Novel synthesis of 2-arylbenzothiazoles

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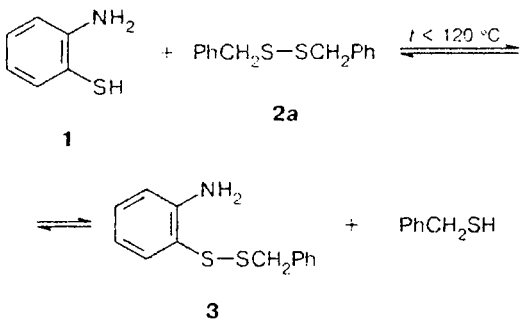
A new method for the synthesis of 2-arylbenzothiazoles by the reaction of dibenzyl disulfides with *o*-aminothiophenol is suggested. A possible mechanism of the new transformation is discussed. 2-Phenylbenzothiazole can also be prepared by reactions of *o*-aminothiophenol with benzyl mercaptane or sodium benzyl thiosulfate.

Key words: 2-arylbenzothiazoles, synthesis; *o*-aminothiophenol, reactions with dibenzyl disulfides, benzyl mercaptan, and sodium benzyl thiosulfate.

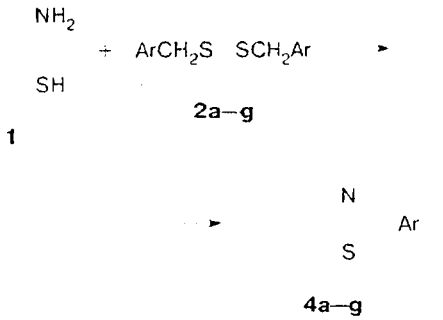
A method commonly used for the synthesis of unsymmetrical disulfides involves the reaction of symmetrical disulfides with thiols proceeding under mild conditions, for example, at room temperature in chloroform.[1] We demonstrated that unsymmetrical disulfides containing the amino group at the α position, which are potential stabilizers in vulcanization of rubbers,[2] are formed in the reaction (Scheme 1) of *o*-aminothiophenol (**1**) with dibenzyl disulfide (**2a**) proceeding upon refluxing of their solutions in ethanol, toluene, or butyl acetate. However, this reaction is unsuitable for preparative purposes because of its reversibility.

Scheme 1



We found that the reaction performed in DMF or 1-methyl-2-pyrrolidone (the **1** : **2a** molar ratio was 2 : 1) at 130—140 °C for 4—10 h afforded 2-phenylbenzothiazole (**4a**) rather than unsymmetrical disulfide **3**. Under the same conditions, other 2-arylbenzothiazoles **4b—g** were synthesized (Scheme 2) in good yields. These compounds are identical in the melting points to those reported in the literature (Table 1). The structures of compounds **4b—g** were also confirmed by ^{1}H NMR spectroscopy and mass spectrometry. The ^{1}H NMR spectrum of 2-phenylbenzothiazole (**4a**) is insufficiently informative due to overlapping of the signals. However, the assignment of most of the signals in the spectra of other 2-arylbenzothiazoles presents no problems. In the mass spectra of 2-arylbenzothiazoles **4a—e**, the molecular ion peaks are most intense. The isotope peaks $[M+1]^{\cdot+}$ and $[M+2]^{\cdot+}$ are also observed. In the case of chlorine-containing compounds **4b,c**, the peaks $[M]^{\cdot+}$, $[M+1]^{\cdot+}$, and $[M+2]^{\cdot+}$ account for the presence of the ^{35}Cl and ^{37}Cl isotopes in the ratio of ~3 : 1. The mass spectrum of nitro-substituted compound **4f** is distinguished by the low intensity of the molecular ion peak. The character of fragmentation of the molecular ions calls for further investigation.

Scheme 2



Additives of bases accelerate the reaction (TLC control). UV irradiation acts the same way, the reaction proceeding at lower temperature (80 °C). Products **4** were not detected in the reaction performed under an inert atmosphere (argon). Probably, irradiation is favorable for the homolytic mechanism of the first reaction step (Scheme 1) and induces electron transfer at one of successive steps. It is known that dibenzyl disulfide

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Table 1. Characteristics of 2-arylbenzothiazoles **4a—g**

Compound	Ar	Yield (%)	M.p./°C	M.p./°C (lit. data)
4a [a]	C_6H_5	54	115—116	114—115 [3]
4b [b]	2-ClC_6H_4	62	81—82	85 [4]
4c [c]	4-ClC_6H_4	65	116—117	120—121 [5]
4d [d]	2,4-$Cl_2C_6H_3$	73	144—145	144 [6]
4e [e]	4-$MeOC_6H_4$	58	131.5—132	134—135 [7]
4f [f]	4-$O_2NC_6H_4$	52	227—2230	229—231 [8]
4g [g]	4-$Me_2NC_6H_4$	60	174—175	173 [9]

[a] ^{1}H NMR, δ: 7.40 (t, 1 H, H(5), $J \approx 8$ Hz); 7.50 (m, 4 H, H(6), H(3′), H(4′), and H(5′)); 7.90 (d, 1 H, H(7), $J \approx 8$ Hz); 8.10 (m, 3 H, H(4), H(2′), and H(6′)). MS, m/z (I_{rel}): 213 [M + 2]$^+$ (7.5); 212 [M + 1]$^+$ (21.3); 211 [M]$^+$ (100); 210 [M − 1]$^+$ (20.4); 184 (4.5); 107 [M − H − PhCN]$^+$ (39.0); 105 (6.8); 81 (8.9); 69 (19.0); 63 (5.8); 57 (7.9); 44 [CS]$^+$ (30.4); 43 (9.8); 42 (12.8); 40 (16.4).

[b] MS, m/z (I_{rel}): 249 ^{37}Cl − [M + 2]$^+$ (4.4); 248 ^{37}Cl − [M + 1]$^+$ (6.4); 247 ^{37}Cl − [M]$^+$; ^{35}Cl − [M + 2]$^+$ (37.8); 246 ^{35}Cl − [M + 1]$^+$ (16.0); 245 ^{35}Cl − [M]$^+$ (100); 210 [M − Cl]$^+$ (24.2); 209 (6.6); 124 (12.3); 123 (13.8); 108 [M − ClC_6H_4CN]$^+$ (52.5); 107 [M − ClC_6H_4CN − H]$^+$ (6.0); 105 (15.3); 83 (6.5); 81 (11.9); 75 (5.5); 69 (34.2); 58 (32.5); 46 (8.1); 45 (5.6); 44 [CS]$^+$ (93.0); 43 (37.9); 42 (35.1); 41 (7.7); 40 (28.7); 39 (6.2).

[c] MS, m/z (I_{rel}): 248 ^{37}Cl − [M + 1]$^+$ (7.6); 247 ^{37}Cl − [M]$^+$, ^{35}Cl − [M + 2]$^+$ (48.5); 246 ^{35}Cl − [M + 1]$^+$ (9.6); 245 ^{35}Cl − [M]$^+$ (73.2); 244 ^{35}Cl − [M − 1]$^+$ (5.2); 212 (5.6); 210 [M − Cl]$^+$ (5.1); 123 (20.4); 108 [M − ClC_6H_4CN]$^+$ (4.2); 107 [M − ClC_6H_4CN − H]$^+$ (52.0); 93 (5.3); 91 (6.1); 81 (9.5); 75 (10.0); 69 (43.2); 63 (16.8); 58 (40.7); 44 [CS]$^+$ (100.0); 43 (28.0); 42 (21.3); 40 (20.3).

[d] ^{1}H NMR, δ: 7.40 (m, 2 H, H(5) and H(6)); 7.50 (m, 2 H, H(3′) and H(5′)); 7.93 (d, 1 H, H(7), $J \approx 8$ Hz); 8.14 (d, 1 H, H(6′)); 8.26 (d, 1 H, H(4), $J \approx 8$ Hz).

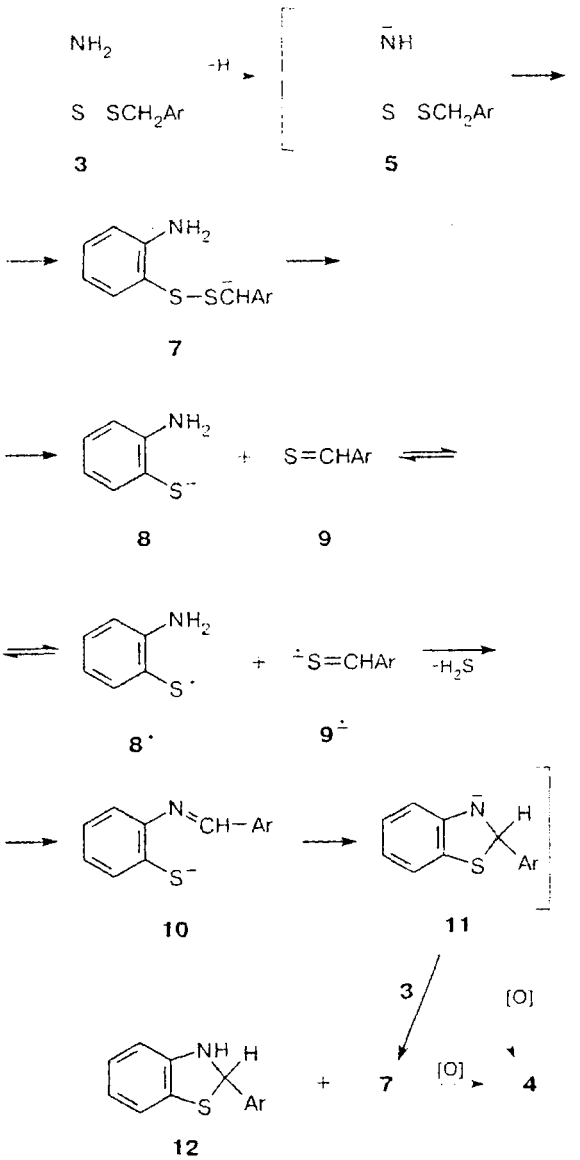
[e] ^{1}H NMR, δ: 3.90 (s, 3 H, MeO); 7.01 (d, 2 H, H(3′) and H(5′), $J \approx 8$ Hz); 7.48 (t, 1 H, H(5), $J \approx 8$ Hz); 7.85 (t, 1 H, H(6), $J \approx 8$ Hz); 7.90 (d, 1 H, H(7), $J \approx 8$ Hz); 8.05 (d, 3 H, H(4), H(2′), and H(6′)). MS, m/z (I_{rel}): 243 [M + 2]$^+$ (6.5); 242 [M + 1]$^+$ (15.3); 241 [M]$^+$ (100.0); 226 (32.4); 198 (30.8); 197 (7.5); 153 (6.0); 107 (6.2); 81 (6.5); 69 (12.4).

[f] MS, m/z (I_{rel}): 258 [M + 2]$^+$ (17.85); 256 [M]$^+$ (44.5); 192 (15.4); 168 (11.5); 160 (43.5); 143 (68.3); 138 (9.5); 130 (6.8); 129 (8.4); 128 (37.0); 109 (11.3); 96 (15.0); 95 (5.6); 86 (5.6); 85 (100); 84 (16.3); 71 (25.4); 70 (8.2); 69 (18.8); 68 (32.3); 67 (6.0); 66 (8.3); 64 (67.5); 59 (16.3); 58 (79.7); 57 (5.6); 56 (9.2); 55 (80.0); 54 (34.1); 53 (53.0); 46 (5.9).

[g] ^{1}H NMR, δ: 2.92 (s, 3 H, MeN); 3.07 (s, 3 H, MeN); 6.76 (d, 2 H, H(3′) and H(5′), $J \approx 8$ Hz); 7.31 (t, 1 H, H(5), $J \approx 8$ Hz); 7.45 (t, 1 H, H(6), $J \approx 8$ Hz); 7.85 (d, 1 H, H(7), $J \approx 8$ Hz); 7.97 (m, 3 H, H(4), H(2′), and H(6′)).

undergoes deprotonation under the action of such bases as NaOH [10] or LDA.[11] The resulting carbanion of the benzyl type undergoes β-scission to form the toluenethiolate anion and thiobenzaldehyde. The latter compound is converted into the corresponding radical anion due to electron transfer from the base to LDA.[11] In unsymmetrical disulfide **3**, the nitrogen atom of the amino group or *N*-anion **5**, which is generated under the action of an external base on disulfide **3**, can act as an "internal base" and the electron transfer from the thiolate anion to thioaldehyde can occur in the solvent "cage." It can be suggested that unsymmetrical disulfide **3**, which is formed in the first stage of the reaction of symmetrical disulfide **2** with aminothiol **1** or bis(2-aminophenyl) disulfide (**6**), gives carbanion **7** upon protonation. Subsequent conversions of anion **7** may involve the cleavage of the S—S bond to form thiolate anion **8** and thioaldehyde **9** or radical **8**$^{\cdot}$ and radical anion **9**$^{\cdot-}$, which react with each other in the "cage" with elimination of a molecule of hydrogen sulfide and the thiolate anion of Schiff's base **10**. The latter undergoes intramolecular cyclization giving rise to *N*-anion **11** whose oxidation affords arylbenzothiazole **4**. The reaction of *N*-anion **11** with disulfide **3** can result in generation of

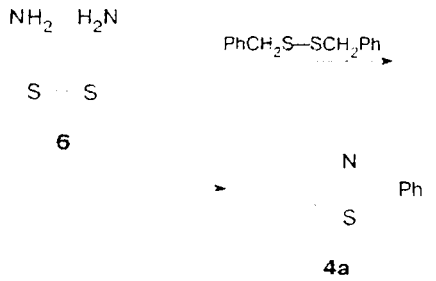
Scheme 3



anion **7**, which continues the process, and 2-aryl-2,3-dihydrobenzothiazole **12**, which is oxidized to 2-arylbenzothiazole **4** (Scheme 3).

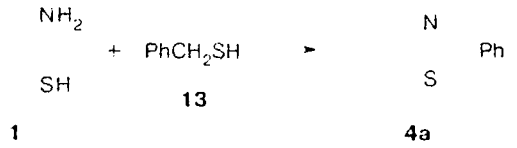
The synthesis of 2-phenylbenzothiazole (the yield was 56%) from bis(2-aminophenyl) disulfide (**6**) under conditions similar to those described above for the preparation of the former compound from aminothiol **1** (Scheme 4) is yet another argument in favor of the possible involvement of **6** in the reaction.

Scheme 4



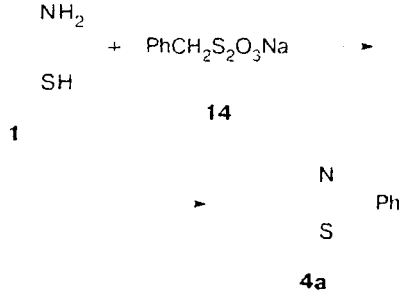
According to the published data,[12] benzyl mercaptan (**13**) can also form radical anion **9**$^{\bullet-}$ under the action of bases. Hence, it was of interest to study the reaction of thiol **13** with *o*-aminothiol **1**. Actually, 2-phenylbenzothiazole (**4a**) was obtained under the same conditions in 42% yield (Scheme 5).

Scheme 5



Since *S*-aryl(alkyl) thiosulfates (Bunte salts) can be considered as precursors of disulfides and it is known that these compounds are converted into disulfides under the action of thiols in the presence of bases,[13] Bunte salts would be expected to give intermediate **9** under these conditions. We performed the reaction of sodium benzyl thiosulfate (**14**) with *o*-aminothiophenol (**1**) and obtained 2-phenylbenzothiazole (**4a**) in 36% yield (Scheme 6).

Scheme 6



To summarize, we developed a simple and convenient procedure for the synthesis of 2-arylbenzothiazoles by the reactions of *o*-aminothiophenol (**1**) or bis(2-aminophenyl) disulfide (**6**) with various bis(arylmethyl) disulfides, thiols, and thiosulfates.

Experimental

The ^{1}H NMR spectra were recorded on a Bruker AC-200 spectrometer in $CDCl_3$. The mass spectra (EI) were obtained on a Kratos instrument (70 eV) with direct introduction of the sample into the ion source. The melting points were measured on a Boetius microtable and were not corrected. The completion of the reactions was monitored by TLC (Silufol UV-254, a 3 : 1 hexane—AcOEt mixture as the eluent).

o-Aminothiophenol (**1**), bis(2-aminophenyl) disulfide (**6**), and benzyl mercaptan (**13**) were purchased from Aldrich. Dibenzyl disulfide (**2a**), 2,2′-dichlorodibenzyl disulfide (**2b**), 4,4′-dichlorodibenzyl disulfide (**2c**), and 2,2′,4,4′-tetrachlorodibenzyl disulfide (**2d**) were prepared from the corresponding benzyl chlorides and Na_2S_2 according to a known procedure.[14] 4,4′-Di(methoxy)dibenzyl disulfide (**2e**) and 4,4′-bis(dimethylamino)dibenzyl disulfide (**2g**) were synthesized from the corresponding substituted benzaldehydes and hydrogen sulfide according to a procedure reported previously.[15] 4,4′-Dinitrodibenzyl disulfide (**2f**) was prepared from the corresponding Bunte salt according to a known procedure.[16] Sodium benzyl thiosulfate (**14**) was prepared from benzyl chloride and $Na_2S_2O_3 \cdot 5H_2O$ according to a procedure reported previously.[17]

2-Phenylbenzothiazole (4a). *A.* *o*-Aminothiophenol (26.25 g, 0.21 mol) and dibenzyl disulfide (24.6 g, 0.1 mol) were heated in anhydrous DMF (30 mL, dried over alkali and distilled *in vacuo*) at 130—140 °C for 4—10 h, cooled to ~20 °C, and poured onto ice. The precipitate that formed was filtered off and recrystallized from 95% EtOH. **2-(2-Chlorophenyl)benzothiazole (4b)**, **2-(4-chlorophenyl)benzothiazole (4c)**, **2-(2,4-dichlorophenyl)benzothiazole (4d)**, **2-(4-methoxyphenyl)benzothiazole (4e)**, **2-(4-nitrophenyl)benzothiazole (4f)**, and **2-(4-*N*,*N*-dimethylaminophenyl)benzothiazole (4g)** were prepared analogously. The yields and characteristics of the resulting compounds are given in Table 1.

B. 2-Phenylbenzothiazole (**4a**) was prepared in 56% yield from bis(2-aminophenyl) disulfide (**6**) (24.8 g, 0.1 mol) and disulfide **2a** (24.6 g, 0.1 mol) under conditions used in procedure *A*.

C. 2-Phenylbenzothiazole (**4a**) was prepared in 42% yield from thiol **13** (12.4 g, 0.1 mol) and *o*-aminothiophenol (**1**) (12.5 g, 0.1 mol) under conditions used in procedure *A*.

D. 2-Phenylbenzothiazole (**4a**) was prepared in 36% yield from sodium benzyl thiosulfate (**14**) (22.6 g, 0.1 mol) and *o*-aminothiophenol (**1**) (12.5 g, 0.1 mol) under conditions used in procedure *A*.

The reaction conditions were varied using the synthesis of 2-phenylbenzothiazole (**4a**) from *o*-aminothiophenol (26.25 g, 0.21 mol) and dibenzyl disulfide (24.6 g, 0.1 mol) as an example. The reaction time was decreased to 1 or 1.5 h in the presence of catalytic amounts (~0.001 mol) of KOH or K_2CO_3, respectively. Irradiation of the mixture in a quartz flask using a PRK-4 mercury-quartz lamp (80 °C, 9 h) afforded phenyl-

benzothiazole **4a** in 58% yield. The reaction performed under argon (20 h) did not give rise to compound **4a**.

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