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# SUBSTITUENT EFFECT ON IR, $^{1}$H- AND $^{13}$C-NMR SPECTRAL DATA IN *N*-(SUBSTITUTED PHENYL)-2-CYANOACETAMIDES: A CORRELATION STUDY

*Linear free energy relationships (LFER) were applied to the IR, $^{1}$H- and $^{13}$C--NMR spectral data of N-(substituted phenyl)-2-cyanoacetamides. A variety of substituents were employed for phenyl substitution and fairly good correlations were obtained using the simple Hammett and the Hammett-Taft dual substituent parameter equations. The correlation results of the substituent induced $^{13}$C-NMR chemical shifts (SCS) of the C1, C=O and N-H atom indicated different sensitivity with respect to electronic substituent effects. A better correlation of the $SCS_{C=O}$ with a combination of electrophilic and nucleophilic substituent constants indicated a significant contribution of extended resonance interaction ($\pi$-delocalization) within the $\pi_1$-unit. The conformations of the investigated compounds were studied using the DFT B3LYP/6-311G** method and, together with the results of $^{13}$C-NMR and IR spectroscopic studies, a better insight into the influence of such a structure on the transmission of electronic substituent effects was obtained.*

*Keywords: N-(substituted phenyl)-2-cyanoacetamides, LFER analysis, IR and NMR spectra, SCS shift, Hammett equation.*

Cyanoacetamides are important compounds, which, due to their high reactivity, are frequently used as intermediates for the preparation of various organic and often heterocyclic compounds [1,2]. The starting cyanoacetamides, as well many derivatives of cyanoacetamides, show diverse biological activity. Examples can easily be found in the literature, *e.g.*, antitumor activity [3], insecticidal activity [4], fungicidal activity [5], or algicidal, bactericidal and fungicidal activities [6-8]. Some derivatives are also used as dyes [9,10].

Previous investigations into the chemistry of amides included the synthesis and identification of new compounds, as well as a mass spectral study [11,12]. In addition, the UV absorption spectra of *N*--(4-substituted phenyl)-2,3-diphenylpropanamides [13] in various solvents, and the mass fragmentation of *N*--alkyl and *N*-(substituted phenyl)-2-cyanoacetamides [14] were recently published.

The conformations of various *N*- and *N,N*-substituted-2-phenylacetamides have been extensively studied in our previous works [15-17]. Studies employing infrared and $^{1}$H-NMR spectroscopy have provided valuable information on the *cis* and *trans* conformational isomers.

In the first part of this work, a series of *N*-(substituted phenyl)-2-cyanocetamides was synthesized (Figure 1), and results of syntheses are given in Table 1. In the second part of the work, linear free energy relationships (LFER) were applied to the IR absorption frequencies, and $^{1}$H- and $^{13}$C-NMR substituent chemical shifts (*SCS*) in *N*-(substituted phenyl)-2-cyanoacetamides, with the aim of obtaining insight into the factors determining the chemical shifts in the investigated compounds. The transmission of polar (field/inductive) and resonance electronic effects in the *N*-(substituted phenyl)-2-cyanoacetamides (Figure 1a) from the substituent (X) in the phenyl group to the carbon atoms of interest, as well as to the N-H hydrogen, were studied using Eqs.(1)-(3):

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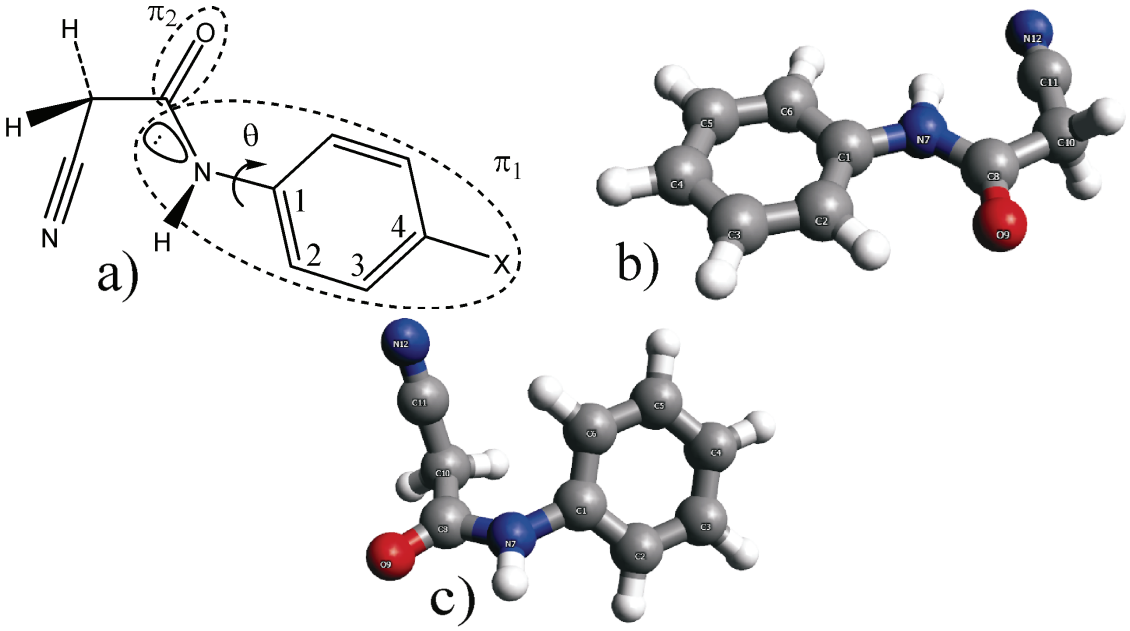


*Figure 1. General structure of the N-(substituted phenyl)-2-cyanoacetamides with labels of the nuclei under investigation and π-resonance units (a), as well as optimized trans- (b) and cis-conformation (c) of N-phenyl-2-cyanoacetamide.*

$$s = \rho\sigma + h \text{ or } s = \rho\nu + h \quad (1)$$

$$s = \rho_I\sigma_I + \rho_R\sigma_R + h \quad (2)$$

$$s = fF + rR + h \quad (3)$$

where $s$ are substituent-dependent values: substituent chemical shifts (*SCS*) or absorption frequencies ($\nu$), $\rho$ is a proportionality constant reflecting the sensitivity of the $^{1}$H- and $^{13}$C-NMR chemical shifts and IR frequencies to the substituent effects, $\sigma$, $F$ and $R$ are the corresponding substituent constants, and $h$ is the intercept (*i.e.*, it describes the unsubstituted member of the series) [18].

Equation (1) (the simple Hammett Equation - SSP) attributes the observed substituent effect to an additive blend of polar and $\pi$-delocalization effects given as corresponding the $\sigma$ values. In the dual-substituent parameter (DSP) Eqs. (2) (the extended Hammett Equation) and (3) (the Swain-Lupton Equation), $s$ are correlated by a linear combination of inductive ($\sigma_I$) and various resonance scales ($\sigma_R^o$, $\sigma_R$ and $\sigma_R^+$), or Swain-Lupton $F$ and $R$ values, depending on the electronic demand of the atom under examination. Calculated values $\rho_I$ and $\rho_R$, as well as $f$ and $r$, are relative measures of the transmission of the inductive and resonance effects through the investigated system.

SSP and DSP equations were applied to study transmission of substituent effects using NMR and IR data in different compounds. For example, *E*-2-benzylidenebenzocycloalkanones [19,20], 6-arylidenedibenzo[*b*,*e*]thiepin-11-one-5,5-dioxides [21], 4,6-disubstituted-3-cyano-2-pyridones [22], 3-cyano-4-(substituted phenyl)-6-phenyl-2(1*H*)pyridones [23], 4-substituted phenyl-4,5-dihydrobenzo [f] [1,4]oxazepin-3(2*H*)-ones(thiones) [24], substituted benzaldehyde [25], 4-bromo-1-naphthyl chalcones [26] were studied in such manner.

As a continuation of the *cis*/*trans* conformational study of amides [15-17], FTIR and DFT studies of *N*-(4-substituted phenyl)-2-cyanoacetamides were performed in this work. In order to examine the state of equilibrium, *i.e.*, equilibrium ratio of *cis*/*trans* isomers in carbon tetrachloride, we wish to report the results of an FTIR spectroscopic study of *N*-(4-substituted phenyl)-2-cyanoacetamides. The results of DFT calculations suggest that the investigated amides achieve nearly planar conformations in *trans* conformation. The contributions from the electronic substituent effects and the other factors that determine chemical shifts are discussed in relation to calculated geometries. Both optimized *trans* and *cis* conformations of *N*-phenyl-2-cyanoacetamide are presented in Figures 1b and 1c, respectively.

## EXPERIMENTAL

### Methods of synthesis of *N*-(substituted phenyl)-2-cyanoacetamides

All the investigated amides were synthesized according to known methods (Figure 2).

*Method A*. Equimolar amounts of amine and ethyl cyanoacetate (0.17 mol) were heated at 150 °C

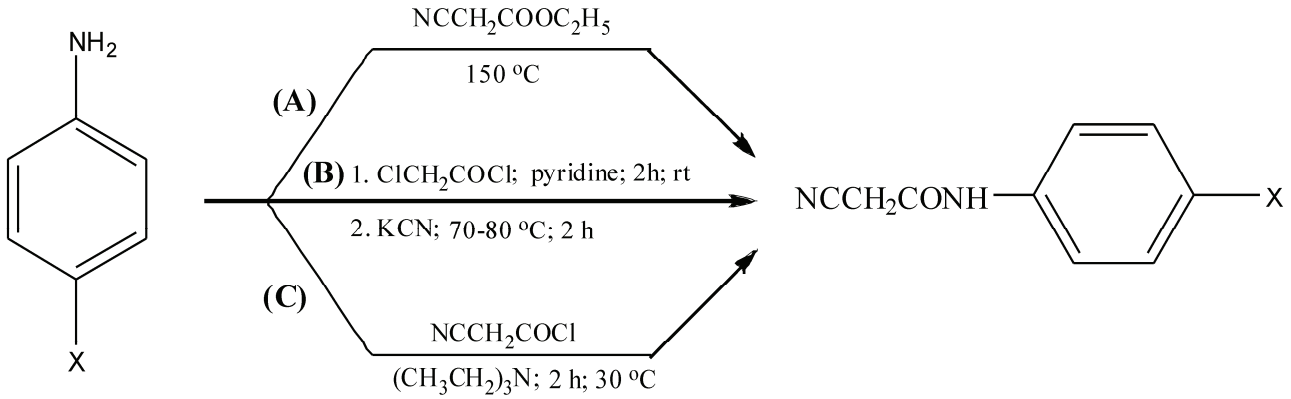


*Figure 2. Methods of N-(substituted phenyl)-2-cyanoacetamides syntheses.*

for 4 h. After cooling to room temperature, the obtained solid was filtrated and purified by crystallization from ethanol [27].

*Method B*. chloroacetyl chloride (0.05 mol) was added to a mixture of benzene (100 cm$^3$), dry pyridine (0.45 mol) and substituted aniline (0.45 mol) under mixing. The mixture was stirred for 2 h at room temperature. The formed solid was then removed by filtration and rinsed with water [28]. After drying, the obtained *N*-(substituted phenyl)-2-chloroacetamide (33 mmol) was dissolved in ethanol (35–120 cm$^3$). A solution of potassium cyanide (46 mmol) in water (5 cm$^3$) was then added drop-wise. The reaction mixture was then mixed at 70–80 °C for 2 h and finely mixed with iced water (100 cm$^3$). The solid was then removed by filtration, rinsed with ethanol and purified by crystallization from ethanol [29].

*Method C*. Cyanoacetyl chloride (11 mmol) was added to a mixture of solvent (50 cm$^3$), triethylamine (1.4 cm$^3$) and substituted aniline (0.45 mol) at 30 °C and stirred for 2 h. The formed solid was then removed by filtration and rinsed with water. The reaction mixture for the preparation of compounds **8** and **9** were acidified before removal of the solid. After drying, the product was purified by crystallization from ethanol [30].

Cyanoacetyl chloride was prepared from cyanoacetic acid and phosporus(V) chloride in dry carbon tetrachloride [31], and used immediately for the synthesis due to its great instability. All other reagents were commercially obtained.

The yields and melting points of the synthesized *N*-(substituted phenyl)-2-cyanoacetamides are given in Table 1.

### Instrumental techniques

Fourier-transform infrared (FTIR) spectra of *N*--(4-substituted phenyl)-2-cyanoacetamides were recorded in the transmission mode, in KBr form and in carbon tetrachloride solution ($10^{-3}$ mol dm$^{-3}$), using a BOMEM (Hartmann&Braun) spectrometer.

$^1$H- and $^{13}$C-NMR spectra were determined in deutared DMSO-$d_6$ using a Varian-Gemini 200 MHz spectrometer using TMS as an internal standard. The chemical shifts are expressed in ppm values referenced to TMS ( $\delta_H$ = 0 ppm) in the $^1$H-NMR spectra, and the residual solvent signal ( $\delta_C$ = 39.5 ppm) in $^{13}$C--NMR spectra. The chemical shifts were assigned by the complementary use of DEPT-, two dimensional $^1$H-$^{13}$C correlation HETCOR- and by selective INEPT

*Table 1. Method of synthesis, yields and melting points of the studied N-(substituted phenyl)-2-cyanoacetamides*

| Compound | Substituent | Method | Lit. m.p., °C | m.p., °C | Yield, % |
|---|---|---|---|---|---|
| **1** | H | A | 198 [32] | 198-200 | 47.3 |
| **2** | $CH_3$ | B | 186-187[30] | 181-183 | 70.2 |
| **3** | $OCH_3$ | B | 134-135 [30] | 133-134 | 59.6 |
| **4** | Br | B | 198-200 [30] | 193-195 | 60.6 |
| **5** | Cl | B | 198-199 [30] | 195-196 | 57.4 |
| **6** | $NO_2$ | C[a] | 198-202 [30] | 214-216 | 45.4 |
| **7**[b] | OH | C[c] | - | 218-220 | 48.5 |
| **8**[b] | COOH | C[d] | - | 168-170 | 65.0 |
| **9**[b] | $SO_3H$ | C[d] | - | 191-193 | 46.2 |
| **10**[b] | $COCH_3$ | C[a] | - | 192-193 | 53.3 |

[a]Diethyl ether; [b]new compounds; [c]2-butanone; [d]water

long-range experiments. All spectra were recorded at ambient temperature.

### Computational details

In order to find the optimal geometry of *cis* and *trans* isomers, conformational search of all possible conformers was done. In both isomers there are two rotatable bonds, C1-N7 and C8-C10 (Figure 1b). Complete potential energy surface (PES) scan was done for each rotatable bond with the DFT method, namely B3LYP functional using triple-zeta basis set, 6-311G** [33]. All the energies were calculated in DMSO and carbon tetrachloride solution using static isodensity surface polarized continuum (IPMC) model with B3LYP/6-311G** method. IR frequencies were calculated on optimized geometry with B3LYP method and 6-311G** basis set. All structures were fully optimized, *i.e.*, with zero negative frequencies. All calculated frequencies were scaled by a factor of 0.9619, as recommended in [34]. NMR chemical shifts were calculated on the gas-phase optimized structure using GIAO calculations in DMSO as a solvent, with the specially parameterized WP04 functional of Cramer *et al.*, using the cc-pVDZ basis set. This method was proven to give best accuracy/cost ratio in NMR chemical shift prediction [35]. The values of chemical shifts presented in Table 2 are calculated relative to TMS. All DFT calculations were done in Gaussian G03 program package [33].

### $^1$H- and $^{13}$C-NMR spectral data

*N-phenyl-2-cyanoacetamide (**1**)*. $^1$H-NMR ($CDCl_3$): $\delta$ 3.91 (2H, *s*, $CH_2$-CN), 7.09 (1H, *t*, $J_{HH}$ = 7.4 Hz, Ar-H), 7.34 (2H, *t*, $J_{HH}$ = 8.2 Hz, Ar-H), 7.57 (2H, *d*, $J_{HH}$ = = 8.2 Hz, Ar-H), 10.33 (1H, *s*, NH). $^{13}$C-NMR ($CDCl_3$): $\delta$ 26.97 ($\underline{C}H_2$-CN), 116.23 (CN), 119.52 (2C ring), 124.17 (1C ring), 129.17 (2C ring), 138.66 (1C ring), 161.31 (CO).

*N-(4-methylphenyl)-2-cyanoacetamide (**2**)*. $^1$H-NMR ($CDCl_3$): $\delta$ 2.25 (3H, *s*, $CH_3$), 3.87 (2H, *s*, $CH_2$-CN), 7.13 (2H, *d*, $J_{HH}$ = 8.4 Hz, Ar-H), 7.44 (2H, *d*, $J_{HH}$ = 8.2 Hz, Ar-H), 10.22 (1H, *s*, NH). $^{13}$C-NMR ($CDCl_3$): $\delta$ 20.65 ($CH_3$), 26.88 ($\underline{C}H_2$-CN), 116.26 (CN), 119.62 (2C ring), 129.56 (2C ring), 133.20 (1C ring), 136.15 (1C ring), 161.12 (CO).

*N-(4-methoxylphenyl)-2-cyanoacetamide (**3**)*. $^1$H-NMR ($CDCl_3$): $\delta$ 3.72 (3H, *s*, $OCH_3$), 3.86 (2H, *s*, $CH_2$-CN), 6.91 (2H, *d*, $J_{HH}$ = 9.0 Hz, Ar-H), 7.47 (2H, *d*, $J_{HH}$ = 8.8 Hz, Ar-H), 10.18 (1H, *s*, NH). $^{13}$C-NMR ($CDCl_3$): $\delta$ 26.74 ($\underline{C}H_2$-CN), 55.38 ($OCH_3$), 114.26 (CN), 116.32 (2C ring), 121.13 (2C ring), 131.74 (1C ring), 155.92 (1C ring), 160.76 (CO).

*N-(4-bromophenyl)-2-cyanoacetamide (**4**)*. $^1$H-NMR ($CDCl_3$): $\delta$ 3.91 (2H, *s*, $CH_2$-CN), 7.18 (2H, *t*, $J_{HH}$ = 9.0 Hz, Ar-H), 7.57 (2H, *d*, $J_{HH}$ = 8.8 Hz, Ar-H), 10.38 (1H, *s*, NH). $^{13}$C-NMR ($CDCl_3$): $\delta$ 20.86 ($\underline{C}H_2$-CN), 115.55 (CN), 116.16 (1C ring), 121.29 (2C ring), 134.98 (2C ring), 156.21 (1C ring), 161.27 (CO).

*N-(4-chlorophenyl)-2-cyanoacetamide (**5**)*. $^1$H-NMR ($CDCl_3$): $\delta$ 3.93 (2H, *s*, $CH_2$-CN), 7.39 (2H, *d*, $J_{HH}$ = 8.6 Hz, Ar-H), 7.59 (2H, *d*, $J_{HH}$ = 8.8 Hz, Ar-H), 10.46 (1H, *s*, NH). $^{13}$C-NMR ($CDCl_3$): $\delta$ 27.03 ($\underline{C}H_2$-CN), 116.06 (CN), 121.07 (2C ring), 127.79 (1C ring), 129.10 (2C ring), 137.57 (1C ring), 161.51 (CO).

*N-(4-nitrophenyl)-2-cyanoacetamide (**6**)*. $^1$H-NMR ($CDCl_3$): $\delta$ 4.04 (2H, *s*, $CH_2$-CN), 7.80 (2H, *d*, $J_{HH}$ = 9.4 Hz, Ar-H), 8.23 (2H, *d*, $J_{HH}$ = 9.0 Hz, Ar-H), 10.93 (1H, *s*, NH). $^{13}$C-NMR ($CDCl_3$): $\delta$ 27.43 ($\underline{C}H_2$-CN), 115.81 (CN), 119.25 (2C ring), 125.33 (2C ring), 142.92 (1C ring), 144.70 (1C ring), 162.51 (CO).

*N-(4-hydroxyphenyl)-2-cyanoacetamide (**7**)*. $^1$H-NMR ($CDCl_3$): $\delta$ 3.82 (2H, *s*, $CH_2$-CN), 6.73 (2H, *d*, $J_{HH}$ = 8.8 Hz, Ar-H), 7.34 (2H, *d*, $J_{HH}$ = 8.8 Hz, Ar-H), 9.31 (1H, *s*, OH), 10.05 (1H, *s*, NH). $^{13}$C-NMR ($CDCl_3$): $\delta$ 26.68 ($\underline{C}H_2$-CN), 115.55 (CN), 116.41 (2C ring), 121.44 (2C ring), 130.27 (1C ring), 154.17 (1C ring), 160.55 (CO).

*N-(4-carboxyphenyl)-2-cyanoacetamide (**8**)*. $^1$H-NMR ($CDCl_3$): $\delta$ 3.98 (2H, *s*, $CH_2$-CN), 7.71 (2H, *t*, $J_{HH}$ = 8.8 Hz, Ar-H), 7.95 (2H, *d*, $J_{HH}$ = 8.8 Hz, Ar-H), 10.63 (1H, *s*, NH), 12.74 (1H, *s*, COOH). $^{13}$C-NMR ($CDCl_3$): $\delta$ 27.26 ($\underline{C}H_2$-CN), 116.06 (CN), 118.89 (2C ring), 126.08 (1C ring), 130.87 (2C ring), 142.67 (1C ring), 161.97 (CO), 167.19 (COOH).

*N-(4-sulfoxyphenyl)-2-cyanoacetamide (**9**)*. $^1$H-NMR ($CDCl_3$): $\delta$ 3.91 (2H, *s*, $CH_2$-CN), 7.39 (2H, *d*, $J_{HH}$ = 8.8 Hz, Ar-H), 7.67 (2H, *d*, $J_{HH}$ = 8.6 Hz, Ar-H), 10.41 (1H, *s*, NH). $^{13}$C-NMR ($CDCl_3$): $\delta$ 27.06 ($\underline{C}H_2$-CN), 116.03 (CN), 121.64 (2C ring), 126.00 (2C ring), 137.82 (1C ring), 138.44 (1C ring), 161.50 (CO).

*N-(4-acetylphenyl)-2-cyanoacetamide (**10**)*. $^1$H-NMR ($CDCl_3$): $\delta$ 2.55 (3H, *s*, $CH_3$), 3.99 (2H, *s*, $CH_2$-CN), 7.70 (2H, *d*, $J_{HH}$ = 8.8 Hz, Ar-H), 7.97 (2H, *d*, $J_{HH}$ = 8.8 Hz, Ar-H), 10.66 (1H, *s*, NH). $^{13}$C-NMR ($CDCl_3$): $\delta$ 26.66 ($\underline{C}H_2$-CN), 27.28 ($CO\underline{C}H_3$), 116.01 (CN), 118.80 (2C ring), 129.87 (2C ring), 132.51 (1C ring), 142.92 (1C ring), 162.02 (CO), 196.85 ($\underline{C}OCH_3$).

## RESULTS AND DISCUSSION

In order to attain better insight into the transmission of particular substituent effects, as well as the influence of their optimal geometry, an analysis of the IR absorption frequencies, $\nu$, of the N-H, CN and C=O groups, and the $^1$H- and $^{13}$C-NMR chemical shifts of N-H proton, C1 and C=O carbons was performed.

The substitutent induced chemical shifts (*SCS*) of the N-H proton, and the C1 and carbonyl carbon

*Table 2. IR stretching frequencies of the N-H, CN and C=O groups and the SCS values of N-H and C1 and C=O in the N-(substituted phenyl)-2-cyanoacetamides*

| Compd. | $\nu_{N-H}$ / cm$^{-1}$ | $\nu_{CN}$ / cm$^{-1}$ | $\nu_{C=O}$ / cm$^{-1}$ | $SCS_{N-H}$ [a] / ppm | $SCS_{C=O}$ / ppm | | | $SCS_{C1}$ / ppm | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | exp.[b] | *trans*[c] | *cis*[c] | exp.[b] | *trans*[c] | *cis*[c] |
| **1** | 3270.12, 3208.40 | 2259.98 | 1669.31 | 10.33 | 161.31 | 157.18 | 160.22 | 136.66 | 136.45 | 134.49 |
| **2** | 3270.93, 3206.29 | 2259.53 | 1613.29 | -0.11 | -0.19 | -0.25 | 0.52 | -3.51 | -1.79 | -1.94 |
| **3** | 3303.84, 3211.01 | 2259.21 | 1610.47 | -0.15 | -0.55 | -0.74 | 1.77 | -4.92 | -6.82 | -7.25 |
| **4** | 3267.67, 3193.45 | 2246.7 | 1666.67 | 0.05 | -0.04 | 0.38 | 0.39 | 0.38 | -0.81 | 0.20 |
| **5** | 3268.26, 3201.04 | 2246.7 | 1666.21 | 0.13 | 0.20 | 0.38 | 0.52 | 0.91 | -1.17 | -0.39 |
| **6** | 3295.30, 3096.84 | 2268.19 | 1712.19 | 0.60 | 1.2 | 1.97 | -0.01 | 8.04 | 5.87 | 7.18 |
| **7** | 3314.06 | 2269.49 | 1671.17 | -0.28 | -0.76 | -0.91 | 1.56 | -6.39 | -6.44 | -7.00 |
| **8** | 3285.84 | 2269.49 | 1691.89 | 0.30 | 0.66 | 1.04 | -0.05 | 6.01 | 6.14 | 5.18 |
| **9** | 3270.96 | 2260.57 | 1669.18 | 0.08 | 0.19 | 1.74 | -0.09 | 1.78 | 5.18 | 5.59 |
| **10** | 3322.27, 3290.97 | 2259.53 | 1655.45 | 0.33 | 0.71 | 1.08 | 0.07 | 6.26 | 4.55 | 4.71 |

[a]$^{13}$C Chemical shifts (in ppm) expressed relative to the unsubstituted compound, downfield shifts are positive; [b]experimental value; [c]calculated chemical shifts for *trans* and *cis* isomer

atoms of all the cyanoacetamides are given in Table 2, in terms of the substituent chemical shifts relative to the parent compound. Theoretical values for C1 and carbonyl carbon are also given in Table 2. In addition, the IR stretching frequencies of characteristic groups N-H, CN and C=O of the *N*-(substituted phenyl)-2-cyanoacetamides, in the KBr form, are also listed in Table 2.

The general conclusion derived from the data in Table 2 is that all substituents influence *via* their electronic and steric effects the value of the $\nu$, $SCS_{N-H}$ and *SCS* carbons of interest. The *SCS* values in Table 2 indicate that substituents at the aniline ring have a pronounced influence on the electron density at the C1 carbon atom and a lower at the carbonyl carbon. Among the factors contributing to the differences in $\nu$ and the *SCS* values, the geometry of the investigated compounds plays an important role, arising from the out-of-plane rotation of the substituted phenyl rings around the C-N bond for the torsion angles $\theta$ (Figure 1a). Thus, a definite molecular geometry is achieved as a consequence of the particular transmission modes of the substituent electronic effects. Considering the calculated and experimental values of $SCS_{C=O}$ and $SCS_{C1}$, it could be assumed that both isomers exist in DMSO solution, and the recorded average experimental value of *SCS* reflects the contribution of both isomers.

## LFER analysis of the $^1$H- and $^{13}$C-NMR data of the *N*-(substituted phenyl)-2-cyanoacetamides

An extensive analysis of the IR frequencies and the $^1$H- and $^{13}$C-NMR chemical shifts was performed to obtain better insight into the influence of their geometry on the transmission of a particular substituent effect. In order to analyze the influences of the substituents on the *SCS* of the atoms of interest, linear free energy relationships in the form of SSP equation with $\sigma$, $\sigma^-$ or $\sigma^+$ substituent constants [36,37] were applied for the *N*-(substituted phenyl)-2-cyanoacetamides, and the best correlation results are presented in Table 3.

*Table 3. Correlation results of the $SCS_{N-H}$, $SCS_{C=O}$ and $SCS_{Cl}$ in N-(substituted phenyl)-2-cyanoacetamides obtained by the use of SSP, Eq. (1)*

| Atom | Scale | $\rho$ | $h$ | $r$[a] | *s.d.*[b] | $F$[c] | $n$[d] |
|---|---|---|---|---|---|---|---|
| N-H | $\sigma$ | 0.645(±0.052) | -0.017(±0.022) | 0.974 | 0.062 | 151 | 10 |
| | $\sigma$ | 0.528(±0.028) | -0.021(±0.014) | 0.990 | 0.040 | 365 | 10[e] |
| C=O | $\sigma$ | 1.454(±0.122) | 0.109(±0.048) | 0.969 | 0.145 | 142 | 10 |
| | $\sigma$ | 1.478(±0.103) | 0.096(±0.045) | 0.983 | 0.122 | 203 | 9[f] |
| | $\sigma^{+/-}$ | 0.836(±0.052) | 0.005(±0.040) | 0.985 | 0.110 | 254 | 10 |
| | $\sigma^{+/-}$ | 0.841(±0.028) | 0.033(±0.020) | 0.996 | 0.060 | 874 | 9[f] |
| C1 | $\sigma$ | 6.865(±0.358) | -0.305(±0.234) | 0.987 | 0.757 | 363 | 10 |
| | $\sigma$ | 17.252(±1.222) | -0.211(±0.298) | 0.996 | 0.333 | 199 | 4[g] |
| | $\sigma$ | 10.812(±0.637) | -0.481(±0.286) | 0.993 | 0.480 | 288 | 7[h] |

[a]Correlation coefficient; [b]standard deviation; [c]Fisher test; [d]number of data included in the correlation; [e]$\sigma^-$ for **6**; [f]without **4**; [g]electron-donor; [h]electron-acceptor

The results of the SSP correlations for all carbons with $\sigma$ are of good precision, while that for C1 is excellent for separate correlations. The good correlation between *SCS* and $\sigma$ indicates that electronic substituent effects affect *SCS* at the C1 and C=O carbons. According to the observed $\rho$ values for both carbons and the N-H proton, it is apparent that the *SCS* of C1 showed an increased susceptibility to substituent effects (Table 3; lines 7-9), and normal substituent effect was observed for all atoms of interest. The correlation for the C=O carbon was improved if a combination of $\sigma^{+}$ and $\sigma^{-}$ [37] (Table 3; lines 5 and 6), so-called electrophilic and nucleophilic substituent constants, respectively, was used. This result undoubtedly indicates a considerable contribution of the extended resonance interaction of both electron-donor and electron-acceptor substituents from the aniline ring with the $\pi$-electronic density of the carbonyl group. This means that the extended resonance interaction ($\pi$-delocalization) within the $\pi_1$-unit could be effectively transmitted to the C=O group by a resonance and a resonance-induced polar effect [38].

The separate correlations for the C1 carbon with the $\sigma$ constant (Table 3; lines 8 and 9) and the positive values of both correlation coefficients indicate a normal substituent effect, but of different magnitudes. The correlation results (Table 3) for the C1 carbon for electron-acceptor substituted compounds indicates an appropriate contribution of n,$\pi$-conjugation (nitrogen lone pair participation) to the overall electronic interaction within the $\pi_1$-unit (Figure 1a). Somewhat lower influences of the electron-acceptor substituents on the electron density changes at the C1 carbon were observed, which could be consistent with the opposing direction of the electron-accepting character of the whole $\pi_1$-unit and the polarization of the carbonyl group. The appropriate extent of planarity of the electron-accepting carbonyl group enables a higher extent of electronic interaction with the aniline ring. The carbonyl group acts as an electron-acceptor and hence the introduction of an electron-donating substituent enhances its electron-withdrawing ability. In this way, a higher extent of resonance interaction is operative within the $\pi_1$-resonance unit.

Although SSP analysis uses an additive blend of the inductive and resonance parameters of the substituents given as $\sigma$, $\sigma^{+}$ and $\sigma^{-}$ values, it presented a satisfactory tool for a description of the electronic effects of the substituent in correlations using Eq. (1). Evaluation of the separate contributions of the inductive and resonance effects of substituent (X), the regression analysis according to Eq. (3), namely DSP analysis, using the Swain-Lupton *F* and *R* substituent constants [37] was performed. The correlation results obtained by the use of Eq. (3) are given in Table 4, and ones obtained with various combinations of $\sigma_I$ and $\sigma_R^{o}$, $\sigma_R$, $\sigma_R^{+}$, using Eq. (2), had lower statistical values and are not presented.

Generally, both the field and resonance substituent effect had different contribution at all atoms (Table 4). The results of the DSP fits are similar to or slightly better than the SSP correlations. The observed $\rho_F$ and $\rho_R$ values for all carbons indicate a similar contribution of the field and resonance effects, considering the $\lambda$ values. The field effect showed a noticeable alternation regarding the position of a particular atom in molecular structure of the investigated compounds.

The principal deficiency of correlations with $\sigma$ arises from the hybrid natures of these substituent constants; likewise, the field factor cannot be ignored in $\sigma$ value. To obtain resonance values that are satisfactory measures of the resonance potential of substituents, pure field contributions may be obtained by the use of Swain-Lupton constants F and R. From that point of view we obtained better correlation with these constants, which indicate that pure resonance is included in correlations.

The substituents exert relatively small influences on the *SCS* of the N-H proton. The spatial position of the N-H atom with respect to the aniline ring indicates that an anisotropic effect could exist, which has a relatively small contribution to the NMR chemical shifts. The anisotropy effect depends on the spatial arran-

*Table 4. Correlations results of the $SCS_{N-H}$, $SCS_{C=O}$ and $SCS_{Cl}$ in N-(substituted phenyl)-2-cyanoacetamides obtained by the use of DSP, Eq. (3)*

| Atom | $\rho_F$ | $\rho_R$ | *h* | *r* | *s.d.* | *F* | $\lambda^{a}$ | *n* |
|---|---|---|---|---|---|---|---|---|
| N-H | 0.690 (±0.059) | 0.690(±0.087) | -0.005(±0.035) | 0.995 | 0.051 | 116 | 1.00 | 10 |
| | 0.738 (±0.053) | 0.683(±0.035) | -0.010(±0.020) | 0.996 | 0.030 | 337 | 0.93 | 9[b] |
| C=O | 1.249 (±0.204) | 1.732(±0.138) | 0.035(±0.081) | 0.984 | 0.118 | 109 | 1.39 | 10 |
| | 1.367 ±(0.105) | 1.701(±0.070) | 0.022(±0.041) | 0.997 | 0.060 | 442 | 1.24 | 9[b] |
| C1 | 10.278(±1.374) | 14.282(±0.931) | 0.898(±0.548) | 0.989 | 0.801 | 162 | 1.39 | 10 |
| | 10.748(±1.307) | 14.160(±1.307) | 0.141(±0.307) | 0.992 | 0.740 | 191 | 1.32 | 9[b] |

[a] $\lambda = \rho_R/\rho_I$; [b] without **4**

gement, but it is independent of the nuclei being observed [39]. Additionally, a steric effect could also be operative, and it includes all those phenomena which result in structural changes at the measured sites, such as bond lengths and angles; effects due to the size of the atom close enough to cause geometrical adaptation. Since the optimized geometry of the investigated compounds counts to the lowest steric interactions, it was assumed that the field effect (polar effect transmitted through space inducing $\pi$-polarization) has a significant contribution causing shielding at the C1, N-H and C=O atoms in the presence of an electron-donor. An electron-donor increases the electron density at the aniline ring and, hence, an increase in the shielding of the N-H proton could be observed. The opposite is true for an electron-acceptor.

Recently, an LFER study was applied to the $\nu$, $^1$H- and $^{13}$C-NMR spectral data in a series of *N*-alkyl and *N*-cycloalkyl-2-cyanoacetamides. In these series, containing alkyl and cycloalkyl substituent attached to the amide nitrogen, the necessity to include the steric factor in the correlation of the *SCS* for the N-H proton and $\nu_{N\text{-}H}$ bond showed that steric interference of the bulky alkyl groups with the N-H proton occurs. An excellent correlation was obtained for the C=O carbon with the Taft set of polar constants $\sigma$ for the alkyl and cycloalkyl substituents. These value quantitatively described the polar, steric and resonance components of the alkyl substituent. Reverse polarization was found to be operative at the carbonyl carbon, as a consequence of $\pi$-polarization. The results of geometry optimization showed that for *trans*-conformation of *N*-alkyl and *N*-cycloalkyl-2-cyanoacetamides, the substituent and amide group are nearly *co*-planar, and the deviations, defined by the torsional angle $\theta$, vary with the type of substitution [40]. Such results indicate the general principle that the substituent influences the conformational state of the amide studied, and the chemical shifts of *N*-alkyl and *N*-cycloalkyl-2-cyanoacetamides are mainly caused by steric and polar substituent effects, while in the series of *N*-(substituted phenyl)-2-cyanoacetamides, the electronic substituent effect is of primary significance.

Taking into account the previous discussion, the transmission of the electronic effects of the substituents could be presented by mesomeric structures (Figure 3, structures **a**-**d**) of the electron-acceptor substituted *N*-(substituted phenyl)-2-cyanoacetamides.

Considering the wave function presented by structure **a** in Figure 3, for an electron-acceptor substituted *N*-(substituted phenyl)-2-cyanoacetamide, a dipole on X (or near the C-X bond) is induced, and interaction of this dipole through a molecular cavity results in the polarization of the $\pi_1$-unit. Resonance interaction within amide group (n,$\pi$-conjugation), presented by wave function **b** in Figure 3, is of appropriate significance and oppositely oriented with respect to the resonance interaction within the $\pi_1$-unit ((Figure 3, structure **d**; n,$\pi$-conjugation). Electron-acceptor substituents induce non-planar conformations of aniline part, by increasing the torsion angle $\theta$, owing to n,$\pi$-conjugation of the nitroaniline type. Namely, this conjugation, which involves the lone pair of the sp$^2$ hybridized amido nitrogen and $\pi$-electrons from the aniline ring, is possible only if the aniline ring with electron-accepting substituents is deflected by a certain angle $\theta$, *i.e.*, if the aniline ring is out-of-plane with the rest of the molecule (Figure 3, structure **d**). A

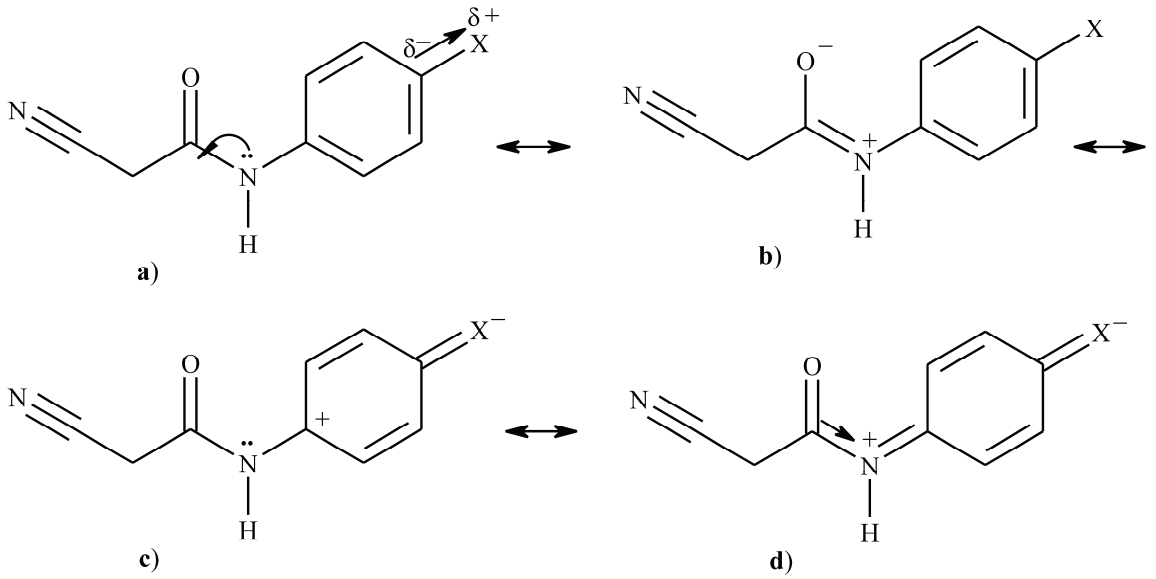


*Figure 3. Mesomeric structures of electron-acceptor substituted N-(substituted phenyl)-2-cyano- acetamides (**a**-**d**).*

non-planar conformation of the aniline ring causes an increase in the contribution of n,π-conjugation and consequently the π-electron density of the carbonyl group is shifted toward amide nitrogen. The net result is that electron-acceptor substituents decrease the electron density at the C1 and C=O carbons and, hence, decrease the shielding. It seems that the extent of resonance interaction within the $\pi_1$-unit is of utmost significance, causing normal and decreased polarization of carbonyl groups, which significantly depend on the planarity of the substituted phenyl ring and the plane of the amide group.

Electron-donor substituents *via* their +R effect, transmitted through the $\pi_1$-resonance unit increase the electronic density at the C1 carbon (Figure 4, **a**), shifting the corresponding signal at C1 carbon towards higher magnetic fields (Table 2). This considerably increases the extent of n,π-conjugation of the nitrogen lone pair with the π-electron of the carbonyl group (Figure 4, **b**).

The results from Table 4 also show that the +R resonance effect reaches the C=O carbon and, probably, may be achieved by resonance- and field-induced *π*-electron transfer modes (Figure 4) [41]. The high contribution of the resonance effect of a substituent at C1, in accordance with the corresponding $\rho_R$ values of 14.282 and 14.160 (Table 4; lines 5 and 6), indicates that the substituent effect on the electron density shift to the C1 atom could be presented as in Figure 4, **a**. The increased electron density on the C1 atom favors the delocalization of the free electron pair from the amide nitrogen atom toward the C=O carbon (Figure 4, **b**); n,π-conjugation in amide group). In this way, the electron density at the C=O carbon increases as the electron-donating power of substituent increases. Namely, this conjugation, which involves the lone pair of the amide nitrogen and *π*-electrons from the C=O carbonyl group, is possible only if an appropriate geometrical adjustment could provide larger electronic interaction of the nitrogen lone pair and the C=O π-electron (Figure 4, **b**).

Transmission of the substituent effect is significantly determined by spatial geometries of studied compound, as well as the *cis*/*trans* isomer ratio. These *cis*/*trans* isomer ratio were studied on the basis of $\nu_{N\text{-}H}$ frequency in the infrared spectra, particularly $\nu_{N\text{-}H}$ stretching vibrations for the amide monomers in carbon tetrachloride at ambient temperature [17]. On the basis of FTIR data for diluted solutions of *N*-(4--substituted phenyl)-2-cyanoacetamides in carbon tetrachloride the exact positions of N-H stretching bond were established. It can be seen that all of the investigated amides show characteristics of *trans* and *cis* forms, and percent of isomers was calculated according to integrated peak area. Additionally calculated IR frequencies for *trans* and *cis* forms, obtained by the use of DFT B3LYP functional with 6-311G** basis set, are given in Table 5.

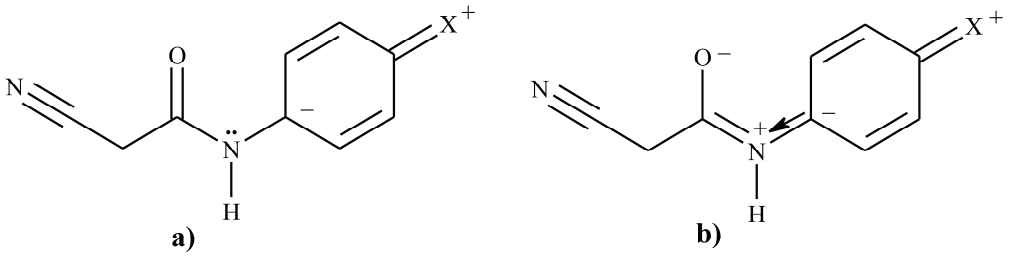


*Figure 4. Mesomeric structures of electron-donor substituted N-(substituted phenyl)-2-cyano-acetamides,* ***a****, with a contribution of the field effect,* ***b****.*

*Table 5. cis/trans isomer ratio of the N-(4-substituted phenyl)-2-cyanoacetamides in carbon tetrachloride*

| Compd. | *Trans* | | | *Cis* | | |
|---|---|---|---|---|---|---|
| | $\nu_{N\text{-}H}$ (exp) / cm$^{-1}$ | $\nu_{N\text{-}H}$ (calcd) / cm$^{-1}$ | % | $\nu_{N\text{-}H}$ (exp) / cm$^{-1}$ | $\nu_{N\text{-}H}$ (calcd) / cm$^{-1}$ | % |
| **1** | 3445.24 | 3447.05 | 2.8 | 3421.69 | 3440.08 | 97.2 |
| **2** | 3443.72 | 3448.04 | 2.5 | 3422.33 | 3439.28 | 97.5 |
| **3** | 3446.70 | 3451.13 | 4.2 | 3422.58 | 3436.19 | 95.8 |
| **4** | 3445.24 | 3446.64 | 2.9 | 3420.55 | 3438.45 | 97.1 |
| **5** | 3445.24 | 3446.70 | 15.9 | 3421.32 | 3438.41 | 84.1 |
| **6** | 3446.56 | 3440.60 | 22.3 | 3419.54 | 3436.81 | 77.7 |
| **7** | 3445.24 | 3450.02 | 53.0 | 3419.85 | 3435.85 | 47.0 |
| **8** | 3446.75 | 3443.51 | 2.2 | 3411.38 | 3438.07 | 97.8 |
| **9** | 3446.54 | 3441.38 | 61.4 | 3421.39 | 3437.24 | 38.6 |
| **10** | 3447.47 | 3442.48 | 26.0 | 3420.41 | 3437.28 | 74.0 |

Although we have shown earlier that the *trans* conformation of *N*-monosubstituted amides predominates over *cis* conformation [40], the presented results indicate that in the studied amides, when substituent as H, $CH_3$, $OCH_3$, Br, and COOH is present, the *cis* isomer largely predominate. On the other hand, for amides with $NO_2$, Cl, OH, $SO_3H$ and $CH_3CO$ substituent there is an equilibrium of *cis*/*trans* isomers, as it was shown earlier for *N*-(4-substituted phenyl)-2,3-diphenylpropanamides [13]. Good agreements and general trend of the experimental and calculated values of $\nu_{N-H}$ were obtained for the *trans* isomer, and somewhat higher calculated value for the *cis* isomer.

Additional support to assess the transmission modes of substituent effects was obtained from calculation of the elements of their optimized geometries and atomic charges (Table 6), obtained by use DFT B3LYP/ 6-311G** method.

Geometry optimization of the *N*-(substituted phenyl)-2-cyanoacetamides showed that *trans* isomers are in the planar conformation (Table 6; torsion angle $\theta$). Oppositely, large deviation was found for *cis* isomers, and the highest rotation observed in compounds **3** and **7** indicates that strong electron-donating groups cause such geometrical adaption to conform higher contribution of π,π-conjugation in defined π-unit (Figure 1a). Based on the MO calculations (HOMO orbitals), electron-donors increases electron density at the $\pi_1$-unit, and in accordance to the increased electron density at the C1 carbon, they act as extended π-donor supporting the transmission of the substituent effect to the amide group (Figure 4, **b**). Such finding is in accordance with the results of their optimal geometries. In other words, the shielding effect of an electron-donor at the C=O carbon is indeed a type of "push-effect" of the electron rich $\pi_1$--unit. On the contrary, an electron-acceptor withdraws electron density, thereby decreasing the shielding at the carbonyl carbon.

Based on the calculated parameters of the geometries of the *N*-(substituted phenyl)-2-cyanoacetamides (Table 6), it could be observed that the introduction of phenyl substituents of different electronic properties causes a noticeable geometrical variations. Some characteristic consequences of the substituent effect on the geometries of *N*-(substituted phenyl)-2-cyanoacetamides, compared to the unsubstituted one, could be summarized as:

1. The C1-N bond length are longer in electron-donor substituted compounds, and generally longer in *cis* isomer. This results is an additional support to the extensive conjugation operative in the $\pi_1$-unit, *i.e.*, the electron-density is shifted toward the C1 carbon in electron-donor substituted compounds (π,π-conju-

*Table 6. Interatomic distances, atomic charges, torsion angle and energies of both isomers in N-(substituted phenyl)-2-cyanoacetamides obtained by the use of DFT B3LYP/ 6-311G** method*

| Compound | | Interatomic distances | | | Atomic charges | | Torsion angle[a] | *E* / kcal |
|---|---|---|---|---|---|---|---|---|
| | | C1-N | N-(C=O) | C=O | C1 | N | | |
| **1** | *Trans* | 1.416 | 1.362 | 1.213 | 0.170 | -0.457 | 0.0 | 0.0 |
| | *Cis* | 1.425 | 1.372 | 1.212 | 0.086 | -0.430 | 55.9 | 1.64 |
| **2** | *Trans* | 1.417 | 1.361 | 1.214 | 0.303 | -0.636 | 0.0 | 0.0 |
| | *Cis* | 1.427 | 1.371 | 1.212 | 0.240 | -0.590 | 59.9 | 1.47 |
| **3** | *Trans* | 1.419 | 1.359 | 1.215 | 0.303 | -0.637 | 0.0 | 2.08 |
| | *Cis* | 1.431 | 1.369 | 1.212 | 0.212 | -0.588 | 70.0 | 0.0 |
| **4** | *Trans* | 1.414 | 1.364 | 1.216 | 0.311 | -0.638 | 0.0 | 0.0 |
| | *Cis* | 1.423 | 1.374 | 1.211 | 0.252 | -0.593 | 56.6 | 2.09 |
| **5** | *Trans* | 1.414 | 1.364 | 1.216 | 0.308 | -0.638 | 0.0 | 0.0 |
| | *Cis* | 1.423 | 1.374 | 1.211 | 0.248 | -0.593 | 57.7 | 2.11 |
| **6** | *Trans* | 1.407 | 1.369 | 1.211 | 0.334 | -0.643 | 0.0 | 0.0 |
| | *Cis* | 1.411 | 1.381 | 1.209 | 0.301 | -0.602 | 43.8 | 3.00 |
| **7** | *Trans* | 1.419 | 1.359 | 1.215 | 0.302 | -0.637 | 0.2 | 0.0 |
| | *Cis* | 1.430 | 1.370 | 1.212 | 0.213 | -0.588 | 69.3 | 0.85 |
| **8** | *Trans* | 1.411 | 1.366 | 1.211 | 0.322 | -0.640 | 0.0 | 0.0 |
| | *Cis* | 1.415 | 1.378 | 1.210 | 0.284 | -0.598 | 45.9 | 2.45 |
| **9** | *Trans* | 1.408 | 1.368 | 1.211 | 0.319 | -0.639 | -0.4 | 0.0 |
| | *Cis* | 1.413 | 1.380 | 1.209 | 0.282 | -0.598 | 45.3 | 3.20 |
| **10** | *Trans* | 1.411 | 1.366 | 1.212 | 0.319 | -0.639 | 0.0 | 0.0 |
| | *Cis* | 1.416 | 1.377 | 2.210 | 0.279 | -0.597 | 47.2 | 2.56 |

gation), contributing to a larger extent of the conjugation in the amide group (Figure 4, **b**). This fact is clearly observable from high value of the correlation coefficient $\rho_R$ for the C1 carbon (Table 4, lines 5 and 6). A decrease in the C1-N bond length in electron-acceptor substituted compounds is a consequence of the contribution of n,π-conjugation (Figure 3, **d**).

2. The existence of a conjugative transfer of electron density toward the carbonyl group from the aniline ring could be clearly observed from the changes in the C1-N and N-C(=O) bond lengths. An electron-donor supports an electron density shift (Figure 4, **b**) from the $\pi_1$-unit toward the carbonyl group causing significant increases in the C1-N bond length and concomitantly decreases in the *N*-C(=O) bond length as the electron-donating capabilities of the substituents increase. The opposite is true for electron-acceptors.

3. Considering the C=O bond length, small bond length changes could be noticed. The polarization operative in the $\pi_2$-unit has an opposite effect on the polarization in the extended conjugative system of the $\pi_1$-unit when an electron-acceptor substituent is present. Accordingly, the increase in $\nu_{C=O}$ can be attributed to a shorter carbonyl bond and therefore increased double bond character of the C=O bond. Both the $^{13}$C-NMR and IR spectroscopic data suggest substituent-induced electron density decreases at the carbonyl carbon in accord with increasing electron-withdrawal capabilities of the phenyl substituents. The length of the C=O bond is a somewhat higher in the *trans* isomer which is a additional evidence about higher contribution of π,π-conjugation in a more planar conformation of *N*-(substituted phenyl)-2-cyanoacetamides.

## LFER analysis of IR absorption frequencies in *N*-(substituted phenyl)-2-cyanoacetamides

The IR stretching frequencies of the characteristic groups in *N*-(substituted phenyl)-2- cyanoacetamides are shown in Table 2. As the correlation with different steric constants failed, it was considered appropriate to correlate with the Hammett $\sigma$ constants, and the obtained correlation results are presented in Table 7.

It is evident from the failure of the correlations with the steric substituent constants and the good correlation with the $\sigma$ Hammett constants, that the electronic substituent effect is the most important factor influencing the IR absorption frequencies of the N-H, C=O and CN groups.

The high sensitivity of the $\nu$ values with respect to the Hammett substituent constant $\sigma$ could be observed (Table 7). The attempt to correlate the asymmetric stretching vibration of the N-H bond gave acceptable separate correlations for electron-donor and electron-acceptor substituents. A reverse substituent effect is operative for electron-donors, and it also showed higher sensitivity than for electron-acceptors. A better correlation was obtained with electrophilic substituent constant $\sigma^+$ for electron-donors and a somewhat lower with the nucleophilic substituent constant $\sigma^-$ for electron-acceptors. These results indicate that electron-donors cause a larger increase in the N-H bond force constant. The shorter bond distance results in a stronger force constant and consequently higher infrared frequency. Similar behavior could be observed for the C=O bond. A lower sensitivity of $\nu_{C=O}$ caused by electron-donors, and a significantly higher for electron-acceptor could be observed. The spectroscopic results suggest that electron-withdrawing substituents increase the force constant of the C=O bond due to an increased contribution of n,π-conjugation (Figure 3, structure **d**). Some results of DFT calculations support the correlation results, verifying both the electron density increase at the carbonyl carbon and the increase in the bond order of the C=O bond caused by electron-withdrawing substituents. Although a small substituent effect on the IR frequency of the distant CN bond

*Table 7. Correlations results of the N-H, C=O and CN stretching frequencies in N-(substituted phenyl)-2-cyanoacetamides obtained by the use SSP, Eq. (1)*

| Group | Scale | $\rho$ | $h$ | $r$ | *s.d.* | $F$ | $n$ |
|---|---|---|---|---|---|---|---|
| N-H | $\sigma$ | -124.21(±22.19) | 3267.10(±5.42) | 0.969 | 6.06 | 31.4 | 4[a] |
| | $\sigma^+$ | -47.37(±3.62) | 3268.41(±2.56) | 0.994 | 2.26 | 171 | 4[a] |
| | $\sigma$ | 50.34(±1.91) | 3257.12(±1.95) | 0.994 | 1.10 | 693 | 6[b] |
| | $\sigma^-$ | 30.12(±3.55) | 3260.72(±2.57) | 0.973 | 3.33 | 72 | 6[b] |
| C=O | $\sigma$ | -28.02(±4.18) | 1659.82(±1.02) | 0.978 | 1.14 | 45 | 4[a] |
| | | 74.84(±8.38) | 1652.04(±3.86) | 0.983 | 4.41 | 80 | 5[b,c] |
| | $\sigma^-$ | 44.12(±2.53) | 1656.62(±1.76) | 0.995 | 2.28 | 305 | 5[b,c] |
| CN | $\sigma$ | 43.50(±9.08) | 2238.31(±4.18) | 0.940 | 4.77 | 23 | 5[b,c] |

[a]Electron-donor; [b]electron-acceptor; [c]without **10**

could be expected, normal and significant influences were observed, meaning that not only a substituent effect but some polar (field) effect plays a significant role on the changes in the $\nu_{CN}$ values.

## CONCLUSION

The applied LFER analysis appears to be a straightforward method for correlations of the *SCS* values of the investigated molecules with appropriate substituent constants. General trends of the contribution of electronic substituent effects, both polar (field/inductive) and resonance, were estimated. The substituted phenyl group and the amide group are highly deviated in *cis* isomer, while they are nearly *co*-planar in *trans* isomer, and that deviations, defined by the torsion angle $\theta$, vary with the type of the substitution. The FTIR conformational study showed presence of both *cis* and *trans* isomers for amides with $NO_2$, Cl, OH, $SO_3H$ and $CH_3CO$ substituent, while for other *cis* isomers largely predominate. DFT B3LYP/6--31G** calculations indicate somewhat higher stability of the *trans* isomers for all compounds, except compound **3**. Good agreement of these results indicate that both forms, *cis* and *trans* isomers, have an appropriate contribution in the values of IR, $^{1}$H- and $^{13}$C-NMR spectral data of *N*-(substituted phenyl)-2--cyanoacetamide. The high sensitivity of the $\nu$ values with respect to the Hammett substituent constant $\sigma$ could be observed and the opposite effect of electron-donors to $\nu_{N-H}$ and $\nu_{C=O}$ was found. The optimized geometries of the investigated compounds and the transmission of individual substituent electronic effects through well defined $\pi$-resonance units indicate that these units behave both as isolated and as conjugated fragments, depending on the substituents present in the corresponding molecules.

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NAUČNI RAD

# UTICAJ SUPSTITUENATA NA IR, $^{1}$H- I $^{13}$C-NMR SPEKTRALNE PODATKE *N*-(SUPSTITUISANIH FENIL)-2-CIJANOACETAMIDA: KORELACIONA ANALIZA

*Principi linearnih korelacija slobodnih energija (LFER) su primenjeni na IR, $^{1}$H- i $^{13}$C--NMR spektralne podatke N-(supstituisanih fenil)-2-cijanoacetamida. Pri sintezi N-(supstituisanih fenil)-2-cijanoacetamida izvršen je zadovoljavajući izbor supstituenata u pogledu elektronskih svojstava kako bi se adekvatno sagledao uticaj elektronskih efekata supstituenata na pomeranja u IR, $^{1}$H- i $^{13}$C-NMR spektralnim podacima. Primenom proste Hametove jednačine dobijene su zadovoljavajuće korelacije. Na osnovu korelacionih rezultata uočen je primaran uticaj elektronskih efekata na SCS (supstituentom indukovana hemijska pomeranja) vrednosti N-H vodonika, C1 i C=O ugljenika ispitivanih jedinjenja. Korelacioni rezultati za C=O ugljenik se značajno popravljaju ako se koristi kombinacija $\sigma^{+}$ i $\sigma^{-}$ konstanti supstituenata, takozvane elektrofilne i nukleofilne konstante supstituenata, što ukazuje na postojanje značajne proširene rezonancione interakcije supstituenata i elektronske gustine karbonilne grupe. Vrednosti konstanti proporcionalnosti $\rho_F$ i $\rho_R$, za sve atome, ukazuju na približno isti doprinos efekta polja i rezonancionog efekta supstituenata. Efekat polja je nešto izraženiji na N-H vodoniku, i za sve atome pokazuje značajne razlike u odnosu na njihov položaj u molekuskoj strukturi ispitivanih jedinjenja. Uticaj efekata supstituenata na IR vibracije istezanja N-H (simetrične i antisimetrične), C=O i CN veze je prevashodno elektronske prirode što se može zaključiti na osnovu dobrih korelacija dobijenih primenom Hametove jednačine i σ parametara supstituenata. Osim toga izvršena je optimizacija geometrije ispitivanih jedinjenja primenom DFT B3LYP/ 6-311G** metode, pri čemu je nađeno da je trans-izomer nešto stabilniji, izuzev u slučaju jedinjenja **3**. Supstituisana fenil-grupa i amidna grupa, kod trans-izomera, su približno koplanarne, dok se kod cis- izomera uočava značajna devijacija koja je značajno određena elektronskim efektima prisutnog supstituenta. Takođe je ispitivan položaj cis/trans ravnoteže u ugljen-tetrahloridu, i na osnovu rezultata FTIR analize, kada je prisutan H, $CH_3$, $OCH_3$, Br, i COOH supstituent, nađeno je da je cis izomer u velikom višku, a za ostala jedinjenja utvrđeno je postojanje ravnoteže cis- i trans-izomera.*

*Ključne reči: N-(supstituisani fenil)-2-cijanoacetamidi; LFER analiza; IR i NMR spektri; SCS pomeraj; Hametova jednačina.*