Theoretical Studies on the Electrophilic Methylation of Five-Membered Heteroaromatic Compounds with Dimethylfluoronium Ion[1]

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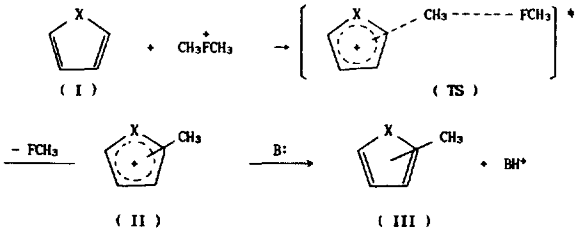
Electrophilic methylation reactions of five-membered heteroaromatic compunds, furan, pyrrole and thiophene, with the dimethylfluoronium ion, $CH_3FCH_3(+)$, have been investigated theoretically by the MNDO method. The site selectivity of α, β and heteroatom (X) is related to charge density of the site, indicting that the site selectivity is dictated by electrosatic interaction between two reaction centers. The reactivity order between the three heteroaromatics can not be determined decisively since the order differs depending on which site is compared, with relatively low activation enthalpies, $\Delta H^* = 20\text{-}30$ kcal/mol, in all cases. These site and substrate selectivity behaviors are consistent with the gas-phase experimental results.

Introduction

In a previous paper,[2] we have reported on the theoretical studies of the electrophilic isopropylation of five-membered heteroaromatics with isopropyl cation. We found that the site selectivities of α, β and heteroatom (X) positions are controlled mainly by charge transfer stabilization[3] between the HOMO of heteroaromatics and the LUMO of the electrophile.

Here we extend our work tö the electrophilic methylation process, Eq. (1), using the MNDO MO method.[4]



X=O NH or S
B : =a base or other substrate molecule

Two types of processes, isopropylation and methylation, differ basically : In the isopropylation process, the isopropyl cation forms an adduct with the substrate,[2,5] five-membered heteroaromatics, whereas in the methylation, Eq. (1), the substrate attacks the carbon center of $CH_3FCH_3(+)$ in an S_N2 type process with concomitant fragmentation of the CH_3F molecule. Thus the electrophilic methylation process of the five-membered heteroaromatics with $CH_3FCH_3(+)$ constitutes an entirely different type from that of the isopropylation with isopropyl cation. In this work, we examined the factors responsible for the site and substrate selectivities in the methylation with $CH_3FCH_3(+)$ and compared the results with those of the gas-phase experiments by Angelini *et al.*[6] The deprotonation of the methylated intermediates (II) by a base, B :, in Eq. (1), is a normal acid-base proton transfer process so that it should proceed rapidly relative to the process I→II. We have therefore only dealt with the slow process, I→II, in this methylation studies.

Table 1. Positonal Activation Energy Barrier (ΔH^*), Heavy Atom Charge Density (q) and HOMO-LUMO Energy Gaps ($\Delta\varepsilon_{FMO}$) of Furan.

Position	ΔH^{*a}	q^b	$\delta\varepsilon_{FMO}{}^c$	$\Delta H_R{}^d$
	24.7	−0.13	5.67	−6.9
C_α	29.4	−0.01(+0.01)^e	4.49	−42.5
β	28.7	−0.13(+0.09)	4.49	−36.9

$^a\Delta H^* = \Delta H_f\,(\text{TS}) + [\Delta H_f\,(\text{furan}) + \Delta H_f(\text{dimethylfluoronium ion})]$ in kcal/mol. ^{b}Charge densities of heavy atoms are in electronic charge unit $^c\Delta\varepsilon_{FMO}$ = LUMO (dimethylfluoronium ion)-HOMO (furan) in eV. $^d\Delta H_R = \Delta H_f\,(\text{Product complex}) - [\Delta H_f\,(\text{furan}) + \Delta H_f\,(\text{dimethylfluoronium ion})]$ in kcal/mol. ^{e}Parenthesis is a charge of the attached hydrogen atom.

Calculations

The calculations were carried out using the standard MNDO procedure[7] with full optimization of all geometrical variables. Transition States (TS) were located by the reaction coordinate method,[8] refined with the gradient norm minimization method[9] and characterized by confirming only one negative eigenvalue in the Hessian matrix.[10]

Results and Dicussion

Methylation of Furan. The activation enthalpy ΔH^*, positional charge density, q, of the ground state and the HOMO-LUMO energy gap, $\Delta\varepsilon_{FMO}$, for methylation of C_α, C_β and O positions of furan with $CH_3FCH_3(+)$ ion are summarized in Table 1; the HOMO of the oxygen atom is the π-lone pair orbital, and that for C_α and C_β is the π-bond orbital of the C_α-C_β bond, while the LUMO is the antibonding σ orbital (σ*) of the C-F bond in $CH_3FCH_3(+)$ since the process proceeds by an S_N2 type TS. The site selectivity of furan determined by ΔH^* decreases as $O > C_\beta > C_\alpha$. This order is exactly in reverse to that found for isopropylation reaction,[2] for which charge transfer interaction $(\varepsilon_{ct})^3$ dictated by $\Delta\varepsilon_{FMO}$ is the major factor controlling the site selectivity.[11] Thus in the methylation with $CH_3FCH_3(+)$ ion, the site sele-

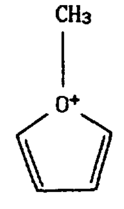
Table 2. Positional Activation Energy Barrier (ΔH^*), Heavy Atom Charge Density (q) and HOMO-LUMO Energy Gaps ($\Delta\varepsilon_{FMO}$) of Pyrrole

Positon	ΔH^{*a}	q^b	$\Delta\varepsilon_{FMO}{}^c$	$\Delta H_R{}^d$
N	24.8	$-0.22(+0.20)^e$	4.68	-31.9
C_α	25.5	$-0.03(+0.09)$	3.91	-55.8
C_β	22.7	$-0.13(+0.08)$	3.91	-31.9

[a] $\Delta H^* = \Delta H_f$ (TS) $-$ [ΔH_f(pyrrole) + ΔH_f (dimethylfluoronium ion)] in kcal/mol. [b] Charge densities of heavy atoms are in electronic charge unit. [c] $\Delta\varepsilon_{FMO}$ = LUMO (dimethylfluoronium ion) $-$ HOMO(pyrrole) in eV. [d] $\Delta H_R = \Delta H_f$ (Product complex) $-$ [ΔH_f (pyrrole) + ΔH_f(dimethylfluoronium ion)] in kcal/mol. [e] Parenthesis is a charge of the attached hydrogen atom.

ctivity is expected to depend more on the electrostatic interaction (ε_{es})[12] between the reacting positions of the substrate and electrophile as can be seen from positional charge densities and the frontier MO (FMO) gap, $\Delta\varepsilon_{FMO}$. Since the FMO gap is relatively large, 4.5 − 5.7 eV, for the methylation process in contrast to the narrower gaps obtained, *ca.* 1-2 eV, for the isopropylation process, the ε_{ct} term will be relatively unimportant in the methylation process. On the other hand we note that the O atom has similar charge density ($q = -0.13$) but has a lower ΔH^* value compared with the C_β position indicating a greater electrostatic stabilization leading to a greater selectivity. This can be rationalized by a net charge density, $q_{net}(\beta) = -0.04$, when the charge of hydrogen attached to the C_β is included in the net charge of the C_β-moiety. This will lead to a higher ε_{es} for O and hence the higher reactivity of O compared to C_β.

The results of our calculation appear to disagree with those of the Angelini and coworker's gas-phase experiment giving methylated product III ratio of O : C_α : C_β = 36 : 35 : 29.[6b] The site selectivity is shown to be in the other, O > C_β > C_α, according to our results in Table 1, whereas the experimental results indicates similar reactivity of O and C_α positions with the lowest reactivity of the C_β position. However, these discrepancies can be easily resolved. We note that the difference in ΔH^* between C_α and C_β is only 0.7 kcal/mol implying very small difference in the product ratio of the methylated species between the two positions. Moreover, even if the O-methylated species, IV, were produced in a greater quantity than the C_α and C_β-methylated species, the amount of IV produced can not be measured directly in the experiment as Angelini *et al.* have reported, since IV is not a neutral species and hence is not stable. The greater incipient yield of species IV would be reduced by methyl transfer to either C_α or C_β.



(IV)

This rapid methyl transfer process is more likely to occur at the C_α than C_β position increasing the product yield of C_α-methylated species in a later rapid stage of the reaction as Angelini *et al.* have pointed out in their report of the experimental results.

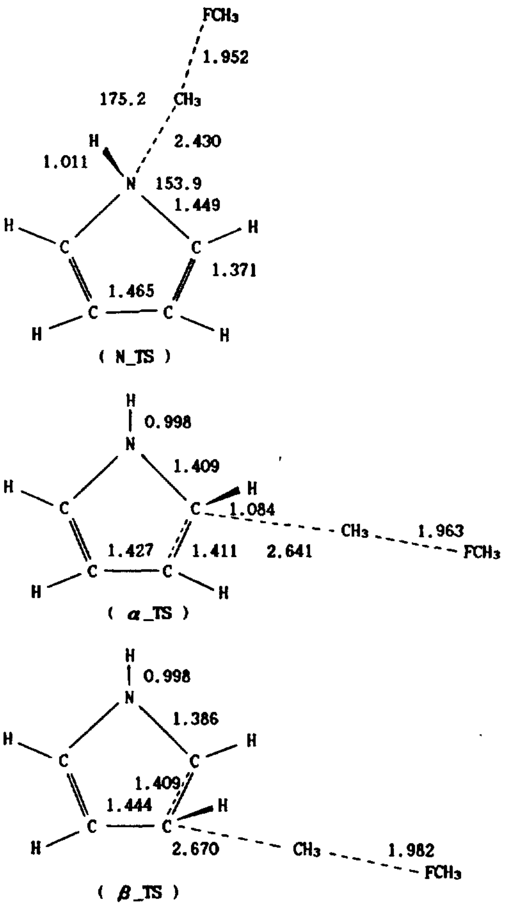


Figure 1. Geometries for TSs in the methylation processes of Pyrrole.

Methylation of Pyrrole. The calculated results relevant to reactivity for the methylation of pyrrole with $CH_3FCH_3(+)$ are presented in Table 2. The site selectivity of pyrrole is shown to be in the order C_β > N > C_α, which indicates that the site selectivity is independent of the charge transfer term, ε_{ct}, which in tern is dictated by $\Delta\varepsilon_{FMO}$. In the reaction of pyrrole with isopropyl cation, the site selectivity was found to be in the order C_β > C_α > N, which is mainly controlled by the charge transfer term, ε_{ct}. In contrast, in the methylation process, as in the reaction of furan, the contribution of charge transfer stabilization is negligible due to a greater interfrontier energy gap, $\Delta\varepsilon_{FMO}$ = 3.9-4.7 eV compared to a smaller gap, $\Delta\varepsilon_{FMO}$ = 0.4-1.2 eV for the isopropylation process. This leads us to the same conclusion as for furan that the site selectivity of pyrrole in the methylation is mainly controlled by the electrostatic interaction, ε_{es}, between the two reaction centers in the substrate and electrophile. In this case, the reactivity of N is lower than C_β despite the greater negative charge, q, on N. The reason for this inconsistency could be due to a net lower negative charge density, $q_{net} = -0.02$, when the highly acidic hydrogen ($q = +0.20$) attached to the N atom is included in the net charge of the N-moiety. This will naturally leads to a lower

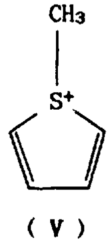
Table 3. Positional Activation Energy Barrier (ΔH^{*}), Heavy Atom Charge Density (q) and HOMO-LUMO Energy Gaps($\Delta\varepsilon_{FMO}$) of Thiophene

Position	ΔH^{*a}	q^{b}	$\Delta\varepsilon_{FMO}{}^{c}$	$\Delta H_R{}^{d}$
S	20.2	+0.31	4.69	−25.2
C_α	27.2	−0.26(+0.10)^e	4.86	−38.7
C_β	29.7	−0.08(+0.08)	4.86	−31.5

^{a} $\Delta H^{*} = \Delta H_f$ (TS) − [ΔH_f(thiophene) + ΔH_f (dimethylfluoronium ion)] in kcal/mol. ^{b} Charge densities of heavy atoms are in electronic charge unit. ^{c} $\Delta\varepsilon_{FMO}$ = LUMO (dimethylfluoronium ion) − HOMO (thiophene) in eV. ^{d} $\Delta H_R = \Delta H_f$ (Product complex) − [ΔH_f (thiophene) + ΔH_f(dimethylfluoronium ion)] in kcal/mol. ^{e} Parenthesis is a charge of the attached hydrogen atom.

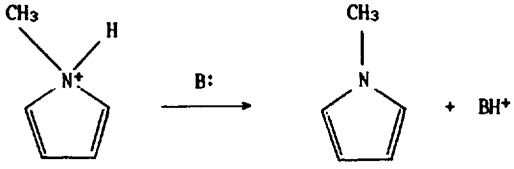
ε_{es} for N and hence the lower reactivity of N compared to C_β. This rationalization will reconcile the calculated site selectivity with that of the gas-phase experiment,[6a] N : C_α : C_β = 35 : 15 : 50. The TS geometries for the methylation of pyrrole are shown in Figure 1.

Methylation of Thiophene. The ΔH^{*} values in Table 3 indicates that the site selectivity for the methylation of thiophene with $CH_3FCH_3(+)$ is in the order S>C_α>C_β. The major factor determining the reactivity for C_α and C_β is similar to that for furan and pyrrole *i.e.,* the relative reactivity between the two position is determined by the negative charge, q. We note that the S atom has a greater site selectivity than C_α and C_β notwithstanding the positive charge on S. Since S is a third row element, it has a greater size as well as a greater polarizability compared to the second row elements of C, N and O. In general the S_N2 reactivity is greater for such reaction center as S with a greater polarizability, so that the greatest site selectivity predicted by our calculation seems reasonable. The site selectivity with respect to C_α and C_β is in good agreement with those of the gas-phase experiment, S : C_α : C_β = 19 : 43 : 38. However, discrepancy is noted in the relative site selectivity of the S-methylated species, V.[13] The situation is similar to the O-methylated species IV in the methylation of furan: species V can not be detected directly due to its instability under the experimental condition, and the species either transforms to α- or β-methylated species or isomerizes to other products in succeeding rapid processes.



(V)

In contrast to the two heteroatom methylated species, IV and V, the N-methylated intermediate, VI, in the case of pyrrole can form the neutral N-methylated pyrrole, VII, by a neutralization process, Eq. (2), so that no methyl transfer or isomerization is likely to take place. This makes the methylation process of pyrrole on N quite different one from those of furan and thiophene on O and S respectively.



(VI) (VII) (2)

Comparison of the Reactivity of the Three Heteroaromatics. The relative reactivity for methylation of the three heteroaromatics with the $CH_3FCH_3(+)$ ion based on the ΔH^{*} values in Tables 1-3 differs depending on which site we are comparing; the reactivity decreases in the order, pyrrole>thiophene>furan, pyrrole>furan>thiophene and thiophene>furan>pyrrole for the C_α, C_β and heteroatom positions respectively. Furthermore, the ΔH^{*} values range 20-30 kcal/mol with little difference between the substrates, *ca.* 4-7 kcal/mol. Thus it is most likely that the reactivity of the three heteroaromatics is in reality approximately equal, as has been concluded in the gas-phase experiment.[6,14]

We can summarize our results as: In the methylation of the three heteroaromatics with $CH_3FCH_3(+)$, (i) the site selectivity is controlled by electrostatic interaction, (ii) the methylation on different sites proceed competitively since the activation barriers, ΔH^{*}, for the three sites do not differ greatly, and (iii) the reactivities of the three heteroaromatics are approximately equal.

Acknowledgement. We thank the Ministry of Education and the Korea Science and Engineering Foundation for support of this work.

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Passive Film on Cobalt: A Three-Parameter Ellipsometry Study During the Film Formation

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Thin film being formed on the surface of cobalt in the early stage of electrochemically induced passivation was studied by the three-parameter ellipsometry. The growth of the passive film was complete in a few seconds from the onset of the passivating potential, and was followed by a slight decrease in the thickness in 4-40 seconds. The optical constants of the passive film changed gradually during the changes in the thickness. The thickness and the optical properties at the steady state of passivation depended on the potential of the electrode. From the coulometric data and the optical properties, the composition of the passive films was deduced to be close to those of CoO, Co_3O_4, and Co_2O_3 depending on the potential. Cathodic reduction in the presence of EDTA was found to be an efficient way to obtain film-free reference surface of cobalt.

Introduction

Surface films formed with passivation of cobalt have been studied by spectroscopic methods,[1,2] electrochemical measurements,[3] the conventional (two-parameter) ellipsometry combined with electrochemical methods,[4–7] and briefly by the three-parameter ellipsometry.[8] The three-parameter ellipsometry has also been used to study surface films on various metals in number of laboratories.[8–15] The method, also called combined ellipsometry-reflectance technique because reflectance change is measured in addition to the usual Δ and Ψ measurements of ellipsometry, proved to be particularly useful for monitoring the changes in passivating layers on iron and nickel electrodes in early stages of the layer formation.[16–18] The earlier study on cobalt using the three-parameter ellipsometry method for the first time[8,14] was mainly to test the feasibility of applying the method for determining the thickness and optical properties of thin films having complex refractive indices, and the method has not been applied to its full advantage for the study of passivation of cobalt.

The present study was conducted in order to study passive film on cobalt, particularly the nature of the passive film during its formation stages, by auto-recording three-parameter ellipsometry. The variations of the optical properties and the thickness of the passive films being formed on cobalt surface were determined in 0.1s to 100s after the potential of the cobalt electrode was stepped to a passivating potential. The optical and electrochemical measurements were made simultaneously to deduce the approximate composition and properties of the passive film. The results are presented here.

Experimental

Materials. Cobalt electrodes were prepared by vacuum deposition of thermally evaporated 99.99% cobalt on glass slides to approximately 1 μm thickness. A thin layer of chromium was first deposited on the glass slide before the cobalt deposition to make the cobalt film more adhering. A buffer solution of 0.08 *M* sodium borate−0.35 *M* boric acid, pH 8.65, was used as the electrolyte solution. The solutions were prepared from reagent grade chemicals and doubly distilled water of specific resistivity greater than 10 M ohm-cm. To remove the fine particles suspended in the prepared solution, which scatter the laser light of the ellipsometer and hence cause noises in the optical measurements, a membrane filter of 0.45 μm pore size (Millipore HAWP-04700) was used prior to the transfer of the solutions into the cell.

Equipment and Measurements. An automatic ellipsometer built in this laboratory was used in the present study. The ellipsometer is equipped with a He-Ne laser of 632.8 nm wavelength as the light source and is capable of recording the reflectance (*R*) change as well as the changes in the usual ellipsometry measurements Δ and ψ as described previously.[16,18] The cobalt electrode was mounted in an electrochemical-optical cell. The cell had a Pt counter elec-

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