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# REARRANGEMENT REACTION OF N-HALO-S-[(1,2-BENZISOXAZOL-3-YL)METHYL]-SULFOXIMINE TO THE CORRESPONDING α-HALO SULFOXIMINE

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The first example of the rearrangement reaction of N-halosulfoximine to α-halo sulfoximine is described.

Since N-halosulfoximines prepared easily by halogenation of N-unsubstituted (free) sulfoximines have been used as halogenating agents,[1] it is expected that N-halosulfoximine containing a benzyl or an active methylene group could bring about the rearrangement of the halogen atom. However, no research has been reported on this possibility.

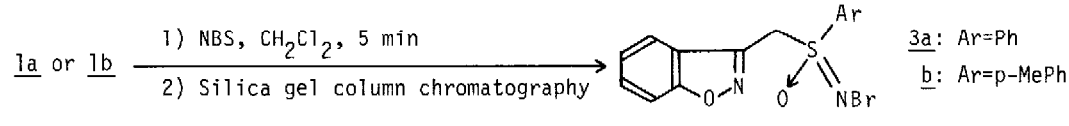
Now we found the rearrangement reaction of N-halosulfoximine having 1,2-benzisoxazole ring whose C=N bond showed the nature of a "masked" carbonyl group[2] to the corresponding α-halo sulfoximine.

The reaction of S-aryl-S-[(1,2-benzisoxazol-3-yl)methyl]sulfoximines 1[3] with an equimolar amount of bromine/pyridine (reaction time, 2-3 hr), N-bromosuccinimide (NBS)(3-4 hr), and N-chlorosuccinimide (24 hr) in commercial chloroform at room temperature gave α-halo "free" sulfoximines 2 in 80-90%(2a-e), ca.60%(2a-c), and ca.70%(2f-h) yields, respectively. All α-halo sulfoximines 2 were isolated as a mixture of diastereomers in the $^1$H-NMR of which two distinct methine singlets were observed; e.g., 2a($CDCl_3$): δ 6.16s and 6.22s(methine), 3.57s and 4.00s(NH), 7.2-8.4m(arom).


1a-e 2a-h

| Compd 1 | a | b | c | d | e | f | g | h | Compd 2 |
|---|---|---|---|---|---|---|---|---|---|
| R | H | H | H | Br | MeO | H | H | H | R |
| Ar | Ph | p-MePh | p-ClPh | Ph | Ph | Ph | p-MePh | p-ClPh | Ar |
| | Br | Br | Br | Br | Br | Cl | Cl | Cl | X |

However, 1a and 1b were treated with NBS in dichloromethane for 5 min at room temperature and then the reaction mixture was chromatographed on silica gel column to afford N-bromosulfoximines 3a and 3b, respectively, in 90% yields.



This suggests that the α-halo sulfoximines 2 were formed via the corresponding N-halo derivatives. Indeed, the bromine transfer reaction of 3 proceeded easily at room temperature in the presence of a light source, even a room light (a fluorescent lamp), as shown in Table.

Table. Products and Yields for the Reaction of N-Bromosulfoximines, 3[a)]

| Compd | Reaction Conditions | Products and Yields(%)[b)] |
|---|---|---|
| 3a | 5%EtOH-$CHCl_3$[c)], 1.5 hr | 1a(38.5), 2a(56.6) |
| | 1%EtOH-$CHCl_3$[c)], 2.5 hr | 1a(35.2), 2a(58.1) |
| | $CH_2Cl_2$, 10 hr | 1a(31.5), 2a(58.5) |
| | 1%EtOH-$CHCl_3$, in the dark, 1 week | no reaction |
| 3b | 5%EtOH-$CHCl_3$, 1.5 hr | 1b(43.4), 1i[d)](trace), 2b(47.1), 2i[e)](trace) |
| | 1%EtOH-$CHCl_3$, 2.5 hr | 1b(34.1), 1i (2.5), 2b(47.8), 2i (5.1) |
| | $CH_2Cl_2$, 10 hr | 1b(24.5), 1i (25.4), 2b(22.5), 2i (16.8) |
| | $CCl_4$, reflux, 10 hr | 1b(31.2), 1i (18.5), 2b(18.6), 2i (9.9) |
| | $CCl_4$, BPO(5%), reflux, 3 hr | 1b(26.0), 1i (15.1), 2b(20.6), 2i (11.2) |

a) The reaction was carried out at room temperature in the presence of a room light unless otherwise stated; b) Determined by HPLC; c) Chloroform containing 5% or 1% of ethanol; d) 1i: R=H, Ar=p-$BrCH_2Ph$; e) 2i: R=H, Ar=p-$BrCH_2Ph$, X=Br.

The effect of solvent was remarkable; the increase of concentration of ethanol in solvent enhanced the rate of this reaction and caused to decrease the yields of radical products. Thus, in dichloromethane and in refluxing carbon tetrachloride 3b gave S-(p-bromomethylphenyl)sulfoximines, 1i(R=H, Ar=p-$BrCH_2Ph$) and 2i(R=H, Ar=p-$BrCH_2Ph$, X=Br), in 10-25% yields in either the absence or presence of a radical initiator, while in chloroform containing 5% of ethanol the yields of 1i and 2i decreased to only trace.

Meanwhile, the reaction of 3a with cyclohexene in chloroform containing 5% of ethanol and in dichloromethane gave 1,2-dibromocyclohexane in 22% and 36% yields, respectively.

These results suggest that the bromine transfer reaction of the N-bromosulfoximines 3 proceeds through an initial photo-induced radical process followed by bromination process with the bromine molecule considered to be formed in the initial step and that the latter process involves two mechanisms, i.e., an ionic process and a radical process similar to brominations of toluene[1b)] and cyclohexene[1c)] using N-bromo-S,S-diphenylsulfoximine, and in the solvent containing ethanol the ionic process is considered to be mainly operative.

Further studies on this reaction are under investigation in these laboratories.

References and Note.

1) a) R. Annunziata, R. Fornasier, and F. Montanari, Chem. Commun., 1133 (1972); b) T. Akasaka, N. Furukawa, and S. Oae, Chem. Letters, 529 (1979); c) Idem, Tetrahedron Letters, 2035 (1979).
2) H. Uno and M. Kurokawa, Chem. Pharm. Bull. (Tokyo), 26, 312 and 3498 (1978).

3) All new compounds gave satisfactory elemental and spectral analyses.

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