Tetrahedron Letters,Vol.25,No.7,pp 757-760,1984
Printed in Great Britain

0040-4039/84 $3.00 + .00

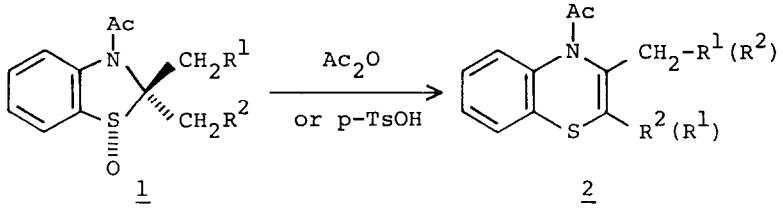
NON-STEREOSPECIFIC RING EXPANSIONS OF 5-MEMBERED HETEROCYCLIC SULFOXIDES

Norihiro Ueda, Hiroshi Shimizu, Tadashi Kataoka, and Mikio Hori*

Gifu College of Pharmacy, 6-1, Mitahora-higashi 5-chome, Gifu 502, Japan

Summary: Non-stereospecific ring expansion reactions of 5-membered heterocyclic sulfoxides, 1,3-benzoxathiole sulfoxides, 1,3-benzodithiole sulfoxides, and 1,3-dithiolane sulfoxides having a heteroatom at β-position to the sulfinyl group with acetic anhydride or p-toluenesulfonic acid are described together with thier reaction mechanism involving a sulfonium ion intermediate.

In our previous papers,[1] dealing with the ring expansion reaction of benzothiazoline sulfoxides (1) with acetic anhydride, we reported that the reaction afforded 1,4-benzothiazines (2) by non-stereospecific mechanism based on the evidence that the reaction underwent the ring expansion in the direction of both cis and trans substituent to the sulfinyl group of 1. Independently, Prota et al. have reported these reactions proceed also with p-toluenesulfonic acid similarly.[2]



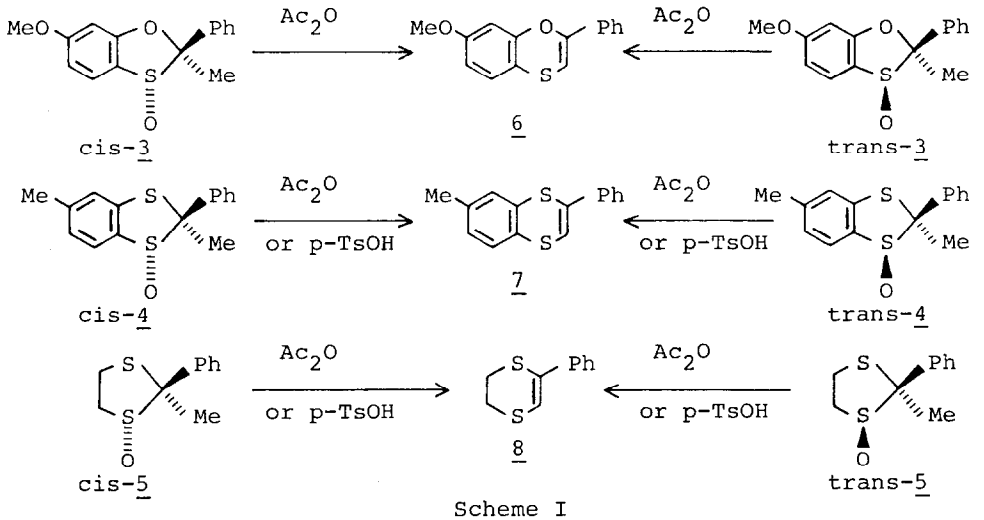
1 2

Concerning to the non-stereospecific mechanism for the ring expansion of benzothiazoline sulfoxides, it is very interesting to investigate the stereospecificity of the ring transformation of other cyclic sulfoxides possessing a heteroatom such as oxygen or sulfur except nitrogen at β-position to the sulfinyl group. Now, in this communication, we describe that the stereospecificity of the ring expansion of 5-membered heterocyclic sulfoxides such as 1,3-benzoxathiole sulfoxide (3), 1,3-benzodithiole sulfoxide (4), and 1,3-dithiolane sulfoxide (5) with acetic anhydride or p-toluenesulfonic acid.

Sulfoxides 3, 4, and 5 were readily obtained by the oxidation of their precursors with m-chloroperbenzoic acid for 30 min in dichloromethane in good yields.[1,3] Cis and trans isomers of these sulfoxides were purely separated by silica gel column chromatography using a mixture of ethyl acetate and n-hexane as an eluent. And the structural assignments of cis and trans isomers were based on their ^{1}H-NMR spectroscopic results, including aromatic solvent-induced shift (ASIS).[4]

Stirring cis-3 (Me is cis to the sulfinyl group) with acetic anhydride at room temper-

ature for 2.5 days afforded the ring expanded product 6 in 48 % yield, and also from trans-3 (Me is trans) the same product 6 was obtained in 27 % yield (runs 1 and 2 in Table I). Similarly, from cis and trans sulfoxides 4 (or 5) the same ring expanded product 7 (or 8) was obtained in 71 and 72 % (or 98, 99 %) yields, respectively (runs 3, 4, 5 and 6 in Table I).



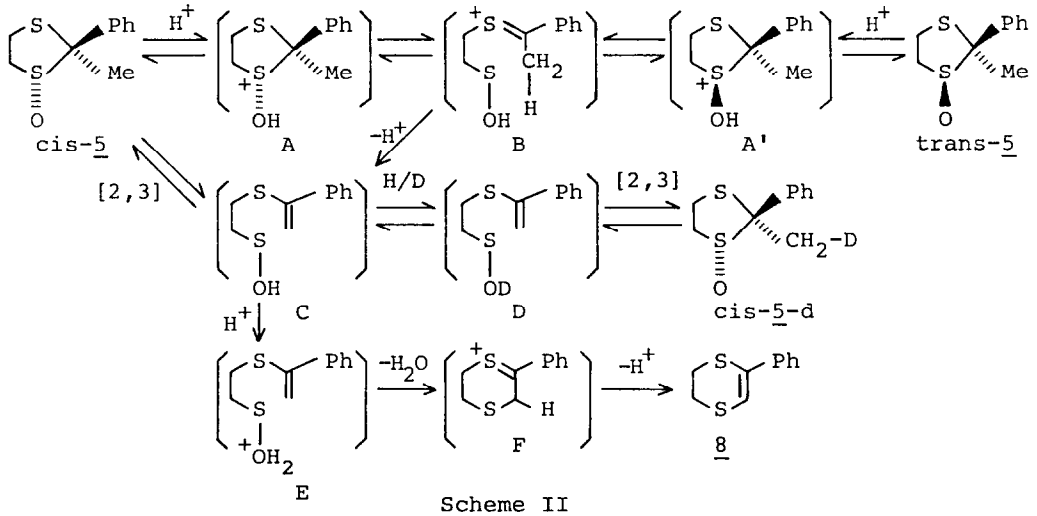
Scheme I

Apparently from these results, cis-3, 4, and 5 expanded in the direction of the cis methyl group to the sulfinyl group, on the contrary, trans-3, 4, and 5 did in the direction of trans methyl group, namely, the ring expansion reaction with acetic anhydride proceeded non-stereospecifically, as well as 1.

Refluxing cis-4 or 5 with p-toluenesulfonic acid (0.25 equiv. for the sulfoxide) in benzene afforded the ring expanded product 7 or 8 in 56 or 77 % yield, respectively, while from trans-4 or 5 the same product 7 or 8 was obtained in 43 or 86 % yield, respectively (runs 7, 8, 9, and 11 in the Table II). And even at room temperature stirring cis-5 for 31 days gave the ring-expanded product 8 besides the unreacted cis-5 in 9 % yield and the isomerized trans-5 in 11 % yield (run 10 in Table II). Consequently, the reaction with p-toluenesulfonic acid also gave the ring-expanded product non-stereospecifically as well as in the case of the reaction with acetic anhydride.

It has been reported that in the thermal reaction of the sulfoxides analogous to 5, the ring expansion proceeded stereospecifically via sulfenic acid intermediate.[3,5] We observed the isomerizations between cis and trans isomers in all cases of the sulfoxides mentioned above in the course of the reaction. This observation offers the possibility that the non-stereospecificity of the ring expanson of the sulfoxides 3, 4, and 5 might come from the isomerization of trans sulfoxides to the cis isomers which ring-open by [2,3] sigmatropy even under the acid- or acetic anhydride-used conditions. In order to examine this possibility, we next carried out the deuterium-incorporation experiments. It was well established that 2-alkyl group substituted sulfoxide is in a thermal equilibrium with the sulfenic acid based on the result that on refluxing a solution of sulfoxide in benzene containing deuterium oxide, deuterium is incorporated into the 2-alkyl group.[5c] We applied this

technique to the above sulfoxide for the examination of a sulfenic acid (cis-5 → C → D → cis-5-d in Scheme II). By refluxing cis-4 for 24 hr with excess deuterium oxide in benzene, deuterium-incorporated products of cis-4 were obtained in 10 % yield in total, and cis-5 afforded 25 % yield of deuterium-incorporated products after refluxing for 6 hr. These yields of deuterated products are rather low, and moreover the deuteration of the methyl group of cis-5 at room temperature was not observed by MS and ^{1}H-NMR spectroscopy, although the ring expansion reaction proceeded even at room temperature in the presence of p-toluenesulfonic acid (Table II,III). From these results, it was confirmed that the ring expansion reaction of cis-4 and 5 proceeded dominantly by the non-stereospecific mechanism in which the C-S bond of the sulfoxide was cleaved by the participation of a heteroatom at β-position via the sulfonium ion intermediate A or A' formed by the initial protonation with p-toluenesulfonic acid or the acylation with acetic anhydride respectively, rather than the stereospecific mechanism through the sulfenic acid intermediate C generated by [2,3] sigmatropy. It was accordingly confirmed that the stereochemistry of cis-5 and trans-5 was lost by the initial formation of the sulfonium ion A or A' followed by ring-opening of it to the heteroatom stabilized carbonium ion intermediate B. The carbonium ion intermediate B is converted to the sulfenic acid C by the loss of the proton, which subsequently leads to the formation of the ring expanded product 8 by acid-catalized ring closure through the intermediate F, as shown in Scheme II.



Scheme II

Thus, it was clarified that the ring expansion reaction of 5-membered heterocyclic sulfoxides having a heteroatom at β-position proceeded non-stereospecifically in the presence of acetic anhydride or p-toluenesulfonic acid and is different from the stereospecific Morin rearrangement in view of the reaction mechanism.

We now continue to investigate the stereospecificity of the ring expansion reaction of 7-membered heterocyclic sulfoxides.

Table I. Ring Expansion Reactions of 3, 4, and 5 with Acetic Anhydride.

run	sulfoxide[a]	temp.	time, day	product[a]	yield, %
1	cis-3	r.t.	2.5	6	48
2	trans-3	r.t.	4	6	27
3	cis-4	r.t.	12	7	71
4	trans-4	r.t.	10	7	72
5	cis-5	r.t.	2	8	98
6	trans-5	r.t.	2	8	99

a. Satisfactory physico-chemical data were obtained for all compounds.

Table II. Ring Expansion Reactions of 4 and 5 with p-Toluenesulfonic Acid.[a]

run	sulfoxide	temp.	time	product	yield, %
7	cis-4	reflux	24 hr	7	56
8	trans-4	reflux	24 hr	7	43
9	cis-5	reflux	3 hr	8	77
10	cis-5	r.t.	31 days	8[b]	22
11	trans-5	reflux	3 hr	8	86

a. 0.25 Equivalent p-toluenesulfonic acid for sulfoxide.

b. Unreacted cis-5 (49 %) and isomerized trans-5 (11 %) remained.

Table III. Deuterium Incorporation of 4 and 5 in Benzene.[a]

run	sulfoxide	temp.	time	rate[b] of deuteration into 2-Me.
12	cis-4	reflux	24 hr	10 %
13	cis-5	reflux	6 hr	25 %
14	cis-5	r.t.	31 days	-

a. Deuterium Oxide - Benzene (1 : 10).

b. Measured by ^{1}H-NMR spectroscopy.

REFERENCES

1)a)M.Hori, T.Kataoka, H.Shimizu, and Y.Imai, Chem. Pharm. Bull.(Tokyo), 27, 1982 (1979).
b)M.Hori, T.Kataoka, H.Shimizu, and N.Ueda, Tetrahedron Lett., 22, 1701 (1981).
2)F.Chioccara, L.Oliva, and G.Prota, Synthesis, 744 (1978).
3)C.H.Chen, Tetrahedron Lett., 25 (1976).
4)a)J.J.Rigau, C.C.Bacon, and C.R.Johnson, J. Org. Chem., 35, 3655 (1970).
b)K.K.Anderson, R.L.Caret, and I.Karup-Nielsen, J. Amer. Chem. Soc., 96, 8026 (1974).
5)a)Although the ring expansion of the similar spiro-1,3-dithiolane sulfoxides in the presence of p-toluenesulfonic acid has been reported, the stereospecificity of the reaction was not discussed in it: C.H.Chen and B.A.Donatelli, J. Org. Chem., 41, 3053 (1976).
b)J.W.A.M.Janssen and H.Kwart, J. Org. Chem., 42, 1530 (1977).
c)R.D.G.Cooper, J. Amer. Chem. Soc., 92, 5010 (1970).

(Received in Japan 2 November 1983)