J. Am. Chem. Soc. **1989**, *111*, 7379–7387

IX. Concluding Remarks

Absolute hardness as an indicator for aromaticity has the advantage that it does not depend on the subtleties of a reference structure. Also, in principle it does not depend on a quantum mechanical model for molecules, because ideally one would simply use experimental ionization potential and electron affinity to determine hardness (eq 2). However, absolute hardness does not provide of itself the prediction that all acyclic polyenes are nonaromatic, or the prediction that some cyclic molecules are antiaromatic, for which purposes relative hardness appears to be useful.

Given that the hardnesses are composed from experimental I and A values, they incorporate, in principle, information about σ electrons as well as about π electrons. This reminds one of the corresponding characteristic of successful semiempirical electronic structure theories. The quantity $I - A$ is the one-center parameter in PPP theory;[26] for an atom or species as a whole it is twice the hardness.[11] For the species as a whole it now appears also to be, in essence, the aromaticity. There is no problem extending the concept to homoaromatic and general nonplanar systems.

The agreement, at least rough agreement, with ring-current ideas is straightforward to demonstrate, and accords with the arguments of Haddon.[9] The "paramagnetic" contributions to magnetic susceptibilities and chemical shifts are second-order-perturbation contributions, the approximate evaluation of which can be accomplished by factoring out an "average energy denominator", and hence these quantities vary inversely as hardness (at least roughly). Alternatively, one sees from the exact density-functional formula for the so-called linear response function in terms of softness kernel[27] that such second-order quantities must have inverse dependence on hardness.

The maximum hardness principle of section V merits careful study. If it can be suitably generalized, it could be of considerable importance.

In summary, in chemical hardness one has a simply defined and straightforwardly determined molecular parameter that measures molecular stability, molecular reactivity, and ring-current effects. We therefore commend hardness and relative hardness as defining measures of aromaticity.

Acknowledgment. This work has been aided by research grants from the National Institutes of Health and the National Science Foundation to the University of North Carolina.

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[26] Pariser, R. *J. Chem. Phys.* **1953**, *21*, 568–569.

[27] Berkowitz, M.; Parr, R. G. *J. Chem. Phys.* **1988**, *88*, 2554–2557; eq 36.

Stereoelectronic Effects in the Gas Phase. 2. Negative Ion Reactions of 1,3-Dithianes and 1,3-Dithiane 1-Oxides

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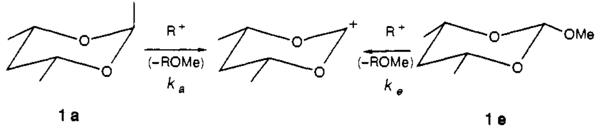
Received November 9, 1987

Abstract: Reactions of gaseous anions (methoxide, hydroxide, and thermal electrons) with *cis*-4,6-dimethyl-1,3-dithiane and the corresponding axial and equatorial 1-oxides have been investigated using the techniques of ion cyclotron resonance (ICR) spectroscopy and pulsed positive–negative ion chemical ionization (PPNICI) spectroscopy. Deprotonation to $(M-H)^-$ ions *and* extensive fragmentation to ions of m/z 99 and 101 were observed for all three compounds with all three reactant anions. When compounds labeled with deuterium specifically at the C2 position were used, it was found that deprotonation occurred at C2 *and* elsewhere in the molecule. The axial hydrogen at C2 was removed as readily or more so than the equatorial hydrogen, depending on the reactants and conditions of ion generation. (These results differ from the corresponding condensed-phase reactions, which show strong selectivity for C2 equatorial deprotonation.) Deuterium isotope effects were estimated to be 1.2 and 1.3 for ions generated by MeO^- and e, respectively. Exchange (H/D) between hydroxide and *cis*-4,6-dimethyl-1,3-dithiane-*2*-d_2 was insignificant, although exchange was observed in comparable reactions of hydroxide with 1,3-dithiane-d_2 and bis(methylthio)methane-d_2. Stereoelectronic effects that may contribute to selectivity in solution do not account for the gas-phase results. Ab initio calculations at the 3-21G(*) level applied to methanedithiol and the anion $(HS)_2CH^-$ (as models for the 1,3-dithiane system) provide insight into the nature of the gas-phase reactions. Possible reaction pathways are discussed.

There is much evidence, largely through the work of Deslongchamps,[1] that certain reactions have demanding stereoelectronic requirements. Yet it is difficult to isolate stereoelectronic effects from effects due to the reaction medium, counterions, and leaving groups, and it remains controversial as to how important they really are.[2] In an earlier investigation, we sought evidence of stereoelectronic control in the gaseous ionic dissociation of cyclic orthoesters **1a** and **1e** using ion cyclotron resonance (ICR) techniques.[3] Eliel and Nader[4] had shown previously that cyclic orthoesters **1** react selectively with Grignard reagents to cleave the *axial* OMe bond (**1e** is unreactive). The axial selectivity is possibly a stereoelectronic effect involving n → σ^* delocalization of nonbonding electrons of the ring oxygens into the σ^* orbital of the axial C–O bond. It is also possible that axial selectivity may be due entirely to reagent and solvent effects.[5] We reasoned that a study of related gas-phase reactions of **1a** and **1e** where perturbations by solvent and counterions are absent might permit isolation of the stereoelectronic effect. However, no significant differences in the rates of ionic cleavage of the exocyclic OMe group of **1a** and **1e** were observed under the conditions of the ICR experiment (eq 1, $k_a = k_e$).[3] A similar result has been found for the related thioorthoesters.[6]



(1)

1a

1e

$R^+ = C_3H_7^+$
$= CH_3SCH_2^+$

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[1] Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry*; Pergamon Press: New York, 1983.

[2] Perrin, C. L.; Nunez, O. *J. Am. Chem. Soc.* **1987**, *109*, 522–7; **1986**, *108*, 5997–6003.

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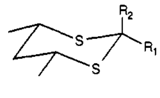
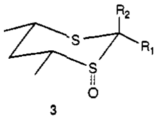
Interpretation of the kinetic data obtained in the ICR experiment is not without ambiguity because the slow step in eq 1 could in fact be ion–molecule association to form a complex. If so, the kinetic data provide little information as to the nature of the transition state leading to products.[7] For a better test of stereoelectronic effects, the bonds to be cleaved should be in the *same* molecule so that rates of bond cleavage correlate directly with product distribution. A suitable system is described in this paper. We chose to study the reactions of *cis*-4,6-dimethyl-1,3-dithiane **2** and its 1-oxides **3** and **4** with gaseous OH^- and MeO^- ions generated by ICR[8] and PPNICI[9] techniques in order to determine the selectivity for abstraction of the equatorial proton at C2 over the axial proton.



2



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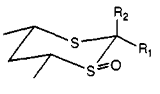
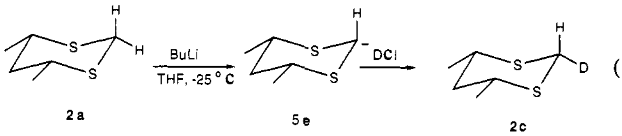


4

2	3	4
a $R_1 = R_2 = H$	a $R_1 = R_2 = H$	a $R_1 = R_2 = H$
b $R_1 = R_2 = D$	b $R_1 = R_2 = D$	b $R_1 = R_2 = D$
c $R_1 = D, R_2 = H$	c $R_1 = D, R_2 = H$	c $R_1 = D, R_2 = H$
d $R_1 = H, R_2 = D$	d $R_1 = H, R_2 = D$	d $R_1 = H, R_2 = D$

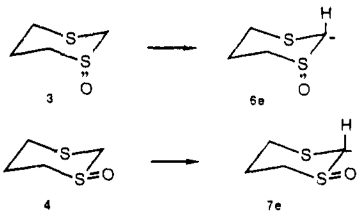
Deprotonation of **2** observed in condensed phase is stereoselective. Eliel and co-workers[10] reported that **2** is selectively deprotonated at the C2 *equatorial* position by strong bases such as butyllithium in tetrahydrofuran; the anion or lithio derivative **5e** produced is reprotonated selectively—also at the equatorial position (eq 2).



(2)

Although ion pairing[11] and solvent effects[12,13] are significant factors in the stereoselectivity of ionic reactions in condensed phase, the kinetic preference for the formation of the equatorial anion **5e** over the axial anion **5a** can be attributed to a stereoelectronic effect, which confers greater stability on the equatorial anion—a conclusion that is supported by theoretical calculations.[14] In terms of the orientation of electron pairs, the effect can be correlated with the number of n → σ* interactions enabled by antiperiplanar orientations of nonbonding electron pairs with bonding electron pairs (six in **5e** but only two in **5a**). Similar arguments lead to the expectation that equatorial anions **6e** and **7e** should be preferred on deprotonation of the axial sulfoxide **3** and the equatorial sulfoxide **4**, respectively (eq 3). These expectations are only partly borne out by experiment.[12] Eliel has suggested that ion-pairing effects and coordination of counterions with heteroatoms exert more control on these reactions than stereoelectronic effects.[11]

Bartmess demonstrated in an ICR study that 1,3-dithiane **9** reacts with gaseous anions by deprotonation and elimination pathways.[13] Also, ICR studies by Nibbering and co-workers of the reactions of thioethers with basic anions document clearly that deprotonation of thioethers to give $(M-H)^-$ anions is a common

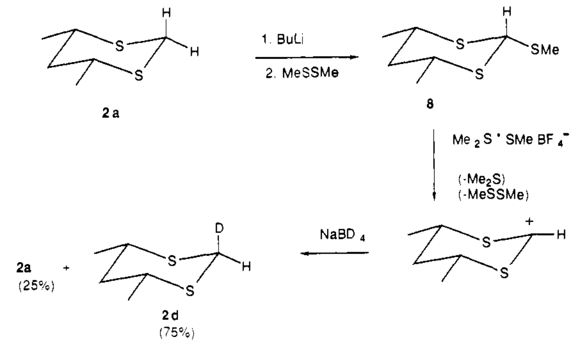


(3)

pathway and is accompanied by elimination and substitution.[15] Assured that a study of gas-phase proton-transfer reactions of **2–4** was feasible, we began the investigation here described in the hope that it would serve as a reliable test of stereoelectronic effects and would resolve some of the ambiguity that now exists with respect to the interpretation of solution data. As will be described, deprotonation of **2–4** by negative ions in the gas phase was found to be more complex than anticipated and the results require careful evaluation for relevancy to the concept of stereoelectronic control. The study was expanded to include chemical ionization techniques, specifically pulsed positive–negative ion chemical ionization (PPNICI)[9] whereby ionization of the dithianes of interest was achieved with methoxide ions or thermal electrons. Even so, the collective results of the ICR and PPNICI experiments do not reproduce the selectivities observed in related solution reactions.

Synthesis

To monitor selectivity in the gas-phase reactions it was necessary to synthesize **2–4** with deuterium labels at specific sites. Published procedures of Eliel and co-workers[10] were followed for the most part, as indicated in the Experimental Section, and led to the preparation of **2a–c** with an isotopic purity of 95% or better. Selective monooxidation of the labeled dithianes led to the corresponding labeled 1-oxides **3a–c** and **4a–c**.[12] However, synthesis of the axially deuterated compound **2d** proved to be difficult. Although selective removal of deuterium from the dideuterated analogue **2b** should give **2d** on reprotonation (by analogy with eq 2) in practice the first step was so slow as to be useless. The route adopted is shown in eq 4. For stereoelectronic reasons[1] it was anticipated that an intermediate cation generated upon methylthiolation of **8**[16-18] would be trapped by an added nucleophile ($NaBD_4$) entering from the *axial* direction. The major product was indeed **2d** but was isolated as a 3:1 mixture with **2a**, as determined by ^1H NMR and mass spectrometry. The 3:1 mixture of **2d** and **2a** was utilized in subsequent experiments, and a correction was made for the unlabeled material present in evaluating the reaction data. Because of the difficulty encountered and the less than optimum purity obtained in the synthesis of **2d**, conversion of **2d** as a mixture with **2a** to the monoxides corresponding to **3d** and **4d** was not attempted.



(4)

It proved necessary in the course of this work to prepare other labeled compounds in order to estimate H/D isotope effects and

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(6) Caserio, M. C.; Shih, P.; Fisher, C. L. *J. Org. Chem.*, in press.

(7) See: *Kinetics of Ion Molecule Reactions*; Ausloos, P., Ed.; Plenum Press: New York, 1979.

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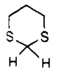
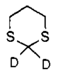
to determine the significance of H/D exchange reactions. 1,3-Dithiane-*2,2*-d_2 (**9b**) and bis(methylthio)methane-*1,1*-d_2 (**12b**) were prepared by routes analogous to the synthesis of **2b**, as described more fully in the Experimental Section.


9a


9b

$(CH_3S)_2CH_2$
12a

$(CH_3S)_2CD_2$
12b

$(CH_3S)_2CH\dot{D}$
12c

Generation of Negative Ions

Gaseous methoxide ions were generated in the ICR experiment from methyl nitrite by *dissociative attachment* of electrons in the energy range 0.1–0.7 eV (eq 5). Hydroxide ions were generated

$$MeONO + e^- \rightarrow [MeONO]^- \rightarrow MeO^- + NO \qquad (5)$$

from neutral water by *ion-pair production* using 10-eV electrons and appropriate trapping voltages on the plates of the ICR cell[19] to quench the positive ions (eq 6). Hydroxide and methoxide

$$H_2O + e^- \rightarrow H^+ + HO^- + e^- \qquad (6)$$

ions generated in this manner served as the reactant ions for subsequent ion–molecule reactions with other neutral reactants introduced into the ICR cell. Since both MeO⁻ and HO⁻ are exceptionally strong bases in the gas phase,[20] their ion chemistry is dominated by proton-transfer (eq 7) and base-induced elimination reactions.

$$RH + MeO^-/HO^- \rightarrow R^- + MeOH/H_2O \qquad (7)$$

Generation of negative ions by pulsed positive–negative ion chemical ionization spectrometry (PPNICI) employed the technique first described by Hunt and co-workers[9] using a Finnigan 4000 mass spectrometer. Methane was used as the reagent gas, which was ionized with a 100-eV electron beam from a heated rhenium filament. Thermal electrons produced as a result of collisional stabilization (eq 8) led to secondary ionization by subsequent reaction with gaseous neutrals introduced into the spectrometer through the inlet system (eq 9).

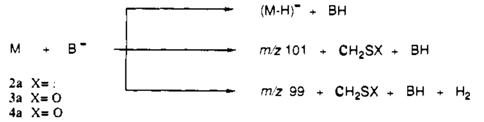
$$CH_4 \xrightarrow{100\text{ eV}} \text{positive ions} + CH_4{}^* + e^- \qquad (8)$$

$$RH + e^- \rightarrow [RH]^- \rightarrow \text{fragmentation} \qquad (9)$$

The 1,3-dithianes **2a–d** and the 1-oxides **3a–c** and **4a–c** were subjected to study under both ICR and PPNICI conditions. Reactions with MeO⁻ generated from methyl nitrite via dissociative attachment were studied by ICR and PPNICI methods, but reactions with HO⁻ formed by ion-pair production from water were observed only by ICR methods. Dissociative attachment reactions (eq 9) were observed with methane as the ionizing reagent gas using the PPNICI method.

Results

The major product ions and their relative amounts formed in the negative ion reactions of labeled and unlabeled 1,3-dithiane derivatives **2–4** are recorded in Table I. The data are inclusive of ICR experiments with MeO⁻ and HO⁻ as reactant ions and PPNICI experiments with MeO⁻ and e as reactant ions. Several important observations can be made. First, product ions corresponding to proton-transfer reactions (M–H)⁻ and (M–D)⁻ are indeed evident (eq 10), but, with one exception, extensive elimination to give ions of *m/z* 101 (eq 11) and *m/z* 99 (eq 12) is seen



(10)
(11)
(12)

Table I. Percentage Distribution of Product Ions in ICR and PPNICI Reactions of *cis*-4,6-Dimethyl-1,3-dithiane and 1-Oxides with Methoxide, Hydroxide, and Thermal Electrons

ICR[a]

	methoxide				hydroxide			
compd	M–H	M–D	*m/z* 101	*m/z* 99	M–H	M–D	*m/z* 101	*m/z* 99
2a	100				66		21	13
2b	73	27			10	41	24	25
2c	86	14			46	5	27	22
2d[b]	89	11			24	31	20	25
3a	15		63	22	21		66	13
3b	13	60	4	23	10	43	47	
3c	14	6	36	44	36	11	34	19
4a	39		48	13	16		62	22
4b	12	21	53	14	15	20	39	26
4c	36	9	10	45	36	6	50	8

PPNICI[a]

	methoxide				e			
compd	M–H	M–D	*m/z* 101	*m/z* 99	M–H	M–D	*m/z* 101	*m/z* 99
2a	44		52	4	37		41	22
2b	21	29	46	4	7	39	33	21
2c	29	11	56	4	52	6	27	15
2d[b]	42	23	31	3	19	29	32	21
3a	44		37	19	22		46	31
3b	8	38	34	21	1	8	32	59
3c	34	13	38	15	2	1	45	52
4a	65		18	17	7		33	60
4b	11	34	21	34	3	8	22	68
4c	52	10	19	17	7	1	29	63

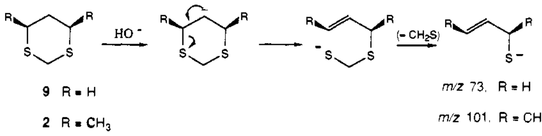
[a] Ion intensities (*I*) reported represent average of duplicate or multiple determinations. Uncertainty in the data is greatest for ions of abundance of 10% or less, where $I \pm 0.2I$. [b] Corrected for 25% of **2a**.

Table II. Ratio of Deprotonation to Fragmentation in Reactions of *cis*-4,6-Dimethyl-1,3-dithiane and 1-Oxides with Gaseous Anions

reactant ion	conditions	ratio (M–H)⁻/(*m/z* 99 + *m/z* 101)		
		2a	**3a**	**4a**
MeO⁻	ICR	100:0	15:85	39:61
MeO⁻	PPNICI	44:56	44:56	65:35
HO⁻	ICR	66:34	21:79	16:84
e	PPNICI	37:63	22:77	7:93

in all cases. Table II lists the ion abundance ratio (M–H)⁻/(*m/z* 99 + *m/z* 101) for the unlabeled compounds **2a**, **3a**, and **4a** as a relative measure of deprotonation to fragmentation. In general, fragmentation is more extensive in the 1-oxides **3a** and **4a** than in the dithiane **2a** and for ions from PPNICI experiments than from ICR experiments. For example, **2a** does not give elimination products on ionization with ICR-generated MeO⁻ but does so extensively (56%) with MeO⁻ under PPNICI conditions. Elimination, in fact, dominated the ion chemistry of the 1-oxides.

A second observation is the appearance of (M–H)⁻ ions from *2,2*-d_2-labeled compounds **2b**, **3b**, and **4b**. Clearly, *there is proton loss at positions other than C2*. This result, and the appearance of fragmentation products, is consistent with the ICR study of 1,3-dithiane **9** reported by Bartmess and co-workers.[13] By labeling the C5 methylene of **9** with deuterium, these investigators determined that deprotonation occurs at C5. A fragment ion (*m/z* 73) was also observed, and the suggestion that *m/z* 73 arises from elimination of CH_2S from the C5 carbanion (eq 13, R = H) is



(13)

supported by the fact that *gem*-dimethyl substitution at C5 blocks the elimination pathway. A related process in the current set of reactions seems very likely (eq 13, R = CH_3). In the present case,

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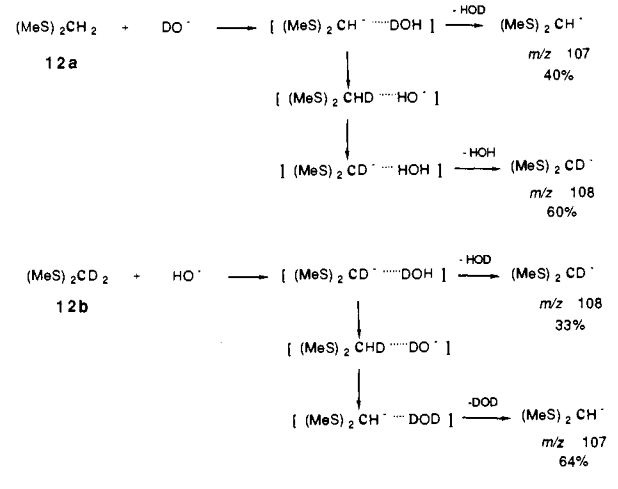
(19) McIver, R. T., Jr. *Rev. Sci. Instrum.* **1970**, *41*, 555–558.

(20) (a) Depuy, C. H.; Bierbaum, V. M.; Damrauer, R. *J. Am. Chem. Soc.* **1984**, *106*, 4051–4053. (b) DePuy, C. H.; Beedle, E. C.; Bierbaum, V. M. *Ibid.* **1982**, *104*, 6483–6488.

Scheme I



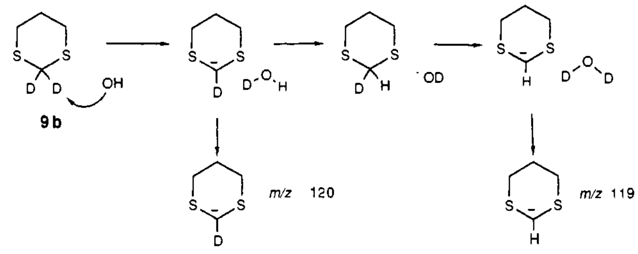
β-deprotonation and C–S bond cleavage would give a thiolate ion (M–H)$^-$ that, on elimination of CH_2S (or CH_2SO), would give the observed fragment ions *m/z* 101. However, in the case of **2** (R = CH_3), further fragmentation to *m/z* 99 corresponding to the loss of both CH_2S and 2 H from (M–H)$^-$ ions is also observed. A third point relates to the data in Table I for the axially deuterated compound **2d**. If deprotonation at C2 is selective for the equatorial proton, then **2d** is not expected to give (M–D)$^-$ ions. Nonetheless, (M–D)$^-$ is formed in significant abundance in the reactions of **2d** with MeO$^-$, HO$^-$, and e. This qualitative assessment of the gas-phase results does not reproduce the selectivities observed in condensed-phase deprotonation reactions of 1,3-dithianes. To analyze the data in more quantitative terms, an estimate of the relative rates of deprotonation at the axial and equatorial positions of C2, k_{ax}/k_{eq}, must be made. To do so requires that the (M–H)$^-$/(M–D)$^-$ data in Table I be corrected for possible H/D exchange reactions, isotope effects, and for the extent of deprotonation at other sites.

Exchange Reactions. Some remarkable H/D exchanges have been described for the reactions of neutral molecules with gaseous HO$^-$/DO$^-$ ions under certain conditions,[21] including reactions of HO$^-$ with thioethers.[15a] To assess the importance of exchange in molecules with the structural feature $-SCH_2S-$, we examined the ICR ion chemistry of bis(methylthio)methane **12a** and **12b**, 1,3-dithianes **9a** and **9b**, and **2b**, with HO$^-$ and DO$^-$. In the case of **12**, exchange was found to be extensive; the unlabeled compound with DO$^-$ led to *m/z* 107 (M–H) and *m/z* 108 in the ratio of 40:60, while the labeled compound **12b** with HO$^-$ led to *m/z* 108 (M–D) and *m/z* 107 in the ratio 33:64. If exchange were negligible, **12a** would lead only to *m/z* 107 and **12b** to *m/z* 108. Exchange is not negligible and probably occurs in the ion–molecule complex before it dissociates, as shown in Scheme I.

Bartmess[13] reported that under ICR conditions 1,3-dithiane **9a** incorporated deuterium on reaction with DO$^-$. Our results with labeled **9b** and HO$^-$ confirm the occurrence of exchange at C2, which, besides producing *m/z* 120 (M–D), produced *m/z* 119, indicating loss of both deuteriums (Scheme II).

However, parallel reactions of HO$^-$ with *cis*-4,6-dimethyl-1,3-dithiane-*2,2-d*$_2$ (**2b**) did *not* produce ions of *m/z* 147 anticipated from H/D exchange. This result is remarkable in comparison with the facile exchange observed in the acyclic case (**12**) and the parent 1,3-dithiane (**9**). Whatever the correct explanation for the lack of multiple H/D exchange in **2**,[22] exchange was not a factor in the estimation of the k_{ax}/k_{eq} selectivity.

Scheme II



Isotope Effects. Estimating k_H/k_D isotope effects in the deprotonation reactions of **2** and related compounds requires that complications arising from H/D exchange, regioselectivity, and stereoselectivity be appropriately corrected for. Measurement of the (M–H)$^-$/(M–D)$^-$ ratios formed in the PPNICI reactions of *mixtures* of **2a** and **2b** with MeO$^-$ and e provided an estimate of the isotope effects involved. The method is described in more detail in the Experimental Section. The isotope effect determined for the reaction of **2** with MeO$^-$ was 1.2 ± 0.1 and with e was 1.3 ± 0.1. Clearly, the isotope effect is not large and does not appear to depend significantly on the reactant ion. By a similar analysis it was determined that the isotope effect k_H/k_D for deprotonation of **9** and **12c** in the gas phase was close to unity. For the purpose of estimating axial–equatorial selectivity in **2** under ICR conditions, values of k_H/k_D = 1.3 for HO$^-$ and 1.2 for MeO$^-$ were assumed. Also, the 1-oxides **3** and **4** were assumed to have isotope effects of the same magnitude as in **2**. The gas-phase values of 1.2 and 1.3 are lower than the value of 2.5 determined for the isotope effect in solution,[10b,11] possibly indicating less C–H bond breaking in the transition state, but are in keeping with isotope effects determined in the FT-ICR base-induced elimination reactions of ethyl sulfide.[15a]

Axial–Equatorial Selectivity. It can be shown that the specific rates of proton loss at the axial and equatorial positions of C2 in **2c**, **3c**, and **4c** are related to ion-abundance ratios (M–D)$^-$/(M–H)$^-$ according to eq 14, where x equals the ion-abundance

$$k_{ax}/k_{eq} = \frac{x - y}{y(1 + [k_H/k_D]x)} \qquad (14)$$

ratio from **2b** (**3b** or **4b**) and y equals that from **2c** (**3c** or **4c**), and k_H/k_D is the kinetic isotope effect. Derivation of this expression is given in the Experimental Section. The comparable expression for the axially substituted dithiane **2d** is given in eq 15 where the terms have the same meaning as in eq 14 except that y is the abundance ratio (M–D)$^-$/(M–H)$^-$ from **2d**.

$$k_{ax}/k_{eq} = \frac{y(1 + [k_H/k_D]x)}{x - y} \qquad (15)$$

The selectivity factors k_{ax}/k_{eq} calculated from eq 14 and 15 using experimentally determined abundance data (see the Experimental Section) are listed in Table III together with pertinent data from solution results. A number of crucial points can be made. First, *removal of the C2 axial hydrogen or deuterium is consistently more important in the gas phase than in solution.* Only in the case of the axial sulfoxide **3c** was axial proton transfer favored in solution whereas, in the gas phase, axial proton transfer is observed in *all* cases and is preferred in most. Second, the differences in selectivity between MeO$^-$, HO$^-$, and e are not striking, but the k_{ax}/k_{eq} ratios overall are somewhat higher for HO$^-$ and e than that for MeO$^-$. Third, the k_{ax}/k_{eq} values from experiments with **2c** and **2d** should be the same under comparable reaction conditions, and, within the error limits of the data, this is the case. For example, Table III reports the axial–equatorial selectivities of **2c** and **2d** with MeO$^-$ under ICR conditions as 0.9 ± 0.5 and 0.7 ± 0.2, respectively.

The results are also expressed in Table IV to show the relative amounts of (M–H)$^-$ formation from deprotonation at three sites, C2 axial, C2 equatorial, and at sites other than C2. The amount of deprotonation at the *axial* site is significant in all cases. But,

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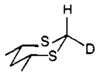
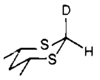
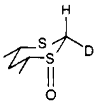
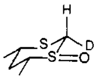
(21) DePuy, C. H.; Bierbaum, V. M. *Acc. Chem. Res.* **1981**, *14*, 146–153.

(22) The reasons for the lack of exchange are unclear, although there are several conceivable explanations. Dissociation of the ion–molecule complex could be faster than exchange, there may be no cross-over between exchange at the equatorial site with that at the axial site, or the (M–H)$^-$ ions may be thiolate ions rather than carbanions. Exchange may occur at C2 but would be undetected if the exchanged site is lost on fragmentation as neutral thioformaldehyde. However, exchange involving positions other than C2 is not significant because no deuterium incorporation was detected in the fragment ions.

Table III. Axial–Equatorial Selectivity k_{ax}/k_{eq} at C2 of 1,3-Dithianes on Reaction with Gaseous Negative Ions[a,b]

		k_{ax}/k_{eq}				
		reactant ion (ICR)		reactant ion (PPNICI)		
compd	no.	MeO^-	HO^-	MeO^-	*e*	solution[c]
	**2c**	0.9 ± 0.5	5.8 ± 2.7	1.0 ± 0.3	5.7 ± 1.6	<0.01
	**2d**[d]	0.7 ± 0.2	2.9 ± 0.9	1.7 ± 0.4	3.1 ± 0.7	<0.01
	**3c**	1.5 ± 0.7	2.0 ± 0.4	1.7 ± 0.3	1.3 ± 0.6	6.7
	**4c**	1.9 ± 0.6	2.6 ± 1.0	3 ± 1	4 ± 1	<0.01

[a] Calculated from eq 13 and 14. [b] Error limits in k_{ax}/k_{eq} reflect the uncertainty in the ion abundance data of Table I and in the estimated isotope effects. [c] See ref 10. [d] Corrected for 25% of **2a**.

Table IV. Percent $(M-H)^-$ Ions from Deprotonation at Various Sites in the Reactions of 1,3-Dithianes and 1-Oxides with Gaseous Negative Ions[a]

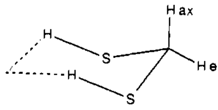
	ion				
compd	ICR	PPNICI	$[M-H]^b$	$[M-H]_{ax}{}^c$	$[M-H]_{eq}{}^d$
2c	MeO^-		69	15	16
2c		MeO^-	38	31	31
2c	HO^-		16	72	12
2c		e	13	74	13
2d	MeO^-		69	13	18
2d		MeO^-	37	40	23
2d	HO^-		16	63	21
2d		e	12	66	22
3c	MeO^-		15	51	34
3c		MeO^-	15	53	31
3c	HO^-		12	60	28
3c		e	9	52	39
4c	MeO^-		33	44	23
4c		MeO^-	21	60	19
4c	HO^-		36	46	18
4c		e	23	61	16

[a] Calculated from k_{ax}/k_{eq} values in Table III, the $(M-D)^-/(M-H)^-$ ratios from Table I, and isotope effects $k_H/k_D = 1.2$ for reactions with MeO^- and 1.3 for reactions with HO^- and e. [b] Percent abundance of M–H ions from sites other than C2. [c] From axial hydrogen loss at C2. [d] From equatorial hydrogen loss at C2.

ICR-generated MeO^- ions produce more $(M-H)^-$ by β-deprotonation (70% in **2**) than at either the axial (14%) or equatorial (16%) position of C2. In contrast, HO^- and thermal electrons produce more $(M-H)^-$ ions from deprotonation at C2 (63–74% axial, 12–22% equatorial in **2**) than elsewhere in the molecule (13–16%). Table II shows that fragmentation to *m/z* 99 and 101 is prominent in all but the reactions with MeO^- under ICR conditions; also, fragmentation is more important in the monoxides **3** and **4** than in the dithiane **2** (93% with e and **4**). The possibility that *m/z* 99 and 101 result from successive fragmentation of short-lived $(M-H)^-$ ions must be considered.

Ab Initio Calculations. Theory provides some insight into the observed differences between the gas-phase and condensed-phase deprotonation reactions of 1,3-dithianes. Ab initio calculations at the STO-3G level were originally reported by Lehn and Wipff[14] using methanedithiol HSCHXSH as a model system, where X = H, Li, or a negative charge. According to these calculations, the HOMO of the pseudoaxial lithio structure is 3.4 kcal higher in energy than the pseudoequatorial structure, and the HOMO of the free axial anion is 9.4 kcal higher than the equatorial anion. The calculated energy difference is nontrivial and should be manifest in our experiments if the gas-phase and condensed-phase reactions are comparable processes. Since calculations at the STO-3G level do not explicitly consider the presence of d orbitals, it appeared worthwhile to recalculate the energies at the 3-21G(*) level,[23a,b] which uses a split-valence basis set with additional d-type atomic orbitals on second-row elements (sulfur) and which is well documented with regard to its ability to reproduce experimental equilibrium geometries for a wide variety of compounds. The methanedithiol chain was constrained to a geometry that simulated a chair conformation, and the geometry was optimized with this restriction. The equatorial and axial anions were next examined by removing the appropriate hydrogen from methanedithiol without further optimization of geometry. Single-point calculations were carried out on equatorial and axial anions both at the 3-21G(*) level and using the 3-21+G basis set in view of previous experience suggesting the importance of diffuse functions in descriptions of anions.[23c] Table V gives the calculated bond lengths and bonds angles for the neutral dithiol and the energies of the C2 anions therefrom. The overall conclusions are (1) the axial anion is higher in energy than the equatorial ion but the energy difference is small (2.1 kcal/mol) and (2) the equatorial CH bond length in the parent methanedithiol is slightly longer than the axial, implying that the equatorial bond is weaker. Overall, the data support the conclusions made from the earlier calculations of Lehn and Wipff.[14] The electron density distribution in the HOMO of methanedithiol is also revealing. Figure 1a shows three perspectives of the HOMO, each of which shows quite clearly that orbital amplitude along the equatorial C–H bond at C2 is *less* than along the axial bond. Only on the basis of the nature of the

Table V. Ab Initio Calculations for Methanedithiol and Carbanions



neutral molecule				anion		
bond length, Å		bond angle, deg		position	energy,[a] hartrees	relative energy, kcal/mol
CS	1.822	SCS	116.6	equatorial	−830.674 42	0^b
CH_{eq}	1.080	CSH	97.6	axial	−830.670 77	2.3^b
CH_{ax}	1.078	SCH_{eq}	105.7	equatorial	−830.644 60	0^c
SH	1.327	SCH_{ax}	110.5	axial	−830.641 26	2.1^c
		$\omega(H_{eq}CSH)$	115.6			

[a] 1 hartree = 627.47 kcal mol^{-1}. [b] Level of calculation: 3-21+G(*)//3-21G(*). [c] Level of calculation: 3-21G(*)//3-21G(*).

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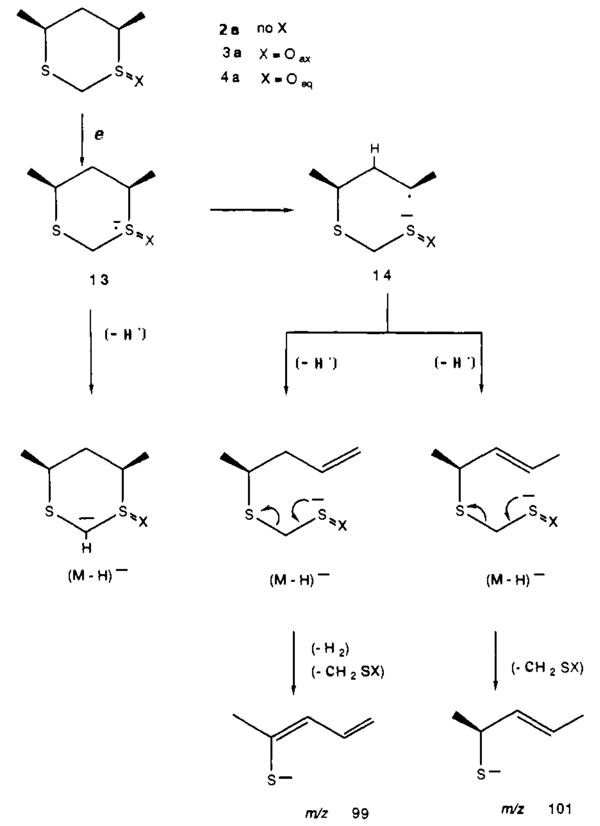
(23) (a) Pietro, W. J.; Francl, M. M.; Hehre, W. J.; DeFrees, D. J.; Pople, J. A.; Binkley, J. S. *J. Am. Chem. Soc.* **1982**, *104*, 5039. (b) Binkley, J. S.; Pople, J. A.; Hehre, W. J. *Ibid.* **1980**, *102*, 939. (c) Spitznagel, G. W.; Clark, T.; Schlever, P. v. R.; Hehre, W. J. *J. Comput. Chem.* **1987**, *8*, 1109–1116. (d) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986; Chapter 4.

Scheme III



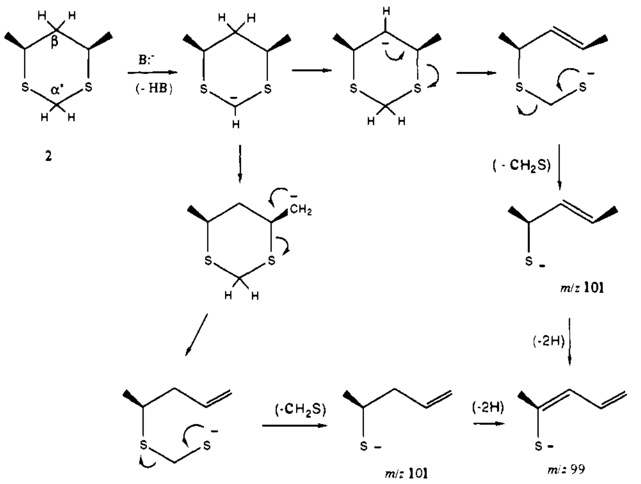
HOMO, proton transfer from the equatorial position should be preferred over the axial.

However, the LUMO of methanedithiol is also revealing. Figure 1b shows three perspectives of this orbital. It is remarkable that the orbital amplitude associated with the C–H bonds at C2 lies entirely along the *axial* bond; there is *no* amplitude along the equatorial bond. Since the LUMO is an *antibonding* orbital, an electron residing in this orbital would weaken the *axial* C–H bond more than the equatorial. The LUMO also shows considerable amplitude along the H–S bond (corresponding to the C4–S or C6–S bond in 1,3-dithiane), and this could be important in understanding the fragmentation processes of 1,3-dithianes in the gas phase. In summary, the calculations confirm that the equatorial C2 anion is modestly lower in energy than the axial anion; but, if the reactions of the dithiane involve electron capture or significant HOMO–LUMO interactions between the attacking anion and the dithiane, the resulting population of the LUMO will weaken preferentially the C2–H_{ax} and the C4–S or C6–S bonds. The outcome of the gaseous reactions can be understood within this framework, as described below.

Discussion of Reaction Mechanisms. A. Reactions with Thermal Electrons. There can be little doubt that, in the ionization of dithianes with thermal electrons, radical anions are formed initially. Since stable radical anions $M^{\bullet-}$ were not detected, they apparently dissociate rapidly to the observed product ions $(M-H)^-$, *m/z* 99 and 101 under the conditions of the experiment. According to the theoretical calculations described above, electron capture by the neutral dithiane molecule would populate the LUMO and create a singly occupied (antibonding) molecular orbital (SOMO) that would weaken the C4–S, C6–S, and C2–H_{ax} bonds preferentially. The observed fragmentation to $(M-H)^-$, *m/z* 99 and 101, can be explained on this basis (Scheme III) where the first-formed radical anion **13** is shown to cleave at the C–SX bond, giving a second radical anion **14**, which, on C–H cleavage (at C5) and elimination of CH_2SX, produces *m/z* 101. Elimination of both CH_2SX and hydrogen produces *m/z* 99.

Of the $(M-H)^-$ ions detected, the major source is from deprotonation at C2 (77–91%; see Table IV). The process is shown in Scheme III as the dissociation of the first-formed radical anion **13** by loss of a hydrogen atom at C2. The experimental results show that hydrogen is lost preferentially but not exclusively from the axial position. This result is consistent with the calculations, which predict that electron density in the σ^* SOMO will concentrate along the axial bond leading to its cleavage.

Scheme IV



Formation of stable $(M-H)^-$ ions by loss of $H^\bullet$ from the radical anion **14** appears minor (only 9–23%; see Table IV). The relatively high abundance of fragment ions *m/z* 99 and 101 and low abundance of $(M-H)^-$ ions from **14** implies that $(M-H)^-$ ions from this source fragment rapidly.

B. Reactions with Basic Anions. The reactions of neutral dithianes with basic anions HO^- and MeO^- appear to be straightforward proton transfers to give $(M-H)^-$ ions and β-eliminations to form thiolate anions. Base-induced elimination reactions are well precedented[13,15,20] and, in the present system, evidently compete well with proton transfer despite the large difference in CH acidity of the C2 versus the β positions, (estimated to be about 21 pK_a units).[24] However, it is conceivable that an α',β-elimination pathway exists analogous to that described by Nibbering for FT-ICR reactions of thioethers with basic anions.[15a] The pathway is shown in Scheme IV and is depicted as an intramolecular proton transfer from a β position (i.e., C5 or a ring methyl group) to the anion formed by *initial* deprotonation at the α' position (i.e., C2) followed or accompanied by C–S bond cleavage and elimination of CH_2S. Nibbering has in fact suggested that $(M-H)^-$ ions from 1,2-dithiane do not retain a carbanion structure but rearrange to the thiolate structure, implying that α',β-elimination for the 1,3-dithiane system is a very efficient process.[15b]

Interpretation of the observed reactions as simple proton transfers and based-induced polar eliminations has powerful precedent, but there are inconsistencies in these reactions that are difficult to account for with this interpretation. According to Bartmess,[13] β-elimination in 1,3-dithianes increases with increasing exothermicity of proton transfer (i.e., with increasing basicity of the gaseous base). In the present case, ICR reactions of **2** certainly yield more elimination with HO^- than with the weaker base MeO^-, but the trend is not upheld with the monoxides **3** and **4** or in PPNICI reactions (see Table II). Also, it is necessary to explain why the gaseous proton-transfer reactions are not selective for the equatorial proton at C2 when, according to the calculations, this should be the more acidic proton.

It is conceivable that the gaseous reactions with HO^- and MeO^- are not simple proton-transfer processes but involve radical-anion intermediates, as in the e reactions. This idea is not unreasonable because the ion chemistry found in the reactions with HO^- and

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(24) The pK_a of 1,3-dithiane in DMSO is estimated to be 39: Bordwell, F. G.; Drucker, G. E.; Andersen, N. H.; Denniston, A. D. *J. Am. Chem. Soc.* **1986**, *108*, 7310–7313. The pK_a of cyclohexane is close to 60, giving a difference of 21 pK_a units or 29 kcal mol^{-1}. The gas-phase acidities of 1,3-dithiane (373 kcal mol^{-1})[13] and ethane (421 kcal mol^{-1})[20] place the difference in acidity of C2 and β positions at 48 kcal mol^{-1}.

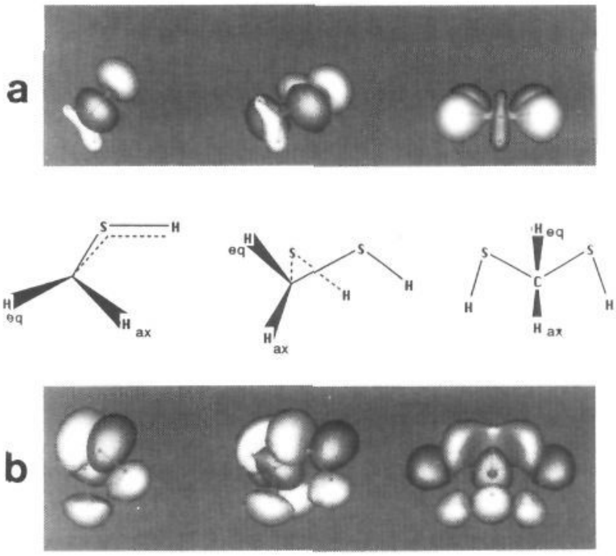

Figure 1. (a) Highest occupied molecular orbital of methanedithiol (three different perspectives). (b) Lowest unoccupied molecular orbital of methanedithiol (three different perspectives).

MeO^- is remarkably similar to that observed with e. However, the process would require an endothermic single electron transfer (SET) from the anionic base to the neutral dithiane within the ion–molecule complex prior to its dissociation.[25-31] In the absence of direct evidence to substantiate or refute this suggestion, further comment is inappropriate. Nonetheless, a qualitative understanding of the selectivity observed can be reached by inspection of the frontier orbitals in Figure 1. As noted previously, the LUMO of $(HS)_2CH_2$ (as a model for 1,3-dithiane) shows significant orbital amplitude along the pseudoaxial C–H bond but not along the equatorial C–H bond. Because the dominant HOMO–LUMO interaction between an attacking anion (as the HOMO component) and the neutral 1,3-dithiane (as the LUMO component) is expected to advance bonding faster at positions with the highest orbital amplitude, there should be a *kinetic* preference for axial C–H proton transfer. That is to say, HOMO–LUMO arguments suggest that the transition state for axial proton loss would be favored over that for equatorial loss, even though anion stability arguments favor the formation of the equatorial anion. The fact that a comparable degree of axial selectivity is *not* seen in solution is taken as evidence that the kinetic selectivity in solution is a manifestation of solvent and counterion effects rather than stereoelectronic effects.

Summary

The objective of this investigation was to test the concept of stereoelectronic control in a system free of the influence of solvent and counterions. Existing evidence of stereoselectivity in the formation and reactions of carbanions from 1,3-dithianes in solution made the study of comparable gas-phase reactions a logical choice. However, the finding that selectivity of proton transfer of 1,3-dithiane derivatives to anionic bases in the gas phase is different from that in solution raises serious questions about the controlling factors in both media.

Contrary to the solution behavior of **2** and related compounds, the gaseous ion–molecule reactions show that proton loss at C2 is *not* selective for the equatorial hydrogen. Loss of the axial hydrogen is prevalent and, in most cases, preferred. Extensive fragmentation is seen—a result that is consistent with earlier findings of based-induced elimination pathways for thioethers. These reactions can be conceptualized as base-induced elimination processes. However, reactions with thermal electrons induce the same gaseous ion chemistry in 1,3-dithianes and 1-oxides as more conventional basic anions (HO^- and MeO^-) but are rationalized in terms of radical-anion formation and fragmentation. While the possibility exists that reactions with anionic bases could also have radical-anion character (as a result of SET pathways), direct evidence is lacking. Extensive proton loss at the C2 axial position is explained in terms of HOMO–LUMO interactions, which affect the axial position more than the equatorial position. We conclude that equatorial selectivity observed in condensed-phase proton-transfer reactions of 1,3-dithianes is more a medium effect than a stereoelectronic effect.

Experimental Section

Instrumentation. The gas-phase reactions investigated by ICR spectrometry employed a trapped-ion analyzer cell[19,32] and a capacitance bridge detector[33] with field sweeping to obtain mass scans. Mass scans were performed at 152.29 kHz for the dithianes and at 137.64 kHz for their oxides. The ICR sample pressures were on the order of 5×10^{-7} Torr for the dithianes and 1×10^{-6} Torr for the H_2O or CH_3ONO. Reaction times were approximately 1.5 s, without quenching.

The PPNICI analyses were performed on a Finnigan 4000 mass spectrometer using the techniques described by Hunt et al.[9] The methane reagent gas pressure was 3×10^{-5} Torr, while the CH_3ONO was leaked into the system until a maximum height for the peak at m/z 31 (CH_3O^- and HNO^-) was found. Otherwise, standard chemical ionization procedures were used. The dithianes and their sulfoxides were introduced to the ionizer area via a direct inlet.

All ^1H and ^{13}C NMR spectra were obtained with a Brüker WM-250 or General Electric QE-300 NMR spectrometer using $CDCl_3$ as the solvent and TMS as an internal standard. The Finnigan 4000 mass spectrometer provided mass spectral data.

Syntheses. 4*r*,6*c*-Dimethyl-1,3-dithiane (**2a**) and 2*r*-deuterio-4*c*,6*c*-dimethyl-1,3-dithiane (**2c**) were synthesized in the fashion described by Eliel and co-workers.[10] The method of Bal and Pinnick[34] was used to synthesize dideuterioformaldehyde di-1-butyl acetal, which was then used in preference to dimethoxymethane to synthesize 2,2-dideuterio-4,6-dimethyl-1,3-dithiane (**2b**). The synthesis designed by Smallcombe and Caserio[18] was employed to obtain dimethyl(methylthio)sulfonium tetrafluoroborate needed to form **2d**. 4*r*,6*c*-Dimethyl-1,3-dithiane 1*c*-oxide (**3a**), 2*r*-deuterio-4*c*,6*c*-dimethyl-1,3-dithiane 1*c*-oxide (**3b**), and 2,2-dideuterio-4*c*,6*c*-dimethyl-1,3-dithiane 1*c*-oxide (**3c**) were synthesized using the peroxide method described by Koskimies.[12] The axial sulfoxides, 4*r*,6*c*-dimethyl-1,3-dithiane 1*t*-oxide (**4a**), 2*r*-deuterio-4*c*,6*c*-dimethyl-1,3-dithiane 1*t*-oxide (**4b**), and 2,2-dideuterio-4*r*,6*c*-dimethyl-1,3-dithiane 1*t*-oxide (**4c**), were prepared from their respective equatorial sulfoxides by the inversion devised by Koskimies.[12]

4*r*,6*c*-Dimethyl-2*c*-(methylthio)-1,3-dithiane (8). Following the procedure of Ellison, Woessner, and Williams,[35] a solution of 0.7148 g (4.820 mol) of **2a** and 10 mL of THF in a flame-dried round-bottomed flask was cooled to −78 °C using an isopropyl alcohol/dry ice bath under dry nitrogen atmosphere. To this was added 3.47 mL (2.09 M, 7.25 mmol) of *n*-butyllithium solution in hexane slowly over a 45-min period. The reaction was left to stir for 2 h at −78 °C and then cannulated into a solution of 0.541 g (5.76 mmol) of dimethyl disulfide in 5 mL of THF (also at −78 °C) over 20 min. The cold bath was removed and the reaction mixture allowed to warm to room temperature. It was then poured into 50 mL of 0.05 M hydrochloric acid and concentrated by

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(25) (a) Pross, A. *Acc. Chem. Res.* **1985**, *18*, 212–219. (b) Pross, A. *Adv. Chem.* **1987**, *215*, 331–338. (c) Pross, A. *Adv. Phys. Org. Chem.* **1985**, **21**, 99–196. (d) Pross, A.; Shaik, S. S. *Acc. Chem. Res.* **1983**, *16*, 363–370. (f) Shaik, S. S. *Prog. Phys. Org. Chem.* **1985**, *15*, 197–337. (g) Pross, A.; Shaik, S. S. *J. Am. Chem. Soc.* **1982**, *104*, 187–195.

(26) Sawyer, D. T.; Roberts, J. L., Jr. *Acc. Chem. Res.* **1988**, *21*, 469–476.

(27) Ashby, E. C. *Acc. Chem. Res.* **1988**, *21*, 414–421.

(28) See: Newcomb, M.; Curran, D. P. *Acc. Chem. Res.* **1988**, *21*, 206–214, and references therein.

(29) (a) Bordwell, F. G.; Harrelson, J. A., Jr. *J. Am. Chem. Soc.* **1987**, *109*, 8112–8113. (b) Bordwell, F. G.; Wilson, C. A. *Ibid.* **1987**, *109*, 5470–5474. (c) Bordwell, F. G.; Clemens, A. H. *J. Org. Chem.* **1982**, *47*, 2510–2516.

(30) A more familiar but analogous process is the key electron-transfer step in the initiation of an $S_{RN}1$ reaction: $N:^- + R{-}X \rightarrow N^\bullet + R{-}X^{\bullet-}$. See: Bunnett, J. F. *Acc. Chem. Res.* **1978**, *11*, 413. Rossi, A. R.; Rossi, R. H. *Aromatic Substitution by the $S_{RN}1$ Mechanism*; ACS Monograph 178, American Chemical Society: Washington, DC, 1983.

(31) The electron affinities of 1,3-dithianes **2–4** are not known but are almost certainly lower than the EA's of $HO^\bullet$ (1.83 eV) and of $MeO^\bullet$ (1.57 eV) such that electron transfer from either HO^- or MeO^- to the dithiane would be endothermic.

(32) McIver, R. T., Jr. *Sci. Am.* **1986**, *243*, 186–196.

(33) McIver, R. T., Jr.; Hunter, R. L.; Ledford, E. B.; Locke, M. J.; Francl, T. J. *Int. J. Mass Spectrosc. Ion Phys.* **1981**, *39*, 65–84.

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rotary evaporation to remove the THF. The resulting solution was then extracted twice with 50 mL of a 1:1 pentane/CH_2Cl_2 solution. The organic layers were combined and washed with 25 mL each of 10% (by weight) aqueous sodium bicarbonate, H_2O, and saturated aqueous NaCl. The organic solution was then dried over Na_2SO_4, filtered, and concentrated on a rotary evaporator. A solid crystallized out, which was removed by filtration and washed with methanol. Separation of the remaining compound was achieved by column chromatography using neutral alumina (Activity Super I) and 90:10 hexanes/$CHCl_3$. The white crystalline solids were combined and recrystallized twice from methanol for a final yield of 0.5674 g (60%), mp 50.5–50.7 °C. ^1H NMR ($CDCl_3$): δ 1.189, 1.208 (C*H* of C-5; part of AB quartet; dt; $J = -13.9$ Hz, 11.5 Hz; 1 H), 1.255 (CH_3 on C-4,6; d; $J = 6.9$ Hz; 6 H), 2.034, 2.089 (C*H* of C-5; part of AB quartet; dt; $J = -13.9$ Hz, 2.3 Hz; 1 H), 2.342 (–SCH_3; s; 3 H), 2.933–3.070 (C*H* of C-4,6; m; $J = 6.9$ Hz, 11.5 Hz, 2.3 Hz; 2 H), 4.939 (C*H* of C-2; s; 1 H). ^{13}C NMR ($CDCl_3$): δ 13.14 (–SCH_3), 21.16 (CH_3 on C-4,6), 41.31 (CH_2 of C-5), 42.40 (*C*H of C-4,6), 49.83 (*C*H of C-2). MS (relative intensity): (EI) *m/z* 194 (2.03), 147 (100.00), 105 (5.66), 92 (9.07), 69 (39.71); (CI) *m/z* 195 (38.12), 147 (100.00). Anal. Calcd for $C_7H_{14}S_3$: C, 43.26; H, 7.26. Found: C, 43.48; H, 7.40.

2*r*-Deuterio-4*t*,6*t*-dimethyl-1,3-dithiane (2d). A method similar to that of Fochi[16] and Nakayama[17] was utilized. A solution of 0.0402 g (0.207 mmol) of **8** and 3 mL of dried dichloromethane in a flame-dried round-bottomed flask was cooled to −78 °C by an isopropyl alcohol/dry ice bath. To this was added 0.0457 g (0.419 mmol) of $(CH_3)_2SSCH_3^+BF_4^-$. The reaction was stirred for 5 h at −78 °C, after which the solution has a slight yellow color. It was then cannulated into a flask containing 0.0220 g (0.582 mmol) of sodium borodeuteride in 0.5 mL of dried diglyme at −78 °C. The yellow color disappeared within 10 min. This mixture was stirred for 1 h at −78 °C, and then 5 mL each of H_2O and diethyl ether were added. The reaction was warmed to room temperature and transferred to a separatory funnel, and the aqueous layer was removed. The ether layer was washed twice with 5 mL of H_2O and then dried over Na_2SO_4. After filtration, the ether was removed under vacuum and a yellowish solid collected. This was chromatographed on a column of Activity Super I neutral alumina using a 90:10 hexanes/$CHCl_3$ solvent system. The resulting white solid was recrystallized from methanol; yield 0.0152 g (49%), mp 80–81 °C. ^1H NMR showed only **2d** and **2a** were present, and, from the mass spectrum, the ratio was 75:25, respectively. ^1H NMR ($CDCl_3$): δ 3.46 (C*H*D of C-2, eq; br s); other signals were the same as that for **2a** for the C-4, -5, -6, and methyl protons.

Formaldehyde Di-1-butyl Acetal. A method similar to that of Eliel et al.[10] was used. To a mixture of 8.73 mL (0.100 mol, 7.61 g) of dimethoxymethane and 73.0 mL (0.800 mol, 59.2 g) of 1-butyl alcohol in a 250-mL round-bottomed flask equipped with a condenser was added 2.85 g (0.015 mol) of *p*-toluenesulfonic acid. The mixture was heated to reflux for 2.5 h and then cooled to room temperature. It was added to 350 mL of 5% (by weight) aqueous sodium bicarbonate solution. The organic layer was separated, added to another 350 mL of 5% $NaHCO_3$, and then separated again. The first 350 mL of aqueous solution was washed with diethyl ether, and the two organic layers were combined. They were extracted once more with 200 mL of 5% $NaHCO_3$ and then dried with sodium sulfate and a small amount of potassium carbonate. After filtration, the solvent was removed by rotary evaporation to give 13.95 g of a mixture of 1-butyl alcohol, the acetal product, and trace amounts of impurities. The mixture was distilled at atmospheric pressure to give one fraction at 113–114 °C (1-butyl alcohol). The residue was distilled under house vacuum (~12 mmHg) to give a fraction between 74–78 °C (99% pure acetal by gas chromatography); yield 6.09 g (38%). ^1H NMR ($CDCl_3$): δ 0.921 (CH_3–; t; 6 H), 1.386 (CH_3CH_2–; m; 4 H), 1.571 (–$CH_2CH_2CH_2$–; m; 4 H), 3.524 (–OCH_2–; t; 4 H), 4.66 (–OCH_2O–; s; 2 H).

Bis(methylthio)methane (Formaldehyde Dimethyl Dithioacetal) (12a). Method 1. A solution of 6.09 g (0.0320 mol) of the acetal formaldehyde di-1-butyl acetal, as prepared above, 12.8 g (0.266 mol) of methanethiol, and 40 mL of chloroform in a 250-mL three-necked round-bottomed flask equipped with an addition funnel and dry ice filled finger condenser was cooled to −78 °C with a dry ice/isopropyl alcohol bath. To this was added 7.9 mL (9.1 g, 0.064 mol) of boron trifluoride etherate in 60 mL of $CHCl_3$ over a period of 15 min. The cold bath was then removed, and the reaction was warmed to room temperature while keeping the condenser cold. The reaction was stirred for 1 h and then put under house vacuum through a bubbler containing hydrogen peroxide to remove any remaining CH_3SH. After 5 h, 100 mL of 20% (by weight) aqueous potassium carbonate solution was added to quench the reaction, which was left stirring under vacuum with the H_2O_2 trap overnight. The mixture was transferred to a 500-mL separatory funnel and the aqueous layer removed. The organic layer was washed with 100 mL of water, 100 mL of 20% K_2CO_3, and again with 100 mL of water. The combined water layers were washed once with 100 mL of $CHCl_3$. The organic layers were then dried with sodium sulfate and filtered, and the solvent was removed by rotary evaporation. The residue was distilled under house vacuum (~12 mmHg) to give two fractions—one between 28 and 32 °C (1-butyl alcohol) and one between 36 and 40 °C, which was mostly dithioacetal. Redistillation at atmospheric pressure gave one fraction between 145 and 147 °C that was 80% pure (lit.[36] bp 148–149 °C). The remaining pot residue was 98% pure dithioacetal: total yield (after gas chromatography) 1.13 g (32%). ^1H NMR ($CDCl_3$): δ 2.16 (CH_3; s; 3 H), 3.62 (CH_2; s; 1 H).

Method 2. A similar synthesis to that above was used, except dimethoxymethane was employed. A solution of 4.37 g (0.0909 mol) of CH_3SH and 1.2 mL (1.1 g, 0.014 mol) of $(CH_3O)_2CH_2$ in 20 mL of chloroform was cooled to −78 °C in a 100-mL three-necked round-bottomed flask equipped with a dry ice finger condenser and gas inlet. Over a 15-min period, 3.4 mL (3.9 g, 0.028 mol) of boron trifluoride etherate in 40 mL of $CHCl_3$ was added. The reaction was stirred for 5 h. It was then warmed to room temperature, transferred into a separatory funnel, and washed with 50 mL of water. The organic layer was separated and then extracted with 50 mL of a saturated aqueous solution of sodium bicarbonate and subsequently three times with 50 mL of water. The chloroform layer was then dried with magnesium sulfate, filtered, and concentrated by rotary evaporation. Distillation under house vacuum (~12 mmHg) gave one fraction that came over all 42–44 °C; yield of pure thioacetal 0.8867 g (59%).

Bis(methylthio)methane-*1,1*-d_2 (Dideuterioformaldehyde Dimethyl Dithioacetal) (12b). Method 1 for **12a** outlined above was used here. A solution of 4.46 g (0.0232 mol) of formaldehyde-d_2 di-1-butyl acetal, 7.57 g (0.158 mol) of methanethiol, and 20 mL of chloroform in a 100-mL three-necked round-bottomed flask equipped with an addition funnel and dry ice filled finger condenser was cooled to −78 °C with a dry ice/isopropyl alcohol bath. To this was added 5.7 mL (6.6 g, 0.046 mol) of boron trifluoride etherate in 40 mL of $CHCl_3$ over a period of 15 min. The cold bath was then removed, and the reaction was warmed to room temperature while keeping the condenser cold. The reaction was stirred for 15 h and then put under house vacuum through a hydrogen peroxide trap to remove any CH_3SH. The reaction was worked up as before. The residue after rotary evaporation was distilled under house vacuum (~12 mmHg) to give 98% pure dithioacetal, which was further purified by gas chromatography; total yield (after gas chromatography) 1.25 g (48%). The ^1H NMR was similar to that of **12a**, except that the formaldehyde protons at δ 3.62 were no longer evident.

2,2-Dideuterio-1,3-dithiane (9b). The method of Eliel et al.[10] was used. A solution of 2.8471 g (0.02631 mol) of freshly distilled 1,3-propanedithiol and 4.6729 g (0.02881 mol) of formaldehyde-d_2 di-1-butyl acetal dissolved in 10 mL of chloroform was added to a refluxing solution of 1.2 mL (1.4 g, 0.0099 mol) of boron trifluoride etherate in 25 mL of $CHCl_3$. After refluxing for 4 h and workup, the chloroform was removed to give a white precipitate. After two recrystallizations from methanol, pure dideuterated material was obtained; yield 0.5239 g (18%). ^1H NMR ($CDCl_3$): δ 2.067 ($CH_2CH_2CH_2$; m; 2 H), 2.821 (CH_2CH_2S; m; 4 H). No peak for the C-2 protons at δ 3.82 was seen.

Calculation of Isotope Effects. The assumption was made that the isotope effect at the C2 axial position of either **2**, **3**, or **4** is equal to that at the C2 equatorial position; that is, $(k_H/k_D)_{eq} = (k_H/k_D)_{ax}$. As shown below, the isotope effect k_H/k_D is related to the composition of a mixture of **2a** and **2b** and to the ratio $(M-D)^-/(M-H)^-$ by the expression in eq 20, where $x = [\mathbf{2b}]/[\mathbf{2a}]$ and $y = (M-D)^-/(M-H)^-$ and c is the ratio of k_S (the rate constant for hydrogen loss at sites other than C2) to k_D (the rate constant for loss of deuterium at C2).

Since the only source of $(M-D)^-$ ions from a mixture of **2a** and **2b** is **2b**, the rate of $(M-D)^-$ formation from, for example, MeO^- can be expressed as:

$$\frac{d(M-D)^-}{dt} = k_D[\mathbf{2b}][MeO^-]$$

There are three sources of $(M-H)^-$ ions: from CH sites at the rear of both **2a** and **2b** and from C2 of **2a**. The rate of $(M-H)^-$ formation is:

$$\frac{d(M-H)^-}{dt} = k_S[\mathbf{2a}][MeO^-] + k_S[\mathbf{2b}][MeO^-] + k_H[\mathbf{2a}][MeO^-]$$

It follows that the ratio of rates of $(M-D)^-$ and $(M-H)^-$ formation is

$$\frac{d(M-D)^-dt}{d(M-H)^-/dt} = \frac{(M-D)^-}{(M-H)^-} = \frac{k_D[\mathbf{2b}]}{k_S[\mathbf{2a}] + k_S[\mathbf{2b}] + k_H[\mathbf{2a}]}$$

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and by substituting in terms of x, y, and c, the expression becomes:

$$x/y = cx + k_H/k_D + c \qquad (16)$$

The linear relationship of the variables x/y and x in eq 16 provides a measure of k_H/k_D from the slope and intercept. Using abundance data determined under PPNICI conditions, values of $k_H/k_D = 1.2 \pm 0.1$ and 1.3 ± 0.1 were determined from eq 16 for reactions with MeO^- and e, respectively.

Calculation of Axial-Equatorial Selectivity. The source of $(M-H)^-$ ions from the reaction of **2c** with a negative ion, for example, methoxide, is through loss of the axial hydrogen at C2 (specific rate = ${}^{H}k_{ax}$) and loss of hydrogen from the rear of the molecule (specific rate = k_S). The source of $(M-D)^-$ is from loss of equatorial deuterium at C2 only (specific rate = ${}^{D}k_{eq}$). The respective rate expressions are:

$$d(M-D)^-/dt = {}^{D}k_{eq}[\mathbf{2c}][MeO^-]$$

$$d(M-H)^-/dt = ({}^{H}k_{ax} + k_S)[\mathbf{2c}][MeO^-]$$

Dividing one expression by the other gives the relative rates in terms of relative ion abundance and specific rates (eq 17). A comparable

$$\frac{d(M-D)^-/dt}{d(M-H)^-/dt} = \frac{(M-D)^-_{2c}}{(M-H)^-_{2c}} = y = \frac{{}^{D}k_{eq}}{({}^{H}k_{ax} + k_S)} \qquad (17)$$

equation relates the ion abundance data from the dideuterated compound **2b** with specific rates of hydrogen loss (eq 18). Eliminating k_S from eq

$$\frac{(M-D)^-_{2b}}{(M-H)^-_{2b}} = x = ({}^{D}k_{ax} + {}^{D}k_{eq})/k_S \qquad (18)$$

17 and 18 and recalling that ${}^{H}k_{ax}/{}^{D}k_{ax} = {}^{H}k_{eq}/{}^{D}k_{eq} = k_H/k_D$, the following expression results:

$$k_{ax}/k_{eq} = \frac{x - y}{y(1 + [k_H/k_D]x)} \qquad (14)$$

The expression for the k_{ax}/k_{eq} value for *axially* substituted **2d** was derived in a comparable manner and is given in eq 15, where y equals the abundance ratio $(M-D)^-/(M-H)^-$ from **2d** and x equals that from **2b**.

$$k_{ax}/k_{eq} = \frac{y(1 + [k_H/k_D]x)}{x - y} \qquad (15)$$

Gas-Phase Base-Induced Elimination Reactions in Onium Intermediates. 1. Competitive Substitution and Elimination Mechanisms in the Attack of Amines on Diethylmethyloxonium Ions

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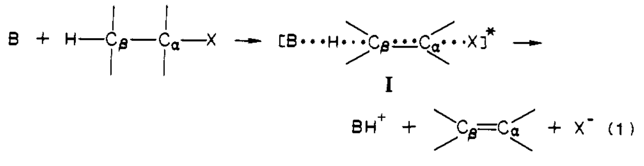
Abstract: The elimination/substitution branching ratio associated with the attack of amines on diethylmethyloxonium ions has been studied in the gas phase by using the method of Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometry. Increasing the base strength causes enhancement of the efficiency of the elimination process relative to substitution. The same trend is observed upon increasing the excitation energy of the encounter between the oxonium ion and the base. At low encounter excitation energies, nucleophilic displacement is flanked by an entropically favored E2 elimination mechanism. At high encounter excitation energies, these reactions are superseded by alternative entropically favored processes, characterized by an initial one-electron transfer from the amine to the oxonium ion leading to a long-lived electrostatically bound adduct involving the amine radical ion and an alkyl radical loosely bound to an ether molecule. Collapse of this adduct may involve an alkyl radical–amine ion-radical recombination (an $S_{RN}1$-like mechanism) or, alternatively, a hydrogen transfer from the present neutrals to the molecular ion of the base (an E_R1 mechanism). These proposed mechanisms are unprecedented in the field of gas-phase positive ion–molecule chemistry.

Since Ingold's first introduction in 1927,[1] base-promoted olefin-forming elimination reactions (E2) have represented an inexhaustible source of mechanistic investigations by many research groups. The interest in this class of reactions derives from the widely held view that these concerted processes involve a rate-determining step proceeding via a complex transition state (I) where both C_α–X (X = leaving group) and C_β–H bonds are partially broken and the $C_\alpha{=}C_\beta$ and B–H (B = base) bonds are partially formed (eq 1).



Concerted E2 mechanisms not necessarily involve synchronous cleavage and formation of bonds in I,[2] which, depending on the base strength of B, may occur via a "variable" transition state, ranging between the E1cB-like and E1-like extremes.[3] Within this concept, refinements are introduced with respect to the geometry of I involving linear C_β···H···B transfer (E2H model),[2] bent proton transfer with loose covalent interaction between nucleophilic B and C_α (E2H-E2C model),[4] and even an intermediate-type proton transfer (McLennan model).[5] In fact, the nature and the

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