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Catalytic activity of ZrO_2–SO_3H as highly efficient recyclable nano-catalyst for the synthesis of tetrahydrobenzo[*b*]pyrans

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Abstract: Application of Nano Zirconia Sulfuric Acid (n-ZrSA), as a catalyst for the synthesis of tetrahydrobenzo[*b*]pyran prepared by the reaction of dimedone, aromatic or aliphatic aldehydes, and malononitrile in solvent-free condition. The catalyst was prepared according to a previously published literature procedure using inexpensive and readily available starting materials. Furthermore, the catalyst could be recovered conveniently and reused efficiently such that a considerable catalytic activity still could be achieved after fourth run. Other beneficial features of this new synthetic approach include short reaction time, high yields, clean reaction profiles, and a simple work-up procedure.

Keywords: Nano Zirconia Sulfuric Acid (n-ZrSA), Tetrahydrobenzo[*b*]pyrans, Fast and green synthesis.

Introduction

Acid-catalysts are one of the most frequently applied processes in chemical industry, which has been a major area of research interest [1–6]. Commonly, liquid inorganic acids including H_2SO_4, HCl and H_3PO_4 are part of the homogeneous acid catalysts. Despite their application in the wide production of industrial chemicals, many disadvantages such as high toxicity, corrosive nature, hazards in handling and difficult separation from the products make them not so useful. Furthermore, the synthesis using homogeneous catalysts have major problem of catalyst recovery and reuse. These difficulties are not in the range of green chemistry. According to these disadvantages, in order to improve drawbacks of these catalysts, replacement of them by novel, nontoxic, eco-friendly, recyclable heterogeneous catalysts with improved efficiency have been the important topics of researchers during the last decades.

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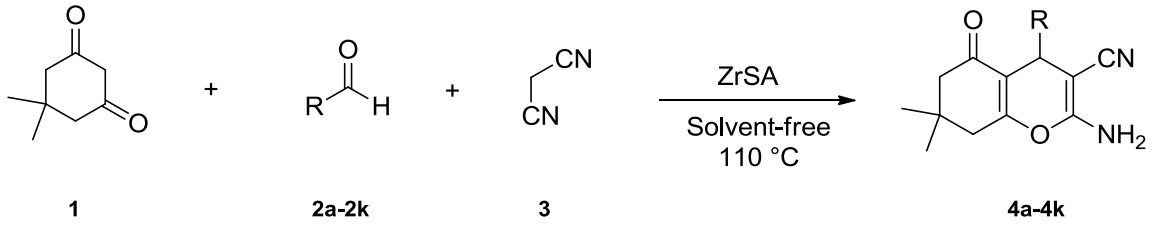
Heterogeneous catalysts show important role in many aspects of environmental and economic in many industrial processes. They presented some excellence including great reactivity, operational simplicity, low toxicity, non-corrosive nature and the potential of the recyclability. Furthermore, most of the heterogeneous catalysts show better product selectivity, so that by-product can be easily separated [7–12]. One of the important routes for developing novel heterogeneous catalysts is immobilizing of homogenous precursors on a solid support [13–15]. The metal oxide nanoparticles such as TiO_2, MgO, Al_2O_3, and ZnO are reported as useful heterogeneous catalyst agents in the synthesis of organic compounds [16, 17]. Zirconia (ZrO_2) is one of the most important metal oxide nanoparticles with high surface area, mechanical strength and thermal stability which have widely application in chemical industry especially as catalyst [18]. Tetrahydrobenzo[*b*]pyrans are an important class of oxygen-containing heterocycles with diverse and interesting biological and pharmacological activities such as anti-coagulant,

spasmolytic, diuretic, anti-cancer, and anti-anaphylactin characteristics [19–25]. They are also used for the treatment neurodegenerative disease, AIDS associated dementia and down's syndrome as well as for the treatment of schizophrenia and myoclonuse [26]. Some 2-amino- 4H-pyrans can be useful as photoactive materials [27]. Whereas polysubstituted 4H-pyran constitutes a structural unit of a series of natural products [28, 29]. According to these excellent properties of the 4H-pyrans, several methods have been reported for the synthesis of these compounds *via* three components one-pot reactions [30–40]. However, many of these methods were associated with use of hazardous organic solvents which is significantly harmful to environment, long duration of reaction, low yield of products, effluent pollution, hard to separate the catalyst and lack of general applicability. Therefore, the development of a new greener and more convenient method using a new catalyst with high catalytic activity for the synthesis of 4H-benzo[*b*]pyrans is highly desirable. During the course of our recent studies directed towards the development of practical and environmentally friendly procedures for the synthesis of organic compounds using reusable catalysts [41–49], and as a result of global interest in the ongoing research towards the development of environmentally friendly methods for the synthesis of organic compounds, we report herein facile and efficient green synthesis of tetrahydrobenzo[*b*]pyrans with short reaction time by the three-component reaction of dimedone, aromatic or aliphatic aldehydes, and malononitrile using Nano Zirconia Sulfuric Acid (n-ZrSA), as heterogeneous catalysts with high catalytic activity under solvent-free condition in high yield (Scheme **1**).



Scheme 1: ZrSA nanoparticles catalyzed synthesis of tetrahydrobenzo[*b*]pyrans.

Results and discussion

Preparation of nano-ZrO_2:

The zirconium dioxide nanoparticles were prepared through chemical precipitation method. 10 g $ZrOCl_2.8H_2O$ was dissolved in 100 mL bidistilled water using hot plate magnetic stirrer. The desired volume of 2 M NaOH was added to the above mentioned precursor solution until the pH value became 10. After 15 minutes, the precipitate was filtered off, washed and dried at 120 °C overnight. The dried $ZrO_2{\cdot}nH_2O$ was calcined at different temperatures from 500 to 1200 °C at a rate of 10 °C/min and kept at the respective temperature for 1h [52].

Preparation of nano-ZrO_2-SO_3H (n-ZrSA):

The chlorosulfonic acid (0.5 mL, 7.5 mmol) was added dropwisely over a period of 30 min under room temperature to the nano-ZrO_2 (3.08 g, 25 mmol) in dry CH_2Cl_2 (20 mL). A suction flask equipped with a constant-pressure dropping funnel and a gas inlet tube for conducting HCl gas over an adsorbing solution (i.e., water) was used. Stirring was continued until HCl evolution was finished. Then, the mixture was shaken for 30 min. A light cream powder of nano-zirconia-supported sulfonic acid was obtained. Afterward, the CH_2Cl_2 was removed under reduced pressure and the solid powder was washed with ethanol (10 mL) and dried at 100 °C [52].

Characterization of the catalyst:

The n-ZrSA catalyst was characterized by FT-IR, and pH analysis. The FT-IR spectrum of the nano-ZrO_2 and nano-ZrO_2–SO_3H are shown in Figure **1**(1) and (2), respectively. In Figure **1**(1), the characteristic vibrational bands of the Zr–O bond at 576 and 752 cm^{-1}, as well band belonging to the Zr–OH group at 1627 cm^{-1}. The FT-IR spectrum of the catalyst also contained absorbance band at 3421 cm^{-1}, which indicated the presence of water. These observations

proved nano-ZrO_2 structures and are consistent with the previously reported evidences [52]. The FT-IR spectrum of the n-ZrSA catalyst prepared in the current study (Figure **1**(2)) revealed new bonds at 820-890 and 1060–1180 cm^{-1} which are related to the O=S=O asymmetric and symmetric stretching vibration and S–O stretching vibration of the sulfonic groups (-SO_3H), respectively. The appeared broad band around 2700–3600 cm^{-1} related to the OH stretching absorption of the SO_3H group. All these specifications acknowledge nano-ZrO_2 structure that has functionalized with sulfonic acid groups. The density of the SO_3H groups was measured using NaOH (0.1 N) as titrant by acid-base potentiometric titration. The amount of SO_3H in the catalyst was 2.45 mmol/g.

The XRD pattern of n-ZrSA catalyst is shown in Figure **2**. The following peak intensities (011), (110), (111), (111), (-111), (002), (200), (021), (211), (-102), (121), (-112), (202), (220), (-202), (013), (113), (311), (222), (-222), (-132) have good agreement with the previous reported evidence [52] which confirm the formation of n-ZrSA.

In the effort to develop an efficient and environmentally benign method for synthesis of tetrahydrobenzo[*b*]pyrans we initiated our studies by adding a catalytic amount of n-ZrSA to a mixture of dimedone (1 mmol), 4-chlorobenzaldehyde (1 mmol), and malononitrile (1 mmol), as model reaction in different solvents such as EtOH, H_2O, MeOH, CH_3CN, CH_2Cl_2, CH_3CO_2Et, and also under solvent-free conditions (Table **1**). We were pleased to see that the reaction was efficiently catalyzed by n-ZrSA under solvent-free conditions at elevated temperature leading to a high yield of the product 4b. The reaction conditions were then optimized by conducting the reaction at different temperatures and using different amounts of catalyst. The results are summarized in Table **1**. Low yield of the product was obtained in the absence of the catalyst at 110 °C after 125 min (entry 1) indicating that the catalyst is necessary for the reaction. The best result was obtained when the reaction was run at 110 °C in the presence of 0.09 g n-ZrSA under solvent-free conditions (entry 15).

Evaluation of catalytic activity of n-ZrSA in the synthesis of Tetrahydrobenzo[b]pyrans:

Table 1: Synthesis of compound 4b in the presence of the n-ZrSA as catalysts under different reaction conditions

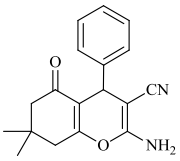
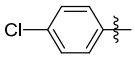
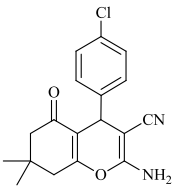
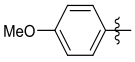
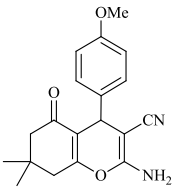
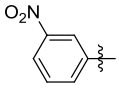
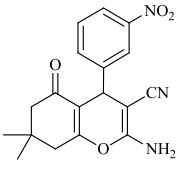
Entry	Catalyst amount (g)	Solvent	T (°C)	Time (min)	Yield* (%)
1	-----	-----	110	125	27
2	0.01	-----	90	85	43
3	0.01	-----	110	80	52
4	0.01	-----	130	77	47
5	0.03	-----	90	73	51
6	0.03	-----	110	70	56
7	0.03	-----	130	70	55
8	0.05	-----	90	56	63
9	0.05	-----	110	44	70
10	0.05	-----	130	45	69
11	0.07	-----	90	36	75
12	0.07	-----	110	33	84
13	0.07	-----	130	35	85
14	0.09	-----	90	19	88
15	0.09	-----	110	16	96
16	0.09	-----	130	17	94
17	0.11	-----	90	15	90
18	0.11	-----	110	15	94
19	0.11	-----	130	16	91
20	0.09	EtOH	Reflux	125	53
21	0.09	MeOH	Reflux	125	46
22	0.09	CH_2Cl_2	Reflux	125	37
23	0.09	CH_3CN	Reflux	125	45
24	0.09	H_2O	Reflux	125	63
25	0.09	CH_3CO_2Et	Reflux	125	56

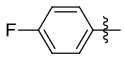
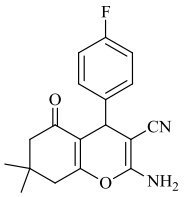
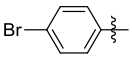
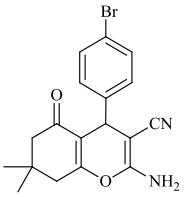
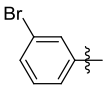
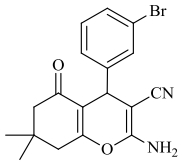
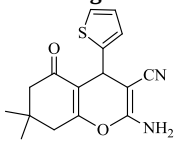
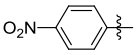
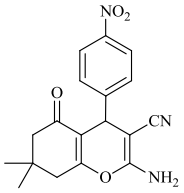
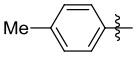
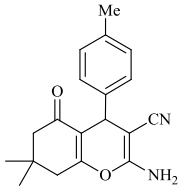
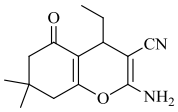
Reaction conditions: dimedone **1** (1 mmol), aldehyde **2a-2k** (1 mmol), malononitrile **3** (1 mmol). *Isolated yields.

Thereafter, the applicability of the method was evaluated for the synthesis of other tetrahydrobenzo[*b*]pyrans using a wide range of aromatic or aliphatic aldehydes (Table **2**). The substituents in the aromatic ring of aldehydes or use of heteroaromatic aldehydes have no significant effect on the time of the reaction and yield of the products. ZrSA nanoparticle efficiently catalyzed the reactions, giving the desired products 4a-k in high yields over relatively short reaction times. Easy separation of obtained products from the catalyst makes this method useful for the synthesis of tetrahydrobenzo[*b*]pyrans. Purity checks with melting points, TLC and the ^{1}H NMR spectroscopic data reveal that only one product is formed in all cases and no undesirable side-products are observed. The structures of all known products **4a-4k** were deduced from their ^{1}H NMR and FT-IR spectral data and a comparision of their melting points with those of authentic samples.

We compared the results we obtained using n-ZrSA as catalyst with previously reported results for the synthesis of tetrahydrobenzo[*b*]pyrans in the presence of various catalysts [30–40]. Our reaction conditions showed shorter reaction times than all the other conditions and gave high yields of the desired products.

Table 2: ZrSA nanoparticles catalyzed synthesis of tetrahydrobenzo[*b*]pyrans [a]

Entry	R	Products[b]	Time/min	Isolated Yield/%	m.p. (ºC)	
					Found	Reported
1		 **4a**	13	93	228-230	228-230 [30]
2		 **4b**	16	96	212-214	211-212 [30]
3		 **4c**	14	91	199-200	200-201 [31]
4		 **4d**	14	90	213-215	213-214 [31]

5		 **4e**	15	97	212-214	210-212 [51]
6		 **4f**	13	90	207-209	207-208 [31]
7		 **4g**	13	94	230-232	228-230 [50]
8		 **4h**	10	91	212-214	210-212 [30]
9		 **4i**	12	94	176-178	176-178 [50]
10		 **4j**	11	89	216-217	215-216 [31]
11		 **4k**	15	88	179-181	178-180 [50]

[a]Reaction conditions: dimedone **1** (1 mmol), aldehyde **2a-2k** (1 mmol), malononitrile **3** (1 mmol), and n-ZrSA (0.09 g), at 110°C under solvent-free condition.
[b]All the products were characterized according to their FT-IR and ^{1}H NMR spectral data and comparision of their melting points with those of authentic samples.

To test the recyclability of n-ZrSA, after completion of the model reaction, the catalyst was recovered according to the procedure described in the experimental section. The separated catalyst was dried at 60 ºC under vacuum for 1 h before being reused in a similar reaction. The catalyst could be used at least four times without significant reduction in its activity (96, 95, 94, 94, % yields in first to fifth use, respectively) which clearly demonstrates the practical reusability of this catalyst. The FT-IR spectra of the

recovered catalysts (Figure **1**(3)–(5)) were almost identical to the spectrum of the fresh catalyst (Figure **1**(2)), indicating that the structure of the catalyst was unchanged by the reaction.

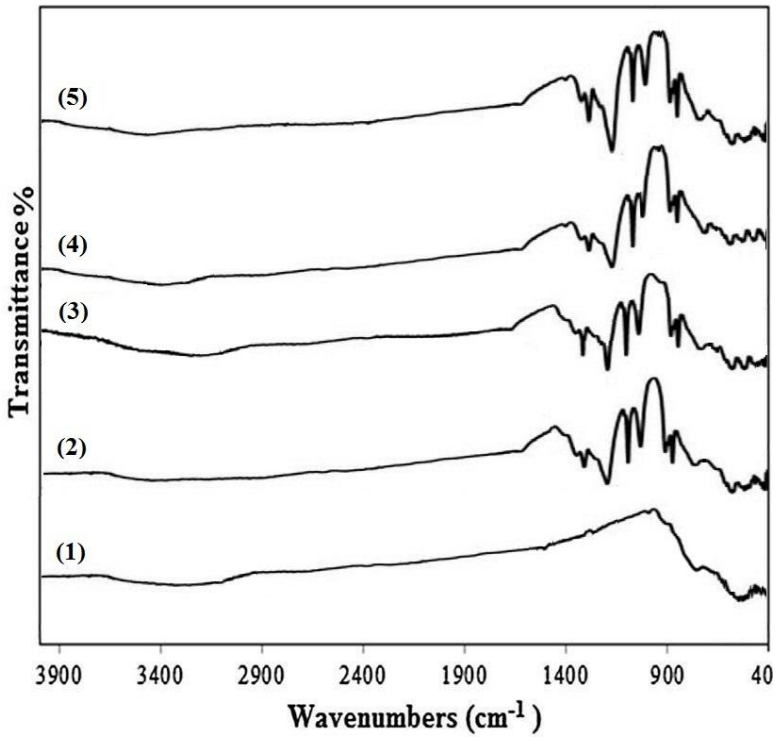


Figure 1: FT-IR spectra of n-ZrO_2 (1), fresh catalyst n-ZrSA ((2), first run), and recovered catalysts (3-5)

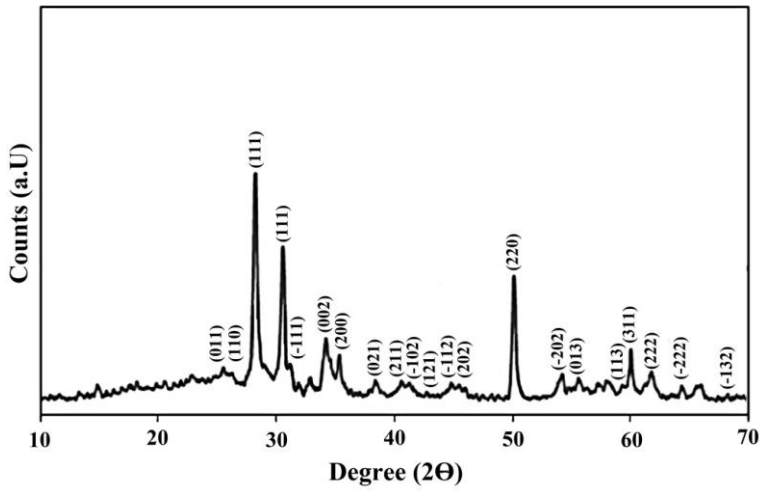
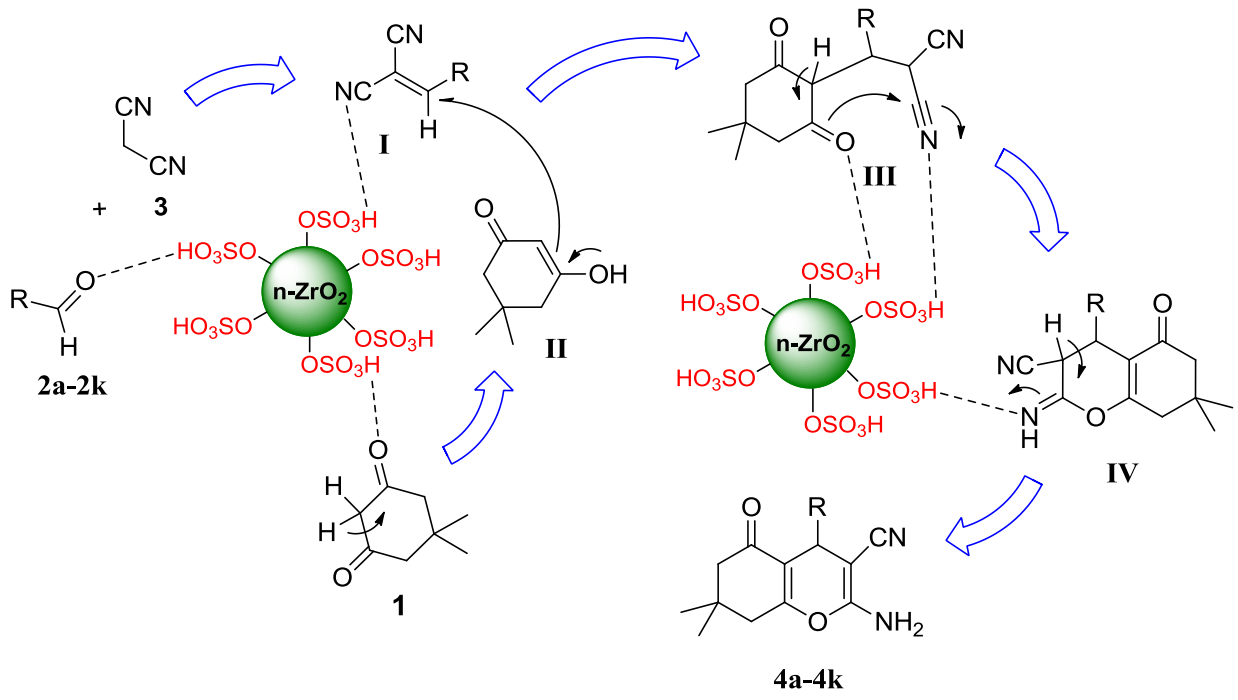


Figure 2: XRD pattern of n-ZrSA.



Scheme 2: Plausible mechanism for the n-ZrSA catalyzed formation of tetrahydrobenzo[*b*]pyrans.

Although we did not investigate the reaction mechanism, the n-ZrSA could act as Brönsted acid and therefore promote the necessary reactions. The catalyst would play a significant role in increasing the electrophilic character of the electrophiles in the reaction. According to this mechanism, the n-ZrSA catalyst would facilitate the formation of intermediates **I**, **II**, **III** and **IV**. Under these conditions, however, attempts to isolate the proposed intermediates

Conclusion

In summary, we showed that n-ZrSA catalyzed the synthesis of tetrahydrobenzo[*b*]pyrans by one-pot, three-component reaction of dimedone, aldehydes, and malononitrile, at 110 °C under solvent-free conditions. The method was relatively fast and high yielding, and the work-up was easy. The catalyst can be recycled after simple handling, and used at least four times without any substantial reduction in its catalytic activity. The procedure is also advantageous in the sense that it is a fast reaction under solvent-free conditions and therefore operates under environmentally friendly conditions

Experimental Section

All chemicals were available commercially and used without additional purification. The catalyst was synthesized according to the literature. Melting points were recorded using a Stuart SMP3 melting point apparatus. The FT-IR spectra of the products were obtained with KBr disks, using a Tensor 27 Bruker spectrophotometer. The ^{1}H NMR (400 and 500 MHz) spectra were recorded using Bruker 400 and 500 spectrometers.

General experimental procedure:

A mixture of dimedone **1** (1 mmol), aromatic or aliphatic aldehyde **2a-2q** (1 mmol), malononitrile **3** (1 mmol) and n-ZrSA (0.09 g) as catalyst was heated under solvent-free condition for the appropriate time. The reaction was monitored by TLC. Upon completion of the transformation, hot ethanol was added and the catalyst filtered through sintered glass Büchner funnel under hot conditions. The catalyst was washed with a small portion of hot ethanol. After cooling, the combined filtrate was allowed to stand at room temperature. The precipitated solid was collected by filtration, and recrystallized from ethanol to give compounds 4a-4k in high yields.

^{1}H NMR and FT-IR data:

2-amino-7,7-dimethyl-5-oxo-4-phenyl-5,6,7,8-tetrahydro-4H-benzopyran-3-carbonitrile (4a):

^{1}H NMR (400 MHz, DMSO-d_6): δ 0.97 (s, 3H, CH_3), 1.05 (s, 3H, CH_3), 2.10 (d, 1H, J = 16.0 Hz, CH_2, diastereotopic proton), 2.27 (d, 1H, J = 16.0 Hz, CH_2,

diastereotopic proton), 2.45–2.55 (m, 2H, CH2, diastereotopic protons overlapped with solvent), 4.18 (s, 1H, CH), 7.03 (s br., 2H, NH_2), 7.10–7.24 (m, 3H, arom-H), 8.16 (t, 2H, *J* = 7.2 Hz, arom-H); FT-IR (KBr disc): ν 3342, 3061, 2982, 1688, 1651, 1489, 1372, 1211, 1167, 828.

2-amino-4-(4-chlorophenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-benzopyran-3-carbonitrile (4b):

^{1}H NMR (500 MHz, DMSO-d_6): δ 0.95 (s, 3H, CH_3), 1.03 (s, 3H, CH_3), 2.10 (d, 1H, *J* = 16.0 Hz, CH_2, diastereotopic proton), 2.24 (d, 1H, *J* = 16.0 Hz, CH_2, diastereotopic proton), 2.45–2.55 (m, 2H, CH2, diastereotopic protons overlapped with solvent), 4.19 (s, 1H, CH), 7.05 (s br., 2H, NH_2), 7.17 (d, 2H, *J* = 8.4 Hz, arom-H), 7.34 (d, 2H, *J* = 8.4 Hz, arom-H); FT-IR (KBr disc): ν 3342, 3061, 2982, 1688, 1651, 1489, 1372, 1211, 1167, 828.

2-amino-4-(4-methoxyphenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-benzopyran-3-carbonitrile (4c):

^{1}H NMR (500 MHz, DMSO-d_6): δ 0.94 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 2.08 (d, 1H, *J* = 16.0 Hz, CH_2, diastereotopic proton), 2.24 (d, 1H, *J* = 16.0 Hz, CH_2, diastereotopic proton), 2.42–2.56 (m, 2H, CH2, diastereotopic protons overlapped with solvent), 3.71 (s, 3H, OCH_3), 4.12 (s, 1H, CH), 6.83 (d, 2H, *J* = 8.7 Hz, arom-H), 6.93 (s br., 2H, NH_2), 7.04 (d, 2H, *J* = 8.7 Hz, arom-H); FT-IR (KBr disc): ν 3342, 3061, 2982, 1688, 1651, 1489, 1372, 1211, 1167, 828.

2-amino-7,7-dimethyl-4-(3-nitrophenyl)-5-oxo-5,6,7,8-tetrahydro-4H-benzopyran-3 carbonitrile (4d):

^{1}H NMR (500 MHz, DMSO-d_6): δ 0.96 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 2.11 (d, 1H, *J* = 16.1 Hz, CH_2, diastereotopic proton), 2.27 (d, 1H, *J* = 16.1 Hz, CH_2, diastereotopic proton), 2.55 (s, 2H, diastereotopic proton), 4.42 (s, 1H, CH), 7.17 (s br., 2H, NH_2), 7.55–7.50 (m, 2H, arom-H), 7.97 (t, 1H, *J* = 1.7 Hz, arom-H), 8.05–8.10 (m, 1H, arom-H); FT-IR (KBr disc): ν 3342, 3061, 2982, 1688, 1651, 1489, 1372, 1211, 1167, 828.

2-amino-4-(4-fluorophenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-benzopyran-3-carbonitrile (4e):

^{1}H NMR (400 MHz, DMSO-d_6): δ 0.96 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 2.11 (d, 1H, *J* = 16.2 Hz, CH_2, diastereotopic proton), 2.26 (d, 1H, *J* = 16.2 Hz, CH_2, diastereotopic proton), 2.41–2.55 (m, 2H, CH2, diastereotopic protons overlapped with solvent), 4.21 (s, 1H, CH), 7.07 (s br., 2H, NH_2), 7.08–7.23 (m, 4H, arom-H); FT-IR (KBr disc): ν 3342, 3061, 2982, 1688, 1651, 1489, 1372, 1211, 1167, 828.

2-amino-4-(4-bromophenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-benzopyran-3-carbonitrile (4f):

^{1}H NMR (400 MHz, DMSO-d_6): δ 0.96 (s, 3H, CH_3), 1.05 (s, 3H, CH_3), 2.11 (d, 1H, *J* = 16.0 Hz, CH_2, diastereotopic proton), 2.26 (d, 1H, *J* = 16.0 Hz, CH_2, diastereotopic proton), 2.45–2.55 (m, 2H, CH2, diastereotopic protons overlapped with solvent), 4.19 (s, 1H, CH), 7.10 (s br., 2H, NH_2), 7.12 (d, 2H, *J* = 8.4 Hz, arom-H), 7.50 (d, 2H, *J* = 8.4 Hz, arom-H); FT-IR (KBr disc): ν 3342, 3061, 2982, 1688, 1651, 1489, 1372, 1211, 1167, 828.

2-amino-4-(3-bromophenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-benzopyran-3-carbonitrile (4g):

^{1}H NMR (400 MHz, DMSO-d_6): δ 0.97 (s, 3H, CH_3), 1.05 (s, 3H, CH_3), 2.14 (d, 1H, *J* = 16.0 Hz, CH_2, diastereotopic proton), 2.27 (d, 1H, *J* = 16.0 Hz, CH_2, diastereotopic proton), 2.45–2.55 (m, 2H, CH2, diastereotopic protons overlapped with solvent), 4.22 (s, 1H, CH), 7.13 (s br., 2H, NH_2), 7.15–7.20 (m, 1H, arom-H), 7.20-7.35 (m, 2H, arom-H), 7.37–7.45 (m, 1H, arom-H); FT-IR (KBr disc): ν 3342, 3061, 2982, 1688, 1651, 1489, 1372, 1211, 1167, 828.

2-amino-7,7-dimethyl-5-oxo-4-(thiophen-2-yl)-5,6,7,8-tetrahydro-4H-benzopyran-3-carbonitrile (4h):

^{1}H NMR (400 MHz, DMSO-d_6): δ 0.99 (s, 3H, CH_3), 1.05 (s, 3H, CH_3), 2.15 (d, 1H, *J* = 16.2 Hz, CH_2, diastereotopic proton), 2.31 (d, 1H, *J* = 16.2 Hz, CH_2, diastereotopic proton), 2.44 (d, 1H, *J* = 17.4 Hz, CH_2, diastereotopic proton), 2.56 (d, 1H, *J* = 17.4 Hz, CH_2, diastereotopic proton), 4.55 (s, 1H, CH), 6.87 (d, 1H, *J* = 2.8 Hz, arom-H), 6.92 (dd, 1H, J = 5.0, 3.4 arom-H), 7.15 (s br., 2H, NH_2), 7.40 (dd, 1H, *J* = 4.8, 0.8 Hz, arom-H); FT-IR (KBr disc): ν 3342, 3061, 2982, 1688, 1651, 1489, 1372, 1211, 1167, 828.

2-amino-7,7-dimethyl-4-(4-nitrophenyl)-5-oxo-5,6,7,8-tetrahydro-4H-benzopyran-3-carbonitrile (4i):

^{1}H NMR (400 MHz, DMSO-d_6): δ 0.97 (s, 3H, CH_3), 1.06 (s, 3H, CH_3), 2.12 (d, 1H, *J* = 16.0 Hz, CH_2, diastereotopic proton), 2.28 (d, 1H, *J* = 16.0 Hz, CH_2, diastereotopic proton), 2.45–2.60 (m, 2H, CH2, diastereotopic protons overlapped with solvent), 4.38

(s, 1H, CH), 7.22 (s br., 2H, NH_2), 7.47 (d, 2H, *J* = 8.4 Hz, arom-H), 8.19 (d, 2H, *J* = 8.4 Hz, arom-H); FT-IR (KBr disc): ν 3342, 3061, 2982, 1688, 1651, 1489, 1372, 1211, 1167, 828.

2-amino-7,7-dimethyl-5-oxo-4-(4-methylphenyl)-5,6,7,8-tetrahydro-4H-benzopyran-3-carbonitrile (4j):

^{1}H NMR (400 MHz, DMSO-d_6): δ 0.95 (s, 3H, CH_3), 1.05 (s, 3H, CH_3), 2.09 (d, 1H, *J* = 16.0 Hz, CH_2, diastereotopic proton), 2.24 (d, 1H, *J* = 16.0 Hz, CH_2, diastereotopic proton), 2.25 (s, 3H, CH_3), 2.43–2.57 (m, 2H, CH2, diastereotopic protons overlapped with solvent), 4.13 (s, 1H, CH), 6.95 (s br., 2H, NH_2), 7.02 (d, 2H, *J* = 8.0 Hz, arom-H), 7.08 (d, 2H, *J* = 8.0 Hz, arom-H); FT-IR (KBr disc): ν 3342, 3061, 2982, 1688, 1651, 1489, 1372, 1211, 1167, 828.

2-amino-4-ethyl-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-benzopyran-3-carbonitrile (4k):

^{1}H NMR (400 MHz, DMSO-d_6): δ 0.70 (t, 3H, *J* = 7.2, CH_3), 1.03 (s, 3H, CH_3), 1.05 (s, 3H, CH_3), 1.30–1.65 (m, 2H, CH_2, diastereotopic proton), 2.20 (d, 1H, *J* = 16.0 Hz, CH_2, diastereotopic proton), 2.30 (d, 1H, *J* = 16.0 Hz, CH_2, diastereotopic proton), 2.37 (d, 1H, *J* = 17.8 Hz, CH_2, diastereotopic proton), 2.46 (d, 1H, *J* = 17.8 Hz, CH_2, diastereotopic proton), 3.19 (t, 1H, *J* = 3.6 Hz, CH), 6.93 (s br., 2H, NH_2); FT-IR (KBr disc): ν 3342, 3061, 2982, 1688, 1651, 1489, 1372, 1211, 1167, 828.

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