

Electron-topological, energetic and π -electron delocalization analysis of ketoenamine-enolimine tautomeric equilibrium

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Abstract The ketoenamine-enolimine tautomeric equilibrium has been studied by the analysis of aromaticity and electron-topological parameters. The influence of substituents on the energy of the transition state and of the tautomeric forms has been investigated for different positions of chelate chain. The quantum theory of atoms in molecules method (QTAIM) has been applied to study changes in the electron-topological parameters of the molecule with respect to the tautomeric equilibrium in intramolecular hydrogen bond. Dependencies of the HOMA aromaticity index and electron density at the critical points defining aromaticity and electronic state of the chelate chain on the transition state (TS), OH and HN tautomeric forms have been obtained.

Keywords Aromaticity · Carbonylamine · Enolimine · Intramolecular hydrogen bond · QTAIM · Tautomeric equilibrium · HOMA

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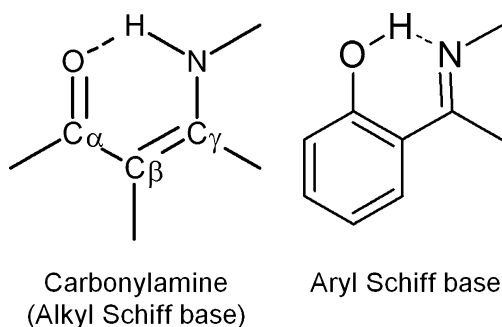
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Introduction

The carbonylamines presented in the paper (Scheme 1) are prototypes of malonaldehydes investigated in a number of experimental and computational studies [1–3]. The given compounds can be referred to so-called resonance assisted hydrogen bond (RAHB) system being elaborated by Gilli et al. [4]. Recently the interest in RAHB has much grown due to the critics presented in refs [5, 6]. It is noteworthy that the aryl Schiff bases were properly studied [7–9]. However, theoretical studies of the carbonylamine (alkyl derivatives of Schiff bases) are not as numerous [10–14]. Both the alkyl Schiff bases and the aryl Schiff bases (Scheme 1) contain a quasi-aromatic formation as a common feature. But, the experimental data [15–23] expose the principle difference between these two types of compounds. What makes them different is that the HN (ketoenamine) tautomeric form prevails for the alkyl derivatives [10–26], meanwhile OH (enolimine) tautomeric form (Scheme 2) prevails for the aryl derivatives [7–9]. The transition from one form to another (the proton transfer) requires energetic expenditure (ΔE_{PT}). The change of tautomeric equilibrium is evoked by an acid-base balance and polarity of the environment. A series of papers [27–40] deals with the ways the tautomeric equilibrium affects the aromatic state of a molecule with intramolecular hydrogen bonding.

To trace a change of a tautomeric equilibrium in carbonylamines experimentally is really challenging. It is also difficult to estimate the substituent influence in the chelate chain ($O=C-C=C-N$) on the hydrogen bonding strength. This task is hampered by complementary phenomena (trans-cis isomerization [11] and $HO-CH=CH-C=NR \rightleftharpoons O=C-CH_2-CH=NR$ equilibrium [15–17]) observed experimentally for carbonylamines. However, quantum-

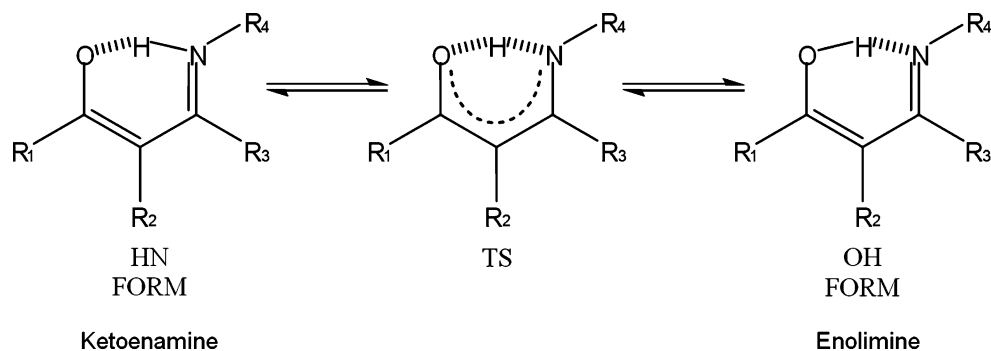


Scheme 1 Alkyl and aryl Schiff bases

mechanical calculations make it possible to describe a complicated nature of hydrogen bond. This paper is concerned with the ketoenamine-enolimine tautomeric equilibrium (Scheme 2) and the calculations of the carbonylamines with various substituents (CH₃, H, NH₂, Cl and F) in the chelate chain. The calculations were performed for the OH and HN tautomeric forms and transition state (Scheme 2) describing two main stages of the proton transfer process [41]. For description of these stages we calculated the difference of energies between them ($\Delta E_{PT}=E_{OH} - E_{HN}$, $\Delta E_{TS}=E_{TS} - E_{HN}$; the energy of HN tautomer is taken as the ground energetic level) and the HOMA aromaticity index [42] and electron-topological parameters [43, 44]. HOMA index is a widely accepted parameter applied in the description of the aromaticity [45, 46]. The merit of HOMA index is in its ability to be used for the experimental [47] and computational [48] results. The difference of energies is one of the most reliable parameters in the description of the hydrogen bonding [49].

As for the HOMA aromaticity index, it has been repeatedly verified by the researchers of intramolecular hydrogen bonding during last decade [26, 27, 30–40]. There are papers dwelling on the influence of tautomeric equilibrium on the aromaticity of phenol, aniline and naphthol complexes [50]. This paper develops these studies with aim to unify the HOMA aromaticity index in the area of hydrogen bonding and electron-topological analysis.

Scheme 2 Where R₁, R₂, R₃ and R₄ are CH₃, H, NH₂, Cl and F substituents



Computational details

The calculations were performed with Gaussian 03 [51] sets of code using the 6-311+G(d,p) basis set [52–55] at the Møller–Plesset second-order perturbation level (MP2) [56]. QTAIM analysis was performed using the AIM2000 program [57] with all the default options.

The HOMA aromaticity index was calculated by the following formula:

$$\text{HOMA} = 1 - \frac{1}{n} \sum_{i=1}^n \alpha_i (R_{opt} - R_i)^2 \quad (1)$$

where n is a number of bonds, α is an empirical constant, R_{opt} and R_i are the optimal and individual bond lengths taken from ref. 42. A higher HOMA aromaticity index corresponds to a more delocalized π -electronic system, hence a more aromatic formation [58].

Results and discussion

The influence of substituents on the intramolecular hydrogen bonding in the carbonylamines

The influence of substituents (R₁ – R₃) in the α , β and γ positions on the ketoenamine-enolimine equilibrium can be described by the inductive constants [59] ($\sigma_F=0, \sim 0, 0.14, 0.44$ and 0.45 for H, CH₃, NH₂, Cl and F, respectively). It is noteworthy, that the π -electron donation of NH₂ group is small due to perpendicular orientation of its lone electron pair with respect to quasi-aromatic formation. This phenomenon was properly described by Sola et al. [60]. The increase of the electron acceptor ability of the R₁ and R₂ substituents (the increase of σ_F constant) in the α and β positions results in the growth of both the energetic barrier of transition state (ΔE_{TS}) and the OH form (ΔE_{PT}), (Fig. 1a and b). This trend is traced for the CH₃ (Fig. 1a) and H (Fig. 1b) substituents at the nitrogen atom, which serve as the basic ones for the predominant HN tautomeric form. An opposite picture is observed for the substituent (R₃) in the γ

Fig. 1 The energy levels of carbonylamine derivatives depending on substituents (black column respect to $R_1=H, CH_3, NH_2, Cl, F$; $R_2=R_3=H$; grey column respect to $R_2=H, CH_3, NH_2, Cl, F$; $R_1=R_3=H$; white column respect to $R_2=R_3=H$)

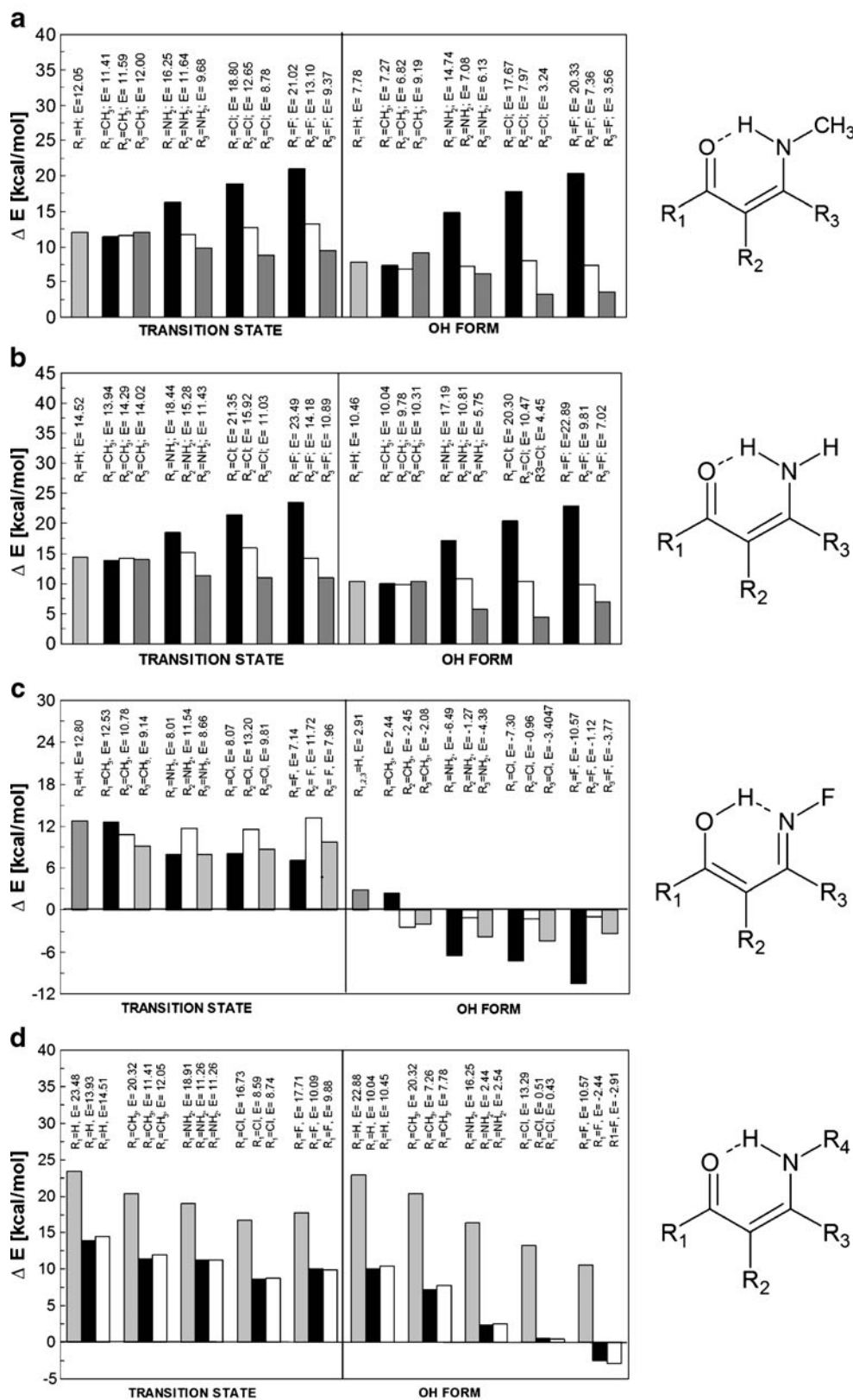
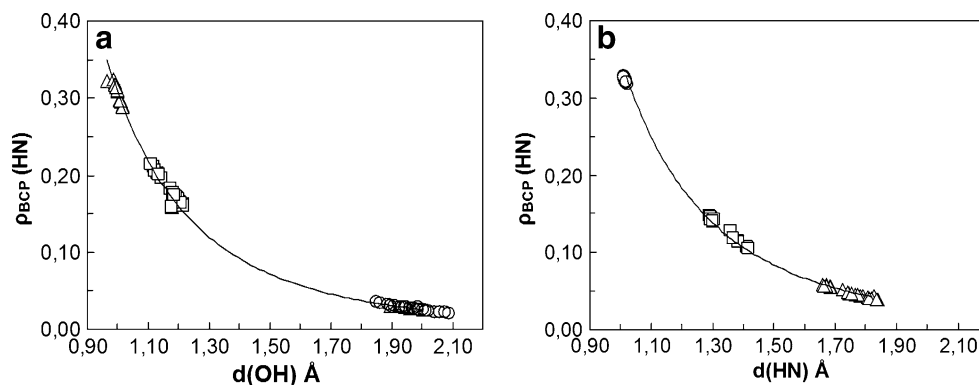


Fig. 2 Correlations between the electron density (**a**) at the OH bond critical point ($\rho_{\text{BCP}}(\text{OH})$, a.u.) and OH bond length ($d(\text{OH})$, Å), and (**b**) at the HN bond critical point ($\rho_{\text{BCP}}(\text{HN})$, a.u.) and HN bond length ($d(\text{HN})$, Å). Circles, squares and triangles correspond to the OH, transition state and HN forms, respectively



position (Fig. 1a and b) which reveals the decrease of the ΔE_{TS} and ΔE_{OH} values under the σ_{F} constants increase. These trends originate in the following phenomena: 1) the substitution (R_1) in the α position greatly affects the C=O group by weakening its basicity, consequently, it attenuates the hydrogen bond strength and enhances the ΔE_{TS} and $\Delta E_{\text{HN-OH}}$ barriers according to the CH_3 , H, NH_2 , Cl and F sequence; 2) the substitution (R_3) in the γ position mostly influences the amine group by increasing its acidity according to the Cl, F, NH_2 and $\text{H}\equiv\text{CH}_3$ sequence. Some exception from the expected CH_3 , H, NH_2 , Cl and F sequence is observed for the fluoro-substituent (R_3) in the γ position. The reason for this disagreement is a marked polarizability effect of the fluorine atom ($\sigma_{\alpha} = -0.25$ [59]) which causes some attenuation of the acidity of the HN group and the intramolecular hydrogen bonding. Remarkably, the substituent (R_2) in the β -position influences but to a lesser extent the ΔE_{TS} and ΔE_{OH} values due to its remote position from the acidic (NR_4) and basic ($\text{O}=\text{C}$) moieties.

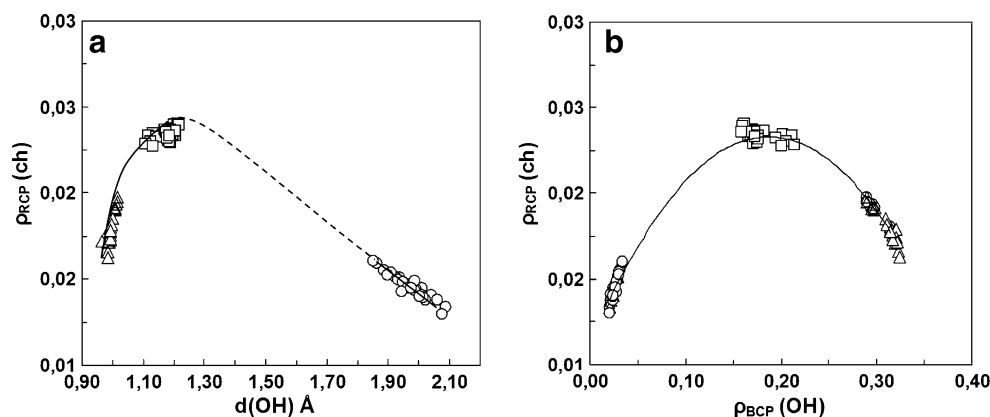
The picture changes for the N-F derivatives (R_4). The majority of these derivatives is characterized by the OH tautomeric form prevailing over the HN tautomeric form (Fig. 1c). The development of the electron acceptor ability of the R_1 substituent (under weak basicity of the nitrogen

atom, at N-F substituent) brings about both the decrease of the ΔE_{TS} values and the strengthening of the OH tautomeric form prevailing. However, the increase of the electron acceptor properties of the substituent (R_2) in the β -position is accompanied by the growth of the ΔE_{TS} values and the weakening of the OH tautomeric form prevailing.

With respect to the substituent impact on the nitrogen atom (R_4), the ΔE_{TS} and ΔE_{OH} values are getting smaller according to the H, CH_3 , NH_2 , Cl and F sequence (Fig. 1d). Some discrepancy as to the expected CH_3 , H, NH_2 , Cl and F sequence is observed for the H substituent which slightly influences the acidity of the amine group. A similar deviation was discovered for ortho-hydroxy aryl Schiff bases and explained by a significant polarization effect of the NH group [41, 60, 61].

In terms of the structural data of the hydrogen bridge ($d(\text{OH})$, $d(\text{HN})$ and $d(\text{OH})$), they are characterized by the following tendencies: 1) the elongation of the HN bond results in the reduction of the hydrogen bond and the OH bond lengths; 2) the elongation of the OH bond also triggers the reduction of the hydrogen bond and the HN bond lengths; 3) the shortest hydrogen bridge is found for the transition state; 4) the position of the TS is more shifted toward the reagents ($d(\text{O-H})_{\text{TS}} < d(\text{N-H})_{\text{TS}}$ for prevailing of the $\text{NH}\cdots\text{O}$ form) according to Leffler-Hammond rule [62, 63].

Fig. 3 Correlations between electron density at the chelate chain critical points ($\rho_{\text{RCP}}(\text{ch})$, a.u.) and (**a**) OH bond length ($d(\text{OH})$, Å), and (**b**) the electron density at the OH bond critical point ($\rho_{\text{BCP}}(\text{OH})$, a.u.)



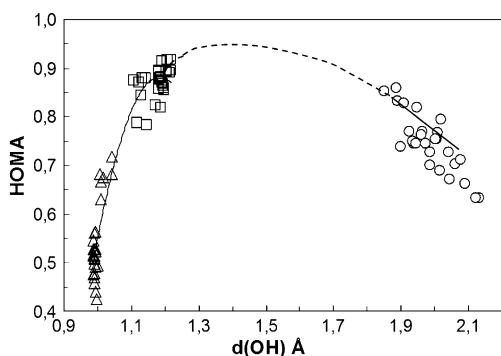


Fig. 4 Scatter plot of the chelate chain aromaticity index HOMA(ch) versus the OH bond length (d(OH), Å)

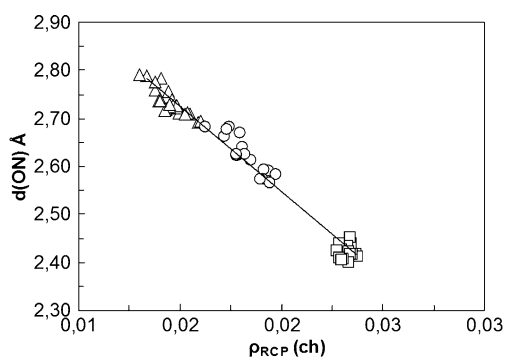
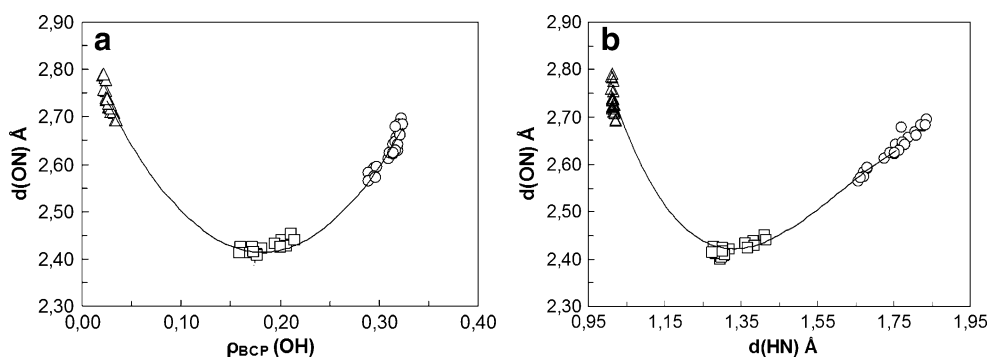
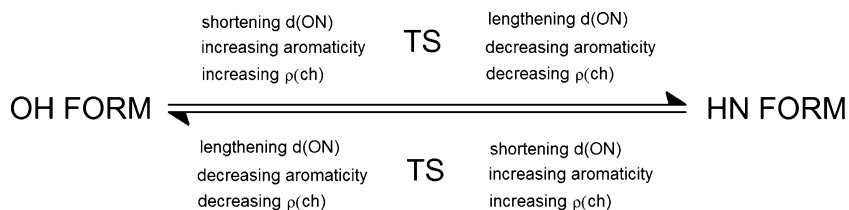


Fig. 5 Correlations between hydrogen bond length (d(ON), Å) and electron density at chelate chain critical points ($\rho_{RCP}(ch)$, a.u.)

Fig. 6 Correlations between hydrogen bond length (d(ON), Å) and electron density at (a) chelate chain critical points ($\rho_{RCP}(ch)$, a.u.), and (b) the HN bond length (d(HN), Å)



Scheme 3 Structural and electron-topological scheme of the tautomeric equilibrium



Analysis of aromatic and AIM parameters vs. tautomeric equilibrium

To verify the calculations obtained by the QTAIM method the $\rho_{BCP}(XH)=f(d(XH))$ ($X=N$ or O atom) dependence was developed (Fig. 2; $\rho_{BCP}(OH)=0.3489 \times (OH)^{-3.522}$, $R^2=0.9991$; $\rho_{BCP}(NH)=0.3071 \times (NH)^{-3.5938}$, $R^2=0.9987$). The dependence taken by means of full optimization for different substituents in α - γ positions appears to be an exponential curve which is in accordance with the results obtained by non-adiabatic approach [41, 64]. Remarkably, the results for different substituents under full optimization are in agreement with those found under non-adiabatic approach for ortho-hydroxy aryl Schiff bases [65].

The next stage of the study was to verify the $\rho_{RCP}(ch)=f(d(OH))$ and $\rho_{RCP}(ch)=f(\rho_{BCP}(OH))$ dependencies (Fig. 3) calculated for the OH, TS and HN states of the compounds. These dependencies look like Morse or bell-shaped curves. A similar shape of the curve is traced for $HOMA(ch)=f(d(OH))$ scatter plot (Fig. 4). The calculated scatter plot conditioned by some scattering of points supports the trends which are not observed under non-adiabatic approach [66]. The correlations reveal that the maximum of the electronic density at quasi-aromatic critical point ($\rho_{RCP}(ch)$) and maximum aromaticity reaches its top in the transition state. This result comes in agreement with the results obtained in paper 66, where the comparison of the aromaticity of hydrogen-bonded and Li bonded aryl Schiff bases derivatives was carried out.

The $d(\text{ON})=f(\rho_{\text{RCP}}(\text{ch}))$ correlation (Fig. 5; $d(\text{ON}) = -35.482 \times (\rho_{\text{RCP}}(\text{ch})) + 3.2575$, $R^2=0.9849$) appears to be one of the most interesting dependencies which states that the shortening of the hydrogen bridge results from the growth of the electron density at the critical point of quasi-aromatic formation. But comparatively, the parabolic dependence $d(\text{ON})=f(\rho_{\text{BCP}}(\text{XH}))$ is more informative with respect to tautomeric equilibrium (Fig. 6) in terms of the basic parameter ($d(\text{ON})$) describing the hydrogen bond strength.

The $\rho_{\text{RCP}}(\text{ch})=f(d(\text{OH}))$, $\rho_{\text{RCP}}(\text{ch})=f(\rho_{\text{BCP}}(\text{OH}))$, $\text{HOMA}(\text{ch})=f(d(\text{XH}))$ and $d(\text{ON})=f(\rho_{\text{RCP}}(\text{OH}))$ dependencies (Figs. 3, 4 and 5) show that strengthening of the hydrogen bond brings about the increase of both electron density at the critical point of quasi-aromatic formation and the chelate chain aromaticity (Scheme 3).

Bearing in mind the fact of mutual increase of aromaticity and π -component in the aromatic formation one can confirm that the increase of $\rho_{\text{RCP}}(\text{ch})$ provokes the active participation of π -component.

Conclusions

It has been shown that for the HN tautomeric form the increase of the electron-acceptor ability of the substituents (R_1 and R_2) in α and β positions evokes a larger prevailing this form. In case of the OH tautomeric form the growth of the electron-acceptor ability of the substituents (R_1) in β position contributes into the OH tautomeric form prevailing, whereas for the substituent (R_2) in β position it reveals a reverse trend. With respect to the influence of substituent (R_3) in the γ -position for carbonylamines, the growth of the electron-acceptor ability hinders the prevailing of the HN tautomeric form. However, for the HN tautomeric form the impact of the substituent (R_3) in γ -position seems quite complicated due to mutual compensating action of the steric, inductive, resonance and polarizability effects, as well as local $\text{N-H}\cdots\text{F}$ hydrogen bond influence.

The $\text{HOMA}(\text{ch})=f(d(\text{OH}))$, $\rho_{\text{BCP}}(\text{ch})=f(d(\text{OH}))$, $d(\text{ON})=f(\rho_{\text{BCP}}(\text{ch}))$ dependencies have been obtained. The $\text{HOMA}(\text{ch})=f(d(\text{OH}))$ and $\rho_{\text{BCP}}(\text{ch})=f(d(\text{OH}))$ dependencies are bell-shaped and indicate that the transfer process from one tautomeric form to another goes via a transition state. According to these dependencies in the transition state one can observe the maximum delocalization of π -component of the chelate chain and the maximum electron density of quasi-aromatic formation. The $d(\text{ON})=f(\rho_{\text{BCP}}(\text{ch}))$ dependence states that the electron density at the critical points of quasi-aromatic formation is a measure of the intramolecular hydrogen bond strength. According to the presented dependencies the enhancement of the hydrogen bond strength leads to the growth of $\rho_{\text{BCP}}(\text{ch})$ and $\text{HOMA}(\text{ch})$ and reaches its maximum in the transition state. Krygowski et al. [58]

stated earlier that the increase of aromaticity strengthens π -component participation. Therefore, the strengthening of the hydrogen bond in the studied compounds is conditioned by the π -electron delocalisation in the chelate chain.

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