

Theoretical Studies of Eliminations. 5. Intermolecular vs Intramolecular Eliminations: An *ab Initio* Study of the Gas-Phase Reaction of NH_2^- with $\text{CH}_3\text{CH}_2\text{SCH}_3$

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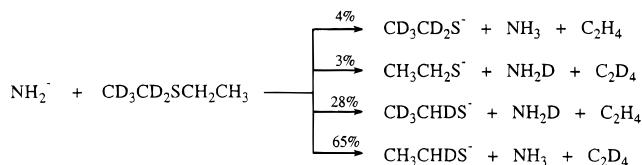
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Ab initio calculations at the MP2/6-31+G**//MP2/6-31+G* level have been completed on the title reaction. The computational results are in good accord with a mechanism suggested by Nibbering and co-workers in 1987. The preferred elimination pathway involves abstraction of an α -proton followed by an intramolecular syn elimination. Although a conventional E2 mechanism is viable, abstraction of an α -proton has a substantial energetic advantage and is effectively irreversible. The intramolecular syn elimination has a higher barrier than a conventional anti E2 pathway, but is the only option after the irreversible α -proton abstraction. Results are also presented for the reaction of fluoride with $\text{CH}_3\text{CH}_2\text{SCH}_3$.

Introduction

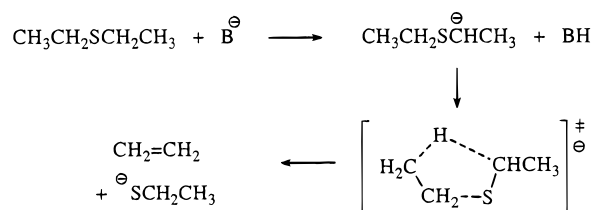
In 1987 Nibbering and co-workers reported a fascinating mechanism for the gas-phase, base-induced eliminations of dialkyl sulfides.¹ When treated with a strong base such as NH_2^- , diethyl sulfide yields ethanethiolate as the major ionic product. Since it is known that alkyl sulfides do not undergo $\text{S}_\text{N}2$ reactions under these conditions,² this result points to an E2 elimination; however, careful deuterium labeling studies¹ indicated that another mechanism must be active. For example, consider the reaction of NH_2^- with $\text{CD}_3\text{CD}_2\text{SCH}_2\text{CH}_3$.



The first two products are the result of a direct E2 elimination, but the latter two require a rearrangement to explain the deuterium scrambling in the thiolate product. Realizing that NH_2^- is a strong enough base to remove an α -proton from an alkyl sulfide (the ΔH_{acid} values for NH_3 and CH_3SCH_3 are 403.6 and 393.2 kcal/mol, respectively),³ they suggested a mechanism that involved abstraction of an α -proton followed by an intramolecular elimination (Scheme 1).

As can be seen from the mechanism, the net result is an elimination with a transfer of a hydrogen from a β -position to an α' -position. This mechanism explains the deuterium scrambling and was referred to as an α',β -elimination.⁴ The branching ratios in Nibbering's experiments suggest that this mechanism accounts for over 90% of the elimination products when NH_2^- or other amides are used as the base. With weaker bases such as HO^- or F^- , only conventional E2 pathways were found. α',β -

Scheme 1



eliminations have also been observed in the reaction of tetrahydrothiophenes with amide.⁵

Given that gas-phase E2 eliminations are generally fast when exothermic,⁶ it is somewhat surprising that the α',β -elimination mechanism would be so dominant. Moreover, the α',β -elimination mechanism requires an unfavorable syn conformation for the elimination transition state.^{7–10} To investigate this effect, we have undertaken an *ab initio* study of the mechanism of the reaction of NH_2^- with $\text{CH}_3\text{CH}_2\text{SCH}_3$. Ion–dipole complexes, E2 transition states, and the transition states of the α',β -elimination mechanism have been located.

Methods

All calculations were carried out on HP-720 or HP-735 computers using the GAUSSIAN92 quantum mechanical package developed by Pople and co-workers.¹¹ All structures were fully optimized using a 6-31+G* basis set. The curvature of the potential energy surface at all minima and transition states was confirmed with analytical

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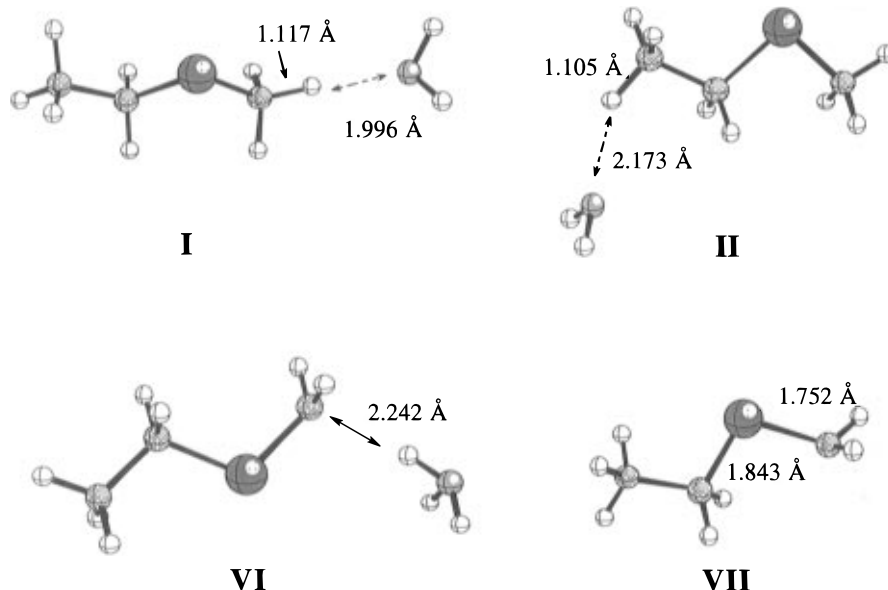


Figure 1. Structures of minima in the reaction of NH_2^- with $\text{CH}_3\text{CH}_2\text{SCH}_3$ (MP2/6-31+G*).

second-derivatives at the Hartree-Fock level. When appropriate, the possibility of multiple rotamers was investigated. To account for correlation effects, the geometries were reoptimized at the MP2/6-31+G* level and final energies are reported at the MP2/6-31+G** level. Using the Hartree-Fock frequencies, corrections were made for zero-point energy differences (scaled by 0.9135).¹²

Results and Discussion

For either reaction path, the first minimum on the potential energy surface will be a loosely bound, ion-dipole complex. For molecules such as diethyl sulfide, there are many energetically similar conformations for the ion-dipole complex. For simplicity, only two structures were located, one leading to an α',β -elimination (**I**) and the other leading directly to an E2 reaction (**II**). The structures are shown in Figure 1 and the energies are given in Table 1. The longer C-H distance and shorter N-H distance in **I** suggest a stronger hydrogen bonding interaction, yet **II** is about 1 kcal/mol more stable. However, both complexation energies are relatively small, indicating an absence of strong, specific interactions.

There are two possible pathways for the conventional E2 elimination. The transition state for the anti elimination (**III**) is shown in Figure 2. At the transition state, proton transfer is well underway (C-H distance = 1.427 Å), yet leaving group expulsion has just begun (C-S distance = 1.867 Å). In comparison to our previous study of the reaction of HO^- with $\text{CH}_3\text{CH}_2\text{OCH}_3$, **III** is an earlier E2(anti) transition state.⁸ This is not unexpected given that the present system involves a stronger base and a better leaving group. At the MP2/6-31+G**//MP2/6-31+G* level, this transition state is 5.9 kcal/mol more stable than the separated reactants. The syn transition state (**IV**) is also shown in Figure 2. As we have noted in the past, E2(syn) eliminations do not require periplanar transition states.⁸⁻¹⁰ To avoid eclipsing interactions, **IV** adopts an almost perfectly staggered transition state ($\text{H}_\beta\text{-C}_\beta\text{-C}_\alpha\text{-S}$ dihedral angle = 59.6°). The conformation

Table 1. Energies of Complexes, Transition States, Reactants, and Products

structure	HF/6-31+G*	MP2/6-31+G**	ZPE	relative energy	
				HF	MP2
I	-571.30449	-572.10863	76.4	-8.5	-11.2
II	-571.30622	-572.11041	76.4	-9.6	-12.3
III	-571.27870	-572.09595	73.7	5.0	-5.9
IV	-571.27138	-572.08654	73.6	9.5	-0.1
V	-571.28777	-572.10117	74.0	-0.4	-8.9
VI	-571.31619	-572.11772	77.1	-15.1	-16.2
VII	-515.11413	-515.71036	54.8	-8.4	-7.6
VIII	-515.07176	-515.69432	51.7	15.2	-0.6
IX	-952.78248	-953.68618	80.6	17.3	2.7
X	-615.16109	-615.96245	61.3	15.3	9.6
XI	-615.14625	-615.94926	61.2	24.5	17.8
$\text{CH}_3\text{SCH}_2\text{CH}_3$	-515.77154	-516.35858	64.2		
NH_2^-	-55.51808	-55.73094	11.4		
NH_3	-56.18950	-56.39198	21.2		
CH_3S^-	-437.12693	-437.40956	22.2		
$\text{CH}_2=\text{CH}_2$	-78.03582	-78.32314	31.3		
HSCH_2^-	-437.04315	-437.33654	19.3		
F^-	-99.41859	-99.62385	0.0		

^a Absolute energies in hartrees and relative energies in kcal/mol. Zero-point energies in kcal/mol and scaled by 0.9135.

is very similar to the one found for the reaction of HO^- with $\text{CH}_3\text{CH}_2\text{OCH}_3$ although the transition state is somewhat earlier on the reaction coordinate. Transition state **IV** is 5.8 kcal/mol less stable than **III**; therefore, the anti pathway should dominate. This is consistent with numerous experimental as well as theoretical studies of E2 eliminations.^{7-10,13-18}

The pathway for the α',β -elimination begins with **I** and leads first to a transition state for proton transfer (**V**). In the transition state, the breaking C-H distance is 1.360 Å and the forming N-H distance is 1.389 Å. Based on these distances, this can be viewed as an earlier transition state than is observed for the E2 eliminations. The transition state is 8.9 kcal/mol more stable than the

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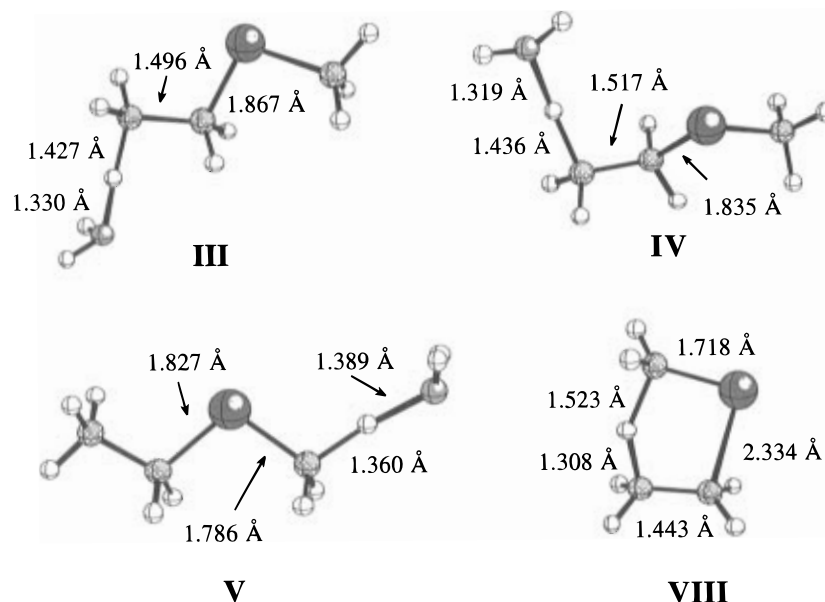


Figure 2. Structures of transition states in the reaction of NH_2^- with $\text{CH}_3\text{CH}_2\text{SCH}_3$ (MP2/6-31+G*).

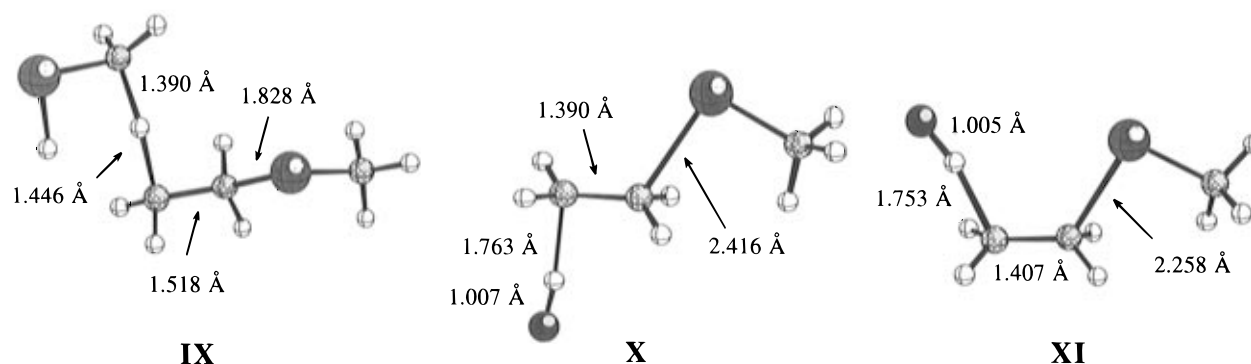


Figure 3. Structures of the E2 transition states of the reaction of HSCH_2^- with $\text{CH}_3\text{CH}_2\text{SCH}_3$ (**IX**) and F^- with $\text{CH}_3\text{CH}_2\text{SCH}_3$ (anti, **X**, and syn, **XI**) at the MP2/6-31+G* level.

reactants or 3 kcal/mol more stable than transition state **III**. Therefore, the lowest energy pathway involves proton transfer from an α -carbon. The initial product complex, **VI**, is 16.2 kcal/mol more stable than the reactants. The separated products of this reaction, **VII** and NH_3 , are 7.6 kcal/mol more stable than the reactants, indicating that proton transfer to form **VII** is viable and favorable under gas phase conditions. The energy of **VII** suggests a ΔH_{acid} of 396.0 kcal/mol for the methyl group of ethyl methyl sulfide. This value seems somewhat high given the experimental ΔH_{acid} of dimethyl sulfide (393.2 kcal/mol)³ and suggests a small error at this theoretical level.

From **VII**, transition state **VIII** leads to the elimination of ethene. The transition state geometry has a perfect synperiplanar arrangement ($\text{H}_\beta\text{-C}_\beta\text{-C}_\alpha\text{-S}$ dihedral angle = 0°). In the transition state, the breaking C-S distance is surprisingly long (2.334 Å) and the breaking C-H distance is surprisingly short (1.308 Å). These distances suggest that the intramolecular elimination has a more E1-like transition state. For comparison, the E2(syn) elimination reaction of HSCH_2^- with $\text{CH}_3\text{CH}_2\text{SCH}_3$ (**IX** in Figure 3), adopts a gauche transition state ($\text{H}_\beta\text{-C}_\beta\text{-C}_\alpha\text{-SCH}_3$ dihedral = 70°) and has bond lengths similar to the other eliminations (C-S breaking = 1.828 Å and C-H breaking = 1.446 Å). The activation energy associated with transition state **IX** is 2.7 kcal/mol whereas the barrier to the intramolecular elimination (**VIII**) is 7.0

kcal/mol with respect to **VII**. In other words, the intramolecular elimination is only slightly less favorable than the bimolecular analog despite the extreme differences in geometry. These results are a testament to the unusual flexibility of the E2 transition state. The unusual geometry for **VIII** can be rationalized in the following way. The five-membered ring of the intramolecular reaction makes it very difficult for the system to maintain a linear proton transfer arrangement as well as reasonable bond angles for the other linkages. One option for maintaining linearity in the proton transfer is to stretch the breaking C-S distance and reduce the breaking C-H distance. It is remarkable that although transition state **VIII** is forced to have an entirely different character (much more E1-like) it suffers only a minor energetic disadvantage. Obviously, the potential energy surfaces of elimination reactions are relatively flat and the transition state can easily be pushed along the E1cb-like $\rightarrow \text{E2} \rightarrow \text{E1}$ -like spectrum.¹⁶

The energy of transition state **VIII** with respect to the reactants, $\text{NH}_2^- + \text{CH}_3\text{CH}_2\text{SCH}_3$, is -0.6 kcal/mol; therefore the α',β -elimination pathway is energetically viable in the gas phase. A plot of the reaction energetics (Figure 4) illustrates the preference for the α',β -elimination pathway. When the NH_2^- attacks, the most favorable transition state, **V**, involves proton transfer from the α -carbon and initially produces a complex of **VII** and NH_3

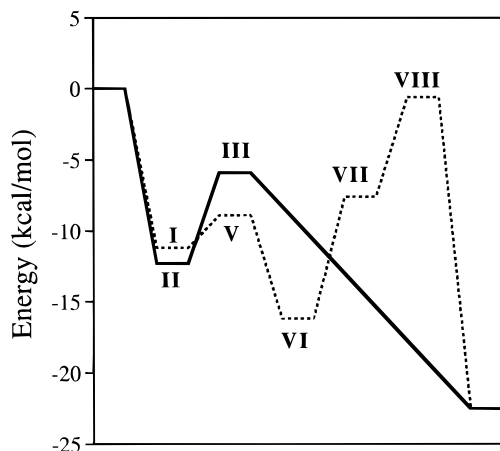
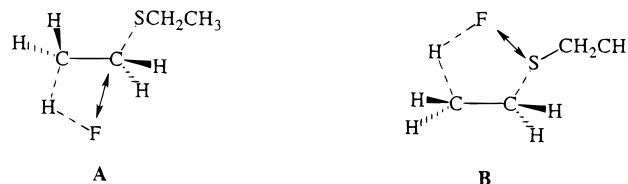


Figure 4. Relative energies of maxima and minima on the potential energy surface for the reaction of NH_2^- with $\text{CH}_3\text{CH}_2\text{SCH}_3$ (MP2/6-31+G**). The conventional E2 path is the solid line and the α,β -elimination path is the dashed line. It should be noted that there is an ion-dipole complex on the reaction coordinate between **III** and the products. This complex was not investigated in the present study.

(complex **VI**). The experimental work gives some important information about this complex.¹ First, no deuterium exchange was seen in the reaction of NH_2^- with $\text{CD}_3\text{CD}_2\text{SCD}_2\text{CD}_3$, indicating that the α -proton abstraction must be effectively irreversible. This suggests that either the lifetime of the complex (with respect to expulsion of NH_3) is too short for exchange or that the intramolecular elimination occurs much faster than the exchange. Both are likely because deuterium exchange is slow with ammonia¹⁹ and complex **VI** has adequate energy for the elimination process.²⁰ The second key experimental observation is that the $\text{M} - 1$ anion of the parent sulfide is formed in small amounts. This indicates that in some cases the NH_3 departs with sufficient energy to leave **VII** as a stable anion. This is not surprising because the calculations indicate that transition state **VIII** is almost at the energy of the entrance channel and therefore any excess energy in the departing NH_3 could inhibit the elimination.²¹ Given this information, it is not possible to discern whether the elimination occurs mainly in the product complex (**VI**) or in free **VII**; however, the preferential and irreversible formation of **VI** explains why the elimination proceeds almost exclusively through **VIII** despite the fact that **III** is a more stable transition state for the elimination. It is not the nature of the elimination transition state that is key, but instead, the greater acidity of the α -position. With weaker bases (such as HO^- or CH_3O^-), the proton transfer to give **VII** becomes endothermic and cannot compete with the conventional E2 pathway.

The reaction of F^- with $\text{CH}_3\text{CH}_2\text{SCH}_3$ was investigated at the same theoretical level. On the basis of experimental isotope effects,¹ unusual transition states were

suggested for the E2 elimination reactions of F^- with $\text{CH}_3\text{CH}_2\text{SCH}_2\text{CH}_3$. Specifically, an E2C path (**A**) was suggested for the anti elimination and a transition state with an $\text{F}-\text{S}$ interaction (**B**) was suggested for the syn elimination (key transition state interactions are noted with double-headed arrows).



However, at the MP2/6-31+G* level, we find transition state geometries that are typical of E2 reactions (**X** and **XI** in Figure 3). Specifically, the $\text{F}-\text{H}-\text{C}$ linkages of the proton transfers are nearly linear. As Jensen and Glad have noted,²² kinetic isotope effects in gas phase eliminations are sometimes misleading because they can be contaminated by large contributions from equilibrium isotope effects. This is particularly important when the frequencies of the breaking and forming bonds are very different ($\text{C}-\text{H}$ vs $\text{F}-\text{H}$).²³ In any case, the $\text{F}-\text{S}$ interaction in structure **B** seems unlikely because both of these atoms should have a partial negative charge. Finally, it should be pointed out that our calculations indicate that the E2 reaction of F^- with $\text{CH}_3\text{CH}_2\text{SCH}_3$ has a high barrier (particularly syn) and therefore the reaction should be too slow to be observed under typical gas phase conditions (Table 1); however, elimination products were observed in the reaction of F^- with $\text{CH}_3\text{CH}_2\text{SCH}_2\text{CH}_3$.¹ This suggests an error in the calculated barrier or the presence of translationally excited fluoride ions in the experiment. Although one cannot rule out an error in the theoretical approach, the present results are supported by calculations up to the MP4/6-31+G**/MP2/6-31+G* level.

Conclusions

Ab initio calculations suggest that in the reaction of NH_2^- with alkyl sulfides, the kinetically favored path involves abstraction of an α -proton. Under gas-phase conditions, this step is irreversible and predisposes the system to an α,β -elimination rather than a conventional E2 elimination despite the fact that the E2 transition state is more stable than the transition state of the intramolecular elimination.

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Supporting Information Available: Tables of Cartesian coordinates for relevant species (5 pages). This material is available in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(20) The reaction of free **VII** has a negative activation barrier, and the presence of the ammonia should further stabilize transition state **VIII** (via ion-dipole interactions) relative to the separated reactants.

(21) Assuming no excitation in the departing NH_3 , **VII** is formed with 7.6 kcal/mol of excess energy and can overcome the 7.0 kcal/mol barrier to elimination. If some of the excess energy is deposited in the NH_3 , **VII** may not have enough internal energy to reach **VIII**.

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(23) Zero-point energy differences do not suggest any unusual isotope effects in these transition states. However, a very low primary isotope effect is observed because the transition state is late and has a nearly fully formed $\text{H}-\text{F}$ bond.