Correlation analysis of IR, ^{1}H NMR and UV spectral data of alkyl and aryl 4,6-disubstituted-3-cyano-2-pyridones. Part I

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Abstract
Spectral characteristics of the two series of previously synthesized and identified 4,6-disubstituted-3-cyano-2-pyridones were determined, and corresponding ^{1}H NMR chemical shifts and IR and UV frequencies were correlated with LFER parameters. A variety of substituents were employed for both alkyl and aryl substitution, and fairly good correlations were obtained, using simple Hammett and Hammett-Taft dual parameter equations, as well as the more sophisticated multiparameter regression approaches. It was established that both polar and steric effects influence the spectra of the investigated compounds.

Keywords : Substituted 2-pyridones, LFER analysis, IR, NMR and UV spectra

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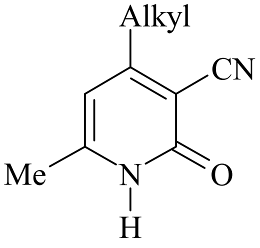
Introduction

Our previous investigations into the chemistry of substituted 3-cyano-2-pyridones included the synthesis and identification of new compounds[1-5], the study of new catalysts for the reaction, and the mechanisms of both chemically and enzyme catalyzed reactions[3,6-7]. These and other papers and communications were summarized in a review[8]. In a recent publication, the UV/VIS absorption spectra of arylazo substituted 3-cyano-2-pyridones in various solvents have been investigated[9]. Other investigators studied the tatomerism of some substituted 2-pyridones by UV/vis, ^{1}H and ^{13}C NMR spectroscopic methods.[10]

It is well known from the literature that 2-pyridones of structure similar to those investigated here, have a broad spectrum of biological activity, and to mention only a few, exhibited vasodilatory, antioxidant, antidiabetic, antimicrobial and antiviral activity[8,11]. Therefore we considered it worthwhile to investigate the effects of substituents in the positions 4 and 6 in the title compounds (Fig. 1) on the spectral features of the groups in investigated molecules, which might be either directly or indirectly involved in molecular interactions in living organisms.



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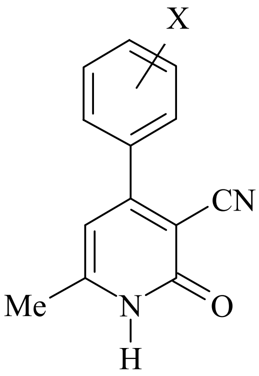

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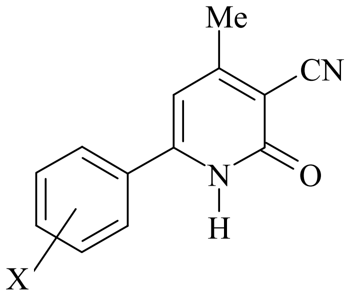

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Compd	Substituent
1a	Me
1b	Et
1c	*n*-P
1d	*i*-Pr
1e	*n*-Bu
1f	*i*-Bu
1g	*t*-Bu
2a	p-OCH_3
2b	H
2c	p-Br
2d	p-Cl
2e	m-NO_2
2f	p-NO_2
3a	p-OCH_3
3b	H
3c	p-Br
3d	p-Cl
3e	m-NO_2
3f	p-NO_2

Figure 1. General structures of investigated 4,6-disubstituted-3-cyano-2-pyridones.

Results and Discussion

A large number of spectral data relating to substituted 3-cyano-2-pyridones, accumulated in the previous investigations, were correlated in the present work using a variety of LFER models, conventionaly used for the study of structure-reactivity and structure-property relationships. It was assumed that it should be possible to find an adequate approach to study the transmission of substituent effects in the multi-substituted 2-pyridone nuclei, considering that their aromaticity has been established[12]. Problems arose from the difficult assignement of the IR stretching frequency bands, low solubility of investigated compounds in the common solvents used for recording the ^{1}H NMR spectra, and the close values of the UV absorption maxima. However, some fairly good correlations were obtained, considering the possibility of interactions between substituents and probable deviations from planarity in some of the investigated molecules. It was always initially attempted to use a simple Hammett Equation as presented in Eq. 1.a., but it was frequently more appropriate to use other approaches, like the Hammett-Taft (Extended Hammett Equation) DSP model, Eq. 1.b., and Swain-Lupton Eq. 1.c., which are usually given in the literature in their general form[13,14]. In these models, *s* is the measured spectral characteristics, $\sigma_{m/p}$[15], σ_I, σ_R and υ[16], F and R[15] are substituent constants, ρ, ρ_I, ρ_R, f and r are the corresponding calculated proportionality constants, which in a broad sense reflect the sensitivity of the spectral characteristics to substituent effects, and s_0 is the intercept. On certain occasions, when other models failed, combined multiparameter equations were applied, the method known to be used before[17,18], and with the same precision as obtained here.

$$\text{a. } s = \rho\sigma + s_0\,; \quad \text{b. } s = \rho_I\sigma_I + \rho_R\sigma_R + s_0 \qquad \text{c. } s = fF + rR + s_0 \qquad (1)$$

For the correlation of spectral data for 4-alkyl substituted-6-methyl-3-cyano-2-pyridones we also applied Charton's steric constants υ corrected for the -C-C- branching in the the corresponding alkyl group[19]. The υ_{corr} parameter stands for $\upsilon(n_1+n_2)$, n_1 and n_2 being the number of branch points at the *alpha*- and *beta*-C-atoms in the alkyl groups, respectively. In some instances, we considered it appropriate to take into account the conformational effects, because of the close proximity of the alkyl groups and the cyano group.

4-Alkyl-6-methyl-3-cyano-2-pyridones

The IR stretching frequencies of characteristic groups in alkyl substituted 3-cyano-2-pyridones 1a-g are shown in Table 1. As the correlation with Hammett σ constants failed, it was considered appropriate to correlate first the very distinctive CN group frequency with steric constants υ and Es, because of its *ortho* position to the 4-alkyl group, as the steric effect was to be expected. However, the best correlation has been obtained with υ_{corr} and this is presented in Eq. 2.

Table 1. IR Streching frequencies and ^{1}H NMR chemical shifts for 4-alkyl-6-methyl-3-cyano-2-pyridones

Compd	Substituent	ν_{CN} (KBr) cm^{-1}	ν_{CO} (KBr) cm^{-1}	ν_{ring} (KBr) cm^{-1}	δ_{5H} (DMSO-d$_6$) ppm
1a	Me	2218.8	1661	1629	6.00
1b	Et	2219	1646	1618	6.22
1c	*n*-Pr	2221	1656	1619	
1d	*i*-Pr	2223	1645	1616	6.29
1e	*n*-Bu	2222	1646	1615	
1f	*i*-Bu	2224	1646	1622	
1g	*t*-Bu	2226.5	1630	1556	6.50

$$\nu_{CN} = (2.05 \pm 0.25)\upsilon_{corr} + (2218.68 \pm 0.51) \quad (2)$$

R=0.964, s=0.79, n=7

It is evident from the failure of correlations with the electronic effect substituent constants, and fairly good one with υ_{corr} steric parameter, that the steric effect of the alkyl groups in the *ortho*-position to the CN group is dominant. Considering that inductive effect of the alkyl groups is weak and practically equal, as examplified by the σ_I values (Table 5, section A), this prompted us to introduce the Swain-Lupton parameters as in Eq. 3, together with the υ_{corr}, particularly because of the recent oppinion which supports the preferential use of the field effect.[21]

$$\nu_{CN} = (13.40 \pm 16.02)F + (-16.35 \pm 9.97)R + (2.22 \pm 0.22)\upsilon_{corr} + (2219 \pm 1.60) \quad (3)$$

R = 0.987, s = 0.61, n=7

The above calculation is not statisticaly perfect, in view of the high standard deviation of the F term, although the standard deviation value and the Fisher test (38.82) are affirmative. Evidently, the steric effect of the *ortho* cyano group restricts the free rotation of the bulkier alkyl groups and hence the iregular field effect and the negative sign of the R-term. It should be mentioned that correlation of the same data with only F and R parameters was completely unacceptable (R=0.40, s=3.10, F=0.36).

Correlation of the ν_{CO} values for the 1a-g series from Table 1 was logically tried with Hammett σ_m constants, as in Eq. 4, but this was improved by the inclusion of the steric parameter υ shown in Eq. 5.

$$\nu_{CO} = (670.73 \pm 88.48)\sigma_m + (1697.93 \pm 6.79) \quad (4)$$

R=0.959, s=3.03, n=7

$$\nu_{CO} = (520.94 \pm 71.19)\sigma_m + (-12.33 \pm 3.91)\upsilon + (1696 \pm 4.11) \quad (5)$$

R=0.988, s=1.82, n=7

The neccessity to include the steric factor in the calculation of the CO group vibration frequencies shows that an interference of the bulky alkyl groups with the CN substituent occurs. The correlation is even better with υ_{corr} as in Eq. 6, which further confirms the importance of conformational effects. It is possible that this causes attenuation of the resonance effect transmission, which is evident also from negative signs of the steric parameters in Equations 5 and 6.

$$\nu_{CO} = (526.98 \pm 47.18)\sigma_m + (-2.51 \pm 0.51)\upsilon_{corr} + (1691.16 \pm 3.16) \qquad (6)$$

R = 0.994, s = 1.27, n = 7

Correlations of the pyridone ring stretching frequencies as influenced by alkyl groups in position 4 of the heterocyclic 2-pyridone nuclei in the 1a-g series, were expected to be reasonably good with the corresponding steric constants constants υ and the Es values, considering the rather weak electronic effects of this groups. However, these models failed, but fairly good results were obtained with the corrected Charton constant υ_{corr} which is shown in Eq. 7. It appears that these constants, corrected for the C-C branching at the *alpha*- and *beta*-carbons in the substituent alkyl groups, also account for the hyperconjugation and its effect on the electron density in the heterocyclic ring. This is consistent to the statement relating to the Eq. 6, that the restriction of the free rotation of the bulkier alkyl groups also affects hyperconjugational resonance interaction.

$$\nu_{ring} = (0.19 \pm 0.01)\upsilon_{corr} + (0.46 \pm 0.03) \qquad (7)$$

R=0.982, s=0.05, n=7

Table 2. IR Streching frequencies for 4(6)-aryl-6(4)-methyl-3-cyano-2-pyridones (KBr)

Compd	Substituent	ν_{CN} (KBr) cm^{-1}	ν_{CO} (KBr) cm^{-1}	ν_{ring} (KBr) cm^{-1}
4-Aryl substitution				
2a	p-OCH_3	2220	1662	1611
2b	H	2222	1661	1626
2c	p-Br	2221	1663	1625
2d	p-Cl	2222.13	1663	1627
2e	m-NO_2	2221.17	1666	1625
2f	p-NO_2	2221	1660	1635
6-Aryl substitution				
3a	p-OCH_3	2218.77	1621	1570
3b	H	2223.38	1626	1577
3c	p-Br	2223.87	1662	1609
3d	p-Cl	2224.81	1667	1598
3e	m-NO_2	2230.00	1657	1621
3f	p-NO_2	2228.74	1660	1625

For the recording of ^{1}H NMR chemical shifts in the series 1a-g the only available hydrogens were those of the 6-methyl group and the heterocyclic 5H. The values for the 6-methyl hydrogens and the 5H were very close in the spectra taken in CF_3COOH, almost equal, and the correlations were pointless. The investigation was also hindered by the low solubility of the compounds in DMSO-d_6 and $CDCl_3$, and it was possible to determine the 5H chemical shifts for four compounds only (Me, Et, i-Pr, t-Bu). These results are presented in Table 1. The data were correlated with Charton's constants's υ, but the regression coefficient was very low (R= 0.909). It was much better with υ_{corr} as shown in Eq. 8. An even better result was obtained with a two parameter equation using both υ and υ_{corr}, R=0.998, s=0.02, but the use of that model was not justified for such a small number of data points. Nevertheless, the qualitative conclusion about the effects of the alkyl groups in the *ortho*- position both upon the hydrogen in the position 5 and to the cyano group is the same as for the IR spectra, namely that the governing factor is the branching in the alkyl group.

$$\delta_{5H} = (0.12 \pm 0.03)\upsilon_{corr} + (6.07 \pm 0.06) \qquad (8)$$

R=0.947, s=0.08, n=4

The UV spectra for 4-alkyl-6-methyl-3-cyano-2-pyridones were recorded in ethanol in the interval 270-400 nm , but the ν_{max} values were very close and impossible to correlate.

Table 3. ^{1}H NMR Chemical shifts for 4(6)-aryl-6(4)-methyl-3-cyano-2-pyridones (CF_3COOD)

Compd	Substituent	δ_{5H} ppm	δ_{CH_3} ppm
4-Aryl substitution			
2a	p-OCH_3	6.92	2.63
2b	H	6.95	2.68
2c	p-Br	6.89	2.70
2d	p-Cl	6.86	2.62
2e	m-NO_2	6.92	2.72
2f	p-NO_2	6.90	2.72
6-Aryl substitution			
3a	p-OCH_3	7.20	2.73
3b	H	7.20	2.72
3c	p-Br	7.15	2.78
3d	p-Cl	7.16	2.78
3e	m-NO_2	7.22	2.78
3f	p-NO_2	7.20	2.80

Table 4. UV Absorption frequencies in the spectra of 4(6)-aryl-6(4)-methyl-3-cyano-2-pyridones*

Compd	Substituent	ν cm^{-1} 10^{-3}
4-Aryl substitution		
2a	p-OCH_3	31.25
2b	H	29.07
2c	p-Br	28.99
2d	p-Cl	28.82
2e	m-NO_2	28.49
2f	p-NO_2	28.33
6-Aryl substitution		
3a	p-OCH_3	27.62
3b	H	28.49
3c	p-Br	28.09
3d	p-Cl	27.93
3e	m-NO_2	28.49
3f	p-NO_2	28.25

*C_o=12x10^{-5} M (ethanol)

(4,6)-Substituted aryl-(6,4)-substituted methyl-3-cyano-2-pyridones (2a-f and 3a-f)

There was initially a dilema what sets of parameters to use for correlations of the effects of substituents in the phenyl ring which are substituents itself on the positions 4 and 6 in the pyridone nucleus. The obvious choice would be the same as those for substituted phenyl groups (Table 5, section C)[15,16] but the corresponding calculation results were not always satisfactory, with few exceptions. Comparison of the two sets of parameters, m/p and F/R scales,[15] both for "ordinary" Hammett substituent constants and for phenyl substituted rings, show that the values of the later are smaller. Except for the unsubstituted phenyl group, for which the substituent constant is determined from the dissociation of substituted benzoic acids,[13] the substituent constants for other substituted rings were determined from dissociation of phenylacetic acids,[16] and this may be the reason for the differences in parameter values. For the substituted phenyl groups, both inductive and resonance effects are attenuated, and probably not proportionally transmitted through the methylene group, and hence the unsatisfactory correlations. Alternatively, one could take substituent effects as transmited from m/p positions in the phenyl ring to the atoms 4 and 6 in the pyridone ring. In these calculations, for the unsubstituted phenyl groups σ constants and steric constants had to be zero, as for hydrogen, taking that the steric effect of the phenyl group is constant. This approach is again not sufficiently precise, as the observed pyridone substituents are in *ortho*-, *meta*- and *para*-positions. This is probably the reason why the correlations with the F/R scale are statistically more satisfactory, because this model describes substituents in the *meta*- and *para*-positions in the same way.

Table 5. Substituent constants used in calculations (Eqs. 2 – 18)

Section	Substituent	σ_m[15]	σ_p[15]	σ_I[16]	σ_R[16]	υ[16]	υ_{corr}	F[15]	R[15]
A	Me	-0.07	-0.17	-0.01	-0.16	0.52	0	0.01	-0.18
	Et	-0.07	-0.15	-0.01	-0.14	0.56	0.56	0.00	-0.15
	n-Pr	-0.06	-0.13	-0.01	-0.16	0.68	1.36	0.01	-0.14
	i-Pr	-0.04	-0.15	0.01	-0.16	0.76	1.52	0.04	-0.19
	n-Bu	-0.08	-0.16	-0.01		0.68	1.36	-0.01	-0.15
	i-Bu	-0.07	-0.12	-0.01		0.98	2.94	-0.01	-0.11
	t-Bu	-0.10	-0.20	-0.01	-0.18	1.24	3.72	-0.02	-0.18
B	OMe	0.12	-0.27	0.30	-0.59	0.36		0.29	-0.56
	H	0.00	0.00	0.00	0.00	0.00		0.03	0.00
	Br	0.39	0.23	0.47	-0.25	0.65		0.45	-0.22
	Cl	0.37	0.23	0.47	-0.25	0.55		0.42	-0.19
	NO_2	0.71	0.78	0.67	0.10	1.39		0.65	0.13
C	p-OMe-C_6H_4	0.05	-0.08					0.13	-0.21
	C_6H_5	0.06	-0.01			2.15		0.12	-0.13
	p-Br-C_6H_4	0.15	0.12					0.18	-0.06
	p-Cl-C_6H_4	0.15	0.12					0.18	-0.06
	m-NO_2-C_6H_4	0.21	0.20					0.23	-0.03
	p-NO_2-C_6H_4	0.25	0.26					0.26	0.00

The characteristic IR stretching frequencies of the CN, CO and ring as influenced by the substituted aryl groups in positions 4 and 6 in the 2-pyridone nucleus are given in Table 2 (2a-f and 3a-f series). In all the equations which follow, the measured frequency item has a superscript which denotes the position of the aryl substituent in the 2-pyridone nucleus, and the subscript which shows the group in the molecule whose frequency has been measured.

Correlations for the CN group were first done with $\sigma_{m/p}$ constants for the phenyl group (Table 5, section C), for compounds in the 2a-f and 3a-f series, but the results were poor. The use of Hammett $\sigma_{m/p}$ constants (Table 5, section B), according to position of substituents in the phenyl groups in 4 and 6 phenyl substituted 2-pyridones, gave satisfactory result for the 6-isomer, and with the steric factor υ for the 4-isomer, as shown in Eqs. 9 and 10.

$$\nu_{CN}^{4} = (4.03 \pm 1.58)\sigma_{m/p} + (-2.90 \pm 0.84)\upsilon + (2222.20 \pm 1.40) \qquad (9)$$

R=0.900, s=0.43, n=6

$$\nu_{CN}^{6} = (10.05 \pm 0.92)\sigma_{m/p} + (2221.95 \pm 0.43) \qquad (10)$$

R=0.983, s=0.84, n=6

The correlation was also performed with F and R parameters (Table 5, section B), but it was statistically acceptable only for the 6-phenyl substituted compounds (3a-f series):

$$\nu_{CN}^{6} = (10.08 \pm 1.08)F + (-1.70 \pm 3.11)R + (2222.43 \pm 0.99) \qquad (11)$$

R=0.985, s=0.92, n=6

With both sets of parameters (Table 5, section B), the results are better for compounds 3a-f, even with steric υ included for the compounds 2a-f (Eq. 9), to compensate for the strong steric interaction with the *orto* phenyl substituent. Besides, by taking the value υ=0 for the unsubstituted phenyl group, it is assumed that the steric effect of the phenyl nucleus is constant in the series, which is probably not entirely true.

It was logical to expect that the correlations for the CO frequencies should be first tried with the Hammett σ_m constants, but the results were poor. Better correlations were obtained with the extended Hammett equation but σ_m and Charton's steric parameter υ had to be included (Table 5, section B) but the results were unacceptable, on the ground of statistical insufficiency, because of too many parameters in the multiparameter equations for only six data points. Swain-Lupton approach was indicated but it was successful only for the 6-aryl isomer (3a-f series) with the substituent parameters for the phenyl group (Table 5, section C), and this is presented in Eq. 12.

$$\nu_{CO}^{6} = (176.00 \pm 42.52)F + (372.63 \pm 31.28)R + (-14.80 \pm 1.63)\upsilon + (1727.53 \pm 10.91) \qquad (12)$$

R = 0.997, s= 2.29, n=6

This equation is also not statistically perfect, the scattering of the data points being high, but at least an idea of the effects of substituents on the CO group in 2-pyridones could be obtained.

Because of the nature of the probable interaction of substituted aryl nuclei with the 2-pyridone heterocyclic ring, it was considered appropriate to correlate corresponding IR frequencies (Table 2) with the extended Hammett equation (DSP equation). The correlations, for the series 2a-f, were only fair, but became better, by inclusion of the steric parameter υ, which lowered its statistical reliability. Therefore the calculation for this series was performed using the Swain Lupton parameters (Table 5, secton C) as in Eq.13:

$$\nu_{ring}^{4} = (-98.36 \pm 43.43)F + (148.98 \pm 31.12)R + (1655 \pm 10.26) \qquad (13)$$

R=0.958, s=2.6, n=6

which is more satisfactory from statistical point of view. The correlation for 3a-f series with DSP equation is fairly good, probably because of less steric perturbancies, Eq.14:

$$v_{ring}^{6} = (66.07 \pm 12.91)\sigma_I + (37.75 \pm 12.16)\sigma_R + (1577.19 \pm 6.95) \quad (14)$$

R=0.971, s=6.95, n=6

For comparison, the calculation with F and R parameters is also done for 3a-f series, Eq.15:

$$v_{ring}^{6} = (217.65 \pm 96.84)F + (145.37 \pm 69.40)R + (1572 \pm 23.00) \quad (15)$$

R=0.982, s=5.52, n=6

This correlation is better in view of correlation coefficient, overal standard deviation, as well as the overal reliability (Fisher test 40.82 as compered with 25.18 for Eq.14) but less favourable if standard errors of F and R terms are considered.

There were not enough data for ^{1}H NMR spectra in DMSO-d$_6$, for 2a-f and 3a-f series of the substitution types due to the insolubility of the compounds, and the spectra for both were taken in CF$_3$COOD.[1] These data are given in Table 3. However, correlation for the heterocyclic 5H was not statistically acceptable for series 2a-f, and not at all possible for series 3a-f. The correlations for the ^{1}H NMR data for methyl hydrogens for both series, were attempted with σ_m constants for the substituted phenyl groups (Table 5, section C) but only that for the 4-methyl group in 6-phenyl substituted isomer was successful and is presented in Eq.16:

$$\delta_{CH_3}^{6} = (0.33 \pm 0.04)\sigma_m + (2.72 \pm 0.01) \quad (16)$$

R=0.965, s=0.01, n=6

The calculations using DSP equation and Swain-Lupton equation, gave rather inferior correlations of the ^{1}H NMR data, the regression coefficients amounting only up to 0.850 and with high standard errors. The results were much better if Charton's steric parameter was included, but these calculations were objectionable because of statistic insuficiency. However, this should be noted because it is still another proof of how important are the steric effects in investigated compounds.

The UV spectra of 4- and 6-substituted aryl, 6- and 4-methyl derivatives were determined in ethanol in the interval 200-400 nm, and the corresponding v cm^{-1} 10^{-3} values are given in Table 4. The correlation for 4-substituted aryl-6-methyl-3-cyano-2-pyridones (series 2a-f) was fairly good with Hammett σ_p values, Eq. 17.

$$v_{UV}^{4} = (-0.05 \pm 0.01)\sigma_P + (15.44 \pm 2.63) \quad (17)$$

R=0.958, s=0.21, n=5

The correlations of the v_{UV}^{4} for the series 2a-f were done also with the three parameter equations comprising σ_I, σ_R, F and R, but needed the inclusion of the steric parameter υ. In both calculations the correlation coefficients were acceptable but the standard errors were large. However, all calculations for 6-substituted aryl-4-methyl-3-cyano-2-pyridones (series 3a-f) were poor.

The apparent differences in the behaviour of the 4- and 6-aryl substituted derivatives in the transmission of substituent effects, as visible in their UV spectra, could be explained by greater symmetry of the 4-aryl substituted molecules and the electronic effect disturbances because of the close proximity of the three substituents, namely 6-substituted aryl, NH and CO group in the 6-aryl substitution.

It was of interest to try the intercorrelation of the data for IR_{ring} stretching frequencies from Table 2. and the UV absorption maxima from Table 4, which we believed to reflect the similarity of substituents' interaction with π-electrons in the 2-pyridone nuclei. The correlation for the 4-aryl substitution (series 2a-f) is fairly good, as presented in Eq. 18, while for the 6-aryl substitution the correlation was poor, probably due to less symetry of the 6-aryl substituted molecules 3a-f.

$$\nu^{4}_{IR_{ring}} = (-5.31 \pm 0.97)\nu^{4}_{UV} + (1778 \pm 28.28) \qquad (18)$$

R=0.940, s=2.31, n=6

Experimental Section

General Procedures. All substances whose spectral characteristics are presented in the present paper and were used for correlations with the LFER parameters, were synthesised by literature methods or by analogy to those, sometimes by modified procedures. They were fully characterized by IR, NMR and UV spectra in our previous communications[1-5] and some of the spectra were rechecked or redetermined on more modern equipment.

The LFER equations[13] and substituent constants[15,16] used for calculation were taken from the standard texts on the subject. Those actually used are presented in Table 5.

The instruments used in the investigation are as follows: IR spectra were recorded on a Bomem MB 100 FTIR spectrophotometer. UV data were obtained using a Shimadzu UV A 160 spectrophotometer. ^{1}H NMR spectra were determined in an appropriate solvent on a Varian-Gemini 200 MHz spectrometer using TMS as internal standard.

Conclusions

The pyridone nucleus of relatively low aromaticity, is very heavily substituted and, practically, only one position the 5H, is free. There are the possibilities for substituent interactions, both electronic and particularly steric, not always adequately accounted for by the used substituent constants. However, the general trends can be estimated. One conclusion is that in both 4- and 6-

aryl substitution, the phenyl and heterocyclic nuclei are not co-planar, and that deviations vary with the type of substitution. Hence, the high standard errors in some of the models employed, although the regression coefficients were fairly satisfactory. We believe that these shortcomings will be overcomed in our further investigations of the effect of substituents on the NH group in the 3-cyano-2-pyridone nucleus, and the study of the ^{13}C NMR spectra.

Acknowledgments

D.Mijin acknowledges the financial support of the Ministry of Science and Environmental Protection of the Republic of Serbia (project 142063). The authors are grateful to professors K.Bowden and J.Shorter for useful suggestions. We are also indebted to Dr Nataša Valentić for discussions and suggestions, on the choice of parameters for LFER analysis.

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