The Reaction of Sulfilimine with Phenyl Grignard Reagent*,[1]

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The reactions of diphenyl (I), phenyl benzyl (II), and phenyl methyl *N*-*p*-tosylsulfilimines (III) with phenylmagnesium bromide were carried out. (I) gave biphenyl and diphenyl sulfide in high yields. A tracer experiment with diphenyl sulfilimine-1-^{14}C revealed that the reaction proceeds *via* the initial formation of triphenylsulfonium salt upon which the attack of phenylmagnesium bromide affords the products. "Benzyne" mechanism is ruled out. (II) and (III) gave various compounds, the major products being α-phenylated sulfides which are presumed to be formed by the Pummerer type rearrangement initiated by the abstraction of α-proton by the Grignard reagent.

N-*p*-Tosylsulfilimines can generally be prepared by allowing the corresponding sulfides to react with chloramine-T[2] (sodium salt of *N*-chloro *p*-toluenesulfonamide). Spectroscopic analysis indicates that the sulfilimine has a semipolar S–N bond similar to the S–O bond in sulfoxides.[3] In contrast to the massive works on sulfoxides,[4] the chemical properties of sulfilimines have not been explored. Recently Cram *et al.*[5] and Johnson *et al.*[6] studied the stereochemistry of nucleophilic substitution reactions of sulfilimines while Petranek and Vecera investigated the sigmatropic rearrangement of allylic *N*-*p*-tosylsulfilimines.[7] We have also studied the substitution,[8] elimination,[9] E*i* reaction[10], and pyrolysis reactions of sulfilimines.[10] Since sulfilimines have a labile S–N bond they are as reactive as the corresponding sulfoxides, and are, therefore, good substrates for examining the possible reactions which occur on the trivalent sulfur atom. This paper describes a detailed account of the reaction of *N*-*p*-tosylsulfilimines with phenyl Grignard reagent.

Reaction of Diphenyl Sulfilimine with Phenylmagnesium Bromide. Diphenyl *N*-*p*-tosylsulfilimine was dissolved in anhydrous THF. Into the resulting solution was added 5 mol excess of phenylmagnesium bromide. When the mixture was allowed to stand at room temperature, no reaction occurred and the sulfilimine was recovered almost quantitatively. The mixture was therefore refluxed in an oil bath for several hours. The reaction mixture was then decomposed with water, and the products were isolated and identified as shown in Table 1.

Table 1. Products and yields of the reaction of $PhS(Ph)NTs^-$ with PhMgBr

Products	Yield (%)	
	A	B
PhSPh	trace	73
Ph–Ph		59
$TsNH_2$	trace	73
Recovered	quantitatively	20
$(Ph)_3S^+X^-$	not identified	not identified

A; Carried out at room temperature.
B; Carried out by refluxing in THF.

Contrary to expectation, the major products are biphenyl and diphenyl sulfide, no sulfonium salt being isolated. Both biphenyl and diphenyl sulfide are known to be obtained by the attack of phenyl anion on triphenylsulfonium salt[12] incipiently formed during the reaction. The mechanism of the reaction was investigated. In a previous paper, it was shown that sulfilimine has two attacking sites, *i.e.* S and N for nucleophiles.[13] If the attack of the Grignard reagent takes place on the sulfur (IV) atom (Path (A), Fig. 1), triphenylsulfonium salt might be formed as an incipient intermediate which is then attacked by another molecule of the Grignard reagent either at the *ortho* proton to form benzyne and diphenyl sulfide (Path (A)-(a)) or at the phenyl carbon attached to the sulfur atom to form directly biphenyl and diphenyl sulfide (Path (A)-(b)). If the attacking site is the sulfilimino nitrogen (Path (B)), diphenyl sulfide would be obtained directly while biphenyl would result from the reaction between *N*-phenyltosylamide and phenylmagnesium bromide. Another alternative path (Path (C)), would be the one which involves the initial attack of the Grignard reagent on the α-hydrogen atom of the sulfilimine giving

* Recently, Manya *et al.* reported the same sort of reaction. They obtained nearly the same results as ours but they could isolate the triphenylsulfonium salt. P. Manya, S. Sekera, and P. Rumpf, *Bull. Soc. Chim. Fr.*, **1971**, 286.

1) Sulfilimine and sulfoximine Part X. Part IX. K. Tsujihara, N. Furukawa, and S. Oae, *Tetrahedron*, in press (1971).
2) B. H. Nicolet and J. Willard, *Science*, **53**, 217 (1921).
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9) S. Oae, K. Tsujihara, and N. Furukawa, *ibid.*, **1970**, 2663.
10) H. Kobayashi, N. Furukawa, T. Aida, and S. Oae, *ibid.*, **1971**, 3109.
11) K. Tsujihara, A. Aida, N. Furukawa, and S. Oae, *ibid.*, **1970**, 3415.
12) K. K. Andersen and N. E. Papanikolaou, *ibid.*, **1966**, 5445.
13) B. S. Wildi, S. W. Taylor, and H. A. Potratz, *J. Amer. Chem. Soc.*, **73**, 1965 (1951).

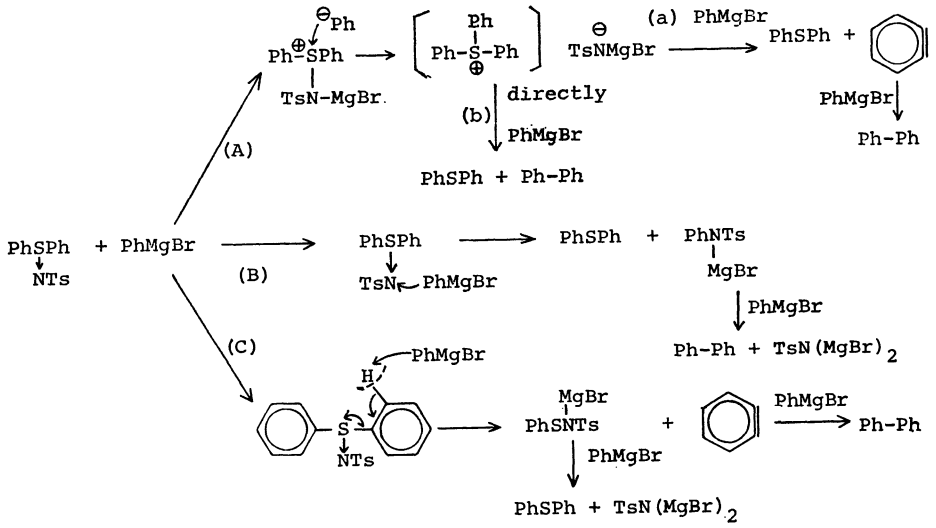


Fig. 1. The mechanism of the reaction.

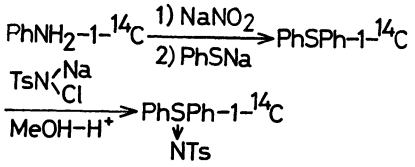


Fig. 2. The synthetic method of sulfilimine-1-^{14}C.

benzyne and *N*-phenylmercaptotosylamide upon which the attack of the Grignard reagent[14] produces diphenyl sulfide. The above four mechanistic schemes are shown in Fig. 1. In order to make a choice from the four mechanisms, the sulfilimine labeled with ^{14}C at 1-position was synthesized and allowed to react with phenylmagnesium bromide. The synthetic procedure to prepare the *N*-*p*-tosylsulfilimine-1-^{14}C is shown in Fig. 2. If the reaction proceeds *via* the formation of triphenylsulfonium ion (Path (A), either (a) or (b)), the original ^{14}C activity of the sulfilimine should be distributed between diphenyl sulfide and biphenyl, 2/3 (66.7%) for the sulfide and 1/3 (33.3%) for biphenyl, if the ^{14}C isotope effect is neglected. The reaction that proceeds *via* path (B) will require all the ^{14}C activity to be found in the diphenyl sulfide alone, that *via* path (C) 50% each in both diphenyl sulfide and biphenyl. A choice between paths (a) and (b) can be made by tracing the ^{14}C activity within the molecule of biphenyl by means of degradation. Thus, diphenyl sulfilimine-1-^{14}C was treated with phenylmagnesium bromide. The ^{14}C analytical data obtained from the above experiment are shown in Table 2.

The distribution of ^{14}C activity among the products indicates that *ca.* 70% is in diphenyl sulfide the rest in biphenyl. These data rule out (B) and (C), leaving the first two plausible mechanisms that involve the initial formation of triphenylsulfonium salt. (A) is consistent with the mechanism proposed by Andersen[15] for the reaction between diphenyl sulfoxide with phenyllithium.

14) T. Mukaiyama, S. Kobayashi, and T. Kumamoto, *Tetrahedron Lett.*, **1970**, 5115.

15) K. K. Andersen and S. A. Yeager, *J. Org. Chem.*, **28**, 865 (1963).

TABLE 2. ^{14}C DISTRIBUTION IN THE PRODUCTS

Compound	^{14}C Activities dpm/mM	(%)
Ph–Ph	4.80×10^{6}	30.0
Ph–S–Ph[a]	1.11×10^{6}	69.2
Ph–S–Ph	1.60×10^{6}	(100)
↓ NTs		
(original)		
(recovered)[b]	1.57×10^{6}	98.2
Ph–S–Ph[c]		
(original)	1.65×10^{6}	(100)
(recovered)	1.61×10^{6}	97.6

a) The activity of diphenyl sulfide was measured, after its oxidation to diphenyl sulfone with H_2O_2.

b) The reaction was interrupted and the activity of the recovered sulfilimine measured.

c) Diphenyl sulfide-1-^{14}C was treated with phenylmagnesium bromide in order to check a possible ^{14}C exchange reaction between the diphenyl sulfide formed and phenyl Grignard reagent.

The fact that the ^{14}C activity of the recovered sulfilimine is practically the same as that of the original one, seems to indicate that the decomposition of the intermediate triphenylsulfonium salt to diphenyl sulfide is faster than the possible reverse reaction to the sulfilimine. Under the same conditions, diphenyl sulfide does not undergo phenyl exchange with phenyl Grignard reagent. Thus, the ^{14}C activity of diphenyl sulfide should come from the sulfilimine alone. All these data support the mechanism involving the initial formation of triphenylsulfonium ion. However, the question still remains through which of the paths (a) and (b) the reaction proceeds.

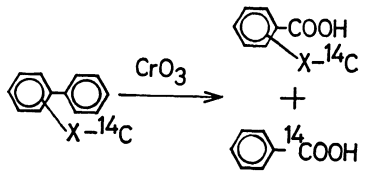
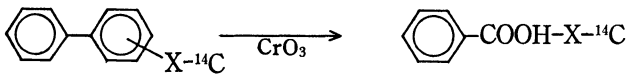


Fig. 3. The degradation of biphenyl.

In order to ascertain this, biphenyl-X-^{14}C obtained from the above experiment was allowed to degrade by the following method.

As shown in Fig. 1, if the reaction proceeds by the nucleophilic attack of phenyl anion at the sulfonium salt (Path (b)), the ^{14}C activity found in biphenyl-X-^{14}C should be the same as that found in benzoic acid-X-^{14}C, since no ^{14}C migration occurs at all during the reaction. On the other hand, the benzyne route (a) requires the ^{14}C activity of benzoic acid to be 3/4 of that of biphenyl. The results obtained from the degradation are shown in Table 3, and indicate that the reaction proceeds *via* path (A)-(b).

Table 3. Degradation data of biphenyl-X-^{14}C



Theor. (%)		
For (Aa)	(100)	(75)
For (Ab)		(100)
Found		
Activities (dmp/mM)		
1.53×10^4		1.58×10^4
	(100)	(103)

The result seems to contradict our earlier observation[16] and also that of Franzen's[17] on the reaction of triarylsulfonium salt with phenyllithium where benzyne route is confirmed. The difference between the above two reactions might be due to the less basic nature of the Grignard reagent than phenyllithium. Namely, phenyllithium is so strong a base that it can attack a proton *ortho* to the sulfonio group to form "benzyne", while the Grignard reagent is not a powerful base but a good nucleophile to attack the phenyl carbon.

Reactions of Phenyl Methyl and Phenyl Benzyl N-*Tosylsulfilimines with Phenylmagnesium Bromide.* These two reactions were carried out in a similar way to that of diphenyl *N*-tosylsulfilimine and phenylmagnesium bromide. After the reaction, the products were separated through a column packed with silica gel. The products and their yields obtained from the above sulfilimines are shown in Table 4.

We see that no sulfonium salt was isolated, however, the products are rather complicated. The results are in a marked contrast to those of diphenyl *N*-*p*-tosylsulfilimine. The pattern of distribution of the products is very close to that for the reaction of the corresponding sulfoxide with phenylmagnesium bromide.[18]

In the case of phenyl benzyl *N*-*p*-tosylsulfilimine, the major product is *N*-benzhydryl-*p*-toluenesulfonamide which was identified by comparing the IR, NMR, and mass spectra with those of the authentic sample prepared from benzhydrylamine and *p*-tosyl chloride. In addition to the *N*-benzhydryl-*p*-toluenesulfonamide, diphenyl sulfide and phenyl benzyl sulfide were isolated, identified and their yields were determined. With the present data only, it is difficult to postulate any plausible mechanism for the reaction. However, as in the case of the sulfoxides α-hydrogen abstraction by phenyl anion (or radical) might be the initial step followed by either the Pummerer or Stevens-type rearrangement as shown

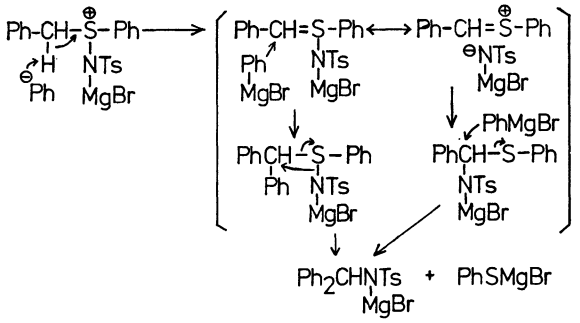


Fig. 4. The mechansim of the reaction.

below. A large excess of the Grignard reagent and a prolonged reaction time gave diphenyl sulfide in an increasing yield and diphenyl disulfide in a smaller amount. Diphenyl sulfide is probably obtained from diphenyl disulfide and not from the direct attack by phenylmagnesium bromide on sulfinyl sulfur. This was

Table 4. Products and yields in the reaction of phenyl benzyl and phenyl methyl *N*-tosylsulfilimines and phenylmagnesium bromide

Sulfilimine	Condition		Products and yields (%)
Ph–S(+)–CH_2–Ph | –NTs (1 mol)	PhMgBr (2 mol)	room temp. 3 hr	Ph–Ph, PhS–Ph(7), PhCHSPh (25) PhSSPh(10), $Ph_2CHNHTs$(17) $TsNH_2$, Recovered (48)
	PhMgBr (5 mol)	room temp. 24 hr	Ph–Ph, PhSPh(38), $PhCH_2SPh$(20) PhSSPh(1.7), $Ph_2CHNHTs$ (40) $TsNH_2$, Recovered (16)
Ph–S(+)–CH_3 | –NTs (1 mol)	PhMgBr (5 mol)	reflux 1 hr	Ph–Ph, $PhSCH_3$(5), PhSPh(16) $PhCH_2SPh$(21), $TsNH_2$(56), PhSH $PhCHCH_2CH_2CH_2OH$, $Ph_2CCH_2CH_2CH_2OH$ OH (16) OH (2.4)

16) Y. H. Khim and S. Oae, This Bulletin, **42**, 1968 (1969).
17) V. Franzen and C. Mertz, *Angew. Chem.*, **72**, 416 (1960).
18) P. Manya, A. Sekera, and P. Rumpf, *Tetrahedron*, **26**, 467 (1970).

found to be the case for the reaction with the diphenyl sulfilimine. In the case of phenyl methyl *N-p*-tosylsulfilimine, the major product is phenyl benzyl sulfide which might be formed by a Pummerer type rearrangement.

Experimental

Preparation of N-p-*Tosylsulfilimines.* The sulfilimines used in the study were prepared according to the known method.[19]

Reaction of Diphenyl N-p-*Tosylsulfilimine with Phenylmagnesium Bromide.* Diphenyl *N-p*-tosylsulfilimine (1 g) was dissolved in 30 m*l* anhydrous THF. To this was added 20 m*l* solution of phenylmagnesium bromide prepared from bromobenzene (1.6 g) and magnesium (0.25 g) in 20 m*l* anhydrous THF. The solution was then refluxed for 12 hr. After the reaction, the solution was decomposed with water and then with dilute hydrochloric acid. The aqueous solution was then extracted with chloroform. The chloroform extract was separated, washed with water, extracted again with 10% of aqueous sodium hydroxide, washed with water and then dried over anhydrous sodium sulfate. After removing the solvent, the residue was chromatographed through a column packed with silica gel.

The chromatogram indicated two spots, each of which was nicely separated; diphenyl sulfide and biphenyl were identified by glc from the first layer and the sulfilimine from the second layer. *p*-Tosylamide was isolated from the aqueous layer after acidifying the solution with hydrochloric acid. All the products were identified by comparing their IR, NMR, and glc with those of the authentic samples. The yields are shown in Table 1.

^{14}C Tracer Study with Diphenyl N-p-*Tosylsulfilimine-1-^{14}C with Phenylmagnesium Bromide.* N-p-*Tosylsulfilimine-1-^{14}C*: Diphenyl sulfide-1-^{14}C (3 g) prepared from diazotizing of aniline-1-^{14}C and thiophenol[20] was dissolved in 10 m*l* methanol containing a drop of acetic acid. To the solution was added 4.6 g of chloramine-T in 5 m*l* methanol. After being kept standing for 1 hr, the solution was poured into ice water. To this was added 10% of aqueous sodium hydroxide. The precipitates were separated. The crude sulfilimine was recrystallized from ethanol, yield 5 g, mp 111—112°C.

Exchange Reaction of Diphenyl Sulfide-1-^{14}C with Phenylmagnesium Bromide. In order to confirm the possibility of phenyl group interchange between the sulfide and phenyl Grignard reagent, a mixture of 0.6 g of diphenyl sulfide-1-^{14}C and phenylmagnesium bromide prepared from bromobenzene (1.6 g) and magnesium (0.24 g) in 10 m*l* of anhydrous THF was treated under the same conditions applied for the above reaction. After the reaction, diphenyl sulfide was recovered and oxidized to diphenyl sulfone by hydrogen peroxide for treatment such as degradation and ^{14}C activity determination.

Degradation of Diphenyl Sulfide-1-^{14}C.[21] In order to locate the specific position of ^{14}C activity of diphenyl sulfide-1-^{14}C the sulfide was oxidized first to the diphenyl sulfone which was then irradiated with 150 W UV lamp in benzene solution for 42 hr to afford biphenyl. After biphenyl was isolated and purified by sublimation, biphenyl (0.55 g) was oxidized by anhydrous chromic acid to benzoic acid, yield 0.16 g (37%). During those reactions no ^{14}C migration was observed. By the above method the labeled position and amount of ^{14}C activity in the diphenyl sulfide were found.

Degradation of Biphenyl-x-^{14}C. Biphenyl-x-^{14}C prepared from the sulfilimine and phenylmagnesium bromide was degraded similarly. After oxidation of biphenyl, benzoic acid-x-^{14}C was obtained in 58% yield. Both biphenyl and benzoic acid were purified by sublimation.

Measurement of ^{14}C Activity. The ^{14}C activity of the products obtained from the above reactions was measured by means of a Packard Tri Carb liquid scintillation counter by dissolving aliquot amounts of the samples in toluene. POP and POPOP were used as scintillators.

Reaction of Phenyl Benzyl N-p-*Tosylsulfilimine with Phenylmagnesium Bromide.* A typical experiment is as follows. Phenyl benzyl *N-p*-tosylsulfilimine (1 g prepared from the sulfide and chloramine-T) was dissolved in 20 m*l* anhydrous THF. To this solution was added phenylmagnesium bromide (2: 1 mol of sulfilimine) in anhydrous THF, and the solution was stirred overnight at room temperature. The solution was then decomposed with aqueous hydrochloric acid solution. The aqueous solution was extracted with chloroform. The chloroform solution was extracted again with an aqueous alkaline solution. The chloroform extract was condensed and the residue was chromatographed through a column packed with silica gel. From the chloroform eluent, a mixture of the sulfide and biphenyl was separated and the sulfilimine was recovered. The mixture was separated by means of glc (diethylene glycol succinate polyester on Neosorb). Their yields were determined by glc. After eluting the above mixture, chloroform was used to separate the polar compounds from which *N*-benzhydryl-*p*-tosylamide was obtained together with the recovered sulfilimine. *N*-Benzhydryl-*p*-tosylamide: mp 152°C; IR νSO_2 1165, 1320 cm^{-1}, νNH 3260 cm^{-1}; NMR methyl proton 7.57, methine C–H and N–H protons 4.30, phenyl protons 2.1—3.0 τ.

Found: C, 70.83; H, 5.81; N, 4.04%. Calcd for $C_{20}H_{19}SNO_2$: C, 71.20; H, 5.67; N, 4.15%.

From the alkaline extract only *p*-tosylamide was isolated.

Reaction of Phenyl Methyl N-p-*Tosylsulfilimine with Phenylmagnesium Bromide.* The reaction was carried out by the same method as for phenyl benzyl sulfilimine and after the usual work up the products given in Table IV were isolated.

19) K. Tsujihara, N. Furukawa, K. Oae, and S. Oae, This Bulletin, **42**, 2631 (1969).

20) S. Oae and N. Furukawa, *ibid.*, **39**, 2260 (1966).

21) S. Oae, M. Nakai, N. Furukawa, and T. Nakabayashi, *ibid.*, **45**, 1268 (1972).