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Synthesis and NMR Studies of (*E*)-1-Aryl-3-(2-pyrrolyl)-2-propenones and (*E*)-3-Aryl-1-(2-pyrrolyl)-2-propenones

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Series of (*E*)-1-aryl-3-(2-pyrrolyl)-2-propenones, that were aldol condensation products between pyrrole-2-carbaldehyde and *m*- and *p*-substituted acetophenones, were prepared and their ^{1}H and ^{13}C NMR spectra were examined to obtain the information on the conformation of the enone system. Similar studies were carried out with (*E*)-3-aryl-1-(2-pyrrolyl)-2-propenones that were prepared from 2-acetylpyrrole and *m*- and *p*-substituted benzaldehydes. The substituent chemical shifts were studied by applying the Hammett relationship.

Key Words : ^{1}H and ^{13}C NMR, Pyrrole, Aldol condensation, Conformation of enones

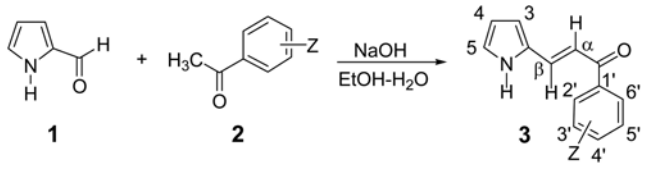
Introduction

Pyrrole is considered unique among the five-membered monoheterocyclic aromatic compounds because of its electron-releasing ability through resonance. For example, ^{1}H chemical shift value of the aldehydic proton in pyrrole-2-carbaldehyde (**1**) is δ 9.60, which is the most up-field value compared to the analogues such as benzene (δ 10.0), thiophene (δ 9.93), and furan (δ 9.68).[1] The resonance contribution like **1'** should decrease the susceptibility of the carbonyl carbon of pyrrole toward the nucleophilic attack. Therefore, **1** fails to undergo Cannizzaro reaction and benzoin condensation.[2]

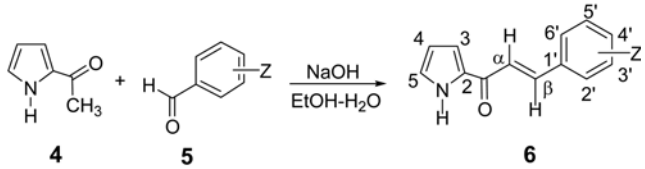
1 **1'**

The hydroxide addition at the carbonyl carbon of **1** is considerably slower than the similar reaction to the furan or thiophene analogues. The rate studies for the sodium methoxide-catalyzed condensations of heteroaromatic aldehydes with phenylacetonitrile in methanol show a reactivity sequence: pyridine-4-carbaldehyde > furan-2-carbaldehyde > benzaldehyde > thiophene-2-carbaldehyde > pyrrole-2-carbaldehyde.[3]

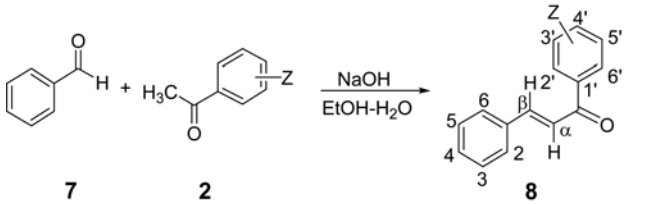
On the other hand, an aldol condensation of **1** with methyl ketones was reported.[4-7] However, the reaction seems not to be straightforward as the stoichiometric equation indicates. An early study reports a reaction time of four weeks with a mixture of **1** (0.9 g), acetophenone (**2k**, 3 mL), and 1 M-KOH solution (3 mL) to give **3k** (no yield given).[4] A similar reaction with identical amounts of **1**, **2k**, and KOH solution was reported to give 2.2 g of **3k** after standing overnight.[5] Although the product might be impure, the yield (118%) is quite unusual. When an 1:2 mixture of **1** and **2k** in ethanolic KOH (20%) was allowed at room temperature for 4 days, a mixture of **3k** and **9** was formed in 29% and 29%, respectively.[6] On the other hand, a solution of **1** (5.26 mmol) and **2k** (5.26 mmol) in ethanol (2.1 mL) was mixed with 10% NaOH solution (0.5 mL) and stirred overnight at room temperature to give **3k** in 48.5% yield.[7] There was no mention about the side product in the report in spite of the low yield of **3k**.



1 **2** **3**

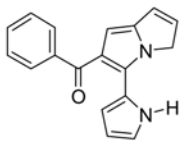


4 **5** **6**



7 **2** **8**

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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Aldol condensation of **1** (100 mmol) with 2-acetylpyridine (100 mmol) in the presence of cetyltrimethylammonium bromide (15 mmol) in 0.5 M-NaOH (200 mL) for 80 min gave the product in 77% yield.[8]

Contrary to the wide reports on the aldol condensation of **1**, a small number of the similar reactions of 2-acetylpyrrole (**4**) with substituted benzaldehyde (**5**) can be found in literature.[8,9]

In the course of our extensive investigation on the chalcone derivatives of aryl and heteroaryl aldehydes we came to be interested in the pyrrole derivatives of the chalcone. The chalcone analogues of pyrrole have been examined for a wide scope of interests such as antibacterial activity,[10] antitumor activity,[11] anticancer activity,[12] determination of volatile components from Maillard reaction in glucose-lysine model,[13,14] and a substrate for copper-catalyzed asymmetric cycloaddition.[15] We were interested in the synthesis and the NMR spectroscopic characteristics of the pyrrole derivatives of chalcone intending to achieve a quantitative assessment of the conjugation effect of the pyrrole ring.

Results and Discussion

There are ample reports describing the conditions for aldol condensation. We were in need of a set of conditions which is suitable for both **1** and **4**. Furthermore, the conditions should give reasonable yields with **2** and **5** having electron-withdrawing and -donating substituents at the meta and para positions. A tolerable reaction time (2-4 h) and a moderate temperature (preferably room temperature) were also desirable because pyrrole compounds tend to be darken upon heating and consequently, lowering yields.

Although the condensation of **1** and **2** is carried out in an ice-bath, the condensation of **4** with **5** usually requires heating at 40 °C for *ca.* 30 min for completion. Apparently, the enolization of the acetyl group linked to pyrrole (**4**) seems to be difficult due to the effect of conjugation like **1'**. So it is understandable that different sets of conditions are necessary. After countless trials we came to develop conditions suitable for **1** and **4**, separately, which are described in the experimental section. The yields and mp are listed in Table 7.

All products were recrystallized from ethanol to analytical purity, which is essential for the NMR spectroscopic analysis. The NMR spectra were obtained with 0.1 M-DMSO-d_6 solutions. Although many of the products were soluble in $CDCl_3$, some were not soluble enough to make 0.1 M solution. Therefore, DMSO-d_6 was employed so that the comparison of the chemical shift values was logical. The chemical shift values are listed in Tables 1-5. The assignments were made with the aid of ^{1}H-^{1}H COSY and ^{1}H-^{13}C HETCOR spectroscopy.

Both **3** and **6** showed very similar splitting patterns for the 3-, 4-, and 5-H of the pyrrole ring. Because of the close values for $J_{4,5}$ (*ca.* 2.6 Hz) and $J_{4,1}$ (*ca.* 2.3 Hz)[16] the splitting pattern for the 4-H appears to be a doublet of triplets with $J_{4,3}$ = 3.8 and $J_{4,5} = J_{4,1}$ = 2.4 Hz. On the other hand, that for the 3-H is a doublet of doublets of doublets with the two lines at the middle overlapping. The typical coupling constants are: $J_{3,1}$ = 2.3, $J_{3,4}$ = 3.8, and $J_{3,5}$ = 1.3 Hz. However, the splitting pattern for the 5-H is a slightly distorted doublet of triplets with $J_{5,3}$ = 1.3 and $J_{5,4} = J_{5,1}$ = 2.5 Hz.

Although the splitting patterns for the 3-, 4-, and 5-Hs in **3** and **6** are similar, the order of appearance of them from the up field is different: 4-H < 3-H < 5-H for **3** and 4-H < 5-H < 3-H for **6**. It is notable that the effect of the carbonyl group in **6** on the chemical shift of the 3-H of the pyrrole ring is far greater ($\Delta\delta$ = 1.37) than those of the typical carbonyl derivatives of pyrrole reported in the literature: $\Delta\delta$ = 0.93 for CHO; 0.78 for $COCH_3$; and 0.79 for $COOCH_3$.[16] The large down field shift of the 3-H signal may be the result of the conformation. There are four possible conformations (**I**-**IV**)

Table 1. ^{1}H Chemical Shift Values (δ) of **3** in 0.1 M-DMSO-d_6

	N-H	3-H	4-H	5-H	α-H	β-H	2'-H	3'-H	4'-H	5'-H	6'-H
a	11.89	6.80	6.26	7.21	7.64	7.70	8.75		8.47	7.86	8.45
b	11.75	6.77	6.24	7.17	7.54	7.63	8.16		7.83	7.53	8.01
c	11.74	6.77	6.24	7.17	7.54	7.63	8.02		7.70	7.60	7.98
d[a]	11.72	6.73	6.23	7.15	7.54	7.60	7.53		7.20	7.48	7.64
e[a]	11.71	6.73	6.22	7.14	7.54	7.60	7.84		7.44	7.45	7.82
f	11.82	6.80	6.25	7.20	7.54	7.65	8.38	8.20		8.20	8.38
g	11.75	6.76	6.23	7.16	7.52	7.61	7.95	7.78		7.78	7.95
h	11.73	6.75	6.23	7.16	7.54	7.62	8.03	7.64		7.64	8.03
i[a]	11.68	6.70	6.21	7.12	7.55	7.59	8.04	7.09		7.09	8.04
j[a]	11.70	6.71	6.22	7.13	7.55	7.59	7.94	7.36		7.36	7.94
k	11.75	6.73	6.22	7.14	7.57	7.61	8.03	7.56	7.63	7.56	8.03
Ave	11.75	6.75	6.23	7.16	7.55	7.62					
k[b]	9.40	6.72	6.33	6.99	7.21	7.78	7.98	7.46	7.55	7.46	7.98
k[c]	10.95	6.74	6.27	7.10	7.54	7.72	8.06	7.53	7.60	7.53	8.06
k[d]	-	6.67	6.25	7.03	7.37	7.68	7.56	7.50	7.58	7.50	7.56
k[e]	9.94	6.72	6.30	7.06	7.35	7.69	8.05	7.56	7.63	7.56	8.05
$\Delta\delta$[f]	2.35	0.07	0.11	0.15	0.36	0.17	0.50	0.10	0.08	0.10	0.50

[a]Methyl signal, δ: **3d**, 3.84; **3e**, 2.41; **3i**, 3.85; **3j**, 2.39. [b]In $CDCl_3$. [c]In CD_3COCD_3. [d]In CD_3OD. [e]In CD_3CN. [f]Difference between the largest value and the smallest value of the chemical shifts in various solvents.

Table 2. ^{13}C Chemical Shift Values (ppm) of **3** in 0.1 M-DMSO-d_6

	C=O	2-C	3-C	4-C	5-C	α-C	β-C	Ipso-C
a	186.73	129.65	118.17	111.44	125.68	113.99	136.13	140.02
b	187.35	129.66	117.61	111.32	125.29	114.43	135.49	140.91
c	187.41	129.64	117.54	111.29	125.26	114.47	135.47	140.71
d[a]	188.54	129.64	117.08	111.12	124.85	115.07	134.81	140.27
e[a]	188.94	129.64	116.86	111.07	124.72	115.18	134.64	138.86
f	187.80	129.71	118.02	111.56	125.82	114.71	136.26	143.89
g	187.91	129.65	117.32	111.29	125.17	114.61	135.29	137.84
h	187.68	129.64	117.25	111.24	125.11	114.64	135.22	137.49
i[a]	187.29	129.72	116.43	110.97	124.41	115.11	133.98	131.61
j[a]	188.36	129.66	116.70	111.03	124.62	115.11	134.41	136.25
k	188.94	129.65	116.96	111.12	124.84	115.12	134.81	138.83
Ave	187.90	129.66	117.27	111.22	125.23	114.77	135.14	138.79
k[b]	190.81	129.29	115.67	111.47	123.42	115.35	135.01	138.61
k[c]	189.69	130.83	117.28	111.96	124.86	116.14	135.21	140.21
k[d]	191.40	129.70	117.17	110.94	124.48	114.33	135.72	139.03
k[e]	189.16	129.14	115.79	110.60	123.55	115.21	133.67	138.65
Δδ[f]	2.46	1.69	1.61	1.36	1.44	1.81	2.05	1.60

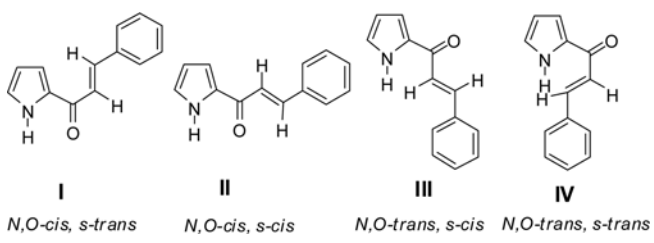
[a]Methyl signal, ppm: **3d**, 55.81; **3e**, 21.49; **3i**, 56.04; **3j**, 21.64. [b]In $CDCl_3$. [c]In CD_3COCD_3. [d]In CD_3OD. [e]In CD_3CN. [f]Difference between the largest value and the smallest value of the chemical shifts in various solvents.

Table 3. ^{1}H Chemical Shift Values (δ) of **6** in 0.1 M-DMSO-d_6

	NH	3-H	4-H	5-H	α-H	β-H	2'-H	3'-H	4'-H	5'-H	6'-H
a	12.06	7.48	6.29	7.20	7.76	7.91	8.71		8.29	7.73	8.23
b	12.02	7.44	6.28	7.18	7.60	7.78	8.14		7.60	7.39	7.82
c	12.02	7.43	6.28	7.18	7.62	7.78	8.01		7.47	7.46	7.78
d[a]	12.00	7.42	6.27	7.17	7.62	7.70	7.40		6.99	7.35	7.41
e[a]	11.99	7.37	6.27	7.16	7.61	7.68	7.67		7.23	7.33	7.61
f	12.09	7.45	6.30	7.21	7.73	7.90	8.27	8.12		8.12	8.27
g	12.01	7.48	6.27	7.17	7.61	7.73	7.81	7.64		7.64	7.81
h	12.01	7.49	6.27	7.17	7.63	7.72	7.88	7.50		7.50	7.88
i[a]	11.94	7.33	6.26	7.14	7.55	7.62	7.79	7.00		7.00	7.79
j[a]	11.96	7.35	6.26	7.15	7.61	7.64	7.72	7.26		7.26	7.72
k	12.01	7.37	6.27	7.17	7.65	7.71	7.84	7.43		7.43	7.84
Ave	12.01	7.42	6.27	7.17	7.62	7.74					
k[b]	9.98	7.13	6.36	7.10	7.37	7.84	7.64	7.41	7.43	7.41	7.64
k[c]	11.07	7.31	6.32	7.23	7.66	7.74	7.79	7.43	7.43	7.43	7.79
k[d]	-	7.26	6.31	7.15	7.55	7.71	7.70	7.41	7.39	7.41	7.70
k[e]	10.10	7.10	6.22	7.04	7.41	7.63	7.65	7.35	7.32	7.35	7.65
Δδ[f]	2.03	0.26	0.14	0.19	0.29	0.21	0.20	0.08	0.06	0.08	0.20

[a]Methyl signal, δ: **3d**, 3.82; **3e**, 2.35; **3i**, 3.81; **3j**, 2.34. [b]In $CDCl_3$. [c]In CD_3COCD_3. [d]In CD_3OD. [e]In CD_3CN. [f]Difference between the largest value and the smallest value of the chemical shifts in various solvents.

for the enone system in **6**.



A pseudo six-membered ring consisting the 3-H and the β-C like **Ia** is possible in the conformation **I**. The β-C is the positive end of the enone due to the resonance form like **Ib**. The influence of the positively charged β-C should result the observed down field shift.

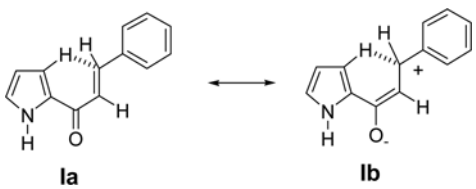


Table 4. ^{13}C Chemical Shift Values (ppm) of **6** in 0.1 M-DMSO-d_6

	C=O	2-C	3-C	4-C	5-C	α-C	β-C	Ipso-C
a	177.84	133.50	118.70	110.84	127.44	126.35	138.81	137.36
b	177.98	133.54	118.42	110.76	127.23	125.12	139.49	137.96
c	178.00	133.54	118.41	110.77	127.23	125.14	139.24	137.70
d[a]	178.23	133.56	118.07	110.68	126.97	123.83	141.19	136.81
e[a]	178.28	133.57	117.88	110.67	126.89	123.35	141.32	131.32
f	177.64	133.52	118.82	110.95	127.71	127.71	138.54	142.03
g	178.06	133.53	118.17	110.75	127.13	123.86	139.87	134.72
h	178.07	133.54	118.17	110.75	127.13	124.34	139.74	135.03
i[a]	178.42	133.64	117.44	110.56	126.53	121.11	141.09	128.02
j[a]	178.33	133.57	117.68	110.61	126.72	122.51	141.19	132.65
k	178.25	133.55	117.95	110.70	126.95	123.46	141.18	135.25
Ave	178.10	133.55	118.16	110.73	127.08	124.25	140.15	134.93
k[b]	179.31	133.59	116.82	111.42	125.90	122.38	141.71	135.44
k[c]	178.26	133.69	116.77	110.53	125.87	123.10	141.33	135.74
k[d]	179.60	133.36	117.92	110.70	126.67	122.52	142.05	135.46
k[e]	177.67	132.56	115.95	109.88	125.11	122.04	140.56	134.62
Δδ[f]	1.93	1.13	1.97	1.54	1.84	1.42	1.49	1.12

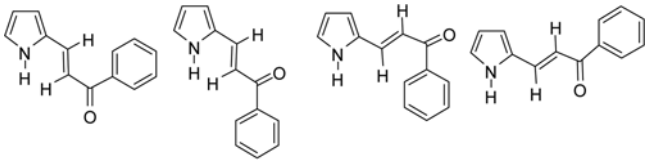
[a]Methyl signal, ppm: **6d**, 55.77; **6e**, 21.41; **6i**, 55.83; **6j**, 21.53. [b]In $CDCl_3$. [c]In CD_3COCD_3. [d]In CD_3OD. [e]In CD_3CN. [f]Difference between the largest value and the smallest value of the chemical shifts in various solvents.

Table 5. ^{13}C Chemical Shift Values (ppm) of Carbon Atoms in Phenyl Ring of **3** and **6** in 0.1 M-$CDCl_3$

	1'-C	2'-C	3'-C	4'-C	5'-C	6'-C
3a	140.02	122.80	148.64	127.33	131.04	134.54
6a	137.36	124.73	148.94	123.20	130.81	135.26
3b	140.91	131.51	122.72	135.63	131.00	127.38
6b	137.96	131.00	122.89	133.04	131.41	128.40
3c	140.71	128.09	134.19	132.71	131.23	127.00
6c	137.70	128.15	134.27	130.15	131.15	128.02
3d	140.27	113.28	160.00	118.86	130.34	120.86
6d	136.81	113.77	160.14	116.55	130.40	121.82
3e	138.86	128.90	138.51	133.63	129.07	125.68
6e	131.32	129.32	135.31	138.60	129.26	126.45
3f	143.89	129.65	124.43	149.99	124.43	129.65
6f	142.03	130.03	124.45	148.28	124.45	130.03
3g	137.84	132.31	130.47	127.09	130.47	132.31
6g	134.72	130.96	132.32	124.39	132.32	130.96
3h	137.49	130.30	129.34	137.93	129.34	130.30
6h	135.03	129.40	130.73	134.39	130.73	129.40
3i	131.61	130.73	114.47	163.31	114.47	130.73
6i	128.02	130.80	114.84	161.42	114.84	130.80
3j	136.25	129.76	128.57	143.34	128.57	129.76
6j	132.65	129.01	129.97	140.15	129.97	129.01
3k	138.83	129.22	128.45	133.05	128.45	129.22
6k	130.59	129.02	129.37	130.59	129.37	129.02

Furthermore, the *syn* conformation of the N-H and C=O in **6** is compatible with the predominant *syn* conformation of 2-formyl- and 2-acetylpyrrole widely reported in the literature.[17]

On the other hand, the difference in the chemical shift of the 3-H of **3** and that in pyrrole itself is 0.70 ppm, which is a smaller magnitude than the effect of HC=O and CH_3-C=O. Such small difference in the chemical shift values may not give any clue for the conformation of **3**, which may be represented like **V-VIII**.



V *N,O-cis, s-trans* **VI** *N,O-trans, s-cis* **VII** *N,O-trans, s-trans* **VIII** *N,O-cis, s-cis*

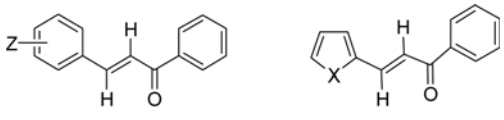
We have examined the correlation of the chemical shift values with the Hammett σ parameters in order to obtain the relevant information on the conformation.

Studies on the correlation of the chemical shift values with the substituent constants have been carried out widely in order to investigate the physico-chemical properties of the five-membered monoheterocyclic aromatic compounds.[18] The substituent effect on the chemical shift is generally analyzed by the single substituent parameter (SSP) and dual substituent parameter (DSP) approach, which are represented by Eq. (1) and (2), respectively.[19]

$$\delta = \rho\sigma + \delta o \quad (1)$$

$$\delta = \rho_I\sigma_I + \rho_R\sigma_R + \delta o \quad (2)$$

Solaniova *et al*. investigated the substituent effect of the chalcones **8** and **10** in chloroform-*d*.[20] Musumarra and Ballistreri reported the substituent effect in the chalcone analogues of thiophene and furan (**11**) in chloroform-*d*.[21]



10 **11** X = S, O

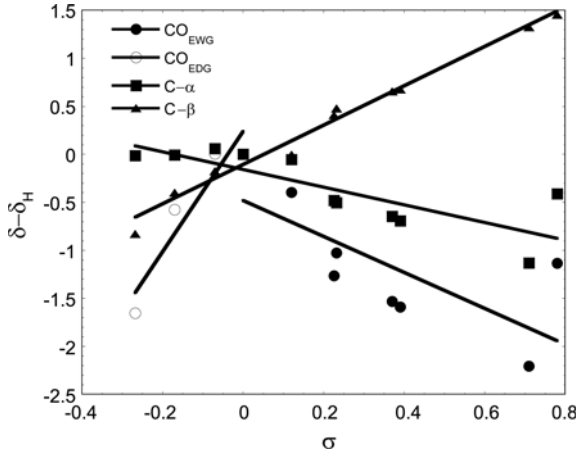


Figure 1. Correlation between σ and $\delta_{C=O}$, $\delta_{C-\alpha}$, and $\delta_{C-\beta}$ in **3**.

Compounds **3** of the present study can be considered the analogues of **8** and **11**, whereas compounds **6** are structurally related to **10**. But there is no report of similar study with the pyrrole series **3** and **6**.

Figure 1 shows the correlation of the chemical shift values of the C=O, α-C, and β-Cs of **3** with the Hammett σ values. The values of the slopes and the correlation coefficients (*r*) from the similar plots for all the protons and carbons in **3** and **6** are listed in Table 6. The values for **8** from the literature[22] are also listed for the purpose of comparison.

Although the comparison between the pyrrole series **3** and the phenyl series **8** in literature[22] may not be reasonable due to the difference in solvents ($CDCl_3$ in the literature *vs.* DMSO-d_6 in the present study), the comparison between **3** and **6** gives a striking contrasts. One of them is a good inverse correlation of the ^{13}C=O of **6** (r = 0.984) with the σ and no correlation of the ^{13}C=O of **3** (r = 0.525). The apparent no correlations of the chemical shifts of the carbonyl carbons with the σ were reported not only fo **8**[22] but also for the series of benzaldehydes and the acetophenones[23] and for the series of benzanilides.[24] However, the clear correlations are apparent if the plottings are made with the electron-donating substituents (−σ values) and with the electron-withdrawing substituents (+σ values), separately, as shown in Figure 1. The ρ values of 633.9 (r = 0.941) and −187.2 (r = 0.735) are obtained from the correlations with the electron-donating groups and electron-withdrawing groups, respectively, as shown in Table 6. Similar observations are reported in the literature for the *m*- and *p*-substituted phenyl ketones.[24,25]

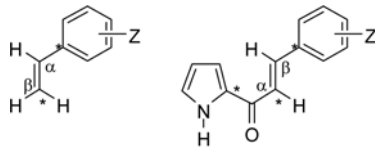
Table 6. Best Fit of the Single Substituent Parameter Equation for the ^1H and ^{13}C Chemical Shifts of **3** and **6** in DMSO-d_6 in Hz

	3		**6**		**8**[a]	
	ρ	r	ρ	r	ρ	r
α-H	11.97	0.328	57.11	0.816	-22.26	0.562
β-H	34.08	0.904	107.93	0.982	22.29	0.761
N-H	60.65	0.878	47.11	0.957		
2-H					10.63	0.764
3-H	41.02	0.989	51.34	0.777	17.45	0.963
4-H	17.19	0.991	13.31	0.960	7.20	0.845
5-H	32.42	0.992	23.89	0.972		
C=O	-111.69	0.525	-67.39	0.984	-142.66	0.573
$C=O_{EDG}$	633.9	0.941			718.1	0.916
$C=O_{EWG}$	-187.2	0.735			-241.9	0.831
α-C	-91.87	0.809	521.75	0.975	-121.42	0.844
β-C	204.68	0.991	-294.59	0.930	268.96	0.994
1-C					-77.66	0.993
2-C	0.04	0.004	-9.45	0.836	35.99	0.995
3-C	158.32	0.991	121.89	0.989	19.42	0.986
4-C	52.70	0.986	30.76	0.963	89.04	0.993
5-C	128.29	0.994	95.26	0.980		
1'-C	739.44	0.794	1070.2	0.898	718.27	0.789

[a]In $CDCl_3$ and are calculated with the data in reference 22 using same σ values as **3** and **6**.

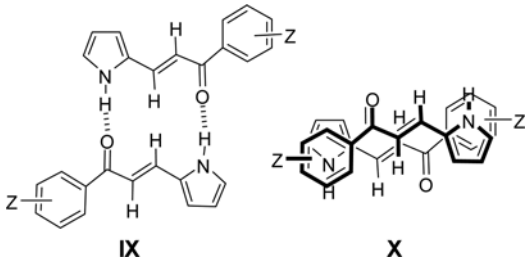
Plotting the chemical shift values of the 2-Cs also shows a striking contrast: absolutely no correlation for **3** (r = 0.04) and a fair correlation for **6** (r = 0.836). The α-Hs of **3** also showed no correlation (r = 0.328), whereas those of **6** showed only a trend (r = 0.816). The position of –HC=CH– moiety, whether it is between the carbonyl and the substituted phenyl ring or between the carbonyl and the 2-pyrrolyl ring, makes a dramatic change in the correlation pattern.

The series **6** can be related to a β-substituted styrene. An inverse correlation for the chemical shifts of the α-C and a normal correlation for those of the β-C with the σ were explained in terms of induced π-polarization.[23,26]

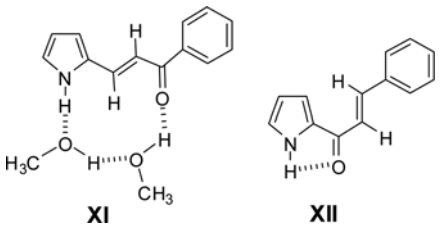


The observed correlations with **6** seem to be consistent with such rationale. But the correlation observed in **3** may not be understood by the induced π-polarization only. Apparently, the carbonyl group seems to play a role of insulator as the electronic effect of the *m*- and *p*-substituent is transmitted through the bonds. Such insulating effect may be the reason why the magnitudes of the ρ values of the α-C and the β-C in **3** are smaller than those in **6**.

Contrary to this, the ρ values of the 3-, 4-, and 5-Cs in **3** are about 30-70% larger than those in **6**. Apparently, the substituent effect should be transmitted not only through the bonds but also through the space. With the conformation like **VIII** the association of the molecules may be possible by intermolecular H-bonding as shown like **IX** and by the stacking like **X**.



In order to prove the presence of such H bonding, we examined the solvent effect on the chemical shifts of **3k** and **6k** having no substituent. The spectra were obtained in 0.1 M solution of CD_3COCD_3, CD_3CN, CD_3OD, and $CDCl_3$ in addition to CD_3SOCD_3, and the data are included in Tables 1-4. The solvent effect seems to appear more profoundly in **3k** than in **6k**, as indicated with the Δδ value which is the difference between the largest value and the smallest value of the chemical shift in solvents employed. The plot of δ_{NH} of **3k** in various solvents against those of **6k** indicates a good correlation (r = 0.989) with a slope of 0.92, as shown in Figure 2, Similar plot with the chemical shift values of CO of **3k** against **6k** shows a slope of 0.64, as shown in Figure 3, implying much more influence of the solvents on the enone system of **3k**. The observation should be consistent with the dimerization of the molecules by the H bonding or stacking. The intermolecular H bonding like **IX** may be unfavorable in the solvent like CD_3OD because the solvent molecule may form stronger H bonding like **XI**, prohibiting dimerization. On the other hand, the intramolecular H bonding in **6k** should be favorable like **XII** and therefore, the solvent effect may not be as much significant as in the case of **3k**.



XI **XII**

In conclusion, the aldol condensation of the carbonyl derivatives of pyrrole with benzaldehydes and acetophenones under basic conditions produced the enone compounds in 37-92% yields. The NMR studies of the products indicate that the enones from pyrrole-2-carbaldehyde and acetophenones prefer *N,O-cis, s-cis* conformation, whereas those from 2-acetylpyrrole and benzaldehydes favor *N,O-cis, s-trans* conformation.

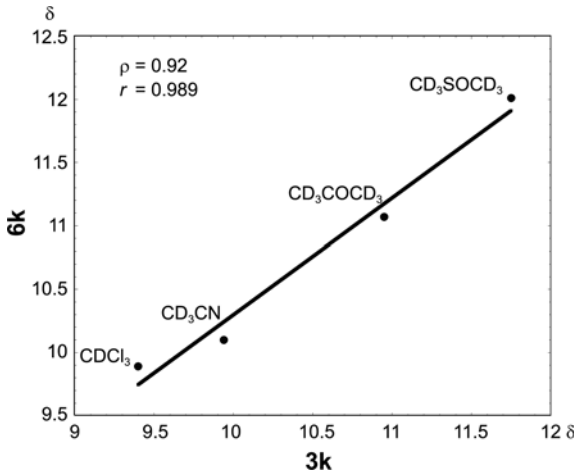


Figure 2. Plot of ^{1}H chemical shifts (δ) of N-H in **3k** against those in **6k** in various solvents.

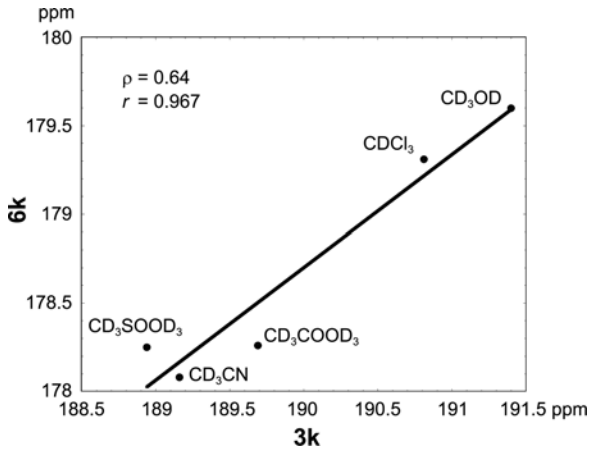


Figure 3. Plot of ^{13}C chemical shifts (ppm) of CO in **3k** against those in **6k** in various solvents.

Experimental Section

Nuclear magnetic resonance (NMR) spectra in chloroform-*d* solution 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 solutions were 0.10 M in DMSO-d_6. Each solution was prepared in a 1 mL cylindrical volumetric flask by weighing the compound into the flask and filling with the solvent containing 1%-TMS. A portion (0.60 mL) of the solution was transferred into a 5 mm NMR tube and the spectrum was obtained at 20 °C. The chemical shift values are listed in Tables 1-5. The σ values for the *m*- and *p*-substituents are from the literature.[27]

2-Pyrrolecarbaldehyde (**1**), 2-acetylpyrrole (**4**), *m*- and *p*-substituted benzaldehydes (**2a-k**), and *m*- and *p*-substituted acetophenones (**5a-k**) were the commercial products and used as delivered. Column chromatography was performed using silica gel and 1:1 mixture of ethyl acetate and hexane as elution solvent.

Preparation of (*E*)-1-Aryl-3-(2-pyrrolyl)-2-propenones. An Illustrative Procedure with 3k: 2-Pyrrolecarbaldehyde (**1**, 12 mmol), acetophenone (**2k**, 13 mmol), and 24 mmol of NaOH in ethanol (20 mL) and water (10 mL) were mixed in

Table 7. Yields and Melting Points of **3** and **6**

	Yield, %	MP, °C		Yield, %	MP, °C
3a	84	154	**6a**	77	200
3b	90	131	**6b**	88	182
3c	37	128	**6c**	88	162
3d	79	96	**6d**	83	144
3e	85	157	**6e**	75	121
3f	55	173	**6f**	78	170
3g	92	183	**6g**	88	162
3h	88	175	**6h**	91	156
3i	53	168	**6i**	84	138
3j	65	157	**6j**	79	153
3k	66	130	**6k**	80	139

an ice-bath and stirred for 4 h in the bath. The mixture was neuteralized with 1 M-HCl aqueous solution to pH 8-9 and then the resulting precipitate was collected and recrystallized from ethanol. The yields and mp are listed in Table 7.

Preparation of (*E*)-3-Aryl-1-(2-pyrrolyl)-2-propenones. An Illustrative Procedure with 6k: 2-Acetylpyrrole (**4**) gave the best results when equal molar (7.6 mmol) mixture of **4** and benzaldehyde (**5k**) was mixed with 2 M-NaOH (5 mL) and ethanol (7 mL) in an ice-bath and stirred for 5 h, and then heated at 40 °C for 30 min. After a similar work-up the crude products were recrystallized from ethanol. The yields and mp are listed in Table 7.

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