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Formation and Reactions of Heteroaromatic Anions in the Gas Phase

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The gas-phase acidities of furan, thiophene, pyridine, 1-methylpyrrole, and a number of their methyl derivatives have been determined in a flowing afterglow apparatus. The ΔG_{acid} (kcal/mol) and site of deprotonation of the parent heterocycles are as follows: furan 380 ± 3 (2-position), thiophene 373 ± 3 (2-position), pyridine 384 ± 3 (3- and/or 4-position), 1-methylpyrrole 386 ± 3 (methyl group). For the methylated species studied the acidities are 2-methylfuran 377 ± 3, 2-methylthiophene 373 ± 3, 3-methylthiophene 373 ± 3, 3-methylpyridine 371 ± 3, 2-methylpyridine 370 ± 3, and 4-methylpyridine 368 ± 3. The relative acidities of the hydrogens in the other sites in these molecules have been estimated by hydrogen–deuterium exchange studies and by other chemical methods. Anions (M − 1) from these molecules have been allowed to react with N_2O, O_2, COS, and CS_2 and the ionic products determined. The gas-phase acidities have been compared with those calculated by the semiempirical methods AM1 and MNDO.

In solution many five- and six-membered heteroaromatic compounds are sufficiently acidic that their conjugate bases can readily be formed by hydrogen abstraction reactions.[1] For example, 2-lithiofuran results from reaction of furan with *n*-butyllithium[2] and lithiopyridines from pyridine and *n*-butyllithium–potassium *tert*-butoxide.[3] In each case, the resulting carbanion can be put to synthetic use to form substituted heteroaromatics in good to excellent yield. Both synthetic and mechanistic investigations have shown that the particular isomeric form of the ion produced by hydrogen abstraction is a function of the experimental conditions. For example, Verbeek and Brandsma[3] found that the relative amounts of 2-, 3-, and 4-lithiopyridine formed "depends strongly upon the length of the time between addition of pyridine to the base and addition of the (quenching) reagent", and Zoltewicz, Grahe, and Smith[4] showed that the relative rates of H,D exchange among the 2-, 3-, and 4-positions of pyridine changes in going from a solution of CH_3OD–CH_3ONa to ND_3–$NaND_2$. Indeed, it appears that for pyridine in solution, hydrogens at the 2,6-positions are kinetically the most reactive, whereas the 4-hydrogen is the most acidic thermodynamically.[3] From these and other data it appears likely that, at least in solution, the kinetic acidity and the thermodynamic acidity are not the same in many of these compounds.

The acidity of a number of heterocyclic molecules has been measured in solution.[5] Such acidities can be quite solvent dependent[6] and in some solvents represent ion pair acidities rather than those of separated ions.[5] In the gas phase ions can be generated in the absence of solvent and counterions. We therefore undertook a study of the gas phase anion chemistry of several of the more common heterocycles; furan, thiophene, 1-methylpyrrole, and pyridine, as well as some of their methyl-substituted derivatives. We have generated carbanions at various positions within these molecules, measured their relative basicities both with respect to isomeric positions within the same molecule and with respect to other heterocyclic carbanions, and examined a number of chemical reactions that they undergo in the gas phase. We have also compared our experimental basicities with those calculated by semiempirical molecular orbital theory.

Experimental Section

For our experiments we used a conventional flowing afterglow (FA) instrument, which has been described in detail previously.[7]

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Ions, initially HO^-, NH_2^-, or F^- are generated by electron impact on appropriate precursors (N_2O and CH_4, NH_3 or NF_3, respectively) added in trace amounts to a (8000 cm/s) (0.4 Torr) helium stream and confined in a 1-m long × 7.6-cm i.d. stainless steel tube. At the end of the flow tube a small fraction of the resulting plasma is sampled through a 0.5-mm orifice into a low-pressure region (10^{-5}–10^{-6} Torr) where the ions are separated in a quadrupole mass filter and detected by an electron multiplier. The neutral reagents are added through inlets attached to the flow tube. For example, addition of furan vapors downstream from the ionizing region rapidly converts HO^- (m/z 17) to $C_4H_3O^-$ (m/z 67). After allowing a further 30 cm for the resulting anion to reach thermal equilibrium with the bath gas, another neutral reagent (e.g., O_2, N_2O, D_2O) is added to investigate the chemical reactions of the anion. Carbanions can also be prepared by reaction of trimethylsilyl derivatives of heterocycles with fluoride ions.[8] For example, an anion $C_5H_6N^-$ (m/z 80) results from addition of 1-methyl-2-(trimethylsilyl)pyrrole to a stream of F^- ions.

All reagent gases were obtained from commercial suppliers and had the following purities: He (99.995%), NH_3 (99.995%), N_2O (99.99%), CH_4 (99.995%), O_2 (99.98%). The heterocyclic compounds were the highest quality commercially available, distilled before use, and dried over $LiAlH_4$ or CaH_2 as necessary. The 2,5-dideuteriofuran and 2-deuterio-1-methylpyrrole were prepared by quenching the corresponding lithium salts with D_2O;[9] similarly for the preparation of the 2-deuteriopyridine.[10] The 1-methylpyrrole-*1*-d_3 was obtained by the alkylation of pyrrylthallium with CD_3I.[11] The 2-trimethylsilyl derivatives of pyridine and 1-methylpyrrole were prepared by allowing their lithium salts to react with trimethylchlorosilane,[3b] while the 1-methyl-2-(trimethylsilyl)pyrrole was photochemically rearranged to the 3-isomer.[12] For molecular orbital calculations the AMPAC program (QCPE 506) was used.[13]

Results and Discussion

In determining the gas-phase acidity of a compound, the simplest method is to use the bracketing technique, in which the neutral reagent is allowed to react with a series of anions of increasing base strength until one is found that is capable of extracting a proton. For example, of all the compounds studied only 1-methylpyrrole fails to form an M − 1 ion upon reaction with HO^-. The rest, therefore, have at least one hydrogen more acidic than those in water ($\Delta G_{acid}(H_2O) = 384.1 \pm 0.4$ kcal/mol).[14] 1-Methylpyrrole forms an M − 1 ion upon reaction with $(CH_3)_2N^-$ ($\Delta G_{acid}((CH_3)_2NH) = 389.2 \pm 0.6$ kcal/mol). So we place its acidity as $\Delta G_{acid} = 386 \pm 3$ kcal/mol, halfway between that of water and dimethylamine.

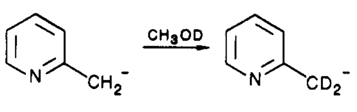
Thiophene, 2-methylthiophene, and 3-methylthiophene are deprotonated by methoxide ion (ΔG_{acid}(methanol) = 374 ± 2 kcal/mol) but not by ethoxide ion (ΔG_{acid}(ethanol) = 371 ± 2 kcal/mol) so they can be assigned $\Delta G_{acid} = 373 \pm 3$ kcal/mol. All three methylpyridines react with ethoxide ion to form detectable amounts of M − 1. However, 3-methylpyridine is the least acidic of the three since some ethoxide ion remains even in the presence of an excess of pyridine. We therefore assign to it $\Delta G_{acid} = 371 \pm 3$ kcal/mol. Next in acidity is 2-methylpyridine ($\Delta G_{acid} = 370 \pm 3$ kcal/mol), which lies between ethanol and 2-propanol ($\Delta G_{acid} = 369 \pm 2$ kcal/mol). The most acidic is 4-methylpyridine; it can be deprotonated by isopropoxide ion and in turn will abstract a hydrogen from acetonitrile ($\Delta G_{acid} = 365 \pm 2$ kcal/mol). We therefore assign to it a gas-phase acidity of 368 ± 3 kcal/mol.

The remaining three compounds, pyridine, furan, and 2-methylfuran, all lie in acidity between water and methanol. This 10 kcal/mol region is one in which there are no well-established standard reference acids for use in comparisons by the bracketing method. These five compounds, the three heterocycles plus water and methanol, appear to span this range rather neatly. If we establish their relative order of acidity, we will have a ladder of acidities through this important region.

At the top end we found that pyridine reacts completely with HO^- when the latter is formed from N_2O and CH_4 so that there is no H_2O present in the flow tube. However, when water is added downstream, so that pyridine and water are present together, both $C_5H_4N^-$ and HO^- are present. It thus appears that pyridine and water have nearly the same acidity. We assign to it $\Delta G_{acid} = 384 \pm 2$ kcal/mol, in good agreement with that reported (382.8 ± 0.4) by Meot-ner.[14] The pyridyl anion will, in turn, abstract a hydrogen from furan, 2-methylfuran, and methanol.

At the lower end of this region an M − 1 anion is obtained readily from furan and 2-methylfuran by reaction with methoxide ion. Since the M − 1 from furan will abstract a hydrogen from 2-methylfuran but the reverse reaction will not take place, furan must be less acidic than the 2-methyl derivative. The order of acidity among these compounds is then pyridine ~ water < furan < 2-methylfuran < methanol. If we use a 3 kcal/mol interval between the acidities we have furan $\Delta G_{acid} = 380 \pm 3$ kcal/mol, and 2-methylfuran $\Delta G_{acid} = 377 \pm 3$ kcal/mol. We have summarized these experimental results in Table I, together with the position within the molecules from which a hydrogen is removed. The evidence upon which these latter conclusions are based is given below.

We next examined the question of the site of the most acidic hydrogen(s) within each molecule and the relative acidity of the various types of hydrogens that they contain. Our first information comes from hydrogen–deuterium exchange reactions. Consider first the anion derived from 2-methylpyridine. Because 2-methylpyridine is so much more acidic than pyridine itself, hydrogen abstraction must occur from the methyl group to form the benzyl-type ion shown in eq 1, rather than from the ring. When CH_3OD is added to the flow tube, this anion rapidly exchanges two and only two of its hydrogens for deuterium, as expected for this structure. An analogous exchange of two hydrogens for deuterium occurs for the anions from 3- and 4-methylpyridine.



(1)

We have discussed gas-phase H–D exchange in carbanions extensively in earlier publications.[15] Briefly, the anion and the neutral exchange reagent are attracted to one another by ion–dipole and ion-induced dipole forces until

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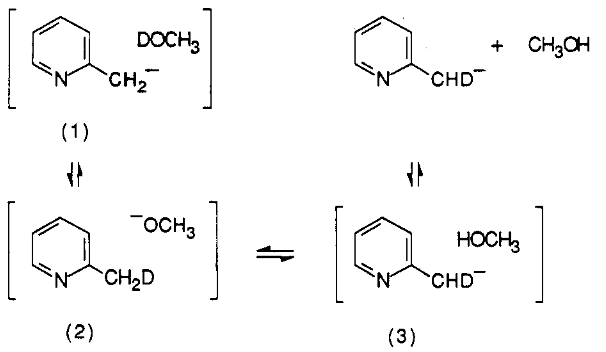
Table I. Experimental and Calculated Gas-Phase Acidities and Heats of Formation of Selected Heterocycles

	acidity[a]				ΔH_{form}		
	ΔG_{exp}	ΔH_{exp}[b]	AM1	MNDO	exp[c]	AM1	MNDO
furan					−8.3	3.0	−8.6
2-anion	380 ± 3	388 ± 3	385	391	14	22.0	16.4
3-anion			403	411		40.5	37.0
thiophene					27.6	36.7	26.5
2-anion	373 ± 3	381 ± 3	390	397	43	60.7	57.6
3-anion			398	403		69.0	64.0
1-methylpyrrole					24.7	44.4	32.6
methyl anion	386 ± 3	394 ± 3	380	386	53	58.9	52.7
2-anion			394	400		72.2	66.7
3-anion			413	418		91.4	85.1
pyridine					34.6	32.1	29.1
2-anion			388	395		54.7	58.5
3-anion	*d*	*d*	394	398		60.5	61.8
4-anion	384 ± 3	392 ± 3	393	398	61	59.6	60.9
2-methylfuran					*e*	−4.0	−19.3
methyl anion	377 ± 3	384 ± 3	371	373		1.3	−12.4
3-anion			403	409		33.0	23.5
4-anion			403	410		33.6	24.8
5-anion			384	388		14.4	3.0
2-methylthiophene					20.0	29.2	15.6
methyl anion	373 ± 3	380 ± 3	365	365	34	28.2	14.9
3-anion			398	401		61.3	50.7
4-anion			398	402		61.5	51.7
5-anion			389	394		52.7	44.2
3-methylthiophene					19.7	28.5	16.5
methyl anion	373 ± 3	381 ± 3	376	376	35	39.1	26.6
2-anion			389	394		52.1	44.6
4-anion			398	402		60.6	52.6
5-anion			390	396		52.4	46.6
2-methylpyridine					23.7	25.7	20.1
methyl anion	370 ± 3	377 ± 3	367	365	35	27.2	19.6
3-methylpyridine					25.4	24.1	20.8
methyl anion	371 ± 3	377 ± 3	365	365	38	24.1	20.2
4-methylpyridine					24.9	24.2	21.1
methyl anion	368 ± 3	375 ± 3	364	362	34	22.2	17.2
benzene					19.8	22.0	21.2[f]
phenide anion	391 ± 1	400 ± 1	403	405	54.0	57.4	60.9[f]
toluene					12.0	14.1	13.5[f]
benzyl anion	374 ± 2	381 ± 2	374	371	27	20.8	18.3[f]

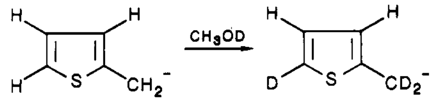
[a] ΔH_{form} [H$^+$] = 365.7 kcal/mol. [b] $\Delta H = \Delta G + T\Delta S$, $\Delta S = 26.0 + R \ln n$. [c] ΔH_{form} of neutral from ref 25. [d] Assuming that 4-position is most acidic. [e] ΔH_{form} not available. [f] Reference 26.

Scheme I



they enter into a relatively long-lived complex, which in these cases will contain ~15 kcal/mol of excess energy. This energy will be lost upon separation of the components, but while they are in the complex it may be used to fuel endothermic hydrogen or deuteron transfer reactions resulting in H–D exchange. For example, as shown in Scheme I, the anion and CH_3OD enter complex **1** in which endothermic deuteron transfer to form **2** may occur, using up about 4 kcal/mol of the complexation energy. This can be regained by hydrogen transfer to form **3** followed by dissociation. Subsequent reaction with another molecule of CH_3OD can result in a second exchange.

In the anion derived from 2-methylfuran and 2-methylthiophene, three hydrogens exchange with CH_3OD, indicating that the methyl group and the remaining α-position are of roughly equal acidity (eq 2). In this

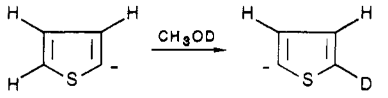


(2)

equation we have arbitrarily written the anion as that arising by hydrogen abstraction from the methyl group. Note that the fact that three rather than four exchanges occur demonstrates that the α-hydrogens are more acidic than the β-hydrogens, since four exchanges would have been observed if the β-hydrogens were more acidic than the α-hydrogens.

In the anion derived from 3-methylthiophene only one exchange occurs with CH_3OD, indicating that the α-hydrogens are more acidic than the methyl group in this case. This is not unexpected since proton abstraction from the methyl group in 2-methylthiophene affords a pentadienyl anion while the 3-isomer only leads to an allylic anion.

The anion from thiophene, to which we assign by analogy the α-anion structure, exchanges a single hydrogen with CH_3OD, as expected (eq 3). It exchanges all three of its hydrogens when D_2O is the exchange reagent (eq 4). Exchange reactions with D_2O, when they occur, can be more complicated than those with CH_3OD and other deuterated alcohols because D_2O brings two exchangeable deuterium atoms into a reaction complex at the same time. Exchange with CH_3OD occurs in the expected way, by



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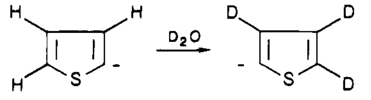


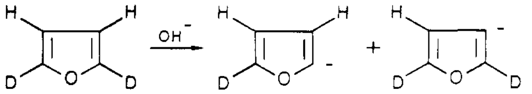
(4)

addition of a deuteron to one α-position and removal of a hydrogen of identical acidity from the other. A similar process can occur with D_2O. However, less acidic hydrogens can also be exchanged with D_2O by the process given in Scheme II. As before, the ion and the exchange reagent enter into a long-lived ion–dipole complex (**4**), which contains ~15 kcal/mol excess energy. A deuteron transfer, which is endothermic by ~10 kcal/mol, produces **5**. A hydrogen transfer from the β-carbon can follow to form **6**. The initial complexation energy can be recovered by adding a deuterium to the β-position (**7**) and reabstracting a hydrogen (or deuterium) from an α-position (**8**). The remaining hydrogen can be exchanged by analogous steps in a subsequent encounter with D_2O.

The anions from 2-methylfuran and from pyridine are both much more basic than methoxide ion and so are neutralized rapidly by CH_3OD. When D_2O is added to the anion from pyridine, DO^- is formed immediately but some pyridyl-d_1 and -d_2 anions are also formed, indicating that exchange and hydrogen transfer are competitive. The exchange data therefore support the conclusion that pyridine and water have approximately the same acidity. When the pyridyl anion is allowed to react with ND_3, two hydrogens are exchanged for deuterium at approximately the same rate. Therefore one set of hydrogens, consisting of the 4- and those in either the 2,6- or 3,5-positions, are more acidic than the other two. The anion from 1-methylpyrrole reacts irreversibly with both CH_3OD and D_2O but exchanges four hydrogens with ND_3. This demonstrates that the methyl hydrogens and either the hydrogens in the 2,5- or 3,4-positions make up the acidic set.

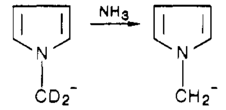
To gain further insight into these relative acidities, we have prepared deuteriated derivatives of some of these heterocycles. Our 2,5-dideuteriofuran contained 65% d_2, 25% d_1, and 10% d_0 as determined by mass spectral analysis, while the NMR spectrum showed that all the deuterium was in the α-position. Hydrogen abstraction by HO^- produced M − 1 ions, which were 15% d_2, 53% d_1, and 32% d_0. Clearly the majority of hydrogen abstraction occurs from the α-position, but the presence of a significant amount of M − 1 with two deuterium atoms shows that the β-hydrogens can also be abstracted. If we neglect any kinetic isotope effect or H–D exchange during the process of hydrogen abstraction, then the data show that abstraction from the α-position is approximately 3 times as likely as abstraction from the β-position. This is probably a maximum value for furan since the kinetic isotope effect is expected to be small[16] but H–D exchange during hydrogen abstraction, which would reduce the observed preference for α-abstraction, is probably occurring since the anion from furan does undergo three exchanges with D_2O. Consequently, all we can conclude is that the α- and β-positions are close in acidity with the former being slightly more acidic.

In order to determine which hydrogens in 1-methylpyrrole exchange, we prepared both the deuteriomethyl



(5)

derivative and the α-deuterio derivative and allowed their anions to react with NH_3 (eq 6 and 7). In both cases, all



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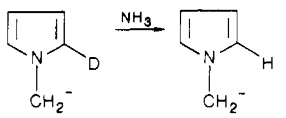
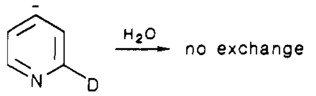


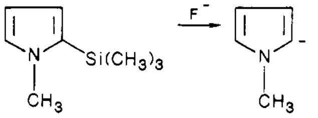
(7)

deuterium was lost by exchange, showing that the α-hydrogens are the most acidic ring hydrogens. An analogous experiment was carried out in the pyridine series where 2-deuteriopyridine was prepared and its anion allowed to react with H_2O (eq 8). Deuterium was not removed from the molecule by exchange, showing that the 3- and 4-positions are the more acidic positions.



(8)

Next we examined anion production from some trimethylsilyl derivatives of these heterocycles. We have shown in earlier work[17] that reaction of such derivatives with F^- is a convenient way to generate carbanions in the gas phase by taking advantage of the great strength of the silicon–fluorine bond (~150 kcal/mol) to drive the reaction. We found previously that the allyl anion (ΔG_{acid}(propylene) = 385 ± 2 kcal/mol) and anions less basic than allyl can be formed in good yield by this reaction. The method is not useful for the generation of species as strongly basic as the phenide ion, (ΔG_{acid}(benzene) = 391 ± 1 kcal/mol). When 1-methyl-2-(trimethylsilyl)pyrrole is allowed to react with fluoride ion, the corresponding 2-pyrrole anion is produced (eq 9), while similar reaction of the 3-derivative does not produce any pyrryl anion (eq 10), thus confirming our previous conclusion that the α-anion is less basic than the β-anion. Nor is a carbanion formed from 2-(trimethylsilyl)pyridine under similar conditions (eq 11). We also used another reaction of these



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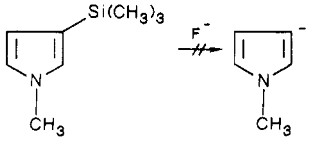

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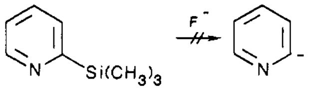

(11)

three trimethylsilyl derivatives as a probe of the relative acidity of the 2- and 3-positions in 1-methylpyrrole and the 2-position in pyridine. When a tetrasubstituted silane is allowed to react with hydroxide ion in the gas phase, a molecule of hydrocarbon is lost, and a siloxide ion is formed. For example, the reaction of tetramethylsilane

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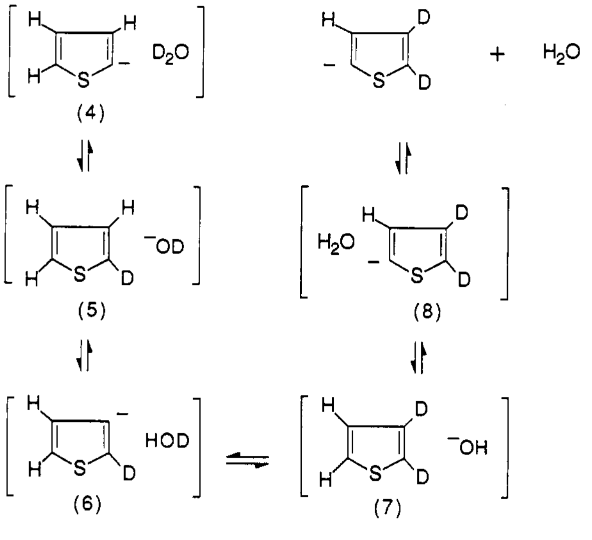
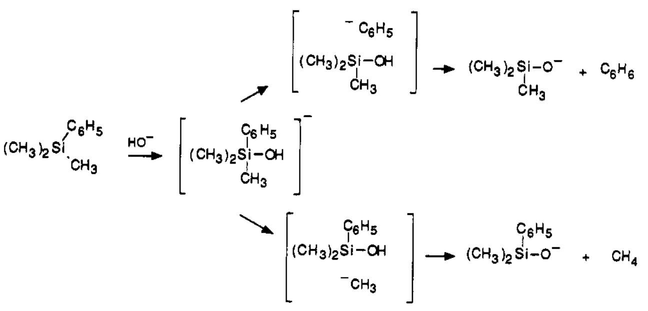
(16) Wellman, K. M.; Victoriano, M. E.; Isolani, P. C.; Riveros, J. M. *J. Am. Chem. Soc.* **1979**, *79*, 2242. Noest, A. J.; Nibbering, N. M. M. *Int. J. Mass Spectrom. Ion Phys.* **1980**, *34*, 383. Klass, G.; Underwood, D. J.; Bowie, J. H. *Aust. J. Chem.* **1981**, *34*, 507.

(17) DePuy, C. H.; Bierbaum, V. M.; Damrauer, R. *J. Am. Chem. Soc.* **1984**, *106*, 4051–4053.

Scheme II



Scheme III



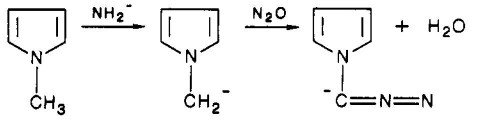
with hydroxide ion forms trimethylsiloxide ion and methane at every collision (eq 12).[17] When the silane has

$$(CH_3)_4Si + HO^- \rightarrow (CH_3)_3SiO^- + CH_4 \qquad (12)$$

two different substituents, as for example phenyltrimethylsilane, then two different siloxides can be formed, trimethylsiloxide by loss of benzene and phenyldimethylsiloxide by loss of methane. We have shown previously that the relative amounts of these two product ions observed correlates well with the relative acidity of the hydrocarbons formed.[17] The overall mechanism of the reactions is shown in Scheme III. The hydroxide ion adds to the silicon atom to form a pentacoordinate anion, which decomposes by attempting to eject either a phenide or a methide ion. These ions, while still in the vicinity of the resulting silanol, react with the hydrogen of the OH group to form the hydrocarbon and the siloxide ion. The more weakly basic the carbanion (i.e., the more acidic the hydrocarbon) the more easily it is lost. Hence in Scheme III more trimethylsiloxide is formed than phenyldimethylsiloxide. For example, under a given set of experimental conditions of resolution and other instrumental settings we observed 12 times as many ions of *m*/*z* 89 than of *m*/*z* 151. Since there are three methyl and only one phenyl groups, the relative rate of loss of benzene and methane is 36:1.

When the same reaction was carried out with 1-methyl-3-(trimethylsilyl)pyrrole, the ratio of siloxide ions, *m*/*z* 89 (resulting from loss of 1-methylpyrrole) to *m*/*z* 154 (resulting from loss of methane), was 27:1 (statistically corrected), suggesting that the hydrogens in the 3-position are slightly less acidic than those in benzene. The ratio of ions of the same two masses in the products from the reaction of 1-methyl-2-(trimethylsilyl)pyrrole with hydroxide ion was 50:1, suggesting that the 2-hydrogens are more acidic than those in benzene and again supporting our conclusion that the 2-position in 1-methylpyrrole is more acidic than the 3-position.

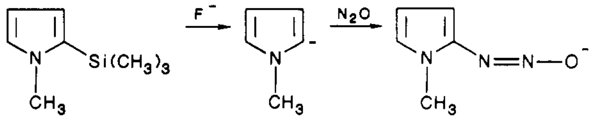
Finally, we examined the chemical reactions of these anions with O_2, N_2O, OCS, and CS_2, reagents that we have found useful in previous studies as probes of ion structure and reactivity. Of these reagents, N_2O is the most versatile since it can react by a number of different mechanisms, depending upon the structure of the anion.[18] For example, a primary anion is converted to a diazoanion upon reaction with N_2O (eq 13) such as that formed from 1-methylpyrrole



(13)

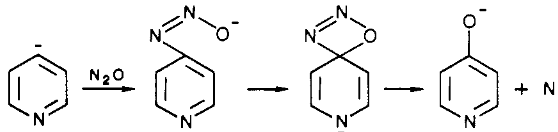
by abstraction of a hydrogen with NH_2^-. A similar reaction occurs with the M − 1 anions from the methylfurans and methylthiophenes. Only a trace of diazoanion was formed from the anion from 3-methylpyridine, while the corresponding anions from 2- and 4-methylpyridine do not react with N_2O at an observable rate. We have previously noted a correlation between anion basicity and rate of reaction with N_2O,[19] and it is not surprising that anions as weakly basic as these latter three react only slowly or not at all under our conditions.

Vinyl anions usually react with N_2O either by forming an adduct or, occasionally, by oxygen atom transfer.[18] In the gas phase the formation of an adduct must be a three-body reaction with the exothermicity of the reaction being removed by collisions with the buffer gas. Under the relatively high pressures of FA conditions such addition reactions of large organic molecules are frequently "saturated" in the sense that each adduct lives long enough to be cooled and the yield of adduct is insensitive to the small changes in helium flow that can be made. For example, the carbanion formed from the reaction of 1-methyl-2-(trimethylsilyl)pyrrole with fluoride ion forms an adduct with N_2O (eq 14). This result confirms our



(14)

assignment of the methyl group as the site of hydrogen abstraction by NH_2^- since that anion forms a diazoanion upon treatment with N_2O. Analogous adducts are formed from the M − 1 anions from thiophene and, in part, pyridine. However, the major product from the reaction of the M − 1 anion from pyridine is an ion $(M + 15)^-$, which corresponds to oxygen transfer from N_2O. We propose that this ion results from the pathway shown in eq 15. An analogous mechanism for an adduct formed at the 3-position could also be written and this result does not distinguish between these two sites.



(15)

The anion from furan reacts with N_2O by yet another pathway to form an $(M + 13)^-$ ion by nitrogen atom transfer (eq 16). This reaction has been discussed pre-

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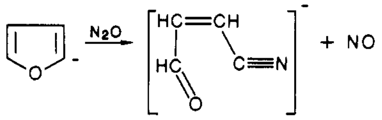
(18) Kass, S. R.; Filley, J.; Van Doren, J. M.; DePuy, C. H. *J. Am. Chem. Soc.* **1986**, *108*, 2849.

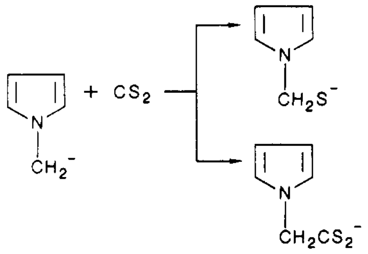
(19) Bierbaum, V. M.; Grabowski, J. J.; DePuy, C. H. *J. Phys. Chem.* **1984**, *88*, 1389–1393.

viously,[18] and the evidence for the structure of the product ion will not be repeated here.



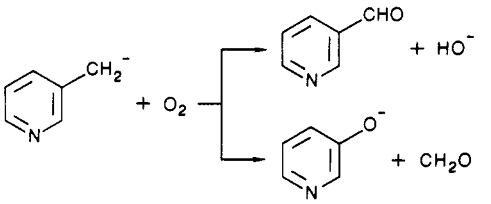
(16)

We also examined the reactions of these anions with COS and CS_2. In complete analogy to our previous work,[20] two competing pathways, addition and sulfur atom transfer, were generally observed, as shown for reaction of 1-methylpyrrole with carbon disulfide (eq 17). In agreement with our earlier work, the more basic the anion the more sulfur atom transfer is observed; as the anion becomes less basic, addition predominates. The anion from 4-methylpyridine, for example, gives exclusively addition with either COS or CS_2. We also examined the reactions of each of these anions with O_2.[21] Those from furan, thiophene, 3-methylthiophene, and 2- and 4-methylpyridine do not react. The anion from 3-methylpyridine reacts slowly to form both hydroxide ion and an ion $C_5H_4NO^-$ corresponding to loss of formaldehyde. By analogy to reactions of benzyl ions, we suggest that these reactions occur as shown in the following equation. Anions from 2-methylthiophene and 2-methylfuran react analogously, but some O_2^- formed by electron transfer is observed in the latter case. The anion from 2,5-dimethylfuran forms O_2^- exclusively. These results suggest that the electron affinity of the 2-methylfuryl anion is very close to that of O_2, namely 10 kcal/mol.[22] By combining this electron affinity with the gas-phase acidity and the ionization potential of the hydrogen atom one can derive the bond dissociation energy of the C–H bond of the methyl group in 2-methylfuran to be 80 kcal/mol. For comparison, the bond dissociation energy of toluene is 88 kcal/mol.



(17a)

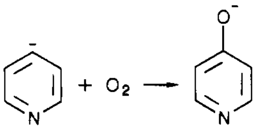
(17b)



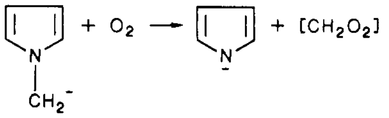
(18a)

(18b)

The anion from pyridine reacts with O_2 exclusively by oxygen atom transfer (eq 19), while that from 1-methylpyrrole loses mass 14 to form what is presumably the pyrrole anion (eq 20). The structure of the neutral product(s) formed in the latter reaction, corresponding to the elemental composition CH_2O_2, is unknown. It appears unlikely to be formic acid since no formate ion is observed among the product ions.



(19)



(20)

We are now in a position to combine data from anion formation, hydrogen–deuterium exchange, and chemical reactions into an overall picture of gas-phase acidity among these heterocycles. The least acidic hydrogens that we have studied appear to be those in the 3-position of 1-methylpyrrole. These hydrogens do not exchange with ND_3, an anion is not produced at this position when the trimethylsilyl derivative is allowed to react with F^-, and the ratio of loss of 1-methylpyrrole to loss of methane upon reaction of this derivative with hydroxide ion is the smallest among the heterocycles studied. The most acidic hydrogens in the molecule are those of the methyl group, which we have established by bracketing as $\Delta G_{\text{acid}} = 386 \pm 3$ kcal/mol. The 2-hydrogens are thus intermediate in acidity.

In pyridine the order of acidity among the hydrogen appears to be $4 \approx 3 > 2$. We were unable to establish for certain whether the 3- or 4-position is the more acidic, but the two appear to be quite similar and one would not expect a large difference between them. On the basis of the ratio of pyridine to methane lost upon treatment of the 2-trimethylsilyl derivative with hydroxide ion, the 2-position appears to be about as acidic as benzene.

In thiophene the 2-position is again more acidic than the 3-position. We have as yet no good way of estimating the acidity of the 3-position in thiophene. However H–D exchange of these hydrogens is observed with D_2O. In 2-methylthiophene the methyl hydrogens and the 5-hydrogen appear to be nearly identical in acidity. In 3-methylthiophene, the 2- and 5-hydrogens are the most acidic, and the methyl hydrogens are likely to be more acidic than water. Finally, among the methylpyridines the order of acidity is $4 > 2 > 3$.

We felt it to be of interest to compare our measured and estimated acidities of these compounds (in terms of ΔH_{acid}) with acidities calculated by the MNDO and AM1 semiempirical molecular orbital methods. We have summarized the results in Table I. There are two different types of carbanions: localized anions resulting from abstraction of a ring hydrogen and delocalized, benzyl-type anions resulting from hydrogen abstraction at a methyl group. It is known that these semiempirical methods tend to underestimate the stability of localized anions somewhat and to overestimate the stability of delocalized anions.[23] This can be seen in the case of benzene, which is calculated to be 2 kcal/mol less acidic than the experimental value (403 vs 401 kcal/mol) while the methyl hydrogens of toluene are calculated to be 7 kcal/mol more acidic than the measured value (374 vs 381 kcal/mol). With few exceptions, this trend persists among the heteroaromatic compounds that we have studied. In general, the calculated acidity of hydrogens attached to methyl groups of heteroaromatics is about 10 kcal/mol greater than the measured acidity throughout the series. In contrast, the ring hydrogens are calculated to be somewhat less acidic than they

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are measured to be. If we take into account these tendencies, then the semiempirical methods do quite well in predicting the relative order of acidities in these compounds. For example, in 1-methylpyrrole they correctly predict that the methyl hydrogens are the most acidic followed by the 2- and then the 3-hydrogens. The ordering of the 2- and 3-hydrogens in furan and thiophene is also predicted correctly, as is the relative acidity of the methyl group in 2-methylfuran. Among the methylpyridines, the 4-methyl is correctly predicted to be the most acidic with the 2- and 3-methylpyridines being nearly the same acidity both by calculation and by experiment. The only major error in the calculations occurs in pyridine itself, where the 2-position is predicted to be much more acidic than either the 3- or 4-position while it is found experimentally to be the least acidic of the three. This calculational error undoubtedly arises from the underestimation of the repulsion between the lone pair on the carbanion and the adjacent lone pair on nitrogen, which are constrained by the geometry of the anion to be in the same plane. An analogous situation occurs in the neutral analogues of these anions, namely the diazabenzenes, in which the nitrogen lone pairs are in the plane of the ring. In pyridazine the two nitrogens are adjacent so that lone-pair repulsion is expected to be large, and this isomer is calculated to be more stable (i.e., to have a lower heat of formation) than is found experimentally by 11 kcal/mol in the case of AM1 and 23 kcal/mol in the case of MNDO.[23] For pyrimidine and pyrazine, where the two nitrogens are farther apart, the discrepancies between theory and experiment are much smaller (3 and 10 kcal/mol for AM1 and MNDO, respectively). In the anion derived from 1-methylpyrrole by abstraction of the 2-hydrogen, the lone pair on the carbon and the lone pair on the adjacent nitrogen are orthogonal, and so interaction is minimized. In this case the calculated and experimental acidities agree quite well, despite the fact that both AM1 and MNDO do poorly in calculating the heat of formation of pyrrole itself. Obviously this error, whatever its source, occurs in both the neutral and the anion and so cancels in the calculation of the acidity.

Taft has noted a similar effect of adjacent lone pairs on the relative basicity of pyridazine and pyrimidine and on the relative gas-phase acidity of pyrazole and imidazole.[24] Catalan and co-workers have carried out both semiempirical and ab initio calculations on these and other heterocycles, including pyridine.[25] They find that among the semiempirical methods, only INDO handles this effect correctly; by this method they predicted the 4- and the 3,5-positions in pyridine to be the most acidic with the 2,6-positions much less acidic, in agreement with our data.

We plan to extend these investigations to other heteroaromatic systems, both to gain experimental insights into the ways carbanions are stabilized and to make further comparisons between experiment and theory.

Acknowledgment. We gratefully acknowledge support of this work by the U.S. Army Research Office (Contract DAAG29-85-K-0046) and the National Science Foundation (Grant CHE-8503505). We also thank Dr. Chris Roberts for help with some of the experiments.

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Postulation of Bis(thiazolin-2-ylidene)s as the Catalytic Species in the Benzoin Condensation Catalyzed by a Thiazolium Salt plus Base

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Thiazolin-2-ylidenes generated by desilylation of 2-(trimethylsilyl)thiazolium ions are used as catalysts for the benzoin condensation. The experimental results together with theoretical calculations lead to the postulate that bis(thiazolin-2-ylidene)s, and not thiazolin-2-ylidenes, are the catalytic species in the benzoin condensation catalyzed by thiazolium salts plus base.

The benzoin condensation can be catalyzed by cyanide ion,[1-3] thiazolium salts **1** plus bases,[4,5] or bis(thiazolin-2-ylidene)s **2**.[6,7] Bis(thiazolin-2-ylidene)s can be formed by deprotonation of thiazolium ions with concomitant nucleophilic attack of the resulting thiazolin-2-ylidenes (or conjugate bases of thiazolium ions) **3** on the thiazolium ions.[8-11] Reaction of **2** with an electrophile gives the same derivative as that from reaction of **1** and the electrophile; the mechanism for this behavior was proposed by Lemal.[12]

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