(PPh₃)Re[μ-(COCHCOH)-*C*¹:*C*³]Re(CO)₄(PMe₃)} (5-OH). X-ray data were collected on a Nicolet R3m/V automated diffractometer system with a dedicated MicroVAX II computer system. Suitable crystals for both compounds were cocrystallized from diffusion of hexanes into a toluene solution and were sealed in glass capillaries under nitrogen. The parameters used during collection of diffractometer data for complexes **5** and **5-OH** are summarized in Table III. No systematic variation in intensities of three standard reflections for either data set were noted. All computations used the SHELXTL PLUS (Version 4.11) program library (Siemens Corp., Madison, WI). For **5**, the initial choice of the centro-symmetric space group *P*T̄ was confirmed by the successful solution and refinement of the structure.

Both structures were solved by direct methods and subsequent Fourier syntheses located all non-hydrogen atoms. All hydrogen atoms were placed isotropically in idealized positions. Although both the Re(1) unit and malonyl bridge of **5-OH** are well-behaved, excessive thermal parameters and distortion of the carbonyl positional parameters in the Re(2) unit suggested a mild disorder problem. Because of this, the carbonyl ligands were placed as rigid groups with fixed isotropic thermal parameters. All other non-hydrogen atoms except the phenyl carbons

were refined anisotropically. The final Fourier difference map revealed a residual electron density peak of 2.87 e, 1.06 form Re(2). For **5**, all non-hydrogen atoms except C(42) and C(6) and the phenyl carbons were refined anisotropically. No excessive thermal motion was noted in this structure; however, uncompensated absorption from the thin plate used for data collection resulted in pairs of residual electron density peaks of 1.47-3.69 e, symmetrically placed about the Re(1) and Re(2) centers.

Gas-Phase Heteroaromatic Substitution. 12.[1] Reaction of Free Trifluoromethyl Cation with Simple Five-Membered Heteroarenes in the Gas Phase

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Abstract: The reactivity features of radiolytically (⁶⁰Co γ-rays) generated unsolvated trifluoromethyl cation CF_3^+ toward pyrrole, *N*-methylpyrrole, furan, and thiophene have been measured under conditions, i.e. 7 Torr of C_2H_4 added, ensuring depletion of concomitant radicalic processes. Experiments have been carried out at atmospheric pressure and in the presence of variable concentrations of a gaseous base (NMe_3, 0-5 Torr). The mechanism of the ionic trifluoromethylation process and of the subsequent isomerization of the relevant ionic intermediates is discussed and the intrinsic positional selectivity of CF_3^+ ions evaluated. The preference of CF_3^+ for the β carbons of pyrroles (ca. 56%) and furan (ca. 78%) and the α carbons of thiophene (ca. 59%) conforms to a substitution route proceeding via the classical donor–acceptor S_E2 mechanism, ruling out alternative substitution pathways, including the two-step process advanced in the case of gas-phase acylation of the same substrates. The selectivity features of the CF_3^+ ion toward pyrroles appear to fit into Klopman's reactivity model, since determined essentially, but not exclusively, by its LUMO energy. The pronounced preference of CF_3^+ toward the β carbons of furan is discussed and compared with the general tendency of other gaseous alkyl carbocations, irrespective of their LUMO energy, to attack predominantly the α carbons of the same substrate. It is concluded that such a tendency is due to the establishment of electrostatic interactions between the n-electrons of the oxygen of furan and the hydrogens of the alkylating electrophile, a process which is prevented in the case of CF_3^+.

Introduction

The essence of Klopman's charge and frontier orbital control concept[2] in a donor–acceptor reaction is that, when the energy gap between the HOMO of the donor and the LUMO of the acceptor is small compared to that between the orbitals of the individual reagents, the reaction is "frontier-orbital controlled", i.e. it is governed by bonding between the atoms carrying the highest charge density in the frontier orbitals. When, instead, the energy gap between the HOMO of the donor and the LUMO of the acceptor progressively increases, the reaction tends to be "charge controlled", i.e. it is regulated by attractive electrostatic interactions between the centers of the two reagents with the highest total charge. If the acceptor is a free, unsolvated ionic electrophile and the donor is a five-membered heteroarene, such as pyrrole and furan, having a HOMO electron density distribution opposite to the total charge-density one,[3] a detailed investigation of their reactivity and selectivity features may represent a powerful

means for ascertaining whether Klopman's model is actually adequate for describing heteroaromatic reactivity, especially if the study is carried out in the gas phase, where solvation and ion-pairing factors normally affecting the intrinsic reactivity properties of both the donor and the acceptor are excluded.

In recent years, intense research effort has been actually channelled in this direction.[1,4] The study allowed for the es-

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tablishment of an approximately linear relationship between the STO-3G SCF calculated LUMO energy of several free ionic electrophiles and their positional selectivity toward the ring carbons of pyrrole (log (β/α)), in qualitative agreement with Klopman's model.[2] In fact, ionic electrophiles with high-energy LUMO's are electrostatically directed toward the ring carbons of pyrrole (ϵ(HOMO) = -6.6 eV) with the highest net negative charge, i.e. the C_β carbons (e.g. t-$C_4H_9^+$ (ϵ(LUMO) = -3.1 eV); log (β/α) = 0.54),[4d] whereas ionic reactants with low-energy LUMO's preferentially establish partial electron exchange with the ring centers of the same heteroarene with the highest HOMO π-electron density, i.e. the C_α atoms (e.g. CH_3^+ (ϵ(LUMO) = -6.4 eV); log (β/α) = -0.51).[4g] However, when unsaturated carbocations, such as acylium (acetylium and benzoylium)[1] and phenylium[4j] ions, are considered, appreciable deviations from the linear correlation are observed, reflecting a measured positional selectivity toward pyrrole well below that expected on the grounds of their STO-3G calculated LUMO energies (ϵ(LUMO) = -2.4 (acylium ions), -3.5 (ground-state phenylium ion), -5.5 eV (vibrationally excited phenylium ion)).

Persuasive experimental evidence points to a two-step substitution mechanism as responsible for the exceedingly high affinity of acylium ions for the α positions of pyrrole (log (β/α) = -1.1).[1] Free acylium ions are, in fact, able to accept an electron from the heteroarene molecule in the encounter complex, yielding an electrostatically bonded acyl radical–heteroarene radical ion pair I (eq 1), which, under the high-pressure conditions adopted, readily

Y = NH(1); NMe(2); O(3); S(4).   (II_β)   (II_α)
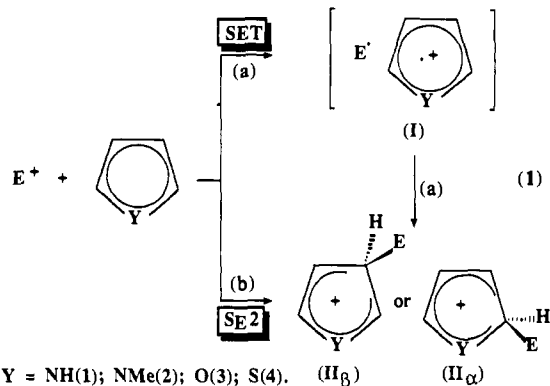
collapses to a covalently bonded σ intermediate II prior to dissociation (eq 1a). Radical–radical ion recombination within I involves predominantly the ring centers of the heteroarene radical ion with the highest spin density, i.e. the C_α carbons.[5] Kinetic predominance of the two-step substitution sequence 1a over the classical donor–acceptor S_E2 mechanism 1b in the attack of gaseous acylium ions on heteroarenes is determined by both favorable entropy factors and limited activation barriers, in view of the energetically quasiresonant (nearly thermoneutral) character of the vertical single-electron transfer (SET) from the heteroarene to the acylium ion (Figure 1).

Thermochemical calculations, visualized in Figure 1, indicate that a SET event in the attack of a nuclear-decay-formed (nucleogenic) phenylium ion Ph_{exc}^+ on simple five-membered heteroarenes is energetically allowed. It follows that, as for acylium ions, the appreciable deviation from Klopman's log (β/α) vs ϵ(LUMO) linear correlation exhibited by nucleogenic phenylium ion (log (β/α) = -0.42)[4j] may be, in principle, rationalized in terms of a kinetic prevalence of the two-step mechanism 1a over the S_E2 mechanism 1b.[4j] However, the substantial difference between the site selectivity of acylium (log (β/α) = -1.1)[1] and nucleogenic phenylium ions (log (β/α) = -0.42)[4j] toward pyrrole throws some doubt upon such a rationale for phenylium ion,[1] in view of the fact that a common two-step mechanism 1a for both electrophiles would lead to the same exceedingly high extent of α substitution, as essentially due to the spin-density distribution on the ring of pyrrole radical ion.[5]

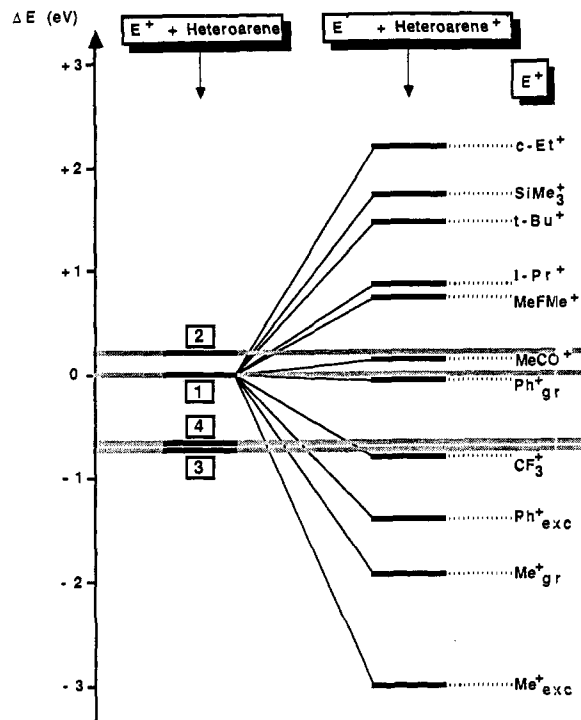(5) Shiotani, M.; Nagata, Y.; Tasaki, M.; Sohma, J.; Shida, T. *J. Phys. Chem.* **1983**, *87*, 1170.

Figure 1. Energetics of the vertical electron transfer from simple five-membered heteroarenes, i.e. pyrrole (1), N-methylpyrrole (2), furan (3), and thiophene (4), to the electrophile E^+ (c-Et$^+$ = bridged ethyl cation; gr = ground state; exc = vibrationally excited). The relevant thermochemistry is equal to IP_v(heteroarene) + EA_v(E^+). For electrophiles E^+ with the same geometry of ground-state E^*, IP_v(heteroarene) + EA_v(E^+) is expressed by IP_v(Heteroarene) - IP_v(E^*). When, instead, the geometry of E^+ significantly differs from that of ground-state E^*, IP_v(heteroarene) + EA_v(E^+) can be approximately expressed by IP_v(heteroarene) - IP_a(E^*) (refs 7 and 14). If the E^*/heteroarene^{*+} pair is considered electrostatically bonded in the encounter complex I of eq 1a, the energetics reported may be further lowered by several kilocalories per mole (Ausloos, P.; Lias, S. G. J. Am. Chem. Soc. **1981**, *103*, 3641).

To gain further insight into the kinetic role of two-step mechanism 1a in gas-phase heteroaromatic substitution by ionic electrophiles for which the preliminary SET step is exothermic, we have now extended the investigation to the trifluoromethyl cation CF_3^+, which can be conveniently generated in the gas phase by γ-radiolysis of CF_4.[6]

On the grounds of purely thermochemical considerations,[7] trifluoromethyl cation is ranked among the "hardest" ionic electrophiles and, thus, is expected to be electrostatically directed toward the ring positions of the heteroarene molecule with the highest net negative charge (e.g. the C_β's of pyrrole), if the classical donor–acceptor S_E2 mechanism 1b is operative. In the meantime, Figure 1 shows that CF_3^+ may undergo an exothermic vertical SET process from the heteroarene, much in the same way as nucleogenic phenylium ion. If, besides being energetically allowed, the two-step sequence 1a involving the preliminary SET event is also kinetically significant for CF_3^+, predominant α substitution on the heteroaromatic molecule would actually be observed, in spite of the allegedly "hard" character of the electrophile.

Additional interest is attached to CF_3^+ as regards to the nature of the primary adducts generated from the interaction of gaseous ionic electrophiles with the heteroatom of substrates, such as furan and thiophene.[4] It was, indeed, generally observed, at variance with the behavior of pyrroles, that these substrates undergo predominant α substitution, irrespective of the LUMO energy of the electrophile employed. For most electrophiles investigated, e.g. t-$C_4H_9^+$,[4d] such a peculiar site selectivity may respond to attractive interactions between the positively charged atoms of

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Table 1. Product Yields from the γ-Radiolysis of Gaseous CF₄–Heteroarene Mixtures

| system composition,[a] Torr | | | | | isomeric distribution of trifluoro-methylated products,[b] % | | overall-G(M) value |
CF₄	hetero-arene	NH₃	C₂H₄	NMe₃	α	β	
50	1, 0.8				47.1	52.9	2.6
150	1, 0.9				48.0	52.0	2.3
300	1, 0.8				48.9	51.1	2.9
500	1, 1.0				48.1	51.9	3.0
760	1, 0.9				48.3	51.7	2.5
760	1, 0.8			2	38.7	61.3	1.3
760	1, 0.7			5	42.3	57.7	0.6
760	1, 0.6			7	42.7	57.3	0.4
760	1, 0.8			10	42.7	57.3	0.1
760	1, 0.9	10			59.3	40.7	1.3
760	1, 1.0		7		51.0	49.0	0.4
760	1, 0.8		7	3	44.5	55.5	0.2
760	1, 0.7		7	5	44.3	55.7	0.1
760	1, 0.2		7	5	45.0	55.0	0.05
760	1, 1.8		7	5	44.8	55.2	0.2
50	2, 0.6				30.6	69.4	2.9
150	2, 0.8				30.8	69.2	3.2
300	2, 1.0				31.5	68.5	3.7
500	2, 1.0				29.4	70.6	3.4
760	2, 0.8				30.7	69.3	3.0
760	2, 0.7			2	32.6	67.4	0.9
760	2, 0.8			5	32.2	67.8	0.4
760	2, 0.9			7	32.9	67.1	0.2
760	2, 0.6			10	32.4	67.6	0.1
760	2, 1.0	10			26.9	73.1	1.9
760	2, 0.7		7		47.3	52.7	0.4
760	2, 0.8		7	3	43.0	57.0	0.2
760	2, 0.9		7	5	43.1	56.9	0.1
760	2, 0.2		7	5	43.8	56.2	0.03
760	2, 2.0		7	5	43.4	56.6	0.2
50	3, 0.7				44.0	56.0	3.0
150	3, 0.6				44.2	55.8	2.8
300	3, 0.7				45.3	54.7	2.6
500	3, 0.9				45.1	54.9	2.7
760	3, 1.0				45.3	54.7	2.5
760	3, 1.0			2	24.2	75.8	1.0
760	3, 0.6			5	23.6	74.4	0.4
760	3, 0.6			7	22.4	77.6	0.2
760	3, 0.8			10	22.4	77.6	0.08
760	3, 1.0	5			45.3	54.7	1.9
760	3, 0.7	10			48.8	51.2	1.6
760	3, 0.6		7		45.3	54.7	0.5
760	3, 0.5		7	3	24.7	75.3	0.2
760	3, 0.7		7	5	22.2	77.8	0.1
760	3, 0.2		7	5	23.0	77.0	0.04
760	3, 2.0		7	5	22.1	77.9	0.1
50	4, 0.6				58.8	41.2	1.4
150	4, 0.7				59.0	41.0	1.2
150	4, 1.0			5	61.6	38.4	0.2
150	4, 0.8		7		62.6	37.4	0.2
300	4, 0.6				63.3	36.7	0.8
500	4, 0.5				54.1	45.9	0.7
760	4, 0.8				56.0	44.0	1.0
760	4, 1.0			2	56.5	43.5	0.6
760	4, 1.0			5	57.7	42.3	0.4
760	4, 0.9			10	59.8	40.2	0.1
760	4, 0.7	10			58.1	41.9	0.6
760	4, 0.6		7		55.0	45.0	0.2
760	4, 0.8		7	3	58.5	41.5	0.1
760	4, 0.7		7	5	58.6	41.4	0.07
760	4, 0.2		7	5	57.9	42.1	0.03
760	4, 1.9		7	5	59.2	40.8	0.1

[a] O₂: 4 Torr. Radiation dose: 3.2 × 10⁴ Gy. Dose rate: 4 × 10³ Gy h⁻¹. [b] Uncertainty level: 10%. N-Trifluoromethylated derivatives of 1 and 2 below the detection 3 (G(M): ca. 0.001. Ca. 30% of an unknown isomeric trifluoromethylated derivative of 3 formed from the runs with NMe₃ (see ref 21). [c] Overall G(M) values defined as the number of molecules M of products formed per 100 eV of absorbed energy. Uncertainty level: 10%.

the electrophile and the n-electrons of the heteroatom, which favor subsequent α substitution by proximity effects. No clear-cut information is available as regards to the nature of such interactions, whether electrostatic involving the protons of the electrophile or rather covalent involving its carbon center. A comparative analysis of the positional selectivity toward furan and thiophene by typical alkyl carbocations, e.g. t-C₄H₉⁺, and by CF₃⁺, for which electrostatic proton bonding is prevented, may help in elucidating the origin of the exceedingly high extent of α substitution observed for these substrates in the gaseous phase.

The kinetic approach adopted in this study involves preparation of stationary concentrations of CF₃⁺ ions from the γ-radiolysis of CF₄ gaseous mixtures, containing several selected additives, such as O₂, C₂H₄, or NH₃, and their reactions with selected five-membered heteroarenes, under conditions, i.e. 50–760 Torr and the presence of a powerful ion trap (NMe₃, 0–10 Torr), ensuring efficient collisional thermalization and rapid deprotonation of the trifluoromethylating electrophile and its daughter heteroarenium intermediates, whose isomeric distribution therefore can be determined from the relative abundance of the corresponding trifluoromethylated neutral derivatives.

Experimental Section

Materials. Carbon tetrafluoride, oxygen, ammonia, ethylene, and trimethylamine were research grade gases from Matheson Co., with a minimum purity of 99.5 mol %. Pyrrole (1), N-methylpyrrole (2), furan (3), and thiophene (4) were research grade chemicals from Fluka AG. These substrates were analyzes by gas chromatography (GC) to check for the absence of trifluoromethylated impurities. Trifluoromethylated derivatives of 1–4 were obtained by conventional synthetic procedures,[8] purified by preparative GC, and identified by conventional IR, NMR, and GC–mass spectrometry (GC–MS).

Procedure. The gaseous samples used in the radiolytic trifluoromethylation were prepared according to standard procedures with use of a greaseless vacuum line and were introduced into carefully evacuated and outgassed 285-mL Pyrex vessels. Typical experimental conditions were the following: CF₄, 50–760 Torr; heteroarene, 0.2–2.0 Torr; O₂, 4 Torr; C₂H₄, 0–7 Torr; NH₃, 0–10 Torr; NMe₃, 0–10 Torr. The irradiations were carried out in a 220 Gammacell (Atomic Energy Canada Ltd.) to a total dose of 3.2 × 10⁴ Gy at a rate of ca. 4 × 10³ Gy h⁻¹, at a temperature of 30 °C. The irradiated samples were analyzed by GC and GC–MS with respectively a Perkin-Elmer 8320 and Sigma 3 gas chromatographs, equipped with FID units, and a Hewlett-Packard 5970B mass selective detector on the following columns: (i) a 2-m long, 3.2-mm i.d., stainless steel column, packed with Carbowax 20M, 10% on 100/120 mesh Chromosorb W-AW, operated at temperatures ranging from 50 to 120 °C; (ii) a 50-m long 0.32-mm i.d., fused-silica column, coated with Superox, operated at temperatures ranging from 60 to 150 °C.

The identity of the products was established by comparison of their retention volumes with those of authentic samples, as well as from their mass spectra in the GC–MS separations. The amounts of the products formed were determined from the areas of the corresponding elution peaks by using the internal standard calibration method.

Computational Details. Standard quantum-mechanical calculations, with the Gaussian 80⁹ set of programs, were performed in order to evaluate the SCF STO-3G¹⁰ eigenvalues of the LUMO orbital for CF₃⁺ ions. Geometry optimization, at the STO-3G level of theory, was performed in order to obtain the optimized wave functions and orbital eigenvalues. D₃ₕ symmetry was assumed. The energy of the LUMO of CF₃⁺ is −5.3 eV.

Results

The composition of the irradiated mixtures and the G(M) values of the final neutral products, i.e. the number of molecules M produced per 100 eV of absorbed energy, are reported in Table I. The listed values represent the average of several separate determinations from irradiations carried out under the same

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conditions, and their uncertainty level is of the order of 10%.

The conditions typical of the radiolytic experiments, in particular the low concentration of the heteroaromatic substrate (<0.3 mol%) and the total pressures used, ensure that the reacting species formed from the γ-radiolysis attain thermal equilibration by multiple unreactive collisions with the bath gas prior to attack on the substrate and that parasitic processes, induced by direct radiolysis on the heteroarene, can be safely neglected.

Analysis of Table I indicates that trifluoromethylation represents the major reaction channel for all selected substrates 1–4, in fact their α- (1α–4α) and β-trifluoromethylated (1β–4β) derivatives are by far the most abundant radiolytic products. Under no circumstances does trifluoromethylation take place at the N center of pyrroles 1 and 2, as shown by the lack of detectable amounts of *N*-(trifluoromethyl)pyrroles among the relevant products.

The relative and absolute yields of the neutral trifluoromethylated heteroarenes, expressed by their overall *G* values, while rather insensitive to large variations of the system pressure (50–760 Torr), are found to depend on the composition of the gaseous system. In particular, while the *G(M)* values of the trifluoromethylated products from 1–4 are dramatically lowered (up to ca. 97%) by addition of variable concentrations of NMe_3 to the gaseous mixture, they seem much less sensitive to addition of equal amounts of NH_3 (up to ca. 50%). A significant decrease of the *G(M)* values of products (up to ca. 87%) is caused as well by addition of ca. 1 mol % of C_2H_4 to the irradiated mixtures. The effect of the above additives on the *G(M)* values of the trifluoromethylated products of 1–4 is paralleled by pronounced variations in their relative distribution. Thus, while addition of either NH_3 or C_2H_4 to the gaseous mixture causes limited shifts in the product distribution, sometimes in opposite directions, addition of NMe_3 may lead to a significant increase of the relative yield of the β-substituted product. The most pronounced effect is observed in the case of furan (3) (from ca. 55% to ca. 78%), while for the other heteroarenes the effect is much less evident (1) or even absent (2 and 4). At any rate, β-trifluoromethylation of pyrroles 1 and 2 and furan (3) prevails over α-substitution under most conditions. The opposite trend is observed in the case of thiophene (4).

Discussion

Nature of the Ionic Reagent. Extensive studies on the radiolysis and the related ion chemistry of gaseous CF_4 indicate that, in the pressure range of interest to the present work, CF_3^+ represents by far the most significant cationic species, formed together with other ions (F^-) and radicals (CF_3 and F).[11] All such species are inert toward the parent CF_4 and, therefore, tend to accumulate in considerable concentrations depending on the purity of CF_4. The presence of an otherwise effective radical scavenger, such as O_2, in the irradiated mixtures cannot ensure that CF_3 does not actually contribute in part to the formation of the observed trifluoromethylated products in view of the fact that CF_3 radicals are only very slowly trapped by O_2[12] and may give rise to daughter oxygenated radicals with still some trifluoromethylating properties toward 1–4. On the other hand, the sharp decrease of the absolute yields of products caused by increasing concentrations of an effective cation trap, such as NMe_3, cannot be taken in this case as evidence of their ionic origin, since NMe_3 is able to lose a hydrogen atom to CF_3 radicals as well.[13] The efficiency of such a process is known to appreciably decrease by decreasing the number of methyls of the amine. In general, a close parallelism is observed between the exothermicity and the rate of hydrogen transfer from the C or the N atom of the amine to CF_3. In the case of NH_3, hydrogen transfer to CF_3 becomes exceedingly slow,

owing to its unfavorable energy requirements.[14] Accordingly, the trifluoromethylated derivatives of 1–4 recovered in the systems with 10 Torr of NH_3 can be taken as originating predominantly from attack of CF_3 radicals on the selected substrates, in view of the fact that NH_3, aside from being inert toward CF_3 radicals, is still a very effective scavenger of carbocations, such as CF_3^+. An estimate of the distribution of isomeric trifluoromethylated products originating from the CF_3^+ ion can instead be obtained from a comparative analysis of the results obtained with and without added ethylene C_2H_4. Ethylene, in fact, competes favorably with the heteroaromatic substrate for the CF_3 (and F) radicals,[15] yielding daughter alkyl radicals that can be effectively trapped by O_2. Therefore, in the presence of relatively large concentrations of ethylene (7 Torr), the trifluoromethylated products of 1–4 can be taken as mostly due to the attack of CF_3^+ ions on the selected substrates. In view of the absolute lack of reactivity of gaseous F^- ions toward electron-rich aromatic molecules, such as 1–4,[16] it can be concluded that the yield and the distribution of products recovered in the systems with C_2H_4 refer essentially to the ionic substitution channel, whereas those measured in the systems with NH_3 concern the radicalic substitution pathway. The results obtained in the absence of both additives refer instead to the combination of both substitution routes.

Use of a large excess (over 60:1) of CF_4 over the heteroaromatic substrate ensures the efficient thermal equilibration of radiolytic CF_3^+ ions by multiple unreactive collisions with the CF_4 molecules before a reactive encounter with the heteroarene and precludes direct radiolysis of the heteroaromatic substrate, as an additional undesired route to the trifluoromethylated products.

In the gas phase, ground-state CF_3^+ is expected to be a planar ion with a D_{3h} symmetry due to trigonal sp^2 hybridization of carbon. At variance with the often combined Bronsted and Lewis acid character of most gaseous alkylating carbocations toward aromatic molecules, CF_3^+ can only add to 1–4 as a pure Lewis-type acid, following energetically allowed substitution pathways.[17]

The Ionic Trifluoromethylation Process. When the extent of the radical route to the trifluoromethylated products is minimized by the combined action of O_2 (4 Torr) and C_2H_4 (7 Torr), it is possible to have a picture of the reactivity and selectivity of the CF_3^+ ion toward the selected heteroarenes. The results of the radiolytic experiments, carried out under such conditions are consistent with a trifluoromethylation pattern, involving the primary attack of a thermally equilibrated CF_3^+ cation on the heteroaromatic substrate, which leads to intermediates II (eq 1, E = CF_3), excited by the exothermicity of their formation process. Excited intermediates II undergo collisional deactivation with the bath CF_4 molecules prior to neutralization by proton transfer to a gaseous base, such as NMe_3 or the substrate itself.[18] In com-

(11) (a) Wilson, J. E. *Radiation Chemistry of Monomers, Polymers, and Plastics*; Marcel Dekker: New York, 1974. (b) Spinks, J. W. T.; Woods, R. J. *An Introduction to Radiation Chemistry*; Wiley: New York, 1964. (c) Vereshchinskii, I. V. *Adv. Radiat. Chem.* **1972**, *3*, 75.

(12) (a) Sieck, L. W.; Gorden, R., Jr.; Ausloos, P. *J. Res. Natl. Bur. Stand. Sect. A* **1974**, *78*, 151. (b) Quick, L. M.; Whittle, E. *Trans. Faraday Soc.* **1971**, *67*, 1727. (c) Orlando, J. J.; Smith, D. R. *J. Phys. Chem.* **1988**, *92*, 5147.

(13) Morris, E. R.; Thynne, J. C. J. *Trans. Faraday Soc.* **1968**, *64*, 3021.

(14) Hydrogen atom transfer from NH_3 to CF_3 is calculated to be thermoneutral or slightly endothermic. Cf.: Lias, S. G.; Bartmess, J. E.; Liebman, J. F.; Holmes, J. L.; Levin, R. D.; Mallard, W. G. *J. Phys. Chem. Ref. Data* **1988**, *17*, Suppl. 1.

(15) (a) Sangster, J. M.; Thynne, J. C. J. *J. Phys. Chem.* **1969**, *73*, 2746. (b) Dixon, P. S.; Szwarc, M. *Trans. Faraday Soc.* **1963**, *59*, 112. Ethylene is also able to compete with the heteroaromatic substrate for CF_3^+ ions. Partial trapping of CF_3^+ by ethylene is supported by the observation that the combined *G*(M) values measured in the presence of 10 Torr of NH_3, reflecting the radicalic route to the trifluoromethylated substrates, and in the presence of 7 Torr of C_2H_4, reflecting the portion of CF_3^+ trapped by the heteroarene to yield its trifluoromethylated derivatives, does not match the *G*(M) value estimated at atmospheric pressure in the absence of both additives, where both radicalic and ionic pathways fully cooperate in the formation of the final products. It should be noted, however, that, owing to the substantial dipole moment associated with the heteroarene molecule, this competes favorably with the apolar ethylene for the CF_3^+ ion.

(16) Smardzewski, R. R.; Fox, W. B. *J. Am. Chem. Soc.* **1974**, *96*, 304.

(17) Even rough thermochemical calculations of processes 1 by $E^+ = CF_3^+$ are prevented, owing to the paucity of reliable thermochemical data concerning neutral and ionic trifluoromethylated heteroarenes. However, observation of highly effective gas-phase trifluoromethylation reactions of benzene and toluene by CF_3^+ (ref 6) ensures that the same substitution process on the more activated heteroaromatic molecules 1–4 is energetically allowed as well.

(18) In view of the electron-withdrawing properties of the CF_3 group, the proton affinities of both 1α–4α and 1β–4β are expected to be appreciably lower than that of the corresponding unsubstituted parent molecule 1–4.

petition with collisional quenching, excited intermediates II may undergo several secondary processes, including isomerization to a more stable structure of fragmentation with loss of HF.[19] Their extent is expected to be minimized in systems with the highest NMe_3 concentration, where rapid neutralization of the primary trifluoromethylated intermediates II takes place. In this view, the isomeric composition of the trifluoromethylated products recovered from the systems at the highest NMe_3 partial pressure (5 Torr) closely reflects the relative population of the primary C-trifluoromethylated intermediates II_α and II_β from attack of CF_3^+ on the C_α's and the C_β's of the selected substrates.

In the absence of NMe_3, namely under longer lived ion conditions, a more or less extensive fraction of the primary intermediates II is able to isomerize to thermodynamically more stable structures. Isomerization can involve either an intramolecular CF_3 group shift within the intermediates II or an intermolecular CF_3 group transfer from II to another heteroarene molecule. Discrimination between these alternative isomerization mechanisms is provided by a study of the dependence of the isomeric distribution of the trifluoromethylated products of each heteroaromatic substrate for a 10-fold variation of the partial pressure of the heteroarene (0.2–2.0 Torr), keeping constant the total pressure of the gaseous mixture (760 Torr) and, especially, the concentration of the base NMe_3 (5 Torr), which would efficiently compete with the heteroaromatic substrate for the intermediates II in a conceivable intermolecular isomerization path. The essential constancy of the relative abundance of the trifluoromethylated products of 1–4, reported in Table I, by increasing the substrate concentration is consistent with an intramolecular isomerization pathway, rather than an intermolecular one. Among the conceivable intramolecular isomerization paths, that involving 1,2-H shifts within II is expected to predominate over the competing 1,2-CF_3 group transfer, in view of its comparatively limited activation barrier reflecting more favorable thermodynamic factors.[20] Relatively slow 1,2-CF_3 group shifts can, in principle, be observed only when much faster alternative isomerization routes are prevented, as for instance when occurring from the heteroatom of furan (3) to its C_α centers. Competition between 1,2-H and 1,2-CF_3 group shifts within II accounts for the significantly different dependence of the product distributions from 1–4 measured with or without added NMe_3 (Table I). Thus, the limited dependence of the relative distribution of trifluoromethylated derivatives of pyrroles 1 and 2 upon the NMe_3 concentration (Table I) is attributed to the kinetic predominance of H-shifts within their primary excited adducts II over CF_3 group migrations, inducing essentially a freeze of the CF_3 group on the specific C center of the heteroarene ring. Extending this view to furan (3), the evident decrease of the relative yield of its α-substituted product 3α from 45.3 to 22.2% by addition of 0.6 mol % of NMe_3 to the relevant gaseous mixture (Table I) can be rationalized only in terms of direct attack of part of the CF_3^+ ions on the heteroatom of furan (3) yielding a primary O-trifluoromethylated intermediate II_O which, in the absence of NMe_3, is able to slowly rearrange to the more stable C_α-substituted isomer II_α. Relatively slow O-to-C_α CF_3 group transfer within II_O is, in fact, easily prevented by the presence of even limited concentrations of NMe_3, which rapidly neutralizes II_O prior to rearrangement to II_α.[21] The apparent result of NMe_3 addition to

(19) Independent FT-ICR experiments revealed that addition of CF_3^+ to 1 with elimination of a HF molecule represents a major process at total pressures of the order of 5×10^{-7} Torr.

(20) (a) McLean, C.; Mackor, E. L. *Discuss. Faraday Soc.* **1962**, *34*, 165. (b) Field, F. H. *Ion–Molecule Reactions*; Franklin, J. L., Ed.; Butterworths: London, 1972.

(21) A product with the same molecular weight and fragmentation pattern of isomeric trifluoromethylated furans is recovered from the corresponding irradiated mixtures containing NMe_3. Its yield relative to the combined yield of isomeric trifluoromethylated furans amounts to ca. 30%, which matches the estimated yield of II_O. It is tempting to identify such a product as an acyclic isomer of trifluoromethylated furans, presumably $CF_3OCH=CH$-$C\equiv CH$, which might derive from transfer of the β hydrogen of II_O to NMe_3 with concomitant ring opening. This hypothesis is supported by the absolute lack of the same product, when the irradiations are carried out in the absence of a sufficiently powerful base, such as NMe_3.
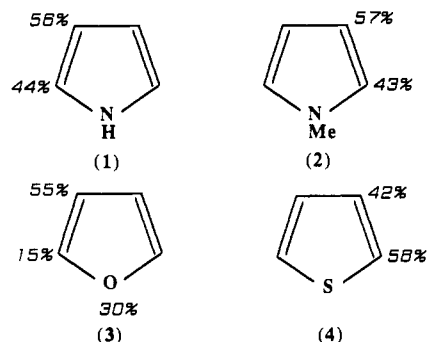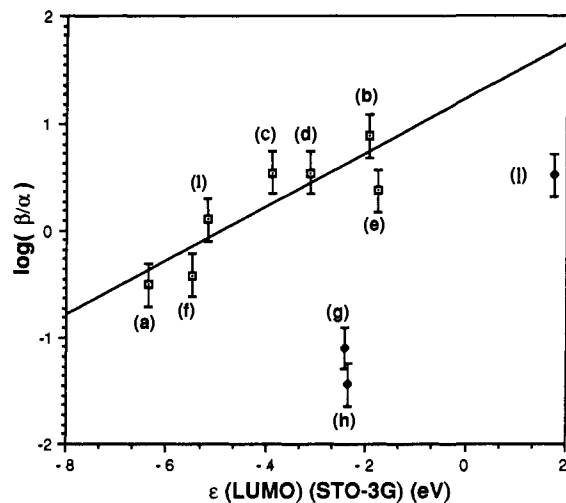

Figure 2. Positional selectivity of gaseous CF_3^+ ions toward simple five-membered heteroarenes.

the mixtures with 3 is, therefore, the sudden decrease of the relative yield of 3α to an extent reflecting the relative abundance of the primary O-trifluoromethylated intermediates II_O from direct attack of CF_3^+ on the oxygen of furan (3). An alternative explanation of the effect of NMe_3 on the product distribution from 3 (Table I), involving extensive reshuffling of the CF_3 moiety among the carbons of the corresponding C-substituted intermediates II, meets with some difficulty, in view of the fact that it would favor formation of the thermodynamically most stable heteroarenium isomer which, according to the electron-withdrawing character of the CF_3 group, is the β-substituted intermediate III (eq 2). It would follow a distinct increase of the β-trifluoromethylated furan 3β under long-lived ion conditions, i.e. in the absence of NMe_3, in contrast with experimental evidence.

$$\text{(2)}$$
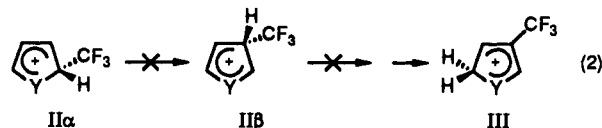
As mentioned above, the initial population of the O-trifluoromethylated intermediate II_O emerges directly from a comparative analysis of the isomeric distribution of the neutral C-substituted products 3α and 3β, as measured under kinetically controlled conditions, i.e. at 760 Torr and in the presence of NMe_3, where $II_O \rightarrow II_\alpha$ is minimized, and at the same pressure but in the absence of NMe_3, when $II_O \rightarrow II_\alpha$ is allowed. The increase of the relative yield of 3α (from 22.2 to 45.3%), as the NMe_3 partial pressure decreases from 5 Torr to zero, is consistent with a relative extent of direct attack at CF_3^+ on the oxygen of 3 amounting to ca. 30%.[21] Similar attack of CF_3^+ on the sulfur atom of thiophene (4) is comparatively ineffective, in view of the relative constancy of the isomeric distribution of its trifluoromethylated derivatives 4α (55.0–58.6%) and 4β (41.4–45.0%), under all experimental conditions (Table I). The same conclusions can be drawn as regards to the N-center of pyrroles 1 and 2 on the bases of the relative insensitivity of the product distribution upon the experimental conditions (Table I), and from the lack of any detectable amounts of N-trifluoromethylated products from 1 and 2, in spite of a specific search. Accordingly, we can evaluate the intrinsic positional selectivity of the CF_3^+ ion toward the selected substrates 1–4, as reported in Figure 2.

Positional Selectivity. The intrinsic site selectivity of gaseous CF_3^+ cation toward the selected heteroarenes 1–4 can be instructive of the detailed substitution mechanism, whether 1a or 1b, and the actual reacting mode of the free CF_3^+ electrophile toward heteroarenes. The site selectivity measured for CF_3^+ is, in fact, consistent with that expected from Klopman's reactivity model[2] for an ionic acceptor with a STO-3G SCF calculated LUMO energy (ϵ(LUMO) = -5.3 eV) lying between that of the "soft" methyl cation (ϵ(LUMO) = -6.4 eV)[4g,j] and that of the very "hard" i-$C_3H_7^+$ ion (ϵ(LUMO) = -3.9 eV).[4f,j] Figure 3, reporting the site selectivity (log (β/α)) of a variety of gaseous ionic electrophiles toward pyrrole (1) vs their STO-3G SCF calculated LUMO energy, visualizes such a consistency. Here, the site selectivity of CF_3^+ toward 1 (log(β/α) = 0.10) is found

Figure 3. Plot of site selectivity of ionic electrophiles toward the β and α carbons of pyrrole, expressed as the log (β/α), as a function of SCF STO-3G calculated LUMO eigenvalues of the ionic electrophiles: (a) ground-state CH_3^+ (ref 4g); (b) proton-bridged $C_2H_5^+$; (c) i-$C_3H_7^+$; (d) t-$C_4H_9^+$; (e) $(CH_3)_3Si^+$; (f) vibrationally excited $C_6H_5^+$ (ref 4j); (g) CH_3CO^+; (h) $C_6H_5CO^+$; (i) CF_3^+; (j) $(CH_3)_2F^+$. The interpolating line refers to the open square points exclusively.

to fall, within the experimental uncertainty of ca. ±0.3, on the linear log (β/α) vs ϵ(LUMO) relationship predicted by Klopman's concept[2] and to substantially diverge from that, characterized by almost exclusive α substitution, of acylium ions which are known to attack pyrroles via mechanism 1a.[1] A conceivably common two-step mechanism 1a for both acylium and CF_3^+ ions toward pyrroles is therefore excluded since it would lead to the same exceedingly high extent of α substitution, determined mainly by the predominant spin density location at the C_α centers of pyrrole radical ion.[5] Instead, the slightly higher affinity of CF_3^+ for the C_β's of pyrroles appears indicative of a substitution pathway following the classical donor–acceptor S_E2 mechanism 1b as for all the other alkylating and arylating electrophiles of Figure 3.

In conclusion, the present trifluoromethylation results confirm previous indications[1] about the energetic requirements necessary to make the entropy-favored two-step mechanism 1a kinetically prevailing over the competing classical S_E2 route 1b in the gas-phase heteroaromatic substitution by ionic electrophiles. Accordingly, the gas-phase SET step of eq 1a, in spite of favorable entropic factors, appears prevented not only when energetically unaccessible, i.e. when markedly endothermic, as for c-$C_2H_5^+$, $(CH_3)_3Si^+$, t-$C_4H_9^+$, and i-$C_3H_7^+$ (Figure 1), but also when energetically allowed, but highly exothermic, as for nucleogenic CH_3^+ and $C_6H_5^+$, and for CF_3^+ ions (Figure 1). A two-step mechanism 1a seems, instead, kinetically prevailing over the S_E2 mechanism 1b only if its entropy-favored SET step is energetically quasiresonant, as for acylium ions (Figure 1), and thus involves only limited energy barriers, if any.

Restricting the analysis to the ionic reactants following the classical S_E2 mechanism 1b, close inspection of Figure 3 confirms the view of a qualitative correspondence with Klopman's reactivity model,[2] in spite of several apparent discrepancies (e.g. *f*). Having excluded that such discrepancies are attributed to a mechanistic changeover, the experimental evidence of Figure 3 can only be rationalized in terms of a novel, more refined reactivity model taking into account the intimate nature of the substitution transition state, whose application is presented in the following paper of this issue.

The tendency of CF_3^+ to attack preferentially the ring sites of the heteroaromatic molecule with the highest net negative charge is documented by the corresponding positional selectivity shown in Figure 2. It should be noted that this tendency extends to furan (3) as well, while other alkylating carbocations, irrespective of their LUMO energies, exhibit an apparently high affinity for the α positions of furan (3).[4] Such an unexpected behavior of alkylating carbocations is attributed to the action of the n-electrons

of the heteroatom of 3 which can effectively interact with the positively charged centers of the electrophile, thus promoting its subsequent attack on the adjacent C_α centers of the substrate by proximity effects. These attractive interactions are electrostatic in nature and involve predominantly the proton rather than the carbocationic center of the electrophile. This view is supported by the observation that, when the same attractive proton–oxygen interactions cannot be established, as in the CF_3^+/3 adduct, α substitution is still observed, but only to the minor extent predicted by Klopman's model. In other words, preliminary electrostatic interactions take place between the n-electrons of 3 and the cationic centers of the electrophile to an extent depending upon the specific charge distribution within the electrophile–furan adduct. If involving the carbocationic center of the electrophile, such as in CF_3^+, the interaction leads to the formation of the covalently bonded oxonium intermediate II_O which, under long-lived ion conditions, may slowly rearrange to its more stable isomer II_α. When, instead, attractive interaction can be established between the n-electron of oxygen of 3 and a hydrogen of the electrophile, as in alkylating carbocations, it may drive the subsequent attack of the carbocationic center of the electrophile on the adjacent C_α sites so efficiently to make its interception very hard even by addition of relatively high concentrations of NMe_3 in the reaction mixture. In this latter case, the intrinsic affinity of the alkylating carbocations toward the α carbons of 3 is magnified by the electrostatic effect of the vicinal heteroatom to an extent that increases with the number and the individual charge fraction of the hydrogens of the electrophile relative to that of its carbocationic center, as demonstrated by the relative extent of α substitution on 3 measured for t-$C_4H_9^+$ (91%),[4d] i-$C_3H_7^+$ (71%),[4f] c-$C_2H_5^+$ (45%),[4h] and $(CH_3)_2F^+$ (35%).[4c] According to the available experimental evidence, when the heteroatom is sulfur, as in the case of thiophene (4), its tendency to establish electrostatic or covalent interactions with the cationic centers of the electrophile appears comparatively unimportant, so that the measured site selectivity by most gaseous ionic electrophiles, including CF_3^+, closely follows that expected on the grounds of the $\alpha > \beta > S$ net negative charge and HOMO electron density distribution of thiophene (4).[22]

Conclusions

The present trifluoromethylation results support the view of gas-phase substitution on simple five-membered heteroarenes by carbocations as mainly proceeding via the classical donor–acceptor S_E2 mechanism 1b, unless an entropy-favored quasi-resonant single-electron transfer (SET step in sequence 1a) from the heteroarene to the ionic electrophile is possible. A SET step appears kinetically prevented not only when highly endothermic but also when exothermic, as in the case of CF_3^+ toward 1–4. The site selectivity of gaseous CF_3^+ toward 1–4 conforms to that expected on the grounds of Klopman's charge and frontier orbital control concept,[2] but in sharp contrast with that expected on the grounds of the allegedly very "hard" character of the electrophile, estimated on the basis of purely thermochemical arguments.[7]

Klopman's reactivity model is found to qualitatively apply as well to the reactivity properties of most ionic electrophiles following the classical S_E2 mechanism 1b toward 1–4. Accordingly, the reactivity properties of the ionic electrophiles considered toward simple five-membered heteroarenes appear largely, but not exclusively, determined by their LUMO energy. Other factors, related to the intimate nature of the relevant energy profile may, in fact, play a role as well, as discussed in the following paper.

For five-membered heteroarenes containing n-electrons, such as furan (3) and, to a much lesser extent, thiophene (4), the kinetic picture is further complicated by establishment of attractive electrostatic interactions between the heteroatom and the cationic centers of the electrophile, which increase the probability of substitution at the vicinal C_α centers, thus altering the intrinsic orienting properties of the ring carbons of the substrate toward

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the incoming electrophile. The importance of this coordination effect by the heteroatom is related to the nature and the probability of the attractive interaction with the ionic electrophile, whether electrostatic involving its protons or covalent involving its carbocationic center.

Gas-Phase Heteroaromatic Substitution. 13.[1] A Quantitative Application of the Curve-Crossing Reactivity Model to Heteroaromatic Substitution

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Contribution from the Istituto di Chimica Nucleare del CNR, Area della Ricerca di Roma, Rome, Italy, and the Dipartimento di Agrobiologia ed Agrochimica, Università della Tuscia, Viterbo, Italy. Received July 26, 1990. Revised Manuscript Received January 21, 1991

Abstract: Gas-phase kinetic data concerning the electrophilic attack of free, unsolvated cations, such as CH_3^+, $C_2H_5^+$, $i\text{-}C_3H_7^+$, $t\text{-}C_4H_9^+$, $C_6H_5^+$, CF_3^+, $(CH_3)_2F^+$, $(CH_3)_3Si^+$, CH_3CO^+, and $C_6H_5CO^+$, toward simple five-membered heteroarenes have been embodied into Klopman's charge and frontier orbital control reactivity model. The origin of the deviations from a linear correlation between the positional selectivity of some of the above electrophiles and their SCF STO-3G calculated LUMO energy has been investigated. The influence of the computational level used for estimating the LUMO eigenvalues of the ionic reactants has been assessed by increasing the basis set dimensions from the STO-3G to the 6-31G*. Similar positional selectivity vs LUMO energy correlations have been obtained at both computational levels, revealing no significant difference at the two levels of theory employed. Direct evaluation of the activation parameters governing the gas-phase electrophilic attack on pyrrole by some representative ionic reactants, such as $i\text{-}C_3H_7^+$, $t\text{-}C_4H_9^+$, CF_3^+, and $(CH_3)_2F^+$, has been derived from their Arrhenius plots, measured within the temperature interval 30–140 °C. The curve-crossing reactivity model has been quantitatively applied to interpret the experimental kinetic results. A satisfying linear relationship between the intramolecular selectivity of the electrophiles considered and their G values has been obtained, the G parameter being a function of the vertical ionization potential IP_v of the heteroarene and of the vertical electron affinity EA_v of the electrophile. The influence of the G parameter in determining the nature of the transition states and the relative height of the activation barriers involved in the attack of the ionic electrophile on the α and β carbons of pyrroles has been discussed and compared with the effects of Klopman's HOMO (donor)–LUMO (acceptor) energy gap on the corresponding positional selectivity. A close relationship between the G parameter and the HOMO–LUMO gap, both reflecting the properties of the unperturbed donor–acceptor pair, has been verified.

Introduction

In earlier Parts of this series, specifically designed radiolytic and nuclear-decay kinetic procedures have been extensively applied to the study of the reactivity and selectivity properties of free, unsolvated ionic electrophiles toward five-membered heteroarenes in the dilute gaseous state, where complications due to interaction with the solvent and the counterion are eliminated.[1,2] The emerging picture characterizes gas-phase heteroaromatic substitution as generally proceeding via the classical S_E2 mechanism, unless a quasiresonant single-electron transfer (SET) from the heteroarene to the electrophile is allowed. Almost exclusive α substitution is observed for those electrophiles undergoing the SET event, e.g. the acylium ions, while the site selectivity of those following the donor–acceptor S_E2 mechanism qualitatively conforms to that expected on the grounds of Klopman's charge and frontier orbital control concept.[3] Accordingly, the selectivity properties of a number of ionic electrophiles toward simple five-membered heteroarenes, such as pyrrole, appear primarily determined by the energy gap between the HOMO of the heteroaromatic donor and the LUMO of the cationic acceptor, as indicated in Figure 1 by the approximately linear correlation between the β vs α substitution ratio (log (β/α)) in pyrrole and

the SCF STO-3G calculated LUMO energy of the electrophile. A similar correlation is found for *N*-methylpyrrole. Although these trends are acceptable, the linear correlation of Figure 1 is rather unsatisfying from the quantitative point of view. In fact, appreciable deviations from the linearity are actually observed for several ionic electrophiles, reflecting a measured positional selectivity toward pyrrole somewhat different from that expected on the grounds of their SCF STO-3G calculated LUMO energy.

The aim of the present investigation is to ascertain whether the origin of such deviations from Klopman's predictions is due to

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