reactions in the absence of a solvent [23]. As part of continuing effort in our laboratory towards the development of environmentally friendly procedures for the synthesis of biologically active heterocyclic molecules [24-26], we now describe the synthesis of 5,6-dihydro-2-(2-oxo-2*H*-chromen-3-yl)-5-phenyl-indolo[2',3':5,6]-pyrano[2,3-d]pyrimidin-4(3*H*)-one derivatives from the reaction of 2-amino-4,5-dihydro-4-phenylpyrano[3,2-b]indole-3-carbonitriles and coumarine-3-carboxylic acid using SuSA as an efficient reusable catalyst under solvent-free conditions. 2-Amino-4,5-dihydro-4-phenyl-pyrano[3,2-b]indole-3-carbonitriles were synthesized from benzaldehydes, 3-hydroxyindole and malononitrile using TUD as an efficient organocatalyst (Scheme 1).



Scheme 1. Synthesis of various 2-amino-4,5-dihydro-4-phenylpyrano[3,2-b]indole-3-carbonitrile derivatives from benzaldehyde, 3-hydroxyindole and malononitrile catalysed by TUD (10 mol %) in water at 70 ºC.

In recent years, TUD is used as the catalyst for the hydrolysis of imines [27], synthesis of naphthopyran derivatives [28], synthesis of a library of novel heterocyclic compounds [29], synthesis of 3,4-dihydropyrimidinones [30] and for the catalytic oxidation of alcohols [31]. We have also reported the application of TUD for the synthesis of 3,4-dihydropyrano[*c*]chromenes and 6-amino-5-cyano-4-aryl-2-methyl-4*H*-pyrans in water [26]. Multicomponent reactions (MCRs) allow the creation of several bonds in a single operation and are attracting increasing attention as one of the most powerful emerging synthetic tools for the creation of molecular diversity and complexity [32-34].

EXPERIMENTAL

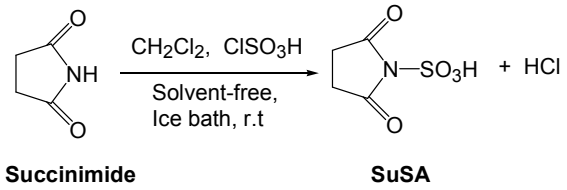
Apparatus and analysis

Chemicals were purchased from Merck, Fluka and Aldrich Chemical Companies. All yields refer to isolated products unless otherwise stated. ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were obtained using Bruker DRX-500 Avance at ambient temperature, using TMS as internal standard. FT-IR spectra were obtained as KBr discs on Shimadzu spectrometer. Mass

spectra were determined on a Varion - Saturn 2000 GC/MS instrument. Elemental analysis was measured by means of Perkin Elmer 2400 CHN elemental analyzer flowchart.

Preparation of succinimide-N-sulfonic acid

Succinimide-*N*-sulfonic acid as a stable reagent was easily prepared by the reaction of succinimide with neat chlorosulfonic acid (Scheme 2) [21].



Scheme 2. Preparation of SuSA.

*General procedure for the synthesis of pyrano[3,2-b]indole derivatives (**4a-j**)*

A mixture of aldehyde (1 mmol), 3-hydroxyindole (1 mmol), malononitrile (1.1 mmol) and TUD (0.1 mmol) in water (5 mL) was stirred at 70 ºC (Scheme 1). After completion of the reaction, as indicated by TLC, ethanol (10 mL) was added and the reaction mixture was filtered. The remaining solution was washed with warm ethanol (3 × 5 mL) in order to separate organo-catalyst. After cooling, the crude products were precipitated. The remaining aqueous thiourea dioxide was collected and reused without any further processing for subsequent runs. The reaction products were identified by comparing their physical and spectral data (i.e., IR, ^{1}H and ^{13}C NMR and MS) with those reported in the literature for the same compounds. The crude products were purified by recrystallization from ethanol (95%) to give **4a-j**.

Spectral date for the synthesized pyranoindole derivatives

*2-Amino-4,5-dihydro-4-phenylpyrano[3,2-b]indole-3-carbonitrile (**4a**)*. IR (KBr, cm^{-1}): 3276 and 3241 (–NH_2), 2213 (–CN), 1660 (–NH); ^{1}H NMR (500 MHz, $CDCl_3$) *δ:* 5.22 (s, 1H, CH), 6.88 (bs, 2H, NH_2), 6.77–6.90 (m, 2H, Ar-H); 7.04–7.13 (m, 5H, Ar-H); 7.52 (d, 1H, *J* = 7.4, Ar-H); 7.77 (d, 1H, *J* = 7.8, Ar-H), 9.80 (bs, 1H, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ:* 30.2, 59.8, 103.1, 111.3, 117.4, 120.5, 122.1, 128.0, 128.9, 130.2, 130.8, 135.0, 135.5, 137.4, 177.0 ppm; MS(ESI): *m/z* 288 $(M+H)^+$. Anal. calcd for $C_{18}H_{13}N_3O$: C, 75.25; H, 4.56; N, 14.63%. Found: C, 75.13; H, 4.52; N, 14.60%.

*2-Amino-4,5-dihydro-4-(4-fluorophenyl)-pyrano[3,2-b]indole-3-carbonitrile (**4b**)*. IR (KBr, cm^{-1}): 3270 and 3234 (–NH_2), 2221 (–CN), 1664 (–NH); ^{1}H NMR (500 MHz, $CDCl_3$) *δ:* 5.15 (s, 1H, CH), 6.93 (bs, 2H, NH_2), 6.80–6.97 (m, 2H, Ar-H); 7.04–7.13 (m, 4H, Ar-H); 7.48 (d, 1H, *J* = 7.4, Ar-H); 7.85 (d, 1H, *J* = 7.8, Ar-H), 9.94 (bs, 1H, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ:* 30.5, 60.3, 102.9, 110.8, 118.2, 121.0, 122.9, 127.6, 128.7, 130.6, 131.1, 135.3, 135.7, 138.0, 176.4 ppm; MS(ESI): *m/z* 306 $(M+H)^+$. Anal. calcd for $C_{18}H_{12}FN_3O$: C, 70.82; H, 3.93; N, 13.77%. Found: C, 70.75; H, 3.90; N, 13.75%.

*2-Amino-4,5-dihydro-4-(3-bromophenyl)-pyrano[3,2-b]indole-3-carbonitrile (**4c**)*. IR (KBr, cm^{-1}): 3268 and 3245 (–NH_2), 2208 (–CN), 1656 (–NH); ^{1}H NMR (500 MHz, $CDCl_3$) *δ:* 5.24 (s, 1H, CH), 6.78 (bs, 2H, NH_2), 6.74–6.89 (m, 2H, Ar-H); 7.14–7.23 (m, 4H, Ar-H); 7.58 (d, 1H, *J*

= 7.4, Ar-H); 7.76 (d, 1H, *J* = 7.8, Ar-H), 9.95 (bs, 1H, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ:* 30.0, 59.5, 102.7, 110.6, 117.6, 120.6, 122.2, 128.1, 128.6, 130.1 130.9, 135.6, 135.9, 137.6, 177.1 ppm; MS(ESI): *m/z* 366.9 $(M+H)^+$. Anal. calcd for $C_{18}H_{12}BrN_3O$: C, 59.03; H, 3.28; N, 11.48%. Found: C, 58.91; H, 3.22; N, 11.44%.

2-Amino-4,5-dihydro-4-(2-chlorophenyl)-pyrano[3,2-b]indole-3-carbonitrile ***(4d)***. IR (KBr, cm^{-1}): 3266 and 3233 (–NH_2), 2219 (–CN), 1669 (–NH); ^{1}H NMR (500 MHz, $CDCl_3$) *δ:* 5.17 (s, 1H, CH), 6.90 (bs, 2H, NH_2), 6.84–6.97 (m, 2H, Ar-H); 7.09–7.19 (m, 4H, Ar-H); 7.45 (d, 1H, *J* = 7.4, Ar-H); 7.90 (d, 1H, *J* = 7.8, Ar-H), 9.78 (bs, 1H, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ:* 30.9, 60.7, 103.0, 111.2, 118.1, 121.2, 122.7, 127.5, 128.5, 130.0, 131.2, 135.1, 135.5, 138.1, 176.7 ppm; MS(ESI): *m/z* 322.5 $(M+H)^+$. Anal. calcd for $C_{18}H_{12}ClN_3O$: C, 67.19; H, 3.73; N, 13.06%. Found: C, 67.10; H, 3.75; N, 13.01%.

2-Amino-4,5-dihydro-4-(4-cyanophenyl)-pyrano[3,2-b]indole-3-carbonitrile ***(4e)***. IR (KBr, cm^{-1}): 3270 and 3238 (–NH_2), 2216 (–CN), 1672 (–NH); ^{1}H NMR (500 MHz, $CDCl_3$) *δ:* 5.14 (s, 1H, CH), 6.85 (bs, 2H, NH_2), 6.76–6.94 (m, 2H, Ar-H); 7.17–7.33 (m, 4H, Ar-H); 7.56 (d, 1H, *J* = 7.4, Ar-H); 7.84 (d, 1H, *J* = 7.8, Ar-H), 9.74 (bs, 1H, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ:* 31.4, 59.6, 102.6, 110.9, 116.8, 117.7, 120.8, 122.0, 128.3, 128.8, 130.4 130.8, 135.4, 135.7, 137.6, 177.3 ppm; MS(ESI): *m/z* 313 $(M+H)^+$. Anal. calcd for $C_{19}H_{12}N_4O$: C, 73.07; H, 3.85; N, 17.95%. Found: C, 73.01; H, 3.83; N, 17.83%.

2-Amino-4,5-dihydro-4-(4-N,N-dimethylaminophenly)-pyrano[3,2-b]indole-3-carbonitrile ***(4f)***. IR (KBr, cm^{-1}): 3274 and 3240 (–NH_2), 2206 (–CN), 1659 (–NH); ^{1}H NMR (500 MHz, $CDCl_3$) *δ:* 2.72 (s, 6H, $N(CH_3)_2$), 5.22 (s, 1H, CH), 6.82 (bs, 2H, NH_2), 6.85–6.94 (m, 2H, Ar-H); 7.19–7.30 (m, 4H, Ar-H); 7.54 (d, 1H, *J* = 7.4, Ar-H); 7.83 (d, 1H, *J* = 7.8, Ar-H), 9.83 (bs, 1H, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ:* 31.3, 42.8, 60.5, 103.4, 111.2, 118.0, 121.3, 122.3, 127.7, 128.4, 130.7, 131.0, 135.7, 136.2, 138.0, 176.6 ppm; MS(ESI): *m/z* 331 $(M+H)^+$. Anal. calcd for $C_{20}H_{18}N_4O$: C, 72.72; H, 5.45; N, 16.96%. Found: C, 72.60; H, 5.46; N, 16.84%.

2-Amino-4,5-dihydro-4-(2-nitrophenyl)-pyrano[3,2-b]indole-3-carbonitrile ***(4g)***. IR (KBr, cm^{-1}): 3271 and 3243 (–NH_2), 2212 (–CN), 1662 (–NH); ^{1}H NMR (500 MHz, $CDCl_3$) *δ:* 5.26 (s, 1H, CH), 6.77 (bs, 2H, NH_2), 6.86–6.98 (m, 2H, Ar-H); 7.12–7.28 (m, 4H, Ar-H); 7.47 (d, 1H, *J* = 7.4, Ar-H); 7.76 (d, 1H, *J* = 7.8, Ar-H), 9.87 (bs, 1H, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ:* 31.5, 59.9, 102.9, 110.7, 117.9, 120.7, 122.7, 128.2, 128.8, 130.3, 130.7, 135.5, 136.1, 137.5, 177.0 ppm; MS(ESI): *m/z* 333 $(M+H)^+$. Anal. calcd for $C_{18}H_{12}N_4O_3$: C, 65.06; H, 3.61; N, 16.87%. Found: C, 64.96; H, 3.57; N, 16.85%.

2-Amino-4,5-dihydro-4-(3-methylphenyl)-pyrano[3,2-b]indole-3-carbonitrile ***(4h)***. IR (KBr, cm^{-1}): 3268 and 3237 (–NH_2), 2217 (–CN), 1670 (–NH); ^{1}H NMR (500 MHz, $CDCl_3$) *δ:* 2.16 (s, 3H, CH_3), 5.13 (s, 1H, CH), 6.95 (bs, 2H, NH_2), 6.80–6.95 (m, 2H, Ar-H); 7.08–7.18 (m, 4H, Ar-H); 7.53 (d, 1H, *J* = 7.4, Ar-H); 7.91 (d, 1H, *J* = 7.8, Ar-H), 9.80 (bs, 1H, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ:* 20.1, 30.4, 60.2, 103.0, 111.0, 118.3, 121.1, 122.5, 127.8, 128.7, 130.2, 131.0, 135.0, 135.7, 138.0, 176.8 ppm; MS(ESI): *m/z* 302 $(M+H)^+$. Anal. calcd for $C_{19}H_{15}N_3O$: C, 75.75; H, 4.98; N, 13.95%. Found: C, 75.66; H, 4.99; N, 13.93%.

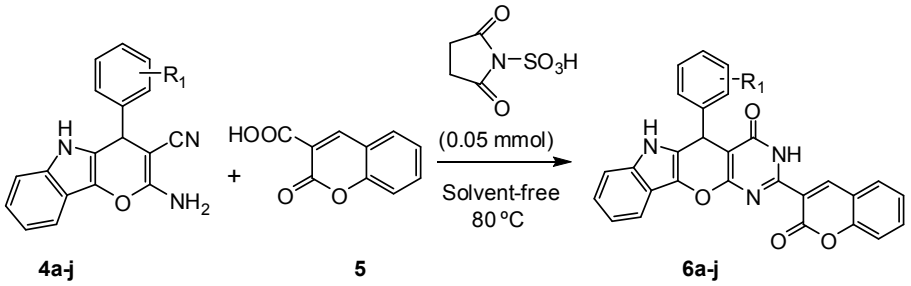
2-Amino-4,5-dihydro-4-(4-chlorophenyl)-pyrano[3,2-b]indole-3-carbonitrile ***(4i)***. IR (KBr, cm^{-1}): 3276 and 3236 (–NH_2), 2212 (–CN), 1667 (–NH); ^{1}H NMR (500 MHz, $CDCl_3$) *δ:* 5.17 (s, 1H, CH), 6.79 (bs, 2H, NH_2), 6.93–7.02 (m, 2H, Ar-H); 7.08–7.19 (m, 4H, Ar-H); 7.38 (d, 1H, *J* = 7.4, Ar-H); 7.83 (d, 1H, *J* = 7.8, Ar-H), 9.81 (bs, 1H, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ:* 30.7, 60.7, 103.7, 111.3, 118.3, 121.3, 122.4, 127.5, 128.3, 130.2, 131.2, 135.0, 135.7, 138.4,

176.5 ppm; MS(ESI): *m/z* 322.5 $(M+H)^+$. Anal. calcd for $C_{18}H_{12}ClN_3O$: C, 67.19; H, 3.73; N, 13.06%. Found: C, 67.13; H, 3.67; N, 12.94%.

2-Amino-4,5-dihydro-4-(4-methylphenyl)-pyrano[3,2-b]indole-3-carbonitrile ***(4j)***. IR (KBr, cm^{-1}): 3266 and 3236 ($–NH_2$), 2216 (–CN), 1669 (–NH); ^1H NMR (500 MHz, $CDCl_3$) *δ:* 2.19 (s, 3H, CH_3), 5.19 (s, 1H, CH), 6.84 (bs, 2H, NH_2), 6.93–7.07 (m, 2H, Ar-H); 7.11–7.18 (m, 4H, Ar-H); 7.53 (d, 1H, *J* = 7.4, Ar-H); 7.88 (d, 1H, *J* = 7.8, Ar-H), 9.88 (bs, 1H, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ:* 18.7, 30.7, 61.2, 102.2, 111.3, 117.3, 121.2, 122.4, 127.6, 128.5, 130.2, 131.1, 134.8, 135.3, 138.4, 176.7 ppm; MS(ESI): *m/z* 302 $(M+H)^+$. Anal. calcd for $C_{19}H_{15}N_3O$: C, 75.75; H, 4.98; N, 13.95%. Found: C, 75.68; H, 4.91; N, 13.89%.

General procedure for the synthesis of 5,6-dihydro-2-(2-oxo-2H-chromen-3-yl)-5-phenyl-indolo[2',3':5,6]pyrano[2,3-d]pyrimidin-4(3H)-one derivatives by SuSA

A mixture of 2-amino-4,5-dihydro-4-phenylpyrano[3,2-*b*]indole-3-carbonitrile **4a-j** (1 mmol), coumarin-3-carboxylic acid (1 mmol) and SuSA (0.05 mmol) were heated at 80 ºC for about 3.0–4.0 h (Scheme 3). After completion of the reaction as indicated by TLC, the insoluble crude product was dissolved in hot ethanol and the SuSA was filtered off. The filtrate was concentrated to dryness, and the crude product was purified by recrystallization from ethanol. The recovered catalyst was washed with acetone, dried and reused for subsequent reactions without loss in its activity and product yield.



4a-j **5** **6a-j**

Scheme 3. Synthesis of various 5,6-dihydro-2-(2-oxo-2*H*-chromen-3-yl)-5-phenyl-indolo[2',3':5,6]pyrano[2,3-d]pyrimidin-4(3*H*)-one derivatives from **4a-j** and coumarine-3-carboxylic acid catalysed by SuSA (0.05 mmol) under solvent-free condition at 80 ºC.

Spectral data for the synthesized compounds ***(6a-j)***

5,6-Dihydro-2-(2-oxo-2H-chromen-3-yl)-5-phenyl-indolo[2',3':5,6]pyrano[2,3-d]pyrimidin-4(3H)-one ***(6a)***. IR (KBr, cm^{-1}): 3266, 1708, 1677, 1660, 1633, 1604, 1200; ^1H NMR (500 MHz, $CDCl_3$) *δ:* 4.96 (s, 1H, CH), 6.82–6.94 (m, 2H, Ar-H); 7.14–7.28 (m, 5H, Ar-H); 7.44 (d, 1H, *J* = 7.6, Ar-H); 7.60 (d, 1H, *J* = 8.0, Ar-H), 7.80–8.00 (m, 4H, Ar-H), 8.26 (s, 1H, coumarin H), 8.77 (s, 1H, NH) 9.94 (s, 1H, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ:* 30.8, 102.1, 103.6, 111.2, 117.7, 120.3, 121.2, 122.5, 125.1, 125.5, 126.2, 127.5, 128.0, 128.2, 128.5, 129.3, 135.6, 137.3, 137.7, 146.4, 150.7, 160.9, 162.4, 164.1, 168.4 ppm; MS(ESI): *m/z* 460 $(M+H)^+$. Anal. calcd for $C_{28}H_{17}N_3O_4$: C, 73.20; H, 3.70; N, 9.15%. Found: C, 73.11; H, 3.66; N, 9.12%.

5,6-Dihydro-2-(2-oxo-2H-chromen-3-yl)-5-(4-fluorophenyl)-indolo[2',3':5,6]pyrano[2,3-d]pyrimidin-4(3H)-one ***(6b)***. IR (KBr, cm^{-1}): 3277, 1704, 1673, 1669, 1635, 1596, 1204; ^1H

NMR (500 MHz, $CDCl_3$) *δ:* 5.06 (s, 1H, CH), 6.75–6.96 (m, 2H, Ar-H); 7.10–7.30 (m, 4H, Ar-H); 7.46 (d, 1H, *J* = 7.6, Ar-H); 7.68 (d, 1H, *J* = 8.0, Ar-H), 7.78–7.96 (m, 4H, Ar-H), 8.30 (s, 1H, coumarin H), 8.86 (s, 1H, NH) 10.06 (s, 1H, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ:* 31.2, 102.6, 103.3, 111.6, 117.5, 120.2, 121.4, 122.9, 124.7, 125.4, 126.7, 127.3, 128.2, 128.3, 128.6, 130.0, 135.0, 137.2, 137.4, 146.3, 151.3, 161.2, 162.1 164.6, 168.2 ppm; MS(ESI): *m/z* 478 $(M+H)^+$. Anal. calcd for $C_{28}H_{16}FN_3O_4$: C, 70.44; H, 3.35; N, 8.80%. Found: C, 70.34; H, 3.30; N, 8.77%.

5,6-Dihydro-2-(2-oxo-2H-chromen-3-yl)-5-(3-bromophenyl)-indolo[2',3':5,6]pyrano[2,3-d]pyrimidin-4(3H)-one ***(6c)***. IR (KBr, cm^{-1}): 3282, 1711, 1685, 1662, 1638, 1605, 1211; ^{1}H NMR (500 MHz, $CDCl_3$) *δ:* 5.08 (s, 1H, CH), 6.84–6.92 (m, 2H, Ar-H); 7.16–7.32 (m, 4H, Ar-H); 7.50 (d, 1H, *J* = 7.6, Ar-H); 7.75 (d, 1H, *J* = 8.0, Ar-H), 7.85–7.99 (m, 4H, Ar-H), 8.42 (s, 1H, Coumarin H), 8.80 (s, 1H, NH) 9.98 (s, 1H, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ:* 30.7, 102.7, 103.2, 110.4, 118.0, 120.4, 121.5, 123.2, 125.7, 125.9, 126.7, 127.7, 128.3, 128.5, 128.7, 130.2, 135.4, 137.7, 137.9, 147.0, 150.6, 160.8, 162.5, 165.0, 167.7 ppm; MS(ESI): *m/z* 538.9 $(M+H)^+$. Anal. calcd for $C_{28}H_{16}BrN_3O_4$: C, 62.46; H, 2.97; N, 7.81%. Found: C, 62.40; H, 2.94; N, 7.80%.

5,6-Dihydro-2-(2-oxo-2H-chromen-3-yl)-5-(2-chlorophenyl)-indolo[2',3':5,6]pyrano[2,3-d]pyrimidin-4(3H)-one ***(6d)***. IR (KBr, cm^{-1}): 3270, 1713, 1680, 1670, 1643, 1592, 1213; ^{1}H NMR (500 MHz, $CDCl_3$) *δ:* 4.92 (s, 1H, CH), 6.78–6.89 (m, 2H, Ar-H); 7.09–7.29 (m, 4H, Ar-H); 7.54 (d, 1H, *J* = 7.6, Ar-H); 7.70 (d, 1H, *J* = 8.0, Ar-H), 7.82–8.01 (m, 4H, Ar-H), 8.30 (s, 1H, coumarin H), 8.73 (s, 1H, NH) 10.10 (s, 1H, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ:* 31.4, 102.0, 104.2, 111.3, 118.3, 120.3, 121.5, 123.4, 125.3, 125.7, 126.3, 127.3, 128.3, 128.6, 128.8, 129.5, 135.2, 138.1, 138.6, 147.2, 151.0, 161.3, 162.7, 164.7, 167.9 ppm; MS(ESI): *m/z* 493.4 $(M+H)^+$. Anal. calcd for $C_{28}H_{16}ClN_3O_4$: C, 68.09; H, 3.24; N, 8.51%. Found: C, 68.01; H, 3.26; N, 8.47%.

5,6-Dihydro-2-(2-oxo-2H-chromen-3-yl)-5-(4-cyanophenyl)-indolo[2',3':5,6]pyrano[2,3-d]pyrimidin-4(3H)-one ***(6e)***. IR (KBr, cm^{-1}): 3262, 1707, 1683, 1668, 1637, 1607, 1202; ^{1}H NMR (500 MHz, $CDCl_3$) *δ:* 4.99 (s, 1H, CH), 6.74–6.92 (m, 2H, Ar-H); 7.18–7.40 (m, 4H, Ar-H); 7.58 (d, 1H, *J* = 7.6, Ar-H); 7.69 (d, 1H, *J* = 8.0, Ar-H), 7.85–7.94 (m, 4H, Ar-H), 8.34 (s, 1H, coumarin H), 8.93 (s, 1H, NH) 9.90 (s, 1H, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ:* 30.5, 102.9, 103.7, 110.7, 117.1, 117.6, 120.8, 121.3, 122.7, 125.4, 125.8, 126.4, 127.8, 128.0, 128.2, 128.6, 130.1, 135.7, 137.7, 137.9, 146.6, 151.3, 160.7, 162.4, 164.8, 168.4 ppm; MS (ESI): *m/z* 485 $(M+H)^+$. Anal. calcd for $C_{29}H_{16}N_4O_4$: C, 71.90; H, 3.30; N, 11.57%. Found: C, 71.78; H, 3.24; N, 11.59%.

5,6-Dihydro-2-(2-oxo-2H-chromen-3-yl)-5-(4-N,N-dimethylaminophenyl)-indolo[2',3':5,6]pyrano[2,3-d]pyrimidin-4(3H)-one ***(6f)***. IR (KBr, cm^{-1}): 3285, 1700, 1678, 1667, 1633, 1599, 1208; ^{1}H NMR (500 MHz, $CDCl_3$) *δ:* 2.66 (s, 6H, $N(CH_3)_2$), 5.11 (s, 1H, CH), 6.79–6.93 (m, 2H, Ar-H); 7.12–7.33 (m, 4H, Ar-H); 7.48 (d, 1H, *J* = 7.6, Ar-H); 7.64 (d, 1H, *J* = 8.0, Ar-H), 7.86–8.00 (m, 4H, Ar-H), 8.29 (s, 1H, coumarin H), 8.84 (s, 1H, NH) 9.99 (s, 1H, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ:* 31.6, 43.4, 102.5, 104.4, 111.1, 118.1, 120.7, 121.2, 123.1, 125.0, 125.5, 126.1, 127.6, 128.4, 128.6, 128.9, 129.7, 135.5, 138.0, 138.4, 147.2, 150.5, 161.0, 162.2, 165.4, 167.6 ppm; MS(ESI): *m/z* 503 $(M+H)^+$. Anal. calcd for $C_{30}H_{22}N_4O_4$: C, 71.71; H, 4.38; N, 11.15%. Found: C, 71.66; H, 4.33; N, 11.12%.

5,6-Dihydro-2-(2-oxo-2H-chromen-3-yl)-5-(2-nitrophenyl)-indolo[2',3':5,6]pyrano[2,3-d]pyrimidin-4(3H)-one ***(6g)***. IR (KBr, cm^{-1}): 3278, 1710, 1684, 1671, 1636, 1603, 1205; ^{1}H NMR (500 MHz, $CDCl_3$) *δ:* 5.00 (s, 1H, CH), 6.83–6.97 (m, 2H, Ar-H); 7.16–7.39 (m, 4H, Ar-

H); 7.55 (d, 1H, *J* = 7.6, Ar-H); 7.72 (d, 1H, *J* = 8.0, Ar-H), 7.80–7.94 (m, 4H, Ar-H), 8.34 (s, 1H, coumarin H), 8.88 (s, 1H, NH) 9.94 (s, 1H, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ:* 30.4, 102.4, 103.8, 110.8, 117.7, 120.3, 121.7, 122.8, 124.9, 125.6, 126.4, 127.6, 128.2, 128.5, 128.7, 130.2, 135.3, 137.5, 137.7, 146.6, 150.7, 160.7, 162.6, 164.9, 168.3 ppm; MS (ESI): *m/z* 505 $(M+H)^+$. Anal. calcd for $C_{28}H_{16}N_4O_6$: C, 66.66; H, 3.17; N, 11.11%. Found: C, 66.56; H, 3.13; N, 11.12%.

5,6-Dihydro-2-(2-oxo-2H-chromen-3-yl)-5-(3-methylphenyl)-indolo[2',3':5,6]pyrano[2,3-d]pyrimidin-4(3H)-one ***(6h)***. IR (KBr, cm^{-1}): 3272, 1712, 1682, 1668, 1635, 1602, 1212; ^{1}H NMR (500 MHz, $CDCl_3$) *δ:* 2.26 (s, 3H, CH_3), 5.09 (s, 1H, CH), 6.74–6.97 (m, 2H, Ar-H); 7.20–7.38 (m, 4H, Ar-H); 7.59 (d, 1H, *J* = 7.6, Ar-H); 7.74 (d, 1H, *J* = 8.0, Ar-H), 7.87–8.05 (m, 4H, Ar-H), 8.37 (s, 1H, coumarin H), 8.85 (s, 1H, NH) 9.90 (s, 1H, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ:* 19.7, 31.5, 102.3, 104.1, 111.4, 117.5, 120.1, 121.8, 123.3, 124.8, 125.7, 126.6, 127.3, 128.2, 128.4, 128.6, 129.9, 135.4, 137.4, 137.8, 147.2, 150.6, 161.3, 162.3, 164.8, 167.7 ppm; MS(ESI): *m/z* 474 $(M+H)^+$. Anal. calcd for $C_{29}H_{19}N_3O_4$: C, 73.57; H, 4.01; N, 8.88%. Found: C, 73.44; H, 4.04; N, 8.82%.

5,6-Dihydro-2-(2-oxo-2H-chromen-3-yl)-5-(4-chlorophenyl)-indolo[2',3':5,6]pyrano[2,3-d]pyrimidin-4(3H)-one ***(6i)***. IR (KBr, cm^{-1}): 3263, 1710, 1688, 1674, 1641, 1596, 1210; ^{1}H NMR (500 MHz, $CDCl_3$) *δ:* 4.88 (s, 1H, CH), 6.80–6.90 (m, 2H, Ar-H); 7.04–7.27 (m, 4H, Ar-H); 7.55 (d, 1H, *J* = 7.6, Ar-H); 7.74 (d, 1H, *J* = 8.0, Ar-H), 7.84–8.03 (m, 4H, Ar-H), 8.33 (s, 1H, coumarin H), 8.77 (s, 1H, NH) 10.12 (s, 1H, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ:* 31.7, 102.2, 104.2, 111.7, 118.5, 120.3, 121.5, 123.3, 125.3, 125.7, 126.5, 127.3, 128.3, 128.7, 129.1, 129.7, 134.9, 138.3, 138.6, 147.2, 151.0, 161.3, 162.5, 164.6, 168.0 ppm; MS(ESI): *m/z* 493.4 $(M+H)^+$. Anal. calcd for $C_{28}H_{16}ClN_3O_4$: C, 68.09; H, 3.24; N, 8.51%. Found: C, 68.05; H, 3.20; N, 8.49%.

5,6-Dihydro-2-(2-oxo-2H-chromen-3-yl)-5-(4-methylphenyl)-indolo[2',3':5,6]pyrano[2,3-d]pyrimidin-4(3H)-one ***(6j)***. IR (KBr, cm^{-1}): 3266, 1703, 1689, 1670, 1638, 1600, 1211; ^{1}H NMR (500 MHz, $CDCl_3$) *δ:* 2.20 (s, 3H, CH_3), 5.04 (s, 1H, CH), 6.77–6.99 (m, 2H, Ar-H); 7.22–7.39 (m, 4H, Ar-H); 7.57 (d, 1H, *J* = 7.6, Ar-H); 7.77 (d, 1H, *J* = 8.0, Ar-H), 7.90–8.07 (m, 4H, Ar-H), 8.39 (s, 1H, coumarin H), 8.81 (s, 1H, NH) 9.90 (s, 1H, NH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ:* 19.4, 31.4, 102.6, 104.6, 111.5, 117.3, 120.3, 121.3, 123.7, 124.7, 125.8, 126.8, 127.5, 128.4, 128.8, 129.4, 129.9, 135.4, 137.4, 137.8, 147.2, 150.3, 161.5, 162.7, 164.8, 168.3 ppm; MS(ESI): *m/z* 474 $(M+H)^+$. Anal. calcd for $C_{29}H_{19}N_3O_4$: C, 73.57; H, 4.01; N, 8.88%. Found: C, 73.49; H, 4.00; N, 8.77%.

RESULTS AND DISCUSSION

The aim of this presented protocol is to highlight the development of a new eco-compatible strategy for the synthesis of 5,6-dihydro-2-(2-oxo-2*H*-chromen-3-yl)-5-phenyl-indolo-[2',3':5,6]pyrano[2,3-*d*]pyrimidin-4(3*H*)-ones by the condensation reaction of 2-amino-4,5-dihydro-4-phenyl-pyrano[3,2-*b*]indole-3-carbonitrile derivatives with coumarine-3-carboxylic acid using SuSA under solvent-free conditions (Scheme 3).

To find out the suitable conditions for the synthesis of 2-amino-4,5-dihydro-4-phenyl-pyrano[3,2-*b*]indole-3-carbonitrile, a series of experiments were performed with the standard reaction of benzaldehyde (**1a),** 3-hydroxyindole (**2**), malononitrile (**3**), as a model reaction (Scheme 1).

Our initial work started with screening of solvent and catalyst loading so as to identify optimal reaction conditions for the synthesis of pyranoindole derivatives. To evaluate the effect of solvent, we studied the reaction of benzaldehyde, 3-hydroxyindole and malononitrile in the presence of catalytic amount of TUD (0.1 mmol). A range of solvents like acetonitrile, 1,4-

dioxane, $CHCl_3$, MeOH, EtOH and water were examined (Table 1, Entries 1-6). The reaction without any solvent at 70 ºC was not very successful (Table 1, Entry 5). The reaction was more facile and proceeded to give highest yield, in the presence of water as solvent (Table 1, Entry 6). Furthermore, the effect of reaction temperature was examined and the reaction proceeded smoothly at 70 ºC (Table 1, Entry 6). The model reaction was conducted in a range of different temperatures, including room temperature, 50, 60, 70 and 80 ºC, in the presence of 0.1 mmol TUD catalyst in water (Table 1, Entries 6–10). As can be concluded from Table 1, the reaction proceeded slowly at room temperature. With increasing temperature to 70 ºC, reaction yield was increased and time of reaction was decreased, when the reaction was heated above 70 ºC, so high temperatures did not further improved yield and decrease time of reaction. The greatest yield in the shortest reaction time was obtained in water at 70 ºC (Table 1, Entry 6). We also evaluated the amount of TUD required for the reaction. Catalyst loadings in the range of 0.00–0.15 mmol were tested (Table 1, Entries 6 and 11–14). The best result was obtained with 0.1 mmol of TUD in water at 70 ºC (Table 1, Entry 6). Among the different catalysts tested, including KF/Al_2O_3, triphenyl phosphine (PPh_3), tetrabutylammonium bromide (TBAB), *p*-toluene sulfonic acid and TUD, TUD was found to be the most efficient in terms of the reaction time and yield of the product (Table 1, Entries 6 and 15-18).

Encouraged by this successful three-component reaction, synthesis of diverse 2-amino-4,5-dihydro-4-phenyl-pyrano[3,2-b]indole-3-carbonitrile derivatives **4a-j** were undertaken. The aromatic aldehydes bearing electron-withdrawing and electron donating groups were found to be equally effective to produce 2-amino-4,5-dihydro-4-phenyl-pyrano[3,2-*b*]indole-3-carbonitrile derivatives **4a-j** in very good yields (Table 2, Entries 1-10).

Table 1. Optimization of the reaction conditions on the synthesis of 2-amino-4,5-dihydro-4-phenyl-pyrano[3,2-b]indole-3-carbonitrile **4a**[a].

Entry	Catalyst	Amount	Solvent	Temperature (ºC)	Time (min)	Yield (%)[b]
1	TUD	0.1 mmol	CH_3CN	Reflux	120	54
2	TUD	0.1 mmol	1,4-Dioxane	Reflux	120	56
3	TUD	0.1 mmol	$CHCl_3$	Reflux	120	39
4	TUD	0.1 mmol	MeOH	Reflux	90	73
5	TUD	0.1 mmol	EtOH	Reflux	90	78
6	TUD	0.1 mmol	H_2O	70	40	94
7	TUD	0.1 mmol	H_2O	rt	120	59
8	TUD	0.1 mmol	H_2O	50	90	69
9	TUD	0.1 mmol	H_2O	60	60	81
10	TUD	0.1 mmol	H_2O	80	40	96
11	TUD	0.0 mmol	H_2O	70	150	25
12	TUD	0.02 mmol	H_2O	70	90	47
13	TUD	0.05 mmol	H_2O	70	65	74
14	TUD	0.15 mmol	H_2O	70	40	94
15	KF/Al_2O_3	0.1 mmol	H_2O	70	120	66
16	PPh_3	0.1 mmol	H_2O	70	90	70
17	TBAB	0.1 mmol	H_2O	70	120	79
18	*p*-TSA	0.1 mmol	H_2O	70	120	38

[a]Reaction conditions: benzaldehyde (1 mmol), 3-hydroxyindole (1 mmol), malononitrile (1.1 mmol), solvent 5 mL. [b]Isolated yield.

After the synthesis of 2-amino-4,5-dihydro-4-phenylpyrano[3,2-b]indole-3-carbonitriles, we have synthesized 5,6-dihydro-2-(2-oxo-2*H*-chromen-3-yl)-5-phenyl-indolo[2',3':5,6]pyrano [2,3-d]pyrimidin-4(3*H*)-one derivatives.

The solvents played an important role in the synthesis of indolo pyrano pyrimidinone derivatives. Various reaction media were screened (methanol, acetonitrile, *t*-BuOH, 1,4-dioxane,

ethanol and THF) using the model reaction (Table 3, Entries 1-6). The reaction was carried out under solvent-free condition at 80 ºC. It was found that the best results were obtained with 0.05 mmol of SuSA under solvent free condition (Table 3, Entry 7). The reaction was completed in 3 h and the expected product was obtained in 90% yield. Next, the effect of temperature was evaluated for the model reaction. It was observed that the reaction did not proceed at room temperature. Elevating the reaction temperature proved helpful, and the yield of desired product increased considerably (Table 3, Entries 7-12).

Table 2. Synthesis of various 2-amino-4,5-dihydro-4-phenyl-pyrano[3,2-b]indole-3-carbonitrile derivatives from benzaldehyde, 3-hydroxyindole, malononitrile catalysed by TUD (0.1 mmol)[a].

Entry	R1	Product	Time (min)	Yield (%)[b]
1	H	**4a**	40	94
2	4-F	**4b**	30	88
3	3-Br	**4c**	30	89
4	2-Cl	**4d**	60	84
5	4-CN	**4e**	40	85
6	4-$N(CH_3)_2$	**4f**	60	87
7	2-NO_2	**4g**	60	85
8	3-CH_3	**4h**	60	84
9	4-Cl	**4i**	60	86
10	4-CH_3	**4j**	60	85

[a]Reaction conditions: benzaldehyde (1 mmol), 3-hydroxyindole (1 mmol), malononitrile (1.1 mmol); TUD 0.1 mmol in water at 70 ºC. Isolated yield[b]

Table 3. Optimization of the reaction conditions on the synthesis of 5,6-dihydro-2-(2-oxo-2*H*-chromen-3-yl)-5-phenyl-indolo[2',3':5,6]pyrano[2,3-d]pyrimidin-4(3*H*)-one **6a**[a].

Entry	Catalyst	Amount	Solvent	Temperature (ºC)	Time (h)	Yield (%)[b]
1	SuSA	0.05 mmol	MeOH	Reflux	4.0	77
2	SuSA	0.05 mmol	CH_3CN	Reflux	5.0	42
3	SuSA	0.05 mmol	*t*-BuOH	Reflux	4.0	32
4	SuSA	0.05 mmol	1,4-Dioxane	Reflux	4.0	65
5	SuSA	0.05 mmol	EtOH	Reflux	4.0	81
6	SuSA	0.05 mmol	THF	Reflux	4.0	47
7	SuSA	0.05 mmol	Solvent-free	80	3.0	90
8	SuSA	0.05 mmol	Solvent-free	Rt	7.0	54
9	SuSA	0.05 mmol	Solvent-free	50	6.0	63
10	SuSA	0.05 mmol	Solvent-free	60	5.0	73
11	SuSA	0.05 mmol	Solvent-free	70	4.0	80
12	SuSA	0.05 mmol	Solvent-free	90	3.0	90
13	SuSA	0.00 mmol	Solvent-free	80	6.0	22
14	SuSA	0.02 mmol	Solvent-free	80	5.0	64
15	SuSA	0.04 mmol	Solvent-free	80	4.0	78
16	SuSA	0.06 mmol	Solvent-free	80	3.0	90
17	MTSA	0.05 mmol	Solvent-free	80	4.0	68
18	CSA	0.05 mmol	Solvent-free	80	4.0	73
19	SPA	0.05 mmol	Solvent-free	80	4.0	76
20	SA	0.05 mmol	Solvent-free	80	4.0	70

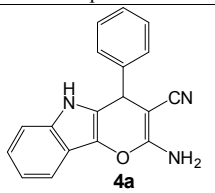
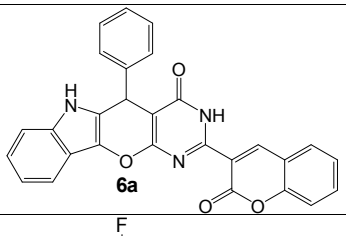
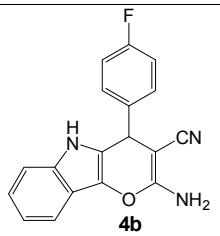
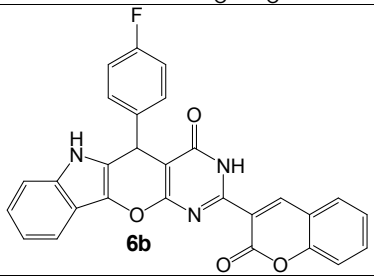
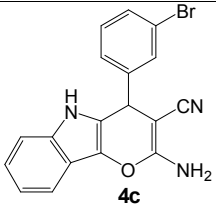
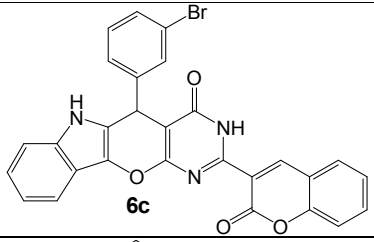
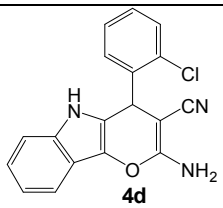
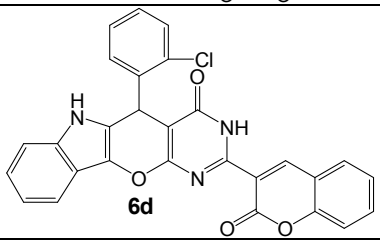
[a]Reaction conditions: **4a** (1 mmol) and coumarin-3-carboxylic acid (1 mmol), solvent 5 mL. [b]Isolated yield.

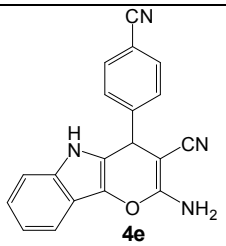
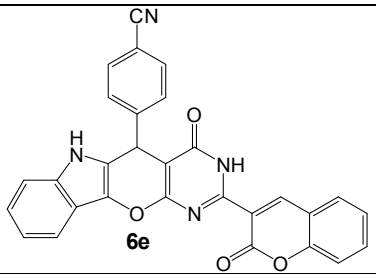
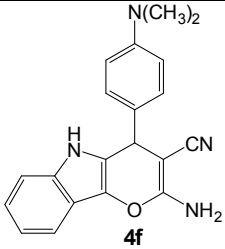
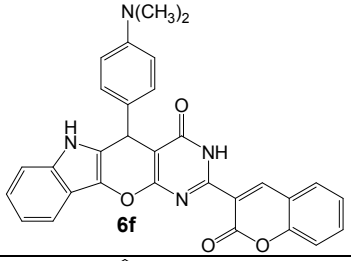
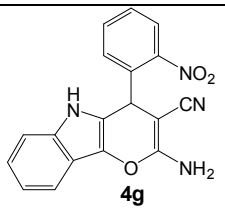
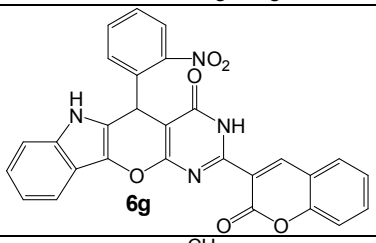
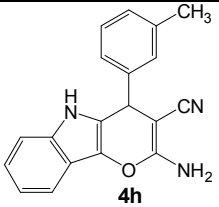
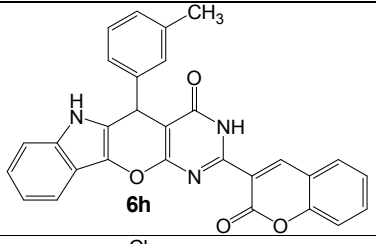
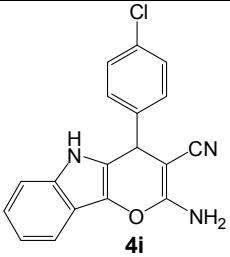
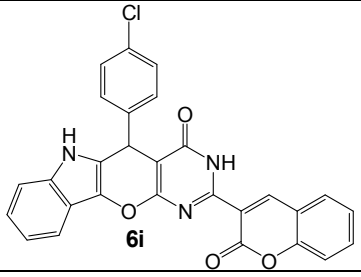
In order to evaluate the appropriate catalyst loading, the model reaction was performed using 0.0 to 0.06 mmol SuSA at 80 ºC without solvent (Table 3, Entries 7 and 13-16). It was found that 0.05 mmol of the catalyst afforded the maximum yield in minimum time. Higher

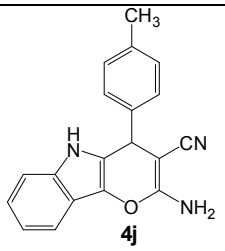
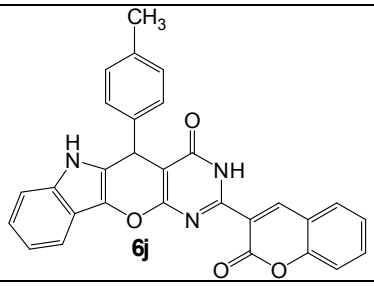
percentages of catalyst loading (0.06 mmol) neither increased the yield nor lowered the conversion time. To show that SuSA is an efficient catalyst, we accomplished the model reaction in the presence of catalysts, such as melamine trisulfonic acid (MTSA), cellulose sulfuric acid (CSA), silica perchloric acid (SPA) and sulfamic acid (SA) (Table 3, Entries 17-20). Tested catalysts gave lower yields compared with SuSA (Table 3, Entry 7). Thus, solvent-free and 0.05 mmol of SuSA were chosen as the optimum system to extend the protocol.

At these optimise conditions (solvent-free, 80 ºC, 0.05 mmol of SuSA) we synthesized various indolo pyrano pyrimidinones **6a-j** (Table 4, Entries 1-10). All the synthesized compounds were confirmed by their analytical and spectroscopic data.

Table 4. Preparation of various 5,6-dihydro-2-(2-oxo-2*H*-chromen-3-yl)-5-phenyl-indolo-[2',3':5,6]pyrano[2,3-d]pyrimidin-4(3*H*)-one derivatives[a].

Entry	Compound **4**	Product	Time (h)	Yield (%)[b]
1	 **4a**	 **6a**	3.0	90
2	 **4b**	 **6b**	3.0	91
3	 **4c**	 **6c**	3.5	91
4	 **4d**	 **6d**	4.0	88

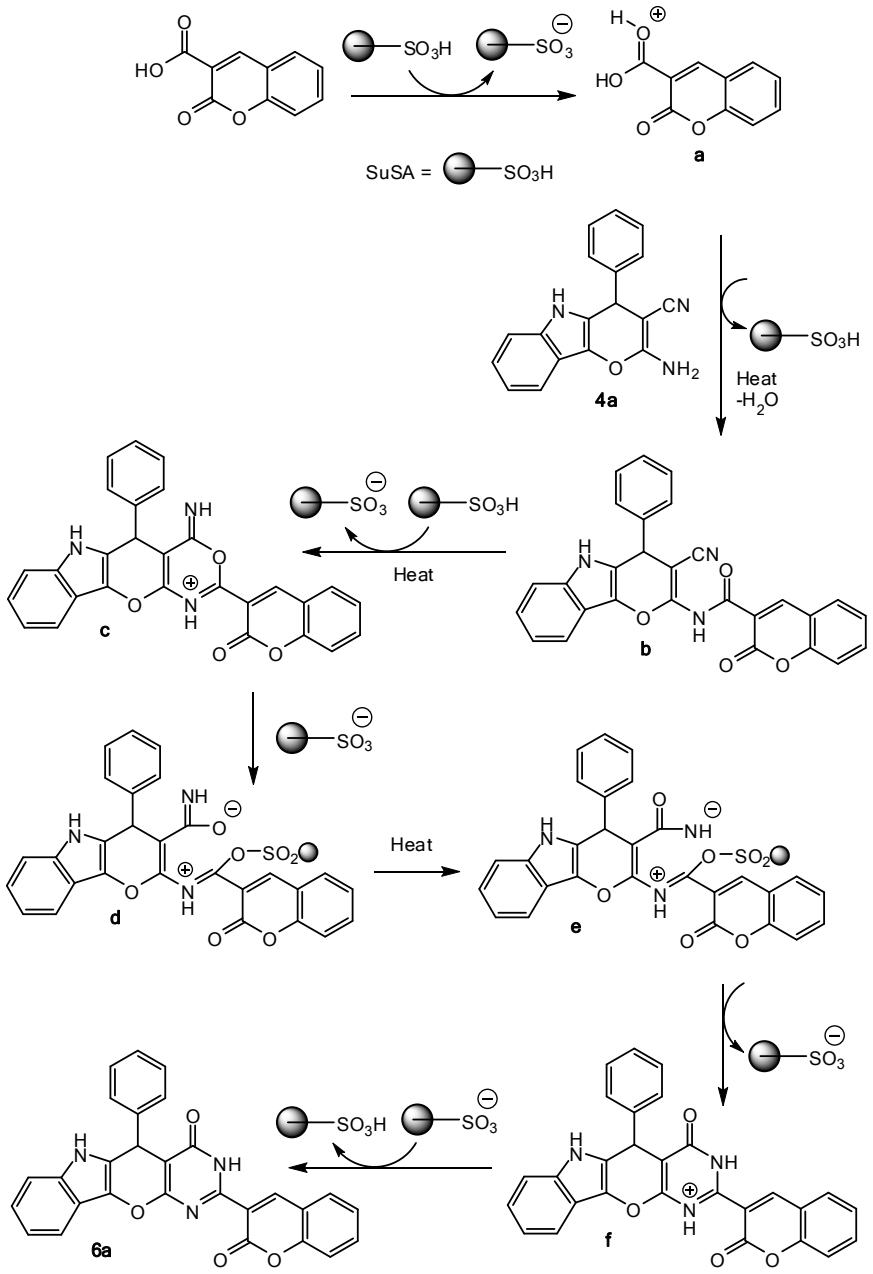
5	 **4e**	 **6e**	3.5	89
6	 **4f**	 **6f**	3.5	89
7	 **4g**	 **6g**	4.0	87
8	 **4h**	 **6h**	3.5	85
9	 **4i**	 **6i**	3.5	89

10	 **4j**	 **6j**	3.5	86

[a]Reaction conditions: **4a-j** (1 mmol) and coumarin-3-carboxylic acid (1 mmol) in the presence of SuSA (0.05 mmol) at 80 ºC. [b]Isolated yield.

The possible mechanism for the synthesis of 5,6-dihydro-2-(2-oxo-2*H*-chromen-3-yl)-5-phenyl-indolo[2',3':5,6]pyrano[2,3-d]pyrimidin-4(3*H*)-one derivatives in the presence of SuSA as a solid catalyst is shown in Scheme 4. SuSA activates the coumarin-3-carboxylic acid by protonation to form a cation intermediate (**a**). In continue, the formation of (**b**) resulting from the amidation of (**a**) with **4a** was established. In the next step, the protonation of nitrile group of intermediate (**b**) following by a cyclo-addition reaction was occurred to form the intermediate (**c**). In continue the addition reaction of $-SO_3^-$ followed by ring opening of the (**c**) to the intermediate (**d**) and (**e**) followed by ring closure of intermediate (**e**) results in the formation of intermediate (**f**) that convert to the (**6a**) as product by the de-protonation reaction. Interestingly, the formation of compound **6a**, obtained from the condensation of coumarin-3-carboxylic acid with **4a**, confirms the mechanism of the reaction which was rarely described in the literature as Dimroth rearrangement [35, 36].

The reusability of the catalyst is one of the most important green aspects by avoiding toxic catalyst [37]. One of the most important advantages of heterogeneous catalysis over the homogeneous counterpart is the possibility of reusing the catalyst by simple filtration, without loss of activity [38-40]. We have studied the recyclability and reusability of the catalyst. After completion of the reaction as indicated TLC, the insoluble crude product was dissolved in hot ethanol and the SuSA was filtered off. The filtrate was concentrated to dryness, and the crude product was purified by recrystallization from ethanol. The recovered catalyst was, washed with acetone, dried and reused for subsequent reactions without significant loss in its activity. The catalyst was recycled for four runs without loss of its activity (Figure 1).



Scheme 4. A possible mechanism for the synthesis of 5,6-dihydro-2-(2-oxo-2*H*-chromen-3-yl)-5-phenyl-indolo[2',3':5,6]pyrano[2,3-d]pyrimidin-4(3*H*)-one derivatives in the presence of SuSA as a catalyst.

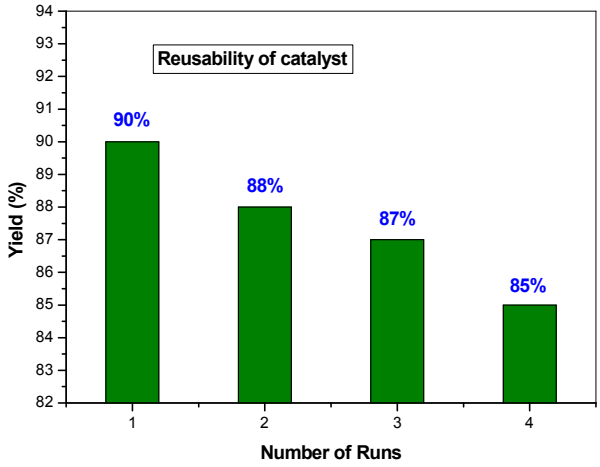


Figure 1. Recyclability of the catalyst: The SuSA catalyst could be reused four times without any loss of its activity towards the synthesis of 5,6-dihydro-2-(2-oxo-2*H*-chromen-3-yl)-5-phenyl-indolo[2',3':5,6]pyrano[2,3-d]pyrimidin-4(3*H*)-one.

CONCLUSIONS

In summary, we have developed a straightforward and efficient method for the preparation of 5,6-dihydro-2-(2-oxo-2*H*-chromen-3-yl)-5-phenyl-indolo[2',3':5,6]pyrano[2,3-*d*]pyrimidin-4(3*H*)-one derivatives by the condensation of 2-amino-4,5-dihydro-4-phenylpyrano[3,2-*b*]indole-3-carbonitriles with coumarin-3-carboxylic acid in the presence of 0.05 mmol of SuSA as catalyst. This method tolerates most of the substrates, and the catalyst can be reused at least four times without significant loss of activity.

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