Rearrangement of 2-Benzothiazolylthioacetyl Hydrazide in Ethanol Solution of Potassium Hydroxide: Synthesis of *s*-Triazolo[3,4-*b*]benzothiazol-3-thiol and Its Derivatives

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A novel rearrangement reaction about 2-benzothiazolylthioacetyl hydrazide (1) to produce *s*-triazolo[3,4-*b*]benzothiazol-3-thiol (3) in the presence of KOH and CS_2 was described. Other way to synthesize 3 from 2-benzothiazolylhydrazine (2) under the same condition was compared and the Mannich reaction of compound 3 was reported too. Their structures were established by elemental analyses, IR, ^1H NMR and MS spectra.

Keywords rearrangement, *s*-triazolo[3,4-*b*]benzothiazol-3-thiol, Mannich reaction

Introduction

2-Substituted-benzothiazoles and their derivatives have attracted much attention of chemists and pharmacologists because of their broad spectrum of biological activities and uses as photographic materials.[1-3] Using 2-benzothiazolylthioacetyl hydrazide (**1**) as a better reactive compound, generally 5-substituted-1,3,4-oxadiazol-2-thiol, is obtained by cyclization of this hydrazide with carbon disulfide in ethanolic solution of KOH.[4] But our experiment about 2-benzothiazolylthioacetyl hydrazide (**1**) exhibited that instead of the expected 5-benzothiazolylthiomethylene-1,3,4-oxadiazole-2-thiol (**3'**),[5] biologically active *s*-triazolo[3,4-*b*]benzothiazol-3-thiol (**3**)[6,7] was formed and isolated. In order to synthesize compound **3**, treatment of 2-benzothiazolylhydrazine (**2**) under the same condition afforded compound **3** too (Scheme 1). Further work was established due to the rearrangement reaction of the hydrazide.

As we know, 1,2,4-triazolo[3,4-*b*]benzothiazol-3-thiol and their derivatives are extensively applied in agrochemistry.[6-11] Their 3-substituted and 3-thiolsubstituted derivatives are often studied because they can be easily obtained. The study of reaction at 2-position is limited. In general, it is a good method to form potential biologically active compounds by Mannich reaction.[12] Thus, we tried to perform Mannich and double Mannich reaction starting from compound **3** to prepare some biologically active Mannich bases (Scheme 2).

Experimental

All reagents were of laboratorial grade and were used without purification. Melting points were uncorrected and taken on an X-4 microscopic melting point apparatus. IR spectra were recorded on a Nicolet AVATAR 360 FT-IR spectrometer in KBr disc. ^1H NMR spectra were recorded on a Bruker AC-80 instrument in DMSO-d_6 with TMS as internal standard. Mass spectra were performed on a ZAB-HS (EI) and VG ZAB-HS (FAB) instruments. Gas chromatography was determined by using a Shimadzu GC-9M. Elemental analyses were performed on an Elementary Vario EL apparatus.

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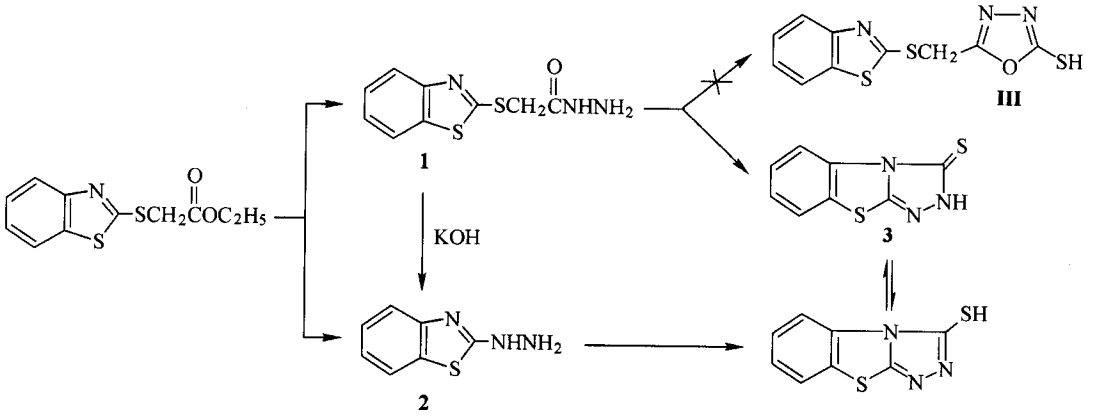
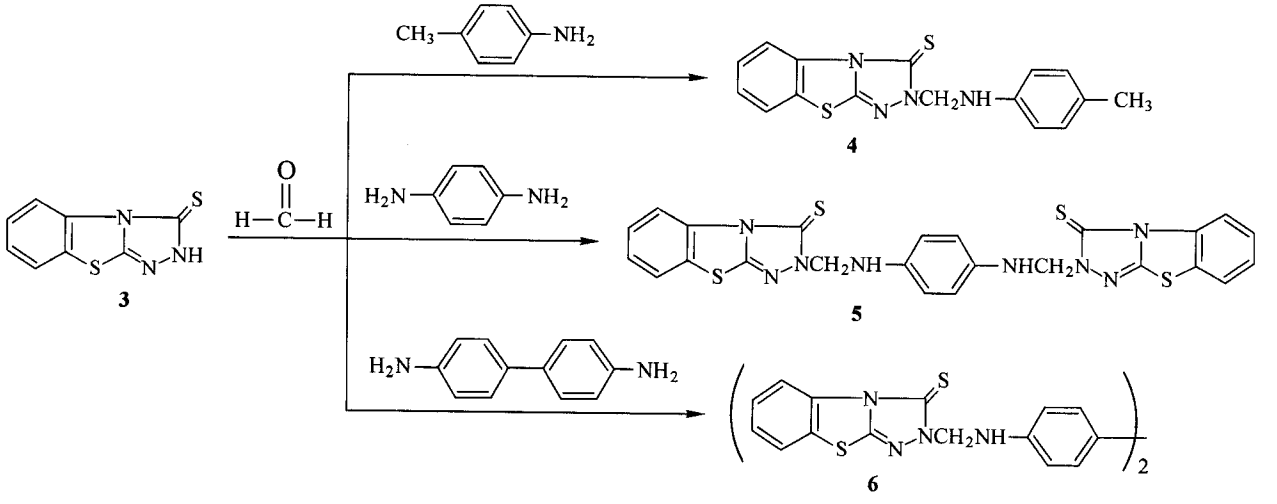
Receved July 12, 2001; revised september 30, 2001; accepted November 5, 2001.
Project supported by the National Natural Science Foundation of China (QT Program).

Scheme 1 Preparation of *s*-triazolo[3,4-*b*]benzothiazol-3-thiol (**3**)



Scheme 2 Preparation of Mannich bases **4**—**6**



Preparation of 2-benzothiazolylthioacetyl hydrazide (**1**) *and 2-benzothiazolyl hydrazine* (**2**)

2-Benzothiazolylthioacetyl hydrazide (**1**) was synthesized following the method in literature[5] with a little account of 2-benzothiazolylhydrazine (**2**) formed.

1 Yield 92%; m.p. 173—175 ℃ (lit.[5a] 175 ℃); ^{1}H NMR δ: 9.42 (s, 1H, NH*), 8.08—7.79 (m, 1H, ArH), 7.49—7.33 (m, 3H, ArH), 4.38 (s, 2H, SCH_2), 4.10 (s, 2H, NH_2*) (*exchangeable with D_2O); IR (KBr) ν: 3284, 1645, 1530, 1456, 1426, 1237, 993, 756, 698 cm^{-1}; MS (70 eV) *m/z* (%): 239 (M^+, 8), 208 (57), 180 (29), 167 (100), 136 (16), 122 (7), 108 (16), 69 (11).

2 White needle, yield 2%; m.p. 195—197 ℃ (lit.[9] 197—198 ℃); ^{1}H NMR δ: 8.98 (s, 1H, NH*), 7.72—6.86 (m, 4H, ArH), 5.01 (s, 2H, NH_2*) (*exchangeable with D_2O); IR (KBr) ν: 3318, 3059, 2870, 1649, 1596, 1561, 1449, 1279, 985, 755, 696 cm^{-1}; MS (70 eV) *m/z* (%): 165 (M^+, 100), 148 (63), 135 (15), 122 (10), 108 (24), 69 (17).

Preparation of s-triazolo[3,4-*b*]*benzothiazol-3-thiol* (**3**)

Method A from **1**: Potassium hydroxide (0.015 mol) was dissolved in hot ethanol (30 mL). Then compound **1** (0.010 mol) was added quickly and the mixture was refluxed. At the beginning, the solution was yellow pellucid and about ten seconds later a lot of white needle crystals **2** appeared and odd odor was released from the mixture. Then carbon disulfide (0.02 mol) diluted by ethanol (10

mL) was added slowly and the mixture was refluxed for 25 h. The solvent was distilled off and the residue was poured into ice-cold water. After filtration, the filtrate upon acidification gave a precipitate which was filtered, washed with water and recrystallized from ethanol to get pale yellow crystal **3**.

Method B from **2**: Similar process was allowed to treat **2** (0.010 mol) with potassium hydroxide (0.015 mol) and carbon disulfide (0.02 mol) in ethanol. And the mixture was refluxed for 2 d to form product **3**.

3 Pale yellow crystal, yield 75% (method A) or 81% (method B); m.p. 252—254 ℃ (lit.[8a] 255 ℃); ^{1}H NMR δ: 14.23 (s, 1H, NH), 8.94—8.82 (m, 1H, ArH), 8.11—7.99 (m, 1H, ArH), 7.61—7.47 (m, 2H, ArH); IR (KBr) ν: 3411, 3083, 1536, 1492, 1333, 749 cm^{-1}; MS (70 eV) *m/z* (%): 207 (M^+, 100), 180 (6), 149 (65), 148 (20), 134 (5), 122 (11); Anal. calcd for $C_8H_5N_3S_2$: C 46.36, H 2.43, N 20.27; found C 46.48, H 2.31, N 20.10.

General procedure for preparation of 2-*p*-*toludinomethyl*-3-*thion*-1,2,4-*triazolo*[3,4-*b*]*benzothiazole* (**4**) *and N,N'-bis*[2-*methylene*-1,2,4-*triazolo*[3,4-*b*]*benzothiazol*-3-*thion*]*phenylenediamine* (**5**)/*diaminobiphenyl* (**6**)

3-Mercapto-*s*-triazolo[3,4-*b*]benzothiazole (**3**) (1 mmol), suspensing in ethanol, was cooled in an ice-water bath. To which, formaldehyde solution (1.5 mmol) was added. An ethanolic solution of *p*-toluidine/phenylenediamine/benzidine (1 mmol) was added dropwise. Needle substrate disappeared when the mixture was stirred in room temperature for a day and the reaction was monitored by TLC. The precipitation was filtered, washed and recrystallized from EtOH or EtOH-DMF.

4 Pale yellow needle, yield 92%; m.p. 142—143 ℃; ^{1}H NMR δ: 8.96—8.85 (m, 1H, ArH), 8.10—7.98 (m, 1H, ArH), 7.60—7.46 (m, 2H, ArH), 6.86 (s, 4H, ArH), 5.54 (s, 2H, CH_2), 4.74 (s, 1H, NH), 2.11 (s, 3H, CH_3); IR (KBr) ν: 3392, 614, 1524, 1401, 1368, 1241, 813, 751 cm^{-1}; MS (70 eV) *m/z* (%): 326 (M^+, 2), 220 (1), 207 (100), 149 (40), 120 (9), 119 (47), 91 (31); Anal. calcd for $C_{16}H_{14}N_4S_2$: C 58.87, H 4.32, N 17.16; found C 58.64, H 4.11, N 17.04.

5 Pale yellow granular, yield 95%; m.p. 260—262 ℃; ^{1}H NMR δ: 8.90—8.66 (m, 2H, ArH), 7.97—7.78 (m, 2H, ArH), 7.57—7.30 (m, 4H, ArH), 6.76 (s, 4H, ArH), 5.49 (s, 4H, $2CH_2$), 4.61 (br, 2H, 2NH); IR (KBr) ν: 3373, 1525, 1400, 1364, 1237, 862, 752 cm^{-1}; FAB-MS *m/z*: 546 (M^+); MS (70 eV) *m/z* (%): 207 (100), 149 (25), 133 (2), 132 (14), 122 (3), 104 (3), 90 (1). Anal. calcd for $C_{24}H_{18}N_8S_4$: C 52.73, H 3.31, N 20.50; found C 52.52, H 2.96, N 20.86.

6 White powder, yield 90%; m.p. 256—257 ℃; ^{1}H NMR δ: 8.97—8.85 (m, 2H, ArH), 8.10—7.98 (m, 2H, ArH), 7.58—7.49 (m, 4H, ArH), 7.31 (d, J = 8.2 Hz, 4H, ArH), 6.94 (d, J = 8.2 Hz, 4H, ArH), 5.60 (s, 4H, $2CH_2$), 4.91 (br, 2H, 2NH); IR (KBr) ν: 3331, 1613, 1532, 1508, 1395, 1373, 1240, 819, 748 cm^{-1}; FAB-MS *m/z*: 622 (M^+); MS (70 eV) *m/z* (%): 210 (2), 209 (20), 208 (82), 207 (100), 196 (10), 180 (7), 152 (17), 149 (24), 148 (8), 122 (14); Anal. calcd for $C_{30}H_{22}N_8S_4$: C 57.86, H 3.56, N 17.99; found C 57.62, H 3.40, N 17.59.

Results and discussion

Throughout the reaction, white needle crystal appeared shortly after **1** dissolved completely in the hot ethanolic solution of potassium hydroxide, and odd odor was released from the mixture. The precipitate **2** was separated and assigned to be 2-benzothiazolyl hydrazine based on the melting point, ^{1}H NMR and standard IR spectra.[12] The compound with odd odor was proved to be mercapto acetic acid by GC upon comparing with the authenic sample. Similar treatment had been done from hydrazine **2** to produce triazolobenzothiazole **3** too. Above all, it could be thought that intramolecular addition-elimination occurred from 2-benzothiazolyl thioacetyl hydrazide (**1**) to form 2-benzothiazolylhydrazine (**2**) in the presence of KOH in hot ethanol, then hydrazine **2** continued to react with KOH and CS_2 to give *s*-triazolo[3,4-*b*]benzothiazol-3-thiol (**3**). The reaction mechanism was proposed as shown in Scheme 3.

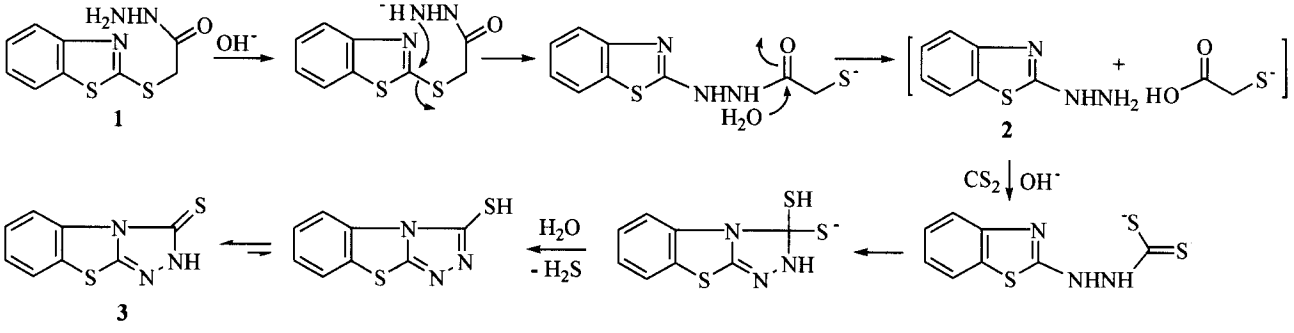
The reasons for compound **3** instead of **3'** from hydrazide **1** might be explained by two factors. First of all, a little account of water in the ethanol without purification acted as the promoting agent. Furthermore, the hot mixture was placed for a period of time when the needle crystal appeared which was enough to finish the rearrangement reaction.

Other methods to synthesize **3** from different sub-

strates had been discussed before.[8] Reynolds[8b] pointed that it might have a double-bonded sulfur rather than a mercapto group in 3-position (Scheme 3). The ^{1}H NMR spectrum of compound **3** showed a singlet at downfield (δ 14.23) which indicated that the proton existed in N—H form rather than S—H form.

The ^{1}H NMR spectra of **4**—**6** exhibited a singlet for NCH_2N protons at δ 5.5. By analyzing the mass spectra, it was found that the molecular ion peak of **4** was low and the molecular ion peaks of **5** and **6** could not been detected by EI mass because of the weak C—N bond of the compounds.

Scheme 3 Process of rearrangement reaction



Acknowledgements

We thank for Mrs Xiao-Ling Jin, National Laboratory of Applied Organic Chemistry, for helpful comments.

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