Anionic α-Perhalogenation of *S*-Alkyl-*S*-aryl-*N*-*p*-toluenesulfonylsulfoximines with Hexahaloethanes

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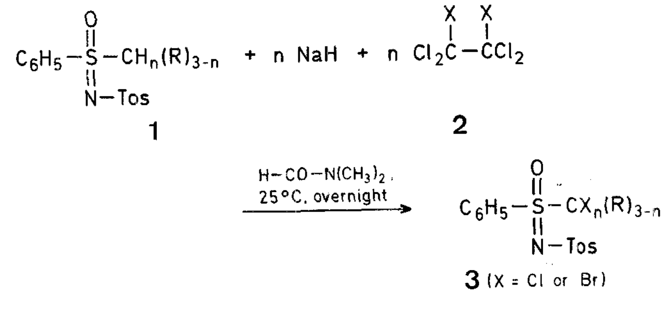
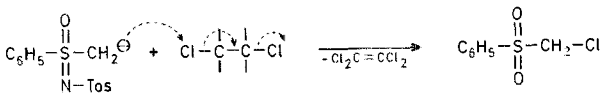
We have previously described the preparation[1] and reactions[2] of α-halosulfoximines prepared by methods based on *t*-butyl hypochlorite. α-Halo-*N*-tosylsulfoximines were prepared indirectly by halogenation of *N*-*H*-sulfoximines followed by *N*-tosylation. Attempts to α-brominate *N*-tosylsulfoximines under radical conditions with *N*-bromosuccinimide resulted in bromination of the tolyl methyl group. In this paper, we describe simple and high yield methods for the preparation of α-halo derivatives of *N*-tosylsulfoximines utilizing hexachloroethane and 1,2-dibromo-1,1,2,2-tetrachloroethane. Hexachloroethane has been previously employed in the halogenation of sulfones[3].

N-Tosylsulfoximines **1** when treated with sodium hydride and the hexahaloethane (**2**) in dimethylformamide overnight at room temperature gave excellent yields of halogenated sulfoximines **3** (Table 1). Reactions with dibromotetrachloroethane (**2**; X = Br) required excess base and dibromide to go to completion due to a bromine-producing side-reaction.



Presumably, the mechanism of these reactions involves nucleophilic attack of the sulfonimidoyl carbanion on the hexahaloethane[3], e.g.:



Under the reaction conditions used, the introduction of each subsequent halogen occurs with increasing rapidity in accordance with the decreasing pK$_a$ of the substrate [**1** (n = 3), pK$_a$ = 24.5; **1** (n = 2), pK$_a$ = 20.7±0.2; **1** (n = 1), pK$_a$ = 16.9±0.3]. Treatment of **1** (n = 3) with one equivalent each of sodium hydride and hexachloroethane under the usual conditions resulted in a 2 : 1 mixture of starting sulfoximine and trichloro product **3a**. Possibly due to a combina-

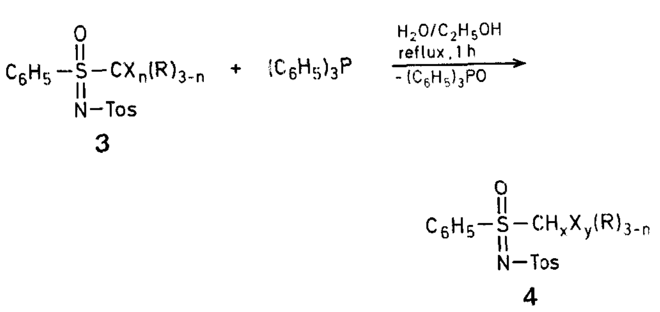
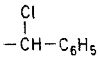
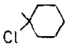
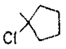


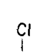
Table 1. α-Halogenation of *N*-Tosylsulfoximines **1** with Hexachloroethane (**2**; X = Cl) or 1,2-Dibromo-1,1,2,2-tetrachloroethane (**2**; X = Br)

$[-CX_n(R)_{3-n}]$ in product **3**		Yield [%]	m.p. [°C]	Molecular formula[a]	¹H-N.M.R. ($CDCl_3$) δ [ppm]	I.R. ($CHCl_3$) ν [cm⁻¹]
3a	$-CCl_3$	82	105–106°	$C_{14}H_{12}Cl_3NO_3S_2$ (412.7)	2.41 (s, 3H); 7.2–8.3 (m, 9H)	1160, 1120, 1090, 1068
3b	$-CCl_2-CH_3$	81	119–120°	$C_{15}H_{15}Cl_2NO_3S_2$ (392.3)	2.36 (s, 3H); 2.39 (s, 3H); 7.1–8.2 (m, 9H)	1159, 1112, 1086, 1060
3c	 $-\overset{Cl}{CH}-C_6H_5$	85[b]	146–147° 134–136°	$C_{20}H_{18}ClNO_3S_2$ (420.0)	2.40 (s, 3H); 6.67 (s, 1H); 7.30 (s, 5H); 7.1–8.0 (m, 9H) 2.40 (s, 3H); 6.70 (s, 1H); 7.30 (s, 5H); 7.1–8.0 (m, 9H)	1153, 1088, 1063 —
3d	$-CCl_2-C_6H_5$	86	120–121°	$C_{20}H_{17}Cl_2NO_3S_2$ (454.4)	2.39 (s, 3H); 7.0–8.0 (m, 14H)	1157, 1105, 1089, 1066
3e		97	39–40°	$C_{19}H_{22}ClNO_3S_2$ (412.0)	1.1–2.4 (m, 10H); 2.40 (s, 3H); 7.1–8.2 (m, 9H)	1154, 1099, 1088, 1064
3f		93	77–78°	$C_{18}H_{20}ClNO_3S_2$ (398.0)	1.6–2.4 (m, 6H); 2.40 (s, 3H); 2.4–3.05 (m, 2H); 7.05–8.1 (m, 9H)	1156, 1100, 1089, 1066
3g	$-CBr_3$	84	104–106°	$C_{14}H_{12}Br_3NO_3S_2$ (546.1)	2.42 (s, 3H); 7.2–8.45 (m, 9H)	1160, 1108, 1089, 1064
3h	$-CBr_2-CH_3$	82	82–83.5°	$C_{15}H_{15}Br_2NO_3S_2$ (481.3)	2.41 (s, 3H); 2.73 (s, 3H); 7.15–8.2 (m, 9H)	—
3i	$-CBr_2-C_6H_5$	76	134–135°	$C_{20}H_{17}Br_2NO_3S_2$ (543.3)	2.38 (s, 3H); 7.05–7.9 (m, 14H)	1153, 1088, 1061

[a] Satisfactory microanalyses obtained: C ±0.30, H ±0.30.

[b] Reaction using 1 equivalent of sodium hydride; 1:1 mixture of diastereomers formed.

Table 2. Reductive Dehalogenation of α-Halosulfoximines **3**

$[-CX_n(R)_{3-n}]$ in substrate **3**	$(C_6H_5)_3P$ equiv. used	$[-CH_xX_y(R)_{3-n}]$ in product **4**	Yield [%]	m.p. [°C]	Molecular formula[a] or Lit. m.p.	¹H-N.M.R. ($CDCl_3$) δ [ppm]	I.R. ($CHCl_3$) ν [cm⁻¹]
$-CCl_3$	1	$-CHCl_2$	99	106–107.5°	$C_{14}H_{13}Cl_2NO_3S_2$ (378.3)	2.41 (s, 3H); 7.41 (s, 1H); 7.2–8.2 (m, 9H)	—
$-CCl_3$	2	$-CH_2Cl$	95	155–156°	155–156°[1]	—	—
$-CCl_2-CH_3$	1	 $-\overset{Cl}{CH}-CH_3$	90[b]	115–117° 95–100°	$C_{15}H_{16}ClNO_3S_2$ (357.8) $C_{15}H_{16}ClNO_3S_2$ (357.8)	1.82 (d, 3H, *J* = 6.5 Hz); 2.40 (s, 3H); 5.51 (q, 1H, *J* = 6.5 Hz); 7.1–8.1 (m, 9H) 1.82 (d, 3H, *J* = 6.5 Hz); 2.40 (s, 3H); 5.65 (q, 1H, *J* = 6.5 Hz); 7.1–8.1 (m, 9H)	1155, 1089, 1068, 1047 1154, 1100 (sh), 1088, 1067, 1050 (sh)
$-CBr_3$	2	$-CH_2Br$	92	156–157.5°	$C_{14}H_{14}BrNO_3S_2$ (388.3)	2.41 (s, 3H); 5.80 (AB-q, 2H); 7.15–8.15 (m, 9H)	1155, 1110, 1088, 1065
$-CH_2Br$	1	$-CH_3$	90	107–109°	107–109°[7]	—	—

[a] Satisfactory microanalyses obtained: C ±0.30, H ±0.30.

[b] Product is a 2:1 mixture of diastereomers.

tion of steric and electronic effects, monochlorination of the benzyl substrate could be achieved (Table 1).

Stepwise reductive dehalogenation of the α-polyhalosulfoximines could be readily achieved using triphenylphosphine[5] in 95% ethanol at reflux for one hour (Table 2). Whereas monobromo compounds were reduced to the parent sulfoximine, the monochloro sulfoximines were inert under these conditions.

Chlorination of *N*-Tosylsulfoximines 1 with Hexachloroethane (2; X = Cl):

To a solution of *N*-tosylsulfoximine **1** (1 mmol) in dry dimethylformamide (5 ml) under a nitrogen atmosphere are added sodium hydride (n mmol; as a 50% oil dispersion) and hexachloroethane (**2**; X = Cl; n mmol: n = number of hydrogens to be substituted). The mixture is stirred overnight at room temperature, quenched with aqueous ammonium chloride solution (10 ml), and extracted with diethyl ether (2 × 10 ml). The ether layer is washed with saturated sodium chloride solution (2 × 10 ml). After drying with anhydrous magnesium sulfate, the ether is evaporated and the crude product **3** is recrystallized from diethyl ether/pentane (Table 1).

Bromination of *N*-Tosylsulfoximines 1 with 1,2-Dibromo-1,1,2,2-tetrachloroethane (2; X = Br):

The procedure followed is similar to that above except (n + 2) mmol of sodium hydride and (n + 1) mmol of 1,2-dibromo-1,1,2,2-tetrachloroethane[6] are used (Table 1).

Reductive Dehalogenation of Halosulfoximines 3 with Triphenylphosphine:

A solution of the halosulfoximine **3** (1 mmol) and triphenylphosphine (1 or 2 mmol) in 95% ethanol (10 ml) is refluxed with stirring for 1 h. In some instances, upon cooling the reaction mixture, the desired sulfoximine **4** crystallizes in pure form, otherwise the alcohol is evaporated and the crude sulfoximine **4** is recrystallized from diethyl ether/pentane or purified by column chromatography on silica gel with dichloromethane as eluent (Table 2).

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