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A GENERAL SYNTHESIS OF SULFENAMIDES[1]

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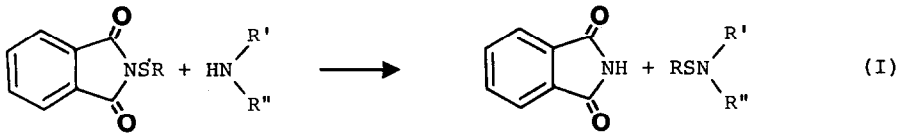
It has recently been shown that thiophthalimides (sulfenimides) (1) undergo displacement of phthalimide when treated with a variety of nucleophiles: thiols[2], hydrodisulfides[2b], alkoxides[3] and phosphines[4] result in the formation of disulfides, trisulfides, sulfenate esters and N-alkylphthalimides. We wish to report that both primary and secondary amines also react with thiophthalimides to give excellent yields (81-100%) of the corresponding sulfenamides (2), (eq. I).



1 2 (I)

Although these compounds may be produced by the reaction of a sulfenyl halide with an amine[5], this method generally suffers from low yields and side reactions when alkyl sulfenyl halides are used. Alkyl sulfenamides have been prepared by treating thiolsulfonates with amines[6]; however, simple alkyl and aryl thiolsulfonates are reported to be unreactive towards aromatic amines[6]. We find that phenyl thiophthalimide reacts with aniline to give sulfenamide (7) in 82% yield.

When benzylamine was allowed to react with i-propyl thiophthalimide, ring opening rather than displacement of the phthalimide group occurred. This anomalous result may be due to the steric hindrance of the i-propyl group, thus preventing attack at the adjacent sulfur atom. The product (10) was isolated in 73% yield.

All compounds obtained are listed in Table I, along with the reaction conditions, yields, and physical data.

A general procedure is as follows: the thiophthalimide (10 mmol) and an equivalent of the amine were stirred (0.5-15.5 hrs.) in 50 ml of an appropriate solvent, either at reflux or at room temperature. Non-polar solvents were preferred as precipitation of phthalimide was facilitated. Phthalimide was then filtered (ca. 90%) and the filtrate was evaporated in vacuo. The resulting residue was then purified (as necessary) by crystallization or distillation. In the case of sulfenamide (7) the solvent was evaporated and the residue was taken up in pentane. Phthalimide was removed by filtration, washed with pentane, and the concentrated pentane solution was chromatographed over alumina to provide the product.

The structures of all products were consistent with their nmr spectra and all new compounds gave satisfactory elemental analyses.

It is seen that alkyl and aryl sulfenamides are readily and cleanly prepared in excellent yield by the reaction of amines with the corresponding thiophthalimide derivatives. The reaction is especially attractive in view of the stability and ease of preparation of the precursor thiophthalimides.

Table I

Products Derived From the Reaction of Amines with Thiophthalimides

No	Thiophtha-limide	Amine	Product	Solvent Rxn time (hr)	(mp) or bp/mm	lit (mp) or bp/mm	Yield
3	$C_6H_5CH_2S$-PHL	morpholine	$C_6H_5CH_2SN\langle\rangle O$	C_6H_6[b](10.5)	(72-74)	(74-76)[6]	90
4	EtS-PHL	N-methyl-n-butylamine	$EtSN(CH_3)(n\text{-}Bu)$	Et_2O[c](1)	70-71 /21	-	91
5	n-BuS-PHL	piperidine	$n\text{-}BuSN\langle\rangle$	Et_2O[c](1)	43-44 /0.15	59-60[7] /0.5	100
6	$C_6H_5CH_2S$-PHL	cyclohexyl-amine	$C_6H_5CH_2SNHC_6H_{11}$	CH_2Cl_2[c](2)	(41-42)	-	87
7	C_6H_5S-PHL	aniline	$C_6H_5SNHC_6H_5$	EtOH[b](6)	(57-59)	(53-55)[8]	82
8	EtS-PHL	piperazine	$EtSN\langle\rangle NSEt$	C_6H_6[b](0.5)	(49-50)	-	90
9	$C_6H_5CH_2S$-PHL	piperazine	$C_6H_5CH_2SN\langle\rangle N\text{-}SCH_2C_6H_5$	C_6H_6[b](15.5)	(140-142)	-	81
10	i-PrS-PHL	benzyl-amine	$o\text{-}C_6H_4(CONHS\text{-}i\text{-}Pr)(CONHCH_2C_6H_5)$	Et_2O[c](1.5)	(143-144)	-	73

(a) PHL = phthalimide

(b) reflux

(c) room temperature

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