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N,N'-THIOBISPHTHALIMIDE - A USEFUL SULFUR-TRANSFER REAGENT[1]

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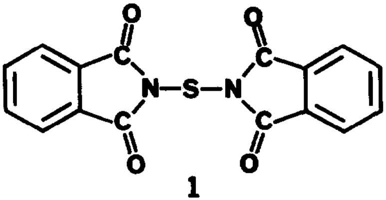
It has recently been demonstrated that alkyl and aryl thioimides act as efficient sulfur-transfer agents. They have been found to react with thiols[2a,b,c], hydrodisulfides[2b], and alkoxides[3] to give disulfides, trisulfides and sulfenate esters respectively. Furthermore, they generate sulfenamides when treated with primary[4] or secondary[4,5] amines. Primary amines have also been shown to react with thioimides to give N-thio-N'-diamides[4,6]. This dichotomy of behaviour in the case of primary amines is under continued investigation.

The above findings prompted us to study the sulfurizing properties of N,N'-thiobisphthalimide (1). We now wish to report that this stable and easily prepared compound[7] reacts with two moles of piperidine or morpholine to afford excellent (88%) yields of the corresponding N,N'-thiobisamines (2a and b). When only one mole of piperidine was used, the N-aminothiophthalimide (3) was obtained in 75% yield. Attempts to obtain unsymmetrical thiobisamines by the treatment of (3) with a second, different amine have heretofore been unsuccessful due to simultaneous disproportionation to mixtures containing the symmetrical counterparts, as shown by gas chromatography.



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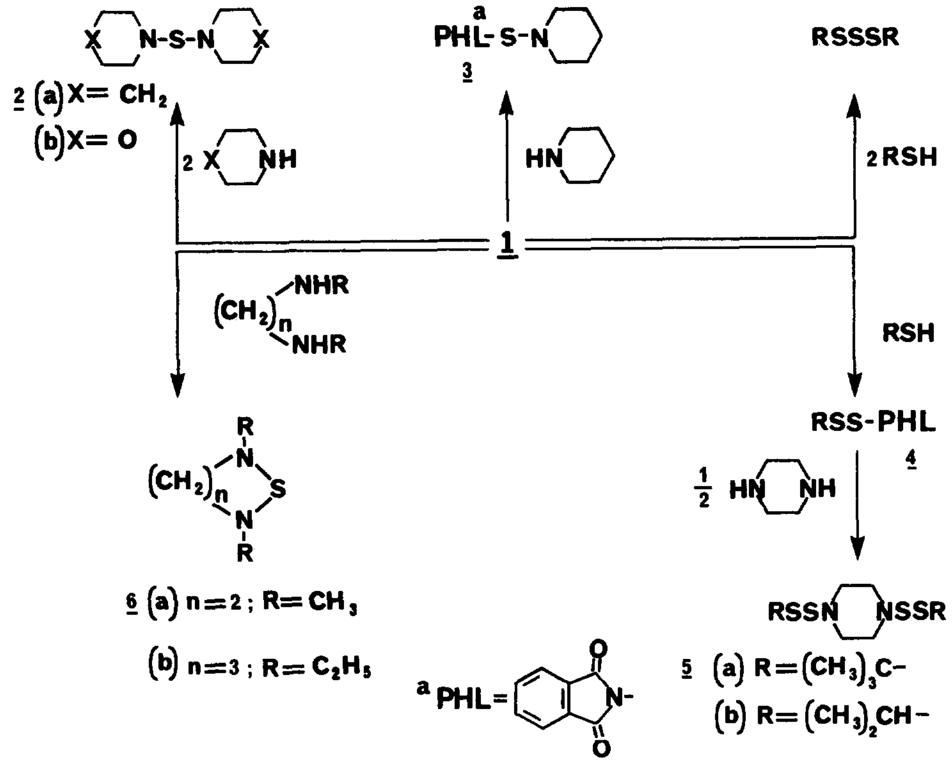
It has also been shown recently that (1) reacts with two moles[8] or with one mole[9] of thiol to afford trisulfides and alkyl phthalimido disulfides (4) respectively. We find that t-butyl and i-propyl phthalimido disulfides react with piperazine to give 87 and 91% yields of the corresponding bisthiosulfenamides (5a and b) respectively.

Furthermore, the sulfur-transferring ability of (1) provides a clean, rapid means of cyclizing secondary ethane and 1,3-propane diamines to the corresponding 1,2,5-thiadiazolidine and 1,2,6-perhydrothiadiazine derivatives (6a and b) respectively. High yields (6a: 70%; 6b: 90%) and absence of concomitant polymer formation make (1) a convenient sulfurizing agent for this purpose. These advantages are generally not afforded by other agents such as sulfur dichloride. The above reactions are illustrated below.



In a typical experiment, 10 mmol of (1) or (4) were stirred with an equivalent amount of amine in refluxing benzene or in methylene chloride at room temperature for 1 to 18 hrs. Phthalimide was then filtered and the filtrate evaporated to dryness. Trituration with pentane or carbon tetrachloride, followed by filtration of the remaining phthalimide (yield: ∿95%) and evaporation of the solvent afforded the desired product. Further purification *via* crystallization was performed as necessary. Purification of (6b) was effected by dissolving the product in petroleum ether and stirring for several minutes with alumina, followed by decantation and evaporation of the solvent. The structures of all products were consistent with their nmr spectra, and all new compounds gave satisfactory elemental analyses. In addition, mass spectrometry showed intense parent peaks for (6a and b) at m/e 118 and 160 respectively. The products, reaction conditions and physical data are listed below.

Products of the Reaction of (1) and (4) with Amines

Compound[a]	Solvent[b]	Rxn. time (hrs.)	(mp) or bp/mm	Yield %
2a	C_6H_6	8.5	(75-76°)[c]	88
2b	C_6H_6	12	(125-127°)[d]	88
3	C_6H_6	6.5	(178-179°)	75
5a	C_6H_6	3.5	(134-135°)	87
5b	C_6H_6	18	(112-113°)	91
6a	CH_2Cl_2	1.5	(125-127°)	70
6b	CH_2Cl_2	1	53-55°/1.2	90

a) Compounds (5a and b) were prepared from (1) *via* (4) and their yields as reported above are based on (4). All other compounds were prepared directly from (1). b) Reactions performed in benzene were refluxed, those in methylene chloride were at room temperature. c) lit[10] 75-76°. d) lit[11] 125-126°.

It can thus be seen that the sulfurizing ability of (1) provides a rapid, clean, and efficient method of preparing N,N'-thiobisamines, aminothiophthalimides and thiosulfenamides. In addition, (1) affords a convenient route for the synthesis of heterocycles containing the $\rangle N{-}S{-}N\langle$ moiety *via* the cyclization of diamines. The reactions of (1) with other nucleophiles is currently being investigated.

References

1) D.N. Harpp and T.G. Back, Organic Sulfur Chemistry, Part XIV. For Part XIII see *Tetrahedron Letters*, (in press).

2) (a) K.S. Boustany and A.B. Sullivan, *Tetrahedron Letters*, 3547, (1970); (b) D.N. Harpp, D.K. Ash, T.G. Back, J.G. Gleason, B.A. Orwig, W.F. VanHorn, and J.P. Snyder, *Tetrahedron Letters*, 3551, (1970); (c) D.N. Harpp and T.G. Back, *J. Org. Chem.*, *36*, 3828, (1971).

3) D.H.R. Barton, G. Page, and D.A. Widdowson, *Chem. Commun.*, 1466, (1970).

4) D.N. Harpp and T.G. Back, *Tetrahedron Letters*, (in press).

5) K.S. Boustany, *Chimia*, 396, (1970).

6) K.S. Boustany and J.P. Vander Kooi, *Tetrahedron Letters*, 4983, (1970).

7) M.V. Kalnins, *Can. J. Chem.*, *44*, 2111, (1966).

8) D.N. Harpp and D.K. Ash, *Intl. J. Sulfur Chem.*, (in press); A.B. Sullivan and K.S. Boustany, *Intl. J. Sulfur Chem.*, (in press).

9) D.N. Harpp and D.K. Ash, *Intl. J. Sulfur Chem.*, *1* 57, (1971).

10) R.G.R. Bacon and R.S. Irwin, *J. Chem. Soc.*, 5079, (1960).

11) E.S. Blake, *J. Am. Chem. Soc.*, *65*, 1267 (1943).

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