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Preparation of α-Bromoketones and Thiazoles from Ketones with NBS and Thioamides in Ionic Liquids

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Abstract

Ketones smoothly reacted with NBS in the presence of a catalytic amount of *p*-toluenesulfonic acid to give α-bromoketones in good yields in typical ionic liquids, such as [bmim]PF_6 and [bmpy]Tf_2N, and the ionic liquids could be repeatedly used for the same reaction after the extraction of the α-bromoketones. Then, the one-pot conversion of ketones into thiazoles by the treatment with NBS, and subsequently with thioamides could be also carried out in [bmim]PF_6 and [bmpy]Tf_2N, respectively Thus, [bmim]PF_6 and [bmpy]Tf_2N could be used as recyclable reaction media for the preparation α-bromoketones and thiazoles from ketones.

Keywords: Ketone, α-Bromoketone, Thiazole, NBS, Thioamide, Ionic Liquid

1. Introduction

Thiazoles are one of the most important heterocycles and known for their broad spectrum of biological activities [1,2]. Many natural and synthetic molecules containing the thiazole moiety play a significant role in the pharmaceutical industry due to their anti-inflammatory [3,4], anti-HIV [5], anti-bacterial [6], anti-cancer [7] properties. Today, there are many methods for the preparation of the thiazole moiety [8-12]. One of the most excellent and efficient method is the Hantzsch thiazole synthesis [13,14] that employs the reaction of α-haloketones or α-tosyloxyketones with thioamides. For the preparation of α-bromonoketones from ketones, NBS (*N*-bromosuccinimide) is well used [15], whereas HTIB [(hydroxy)(tosyloxy)iodobenzene] is the sole reagent for the direct preparation of α-tosyloxyketones from ketones [16-22].

On the other hand, ionic liquids have grown in popularity as organic reaction media due to the promotion of ionic reactions and in view of environmental safety [23-30]. Ionic liquids offer interesting and useful features that are advantageous to organic reactions such as negligible vapor pressure, nonflammability, high thermal stability, and easy reusability. In this regard, ionic liquids have been successfully used in the Friedel-Crafts reaction [31-33], hydrogenation [34-36], Diels-Alder reactions [37-39], Mizoroki-Heck, Suzuki-Miyaura, Sonogashira, and olefin metathesis reactions [40-44], Michael additions [45], oxidation [46-54], condensation reaction [55-59], formation of imines [60], 1,2-rearrangement [61], esterification of carboxylic acids and carboxylates [62-65], Williamson ether synthesis [66-72], and the Grignard reaction [73,74]. We have reported efficient methods for the esterification of carboxylic acids and phosphonic acids with trialkyl orthoacetate in ionic liquid [75], the demethylation of *N,N*-dimethylanilines with phenyl chloroformate in ionic liquids [76], and the 3-*exo*-*tet* cyclization of 2,2-disubstituted 1,3-dihalopropanes with indium in ionic liquid [77], The α-bromination of β-dicarbonyls and cyclic ketones with NBS in ionic liquids [78], and the aromatic ring bromination with NBS in ionic liquids [79,80] have been reported as well. However, to the best of our knowledge, there are no synthetic studies that deal with the preparation of thiazoles from ketones with NBS and thioamides in ionic liquids. Here, as a part of our synthetic study of ionic liquids, we would like to report the preparation of α-bromoketones and thiazoles from ketones, with NBS and thioamides in typical room-temperature ionic liquids.

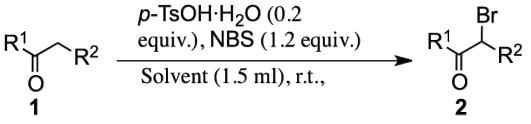
2. Results and Discussion

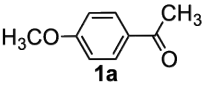
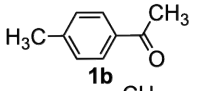
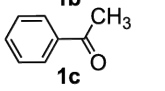
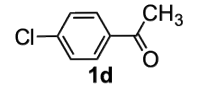
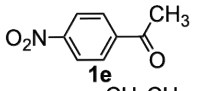
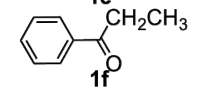
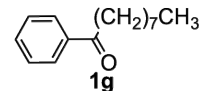
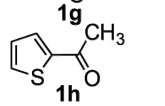
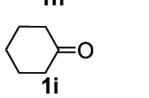
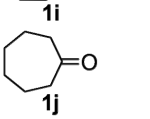
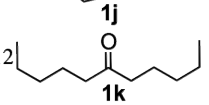
The α-bromination of ketones with NBS in the presence of a catalytic amount of *p*-toluenesulfonic acid (*p*-TsOH) was carried out at room temperature in both chloroform and typical room-temperature ionic liquids, such as 1-butyl-3-methylimidazolium hexafluorophosphate ([bmim]PF_6), *N*-butyl-*N*-methylpyrrolidinium bis(trifluoromethanesulfonyl)imidate ([bmpy]Tf_2N), and 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim]BF_4), as shown

in **Table 1**. As a result, the corresponding α-bromoketones were obtained in good to high yields in chloroform, [bmim]PF_6, and [bmpy]Tf_2N, respectively. In contrast, the α-bromination of ketones did not proceed at all in [bmim]BF_4. It is probable that the proton derived from *p*-TsOH could not promote the formation of enol forms of ketones due to the interaction between the proton of *p*-TsOH and BF_4^-. Practically, chemical shift of a hydrogen atom at 2-position of [bmim]BF_4 is 9.42 ppm ($CDCl_3$, TMS), and is lower field than that of [bmim]PF_6 (8.42 ppm, $CDCl_3$, TMS). This suggests that BF_4^- in [bmim]BF_4 interacts strongly with a proton of *p*-TsOH. Moreover, the yields of α-bromoketones in [bmim]PF_6 and [bmpy]Tf_2N are higher overall than those in chloroform, especially when propiophenone and nonanophenone were used as substrate (entries 6, 7). When an ionic liquid such as [bmim]PF_6 was used, α-bromoketone was obtained in good yields with good purity (>80%) by simple ether extraction of the reaction mixture and the ionic liquid reaction medium could be reused for the same reaction up to the 7th time while maintaining the high yields of α-bromoketone, as shown in **Table 2**.

Then, the one-pot conversion of ketones to thiazoles in both chloroform and ionic liquids, such as [bmim]PF_6 and [bmpy]Tf_2N, was studied, as shown in **Table 3**. After the α-bromination of ketones with NBS, thioamide and potassium carbonate were added to the reaction mixture, and the obtained mixture was stirred at room temperature. Overall, the yields in [bmim]PF_6 and [bmpy]Tf_2N were higher than those in chloroform, particularly, when propiophenone with thiobenzamide, acetophenone with *p*-methoxythiobenzamide, and acetophenone with thioacetamide were used (entries 6, 10, 12). In the reaction with acetophenone in [bmim]PF_6, thiazoles were obtained in good yields with moderate purity (>70%) by ether extraction, and the ionic liquid reaction medium could be reused for the same reaction, maintaining the good yields of thiazole up to the 5th time, as shown in **Table 4**.

Table 1. Conversion Ketones into α-Bromoketones in ILs or $CHCl_3$.



Entry	Substrate	Times (h)	Yields (%) [Bmim]PF_6	[Bmpy]Tf_2N	[Bmim]BF_4	$CHCl_3$
1	 **1a**	9	86	85	0	92
2	 **1b**	9	84	89	0	96
3	 **1c**	9	90	84	0	81
4	 **1d**	10	93	95	0	94
5	 **1e**	35	85	96	0	62
6	 **1f**	9	74	75	0	26
7	 **1g**	32	83	92	0	53
8	 **1h**	9	81	74	0	67
10	 **1i**	2	78	68	0	57
11	 **1j**	2	73	68	0	64
12	 **1k**	2	82	83	0	66

3. Conclusions

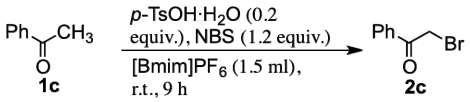
Typical room temperature ionic liquids, such as [bmim]PF_6 and [bmpy]Tf_2N could be used for the conversion of ketones to α-bromoketones with NBS and the conversion of ketones to thiazoles with NBS and subsequently thioamides in a one-pot manner. α-Bromoketones and thiazoles could be obtained in good yields with good purity by simple ether extraction, and the ionic liquid reaction media could be reused for the same reaction while maintaining good yields and purity of the products. The present method offers a green approach to the preparation of α-bromoketones and thiazoles in good yields with good purity from ketones with NBS and subsequently thioamides at room temperature.

4. Experimental Section

4.1. General

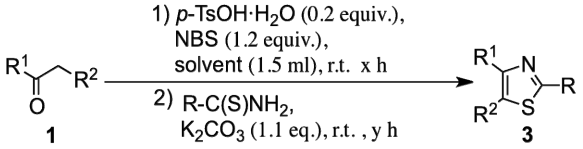
^{1}H NMR and ^{13}C NMR spectra were obtained on JEOL-

Table 2. Recyclic Use for conversion of acetophenpne to α-Bromoketones from acetophenone in [Bmim]PF_6.

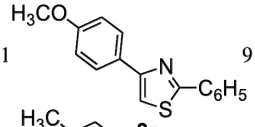
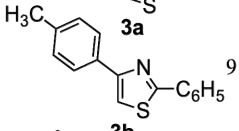
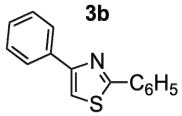
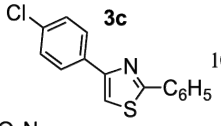
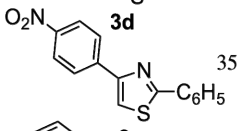
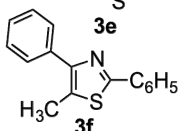
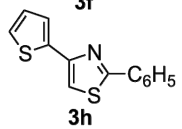
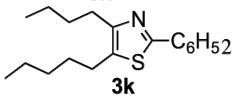
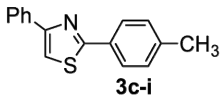
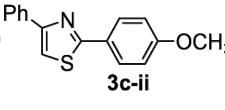
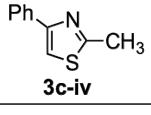


Reuse	0	1	2	3	4	5	6	7
Yields (%)	90	81	78	91	92	96	93	95

Table 3. Conversion of Ketones into Thiazols with NBS and Thibenzamide in ILs and $CHCl_3$.

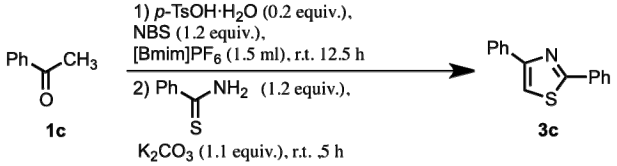


R = C_6H_5, *p*-$CH_3C_6H_4$, *p*-$CH_3OC_6H_4$, *p*-$O_2NC_6H_4$, CH_3

Entry	product	x (h)	y (h)	Yields (%) [Bmim]PF_6	[Bmpy]Tf_2N	$CHCl_3$
1	 **3a**	9	12	81	89	86
2	 **3b**	9	5	94	96	87
3	 **3c**	9	5	96	94	73
4	 **3d**	10	5	89	69	73
5	 **3e**	35	12	85	83	74
6	 **3f**	9	11	73	63	30
7	 **3h**	9	3	99	-	71
8	 **3k**	2	11	77[a]	71	64
9	 **3c-i**	9	5	94	-	90
10	 **3c-ii**	9	4	84	61	26
11	 **3c-iii**	9	4	85	-	78
12	 **3c-iv**	9	6	83	75	44

a) Reaction temperature was 50˚C.

Table 4. Recyclic Use of [Bmim]PF6 for preparation of 2,4-diphenylthiazol from acetophenone.



Reuse	0	1	2	3	4	5
Yields (%)	95	97	91	85	89	96

JNM-ECX400, JEOL-JNM-ECS400, and JEOL-JNM-ECA500 spectrometers. All chemical shifts were expressed in ppm, δ units down field from TMS (Me_4Si). Mass spectra were recorded on JEOL-HX-110 and JEOL-JMS-AT15 spectrometers. Melting points were determined on Yamato melting points apparatus Model MP-21. Silica Gel 60 (Kanto Kagaku Co.) and Wakogel B-5F were used for column chromatography and preparative TLC, respectively.

4.2. Typical Procedure for Conversion of Acetophenone into *p*-bromoacetophenone with NBS and *p*-TsOH·H_2O in Ionic Liquids

To a solution of acetophenone (1 mmol) in [Bmim]PF_6 (1.5 mL) were added *p*-TsOH·H_2O (0.2 mmol) and NBS (1.2 mmol). The mixture was stirred for 9.5 h at room temperature. After the reaction, the reaction mixture was extracted with diethyl ether (10 mL × 7). Then, the extract was poured into sat. aq. Na_2SO_3 solution. The organic layer was dried over Na_2SO_4. After removal of the solvent under reduced pressure, α-bromoacetophenone was obtained in the crude state. Purity was estimated by ^{1}H-NMR to be in the range of 70% - 80%. Pure α-bromoacetophenone was obtained by flash short column chromatography on silica gel ($CHCl_3$:Hexane = 1:1) in 90% yield.

4.3. Typical Reuse of [Bmim]PF_6

After the extraction with diethyl ether, the ionic liquid was dried with a vacuum pump for 2 h at 80˚C. To a solution of acetophenone (1 mmol) in [Bmim]PF_6 (1.5 mL) were added *p*-TsOH·H_2O (0.2 mmol) and NBS (1.2 mmol). The mixture was stirred for 9 h at room temperature. After the reaction, the reaction mixture was extracted with diethyl ether (10 mL × 7). Then, extract was poured into sat. aq. Na_2SO_3 solution. The organic layer was dried over Na_2SO_4. After removal of the solvent under reduced pressure, α-bromoacetophenone was obtained in the crude state. Purity was estimated by ^{1}H-NMR to be in the range of 70% - 80%. Pure α-bromoacetophenone

was obtained by flash short column chromatography on silica gel ($CHCl_3$:Hexane = 1:1) in 91 % yield.

α-Bromoacetophenone: mp 54˚C - 55˚C (lit. [81] mp 49˚C - 50˚C); IR(Nujol) 2319, 1690, 1594, 1308, 1276, 1199, 991, 745, 685 cm^{-1}; ^1H NMR(500 MHz, $CDCl_3$): δ = 7.99 (d, 2H, *J* = 7.4 Hz, ArH), 7.62 (t, 1H, *J* = 7.4 Hz, ArH), 7.50 (t, 2H, *J* = 7.4 Hz, ArH), 4.46 (s, 2H, -CH_2-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.2, 133.9 (3C), 128.9, 128.8, 30.8.

α-Bromo-4'-chloroacetophenone: mp 101˚C - 103˚C (lit. [82] mp 95˚C - 96˚C); IR(Nujol) 3853, 3749, 3648, 1690, 1540, 1507, 1092, 721, 509 cm^{-1}; ^1H NMR(400 MHz, $CDCl_3$): δ = 7.99 (d, 2H, *J* = 7.3 Hz, ArH), 7.62 (t, 1H, *J* = 7.3 Hz, ArH), 7.50 (t, 2H, *J* = 8.0 Hz, ArH), 4.46 (s, 2H, -CH_2Br); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 190.2, 140.5, 132.2, 130.3, 129.2, 30.3.

α-Bromo-4'-methoxyacetophenone : mp 70˚C (lit. [83] mp 69˚C - 73˚C); IR(Nujol) 3853, 3749, 3648, 2309, 1683, 1598, 1508, 1322, 1306, 1260, 1205, 1170, 1116, 1020, 986, 840, 816, 721 cm^{-1}; ^1H NMR(400 MHz, $CDCl_3$): δ = 7.97 (d, 2H, *J* = 7.8 Hz, ArH), 6.96 (d, 2H, *J* = 7.8 Hz, ArH), 4.40 (s, 2H, -CH_2-), 3.88 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 189.8, 163.9, 131.1, 126.7, 113.9, 55.5, 30.7.

α-Bromo-4'-methylacetophenone: mp 56˚C - 58˚C (lit. [84] mp 48˚C - 50˚C); IR(Nujol) 1687, 1608, 1282, 1179, 799, 723 cm^{-1}; ^1H NMR(500 MHz, $CDCl_3$): δ = 7.88 (d, 2H, *J* = 8.6 Hz, ArH), 7.28 (d, 2H, *J* = 8.6 Hz, ArH), 4.42 (s, 2H, -CH_2Br), 2.42 (s, 3H, -CH_3) ; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 190.9, 144.9, 131.4, 129.5, 129.0, 30.9, 21.7.

α-Bromo-4'-nitroacetophenone: mp 98˚C - 101˚C (lit. [85] mp 98˚C); IR(Nujol) 3853, 3748, 3647, 2309, 1698, 1507, 966, 844, 720 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.35 (d, 2H, *J* = 8.9 Hz, ArH), 8.16 (d, 2H, *J* = 8.44 Hz, ArH), 4.46 (s, 2H, -CH_2Br); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 189.8, 150.7, 138.3, 130.0, 124.0, 30.1.

α-Bromopropiophenone: Oil; IR(Neat) 3062, 2978, 2925, 1686, 1595, 1448, 1346, 1238, 1160, , 994, 949, 707 cm^{-1} ; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.03 (d, 2H, *J* = 7.4 Hz, ArH), 7.59 (t, 1H, *J* = 6.9 Hz, ArH), 5.29 (q, *J* = 6.30 Hz, 1H, -CH-), 1.91 (d, *J* = 6.30 Hz, 3H, -CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 193.2, 134.0, 133.6, 128.8, 128.6, 41.4, 20.0.

α-Bromononanophenone: Oil; IR(Neat) 2926, 2855, 1687, 1264, 702, 685 cm^{-1} ; ^1H NMR(500 MHz, $CDCl_3$): δ = 8.01 (d, 2H, *J* = 7.4 Hz, ArH), 7.59 (t, 1H, *J* = 7.4 Hz, ArH), 7.48 (t, 2H, *J* = 7.4 Hz, ArH), 5.13 (t, 1H, *J* = 6.8 Hz, -CHBr-), 2.24-2.07 (m, 2H, -CH_2-), 1.53-1.48 (m, 1H, -CH-), 1.43-1.27 (m, 9H, -CH_2-), 0.89-0.86 (t, 3H, *J* = 6.8 Hz, -CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 193.3, 134.5, 133.6, 128.8, 128.7, 47.3, 33.5, 31.6, 29.1, 29.0, 27.5, 22.5, 14.0.

2-(α-Bromacetyl)thiophene: Oil; IR(Neat) 3544, 3297, 3091, 2942, 2469, 2319, 1660, 1517, 1412, 1355, 1289, 1238, 1193, 1112, 1079, 1061, 1041, 972, 940, 885, 859, 727, 686, 664, 632, 614 cm^{-1}; ^1H NMR(500 MHz, $CDCl_3$): δ = 7.81 (d, 1H, *J* = 4.0 Hz, thiophene), 7.72 (d, 1H, *J* = 4.6 Hz, thiophene), 7.17 (t, 1H, *J* = 4.5 Hz, thiophene), 4.36 (s, 2H, -CH_2Br); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 184.3, 140.7, 135.2, 133.5, 128.3, 30.5.

α-Bromocyclohexanone: Oil; IR(Neat) 2927, 2867, 1715, 1448, 1430, 962 cm^{-1} ; ^1H NMR(400 MHz, $CDCl_3$): δ = 4.44 (t, 1H, *J* = 5.1 Hz, -CHBr-), 3.01 - 2.95 (m, 1H, -CH_2-), 2.36 - 2.29 (m, 2H, -CH_2-), 2.27 - 2.19 (m, 1H, -CH_2-), 2.06 - 1.92 (m, 2H, -CH_2-), 1.85 - 1.70 (m, 2H, -CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 203.4, 53.4, 37.9, 36.7, 26.7, 22.1

α-Bromocycloheptanone: Oil; IR(Neat) 2933, 2857, 1709, 1454, 1322, 1186, 1159, 935 cm^{-1}; ^1H NMR(400 MHz, $CDCl_3$): δ = 4.38 (q, 1H, *J* =4.6 Hz, -CHBr-), 2.89 - 2.82 (m, 1H, -CH-), 2.49 (qd, 1H, *J* = 8.0 Hz, *J* = 2.96, -CH-), 2.40 - 2.32 (m, 1H, -CH-), 2.06 - 1.90 (m, 3H, -CH-), 1.81 - 1.73 (m, 1H, -CH-), 1.62 - 1.51 (m, 2H, -CH-), 1.43 - 1.34 (m, 1H, -CH-); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 206.2, 53.6, 39.3, 34.2, 29.5, 26.7, 24.9.

5-Bromoundecan-6-one: Oil ; IR (Neat) 2958, 2860, 1717, 1464, 1406, 1377, 1241, 1125, 1053, 731; ^1H NMR (400 MHz, $CDCl_3$): δ = 4.23 (dd, 1H, *J* = 6.6 Hz, *J* = 8.2 Hz,-CHBr-), 2.74 - 2.58 (m, 2H, -CH_2-), 2.04 - 1.88 (m, 2H, -CH_2-), 1.62 (quant, 2H, *J* = 7.3 Hz,-CH_2-), 2.04 - 1.27 (m, 8H, -CH_2-), 0.90 (q, *J* = 5.5 Hz, 6H, -CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 204.4, 53.7, 38.9, 33.1, 31.2, 29.4, 23.6, 22.4, 22.1, 13.9, 13.8.

4.4. Typical Procedure for Conversion of Acetophenone into 2,4-diphenylthiazole in Ionic Liquid with NBS and Benzthioamide

To a solution of acetophenone (1 mmol) in [Bmim]PF_6 (1.5 mL) were added *p*-TsOH·H_2O (0.2 mmol) and NBS (1.2 mmol). The mixture was stirred for 9 h at room temperature. Then, benzthioamide (1.2 mmol) and K_2CO_3 (1.1 mmol) were added to the reaction mixture and the obtained mixture was stirred for 5 h at room temperature. After the reaction, the reaction mixture was extracted with diethyl ether (10 mL × 10). Then, the extract was washed with sat. aq. Na_2SO_3 solution. The organic layer was dried over Na_2SO_4. After removal of the solvent under reduced pressure, 2,4-diphenylthiazole was obtained in the crude state. Pure 2,4-diphenylthiazol was obtained by flash short column chromatography on silica gel ($CHCl_3$:Hexane = 1:1) in 96 % yield.

4.5. Reuse of [Bmim]PF_6

After extraction with diethyl ether, the ionic liquid was

washed with water (1 mL). The mixture was dried with a vacuum pump for 2 h at 80˚C. To a solution of acetophenone (1 mmol) in [Bmim]PF_6 (1.5 mL) were added *p*-TsOH·H_2O (0.2 mmol) and NBS (1.2 mmol). The mixture was stirred for 12.5 h at room temperature. Then, benzthioamide and K_2CO_3 (1.1 mmol) were added and the obtained mixture was stirred for 5 h at room temperature. After the reaction, the reaction mixture was extracted with diethyl ether (10 mL × 10). Then, the extract was washed with sat. aq. Na_2SO_3 solution. The organic layer was dried over Na_2SO_4. After removal of the solvent under reduced pressure, 2,4-diphenylthiazole was obtained in the crude state. Pure 2,4-diphenylthiazole was obtained by flash short column chromatography on silica gel ($CHCl_3$:Hexane = 1:1) in 97% yield

2-Phenyl-4-(4'-methoxyphenyl)thiazole: mp 126˚C - 127˚C (lit. [86] mp 134˚C - 135˚C). IR(Nujol); 3748, 3648, 2309, 1607, 1520, 1307, 1255, 1172, 1029, 979, 833, 737, 722 cm^{-1}; ^1H NMR(500 MHz, $CDCl_3$): δ = 8.03 (d, 2H, *J* = 6.3 Hz, ArH), 7.93 (d, 2H, *J* = 8.6 Hz, ArH), 7.45-7.43 (m, 3H, ArH), 7.34 (s, 1H, thiazole), 6.97 (d, 2H, *J* = 9.1 Hz, ArH), 3.86 (s, 3H, -OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.6, 159.6, 156.1, 133.8, 129.9, 128.8, 127.7, 127.5, 126.5, 114.0, 110.8, 55.3.

2-Phenyl-4-(4'-methylphenyl)thiazole: mp 108˚C (lit. [86] mp 116˚C); IR(Nujol) 3853, 3749, 3648, 2309, 1698, 1540, 1507, 973, 722 cm^{-1} ; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.04 - 8.02 (d, 2H, *J* = 6.3 Hz, ArH), 7.89 - 7.87 (d, 2H, *J* = 8.0 Hz, ArH), 7.46 - 7.41 (m, 3H, ArH), 7.40 (s, 1H, thiazole), 7.25 - 7.23 (d, 2H, *J* = 6.3 Hz, ArH), 2.39 (s, 3H, -CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.6, 156.3, 137.9, 133.8, 131.8, 129.9, 129.3, 128.8, 126.5, 126.3, 111.8, 21.2.

2,4-Diphenylthiazole: mp 78˚C (lit. [87] mp 75˚C - 78˚C). IR(Nujol) 760, 725, 465 cm^{-1}; ^1H NMR(500 MHz, $CDCl_3$): δ = 8.05 (d, 2H, *J* = 8.0 Hz, ArH), 8.00 (d, 2H, *J* = 8.0 Hz, ArH), 7.49 - 7.42 (m, 6H, thiazole, ArH), 7.35 (t, 1H, *J* = 7.4 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.8, 156.2, 134.4, 133.7, 130.0, 128.8, 128.7, 128.1, 126.5, 126.4, 112.5.

2-Phenyl-4-(4'-chlorophenyl)thiazole: mp 128˚C (lit. [86] mp 131˚C - 132˚C). IR(Nujol) 1235, 1051, 766, 722 cm^{-1}; ^1H NMR(500 MHz, $CDCl_3$): δ = 8.03 (d, 2H, *J* = 8.0 Hz, ArH), 7.93 (d, 2H, *J* = 8.5 Hz, ArH), 7.48-7.44 (m, 4H, ArH, thiazole), 7.41 (d, 2H, *J* = 8.5 Hz, ArH); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.1, 155.0, 133.9, 133.5, 132.9, 130.1, 128.9, 128.8, 127.6, 126.5,112.8.

2-Phenyl-4-(4'-nitrophenyl)thiazole: mp 125˚C - 127˚C (lit. [88] mp 122˚C); IR(Nujol) 1597, 1509, 1341, 1058, 974, 842, 734, 665 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.31 (d, 2H, *J* = 8.8 Hz, ArH), 8.17 (d, 2H, *J* = 8.8 Hz, ArH), 8.06 - 8.03 (m, 2H, ArH), 7.69 (s, 1H, thiazole), 7.52 - 7.48 (m, 3H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.7, 153.7, 147.2, 140.2, 133.1, 130.5, 129.0, 126.9, 126.6, 124.1, 115.9.

2,4-Diphenyl-5-methylthiazole: mp 75˚C - 76˚C (lit. [89] mp 76˚C); IR(Nujol) 2723, 1306, 970, 760, 721, 690 cm^{-1}; ^1H NMR(400 MHz, $CDCl_3$): δ = 7.96 (d, 2H, *J* = 6.4 Hz, ArH), 7.73 (d, 2H, *J* = 6.8 Hz, ,ArH), 7.48 - 7.39 (m, 6H, ArH, thiazole), 2.61 (s, 3H, -CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.5, 151.9, 135.1, 133.8, 129.5, 128.7, 128.6, 128.3, 127.5, 126.2, 12.8.

2-Phenyl-4-(2'-thienyl)thiazole: mp 58 - 60 (lit. [90] mp 69˚C - 71˚C); IR(Nujol) 1664, 1024, 970, 763, 691, 740 cm^{-1}; ^1H NMR(400 MHz, $CDCl_3$): δ = 8.04 - 8.01 (m, 2H, ArH), 7.53 (dd, 1H, *J* = 3.6 Hz, *J* = 1.1 Hz, thienyl), 7.49 - 7.45 (m, 3H, ArH), 7.35 (s, 1H, thiazol), 7.32 (dd, 1H, *J* = 5.0 Hz, *J* = 1.1 Hz, thienyl), 7.10 (dd, 1H, *J* = 3.6 Hz, *J* = 5.2 Hz, thienyl); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.9, 150.7, 138.3, 133.3, 130.1, 128.9, 127.6, 126.6, 125.3, 124.2, 111.3.

4-Butyl-2-phenyl-5-pentylthiazole: Oil. IR (neat) 2928, 2857, 1536, 1461, 1248, 991, 760, 689 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.87 (d, 2H, *J* = 6.6 Hz, ArH), 7.41-7.33 (m, 3H, ArH), 2.75 (t, 2H, *J* = 7.5 Hz, -CH_2-), 2.68 (t, 2H, *J* = 7.5 Hz, -CH_2-), 1.71 (quant, 2H, *J* = 7.5 Hz, -CH_2-), 1.63 (quant, 2H, *J* = 7.8 Hz, -CH_2-), 1.46 - 1.33 (m, 6H, -CH_2-), 0.95 (t, 3H, *J* = 7.3 Hz, -CH_3), 0.90 (t, 3H, *J* = 7.1 Hz, -CH_3) ; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.5, 153.4, 134.2, 132.7, 129.2, 128.7, 126.1, 34.2, 31.7, 29.6, 29.2, 26.1, 22.5, 22.2, 14.0, 13.8; HRMS Calcd for $C_{18}H_{26}NS$ 288.1780, Found; 288.1774.

4-Phenyl-2-(4'-methylphenyl)thiazole: mp 120˚C - 122˚C (lit. [91] mp 127˚C - 128˚C); IR(Nujol) 1056, 972, 814, 739, 689 cm^{-1}; ^1H NMR(400 MHz, $CDCl_3$): δ = 7.99 (d, 2H, *J* = 7.3 Hz, ArH), 7.93 (d, 2H, *J* = 8.2 Hz, ArH), 7.46 - 7.42 (m, 2H, ArH, thiazol), 7.34 (t, 1H, *J* = 7.3 Hz, ArH) 7.26 (d, 1H, *J* = 6.4 Hz, ArH) 2.41 (s, 3H, -CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.0, 156.1, 140.2, 134.6, 131.1, 129.5, 128.6, 128.0, 126.5, 126.4, 112.1, 21.4.

4-Phenyl-2-(4'-methoxyphenyl)thiazole: mp 96˚C - 98˚C (lit. [91] mp 101˚C); IR(Nujol) 1519, 1254, 979, 833, 737 cm^{-1}; ^1H NMR(400 MHz, $CDCl_3$): δ = 7.98 (d, 2H, *J* = 9.1 Hz, ArH), 7.44 (t, 2H, *J* = 7.3 Hz, ArH), 7.41 (s, 1H, thiazole), 7.34 (t, 1H, *J* = 7.3 Hz, ArH), 3.86 (s, 3H, -OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.6, 161.1, 155.9, 134.6, 128.6, 128.0, 126.7, 126.3, 114.2, 111.7, 55.3.

2-(4'-Nitrophenyl)-4-Phenylthiazol: mp 162˚C - 164˚C (lit. [91] mp 164˚C - 165˚C); IR(Nujol) 1595, 1512, 1340, 848, 751, 722, 687 cm^{-1}; ^1H NMR(500 MHz, $CDCl_3$): δ = 8.33 (d, 2H, *J* = 9.2 Hz, ArH), 8.22 (d, 2H, *J* = 9.2 Hz, ArH), 8.00 (d, 2H, *J* = 6.8 Hz, ArH), 7.62 (s, 1H, thiazol), 7.47 (t, 1H, *J* = 7.4 Hz, ArH), 7.39 (t, 1H, *J* = 7.4 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.7, 157.3,

148.4, 139.1, 133.8, 128.8, 128.6, 127.1, 126.4, 124.3, 114.5.

2-Methyl-4-phenylthiazole: mp 64˚C (lit. [92] mp 64˚C); IR(Nujol) 740, 726, 692, 675 cm^{-1}; ^1H NMR(400 MHz, $CDCl_3$): δ = 7.87 (d, 2H, J = 6.8 Hz, ArH), 7.41 (t, 2H, J = 7.8 Hz, ArH), 7.33-7.30 (m, 2H, ArH, thiazole), 2.78 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.7, 155.1, 134.5, 128.6, 127.9, 126.2, 112.2, 19.3.

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