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A FACILE SYNTHESIS OF TETRAHYDROBENZO[b]PYRANS AND PYRANO [2,3-d] PYRIMIDINE DIONES IN WATER USING CERIUM CHLORIDE HEPTAHYDRATE AS CATALYST

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Abstract

A series of tetrahydrobenzo[b]pyrans and pyrano [2,3-d] pyrimidine diones were synthesised in water using Cerium chloride heptahydrate ($CeCl_3.7H_2O$), a water tolerant Lewis acid with low toxicity, as a catalyst. This protocol provides a clean, safe, quick and efficient one pot route for the synthesis of the target molecules.

Keywords: Tetrahydrobenzopyrans, pyranopyrimidine, $CeCl_3.7H_2O$, Lewis acid, water

Introduction

Pyran derivatives are structural subunits in a variety of important natural products, including carbohydrates, alkaloids, polyether antibiotics, pheromones, and iridoids.[i] Many natural products containing benzopyran core structure display a wide array of pharmacological activities such as antibacterial, antitumor, antiallergic, anticoagulant, spasmolytic, diuretic, and potassium channel activators.[ii-vii] Pyrans and their derivatives are also key synthons[viii] in the fields of pharmaceuticals, cosmetics, and perfumes. Some 2-amino-4*H*-pyrans are also employed as photoactive materials.[ix]

Pyrano [2,3-d] pyrimidine is an unsaturated heterocycle formed by the fusion of pyran and pyrimidine rings. The biological importance of these compounds has evoked widespread interest in the development of new methodologies for their synthesis. Some of the reported procedures for the synthesis of tetrahydrobenzopyrans use DMF/acetic acid as solvents,[x] which make the

workup tedious and result in poor yields of products. In spite of merits involved in the use of reactants in the solid or molten state,[xi] they have their disadvantages such as very high temperatures and long reaction times.[xii-xiii] Generally, these compounds are synthesized by three-component reactions of dimedone with malononitrile and aryl aldehydes. Several catalytic reagents such as piperidine,[xiv] $BF_3.SiO_2$,[xv] choline hydroxide,[xvi] DABCO,[xvii] L-Proline,[xviii] Mg-Al hydrotalcite,[xix] $MnSO_4.4H_2O$,[xx] $Ni(NO_3)_2.6H_2O$,[xxi] sucrose,[xxii] and lipase[xxiii] have been used as a catalyst in these reactions. Most of these methods also involve the use of volatile solvents, long reaction times and harsh work-up procedures.

Likewise, for the synthesis of pyranopyrimidines, efforts have been directed towards the synthetic manipulation of uracils. These require drastic conditions, long reaction times and complex synthetic pathways and the yields are poor.[xxiv-xxvi] The general procedure for the preparation of pyrano [2,3-d] pyrimidine-2,4-(1*H*,3*H*)-diones include the reaction of arylidenemalononitriles with barbituric acid under traditional hot reaction conditions[xxvii-xxviii] or microwave irradiation.[xxix] In these methods the arylidenemalononitriles are previously derived from malononitrile and aldehydes. Direct condensation of aldehydes, malononitrile and barbituric acid in aqueous media has also been reported under ultrasound irradiation, [xxx] heating with water[xxxi] and using the ball-milling technique.[xxxii] Different catalysts such as L-proline,[xxxiii] N-methyl morpholine,[xxxiv] $[BMIm]BF_4$,[xxxv] 1,4-dioxane,[xxxvi] heteropolyacid like $H_{14}[NaP_5W_{30}O_{110}]$, [xxxvii] K $Al(SO_4)_2$ [xxxviii] under heating, dibutyl amine [xxxix] and SBA-Pr-SO_3H as a nanocatalyst [xl] have been studied for this synthesis.

In the last few years, there has been substantial interest in the organic reactions promoted by cerium chloride.[xli] Unlike common Lewis acids, trivalent lanthanide salts are stable in aqueous solutions. Cerium chloride heptahydrate ($CeCl_3.7H_2O$), the most common commercially available source of Ce^{+3}, finds useful application as a catalyst in heterocyclic synthesis. [xlii] $CeCl_3.7H_2O$ is a mild Lewis acid, has low toxicity and is relatively inexpensive. Hence $CeCl_3.7H_2O$ is a good candidate for use in green organic transformations.[xliii-xliv] Our studies have demonstrated the effective use of $CeCl_3.7H_2O$ as a catalyst in the synthesis of imines [xlv] as well as reductive amination reactions.[xlvi] Further, we have synthesised 3-methyl isoxazolone derivatives[xlvii] as well as 1,3,5-triaryl-2-pyrazoline derivatives[xlviii] catalysed by $CeCl_3.7H_2O$ using 70% ethyl lactate as a solvent. Recently we have reported the use of low melting mixtures of sugars, urea and $CeCl_3$ $.7H_2O$ as efficient green solvents for the synthesis of 1,4-dihydropyridines.[xlix]

Solvents are an important constituent of any organic synthesis and often account for the maximum amount of waste that is generated. The conventional solvents like benzene, DMSO, etc., have detrimental environmental impacts. Hence, the use of green solvents in organic synthesis is an area of extensive research and several green solvents like water, ionic liquids, polyethylene glycol and some biomass based solvents in organic synthesis have been reported in the literature.[l] Water is the solvent in which biochemical reactions are performed in nature, and it is environmentally benign.[li]

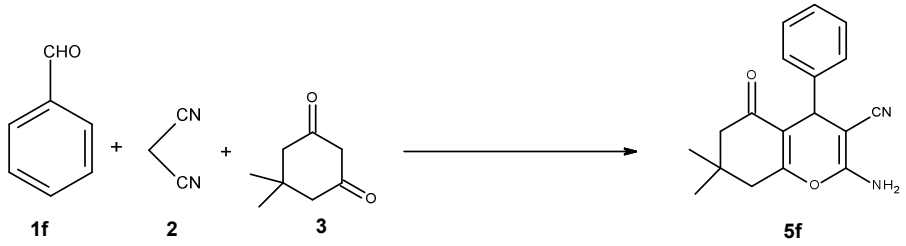
In continuation with our previous work on the use of Cerium chloride heptahydrate ($CeCl_3.7H_2O$) as a mild, low cost and high performance catalyst in the green synthesis of heterocyclic compounds, we now report a facile synthesis of a number of benzopyrans and pyranopyrimidines from substituted aldehydes, malononitrile and dimedone/barbituric acid respectively. In a previously reported paper, $CeCl_3$ $.7H_2O$ has been employed as a catalyst for synthesis of benzopyrans.[lii] However, to the best of our knowledge, the use of $CeCl_3$ $.7H_2O$ in

water under reflux conditions for the synthesis of benzopyrans and pyranopyrimidines is not reported in the literature.

Results and Discussion:

In the initial experiment, the synthesis of 2-amino-3-cyano-7,7-dimethyl-5-oxo- 4-phenyl- 4*H*-5,6,7,8-tetrahydrobenzo[b]pyran (**5f**) was carried out using benzaldehyde (**1f**), malononitrile (**2**) and dimedone (**3**) as model substrates for exploring the optimum conditions (**SCHEME 1**). Water was used as the solvent and the reaction was conducted at R.T and reflux conditions with different concentrations of the catalyst $CeCl_3.7H_2O$. The results are summarised in **Table 1**.

The reaction gave very poor yields at room temperature (**Table 1**, Entries **1- 4**). However, the yields increased under reflux conditions. The amount of catalyst was also found to influence the yields. The highest yield was obtained with a 15 mol% concentration of the catalyst (**Table 1**, Entry **7**) and a further increase in catalyst concentration did not change the yield appreciably. On the basis of these results, the optimum conditions for the synthesis were determined to be refluxing in water in the presence of 15mol % $CeCl_3 .7H_2O$ as a catalyst.



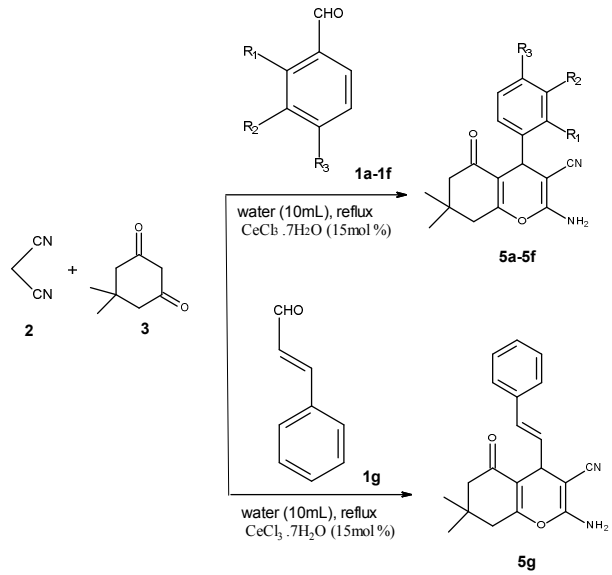
SCHEME 1: Model reaction for the optimisation of reaction conditions

Table 1: Optimisation of reaction conditions using the model reaction

Entry	Catalyst (mol %)	Condition(°C)	Time(min.)	Yield[a] (%)
1.	5	R.T.	120	30
2.	10	R.T.	100	30
3.	15	R.T.	100	35
4.	20	R.T.	90	35
5.	5	Reflux	110	54
6.	10	Reflux	100	68
7.	15	Reflux	90	89
8.	20	Reflux	90	85

[a] All yields are of pure isolated products.

By using the optimised conditions described above, condensation reactions to produce the other tetrahydrobenzo[b] pyran derivatives (**5a-5g**) were studied (**SCHEME 2)**. The results are enumerated in **Table 2**.



Aldehyde/Product	R_1	R_2	R_3
1a/5a	H	H	Cl
1b/5b	H	NO_2	H
1c/5c	H	H	NO_2
1d/5d	Cl	H	H
1e/5e	H	H	OH
1f/5f	H	H	H

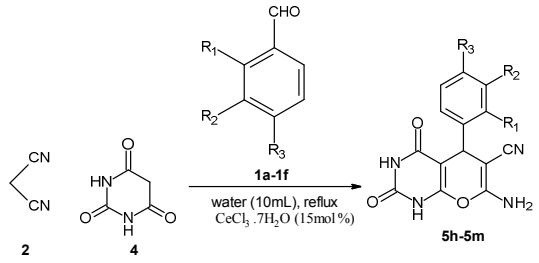
SCHEME 2: Synthesis of tetrahydrobenzo[b]pyrans

Table 2: Synthesis of tetrahydrobenzo[b]pyrans using substituted benzaldehydes, malononitrile and dimedone.

Aldehyde /Product	Time (min)	Melting point (◦C)		Yield[a] (%)
		Found	Reported	
1a/5a	90	206-207	209-211 [liii]	96
1b/5b	15	207-208	208-210[liii]	88
1c/5c	20	176-177	175-177 [liii]	87
1d/5d	150	211-212	214-215 [liii]	94
1e/5e	75	213-214	214-215 [liv]	79
1f/5f	150	226-227	227-229 [liii]	89
1g/5g	90	184-185	183-185 [liii]	88

[a] All yields are of pure isolated products.
Reaction conditions: aldehyde (1mmol), malononitrile (1.1mmol,) dimedone (1mmol) in water (10mL), $CeCl_3 .7H_2O$, (15mol %) refluxed

The same conditions were used for the synthesis of pyrano [2,3-d] pyrimidine diones (**5h-5m**) by replacing dimedone with barbituric acid (**SCHEME 3**). The results are enumerated in **Table 3**.



Aldehyde/Product	R_1	R_2	R_3
1a/5h	H	H	Cl
1b/5i	H	NO_2	H
1c/5j	H	H	NO_2
1d/5k	Cl	H	H
1e/5l	H	H	OH
1f/5m	H	H	H

SCHEME 3: Synthesis of pyrano [2,3-d] pyrimidine diones

Table 3: Synthesis of pyrano [2,3-d] pyrimidine diones using substituted benzaldehydes, malononitrile and barbituric acid

Aldehyde /Product	**Time (min)**	**Melting point (◦C)**		**Yield[a] (%)**
		Found	Reported	
1a/5h	45	230-232	234-235 [lv]	92
1b/5i	60	256-257	258-260 [xxxix]	91
1c/5j	90	227-228	227-229 [xxxix]	84
1d/5k	45	209-210	208-211 [lv]	94
1e/5l	60	162-163*	163-167[xxxix]	84
1f/5m	30	203-204	205-207 [xxxix]	93

* decomposition

[a] All yields are of pure isolated products.

Reaction conditions: aldehyde (1mmol), malononitrile (1.1mmol,) barbituric acid (1mmol) in water (10mL), $CeCl_3$.$7H_2O$, (15mol %) refluxed

The reaction proceeded in a clean manner and after completion of the reaction the solid product was collected by simple filtration. The products obtained in most cases were pure. Wherever required the products were purified by recrystallisation from hot ethanol. The structures of the compounds were established by spectral data and comparison of their physical properties with that reported in the literature.

All the products were characterized by comparison of their melting points with the literature value as well as IR, PMR and CMR data. The infrared spectrum of all the synthesised compounds showed a characteristic sharp peak in the region 1650-1750 cm^{-1} corresponding to the >C=O group. Another characteristic sharp peak corresponding to - C≡N group was observed in the region 2190-2220 cm^{-1} for all the compounds. In the case of the tetrahydrobenzopyrans **(5a-5g)** two peaks were observed in the range 3300-3450 cm^{-1} which clearly indicates the $–NH_2$ group. In the products from barbituric acid, a series of upto four peaks were observed in the range 2800-3500 cm^{-1} which may be due to the $–NH_2$ and –NH groups.

^{1}H NMR spectrum of the tetrahydrobenzopyran derivatives showed the characteristic peak in the region of 3.85-4.85 ppm corresponding to the methine proton at C-4 of the pyran ring. (**Fig.1**) The two protons at C-6 are diastereotopic in nature and appear as two doublets with large coupling constants (J = 12-16 Hz) in the region 2.02-2.45 ppm. The two methyl groups on C-7 are also diastereotopic and appear as two separate singlets very close to each other in the region 1.02-1.13 ppm. The two protons at C-8 appear as a singlet in the region 2.41-2.54 ppm. The

protons of $-NH_2$ group at C-2 appear as a singlet in the range 6.63-7.26 ppm and the signals due to the aromatic protons are observed at their characteristic positions.

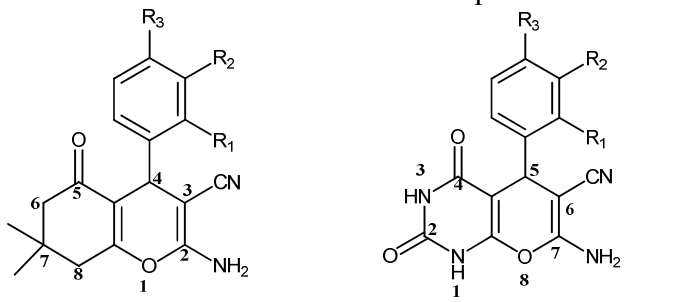
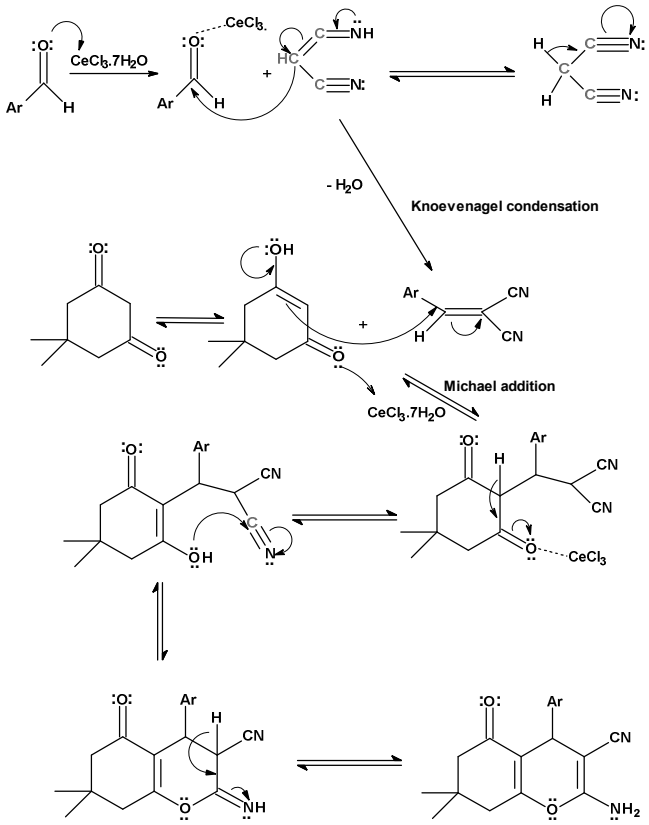


Fig.1: General structures of synthesised compounds

The tetrahydrobenzopyran derivative obtained from cinnamaldehyde **(5g)** shows a doublet at 6.35 ppm which has been assigned to the olefinic protons, and it has a coupling constant of 14.2 Hz. In the ^1H NMR spectrum of the pyrano [2,3-d] pyrimidine diones, the protons on the nitrogens at positions 1 and 3 of the pyrimidine ring appear as two separate singlets between 9.00-11.00 ppm and 12-13 ppm. The methine proton at C-5, the amino protons at C-7 and the aromatic protons appear at their characteristic values. Each of these spectral assignments are in good agreement with values reported in the literature.

^{13}CNMR of the tetrahydrobenzopyran derivatives showed characteristic peaks in the regions, 25-30 ppm (-CH_3 at C-7), 36-40 ppm (methine carbon at C-4), 118-120 ppm (carbon of -CN), 125-140 ppm (aromatic carbons) and at 185-195 ppm (>C=O group). In the ^{13}CNMR spectrum of the pyrano [2,3-d] pyrimidine diones, the peak attributed to the >C=O group appears in the range 160-165 ppm due to resonance with the adjacent –NH group. Other ^{13}CNMR peaks are in line with reported values. Thus the structures of the synthesised derivatives have been unambiguously confirmed.

A reasonable pathway for the reaction between aldehyde, malononitrile and dimedone/barbituric acid in the presence of $CeCl_3.7H_2O$ is proposed based on the results obtained and information in the literature. $CeCl_3.7H_2O$ is a mild Lewis acid capable of coordinating with carbonyl oxygen which enhances its reactivity. Based on mechanisms proposed by Ziarani *et al* in the synthesis of pyrano [2,3-d] pyrimidine diones facilitated by sulphonic acid nanoporous silica (SBA-Pr-SO_3H)[xl] and by Kidwai and Jahan in Mannich reaction catalysed by $CeCl_3.7H_2O$,[lvi] we propose the following likely mechanism for this reaction. **(Scheme 4)** A similar mechanism can be put forward to explain the synthesis of pyrano [2,3-d] pyrimidine diones.



SCHEME 4: Plausible mechanism for the synthesis of tetrahydrobenzo[b]pyran derivatives using $CeCl_3.7H_2O$ as catalyst.

Conclusion:

The paper describes a simple methodology for the synthesis of tetrahydrobenzopyran and pyrano [2,3-d] pyrimidine dione derivatives using cerium chloride heptahydrate in water. This protocol uses a safe solvent and $CeCl_3.7H_2O$, which is a water tolerant Lewis acid. Unlike the previously reported synthesis of these compounds in water in the absence of a catalyst, [xxxiii] the present methodology gives the desired products in comparable time and works well for all systems giving better yields. As compared to reported methods, the current methodology provides a clean, safe, quick and efficient route for the synthesis of the target molecules.

Experimental Section

All the reagents were obtained from commercial sources and were used directly, without any further purification. The characterization of the products was done by comparing their physical constants with the literature values and by recording their spectra. ^1H and ^{13}C NMR spectra were measured at ambient temperatures using $CDCl_3$ or DMSO- d_6 as the solvent on a 600MHz BRUKER AVANCE DRX-500. FT-IR spectra were recorded on Perkin Elmer RXI spectrometer.

General procedure for the synthesis of tetrahydrobenzo[b]pyrans (5a-5g) and pyrano [2,3-d] pyrimidine diones (5h-5m): (SCHEME 1,2)

A suspension of aldehyde (1mmol, **1a – 1g**), malononitrile (1.1mmol, **2**) and dimedone (1mmol, **3**) or barbituric acid (1mmol, **4**) in water (10mL) and ($CeCl_3.7H_2O$, 15mol %) was refluxed. The progress of the reaction was monitored by thin layer chromatography (TLC) using hexane:ethyl acetate (7:3) as the solvent system. The precipitated solid was collected by filtration, washed with water and dried. Further purification when required was accomplished by recrystallisation from ethanol.

Physical and spectral characterization of 4-aryl 2-amino-3-cyano-7,7-dimethyl-5-oxo-4*H*-5,6,7,8-tetrahydrobenzo[b]pyran derivatives (5a-5g) and 5-aryl-7-amino-6-cyano-5*H*-pyrano[2,3-d]pyrimidine-2,4(1*H*,3*H*)-dione derivatives (5h-5m)

1. 2-amino-4-(4'-chlorophenyl)-3-cyano-7,7-dimethyl-5-oxo-4*H*-5,6,7,8-tetrahydrobenzo[b]pyran (5a)

The compound was obtained as a yellow solid (M.P.206 - 207◦C) with a yield of 96%.

^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm): 7.25 (d, 2H, *J* = 12Hz, Ar-H), 7.17 (d,2H, *J* = 12Hz, Ar-H), 7.09 (s, 2H, -NH_2), 4.40 (s, 1H, H-4), 2.45 (s, 2H, H-8), 2.25 (d, *J* = 18 Hz, 1H, H-6),2.20 (d, *J* = 18 Hz, 1H, H-6') 1.13 (s, 3H, CH_3 on C-7), 1.02 (s, 3H, CH_3 on C-7).

^{13}C NMR (151 MHz, $CDCl_3$, δ, ppm):196.0, 161.8, 157.4, 134.1, 128.7, 121.9, 118.2, 112.8, 61.1, 50.3, 40.3, 37.0, 31.6, 28.7, 26.9.

2. 2-amino-3-cyano-7,7-dimethyl-4-(3'-nitrophenyl)-5-oxo-4*H*-5,6,7,8-tetrahydrobenzo[b]pyran (5b)

The compound was obtained as a yellow solid (M.P.207 - 208◦C) with a yield of 88%.

^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm): 8.08 (m, 1H, Ar-H), 8.03 (m,1H, Ar-H), 7.67 (m,1H, Ar-H), 7.48 (m,1H, Ar-H), 7.26 (s, 2H, NH_2), 4.51 (s, 1H, H-4), 2.50 (s, 2H, H-8), 2.26 (d, *J* = 16.4 Hz, 1H, H-6), 2.20 (d, *J* = 16.4 Hz, 1H, , H-6'), 1.12 (s, 3H, CH_3 on C-7), 1.03 (s, 3H, CH_3 on C-7).

^{13}C NMR (151 MHz, $CDCl_3$, δ, ppm): 196.3, 163.1, 159.0, 148.6, 134.3, 129.9, 122.7, 118.5, 112.5, 57.7, 50.5, 40.7, 39.1, 32.4, 28.9, 27.8.

3. 2-amino-3-cyano-7,7-dimethyl-4-(4'-nitrophenyl)-5-oxo-4*H*-5,6,7,8-tetrahydrobenzo[b]pyran (5c)

The compound was obtained as a yellow solid (M.P.176-177◦C) with a yield of 87%.

^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm): 8.17 (d, *J* = 8.7 Hz, 2H, Ar-H), 7.42 (d, *J* = 8.7 Hz, 2H, Ar-H), 7.26 (s, 2H, -NH_2), 4.52 (s, 1H, H-4), 2.48 (s, 2H, H-8), 2.26 (d, *J* = 16.4 Hz, 1H, H-6), 2.20 (d, *J* = 16.4 Hz, 1H, H6'), 1.13 (s, 1H, CH_3 on C-7), 1.03 (s, 1H, CH_3 on C-7).

^{13}C NMR (151 MHz, $CDCl_3$, δ, ppm): 196.0, 162.1, 157.4, 145.4, 134.6, 128.9, 122.3, 118.2, 113.2, 61.9, 50.5, 40.7, 39.1, 32.4, 28.6, 27.1.

4. 2-amino-4-(2'-chlorophenyl)-3-cyano-7,7-dimethyl-5-oxo-4*H*-5,6,7,8-tetrahydrobenzo[b]pyran (5d)

The compound was obtained as a yellow solid (M.P.211 - 212◦C) with a yield of 94%.

^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm): 7.33 - 7.19(m, 4H, Ar-H), 7.07(s,2H,NH_2), 4.85(s,1H,H-4), 2.45(s,2H,H-8), 2.24(d, *J* = 18Hz,1H,H-6), 2.18(d, *J* = 18Hz,1H,H-6'), 1.11(s,3H,CH_3), 1.07(s,3H,CH_3).

^{13}C NMR (151 MHz, $CDCl_3$, δ, ppm): 195.8, 162.0, 158.0, 140.0, 133.1 ,129.7, 128.6, 118.5, 112.7, 58.1, 50.5, 40.3, 39.1, 33.4, 28.4, 27.4.

5. 2-amino-3-cyano-4-(4'-hydroxyphenyl)-7,7-dimethyl-5-oxo-4*H*-5,6,7,8-tetrahydrobenzo[b]pyran (5e)

The compound was obtained as a light yellow solid (M.P.213 - 214◦C) with a yield of 79%.
^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm): 9.41 (s,1H, -OH), 6.80 – 6.96 (m,4H), 6.63 (s,2H,NH_2), 4.13 (s,1H,H-4), 2.54 (s,2H,H-8), 2.25 (d, *J* = 16.3Hz,1H,H-6), 2.02 (d, *J* = 16.3Hz,1H,H-6'), 1.11(s,3H,CH_3), 1.04 (s,3H,CH_3).

^{13}C NMR (151 MHz, $CDCl_3$, δ, ppm): 195.1, 161.5, 157.7, 148.2, 134.0, 128.6, 121.6, 118.4, 112.7, 62.8, 50.1, 40.3, 35.3, 31.8, 28.6, 26.7.

6. 2-amino-3-cyano-7,7-dimethyl-5-oxo-4-phenyl-4*H*-5,6,7,8-tetrahydrobenzo[b]pyran (5f)

The compound was obtained as a white solid (M.P.226 - 227◦C) with a yield of 89%.
^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm): 7.30 - 7.18(m,5H), 6.91(s,2H,NH_2), 4.40(s,1H,H-4), 2.45(s,2H,H-8), 2.24(d, *J* = 16.3Hz,1H,H-6), 2.19(d, *J* = 16.3Hz,1H,H-6'), 1.11(s,3H,CH_3), 1.04(s,3H,CH_3).

^{13}C NMR (151 MHz, $CDCl_3$, δ, ppm): 195.8, 162.5, 158.1, 148.2, 134.3, 129.6, 122.7, 118.2, 110.6, 61.9, 50.1, 40.3, 39.1, 31.8, 28.3, 27.1.

7. 2-amino-3-cyano-7,7-dimethyl-5-oxo-4-[(E)-styryl]-4*H*-5,6,7,8-tetrahydrobenzo[b]pyran (5g)

The compound was obtained as a light yellow solid (M.P.184-185◦C) with a yield of 88%.
^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm): 7.20 -7.33 (m,5H,Ar-H), 7.03 (s,2H,NH_2),6.35 (d,*J* = 14.2Hz, 2H,CH=CH), 3.85(s,1H,H-4), 2.41 (s,2H,H-8), 2.21(d, *J* = 16.3Hz,1H,H-6), 2.06(d, *J* = 16.3Hz,1H,H-6'),1.07(s,3H,CH_3), 1.03 (s,3H,CH_3).
^{13}C NMR (151 MHz, $CDCl_3$, δ, ppm): 196.3, 163.0, 158.2, 149.0, 145.3, 134.4, 129.2, 123.5, 118.1, 112.9, 61.7, 50.7, 40.7, 35.5, 32.0, 28.8, 27.3.

8. 7-amino-6-cyano-5-(4'-chlorophenyl)-5*H*-pyrano[2,3-d]pyrimidine-2,4(1*H*,3*H*)-dione (5h)

The compound was obtained as a yellow solid (M.P.230 - 232◦C) with a yield of 92%.
^{1}H NMR (600 MHz, DMSO-d_6, δ, ppm): 11.86(s, 1H, NH), 10.85(s, 1H, NH), 7.46(d, 2H, *J* = 6.3 Hz, ArH), 7.25(d, 2H, *J* = 6.3 Hz, ArH),, 7.16(s, 2H, NH_2), 4.40(s, 1H, CH).

^{13}C NMR (151 MHz, DMSO- d_6, δ, ppm): 175.15, 170.07, 155.30, 150.99, 148.51, 145.32, 129.13, 122.59, 118.27, 106.82, 73.68, 67.99.

9. 7-amino-6-cyano-5-(3'-nitrophenyl)-5*H*-pyrano[2,3-d]pyrimidine-2,4-(1*H*,3*H*)-dione (5i)

The compound was obtained as a yellow solid (M.P.256 - 257◦C) with a yield of 91%.

^{1}H NMR (600 MHz, DMSO- d_6, δ, ppm): 12.14 (s, 1H, NH), 10.23 (s, 1H, NH), 8.29 (s, 1H, ArH), 8.09 (m, 3H, ArH),6.84(s, 2H, NH_2), 3.88(s, 1H, CH).

^{13}C NMR (151 MHz, DMSO-d_6, δ, ppm): 163.9, 160.3, 156.9, 151.7, 150.6, 146.1, 129.5, 123.9, 118.1, 105.0, 79.1, 70.5.

10. 7-amino-6-cyano-5-(4'-nitrophenyl-5*H*-pyrano[2,3-d]pyrimidine-2,4-(1*H*,3*H*)-dione (5j)

The compound was obtained as a yellow solid (M.P.227 - 228◦C) with a yield of 84%.

^{1}H NMR (600 MHz, DMSO-d_6, δ, ppm): 12.96(s, 1H, NH), 8.86(s, 1H, NH), 7.89(d, 2H, *J* = 6.3 Hz, ArH), 7.39(d, 2H, *J* = 6.3 Hz, ArH), 6.77(s, 2H, NH_2), 4.82(s, 1H, CH).

^{13}C NMR (151 MHz, DMSO- d_6, δ, ppm): 176.8, 170.1, 154.9, 151.8, 149.6, 146.7, 128.4, 123.7, 120.0, 104.3, 75.1, 70.8.

11. 7-amino-6-cyano-5-(2'-chlorophenyl)-5*H*-pyrano[2,3-d]pyrimidine-2,4-(1*H*,3*H*)-dione (5k)

The compound was obtained as a light yellow solid (M.P.209 - 210◦C) with a yield of 94%.

^{1}H NMR (600 MHz, DMSO- d_6, δ, ppm): 12.06(s, 1H, NH), 10.95(s, 1H, NH),7.46(d, 1H, J = 6.3 Hz, ArH),7.24(m, 3H, ArH),7.04(s, 2H, NH_2), 4.68(s, 1H, CH).

^{13}C NMR (151 MHz, DMSO- d_6, δ, ppm): 162.6, 157.5, 155.3, 151.0, 142.0, 136.7, 134.1, 130.8, 129.8, 128.4, 118.3, 88.8, 61.8, 32.0.

12. 7-amino-6-cyano-5-(4'-hydroxyphenyl)-5*H*-pyrano[2,3-d]pyrimidine-2,4-(1*H*,3*H*)-dione (5l)

The compound was obtained as a white solid (M.P.162 - 163◦C) with a yield of 96%.The substance decomposed on melting.

^{1}H NMR (600 MHz, DMSO-d_6, δ, ppm): 11.04 (s, 1H, NH), 10.67 (s,1H, NH), 7.14 (d, *J* = 6.3 Hz, 2H, Ar-H), 6.82 (s, 2H,NH_2), 6.54 (d, *J* = 6.3 Hz, 2H, Ar-H), 6.00 (s, 1H, OH), 4.40 (s, 1H, CH)

^{13}C NMR (151 MHz, DMSO- d_6, δ, ppm): 169.4, 157.5, 155.5, 152.4, 150.2, 129.3, 128.4, 118.2, 115.0, 97.6, 61.9, 50.8.

13. 7-amino-6-cyano-5-phenyl-5*H*-pyrano[2,3-d]pyrimidine-2,4-(1*H*,3*H*)-dione (5m)

The compound was obtained as a light yellow solid (M.P.203 - 204◦C) with a yield of 93%.

^{1}H NMR (600 MHz, DMSO-d_6, δ, ppm): 11.04 (s, 1H, NH), 10.81(s,1H, NH), 7.35 (t, *J* = 6.3 Hz, 2H, Ar-H), 7.05 (m, 3H, Ar-H), 6.83 (s, 2H,NH_2), 4.40 (s, 1H, CH)

^{13}C NMR (151 MHz, DMSO-d_6, δ, ppm): 162.1, 157.7, 152.6, 150.8, 145.4, 129.6, 128.4, 125.8, 118.5, 93.2, 58.4, 50.1.

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