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Convenient synthesis of 2-arylbenzothiazoles and 2-arylnaphthothiazoles

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Abstract

Thiazoles including five 2-arylbenzothiazoles and two 2-arylnaphthothiazoles were synthesized using a simple synthetic strategy in this work. 2-Arylbenzothiazoles and 2-arylnaphthothiazoles can be prepared by the reaction of methylaromatics with aniline or naphthylamine in the presence of elemental sulfur, respectively. All the seven thiazoles were characterized by the melting point measurement, FTIR, ^{1}H NMR, ^{13}C NMR and GC–MS analysis.

Keywords: Thiazoles; Synthesis; Methylaromatics; Arylamines; Sulfur

The design, synthesis and property of thiazoles as a class of the most important heterocyclic systems have been paid extensive and continuous attention in the fields of industry, agriculture and pharmacy [1–3]. For example, 2-arylbenzothiazoles play significant role in medicine as imaging agents for β-amyloid, antitumor agents, antituberculotics, antiparasitics and calcium channel antagonists [4–6], and in chemical detection as chemiluminescent agents and photosensitizers [7,8], and naphthothiazoles found their merits in antitumor [9] or sensitizer dye [10].

Up to date, many synthetic strategies have been developed for the synthesis of 2-arylbenzothiazoles, among which the ways starting from 2-aminothiophenol [11–19] and *N*-phenyl thioamide [20–23] are the most common methods. Other reasonable and effective methods include condensation of copper(I) thiobenzoates and 2-iodoanilines [24], conversion from other heterocycles [25,26] and Suzuki coupling of 2-bromobenzothiazole with aryl boronic acids [4]. There is also the approach involving sulfur [27,28], which is in time out of mind and was not investigated deeply. Generally, these methods usually employ expensive starting materials or special catalysts, or require multistep synthetic process. Therefore, the convenient method of 2-arylbenzothiazoles would be favorable.

In the present work, we report the convenient synthesis of a series of 2-arylbenzothiazoles and 2-arylnaphthothiazoles (Scheme 1) using available and cheap starting materials methylaromatics, arylanilines and sulfur.

As shown in Table 1, 2-arylbenzothiazoles and 2-arylnaphthothiazoles can be formed from the reaction of methylaromatics and aniline or naphthylaniline with sulfur (Scheme 1). In this reaction, thiazole cycle was formed from three facile chemical materials in the absence of any catalyst [29]. The employed methylaromatics include toluene, *p*-xylene, 1-methylnaphthalene and *p*-methylphenol. At low temperatures, the reactions proceeded

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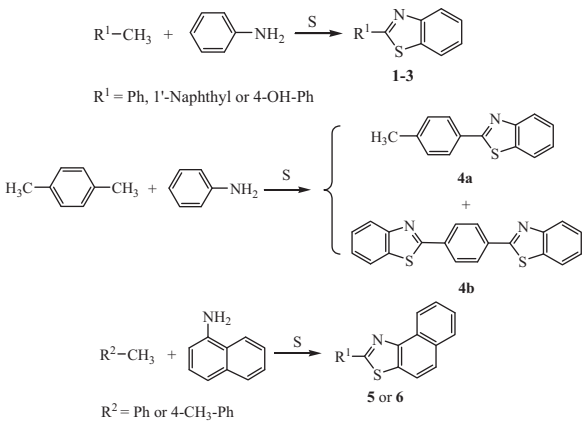

Scheme 1. Synthesis of the title compounds.

Table 1
Results and conditions of the reaction of methylaromatics with arylamines in the presence of sulfur.[a]

Reactant	Temperature (°C)	Time (h)	Product	Yield (%)
Toluene, aniline	275	3.5	**1**	74
1-Methylnaphthalene, aniline	275	0.5	**2**	42
p-Methylphenol, aniline	275	0.5	**3**	62
p-Xylene, aniline	275	3.5	**4a**	61
			4b	14
p-Xylene, aniline[b]	275	3.5	**4a**	15
			4b	70
Toluene, 1-naphthylamine	275	3.5	**5**	50
p-Xylene, 1-naphthylamine	250	1.5	**6**	41

[a] Arene:arylamine:sulfur (mol ratio) = 1:1:4.
[b] Arene:arylamine:sulfur (mol ratio) = 1:2:8.

insignificantly, affording target products in low yields, but at high-temperature reactions tended to produce more byproducts. Optimum temperature was determined to be 275 °C.

For mono-methylaromatics, there is only one expected products (**1**–**3**) [30] with reasonable yields. However, if there are two methyl groups on the aromatics, there will be two possible products with one or two benzothiazole segment(s) whose yields are determined by the ratio of the materials. For *p*-xylene, when less aniline and sulfur were provided with mol ratio of *p*-xylene:arylamine:sulfur = 1:1:4, compounds **4a** [31] or **6** containing one benzothiazole segment were obtained as the dominating products; and when, there were enough aniline and sulfur, namely, the ratio of arene:arylamine:sulfur (mol ratio) = 1:2:8, compound **4b** [31] with two benzothiazole segments are the main product.

Besides aniline, 1-naphthylamine was also introduced for the synthesis of 2-arylnaphthothiazoles. Toluene and *p*-xylene were adopted to react with 1-naphthylamine, giving the expected products **5** and **6** [32] with relative lower yields than those of 2-arylbenzothiazoles.

In conclusion, a series of thiazoles including five 2-arylbenzothiazoles and two 2-arylnaphthothiazoles were conveniently synthesized by the reaction of methylaromatics with aniline or naphthylamine in the presence of elementary sulfur. The products were characterized by various means. Further and detailed study of relevant work will be carried out.

Acknowledgments

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[28] A. Muller, Y. Sulej, S. Hebzr, Z. Chem. 25 (1985) 23.
[29] General synthesis for 2-arylbenzothiazoles and 2-arylnaphthothiazoles: Methylaromatics (50.0 mmol), aniline or 1-naphthylamine (50.0 mmol) and sulfur (200.0 mmol) were put into a 50.0 mL autoclave. The air in the autoclave was replaced several times with nitrogen, then the autoclave was heated to the set temperature and kept at that temperature for 0.5, 1.5 or 3.5 h. Finally, the autoclave was cooled to room temperature and the resulted mixture was analyzed by GC instrument. The result brown mixture was distilled under reduced pressure to give three distillates.
[30] The purification procedures and spectral data for compounds **1**–**3**. 2-Phenylbenzothiazole (**1**): The yellow intermediate distillated was recrystallized in methanol for four times, giving pale yellow needles. mp 113.5−114.0 °C (115.0 °C [11]). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36−7.39 (t, 1 H, J = 7.5 Hz), 7.47−7.49 (m, 4 H), 7.89−7.90 (d, 1 H, J = 8.0 Hz), 8.05−8.09 (m, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.1, 154.2, 135.1, 133.7, 131.0, 129.0, 127.6, 126.3, 125.2, 123.3, 121.6. FTIR: 3063, 1510, 1479, 1433, 1313, 1225, 1070, 964, 764, 731, 690, 623 cm^{-1}. MS: m/z (%) 212 (33, $(M+1)^+$), 211 (100, M^+), 210 (43), 108 (42), 82 (15), 69 (27). 2-(1′-Naphthyl)benzothiazole (**2**): The intermediate distillate was purified by chromatography (silica gel, 100–200 mesh, eluted with petroleum ether to eliminate the impurity and secondly with acetone) and recrystallization from the mixture solvent of petroleum ether and acetone for three times to give fawn crystal of **2**. mp 78.5–79.5 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43–7.46 (t (d, d, d), 1 H, J = 7.5, 1.0 Hz), 7.53–7.57 (m, 3 H), 7.59–7.63 (t (d, t, d), 1 H, J = 7.5, 1.5 Hz), 7.91–7.93 (t (d, s, s), 2 H, J = 7.5 Hz), 7.95–7.99 (t, 2 H, J = 8.5 Hz), 8.18–8.20 (d, 1 H, J = 8.5 Hz), 8.91–8.930 (d, 1 H, J = 8.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.6, 154.2, 135.5, 134.0, 131.1, 130.9, 130.7, 129.4, 128.4, 127.6, 126.5, 126.3, 125.9, 125.3, 125.0, 123.6, 121.4. FTIR: 3045, 1506, 1458, 1429, 1306, 1230, 1176, 1096, 933, 802, 768, 733, 694 cm^{-1}. MS: m/z (%) 262 (22, $(M+1)^+$), 261 (78, M^+), 260 (100), 130 (21), 69 (12). 2-p-Hydroxyphenylbenzothiazole (**3**): The intermediate distillated was dissolved in hot acetone, deleting impurity by filtration, the pale yellow flaky crystals was obtained when cooling the filtrate. mp 234.5–235.5 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.87 (s, 1 H), 6.99–7.02 (d (t, t), 2 H, J = 9.0, 2.0 Hz), 7.37–7.40 (t (d, d, d), 1 H, J = 7.5, 1.0 Hz), 7.47–7.51 (t (d, d, d), 1 H, J = 7.5, 1.0 Hz), 7.95–8.02 (m, 4 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.4, 161.2, 155.3, 135.6, 130.0, 127.1, 126.3, 125.7, 123.4, 122.6, 116.8. FTIR: 3057, 1605, 1483, 1433, 1283, 1225, 1163, 978, 830, 756, 723 cm^{-1}. MS: m/z (%) 228 (16, $(M+1)^+$), 227 (100, M^+), 198 (10), 108 (18), 69 (16).
[31] The purification procedures and spectral data for compounds 2-p-methylphenylbenzothiazole (**4a**) and 1, 4-bi(2,2′-benzothiazolyl)benzene (**4b**). The intermediate distillate was purified in the way of **1** to give **4a** as pale yellow needles, and the heavy distillate was washed with petroleum ether and methanol for times and give yellow powder of **4b**. The melting point of **4b** was not observed for there was a wide melting range of 240–268 °C which may be explained by decomposition according to a previous report [1]. **4a**: mp 83.5–85.0 °C (85.0–85.5 °C [14]). ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.41 (s, 3 H), 7.27–7.29 (d, 2 H, J = 8.0 Hz), 7.37–7.37 (t (d, s, d), 1 H, J = 7.5, 1.0 Hz), 7.45–7.48 (t (d, d, d), 1 H, J = 7.5, 1 Hz), 7.87–7.88 (d (d, d), 1 H, J = 8.0, 0.5 Hz), 7.96–7.98 (d, 2 H, J = 8.0 Hz), 8.03–8.05 (d, 1 H, J = 8.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.2, 154.2, 141.4, 135.0, 131.0, 129.7, 127.5, 126.2, 125.0, 123.1, 121.5, 21.5. FTIR: 3057, 3024, 2914, 1608, 1483, 1313, 1228, 1184, 962, 820, 759, 731, 625 cm^{-1}. MS: m/z (%) 226 (20, $(M+1)^+$), 225 (100, M^+), 224 (42), 69 (12). **4b**: ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.51–7.54 (m, 2 H), 7.59–7.62 (m, 2 H), 8.13–8.14 (d, 2 H, J = 8.0 Hz), 8.21–8.22 (d, 2 H, J = 7.5 Hz), 8.32 (s, 4 H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 166.1, 153.5, 135.0, 134.6, 128.1, 126.8, 125.9, 123.1, 122.4. FTIR: 3055, 1497, 1477, 1433, 1404, 1313, 1250, 1223, 1113, 964, 843, 748, 725, 682, 623 cm^{-1}. MS: m/z (%) 345 (25, $(M+1)^+$), 344 (100, M^+), 343 (13), 108 (29), 82 (14), 69 (22).

[32] The purification procedures and spectral data for compounds 2-phenylnaphtho[1,2-d]thiazole (**5**) and 2-*p*-methylphenyl-naphtho[1,2-d]thiazole (**6**). **5**: The intermediate distillate was leached with hot methanol for three times, and the filtrate was evaporated and the residue was recrystallized from mixed solvent of methanol and tetrahydrofuran (vol ratio about 5:1) to give grey needles. mp 99.5–101.0 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.47–7.53 (m, 3 H), 7.56–7.59 (t (d, d, d), 1 H, J = 7.5, 1.0 Hz), 7.66–7.69 (t (d, s, d), 1 H, J = 7.5, 1.0 Hz), 7.78–7.80 (d, 1 H, J = 8.5 Hz), 7.89–7.91 (d, 1 H, J = 9.0 Hz), 7.93–7.95 (d, 1 H, J = 8.0 Hz), 8.17–8.20 (d (d, d), 2 H, J = 8.0, 1.5 Hz), 8.90–8.92 (d, 1 H, J = 8.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.1, 150.5, 134.0, 132.1, 131.7, 130.6, 129.0, 128.8, 128.1, 127.3, 126.9, 126.1, 125.9, 124.0, 119.0. FTIR: 3048, 1510, 1473, 1443, 1363, 1252, 1070, 972, 906, 797, 758, 738, 681, 605 cm^{-1}. MS: m/z (%) 262 (20, $(M+1)^+$), 261 (100, M^+), 158 (29), 114 (19). **6**: The intermediate distillate was dissolved in tetrahydrofuran, filtrated and evaporated. The residue was recrystallized from mixed solvent of methanol and tetrahydrofuran (vol ratio about 4:1) to give pale green needles. mp 97.0–98.5 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.43 (s, 3 H), 7.30–7.31 (d, 2 H, J = 8.0 Hz), 7.55–7.58 (t (d, s, d), 1 H, J = 7.5, 1.0 Hz), 7.65–7.68 (t (d, s, d), 1 H, J = 7.5, 1.0 Hz), 7.77–7.79 (d, 1 H, J = 9.0 Hz), 7.88–7.90 (d, 1 H, J = 8.5 Hz), 7.92–7.94 (d, 1 H, J = 8.0 Hz), 8.06–8.08 (d, 2 H, J = 8.0 Hz), 8.89–8.90 (d, 1 H, J = 8.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.3, 150.5, 141.0, 132.1, 131.5, 131.4, 129.7, 128.8, 128.0, 127.3, 126.9, 126.0, 125.7, 124.1, 119.0, 21.5. FTIR: 3051, 2916, 1502, 1473, 1363, 1240, 1178, 1080, 972, 906, 802, 739, 690 cm^{-1}. MS: m/z (%) 276 (22, $(M+1)^+$), 275 (100, M^+), 274 (15), 158 (15), 114 (14).