Structural Effects on the Rates of the Ion Molecule Reactions of Organic Heterocycles

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Rate constants for proton transfer reactions of seven heterocyclic amines, eight heterocyclic ethers and propylene sulfide have been measured by photoionization mass specrometry. Rate constants for dimerization of four sulfides have also been measured. The measured rate constants have also been compared to the theoretical (ADO) rate constants. In all cases the ADO rate constants show only small variations with structure. In fact for the mono-heterocycles all but one of the ADO rate constants are between 2.0 and 1.5×10^{-9} cc molec^{-1} sec $^{-1}$. The observed rate constants show considerable dependence on chemical structure. The amines react faster than the oxides which in turn react faster than the sulfides. *N*-Methyl substitution on pyrrolidine and piperidine lowers their rate constants by about a factor of two while, propylene oxide reacts eighteen percent faster than ethylene oxide. Examination of the variation in the observed rate constants as a function of ring size for each group of heterocycles indicates a distinct structure-reactivity correlation although we have not attempted to rationalize this correlation. There is also a structure-reactivity dependence observed in the six-membered oxygen heterocycles having a second heteroatom O, NH, or S in the 4-position. The rate constants increase with the electronegativity of the second heteroatom.

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Intruduction.

Most exothermic ion-molecule reactions in the gas phase occur at rates which are close to the collision rate. The most satisfactory theoretical method for calculating collision rates is the average dipole orientation (ADO) method of Su and Bowers [1]. This theory includes an ion-dipole interaction which considers dipole orientation as well as the classical ion-induced dipole interaction originally considered by Langevin [2,3]. Agreement between experimental rates and theoreticl rates calculated by the ADO theory is quite excellent for small molecules and may be improved for larger molecules by requiring the conservation of angular momentum (AADO) [4]. This extension of the theory introduces the third term into the equation below.

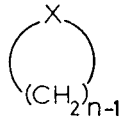
$$k_2 = \frac{2\pi q}{\mu^{1/2}}\left[\alpha^{1/2} + c\mu_D\left(\frac{2}{\pi k T}\right)^{1/2} + \frac{Z\mu_D I^{1/2}}{\alpha^{1/4}}\right]$$

Where q is the charge on the ion, μ is the reduced mass, α is the polarizability of the neutral, C is locking constant which is a function of $\mu_D/\alpha^{1/2}$, μ_D is the dipole moment of the neutral, k is Boltzman's constant, Z is the angular momentum parameter which is a function of T, the temperature, only and I is the moment of inertia. The AADO collision rates for larger molecules appear to add approximately thirty percent to the ADO collision rate. The AADO calculation requires a knowledge of the moment of inertia, (I), of the dipolar molecule. Since moments of inertia are not readily available for the molecules investigated in this work, only the collision rates calculated by the ADO theory have been presented with the results.

The purpose of this work was to examine to what extent chemical structure affects the rates of ion-molecule reactions of similar and related organic compounds. The rates of reaction have been measured for a series of organic heterocycles which are listed in Table 1. The selection of compounds studied permits, a systematic evaluation of

Table 1

Heterocycles Studied



	X	n
Oxides	O	3,3(CH$_3$),4,5,6
Amines	NH	3,4,5,5(CH$_3$),6, 6(CH$_3$),7
Sulfides	S	3,3(CH$_3$),4,5,6

ring size and heteroatom effects on the rates of ion-molecule reactions, as well as a comparison of experimental and theoretical rate constants.

EXPERIMENTAL

The instrument used for this study is similar to that described by Sieck [5]. The light source was a Krypton resonance lamp with either a calcium fluoride window, (10.0eV), or a lithium fluoride window, (10.0 and 10.6 eV), depending upon the ionization potential of the molecule being studied. Pressure in the reaction chamber was measured by a Baratron Capacitance Manometer and was corrected by up to a few tenths of a millitorr so that the least squares straight line through the points corresponding to ninety percent reaction, went through the point corresponding to one hundred percent primary ion at zero millitorr. All rate constants reported are relative to a value of 2.50×10^{-9} cc molec^{-1} sec^{-1} for the proton transfer reaction [b], which was run periodically during the course of

$$NH_3^+ + NH_3 \rightarrow NH_2^+ + NH_2 \qquad (1)$$

Table 2

Theoretical Collision Rate Constants (ADO) and Observed Rate Constants for Heterocycles [a]

Compound	(IPeV)	$\alpha^{1/2}$	μD	C	kADO × 10^9	kOBS × 10^9
Ethyleneimine	(9.9)	2.248	1.90	.235	2.02	2.25
Azetidine	(9.1)	2.614	1.75	.178	1.65	1.43
Pyrrolidine	(8.4)	2.926	1.58	.206	1.65	3.78
N-Methylpyrrolidine		3.227	(1.19) [b]	.178	1.46	2.16
Piperidine	(8.7)	3.216	1.19	.178	1.45	2.88
N-Methylpiperidine		3.507	0.80	.0728	1.24	1.10
Hexamethyleneimine	(8.5)	3.483	(1.20)	.173	1.43	2.95
Ethylene oxide	(10.6)	2.087	1.74	.235	1.84	1.42
Propylene oxide	(10.2)	2.354	2.00	.236	1.82	1.67
Oxetane	(9.7)	2.478	1.93	.231	1.83	.858
Tetrahydrofuran	(9.4)	2.804	1.75	.217	1.64	2.09
Tetrahydropyran	(9.3)	2.805	1.63	.213	1.48	2.48
Ethylene sulfide	(8.9)	2.584	1.84	.226	1.79	.860
Propylene sulfide	(8.6)	2.804	1.95	.224	1.73	1.32
Thietane	(8.9)	2.909	1.78	.216	1.69	.328
Tetrahydrothiophene	(8.6)	3.192	1.90	.214	1.68	.366
Pentamethylene sulfide		3.460	1.71	.201	1.57	1.28
1,4-Dioxane	(9.1)	2.924	(0.46)	.093	1.09	1.27
Morpholine		3.041	(0.45)	.105	1.14	.839
1-Oxa-4-thiacyclohexane		3.297	(0.47)	.103	1.13	.284

[a] Rate constants cm^3 $molec^{-1}$ sec^{-1}. [b] Dipole moments in parentheses are estimated.

this work for calibration. [6] The ideal gas law was used to convert pressure into concentration and the residence time of the ion in the reaction cell was assumed, according to kinetic theory, to be inversely proportional to the square root of the mass of the ion. At least three kinetic runs were made for each compound and the relative precision of the reported rate constants is ±5%. The accuracy of the rate constants is believed to be limited by the accuracy with which the rate constant for the calibration reaction is known *i.e.* ± 20% [6].

Results.

The rate constants for all compounds studied are presented in Table 2 along with the ionization potential of the neutral, its polarizability and dipole moment, the locking constant, C, used to calculate the ADO rate constant and the calculated ADO capture rate constant. The amines and oxides undergo proton transfer, reaction 3, while dimerization, reaction 4, was the reaction observed for the sulfides. Of the sulfides only propylene sulfide reacted by proton transfer rather than dimerization. Proton bound dimers were observed for propylene sulfide, propylene oxide, morpholine and *p*-dioxane. The signal for the proton bound dimer always accounted for less than ten percent of the total ions until at least seventy percent of the primary reaction had occured. The data for these compounds was treated based upon the reasonable assumption that the proton bound dimers are formed by subsequent solvation of the protonated organic by the neutral molecule, reaction 2.

$$MH_2^+ + MH \rightarrow (MH)_2H^+ \quad (2)$$

The signal due to $(MH)_2H^+$ did increase with increasing pressure, relative to the MH_2^+ signal.

Discussion.

The parent ions of the molecules studied undergo either proton transfer, or dimerization, reactions 3 and 4 respectively.

$$MH^+ + MH \rightarrow M\cdot + MH_2^+ \quad (3)$$

$$MH^+ + MH \rightarrow (MH)_2^+ \quad (4)$$

All of the parent ions of the amines and oxides studied undergo the proton transfer reaction. In addition propylene sulfide also undergoes the proton transfer reaction. All of the other sulfides except 1-oxa-4-thiacyclohexane undergo only the dimerization reaction [7]. The latter compound behaves like an oxide and undergoes the proton transfer reaction. These observations are consistent with the thermodynamics of reaction 3, which are summarized below [8]:

$$\Delta H(3) = PA(M\cdot) - PA(MH) = BDE(MH) - HA(MH^+)$$

$$\Delta H(3)\,[\text{Amines}] = -\ (12\text{-}23)\ \text{kcal/mole}$$

$$\Delta H(3)\,[\text{Oxides}) = -\ (12\text{-}25)\ \text{kcal/mole}$$

$$\Delta H(3)\,[\text{Sulfides}] = +\ (3\text{-}10)\ \text{kcal/mole}$$

Since the proton affinities of the radicals (M·) are not readily available the results given above were calculated using the bond dissociation energies (BDE) of M-H and the hydrogen atom affinities of the parent ions MH^+ [8]. The major uncertainty is the bond dissociation energy of M-H, which was assumed to be 93 kcal/mole in all cases. This is an approximate, though reasonable, estimate for the se-

condary C-H and N-H bonds [9]. The results shown above indicate that proton transfer is clearly exothermic for the amines and oxides. The least endothermic proton transfer reaction for the sulfides is that of propylene sulfide, which does undergo proton transfer. For the other sulfides, in which reaction 3 is more endothermic, proton transfer does not occur but rather dimerization, reaction 4, occurs.

Since chemical structure beyond polarizability and dipole moment cannot affect the collision probability, and since all collision processes are quite similar as indicated by the ADO collision rates given in Table 2, the variations in the observed rate constants must reflect the dynamics of the collision complex and the probability that the complex decomposes to products [10]. The rates of dimerization are considerably slower than the proton transfer rates because the associative nature of the dimer makes dissociation of the complex back to reactants more probable. The propensity of sulfur radical ions to form dimers has been observed in other systems and has been ascribed to the formation of a three electron bond between sulfur atoms [11].

Figures 1, 2 and 3 graphically present the data in Table 2 with the observed and ADO rate constants plotted as a function of ring size for each series of compounds. Although the theoretical ADO rate constants show only minor dependence upon ring size, the observed rate constants show a distinct dependence on structure which is

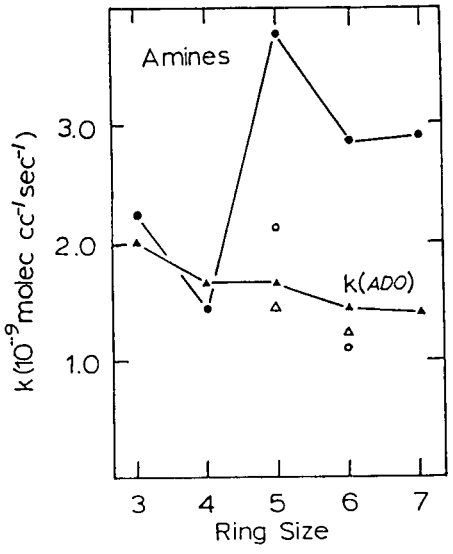


Figure 1. Observed, ●, and Theoretical (ADO), ▲, Rate Constants for Heterocyclic Amines as a Function of Ring Size. Open symbols are *N*-methyl compounds.

quite similar for both the amines and oxides, Figures 1 and 2 respectively. The observed rate constants seem to vary inversely with ring strain although the slowest rates are observed with the four membered rings which are

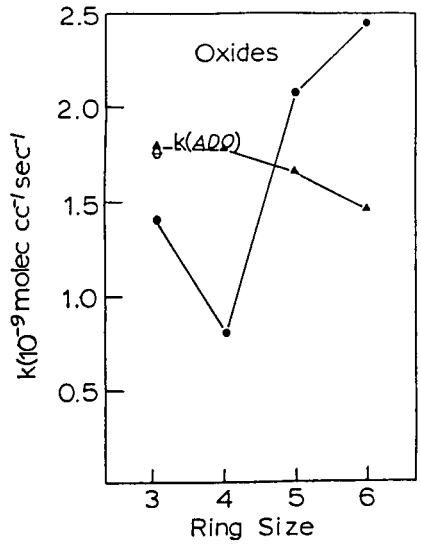


Figure 2. Observed, ●, and Theoretical (ADO), ▲, Rate Constants for Heterocyclic Ethers as a Function of Ring Size. Open symbols are propylene oxide.

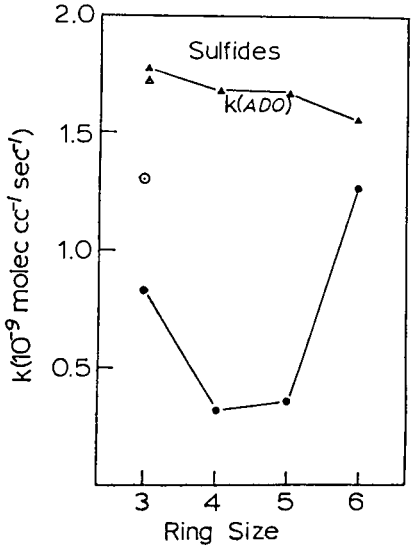


Figure 3. Observed, ●, and Theoretical (ADO), ▲, Rate Constants for Heterocyclic Sulfides as a Function of Ring Size, Open symbols are propylene sulfide.

slightly less strained than the three membered rings. It is difficult and probably unwise to try to rationalize in any detail the correlation observed because although all four species involved in reaction 3 may contain the same ring system, the structural features of the reactant ion and the products are uncertain. Suffice to say that the dependence observed is very similar for both the amines and oxides.

Another structural feature which affects the rates of

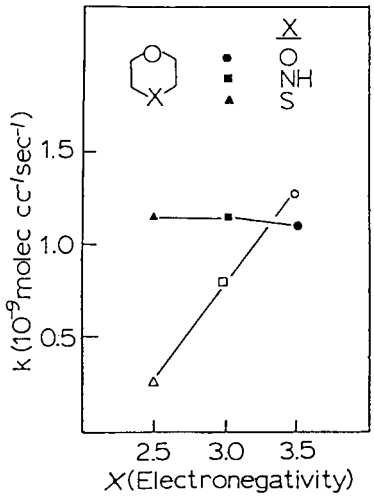


Figure 4. Observed, open symbols, and Theoretical (ADO), filled symbols, Rate Constants for Six-Membered Ring Oxides as a Function of the Electronegativity of the Heteroatom in the 4-Position.

these reactions is the substitution of methyl for hydrogen. Comparison of ethylene and propylene, oxides and sulfides reveals that substitution of a methyl group for a hydrogen on carbon raises the rate constant slightly, perhaps due to the introduction of two additional acid sites, *i.e.* C-H bonds. Comparison of the rate constants for pyrrolidine and piperidine with their N-CH_3 analogs indicates that substitution of methyl for a hydrogen on nitrogen reduces the rate constants significantly. This latter effect is most likely a function of the relative acidity of carbon acids and nitrogen acids. This effect has been observed before in aliphatic amines [12].

Another interesting structural effect can be seen in Figure 4 where the observed and theoretical ADO rate constants for three six membered ring oxygen heterocycles, containing a second heteroatom in the 4-position *i.e.*, 1,4-dioxane, morpholine and 1-oxa-4-thiacyclohexane are plotted against the electro-negativity of the second hetero atom. Although the ADO rate constants change little for this series, there is a definite correlation of the observed rate constants with the electro-negativity of the second heteroatom.

Although the effects observed are not large compared to thermal reactions with activation barriers, the results presented, specifically the effects of ring size, methyl substitution and a second heteroatom on the rate constants of ion-molecule reactions of heterocycles leaves no doubt that structural effects play an important, although not large role in determining the rates of ion molecule reactions. In all cases, because the polarizabilities and dipole moments tend to vary continuously with structure, the ADO theory does not predict anything other than a smooth, continuous and small variation of the rate constants for these reactions. This is to be expected because the ADO theory is based solely on physical interactions, and does not consider the dynamics of the collision complex.

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