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AN EFFICIENT SOLVENT FREE GREEN SYNTHESIS OF 2- ARYL BENZOTHIAZOLE DERIVATIVES USING IONIC LIQUID

Nayana V. Pahade[1], Mangesh A. Kulkarni[1], Sangeeta P. Pawar, Dinesh L. Lingampalle[1]

"Department of Chemistry, Vivekanand Arts, Sardar Dalipsingh Commerce and Science college, Samarth nagar Aurangabad, Maharashtra, India."

Abstract-:
A convenient solvent free method for the synthesis of 2-aryl benzothiazole derivatives on reaction with 2- Aminothiophenol and various aromatic aldehydes has been developed by using recyclable N- methyl pyridinium tosylate as an ionic liquid.

Keywords-: Aromatic aldehydes, ionic liquid-NMPYT, Benzothiazole, 2- Aminothiophenol

Introduction

Benzothiazoles and their derivatives are very important group of fused heterocyclic systems [i], which plays a fundamental role in organic and bioorganic chemistry [ii].They constitutes an important class of compounds with profound interest to medicinal or industrial chemist. Compounds with benzothiazole moiety exhibit diverse biological properties such as anticancer[i,ii,]antitumor[iii,iv],antimaterial[v],fungicidal[vi],antimicrobial[vii],anticonvoluscent, [viii,ix],antiglutamate/ antiparkinson[x],antihelmintic activity[xi],broad spectrum Ca channel antagonist[xii],inhibition of enzymes like monoamine oxidase[xiii],lipoxygenase[xiv] etc.

Several methods have been reported in the literature for the synthesis of benzothiazoles [xv, xvi]. Two common strategies have been used generally for the synthesis of 2-arylbenzothiazoles. The first method is by arylation of benzothiazole with aryl halides using different catalysts like Cs_2CO_3, Pd $(OAc)_2$ and CuBr with P(*t*-Bu)$_3$, as a ligand at 150 °C in a sealed tube [xvii], or by Suzuki coupling of arylboronic acids with 2-bromothiazoles [xviii].The second method is via condensation of 2-aminothiophenols with substituted nitriles, carboxylic acids, aryl chlorides, esters or aldehydes [xix]. A number of catalysts such as $ZrOCl_2 \cdot 8H_2O$ [xx], TMSCl [xxi], CAN [xxii], I2 [xxiii], H2O2 [xxiv], MnO2 [xxv], PCC [xxvi], animal bone meal [xxvii], Baker's yeast [xxviii] have been used to perform the cyclization step. Now a day's different green approaches for the preparation of 2-arylbenzothiazoles by direct condensation of 2-aminothiophenols with aromatic aldehydes have been reported. They involve the use of Cu $(OAC)_2$/MCM41 supported catalyst under ultrasound irradiation [xxix], PTSA either in water at 70 °C or PEG, 200/400 using microwave irradiation [xxx].

Result and discussion

Ionic liquid NMPYT [xxxi] is used for oxidative cyclization and intramolecular cyclization. Ionic liquid is proved as very effective media for biotransformation.

In our endeavourer to develop new synthetic route we report a simple and efficient green methodology for the cyclocondensation of 2-Aminothiophenol with various aromatic aldehydes in the presence of freshly prepared N-methyl pyridinium tosylate (ionic liquid).(scheme-1,table-1).It is noticed that ionic liquid was easily recyclable and reusable without loss of activity .The several aromatic aldehydes bearing either electron donating or withdrawing group were smoothly employed to prepare the corresponding benzothiazole derivatives with 90-95% yields. In same manner other heteroatomic aldehydes such as furfural, pyridine 2-carboxy aldehyde have also been condensed with 2-Aminothiophenol to afford corresponding benzothiazoles with 87-90% yield.

To optimise reaction condition the cyclocondensation of 2-Aminithiophenol and 4-Cl benzaldehyde was choosen as a model reaction.

Conclusion

We have developed a simple, solvent free and efficient ionic liquid mediated protocol for the synthesis of 2-aryl benzothiazole derivatives. The ionic liquid is non-volatile and easily prepared. The present ionic liquid mediated method has several advantages, short reaction time, easy product isolation and purification, high yields, use of nontoxic, inexpensive material, Solvent free conditions, and recyclable ionic liquid. There is no need to add any catalyst, which is generally required in the methodologies reported so far. Hence we claim that this route is economical, rapid and green.

Experimental

Chemicals used were of synthetic grade and made by S.D. fine or spectrochem .1H-NMR spectra were recorded on a Bucker DRX-300 instrument and Mass spectra was recorded on a Jeol SX-102 (FAB) instrument. Melting points were taken open capillaries and are uncorrected.IR were recorded in KBr on a Nicolet impact 410.

General experimental procedure-:

2-Aminothiophenol(1mmol) and aromatic aldehyde(1mmol) was added in premolten N-methyl pyridinium tosylate, an ionic liquid(3mmol) and the resulting reaction mixture was stirred at 120^0C for 3hr.The progress of reaction was monitored by TLC.After the completion of reaction, the reaction mixture was poured into ice water, product was filtered. The solid obtained was dried, and recrystallized from ethanol.

Recovery of ionic liquid-:

After the completion of reaction, the product was filtered off. The filtrate was extracted with ethyl acetate to recover reactants and the aqueous layer was evaporated to give sticky fluid which on cooling gave the ionic liquid. The recovered ionic liquid was reused for two more reactions and found to act satisfactorily.

Physical Data

2-Phenylbenzothiazole(a): light yellow crystals ,Mp = 113-115^0c , IR (KBr, cm_1):3060, 1587, 1512, 1479, 1454, 1430, 1280, 1255, 1226, 1200,960, 763; 1H NMR, δ ppm: dH 8.10–8.13 (m, 3H), 7.90 (d, J = 8.0 Hz,1H), 7.52–7.56 (m, 4H), 7.43 (t, J = 8.0 Hz, 1H); 13C NMR: dC 168.2, 155.3, 135.3, 133.8, 131.2, 129.3, 127.8, 126.5,125.0, 123.2, 121.8; m/z (ESI): 212 [M+H]+.

2-(4-Nitrophenyl)-benzothiazole (b)
Yellow solid; M.P = 226–228◦C) [20]; IR (KBr)/υ(cm−1): 3040, 2936, 1521, 1460,1340 , 1107,850 ,763 ; 1H NMR(400 MHz, CDCl3)/δ ppm: 8.34 (d, 2H, *J* = 8.0 Hz), 8.25 (d, 2H, *J* = 8.0 Hz) , 8.15 (d, 1H, *J* = 7.6 Hz), 7.95, (d, 1H, *J* = 7.6 Hz),7.52–7.56 (t, 1H, *J* = 7.2 Hz),7.44-7.48 (t, 1H, *J* = 7.2 Hz), 13C NMR/(100 MHz, DMSO)/δ ppm: 164.8, 154.1, 148.6, 135.42, 133.2, 128.22, 126.95, 126.25, 124.30,123.92,121.84.

2-(4-Hydroxyphenyl)benzothiazole: (c) brown crystals ,M.P. = 224-226^{0}C , IR (KBr,cm_1): 3064, 2996, 1604, 1542, 1523, 1480, 1463, 1432, 1380,1315, 1285, 1250, 1225, 1165, 1106, 1075, 976, 826, 797, 756; 1HNMR (DMSO-d6) δ ppm: dH 10.23 (s, 1H), 8.05 (d, J = 7.9 Hz, 1H), 7.96 (d, J = 8.1 Hz, 1H), 7.92 (d, J = 8.5 Hz, 2H),7.50–7.53 (m, 1H), 7.40–7.42 (m, 1H), 6.92–6.94 (m,2H); 13C NMR (DMSO-d6): dC 167.7, 161.2, 160.6, 154.3,134.7, 129.6, 126.8, 125.5, 124.7, 122.9, 122.7, 116.5, 116.3; m/z(ESI): 228 [M+H]

2-(4-Chlorophenyl)benzothiazole: (d) white crystals, Mp = 117-118^{0}c, IR (KBr,cm_1): 3053, 1588, 1505, 1472, 1435, 1397, 13156, 1286, 1250,1091, 1013, 963, 827, 755; 1H NMR, δ ppm: dH 8.07 (d, J = 8.1 Hz, 1H), 8.03 (d, J = 8.5 Hz, 2H), 7.90 (d, J = 8.0 Hz, 1H),7.52–7.55 (m, 1H), 7.47 (d, 1H, J = 8.6 Hz), 7.40–7.43(m, 1H); 13C NMR: dC 166.5, 154.2, 137.3, 134.7, 132.3,129.5, 128.5, 126.3, 125.2, 123.1, 121.6; m/z (ESI): 246 [M+H]

2-(4-Methoxyphenyl) benzothiazole: (e) light yellow crystals,Mp 120-122^{0}c, IR(KBr, cm_1): 3063, 2996, 2936, 2834, 1603, 1590, 1554, 1520,1482, 1465, 1453, 1435, 1410, 1311, 1305, 1285, 1256, 1224,1180, 1170, 1075, 1025, 967, 830, 792; 1H NMR, δ ppm: dH 8.06–8.08(m, 3H), 7.92 (d, J = 8.0 Hz, 1H), 7.49–7.52 (m, 1H), 7.35–7.39 (m, 1H), 7.03–7.04 (m, 2H), 3.92 (s, 3H); 13C NMR: dC 167.7, 161.8, 154.1, 134.7, 129.2, 126.6,126.3, 124.81, 122.9, 121.6, 114.5, 55.6; m/z (ESI): 242 [M+H]+.

2-(4-Methylphenyl)benzothiazole: (f) white crystals ,Mp 86-87^{0}c ,IR (KBr,cm_1): 3057, 3025, 1606, 1482, 1455, 1432, 1310, 1287, 1255,1229, 1120, 958, 835, 816, 760; 1H NMR, δ ppm: dH 8.12 (d, J = 7.9 Hz,1H), 8.04 (d, J = 8.2 Hz, 2H), 7.90 (d, J = 8.0 Hz, 1H), 7.51–7.54 (m, 1H), 7.37–7.40 (m, 1H), 7.34 (d,J = 7.9 Hz, 2H), 2.5 (s, 3H, CH3); 13C NMR: dC 168.2, 154.4,141.3, 134.7, 131.2, 129.5, 127.4, 125.1, 126.5, 123.2, 121.7, 21.7;
m/z (ESI): 226 [M+H]+.

2-(3-Chlorophenyl) benzothiazole: (g) white crystals ,Mp 96-98^{0}c , IR (KBr, cm_1): 3055, 1623, 1587, 1568, 1540, 1502, 1472, 1456, 1432,1420, 1296, 1266, 1243, 1233, 1160, 1077, 944, 885, 865, 785,757, 730; 1H NMR, δ ppm: dH 8.12 (t, 1H, J = 1.8 Hz), 8.10 (d, 1H,J = 8.2 Hz), 7.95–7.98 (m, 1H), 7.92 (d, 1H, J = 8.4 Hz), 7.53–7.56 (m, 1H), 7.45–7.48 (m, 1H), 7.40–7.43(m, 2H); 13C NMR: dC 166.2, 154.2, 135.5, 135.3, 135.0,130.7, 130.0, 127.2, 126.4, 125.5, 125.5, 123.4, 121.5; m/z (ESI):246 [M+H]+.

2-(2-Chlorophenyl)benzothiazole: (h) white crystals, Mp 72-74^{0}c , IR (KBr,cm_1): 3054, 1592, 1560, 1490, 1454, 1434, 1315, 1300, 1275,1249, 1057, 1012, 964, 755, 746; 1H NMR, δ ppm: dH 8.24–8.27 (m, 1H), 8.15 (d, J = 8.1 Hz, 1H), 7.96 (d, J = 8.0 Hz, 1H),7.56–7.59 (m, 2H), 7.45–7.49 (m, 3H); 13C NMR: dC164.0, 153, 136.3, 132.5, 132.0, 131.6, 131.0, 130.6, 127.0,126.5, 125.6, 123.3, 121.2; m/z (ESI): 246 [M+H]+.

2-(2-Hydroxyphenyl)benzothiazole: (i) white crystals,Mp 129-130^{0}c , IR (KBr,cm_1): 3056, 2922, 1620, 1587, 1541, 1520, 1482, 1455, 1435,1417, 1316, 1270, 1250, 1217, 1163,

1152, 1035, 974, 870, 862,756, 740; 1H NMR, δ ppm: dH 12.53 (s, 1H, OH), 8.03 (d, 1H, J = 8.0 Hz), 7.90(d, 1H, J = 7.9 Hz), 7.70 (dd, 1H, J1 = 7.9 Hz,J2 = 1.1 Hz), 7.52–7.55 (m, 1H), 7.41–7.45 (m, 2H),7.15 (dd, 1H, J1 = 8.3 Hz, J2 = 0.8 Hz), 6.95–6.97 (m, 1H);13C NMR: dC 169.6, 158.2, 151.7, 132.5, 132.5, 128.6, 126.5, 125.3,122.3, 121.4, 119.4, 117.7, 116.7; m/z (ESI): 228 [M+H]+.

2-(2-Furanyl)benzothiazole: (j) brown crystals, Mp 102-103^{0}c IR (KBr, cm_1):3142, 3120, 3046, 1600, 1540, 1520, 1500, 1472, 1454, 1433,1422, 1384, 1310, 1252, 1242, 1217, 1155, 1010, 896, 884, 767,760, 745; 1H NMR, δ ppm: dH 8.07 (d, J = 8.2 Hz, 1H), 7.92 (d,J = 7.9 Hz, 1H), 7.60 (s, 1H), 7.50 (t, J = 7.3 Hz, 1H), 7.42 (t, J = 7.3 Hz, 1H), 7.20 (d, J = 2.8 Hz, 1H),6.62 (d, J = 1.5 Hz, 1H); 13C NMR: dC 157.2, 153.8, 148.3,144.5, 134.2, 126.4, 125.0, 123.2, 121.8, 112.7, 111.8; m/z (ESI):202 [M+H]+.

2-(Pyridin-4-yl) benzothiazole: (k) brown crystals, Mp 130-132^{0}c; 1H NMR, δ ppm (300 MHz, DMSO-d6): d 7.46–7.48 (d, 2H), 7.55–7.62 (m, 1H), 8.02–8.04 (d,2H), 8.12–8.53 (m, 1H), 8.42–8.58 (m, 2H). 13C NMR (75 MHz, DMSO-d6): d121.6, 123.5, 123.7, 125.8, 126.8, 129.7, 134.2, 135.2, 148.7, 151.8, 154.2, 164.5., EI MS (m/z): 212.9 (M+).

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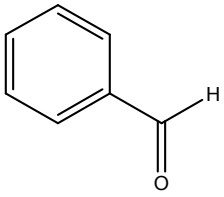
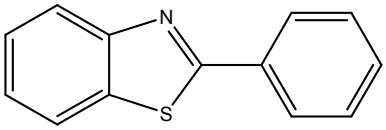
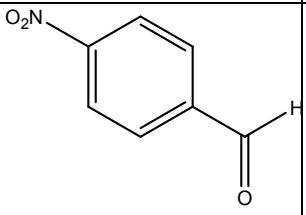
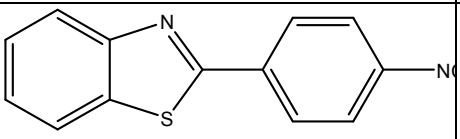
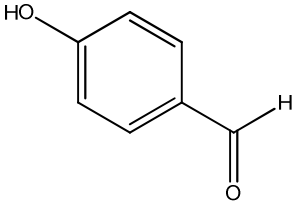
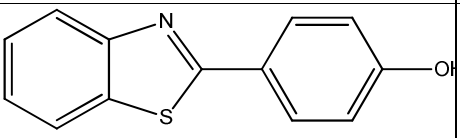
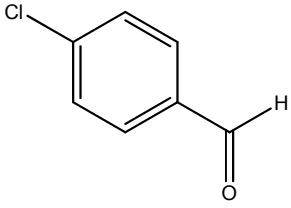
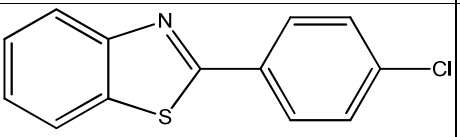
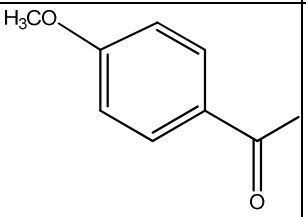
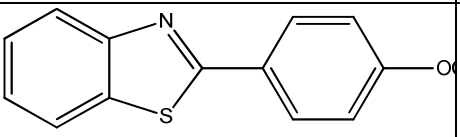
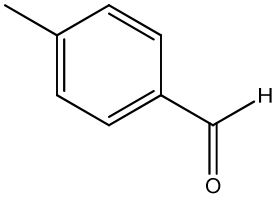
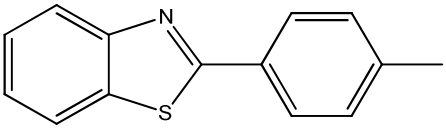
Table.1 Ionic liquid mediated synthesis of 2-aryl benzothiazole derivatives-:

Entry	Aldehydes	Time (hrs)	Product	Yield (%)	M.P [Lit.]
a		3		91	113-115 [xxxi]
b		3		90	230-232 [xxxiii]
C		3		90	224-226 [xxxii]
d		3		92	117-118 [xxxii]
e		3		94	120-122 [xxxii]
f		3		94	86-87 [xxxiii]

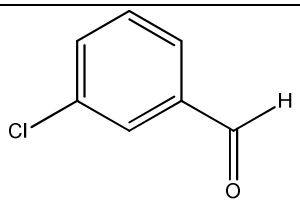
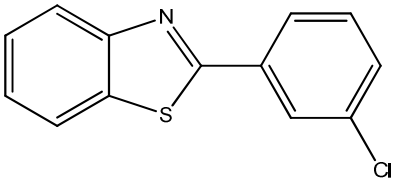
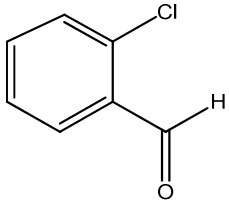
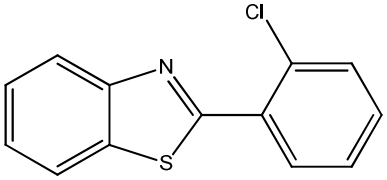
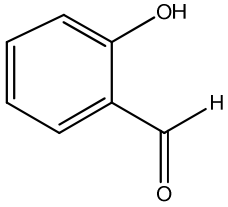
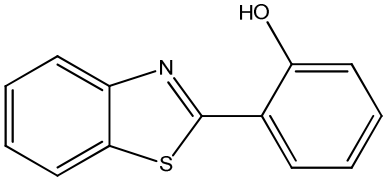
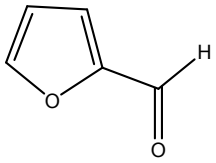
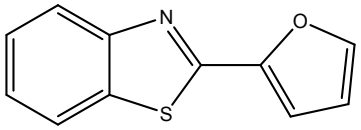
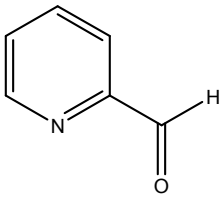
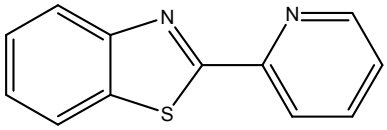
g		3.5		90	96-98 [xxxvii]
h		3.5		90	72-74 [xxxvii]
i		4		92	129-130 [xxxv]
j		4		82	102-103 [xxxvi]
K		4		89	130-132 [xxxv]

Figure1. Synthesis of 2-aryl benzothiazole derivatives using NMPYT as an ionic liquid.