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An Expeditious Catalyst Free Synthesis of 2-Amino Thiazoles

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ABSTRACT

Synthesis of 2-aryl amino thiazoles (III) by carrying the condensation of substituted phenacyl halide and thioureas in the presence of N-methyl pyridinium tosylate as an ionic liquid.

Keywords: 2-amino thiazole, Phenacyl halides, N-methyl pyridinium tosylate, Thiourea

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INTRODUCTION

The thiazoles derivatives play an important role in the synthesis of different natural compounds having biological significance [1]. It is assumed that an important moiety of several drug discovery molecule. Thiazoles derivatives exhibits various biological activities such as analgesic, anticancer [2,3], anti-inflammatory, arthymatic [4], antipsychotic [5], anesthetic, anti-bacterial, anti-hypertensive, anti-tuberculoutic [6], anti-fungal [7], anti-viral [8] and anti-tumour [9]. Thiazole derivatives inhibits the growth of xanthomonas and are also used as herbicides or as sschistosomicidal and antheminitic drug [10], which are also used as sodium channel blockers [11] and also used as precursor HIV inhibitors [12].

Amino thiazole have found their applications in drug development for the treatment of allergy [13], hypertension [14], schizophrenia [15], inflammation [16], bacterial [17], and HIV [18] infections. Amino thiazole derivatives are also used as estrogen receptor [19] & adenosine receptor antagonist [20,21]. For the synthesis of amino thiazole derivatives different synthetic strategies are reported in the literature are as: In the presence of molecular halogen, thiourea on reaction with ketone gives amino thiazole but this reaction is time consuming as it requires 15 h and its purification is also difficult [22].

In presence of NBS in which Benzoyl peroxide is used as radical initiator [23] which reacts with methyl ketone to give α-halo ketone which on further reaction with thioamides [24,25] or thiourea in the presence of hyper valent iodine analogue [26] as a reagent gives amino thiazole but this method is time consuming & gives low yield.

Amino thiazole derivatives are also synthesized by using ketones and thioureas in the presence of silica chloride as a heterogeneous catalyst [27].

EXPERIMENTAL

Chemicals used were of synthetic grade and made by S.D. fine or spectrochem and used as it is without purification. ^{1}H-NMR spectra were recorded on a Bucker DRX-400 instrument and Mass spectra were recorded on a Jeol SX-102 (FAB) instrument. Melting Points were taken open capillaries and are uncorrected. IR was recorded in KBr on a Nicolet impact 410.

General experimental procedure for synthesis of 2-amino thiazoles

To a round bottom flask (25 ml) containing premolten N-methyl pyridinium tosylate (NMPYT) ionic liquid (1 g) was added phenacyl chloride (10 mmol) and thiourea (11 mmol) and the reaction mass was stirred at 110ºC until the reaction gets completed. Reaction is found to be completed in 6-8 min. Progress of the reaction was monitored by TLC then ice water was poured on reaction mixture by adding drop wise ammonia solution until pH gets adjusted to 9-10. The solid obtained was filtered and recrystallized from absolute ethanol (Figure 1 and Table 1) [28].

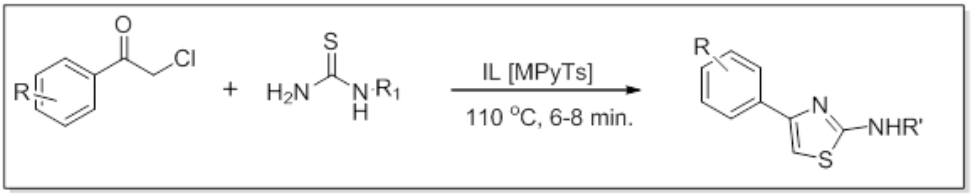

Figure 1: One pot synthesis of 2-aminothiazoles using NMPYT as an ionic liquid

Table 1: Physical data of Ionic liquid mediated synthesis of 2-Aminothiazole derivatives

Sr. No.	R	R'	Yields (%)	M.P.(°C)
1	4-H	H	84	150-151
2	4-Cl	H	91	176-177
3	4-Br	H	93	165-166
4	4-F	H	88	100-101
5	4-CH_3	H	81	135-136
6	4-Cl	C_6H_5	78	150-151
7	4-F	C_6H_5	75	110-111
8	4-CH_3	C_6H_5	73	168-169
9	4-Br	C_6H_5	75	142-143
10	4-OCH_3	C_6H_5	69	140-141

Spectral data

4-Phenyl-thiazol-2-ylamine (1)

M.P=150-151ºC. 5.31 (br s, 2H, NH_2, exchangeable with D_2O), 6.63 (s, 1H, thiazole H), 7.21-7.79 (m, 5H, ArH). ^{13}C NMR (CDCl3, 100 MHz) δ [4] 168.2 (C), 149.7 (C), 134.5 (C), 128.3 (2CH), 127.1 (C), 125.4 (2CH), 101.5 (CH). HRMS (EI, 70 eV) Yield: 84%.

4-(4-Chloro-phenyl)-thiazol-2-ylamine (2)

M.P=176-177ºC. 5.18 (br s, 2H, NH_2, exchangeable with D_2O), 6.62 (s, 1H, thiazole H), 7.28 (d, 2H, J=8.60 Hz, ArH), 7.76 (d, [10] 2H, J = 8.60 Hz, ArH). ^{13}C NMR (CDCl3, 100 MHz) δ 168.7 (C), 146.1 (C), 132.3 (C), 132.0 (C), 128.7 (2CH), 127.3 (2CH), 102.6 (CH). HRMS (EI, 70 eV) Calcd for $C_9H_7N_2SCl$ [M]+: 210.0018. Found: 210.0007. Yield: 91%.

4-(4-Bromo-phenyl)-thiazol-2-ylamine (3)

M.P. = 165-166ºC. 1H NMR ($CDCl_3$, 400 [4] MHz) δ5.06 (br s, 2 H, NH_2, exchangeable with D_2O), 6.68 (s, 1H, thiazole H), 7.42 (d, 2H, [12] J = 7.80 Hz, ArH), 7.67 (d, 2H, J = 8.0 Hz, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.3 (C), 148.8 (C), 134.1 (C), 131.3 (2CH), 127.5 (2CH), 120.0 (C), 102.1 (CH). HRMS (EI, 70 eV) Calcd for $C_9H_7N_2SBr$ [M]+: 255.9493. Found: 255.9476. Yield: 93%.

4-Tolyl-thiazol-2-ylamine (5)

M.P=135-136ºC. ^{1}H NMR ($CDCl_3$, 400 MHz) δ2.40 (s, 3H, CH3), 5.62 (br s, 2H, NH_2, exchangeable with D_2O), 6.67 (s, 1H, thiazole H), 7.16 (d, 2H, J=7.30 Hz, ArH), 7.58 (d, 2H, J=7.30 Hz, ArH). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.1 (C), 150.2 (C), 136.3 (C), 132.6 (C), 129.4 (2CH), 125.1 (2CH), 100.5 (CH), 20.7 (CH_3). HRMS (EI, 70 eV) Calcd for $C_{10}H_{10}N_2S$ [M]+: 190.0565. Found: 190.0565. Yield: 81%.

RESULTS AND DISCUSSION

Potential biological activities of different derivatives of amino thiazoles encourage us to synthesize some new heterocycles easily under laboratory conditions. The different reported methods discuss earlier shows some drawbacks like reactions are time consuming, use of hazardous solvents, expensive catalysts, harsh condition, and gives low yield.

CONCLUSION

The present work describes synthesis of 2-amino thiazole using N-Methyl Pyridinium Tosylate (NMPYT) as an ionic liquid which plays dual role as a catalyst as well as solvent. The developed protocol exhibits following merits

1. Reaction course is short.
2. Require no use of catalyst.
3. Require no use of volatile organic solvents.
4. It is cost effective.

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REFERENCES

[1] R. Borane, M. Chanon, R. Gallo, New York, USA, **1979**, 34.
[2] G. Holfle, N. Glaser, T. Leibold, M. Sefkow, *Pure. Appl. Chem*., **1999**, 71, 2019.
[3] H.I. E1-Subbagh, *Saudi. Pharm. J*., **1999**, 7, 14.
[4] M. Attimarad, G. Bagavant, *Indian. J. Pharm. Sci*., **1999**, 61, 152.
[5] S. Chaki, T. Funakoshi, R. Yoshikawa, S. Okuyama, T. Kunangi, A. Nakagato, M. Nagamine, K. Tomisawa, *Neuropharmacol*., **1999**, 138, 1185.
[6] K.H. Chichalia, K.R. Desai, *J. Inst. Chem*., **1998**, 70, 121.
[7] P. Beuchat, L.M. Varache, A. Nereu, J.M. Leger, J. Vercauteren, S. Larrouture, G. Deffieu, A. Nuhrich, *Eur. J. Med. Chem*., **1999**, 34, 773.
[8] J.A. Flygare, J.C. Jean, P.C. Koarney, J.C. Medium, M. Shivraja, *Chem. Abstr*., **1999**, 131, 184944.
[9] P. Paolo, R. Amici, M. Villa, B. Salom, A. Veupetti, M. Versai, *Chem. Abstr*., **2000**, 133.
[10] Biswanath Das, V. Saidi Reddy, R. Ramu, *J. Mol. Catal. A*., **2006**, 235-237.
[11] D.J. Hogenkamp, R. Upasami, P. Nguyen, US patent, 794424, **2000**, *Chem. Abstr*., 133, **2000**, 281779.
[12] V.A. Ryabinin, O.D. Zakharova, E.Y. Yurchenko, L. Tarrago Litvak, M.L. Andreola, A.N. Sinyakov, *Bioorg. Med .Chem*., 8, **2000**, 985.
[13] K.D. Hargrave, K.K. Hess, J.T. Oliver, *J. Med. Chem*., **1983**, 26, 1158.
[14] W.C. Patt, H.W. Hamilton, M.D. Taylor, M.J. Ryan, D.G. Taylor, B.L. Batley, C.A. Painchand, S.T. Rapundalo, B. M. Michiewilz, S.C.J. Olzon, *J. Med. Chem*., **1992**, 35, 2562.
[15] J.C. Jean, L.D. Wise, B.W. Carprathe, S.C.J. Olzon, *J. Med. Chem*., **1990**, 33, 311.
[16] F. Clemence, O.L. Marter, F. Delevalle, M. Mouren, R. Deraedt, *J. Med. Chem*., **1988**, 31,1453.
[17] K. Tsuji, H. Ishikawa, *Bioorg. Med. Chem. Lett*., **1994**, 4, 1601.
[18] F.W. Bell, A.S. Cantrell, M. Hogberg, S.R. Jaskunas, N.G. Johansson, C.L. Jordon, M.D. Kinnick, P. Lind, J.M. Jr. Morin, R. Noreen, J.A.B. Oberg, C.A. Palkowitz, P. Pranc. Parrish, *J. Med. Chem*., 1995, 38, 4929.
[19] B.A. Fink, D.S. Mortensen, S.R. Stauffer, Z.D. Aron, J.A. katzenellenbogen, *Chem. Biol*., **1999**, 6, 205.
[20] J.E. Van Muiilwijk-Koezen, H. Tiemmermon, R.C. Vollinga, J.F. Von Drabbe Kunzel, M. De Groote, S. Visser, A.P. Ijzerman, *J. Med. Chem*., **2001**, 44, 749.
[21] J.V. Metzger, Pergamon Press, **1984**, 6, 328.
[22] A. Hantch, *Leibig's Ann*., **1888**, 1, 24.
[23] K. Pattrick, F. Monica A.F. John, *J. Org. Chem*., **1998**, 63, 196-200.
[24] B.K. Said, B.R. Sabive, M. Abderrahim, Gerald, *Tetraheron, Lett*., **2002**, 43, 3193-3196.
[25] G. Kamran, Srecjalekshmi, K.C. Satyabhama, K.N. Rajshekharan, *Tetraheron. Lett*., **2006**, 47, 6179-6182
[26] H. Karade, M. Sathe, M.P. Kaushik, *Catalysis. Commun*., **2007**, 8, 741-746.
[27] T.M. Potewar, S.A. Ingale, K.V. Shrinivasan, *Tetrahedron*, **2007**, 63, 11066-11069.
[28] D. Lingampalle, R. Jawale, R. Waghmare, R.A. Mane, *Syn. Commun*., **2010**, 40, 2397-2400.