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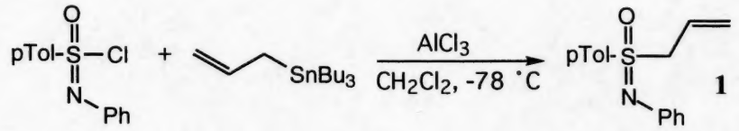
A THEORETICAL ANALYSIS OF 2,3 SIGMATROPIC SHIFTS IN ALLYLIC SULFILIMINES AND SULFOXIMINES

Michael Harmata,* Rainer Glaser,* and Grace Shiahuy Chen

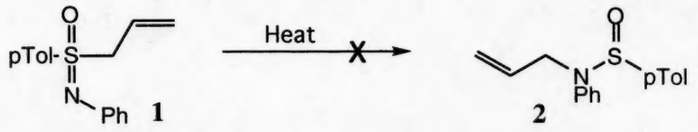
Department of Chemistry, University of Missouri-Columbia, Columbia, Missouri 65211

Abstract: Ab initio calculations at the level MP4(SDTQ,full)/6-31G*//MP2(full)/6-31G* + ΔVZPE(MP2(full)/6-31G*) support the experimental observation that allylic sulfoximines do not undergo 2,3 sigmatropic shifts. This process is hindered by a high kinetic barrier although the reaction is strongly exothermic.

Recently, we reported the synthesis of some allylic sulfoximines by the reaction of sulfonimidoyl chlorides with tributylallyltin in the presence of aluminum chloride (Eq. 1).[1] Anions of some of these compounds were prepared and found to react without appreciable stereoselectivity. Subsequent to our studies, several other groups reported the alkylations of different classes of allylic sulfoximine anions and found them



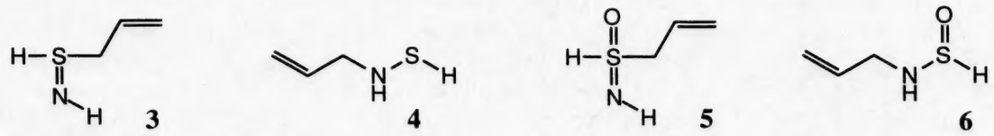
Equation 1



Equation 2

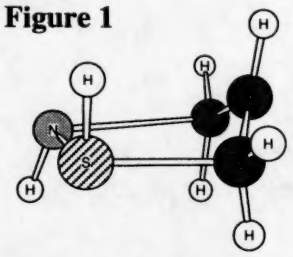
to react with high stereoselectivity.[2] More relevant to the present work is the finding that **1** was stable in refluxing toluene and did not undergo a 2,3 sigmatropic shift to the sulfinamide **2** (Eq. 2). Semi-empirical calculations suggested the reaction to be exothermic[1] and we concluded that a substantial kinetic barrier must exist for the process. Pyne and Boche have also found an allylic sulfoximine which does not experience a 2,3-shift upon thermolysis and they have performed semi-empirical calculations which agree with our own.[2a] Recently, Gais et al. reported that in fact certain allylic sulfoximines are apparently capable of forming allylic sulfinamides via a thermal process in low yield.[3] The mechanism of this rearrangement has yet to be established. Pyne et al. reported a facile rearrangement of allylic sulfoximines catalyzed by palladium.[4]

To further examine this rearrangement, we examined the reaction using ab initio theory and report herein equilibrium structures of the starting materials and products for the 2,3 sigmatropic shift of allylic sulfilimines (**3** and **4**) and sulfoximines (**5** and **6**) and on the transition state structures **3**‡ and **5**‡, respectively, for their interconversion (Figure 1). Reaction energies and activation barriers are listed in Table 1. Bond lengths and atomic charges are summarized in Tables 2 and 3, respectively.

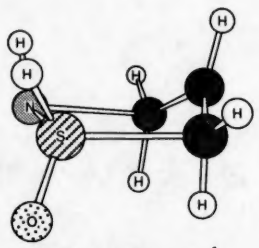


Structures were optimized at the correlated level MP2(full)/6-31G* and first and second energy derivatives were computed analytically in each case at the level of optimization to confirm that a stationary structure indeed had been located and to obtain vibrational frequencies and zero-point energies.[5] Relative energies were refined at the MP4(SDTQ,full)/6-31G* level and, in some instances, QCISD(T,full)/6-31G* energies also were determined. The deviations between the state-of-the-art quadratic CI calculations and the results of the perturbational treatment are within 2 kcal/mol and emphasize the suitability of the latter.

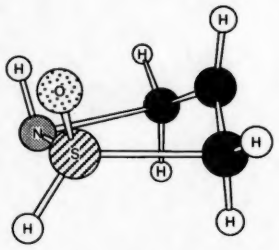
Figure 1



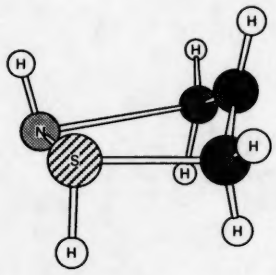
3a‡ (-256 cm^{-1})
HS-endo,HN-exo



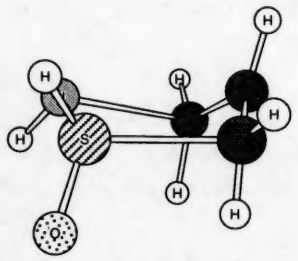
5a‡ (-543 cm^{-1})
OS-exo,HN-endo



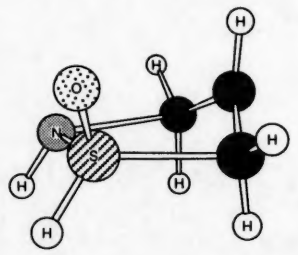
5c‡ (-547 cm^{-1})
OS-endo,HN-endo



3b‡ (-244 cm^{-1})
HS-exo,HN-endo



5b‡ (-529 cm^{-1})
OS-exo,HN-exo



5d‡ (-593 cm^{-1})
OS-endo,HN-exo

Table 1. Relative Energies of Transition State Structures and Products.[a]

	MP2[b]	MP4[c]	QCISD[d]	$MP2_{corr}$[b]	$MP4_{corr}$[c]	$QCISD_{corr}$[d]
4	-40.54	-40.83	-41.33	-39.58	-39.87	-40.37
6	-22.38	-24.56	-25.25	-21.93	-24.11	-24.80
3a‡	5.38	5.77	7.41	4.80	5.19	6.83
3b‡	5.67	5.70		5.05	5.08	
5a‡	35.86	34.32		34.31	32.77	
5b‡	32.92	31.49		31.35	29.92	
5c‡	30.67	29.32		29.30	27.95	
5d‡	37.15	36.13		35.62	34.60	

[a]In kcal/mol, relative to **3** or **5** without and with vibrational zero-point energy corrections. [b]MP2(full)/6-31G*. [c]MP4(SDTQ,full)/6-31G*//MP2(full)/6-31G*. [d]QCISD(T,full)/6-31G*//MP2(full)6-31G*.

Four transition states **5**‡ were optimized. **5a**‡ and **5b**‡ are exo with regard to the O attached to S and **5c**‡ and **5d**‡ are the respective OS-endo structures. For **5a**‡ and **5c**‡, the amino-H is endo. For both pairs, we find a clear preference for those isomers in which the S-O and N-H bonds are cis, **5b**‡ and **5c**‡. The best O-endo transition state structure **5c**‡ is 2.0 kcal/mol preferred over the best O-exo transition state structure **5b**‡. The basis for this energy difference is not clear but we speculate that the origin of this effect might lie in a repulsive interaction between the N lone pair and the developing negative charge at C2. With regard to this lowest-energy transition state **5c**‡, our best estimate of the activation energy is 28.0 kcal/mol. The conversion of **5** to **6** is exothermic by 24.1 kcal/mol at the same level of theory. As with **5**‡, there also are four isomeric transition state structures of **3**‡ that a priori would need to be considered. Of these, we optimized only those structures in which the S-H and N-H bonds are not eclipsed which should reduce lone pair and steric repulsions. The structures **3a**‡ and **3b**‡ are nearly isoenergetic. For the process **3** → **3b**‡ → **4** we determined an activation barrier of 5.1 kcal/mol and an exothermicity of the reaction of 39.9 kcal/mol.

The most important finding concerns the dramatic difference in energy barriers between allylic sulfilimines and sulfoximines for their 2,3 rearrangement. Allylic sulfilimines are known to rearrange at or below room temperature to the corresponding sulfenamides spontaneously and completely.[6] The experimental observation is in complete agreement with the very low activation barrier computed for this process.

Nevertheless, it must be recalled that these are gas phase calculations and that solvent effects may play an important role in altering the activation energy of the process. Notwithstanding this caveat, it is clear that the difference between the barriers calculated for the 2,3 sigmatropic rearrangements of **3** and **5** is enormous and we conclude that a large kinetic barrier does exist for the 2,3 shift of allylic sulfoximines to sulfinamides. Analysis of the structures and of the electronic relaxation along the reaction paths might permit an answer to the question as to the origin of this barrier.

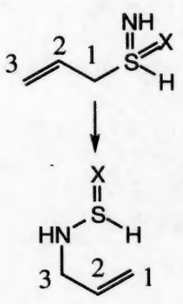


Table 2. Pyramidalization Parameters (P) and Bond Lengths (Å).

	P_N	P_{C2}	S-C	S-O	S-N	N-C	C=C	C-C
3			1.836		1.594		1.340	1.489
3a‡	301.4	355.8	2.159		1.612	2.409	1.366	1.422
3b‡	298.3	356.8	2.153		1.607	2.475	1.362	1.429
4					1.735	1.473	1.337	1.500
5			1.785	1.478	1.533		1.337	1.493
5a‡	310.2	354.3	2.266	1.487	1.591	2.118	1.385	1.400
5b‡	309.8	354.2	2.281	1.496	1.583	2.151	1.383	1.396
5c‡	300.4	354.5	2.277	1.493	1.597	2.144	1.386	1.398
5d‡	312.2	352.3	2.183	1.486	1.595	2.077	1.386	1.405
6				1.497	1.711	1.475	1.337	1.500

Table 3. Atomic Charges from Natural Population Analysis.

	C1	C2	C3	S	N	H(N)	H(S)	O	SH	NH
3	-0.68	-0.26	-0.40	0.86	-1.14	0.37	0.06		0.92	-0.77
3a‡	-0.60	-0.29	-0.42	0.65	-0.96	0.38	0.12		0.77	-0.59
3b‡	-0.61	-0.29	-0.42	0.67	-0.98	0.38	0.12		0.79	-0.60
4	-0.40	-0.26	-0.29	0.12	-0.82	0.40	0.13		0.24	-0.42
5	-0.72	-0.26	-0.40	1.85	-1.18	0.40	0.01	-0.95	1.86	-0.78
5a‡	-0.55	-0.33	-0.36	1.50	-1.00	0.40	0.07	-0.91	1.57	-0.60
5b‡	-0.54	-0.30	-0.37	1.48	-1.02	0.41	0.09	-0.94	1.57	-0.61
5c‡	-0.54	-0.32	-0.38	1.47	-0.99	0.41	0.09	-0.93	1.56	-0.59
5d‡	-0.54	-0.34	-0.34	1.50	-1.02	0.40	0.07	-0.92	1.57	-0.62
6	-0.41	-0.25	-0.30	1.21	-0.90	0.40	0.04	-0.94	1.25	-0.50

The S and N atoms experience the greatest change in charge. The values q(S)-q(N) are reduced from 2.0 (**3**) to 0.9 (**4**) and from 3.0 (**5**) to 2.1 (**6**) during the rearrangements and these changes are virtually the same if the H charges are included (1.7 to 0.7, 2.6 to 1.7). In both cases, the polarity of the initial S=N bonds is greatly diminished in going to the S-N single bond and this relaxation occurs smoothly. In the transition states, the charge relaxation at N has progressed less compared to the charge relaxation at S. Since the SH charge is reduced more than the NH charge, it follows that the overall negative charge of the allyl system also is reduced during the rearrangements. We find a common pattern in that the rearrangements essentially maintain the charges of the central C2 atom (0.26) while the negative charges of the terminal C atoms are reduced and significantly more so for C1 (by ≈0.3) than for C3 (by ≈0.1). All transition state structures show a significant lengthening of the C-S bond and the bond lengths are very similar compared to transition state structures of related sigmatropic rearrangements of hydrocarbon systems as well as allylic sulfoxide/sulfenate systems.[7] However, the two rearrangements are clearly distinct with regard to the C-N bond lengths. The relative lengths of the C-N bonds in the transition states indicate that S-C bond breaking has progressed more than C-N bond formation and more so in the case of the sulfilimine (CN > 2.4 Å) than for the sulfoximine (CN < 2.2 Å). The attack of N at C3 is difficult in both cases because C3 and the entire allyl group are negatively charged for both systems. In the case of the oxygenated systems, however, the oxygen effectively reduces the negative charge on the allyl system and, hence, shorter CN bond distances are realized in the **5**‡ structures. If the CN bond formation is more progressed in the slower reaction, then it is clear that the higher activation barrier must be due to the higher energy requirements for breaking the C-S bond in the oxygenated systems compared to the sulfilimine. We can offer two rationales for the higher barrier to S-C

cleavage. The NP analysis shows that the C-S bond in **5** is more polar than in **3** and the barrier may be related to the increased charge relaxation. On the other hand, the presence of oxygen at sulfur might require a higher activation for C-S bond cleavage because of increased electron-electron repulsion between the O lone pairs and the lone pair forming at S. A similar argument has been put forth to explain the high barrier to racemization in sulfoxides.[8] Finally, it is worthwhile noting that the charges at C2 become more negative in the transition state structures before they are again reduced in the products and this effect is particularly strong for the reaction **5** → **6**. As a consequence of this electron distribution, the central C2 atom slightly pyramidalizes as is reflected in the P_{C2} values given in Table 2 which are the sums of the angles at C2.

In summary, these theoretical results suggest that a large kinetic barrier exists for the 2,3 sigmatropic shift of allylic sulfoximines to sulfinamides. The analysis suggests that the differences are due primarily to the higher activation required for C-S cleavage in the oxygenated system. It may be possible to facilitate this rearrangement by substituting the allyl system with an electron withdrawing group or by attachment of an electron-withdrawing group to S.[9] Further, a similar rearrangement of the selenium analogues of sulfoximines might be feasible due to the decreased strength of the C-Se bond.[10] Electron-withdrawing substituents (π acceptors) might best be introduced in the C2 position as such placement would not only reduce the overall negative allyl charge but also would effectively moderate the charge built-up at C2 on the way to the transition state. These possibilities are under active consideration and the results will be reported in due course.

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