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Ru(III)-catalyzed oxidative reaction in ionic liquid: an efficient and practical route to 2-substituted benzothiazoles and their hybrids with pyrimidine nucleoside

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ABSTRACT

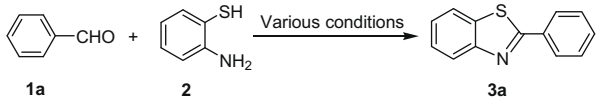
An efficient, practical and environmentally benign synthesis of 2-substituted benzothiazoles was developed through $RuCl_3$-catalyzed oxidative condensation of 2-aminothiophenol with aldehyde in ionic liquid by using air as the oxidant. With this procedure, a series of 2-substituted benzothiazoles and benzothiazole/pyrimidine nucleoside hybrids with antimicrobial activities were efficiently prepared from easily accessible starting materials.

With inherent affinity for diverse biological receptors, 2-substituted benzothiazoles have shown amazing intrinsic pharmacological and biological activities by acting as efficacious antitumor,[1] antiviral,[2] antimicrobial,[3] and antioxidant[4] agents. In addition, they have also found wide applications in the area of organic optoelectronic materials.[5] Due to their importance, numerous methods for the preparation of 2-substituted benzothiazoles have been developed. Among them, one often used procedure involves the condensation of *o*-aminothiophenol with carboxylic acids, acyl chlorides, or esters. But these processes were often accomplished under drastic reaction conditions. An alternative route starting from *o*-aminothiophenol and aldehyde with the assistance of oxidants such as $Sc(OTf)_3$,[6] O_2/activated carbon,[7] PCC,[8] H_2O_2/CAN,[9] and persulfate/$CuSO_4$[10] was then developed. More recently, a Bakers' yeast[11a] and a trichloroisocyanuric acid (TCCA) catalyzed[11b] high efficient preparation of 2-substituted benzothiazoles from *o*-aminothiophenol and aldehyde under mild conditions was also reported. In spite of the merits showed by these procedures, some of them suffer drawbacks such as tedious workup, low yields, use of stoichiometric or excessive metal reagents, and volatile harmful organic solvents. Therefore, the development of new route with significant practical value still remains a challenge.

On the other hand, organic transformations catalyzed by ruthenium(III) species have emerged as a focus of attention in recent years due to their high efficiency and excellent chemoselectivity. A catalytic amount of ruthenium(III) together with oxidants such as H_2O_2,[12] CH_3CO_3H,[13] $NaIO_4$,[14] oxygen,[15] (diacetoxyiodo)benzene (DIB),[16] bromamine-T,[17] $CeCl_3/NaIO_4$,[18] and oxygen/sodium cyanide[19] has been successfully used in an array of oxidative transformations. Meanwhile, the concept of green solvent is of rapidly growing popularity due to the increasing awareness of the adverse effect of volatile organic solvents on the environment, and an expectation has been built up on the use of ionic liquids (ILs) as the solvent for future due to their nonvolatility, nonflammability, thermal stability, and controlled miscibility.[20,21] Furthermore, they are marching beyond the boundary of green solvent by showing significant role in promoting or improving various organic transformation.[22]

As part of our ongoing research efforts toward the development of synthetic methodologies for biologically important heterocycles,[23] we set to develop a more efficient and practical procedure for the preparation of 2-substituted benzothiazoles through $RuCl_3$-catalyzed oxidative condensation of 2-aminobenzenethiol with aldehyde by using ionic liquid as the reaction medium.

Initially, the reaction of benzaldehyde (**1a**) and *o*-aminobenzenethiol (**2a**) was studied under various conditions with regard to different catalyst, solvent, temperature, and reaction time (Scheme 1). The results are summarized in Table 1. It firstly turned out that **3a** could be obtained in a yield of 65% after the mixture of **1a** and **2a** in [bmim]PF_6 (1-butyl-3-methylimidazolium hexafluorophosphate) being stirred at 60 °C for 0.5 h in the presence of 3% of $RuCl_3$ (Table 1 entry 1). It should be noted that no added stoichiometric or excessive oxidant other than air was provided, indicating that the combination of catalytic amount of $RuCl_3$ and air serves as efficient oxidant for the formation of **3a**. To our knowledge, this is the



Scheme 1.

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Table 1
Oxidative condensation of **1a** and **2a** under different reaction conditions[a]

Entry	Solvent	Catalyst	Amount of catalyst (equiv)	Time (h)	Temp. (°C)	Yield[b] (%)
1	[bmim]PF_6	$RuCl_3$	0.03	0.5	60	65
2	[bmim]PF_6	$RuCl_3$	0.03	0.5	80	72
2	[bmim]PF_6	$RuCl_3$	0.03	0.5	100	70
3	[bmim]PF_6	$RuCl_3$	0.05	0.5	60	78
4	**[bmim]PF_6**	**$RuCl_3$**	**0.05**	**0.5**	**80**	**83**
5	[bmim]PF_6	$RuCl_3$	0.1	0.5	80	84
6	[bmmim]PF_6	$RuCl_3$	0.05	0.5	80	63
7	[bmim]BF_4	$RuCl_3$	0.05	0.5	80	75
8	[bmim]PF_6	—	—	3	80	Trace
9	[bmim]PF_6	$RuCl_3$	0.05	3	80	Trace[c]
10	[bmim]PF_6	$InCl_3$	0.05	2	80	Trace
11	[bmim]PF_6	$CeCl_3$	0.05	2	80	66
12	THF	$RuCl_3$	0.05	3	Reflux	68
13	CH_3CN	$RuCl_3$	0.05	3	Reflux	62
14	Toluene	$RuCl_3$	0.05	3	80	50
15	CH_2Cl_2	$RuCl_3$	0.05	3	Reflux	61

[a] Reaction conditions: 1 mmol of **1a** was used.
[b] Isolated yields.
[c] Under nitrogen atmosphere.

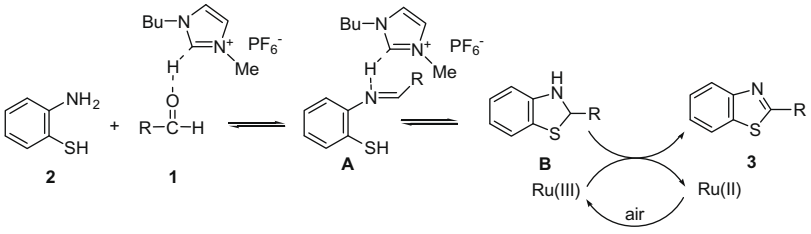


Figure 1.

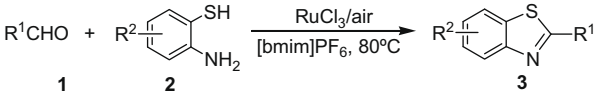
first example in which $RuCl_3$/air acts as an oxidant for the formation of heterocycles. Further studies showed that under optimized reaction conditions, **3a** could be obtained in a yield of 83% (entry 4). Studies also revealed that in the absence of either $RuCl_3$ (entry 8) or air (entry 9), only trace amount of **3a** was formed as indicated by TLC.

In addition, two more ILs, namely [bmim]BF_4 (1-tutyl-3-methylimidazolium tetrafluoroborate) and [bmmim]PF_6 (1,2-dimethyl-3-butyl imidazolium hexafluorophosphate), were employed. It showed that [bmim][PF_6] was superior to [bmim][BF_4] in its efficiency (Table 1, entries 4 and 7), presumably due to its hydrophobic activation activity. It is postulated that water formed from the condensation is miscible with hydrophilic [bmim][BF_4] and thus detained, which prevents the reaction from reaching completion. In contrast, the hydrophobic nature of [bmim][PF_6] would create a micro-environment to drive the equilibrium forward by extruding water out of the ionic liquid phase and thus result in a higher conversion. In the case of [bmmim]PF_6, with the proton of C-2 on the imidazole ring being replaced by a methyl group compared with [bmim]PF_6, the yield of **3a** dropped to 63% under similar conditions (entry 6).

The oxidative condensation was also run in several conventional organic solvents (Table 1, entries 12–15). It followed that compared with CH_2Cl_2, CH_3CN, Toluene, or THF, [bmim]PF_6 and [bmim]BF_4 not only exhibited an environmental benign nature but also showed enhanced reactivity by reducing reaction time and improving the yields significantly.

Based on the above observations, a plausible mechanism for the $RuCl_3$-catalyzed oxidative formation of 2-substituted benzothiazole is depicted in Figure 1. Firstly, the accelerating effect showed by [bmim]PF_6 and [bmim]BF_4 compared with conventional organic solvents and [bmmim]PF_6 was attributed to the acidity of the hydrogen on the 2-position of the imidazolium cation and its ability to act as a hydrogen bond donor. The formation of the O–H hydrogen bond from [bmim]$^+$ to the carbonyl oxygen of **1** induces electrophilic activation of aldehyde, which benefits the initial condensation of **1** with **2** to form an imine intermediate **A**. Moreover, it may further form an N–H hydrogen bond with the in situ-formed imine **A** and it would accelerate the subsequent *intramolecular* nucleophilic cyclization to form intermediate **B**. Intermediate **B** is then oxidized by Ru(III) to give the final product **3**. The in situ-formed Ru (II) could be oxidized by air to regenerate Ru(III) for the next catalytic cycle, accounting for the necessity of the presence of catalytic amount of Ru(III) and air.

With the optimized reaction conditions, the oxidation of a range of substrates was then tried to study the scope and limitation of this new procedure (Scheme 2) and the examples are summarized in Table 2. It was observed that, with either aromatic or aliphatic aldehydes, the reactions underwent smoothly, and the corresponding products were obtained in good yields. For aromatic aldehydes and aminobenzothiols with electron-withdrawing or electron-donating groups on the phenyl rings, the reactions were run with almost equal efficiency (Table 2, entries 1–19). On the other hand, for aminobenzothiol with steric hindered group, the reactions were slowed down and the yields were lower (Table 2, entries 22–25). Moreover, various functional groups, such as nitro, methyl, methoxy, and halide groups on the phenyl rings, were well tolerated under this condition.[24]



Scheme 2.

Table 2
Preparation of **3** with $RuCl_3$/air in $[bmim]PF_6$[a]

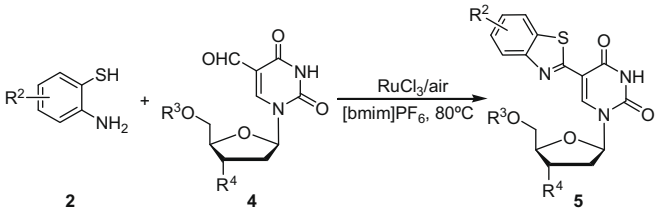
Entry	R^1	R^2	Product	Time (h)	Yield[b] (%)
1	C_6H_5	H	**3a**	0.5	83
2	4-BrC_6H_4	H	**3b**	0.5	85
3	4-$CH_3OC_6H_4$	H	**3c**	0.5	80
4	4-CNC_6H_4	H	**3d**	0.5	85
5	2-BrC_6H_4	H	**3e**	1	81
6	2-$NO_2C_6H_4$	H	**3f**	0.5	82
7	2-ClC_6H_4	H	**3g**	1	81
8	3-$NO_2C_6H_4$	H	**3h**	0.5	86
9	3-BrC_6H_4	H	**3i**	0.5	84
10	3-$CH_3C_6H_4$	H	**3j**	0.5	79
11	C_6H_5	4-Cl	**3k**	0.5	83
12	4-$NO_2C_6H_4$	4-Cl	**3l**	0.5	88
13	4-BrC_6H_4	4-Cl	**3m**	0.5	83
14	4-$CH_3OC_6H_4$	4-Cl	**3n**	0.5	82
15	3-ClC_6H_4	4-Cl	**3o**	0.5	83
16	3-BrC_6H_4	4-Cl	**3p**	0.5	80
17	2-$NO_2C_6H_4$	4-Cl	**3q**	0.5	80
18	2-ClC_6H_4	4-Cl	**3r**	1	80
19	2-BrC_6H_4	4-Cl	**3s**	1	79
20	$CH_3CH_2CH_2$	H	**3t**	2	75
21	$CH_3CH_2CH_2$	4-Cl	**3u**	2	76
22	C_6H_5	3-Cl	**3v**	4	62
23	4-$NO_2C_6H_4$	3-Cl	**3w**	3	75
24	3-$CH_3C_6H_4$	3-Cl	**3x**	4	60
25	2-$NO_2C_6H_4$	3-Cl	**3y**	6	43
26	4-BrC_6H_4	4-CH_3	**3z**	2	80
27	3-$CH_3C_6H_4$	4-CH_3	**3aa**	2	78

[a] Reaction conditions: 1 mmol of **1** and **2**, 1 mL of $[bmim]PF_6$, 80 °C.
[b] Isolated yields.

In a further aspect, Loiseau and co-workers[25] recently reported a synthesis and in vitro antileishmanial evaluation of a small library of 5-heteroaryl-substituted-2′-deoxyuridine. The nucleoside derivatives were synthesized therein through two to three steps and the key step is based on a palladium and cupric salt-catalyzed Stille cross coupling of protected 5-iodo-2′-deoxyuridine with premade aryltin derivatives (Scheme 3).

Considering the tedious procedure, expensive catalyst, and specially made starting material it involved, we thought it would benefit both synthetic and medicinal chemistries to develop a more practical method to prepare these nucleoside derivatives. A new synthetic route was then envisioned by using the methodology developed in this Letter. Thus, a mixture of the easily made 5-formyl-pyrimidine nucleoside (**4**)[26] and commercially available **2** was treated with $[bmim]PF_6$ at 80 °C in the presence of 5% of $RuCl_3$ (Scheme 4). Very encouragingly, the reactions underwent smoothly and afforded the pyrimidine nucleoside-benzothiazole hybrids with good yields (Table 3). The structures of the hybrid compounds were fully characterized by their spectra data.[27]

Finally, the recyclability of $RuCl_3$ together with $[bmim]PF_6$ was studied by using **1a** and **2a** as the substrates. It turned out that $RuCl_3$/$[bmim]PF_6$ could be reused directly for a new cycle after the IL phase was extracted with diethyl ether (10 mL × 3) and dried under vacuum at 90 °C overnight. The recovered $RuCl_3$/$[bmim]PF_6$ was recycled and reused for three times. Only slight drop in its catalytic activity was observed over each reuse. In these reactions, the ionic liquid acts as not only solvent and co-catalyst but also an immobilizing agent for facilitating catalyst recycling.



Scheme 4.

Table 3
Preparation of **5** with $RuCl_3$/air in $[bmim]PF_6$[a]

Entry	R^2	R^3	R^4	Product	Time (h)	Yield[b] (%)
1	H	Ac	OAc	**5a**	2	75
2	4-Cl	Ac	OAc	**5b**	2	77
3	H	Ac	N_3	**5c**	2	75
4	4-Cl	Ac	N_3	**5d**	2	71
5	H	H	OH	**5e**	3	70
6	4-Cl	H	OH	**5f**	3	71
7	H	H	N_3	**5g**	3	68
8	4-Cl	H	N^3	**5h**	3	66
9	3-Cl	Ac	OAc	**5i**	6	50

[a] Reaction conditions: 1 mmol of **2** and **4**, 1 mL of $[bmim]PF_6$, 80 °C.
[b] Isolated yields.

Acknowledgments

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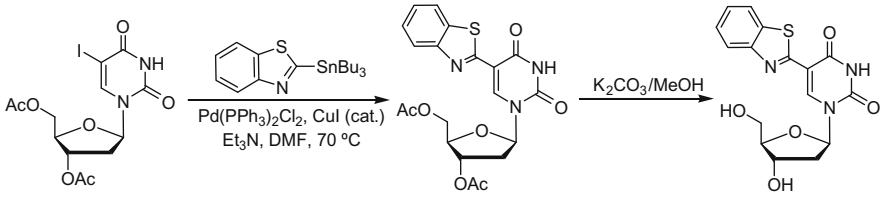

Scheme 3.

References and notes

1. Lion, C. J.; Matthews, C. S.; Wells, G.; Bradshaw, T. D.; Stevens, M. F. G.; Westwell, A. D. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 5005.
2. Vicini, P.; Geronikaki, A.; Incerti, M.; Busonera, B.; Poni, G.; Cabras, C. A.; Colla, P. L. *Bioorg. Med. Chem.* **2003**, *11*, 4785.
3. Zajac, M.; Hrobárik, P.; Magdolen, P.; Foltínová, P.; Zahradník, P. *Tetrahedron* **2008**, *64*, 10605.
4. Cressier, D.; Prouillac, C.; Hernandez, P.; Amourette, C.; Diserbo, M.; Lion, C.; Rima, G. *Bioorg. Med. Chem.* **2009**, *17*, 5275.
5. (a) Zhang, X. H.; Wong, O. Y.; Gao, Z. Q.; Lee, C. S.; Kwong, H. L.; Lee, S. T.; Wu, S. K. *Mater. Sci. Eng.* **2001**, *B85*, 182; (b) Zhang, L.; Xu, Q. F.; Lu, J. M.; Li, N. J.; Yan, F.; Wang, L. H. *Polymer* **2009**, *50*, 4807; (c) Bae, J. S.; Gwon, S. Y.; Son, Y. A.; Kim, S. H. *Dyes Pigments* **2009**, *83*, 324; (d) Dutta, G. K.; Guha, S.; Patil, S. *Org. Electron.* **2010**, *11*, 1; (e) Chen, L. Q.; Yang, C. L.; Qin, J. G. *Spectrochim. Acta, Part A* **2007**, *68*, 317.
6. Itoh, T.; Nagata, K.; Ishikawa, H.; Ohsawa, A. *Heterocycles* **2004**, *63*, 2769. and references cited therein.
7. Kawashita, Y.; Ueba, C.; Hayashi, M. *Tetrahedron Lett.* **2006**, *47*, 4231.
8. Praveen, C.; Kumar, K. H.; Muralidharan, D.; Perumal, P. T. *Tetrahedron* **2008**, *64*, 2369.
9. Bahrami, K.; Khodaei, M. M.; Naali, F. *J. Org. Chem.* **2008**, *73*, 6835.
10. Kumar, A.; Maurya, R. A.; Saxena, D. *Mol. Divers.* **2009**. doi:10.1007/s11030-009-9170-8.
11. (a) Pratap, U. R.; Mali, J. R.; Jawale, D. V.; Mane, R. A. *Tetrahedron Lett.* **2009**, *50*, 1352; (b) Xiao, H. L.; Chen, J. X.; Liu, M. C.; Zhu, D. J.; Ding, J. C.; Wu, H. Y. *Chem. Lett.* **2009**, *38*, 170.
12. Ito, S.; Aihara, K.; Matsumoto, M. *Tetrahedron Lett.* **1983**, *24*, 5249.
13. Komiya, N.; Noji, S.; Murahashi, S.-I. *Chem. Commun.* **2001**, 65.
14. Sharma, N. K.; Ganesh, K. N. *Tetrahedron Lett.* **2004**, *45*, 1403.
15. Mashraqui, S. H.; Karnik, M. A. *Tetrahedron Lett.* **1998**, *39*, 4895.
16. Yusubov, M. S.; Chi, K.-W.; Park, J. Y.; Karimov, R.; Zhdankin, V. V. *Tetrahedron Lett.* **2006**, *47*, 6305.
17. Sharma, V. B.; Jain, S. L.; Sain, B. *Tetrahedron Lett.* **2004**, *45*, 4281.
18. Plietker, B.; Niggemann, M. *J. Org. Chem.* **2005**, *70*, 2402.
19. Murahashi, S.-I.; Komiya, N.; Terai, H.; Nakae, T. *J. Am. Chem. Soc.* **2003**, *125*, 15312.
20. (a) Ranke, J.; Stolte, S.; Strörmann, R.; Arning, J.; Jastorff, B. *Chem. Rev.* **2007**, *107*, 2183; (b) Stolte, S.; Matzke, M.; Arning, J.; Böschen, A.; Pitner, W. R.; Welz-Biermann, U.; Jastorff, B.; Ranke, R. *Green Chem.* **2007**, *9*, 1170.
21. (a) Afonso, C. A. M.; Branco, L. C.; Candeias, N. R.; Gois, P. M. P.; Lourenco, N. M. T.; Mateus, N. M. M.; Rosa, J. N. *Chem. Commun.* **2007**, 2669; (b) Pârvulescu, V. I.; Hardacre, C. *Chem. Rev.* **2007**, *107*, 2615.
22. (a) Martins, M. A.; Frizzo, C. P.; Moreira, D. N.; Zanatta, N.; Bonacorso, H. G. *Chem. Rev.* **2008**, *108*, 2015; (b) Charkraborti, A. K.; Roy, S. R. *J. Am. Chem. Soc.* **2009**, *131*, 6902.
23. (a) Fan, X.; Hu, X.; Zhang, X.; Wang, J. *Aust. J. Chem.* **2004**, *57*, 1067; (b) Fan, X.; Hu, X.; Zhang, X.; Wang, J. *Can. J. Chem.* **2005**, *83*, 16; (c) Fan, X.; Li, Y.; Zhang, X.; Wang, J. *Can. J. Chem.* **2006**, *84*, 794; (d) Zhang, X.; Fan, X.; Niu, H.; Wang, J. *Green Chem.* **2003**, *5*, 267.
24. *Typical procedure for the preparation of* **3a**: A mixture containing aldehyde (**1a**, 1 mmol), *o*-aminobenzenethiol (**2a**, 1 mmol), and $RuCl_3$ (0.05 mmol) in [bmim]PF_6 (1 mL) was stirred at 80 °C for 0.5 h. Upon completion, the mixture was extracted with diethyl ether (10 mL × 3). The combined organic phases were washed with H_2O and dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude product was purified by column chromatography eluting with hexane/ethyl acetate (5–20%) to give **3a**. Other 2-substituted benzothiazoles were obtained in a similar manner. Details of analytical data of selected compounds are presented as follows: *Compound* **3d**: mp 165–167 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.47 (t, 1H, J = 7.6 Hz, ArH), 7.56 (t, 1H, J = 7.6 Hz, ArH), 7.80 (d, 2H, J = 8.0 Hz, ArH), 7.96 (d, 1H, J = 8.0 Hz, ArH), 8.13 (d, 1H, J = 8.0 Hz), 8.22 (d, 2H, J = 8.0 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 114.1, 118.3, 121.8, 123.8, 126.1, 126.8, 127.9, 132.8, 135.3, 137.5, 154.0, 165.3. MS: m/z 237 $(MH)^+$. *Compound* **3l**: mp 185–187 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.43 (dd, 1H, J_1 = 2.0 Hz, J_2 = 8.4 Hz, ArH), 7.87 (d, 1H, J = 8.4 Hz, ArH), 8.10 (d, 1H, J = 2.0 Hz, ArH), 8.24 (d, 2H, J = 8.4 Hz), 8.36 (d, 2H, J = 8.4 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 122.6, 123.6, 124.4, 126.7, 128.3, 132.9, 133.7, 138.7, 149.1, 154.8, 166.6. MS: m/z 291 $(MH)^+$. *Compound* **3t**: oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.07 (t, 3H, J = 7.6 Hz, CH_3), 1.90–1.96 (m, 2H, CH_2), 3.11 (t, 2H, J = 7.6 Hz, CH_2), 7.35 (t, 1H, J = 7.6 Hz, ArH), 7.46 (t, 1H, J = 7.6 Hz, ArH), 7.85 (d, 1H, J = 8.0 Hz, ArH), 7.98 (d, 1H, J = 8.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.7, 23.1, 36.2, 121.4, 122.5, 124.6, 125.8, 126.6, 126.8, 135.1, 153.2, 172.2. MS: m/z 178 $(MH)^+$. *Compound* **3w**: mp 207–210 °C; ^{1}H NMR (400 MHz, CDCl3) δ: 7.39 (t, 1H, J = 8.0 Hz, ArH), 7.58 (dd, 1H, J_1 = 8.0 Hz, J_2 = 0.8 Hz, ArH), 7.85 (dd, 1H, J_1 = 8.0 Hz, J_2 = 0.8 Hz, ArH), 8.30 (d, 2H, J = 8.8 Hz, ArH), 8.36 (d, 2H, J = 8.8 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 120.3, 124.3, 126.7, 127.1, 128.5, 129.0, 136.8, 138.6, 149.3, 151.1, 165.5. MS: m/z 291 $(MH)^+$. *Compound* **3z**: mp 193–195 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.49 (s, 3H, CH_3), 7.30 (d, 1H, J = 8.0 Hz, ArH), 7.60 (d, 2H, J = 8.0 Hz, ArH), 7.66 (s, 1H, ArH), 7.91–7.94 (m, 3H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.5, 121.3, 122.8, 125.1, 128.0, 128.7, 132.1, 132.7, 135.2, 135.6, 152.2, 165.5. MS: m/z 304 $(MH)^+$.
25. Peyron, C.; Benhida, R.; Bories, C.; Loiseau, P. M. *Bioorg. Chem.* **2005**, *33*, 439.
26. Ono, A.; Okamoto, T.; Inada, M.; Nara, H.; Matsuda, A. *Chem. Pharm. Bull. (Tokyo)* **1994**, *42*, 2231.
27. *Typical procedure for the preparation of* **5a**: A mixture containing 3′,5′-diacetyl-5-formyl-2′-deoxyuridine (1 mmol), *o*-aminobenzenethiol (**2**, 1 mmol), and $RuCl_3$ (0.05 mmol) in [bmim]PF_6 (1 mL) was stirred at 80 °C for 2 h. Upon completion, the crude product was purified by column chromatography eluting with hexane/ethyl acetate (20–50%) to give **5a**. Details of analytical data of selected compounds are presented as follows: *Compound* **5a**: mp 223–225 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.16 (s, 3H, CH_3), 2.28 (s, 3H, CH_3), 2.32–2.62 (m, 2H, CH_2), 4.40–4.49 (m, 3H, CH, CH_2), 5.36–5.38 (m, 1H, CH), 6.48–6.52 (m, 1H, CH), 7.38 (t, 1H, J = 7.6 Hz, ArH), 7.49 (t, 1H, J = 7.6 Hz, ArH), 7.92–7.95 (m, 2H, ArH), 9.01 (s, 1H, CH), 9.36 (s, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.9, 21.1, 38.5, 64.2, 74.7, 83.0, 85.9, 109.4, 121.6, 122.2, 124.7, 126.3, 135.7, 139.3, 149.2, 151.8, 158.4, 160.8, 170.4, 170.6. MS: m/z 446 $(MH)^+$. *Compound* **5c**: mp 206–207 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.15 (s, 3H, CH_3), 2.50–2.62 (m, 2H, CH_2), 4.21–4.55 (m, 4H, 2 × CH, CH_2), 6.13–6.18 (m, 1H, CH), 7.39 (t, 1H, J = 7.6 Hz, ArH), 7.51 (t, 1H, J = 7.6 Hz, ArH), 7.89 (d, 1H, J = 7.6 Hz, ArH), 8.09 (d, 1H, J = 7.6 Hz, ArH), 8.85 (s, 1H, CH), 12.12 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 21.2, 37.7, 60.5, 63.6, 82.3, 86.4, 107.4, 121.9, 122.4, 124.9, 126.8, 135.2, 140.8, 149.5, 151.8, 159.9, 161.8, 170.8. MS: m/z 429 $(MH)^+$. *Compound* **5d** mp: 224–226 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.10 (s, 3H, CH_3), 2.48–2.63 (m, 2H, CH_2), 4.21–4.48 (m, 4H, 2 × CH, CH_2), 6.11–6.14 (m, 1H, CH), 7.40 (d, 1H, J = 8.4 Hz, ArH), 7.85 (s, 1H, ArH), 8.09 (d, 1H, J = 8.4 Hz, ArH), 8.82 (s, 1H, CH), 12.10 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 21.1, 37.8, 60.6, 63.6, 82.4, 86.7, 107.1, 121.2, 124.0, 124.9, 131.4, 134.0, 141.3, 149.5, 152.8, 161.9, 162.4, 170.7. MS: m/z 463 $(MH)^+$. *Compound* **5i**: mp: 199–202 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 2.01 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 2.48–2.50 (m, 2H, CH_2), 4.26–4.38 (m, 3H, CH_2, CH), 5.25 (s, 1H, CH), 6.18–6.22 (m, 1H, CH), 7.35 (t, 1H, J = 8.0 Hz, ArH), 7.55 (d, 1H, J = 8.0 Hz, ArH), 8.04 (d, 1H, J = 8.0 Hz, ArH), 8.90 (s, 1H, CH), 12.14 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 21.1, 21.2, 38.0, 64.1, 74.7, 82.9, 87.2, 107.3, 121.4, 125.7, 126.0, 126.7, 136.9, 141.2, 148.6, 149.6, 161.2, 161.9, 170.4, 170.5. MS: m/z 480 $(MH)^+$.