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THE MECHANISM OF PUMMERER REARRANGEMENTS[1, 2]

Carl R. Johnson,[3a] John C. Sharp, and W. Gary Phillips[3b]
Department of Chemistry, Wayne State University, Detroit, Michigan 48202

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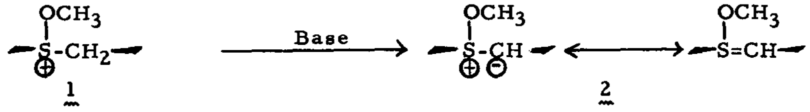
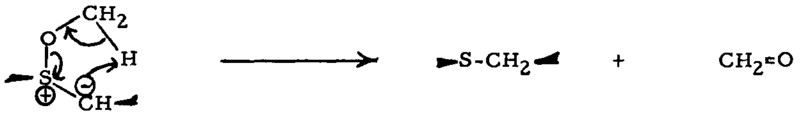
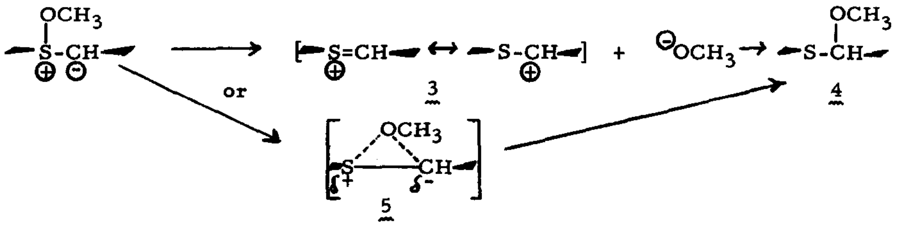
Recently we reported[4] that alkoxysulfonium salts (1) upon treatment with alkoxides undergo alkoxy exchange followed by (a) base-catalyzed collapse to carbonyl compounds and sulfides and/or (b) α-rearrangements (analogous to the Pummerer reaction) to produce monothioacetals. Deuterium experiments revealed that the elimination to carbonyl compounds proceeds via a cyclic transition state involving the sulfur ylid 2. The preponderance of the α-rearrangement product 4 appeared to be a function of the stability of the carbonium ion 3 formed by elimination of alkoxide from the ylid intermediate. However, a transition state (5) involving direct transfer could not be excluded. We now wish to present additional evidence for the intermediary of 3 in the postulated mechanistic pathway b and to relate this pathway to the familiar Pummerer reaction.



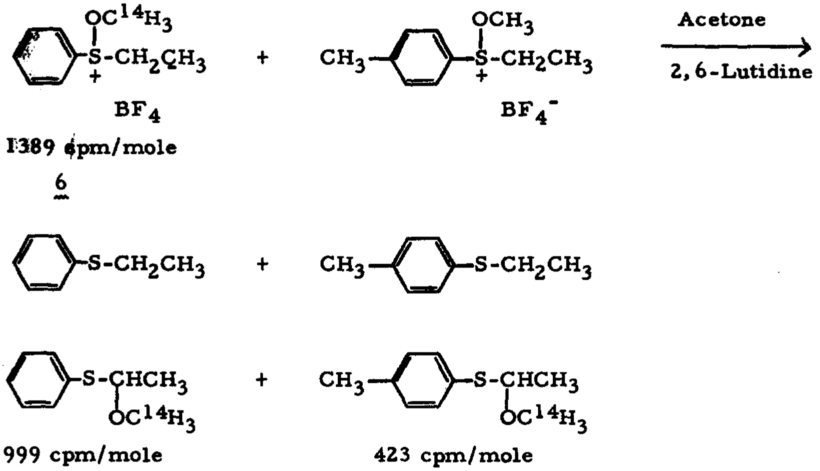
Pathway a



Pathway b



Evidence ruling out direct transfer of the alkoxide group to the neighboring carbon was obtained from the crossover experiment illustrated in equation 1. Appropriate control experiments eliminated the possibility of scrambling of the label after the products were formed. These results provide obligatory evidence



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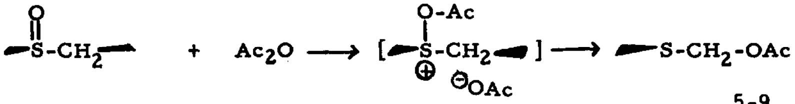
that the alkoxy group escapes to the solution in the α-rearrangement reaction. Scrambling would not be expected to be statistical with short-lived ions such as 3. Solvent effects are also consistent with the intervention of a cation intermediate. With salt 6 (without label) the ratio of products of pathway a to that of b is a linear function of the methyl alcohol concentration in a methyl alcohol-tetrahydrofuran mixture with the preponderance of α-rearrangement product increasing with solvent polarity.

The analogy of these rearrangements to the Pummerer reaction which yields α-acyloxysulfides when the corresponding sulfoxide is treated with an acid anhydride is noteworthy (Eq. 2). Here the acyloxysulfonium salt is believed to be an intermediate which subsequently decomposes to the product. The mechanistic



details of this reaction have been the subject of much speculation.[5-9] There have been only two examples reported of the reaction of simple unsymmetrical sulfoxides with acetic anhydride. Oae and coworkers[10] obtained only 9 percent of acetoxymethyl n-butyl sulfide along with several unidentified products on treatment of methyl n-butyl sulfoxide with refluxing acetic anhydride. Such data makes their conclusion that migration takes place exclusively to the methyl group questionable. Results with methionine sulfoxide were likewise undefinitive.[10]

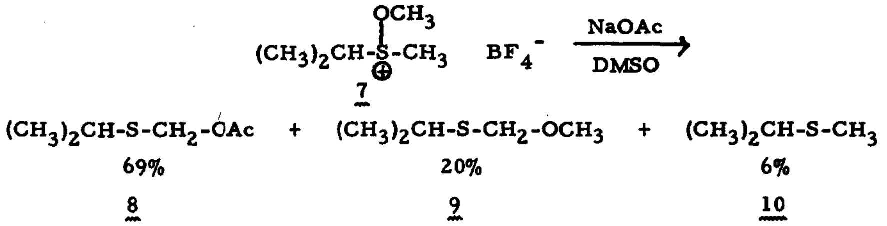
Our results obtained upon reaction of unsymmetrical sulfoxides with acetic anhydride in refluxing benzene are shown in Table I. In each case only one product was formed; the yields are not corrected for recovered starting materials. Thus, it appears that migration does indeed proceed to the least substituted α-carbon. This result is undoubtedly a reflection of the difference in acidities of the α-protons of the intermediate acetoxysulfonium salt. Removal of the proton is the product-determining (and possibly rate-determining) step of the reaction. This conclusion seems reasonable since ylids of this type are not reprotonated to any significant extent.[4]

TABLE I

RESULTS OF PUMMERER REARRANGEMENT ON UNSYMMETRICAL SULFOXIDES

Sulfoxide	Product	% Yield
Methyl isopropyl	α-acetoxymethyl isopropyl sulfide	69
Methyl n-propyl	α-acetoxymethyl n-propyl sulfide	73
Methyl n-butyl	α-acetoxymethyl n-butyl sulfide	64

It would be expected by analogy to rapid alkoxy interchange[4] that an intermediate acetoxysulfonium salt would be formed when an alkoxysulfonium salt is reacted with acetate ion. In fact, when isopropylmethylmethoxysulfonium fluoroborate (7) was treated with sodium acetate in DMSO acetoxymethyl isopropyl sulfide was formed as the major product (Eq. 3). A small amount of highly volatile but unidentified fourth product (probably isopropyl mercaptan) was also obtained. (Similar results have been obtained by treatment of a number of alkoxysulfonium salts with a variety of carboxylates.) It is important to note that the acetate migrated to the least substituted carbon atom as did the methoxy group suggesting similar mechanisms for their formation.

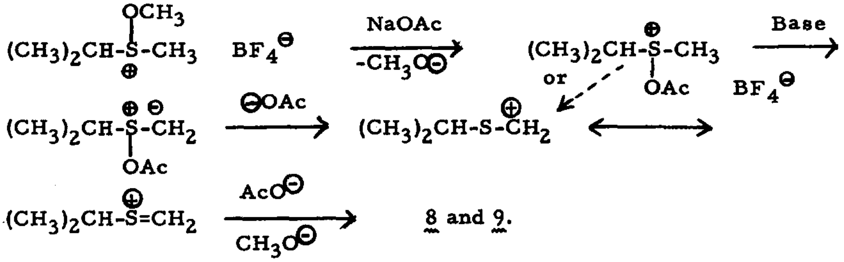


$$\underset{7}{(CH_3)_2CH\text{-}\overset{OCH_3}{\underset{\oplus}{S}}\text{-}CH_3}\quad BF_4^- \xrightarrow[DMSO]{NaOAc}$$

$$\underset{\underset{8}{69\%}}{(CH_3)_2CH\text{-}S\text{-}CH_2\text{-}OAc} + \underset{\underset{9}{20\%}}{(CH_3)_2CH\text{-}S\text{-}CH_2\text{-}OCH_3} + \underset{\underset{10}{6\%}}{(CH_3)_2CH\text{-}S\text{-}CH_3}$$

The sulfide 10 is formed via pathway a. Compounds 8 and 9 are derived from pathway c. It is unlikely that 9 is formed from the ylid derived from alkoxysulfonium salt since S-methyl salts of this type react almost entirely via pathway a to give the parent sulfide.[4] Our comparative data points to the fact that the Pummerer reaction follows an entirely analogous mechanistic scheme involving carbonium ion intermediates.[7]

Pathway c



$$(CH_3)_2CH\text{-}\overset{OCH_3}{\underset{\oplus}{S}}\text{-}CH_3\quad BF_4^{\ominus} \xrightarrow[-CH_3O^{\ominus}]{NaOAc} (CH_3)_2CH\text{-}\overset{\oplus}{\underset{OAc}{S}}\text{-}CH_3\quad BF_4^{\ominus} \xrightarrow{Base}$$

$$(CH_3)_2CH\text{-}\overset{\oplus\ \ominus}{\underset{OAc}{S}}\text{-}CH_2 \xrightarrow{\ominus OAc} (CH_3)_2CH\text{-}S\text{-}\overset{\oplus}{C}H_2 \longleftrightarrow$$

$$(CH_3)_2CH\text{-}\overset{\oplus}{S}{=}CH_2 \xrightarrow[CH_3O^{\ominus}]{AcO^{\ominus}} 8 \text{ and } 9.$$

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