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Preparation of α-Halo Sulfoximines

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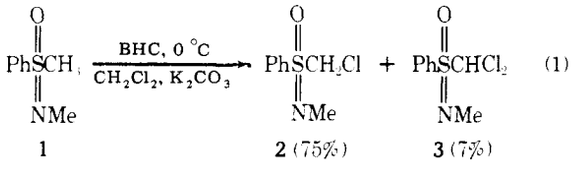
α-Halo sulfoximines have been prepared by the chlorination of *N*-methyl- and *N*-chlorosulfoximines with *tert*-butyl hypochlorite (BHC) and by amination of α-halo sulfoxides with mesitylsulfonyloxyamine. α-Chlorination of *S*-butyl-*N*,*S*-dimethylsulfoximine with BHC occurred only at the *S*-methyl. Reaction of *S*-butyl- or *S*-ethyl-*N*-methyl-*S*-phenylsulfoximine with BHC gave a single diastereomer.

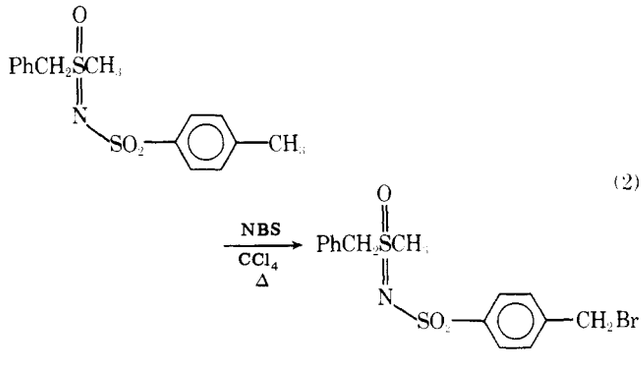
This paper describes the preparation of a new class of compounds, α-halo sulfoximines.

Chlorination of Sulfoximines. We have found that *S*-(chloromethyl)-*N*-methyl-*S*-phenylsulfoximine (**2**) is produced by reaction of **1** with *tert*-butyl hypochlorite (BHC) in dichloromethane with potassium carbonate present (eq 1).



1 2 (75%) 3 (7%) (1)

The base suppresses the formation of the hydrochloride of **1** (isolated in about 10% yield in the absence of base), which results from HCl production in a side reaction. Production of the hydrochloride increases to about 50% when the reaction is conducted at ambient temperature in *tert*-butyl alcohol. The presence of added hydroquinone has little effect on the product distribution, suggesting that a radical process is not operating. The ability of the sulfonimidoyl group to deactivate the α position in radical reactions is revealed by the lack of production of a bromomethylsulfoximine when **1** is treated with *N*-bromosuccinimide in the presence of light and peroxide and by the result shown in eq 2. We suggest the mechanism shown in Scheme I (X = O-*t*-Bu) for the BHC reaction. Support for the ylide mechanism comes from an independent generation of **5**. When *N*-chloro-*S*-methyl-*S*-phenylsulfoximine is treated with trimethyloxonium fluoroborate and the



(2)

Scheme I

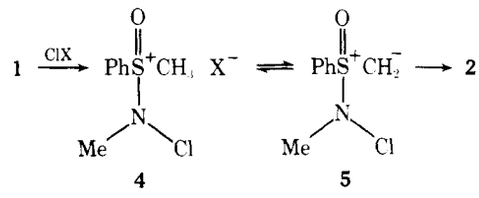


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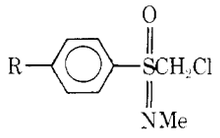
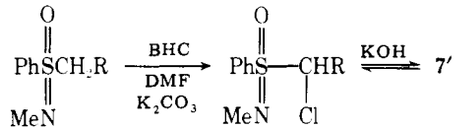
Table I. Products of Reaction of *tert*-Butyl Hypochlorite and *S*-Aryl-*N*,*S*-dimethylsulfoximes in Dichloromethane/K_2CO_3 at 0 °C



R	registry no.	isolated yield, %	mp [bp], °C
H	67069-79-8	75	[122–125 (0.2 mm)]
CH_3	67087-28-9	61	99.5–100
OCH_3	67087-58-5	56	75.5–76.5
Cl	67087-56-3	58	[95–98 (0.1 mm)]
NO_2	67087-55-2	60	136.5–138

resulting salt (**4**, X = BF_4) is subjected to base, **2** is produced. Various *S*-aryl-*N*,*S*-dimethylsulfoximines were halogenated with BHC. The summary in Table I shows that chlorination occurs in good yield with either electron-donating or -withdrawing substituents on the aryl group.

The reaction of BHC with the *S*-ethylsulfoximine **6a** in dichloromethane/K_2CO_3 was unsatisfactory; the major product was the hydrochloride of **6**. α-Chlorination was achieved in fair yield with BHC in dimethylformamide (DMF); interestingly, this chlorination resulted in the production of a single diastereomer, **7a** (eq 3). This diastereomer could be equilibrated with its epimer **7'a** in refluxing methanolic KOH. The well-separated *N*-methyl singlets in the NMR spectra of mixtures of **7a** and **7'a** provided a sensitive probe for analysis. Under the above conditions an equilibrium ratio of 56% **7a**/44% **7'a** was observed. The *S*-butylsulfoximine **6b** also gave rise to a single α-halo diastereomer **7b**, which could be equilibrated to a 58% **7b**/42% **7'b** mixture in refluxing methanolic KOH (eq 3). At this time we cannot provide in-



(3)

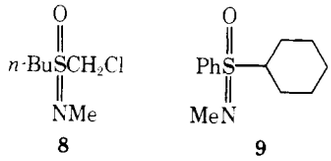
6 **7**

a, R = CH_3; b, R = $CH_2CH_2CH_3$

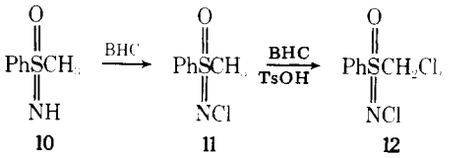
formation about the relative stereochemistries of the chiral sulfur and carbon centers in **7a** and **7b**. The remarkable stereoselectivity in these halogenations may stem from an intramolecular halogen transfer, e.g., from **5** to **2**, Scheme I.

Chlorination of *S*-butyl-*N*,*S*-dimethylsulfoximine with BHC resulted only in substitution at the *S*-methyl to yield **8**. We were unable to achieve chlorination with BHC at the methine of **9**. The reactivity and regiochemistry appear to be controlled by α-CH acidity.[1]

The reaction of BHC with *S*-methyl-*S*-phenylsulfoximine (**10**) yields the *N*-chloro derivative **11**, as expected (eq 4).[2]



8 **9**



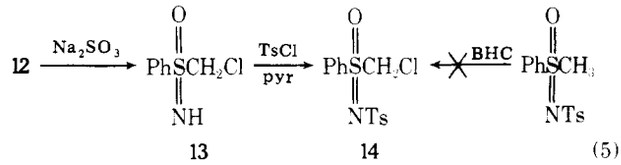
(4)

10 **11** **12**

Compound **11** is recovered after being subjected to a refluxing solution of excess BHC in dichloromethane for 3 days. No reaction had occurred after **11** had stood for 18 h at room temperature in the dark in neat BHC. If, however, a crystal of *p*-toluenesulfonic acid (TsOH) is added to either a neat or dichloromethane solution of the reactants at room temperature, a rapid reaction ensues resulting in a 90% yield of *N*-chloro-*S*-(chloromethyl)-*S*-phenylsulfoximine (**12**) (eq 4). The two most obvious possibilities for the role of the acid are: (1) protonation of BHC at oxygen to generate a more powerful electrophilic reagent; and/or (2) protonation of the sulfoximine at nitrogen to give a salt, the precursor of an ylide which accepts a positive halogen in an intra- or intermolecular reaction.

N-Tosyl- and *N*-benzoylsulfoximines failed to yield α-chloro derivatives when exposed to BHC at room temperature or above. Addition of acid had no effect.

α-Chloro derivatives of "free" sulfoximines were prepared by reduction of the above mentioned *N*,α-dichloro compounds with sodium sulfite. Such "free" sulfoximines can be transformed to *N*-tosyl derivatives by reaction with *p*-toluenesulfonyl chloride in pyridine (e.g., eq 5).



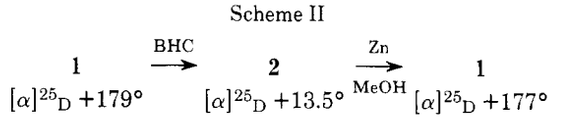
13 **14** (5)

Although it was anticipated that all of the reactions described above occur without perturbation of the configuration of the sulfonimidoyl sulfur, several stereochemical reaction cycles were completed to verify this expectation (Schemes II and III).

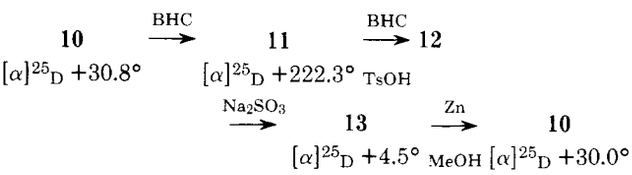
Amination of α-Halo Sulfoxides. An alternative approach to the synthesis of the unsubstituted α-halo sulfoximines was developed which differs from those descirbed above in that the halogen is added at the sulfoxide stage. Recent reports in the literature indicate several good methods are available for preparing the acid-sensitive halo sulfoxide.[3] For example, chloromethyl phenyl sulfoxide can be obtained in 55% yield by treating methyl phenyl sulfoxide with *N*-chlorosuccinimide in the presence of a catalytic amount of *p*-toluenesulfonic acid. α-Halo sulfoxides can be converted to sulfoximines by successive treatment with mesitylsulfonyloxyamine (MSA) and base, usually sodium hydroxide.[4]

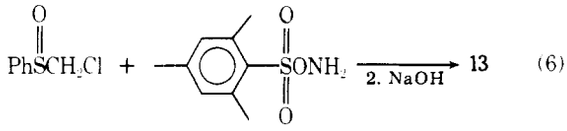
Although high yields of sulfoximines are generally obtained by the "MSA method",[4] the introduction of an α-halo substituent was found to reduce the yield substantially. For example, treatment of the chloromethyl phenyl sulfoxide with excess MSA in dichloromethane followed by basic workup resulted in only 30% of α-halo sulfoximine **13** with a considerable recovery of starting halo sulfoxide (eq 6). By comparison, methyl phenyl sulfoxide is converted to the *S*-methyl-*S*-phenylsulfoximine under these conditions in 95% yield. The

Scheme II



Scheme III





(6)

addition of more MSA (2–3 equiv) over a period of 18 h did not increase the yield of chloro sulfoximine. Presumably the lower yield of halo sulfoximines results from a decrease in reactivity of the halo sulfoxide toward MSA due to the inductive effect of the halide. The slower reaction between these reagents allows decomposition of the oxidizing agent, MSA, to compete with amination.

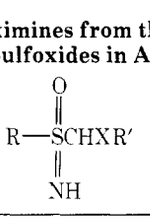
The nature of the MSA decomposition is thought to proceed according to Scheme IV. The stoichiometric ratio of MSA to nitrogen determined experimentally (4:1, respectively) is consistent with that indicated. A benzene solution of MSA at room temperature gives off nitrogen slowly. A white precipitate is formed in the reaction, presumably the salt of mesitylenesulfonic acid and hydrazine. The presence of diimide was inferred by carrying out the decomposition in the presence of cyclohexene. Cyclohexane was identified by VPC. A similar decomposition of hydroxylamine-*O*-sulfonic acid has been observed.[5]

It was found that yields up to ~60% of halo sulfoximines can be obtained if the amination is carried out in acetonitrile or nitromethane. These results are summarized in Table II.

Experimental Section

The following *N*-methylsulfoximines were prepared by the Eschweiler–Clarke methylation of the corresponding N-unsubstituted sulfoximines:[6] *N,S*-dimethyl-*S*-phenylsulfoximine, 77.5% yield, colorless oil, bp 110 °C (0.4 mm) (Kugelrohr distillation); (+)-(*S*)-*N,S*-dimethyl-*S*-phenylsulfoximine, $[\alpha]_D$ +179° (*c* 1.02, acetone);[6] *N,S*-dimethyl-*S*-*p*-tolylsulfoximine, 80.3% yield, colorless oil, bp 108–110 °C (0.5 mm) (Kugelrohr distillation); *S*-(*p*-methoxyphenyl)-*N,S*-dimethylsulfoximine, 75% yield, colorless oil, bp 123–126 °C (0.5 mm) (Kugelrohr distillation); *S*-(*p*-chlorophenyl)-*N,S*-dimethylsulfoximine, 68% yield, colorless oil; *N,S*-dimethyl-*S*-(*p*-nitrophenyl)sulfoximine, 48.8% yield, pale yellow needles, mp 128–129 °C; *S*-butyl-*N,S*-dimethylsulfoximine, 64.5% yield, colorless oil, bp 89–92 °C (0.1 mm) (Kugelrohr distillation); *S,S*-dibutyl-*N*-methylsulfoximine, isolated by column chromatography (Al_2O_3/$CHCl_3$) in 20.5% yield, colorless oil, bp 98–101 °C (0.1 mm) (Kugelrohr distillation); *S*-ethyl-*N*-methyl-*S*-phenylsulfoximine, 77% yield, colorless oil, bp 97–100 °C (0.1 mm) (Kugelrohr distillation); *S*-butyl-*N*-methyl-*S*-phenylsulfoximine, 75% yield, colorless oil, bp 100–110 °C (0.2 mm) (Kugelrohr distillation). *S*-Cyclohexyl-*N*-methyl-*S*-phenylsulfoximine, bp 108–110 °C (0.1 mm), was prepared by methylating *S*-cyclohexyl-*S*-phenylsulfoximine with trimethyloxonium fluoroborate.

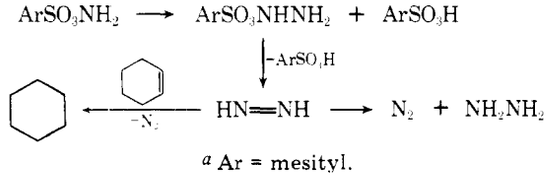
Table II. α-Halosulfoximines from the Reaction of MSA and α-Halo Sulfoxides in Acetonitrile



R	R′	X	registry no.	isolated yield, %	mp, °C
n-Pr	Et	Cl	67087-46-1	45	50–53[a]
n-Bu	*n*-Pr	Cl	67069-95-8	60	42–43[a]
Ph	H	Cl	67087-40-5	63	47.5–48.5
Ph	H	Br	67087-42-7	20[b]	63–64

[a] Single diastereomer. [b] Reaction in dichloromethane.

Scheme IV[a]



[a] Ar = mesityl.

***S*-Benzyl-*S*-methyl-*N*-tosylsulfoximine.** This material was isolated in 36.9% yield as a white solid, mp 128–129 °C, by reacting benzyl methyl sulfoxide with *p*-toluenesulfonyl azide in the presence of Raney-copper catalyst.[7]

Chlorination of *N*-Methylsulfoximines with *tert*-Butyl Hypochlorite[8] (BHC). The apparatus used in this experiment was protected from light by wrapping in aluminum foil. The addition of BHC was made in subdued light. To a solution of the sulfoximine (2.43 mmol) in dichloromethane (10 mL) was added 1.5 equiv of anhydrous potassium carbonate. The stirring mixture was cooled in an ice bath and BHC (5% excess) added slowly via syringe. The ice bath was removed and the mixture was stirred for 15–20 min. After filtration the solution was concentrated by rotary evaporation to give a crude product. The chloro sulfoximines were isolated by either column or thick-layer chromatography (silica gel/ether). If desired small amounts of dichloro sulfoximines and unreacted starting materials could be isolated from the chromatography. The compounds listed in Table I and *S*-butyl-*S*-(chloromethyl)-*N*-methylsulfoximine, bp 93–95 °C, (0.1 mm) were prepared by this method.

***S*-(1-Chloroethyl)-*N*-methyl-*S*-phenylsulfoximine (7a)** was prepared according to the above procedure using DMF as the solvent (4.0 mL/0.2 mmol of sulfoximine) and leaving out the carbonate. After the slow addition of BHC to a cold solution of the sulfoximine, the ice bath was removed and the solution was stirred for 5 h. The colorless solution was poured into an equal volume of saturated sodium chloride solution and extracted with three volumes of diethyl ether. Washing the combined ether extracts with water, drying ($MgSO_4$), and concentrating by rotary evaporation gave a crude oil. The chloro sulfoximine was isolated by thick-layer chromatography (silica gel/diethyl ether) in 44.5% yield as a colorless oil, bp 95–96 °C (0.1 mm) (Kugelrohr distillation). NMR showed this material to be only one diastereomer.

***S*-(1-Chlorobutyl)-*N*-methyl-*S*-phenylsulfoximine (7b).** Using the procedure described for **7a, 7b** was isolated by thick-layer chromatography (silica gel/diethyl ether) in 43.5% yield as a colorless oil, bp 86–87 °C (0.1 mm) (Kugelrohr distillation). NMR showed this material to be one diastereomer.

Epimerization of *S*-(1-Chloroethyl)-*N*-methyl-*S*-phenylsulfoximine (7a). To 0.138 g (0.689 mmol) of diastereomerically pure **7a** in 6.6 mL of methanol was added 4.2 mL of 1 M KOH. The solution was refluxed for 8.5 h. After cooling, the reaction mixture was concentrated to half its volume by rotary evaporation, saturated with sodium chloride, and extracted with three equal volumes of diethyl ether. The combined ether extracts were washed with 5 mL of water, dried ($MgSO_4$), and concentrated to give 0.125 g (90.6%) of crude oil, bp 96–98 °C (0.1 mm) (Kugelrohr distillation). NMR data revealed a 44:56 mixture of chloro sulfoximines **7a/7′a.**

Epimerization of *S*-(1-Chlorobutyl)-*N*-methyl-*S*-phenylsulfoximine (7b) under reflux for 27 h in methanolic KOH resulted in a 43:57 mixture of chloro sulfoximines **7b/7′b** as ascertained by integration of the *N*-methyl singlets after the addition of europium shift reagent [Eu(fod)$_3$].

Methylation of *N*-Chloro-*S*-methyl-*S*-phenylsulfoximine. To 0.621 g (4.0 mmol) of trimethyloxonium fluoroborate slurried in 25 mL of dichloromethane was added 0.753 g (4.0 mmol) of **11.** The mixture was warmed in hot water for 5 min and then allowed to stir at room temperature for 2 h. A small amount of a white precipitate was removed by filtration. Addition of anhydrous ether to the filtrate caused precipitation of the fluoroborate salts, mp 76–81 °C. After collecting by filtration, the salts were washed with a copious amount of anhydrous ether to remove any unreacted starting sulfoximine. Attempts at recrystallization of the white solid were unsuccessful. The NMR spectrum of this white solid as well as its chemistry was consistent with a mixture of (*N*-chloro-*N*-methylamino)methylphenyloxosulfonium fluoroborate (**4,** X = BF_4) and *N,S*-dimethyl-*S*-phenylsulfoximine hydrofluoroborate.

Reaction of Fluoroborate 4 with Base. A. To 0.254 g of the above mixture of fluoroborate salts dissolved in 20 mL of dichloromethane and cooled to 0 °C with added 0.120 g (0.87 mmol) of anhydrous potassium carbonate and 0.097 g (0.87 mmol) of potassium *tert*-butoxide. After stirring 1 h at 0 °C and 11 h at room temperature, the mixture was filtrated and concentrated to give 0.154 g of crude oil. The *S*-(chloromethyl)-*N*-methyl-*S*-phenylsulfoximine and *N,S*-dimethyl-*S*-phenylsulfoximine were found to be components of the oil by TLC and NMR by comparison to that of authentic materials.

B. To 0.202 g of sodium hydride slurried in 10 mL of dry THF was added 0.296 g of the above mixture of fluoroborate salts. A smooth evolution of hydrogen was observed. After stirring at room temperature 30 min the excess hydride was destroyed by the addition of 10 mL of saturated aqueous sodium chloride. Extraction with diethyl ether, drying ($MgSO_4$), and concentrating by rotary evaporation resulted in 0.208 g of oil. The NMR spectrum and TLC of this oil showed the presence of *S*-(chloromethyl)-*N*-methyl-*S*-phenylsulfoximine along with *N,S*-dimethyl-*S*-phenylsulfoximine by comparison to that of authentic materials. The relative percentages of the sulfoximines were 42.3 and 57.7%, respectively.

Radical Bromination. To 0.3254 g (1.00 mmol) of *S*-benzyl-*S*-methyl-*N*-(*p*-tolylsulfonyl)sulfoximine in 10 mL of benzene was added 0.1869 g (5% excess) of *N*-bromosuccinimide and a few milligrams of benzoyl peroxide. After refluxing 35 min and cooling, the reaction mixture was washed with 5 mL of 5% NaOH and water and dried ($MgSO_4$). Concentration by rotary evaporation gave 0.450 g of crude oil which showed two components by TLC. Thick-layer chromatography of 0.300 g of this oil gave 0.246 g of a mixture of *S*-benzyl-*N*-[(*p*-bromomethyl)phenylsulfonyl]-*S*-methylsulfoximine (63%) and starting sulfoximine (37%). The brominated and unbrominated sulfoximines were not separable to TLC.

***N*-Chloro-*S*-(chloromethyl)-*S*-phenylsulfoximine (12).** To 0.262 g (1.38 mmol) of *N*-chloro-*S*-methyl-*S*-phenylsulfoximine in 2 mL of *tert*-butyl hypochlorite was added a small crystal of *p*-toluenesulfonic acid. After 5 min the solution was concentrated by rotary evaporation. The resulting oils were dissolved in chloroform (10 mL) and washed with 10 mL of 0.5% NaOH and 5 mL of water. Drying ($MgSO_4$) and concentrating gave 0.307 g of crude oil. Spectral data (NMR) showed this oil to be a mixture of 88.7% *N*-chloro-*S*-(chloromethyl)-*S*-phenylsulfoximine, 10.5% *N*-chloro-*S*-(dichloromethyl)-*S*-phenylsulfoximine, and 0.7% starting material. Longer reaction time, e.g., 15 min, results in an increased yield of the dichloromethylsulfoximine (26.1%) at the expense of the chloromethyl derivative (61.2%).

Reduction of *N*-Chloro-*S*-(chloromethyl)-*S*-phenylsulfoximine. A solution of the sulfoximine (1.38 mmol) in diethyl ether (6 mL) was shaken with 3.0 mL of 1 M Na_2SO_3 for 2 min. The progress of the reduction was monitored by TLC (silica gel/ether) of the ether layer. The aqueous phase was removed and extracted with 6 mL of ether. The combined ether layers were washed with water, dried ($MgSO_4$), and concentrated via rotary evaporation to give 0.219 g (86.6%) of an oil. Spectral data (IR and NMR) of this oil were identical with that of an authentic sample of *S*-(chloromethyl)-*S*-phenylsulfoximine prepared by another method.

(+)-(*S*)-*S*-(Chloromethyl)-*N*-methyl-*S*-phenylsulfoximine. Reaction of (*S*)-*N,S*-dimethyl-*S*-phenylsulfoximine, $[\alpha]^{25}_D$ +179° (*c* 1.02, acetone) (98% optically pure),[6] with BHC by the general procedure gave the product as a colorless oil: 69%; bp 110–115 °C (0.1 mm); $[\alpha]^{25}_D$ +13.5° (*c* 1.26, acetone). In addition (−)-(*S*)-*S*-(dichloromethyl)-*N*-methyl-*S*-phenylsulfoximine (**3**) was isolated by chromatography in 7% yield as a colorless oil: bp 125–130 °C (0.1 mm); $[\alpha]^{25}_D$ − 32.6° (*c* 1.55, acetone).

Reduction of (+)-(*S*)-*S*-(Chloromethyl)-*N*-methyl-*S*-phenylsulfoximine. The chlorosulfoximine (0.357 g, 1.75 mmol), $[\alpha]^{25}_D$ +13.5° (*c* 1.26, acetone), in 10 mL of methanol was treated with 0.660 g (0.01 g-atom) of powdered zinc under reflux for 5 h. The progress of the reaction was monitored by thin-layer chromatography (silica gel/diethyl ether). After cooling, the mixture was filtered. The filtrate was made acidic by the addition of 10 mL of 10% HCl and washed with two portions (10 mL) of chloroform. The aqueous phase was then made basic with 10% NaOH and extracted with three equal volumes of chloroform, dried ($MgSO_4$), and concentrated by rotary evaporation. The resulting crude oil was subjected to preparative TLC to give 0.200 g (67.8%) of (+)-(*S*)-*N,S*-dimethyl-*S*-phenylsulfoximine, $[\alpha]^{25}_D$ +176.7° (*c* 1.695, acetone).

(+)-(*S*)-*N*-chloro-*S*-methyl-*S*-phenylsulfoximine (11). To 0.712 g (4.6 mmol) of (+)-(*S*)-*S*-methyl-*S*-phenylsulfoximine, $[\alpha]^{25}_D$ 30.8° (*c* 1.060, acetone), in dichloromethane (15 mL) was added 1 equiv (0.635 g) of anhydrous potassium carbonate. The mixture was cooled in an ice bath while 0.55 mL (0.497 g, 4.6 mmol) of BHC was added dropwise. After stirring for 30 min the mixture was filtered and concentrated by rotary evaporation. The resulting oil was chromatographed (column, silica gel/ether) to give 0.667 g (76.0%) of **11** as yellow needles: mp 50.5–51 °C; $[\alpha]^{25}_D$ +222.3° (*c* 1.64, acetone).

(+)-(*S*)-*S*-(Chloromethyl)-*S*-phenylsulfoximine (13). To 0.286 g (22.7 mmol) of (+)-(*S*)-*N*-chlorosulfoximine **11** in dichloromethane (1 mL) was added a crystal of *p*-toluenesulfonic acid; 9 equiv of BHC was added in three portions while the progress of the reaction was monitored by TLC (silica gel/ether). The solution was then concentrated by rotary evaporation. The residual oil was dissolved in diethyl ether (5 mL) and shaken for 2 min with 4 mL of 1 M Na_2SO_3 solution. Washing with 3 mL of 0.5% NaOH and 3 mL of water followed by drying ($MgSO_4$) and concentration gave 0.202 g (70.6%) of **13** as a white solid. Recrystallization from diethyl ether gave white needles: mp 76–77 °C; $[\alpha]^{25}_D$ +4.5 ° (*c* 0.95, acetone).

Reduction of (+)-(*S*)-*S*-(Chloromethyl)-*S*-phenylsulfoximine (13). To a solution of **13** (0.155 g, 0.81 mmol) in methanol (10 mL) was added 0.582 g (8.63 mmol) of powdered zinc. The mixture was refluxed for 18 h. After cooling, the mixture was filtered and the filtrate was concentrated by rotary evaporation. The residual oil was dissolved in chloroform and washed with two 10-mL portions of 10% HCl. The acidic aqueous phase was then made basic by the addition of solid Na_2CO_3 (caution: foaming) and 1 mL of 10% NaOH. Extraction with three equal volumes of chloroform was followed by washing the combined extracts with saturated sodium chloride solution (5 mL). Drying ($MgSO_4$) and concentrating gave 0.041 g of *S*-methyl-*S*-phenylsulfoximine, $[\alpha]^{25}_D$ +29.9° (*c* 0.74, acetone). The product was identified by comparison with spectral data (IR and NMR) of authentic material.

Amination of Halo Sulfoxides with Mesitylsulfonyloxyamine (MSA). To a cooled (0 °C) solution of the halo sulfoxide (0.02 mol) in acetonitrile (120 mL) was added 1.4 quiv of MSA. The solution was stirred at 0 °C for 4 h and at room temperature for 48 h. A white precipitate was observed after 30 min. Concentration by rotary evaporation gave a semisolid which was slurried in dichloromethane (40 mL). While cooling in an ice bath, 11.2 mL of 10% NaOH solution was added and the two-phased system was stirred vigorously for 15 min. After removal of the organic layer, the aqueous phase was extracted with an equal volume of dichloromethene. The combined extracts were washed with two 5-mL portions of saturated sodium chloride, dried ($MgSO_4$), and concentrated to give crude product. The halo sulfoximines were then purified by column chromatography (silica gel/30% ether–cyclohexane) and/or recrystallization. The following halo sulfoximines were prepared by this method: *S*-(1-chlorobutyl)-*S*-butylsulfoximine, 59.9% yield (isolated), white crystals, mp 42–43 °C (ether–pentane) (addition of europium shift reagent in progressively increasing amounts showed the presence of one diastereomer); *S*-(1-chloropropyl)-*S*-propylsulfoximine, 45% yield (isolated), white crystals, mp 50–53 °C (ether–cyclohexane) (one diastereomer); *S*-(chloromethyl)-*S*-phenylsulfoximine, 63% yield, as white needles, mp 47.5–48.5 °C (ether–pentane); *S*-(bromomethyl)-*S*-phenylsulfoximine, use of dichloromethane as the solvent gave 22.3% yield of the bromo sulfoximine as a white solid, mp 63–64 °C (ether–pentane).

Preparation of *N*-(*p*-Tolylsulfonyl)-α-chlorosulfoximines from Free α-Chloro Sulfoximines. To a stirring solution of the chloro sulfoximine (1.0 mmol) in pyridine (5 mL) was added *p*-toluenesulfonyl chloride (1.0 mmol). A bright yellow solution was obtained which turned pale yellow after 15 h. The solution was concentrated by rotary evaporation to a semisolid. Addition of 10 mL of chloroform and 10 mL of water resulted in a two-phase system. After removal of the aqueous phase the chloroform layer was washed with 2 mL of 5% HCl, 2 mL of 5% NaOH, and 2 mL of saturated sodium chloride. Drying ($MgSO_4$) and concentrating by rotary evaporation gave pale yellow crystals which were recrystallized from methanol. The following *N*-tosylsulfoximines were prepared by this procedure: *S*-(chloromethyl)-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine, 85.4% yield (white needles, mp 155–156 °C); *S*-butyl-*S*-(1-chlorobutyl)-*N*-(*p*-tolylsulfonyl)sulfoximine, 90% yield, white crystals, mp 102–105 °C (one diastereomer); *S*-(1-chloropropyl)-*S*-propyl-*N*-(*p*-tolylsulfonyl)sulfoximine, 90.2% yield, as white crystals, mp 116–118 °C (one diastereomer).

***N*-Chloro-*S*-methyl-*S*-phenylsulfoximine (11).** Treatment of S-methyl-S-phenylsulfoximine as described in the procedure for chlorinating *N*-methylsulfoximine derivatives with BHC gave **11**, white needles from methanol, mp 84–84.5 °C (70% yield).

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Registry No.—**1**, 30004-67-2; (*S*)-(+)-**1**, 33993-53-2; **1** HBF_4, 67087-54-1; (*S*)-(+)-**2**, 67087-45-0; **3**, 67087-44-9; **4** (X = BF_4^-), 67124-64-5; **6a**, 67087-37-0; **6b**, 67087-36-9; **7a** isomer 1, 67087-33-6; **7a** isomer 2, 67087-32-5; **7b** isomer 1, 67087-31-4; **7b** isomer 2, 67087-57-4; **8**, 67087-34-7; **9**, 67124-65-6; **10**, 4381-25-3; (*S*)-(+)-**10**, 33903-50-3; **11**, 67087-35-8; (*S*)-(+)-**11**, 39830-45-0; **12**, 67087-49-4; (*S*)-(+)-**13**, 67087-43-8; **14**, 67087-38-1; *N,S*-dimethyl-*S*-*p*-tolylsulfoximine, 67087-52-9; *S*-(*p*-methoxyphenyl)-*N,S*-dimethylsulfoximine, 67087-51-8; *S*-(*p*-chlorophenyl)-*N,S*-dimethylsulfoximine, 67087-50-7; *N,S*-dimethyl-*S*-(*p*-nitrophenyl)sulfoximine, 67087-48-3;

S-butyl-N,S-dimethylsulfoximine, 67087-39-2; S,S-dibutyl-N-methylsulfoximine, 35362-76-6; S-benzyl-S-methyl-N-tosylsulfoximine, 38401-39-7; benzyl methyl sulfoxide, 824-86-2; p-toluenesulfonyl azide, 941-55-9; S-benzyl-N-[(p-bromomethyl)phenylsulfonyl]-S-methylsulfoximine, 67087-53-0; N-chloro-S-dichloromethyl-S-phenylsulfoximine, 67087-47-2; S-butyl-S-(1-chlorobutyl)-N-(p-tolysulfonyl)sulfoximine, 67070-02-4; S-(1-chloropropyl)-S-propyl-N-(p-tolylsulfonyl)sulfoximine, 67070-01-3; propyl 1-chloropropyl sulfoxide, 67087-41-6; butyl 1-chlorobutyl sulfoximine, 21128-90-5; phenyl chloromethyl sulfoxide, 7205-94-9; phenyl bromomethyl sulfoxide, 31268-20-9.

Supplementary Material Available: Analytical and spectral data of the compounds discussed in this paper (9 pages). Ordering information is given on any current masthead page.

References and Notes

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Alkenes from Base-Promoted Eliminations of α-Halo Sulfoximines

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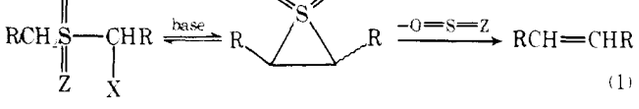
Upon treatment with base α-halo N-(p-tolylsulfonyl)sulfoximines bearing α hydrogens undergo 1,3 eliminations to yield alkenes in analogy to the Ramberg–Bäcklund reaction of α-halo sulfones. Treatment of benzylic α-bromo N-(p-tolylsulfonyl)sulfoximines with refluxing methanolic potassium hydroxide gave *cis*-alkenes as the major product, whereas under the same conditions α-chloro dialkylsulfoximines gave largely *trans*-alkenes. Neither NH nor N-methyl sulfoximines gave alkenes under the above conditions.

α-Halo sulfones undergo an interesting and facile 1,3 elimination which has occupied the attention of chemical laboratories since its discovery by Ramberg and Bäcklund in 1940.[1] (eq 1, Z = O). The question may then be asked as to



(1)

whether halo sulfoximines undergo a similar transformation (eq 1, Z = NR'). If so, how do various nitrogen substituents effect the reaction?

The stereochemistry observed in the alkene produced upon 1,3 elimination of α-halo dialkyl sulfones may vary from predominantly cis to equal amounts of isomeric alkenes.[2] If indeed, a similar 1,3 elimination may be made to occur with α-halo sulfoximines, bulky nitrogen substituents may promote the formation of *cis*-alkenes.

A series of N-substituted α-halo sulfoximines were prepared[3] and treated with base in order to determine to what extent the reaction occurs. Refluxing diastereomerically pure α-chloro sulfoximines in methanolic potassium hydroxide (6 equiv) gave the results shown in Scheme I.

The differences in the reactions of the various N-substituted sulfoximines in Scheme I with methanolic potassium hydroxide is curious. The production of 1-butanesulfinamide in reaction a can be rationalized in a number of ways, including the transient production of a three-membered S–N heterocycle. At this time, we have insufficient data to justify further speculation. The failure of the N-methyl derivative to undergo 1,3 elimination under the conditions of methanolic potassium hydroxide is surprising, since the leaving group, N-sulfinylmethylamine, is a stable compound. When the reaction is carried out with potassium deuterioxide in methanol-*O*-*d*, recovered starting material shows complete exchange of the α and α' protons with deuterium. Thus, the anion is capable of being formed, but apparently the elimination is slow under these conditions. A similar situation has been noted in the literature. 2-Bromothiacyclohexane 1,1-dioxide was initially reported not to undergo elimination after prolonged heating in a sodium hydroxide–dioxane solution, but later was found to give cyclopentene in 82% yield when exposed to potassium *tert*-butoxide in THF at 0 °C (eq 18).[4] It may very well turn out that elimination in the present case will occur under other conditions.

The isolation of 4-octene when the N-tosyl derivative (Scheme I) was treated with potassium hydroxide suggests that a reaction analogous to the Ramberg–Bäcklund reaction is operative. Several α-halo N-tosylsulfoximines were prepared and treated with potassium hydroxide. The cis–trans ratios of the alkenes produced were determined by gas chromatography. The compounds studied can be separated into two structural groups, the benzylic α-bromo and the α-chloro dialkylsulfoximines. The results are summarized in Table I.

In the reactions of the α-bromo sulfoximines **1c–e** and potassium hydroxide approximately 80% of the starting sulfoximines can be accounted for by two reaction pathways. One involves the desired 1,3-dehydrobromination leading to alkene, sulfonamide, and potassium sulfite, while the other is a reduction of the bromo sulfoximines to **4c–e**. The stereochemistry of the alkene produced from **1d** and **1e** is found to be predominately cis. From the α-chloro dialkylsulfoximines **1a** and **1b** only elimination to the alkene was observed. The

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