

# Consequence of one-electron oxidation and one-electron reduction for aniline

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**Abstract** Quantum-chemical calculations were performed for all possible isomers of neutral aniline and its redox forms, and intramolecular proton-transfer (prototropy) accompanied by  $\pi$ -electron delocalization was analyzed. One-electron oxidation ( $\text{PhNH}_2 - e \rightarrow [\text{PhNH}_2]^{+\bullet}$ ) has no important effect on tautomeric preferences. The enamine tautomer is preferred for oxidized aniline similarly as for the neutral molecule. Dramatical changes take place when proceeding from neutral to reduced aniline. One-electron reduction ( $\text{PhNH}_2 + e \rightarrow [\text{PhNH}_2]^{-\bullet}$ ) favors the imine tautomer. Independently on the state of oxidation,  $\pi$ - and n-electrons are more delocalized for the enamine than imine tautomers. The change of the tautomeric preferences for reduced aniline may partially explain the origin of the CH tautomers for reduced nucleobases (cytosine, adenine, and guanine).

**Keywords** Aniline · Charged radicals · DFT ·  $\pi$ -Electron delocalization · Prototropy · One-electron oxidation · One-electron reduction

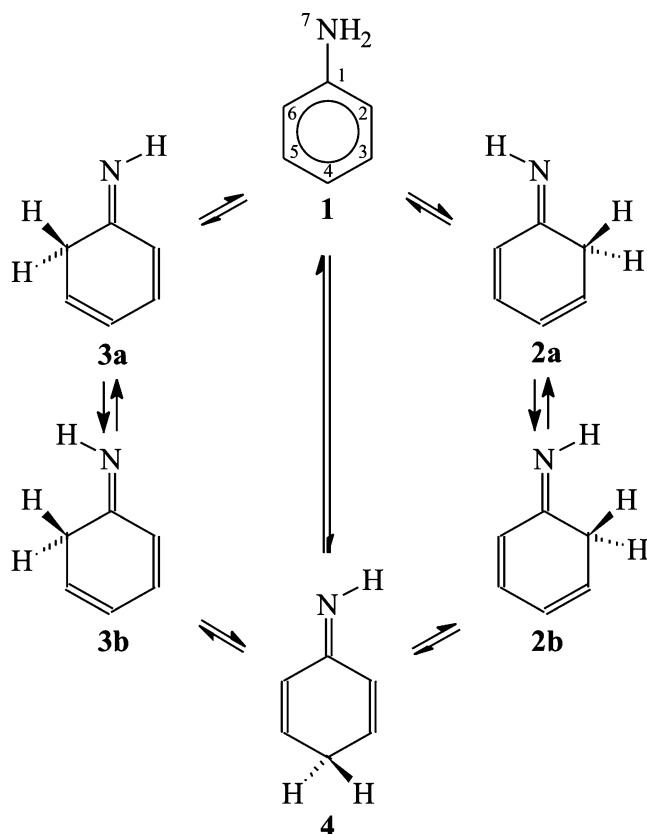
## Introduction

Aniline is a model compound that can be used to understand the structure and physicochemical properties of many biologically active aromatic derivatives such as nucleobases (cytosine, adenine, and guanine) containing the amine group in the ring. Similar to other models of nucleobases (phenol, hydroxypyridine, aminopyridine, imidazole, purine, *etc.*), aniline exhibits prototropic tautomerism (Scheme 1) [1–5]. This phenomenon influences the physicochemical properties of aniline. For the neutral molecule, the enamine tautomer (**1**) is preferred due to strong delocalization of  $\pi$ -electrons. The proton transfer from the *exo*-amine group to the *endo*-carbon atom destroys the aromaticity of the ring and strongly destabilizes the imine forms (**2–4**) in comparison to the enamine one. Usually, the imine tautomers are neglected for aniline [6]. However, investigations of many important biological transformations showed that the energetically less stable tautomer for the neutral form, with particular acid-base, electrophilic-nucleophilic, redox, or even just geometric properties, is often an active intermediate and dictates the mechanism and the product formed. For this reason, complete tautomeric equilibria should be considered for model compound to understand the mechanisms of various biochemical transformations for more complex aromatic biomolecules containing the amine group in the ring.

In this paper, we investigated the consequences of one-electron oxidation and one-electron reduction on tautomeric equilibria for aniline and on composition of its tautomeric mixture. We considered various oxidation states of aniline, neutral ( $\text{PhNH}_2$ ), oxidized ( $\text{PhNH}_2 - e \rightarrow [\text{PhNH}_2]^{+\bullet}$ ), and reduced state ( $\text{PhNH}_2 + e \rightarrow [\text{PhNH}_2]^{-\bullet}$ ). The redox forms of aniline may be formed in the presence of oxidizing or reducing agents. They may also be generated electrochemically, photochemically, or with solvated electrons in liquid ammonia

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**Scheme 1** Prototropic equilibria for aniline

{e.g.,  $K(\text{NH}_3) \rightarrow K^+(\text{NH}_3) + e(\text{NH}_3)$ } [7–14]. They may be identified by various spectroscopic techniques, e.g., zero kinetic energy photoelectron spectroscopy [15, 16], or infrared depletion spectroscopy [17–19]. The charged radicals may be also generated in various types of mass spectrometers during positive ( $M - e \rightarrow M^+$ ) or negative ( $M + e \rightarrow M^-$ ) ionization ( $M - \text{whole molecule}$ ) [20]. In such conditions, an electron may be transferred from or to aniline and change stabilities of the enamine and imine tautomers. Consequently, they may change prototropic equilibria, composition of the tautomeric mixture, and mechanisms of ion-radical reactions.

However, the redox imine forms of aniline have been usually omitted in the literature. For example, the imine radical cations and the imine radical anions have not been considered as intermediates in various mechanisms of aromatic substitution for aniline derivatives. In these reactions, solely the enamine forms, the radical cation and the radical anion, have been taken into account [21–24]. Similarly, the electronic structures, vibrational spectra, and infrared and Raman intensities have been studied by quantum-chemical methods only for the enamine tautomer of the aniline radical cation [15, 25]. The imine isomers have not been considered.

Investigation of the distonic radical cation isomers of ionized aniline,  $\bullet\text{C}_6\text{H}_4\text{-NH}_3^+$ , is a particular case in which

the enamine and imine radical cation isomers have been taken into account [26]. The distonic radical cation is a very stable reactive intermediate in the gas phase with a spatial separated radical and charge site. It can be formed during collisional activation in mass spectrometer from 2-, 3-, or 4-iodoanilinium ion,  $\text{I-C}_6\text{H}_4\text{-NH}_3^+ \rightarrow \bullet\text{C}_6\text{H}_4\text{-NH}_3^+$  [26–28]. Although the DFT relative energies of various distonic radical cation isomers are close to those for the imine radical cation isomers and considerably larger than that of the enamine radical cation isomer [26], isomerization has not been detected by mass spectrometry [26–28]. It has been suggested that the  $\bullet\text{C}_6\text{H}_4\text{-NH}_3^+$  radical cation, generated by a protonation-deiodination sequence on iodoanilines, is protected against H• shifts rearrangements to the conventional aniline radical cation,  $\text{C}_6\text{H}_5\text{NH}_2^+$ , by large energy barriers [26].

For our investigations on prototropy of neutral and redox forms of aniline, we chose quantum-chemical methods, because experimental techniques are incapable of detecting less than 0.1% of minor tautomer(s). We applied the DFT method [29] with the B3LYP functional [30, 31]. The DFT method has been successfully applied for proton-transfer reactions, including tautomeric conversions in the gas phase that models apolar environment [32–36]. For B3LYP calculations, the 6-311+G(d,p) basis set [37] with the diffuse and polarization functions was employed. For selected structures, the G2 theory [38, 39], recommended for the proton-transfer reactions [40, 41], was also applied. The G2 theory corresponds effectively to QCISD(T)/6-311+G(3df,2p)//MP2/6-31 G(d) calculations with zero-point vibrational and 'higher level' corrections [38, 39]. The extended basis sets, 6-311++G(3df,3pd) and aug-cc-pVDZ [37, 42], were additionally tested for DFT calculations. Since prototropy is always accompanied by  $\pi$ -electron transfer(s), we analysed  $\pi$ - and n-electron delocalization for the neutral and redox isomers of aniline optimized at the B3LYP/6-311+G(d,p) level.

### Computational details

Geometries of neutral isomers of aniline (1–4), and its oxidized and reduced forms (radical cations and anions, respectively) were fully optimized without symmetry constraints using the DFT(B3LYP) method [29–31] and the 6-311+G(d,p) basis set [37]. The real minima (with all positive frequencies) were found for each isomer, and thermodynamic parameters calculated using the same level of theory. For selected isomers, additional calculations were performed using the G2 theory [38, 39], and also the extended basis sets, 6-311++G(3df,3pd) and aug-cc-pVDZ [37, 42], for the DFT(B3LYP) method. For all calculations, the Gaussian 03 program [43] was employed.

## Results and discussion

### Choice of quantum-chemical method

For two isomers (**1** and **4**) of neutral aniline, calculations were performed at various levels of theory: B3LYP/6-311+G(d,p), B3LYP/6-311++G(3df,3pd), B3LYP/aug-cc-pVDZ, and G2. The calculated CC and CN bond lengths and the relative Gibbs energies ( $\Delta G$ ) are compared in Table 1. The comparison shows that the B3LYP/6-311+G(d,p) level, frequently employed for the proton-transfer reactions in the gas phase, is sufficient for the tautomeric system for which the relative Gibbs energies are very different from zero. The use of different basis sets for DFT calculations has no important influence on the values of geometric and energetic parameters. The DFT relative Gibbs energies are close to those computed using the G2 theory. Differences in bond lengths are not larger than 0.01 Å and differences in relative energies are not larger than 3 kcal mol<sup>-1</sup>. The DFT  $\Delta G$  values only slightly overestimate (by ca. 10 %) those estimated by the G2 theory. The CC and CN bond lengths calculated for the neutral enamine isomer **1** are close to the literature experimental gas-phase microwave bond lengths [44]. They are also in good agreement with those calculated by Michalska and co-workers at the B3LYP/6-311++G(df,pd) and MP2/6-311++G(df,pd) levels [25]. There is no literature

**Table 1** Comparison of the CC and CN bond lengths (in Å) and relative energies ( $\Delta G$  in kcal mol<sup>-1</sup>) for **1** and **4** of neutral aniline

Isomer	C <sup>1</sup> C <sup>2</sup>	C <sup>2</sup> C <sup>3</sup>	C <sup>3</sup> C <sup>4</sup>	C <sup>4</sup> C <sup>5</sup>	C <sup>5</sup> C <sup>6</sup>	C <sup>1</sup> C <sup>6</sup>	C <sup>1</sup> N <sup>7</sup>	$\Delta G^a$
a) B3LYP/6-311+G(d,p)								
<b>1</b>	1.40	1.39	1.39	1.40	1.39	1.40	1.40	0.0
<b>4</b>	1.47	1.34	1.50	1.50	1.34	1.47	1.29	26.5
b) B3LYP/6-311++G(3df,3pd)								
<b>1</b> <sup>b</sup>	1.40	1.39	1.39	1.39	1.39	1.40	1.40	0.0
<b>4</b>	1.47	1.33	1.49	1.49	1.33	1.47	1.28	26.7
c) B3LYP/aug-cc-pVDZ								
<b>1</b>	1.41	1.40	1.40	1.40	1.40	1.41	1.40	0.0
<b>4</b>	1.48	1.34	1.50	1.50	1.34	1.47	1.29	26.3
d) G2 {with MP2/6-31G(d) geometry}								
<b>1</b> <sup>c</sup>	1.40	1.39	1.39	1.39	1.39	1.40	1.40	0.0
<b>4</b>	1.47	1.34	1.50	1.50	1.34	1.46	1.30	23.9 <sup>d</sup>
f) experiment <sup>e</sup>								
<b>1</b>	1.40	1.39	1.40	1.40	1.39	1.40	1.40	-

<sup>a</sup>  $\Delta G=G(4)-G(1)$

<sup>b</sup> The same CC and CN bond lengths as in ref. [25]

<sup>c</sup> The same CC and CN bond lengths at the MP2/6-311++G(df,pd) level were reported in ref. [25]

<sup>d</sup> The following  $\Delta G$  values were found at the G1 and G2(MP2) levels: 24.1 and 23.8 kcal mol<sup>-1</sup>, respectively

<sup>e</sup> Taken from ref. [44]

data for the neutral imine isomer **4** and no comparison can be made.

### Delocalization of n- and $\pi$ -electrons

First perusal of the bond lengths calculated at the B3LYP/6-311+G(d,p) level for the neutral and charged radicals of **1** shows that addition of one electron to aromatic system does not alter the geometric parameters significantly (Table 2). The CC bond lengths for the radical anion (1.39–1.41 Å) are close to those for the neutral form (1.39–1.40 Å), and the CN bond length for the radical anion (1.40 Å) is the same as that for the neutral molecule (1.40 Å). Important differences take place for the radical cation. Loss of one electron shortens the CN bond (1.33 Å) in comparison to the neutral molecule. It also differentiates the CC bond lengths, which vary from 1.37 to 1.43 Å, indicating some kind of  $\pi$ -electron localization. For the imine tautomers **2–4**, one-electron oxidation and one-electron reduction seem to have only slight effect on some CC bond lengths. For the neutral forms, they vary from 1.34 to 1.53 Å, and for the charged forms, they vary from 1.35 to 1.54 Å. Moreover, the CN bonds are slightly longer for the charged radicals (1.30–1.35 Å) than for the neutral forms (1.28–1.29 Å).

To quantitatively measure  $\pi$ -electron delocalization for all isomers of aniline, the geometry-based HOMED index [45, 46] can be applied. This index describes well various types of conjugations ( $\pi$ - $\pi$ , n- $\pi$ , and  $\sigma$ - $\pi$ ) possible in systems containing heteroatoms [46]. The HOMED index can be obtained from the theoretically derived bond lengths [B3LYP/6-311+G(d,p)] using Eq. 1. In this equation,  $\alpha$  is a normalization constant,  $R_o$  is the optimum bond length

**Table 2** The DFT calculated CC and CN bond lengths (in Å) for isomers of aniline

Isomer	C <sup>1</sup> C <sup>2</sup>	C <sup>2</sup> C <sup>3</sup>	C <sup>3</sup> C <sup>4</sup>	C <sup>4</sup> C <sup>5</sup>	C <sup>5</sup> C <sup>6</sup>	C <sup>1</sup> C <sup>6</sup>	C <sup>1</sup> N <sup>7</sup>
a) neutral							
<b>1</b>	1.40	1.39	1.39	1.40	1.39	1.40	1.40
<b>2a/3a</b>	1.52	1.50	1.34	1.46	1.35	1.47	1.28
<b>2b/3b</b>	1.53	1.50	1.34	1.46	1.35	1.46	1.28
<b>4</b>	1.47	1.34	1.50	1.50	1.34	1.47	1.29
b) radical cation							
<b>1</b>	1.43	1.37	1.41	1.41	1.37	1.43	1.33
<b>2a/3a</b>	1.50	1.47	1.38	1.41	1.39	1.44	1.30
<b>2b/3b</b>	1.51	1.48	1.38	1.41	1.39	1.44	1.30
<b>4</b>	1.44	1.35	1.48	1.48	1.35	1.44	1.32
c) radical anion							
<b>1</b>	1.41	1.39	1.40	1.40	1.39	1.41	1.40
<b>2a/3a</b>	1.53	1.51	1.38	1.42	1.41	1.42	1.32
<b>2b/3b</b>	1.54	1.51	1.38	1.42	1.40	1.42	1.32
<b>4</b>	1.44	1.37	1.51	1.51	1.36	1.45	1.35

(assumed to be realized when full delocalization of  $\pi$  electrons takes place),  $R_i$  are the running bond lengths in the system, and  $n$  is the number of bonds taken into account.

$$\text{HOMED} = 1 - \left[ \alpha \cdot \Sigma(R_o - R_i)^2 \right] / n \quad (1)$$

For the system containing the even number of bonds ( $n=2i$ ), i.e., the same number of single ( $i$ ) and double ( $i$ ) bonds, the normalization  $\alpha$  constant can be calculated from Eq. 2 proposed for the HOMA index [47], where  $R_s$  and  $R_d$  are the single and double bond lengths of the reference compounds [46]. For the system containing the odd number of bonds ( $n=2i+1$ ), i.e., ( $i+1$ ) single bonds and ( $i$ ) double bonds, the normalization  $\alpha$  constant can be calculated from Eq. 3 [46]. The following  $R_s$ ,  $R_d$ , and  $R_o$  values (in Å), calculated at the B3LYP/6-311+G(d,p) level [46] were taken here: 1.5300 (ethane), 1.3288 (ethene) and 1.3943 (benzene) for the CC bonds, and 1.4658 (methylamine), 1.2670 (methylimine) and 1.3342 (1,3,5-triazine) for the CN bonds. On the basis of these  $R$  values, the normalization  $\alpha$  constant equal to 88.09 was used for the ring (six C-atoms). For the whole tautomeric system (seven atoms, one N-atom and six C-atoms), the following  $\alpha$  constants were applied: 80.90 for the CC bonds and 84.52 for the CN bonds.

$$\alpha_{2i} = 2 \cdot \left[ (R_o - R_s)^2 + (R_o - R_d)^2 \right]^{-1} \quad (2)$$

$$\alpha_{2i+1} = (2i + 1) \cdot \left[ (i + 1) \cdot (R_o - R_s)^2 + i \cdot (R_o - R_d)^2 \right]^{-1} \quad (3)$$

The HOMED indices (Table 3) calculated for the ring are close to unity for the neutral enamine tautomer **1** (0.9976) and for its radical anion (0.9944). For the radical cation of **1**, the HOMED index is slightly lower (0.9265). Presence of the C-sp<sup>3</sup> atom in the ring for the imine tautomers (**2-4**) destroys aromatic character of the ring, and decreases the

**Table 3** The DFT estimated HOMED indices for isomers of aniline

Isomer	Neutral form	Radical cation	Radical anion
a) for the ring (six C-atoms)			
<b>1</b>	0.9976	0.9265	0.9944
<b>2a/3a</b>	0.3844	0.7109	0.4904
<b>2b/3b</b>	0.3533	0.6698	0.4704
<b>4</b>	0.4130	0.6802	0.5135
b) for the whole tautomeric system (seven atoms, one N-atom and six C-atoms)			
<b>1</b>	0.9479	0.9422	0.9520
<b>2a/3a</b>	0.4825	0.7598	0.5973
<b>2b/3b</b>	0.4591	0.7248	0.5820
<b>4</b>	0.5106	0.7471	0.5949

HOMED indices in higher degree for the neutral (0.35-0.41) than for the charged radicals, anions (0.47-0.51) and cations (0.67-0.71). When proceeding from the ring (six C-atoms) to the whole tautomeric system (seven atoms), the HOMED indices decrease for the neutral enamine tautomer **1** (from 0.9976 to 0.9479) and for its radical anion (from 0.9944 to 0.9520) due to cross  $n$ - $\pi$  and  $\pi$ - $\pi$  conjugations possible in the whole tautomeric system, i.e., conjugation of  $n$ -electrons of the NH<sub>2</sub> group with  $\pi$ -electrons of the ring. Exception is the enamine radical cation, for which conjugation of the positive charge with  $\pi$ - or  $n$ -electrons increases the number of resonance structures, and consequently, increases the  $\pi$ -electron delocalization and the HOMED index (from 0.9265 to 0.9422). For the imine forms **2-4**, the HOMED indices increase. This increase may be explained by additional  $\pi$ - $\pi$  cross conjugation of the *exo*-C=NH group with  $\pi$ -electrons of the ring. The  $\pi$ - $\pi$  conjugation leads usually to greater  $\pi$ -electron delocalization than  $\sigma$ - $\pi$  hyperconjugation possible in the ring for the  $-\text{CH}=\text{CH}-\text{CH}_2-$  group(s).

### Relative stabilities

For all isomers, the DFT minima (with real frequencies) were found and the thermodynamic parameters such as the energy ( $E$ ), enthalpy ( $H$ ), entropy ( $S$ ), and Gibbs (free) energy ( $G$  for  $T=298.15$  K) were calculated. The  $G$  value includes the electronic energy, the zero-point energy (ZPE), and the thermal corrections (vibrational, rotational, and translational) to the energy and entropy. For the enamine-imine conversions, the relative energies ( $\Delta E_T$ ), enthalpies

**Table 4** The DFT calculated thermodynamic parameters ( $\Delta E_T$ ,  $\Delta H_T$ ,  $T\Delta S_T$ , and  $\Delta G_T$  in kcal mol<sup>-1</sup>) for the enamine-imine conversions in aniline and the percentage contents ( $x$  in %) of the imine tautomers

Conversion	$\Delta E_T^{a,b}$	$\Delta H_T^{b,c}$	$T\Delta S_T^{b,c}$	$\Delta G_T^{b,c}$	$x$
a) neutral form					
<b>1</b> → <b>2a/3a</b>	28.7	28.8	0.6	28.2	1·10 <sup>-19</sup>
<b>1</b> → <b>2b/3b</b>	29.0	29.1	0.7	28.4	1·10 <sup>-19</sup>
<b>1</b> → <b>4</b>	26.6	26.6	0.2	26.5	4·10 <sup>-18</sup>
b) radical cation					
<b>1</b> → <b>2a/3a</b>	43.5	43.8	0.7	43.1	1·10 <sup>-30</sup>
<b>1</b> → <b>2b/3b</b>	43.4	43.6	0.7	43.0	1·10 <sup>-30</sup>
<b>1</b> → <b>4</b>	48.2	48.5	0.6	47.9	8·10 <sup>-34</sup>
c) radical anion					
<b>1</b> → <b>2a/3a</b>	-3.9	-3.6	1.0	-4.7	89.0
<b>1</b> → <b>2b/3b</b>	-2.9	-2.7	0.8	-3.4	11.0
<b>1</b> → <b>4</b>	4.9	5.1	0.5	4.6	1.4·10 <sup>-5</sup>

<sup>a</sup> ZPE included. At 0 K

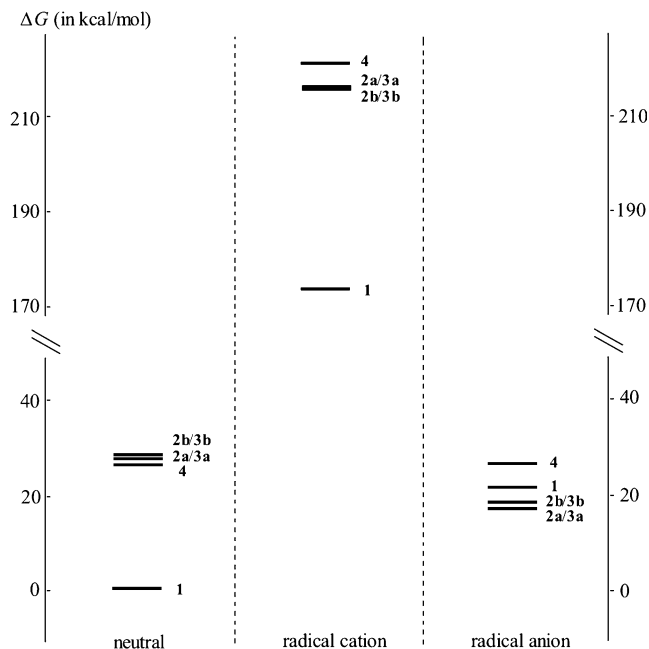
<sup>b</sup>  $\Delta Q_T = Q(i) - Q(1)$ ,  $Q = E, H, S$ , or  $G$

<sup>c</sup> Thermal corrections included. At 298.15 K

( $\Delta H_T$ ), entropy terms ( $T\Delta S_T$ ), Gibbs energies ( $\Delta G_T$ ), and also the percentage contents ( $x$ ) of the imine tautomers were calculated on the basis of Eq. 4, where  $K_T$  is the tautomeric equilibrium constant. They are given in Table 4.

$$-\log[x/(100-x)] = pK_T = \Delta G_T/2.302RT \quad (4)$$

According to DFT calculations, the enamine tautomer (**1**) has the lowest  $G$  value for the neutral molecule. This form is the most stable one in the gas-phase as well as in solution [1–6, 44]. The percentage contents of the imine tautomers (**2–4**) in the tautomeric mixture are exceptionally small ( $< 10^{-15}\%$ ), and from a physicochemical point of view they may be neglected. For the simplest acyclic enamine-imine tautomeric system, the E-isomer of acetaldimine ( $\text{CH}_3\text{-CH=NH}$ ) is more stable than vinylamine ( $\text{CH}_2\text{=CH-NH}_2$ ) with energy difference of 4 kcal mol $^{-1}$  at the G2 level [48]. The Z-isomer of acetaldimine is also more stable than vinylamine, but it has larger energy than the E-isomer by 1 kcal mol $^{-1}$  at the MP4/6-311++G(d,p)/MP2/6-31G(d) level (ZPVE included) [48]. The tautomeric preference for aliphatic derivative is not the same as that for aromatic system for which a part of the tautomeric moiety, the  $\text{NH}_2$  group, is not included in the ring according to the *exo*-mode. This change of the tautomeric preference when proceeding from aliphatic to aromatic system may be explained by the energies describing aromatic stability, e.g., resonance energy (RE 30–50 kcal mol $^{-1}$ ) for simple aromatics [3, 4, 49, 50], which are considerably larger than the tautomeric energy for the parent system.



**Fig. 1** The DFT relative Gibbs energies ( $\Delta G$ ) for isomers of neutral and charged aniline

**Table 5** The DFT calculated thermodynamic parameters (in kcal mol $^{-1}$ ) for oxidation and reduction reactions of individual isomers of aniline

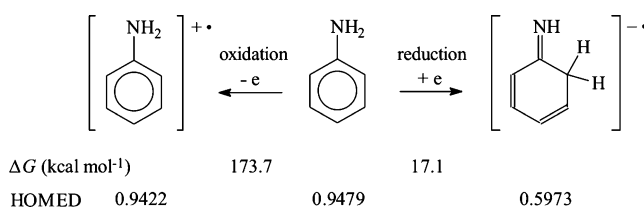
Isomer	$\Delta E^{a,b}$	$\Delta H^{b,c}$	$T\Delta S^{b,c}$	$\Delta G^{b,c}$
a) oxidation				
<b>1</b>	174.1	174.0	0.3	173.7
<b>2a/3a</b>	188.9	189.0	0.4	188.7
<b>2b/3b</b>	188.5	188.6	0.3	188.3
<b>4</b>	195.7	196.0	0.8	195.2
b) reduction				
<b>1</b>	22.2	22.2	0.4	21.8
<b>2a/3a</b>	-10.4	-10.2	0.9	-11.0
<b>2b/3b</b>	-9.7	-9.6	0.5	-10.0
<b>4</b>	0.5	0.7	0.7	0.0

<sup>a</sup> ZPE included. At 0 K

<sup>b</sup>  $\Delta Q_T = Q(\text{charged form}) - Q(\text{neutral form})$ ,  $Q = E, H, S$ , or  $G$ ; the charged form is the radical cation for oxidation and the radical anion for reduction

<sup>c</sup> Thermal corrections included. At 298.15 K

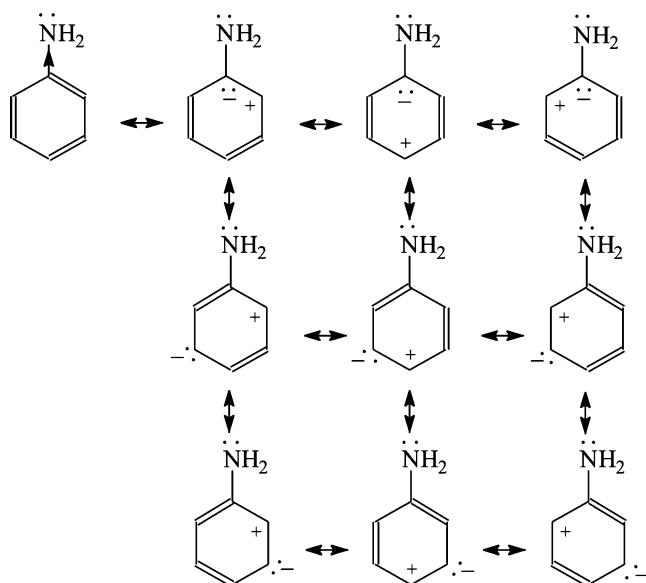
One-electron oxidation has no effect on the tautomeric preference for aniline. The enamine tautomer (**1**) predominates in the tautomeric mixture. It has the lowest energy [26]. One-electron oxidation influences solely the relative energies, and consequently, the amounts of the imine isomers. The  $\Delta G_T$  values for the imine radical cation isomers are ca. one and a half larger than those for the neutral forms, and the percentage contents of the imine isomers are not larger than  $10^{-30}\%$ . Change of the H atom configuration at the N atom when going from **2a/3a** to **2b/3b** has no important effect on the relative stabilities ( $< 0.3$  kcal mol $^{-1}$ ) of the neutral and oxidized forms. This effect has not been discussed by Nguen and co-workers [26]. However, similar relative energies {B3LYP/6-311++G(d,p) + ZPE} between the enamine and imine tautomers have been reported. The orders of stabilities are as follows: **1** > **4** > **2a/3a**  $\approx$  **2b/3b** for the neutral molecule and **1** > **2b/3b**  $\approx$  **2a/3a** > **4** for oxidized aniline. For the oxidized aliphatic parent system, the order of stabilities is reversed in comparison to that for the neutral molecule [51]. The vinylamine radical cation is considerably more stable than the acetaldimine radical cation by 29 kcal mol $^{-1}$  at the G2(MP2) level [51], indicating that enamine-imine isomerization is endothermic for the oxidized acyclic system, similarly as for oxidized aniline.



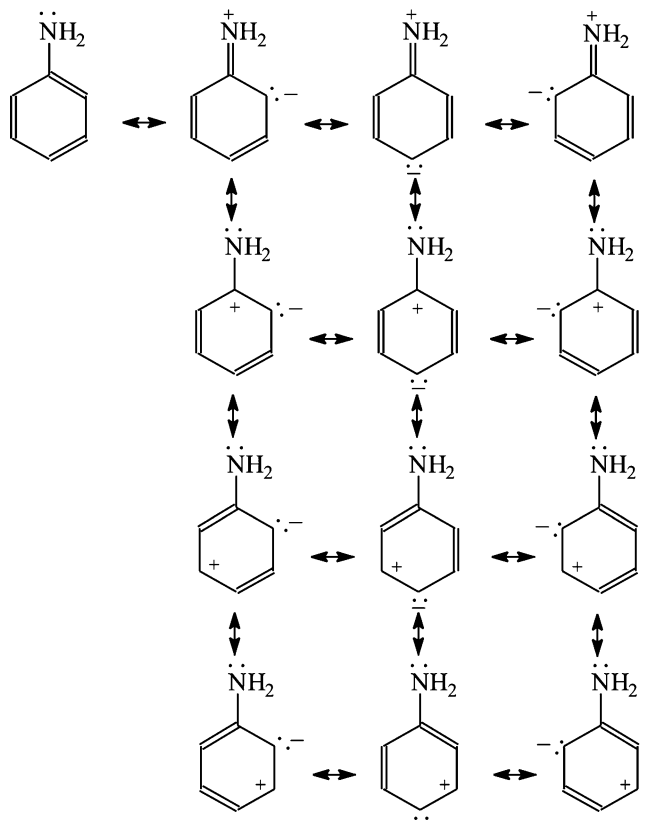
**Scheme 2** The tautomeric preference and  $\pi$ -electron delocalization for redox forms of aniline estimated at the B3LYP/6-311++G(d,p) level

An interesting change of the tautomeric preference occurs for reduced aniline. One-electron reduction favors the imine isomer **2a/3a**. The other imine radical anion isomers **2b/3b** and **4** have larger  $G$  values than **2a/3a**. The

### a inductive effect



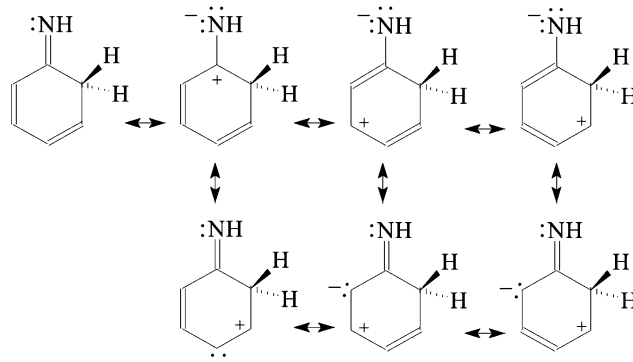
### b resonance effect



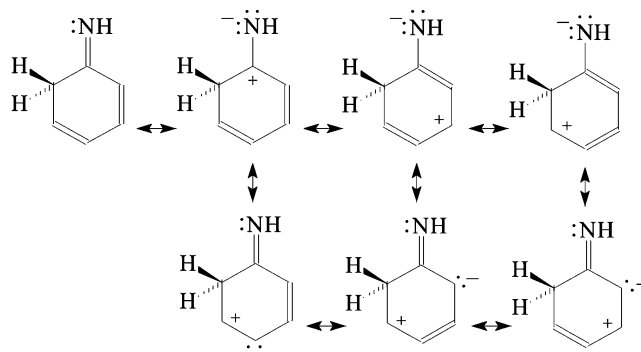
**Scheme 3** Electronic effects of the *exo*-NH<sub>2</sub> group for the neutral enamine isomer **1**

enamine radical anion isomer **1** also has larger  $G$  value. The tautomeric mixture of reduced aniline consists mainly of the imine isomers **2a/3a** (89%) and **2b/3b** (11%). These isomers have to be considered for all electron transfer reactions for which aniline gains one electron. The percentage contents of other tautomers are lower than 0.05%. The order of stabilities for the reduced forms of aniline (**2a/3a**  $\approx$  **2b/3b**  $>$  **4**  $>$  **1**) is completely reversed to that (**1**  $>$  **4**  $>$  **2a/3a**  $\approx$  **2b/3b**) for the neutral molecule. Change of the H configuration at the N atom when going from **2a/3a** to **2b/3b** has only a slight effect on the relative stabilities (1.3 kcal mol<sup>-1</sup>). There are no reports on reduced aniline, so

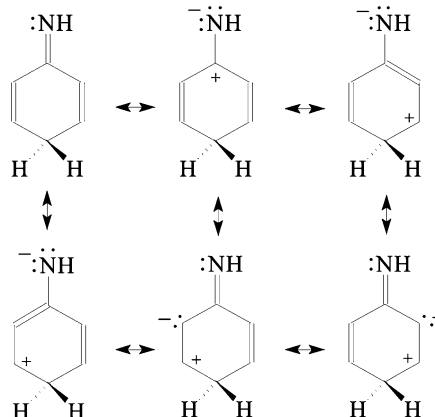
### a isomer 2



### b isomer 3



### c isomer 4



**Scheme 4** Electronic effects of the *exo*=NH group for the neutral imine isomers **2-4**

no comparison can be made. For the reduced aliphatic parent system, the order of stabilities is the same as for the neutral molecule. The acetaldimine radical anion is more stable than the vinylamine radical anion by 1 kcal mol<sup>-1</sup> at the B3LYP/6-311+G(d,p) level. One-electron reduction stabilizes the imine tautomer for the parent system similarly as for aniline.

The relative entropy terms ( $T\Delta S_T$ ) for the reduced forms of aniline are not larger than  $\pm 1$  kcal mol<sup>-1</sup>, similarly as for the neutral and oxidized molecule. This suggests that tautomeric enamine-imine conversions are isoentropic in the gas phase and do not depend on the oxidation or reduction state of aniline. Generally, there are not large structural changes during tautomerization. Some exceptions are those resulting from loss of the ring planarity for the imine tautomers.

### Oxidation and reduction energies

When oxidizing agents are present, the neutral aniline may lose one electron. Consequently, it may be transferred to its

oxidized (ionized) very reactive state ( $\text{PhNH}_2 - e \rightarrow [\text{PhNH}_2]^{+\bullet}$ ). The mechanisms of chemical and anodic oxidations of aniline and formation of polymeric products are very complex and depend on conditions of reaction such as solvent, reagents, catalysts, etc. (see for example refs. [8–14, 52–59]). These processes may pass through different intermediates among which the radical cation of aniline ( $\text{PhNH}_2^{+\bullet}$ ) is possible [8–14, 52–57]. Oxidation of aniline by oxygen from air, catalyzed by sunlight or UV light, is also a very complex process [13, 60–62]. It may occur even in a closed bottle of aniline when colored products appear. A simple loss of one electron may also be observed for aniline during positive ionization in the mass spectrometer, when the molecular ion ( $\text{PhNH}_2^{+\bullet}$ ) is generated [20].

The relative Gibbs energies calculated at the B3LYP/6-311+G(d,p) level for the neutral, oxidized and reduced enamine and imine tautomers of aniline are compared in Fig. 1, where the  $\Delta G$  values are relative to the  $G$  value of the neutral enamine tautomer **1**. The comparison indicates that one-electron oxidation process is very endothermic and

**Table 6** DFT calculated Mulliken charges for isomers of aniline

Isomer	Atom	Neutral form	Radical cation	$\Delta^a$	Radical anion	$\Delta^a$
<b>1</b>	C1	-0.161	0.012	0.17	-7.499	-7.34
	C2	0.025	0.038	0.01	6.874	6.85
	C3	-0.199	-0.182	0.02	-5.617	-5.42
	C4	-0.145	-0.001	0.14	2.388	2.53
	C5	-0.199	-0.182	0.02	-5.615	-5.42
	C6	0.026	0.038	0.01	6.873	6.85
	N7	-0.360	-0.265	0.09	0.529	0.89
<b>2a/3a</b>	C1	-0.066	0.025	0.09	-0.326	-0.26
	C2/C6	-0.484	-0.659	-0.18	-0.228	0.26
	C3/C5	0.134	0.290	0.16	-0.098	-0.23
	C4	-0.219	-0.134	0.08	-0.162	0.06
	C5/C3	0.005	0.005	0.00	-0.198	-0.20
	C6/C2	-0.167	-0.001	0.16	-0.172	-0.01
	N7	-0.293	-0.132	0.16	-0.447	-0.15
<b>2b/3b</b>	C1	0.019	0.165	0.15	-0.299	-0.32
	C2/C6	-0.675	-0.817	-0.14	-0.516	0.16
	C3/C5	0.124	0.301	0.18	-0.130	-0.25
	C4	-0.191	-0.143	0.05	-0.147	0.04
	C5/C3	-0.073	-0.015	0.06	-0.228	-0.16
	C6/C2	0.000	0.034	0.03	0.139	0.14
	N7	-0.308	-0.154	0.15	-0.465	-0.16
<b>4</b>	C1	-0.158	0.174	0.33	-0.597	-0.44
	C2	-0.089	-0.219	-0.13	0.002	0.09
	C3	0.151	0.261	0.11	-0.077	-0.23
	C4	-0.770	-0.938	-0.17	-0.731	0.04
	C5	0.124	0.310	0.19	-0.005	-0.13
	C6	-0.034	-0.110	-0.08	0.231	0.26
	N7	-0.289	-0.070	0.22	-0.463	-0.17

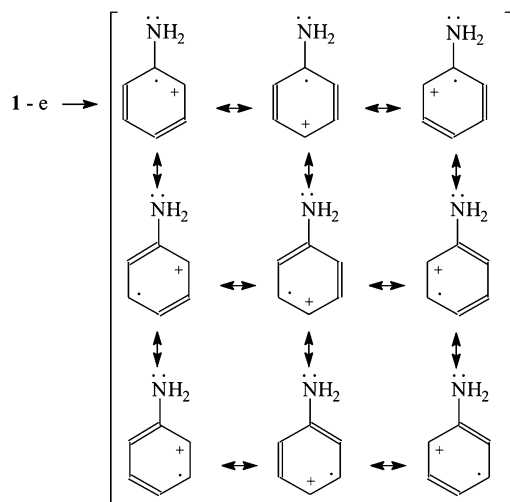
<sup>a</sup>  $\Delta$  is the difference of the Mulliken charges on the C and N atoms between the charged and neutral form

requires ca. 200 kcal mol<sup>-1</sup>. Indeed, the experimental ionization energy for aniline is equal to 178 kcal mol<sup>-1</sup> [63]. Similar results have been reported by Nguyen and co-workers [26] who calculated the adiabatic ionization energy for **1** as equal to 174 {B3LYP/6-311++G(d,p)} and 175 kcal mol<sup>-1</sup> {CCSD(T)/6-311++G(d,p)}. On the other hand, one-electron gain is possible in the presence of reducing agents or during negative ionization in the mass spectrometer, where the neutral molecule is transferred to its reduced state (PhNH<sub>2</sub> + e → [PhNH<sub>2</sub>]<sup>-</sup>) [7, 20]. This process is less endothermic than oxidation and requires ca. 20 kcal mol<sup>-1</sup>. Unfortunately, there

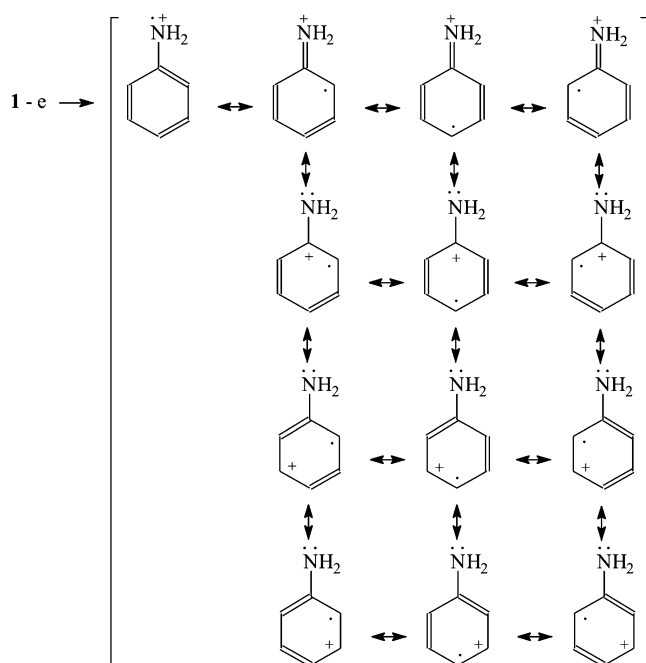
is no experimental data for the electron affinity of aniline [63] and no comparison can be made.

For each individual isomer, the thermodynamic parameters of one-electron oxidation and of one-electron reduction can be estimated as differences between the parameters of the corresponding charged radicals (cations and anions) and the neutral forms (Table 5). The  $\Delta E$ ,  $\Delta H$ , and  $\Delta G$  values for the oxidized enamine tautomer **1** are lower than those for the oxidized imine tautomers **2-4** by ca. 20 kcal mol<sup>-1</sup>. On the other hand, they are negative for reduced **2a/3a** and **2b/3b**, close to zero for reduced **4**, and positive for reduced **1**. The variations of the oxidation and reduction parameters confirm the orders of stabilities for oxidized and reduced aniline isomers. They confirm also the change of the tautomeric preference for the reduced aniline. The entropy terms for both oxidation and reduction reactions are not larger than 1 kcal mol<sup>-1</sup>, indicating that the electron-transfer processes are isoentropic in the gas phase for

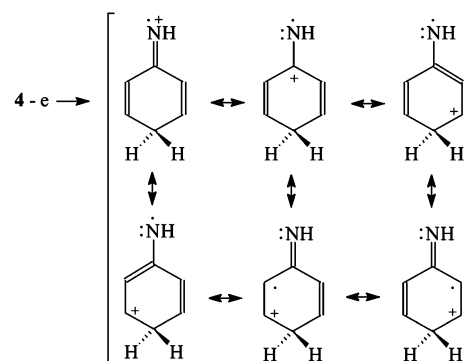
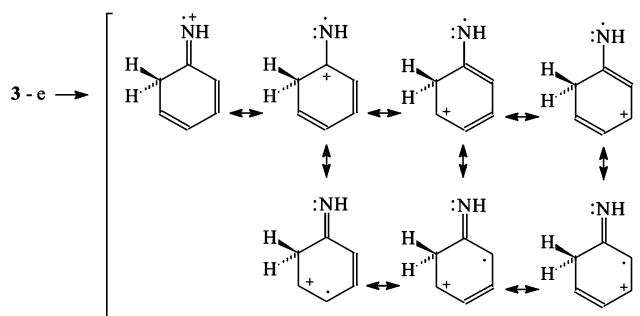
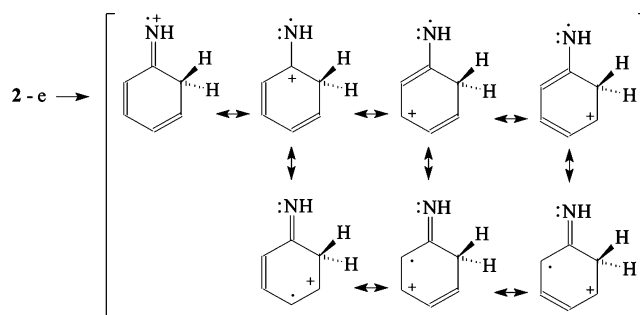
**a** loss of one electron from the  $\pi$ -orbital of the C atom



**b** loss of one electron from the n-orbital of the N atom

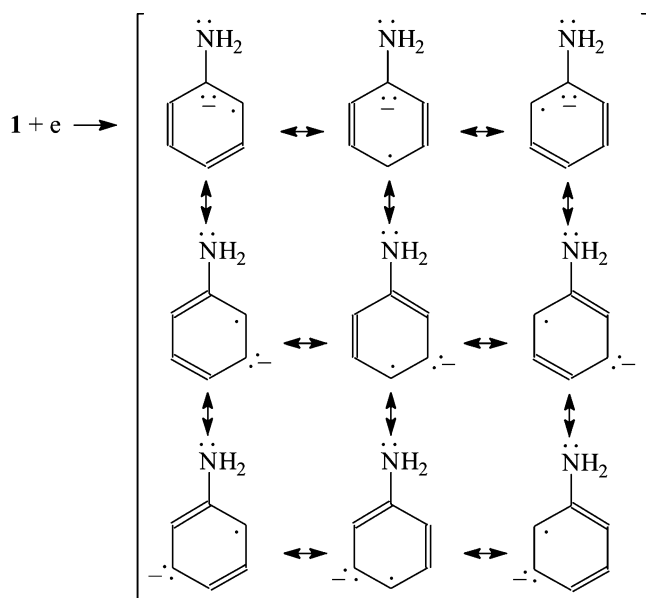


**Scheme 5** Loss of one electron for enamine isomer **1**, and delocalization of electrons and positive charge for its radical cation



**Scheme 6** Loss of one electron for the imine isomers **2-4**, and delocalization of electrons and positive charge for its radical cation





**Scheme 7** Gain of one electron for aniline (**1**), and delocalization of electrons and negative charge for its radical anion

aniline similarly as the proton-transfer interconversions. The relative thermal corrections are also close to zero, and thus  $\Delta E \approx \Delta H \approx \Delta G$ .

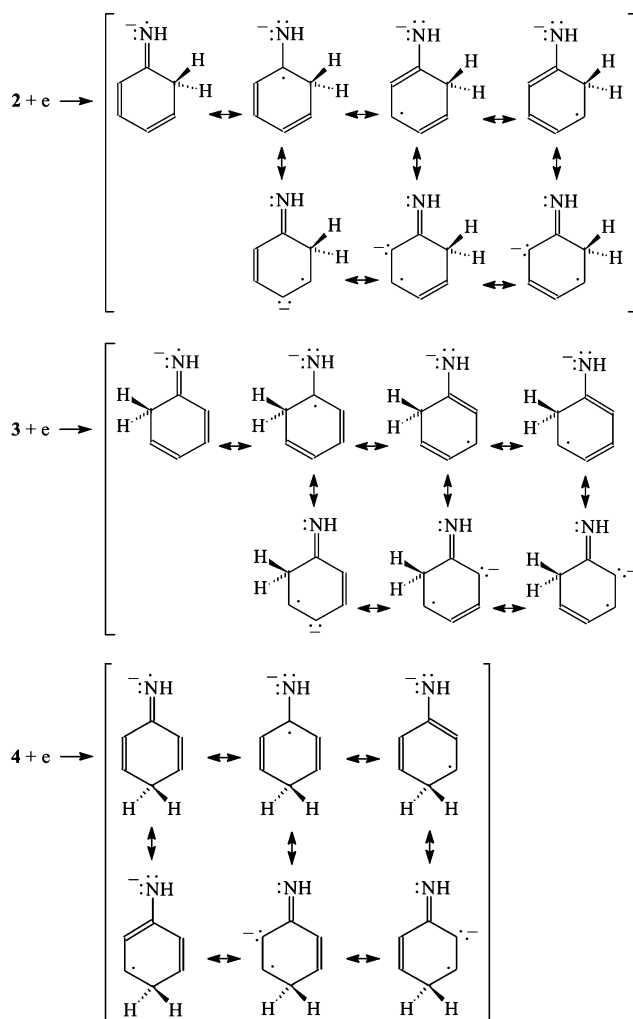
If we consider solely the favored neutral and redox forms of aniline, i.e., the enamine isomer **1** for the neutral and oxidized form (radical cation), and the imine isomer **2a/3a** for the reduced form (radical anion), the following scheme of the redox reactions can be drawn (Scheme 2). The relative Gibbs energies calculated at the B3LYP/6-311+G(d,p) level and the HOMED indices estimated for the geometries optimized at the same level of theory are also given in this scheme. The oxidation energies are close to 170 kcal mol<sup>-1</sup> and the reduction energies are ten times lower (17 kcal mol<sup>-1</sup>). The variation of the tautomeric preferences and  $\pi$ -electron delocalization when proceeding from the neutral molecule to its redox forms may be helpful in understanding the mechanisms of various organic reactions for aniline and of biochemical transformations for aromatic biomolecules containing the NH<sub>2</sub> group in the ring.

#### Mulliken charges

It is well known that for the neutral enamine isomer **1**, the *exo*-NH<sub>2</sub> group influences the phenyl ring by its electronic inductive and resonance effects (Scheme 3). These effects are not parallel. The inductive effect is electron-accepting due to greater electronegativity of the N atom than the C atom, whereas the resonance effect is electron-donating due to presence of n-electrons at the N atom. The n-electrons conjugate with  $\pi$  electrons of the phenyl ring. The mixture of the inductive and resonance effects of the NH<sub>2</sub> group

differentiates the charge distribution at the phenyl C atoms. In the case of the neutral imine isomers **2-4**, the *exo*=NH group also affects the phenyl ring (Scheme 4) but not in the same way as the NH<sub>2</sub> group for **1**. Both, the inductive and resonance effects of the =NH group are electron-accepting. The orientation of the imine H atom and possible intramolecular interactions (repulsion of the CH and NH groups, or interaction of the CH group with n-electrons of the N atom) additionally polarize  $\pi$ -electrons in the ring and influence the charge distribution at the phenyl C atoms. Taking the resonance structures of **1-4** into account, one can assume that the atom possessing the negative charge in the resonance structure may lose one electron and the atom possessing the positive charge may gain one electron during the oxidation and reduction process, respectively.

To obtain more information on the mechanism of one-electron oxidation and one-electron reduction processes, the Mulliken charges, calculated for the neutral and redox



**Scheme 8** Gain of one electron for the imine isomers **2/3**, and delocalization of electrons and negative charge for its radical anion

forms of aniline at the B3LYP/6-311+G(d,p) level, are compared in Table 6. The comparison shows that for all neutral forms (**1-4**), the N atom possesses the negative Mulliken charge. For the C-sp<sup>2</sup> atoms, the Mulliken charges are negative or positive according to various effects of the –NH<sub>2</sub>/=NH group. For the C-sp<sup>3</sup> atom, which takes the moving proton (C2/C6-sp<sup>3</sup> in **2/3** and C4-sp<sup>3</sup> in **4**), its charge becomes more negative. This increase of the negative charge at *ortho*- and *para*-position may partially explain the mechanisms of electrophilic substitutions of aniline [6, 7] and possible participation of the imine forms as intermediates. When proceeding from the neutral form to the radical cation, the negative charge of the C-sp<sup>3</sup> atom additionally augments. Great changes of the Mulliken charges ( $\Delta$  values) take also place for the N atom which loses partially its negative charge in the radical cation isomers. This may suggest that during oxidation the N atom loses one electron from its n-orbital. However, an increase of the positive charge for some C atoms may also indicate that the C atom loses one electron from its  $\pi$ -orbital.

Indeed, for the enamine radical cation isomer **1**, the  $\Delta$  values are positive for the N7 atom and also for all C atoms (with larger  $\Delta$  values for the C1 and C4 atoms). Similar changes of the Mulliken charges {B3LYP/6-311+G(df, pd)} have been observed by Michalska and co-workers [25]. These variations confirm a loss of one electron from the n-orbital of the N atom as well as from the  $\pi$ -orbital of the ring C atom (Scheme 5). In the case of the imine radical cation isomers **2/3**, larger positive  $\Delta$  values for the N7, C1, and C3 atoms suggest that one electron may be taken from the n-orbital of the N atom. However, taking into account all possible resonance structures (Scheme 6), where unpaired electron is delocalized to the ring, one may also conclude that the C atom loses one electron from its  $\pi$ -orbital. Similar conclusion can be derived for the imine radical cation isomer **4**. The  $\Delta$  values are positive for the N7, C1, C3, and C5 atoms, and they are negative for the C2 and C6. This indicates that one electron can be taken from the n-orbital of the N atom, and the positive charge can be delocalized at the N7, C1, C3, and C5 atoms (Scheme 6). For two resonance structures, unpaired electron is placed at the C2 or C6 atom. This may suggest that one electron may also be taken from the  $\pi$ -orbital of the C atom.

In the case of the radical anion isomers, the positive charge for the N atom of **1** suggests that this atom does not participate in electron gain, nor in delocalization of the negative charge. One excess electron seems to be taken by the phenyl ring (Scheme 7). The negative charge is delocalized at the C1, C3, and C5 atoms. Quite a different situation takes place for the imine forms (**2-4**). One-electron reduction increases the negative charge at the C1, C3, and C5 atoms and also at the N7 atom. This indicates that the  $\pi$ -

$\pi$  conjugated fragment, –C=C–C=C–C=NH in **2a/3a** and **2b/3b** and –(C=C–)<sub>2</sub>C=NH in **4**, gains the excess electron (Scheme 8).

## Conclusions

Quantum-chemical calculations performed for the neutral, oxidized, and reduced enamine and imine forms of aniline (Scheme 1) showed evidently that one-electron oxidation does not change the tautomeric preference in the gas phase. The enamine tautomer **1** predominates for the oxidized mixture, similarly as for the neutral one.  $\pi$ -Electron delocalization seems to play a principal role in tautomeric system and affects the tautomeric preference. However, for unknown reason, other internal effect changes this trend for the reduced mixture for which the less delocalized imine isomers **2a/3a** (89%) and **2b/3b** (11%) dominate. This variation of the tautomeric preference and  $\pi$ -electron delocalization may be helpful in understanding the mechanisms of spontaneous point mutations in DNA [64–66] as well as the mechanisms of aniline oxidation polymerization and polycondensation [52–62].

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## References

- Patai S (ed) (1982) The Chemistry of Amino, Nitroso, Nitro Compounds and their Derivatives. Wiley, New York
- Patai S (ed) (1996) The Chemistry of Amino, Nitroso, Nitro and Related Groups, Supplement F2. Wiley, Chichester
- Katritzky AR, Jug K, Oniciu DC (2001) Chem Rev 101:1421–1450
- Balaban AT, Oniciu DC, Katritzky AR (2004) Chem Rev 104:2777–2812
- Raczyńska ED, Kosińska W, Ośmiałowski B, Gawinecki R (2005) Chem Rev 105:3561–3612
- Carey FA, Sundberg RJ (1993) Advanced Organic Chemistry, 3rd edn. Plenum, New York
- Lowry TH, Richardson KS (1987) Mechanism and Theory in Organic Chemistry. Harper & Row, New York
- Dunsch L (1975) J Electroanal Chem 61:61–80
- Dunsch L (1996) J Electroanal Chem 419:55–59
- Omelka L, Ondrášová S, Dunsch L, Petr A, Staško A (2001) Monatsh Chem 132:597–606
- Pron A, Rannou P (2002) Prog Polym Sci 27:135–190
- Kim Y, Fukai S, Kobayashi N (2001) Synth Met 119:337–338
- Karunakaran C, Senthilvelan S (2006) Electrochem Commun 8:95–101, and references cited therein
- Koval'chuk EP, Whittingham S, Skolozdra OM, Zavalij PY, Zavalij IYu, Reshetnyak OV, Błażejowski J (2001) Mater Chem Phys 70:38–48

15. Song X, Yang M, Davidson ER, Reilly JP (1993) *J Chem Phys* 99:3224–3233
16. Müller-Dethlefs K, Schlag EW (1991) *Annu Rev Phys Chem* 42:109–136
17. Piest H, von Helden G, Meijer G (1999) *J Chem Phys* 110:2010–2015
18. Gée C, Douin S, Crépin C, Bréchnignac P (2001) *Chem Phys Lett* 338:130–136
19. Nakanaga T, Piracha NK, Ito F (2001) *J Phys Chem A* 105:4211–4215
20. McLafferty FW, Tureček F (1993) *Interpretation of Mass Spectra*. University Science Books, Mill Valley, California
21. Perrin CL (1977) *J Am Chem Soc* 99:5516–5518
22. Bunnett JF (1978) *Acc Chem Res* 11:413–420
23. Alder RW (1980) *J Chem Soc Chem Commun* 1184–1186
24. Ebersen L, Jönsson L, Wistrand LG (1982) *Tetrahedron* 38:1087–1093, and references cited therein
25. Wojciechowski PM, Zierkiewicz W, Michalska D, Hobza P (2003) *J Chem Phys* 118:10900–10911
26. Le HT, Flammang R, Barbioux-Flammang M, Gerbaux P, Nguyen MT (2002) *Int J Mass Spectrom* 217:45–54
27. Chyall LJ, Kenttämaa HI (1994) *J Am Chem Soc* 116:3135–3136
28. Chyall LJ, Kenttämaa HI (1995) *J Mass Spectrom* 30:81–87
29. Parr RG, Yang W (1989) *Density Functional Theory of Atoms and Molecules*. Oxford University Press, New York
30. Becke AD (1993) *J Chem Phys* 98:5648–5652
31. Lee C, Yang W, Parr RG (1988) *Phys Rev B* 37:785–789
32. Bertrand W, Bouchoux G (1998) *Rapid Commun Mass Spectrom* 12:1697–1700
33. Rodríguez-Santiago L, Vendrell O, Tejero I, Sodupe M, Bertran J (2001) *Chem Phys Lett* 334:112–118
34. Exner O, Bohm S (2006) *Collect Czech Chem Commun* 71:1239–1255
35. Raczynska ED, Zientara K, Kolczyńska K, Stepniowski TM (2009) *Pol J Chem* 83:821–834
36. Raczynska ED, Kamińska B (2010) *J Phys Org Chem* 23:828–835
37. Hehre WJ, Radom L, Schleyer PvR, Pople JA (1986) *Ab initio Molecular Theory*. New York
38. Curtiss LA, Raghavachari K, Trucks WG, Pople JA (1991) *J Chem Phys* 94:7221–7230
39. Curtiss LA, Raghavachari K, Pople JA (1993) *J Chem Phys* 98:1293–1298
40. Smith BJ, Radom L (1993) *J Am Chem Soc* 115:4885–4888
41. Smith BJ, Radom L (1995) *J Phys Chem* 99:6468–6471
42. Woon DE, Dunning TH (1993) *J Chem Phys* 98:1358–1371
43. Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Montgomery JA, Vreven T, Kudin KN, Burant JC, Millam JM, Iyengar SS, Tomasi J, Barone V, Mennucci B, Cossi M, Scalmani G, Rega N, Petersson R, Nakatsuji H, Hada M, Ehara M, Toyota K, Fukuda R, Hasegawa J, Ishida M, Nakajima T, Honda Y, Kitao O, Nakai H, Klene M, Li X, Knox JE, Hratchian HP, Cross JB, Bakken V, Adamo C, Jaramillo R, Gomperts R, Stratmann RE, Yazyev O, Austin AJ, Cammi R, Pomelli C, Ochterski JW, Ayala PY, Morokuma K, Voth GA, Salvador P, Dannenberg JJ, Zakrzewski VG, Dapprich S, Daniels AD, Strain MC, Farkas O, Malick DK, Rabuck AD, Raghavachari K, Foresman JB, Ortiz JV, Cui Q, Baboul AG, Clifford S, Cioslowski J, Stefanov BB, Liu G, Liashenko A, Piskorz P, Komaromi I, Martin RL, Fox DJ, Keith T, Al-Laham MA, Peng CY, Nanayakkara A, Challacombe M, Gill PMW, Johnson B, Chen W, Wong MW, Gonzalez C, Pople JA (2004) *Gaussian-03, Revision E.01*. Gaussian, Inc, Wallingford CT
44. Lister DG, Tyler JK, Hög JH, Larsen NW (1974) *J Mol Struct* 23:253–264
45. Raczynska ED, Krygowski TM, Duczmal K, Hallmann M (2006) XVIII International Conference on Physical Organic Chemistry, Warsaw, Book of abstracts, p. 31
46. Raczynska ED, Hallmann M, Kolczyńska K, Stepniowski TM (2001) *Symmetry* 2:1485–1509
47. Krygowski TM (1993) *J Chem Inf Comput Sci* 33:70–78
48. Lammertsma K, Prasad BV (1994) *J Am Chem Soc* 116:642–650
49. Hehre WJ, Taylor RT, Pople JA, Schleyer PvR (1974) *J Am Chem Soc* 96:7162–7163
50. Schleyer PvR, Pühlhofer F (2002) *Org Lett* 4:2873–2876
51. Henriksen J, Hammerum S (1998) *Int J Mass Spectrom* 179/180:301–308
52. Genies EM, Lapkowski M (1987) *J Electroanal Chem* 236:189–197
53. Lapkowski M, Genies EM (1990) *J Electroanal Chem* 279:157–168
54. MacDiarmid AG, Epstein AI (1989) *Faraday Discuss Chem Soc* 88:317–332
55. Koval'chuk EP, Whittingham S, Skolozdra OM, Zavalij PY, Zavalij IYu, Reshetnyak OV, Seledets M (2001) *Mater Chem Phys* 69:154–162
56. Čirić-Marjanović G, Konyushenko EN, Trchová M, Stejskal J (2008) *Synth Met* 158:200–211
57. de Barros RA, Areias MCC, de Azevedo WM (2010) *Synth Met* 160:61–64, and references cited therein
58. Madathil R (2005) *Synth Met* 150:123–126
59. Cristovan FH, Lemos SG, Santos JS, Trivinho-Strixino F, Pereira EC, Mattoso LHC, Kulkarni R, Manohar SK (2010) *Electrochim Acta* 55:3974–3978, and references cited therein
60. Santhanam M, Ramakrishnan V (1968) *Indian J Chem* 6:88–90
61. Santhanam M, Ramakrishnan V (1972) *Indian J Chem* 10:927–928
62. Davidson RS, Lambeth PF, Santhanam M (1972) *J Chem Soc Perkin Trans* 2:2351–2355
63. Mallard WG, Linstrom PJ (eds) (2005) *NIST Chemistry WebBook*. NIST Standard Reference Database. National Institute of Standards and Technology, Gaithersburg, MD
64. Kryachko ES (2002) *Int J Quantum Chem* 90:910–923
65. Müller-Dethlefs K, Hobza P (2000) *Chem Rev* 100:143–168
66. Grebneva HA (2003) *J Mol Struct* 645:133–143