**HETEROCYCLES, Vol. 60, No. 12, 2003, pp. 2685 - 2705**
**Received, 15th August, 2003, Accepted, 26th September, 2003, Published online, 30th September, 2003**

# NUCLEAR MAGNETIC RESONANCE SPECTROSCOPICAL STUDIES OF 2-CARBONYL DERIVATIVES OF FIVE-MEMBERED MONOHETERO-CYCLES AND DETERMINATION OF AROMATICITY INDICES

Kyu Ok Jeon, Ji Sook Yu, and Chang Kiu Lee*

Department of Chemistry, Kangwon National University, Chuncheon 200-701, S. Korea

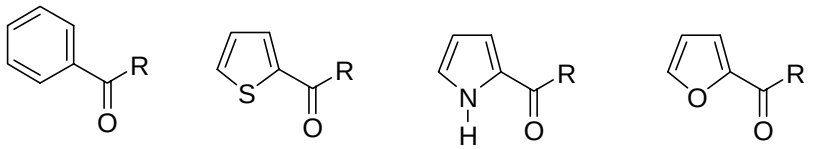
E-mail: cklee410@kangwon.ac.kr

**Abstract**- $^{1}H$ And $^{13}C$ chemical shifts of formyl, acetyl, benzoyl, and methoxycarbonyl derivatives of benzene, thiophene, pyrrole and furan in chloroform-*d*, methanol-$d_4$, and DMSO-$d_6$ are examined. Deviation of the signals of the ring protons and carbonyl carbons provide bases for estimating the indices of aromaticity of the heterocycles. The exceptionally large carbonyl stretching vibration of furan derivatives and correlations of the stretching frequencies with the reactivities of the carbonyl groups are discussed.

## INTRODUCTION

Ring current is one of the bases for determining the aromaticity of heterocyclic compounds.[1,2] For five-membered monoheterocyclic compounds the chemical shifts of α-H are in downfield than those of β-H. The difference in chemical shift of α-H and β-H is considered to be related to the index of aromaticities. In the course of our study on the aromaticities of five-membered heterocycles using NMR spectroscopy, we observed the order of chemical shifts of 3-H and 5-H of 2-thiophenecarboxylate esters (**2**, R = $OC_6H_4$-Z) were reversed from chloroform-*d* to DMSO-$d_6$.[3] For example, the signals of 3-H and 5-H of phenyl 2-thiophenecarboxylate (**2**, R = $OC_6H_5$) appear at δ 7.98 and 7.66 in chloroform-*d*, respectively,

showing the downfield shift of the signal of 3-H compared to that of 5-H. In DMSO- $d_6$, however, the signal of 5-H (δ 8.10) appears more down field than that of 3-H (δ 8.03). The assignment was based on the characteristic coupling constants of $J_{3,4}$ (3.8-3.9 Hz) and $J_{4,5}$ (4.9-5.0 Hz).[4] $^{13}$C signals of the same compound also show similar trends: 3-C at 134.66 ppm (down) and 5-C at 133.46 ppm (up) in chloroform-*d* whereas 3-C at 135.66 ppm (up) and 5-C at 135.79 ppm (down) in DMSO-$d_6$.[3] The assignments were based on their $^1$H-$^{13}$C HETCOR spectra.




**1** **2** **3** **4**

R: **a**, H; **b**, $CH_3$; **c**: $C_6H_5$; **d**, $OCH_3$

The reversal in the chemical shifts of $^{13}$C signals of thiophene derivatives has been reported in the literatures.[5,6] For example, the orders of 3-C and 5-C are opposite in the aldehyde (**2a**) and the methyl ketone (**2b**). They are 137.7 and 135.2 ppm for **2a**[5] in $CHFCl_2$-$CCl_2F_2$ and 132.5 and 133.8 ppm for **2b**,[6] respectively, in the same solvent. There are other reports of same or very close values of chemical shifts for **2b** in chloroform-*d*.[7] Apparently, the change in the order of appearance of **2a** and **2b** is not due to the effect of temperature or solvent. Furthermore, the preferred *syn* conformation was more than 97% even at –100 $^o$C.[6] Therefore, the assignments for the chemical shifts seem to deserve reexamination. In addition, such examination may provide information on the aromaticity of the heterocycles.

## RESULTS AND DISCUSSION

First, we examined the trends in chemical shifts of benzene, thiophene, pyrrole and furan in chloroform-*d*, DMSO-$d_6$, and methanol-$d_4$ at 0.1 M in order to clarify the solvent effect on the heterocyclic rings. The results are summarized in Table 1. Chloroform-*d* was chosen not only because it is the most commonly used solvent for NMR experiment but because it also has a rather small dielectric constant (ε

4.8).[8] DMSO, on the other hand, is the most polar organic solvent (ε 47). Methanol (ε 32.7) has about medium polarity as well as hydrogen bonding ability.

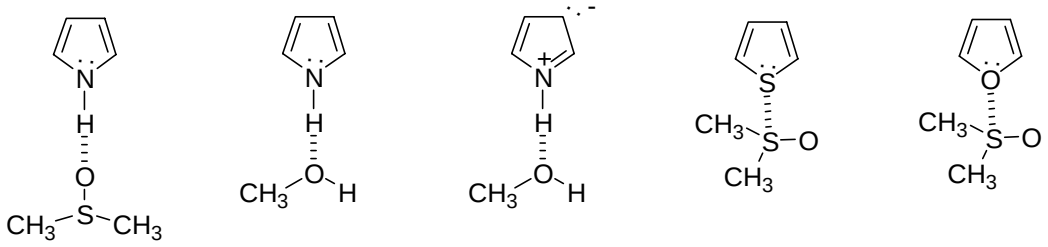
**Table 1.** Chemical Shift Values of 0.1 M Solutions of Benzene, Thiophene, Pyrrole, and Furan in Various Solvents

| | | *α*-H | *β*-H | Δ(α-β) | *α*-C | *β*-C | Δ(α-β) |
|---|---|---|---|---|---|---|---|
| Benzene | $CDCl_3$ | 7.36 | 7.36 | 0 | 128.33 | 128.33 | 0 |
| | DMSO-$d_6$ | 7.37 | 7.37 | 0 | 128.80 | 128.80 | 0 |
| | $CD_3OD$ | 7.32 | 7.32 | 0 | 127.35 | 127.35 | 0 |
| Thiophene | $CDCl_3$ | 7.35 | 7.13 | 0.22 | 125.11 | 126.86 | -1.75 |
| | DMSO-$d_6$ | 7.57 | 7.15 | 0.42 | 126.20 | 127.56 | -1.36 |
| | $CD_3OD$ | 7.40 | 7.11 | 0.29 | 124.96 | 126.78 | -1.82 |
| Pyrrole | $CDCl_3$ | 6.82 | 6.26 | 0.56 | 117.68 | 108.19 | 9.49 |
| | DMSO-$d_6$ | 6.73 | 6.02 | 0.71 | 117.68 | 107.43 | 10.25 |
| | $CD_3OD$ | 6.72 | 6.07 | 0.65 | 118.31 | 108.15 | 10.16 |
| Furan | $CDCl_3$ | 7.45 | 6.39 | 1.06 | 142.52 | 109.44 | 33.08 |
| | DMSO-$d_6$ | 7.67 | 6.48 | 1.19 | 143.37 | 110.17 | 33.20 |
| | $CD_3OD$ | 7.49 | 6.40 | 1.09 | 143.79 | 110.40 | 33.39 |

As shown in Table 1, the effect of solvent on the $^1H$ shift of benzene is almost minimal as it changes from chloroform to DMSO (Δδ 0.01 ppm) or to methanol (Δδ -0.04 ppm). However, the effects are significant on α-Hs of thiophene and furan by changing from chloroform to DMSO-$d_6$ (Δδ 0.22 ppm for both). But the effect of such change is insignificant on β-Hs (Δδ 0.02 ppm in DMSO-$d_6$ and 0.09 ppm in methanol-$d_4$).

In contrast, the signals of protons in pyrrole are shifted upfield by 0.09 and 0.24 ppm for α- and β-H,

respectively, in DMSO-$d_6$. It should be pointed out that the signals of α-H of thiophene and furan are shifted more downfield than those of β-H by the polar solvent whereas the opposite is the case with pyrrole. The upfield shifts of the signals of pyrrolic-Hs in DMSO-$d_6$ and methanol-$d_4$ may be due to the hydrogen bonding like **I** or **II**.



**I** **II** **III** **IV** **V**

Such hydrogen bonding should enhance the electron density around β-C and β-H like **III**. With thiophene and furan on the other hand, complexations like **IV** and **V** should cause a partial positive charge in the ring, and the closest α-C and α-H should be more influenced than β-C and β-H.

As mentioned in the introduction section the order of the 3-H and 5-H shifts of phenyl 2-thiophenecarboxylate changes from chloroform to DMSO. Although the spectra of the phenyl ester had not been reported prior to our report[3] the methyl ester (**2d**) was reported in the literature. For example, Satonaka reported a set of values for the compound: δ 7.80 (3-H), 7.10 (4-H), 7.55 (5-H) and 3.89 ($COOCH_3$) with $J_{3,4}$ = 3.70, $J_{3,5}$ = 1.30, and $J_{4,5}$ = 5.00 Hz in 0.3 M-chloroform-*d*.[4] The $^{13}C$ shifts of the compound was reported by Hearn: 136.0 (2-C), 132.7 (3-C), 128.1 (4-C), 135.0 (5-C), 162.5 (CO), and 52.1 ($CH_3$) in the same solvent as 20-25% (w/v) solution.[9] Therefore, we reexamined the NMR spectra of derivatives of benzene, thiophene, pyrrole and furan, including methyl 2-thiophenecarboxylate (**2d**), in chloroform-*d*, DMSO-$d_6$, and methanol-$d_4$ at 0.1 M. The results are listed in Tables 2 and 3 for protons and carbons, respectively.

As shown in Table 2, the proton chemical shift values of **2d** are almost same to those in the literature[9] despite the difference in concentration of 0.1 M in our study and 0.3 M in the literature in chloroform-*d*. The chemical shift of the 3-H is not influenced by changing the solvents (δ 7.80-7.82) as shown in Figure 1. On the other hand, 4-H signals shift noticeably (δ 7.10-7.23). The effect of the solvent is

quite remarkable on the signals of 5-H (δ 7.55-7.96).

**Table 2.** $^{1}$H Chemical Shift Values of Formyl (**a**), Acetyl (**b**), Benzoyl (**c**), and Methoxycarbonyl (**d**) Derivatives (**1**-**4**) in Various Solvents (0.1 M)

| | | *o*-H | *m*-H | *p*-H | R | $J_{3,4}$ | $J_{3,5}$ | $J_{4,5}$ |
|---|---|---|---|---|---|---|---|---|
| **1a** | $CDCl_3$ | 7.89 | 7.54 | 7.64 | 10.03 | 7.69 | 2.05 | 7.37 |
| **1a** | DMSO-$d_6$ | 7.92 | 7.62 | 7.73 | 10.03 | 7.70 | 1.89 | 7.35 |
| **1a** | $CD_3OD$ | 7.91 | 7.57 | 7.68 | 9.99 | 7.77 | 2.00 | 7.33 |
| **2a** | $CDCl_3$ | 7.79 | 7.22 | 7.77 | 9.95 | 3.86 | 1.17 | 4.87 |
| **2a** | DMSO-$d_6$ | 8.04 | 7.34 | 8.15 | 9.96 | 3.63 | 0.83 | 4.98 |
| **2a** | $CD_3OD$ | 7.93 | 7.28 | 7.96 | 9.91 | 3.78 | 1.15 | 4.90 |
| **3a**[a] | $CDCl_3$ | 7.00 | 6.36 | 7.16 | 9.53 | 3.74 | 1.55 | 2.67 |
| **3a**[b] | DMSO-$d_6$ | 7.00 | 6.28 | 7.22 | 9.48 | 3.60 | 1.46 | 2.50 |
| **3a** | $CD_3OD$ | 7.02 | 6.31 | 7.17 | 9.43 | 3.80 | 1.34 | 2.40 |
| **4a** | $CDCl_3$ | 7.26 | 6.68 | 7.70 | 9.68 | 3.55 | 0.92 | 1.64 |
| **4a** | DMSO-$d_6$ | 7.55 | 6.79 | 8.11 | 9.62 | 3.56 | 1.23 | 1.62 |
| **4a** | $CD_3OD$ | 7.42 | 6.70 | 7.88 | 9.60 | 3.54 | 1.03 | 1.56 |
| **1b** | $CDCl_3$ | 7.96 | 7.47 | 7.57 | 2.61 | 7.86 | 1.49 | 7.28 |
| **1b** | DMSO-$d_6$ | 7.96 | 7.53 | 7.64 | 2.59 | 7.70 | 1.50 | 7.36 |
| **1b** | $CD_3OD$ | 7.97 | 7.53 | 7.64 | 2.59 | 7.73 | 1.54 | 7.36 |
| **2b** | $CDCl_3$ | 7.70 | 7.13 | 7.64 | 2.57 | 3.86 | 0.76 | 4.97 |
| **2b** | DMSO-$d_6$ | 7.94 | 7.24 | 7.99 | 2.54 | 3.84 | 0.90 | 4.98 |
| **2b** | $CD_3OD$ | 7.86 | 7.19 | 7.82 | 2.56 | 3.96 | 0.97 | 4.96 |
| **3b**[c] | $CDCl_3$ | 6.92 | 6.28 | 7.04 | 2.44 | 3.45 | 1.70 | 2.59 |
| **3b**[d] | DMSO-$d_6$ | 6.96 | 6.18 | 7.06 | 2.34 | 3.30 | 1.68 | 2.81 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **3b** | $CD_3OD$ | 7.00 | 6.23 | 7.25 | 2.39 | 3.66 | 1.14 | 2.32 |
| **4b** | $CDCl_3$ | 7.18 | 6.54 | 7.59 | 2.49 | 3.51 | 1.08 | 1.61 |
| **4b** | DMSO-$d_6$ | 7.44 | 6.71 | 7.98 | 2.42 | 3.52 | 1.34 | 1.66 |
| **4b** | $CD_3OD$ | 7.34 | 6.63 | 7.77 | 2.46 | 3.55 | 2.10 | 1.59 |
| **1c** | $CDCl_3$ | 7.81 | 7.48 | 7.59 | | 7.73 | 1.47 | 7.38 |
| **1c** | DMSO-$d_6$ | 7.74 | 7.57 | 7.69 | | 7.70 | 1.40 | 7.43 |
| **1c** | $CD_3OD$ | 7.76 | 7.52 | 7.64 | | 7.64 | 1.41 | 7.37 |
| **2c** | $CDCl_3$ | 7.65 | 7.17 | 7.73 | | 3.75 | 0.95 | 5.00 |
| **2c** | DMSO-$d_6$ | 7.73 | 7.30 | 8.13 | | 3.75 | 0.92 | 4.88 |
| **2c** | $CD_3OD$ | 7.70 | 7.23 | 7.93 | | 3.78 | 0.96 | 4.94 |
| **3c** | $CDCl_3$ | 6.90 | 6.34 | 7.16 | | 3.70 | 1.13 | 2.82 |
| **3c** | DMSO-$d_6$ | 6.78 | 6.27 | 7.22 | | 3.89 | 1.01 | 2.31 |
| **3c** | $CD_3OD$ | 6.84 | 6.30 | 7.19 | | 3.80 | 1.16 | 2.32 |
| **4c** | $CDCl_3$ | 7.24 | 6.60 | 7.71 | | 3.55 | 1.20 | 1.75 |
| **4c** | DMSO-$d_6$ | 7.40 | 6.80 | 8.13 | | 3.56 | 1.36 | 1.70 |
| **4c** | $CD_3OD$ | 7.34 | 6.71 | 7.90 | | 3.65 | 1.26 | 1.72 |
| **1d** | $CDCl_3$ | 8.05 | 7.44 | 7.56 | 3.92 | 8.02 | 1.49 | 7.47 |
| **1d** | DMSO-$d_6$ | 7.97 | 7.54 | 7.67 | 3.86 | 8.51 | 1.10 | 7.63 |
| **1d** | $CD_3OD$ | 8.01 | 7.47 | 7.60 | 3.90 | 7.05 | 1.26 | 7.62 |
| **2d** | $CDCl_3$(lit.[4]) | 7.80 | 7.10 | 7.55 | 3.89 | 3.70 | 1.30 | 5.00 |
| **2d** | $CDCl_3$ | 7.81 | 7.10 | 7.55 | 3.89 | 3.87 | 1.33 | 4.99 |
| **2d** | DMSO-$d_6$ | 7.82 | 7.23 | 7.96 | 3.82 | 4.00 | 0.96 | 4.98 |
| **2d** | $CD_3OD$ | 7.80 | 7.15 | 7.74 | 3.87 | 3.85 | 1.20 | 5.00 |
| **3d** | $CDCl_3$ | 6.92 | 6.29 | 6.96 | 3.86 | 3.74 | 1.49 | 2.54 |
| **3d** | DMSO-$d_6$ | 6.79 | 6.17 | 7.01 | 3.75 | 3.56 | 1.60 | 2.62 |
| **3d** | $CD_3OD$ | 6.85 | 6.18 | 6.95 | 3.81 | 3.71 | 1.39 | 2.02 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **4d** | $CDCl_3$ | 7.19 | 6.51 | 7.58 | 3.90 | 3.49 | 0.87 | 1.84 |
| **4d** | DMSO-$d_6$ | 7.31 | 6.70 | 7.98 | 3.81 | 3.52 | 0.82 | 1.89 |
| **4d** | $CD_3OD$ | 7.23 | 6.59 | 7.74 | 3.86 | 3.48 | 0.89 | 1.57 |

[a] NH: 9.97. [b] NH: 12.09. [c] NH: 9.63. [d] NH: 11.76.

**Table 3.** $^{13}C$ Chemical Shift Values of Formyl (**a**), Acetyl (**b**), Benzoyl (**c**), and Methoxycarbonyl (**d**) Derivatives (**1**-**4**) in Various Solvents (0.1 M)

| | | *i*-C | *o*-C | *m*-C | *p*-C | C=O | $CH_3$ |
|---|---|---|---|---|---|---|---|
| **1a** | $CDCl_3$ | 136.43 | 129.76 | 129.01 | 134.47 | 192.40 | |
| **1a** | DMSO-$d_6$ | 137.05 | 130.35 | 130.03 | 135.45 | 194.12 | |
| **1a** | $CD_3OD$ | 138.09 | 130.72 | 130.21 | 135.70 | 194.28 | |
| **2a** | $CDCl_3$ | 144.09 | 136.27 | 128.31 | 135.41 | 182.99 | |
| **2a** | DMSO-$d_6$ | 143.44 | 137.87 | 128.88 | 136.03 | 184.21 | |
| **2a** | $CD_3OD$ | 145.39 | 138.54 | 129.70 | 136.69 | 185.22 | |
| **3a** | $CDCl_3$ | 132.91 | 121.44 | 111.37 | 126.50 | 179.37 | |
| **3a** | DMSO-$d_6$ | 133.19 | 120.91 | 110.86 | 127.36 | 179.46 | |
| **3a** | $CD_3OD$ | 134.40 | 122.53 | 111.95 | 128.35 | 180.84 | |
| **4a** | $CDCl_3$ | 153.03 | 120.92 | 112.59 | 148.07 | 177.90 | |
| **4a** | DMSO-$d_6$ | 152.42 | 122.95 | 112.84 | 149.13 | 178.34 | |
| **4a** | $CD_3OD$ | 154.60 | 123.33 | 113.83 | 150.17 | 179.72 | |
| **1b** | $CDCl_3$ | 137.14 | 128.58 | 128.32 | 133.11 | 198.17 | 26.63 |
| **1b** | DMSO-$d_6$ | 137.68 | 129.55 | 129.01 | 134.05 | 198.81 | 27.58 |
| **1b** | $CD_3OD$ | 137.36 | 128.72 | 128.42 | 133.40 | 199.52 | 25.68 |
| **2b** | $CDCl_3$ | 144.63 | 132.47 | 128.13 | 133.78 | 190.75 | 26.96 |
| **2b** | DMSO-$d_6$ | 144.48 | 134.27 | 129.07 | 135.21 | 191.12 | 27.07 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **2b** | $CD_3OD$ | 145.52 | 134.79 | 129.15 | 135.60 | 193.19 | 26.86 |
| **3b** | $CDCl_3$ | 132.23 | 116.76 | 110.64 | 124.63 | 188.04 | 25.43 |
| **3b** | DMSO-$d_6$ | 131.84 | 116.76 | 109.56 | 125.15 | 186.78 | 25.46 |
| **3b** | $CD_3OD$ | 133.24 | 118.92 | 111.25 | 126.78 | 189.96 | 25.50 |
| **4b** | $CDCl_3$ | 152.90 | 117.21 | 112.26 | 146.41 | 186.83 | 26.04 |
| **4b** | DMSO-$d_6$ | 151.98 | 118.48 | 112.39 | 147.58 | 185.76 | 25.90 |
| **4b** | $CD_3OD$ | 154.05 | 119.46 | 113.54 | 148.70 | 188.85 | 26.02 |
| **1c** | $CDCl_3$ | 137.59 | 130.06 | 128.28 | 132.43 | 196.79 | |
| **1c** | DMSO-$d_6$ | 137.88 | 130.47 | 129.44 | 133.56 | 196.69 | |
| **1c** | $CD_3OD$ | 138.88 | 131.04 | 129.55 | 133.84 | 198.66 | |
| **2c** | $CDCl_3$ | 143.60 | 134.84 | 127.94 | 134.20 | 188.24 | |
| **2c** | DMSO-$d_6$ | 143.06 | 135.91 | 129.19 | 136.06 | 187.71 | |
| **2c** | $CD_3OD$ | 144.51 | 136.72 | 129.45 | 136.14 | 190.11 | |
| **3c** | $CDCl_3$ | 131.14 | 119.58 | 111.06 | 125.35 | 184.88 | |
| **3c** | DMSO-$d_6$ | 130.87 | 119.68 | 110.63 | 126.75 | 184.00 | |
| **3c** | $CD_3OD$ | 132.23 | 121.52 | 111.64 | 127.55 | 186.78 | |
| **4c** | $CDCl_3$ | 152.24 | 120.55 | 112.17 | 147.08 | 182.54 | |
| **4c** | DMSO-$d_6$ | 151.65 | 121.66 | 113.11 | 148.92 | 181.92 | |
| **4c** | $CD_3OD$ | 153.48 | 122.52 | 113.62 | 149.38 | 184.32 | |
| **1d** | $CDCl_3$ | 130.17 | 129.58 | 128.37 | 132.92 | 167.13 | |
| **1d** | DMSO-$d_6$ | 129.95 | 129.45 | 129.12 | 133.66 | 166.58 | |
| **1d** | $CD_3OD$ | 131.40 | 130.52 | 129.62 | 134.26 | 168.59 | |
| **2d** | $CDCl_3$(lit.[9]) | 136.0 | 132.7 | 128.1 | 135.0 | 162.5 | 52.1 |
| **2d** | $CDCl_3$ | 133.59 | 133.47 | 127.75 | 132.34 | 162.71 | 52.16 |
| **2d** | DMSO-$d_6$ | 133.59 | 134.60 | 129.26 | 134.80 | 162.77 | 53.05 |
| **2d** | $CD_3OD$ | 134.97 | 135.06 | 129.37 | 134.46 | 164.60 | 53.03 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **3d** | $CDCl_3$ | 122.63 | 115.25 | 110.48 | 122.89 | 161.64 | 51.47 |
| **3d** | DMSO-$d_6$ | 121.63 | 114.96 | 109.45 | 123.97 | 160.74 | 50.89 |
| **3d** | $CD_3OD$ | 123.38 | 116.64 | 110.72 | 124.69 | 163.35 | 51.69 |
| **4d** | $CDCl_3$ | 144.61 | 117.95 | 111.86 | 146.30 | 159.16 | 51.95 |
| **4d** | DMSO-$d_6$ | 144.06 | 118.71 | 112.66 | 147.98 | 158.71 | 52.10 |
| **4d** | $CD_3OD$ | 146.18 | 119.54 | 113.38 | 148.64 | 161.12 | 52.71 |

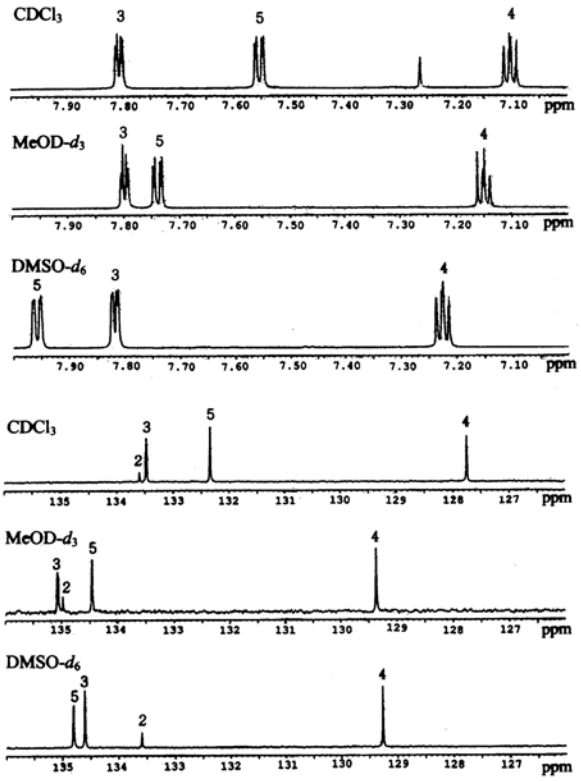



Figure 1. $^{1}H$ and $^{13}C$ spectra of methyl 2-thiophenecarboxylate (**2d**).

Interestingly, a plot of the chemical shift of 5-H against the dielectric constant of the solvent show a straight line with a fair correlation coefficient (r = 0.975) as shown in Figure 2. The observation is best explained by the S,O-*syn* conformation. With S,O-*anti* conformation 3-H should lie under the influence of the diamagnetic anistropic effect of the carbonyl group. Such an effect should vary linearly as the polarity of solvent changes. Therefore, the negligible difference (r = 0.333) in the chemical shift of 3-H is an evidence of the preference of the *syn* conformation.

Then, a question may be raised: why is the signal of 5-H significantly influenced by the nature of solvent? With polar solvent such as DMSO the interaction between the solute and the solvent should be enhanced by dipole-dipole interaction, leading to a strong association among molecules. Sulfur atom is likely to behave as an electron pair acceptor using its *d* orbital. Therefore, association like **VI** and **VII** are possible.

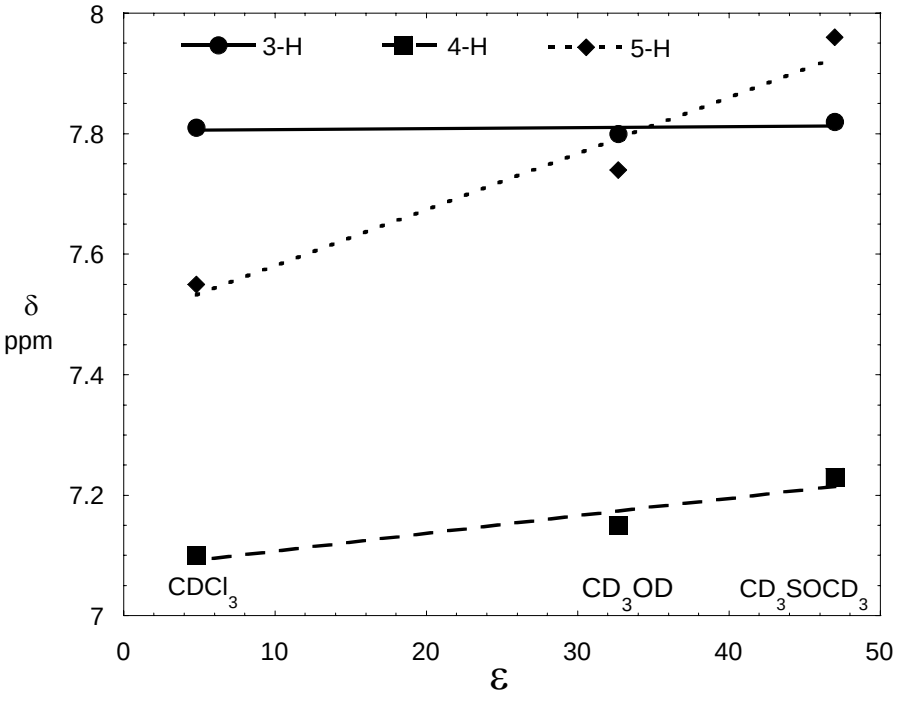
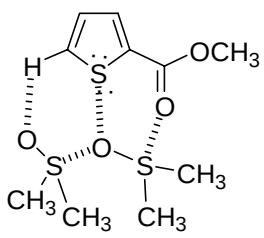
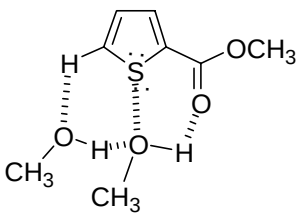



Figure 2. Dependence of the $^{1}$H chemical shift of methyl 2-thiophenecarboxylate (**2d**) on the dielectric constant of solvent. The correlation coefficients are: 3-H, 0.333; 4-H, 0.950; and 5-H, 0.975.



**VI**



**VII**

The $^{1}$H and $^{13}$C chemical shift values of the formyl (**a**), acetyl (**b**), and benzoyl (**c**) derivatives are also

listed in Tables 2 and 3, respectively. The benzene derivatives (**1a-c**) show very insignificant changes in $^1$H chemical shifts of the benzene ring by changing solvents from chloroform to MeOH-$d_4$ or DMSO-$d_6$. The phenomena are similar to the negligible solvent effect on benzene itself. Though small, DMSO causes more downfield shift (Δδ 0.03-0.09 ppm) than methanol (Δδ 0.02-0.04 ppm) does. The *para*-protons seem to be more affected (Δδ 0.04-0.09 ppm) than *ortho*-protons (Δδ 0.02-0.03 ppm).

Unlike $^1$H, there are unusual discrepancies among the reported values of $^{13}$C signals[9] and our values especially with 2-C and 5-C of **2d** as shown in the Table 3. The discrepancies are serious because the literature values are 2.41 and 2.66 ppm downfield for 2-C and 5-C, respectively from the present observation. In order to examine the possible effect of concentration we obtained the spectra at 0.1, 0.5, and 1.0 M solutions. But the signals shifted to upfield as the concentration was increased. Therefore, the values in the literature[9] seem to be inaccurate.

The assignment of $^{13}$C signals in the literature for 3-C and 5-C of **2d** in chloroform-*d* are also incorrectly reversed. The accurate assignment could be made by the $^1$H-$^{13}$C HETCOR spectroscopy. As shown in Figure 1 the order of the appearance of the signals from the upfield are 4-C < 5-C < 3-C < 2-C in chloroform-*d*; 4-C < 5-C < 2-C < 3-C in methanol-$d_4$; and 4-C < 2-C < 3-C < 5-C in DMSO-$d_6$. The chemical shift differences between 3-C and 5-C are 1.13, 0.60, and 0.20 ppm in chloroform-*d*, methanol-$d_4$, and DMSO-$d_6$, respectively. Such difference alone can hardly seem to justify the association of the solvent molecules around the substrate. However, if we compare the chemical shift of thiophene itself (Table 1), the introduction of methoxycarbonyl group at 2-C causes the signal of 5-C (α-C) shift to downfield by 7.23 (chloroform-*d*), 9.50 (methanol-$d_4$), and 8.60 (DMSO-$d_6$) ppm. On the other hand, the effects on the 3-C (β-C) are 6.61, 8.28, and 7.04 ppm, respectively. Clearly, the effect of the 2-substituent is more dramatic at 5-C in DMSO-$d_6$ and methanol-$d_4$ than in chloroform-*d*.

As mentioned earlier, the solvent effect on the chemical shift is minimal in benzene but it is quite significant in thiophene, pyrrole, and furan. Therefore, the combination of the effect of the solvent and that of 2-carbonyl group should result a significant change in chemical shift of the ring protons and carbons. Introducing an aldehyde group results in the downfield shift of the *ortho*-H (3-H). Such a

shift is the most significant with the furan (**4a**) in DMSO-$d_6$ (Δδ 1.07 ppm) and the least with benzene (**1a**) in chloroform-*d* (Δδ 0.53 ppm). It is noticeable that the order of the chemical shift of 3-H and 5-H of 2-thiophenecarboxaldehyde (**2a**) is reversed: 3-H > 5-H in chloroform-*d*, and 5-H > 3-H in DMSO-$d_6$ and methanol-$d_4$, as shown in Figure 3. If we consider the much greater effect of DMSO-$d_6$ to the shift of α-H (2,5-Hs) of thiophene than to that of β-H (3,4-Hs) (Δδ 0.42 ppm, see Table 1), the revered order of the signal is understandable. Such reversed order does not appear in pyrrole and furan series because α-H is mostly influenced by the hetero atom.

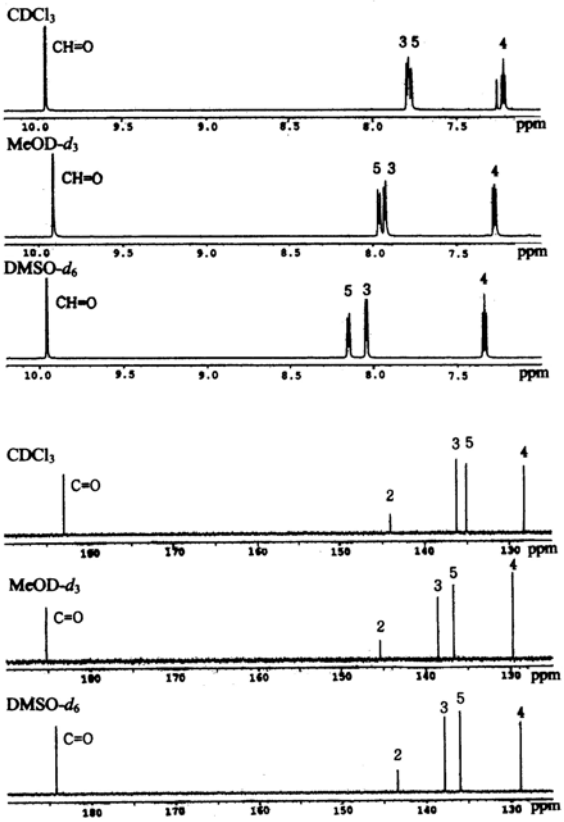



Figure 3. $^{1}H$ and $^{13}C$ spectra of 2-thiophenecarboxaldehyde (**2a**).

With 2-acetylthiophene (**2b**) the order of the chemical shift is 3-H > 5-H in chloroform-*d* and methanol-$d_4$, but the order is reversed in DMSO-$d_6$. On the other hand, the signal corresponding to 5-H of 2-benzoylthiophene (**2c**) is always in downfield regardless of the solvents.

Combination of solvent effect and the electronic effect of the carbonyl group on the chemical shift of

*ortho*-H show several interesting phenomena. As shown in Table 4 the difference was the smallest in the benzene series (**1**) and the largest in the furan series (**4**) in all solvents with exception of **2b**, **2d**, and **3d** in chloroform-*d*. By setting the difference in the benzene series 1.00 and dividing the value with the difference observed in the heterocycle a set of values can be obtained for each functional group in each solvent, as listed in Table 4.

Table 4. Deviations of the Chemical Shifts of 3-H (*ortho*-H) from the Parent Compounds upon Introduction of Carbonyl Groups and Calculated Aromaticity Indices of **1**-**4** Using the Values (in Parenthesis)[a]

| | **1** | | **2** | | **3** | | **4** | |
|---|---|---|---|---|---|---|---|---|
| CH=O | | | | | | | | |
| $CDCl_3$ | 0.53 | (1.00) | 0.66 | (0.81) | 0.74 | (0.72) | 0.87 | (0.61) |
| DMSO-$d_6$ | 0.55 | (1.00) | 0.89 | (0.62) | 0.98 | (0.56) | 1.07 | (0.51) |
| $CD_3OD$ | 0.59 | (1.00) | 0.82 | (0.72) | 0.95 | (0.62) | 1.02 | (0.58) |
| average | 0.56 | (1.00) | 0.79 | (0.70) | 0.89 | (0.63) | 0.99 | (0.56) |
| $CH_3C$=O | | | | | | | | |
| $CDCl_3$ | 0.60 | (1.00) | 0.57 | (1.05) | 0.66 | (0.91) | 0.79 | (0.76) |
| DMSO-$d_6$ | 0.59 | (1.00) | 0.79 | (0.75) | 0.93 | (0.63) | 0.96 | (0.62) |
| $CD_3OD$ | 0.65 | (1.00) | 0.75 | (0.87) | 0.93 | (0.70) | 0.94 | (0.69) |
| average | 0.61 | (1.00) | 0.70 | (0.87) | 0.84 | (0.73) | 0.90 | (0.68) |
| $C_6H_5C$=O | | | | | | | | |
| $CDCl_3$ | 0.45 | (1.00) | 0.52 | (0.87) | 0.64 | (0.70) | 0.85 | (0.53) |
| DMSO-$d_6$ | 0.37 | (1.00) | 0.58 | (0.63) | 0.76 | (0.49) | 0.92 | (0.40) |
| $CD_3OD$ | 0.44 | (1.00) | 0.59 | (0.75) | 0.77 | (0.57) | 0.94 | (0.47) |
| average | 0.42 | (1.00) | 0.56 | (0.72) | 0.72 | (0.56) | 0.90 | (0.45) |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| $CH_3OC=O$ | | | | | | | | |
| $CDCl_3$ | 0.69 | (1.00) | 0.68 | (1.01) | 0.66 | (1.05) | 0.80 | (0.86) |
| DMSO-$d_6$ | 0.60 | (1.00) | 0.67 | (0.90) | 0.77 | (0.78) | 0.83 | (0.72) |
| $CD_3OD$ | 0.69 | (1.00) | 0.69 | (1.00) | 0.78 | (0.88) | 0.83 | (0.83) |
| average | 0.66 | (1.00) | 0.68 | (0.97) | 0.74 | (0.90) | 0.82 | (0.80) |
| Average | | | | | | | | |
| $CDCl_3$ | 0.57 | (1.00) | 0.61 | (0.93) | 0.68 | (0.84) | 0.83 | (0.69) |
| DMSO-$d_6$ | 0.53 | (1.00) | 0.73 | (0.73) | 0.86 | (0.61) | 0.95 | (0.56) |
| $CD_3OD$ | 0.59 | (1.00) | 0.71 | (0.84) | 0.86 | (0.72) | 0.93 | (0.64) |
| Total Average | 0.56 | (1.00) | 0.68 | (0.82) | 0.80 | (0.71) | 0.90 | (0.62) |
| Lit (ring current)[10] | | (1.00) | | (0.75) | | (0.59) | | (0.46) |
| Lit (bond length)[11] | | (1.00) | | (0.93) | | (0.91) | | (0.87) |
| Average of Lit. | | (1.00) | | (0.84) | | (0.75) | | (0.66) |

*a* The indices are calculated by dividing the deviation in **1** by the deviation in **2**-**4**.

The average values for each functional group in each solvent and the average values for each solvent for all functional groups are also listed in the Table. The methoxycarbonyl derivatives (**d**) show the largest set of values whereas the benzoyl derivatives (**c**) show the smallest. The largest values of a set is observed in chloroform-*d* and the smallest one is in DMSO-$d_6$ for all functional groups. The overall average is benzene 1.00, thiophene 0.82, pyrrole 0.71, and furan 0.62. The values are very close to the average of two most commonly referred values for the indices of aromaticity,[10,11] as listed in Table 4 for the purpose of comparison.

Unlike $^1H$ it is difficult to estimate the indices of aromaticity by correlating the deviation of the $^{13}C$ chemical shift of the ring carbons. However, when the chemical shift values of the C=O of the heterocycles (**2**-**4**) is plotted against those of **1** in the three solvents as shown in Figure 4, good correlations are apparent. A set of indices of aromaticity can be calculated from the slope and they are

1.00, 0.71, and 0.62 for benzene, thiophene, and pyrrole, respectively. But a value of 0.61 is obtained for furan, which is quite close to the value for pyrrole. This may be the result of strong interaction of 2-acylfurans with solvents.

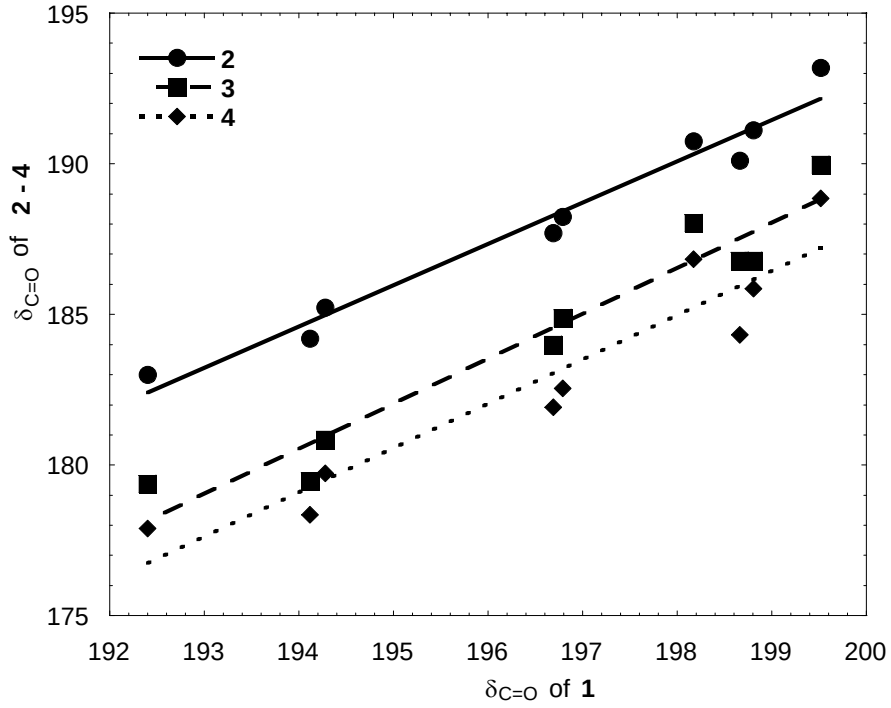



Figure 4. Plots of the $\delta_{C=O}$ of **1a-c** vs. $\delta_{C=O}$ of **2-4** in all solvents. The slopes and correlation coefficients are: **2**, 1.371 (0.994); **3**, 1.496 (0.966); and **4**, 1.470 (0.948).

Recently Neuvonen *et al*. reported the inverse relationship between $^{13}C$ chemical shift and IR stretching frequency of the carbonyl group.[12] For *m*- and *p*-substituted phenyl esters of trifluoroacetates, dichloroacetates and acetates, it was observed that the electron-withdrawing substituent caused an upfield shift of $^{13}C$=O and increased C=O stretching frequency in IR spectrum. Based on the calculation of the reaction energies of the isodesmic reaction, they proposed a new concept which is the decreased resonance stabilization as an explanation for the inverse reactivity and the changes in the chemical shifts and carbonyl frequencies.

The report prompted us to examine the trends in the $^{13}C$ chemical shifts and the stretching frequencies of

the carbonyl group of **1**-**4** in chloroform-*d* solution. As shown in Figure 5, benzene, thiophene, and pyrrole derivatives show good correlations (r = 0.930-0.993) for aldehyde and ketone series, but the ester series show only a fair trend (r = 0.820).

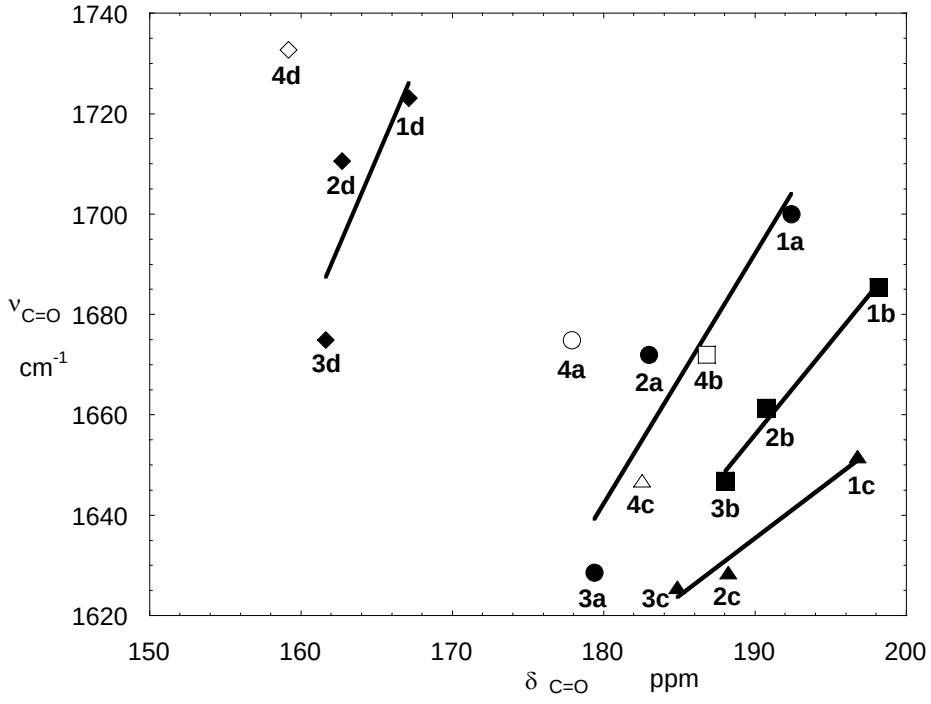
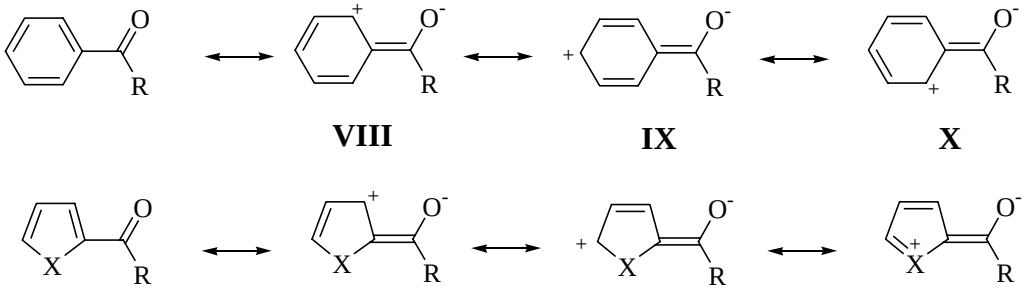



Figure 5. Plots of the chemical shifts of the carbonyl carbons against the stretching vibrational frequencies of the carbonyl group. The slopes and correlation coefficients are: **a**, 4.973 (r = 0.930); **b**, 3.689 (r = 0.993); **c**, 2.288 (r = 0.945); **d**, 7.049 (r = 0.820).

The furan compounds are far apart from the straight lines in all cases. For each series of **a**-**d** the furanyl compound, in general, has the smallest $\delta_{C=O}$ whereas its $\nu_{C=O}$ is a little larger than that of the thiophene counterpart. Apparently, the resonance argument may explain the trends in benzene (**1**), thiophene (**2**), and pyrrole (**3**).

The resonance contribution of **VIII**-**X** should be insignificant because the benzene ring loses the aromatic sextet of electrons. Therefore, the double bond character of the carbonyl group should be the

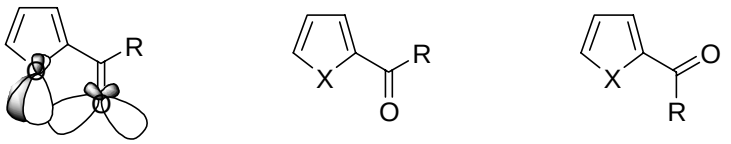
largest, which reflects the highest $\delta_{C=O}$ and $\nu_{C=O}$ in **1**. On the other hand, the contribution of **XI**-**XIII** should be favorable because the *p* orbital of N atom can overlap with the π orbital of the conjugated system in **3** (X = NH). Such conjugation should make the carbonyl bond have more single bond character than a double bond character. A similar kind of rationale may be applicable to the thiophene (X = S), but the contribution of **XIII** should be very unlikely because of the difference in sizes of C and S atoms.



**VIII** **IX** **X**

**XI** **XII** **XIII**

The exceptional behavior of the furan series cannot be explained by the contribution of **XI**-**XIII** (X = O). The spectroscopic behavior of the carbonyl group of **4a**-**d** can be explained better by the interaction of the lone pairs of electrons originated from the *syn* conformation like **XIV**. The conformations of 2-carbonyl derivatives of five-membered monoheterocyclic aromatic compounds have been widely investigated.[13] Generally, X,O-*syn* (**XV**) is the preferred conformation at ambient temperature for furan and thiophene. But about 10% of X,O-*anti* form (**XVI**) presents in furan series (X = O) at –115 $^{o}$C in deuterated diethyl ether solution. The free energy of activation ($\Delta G^{\neq}$) for the exchange of *syn* to *anti* form of 2-furaldehyde (**4a**) is 10.9 kcal mole$^{-1}$ at -115 $^{o}$C.[5,6]



**XIV** **XV** **XVI**

X,O-*syn* X,O-*anti*

With O,O-*syn* conformation in **4** the lone pair orbitals of both O atoms are in close proximity. Such interaction of the lone pair electrons should push the electrons on the carbonyl oxygen atom into the π* orbital of the C=O bond. Consequently, the electron density around the carbonyl carbon should be

dramatically increased and the $^{13}C$=O signal moves to upfield. The result of such move should enhance the force constant of the C=O bond, which, in turn, increase the C=O stretching frequency. This is very similar to α-chlorocyclohexanone of which the equatorial chlorine atom enhances the carbonyl frequency by about 20 $cm^{-1}$.[14]

In order to correlate the chemical shift and the stretching vibrational frequencies of the carbonyl groups in **1**-**4** with the reactivity, we measured the rate of the reduction of **a**-**c** by sodium borohydride in ethanol. The pseudo-first order rate constants are listed in Table 5.

Table 5. Stretching Vibrational Frequencies of Carbonyl Groups and Pseudo-first Order Rate Constants for the Reduction of **1**-**4** by Sodium Borohydride in Ethanol at 25 °C

| | $\nu_{C=O}$, $cm^{-1}$ | $k_{obs}$, $sec^{-1}$ |
|---|---|---|
| **1a** | 1700 | $2.40 \times 10^{-1}$ |
| **2a** | 1659 | $1.88 \times 10^{-2}$ |
| **3a** | 1629 | $2.60 \times 10^{-3}$ |
| **4a** | 1687 | $9.65 \times 10^{-2}$ |
| **1b** | 1685 | $6.22 \times 10^{-2}$ |
| **2b** | 1661 | $2.28 \times 10^{-2}$ |
| **3b** | 1647 | $1.30 \times 10^{-2}$ |
| **4b** | 1672 | $4.25 \times 10^{-2}$ |
| **1c** | 1652 | $1.30 \times 10^{-2}$ |
| **2c** | 1629 | $1.92 \times 10^{-3}$ |
| **3c** | 1626 | $4.69 \times 10^{-4}$ |
| **4c** | 1647 | $3.98 \times 10^{-3}$ |

Figure 6 shows the correlation of ln $k_{obs}$ with $\nu_{C=O}$. The correlation is excellent with the acetyl series **b**.

The larger the $\nu_{C=O}$ values are the faster the rates of the reduction are in the same series. The relative order of the rates of the reduction is benzoyl (**c**) < acetyl (**b**) < formyl (**a**). Apparently, the electron-withdrawing effect of the phenyl group is far less important than the steric effect for the reaction.

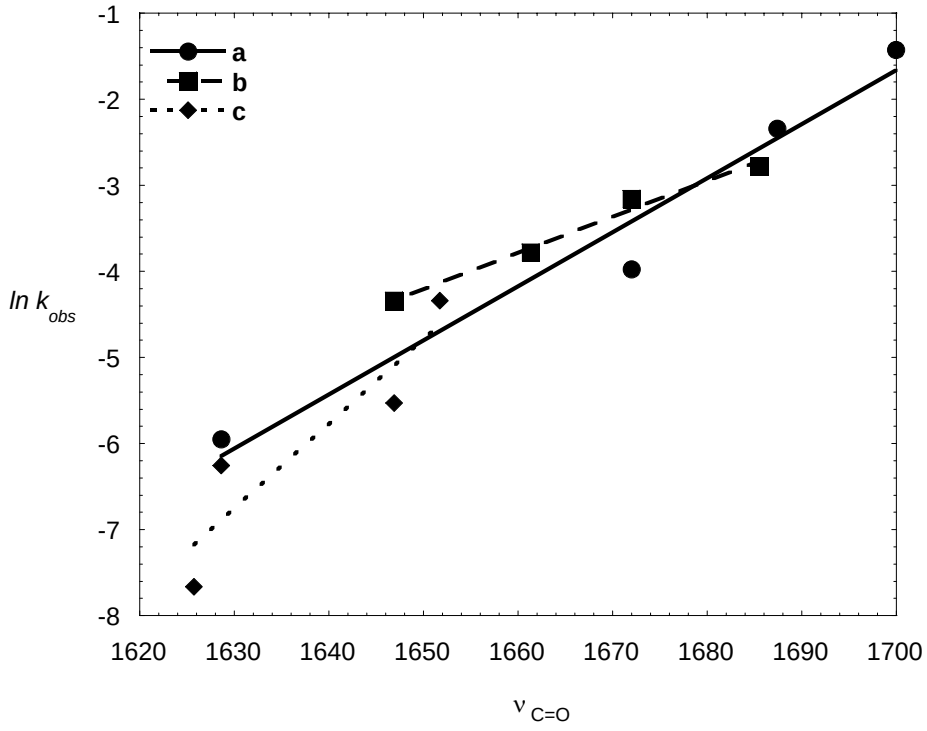



Figure 6. Correlations of ln $k_{obs}$ with the stretching frequencies of the carbonyl group. The slopes and correlation coefficients are: **a**, 0.0628 (r = 0.982); **b**, 0.0419 (r = 0.992); **c**, 0.0981 (r = 0.918).

In summary, the chemical shifts of 2-carbonyl derivatives are significantly affected by solvents. A set of aromaticity indices can be calculated using the deviation of *ortho*-H of the carbonyl compounds from the parent heterocycles. Correlations of the $^{13}$C=O of benzene derivatives and those of heterocycles also provide a reasonable values of indices.

## EXPERIMENTAL

Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker DPX-400 FT NMR spectrometer in the Central Lab of Kangwon National University at 400 MHz for $^{1}$H and 100 MHz for $^{13}$C and were

referenced to tetramethylsilane. The concentration of the solution was 0.10 M in all solvents. Infrared spectra were recorded on a JASCO FT/IR-460 Plus spectrophotometer. Ultraviolet spectroscopic measurement was carried out using Hitachi U-2000 spectrophotometer. All aldehydes (**1a**-**4a**) and methyl ketones (**1b**-**4b**) are commercially available. Benzoyl derivatives (**1c**) and (**2c**) and methyl esters (**1d**) and (**4d**) are also commercial products. 2-Benzoylpyrrole (**3c**) and 2-benzoylfuran (**4c**) were prepared by benzoylation with benzoyl chloride in the presence of aluminum chloride as reported in literatures.[15,16] Methyl esters (**2d**), (**3d**) and (**4d**) were also prepared by literature methods.[17,18]

**Preparation of 0.1 M solution and NMR experiment**

Each solution was prepared in 1 mL cylindrical volumetrical flask by weighing the compound into the flask and filling with solvent containing 1%-TMS. A portion (0.6 mL) of the solution was transferred into an NMR tube and the spectrum was obtained at 20 $^{o}$C.

**Measurement of the rate of reduction**

Ethanol solutions of the carbonyl compound ($1.0 \times 10^{-3}$ M) and sodium borohydride ($2.0 \times 10^{-3}$ M) were prepared. To 1 mL of the substrate solution 10 mL of the sodium borohydride solution was added and the resulting solution was monitored at the wavelength of which the $\lambda_{max}$ of the substrate was predetermined. The decrease in the absorption was recorded until 95% of the substrate was disappeared. The pseudo-first order rate constant was obtained from the slope of the plot of ln ($A - A_{\infty}$) against time.[19]

ACKNOWLEDGEMENT

We thank Dr. Gary Kwong of the 3M Co. for help in preparing the manuscript. This research was supported by Korea Research Foundation (KRF-2001-005-D20012).

EFERENRCE

1. A. R. Katritzky, M. Karelson, and N. Malhotra, *Heterocycles*, 1991, **32**, 127.
2. B. Y. Simkin, V. I. Minkin, and M. N. Glukhovtsev, *Adv. Heterocyclic Chem.*, 1993, **56**, 303.

3. C. K. Lee, J. S. Yu, and H.-J. Lee, *J. Hererocycl. Chem.*, 2002, **39**, 1207.
4. H. Satonaka, *Bull. Chem. Soc. Jpn.*, 1983, **56**, 2463.
5. L. Lunazzi, G. Placucci, C. Chatgilialiglu, and D. Macciantelli, *J. Chem. Soc., Perkin Trans. II*, 1984, 819.
6. D. Casarini, L. Lunazzi, and D. Macciantelli, *J. Chem. Soc., Perkin Trans. II*, 1985, 1839.
7. M. T. W. Hearn, *Tetrahedron Lett.*, 1975, 2787.
8. F. A. Carey and R. J. Sundbert, 'Advanced Organic Chemistry,' 4th ed., part A, Kluwer Academic/Plenum Pub., New York, 2000, p. 237.
9. M. T. W. Hearn, *Aust. J. Chem.*, 1976, **29**, 107.
10. J. A. Elvidge, *Chem. Commun.*, 1965, 160.
11. A. Julg and P. Francois, *Theor. Chim. Acta*, 1967, **8**, 249.
12. H. Neuvonen, K. Neuvonen, A. Koch, E. Kleinpeter, and P. Pasanen, *J. Org. Chem.*, 2002, **67**, 6995.
13. C. W. Bird and G. W. H. Cheesman, 'Comprehensive Heterocyclic Chemistry,' vol. 4, ed. by A. R. Katritzky, Pergamon, New York, 1984, p. 33.
14. N. B. Colthup, L. H. Daly, and S. E. Wiberley, 'Introduction to Infrared and Raman Spectroscopy,' Academic Press, New York, 1964, p. 243.
15. R. A. Jones and R. L. Laslett, *Aust. J. Chem.*, 1964, **17**, 1056.
16. R. Grigg, J. A. Knight, and M. V. Sargent, *J. Chem. Soc.*, 1965, 6057.
17. F. Blicke and E. Blake, *J. Am. Chem. Soc.*, 1930, **52**, 235.
18. References 4 and 8.
19. F. Ruff and I. G. Csizmadia, 'Organic Reactions, Equilibria, Kinetics and Mechanism,' Elsevier, Amsterdam, 1994, p. 61.