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THE PREPARATION OF N-(ALKYL AND ARYLSULFINYL)-PHTHALIMIDES. A NEW CLASS OF SULFINYL-TRANSFER REAGENTS[1]

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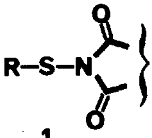
It has recently been found that alkyl and aryl thioimides 1 act as efficient sulfur-transfer agents. They react with thiols[2a,b,c], hydrodisulfides[2b], alkoxides[3], amines[4], and arenesulfinates[5] to give disulfides, trisulfides, sulfenate esters, sulfenamides and thiolsulfonates respectively. Moreover, N,N'-thiobisphthalimide (2) generates N,N'-thiobisamines when treated with amines[6] and efficiently cyclizes 1,2 and 1,3-diamines to the corresponding 1,2,5-thiadiazolidines and 1,2,6-perhydrothiadiazines respectively[6]. In addition, it has been reported that N-(phenylthio)-imides act as sulfurizing agents with active methylene compounds[7].



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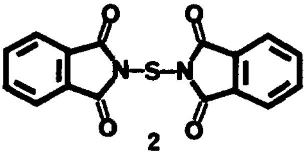

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In view of the successful preparation of a wide variety of sulfenyl compounds with the above methods, we attempted to synthesize N-(alkyl and arylsulfinyl)-phthalimides 3 for possible use as sulfinyl-transfer reagents. We wish to report that thiophthalimides 4 may be conveniently oxidized to the corresponding sulfinyl analogues in high yield (80-100%) by treatment with one equivalent of m-chloroperbenzoic acid.

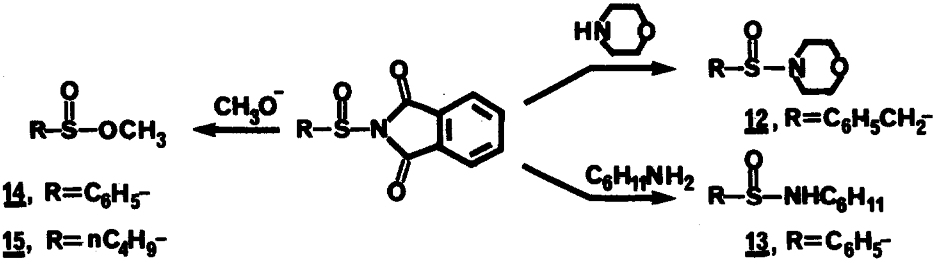
4 3

The products obtained by this method are listed in Table I, along with yields and physical data. All compounds gave satisfactory elemental analyses and had nmr spectra consistent with their structures.

A general procedure for their preparation is as follows: A solution of 10 mmol of the peracid (assumed 85%) in 20 ml of chloroform was added dropwise over 0.5 hr. to a cooled (0-5°) solution of 10 mmol of the thiophthalimide in 40 ml of chloroform. Stirring and cooling was continued for 0.5-1 hr. The solution was then washed with 5% sodium bicarbonate solution, dried over anhydrous sodium sulfate, and the solvent evaporated to provide the sulfinylphthalimide. Alternately, the chloroform solution was evaporated to dryness and the residue was stirred several minutes with 30 ml of ether. Filtration of the insoluble product effected efficient separation from the highly soluble m-chlorobenzoic acid. In the case of unhindered sulfinylphthalimides (e.g. 5 and 6), the latter procedure is the method of choice as contact with bicarbonate solution causes rapid decomposition. Further purification via crystallization was performed as necessary. Sulfinylphthalimides may be stored for months at -10° with no detectable decomposition.

Our preliminary investigations have also shown that sulfinylphthalimides are extremely efficient sulfinyl-transfer reagents. Reaction of 7 and 8 with one equivalent of morpholine or cyclohexylamine gave the corresponding sulfinamides 12 and 13 in yields of 94% and 89% respectively (eq.II).

Similarly, 8 and 9 reacted with sodium methoxide to give sulfinate esters 14 and 15 in yields of 90% and 80%.



The products of these reactions, as well as reaction conditions, yields, and physical data are listed in Table II. All products had nmr spectra consistent with their structures and in addition, 12 gave a satisfactory elemental analysis.

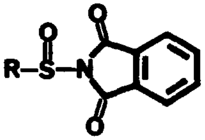
Sulfinamides 12 and 13 were prepared by stirring equivalent amounts of the reactants in benzene. On completion of the reaction, phthalimide was filtered and the solvent was evaporated. The residue was triturated with carbon tetrachloride and additional phthalimide (total: 90-95%) was filtered. The solvent was then evaporated and the product was purified by crystallization.

Sulfinate esters 14 and 15 were obtained by stirring the corresponding sulfinylphthalimide with 1.0 equivalent of sodium methoxide in methanol. The methanol was then evaporated and the residue washed well with pentane. Evaporation of the pentane provided the product as a clear oil.

It has been shown that N-(alkyl and arylsulfinyl)-phthalimides are conveniently prepared in excellent yield by oxidation of the corresponding thiophthalimide with m-chloroperbenzoic acid. Furthermore, sulfinylphthalimides behave as efficient sulfinyl-transfer reagents as evidenced by the high yields of sulfinamides and sulfinate esters generated via treatment with amines and methoxide ion respectively. The use of sulfinylphthalimides in such reactions is especially attractive in view of the instability of conventional sulfinyl-transfer agents such as sulfinyl chlorides[9].

TABLE I

Preparation of Sulfinylphthalimides

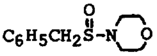
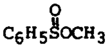


No	R	Yield %	mp
5	C_2H_5	85^a	132-134
6	CH_3	$91^{a,b}$	167-170
7	$C_6H_5CH_2$	96^c	154-155
8	C_6H_5	89^a	150-153
9	$n\text{-}C_4H_9$	$80^{a,d}$	87- 88
10	$t\text{-}C_4H_9$	100^c	133-136
11	$i\text{-}C_3H_7$	94^c	125-127

(a) Ether work-up; (b) The precursor is a new compound, mp 180-182°; (c) Work-up with bicarbonate solution; (d) A significant second crop was obtained by cooling the ether filtrate.

TABLE II

Reaction of Sulfinylphthalimides with Amines and Methoxide Ion

No.	Product	Solvent Rxn time (hrs)	Yield	(mp) or bp/mm	lit. (mp) or bp/mm
12		C_6H_6 $(1)^a$	94	(83-85)	
13	 $C_6H_5\overset{O}{\overset{\|}{S}}NHC_6H_{11}$	C_6H_6 $(0.5)^{b,c}$	89	(114-115)	(116)[8]
14	 $C_6H_5\overset{O}{\overset{\|}{S}}OCH_3$	CH_3OH $(0.5)^b$	90	d	
15	 $n\text{-}C_4H_9\overset{O}{\overset{\|}{S}}OCH_3$	CH_3OH $(0.5)^b$	80	84-85/12	72-73/10[9]

(a) Reflux; (b) Room temperature; (c) A solution of the sulfinylphthalimide was added dropwise over 10 min to the amine in benzene; (d) The product had ir and nmr spectra as well as refractive index identical to those of a genuine sample prepared by the method of Douglass[9]; tlc confirmed purity.

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