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Reaction of Sulfilimine and Sulfonium Ylide with Hydroxide or Methoxide Ion in Methanol

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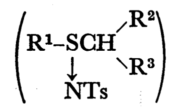
The reactions of dialkyl and alkyl aryl *N-p*-tosylsulfilimines with hydroxide or methoxide in methanol afforded either *S*-substitution products or Pummerer type products or a mixture of both, their distribution being dependent on the structure of the sulfilimine. From the results of analyses, the mechanisms of the formation of these products are discussed. A similar alkaline methanolysis of sulfonium ylides was also investigated.

Cram and his co-workers investigated the hydrolysis of methyl *p*-tolyl *N-p*-tosylsulfilimine with sodium hydroxide in methanol to afford the corresponding sulfoxide in a high yield and suggested the reaction to proceed *via* the nucleophilic attack of hydroxide anion on *S*(III) atom.[1] We found that a similar alkaline treatment of cyclic *N-p*-tosylsulfilimines gave α-methoxysulfides as the main product without forming any detectable amount of the corresponding sulfoxides.[2] The marked difference in the mode of reaction by the change of the sulfilimine is of interest, and deserves further investigation with various sulfilimines in order to clarify the nature of the two reactions, the substitution on *S*(III) atom and the Pummerer type rearrangement. We have carried out the alkaline hydrolyses of various sulfilimines with both hydroxide and methoxide in methanol.

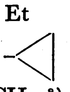
Results and Discussion

Reaction of Dialkyl or Alkyl Aryl N-p-*Tosylsulfilimines with Potassium Hydroxide in Methanol.* The reaction was carried out as follows: A mixture of a *N-p*-tosylsulfilimine with 20 mol excess of potassium hydroxide in methanol was kept for 24 hr at room temperature. The products were then isolated and identified by comparing their IR and NMR spectra with those of authentic samples. The yields of products are summarized in Table 1. The scheme of the reaction is as follows.

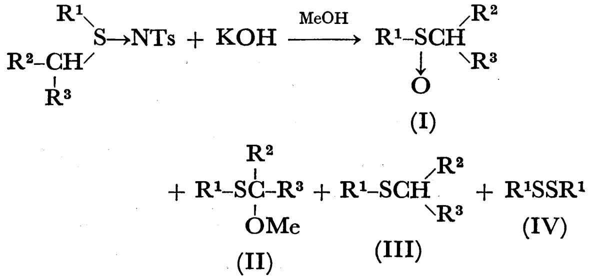
Table 1. Reaction of dialkyl or alkyl aryl *N-p*-tosylsulfilimines with potassium hydroxide in methanol for 24 hr at room temperature



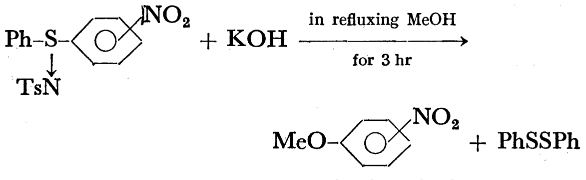
$\left(R^1\text{-}\overset{\downarrow}{S}CH(R^2)(R^3)\,\text{NTs}\right)$

Sulfilimines			Products and yields			
R^1	R^2	R^3	I	II	III	IV
Me	H	H	56	—		
n-Pr	H	H	trace	45		
n-Bu	H	H	trace	41		
Ph	H	H	98	trace	trace	—
Ph	H	Me	27	45	trace	trace
p-$MeOC_6H_4$	H	Me	52	38	trace	ttace
Ph	H	Et	26	42	6	8
Ph	H		32	65	—	
Ph	$-CH_2CH_2-$[a)]		96	—	—	
Ph	Me	Me	3	53	10	21
Ph	H	Ph[b)]	9	44	12	16

a) This reaction was carried out by refluxing methanol for 24 hr. b) A trace amount of benzaldehyde was detected.

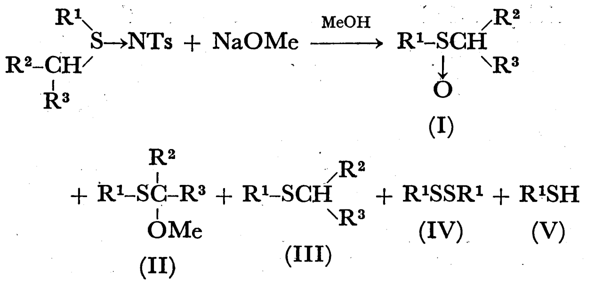


Reaction of Diaryl N-p-*Tosylsulfilimines with Potassium Hydroxide in Methanol.* Diphenyl *N-p*-tosylsulfilimine did not react even under refluxing with its alkaline methanol solution for 48 hr. However, *o*- or *p*-nitrophenyl phenyl *N-p*-tosylsulfilimine gave *o*- or *p*-nitroanisole in a quantitative yield as shown below.



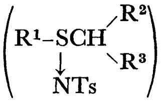
quantitative yield

Reaction of Alkyl Phenyl N-p-*Tosylsulfilimines with Sodium Methoxide in Methanol.* The reactions of alkyl phenyl *N-p*-tosylsulfilimines with sodium methoxide were carried out in methanol at 40—50 °C for 20—35 hr. The distributions of products are summarized in Table 2.



The following results were obtained. 1) The treatment of dimethyl, methyl phenyl and cyclopropyl phenyl sulfilimines with potassium hydroxide in methanol gave

Table 2. Reaction of alkyl phenyl *N*-*p*-tosylsulfilimines with sodium methoxide in methanol

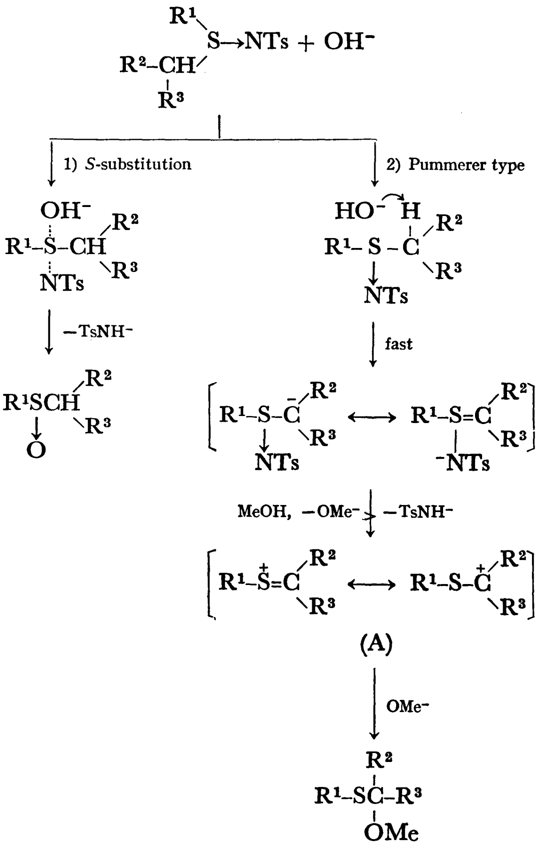


$\left(\begin{array}{l}\mathrm{R^1\text{-}SCH}\begin{smallmatrix}\mathrm{R^2}\\ \mathrm{R^3}\end{smallmatrix}\\ \quad\downarrow\\ \quad\mathrm{NTs}\end{array}\right)$

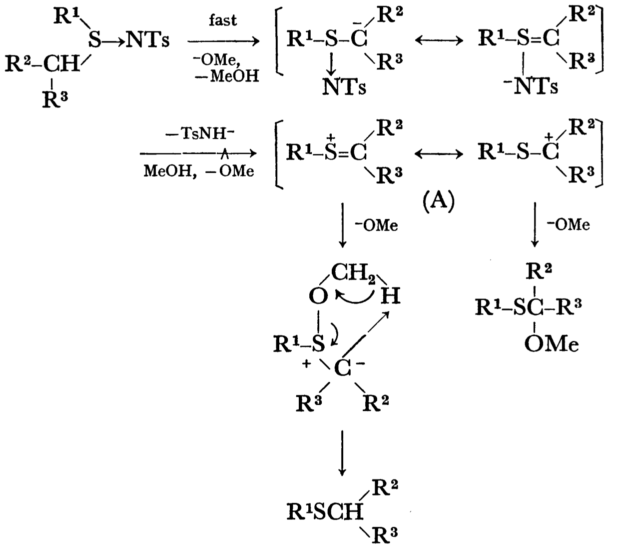
Sulfilimines			Reaction conditions		Products and Yields (%)				
R¹	R²	R³	Time (hr)	Temp. (°C)	I	II	III	IV	V
Ph	H	H	35	50	trace	9	70	—	trace
Ph	H	Me[a)]	35	50	trace	62	22	—	5
Ph	Me	Me	35	50	trace	25	trace	61	10
Ph	Me	Me[b)]	20	40	trace	32	trace	19	trace
Ph	H	Ph[c)]	35	50	trace	58	trace	34	4

a) Phenyl vinyl sulfide was isolated in 5% yield. b) 42% sulfilimine was recovered. c) Benzaldehyde was obtained in 20% yield.

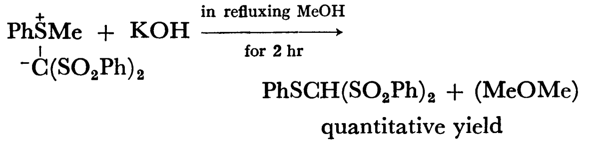
only the substitution products, *i.e.*, the corresponding sulfoxide. 2) A similar treatment of sulfilimines having α-ethyl, *n*-propyl or *i*-propyl groups gave both the sulfoxides and the Pummerer type rearranged products (α-methoxysulfides). The yield of the Pummerer type rearranged product increased in expense of the substitution product, the sulfoxide, with increasing bulkiness of alkyl substituents. 3) In the reactions with methoxide ion, however, the major products were the Pummerer type rearranged products and the reduced sulfides. 4) Diphenyl *N*-*p*-tosylsulfilimine did not react even under treatment with potassium hydroxide in refluxing methanol for 48 hr, while *o*- or *p*-nitrophenyl phenyl *N*-*p*-tosylsulfilimines reacted with potassium hydroxide readily affording unexpectedly either the *o*- or *p*-nitroanisole quantitatively. Thus, except for diaryl *N*-*p*-tosylsulfilimines, most sulfilimines react smoothly in alkaline methanol giving either the *S*(III)-substitution products or the Pummerer type rearrangement products or both. Both steric and electronic effects appear to control the reaction paths. In the case of nucleophilic attack on *S*(III) atom, *viz.*, route (1), the steric hindrance of alkyl group in the approach of hydroxide ion on *S*(III) atom plays an important role. Thus the yield of the sulfoxide in the series of alkyl phenyl sulfilimines, $\left(\begin{array}{l}\mathrm{PhSCH}\begin{smallmatrix}\mathrm{R^2}\\ \mathrm{R^3}\end{smallmatrix}\\ \quad\downarrow\\ \quad\mathrm{NTs}\end{array}\right)$, falls in the order: Me(R^2,R^3; H,H)≫Et (R^2,R^3; H,Me)~*n*-Pr (R^2,R^3; H, Et)>*i*-Pr (R^2,R^3; Me,Me). This postulate also explains the higher reactivity of methyl phenyl sulfilimine as compared to cyclopropyl phenyl derivative and the lack of reactivity of diphenyl derivative. Since the Pummerer type rearrangement (2) is known to proceed *via* an E_1CB process the rate of the reaction depends on the stability of the postulated intermediate (A). Apparently (A) formed during the Pummerer rearrangement is stabilized mostly by the *S*(II) atom bonded to the α-carbon atom since the cyclopropylmethyl phenyl derivative afforded the corresponding cyclopropyl-α-methoxymethyl phenyl sulfide and not the ring enlargement or fission products. However the intermediary carbonium ion (A) could be stabilized further by the alkyl or aryl group attached to the α-carbon, thus yielding the Pummerer type products from alkyl phenyl *N*-*p*-tosylsulfilimines, $\left(\begin{array}{l}\mathrm{PhSCH}\begin{smallmatrix}\mathrm{R^2}\\ \mathrm{R^3}\end{smallmatrix}\\ \quad\downarrow\\ \quad\mathrm{NTs}\end{array}\right)$, in the order: *i*-Pr ($R^2$,$R^3$; Me,Me)>$PhCH_2$ (R^2,R^3; H,Ph)~Et (R^2,R^3; H,Me)~*n*-Pr (R^2,R^3; H,Et)≫Me (R^2,R^3; H,H), which is in line with the order of ability to stabilize the carbonium ion by hyperconjugation.



Apparently *o*- or *p*-nitroanisole is formed *via* an aromatic S_N reaction of the corresponding sulfilimine by the attack of methoxide anion on the phenyl carbon atom, with phenylsulfenamide as leaving group. When methoxide ion is used instead of hydroxide, the exchange of methoxide with NTs group might take place to form the alkoxy sulfonium salt from which both the Pummerer rearrangement and the reduction take place analogously as in the case of alkoxy sulfonium salt[3] as shown below.

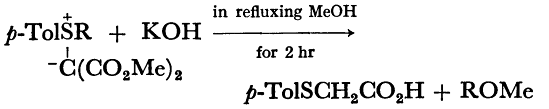


Reaction of Sulfonium Ylide with Potassium Hydroxide in Methanol. The hydrolysis of the sulfonium ylide with hydroxide proceeds *via* an entirely different route from that of the sulfilimine. When methyl *p*-tolyl or benzyl bis(methoxycarbonyl)sulfonium methylides or methyl phenyl bis(phenylsulfonyl)sulfonium methylide was refluxed with an excess potassium hydroxide in methanol, quantitative formation of *p*-toluenethioacetic acid or bis(phenylsulfonyl)methyl phenyl sulfide and benzyl methyl ether or dimethyl ether was observed, while the diphenyl derivative gave diphenyl sulfide in a poor yield.



$$\mathrm{Ph}\underset{^{-}\mathrm{C(SO_2Ph)_2}}{\overset{+}{\mathrm{S}}}\mathrm{Me} + \mathrm{KOH} \xrightarrow[\text{for 2 hr}]{\text{in refluxing MeOH}} \mathrm{PhSCH(SO_2Ph)_2} + (\mathrm{MeOMe})$$

quantitative yield

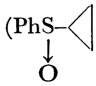


$$p\text{-}\mathrm{Tol}\underset{^{-}\mathrm{C(CO_2Me)_2}}{\overset{+}{\mathrm{S}}}\mathrm{R} + \mathrm{KOH} \xrightarrow[\text{for 2 hr}]{\text{in refluxing MeOH}} p\text{-}\mathrm{TolSCH_2CO_2H} + \mathrm{ROMe}$$

R	products yields	
Me	quantitative	—
CH_2Ph	quantitative	quantitative

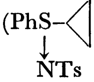
The mechanism completely differs from that of the corresponding sulfilimine, the attacking site by methoxide being the α-carbon atom in this case. Although the mechanisms of all these reactions are by no means unambiguously clarified, our results indicate that the reactions of trivalent sulfur compounds are very sensitive to the minor change in the structure of both the attached substituents on the trivalent sulfur atom and the attacking bases.

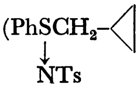
Experimental

Materials. Methanol was purified by the standard procedure. Potassium hydroxide was of special grade. Sodium methoxide, sulfides and disulfide were prepared by the usual procedures. α-Methoxysulfides were prepared by the reaction of the corresponding α-chlorosulfides[4] with sodium methoxide in methanol. Sulfoxides were prepared by treating the corresponding sulfides with hydrogen peroxide in acetic acid;[5] ( ; bp 137—138 °C/1 mmHg).

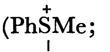
p-Toluenethioacetic acid was synthesized by first dissolving *p*-toluenethiol in an excess of aqueous sodium hydroxide, into which was then added a slight excess of chloroacetic acid; mp 93—94 °C (lit,[6] 94.0—94.4 °C).

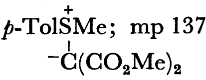
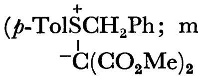
Preparation of Starting Materials. All the *N*-*p*-tosylsulfilimines were prepared as usual by the reaction of the corresponding sulfides with Chloramine-T.[7]

( ; mp 135.0—135.5 °C; Found: C, 60.11; H, 5.47; N, 4.36%. Calcd for $C_{16}H_{17}NS_2O_2$: C, 60.12; H, 5.33; N, 4.39%.)

( ; mp 117.5—118.0 °C; Found: C, 61.19; H, 5.82; N, 4.22%. Calcd for $C_{17}H_{19}NS_2O_2$: C, 61.22; H, 5.71; N, 4.20%.)

All the sulfonium ylides were synthesized by the reaction of the corresponding sulfides with diazo-compounds in the presence of copper sulfate catalyst.[8]

( $\mathrm{Ph}\underset{^{-}\mathrm{C(SO_2Ph)_2}}{\overset{+}{\mathrm{S}}}\mathrm{Me}$; decomp. 160.5—161.5 °C; Found: C, 57.14; H, 4.27%. Calcd for $C_{20}H_{18}O_4S_3$: C, 57.42; H, 4.31%.)

( $p\text{-}\mathrm{Tol}\underset{^{-}\mathrm{C(CO_2Me)_2}}{\overset{+}{\mathrm{S}}}\mathrm{Me}$; mp 137—138 °C) ( $p\text{-}\mathrm{Tol}\underset{^{-}\mathrm{C(CO_2Me)_2}}{\overset{+}{\mathrm{S}}}\mathrm{CH_2Ph}$; mp 154—155 °C)

Reaction of Dialkyl or Alkyl Aryl N-p-*Tosylsulfilimines with Potassium Hydroxide or Sodium Methoxide in Methanol.* About 10 mmol of each of the *N*-*p*-tosylfulfilimines was reacted with 20 mol excess of potassium hydroxide or sodium methoxide in methanol (40 ml). The reaction mixture was then neutralized with a 10% aqueous hydrochloric acid and the products were extracted with chloroform except in the case of dialkyl derivatives. In the case of dialkyl derivatives, after the solvents were evaporated, the products were extracted from the residue with chloroform. The products obtained were separated by chromatography through a silica-gel packed column and identified by comparing their IR and NMR spectra with those of authentic samples. The yields and products are given in Tables 1 and 2, respectively. In all the reactions, the corresponding *p*-tosylamide was obtained quantitatively.

Reaction of o- *or* p-*Nitrophenyl Phenyl* N-p-*Tosylsulfilimine with Potassium Hydroxide in Methanol.* About 10 mmol of *o*- or *p*-nitrophenyl phenyl *N*-*p*-tosylsulfilimine was heated with 20 mol excess of potassium hydroxide in refluxing methanol for 3 hr. The reaction solution was then poured into a large amount of water and acidified with 10% aqueous hydrochloric acid and the products were extracted with chloroform. The products obtained were separated by column chromatography and identified by comparing their IR and NMR spectra with those of authentic samples. Yields of *o*- or *p*-nitroanisole, *p*-tosylamide and diphenyl disulfide were quantitative.

Reaction of Bis(methoxycarbonyl)sulfonium Methylides or Bis(phenylsulfonyl)sulfonium Methylide with Potassium Hydroxide in Methanol. About 20 mmol of each of the sulfonium ylides was heated with 20 mol excess of potassium hydroxide for 2 hr in refluxing methanol (80 ml). The reaction solution was then neutralized with 10% aqueous hydrochloric acid and the products were separated by passing the chloroform extract through a silica-gel packed column. The products obtained were identified by comparing their IR and NMR spectra with those of authentic samples. In all the reactions yields of bis(phenylsulfonyl)methyl phenyl sulfide, *p*-toluenethioacetic acid and benzyl methyl ether were quantitative.

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