74. The HCL-Catalyzed Stereomutation of Cyclic Sulfoxides.[1])

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Summary. The critical step in the HCl-catalyzed stereomutation of sulfoxides is a nucleophilic substitution at the sulfur atom [7]. The rate of this reaction has been determined for cyclic sulfoxides as a function of ring size. The trend closely matches that long since established for substitution at alicyclic carbon [11], which confirms the similarity of the geometries of the transition states for substitution at carbon and at sulfur. The results are compared to those for the analogous silicon and phosphorous compounds, and the question of formation of pentacovalent intermediates for substitutions at sulfur is briefly discussed.

The mechanism of nucleophilic substitution reactions at those atoms of the third period which are important in organic chemistry, namely silicon, phosphorus and sulfur, is of active current interest. As a result of numerous investigations, these mechanistic features have taken rather well defined shapes, outlined in a number of recent monographs and reviews (see [1] for silicon, [2] for phosphorus, and [3] for sulfur). However, several finer details of mechanism are not yet fully elucidated require further investigation.

One of these details concerns the geometry of the transition state for substitution at sulfur. The gross geometrical features were inferred long ago [4] as being those of a trigonal bipyramid where nucleophile and leaving group occupy the apical positions. This was based upon the strict parallelism of steric effects observed for substitution at sulfur [4] and at saturated carbon [5] respectively, which strongly suggested similar arrangements of ligands around the reaction centers in the transition state. This geometry is clearly consistent (although it is not specifically required) with the long established stereochemistry, *i.e.* inversion [6], for substitution at sulfur.

More recent investigations have confirmed the trends of steric effects [7] previously observed [4], and established on a wide basis the stereochemical course of inversion during substitution [8][3]).

We hoped to obtain a deeper insight into the geometry of the transition state by the study of substitution reactions at cyclic sulfur atoms. The constraint imposed by the cycle may give rise to rate effects amenable to rationalization in terms of factors such as angular and torsional strain, which in turn may be reasonably traced

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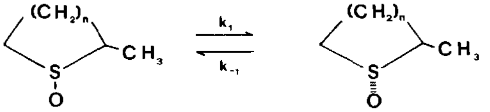
[3]) To the best of our knowledge there is only one report of unambiguous nucleophilic substitution at sulfur with retention of configuration: the conversion of *p*-tolyl and *n*-butyl methyl sulfoxides to the *N*-tosyl sulfimines with *bis*-tosyl-sulfur diimide in benzene [9].

to ring size. Therefore we have examined the effect of ring size on the rate of a nucleophilic substitution at sulfoxidic sulfur. In this first paper we report the results obtained for five-, six-, and seven-membered cyclic sulfoxides.

The reaction chosen was the HCl-catalyzed stereomutation of sulfoxides initially studied by *Mislow et al.* [7a]. Although there is some ambiguity concerning the actual sequence of reactions by which racemization occurs [7c], there can be little doubt that the slow step of this acid and halide catalyzed reaction, like that of the concomitant reduction, is a nucleophilic substitution by halide on the protonated sulfoxide, leading to the (reversible) displacement of the oxygen atom [7].

Results and Discussion. – The rate of stereomutation of the sulfoxide function was obtained by measuring the rate of attainment of equilibrium between diastereomeric 2-methyl-thiacycloalkane 1-oxides in aqueous dioxane containing HCl.



Under these conditions, equilibration is a first-order process which was followed by quantitative gas-liquid chromatography (GLC.).

The equilibrium constant between *cis* and *trans* diastereomers, $K = k_1/k_{-1}$, was obtained by direct measurement of the *cis/trans* ratio at infinite time, and it permits the repartition of the equilibration rate into its components, $k_{eq} = k_1 + k_{-1}$. The Table summarizes the results.

Rates of HCl-Catalyzed Equilibration of Diastereomeric 2-Methylthiacycloalkane 1-oxides in Aqueous Dioxane a)

Ring size	Temp. °C	Isomer ratio initial	Isomer ratio at equilibrium	$10^6 k_{eq}$ s^{-1}	Relative rate
b)	25.0			70.3 c)	19
5	25.0	0.44	2.6	1450	390
6	25.0	100/0	1.8	3.72	1
7	25.0	0.02	0.45	116	31
6	45.0	100/0	1.7	52.7	
6	55.0	100/0	1.8	223	

a) Solvent: H$_2$O, 37% aqueous HCl and dioxane 1:1:0.9 vol.
b) (+)-Methyl 2-butyl sulfoxide.
c) Racemization rate.

From the data at 25, 45 and 55° the activation energy for the six-membered sulfoxide is calculated to be 26.3 kcal/mole. The data, however, are not sufficiently precise to detect any temperature dependence of the isomer ratio at equilibrium.

The isomer ratios reported in the Table are those between the isomer with lower retention time in GLC. compared with the other. Only for the 5-membered sulfoxide this is known to be the *cis/trans* ratio [10]4). For the other systems no configuration can yet be assigned.

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4) The value of the equilibrium constant for the 5-membered cyclic sulfoxide is in excellent agreement with that reported in the literature [10].

The data indicate that ring size affects the rate of stereomutation in the order $5 > 6 < 7$ while the open chain methyl 2-butyl sulfoxide has a reactivity (racemization rate) comparable to that of the seven-membered ring sulfoxide.

It is obvious that ring size has no drastic effect, however. Moreover the order and range of reactivities resembles that found in bimolecular substitution at carbon substrates. For example, for cyclopentyl, cyclohexyl, cycloheptyl and isopropyl bromides reacting with iodide ion, the relative reactivities are: 160, 1, 99, 100 [11].

These findings lend further support to the notion that the geometry of the transition state for direct substitution at sulfur is very similar to that for substitution at carbon, and that displacement occurs from the back side [4].

There is one further point of interest. In the pyramidal inversion of cyclic sulfonium cations, those with five and six members react at very nearly the same rate [12]. In the substitution reaction under investigation here, the rates of the two ring systems differ by a factor of 390. Thus the two reactions have different geometrical requirements and probably involve different degrees of rehybridization of the reaction centre. As the transition state for pyramidal inversion is likely to be very close to planarity with sp^2 hybridization [13], it may be concluded that the transition state for substitution does not achieve complete rehybridization. The close parallelism of steric effects at sulfur and at carbon makes one wonder how general this phenomenon may be.

A comparison of our results for sulfur with those for comparable systems involving other third-period atoms which are important in organic chemistry (Si, P) is permissible.

For nucleophilic substitution at silicon in silacycloalcanes (H^- as the leaving group) the same sequence of ring size and a closely similar range of reactivities have been established by *West* for the 5-, 6-, 7-ring systems and acyclic silanes [14]. However the silacyclobutane system reacts more rapidly [15]⁵) as do other strained systems [15].

Substitution at cyclic phosphorous is complex. Extraordinary increased rates are common in certain five- with respect to corresponding six-membered systems [16], although other 5-membered systems do not display such rate increase [16] [17]⁶).

Similarly, for four-membered systems both high rate increases are recorded [18], as well as rate reductions [19], depending on the nature of the leaving groups and the nucleophile [19].

Thus the behaviour we have found displayed by sulfur, which is analogous to that of saturated carbon, *may* be reproduced, under certain conditions, by silicon and phosphorus. If similar rate trends indicate a similarity in the geometry of transition states then, besides sulfur, silicon and phosphorus also may undergo nucleophilic substitution through a transition state resembling that for S_N2 at carbon. However,

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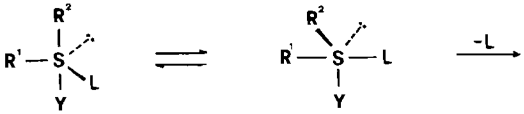
5) Preliminary evidence indicates that, in our system, a four-membered cyclic sulfoxide reacts at a reduced rate with respect to its higher homologues.

6) *Askens & Bergesen* [17] have found that a five-membered cyclic phosphonium cation undergoes displacement (with preservation of the ring) some 1300 times faster than the corresponding six-membered analogue. We tend to consider this factor as 'normal' insofar as it is only one order of magnitude greater than that for substitution at alicyclic carbon, but it is several orders of magnitude *smaller* than that observed for systems where the 'steric acceleration' appears to operate.

if this geometry appears to be necessary for carbon and certainly most common for sulfur, it is neither necessary nor the most common for P and Si. Evidence is furnished not only by the rate trends discussed above (*i.e.* the increased rate in certain strained systems) but also by stereochemical studies: whereas for sulfur there is only one unambiguous report of a substitution with retention of configuration [9], such retention is common for silicon [1b] and has been established for phosphorus in a great variety of cases which include both cyclic and acyclic systems [20]. These two elements must then be capable of a different type of bonding which allows a different geometry. It is a common notion that nucleophilic substitution at Si or P is dominated by the ease of formation of a penta-coordinated trigonal bipyramidal intermediate [16] [1b]. Of its five ligand positions, the basal ones (**b**) will preferentially accomodate the least, and the apical ones (**a**) the most electronegative ligands [16] [21]. On this basis and by further taking into account the strain which may be introduced when a small ring spans the **bb** positions, or relieved when it spans the **ab** positions, that certain substitutions occur with retention and others with inversion, and that certain strained systems yield increased rates and others reduced rates [19] [20f] [22] can be rationalized.

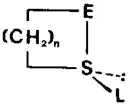
The question then is: why does sulfur not behave more like silicon and phosphorus, rather than more like carbon, as it does? The answer may simply be that sulfur has not yet been sufficiently investigated for revealing the behaviour expected from that of its congeners Si and P.

Let us assume that, just as Si and P, sulfur can form pentacovalent intermediates in a nucleophilic substitution [23][7]. Then when a tricoordinated sulfur compound (R^1R^2S–L, with L as the leaving group) reacts with a nucleophile, Y:, retention of configuration implies an intermediate where an alkyl group (or an electron pair) occupies an **a** position. This is an energetically unfavorable situation [16] [25], so much so that in fact it cannot apparently be reached, with an alkoxide leaving group, even when R^1 and R^2 are part of a highly strained from 4-membered cycle: In fact the alkaline hydrolysis of *cis*- and *trans*-1-ethoxy-3-methyl-thietanium cation gives respectively *trans*- and *cis*-3-methylthietane 1-oxide, *i.e.* the product expected for displacement at sulfur with inversion of configuration [26].



Substitution product (of retained configuration)

In order to be able to regularly observe the phenomena of retention of configuration and increased rate in strained systems (with preservation of the ring) it seems



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[7] The recent isolation of dialkoxy-diaryl-sulfuranes [24] and their preliminarly established structure [24b] give strong support to this hypothesis.

necessary that at least one of the ring atoms alpha to sulfur be an electronegative atom, this must not, however, be more mobile, as a leaving group, than the group L as defined above.

Compounds for which n, E and L would meet the above requirements are mostly unknown and presumably unstable. We are exploring the possibilities of preparing such compounds.

Experimental. – *Materials.* 2-Methylthiolane and 2-methylthiane were prepared according to the procedure of *Whithead et al.* [27]. 2-Methylthiepane was prepared according to the general procedure of *Tuleen & Bennet* [28] through chlorination of thiepane with N-chlorosuccinimide followed by *in situ* methylation with methyl magnesium iodide.

The sulfoxides were obtained by oxidation of the sulfides with H_2O_2 in acetone [29] and purified by distillation. The isomer ratios for 5-, 6- and 7-membered sulfoxides thus obtained were 28/72, 25/75 and 2/98, respectively (the first number is percentage of the isomer with the lower GLC. retention time). Spinning band distillation of 2-methylthiane 1-oxide afforded the first isomer in a pure state.

Kinetics. The equilibration of the isomer mixtures was followed by GLC. analysis on 6 ft × $^1/_8$ in. 2,5% silicon gum nitrile (GEXE-60) on chromosorb G column at 170° [30].

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75. The Gas-Phase Thermal Decomposition of 5-Ethyl-1-pyrroline

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(13. 1. 72)

Summary. The gas-phase thermal decomposition of 5-ethyl-1-pyrroline has been studied in the temperature range 721–786 K. The decomposition appears to proceed by two pathways, one a radical route yielding pyrrole, ethylene and ethane as major products, and the other a molecular hydrogen elimination to form initially 2-ethyl-3*H*-pyrrole which rapidly rearranges to other ethylpyrroles *via* a series of 1,5-hydrogen shifts. Approximate rate constants for the unimolecular hydrogen elimination have been calculated and fit the *Arrhenius* relationship:

$$\log(k/\mathrm{s}^{-1}) = 12.5 \pm 0.4 - (55.5 \pm 1.4\ \mathrm{kcal\ mol}^{-1})/\Theta \text{ where } \Theta = 2.303\ RT.$$

Approximate calculations based on the radical pathway yield a value of $\sim$14 kcal mol^{-1} for the stabilization energy in the 1-pyrrolin-5-yl radical, in good agreement with that reported earlier for the substituted 2-aza-allyl radical.

Introduction. – Kinetic parameters for thermal 1,4-hydrogen elimination reactions have been reported for cyclopentene [1] [2], 1-methylcyclopentene [3], 3-pyrroline [4], 2,5-dihydrofuran [5], and 2,5-dihydrothiophene [6]. In all these reactions, the eliminating hydrogens involved in the orbital symmetry allowed process [7] are in essentially identical environments, and it is of interest to examine the effects of enforced asymmetry on the activation parameters. In 5-ethyl-1-pyrroline, the presence of nitrogen in a terminal position of the double bond, together with the 5-ethyl substituent, render the hydrogen atoms in the 3- and 5-positions non-equivalent.