Available online at www.sciencedirect.com
ScienceDirect
Chinese Chemical Letters 20 (2009) 1408–1410
CHINESE CHEMICAL LETTERS
www.elsevier.com/locate/cclet

A simple and efficient synthesis of 2-substituted benzothiazoles catalyzed by H_2O_2/HCl

Hong Yun Guo *, Ji Chao Li, You Le Shang

College of Chemical Engineering and Materials Science, Zhejiang University of Technology, Hangzhou 310014, China

Received 20 April 2009

Abstract

A simple and efficient procedure for the synthesis of substituted benzothiazoles through condensation of 2-aminothiophenol with aromatic aldehydes in the presence of H_2O_2/HCl system in ethanol at room temperature is described. The target compounds have been characterized by ^{1}H NMR, ^{13}C NMR, IR and MS. Short reaction time, easy and quick isolation of the products, and excellent yields are the main advantages of this procedure.

Keywords: 2-Substituted benzothiazoles; Heterocyclic compounds; H_2O_2/HCl

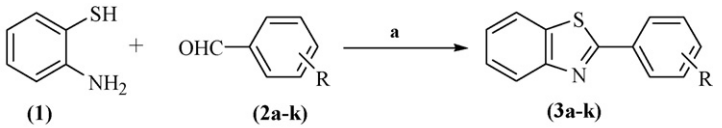
Benzothiazole and their derivatives are very important groups of heterocyclic compounds [1], and are well known for their biological and pharmaceutical activities, such as antitumour [2], antimicrobial [3] and antiglutamate/antiparkinsonism agents [4]. Recently, they have also found applications in organic optoelectronic materials, such as second-order nonlinear optical (NLO) materials [5], liquid crystals [6], and fluorophores [7] as well as used for organic light-emitting diodes (OLEDs) by the formation of cyclometalated ligands with heavy metal ions, such as Ir [8] and Pt [9].

Some of the typical reported methods for the synthesis of benzothiazoles include the reaction of 2-aminothiophenol with carboxylic acids in the presence of polyphosphoric acid at 150 °C for 2 h [10], or in the presence of Lawesson's reagent: 2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane 2,4-disulfide at 190 °C [11], or catalyzed by 4-methoxy-2,2,6,6-tetramethyl-1-piperidinyloxy at 100 °C for 9 h [12], condensation of 2-aminothiophenol with thioamides [13] or benzoyl chloride [14], the coupling reaction of Grignard reagents catalyzed by nickel [15] or palladium [16], ligand-accelerated copper-catalyzed cyclizations of ortho-halobenzanilides [17], reaction of benzonitrile with benzenethiol mediated by ceric ammonium nitrate [18], gas-phase thermolysis of condensed-1,2,4-triazines at 350 °C and 0.06 mbar [19].

However, a number of these methods have some drawbacks such as high temperature, low yields, long reaction times, drastic reaction conditions, toxic metallic compounds that result in generation of waste streams, and co-occurrence of several side reactions. As a consequence, the introduction of new methods and/or further work on technical improvements to overcome the limitations is still an important challenge.

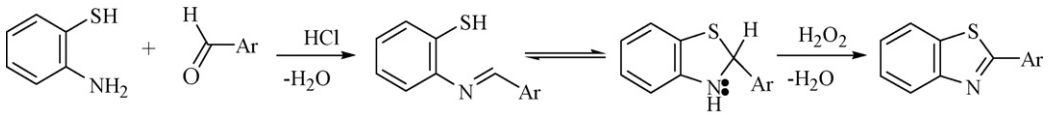
* Corresponding author.
E-mail address: guohy63@163.com (H.Y. Guo).

1001-8417/$ – see front matter
doi:10.1016/j.cclet.2009.06.037



(a) H_2O_2/HCl, 30% and 37% respectively; r.t, -H_2O

Scheme 1. Synthetic route of the 2-substituted benzothiazoles.



Scheme 2. The possible mechanism for the synthesis of 2-arylbenzothiazoles.

Table 1
Aromatic aldehydes and corresponding 2-substituted benzothiazoles.

Entry	Aldehydes	Time (min)	Products	Yield (%)[a,b]
1	Benzaldehyde	45	**3a**	90
2	2-Hydroxybenzaldehyde	45	**3b**	91
3	4-Hydroxybenzaldehyde	45	**3c**	94
4	3-Nitrobenzaldehyde	45	**3d**	92
5	4-Nitrobenzaldehyde	45	**3e**	91
6	3,4-Dimethoxybenzaldehyde	45	**3f**	90
7	2,4-Dichlorobenzaldehyde	45	**3g**	91
8	3,5-Di-tert-butyl-4-hydroxybenzaldehyde	45	**3h**	90
9	1-Naphthaldehyde	60	**3i**	88
10	5-Nitro-1-naphthaldehyde	60	**3j**	89
11	9-Anthrayldehyde	60	**3k**	85

[a] The products were characterized by comparison of their spectroscopic and physical data.
[b] Yields refer to pure isolated products.

Recent report by Neumann and coworkers [20] on the use of a combination of hydrogen peroxide and hydrohalic acid as a green halogenating agent for arenes inspired us to explore the potential of this system for the synthesis of 2-substituted benzothiazoles. To our delight, this system is very effective.

The route for the synthesis of 2-substituted benzothiazoles is shown in Scheme 1.

Several solvents including acetonitrile, dichloromethane, 1,4-dioxane and ethanol were investigated during the course of this study. The best results were achieved using ethanol. The applicability of the H_2O_2/HCl system was then examined for the synthesis of 2-phenylbenzothiazoles in ethanol at room temperature. A ratio of 1:1:6:3 of 2-aminothiophenol/aromatic aldehyde/H_2O_2/HCl was found to be optimum for the coupling. The results are presented in Table 1. Typical experimental procedure and selected characterization data could be seen in [21].

As shown, both aldehydes bearing electron-donating substituents (entries 2, 3, 6 and 8) and electron-withdrawing (entries 4, 5, 7 and 10) substituents gave desired benzothiazoles in excellent yields. This procedure is also applicable to 2-(1-naphthyl)benzothiazole and 2-(9-anthracenyl)-benzothiazole which produced smoothly in good to excellent yields (entries 8–10).

Regarding the mechanism of the oxidation step, the reaction probably involves the formation of benzothiazoline, followed by the abstraction of hydrogen to yield the corresponding benzothiazoles (Scheme 2).

In summary, a simple and efficient procedure for the synthesis of 2-substituted benzothiazoles has been explored. Short reaction time, easy and quick isolation of the products, and excellent yields are main advantages of this procedure which make this method an attractive and useful methodology.

Acknowledgment

We are thankful Education Department of Zhejiang Province (No. 20060811) for the financial support of this work.

References

[1] D.A. Horton, G.T. Bourne, M.L. Smythe, Chem. Rev. 103 (2003) 893.
[2] V. Bénéteau, T. Besson, J. Guillard, S. Léonce, B. Pfeiffer, Eur. J. Med. Chem. 34 (1999) 1053.
[3] P.J. Palmer, R.B. Trigg, J.V. Warrington, J. Med. Chem. 14 (1971) 248.
[4] A. Benazzouz, T. Boraud, P. Dubédat, A. Boireau, J.M. Stutzmann, C. Gross, Eur. J. Pharmacol. 284 (1995) 299.
[5] W.N. Leng, Y.M. Zhou, Q.H. Xu, J.Z. Liu, Polymer 42 (2001) 923.
[6] A. Mori, A. Sekiguchi, K. Masui, T. Shimada, M. Horie, K. Osakada, M. Kawamoto, T. Ikeda, J. Am. Chem. Soc. 125 (2003) 1700.
[7] P.F. Barbara, L.E. Brus, P.M. Rentzepis, J. Am. Chem. Soc. 102 (1980) 5631.
[8] S. Lamansky, P. Djurovich, D. Murphy, F. Abdel-Razzaq, R. Kwong, I. Tsyba, M. Bortz, B. Mui, R. Bau, M.E. Thompson, Inorg. Chem. 40 (2001) 1704.
[9] J. Brooks, Y. Babayan, S. Lamansky, P. Djurovich, I. Tsyba, R. Bau, M.E. Thompson, Inorg. Chem. 41 (2002) 3055.
[10] X.Q. Zhu, M.T. Zhang, A. Yu, C.H. Wang, J.P. Cheng, J. Am. Chem. Soc. 130 (2008) 2501.
[11] J.A. Seijas, M.P. Vazquez-Tato, M.R. Carballido-Reboredo, J. Crecente-Campo, L. Romar-Lopez, Synlett 19 (2007) 313.
[12] Y.X. Chen, L.F. Qian, W. Zhang, B. Han, Angew. Chem. Int. Ed. 47 (2008) 9330.
[13] K.R. Nivalkar, S.H. Mashraqui, Synth. Commun. 26 (1996) 3535.
[14] T.C. Harrop, K. Rodriguez, P.K. Mascharak, Synth. Commun. 33 (2003) 1943.
[15] H. Sugimura, H. Okamura, M. Miura, M. Yoshida, H. Takei, Nippon Kagaku Kaishi 59 (1985) 416.
[16] A. Yokooji, T. Okazawa, T. Satoh, M. Miura, M. Nomura, Tetrahedron 59 (2003) 5685.
[17] G. Evindar, R.A. Batey, J. Org. Chem. 71 (2006) 1802.
[18] R.H. Tale, Org. Lett. 4 (2002) 1641.
[19] H. Al-Awadi, M.R. Ibrahim, N.A. Al-Awadi, Y.A. Ibrahim, Tetrahedron 63 (2007) 12948.
[20] R. Ben-Daniel, S.P. de Visser, S. Shaik, R. Neumann, J. Am. Chem. Soc. 125 (2003) 12116.
[21] Typical experimental procedure for the synthesis of 2-substituted benzothiazoles: In a round-bottomed flask (25 mL) equipped with a magnetic stirrer, a solution of 2-aminothiophenol (1.0 mmol), and aromatic aldehyde (1.0 mmol) in ethanol (10 mL) was prepared. Aq 30% H_2O_2 (6.0 mmol) and aq 37% HCl (3.0 mmol) were added and the mixture was stirred at room temperature monitored by TLC (eluent: n-hexane/EtOAc = 7:3). When the starting materials had completely disappeared, the mixture was quenched by adding H_2O (10 mL), extracted with EtOAc (3× 5 mL), and the combined extracts were dried ($MgSO_4$). The corresponding benzothiazoles were obtained after removal of solvents and purified by silica gel chromatography (eluent: n-hexane/EtOAc = 7:3). *Selected characterization data*: Compound **3i**: white solid, yield 88%, IR(KBr): 3407, 3020, 1590, 1512, 1406, 1215, 759 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, δ ppm): 7.42–7.47 (m, 2H), 7.54–7.59 (m, 2H), 7.62 (t, 1H, J = 8.00 Hz), 7.94 (d, 2H, J = 8.50 Hz), 7.98 (t, 2H, J = 8.50 Hz), 8.19 (d, 1H, J = 8.00 Hz), 8.94 (d, 1H, J = 8.50 Hz). ^{13}C NMR (500 MHz, $CDCl_3$, δ ppm): 121.38, 123.54, 124.97, 125.28, 125.88, 126.26, 126.49, 127.62, 128.39, 129.38, 130.64, 130.75, 131.06, 134.0, 135.43, 154.14, 167.61; MS (ESI): m/z = 262.34 $[M+1]^+$. Compound **3j**: white solid, yield 89%, IR(KBr): 3418, 3055, 1516, 1344, 1224, 1125, 790, 749, 723 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, δ ppm): 7.48–7.59 (m, 2H), 7.68 (t, 1H, J = 8.00 Hz), 7.81 (t, 1H, J = 7.50 Hz), 8.06 (d, 1H, J = 8.00 Hz), 8.21 (d, 1H, J = 8.00 Hz), 8.27 (d, 1H, J = 8.00 Hz), 8.67 (d, 1H, J = 9.00 Hz), 8.79 (d, 1H, J = 9.00 Hz), 9.03 (d, 1H, J = 9.00 Hz). ^{13}C NMR (500 MHz, $CDCl_3$, δ ppm): 121.53, 123.76, 124.18, 125.55, 125.72, 125.76, 125.80, 126.63, 128.31, 130.61, 131.52, 131.56, 132.58, 135.46, 147.22, 154.06, 166.44; MS (ESI): m/z = 307.05 $[M+1]^+$.