# A Basic Ionic Liquid Catalyzed Reaction of Benzothiazole, Aldehydes, and 5,5-Dimethyl-1,3-cyclohexanedione: Efficient Synthesis of Tetrahydrobenzo[*b*]pyrans

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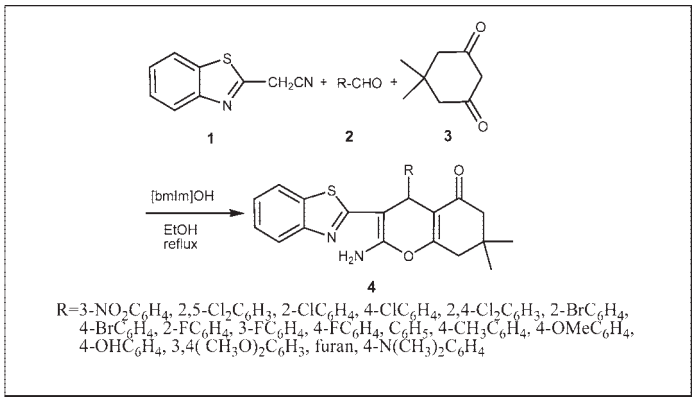


A fast, mild, and quantitative procedure for the preparation of tetrahydrobenzo[*b*]pyran derivatives in the presence of an easily accessible basic ionic liquid—[bmIm]OH(3-butyl-1-methylimidazoliumhydroxide) as the catalyst has been developed. The ionic liquid was stable during the reaction process and could also be reused at least nine times with consistent activity. This procedure may be a practical alternative to the existing procedures to meet the need of academe as well as industries.

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## INTRODUCTION

The exploration of privileged structures in drug discovery is a rapidly emerging theme in medicinal chemistry [1]. 4*H*-Benzopyran derivatives constitute a structural unit of a number of natural products [2] and are versatile synthons because of the inherent reactivity of the pyran ring [3]. In addition, 4*H*-benzo[*b*]pyran derivatives are biologically interesting compounds that possess various pharmacological activities [4], such as, anticoagulant, spasmolytic, diuretic, anticancer, and antianaphylactin characteristics [5]. These ubiquitous applications of 4*H*-benzo[*b*]pyrans stimulated several groups [6–8] to develop new and efficient synthetic protocols for these two bioactive units.

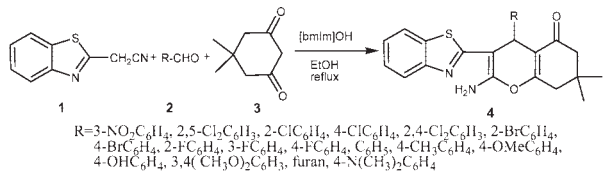
Besides, because of the great pharmacological significance of benzothiazole, which is of particular interest especially within the realm of medicinal chemistry, many useful therapeutic agents also contain the benzothiazole moiety, and these substitution patterns were introduced with efficiency [9].

Because of the vast utility of these kinds of compounds, a number of synthetic routes have been developed for the expedition of these structure frameworks. Some of these reactions were catalyzed by a plethora of reagents including solid or molten state [6], sodium bromide under microwave irradiation [7], [bmIm][$BF_4$] [8]. However, despite the potential utility of these catalysts, many of these methodologies for the synthesis of 4*H*-benzo[*b*]pyrans are associated with several shortcomings, such as, long reaction time, high temperature, harsh reaction conditions, and using of expensive reagents. Gaps remain in terms of the search for economical and environmentally benign methods.

Multicomponent reactions (MCRs), an important subclass of tandem reaction [10], are one-pot processes in which several easily accessible components react to form a single product. They offer significant advantages over conventional linear step synthesis, by reducing time, saving money, energy, and raw materials, thus resulting in both economical and environmental benefits. At the same time, diversity can be achieved from building up libraries by simply varying each component [11].

Recently, ionic liquids have attracted increasing interest in the context of green synthesis [12]. Choline hydroxide has been used as a basic catalyst for aldol condensation reactions between several ketones and aldehydes [13], whereas the basic ionic liquid

**Scheme 1**




[bmIm]OH has been successfully applied to catalyze Michael additions of active methylene compounds to conjugated ketones, carboxylic esters, and nitriles [14]. The synthesis of new and important types of heterocyclic compounds using the basic ionic liquid [bmIm]OH continues to attract wide attention among synthetic chemists.

Thus, in view of the advantages of MCRs and Tandem reactions, and promoted by our earlier researches on MCRs [15], herein, we wish to disclose a green protocol for the synthesis of a variety of biologically important 4*H*-Benzo[*b*]pyrans using the catalyst [bmIm]OH under reflux condition (Scheme 1).

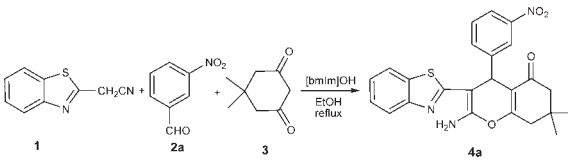
## RESULTS AND DISCUSSION

We first studied the effects of a variety of catalysts on the reaction using *m*-nitrobenzaldehyde as the substrate in ethanol to develop the optimal reaction conditions. The results are summarized in Table 1. Although the reaction could take place without any catalyst, the yield of **4a** was relatively low 39.6%, and the reaction time was long (Table 1, entry 1). The yields of **4a** were also unsatisfactory when using $Et_3N$ or piperidine as catalysts (45.2–52.5%; Table 1, entries 2 and 3). To obtain the higher yield, inorganic catalysts were studied; however, the result was disappointing. It turned out that using KF or $KF/Al_2O_3$ (1:1) as the catalyst, only moderate yields of **4a** were obtained (52.5–55.0%; Table 1, entries 4 and 5). Thus, ionic liquids were tried. Utilizing $[bmIm]BF_4$ and $[bmIm]BF_4$/KOH (1:1), the yields of the products were not obviously improved (50.2–68.0%; Table 1, entries 6 and 7), but when the [bmIm]OH was used as the catalyst, the yield of **4a** was dramatically improved to 83% in 0.5 h. Then, it was observed that when the quantity of [bmIm]OH increased from 20 to 60 mol %, the yield of **4a** improved accordingly to 95% (Table 1, entries 8–10). However, with increasing the amount of the catalyst, the yields of **4a** were not further improved but reduced (Table 1, entries 11 and 12). Therefore, we selected 60 mol % of [bmIm]OH as the catalyst. It was showed that the basic ionic liquid [bmIm]OH plays a significant catalytic role, as well as the acceleration of the reaction rate and improvement of selectivity.

To extend the scope of this new procedure for the synthesis of 4*H*-benzo[*b*]pyrans, a series of reactions were carried out under optimized conditions. We were pleased to find that the reactions proceeded smoothly, and desired products were afforded in excellent yields (77–95%) and in short time (30–50 min) (Table 2). When aromatic aldehydes **2** with more electron-

**Table 1**

Optimization of reaction conditions for compound **4a**.




| Entry | Catalyst (equiv) | EtOH (mL) | Time (h) | Yield (%)[a] |
|---|---|---|---|---|
| 1 | –[b] | 15 | 24 | 39.6 |
| 2 | $Et_3N$(0.2) | 15 | 10 | 52.5 |
| 3 | Piperidine(0.2) | 15 | 24 | 45.2 |
| 4 | KF(0.2) | 15 | 9 | 52.5 |
| 5 | $KF/Al_2O_3$(0.2) | 15 | 8 | 55.0 |
| 6 | $[bmIm]BF_4$(0.2) | 15 | 8 | 50.2 |
| 7 | $[bmIm]BF_4$/KOH(0.2) | 15 | 8 | 68.0 |
| 8 | [bmIm]OH(0.2) | 3.0 | 0.5 | 83.0 |
| 9 | [bmIm]OH(0.4) | 3.0 | 0.5 | 87.3 |
| 10 | [bmIm]OH(0.6) | 3.0 | 0.5 | 95.0 |
| 11 | [bmIm]OH(0.8) | 3.0 | 0.5 | 86.6 |
| 12 | [bmIm]OH(1.0) | 3.0 | 0.5 | 73.0 |

[a] Isolated.
[b] No catalyst.

**Table 2**

Synthesis of compounds **4** by [bmIm]**OH** as catalyst.

| Entry | Product | R | Time (min) | Yeild (%)[a] |
|---|---|---|---|---|
| 1 | **4a** | 3-$NO_2C_6H_4$ | 30 | 95 |
| 2 | **4b** | 2,5-$Cl_2C_6H_3$ | 30 | 90 |
| 3 | **4c** | 2-$ClC_6H_4$ | 40 | 88 |
| 4 | **4d** | 4-$ClC_6H_4$ | 30 | 91 |
| 5 | **4e** | 2,4-$Cl_2C_6H_3$ | 35 | 89 |
| 6 | **4f** | 2-$BrC_6H_4$ | 30 | 94 |
| 7 | **4g** | 4-$BrC_6H_4$ | 30 | 94 |
| 8 | **4h** | 2-$FC_6H_4$ | 30 | 90 |
| 9 | **4i** | 3-$FC_6H_4$ | 35 | 89 |
| 10 | **4j** | 4-$FC_6H_4$ | 30 | 92 |
| 11 | **4k** | $C_6H_5$ | 40 | 87 |
| 12 | **4l** | 4-$CH_3C_6H_4$ | 50 | 80 |
| 13 | **4m** | 4-$OMeC_6H_4$ | 40 | 83 |
| 14 | **4n** | 4-$OHC_6H_4$ | 50 | 77 |
| 15 | **4o** | 3,4$(CH_3O)2C_6H_3$ | 50 | 79 |
| 16 | **4p** | Furan | 40 | 82 |
| 17 | **4r** | 4-$N(CH_3)_2C_6H_4$ | 60 | Trace |

[a] Isolated.

withdrawing substituents or higher electronegativity were used, the yields of **4** were higher (Table 2, entries 1–10). The heterocyclic aldehyde (furan formaldehyde) was also used to support this reaction (Table 2, entry 16). In a further study, 4-$N(CH_3)_2C_6H_4$ was used in this case, however, though the reactions proceeded smoothly, the 2-(benzo[*d*]thiazol-2-yl)-3-(4-*N*,*N*-dimethyl-phenzyl)-acrylonitrile instead of the desired product **4r** was observed (Table 2, entry17). Presumably, it was arrested at the Knoevenagel condensation product stage, as further aromatization did not occur due to electronic effect.

We also investigated the reusability and the recycling of the basic ionic liquid [bmIm]OH, and found that the catalyst could be easily recovered after completion of the reaction and reused in subsequent reactions. Using the reaction of 2-(benzo[*d*]thiazol-2-yl)acetonitrile **1**, 4-chlorobenzaldehyde **2d** and 5,5-dimethyl-1,3-cyclohexanedione **3** as a model reaction, after completion of the reaction, the mixture was filtrated and the filtrate was evaporated under reduced pressure, then extracted with ethyl acetate:ether (1:1). The ionic liquid left in the reaction vessel was rinsed with ether and dried under vacuum at 90°C for 8 h to remove water leaving behind the ionic liquid. The recovered [bmIm]OH was recycled and reused nine times to carry out the same experiment. The activity of the catalyst did not show any significant decrease after nine runs (Fig. 1).

A plausible mechanism for the reaction is outlined in Scheme 2. The initial event can be considered as a Knoevenagel condensation of aldehydes **2** with benzothiazole **1** to form the intermediate [**A**], followed by the elimination to afford the 2-(benzo[*d*]thiazol-2-yl)-3-(aryl)acrylonitrile under the basic ionic liquid [bmIm]OH. The latter then undergoes Michael addition with 5,5-dimethyl-1,3-cyclohexanedione **3** tautomer to give the intermediate [**B**], followed by a intramolecular O-cyclization to give the products 4*H*-Benzo[*b*]pyrans **4** (Scheme 2).

It may be speculated that the difference in basicity of [bmIm]OH used in this reaction compared with $Et_3N$ and piperidine may play a crucial role in accelerating the reaction and improving the yield.

In conclusion, this procedure using the task-specific basic ionic liquid [bmIm]OH as the catalyst provides a very efficient and convenient methodology for synthesis of 4*H*-benzo[*b*]pyrans through three-component reaction. This method offers remarkable improvements with

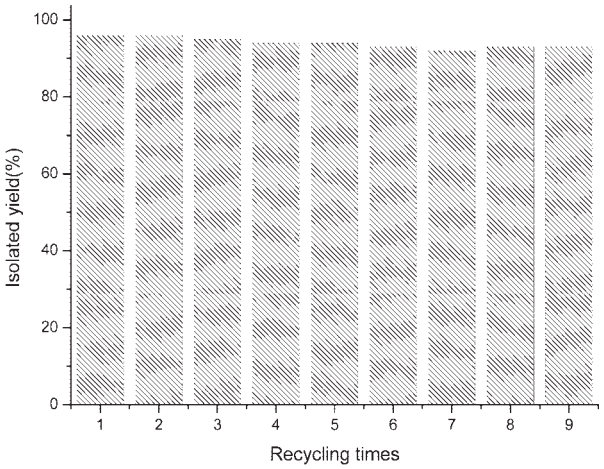
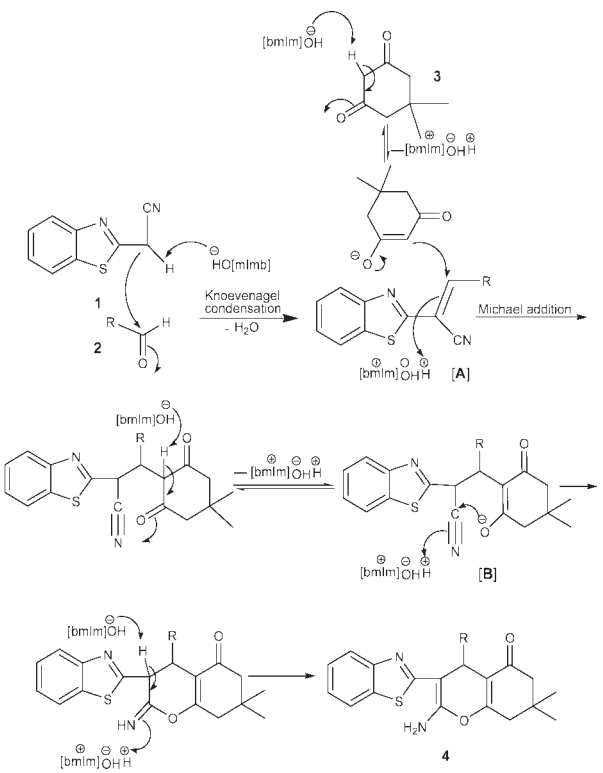



**Figure 1.** Recycling times of [bmIm]OH and the isolated yields of product **4d**.

**Scheme 2**




regard to operational simplicity, reaction time, reaction conditions, general applicability, and greenness of procedure, especially high isolated yields of products and the selectivity. Thus, we believe that this simple and green procedure will be a practical alternative to the existing procedures to cater the need of academe as well as industries.

## EXPERIMENTAL

**General remarks.** Melting points were measured by using a RY-1 apparatus and were uncorrected. IR spectra were recorded on a Nicolet 510P FTIR spectrophotometer as KBr pellets. $^1$H and $^{13}$C NMR were recorded in DMSO-$d_6$ and $CDCl_3$ on a Bruker AC-500 instrument and TMS as internal standard. Mass spectra were performed on a Bruker Esquire Hct spectrometer with an ESI source. Elemental analyses were carried out on a Vario EL III analyzer. All chemicals were purchased and used without further purification.

**The synthesis of 2-cyanomethy-1,3-benzothiazloe [16].** mp 101–102°C; IR (KBr) υ: 2250 cm$^{-1}$; $^1$H NMR (500 MHz, DMSO-$d_6$) δ: 7.80–8.27 (m, 2H), 7.00–7.80 (m, 2H), 4.72 (s, 2H, $CH_2$). Anal. calcd. for $C_9H_2N_2S$: C, 62.07; H, 3.47; N, 16.09; found: C, 62.16; H, 3.44; N, 16.11.

**General procedure for the synthesis of basic ionic liquid.** The basic ionic liquid [bmIm]OH was prepared by anion change of [bmIm]Br using 1 mol equivalent KOH. The ionic liquid was dried under vacuum for 24 h and stored in desiccators. The ionic liquid was characterized by IR, $^1$H NMR, and $^{13}$C NMR spectroscopy. $^1$H NMR (500 MHz, $CDCl_3$): δ = 10.24 (s, 1 H), 7.62 (t, $J$ = 1.7 Hz, 1 H), 7.50 (t, $J$ = 1.7, 1 H), 4.34 (t, $J$ = 7.4 Hz, 2 H), 4.12 (s, 3 H), 3.32–3.25 (br s, 1H), 1.93–1.87 (m, 2 H), 1.40–1.36 (m, 2 H), 0.96 ppm (t, $J$ = 7.4 Hz, 3 H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 137.2, 123.8, 122.1, 49.7, 36.7, 32.1, 19.4, 13.4 ppm; IR (neat) υ: 3422, 3079, 1571, 1169 cm$^{-1}$.

**General procedure for the synthesis of 2-amino-3-(benzo[*d*]thiazol-2-yl)-4-aryl-7,7-dimethyl–5–carbonyl-5,6,7,8-4*H*-benzo[*b*]pyrans (4).** To a mixture of 2-(benzo[*d*]thiazol-2-yl)acetonitrile **1** (1 mmol), aromatic aldehydes **2** (1 mmol), 5,5-dimethyl-1,3-cyclohexanedione **3** (1 mmol) dissolved in a minimum amount (3.0 mL) of ethanol, the basic ionic liquid, [bmIm]OH (60 mol %) was added, and the mixture was refluxed for appropriate time. The progress of reaction was monitored by TLC. After completion of reaction aqueous, the mixture was allowed to cool to room temperature, and filtered to give the crude products, which was further purified by recrystallization (THF/ethanol) to give pure products **4**.

***2-Amino-3-(benzo[d]thiazol-2-yl)-4-(3-nitrophenyl)-7,7-dimethyl-5-carbonyl-5,6,7,8-4H-benzo[b]pyran (4a).*** mp 218–219°C. IR (KBr) υ: 3429, 1679, 1624, 1525, 1473, 822, 696 cm$^{-1}$; $^1$H NMR (500 MHz, DMSO-$d_6$) δ: 0.67 (s, 3H, $CH_3$), 0.92 (s, 3H, $CH_3$), 2.07 (d, $J$ = 16.5 Hz, 1H), 2.29 (d, $J$ = 16.0 Hz, 1H), 2.50 (d, $J$ = 17.5 Hz, 1H), 2.59 (d, $J$ = 17.5 Hz, 1H), 4.70 (s, 1H) 7.14–8.09 (m, 8H, ArH), 8.52 ppm (s, 2H, $NH_2$); $^{13}$C NMR (125 MHz, DMSO-$d_6$) δ: 25.5, 25.6, 26.6, 29.0, 32.4, 37.4, 50.2, 67.4, 80.5, 114.4, 120.6, 121.9, 122.2, 123.4, 126.6, 130.1, 131.7, 135.3, 147.0, 147.9, 154.6, 162.8, 168.3, 196.3 ppm; ms (ESI) *m/z*: 448.4 [M +H]$^+$. Anal. calcd. for $C_{24}H_{21}N_3O_4S$: C, 64.42; H, 4.73; N, 9.40. Found: C, 64.49; H, 4.75; N, 9.42.

***2-Amino-3-(benzo[d]thiazol-2-yl)-4-(2,5-dichlorophenyl)-7,7-dimethyl-5-carbonyl-5,6,7,8-4H-benzo[b]pyran (4b).*** mp 217–218°C. IR (KBr) υ: 3446, 1679, 1661, 1626, 1477, 820, 669 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$) δ: 1.007 (s, 3H, $CH_3$), 1.09 (s, 3H, $CH_3$), 2.23 (d, $J$ = 16.0 Hz, 1H), 2.29 (d, $J$ = 16.0 Hz, 1H), 2.50 (d, $J$ = 17.5 Hz, 1H), 2.59 (d, $J$ = 17.5 Hz, 1H), 5.07 (s, 1H) 7.04–7.30 (m, 7H, ArH), 7.35 ppm (s, 2H, $NH_2$); $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 26.6, 29.2, 32.2, 36.8, 50.5, 79.7, 112.7, 120.5, 121.9, 123.4, 126.6, 128.8, 131.3, 132.2, 142.5, 153.0, 154.8, 163.1, 168.4, 196.1 ppm; ms (47 eV) *m/z*: 493.40 (100%, M +Na). Anal. calcd. for $C_{24}H_{21}N_2O_2SCl_2$: C, 61.02; H, 4.48; N, 5.93. Found: C, 60.89; H, 4.47; N, 5.95.

***2-Amino-3-(benzo[d]thiazol-2-yl)-4-(2-chlorophenyl)-7,7-dimethyl-5-carbonyl-5,6,7,8-4H-benzo[b]pyran (4c).*** mp 204–205°C. IR (KBr) υ: 3445, 1678, 1658, 1624, 1475, 748, 666 cm$^{-1}$; $^1$H NMR (500 MHz, DMSO-$d_6$) δ: 0.83 (s, 3H, $CH_3$), 0.99 (s, 3H, $CH_3$), 2.01 (d, $J$ = 16.0 Hz, 1H), 2.23 (d, $J$ = 16.0 Hz, 1H), 2.40 (d, $J$ = 17.5 Hz, 1H), 2.57(d, $J$ =17.5 Hz, 1H), 4.82 (s, 1H), 7.06–7.83 (m, 8H, ArH), 8.48 ppm (s, 2H, $NH_2$); $^{13}$C NMR (125 MHz, DMSO-$d_6$) δ: 26.6, 29.3, 32.1, 36.4, 39.4, 50.5, 80.4, 113.4, 120.4, 121.7, 123.2, 126.4, 127.0, 128.7, 126.6, 131.9, 133.1, 133.3, 140.5, 153.0, 154.7, 162.6, 168.6, 195.9 ppm; ms (ESI) *m/z*: 437.8 [M +H]$^+$. Anal. calcd. for $C_{24}H_{21}N_2O_2SCl$: C, 65.97; H, 4.84; N, 6.41. Found: C, 66.11; H, 4.85; N, 6.43.

***2-Amino-3-(benzo[d]thiazol-2-yl)-4-(4-chlorophenyl)-7,7-dimethyl-5-carbonyl-5,6,7,8-4H-benzo[b]pyran (4d).*** mp 173–174°. IR (KBr) υ: 3451, 1667, 1618, 1531, 1469, 835, 672 cm$^{-1}$; $^1$H NMR (500 MHz, DMSO-$d_6$) δ: 0.85 (s, 3H,

$CH_3$), 1.12 (s, 3H, $CH_3$), 2.18 (d, $J$ = 16.5 Hz, 1H), 2.25 (d, $J$ = 16.0 Hz, 1H), 2.41 (d, $J$ = 17.5 Hz, 1H), 2.46 (d, $J$ = 17.5 Hz, 1H), 4.76 (s, 1H), 7.24–7.77 (m, 8H, ArH), 7.79 ppm (s, 2H, $NH_2$); $^{13}$C NMR (125 MHz, DMSO-$d_6$) δ: 26.7, 29.2, 32.4, 36.9, 50.4, 81.2, 115.1, 120.6, 121.9, 123.4, 126.6, 128.5, 130.5, 131.5, 131.9, 143.8, 153.3, 154.5, 162.4, 168.7, 196.3 ppm; ms (ESI) *m/z*: 437.5 $[M+H]^+$. Anal. calcd. for $C_{24}H_{21}N_2O_2SCl$: C, 65.97; H, 4.84; N, 6.41. Found: C, 65.89; H, 4.83; N, 6.39.

***2-Amino-3-(benzo[d]thiazol-2-yl)-4-(2,4-dichlorophenyl)-7,7-dimethyl-5-carbonyl-5,6,7,8-4H-benzo[b]pyran (4e).*** mp 209–210°C. IR (KBr) υ: 3454, 1681, 1618, 1468, 1454, 855, 672 $cm^{-1}$; $^1$H NMR (500 MHz, DMSO-$d_6$) δ: 0.85 (s, 3H, $CH_3$), 1.02 (s, 3H, $CH_3$), 2.05 (d, $J$ = 16.5 Hz, 1H), 2.29 (d, $J$ = 16.5 Hz, 1H), 2.46 (d, $J$ = 17.5 Hz, 1H), 2.60 (d, $J$ = 17.5 Hz,1H), 4.832 (s, 1H), 7.14–7.85 (m, 7H, ArH), 8.53 ppm (s, 2H, $NH_2$); $^{13}$C NMR (125 MHz, DMSO-$d_6$) δ: 26.6, 29.2, 32.2, 36.7, 50.4, 79.9, 113.0, 120.4, 121.7, 123.3, 126.5, 127.3, 129.6, 130.3, 132.3, 134.0, 139.8, 152.9, 154.7, 162.9, 168.4, 196.0 ppm; ms (ESI) *m/z*: 472.2 $[M+H]^+$. Anal. calcd. for $C_{24}H_{20}N_2O_2SCl_2$: C, 61.15; H, 4.28; N, 5.94. Found: C, 61.45; H, 4.27; N, 5.91.

***2-Amino-3-(benzo[d]thiazol-2-yl)-4-(2-bromophenyl)-7,7-dimethyl-5-carbonyl-5,6,7,8-4H-benzo[b]pyran (4f).*** mp 177–178°C. IR (KBr) υ: 3446, 1677, 1658, 1475, 1454 $cm^{-1}$; $^1$H NMR (500 MHz, DMSO-$d_6$) δ: 0.90 (s, 3H, $CH_3$), 1.05 (s, 3H, $CH_3$), 2.06 (d, $J$ = 16.0 Hz, 1H), 2.29 (d, $J$ = 16.0 Hz, 1H), 2.45 (d, 1H), 2.60 (d, $J$ = 17.5 Hz, 1H), 4.87 (s, 1H), 7.03–7.88 (m, 8H, ArH), 8.53 ppm (s, 2H, $NH_2$); $^{13}$C NMR (125 MHz, DMSO-$d_6$) δ:26.8, 29.3, 32.2,38.4, 50.6, 80.6, 80.7, 113.6, 115.7, 120.5, 121.7, 123.3, 126.5, 127.7, 129.0, 132.1, 133.8, 142.1, 147.2, 152.9, 154.8, 162.6, 168.7, 196.0 ppm; ms (ESI) *m/z*: 483.2 $[M+H]^+$. Anal. calcd. for $C_{24}H_{21}BrN_2O_2S$: C, 59.88; H, 4.40; N, 5.82. Found: C, 59.70; H, 4.39; N, 5.83.

***2-Amino-3-(benzo[d]thiazol-2-yl)-4-(4-bromophenyl)-7,7-dimethyl-5-carbonyl-5,6,7,8-4H-benzo[b]pyran (4g).*** mp 175–176°C. IR (KBr) υ: 3418, 1676, 1652, 1621, 1477, 1456 $cm^{-1}$; $^1$H NMR (500 MHz, DMSO-$d_6$) δ: 0.84 (s, 3H, $CH_3$), 1.03 (s, 3H, $CH_3$), 2.08 (d, $J$ = 16.0 Hz, 1H), 2.29 (d, $J$ = 16.0 Hz, 1H), 2.46 (d, $J$ = 18.0 Hz, 1H), 2.59 (d, $J$ = 17.5 Hz,1H), 4.56 (s, 1H), 7.17–7.86 (m, 8H, ArH), 8.45 ppm (s, 2H, $NH_2$); $^{13}$C NMR (125 MHz, DMSO-$d_6$) δ: 26.7, 29.2, 32.4, 37.1, 50.4, 81.2, 115.0, 120.0, 120.1, 121.9, 123.4, 126.6, 130.9, 131.4, 131.9, 144.2, 153.3, 154.5, 162.4, 168.7, 196.3 ppm; ms (ESI) *m/z*: 483.2 $[M+H]^+$. Anal. calcd. for $C_{24}H_{21}BrN_2O_2S$: C, 59.88; H, 4.40; N, 5.82. Found: C, 59.64; H, 4.41; N, 5.83.

***2-Amino-3-(benzo[d]thiazol-2-yl)-4-(2-fluorophenyl)-7,7-dimethyl-5-carbonyl-5,6,7,8-4H-benzo[b]pyran (4h).*** mp 173–174°C. IR (KBr) υ: 3429, 1674, 1652, 1614, 1476, 1453 $cm^{-1}$; $^1$H NMR (500 MHz, DMSO-$d_6$) δ: 0.88 (s, 3H, $CH_3$), 1.06 (s, 3H, $CH_3$), 2.06 (d, $J$ = 15.5 Hz, 1H), 2.30 (d, $J$ = 16.0 Hz, 1H), 2.46 (d, 1H), 2.64 (d, $J$ = 18.0 Hz,1H), 4.75 (s, 1H), 7.02–7.91 (m, 8H, ArH), 8.46 ppm (s, 2H, $NH_2$); $^{13}$C NMR (125 MHz, DMSO-$d_6$) δ: 26.5, 29.2, 32.1, 32.3, 50.4, 80.5, 99.9, 113.7, 115.9, 120.4, 121.7, 123.3, 124.4, 126.5, 128.9,129.0, 131.0, 131.1, 131.6, 131.8, 153.2, 154.5, 159.6, 161.6, 168.7, 195.9 ppm; ms (ESI) *m/z*: 421.2 $[M+H]^+$. Anal. calcd. for $C_{24}H_{21}FN_2O_2S$: C, 68.55; H, 5.03; N, 6.66. Found: C, 68.34; H, 5.02; N, 6.67.

***2-Amino-3-(benzo[d]thiazol-2-yl)-4-(3-fluorophenyl)-7,7-dimethyl-5-carbonyl-5,6,7,8-4H-benzo[b]pyran (4i).*** mp 181–182°C. IR (KBr) υ: 3427, 1679, 1663, 1616, 1480, 1452 $cm^{-1}$; $^1$H NMR (500 MHz, DMSO-$d_6$) δ: 0.85 (s, 3H, $CH_3$), 1.05 (s, 3H, $CH_3$), 2.10 (d, $J$ = 16.0 Hz, 1H), 2.31 (d, $J$ = 16.5 Hz, 1H), 2.53 (d, 1H), 2.60 (d, $J$ = 17.5 Hz,1H), 4.61 (s, 1H), 6.94–7.89 (m, 8H, ArH), 8.46 ppm (s, 2H, $NH_2$); $^{13}$C NMR (125 MHz, DMSO-$d_6$) δ: 26.6, 29.1, 32.4, 37.2, 50.4, 81.0, 99.9, 113.8, 113.9, 114.9, 115.2, 115.4, 120.6, 121.9, 123.4, 124.5, 126.5, 130.4, 130.5, 131.9, 147.7, 147.8, 153.3, 154.6, 161.3, 162.5, 163.3, 168.6, 196.2 ppm; ms (ESI) *m/z*: 421.2 $[M+H]^+$. Anal. calcd. for $C_{24}H_{21}FN_2O_2S$: C, 68.55; H, 5.03; N, 6.66. Found: C, 68.75; H, 5.04; N, 6.65.

***2-Amino-3-(benzo[d]thiazol-2-yl)-4-(4-fluorophenyl)-7,7-dimethyl-5-carbonyl-5,6,7,8-4H-benzo[b]pyran (4j).*** mp 192–193°C. IR (KBr) υ: 3423, 1664, 1617, 1480, 1453 $cm^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$) δ: 0.96 (s, 3H, $CH_3$), 1.13 (s, 3H, $CH_3$), 2.20 (d, $J$ = 16.5 Hz, 1H), 2.27 (d, $J$ = 16.0 Hz, 1H), 2.44(d, $J$ = 17.5 Hz, 1H), 2.52 (d, $J$ = 17.5 Hz, 1H), 4.81 (s, 1H), 6.90–7.81 (m, 8H, ArH), 8.45 ppm (s, 2H, $NH_2$); $^{13}$C NMR (125 MHz, $CDCl_3$) δ: 27.3, 29.2, 32.3, 36.6, 40.8, 50.8, 83.4, 114.8, 115.0, 116.1, 120.5, 121.2, 123.2, 125.9, 130.1, 130.2, 132.5, 139.6, 152.9, 160.6, 161.2, 162.6, 168.7, 196.4 ppm; ms (ESI) *m/z*: 421.3 $[M+H]^+$. Anal. calcd. for $C_{24}H_{21}FN_2O_2S$: C, 68.55; H, 5.03; N, 6.66. Found: C, 68.28; H, 5.04; N, 6.67.

***2-Amino-3-(benzo[d]thiazol-2-yl)-4-phenyl-7,7-dimethyl-5-carbonyl-5,6,7,8-4H-benzo[b]pyran (4k).*** mp 185–186°C. IR (KBr) υ: 3428, 1654, 1620, 1532, 1474, 833, 672 $cm^{-1}$; $^1$H NMR (500 MHz, DMSO-$d_6$) δ: 0.897 (s, 3H, $CH_3$), 1.021 (s, 3H, $CH_3$), 2.055 (d, $J$ = 16.0 Hz, 1H), 2.274 (d, $J$ = 16.0 Hz, 1H), 2.47 (d, $J$ = 17.5 Hz, 1H), 2.58 (d, $J$ = 17.0 Hz, 1H), 4.53 (s, 1H), 7.04–7.85 (m, 9H, ArH), 8.519 ppm (s, 2H, $NH_2$); $^{13}$C NMR (125 MHz, DMSO-$d_6$) δ: 26.6, 29.2, 32.3, 37.4, 50.4, 81.7, 115.5, 120.5, 121.8, 123.2, 126.4, 126.9, 128.4, 128.56, 131.9, 144.8, 153.2, 162.1, 168.8, 196.1 ppm; ms (47 eV) *m/z*: 425.20 (100%, M +Na). Anal. calcd. for $C_{24}H_{22}N_2O_2S$: C, 71.62; H, 5.51; N, 6.96. Found: C, 71.55; H, 5.49; N, 6.94.

***2-Amino-3-(benzo[d]thiazol-2-yl)-4-p-tolyl-7,7-dimethyl-5-carbonyl-5,6,7,8-4H-benzo[b]pyran (4l).*** mp 189–190°C. IR (KBr) υ: 3430, 1658, 1628, 1542, 1470, 822, 692 $cm^{-1}$; $^1$H NMR (500 MHz, DMSO-$d_6$) δ: 0.79 (s, 3H, $CH_3$), 0.98 (s, 3H, $CH_3$), 2.03 (d, $J$ = 16.0 Hz, 1H), 2.11 (s, 3H) 2.24 (d, $J$ = 16.5 Hz, 1H), 2.42 (d, $J$ = 17.5 Hz, 1H), 2.58(d, $J$ = 17.5 Hz, 1H), 4.46 (s, 1H), 6.95–7.82 (m, 8H, ArH), 8.32 ppm (s, 2H, $NH_2$); $^{13}$C NMR (125 MHz, DMSO-$d_6$) δ: 20.9, 26.6, 29.2, 32.3, 36.9, 50.4, 66.8, 81.8, 115.6, 117.6, 121.8, 123.2, 126.4, 128.5, 128.9, 131.9, 135.9, 141.8, 153.2, 154.7, 161.9, 168.9, 196.2 ppm; ms (47 eV) *m/z*: 439.24 (100%, M +Na). Anal. calcd. for $C_{24}H_{24}N_2O_2S$: C, 71.26; H, 5.98; N, 6.92. Found: C, 71.39; H, 5.99; N, 6.94.

***2-Amino-3-(benzo[d]thiazol-2-yl)-4-(4-methoxyphenyl)-7,7-dimethyl-5-carbonyl-5,6,7,8-4H-benzo[b]pyran (4m).*** mp 177–178°C. IR (KBr) υ: 3396, 1675, 1656, 1621, 1474, 754, 665 $cm^{-1}$; $^1$H NMR (500 MHz, DMSO-$d_6$) δ: 0.85 (s, 3H, $CH_3$), 1.03 (s, 3H, $CH_3$), 2.06 (d, $J$ = 16.0 Hz, 1H), 2.28 (d, $J$ = 16.0 Hz, 1H), 2.48 (d, $J$ = 17.5 Hz, 1H), 2.58(d, $J$ = 17.5 Hz, 1H), 3.63(s 3H), 4.49 (s, 1H), 6.75–7.86 (m, 8H, ArH), 8.35 ppm (s, 2H, $NH_2$); $^{13}$C NMR (125 MHz, DMSO-$d_6$) δ: 26.2, 28.7, 31.9, 36.0, 49.9, 54.9, 81.5, 113.3, 115.2, 119.9, 121.9, 123.8, 125.9, 129.1, 131.5, 136.2, 152.7, 153.9, 157.7, 162.5, 168.4, 195.7 ppm; ms (ESI) *m/z*: 433.4 $[M+H]^+$. Anal.

calcd. for $C_{25}H_{24}N_2O_3S$: C, 69.42; H, 5.59; N, 6.48. Found: C, 69.34; H, 5.61; N, 6.46.

***2-Amino-3-(benzo[d]thiazol-2-yl)-4-(4-hydroxyphenyl)-7,7-dimethyl-5-carbonyl-5,6,7,8-4H-benzo[b]pyran (4n).*** mp 200–201°C. IR (KBr) υ: 3451, 1677, 1652, 1616, 1474, 757, 538 $cm^{-1}$; $^1H$ NMR (500 MHz, DMSO-$d_6$) δ: 0.82 (s, 3H, $CH_3$), 1.02 (s, 3H, $CH_3$), 2.06 (d, $J$ = 16.0 Hz, 1H), 2.26 (d, $J$ = 16.0 Hz, 1H), 2.44 (d, $J$ = 17.5 Hz, 1H), 2.53 (d, $J$ = 17.0 Hz, 1H), 4.42 (s, 1H), 6.55–7.84 (m, 8H, ArH), 8.30 (s, 2H, $NH_2$), 9.15 ppm (s, 1H); $^{13}C$ NMR (125 MHz, DMSO-$d_6$) δ: 18.9, 26.3, 29.2, 32.3, 36.5, 50.5, 56.5, 81.5, 115.1, 115.9, 120.4, 123.2, 126.4, 129.5, 132.0, 135.0, 153.2, 154.3, 156.2, 169.1, 196.1 ppm; ms (ESI) *m/z*: 419.2 $[M+H]^+$. Anal. calcd. for $C_{24}H_{22}N_2O_3S$: C, 68.88; H, 5.30; N, 6.69. Found: C, 68.75; H, 5.29; N, 6.72.

***2-Amino-3-(benzo[d]thiazol-2-yl)-4-(3,4-dimethoxyphenyl)-7,7-dimethyl-5-carbonyl-5,6,7,8-4H-benzo[b]pyran (4o).*** mp 191–192°C. IR (KBr) υ: 3443, 1662, 1624, 1615, 1560, 838, 669 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) δ: 1.20 (s, 3H, $CH_3$), 1.216 (s, 3H, $CH_3$), 2.19 (d, $J$ = 16.0 Hz, 1H), 2.24 (d, $J$ = 16.5 Hz, 1H), 2.39 (d, $J$ = 17.5 Hz, 1H), 2.44 (d, $J$ = 17.5 Hz, 1H), 3.75 (s, 3H, $OCH_3$), 3.85 (s, 3H, $OCH_3$), 4.74 (s, 1H), 6.24–7.67 (m, 7H, ArH), 7.67 ppm (s, 2H, $NH_2$); $^{13}C$ NMR (125 MHz, $CDCl_3$) δ: 26.7, 29.3, 33.4, 36.9, 32.4, 55.9, 55.9, 81.9, 111.9, 112.7, 115.7, 120.5, 120.7, 121.8, 123.3, 126.5, 132.1, 137.2, 147.9, 148.6, 153.3, 154.5, 161.9, 196.1, 196.3 ppm; ms (ESI) *m/z*: 463.8 $[M+H]^+$. Anal. calcd. for $C_{26}H_{26}N_2O_4S$: C, 67.51; H, 5.67; N, 6.06. Found: C, 67.49; H, 5.68; N, 6.05.

***2-Amino-3-(benzo[d]thiazol-2-yl)-4-(furan-2-yl)-7,7-dimethyl-5-carbonyl-5,6,7,8-4H-benzo[b]pyran (4p).*** mp 201–202°C. IR (KBr) υ: 3458, 1684, 1668, 1621, 1477, 1454 $cm^{-1}$; $^1H$ NMR (500 MHz, DMSO-$d_6$) δ: 0.95 (s, 3H, $CH_3$), 1.06 (s, 3H, $CH_3$), 2.16 (d, $J$ = 16.0 Hz, 1H), 2.33 (d, $J$ = 16.0 Hz, 1H), 2.48 (d, 1H), 2.59 (d, $J$ = 17.5 Hz,1H), 4.73 (s, 1H), 6.18 (s, 1H), 6.27 (s, 1H), 7.20 (s, 1H), 7.22–7.92 (m, 4H, ArH), 8.39 ppm (s, 2H, $NH_2$); $^{13}C$ NMR (125 MHz, DMSO-$d_6$) δ: 26.7, 29.2, 32.4, 50.4, 79.2, 107.1, 110.8, 112.6, 120.6, 121.9, 123.4, 126.5, 131.9, 142.1, 153.4, 154.8, 155.5, 163.6, 168.7, 195.9 ppm; ms (ESI) *m/z*: 393.2 $[M+H]^+$. Anal. calcd. for $C_{22}H_{20}N_2O_3S$: C, 67.33; H, 5.14; N, 7.14. Found: C, 67.53; H, 5.13; N, 7.15.

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