On the Mechanism of Base-Induced Gas-Phase Elimination Reactions of Cyclic Thioethers

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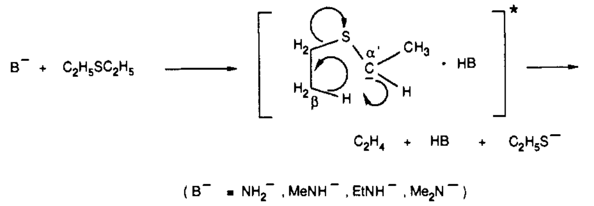
Abstract: The base-induced gas-phase reactions of a series of four cyclic thioethers have been studied with use of the method of Fourier Transform Ion Cyclotron Resonance. Products and mechanisms have been probed by using specifically deuterium labeled substrates as well as bases. Three types of reactions are found to occur: E2, α'-proton abstraction followed by α',β-elimination, and S_N2 substitution. The branching ratios of the primary reaction channels as well as the fraction of α'-deprotonated sulfide reacting further via an α',β-elimination have been determined as a function of the base strength and the sulfide ring size. The results show that the gas-phase acidity of cyclic sulfides diminishes as the sulfides become more strained. Furthermore, both E2 and α',β-elimination appear to be under strict stereoelectronic control, which is also characteristic of condensed phase concerted β-elimination reactions. Finally, it is shown that the S_N2 reaction rates of cyclic sulfides decrease if the sulfide ring size is drastically reduced. This behavior has been explained by the electron distribution in small ring systems, which tends to project away from the molecule, thereby shielding it from nucleophilic attack.

Our studies concerning the mechanism of base-induced gas-phase elimination reactions of simple ethers[1] and thioethers[2] have revealed that the applicability of the concept of the variable transition state structure is not limited to condensed phase β-elimination reactions. Perturbations in transition-state character effected by changing the leaving group or the base as indicated by our gas-phase kinetic deuterium isotope and leaving group effect data indeed follow the rules established for base-induced elimination reactions in the condensed phase.[3,4]

Moreover the studies, referred to above, indicate that the overall exothermicity may be a selection criterion for the mechanistic "mode" of the elimination reactions. That is, relatively highly exothermic elimination reactions prefer an entropically favored linear proton transfer transition state as in the E2H mechanism,[5] whereas close to thermoneutral elimination reactions prefer an enthalpy favored transition state characterized by a bent proton transfer and a two-side attack of the base on the substrate as in the E2C[6] and syn mechanism (Figure 1).

For example, the close to thermoneutral reactions of OH^- with diethyl ether and F^- with diethyl sulfide are considered to proceed via two competing elimination mechanisms, namely the E2H and syn mechanism for the OH^-/diethyl ether reaction system and the E2C and syn mechanism for the F^-/diethyl sulfide reaction system.[1,2]

On the other hand, the *direct* elimination reactions induced by the strong nitrogen bases NH_2^-, $MeNH^-$, $EtNH^-$, and Me_2N^-, for both substrates, exclusively proceed via an E2H mechanism.[1,2] However, only about 7% of the ethyl thiolate product anions in the reaction of the nitrogen bases and diethyl sulfide are formed via a *direct* elimination reaction. The remaining 93% are formed via a not so common α',β-elimination mechanism[2] initiated by α'-proton abstraction of the sulfide and followed by a proton transfer from the β-carbon to the α'-carbon (eq 1). This α',β-elimination mechanism, which has been detected in the reactions of specifically deuterium labeled ethyl sulfides, can enter into competition with the direct elimination mechanism because the initiating α'-proton abstraction is exothermic (at least 3 kcal/mol for the weakest nitrogen base used, Me_2N^-).[7]



(1)

The present Fourier Transform Ion Cyclotron Resonance (FT–ICR) study is concerned with the properties of this α',β-elimination mechanism in relation with the direct β-elimination mechanism. Especially the geometric restrictions of both mechanisms have been investigated by studying the base-induced eliminations of cyclic sulfides, where the ratio direct elimination/α'-proton abstraction and the fraction of α'-deprotonated sulfide reacting further via an α',β-elimination have been determined as a function of the base strength and the sulfide ring size.

Experimental Section

Experiments were performed with our home-made Fourier transform ion cyclotron resonance mass spectrometer.[11] The experimental procedures were as described in previous papers on related studies.[1,2]

Materials. Most of the chemicals used were commercially available. The specifically deuterium labeled cyclic sulfides were prepared following a literature procedure.[12] All sulfides were purified by preparative GC before use (GC conditions: column O.V. 17; temperature 90–130 °C).

For all deuterium labeled sulfides the label content was better than 97%.

Results

Hexamethylene Sulfide. Reaction of NH_2^- with α,α-dideuterio-α',α'-dideuteriohexamethylene sulfide (**1**) proceeds both by E2 elimination and α'-deuterium abstraction resulting in the formation of $(M - H)^-$ and $(M - D)^-$ ions, respectively. The product ion distribution, however, varies with the reaction time as a consequence of consecutive reactions. By extrapolating the product ion distribution to zero reaction time, it has been established that reaction of NH_2^- with **1** yields 87% $(M - D)^-$ and 13% $(M - H)^-$ ions. In order to selectively study the chemistry of these

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(1) Koning, L. J. de; Nibbering, N. M. M. *J. Am. Chem. Soc.* **1987**, *109*, 1715.

(2) Berkel, W. W. van; Koning, L. J. de; Nibbering, N. M. M. *J. Am. Chem. Soc.* **1987**, *109*, 7602.

(3) Thornton, E. R. *J. Am. Chem. Soc.* **1967**, *89*, 2915.

(4) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 2nd ed.; Harper and Row: New York, 1981; pp 197-210.

(5) (a) Bunnett, J. F. *Angew. Chem., Int. Ed. Engl.* **1962**, *1*, 225; *Angew. Chem.* **1962**, *74*, 931. (b) Barthsch, R. A.; Bunnett, J. F. *J. Am. Chem. Soc.* **1968**, *90*, 408.

(6) (a) Parker, A. J.; Ruane, M.; Biale, G.; Winstein, S. *Tetrahedron Lett.* **1968**, 2113. (b) Biale, G.; Cook, D.; Lloyd, D. J.; Parker, A. J.; Stevens, I. P. R.; Takahashi, J.; Winstein, S. *J. Am. Chem. Soc.* **1971**, *93*, 4735.

(7) Heats of formations of the reactants and products are calculated from the data in ref 8 and 9. The gas-phase acidity $\Delta H°_{acid}$ of EtSEt is estimated to be less than 3 kcal/mol lower than that for MeSMe (see ref 10).

(8) The gas-phase acidity data has been taken from: Bartmess, J. E.; McIver, R. T. *Gas Phase Ion Chemistry*; Bowers, M. T., Ed.; Academic: New York, **1979**; Vol. 2, Chapter 11, p 87.

(9) Heats of formation of the neutrals have been calculated or taken from: Benson, S. W. *Thermochemical Kinetics*, 2nd ed.; Wiley-Interscience: New York, 1976.

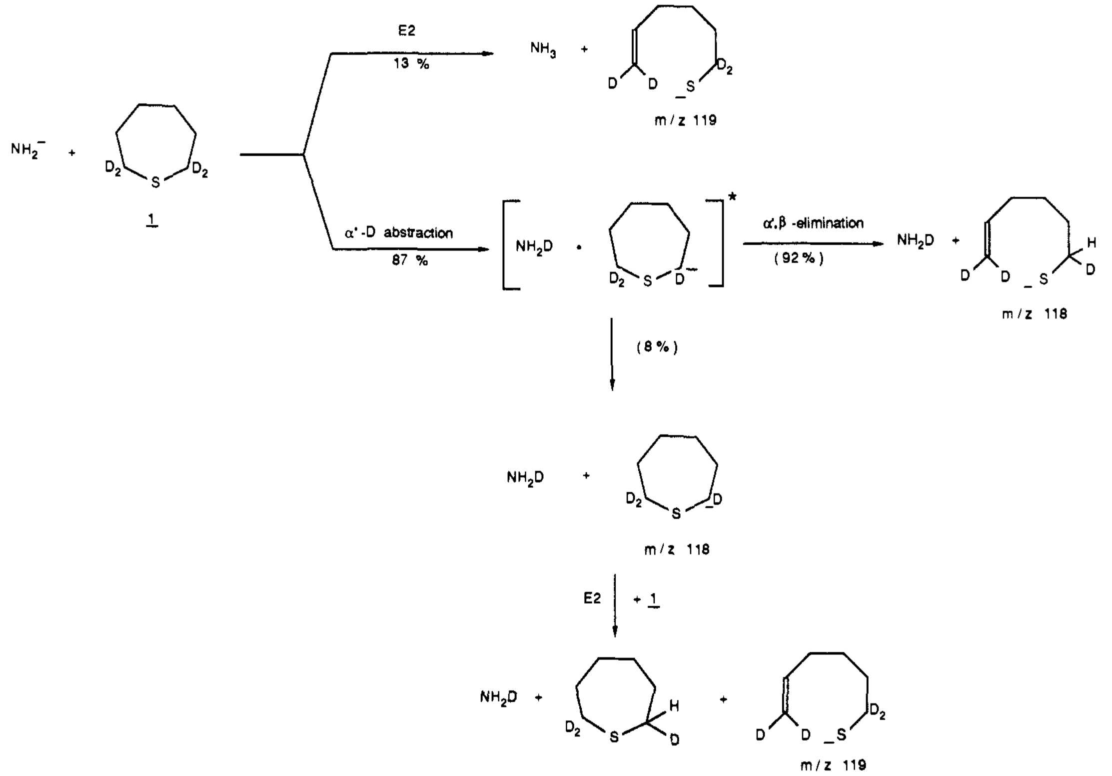
(10) Ingemann, S.; Nibbering, N. M. M. *Can. J. Chem.* **1984**, *62*, 2773.

(11) (a) For hardware see: Dawson, J. H. J. *Lect. Notes Chem.* **1982**, *31*, 331. (b) For software see: Noest, A. J.; Kort, C. W. F. *Comput. Chem.* **1982**, *6*, 111.

(12) Smakman, R.; de Boer, Th. J. *Adv. Mass Spectrom.* **1968**, *4*, 357.

0002-7863/88/1510-2066$01.50/0

Scheme I



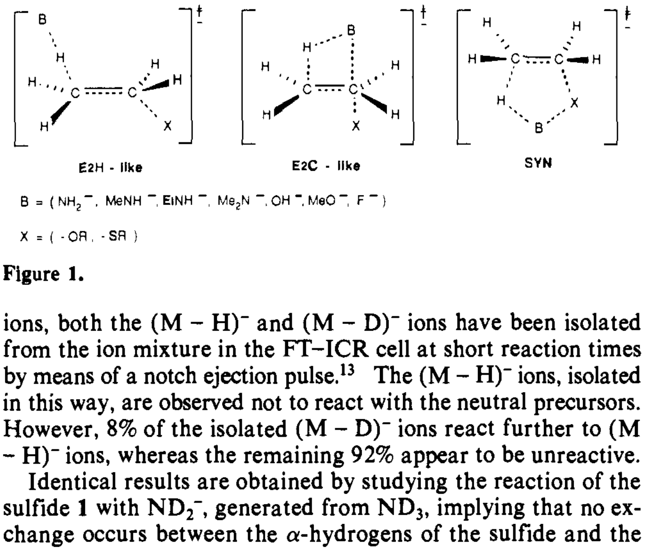


Figure 1.

ions, both the $(M - H)^-$ and $(M - D)^-$ ions have been isolated from the ion mixture in the FT-ICR cell at short reaction times by means of a notch ejection pulse.[13] The $(M - H)^-$ ions, isolated in this way, are observed not to react with the neutral precursors. However, 8% of the isolated $(M - D)^-$ ions react further to $(M - H)^-$ ions, whereas the remaining 92% appear to be unreactive.

Identical results are obtained by studying the reaction of the sulfide **1** with ND_2^-, generated from ND_3, implying that no exchange occurs between the α-hydrogens of the sulfide and the hydrogens of the amide ion. Consequently, the α'-deuteron abstraction is considered to be irreversible. The above results, therefore, are best explained by the Scheme I. Thirteen percent of the primary product ions are formed via a direct E2 elimination, yielding thiolate anions with *m/z* 119. These thiolate anions are expected to be unreactive toward sulfides, since MeS^- is observed not to react with any of the sulfides studied. The remaining 87% of the primary product ions are formed via α-deuteron abstraction resulting in α'-thio carbanions. Ninety two percent of these α'-thio carbanions react further via an intramolecular α',β-elimination, again yielding unreactive thiolate anions, this time with *m/z* 118. Apparently 8% of the α'-thio carbanions succeed in escaping from the reaction complex and subsequently induce an E2 elimination reaction of the parent neutral precursor, again yielding thiolate anions with *m/z* 119. These results indicate that the intrinsic barrier toward α',β-elimination is substantial, since 8% of the α-thio carbanions prefer to induce a bimolecular elimination rather than to undergo a unimolecular elimination reaction. This is at variance with the previously studied reaction of NH_2^- with diethyl sulfide where it was observed that 100% of the initially formed α'-thio carbanions react further via an α',β-elimination.[2]

Reaction of OH^- with α,α-dideuterio-α',α'-dideuteriohexamethylene sulfide (**1**) exclusively proceeds via an E2 mechanism as follows from the observation that reaction of **1** induced by OD^- exclusively yields $(M - H)^-$ ions. However, when the reaction of **1** is induced by OH^- itself, both $(M - H)^-$ and $(M - D)^-$ ions are formed in a ratio of 44 to 56. This ratio is observed to be independent of the reaction time and partial pressures of the neutral precursors, while both the $(M - H)^-$ and $(M - D)^-$ ions, selectively isolated from the ion mixture, show no reactivity. These results indicate a fast exchange between the α-hydrogens and the hydroxide hydrogen within the reaction complex prior to E2 elimination, in the course of which the back transfer of a proton or deuteron from water to the α'-thio carbanion is much faster than the unobserved α'β-elimination reaction (Scheme II).

If the hydrogen/deuterium exchange is very fast relative to the E2 reaction channel, a statistical distribution of 20% $(M - H)^-$ and 80% $(M - D)^-$ ions is to be expected. Therefore, the observed nonstatistical distribution of 44% $(M - H)^-$ and 56% $(M - D)^-$ ions implies that the direct E2 reaction is in competition with the hydrogen/deuterium exchange. Again, this is at variance with the previously studied reaction of OH^- with diethyl sulfide, where it was observed that statistical exchange between the α-hydrogens and the hydroxide hydrogen occurs prior to E2 elimination.[2]

Finally MeO^-, EtO^-, and F^- react with **1** only via an E2 mechanism, exclusively generating $(M - H)^-$ ions.

Tetramethylene Sulfide. Following the same experimental procedures described in the previous section of this paper, the reactions of a base with β,β-dideuterio-β',β'-dideuteriotetramethylene sulfide (**2**) have been studied.

The results show that 54% of the product ions in the reaction of NH_2^- with **2** are formed via a direct E2 mechanism generating unreactive thiolate anions. The remaining 46% of the product ions are formed via α'-proton abstraction resulting in α'-thio carbanions (see Scheme III). Only 12% of these α'-thio carbanions react further via an intramolecular α',β-elimination, whereas 88% escape from the reaction complex and subsequently induce an intermolecular E2 reaction of the parent neutral tet-

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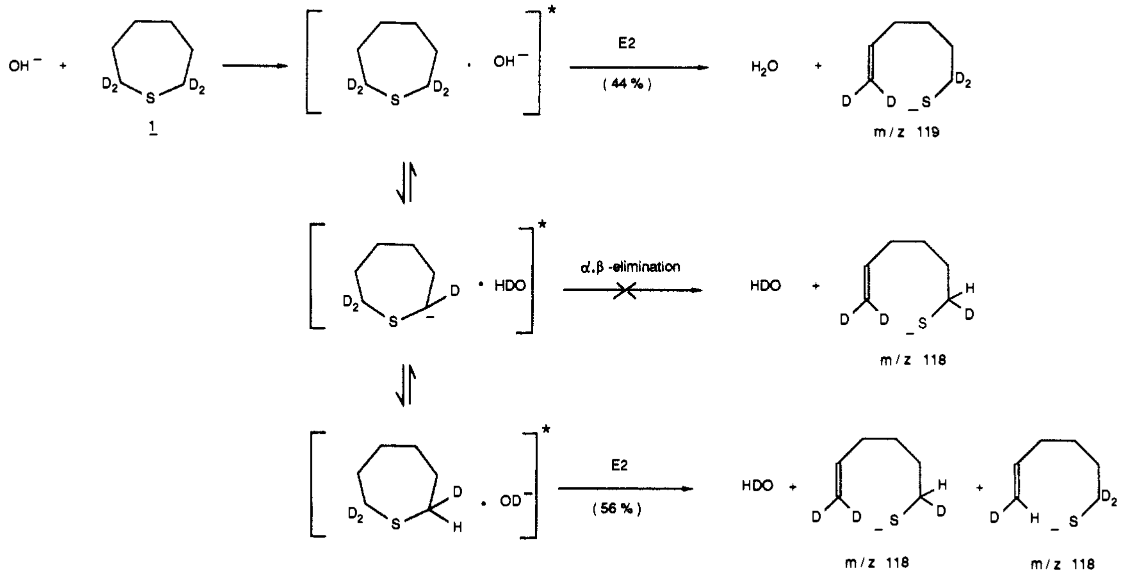
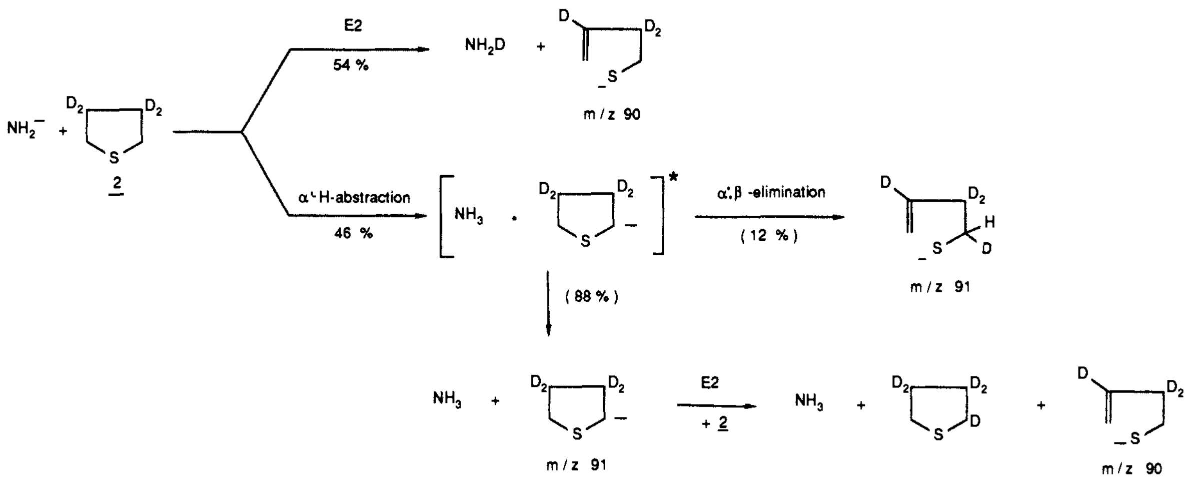
[13] (a) Noest, A. J.; Kort, C. W. F. *Comput. Chem.* **1983**, *7*, 81. (b) Kleingeld, J. C.; Nibbering, N. M. M. *Tetrahedron* **1983**, *39*, 4193.

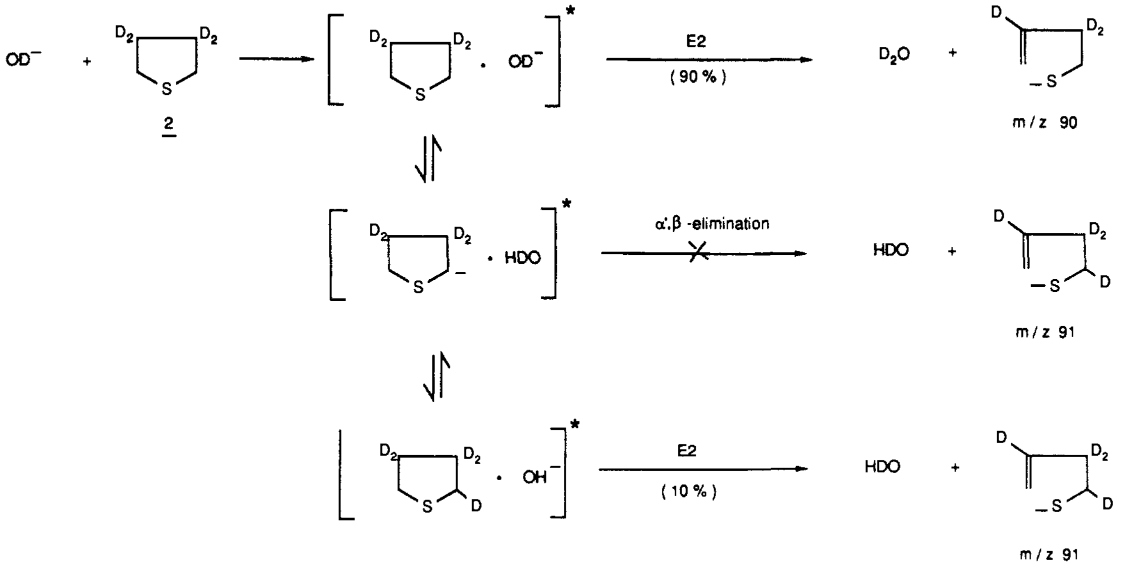
Scheme II



Scheme III

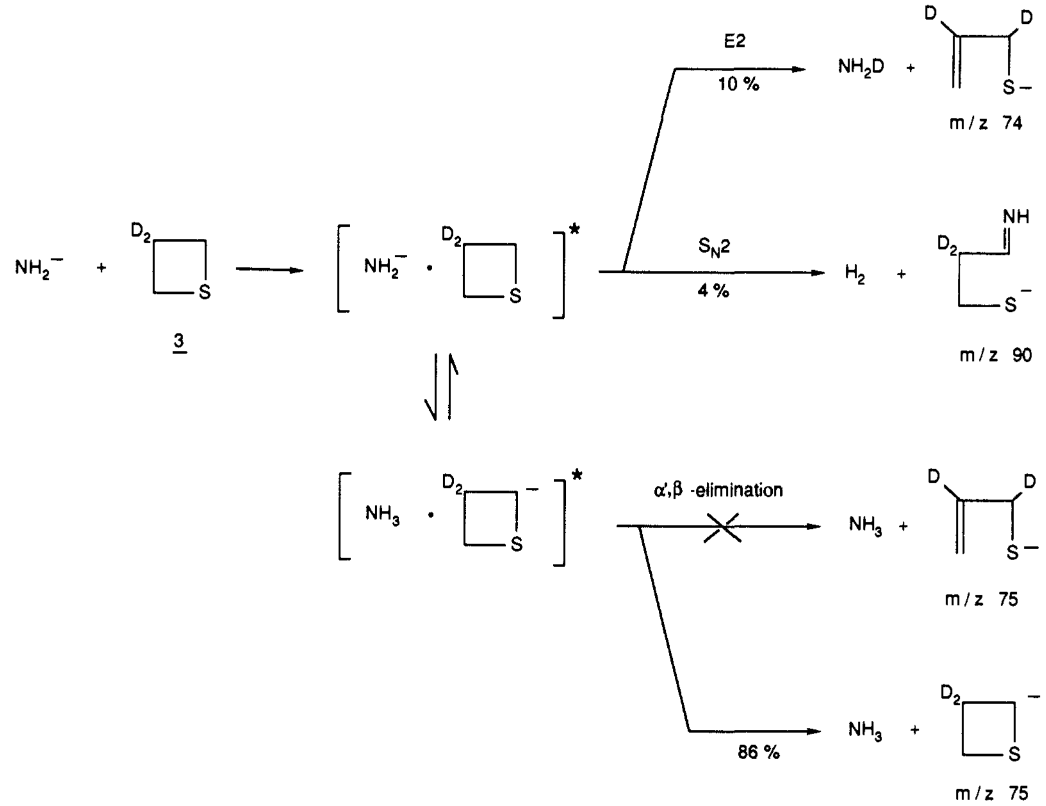


Scheme IV



ramethylene sulfide **2** (see Scheme III). Since reaction of ND_2^- with **2** exhibits identical results, no exchange is expected to occur between the α-hydrogens of the sulfide and the hydrogens of the amide ion. Like hexamethylene sulfide **1**, tetramethylene sulfide **2** reacts with OH^- exclusively by an E2 mechanism, yielding $(M - D)^-$ ions. Reaction of OD^-, on the other hand, produces both $(M - D)^-$ and $(M - H)^-$ ions in a ratio of 90 to 10, illustrating the rapid exchange of the α-hydrogens of the sulfide with the hydroxide hydrogen within the reaction complex prior to E2 elimination (see Scheme IV). Moreover, since statistical distribution of these hydrogens would result in a ratio $(M - D)^-/(M - H)^-$ of 80 to 20, the observed ratio indicates that the rates of

Scheme V



E2 and reversible α-proton abstraction are comparable.

Reactions of MeO^-, EtO^-, and F^- with **2** only generate $(M - D)^-$ ions via an E2 mechanism.

Trimethylene Sulfide. Reaction of NH_2^- with β,β-dideuteriotrimethylene sulfide (**3**) proceeds via three initially competing reaction channels, where 86% of the product ions are formed by α-proton abstraction, yielding $(M - H)^-$ ions, 10% are formed via direct E2 elimination, generating $(M - D)^-$ ions, while the remaining 4% of the product ions are formed by a displacement reaction (S_N2) of NH_2^- on the α-carbon followed by selective loss of H_2, resulting in product ions with *m/z* 90 (see Scheme V). Reaction of ND_2^-, generated from ND_3, with **3** reveals a rapid exchange between the α-hydrogens and the amide ion hydrogens, which finds expression in the replacement of maximally two original α-hydrogens in the product ions.

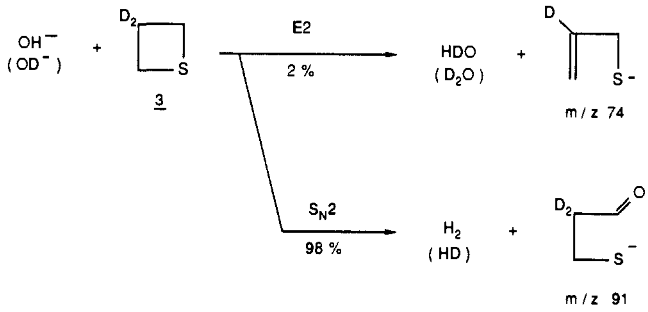
Furthermore, the α′-thio carbanion does not undergo an α′,β-elimination reaction as may be concluded from the observation that *all* of the $(M - H)^-$ ions, initially formed in the reaction of **3** with NH_2^-, react further with both NH_3 and **3**.

Reaction of the $(M - H)^-$ ion with NH_3 again yields the E2 elimination and S_N2 substitution product ions with *m/z* 74 and 90, which once more demonstrates the reversible proton transfer within the NH_2^-/trimethylene sulfide reaction complex. On the other hand, reaction of the $(M - H)^-$ ion with its neutral parent precursor yields a product ion with *m/z* 107, presumably formed via a substitution process followed by loss of CS. However, the structure of this product ion and the nature of its formation are unclear.

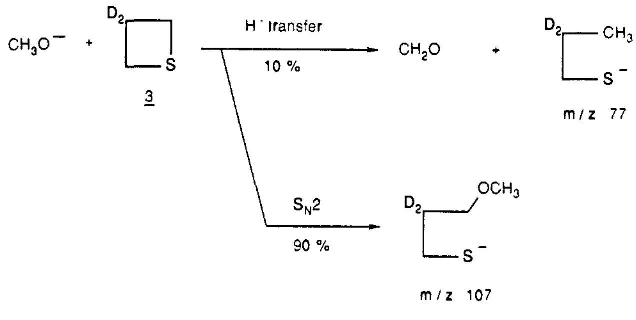
In the reaction of OH^- with **3** only 2% of the product ions are formed via a direct E2 mechanism. The main process here is a displacement reaction (S_N2) of OH^- on the α-carbon of the sulfide followed by selective loss of H_2. Reaction of OD^- with **3** exhibits indentical results with the exception that the displacement reaction of OD^- on the α-carbon of the sulfide is now followed by selective loss of HD (see Scheme VI). This implies that no reversible proton transfer from the α-carbon to OH^- occurs prior to the E2 and S_N2 reactions.

In the reaction of CH_3O^- with **3**, the E2 elimination channel is completely suppressed. Instead, 10% of the product ions arise from a hydride transfer from CH_3O^- to the sulfide in the course of which the hydride probably performs a nucleophilic attack on the α-carbon followed by loss of formaldehyde from the collision complex and resulting in the formation of a propyl thiolate anion with *m/z* 77 (see Scheme VII).[14]

Scheme VI



Scheme VII



Surprisingly, the remaining 90% of the product ions correspond with the adduct of CH_3O^- and the sulfide. Adduct ion formation is an extremely rarely observed process under the presently used very low pressure conditions, since the reaction complex is thermally isolated as a consequence of which the excess reaction

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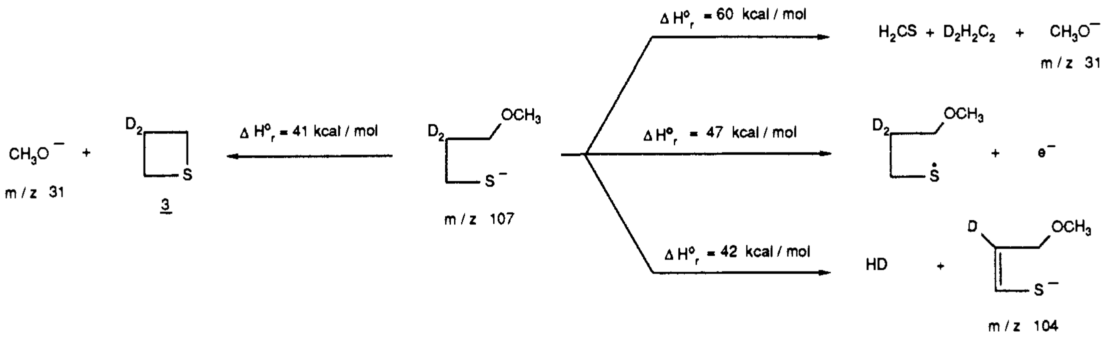
[14] The hydride affinity HA(X) for X = CH_2O is 41.2 kcal/mol. See: Moylan, C. R.; Braumann, J. I. *J. Phys. Chem.* **1984**, *88*, 3175. For hydride transfer reactions of methoxide, see: Ingemann, S.; Kleingeld, J. C.; Nibbering, N. M. M. *J. Chem. Soc., Chem. Commun.* **1982**, 1009.

Scheme VIII



enthalpy is dissipated in the adduct ion and as a rule drives a fragmentation reaction of the adduct ion into products or back to reactants. Nevertheless, the presently studied reaction of the small cyclic sulfide **3** may be an exception, since a nucleophilic attack on the α-carbon is attended with ring strain release (see Scheme VII) which hampers the reverse reaction. On the other hand, electron detachment or fragmentation of the adduct ion with m/z 107 would eventually result in overall endothermic reactions as follows from the estimated reaction enthalpies[8,9] of the least endothermic chemically reasonably fragmentation channels as shown in Scheme VIII.

Therefore, some of the excited adduct ions may have sufficiently long lifetime allowing collisional deactivation even at a low pressure. Collision-induced dissociation (CID)[15] of the adduct ion selectively shows the reappearance of MeO^-, probably arising from the back reaction of the adduct ion, being the lowest endothermic fragmentation channel (see Scheme VIII). Compatible with reaction Scheme VII, CD_3O^- both transfers D^- to the sulfide **3** to give the ion with m/z 78 and generates the adduct ion with m/z 110, which upon CID exclusively regenerates CD_3O^-.

Also $C_2H_5O^-$ reacts with **3** via both hydride transfer and substitution generating the $(M + H)^-$ and adduct ion with m/z 77 and 121, respectively, in a ratio of 31 to 69, while CID of the adduct ion with m/z 121 selectively regenerates the ethoxy anion.

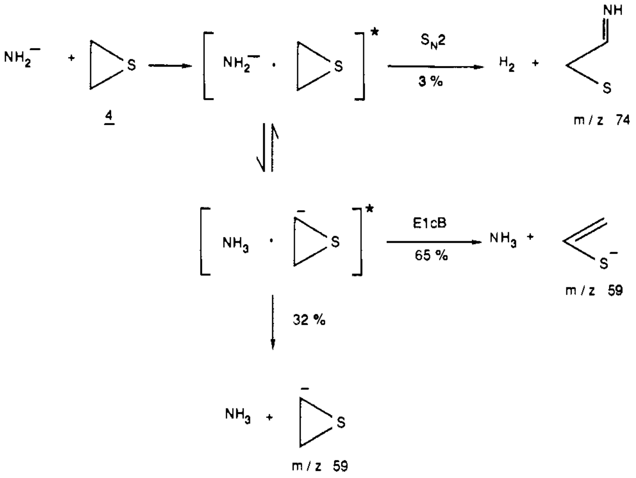
F^- shows no reactivity toward the sulfide **3** in contrast with the larger ring sulfides (vide supra).

Dimethylene Sulfide. Three percent of the initial product ions in the reaction of NH_2^- with dimethylene sulfide (**4**) are formed via an S_N2 substitution on each of the carbon atoms, followed by loss of H_2, thereby yielding thiolate anions with m/z 74 (see Scheme IX). The remaining 97% arise from α-proton abstraction generating $(M - H)^-$ ions with m/z 59. Sixty seven percent of these $(M - H)^-$ ions appear to be nonreactive and therefore are assumed to have a thiolate anion structure arising from ring opening of the initially formed α-thio carbanions. Evidence for this two-step E1cb elimination mechanism arises from the incorporation of maximally two deuterium atoms in the thiolate anion when the reaction is induced by ND_2^- instead of NH_2^-. This deuterium incorporation clearly demonstrates that a reversible proton abstraction step precedes ring opening of the sulfide (see Scheme IX).

Thirty three percent of the initially formed $(M - H)^-$ ions have retained the original α-thio carbanion structure as may be concluded from the observation that they react with their neutral parent precursor to give secondary product ions with m/z 91 and 73. These ions presumably are formed via a nucleophilic attack of the carbanion on the sulfide **4** where the ring strain release drives a second nucleophilic attack generating a four- and a five-membered sulfide, which eliminate SCH_2 and C_2H_4, respectively. This has been visualized in Scheme X.

Reaction of OH^- with **4** exclusively proceeds via a substitution process followed by loss of H_2 resulting in product ions with m/z 75. Reaction of OD^-, however, generates product ions with both m/z 76 and 75 in a 1:1 ratio, implying that the collision complex loses either H_2 or HD. Since it is very unlikely that hydrogen/deuterium exchange occurs prior to S_N2 substitution (see discussion) it thus appears that the product ion may have a conjugated and nonconjugated thiolate anion structure, respectively (see Scheme XI). CH_3O^- reacts extremely slow with **4** via a substitution process, yielding the adduct ion with m/z 91 which shifts to m/z 94 when the reaction is induced by CD_3O^-.

Scheme IX



Finally, like trimethylene sulfide (**3**), dimethylene sulfide (**4**) is observed not to react with F^-.

Discussion

In Table I the relative importance of the various primary reaction channels for the B^-/sulfide reaction systems, as reported in the previous section of this paper, is summarized. It must be noted that the reaction branching ratios refer to the reactions of the specifically deuterium labeled sulfides, with the exception of dimethylene sulfide (**4**). The reaction branching ratios for the correspondingly unlabeled sulfides may differ therefore from the observed values, since the E2, S_N2, and α-proton abstraction reactions are all expected to suffer from a kinetic deuterium isotope effect.[1,2] However, since the studied sulfides are labeled arbitrarily in the α or β position, the large variations in branching ratios as a function of the base strength and sulfide ring size cannot exclusively be explained in terms of kinetic isotope effects and therefore indicate that geometric restrictions have an important influence on the heights of the various intrinsic reaction barriers.

A first conclusion concerning the gas-phase acidity of the sulfides can be drawn on the basis of the observed reversibility of the α-proton abstractions, from which it appears that the acidity diminishes as the sulfide becomes more strained. The gas-phase acidity difference between diethyl sulfide and water is estimated to be not more than 2 kcal/mol.[2,10] Consequently, a statistical exchange is observed between the α-thio hydrogens and the hydroxide hydrogen within the reaction complex prior to the E2 elimination.[2] When going from diethyl sulfide to the seven- and even five-membered ring sulfides, the hydrogen exchange is found to slow down relative to the E2 reaction channel, whereas for the four- and three-membered ring sulfides the hydrogen exchange has completely stopped. Instead, the stronger base NH_2^- now

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(15) (a) Cody, R. B.; Burnier, R. C.; Freiser, B. S. *Anal. Chem.* **1982**, *54*, 96. (b) Carlin, T. J.; Freiser, B. S. *Anal. Chem.* **1983**, *55*, 571.

Scheme X

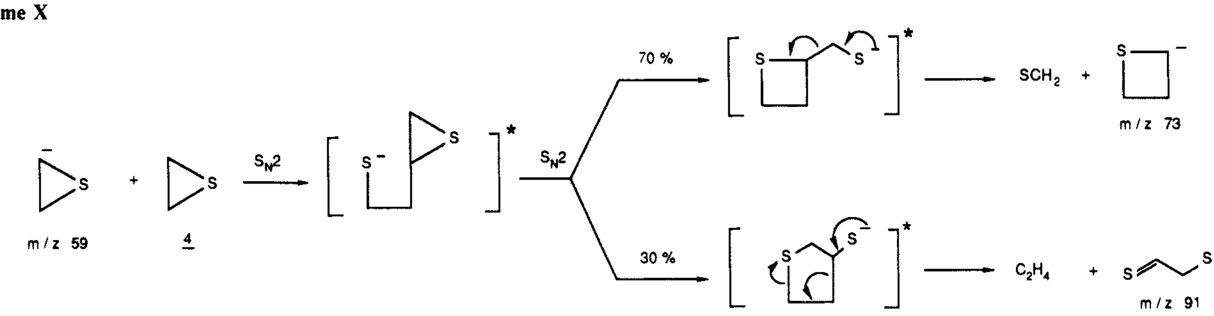
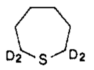
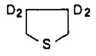
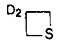
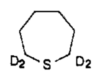
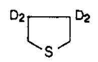
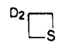
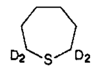
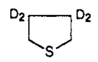
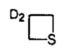
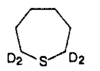
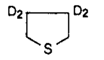
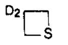


Table I. Relative Importance of Primary Reaction Channels for the B^-/Sulfide Reaction Systems

base/ substrate	E2 (%)	ΔH°_r[a] (kcal/mol)	S_N2 (%)	ΔH°_r[b] (kcal/mol)	α′-H abstraction[c]	unimolecular reaction of α′-thio carbanion (%)
NH_2^-/ $C_2D_5SC_2H_5$[d]	7	-24.9	0	-37.8	93	~100 (α′,β-elimination)
	13	-35.7	0	-46.4	87	92 (α′,β-elimination)
	54	-39.4	0	-44.2	46	12 (α′,β-elimination)
	10	-55.2	4	-62.0	86[e]	0
	0	-60.0	3	-63.3	97[e]	67 (E1cb)
OH^-/ $C_2D_5SC_2H_5$[d]	100	-12.0	0	-22.7	0[e]	
	100	-22.8	0	-31.0	0[e]	
	100	-26.5	0	-28.2	0[e]	
	2	-42.3	98	-47.5	0	
	0	-47.1	100	-48.8	0	
CH_3O^-/ $C_2D_5SC_2H_5$[d]	100	-0.5	0	-16.5	0	
	100	-11.9	0	-25.4	0	
	100	-14.8	0	-22.2	0	
	0	-30.8	100	-40.9	0	
	0	-35.6	100	-42.3	0	
F^-/ $C_2D_5SC_2H_5$[d]	100	7.4	0	-1.7	0	
	100	-3.4	0	-9.8	0	
	100	-6.9	0	-7.5	0	
		-22.7		-26.3		
		-27.5		-27.6		

[a] Reaction enthalpies calculated from known and estimated (ref 8 and 9) heats of formation of reactants and products. [b] Calculated reaction enthalpies (see footnote *a*) for the S_N2 processes, disregarding possible fragmentation of the substitution product ion (see text). [c] Percentage of initially formed α′-thio carbanions. [d] Data taken from our previous study (see ref 2). [e] Reversible α-proton abstraction is observed.

shows a reversible α-proton abstraction reaction with the four- and three-membered ring sulfides, indeed illustrating that the sulfides become less acidic with decreasing ring size. In the condensed phase the reverse effect is normally found.[16] Bordwell, however, has argued that this phenomenon is best explained by differences in solvation of the anions rather than by stereoelectronic effects.[17] This explanation is indeed supported by the present gas-phase data.

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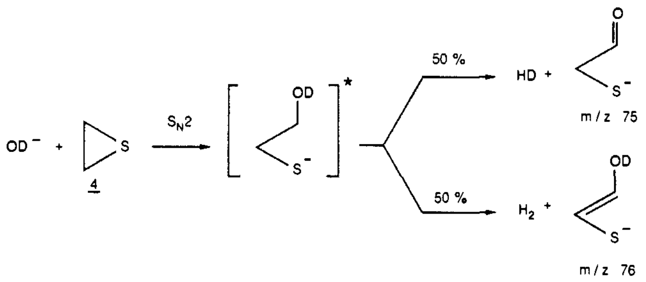
(16) Block, E. *Reactions of Organosulfur Compounds*; Academic: New York, 1978; Chapter 2, p 36.

(17) Bordwell, F. G.; Bares, J. E.; Bartmess, J. E.; Drucker, G. E.; Gerhold, J.; McCollum, G. J.; Van der Puy, M.; Vanier, N. R.; Matthews, W. S. *J. Org. Chem.* **1977**, *42*, 326.

Scheme XI



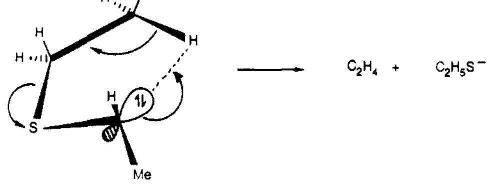
As a result of the decreasing acidity with decreasing sulfide ring size, the importance of the α-proton abstraction channel in the reaction with NH_2^- diminishes down the series diethyl sulfide, hexamethylene sulfide, and tetramethylene sulfide, in favor of the E2 channel, which gains importance in agreement with the increasing exothermicity of this reaction channel with decreasing sulfide ring size (see Table I). In a previous paper[1] it was demonstrated for the OH^-/*cis*- and *trans*-1,4-*tert*-butylmethoxycyclohexane reaction systems that also gas-phase E2 eliminations are under stereoelectronic control, favoring a transition state in which the C_β–H and C_α–leaving group bonds are periplanar. In view of this the present results suggest that down to a five-membered ring size a periplanar E2 transition state can easily be realized. This also holds for the reactions induced by the weaker bases OH^-, MeO^-, and F^-, which even exclusively proceed by E2 elimination.

A further reduction of the sulfide ring size drastically minimizes the importance of the E2 channel in the reaction with all bases used. In the reaction of NH_2^- with tetramethylene sulfide, the α-proton abstraction channel once again is the dominant process in spite of the unfavorable exothermicity, while a minor contribution of an S_N2 substitution channel in addition demonstrates the enormous effect of the ring size reduction from five to four on the reaction branching ratio. This also finds expression in the reaction induced by OH^-, where the contribution of the E2 channel is exceedingly minimized in favor of the S_N2 substitution, whereas in the reaction with MeO^- the E2 elimination is completely superseded by S_N2 substitution.

Since F^- as the weakest base used is observed not to react with either tri- or dimethylene sulfide, it may be concluded that both the E2 and S_N2 reactivity of cyclic sulfides decreases upon reducing the sulfide ring size, notwithstanding the enhancement of the exothermicity of both reaction channels (see Table I). Evidently, the reactions are kinetically controlled, suffering from an increase of the activation energies as the sulfide becomes more strained. For the E2 reaction the most plausible explanation of this effect seems to be the rigidity of the ring strained sulfide so that a periplanar E2 transition state structure is difficult to realize. The limited S_N2 reactivity of the small cyclic sulfides may be due to the electron distribution in small ring systems which tends to project away from the molecule, thereby shielding it from nucleophilic attack. Both aspects more clearly emerge in the reactions of the three-membered ring sulfides, where even NH_2^- is unable to induce a highly exothermic E2 elimination, while also the highly exothermic S_N2 reaction has lost importance relative to the thermodynamically unfavored α-proton abstraction. Yet, the S_N2 substitution is still observed in the reactions of OH^- and MeO^- with dimethylene sulfide. However, the overall reaction rates are observed to decrease drastically as the sulfide becomes more strained. The sudden loss of E2 reactivity accompanying the reduction of the ring size from five to four is not only characteristic for the presently studied cyclic sulfides. With respect to the S_N2 and E2 gas-phase reactivity of heterocyclic compounds it is interesting to compare the results of the present study with those of flowing afterglow studies of DePuy et al. concerning cyclic ethers.[18] Analogous to the present results, it was demonstrated that the gas-phase reactions of NH_2^- and OH^- with tetrahydrofuran in a helium atmosphere at relatively high pressures exclusively proceeded by E2 elimination, whereas the reactions with oxetane yielded only product ions that were formed via a nucleophilic displacement (S_N2). Also ethylene oxide was found to react with NH_2^- and OH^- by a nucleophilic displacement followed by loss of H_2, in this case exclusively over the newly formed C–N and C–O bond, respectively.

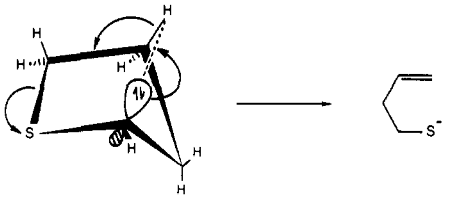
Moreover, reaction of OH^- with oxetane partly resulted in the formation of an adduct ion, whereas reaction of MeO^- with ethylene oxide exclusively generated the adduct ion in an S_N2 reaction. In this case, however, the excess energy of these adduct ions could be removed by collisions with the He buffer gas, which is much less effective for the adduct ions formed in the reaction of CH_3O^- with trimethylene and dimethylene sulfide under the present low-pressure FT–ICR conditions.

Finally, the present study has revealed that intramolecular reaction of the α-thio carbanions via an α',β-elimination process is also under stereoelectronic control. For the α-thio carbanion of diethyl sulfide a perfect syn-periplanar relationship between the C_β–H and C_α–S bonds can easily be realized in an α',β-elimination in which the β-proton is transferred to the α'-carbon under an angle of about 120° as visualized in eq 2.[19]



(2)

Notwithstanding this favorable geometry, the activation energy associated with this process can still be considerable. Consequently, the occurrence of the α',β-elimination is coupled with the exothermicity of the preceding α'-proton abstraction. In the reaction of OH^- this α'-proton abstraction is close to thermoneutral by which the α',β-elimination cannot be activated. In the reaction of NH_2^-, the α'-proton abstraction is at least 12.5 kcal/mol exothermic, which apparently is sufficient to fuel an α',β-elimination of all initially formed α'-thio carbanions (see Table I). For the more rigid hexamethylene sulfide a syn-periplanar transition state for the α',β-elimination is more difficult to realize by which the percentage of initially formed α'-thio carbanions, in the reaction with NH_2^-, undergoing rearrangement to the thiolate anion structure is reduced to 92%. In the case of the α'-thio carbanions formed in the reaction of NH_2^- with tetramethylene sulfide this percentage is further reduced to 12%. In theory, however, even this limited α',β-elimination reactivity of the five-membered ring sulfide may be considered to be amazing, since the rigidity of the system does not allow a syn-periplanar α',β-proton transfer as visualized in eq 3.[19] Apparently, the free energy gained upon ring-opening of the thio carbanion still can fuel this kinetically unfavored reaction.



(3)

In line with the assumed geometric restrictions of the α',β-elimination, all of the α'-thio carbanions initially formed in the reaction of NH_2^- with trimethylene sulfide are observed to retain the carbanion structure in spite of the increasing exothermicity of the α',β-elimination with decreasing sulfide ring size and the

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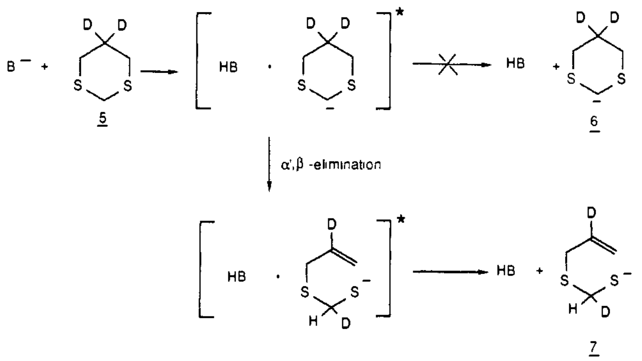
(18) (a) DePuy, C. H.; Beedle, E. C.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1982**, *104*, 6583. (b) Bierbaum, V. M.; DePuy, C. H.; Shapiro, R. H.; Stewart, J. H. *J. Am. Chem. Soc.* **1976**, *98*, 4229.

(19) Although the precise mechanism of stabilization of carbanions by adjacent sulfur is a subject of some controversy, both experiments and calculations point to an sp^3 carbanion structure (see ref 16). Following this, also the α-thio carbanions represented in eq 2–4 are assumed to have an sp^3 structure rather than an sp^2 structure.

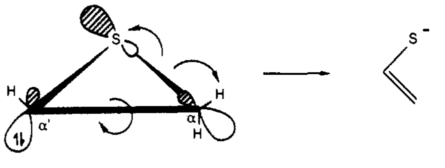
Scheme XII



favorable short distance between the lone electron pair on the α′-carbon and the β-hydrogen.

Bartmess et al.[20] have reported an ICR study of the base-induced reactions of 1,3-dithiane and 1,3-dithiolane. These reactions were observed to proceed via both proton abstraction and β-elimination followed by fragmentation of the initially formed thiolate anion. Indeed, both $(M - H)^-$ and $(M - D)^-$ ions were observed in the reaction of 1,3-dithiane-*5,5-d*$_2$ (**5**) with relatively strong bases. However, the $(M - H)^-$ ions were observed not to react with their neutral precursors as was expected from the observation that neopentoxide, having about the same basicity as the thio carbanion **6**, did react with **5** with a β-elimination. Moreover, no acid/base equilibrium was observed between **5** and any of the bases used in this study. Therefore, we believe that the $(M - H)^-$ ions did not retain the assumed carbanion structure but have rearranged via an α′,β-elimination to the less reactive thiolate anion structure (see Scheme XII). This implies that also for 1,3-dithiane/base reaction systems that α′,β-elimination can be a very efficient process.

Dimethylene sulfide occupies a special position in the series of cyclic sulfides studied, since all hydrogens can be considered to be α- as well as β-hydrogens. Consequently, β-elimination can be described by α′-proton abstraction followed by C_α–S bond breaking. Evidence for this stepwise β-elimination known as an E1cb-elimination has been derived from the observation that deuterium is incorporated in the thiolate product ion, when the reaction of dimethylene sulfide is induced by ND_2^-, revealing a reversible proton transfer prior to C_α–S bond breaking (vide supra). Moreover, 33% of the deprotonated sulfide molecules have retained the original carbanion structure, illustrating a substantial barrier toward C_α–S bond breaking. This may not be surprising, since weakening of the C_α–S bond requires overlap of the lone pair orbital with the LUMO of the C_α–S bond, which can only be achieved by rotating the rigid C_α–$C_{\alpha'}$ bond (eq 4).[19]



(4)

Conclusions

It appears that both E2 and α′,β gas-phase elimination reactions are under strict stereoelectronic control. This finds expression in the extremely low E2 reactivity of small strained cyclic sulfides by which S_N2 substitution, not observed in the reactions of the unstrained sulfides, can enter into competition with E2 elimination. Yet, the S_N2 reaction rates decrease if the sulfide ring size is drastically reduced. This behavior probably originates from the electron distribution in small ring systems which tends to project away from the molecule thereby shielding it from nucleophilic attack, which is in line with the generally held view that gas-phase reactivity to a great extent is influenced by electrostatic repulsion of the reactants.

Finally, it is found that the gas-phase acidity of simple cyclic sulfides decreases with decreasing ring size, i.e., the stability of the α-thio carbanion diminishes with increasing ring strain. Possibly this gas-phase behavior is a direct consequence of the mechanism of stabilization of carbanions by adjacent sulfur, which still is a subject of some controversy.[16]

Acknowledgment. We thank F. A. Pinkse for his expert technical assistance and the Netherlands Organization for Pure Research (SON/ZWO) for financial support.

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(20) Bartmess, J. E.; Hays, R. L.; Khatri, H. N.; Misra, R. N.; Wilson, S. R. *J. Am. Chem. Soc.* **1981**, *103*, 4746.