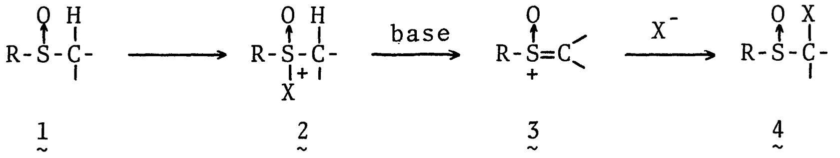
CHEMISTRY LETTERS, pp. 1587-1590, 1980. © The Chemical Society of Japan 1980

CONTROL OF REGIOSELECTIVITY IN α-CHLORINATION OF AN UNSYMMETRICAL DIALKYL SULFOXIDE WITH N-CHLOROSUCCINIMIDE

Katsuyuki OGURA,* Jun-ichi IMAIZUMI, Hirotada IIDA, and Gen-ichi TSUCHIHASHI†
Department of Synthetic Chemistry, Faculty of Engineering,
Chiba University, Yayoi-cho 1-33, Chiba 260
†Sagami Chemical Research Center, Nishi-Ohnuma 4-4-1,
Sagamihara, Kanagawa 229

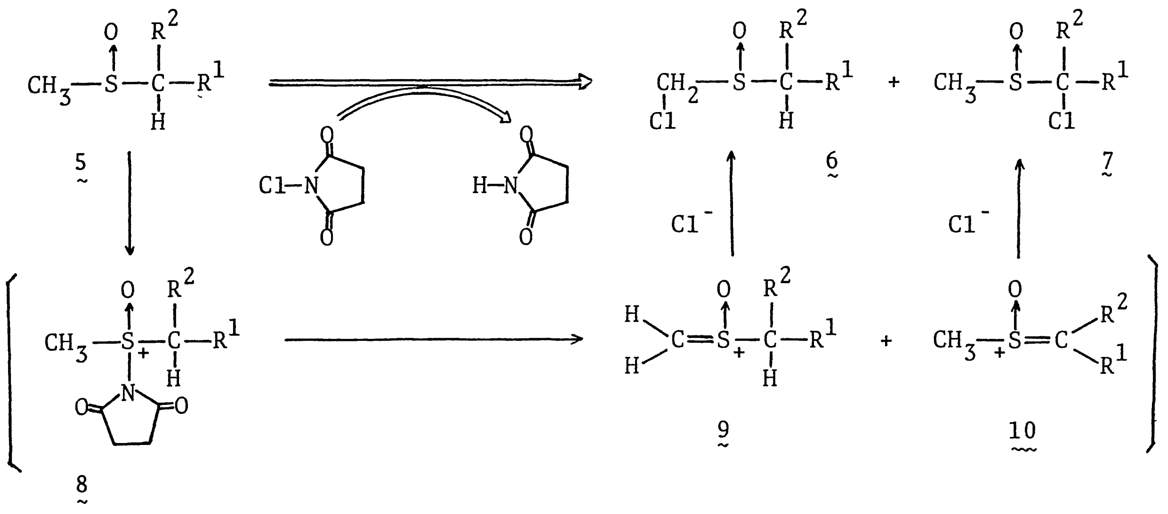
In chlorination of an alkyl methyl sulfoxide (the alkyl = ethyl, isobutyl, or isopropyl) with N-chlorosuccinimide, the corresponding 1-chloroalkyl methyl sulfoxide was predominantly formed, while addition of pyridine into the reaction system reversed the regioselectivity to give an alkyl chloromethyl sulfoxide as a major product.

For halogenation of a sulfoxide (**1**) leading to the corresponding α-halo derivative (**4**), a variety of reagents were reported1) and many probable mechanisms have been presented on the basis of the kinetic and stereochemical studies. Usually such a base as pyridine is added to the reaction system in order to prevent decomposition of the sulfinyl group with the concurrently formed hydrogen halide and, in all the proposed mechanisms, the base plays an important role. For example, the next one which can account for all the experimental results already reported involves a base-assisted elimination of an element of hydrogen halide (HX) from the initially formed oxosulfonium salt (**2**), followed by attack of a halide anion to give **4**.2)



(X = halogen atom)

When this halogenation is applied to an unsymmetrical dialkyl sulfoxide,7) formation of two positionally isomeric products is possible in principle and the crucial step determining the product ratio seems to be the elimination of HX of the oxosulfonium salt (**2**). If so, it is expected that the product ratio can be affected by the absence or presence of a base. To examine this expectation, we carried out chlorination of an alkyl methyl sulfoxide [the alkyl = ethyl (**5a**), isobutyl (**5b**), or isopropyl (**5c**)] with N-chlorosuccinimide (NCS)1i) because this reagent was thought from stoichiometrical consideration not to produce hydrogen chloride. Now we would like to describe our finding that the regioselectivity can be reversed by addition of such a base as pyridine into the reaction system.

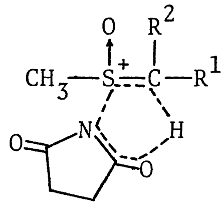


[a: $R^1 = CH_3$ $R^2 = H$, b: $R^1 = (CH_3)_2CH$ $R^2 = H$, c: $R^1 = R^2 = CH_3$]

The reaction was performed by portionwise addition of NCS (1.03 - 1.05 equiv) to a dichloromethane solution of 5 in the presence or absence of pyridine (about 2 equiv) at room temperature, followed by stirring the resulting mixture. After evaporation under reduced pressure, the residue was separated by column chromatography on silica gel to give the chlorinated products (6 and 7). The isolation yield and the ratio of the products are summarized in Table 1.

In every case, an alkyl chloromethyl sulfoxide (6) was predominantly formed in the presence of pyridine, whereas the major product was 7, which was derived from chlorination at the 1-position of the alkyl group, in the absence of any base. It is also noteworthy that insoluble potassium carbonate as well as potassium acetate can behave as a base in analogous manner to give mainly 6.

The predominant formation of 6 in the presence of a base may be accounted for by abstraction of a more acidic and less hindered proton with the base. Thus, the base-assisted elimination of an element of succinimide from the initially formed oxosulfonium salt (8)[8] proceeds mainly in the direction of an alkyloxosulfonium methylide (9) which is transformed to 6 by attack of chloride anion. When any base is not available, it may be reasonable to assume that an element of succinimide eliminates intramolecularly from 8 *via* the stable transition state (11) which possesses considerable double bond character stabilized by more alkyl substituents, resulting in preferable formation of a methyloxosulfonium alkylide (10).



11

Table 1. Chlorination of **5** with NCS

R^1	R^2	Base	Reaction Time (h)	Yield (%)		**6** : **7**
				6	**7**	
CH_3	H	pyr.	12	51	16	75 : 25[a]
		K_2CO_3	2.5	22	10	65 : 35[a]
		AcOK	1	-------[b]		67 : 33[a]
		----	1	14	34	36 : 64[a]
$(CH_3)_2CH$	H	pyr.	23	51	16	76 : 24
		----	1.5	22	34	40 : 60
CH_3	CH_3	pyr.	18	61	7	84 : 16[a]
		----	18	12	46	20 : 80[a]

[a] determined by NMR analysis of the reaction mixture.

[b] not isolated.

Thus, we found the way of controlling the regioselectivity in α-chlorination of an unsymmetrical dialkyl sulfoxide and this will be a useful contribution to the synthesis of new derivatives of sulfoxides *via* α-chlorination.10)

References and Notes

1) (a) p-Toluenesulfonyl Chloride-Pyridine (Pyr.): M. Hojo and Z. Yoshida, *J. Am. Chem. Soc.*, 90, 4496 (1968); (b) NOCl-Pyr.: R. N. Loeppky and D. C. K. Chang, *Tetrahedron Lett.*, 1968, 5415; (c) PhICl$_2$-Pyr.: M. Cinquini, S. Colonna, and F. Montanari, *J. Chem. Soc., Chem. Commun.*, 1969, 607; (d) *t*-BuOCl-Pyr. or AcOK: S. Iriuchijima and G. Tsuchihashi, *Tetrahedron Lett.*, 1969, 5259; (e) Cl$_2$-Pyr.: G. Tsuchihashi and S. Iriuchijima, *Bull. Chem. Soc. Jpn.*, 43, 2271 (1970); (f) Br$_2$-Pyr.: S. Iriuchijima and G. Tsuchihashi, *Synthesis*, 1970, 588; (g) SO$_2$Cl$_2$: K.-C. Tin and T. Durst, *Tetrahedron Lett.*, 1970, 4643; (h) SO$_2$Cl$_2$-Pyr.: G. Tsuchihashi, K. Ogura, S. Iriuchijima, and S. Tomisawa, *Synthesis*, 1971, 89; (i) NCS-Pyr. or K$_2$CO$_3$: G. Tsuchihashi and K. Ogura, *Bull. Chem. Soc. Jpn.*, 44, 1726 (1971).

2) Tsuchihashi,3) Marquet,4) and Klein5) had presented this mechanistic scheme and recently Klein6) proposed this as a general mechanism for halogenation of sulfoxides.

3) S. Iriuchijima, M. Ishibashi, and G. Tsuchihashi, *Bull. Chem. Soc. Jpn.*, 46, 921 (1973).

4) S. Bory, R. Lett, B. Moreau, and A. Marquet, *C. R. Acad. Sci. Ser. C*, 1973,

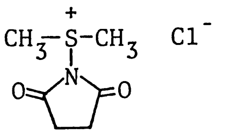
1323.

5) J. Klein and H. Stollar, *J. Am. Chem. Soc.*, 95, 7437 (1973).

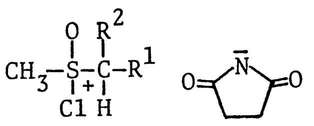
6) J. Klein, *Chem. Lett.*, 1979, 359.

7) Although chlorination of unsymmetrical dialkyl sulfoxides such as benzyl methyl sulfoxide,1c,d,g,i) butyl methyl sulfoxide,1g) and 4-*t*-butyl-2-methylthiane S-oxide4) was reported, the relationship between the regioselectivity of the reaction and a role of the base has received scant attention.

8) The intermediary formation of 8 was supposed, based on the fact that S-(N-succinimido)dimethylsulfonium chloride (12) was isolated in the reaction of dimethyl sulfide with NCS.9) However, the possibilities that a chlorooxosulfonium salt (13) is produced as an intermediate and that 8 is in equilibrium with 13 cannot be excluded. If these possibilities are taken into consideration, "elimination of an element of succinimide" must be replaced by "elimination of an element of hydrogen chloride".



12



13

9) E. Vilsmaier and W. Sprügel, *Justus Liebigs Ann. Chem.*, 747, 151 (1971).

10) For reactions of α-halo sulfoxides see T. Durst and K.-C. Tin, *Tetrahedron Lett.*, 1970, 2369; D. F. Tavares, R. E. Estep, and M. Blezard, *Tetrahedron Lett.*, 1970, 2373; G. Tsuchihashi and K. Ogura, *Bull. Chem. Soc. Jpn.*, 45, 2023 (1972); K. Ogura and G. Tsuchihashi, *J. Chem. Soc., Chem. Commun.*, 1970, 1689; T. Numata and S. Oae, *Bull. Chem. Soc. Jpn.*, 45, 2794 (1972); M. Cinquini, D. Landini, and A. Maia, *J. Chem. Soc., Chem. Commun.*, 1972, 734; H. C. J. Ottenheijm and R. M. J. Liskamp, *Tetrahedron Lett.*, 1978, 2437; V. Reutrakul and W. Kanghae, *Tetrahedron Lett.*, 1977, 1377; V. Reutrakul, A. Tiensripojamarn, K. Kusamran, and S. Nimgirawath, *Chem. Lett.*, 1979, 209.

(Received September 12, 1980)