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THE ZWITTERION-ACCELERATED [3,3]-SIGMATROPIC REARRANGEMENT OF ALLYL VINYL SULFOXIDES TO SULFINES. A SPECIFIC CLASS OF CHARGE-ACCELERATED REARRANGEMENT

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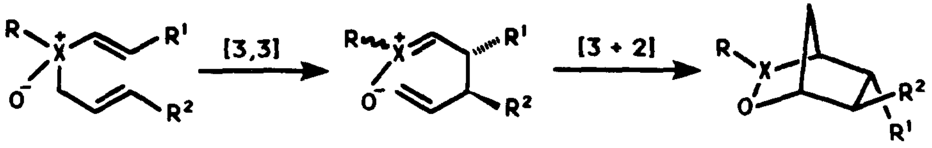
Abstract: *Conversion of allyl vinyl sulfoxides* **5** *and* **8** *to* γ,δ*-unsaturated sulfines* **6** *and* **9**, *respectively, under neutral conditions shows that the accelerating effects of the charges in a zwitterionic moiety do not cancel, instead the sulfoxide functionality significantly facilitates the rearrangement.*

Uncatalyzed [3,3]-sigmatropic rearrangement reactions can be accelerated by placing electron donating or withdrawing groups in the substrate, or more remarkably by introducing a positive or a negative charge into the system. Examples of cation-accelerated rearrangements include Breslow's carbocationic Cope rearrangement[1] and the ammonium-iminium rearrangements.[2] Anion-accelerated rearrangements include Ireland's ester enolate-Claisen rearrangement,[3] Evans' anionic oxy-Cope rearrangement,[4] and carbanionic Claisen rearrangements.[5] Herein, we provide solid evidence that the conversion of allyl vinyl sulfoxides to γ,δ-unsaturated sulfines belongs to a third class of charge-accelerated rearrangements;[6] that is "zwitterion-accelerated rearrangement".

In a zwitterion-accelerated [3,3]-sigmatropic rearrangement, the accelerating factor comes from a moiety that is either a betaine[7] or an ylide.[8] In the latter category, conversion of **1** to **2** offers a unique system that provides valuable information to theoretical chemists about the effects of a zwitterionic moiety on rearrangement rate and offers an expedient route to synthetic chemists for the construction of heterobicyclic [2.2.1]heptanes **3** (Scheme 1).[9] We are specifically interested in investigating the rearrangements of allyl vinyl sulfoxides[10] and allyl enamine oxides. Concerned that the preparation of enamine oxides may be difficult,[11] we initially concentrated our efforts on the sulfoxide system. Since the semipolar S-O bond linkage in sulfoxides[12] results in zwitterionic character, this system can determine what effect a dipolar ionic moiety has on rearrangement rate. Sulfoxide **1a** may utilize the charge accelerating effects of both the sulfonium salt rearrangement[13] and the anionic oxy-Cope process,[4] having both the tricoordinated sulfur (*S*⁺) and the oxide (*O*⁻) at the appropriate positions. Alternately, the effects of the charges may cancel to yield no rate acceleration.



1a X = S; R = electron pair
b X = N

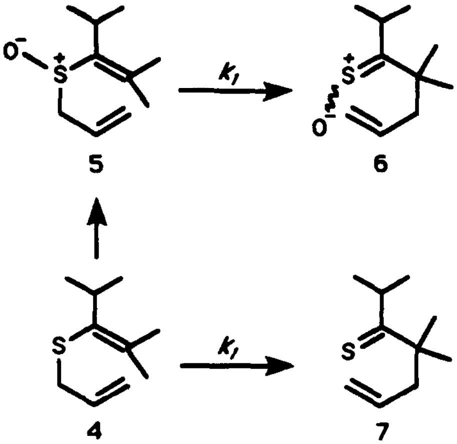
2

3

Scheme 1

If the rearrangement rate of sulfoxide **1a** is significantly faster than that of the corresponding sulfide, it demonstrates the existence of a zwitterion-accelerated rearrangement.

We studied the kinetics of reactions **5** → **6** and **4** → **7** (Scheme 2) under neutral conditions in $CDCl_3$, by monitoring them with ^{1}H-NMR. Sulfoxide **5** was prepared by oxidizing sulfide **4**[14] with one equivalent of *m*-chloroperbenzoic acid (*m*-CPBA) in $CHCl_3$ at 23 °C for 0.5 h. The reaction mixture was then diluted with ether, neutralized with 10% $KOH_{(aq)}$, followed by continued normal neutral workup to give anhydrous products **5** and **6**. We determined the rate constant for the first order reaction of **5** → **6**[15] at 23 °C to be 0.156 ± 0.004 h^{-1}.[16a,17] Comparing that to the k_1 (= 0.0035 ± 0.0001 h^{-1}[16b,17]) for **4** → **7** at 23 °C, the zwitterion-accelerated rearrangement of **5** → **6** is 45 times faster.[18] Thus the effects of the two opposite charges on *S* and *O* do not cancel but rather add to enhance the reaction rate.



Scheme 2

Conversion of **5** to **6** was also carried out under acidic and basic conditions.[19] In acidic medium, the sulfoxide moiety can form hydrogen bonds,[12] thus reducing the accelerating effect of the oxide (O^-) on the [3,3] pathway. However, the sulfonium center (S^+) can still fully contribute to the rate enhancement. Consequently, the rearrangement of **5**, prepared from the oxidation of **4** with *m*-CPBA without neutralizing the acidic media, to give **6** may proceed via a cation-like process. The k_1 for **5** → **6** at 23 °C in the presence of *m*-chlorobenzoic acid (*m*-CBA), resulting from the oxidant *m*-CPBA, was found to be 0.135 ± 0.006 h^{-1}.[16c,17] Alternately, removal of the acidic proton in *m*-CBA by adding a strong base, such as $LiH_{(s)}$, $NaH_{(s)}$ or $KH_{(s)}$, to the reaction mixture in order to make the matrix basic resulted in a slower rearrangement (15-17% conversion of **5** under basic conditions versus 35% conversion under neutral conditions at 0 °C for 0.5 h, followed by warming the solution to room temperature and allowing the rearrangement to proceed for an additional 2.5 h). Therefore, we conclude that the rearrangement rate for the conversion of allyl vinyl sulfoxide **5** to γ,δ-unsaturated sulfine **6** under various conditions decreases along the series neutral ≥ acidic > basic. Under neutral reaction conditions, the observed accelerating effect results from a genuine zwitterionic moiety. In contrast, the different reaction rates for **5** → **6** under acidic and basic conditions indicate the possible existence of alternative mechanisms.

We believed that the presence of various cation species in the reaction mixture should not significantly effect the rate of the zwitterion-accelerated rearrangement of **5** to **6**.[20] Indeed,

Table 1: Conversion of 5 → 6 (3.5 h) in the presence of various cations

cation	% conversion 5 → 6
Li^+	41.1
Na^+	42.9
K^+	38.4

in the presence of Li^+, Na^+ or K^+, the difference in the rearrangement rate, as reflected by percent conversion in 3.5 h (see Table 1), was insignificant. The reaction was performed by oxidizing **4** with *m*-CPBA in chloroform at 0 °C for 0.5 h followed by washing the solution with $LiOH_{(aq)}$ and then drying with $LiOH_{(s)}$, resulting in a total time at room temperature of 3 h; or with $NaOH_{(aq)}$-$Na_2SO_{4(s)}$ and $KOH_{(aq)}$-$KOH_{(s)}$ combinations, respectively.

Sulfoxide **5** completely rearranged to sulfine **6** over a wide range of temperatures (8 °C to 101 °C). The corresponding sulfide **4**, however, rearranged to give equilibrium compositions of 67% of thioketone **7** at 101 °C[14] and 87% at 23 °C. The sulfoxide rearranges more rapidly[21] and also more completely than the uncharged sulfide, making the reaction synthetically useful.[19] We also observed that, after 78% conversion, the rearrangement of **5** → **6** at -23 °C moved towards equilibrium with an extremely sluggish rate. Attempts to experimentally demonstrate the reversibility of the rearrangement by converting **6** to **5** in chloroform solution at -23 °C resulted in decomposed material.

We also successfully converted allyl vinyl sulfoxide **8** to thioaldehyde *S*-oxide **9**[19] (Scheme 3) under neutral, acidic, and basic conditions. Consistent with the results obtained for **5** → **6**, neutral conditions provided the most rapid rearrangement rate.

8 **9**

Scheme 3

In summary, conversion of allyl vinyl sulfoxides **5** and **8** to γ,δ-unsaturated sulfines **6** and **9**, respectively, under neutral conditions with an accelerating effect demonstrates the existence of zwitterion-accelerated rearrangements. The accelerating effects of the charges in a dipolar ionic moiety do not cancel, instead the sulfoxide functionality significantly facilitates the rearrangement. The sulfoxide-sulfine system provides valuable information on the role of multiple charges in [3,3]-sigmatropic processes.

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(15) For compound **6**: ^{1}H-NMR (80 MHz, $CDCl_3$, TMS) δ = 1.18 (s, $C(CH_3)_2$); 1.50 (d, $CH(\underline{CH_3})_2$); 2.25 (d, CH_2); 2.87 (m, $CHMe_2$); 4.94-5.19 (m, $=CH_2$); 5.47-6.0 (m, CH=); ^{13}C-NMR (100 MHz, $CDCl_3$, TMS) δ = 19.66 (q, CH_3); 26.33 (q, CH_3); 35.43 (d, $CHMe_2$); 42.79 (s, CMe_2); 44.89 (t, CH_2); 119.34 (t $=CH_2$); 133.73 (d, HC=); 213.92 (s, S=C); MS, *m/z* 186.1075 (M^+); IR (neat) 2960, 1720, 1460, 1370, 1270, 1090, 1000, 920 cm^{-1}.

(16) (a) correlation coefficient $\geq$ 0.998; (b) correlation coefficient $\geq$ 0.992; (c) correlation coefficient $\geq$ 0.993.

(17) Standard deviations from regression analysis.

(18) This acceleration is comparable to that of an allyl aryl sulfoxide, which rearranges *ca.* 50 times faster than the corresponding sulfide at 100 °C, see (8).

(19) For previous work on related substrates under acidic conditions, see: Block, E.; Ahmad, S. *J. Am. Chem. Soc.* **1985**, *107*, 6731.

(20) In the anionic oxy-Cope process, counterion has a remarkable effect on the rearrangement rate, see (4).

(21) At room temperature, rearrangement of **5** → **6** reached equilibrium in *ca.* 30 h while **4** → **7** took *ca.* 34 days to equilibrate.

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