Mass Spectroscopical Properties of Benzoyl Derivatives of Five-membered Monoheterocycles and Determination of Aromaticity Indices

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The mass spectra of benzophenones, 2-benzoylthiophenes, 2-benzoylpyrroles, and 2-benzoylfurans which have substituents at the *m*- and *p*-positions of the benzoyl ring were analyzed to find correlations against the Hammett substituent parameter σ and σ^+. The slopes of the plots of the intensities of the fragments from the heterocycles against those of the benzene gave sets of meaningful values for the indices of aromaticity of the heterocycles: benzene 1.00; thiophene 0.94, pyrrole 0.82, and furan 0.74.

Key Words : Heterocycles, Aromaticity indices, Hammett equation, Mass spectral fragments

Introduction

One of the criteria for classification of heterocyclic compounds is the aromaticity. For example, five-membered monoheterocyclic compounds such as thiophene, pyrrole, and furan are considered aromatic because they are cyclic planar molecule with 6π electrons in the ring, satisfying the rule of $(4n + 2)$ π electrons.[1] Quantitative estimation of the degree of aromaticity of the heterocyclic compounds has been of interest to theoretical chemists as well as physical organic chemists because such compounds are the structural parts of many naturally occurring and biologically active compounds.

Because the term aromaticity was first coined to characterize the unique chemical and physical properties of benzene, it has been a customary practice to compare any specific property of a heterocycle to that of benzene. For example, comparison of the ring currents measured by the chemical shift of the protons led to a set of aromaticity indices of 0.75, 0.59, and 0.46 for thiophene, pyrrole, and furan, respectively, by setting that of benzene 1.[2] Consideration of bond length and the number of π electrons in the ring gave a different set of the indices: benzene 1, thiophene 0.93, pyrrole 0.91, and furan 0.87.[3] There are a number of different sets of the indices reported in the literature.[1]

We have reported methods for estimating the aromaticity indices by comparing the chemical shifts of ^1H and ^{13}C of five-membered monoheterocyclic compounds (*eg.*, 2-4) to those of structurally related derivatives of benzene (*eg.*, 1).[4] The chemical shift of the aromatic compound is related to the ring current. Therefore, the chemical shift of a proton or carbon in a substituted compound (δ) should be linearly related to that in an unsubstituted one (δ_o), as shown in Eq. (1), which represents single substituent parameter treatment.[5]

$$\delta = \rho\sigma + \delta_o \qquad (1)$$

Since the substituent parameter reflects the electronic

nature of that substituent, it is conceivable that the intensity of a fragment may be affected by the substituent. This notion led us to examine the possibility of correlating the intensities of the fragments originated from the benzoyl ketones of five-membered monoheterocyclic compounds (2-4) to the Hammett parameters. Here we report the results and a new sets of indices of aromaticity derived from such correlation.

Results and Discussions

The probe of a mass spectrometer is considered as a test tube or a flask in which a reaction takes place. The molecular ion and the fragment ions derived from a molecule are like species that follow the general principles of organic reactions. In this regard the intensity of the base fragment peaks in the spectra of aromatic compounds can be correlated with Hammett σ values.[6,7] However, it should be pointed out that the Hammett σ values were originated from the classical studies of equilibrium and rates in solution reactions. Despite this limitation, attempts were made to correlate the mass spectral data with the Hammett σ constants. For example, McLafferty *et al.* reported excellent correlation of the benzoylium ion intensity in the mass spectra of substituted benzophenones (**1**) with the Hammett σ constants.[8] They also observed correlation of the acetylium ion intensity in the mass spectra of substituted acetophenones
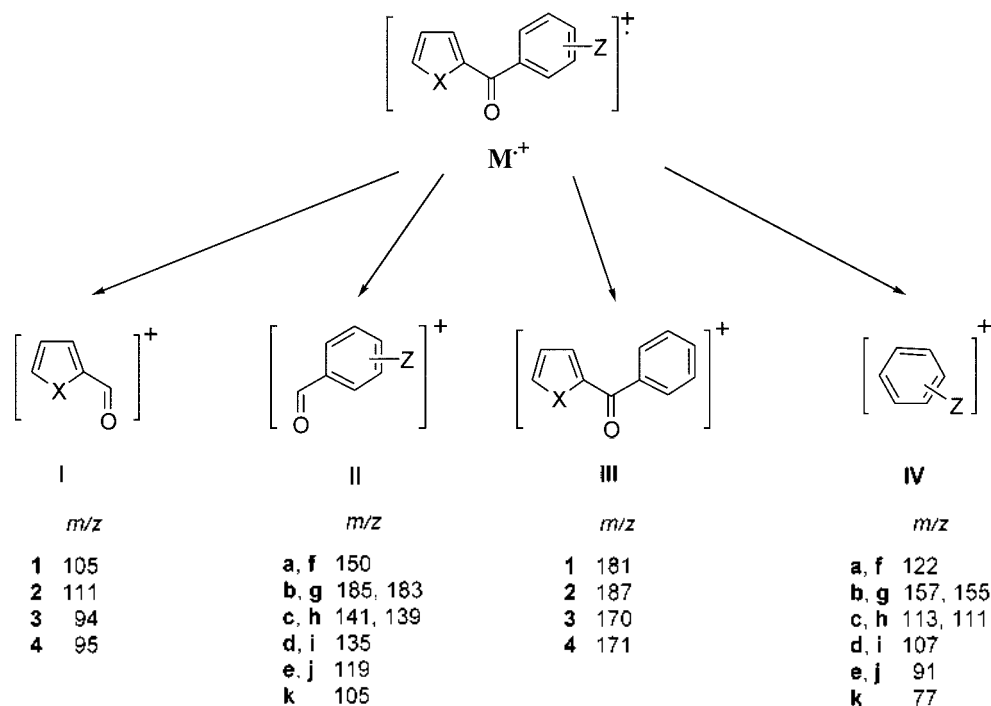

1   2

3   4
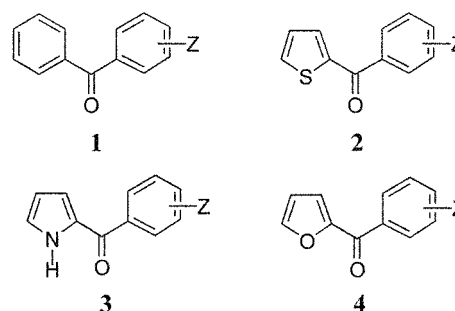
Z: **a**, *m*-NO$_2$; **b**, *m*-Br; **c**, *m*-Cl; **d**, *m*-OCH$_3$; **e**, *m*-CH$_3$;

f, *p*-NO$_2$; **g**, *p*-Br; **h**, *p*-Cl; **i**, *p*-OCH$_3$; **j**, *p*-CH$_3$; **k**, H

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Table 1. Relative Intensities (%) of the fragments of 1–4 in their low-resolution mass spectra

	M⁻	I	II	III	IV		M⁻	I	II	III	IV
1a	39.0	100.0	16.2	0.0	1.0	**2a**	51.2	100.0	6.0	2.3	0.6
1b	63.2	100.0	34.3	9.8	19.4	**2b**	71.0	100.0	14.9	14.5	15.5
1c	62.4	100.0	33.2	7.3	24.1	**2c**	59.4	100.0	21.9	11.9	56.1
1d	100.0	77.0	82.3	11.7	19.6	**2d**	71.9	100.0	30.0	16.2	14.7
1e	84.0	58.7	100.0	14.7	38.6	**2e**	93.8	100.0	58.6	29.1	40.3
1f	44.2	100.0	15.5	3.1	0.0	**2f**	78.8	100.0	7.3	4.2	0.5
1g	101.7	100.0	92.5	23.1	32.8	**2g**	74.4	100.0	33.7	22.9	20.4
1h	99.2	100.0	92.5	16.8	43.3	**2h**	119.6	100.0	68.7	26.4	58.0
1i	54.5	15.2	100.0	3.5	6.5	**2i**	76.4	35.8	100.0	14.9	11.3
1j	65.4	32.0	100.0	11.8	28.7	**2j**	100	81.2	93.7	34.0	41.3
1k	153.9	100.0	100.0	9.5	78.4	**2k**	72.5	100.0	35.7	9.7	37.5
3a	83.5	100.0	6.8	17.0	0.0	**4a**	100.0	100.0	48.5	6.1	2.0
3b	113.5	100.0	7.2	6.3	1.7	**4b**	116.3	73.7	200.0	21.0	37.9
3c	102.2	100.0	11.8	46.3	17.9	**4c**	15.1	11.3	132.5	3.6	39.0
3d	100.0	49.0	12.4	23.4	3.4	**4d**	18.0	8.7	100.0	2.1	25.4
3e	100.0	58.1	11.7	44.5	19.5	**4e**	73.4	24.1	100.0	10.6	48.0
3f	83.8	100.0	2.2	13.5	0.3	**4f**	100.0	84.6	43.2	5.7	4.8
3g	128.4	100.0	16.2	58.5	3.9	**4g**	106.3	42.8	197.7	11.7	29.6
3h	111.6	100.0	24.4	57.7	30.7	**4h**	107.7	68.7	132.7	13.8	47.0
3i	100.0	37.0	47.5	36.2	6.2	**4i**	41.1	7.1	100.0	1.9	43.0
3j	100.0	55.2	21.7	69.4	26.1	**4j**	13.9	6.7	100.0	3.6	43.0
3k	100.0	85.7	18.4	40.7	26.5	**4k**	41.8	18.6	100.0	6.1	55.2

Scheme 1

	I		II		III		IV
	m/z		*m/z*		*m/z*		*m/z*
1	105	**a, f**	150	**1**	181	**a, f**	122
2	111	**b, g**	185, 183	**2**	187	**b, g**	157, 155
3	94	**c, h**	141, 139	**3**	170	**c, h**	113, 111
4	95	**d, i**	135	**4**	171	**d, i**	107
		e, j	119			**e, j**	91
		k	105			**k**	77

with the σ constants. Furthermore, the two sets of mass spectral intensities are correlated with one other by the following equation:

$$\text{Log } (Z/Z_o)_{R=Me} = 0.782 \log (Z/Z_o)_{R=Ph} + 0.007 \qquad (2)$$

where $Z=[RCO^-]/[YC_6H_4COR^+]$ and $Z_o= [RCO^+]/[C_6H_5COR^+]$.

We obtained the low resolution mass spectra for the

substituted (*m*- and *p*-NO₂, Br, Cl, OCH₃, CH₃, H) benzoyl derivatives of benzene (benzophenone, **1**), thiophene (**2**), pyrrole (**3**), and furan (**4**). The results are listed in Table 1.

Besides the molecular ion M⁻, the fragment ions are the results of the unimolecular ion decomposition illustrated in Scheme 1. The molecular ions of the bromo (**b** and **g**) and the chloro (**c** and **h**) compounds were calculated by adding

the intensities of M^+ and $M^- + 2$ ions. Similarly, the intensities of the fragment ions having the halogen atoms were calculated by adding the intensities of the isotope peaks.

As shown in Table 1, the benzoylium (1-I) and the 2-thienoylium (2-I) ions are relatively more abundant than the molecular ions in general. But the trend is the opposite in the 2-pyrroloyl compounds favoring the molecular ions over 2-pyrroloylium ions (3-I). On the other hand, the substituted benzoylium ions (II) seem to be the most stable ions in the 2-furoyl series (4) with the exceptions of *m*- and *p*-nitro derivatives (4a and 4f). The electron-withdrawing nitro group should destabilize the benzoylium ions IIa and IIf. In contrast to the destabilizing effect of the nitro group, the *p*-methoxy group should stabilize the benzoylium ion. Indeed IIi is the base peak in the cases 1i, 2i, and 4i. For 3i the base peak is M^-, but the *p*-methoxybenzoylium ion is favored over 2-pyrroloylium ion by a ratio of 47.5 : 37.0.

The relative ratio of the aroylium ion (I) to benzoylium ion (II) may be considered as an indicator of the relative stability of the ions in the case of unsubstituted aroyl ketones (1k, 2k, 3k, and 4k). The tendency for cleavage of the acyl-carbon bonds (i or ii) can be summarized as follows:

	X	(i)	(ii)
1	HC=CH	1	1
2	S	1	2.72
3	N-H	1	4.66
4	O	1	0.19
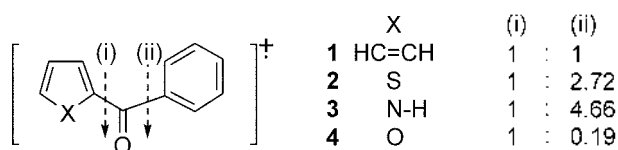
It is not surprising that the 2-pyrroloylium ion is the most stable because of the favorable resonance contribution as follows:

favorable

unfavorable
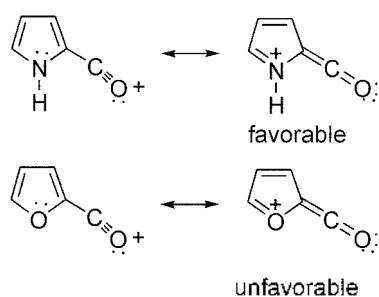
A similar kind of conjugation with the 2-furoylium ion contributes less because of the greater electronegative effect
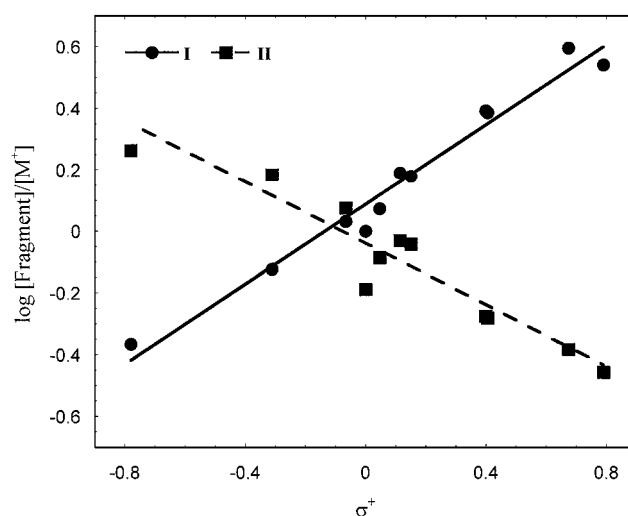

Figure 1. Correlation of the intensities of the benzoyl (I) and substituted benzoyl (II) ions in the mass spectra of substituted benzophenones (1) with σ^+ constants. The slopes are: 0.82 (r = 0.965) for I; −0.63 (r = 0.928) for II.

of the O atom. Furthermore, the C–O double bond in the furan ring is less likely to form than C–N double bond in pyrrole ring. A sulfur atom has little electron-donating ability through conjugation, but it is also much less electronegative than O or N atom. Yet the S atom has d orbitals where it can delocalize the positive charge. Therefore, 2-thienoylium ion formation seems to be preferable to the formation of benzoylium ion.

Fragmentation processes are considered as a set of competing consecutive unimolecular decompositions, and therefore, the relative intensity of a fragment ion should be related to the rate constant for the formation of the ion. The Hammett equation which reflects the linear free energy relationship may be rewritten as Eq. (3) to correlate the mass spectral intensity with the substituent constant σ.

$$\log [\text{fragment}]/[M^+] = \rho\sigma + \log [\text{fragment}]_o/[M^-]_o \quad (3)$$

where $[M^+]$ is the intensity of the molecular ion of a substituted ketone and $[M^+]_o$ is that of an unsubstituted ketone. Likewise, [fragment] and [fragment]$_o$ are the intensities of fragment ions derived from the molecular ion of the substituted and unsubstituted ketones, respectively. Figure 1 shows a plot according to Eq. (3) with the substituted benzophenes (1). Here, σ^+ was used instead of σ to show a better correlation.

Table 2 list the slopes (*ρ*) and correlation coefficients (r)

Table 2. Slopes and correlation coefficients (in Parenthesis) of the plots of log [Fragment] against σ and σ^- of Benzophenones (1), 2-Benzoylthiophenes (2), 2-Benzoylpyrroles (3), and 2-Benzoylfurans (4)
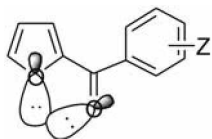
	[ArC=O⁺]/[M⁻]		[Z-C₆H₄C=O⁻]/[M⁻]		[ArC=O⁺]/[Z-C₆H₄C=O⁺]	
	σ	σ^+	σ	σ^+	σ	σ^+
1	0.82 (0.965)	0.65 (0.985)	−0.63 (0.928)	−0.50 (0.944)	−1.45 (0.968)	−1.15 (0.986)
2	0.35 (0.692)	0.32 (0.825)	−0.99 (0.960)	−0.76 (0.948)	−1.34 (0.927)	−1.08 (0.965)
3	0.42 (0.879)	0.34 (0.910)	−0.76 (0.812)	−0.64 (0.881)	−1.19 (0.901)	−0.98 (0.962)
4	0.55 (0.868)	0.44 (0.903)	−0.68 (0.545)	−0.46 (0.578)	−1.23 (0.800)	−0.91 (0.860)

obtained from the plots of log [fragment]/[M⁻] *vs.* σ and σ^+ values. like Figure 1.

The fragments **III** were excluded not only because their intensities were small and there was no apparent correlation but the process to form **III** from M⁺ should be irrelevant to the present discussion. The breaking of the C-Z bond seems to be more related to the nature of Z than to the nature of the heterocycles.

The fragment **IV** also did not show any correlation with either σ or σ^-. The stability of the substituted phenyl cation is known to be affected by not only electronic effect of Z but other factors. such as conjugation in the case of methyl group.[9]

There are several observations worth mentioning in Table 2. First of all. the correlation. in general. is fairly good for the benzenes but it becomes poorer in the order of benzene > thiophene > pyrrole > furan. As mentioned earlier the molecular ions of furyl ketones are not stable. They undergo decomposition. The instability may be due to $O,O\text{-}syn$ conformation in which the lone pair orbitals on the two O atoms repel each other.[10] Such interaction should facilitate C-acyl bond cleavage and therefore. the electronic effect of the substituent in **4** should not be as significant as it is in other series **1-3**.

Secondly. the correlations with σ^+ are better than those with σ. McLafferty *et al.* reported a correlation of the mass fragment ion abundance with σ^+ for the substituted 1.2-
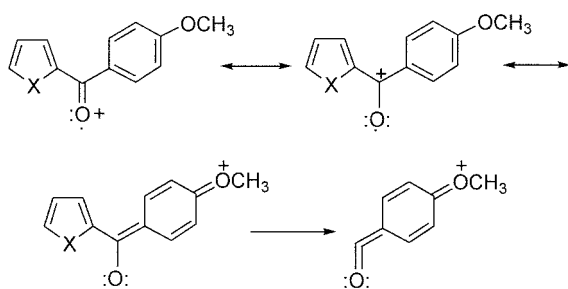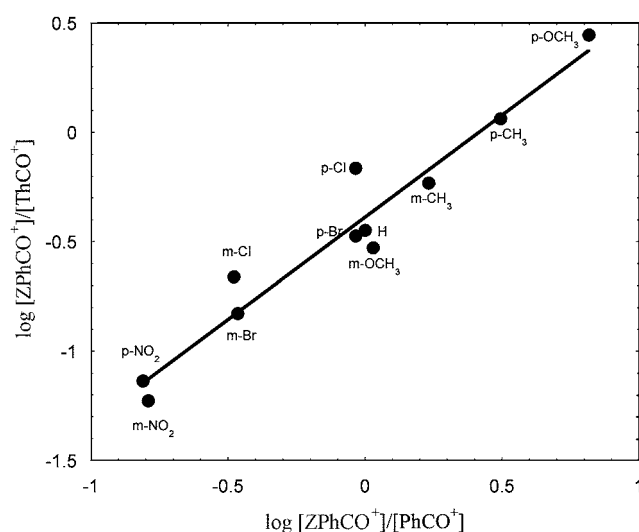
Figure 2. Linear free-energy relationship between the benzoyl ion intensity in substituted benzophenones (1) and the 2-thienoyl ion intensity in substituted benzoylthiophene (2). The slope is 0.93 with a correlation coefficient r = 0.969.

diphenylethanes. Y-C₆H₄CH₂CH₂C₆H₅.[11] This seems reasonable considering that the σ^- values are usually employed for a reaction where a partial positive is building up in the transition state. However. formation of molecular ion of any carbonyl compound is believed to be a result of the loss of one electron from the lone pair orbitals of O atom. Apparently. the electron-donating Z stabilizes not only M⁺ but also $^-O{=}C\text{-}C_6H_4\text{-}Z$ (**II**) by conjugation. This may be the reason that σ^- gives better correlation.

Thirdly. the slopes of log [Ar-C≡O⁻]/[M⁻] are positive while those of log [Z-C₆H₄C≡O⁺]/[M⁻] are negative. This means that the electron-donating substituents favor the bond cleavage of (i).

In order to determine the aromaticity indices of the heterocycles log [fragment] of each series of the heterocycle (**2-4**) was plotted against those of the series of the benzene (**1**). A representative plot is shown in Figure 2. and the results are listed in Table 3. The slopes of the plots are increasing in the order of thiophene < pyrrole < furan when the aroylium intensities are considered. As expected. the slopes are decreasing in the order of thiophene > pyrrole > furan for the substituted benzoylium ion values. The average

Table 3. Slopes and correlation coefficients of the plots of log [ArC=O⁻]/[Z-C₆H₄C=O⁻] of the 2-Benzoylthiophenes (2), 2-Benzoylpyrroles (3), and 2-Benzoylfurans (4) *vs.* Those of the Benzophenones (1)

	2			3			4		
	ρ	r	sd	ρ	r	sd	ρ	r	sd
[ArC=O⁺]/[M⁺]	0.47	0.797	0.11	0.51	0.906	0.12	0.69	0.905	0.09
[Z-C₆H₄C=O⁺]/[M⁻]	1.43	0.945	0.12	1.12	0.808	0.18	0.76	0.518	0.38
Average	0.95			0.82			0.72		
[ArC=O⁺]/[Z-C₆H₄C=O⁻]	0.93	0.969	0.12	0.82	0.933	0.16	0.76	0.844	0.35
Overall Average	0.94			0.82			0.74		

sd: standard deviation

Kyu Ok Jeon et al.

values of the slopes are 0.95, 0.82, and 0.72 for thiophene, pyrrole, and furan, respectively. On the other hand, the plots of log [aroylium]/[benzoylium] (cf. Figure 3) show the slopes of 0.93 (s.d. 0.12), 0.82 (s.d. 0.16), and 0.76 (s.d. 0.35) for thiophene, pyrrole, and furan, respectively. Although the standard deviation (s.d.) for for the furan series is much larger than those for the thiophene and the pyrrole the values are reasonable as indices of aromaticity.

In conclusion, we were able to determine the indices of aromaticity of five-membered monoheterocyclic compounds by mass spectral fragment ion intensities of a series of *m*- and *p*-substituted benzoyl derivatives. It was possible because the fragmentation process is a unimolecular decomposition of the molecular ion. Consequently, the rate of such process should follow the linear free energy relationship. The calculated average values of the indices are: benzene 1.00; thiophene 0.94, pyrrole 0.82, and furan 0.74.

Experimental Section

Preparations of the benzoyl ketones **1-4** were described previously.[4d] Mass spectra were obtained using a Micromass Autospec M363 in the Central Lab of Kangwon National University. The ionization conditions were at 60 °C and 70 eV.

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