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REACTION OF A PHENOXYSULFOXONIUM SALT WITH NUCLEOPHILES

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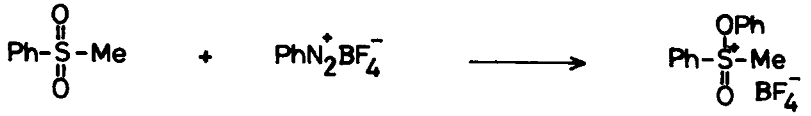
It has been shown that methylation of *p*-toluenesulfonpyrrolidide takes place on nitrogen and the resulting species can be used as an selective tosylating reagent.$^{1)}$ On the other hand, Whiting and his co-workers have reported that both sulfonamides and sulfones react with aryldiazonium salts to give the corresponding O-arylated compounds.$^{2)}$ We particularly interested in the reactivities of the O-arylated species in connection with those of the N-methylated species. We report here the reaction of the salt(2) prepared from methylphenylsulfone(1) with various nucleophiles.

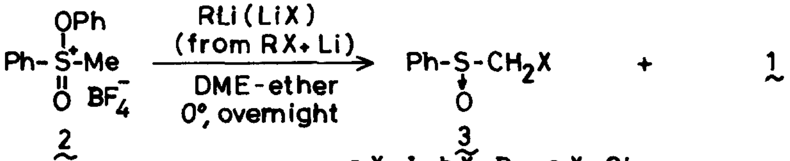


1 2

Expecting the reaction *via* the oxosulfonium ylide, 2 was treated with triethylamine or lithium diisopropylamide and the resulting mixture was subjected to the reaction with electrophiles but none of the desired products were obtained. So the direct nucleophilic reaction with alkyllithiums, dialkyl cupper lithiums, amines, thiols and alcohol was examined.

Reaction of 2 with alkyllithiums and dialkyl cupper lithiums

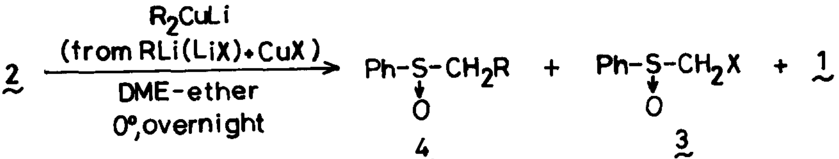
When 2 was treated overnight with methyllithium(*ca*. 3 mol. eq.) in dimethoxyethane-ether(*ca*. 4:1) at 0°, the iodomethyl sulfoxide(3a) was obtained in 70.9 % yield. The iodine introduced must be originated from lithium iodide produced in the preparation of methyllithium. In the same way, the reaction of 2 with ethyllithium prepared from ethyl iodide and lithium afforded the same product in high yield. However, when ethyl bromide was used to prepare ethyllithium, the yield of the corresponding bromo-compound(3b) decreased appreciably and furthermore, none of the chloro-compound(3c) was obtained when ethyl chloride was used. The same tendency was observed by the reaction with phenyllithium. The sulfone (1) was usually obtained, which could be formed by the hydrolysis of the remaining starting material(2) during work up.



a X=I, b X=Br, c X=Cl,

RLi	X used for RX	Products(%)	
		3	1
MeLi	I	70.9	—
EtLi	I	77.8	8.0
	Br	45.3	10.7
	Cl	—	43.4
PhLi	I	60.5	21.0
	Br	13.3	4.3

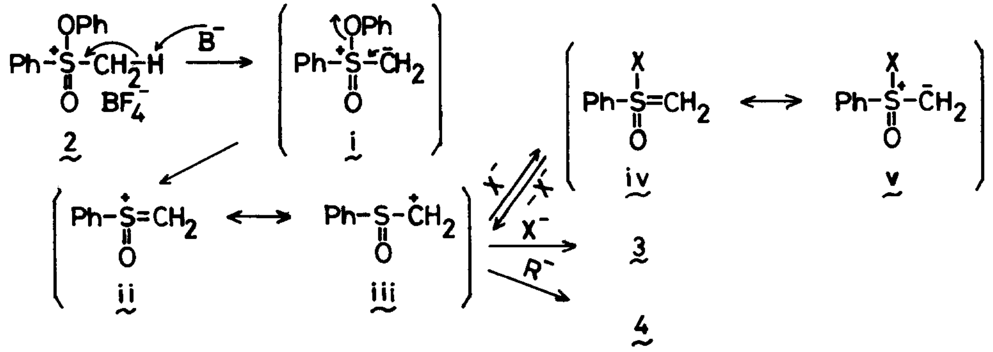
Then, the reaction of 2 with dialkyl cupper lithiums in dimethoxyethane-ether(*ca.* 3:1-2:1) was examined. Contrary to the above results, dimethyl cupper lithium prepared from methyl iodide, lithium and cuprous iodide afforded ethylphenyl sulfoxide(4a) in 69.3% yield. On the other hand, diethyl cupper lithium prepared from ethyl iodide afforded the iodomethyl sulfoxide(3a) in excellent yield(71.1%). When ethyl bromide or chloride was used to prepare diethyl cupper lithium, alkylation again took place to give phenylpropyl sulfoxide(4b) in 30.2% and 28.7% yields, respectively. Reactions of 2 with diphenyl cupper lithium also afforded the phenylated product(4c) in fair yields. These results show that the order of nucleophilicity in these particular reactions is roughly estimated as follows: Me_2CuLi, $Ph_2CuLi > I^- > Et_2CuLi > Br^- > Cl^-$.



a R=Me, b R=Et, c R=Ph; a X=I, b X=Br

R_2CuLi	X used for RX and CuX	Products(%)		
		4	3	1
Me_2CuLi	I	69.3	—	—
Et_2CuLi	I	—	71.1	16.6
	Br	30.2	—	ca.7
	Cl	28.7	—	ca.7
Ph_2CuLi	I	63.6	—	13.9
	Br	59.1	—	5.7

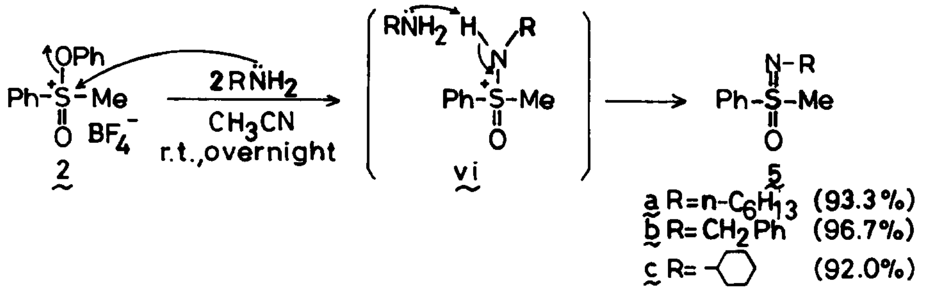
The mechanism of the formation of halo- and alkyl-sulfoxides(3 and 4) is considered as follows. The ylide(i) initially produced from 2 by the reaction of base is very unstable and phenoxide anion is spontaneously removed to afford a sulfoxonium ion(ii or iii), which reacts with nucleophiles affording the final product(3 or 4). There is another possibility that electron deficient sulfur



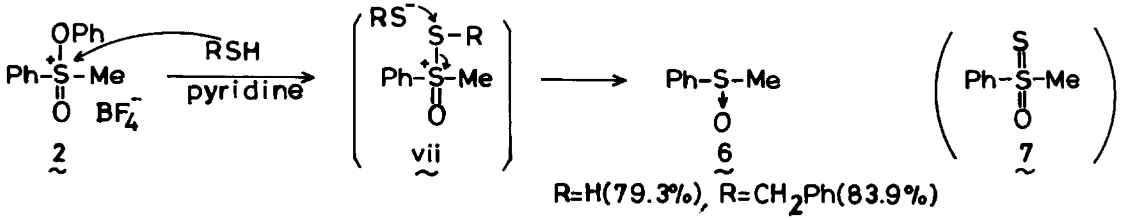
atom of ii may react with a halide anion to afford iv or v. However, it is reasonable to consider that even if they are formed, they are in equilibrium with ii or iii and hence the thermodynamically more stable products(3) are eventually accumulated. Anyway, the reason for the failure of an earlier attempt to trap the oxosulfonium ylide(i) is now apparent.

Reaction of 2 with amines, thiols and alcohol

When 2 molar eq. of primary amines such as *n*-hexyl, benzyl and cyclohexyl amines were used as a nucleophile, the different type of reaction took place and the corresponding N-alkyl sulfoximines(5a,b and c) were obtained in high yields. The particular feature of the present reaction is that the various N-substituted sulfoximines(5) can directly be obtained from 2.[3] However, the progress of the reaction is being governed by the basisity of amines, that is, a weak basic aniline did not react with 2.

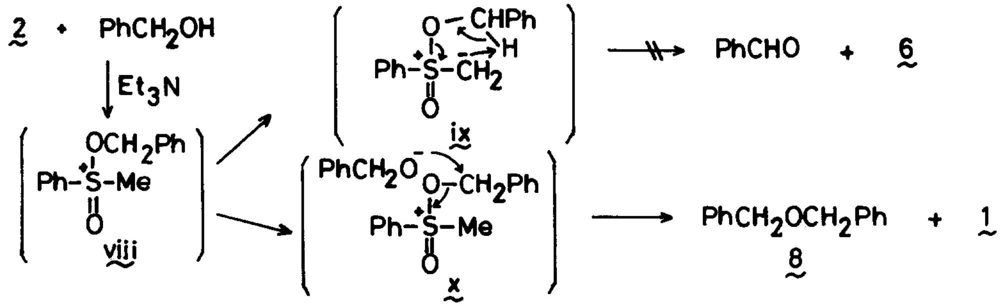


The reaction of 2 with liquid sulfur dioxide[4] in the presence of pyridine was then carried out expecting the formation of monothiosulfone(7),[5] but the product obtained was methylphenyl sulfoxide(6)(79.3% yield). The same type of



reaction occurred by treatment of 2 with benzylmercaptane to give 6 in 83.9% yield. Although the yield of the O-phenylation of 1 is unsatisfactory, the present method may be useful for the selective reduction of sulfone to sulfoxide without using any normal reducing reagent.

The salt(2) is structurally related to dimethylchloroxosulfonium salt which is used as an oxidizing reagent of alcohols.$^{6)}$ Expecting such oxidation, benzyl alcohol was treated with 2 in the presence of triethylamine. However, no oxidation took place but dibenzyl ether(8) was obtained in 43% yield.



These data clearly show that amine, mercaptane and alcohol attacked directly on sulfur of 2 affording the salts(vi, vii and x). The resulting compounds are still reactive enough and again react *in situ* with the second molecule of nucleophiles affording the final products. It is especially interesting that the sites attacked by nucleophiles are particular to each intermediary salt giving different type of products.

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2) G. R. Chalkley, D. J. Snodin, G. Stevens, M. C. Whiting, *J. Chem. Soc. (C)*, 1970, 682.
3) *cf.* Previously N-alkyl sulfoximines have been prepared by alkylation of the corresponding N-unsubstituted sulfoximines by Meerwein reagent or formic acid-aldehyde(or ketone): C. R. Johonson, M. Haake, C. W. Schroeck, *J. Am. Chem. Soc.*, 92, 6594(1970); H. Schmidbaur, A. Kammel, *Chem. Ber.*, 104, 3234(1971); T. R. Williams, R. E. Booms, D. J. Cram, *J. Am. Chem. Soc.*, 95, 7424(1973). When R in 5 are sufficiently bulky, the ylides obtained from them after N-alkylation followed by base treatment are expected to have unique reactivity towards sterically hindered electrophiles.
4) *cf.* T. Ueda, S. Shibuya, *Chem. Pharm. Bull.(Tokyo)*, 22, 930(1974).
5) *cf.* G. Höfle, J. E. Baldwin, *J. Am. Chem. Soc.*, 93, 6307(1971).
6) E. J. Corey, C. U. Kim, *Tetrahedron Letters*, 1973, 919.

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