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NOTE

Synthesis of 2,3-*Bis*(2-benzothiazolyldisulfanyl)-1-propanol

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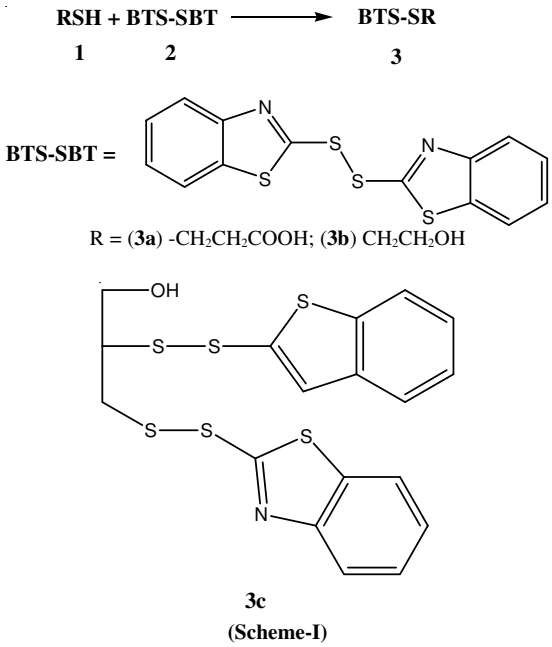
The TLC monitored reaction of 2,2'-dithiobisbenzothiazole with 2,3-dithiopropanol resulted in the formation of unsymmetrical disulfides *i.e.*, 2,3-*bis*(2-benzothiazolyldisulfanyl)-1-propanol (**3**). The molecule is characterized using proton NMR study. The molecular model study of the compound **3** reveals the proximity of the -OH proton to the nitrogen atom of the benzothiazole ring providing the probable hydrogen bond formation which is further confirmed by the study of hydrogen-deuterium exchange reaction.

Key Words: 2,3-*Bis*(2-benzothiazolyldisulfanyl)-1-propanol, 2,2'-Dithiobisbenzothiazole, 2,3-Dithiopropanol.

Nitrogen heterocyclic compounds play an important role with respect to their potential biological activity. Many pharmacologically active molecules have been widely utilized as potent drugs in the market. Molecules containing benzothiazole moiety are reported for their various potential activities[1,2]. For example, unsymmetrical disulfides with a benzothiazole fragment[3] have been reported as an active agent against weapons of mass destructions (WMD's) and this area of research is considered to be the thrust area recently. Also, use of benzothiazole moiety in the construction of some electronic devices has also been reported[4,5]. A number of unsymmetrical disulfides were also reported to have a broad spectrum of biological activities[6-8]. The disulfides also provide an intriguing subject for investigation because of their use as additives for lubricating oils and for tanning of leather. There exist various standard methods of synthesis of unsymmetrical disulfides. But it has been observed that none of them absolutely provide a general method to synthesize all categories of unsymmetrical disulfides. These provide a challenge for the fraternity to look for a general methodology.

In present search for a general methodology to synthesize unsymmetrical disulfides, we have synthesized some unsymmetrical and symmetrical disulfides. One among them is 2,3-*bis*(2-benzothiazolyldisulfanyl)-1-propanol (**3**) (**Scheme-I**).

Melting points were determined in open capillary tubes and are uncorrected. NMR spectra (DMSO-d_6/$CDCl_3$) on a Bruker DRX 300 spectrometer using TMS as internal standard.



(Scheme-I)

All the chemicals are used as such obtained from the commercial sources.

Synthesis of unsymmetrical disulfide: To the suspension of 2,2'-dithiobisbenzothiazole (6.64 g, 0.02 mol) in 75 mL chloroform a solution of thiol (0.01 mol) in 50 mL chloroform was added dropwise and with stirring. The progress of the

reaction was monitored by TLC (silica gel, chloroform as eluent) with respect to the starting material. The reaction mixture was stirred for an additional 3 h. The mixture was then washed with 5 % NaOH solution (2 mL × 40 mL) followed by water (2 mL × 40 mL) and dried (Na_2SO_4). Removal of solvent resulted in the crude product. It was then subjected to column chromatography (silica gel, chloroform as eluent and iodine visualization). Work up of the required portion results in the product in pure form. The schematic procedure for the synthesis of the material 2,3-*bis*(2-benzothiazolyldisulfanyl)-1-propanol (**3**) is given in **Scheme-I**.

The reaction involves a simple nucleophilic substitution reaction. The progress of the reaction was monitored by TLC (silica gel, chloroform as eluent) with respect to the starting material. The crude compound was subjected to column chromatography using chloroform as eluent to give the pure product. The structure of the compound was confirmed on the basis of its detailed spectral analysis.

Compound 3a: ^{1}H NMR (300 MHz in DMSO-d_6, TMS at 0 ppm): δ 2.8 (t, 2H, CH_2); 3.2 (t, 2H, CH_2); 7.5 (m, 2H, ArH); 7.9 (m, 2H, ArH); 8.1 (t, 1H, ArH); ^{13}C NMR (300 MHz in DMSO-d_6, TMS at 0 ppm): 121-126, 135.2, 154.5, 172; anal calcd. (%) for $C_{10}H_9NS_3O_2$: C, 44.26; H, 3.34; N, 5.16; found. (%): C, 44.16; H, 3.49; N, 4.99.

Compound 3b: ^{1}H NMR (300 MHz in $CDCl_3$, TMS at 0 ppm): δ 3.8 (q, 2H, CH_2); 3.9 (q, 2H, CH_2); 4.3 (t, 1H, OH); 7.35 (m, 1H, ArH); 7.46 (m, 1H, ArH); 7.77 (t, 1H, ArH); 7.9 (t, 1H, ArH); ^{13}C NMR (300 MHz in $CDCl_3$, TMS at 0 ppm): 43.1, 59.1, 121-126; anal calcd. (%) for $C_9H_9NS_3O$: C, 44.42; H, 3.72; N, 5.75; found. (%): C, 44.36; H, 3.57; N, 5.78.

Compound 3c: ^{1}H NMR (300 MHz in $CDCl_3$, TMS at 0 ppm): δ 3.2(m, 2H, CH_2); 3.5 (m,1H, CH); 3.7-4.0 (m, 2H, CH_2); 7.2-7.8 (m, 8H, ArH); ^{13}C NMR (300 MHz in $CDCl_3$, TMS at 0 ppm): 44.2, 121-129; anal calcd. (%) for $C_{16}H_{15}NS_4O_3$: C, 44.91; H, 3.10; N, 6.16; found. (%): C, 44.56; H, 2.89; N, 5.88, ^{1}H NMR (300 MHz in $CDCl_3$, TMS at 0 ppm) data after deuterium exchange: δ 3.2 (m, 2H, CH_2); 3.5 (m, 1H, CH); 3.80 (dd, 1H, CH_2, J = 7.2 and 12.6 Hz); 4.02 (dd, 1H, CH_2, J = 3.6 and 12.6 Hz); 7.2-7.8 (m, 8H, ArH).

The detailed study of the ^{1}H NMR spectra reveals that the methylene proton adjacent to the -OH group undergoes shielding or deshielding depending on the orientation of the proton with respect to the lone pair of oxygen. The multiplets observed in the region of δ 3.80 and 4.02 corresponds to this effect. The existence of the multiplet clearly signifies the coupling of the -OH proton with the methylene proton. The occurrence of a triplet at δ 5.19 corresponding to the -OH proton clearly establishes the coupling of the methylene proton. Further, we have subjected the compound to deuterium exchange reaction by taking the spectra in presence of a small amount of D_2O. It was observed that the exchange rate is significantly low and with respect to the exchange the multiplet for the methylene proton which is clearly changed into the much expected double doublet with the requisite J-value 7.2, 12.6, 3.6 and 12.6 Hz. The slow exchange rate is attributed to the fact that the -OH proton is bonded to the nitrogen atom of the benzothiazole nucleus through a weak interaction such as hydrogen bond. The molecular model study of the compound **3**, which reveals the proximity of the -OH proton to the nitrogen atom of the benzothiazole ring provides the probable hydrogen bond formation in the compound. However, this is not being seen when we consider the molecule **3a** with ethanol moiety being the part of the unsymmetrical disulfide.

Conclusion

In this investigation, synthesis of unsymmetrical disulfides 2,3-*bis*(2-benzothiazolyldisulfanyl)-1-propanol (**3**) using a simple, general reaction scheme has been explored. The molecular model study of the compound **3** reveals the proximity of the -OH proton to the nitrogen atom of the benzothiazole ring thus providing the scope for probable hydrogen bond formation in the compound. In recent research, the existence of either intermolecular hydrogen bonding forming an array of compounds or intramolecular hydrogen bonding is interesting because this can be helpful in construction of electronic devices. Hence the scope of the present investigation provides an opportunity for adopting a simple general scheme of reaction procedure for the synthesis of all type of unsymmetrical disulfides.

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REFERENCES

1. A. Rana, N. Siddiqui and S.A. Khan, *Ind. J. Pharm. Sci.*, **69**, 10 (2007).
2. S. Hout, N. Azas, A. Darque, M. Robin, C. Di Giorgio, M. Gasquet, J. Galy and P. Timon-David, *Parasitology*, **129**, 525 (2004).
3. S.I. Baskin, D.W. Porter, G.A. Rockwood, J.A. Romano Jr., H.C. Patel, R.C. Kiser, C.M. Cook and A.L. Ternay Jr., *J. Appl. Toxicol*., **19**, 173 (1999).
4. H.Y. Fu, X.-Y. Sun, X.-D. Gao, F. Xiao and B.X. Shao, *Synth. Met*., **159**, 254 (2009).
5. Y. Qian, *Dyes Pigm*., **76**, 277 (2008).
6. A. Hasgash, D. Lyn Kirkpatrick, J.S. Lazo and L.H. Block, *J. Pharm. Sci*., **91**, 1686 (2002).
7. K.F. Faull, J. Higginson, A.J. Waring, J. Johnson, J. Jo, J.P. Whitelegge, R.L. Stevens, C.B. Fluharty and A.L. Fulharty, *Arch. Biochem. Biophys*., **376**, 266 (2000).
8. E. Brzezinska and A.L. Ternay Jr., *J. Org. Chem*., **59**, 8239 (1994).