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^{13}C-NMR Based Evaluation of the Electronic and Steric Interactions in Aromatic Amines

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Abstract: Chemical shifts of the *para* carbon atoms, δ(^{13}C-4), in a series of aromatic amines were used to calculate the σ_p, σ_R and σ_R^O substituent constants for different amino groups. 1-Pyrrolidino, *N,N*-di-*n*-butylamino and *N,N*-diethylamino groups were found to be the most strong electron-donors. *ortho*-Substitution decreases the donor properties of the amino group. The amino groups in 2,6-di-*i*-propylaniline and *N,N*-2,6-tetramethylaniline have very weak electron-donor properties. The nitrogen atom in benzoquinuclidine and *N,N*-dimethyl-2,6-di-*i*-propylaniline have an electron-acceptor character. The calculated substituent constants of the amino groups studied are consistent with the spectral and reactivity data available in literature. Values of δ(^{15}N) cannot be used as a direct measure of electronic effects of the N atom in anilines.

Keywords: Amino groups, substituent effects, steric inhibition to resonance, ^{13}C- and ^{15}N-NMR, aromatic amines.

Introduction

The nature of the interactions between different molecular moieties is well known for aniline and its common derivatives [1,2]. Little is known, however, about electronic and steric effects of

uncommon amino groups. Due to its +R effect the primary amino group is a strong electron-donor (σ_R = -0.76 [3-5], -0.78 [6]). The inductive effect of NH_2 (σ_I = 0.10 [7], 0.11 [6]) slightly moderates its donating power (σ_p = -0.66 [8]). Further, amino group is much stronger electron donor (σ_p^+ = -1.3 [9]) when there is another substituent of the -R type at the *para* position of the benzene ring. Due to the inductive (+I) effect of the *N*-alkyl groups, alkylamino substituents are even stronger electron-donors [6,8,9].

In addition to common amino groups, *e.g.* NH_2, NHR, NR_2 (R = alkyl) and cyclic polymethyleneimino derivatives, $N(CH_2)_n$, some aromatic amines, *e.g.* indoline and julolidine, contain alkane bridges between the amino nitrogen and the ring *ortho*-carbon atom(s). In consequence, their molecules are conformationally rigid and therefore reveal very interesting properties. It is noteworthy, that although some important aspects of the electronic effect of the amino groups were discussed by Chuchani [1] and recently by Shorter [2], some interesting uncommon amino derivatives were, however, not included there.

The energetically optimal conformation of aromatic amines is a compromise between the tendency of the amine nitrogen atom to be pyramidal (sp^3) and its tendency to assume the planar sp^2-hybridization in order to maximize the resonance interaction with aromatic part of the molecule. The term "steric inhibition of resonance" refers to a non-planar sterically hindered molecule while the unhindered reference molecule is planar [10].

An extent of the conjugation of aromatic part of the molecule with its amino substituent is an indicator for the ability of the nitrogen atom to possess the sp^2-hybridization. In the Hückel MO theory this property is expressed by the overlap integral of the lone-pair orbital, n_N, and the π-orbital of the benzene ring, π_{Ar} [11]. On the other hand, the coulomb integral reflects the electro-negativity of the amino nitrogen atom. It has been found [11] that different N,N-dialkylamino and polymethyleneimino, $N(CH_2)_n$, groups reveal similar inductive effects. Thus, the donor strength of the amino group depends mainly on its resonance interactions with aromatic ring, which are related to the C_{Ar}-N bond length, R-N-R bond angle and other geometrical parameters such as torsion angle of the amino group with respect to benzene ring.

Since the chemical shifts of heavy nuclei (other than protons) depend both on the diamagnetic and paramagnetic shielding tensors of the nuclei [12], their δ values are related to the electronic charges at these atoms and interatomic bond orders. Thus, one may expect that there are more or less direct relations between the σ substituent constants and the NMR chemical shifts for substituted aromatic amines. So, the knowledge of the electronic and steric properties of substituents is very important in interrelating the structural and spectral data. Since Exner [13] has stated that "… a single scale of mesomeric constants is an unrealizable objective", we intended to differentiate various amino groups from a point of view of their electronic and steric properties rather than to determine the absolute σ constants.

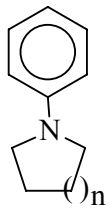
Results and Discussion

The chemical shifts of nitrogen (N) and *para* (with respect to the amino group) carbon (C-4) atoms in the NMR spectra of anilines are collected in Table 1. π-Electron density at the *para* carbon atom in aromatic compounds depends on the twist angle of the substituent [14] and thus, its chemical shift can be used to calculate these angles for the amino groups in anilines. ^{13}C-NMR chemical shifts for

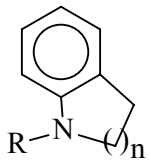
unsubstituted aniline were found to be quite sensitive to the orientation of the NH_2 group [15]. This relation was also confirmed by both theoretical (GIAO, Gauge-Independent Atomic Orbital) and experimental results [15]. The amino group in aniline itself is tilted away from the ring plane by 42°[15]. The chemical shift values increase (deshielding effect) as the amino group is moved away from the planar orientation with the largest changes appearing at the *ipso*, *ortho* and *para* positions [15]. ^{13}C-NMR spectra show that *N*-phenylaziridine is the least conjugated among *N*-phenyl cyclic polymethyleneimines [16]. It has been found that *p*-substituent in *N*-phenylaziridines only slightly affects electron distribution in aziridine ring [17]. This proves that n_N-π_{Ar} conjugation in these compounds is insignificant. The chemical shifts of *para* carbon atom in the spectra *N,N*-dimethyl- and *N,N*-diethylanilines and 1-phenylaziridine, 1-phenylpyrrolidine and 1-phenylpiperidine correlate well with other known measures of benzene ring-nitrogen resonance such as oscillator strength of the UV bands and exaltation of molar refraction [16,18].

Scheme 1

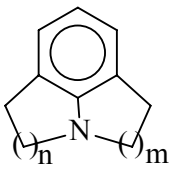
Structures of selected amines



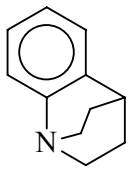
1: n = 1
25: n = 2



4: R = Me, n = 2
6: R = H, n = 2
7: R = Me, n = 3
13: R = Me, n = 1
19: R = H, n = 1



5: n = 2, m = 2
26: n = 2, m = 1
27: n = 1, m = 1



31

Numerous papers have been published on correlations of NMR chemical shifts with Hammett σ values [19-21]. σ_p values for the NMe_2 and NH_2 [8] as well as these for other non-amine substituents [22] are known [8]. Since in chloroform solutions δ(^{13}C-4) values are 117.68, 116.38, 120.72, 125.38, 128.36, 126.43, 126.82, 132.84 and 134.72 ppm for aniline, *N,N*-dimethylaniline, anisole, toluene, benzene, chlorobenzene, bromobenzene, benzonitrile and nitrobenzene [23], respectively, the dependence between the substituent constant and the chemical shift of *para* carbon atom is $\sigma_p = 0.089\ \delta(^{13}\text{C-4}) - 11.22$. This equation can be used to calculate the substituent constants for other groups (Table 1). It is known that different *N,N*-dialkylamino and polymethyleneimino, $N(CH_2)_n$, groups reveal similar inductive effects [11].

Table 1. Selected ^{15}N- and ^{13}C- chemical shifts [ppm] in the NMR spectra of substituted anilines for 0.1-0.2 M solutions in chloroform-d_1 and substituent constants for the amino groups

Compound	Amino group and additional substituents	$\delta(^{15}N)$	$\delta(^{13}C4)$	σ_p	σ_R	σ_R^O
1	$N(CH_2)_4$	-308.7	115.20	-0.92	-1.02	-0.57
2	$N(n\text{-}Bu)_2$	-312.4	115.13	-0.91	-1.01	-0.57
3	NEt_2	-309.7	115.32	-0.91	-1.01	-0.57[a]
4	$N(Me)[2\text{-}(CH_2)_3]$	-319.0	115.33	-0.91	-1.01	-0.57
5	$N[2\text{-}(CH_2)_3][6\text{-}(CH_2)_3]$	-318.5	115.61	-0.89	-0.99	-0.56
6	$NH[2\text{-}(CH_2)_3]$	-320.8	115.90	-0.86	-0.98	-0.55
7	$N(Me)[2\text{-}(CH_2)_4]$	-330.9	116.03	-0.85	-0.95	-0.55
8	NMe_2	-337.7	116.38	-0.82[b]	-0.92	-0.54[a,c]
9	N(Me)Et	-325.0	116.86	-0.77	-0.87	-0.52
10	NHMe	-329.2	116.98	-0.76	-0.88	-0.52[a]
11	NHEt	-310.4	117.02	-0.76	-0.88	-0.52[a]
12	$1\text{-}NH_2,2,6\text{-}Me_2$	-331.2	117.34	-0.73	-0.87	-0.51
13	$N(Me)[2\text{-}(CH_2)_2]$	-316.2	117.53	-0.71	-0.81	-0.51
14	$1\text{-}NH_2,2,6\text{-}Et_2$	-333.2	117.54	-0.71	-0.85	-0.51
15	$1\text{-}NH_2$,2-Me,6-Et	-332.4	117.67	-0.70	-0.84	-0.50
16	NH_2	-325.5	117.68	-0.70[d]	-0.84	-0.50
17	$1\text{-}NH_2$,2-Me	-328.1	117.86	-0.68	-0.82	-0.50
18	1-NHMe,2-Me	-327.1	117.86	-0.68	-0.80	-0.50
19	$NH[2\text{-}(CH_2)_2]$	-314.3	117.89	-0.68	-0.80	-0.50
20	$1\text{-}NMe_2$,2-Me	-347.3	118.23	-0.65	-0.75	-0.49
21	$1\text{-}NH_2$,2-Et	-329.4	118.36	-0.64	-0.78	-0.48
22	$1\text{-}NH_2$,2-*t*-Bu	-322.9	118.37	-0.64	-0.78	-0.48
23	$1\text{-}NH_2$,2-*i*-Pr	-329.4	118.49	-0.63	-0.77	-0.48
24	$N(i\text{-}Pr)_2$	-299.1	118.56	-0.62	-0.72	-0.48
25	$N(CH_2)_5$	-313.2	118.91	-0.59	-0.69	-0.47[a]
26	$N[2\text{-}(CH_2)_2][6\text{-}(CH_2)_3]$	-307.8	119.06	-0.58	-0.68	-0.46
27	$N[2\text{-}(CH_2)_2][6\text{-}(CH_2)_2]$	-	120.0[e]	-0.49	-0.59	-0.44
28	$1\text{-}NH_2,2,6\text{-}(i\text{-}Pr)_2$	-370.8	123.97	-0.14	-0.28	-0.33
29	$1\text{-}NMe_2,2,6\text{-}Me_2$	-364.8	124.72	-0.07	-0.17	-0.31
30	$1\text{-}NMe_2,2,6\text{-}(i\text{-}Pr)_2$	-370.2	126.26	0.07	-0.03	-0.27
31	$1\text{-}N(CH_2CH_2)_2CH\text{-}2$[f]	-339.0[g]	127.00[h]	0.13	0.03	-0.25

[a] Substituent constants based on intensity of the IR bands for anilines [25-27] or ^{19}F NMR chemical shifts for *p*-fluoroanilines [28]. [b] -0.83 [8]. [c] σ_R^O value based on reactivity measurements is -0.52 [28]. [d] -0.66 [8]. [e] In $CDCl_3$ [29]. [f] Benzoquinuclidine. [g] In methylene chloride-d_2 [30]. [h] In benzene-d_6 [31].

Available σ_I values are equal to 0.14, 0.12, 0.10 and 0.10 for *p*-NH_2, *p*- NHMe, *p*-NMe_2 and *p*-NEt_2, respectively [24]. This shows that the resonance effect of the N atom in anilines considerably predominates over its inductive effect.

Values of σ_R (resonance substituent constants) collected in Table 1 were obtained by subtraction of σ_I from σ_p ($\sigma_R = \sigma_p - \sigma_I$). σ_I values used to calculate the σ_R constants are equal to 0.14 for *p*-NH_2 with or without *ortho*-substituent(s), 0.12 for *p*-NHR (R = alkyl and polymethylene bridge in indoline or 1,2,3,4-tetrahydroquinoline) with or without *ortho*-substituent(s), 0.10 for *p*-NR_2 (R = alkyl and/or polymethylene bridge in 1-methylindoline, 1-methyl-1,2,3,4-tetrahydroquinoline, 1-methyl-2,3-benzohexamethyleneimine, lilolidine, *i.e.* 1,2,5,6-tetrahydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline, julolidine, *i.e.* 2,3,6,7-tetrahydro-1*H*,5*H*-pyrido[3,2,1-*ij*]quinoline, and benzoquinuclidine, *i.e.* 3,4-dihydro-2*H*-1,4-ethanoquinoline, with or without *ortho*-substituent(s).

Analysis of the $\delta(^{13}C\text{-}4)$ values in Table 1 shows that σ_p substituent constants for different dialkylamino groups change in the following order: $N(n\text{-}Bu)_2 \approx NEt_2 < NMe_2 < N(Me)Et < N(i\text{-}Pr)_2$. Thus, in general, those containing longer alkyls are stronger electron-donors. On the other hand, dialkylamino groups including secondary alkyl, *e.g.* *i*-propyl, are weaker donors. This may be caused by the strong steric interaction of the N-*i*-propyl group with *ortho*-hydrogen atoms. It seems interesting that $\sigma_{p\text{-}N(Me)Et} \approx \sigma_{p\text{-}NHMe} = \sigma_{p\text{-}NHEt}$.

Substitution at the *ortho* carbon in *N,N*-dimethylaniline causes NMe_2 group to twist out of the ring plane, so the nitrogen valences become more pyramidal [28]. Thus, *ortho*-substitution decreases the donor properties of the amino group. Comparison of $\delta(^{13}C\text{-}4)$ values for different *ortho*-substituted anilines, *o*-R-C_6H_4-NH_2 (**17** and **21-23** in Table 1) with that of the aniline itself (**16**), shows that σ_p substituent constants depend on R in the following order: H < Me < Et ≈ *t*-Bu < *i*-Pr. On the other hand, substitution in both *ortho* positions (**12**, **14** and **15**) increases the donor properties of the amino (NH_2) group as compared to parent aniline **16**. 2,6-Di-*i*-propyloaniline (**28**) is an exception: the amino group in this compound seems to have very weak electron-donor properties. This may be caused by the strong steric interaction of the *ortho*-*i*-propyl and NH_2 groups. When comparing different 2,6-R,R'-substituted anilines **12**, **14-17**, **21-23** and **28** one can see that σ_p substituent constant of the amino group change in the following order: R,R' = Me,Me < Et,Et < Me,Et = H,H < H,Me < H,Et = H,*t*-Bu ≈ H,*i*-Pr << *i*-Pr,*i*-Pr. Due to strong steric interactions, the amino group in 2,*N,N*-trimethylaniline (**20**) is a weak electron-donor (calculations based on the band intensities show *ortho*-methyl group in ethyl N,N,3-trimethyl-4-aminobenzoate to produce a 56 % steric inhibition to resonance [32]). These interactions are much stronger in 2,6-dialkyl-*N,N*-dimethylanilines **29** and **30**. It is noteworthy that the twist angles in 2,6-diethyl- and 2,6-di-*i*-propyl-*N,N*-dimethylanilines were found to be equal to 77 and 88°, respectively [33].

The length of the polymethylene bridge between N and C_{ortho} in anilines **4**, **7**, **13**, **6** and **19** has a considerable effect on the electronic properties of the N atom in these compounds. Thus, it is the strongest donor in 1,2,3,4-tetrahydroquinolines **4** and **6**. The amino nitrogen atom in indolines **13** and **19** is much weaker donor. This tendency is also seen in $\delta(^{13}C\text{-}4)$ values for julolidine (**5**) and lilolidine (**26**). The N atom in 1,2,4,5-tetrahydropyrrolo[3,2,1-*hi*]indole (**27**) is a weak electron-donor.

The nitrogen atom in benzoquinuclidine (**31**) clearly reveals electron-acceptor properties. Studies of molecular structures of benzoquinuclidine and its 6-cyano derivative in the crystal state confirm that there is no n_N-π_{Ar} conjugation in these compounds (the aromatic π and nitrogen electron lone pair

orbitals are orthogonal) [31,34]. Thus, there is no resonance interaction between the amino nitrogen atom and the benzene ring in benzoquinuclidine [35].

Molecular models show that due to the angle strain in the five-membered ring, the C_{Ar}-C_{Ar}-N valence angle in indoline (**19**) and its *N*-methyl derivative **13** is expected to be much smaller than 120°. Bicyclic structures in *N*-methylindoline (**13**) and *N*-methyl-1,2,3,4-tetrahydroquinoline (**4**) were shown to be planar [36]. On the other hand, the seven-membered ring in *N*-methyl-*homo*-tetrahydroquinoline (**7**) is highly puckered [36]. The UV spectrum of this compound shows considerable difference from the spectra of two lower homologues, and this difference is certainly due to the conformational freedom of the seven-membered ring [37].

Although large differences in basic properties were found for *N,N*-diethylaniline and *N*-phenylpyrrolidine, close similarity of their ^{13}C-NMR spectra (Table 1) shows that electron distributions in the benzene rings are nearly the same in these two compounds [16]. 1-Pyrrolidino group (**1**) was found to be a very powerful electron-donor [38]. It is much stronger electron-donor than 1-piperidino group (**25**). Decreased n_N-π_{Ar} interaction in 1-(*p*-nitrophenyl)piperidine, which reflects the relative rigidity of the chair conformation of the six-membered piperidine ring, is also consistent with the downfield shift for signals of protons *2* and *6* in spectra of 1-(*p*-nitrophenyl)pyrrolidine, 1-(*p*-nitrophenyl)hexamethyleneamine and *N,N*-dialkylanilines, where alkyl = Me, Et [39]. Low ε_{max} value of the band at 425 nm in the spectrum of *N*-(*p*-nitrophenyl)piperidine, as compared to the spectra of *N*-(*p*-nitrophenyl)pyrrolidine and *N*-(*p*-nitrophenyl)hexamethyleneimine, proves there is a serious steric inhibition to resonance in its molecule. The angle of twist of the CNC plane with respect to that of the benzene ring in *N*-(*p*-nitrophenyl)piperidine is equal to 33° [40]. Due to interaction between the nitrogen atom and phenyl ring, the resonance energy in *N*-phenylcyclopolymethyleneimines changes in the following order of the ring size: n = 3 < 6 < 4 < 5 [41]. Analysis of the chemical shift values for the ring protons in ^{1}H-NMR spectra of aniline derivatives shows that donor strength of the amino substituents in the ground state of aromatic amines change in the following order [11]: 1-pyrrolidino > dimethylamino >1-piperidino.

Of course, confusion may result from the above discussion having its source in the dispersion of the substituent constants available for the amino groups [13]. One should be aware of differentiation between these parameters depending *e.g.* on application (or not) of the correction for the tautomeric equilibria possible in solutions of such compounds [13]. Thus, the amino substituent in *N,N*,2,6-tetramethylaniline (**29**) was found to be a very weak electron-donor. However, comparison of the $\delta(^{13}$C-4) values for this compound (124.72 ppm) and unsubstituted benzene (128.5 ppm) shows that this cannot be true. We have found that σ_R^O values for some amino groups known [25-27] (Table 1) are linearly related to the obtained NMR chemical shifts of C-4 (Table 1): $\delta(^{13}$C-4) = 36.401 σ_R^O + 135.922 (R = 0.9931 for five correlation points). This equation was used by us to calculate the respective substituent constants for other amino substituents (Table 1). It can be seen that all substituents studied are electron-donor by character but, as expected, their releasing properties are very much differentiated.

The obtained substituent constants seem worthy to be compared to the results of earlier studies (only some amino groups were studied by other authors). Substituent σ_R^O constants for the amino and dimethylamino groups, based on fluorine chemical shift in the NMR spectra of the respective fluoroanilines, are equal to -0.48 and -0.53, respectively [42,43]. Due to the steric inhibition to resonance of the *ortho*-methyl group in *N,N*,2-trimethyl-4-fluoroaniline the σ_R^O constant for the

twisted *p*-dimethylamino substituent in this compound is equal to -0.24 [28]. ^{19}F-NMR chemical shifts of 4-amino-3,5-dimethylfluorobenzene and of its *N,N*-dimethyl derivative were interpreted in terms of a strong steric inhibition to resonance in their molecules but they are insufficient to push these amino groups out of conjugation with the benzene ring [44].

The square roots of integrated absorbancies of the skeletal vibrations, involving the carbon-carbon stretching within the ring, in the 1600-1585 and 1500-1400 cm^{-1} regions, are a good measure of the extent of resonance interaction between benzene ring and unsaturated substituent [45]. It has been found that the resonance interactions between the N atom and benzene ring change in the following order: $N(CH_2)_2 < N(CH_2)_5 < NMe_2 < N(CH_2)_3 < NEt_2 < N(CH_2)_4$. The σ_R^O values for such groups are equal to -0.38 for $N(CH_2)_2$, -0.47 for $N(CH_2)_5$, -0.52 for NHEt and NHMe, -0.53 for NHPr-*i* and NMe_2, -0.54 for NHBu-*n*, -0.55 for $N(CH_2)_3$, -0.57 for NEt_2 and -0.63 for $N(CH_2)_4$ [25-27]. Other σ_R^O values found for the NMe_2 group are equal to -0.54 (based on ^{19}F NMR spectra) [46], -0.52 (based on reactivity measurements) [28] and -0.50 (evaluated by means of equation $\sigma_R^O = 2.0\sigma_R^m$) [47].

Dipole moment of aniline (1.15 D [48]) was found to be only slightly affected by the *ortho*- and *N*-methyl groups: its value is appreciably diminished only in 2,6,*N*-trimethylaniline and especially in 2,*N,N*-trimethyl- and 2,6,*N,N*-tetramethylanilines [46,49]. Charge distribution in the molecules of aromatic amines shows the order of electron-donor strength of the amino groups to be $(CH_2)_4N > Et_2N > (CH_2)_5N$ [50,51] and $NEt_2 > N(CH_2)_4 > NMe_2 > N(CH_2)_5$ [50]. The calculated and measured dipole moments confirm the considerable twist of NMe_2 group in *ortho*-methyl substituted *N,N*-dimethylanilines [52]. Thus, there is a strong steric inhibition to resonance in these molecules [53]. Comparison of the experimentally observed and theoretically calculated dipole moments of 2,*N,N*-trimethylaniline shows the hybridization of the nitrogen atom to be close to sp^3 [14].

The sequence of the base strength of anilines of formula C_6H_5-NR^1R^2 in water changes in the following order [54]: R^1/R^2 = H/H < H/Me < Me/Me < H/Et < H/*i*-Pr < Et/Et. These results confirm that *N*-alkyl groups cause an increase in basicity of aniline due to their +I effect. On the other hand, *N*-alkylation may significantly change effectiveness of solvation of both amine and its conjugate acid. Alkyl groups in the *ortho* positions in aniline always decrease its pK_a [55]. On the other hand, substitution of the amino hydrogen atom(s) by alkyl(s) causes an increase of the base strength of aromatic amines. *Ortho* alkyl groups in *N,N*-dialkylanilines prevent the dialkylamino group from assuming coplanarity with the ring and hence decrease its resonance effect and increase the basicity of the compound. On the other hand, 2,*N*-dimethylaniline is weaker and 2,*N,N*-trimethylaniline is a stronger base than *N*-methylaniline. Unexpectedly, 2,6,*N,N*-tetramethylaniline has a lower pK_a than 2,*N,N*-trimethylaniline [55].

Benzoquinuclidine (**31**, Scheme 1), is a particular aromatic amine. As expected, it is relatively strong base, its pK_a value being the greatest one in a series of selected anilines measured in 50 % aqueous ethanol at 25°C [56]: pK_a: C_6H_5-NH_2 < C_6H_5-NMe_2 < *o*-Me-C_6H_4-NMe_2 < C_6H_5-NHBu-*t* << C_6H_5-N(Me)Bu-*t* < benzoquinuclidine. 1,2,4,5-Tetrahydropyrrolo[3,2,1-*hi*]indole (**27**) was unexpectedly found to be stronger base (pK_a = 4.1, in 50 % aqueous ethanol) than julolidine (**5**) (pK_a~3.6) [57]. Perhaps, in this case the pK_a value also reflects both the conformational changes in the molecule and differences in steric hindrance to solvation [58]. It has been found that linear correlation between the twist angle of the amino group and pK_a values of aniline derivatives is very rough due to peculiar solvation effects [31]. Thus, the anomalies in the base strength attributed to the steric hindrance of solvation [58] also enable evaluation of the conformation of aromatic amines

[26,59]. Acidities of *p*-aminobenzoic acids, R_2N-C_6H_4-CO_2H, and the rates of reduction of *p*-nitroanilines, R_2N-C_6H_4-NO_2, show the following order of the electron donating effect for different amino substituents [60]: $N(CH_2)_5 < NMe_2 < N(CH_2)_4 < NEt_2 < N(i\text{-}Pr)_2$. Decreased mesomerism that results from the twisting of the NCC plane out of the benzene ring plane, is illustrated by the pK_a value for *p*-(*N*-piperidino)benzoic acid, which is lower as compared to other *p*-aminobenzoic acids, *p*-R_2N-C_6H_4-CO_2H [39] (see also ref. [60]) : pK_a: $Et_2N > (CH_2)_4N > Me_2N > (CH_2)_5N$.

The σ substituent constants for some amino groups defined on the basis of dissociation constants of *p*-aminobenzoic acids, *p*-R_2N-C_6H_4-CO_2H, are equal to -0.41 for $N(CH_2)_5$, -0.62 for NH_2, -0.69 for NMe_2 and $N(CH_2)_4$, and -0.71 for NEt_2 [61]. The pK_a values of 4-amino-3,5-dimethylbenzoic acid and its *N,N*-dimethyl derivative, as well as saponification rates for the respective ethyl esters, have been interpreted in terms of steric inhibition to resonance [62].

Although benzoquinuclidine (**31**) is an aromatic amine, there is no resonance interaction between the amino nitrogen and the benzene ring in its molecule. It has been proven by its unsuccessful diazo coupling with *p*-nitrobenzenediazonium salts [35]. The σ_R^o for the twisted -N< group in benzoquinuclidine is equal to -0.134 [63] (as compared to -0.53 for NMe_2 group [64]). On the other hand, another hindered amine, *i.e.* 2,6-di-(*t*-butyl)aniline, can be readily coupled with arenediazonium salts to give the respective *p*-aminoazobenzenes [35,59,65]. Due to steric inhibition to resonance in *N*-*t*-butyl-*N*-methylaniline, this compound does not react with nitrous acid nor with ethyl nitrite to give the *para*-nitroso derivative [65]. The formation of 4'-nitro-4-(*N*-*t*-butyl-*N*-methylamino)azobenzene from this compound and *p*-nitrobenzenediazonium chloride proceeds extremely slowly with only 10 % yield [65]. None of *N,N*-dimethylanilines containing 2-*t*-butyl and 2,6-dimethyl groups can be nitrosated [65].

The nitrogen chemical shifts are influenced by the substituent *via* polar [66] and steric effects [67] and thus can be useful to estimate the degree of *n*-π interaction in anilines [68]. The effect of *N*-methylation on the ^{15}N-NMR chemical shift of aniline is known for long and consistent with the present data (**8**, **10** and **16** in Table 1) [69]. *Ortho*-substitution in *N,N*-dimethylaniline causes a considerably large shift of its ^{15}N-signal [33]. This has been attributed to the torsional distortion of the NMe_2 group [33], which results in a decreased electron delocalization in the molecule [67]. The data in Table 1 show that the changes of $\delta(^{15}N)$ may be both positive (cf. **10** *vs*. **18**; **16** *vs*. **22**; **19** *vs*. **13**) and negative (**4** *vs*. **6**; **8** *vs*. **20**, **29** and **30**; **16** *vs*. **12**, **14**, **15**, **17**, **21**, **23** and **28**). Thus, $\delta(^{15}N)$ cannot be used as a direct quantitative measure of electronic effects of the N atom in anilines, although $\delta(^{15}N)$ of *N*-(*p*-R-phenyl)aziridines qualitatively show, that the lone-pair electrons of aziridine nitrogen interact less effectively with benzene ring than those in the corresponding *N,N*-dimethylanilines [68].

Conclusions

In summary, one can see that the NMR chemical shifts of the C-4 aromatic carbon atom in aromatic amines is a very helpful tool to evaluate the substituent effects of different amino groups. The available literature data concerning the molecular structure of aromatic amines as well as their spectral and reactivity data support the correctness of evaluated substituent constants. The determined substituent constants for different amino groups are not absolute by character. To show the correctness of the determined substituent constants, in our next papers we are going to present also the correlations

between these parameters and other physical data of aromatic amines, *e.g.* the fluorine NMR chemical shifts for *p*-fluroanilines.

Experimental

Most anilines are commercially available and known procedures were used to prepare others [38]. They were recrystallized or distilled *in vacuum* before use. Their physical constants are consistent with these found in literature. All NMR spectra were recorded for 0.1 – 0.2 M $CDCl_3$ solutions at 303 K (unless otherwise stated) with a Bruker Avance DRX 500 FT NMR spectrometer equipped with an inverse detection 5 mm diameter broad band probehead and z-gradient accessory working at 500.13 MHz (^{1}H-), 125.76 MHz (^{13}C-) and 50.59 MHz (^{15}N-), respectively. In proton composite pulse decoupled (Waltz-16) ^{13}C-NMR experiments the spectral width was 30300 Hz (240 ppm), the number of data points 65 K, the flip angle 30°, and the number of scans typically > 10000 in order to observe reliably also the weak signals of the minor contributors. The FIDs were multiplied by an exponential window function of the digital resolution (0.92 Hz) prior to Fourier Transform (FT). The ^{13}C-NMR chemical shifts are referenced to the signal of $CDCl_3$ (δ = 77.00 ppm from TMS).

2D z-pulsed field gradient (PFG) selected ^{1}H,^{13}C HMQC [70,71], and ^{1}H,^{13}C HMBC [72] experiments were run to assign reliably the ^{13}C-NMR spectra. In HMQC the matrix size typically was 2500 Hz/512 points (^{1}H = f_2-axis) x 10000 Hz/512 points (^{13}C = f_1-axis), which was multiplied by a sine-bell window function along both axes prior to FT. The number of scans was 32 and a composite pulse decoupling (garp) was used to remove proton couplings. In HMBC measurements 64 scans were accumulated for each f_1-increment, the matrix size and windowing were the same as in HMQC. A low-pass filter to remove correlations transmitted via direct couplings and a 50 msec delay for an evolution of ^nJ(C,H) couplings was included in the HMBC pulse sequence. In order to determine ^{15}N NMR chemical shifts, z-PFG ^{1}H,^{15}N HMBC experiments were run. In these experiments the size of data matrix was 2500 Hz/512 points (^{1}H) x 22500 Hz/1024 points (^{15}N-axis). The ^{15}N-NMR chemical shifts were referenced to an external nitromethane (δ = 0.0 ppm) sample in a 1 mm diameter capillary tube inserted coaxially inside the 5 mm NMR sample tube. A sine-bell multiplication was done along both axes prior to FT. 64 scans were accumulated for every ^{15}N = f_1-increment. A 100 msec delay for an evolution of ^nJ(N,H) couplings was included in this HMBC pulse sequence.

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